CHAPTER-I

INTRODUCTION

Digital micro-macro dynamics seeks to describe broad characteristics of the flow field, with the goal of understanding the differences between the velocity and shear environments in vascular regions [1]. Through macro dynamics, we can identify the salient characteristics of the flow field in susceptible and protected regions of the vasculature. This approach can also identify the influence on the shear environment of hemodynamic, vessel dynamic, geometric, rheological, and wall mechanical variables, and indicate which variables are more or less controlling different hemodynamic stresses and in different vascular regions.

As the interdisciplinary subject chosen is bio-informatics, the study of the flow of blood in arteries is considered and it is also called as bio-fluid dynamics. One of the oldest branches of applied mathematics is Fluid dynamics. It is also the branch in which some of the most significant advances have been made during the last fifty years and it is one of the most important parts of the interdisciplinary activities concerning engineering and technological developments. These advances have been motivated by exciting developments in science and technology and have been facilitated by growth of computer capabilities and developments of sophisticated mathematical techniques.

In fact, one role of mathematicians interested in biological and medical problems is to evolve new mathematical methods for dealing with the complex situations in life sciences. Since situations in life sciences are quite complex, mathematicians have to formulate a new mathematical model. Once a model is
formulated, its consequence can be deduced by using mathematical techniques and the results can be compared with observations. The discrepancies between theoretical conclusions and observations suggest further improvements in the model.

The mathematical techniques used in this study are Classical mathematical techniques such as the solution of ordinary and partial differential equations, integral equations, Probabilistic and Statistical techniques and Computer techniques confining to Research Methodology. Very often the differential and integral equations arising in mathematical biosciences can be solved only with the help of computers.

For this study the basic concepts about Blood, basic concepts of fluid flows, cardiovascular system, biological fluids, cardiac diseases and cardiac diagnostic methods have been considered as necessary research tools.

1.1 CONCEPTS ABOUT BLOOD

1.1.1 Constitution of Blood

Blood consists of a suspension of cells in an aqueous solution called plasma which is composed of about 90 percent water and 7 per cent protein. There are about $5 \times 10^9$ cells in a milliliter (1cc) of healthy human blood, of which about 95 per cent are red cells or erythrocytes whose main function is to transport oxygen from the lungs to all the cells of the body and the removal of carbon dioxide formed by metabolic processes in the body to the lungs. About 45 per cent of the blood volume in an average man is occupied by red cells. This fraction is known as hematocrit. Of the remaining, white cells or
leukocytes constitute about one-sixth or 1 per cent of the total, and these play a role in the resistance of the body to infection; platelets form 5 per cent of the total, and they perform a function related to blood clotting [2].

In 5 litres of blood in the human body, there are about $25 \times 10^{12}$ red cells [3]. The mean life of a red cell is about 120 days and the total number of red cells which die per second is

$$\frac{(25 \times 10^{12})}{(120 \times 24 \times 60 \times 60)} = 2.4 \times 10^6$$

[3].

These cells supply oxygen to about 60 million cells of the body. The number of red cells in 1 cc of blood is more than the number of living human beings on the planet Earth.

Oxygen is carried by blood in two forms:

(i) Dissolved in plasma.

(ii) Bound with hemoglobin in red cells.

In every 100 ml of blood, 0.48 ml of $O_2$ (oxygen) carried in dissolved form, 20 ml is carried in combination with hemoglobin. Hence, the oxygen binding capacity of completely saturated blood is about 40 times greater than the capacity of plasma for dissolved oxygen. Five litres of blood therefore carry about 24 ml of $O_2$ in dissolved form and about 1,000 ml of $O_2$ in bound form. Thus, blood can carry more than one liter of oxygen per minute, though the requirement of a man at rest is only 250 ml of $O_2$ per minute.

1.1.2 Viscosity of Blood

Viscosity is the internal resistance against the free flow of liquid due to frictional forces between the fluid layers moving over one another at different velocities. Newton defined it as the ratio of shear stress (force resisting or
pushing flow) to the shear strain rate of a moving fluid. Blood is considered neither homogeneous nor Newtonian regarding viscosity. Plasma in isolation may be considered Newtonian with a viscosity of about 1.2 times that of water.

Blood is a viscous fluid having cells and plasma in the ratio of 45:55 and the percent of blood cells, i.e. 45 per cent, is called the hematocrit. More than 99 per cent of the cells are red blood cells which indicate that white blood cells do not have any role in determining the physical characteristics of the blood. The normal count is 5 million/mm$^3$ and 40 per cent of the volume of blood. The red blood cells which are suspended on the viscous fluid plasma and their characteristics have an important influence on the viscosity [4].

The effective viscosity is found to change with the anticoagulants added to prevent clotting. It is also found to change with the type of Viscometer used (coaxial rotating cylinders, cone-plane, or capillary tube). The viscosities of blood samples from different individuals also show more significant variations than are found in samples of non-biological fluids.

**1.1.3 Velocity of blood**

The velocity of blood means the rate of blood flow through a given vessel, i.e., displacement per unit time which is in cm/s. Blood flow means the volume of blood flowing through a given vessel is given interval of time, i.e., volume per unit time which is in cm$^3$/s.

Velocity ($V$) is proportionate to flow ($Q$) divided by the area of the conducting vessel ($A$): $V = Q/A$. The average velocity of fluid movement at any point in a system of tubes is inversely proportional to the total cross-sectional area of the vessel at that point, whereas, the blood flow is directly proportional
to the total cross-sectional area of the vessel. If the vessel is constricted by any means (e.g. Atherosclerosis), the velocity increases to a higher level known as “critical velocity” and laminar flow becomes turbulent at or above this velocity and creates sounds.

1.2 CONCEPTS OF FLUID FLOWS

The foundational axioms of fluid dynamics are the conservation laws, specifically, conservation of mass, conservation of linear momentum (also known as Newton's Second Law of Motion), and conservation of energy (also known as First Law of Thermodynamics). In addition to the above, fluids are assumed to obey the continuum assumption. Fluids are composed of molecules that collide with one another and solid objects. However, the continuum assumption considers fluids to be continuous, rather than discrete. Consequently, properties such as density, pressure, temperature, and velocity are taken to be well-defined at infinitesimally small quantified points, and are assumed to vary continuously from one point to another. The fact that the fluid is made up of discrete molecules is ignored [4]. For fluids which are sufficiently dense to be a continuum, do not contain ionized species, and have velocities small in relation to the speed of light, the momentum equations for Newtonian fluids are the Navier-Stokes equations, which is a non-linear set of differential equations that describes the flow of a fluid whose stress depends linearly on velocity gradients and pressure.
1.2.1 Compressible vs. Incompressible flow

All fluids are compressible to some extent that is variations in pressure or temperature will result in variations in density. However, in many situations the variations in pressure and temperature are sufficiently small so that the variations in density are negligible. In this case the flow can be modeled as an incompressible flow. Otherwise the more general compressible flow equations must be used [5].

Mathematically, incompressibility is expressed by saying that the density $\rho$ of a fluid parcel does not change as it moves in the flow field, i.e.

$$\frac{d\rho}{dt} = 0$$

where $\frac{d}{dt}$ is the substantial derivative, which is the sum of local and convective derivatives. This additional constraint simplifies the governing equations, especially in the case when the fluid has a uniform density.

1.2.2 Viscous vs. Inviscid flow

Viscous problems are those in which fluid friction has significant effects on the fluid motion. The Reynolds number, which is a ratio between inertial and viscous forces, can be used to evaluate whether viscous or inviscid equations are appropriate to the problem. Stokes flow is flow at very low Reynolds numbers, $Re<<1$, such that inertial forces can be neglected compared to viscous forces. On the contrary, high Reynolds numbers indicate that the inertial forces are more significant than the viscous (friction) forces. Therefore,
we may assume the flow to be an inviscid flow, an approximation in which we neglect viscosity completely, compared to inertial terms. This idea can work fairly well when the Reynolds number is high. However, certain problems such as those involving solid boundaries may require that the viscosity be included. Viscosity often cannot be neglected near solid boundaries because the no-slip condition can generate a thin region of large strain rate (known as Boundary layer) which enhances the effect of even a small amount of viscosity, and thus generating vorticity which is a vector that describes the local spinning motion of a fluid near some point, as would be seen by an observer located at that point and traveling along with the fluid [6].

1.2.3 Steady vs. unsteady flow

When all the time derivatives of a flow field vanish, the flow is considered to be a steady flow. Steady-state flow refers to the condition where the fluid properties at a point in the system do not change over time. Otherwise, the flow is called unsteady [7].

1.2.4 Reynolds number of flows

When two geometrically similar flow patterns, in perhaps different fluids with possibly different flow rates, have the same values for the relevant dimensionless numbers, they are said to be dynamically similar [8].

Typically it is given as follows:

\[ R_s = \frac{\rho v_s^2}{\mu} = \frac{\rho v_1 L}{\mu} = \frac{v_1 L}{v} \]
where

- \( v_s \) - mean fluid velocity, [m s\(^{-1}\)]
- \( L \) - characteristic length, [m]
- \( \mu \) - (absolute) dynamic fluid viscosity, [N s m\(^{-2}\)] or [Pa s]
- \( \nu \) - kinematic fluid viscosity: \( \nu = \frac{\mu}{\rho} \), [m\(^2\) s\(^{-1}\)]
- \( \rho \) - fluid density, [kg m\(^{-3}\)]

### 1.2.5 Laminar flow

Laminar flow, sometimes known as streamline flow, occurs when a fluid flows in parallel layers, with no disruption between the layers. When a fluid is flowing through a closed channel such as a pipe or between two flat plates, either of two types of flow may occur depending on the velocity of the fluid: laminar flow or turbulent flow. Laminar flow is the opposite of turbulent flow which occurs at higher velocities where eddies or small packets of fluid particles form leading to lateral mixing [9]. In nonscientific terms laminar flow is "smooth", while turbulent flow is "rough". When the Reynolds number is much less than one creeping motion or Stokes flow occurs [10]. This is an extreme case of laminar flow where viscous (friction) effects are much greater than inertial forces. The common application of laminar flow would be in the smooth flow of a viscous liquid through a tube or pipe. In that case, the velocity of flow varies from zero at the walls to a maximum along the centerline of the vessel. The flow profile of laminar flow in a tube can be calculated by dividing the flow into thin cylindrical elements and applying the viscous force to them.
1.3 INTRODUCTION TO THE HUMAN CIRCULATORY SYSTEM

The human circulatory system pumps five litres of blood through a complex network of passages that passes through the vital organs of the human body, providing nutrients and oxygen that these organs use and carry out the waste products and potentially harmful chemicals away from these organs. The heart is responsible for providing the driving push to move all this blood whereas the lungs allow for the exchange of gases: providing oxygen to be carried to the vital and peripheral organs and taking away the carbon dioxide build-up. Therefore, the circulatory system itself can be separated into three distinct portions: the pulmonary system, encompassing the lungs; the coronary system, encompassing the heart and the systemic system, which covers the rest of the system. It is common to combine both the pulmonary system with the coronary system to a system by itself called the cardiopulmonary system. Cardiopulmonary circulation involves the movement of blood from heart to lungs and back again and is important for removing waste gases and saturating
the blood with oxygen prior to being pumped from the heart to other portions of the body. The veins bring in blood rich in waste materials, particularly carbon dioxide which results from the combustion processes necessary to generate energy carried out throughout the body. This enters the right atrium of the heart (lower chamber) via two large veins called the venacavae, which then contracts (systole) and pushes the blood into the right ventricle (upper chamber) via a one-way valve. The right ventricle then contracts to force the fluids out through the pulmonary artery into the lungs, whereby the aforementioned exchange of gases occurs. This blood, now rich in oxygen is further pumped into the left atrium via the pulmonary vein, which is pumped into the left ventricle of the heart and expelled through the aorta, the largest artery in the body (to withstand the high pressures), to the other portions of the body [11]. It is important to note that there are series of valves within the heart and within the veins around the body that prevent backflow from occurring by sealing off the vessels when the heart is expanding (diastole), causing a lower pressure upstream. The systemic circulation covers the blood flow immediately after it leaves the heart to circulate around the body, depositing oxygen and nutrients while collecting waste products, as and when it returns back into the heart. Within this flow, the blood will absorb nutrients attained from the digestion process, which is then used to provide fuel for energy as well as for cell growth and storage. The blood will deposit any unnecessary waste through the liver within this circulation as well, which will be expelled from the body. All the vessel walls are smooth to allow for ease of flow and strong enough to withstand the varying pulses of the flow. Within the systemic circulation, it can be seen how the arteries, which transfer
oxygen rich blood, become veins that take away the waste gases. Where this transfer occurs, the relatively large arteries branch up into arterioles which branch further into capillaries. These small branches allow for the maximum transfer of materials carried within the blood to the parts of the body that need them [12]. Capillaries have extremely thin walls to allow for this transfer, and they eventually come together to form venules. Venules join together to form veins. Veins are notably smaller in diameter than arteries as they need not withstand as high pressures and do not transfer as much materials, but they do have valves along the vessel to prevent flow reversal.

1.3.1 Cardiovascular System

The cardiovascular system consists of the following:

(i) The heart (which acts as a pump, whose elastic muscular walls contract rhythmically, making possible the pulsatile flow of blood through the vascular system)
(ii) The distributory system (comprising arteries and arterioles for sending blood to the various organs of the body)
(iii) The diffusing system (made up of fine capillaries which are in contact with the cells of the body)
(iv) The collecting system of veins (which collects blood depleted of oxygen and full of products of metabolic processes of the system).

The organs which supplement the function of the cardiovascular system are
(i) The lungs which provide a region of inter phase transfer of $O_2$ to the blood and removal of $CO_2$ from it, and

(ii) The kidney, liver and spleen which help in maintaining the chemical quality of blood under normal conditions and under conditions of extreme stress [13].

![Coronary artery]

**Figure 1.2 Coronary artery**

The heart sends out about 5.5 litres of blood per minute, of which about 0.75 litre is received by the brain, 1.1 litres by the kidneys, 1.1 litres by the liver, 0.25 litre by the heart muscles, and so on. The oxygen supplied by blood to different organs of the body depends on their requirement. Thus the brain, which has only about 2 per cent of body weight, receives about 20 percent of oxygen. There are also control mechanisms to change the distribution proportions at times of stress.

### 1.3.2 Diastole

Diastole is the time period when the heart is in a state of relaxation and dilatation (expansion). The final letter in "diastole" is pronounced as a long "e" as in "lee." The adjective for diastole is diastolic. The diastolic pressure is
specifically the minimum arterial pressure during relaxation and dilatation of the ventricles of the heart.

Diastole is the time when the ventricles are filled with blood. In a blood pressure reading, the diastolic pressure is typically the second number recorded. For example, with a blood pressure of 120/80 ("120 over 80"), the diastolic pressure is 80. By "80" it is meant 80 mm Hg (millimeters of mercury).

1.3.3. Systole

Systole is the time period when the heart is contracting. It is the period specifically during which the left ventricle of the heart contracts. The final letter in "systole" is pronounced as a long "e" as in "lee." The adjective for systole is systolic. The systolic pressure is specifically the maximum arterial pressure during contraction of the left ventricle of the heart. In a blood pressure reading, the systolic pressure is typically the first number recorded. For example, with a blood pressure of 120/80 ("120 over 80"), the systolic pressure is 120. By "120" it is meant 120 mm Hg (millimeters of mercury).
Table 1.1: Approximate Dimensions of Human Blood vessels and Reynolds number of flows [11].

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter (cm)</th>
<th>Length (cm)</th>
<th>Wall thickness</th>
<th>Average velocity (cm/sec)</th>
<th>Average Reynolds number</th>
<th>Maximum velocity (cm/sec)</th>
<th>Maximum Reynolds number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>2.5</td>
<td>50</td>
<td>0.2</td>
<td>48</td>
<td>3400</td>
<td>120</td>
<td>8500</td>
</tr>
<tr>
<td>Arteries</td>
<td>0.40</td>
<td>50</td>
<td>0.1</td>
<td>45</td>
<td>500</td>
<td>90</td>
<td>1000</td>
</tr>
<tr>
<td>Arterioles</td>
<td>0.005</td>
<td>1</td>
<td>0.02</td>
<td>5</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.0008</td>
<td>0.1</td>
<td>0.0001</td>
<td>0.1</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venules</td>
<td>0.002</td>
<td>0.2</td>
<td>0.0002</td>
<td>0.2</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veins</td>
<td>0.5</td>
<td>2.5</td>
<td>0.05</td>
<td>1.0</td>
<td>140</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vena cava</td>
<td>3.0</td>
<td>50</td>
<td>0.15</td>
<td>38</td>
<td>3300</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.4 CHARACTERISTICS OF BIOLOGICAL FLUIDS

1.4.1. Shear Stress

A shear stress, denoted $\tau$ (Greek: tau), is defined as the component of stress coplanar with a material cross section. Shear stress arises from the force vector component parallel to the cross section. Normal stress, on the other hand, arises from the force vector component perpendicular or anti parallel to the material cross section on which it acts.

The formula to calculate average shear stress is

$$\tau = \frac{F}{A}$$

where
\( \tau = \) the shear stress;
\( F = \) the force applied;
\( A = \) the cross-sectional area of material with area parallel to the applied force vector.

1.4.2. Shear Stress in Fluids

Any real fluids (liquids and gases included) moving along solid boundary will incur a shear stress on that boundary. The no-slip condition dictates that the speed of the fluid at the boundary (relative to the boundary) is zero, but at some height from the boundary the flow speed must equal that of the fluid. The region between these two points is aptly named the boundary layer. For all Newtonian fluids in laminar flow the shear stress is proportional to the strain rate in the fluid where the viscosity is the constant of proportionality [14]. However for Non Newtonian fluids, this is no longer the case as for these fluids the viscosity is not constant. The shear stress is imparted onto the boundary as a result of this loss of velocity. The shear stress, for a Newtonian fluid, at a surface element parallel to a flat plate, at the point \( y \) is given by

\[
\tau(y) = \mu \frac{\partial u}{\partial y}
\]

where

\( \mu \) is the dynamic viscosity of the fluid;
\( u \) is the velocity of the fluid along the boundary;
\( y \) is the height above the boundary [15].

Specifically, the wall shear stress is defined as
\[ \tau_w = \tau(y = 0) = \mu \frac{\partial u}{\partial y} \bigg|_{y=0} \]

1.4.3. Viscosity

Viscosity is a measure of the resistance of a fluid which is being deformed by either shear or tensile stress. In everyday obvious terms (for fluids only), viscosity is "thickness" or "internal friction". Thus, water is "thin", having a lower viscosity, while honey is "thick", having a higher viscosity. Put simply, the less viscous the fluid is, the greater its ease of movement (fluidity) [16].

Viscosity describes a fluid's internal resistance to flow and may be thought of as a measure of fluid friction. For example, a fluid with high-viscosity called felsic magma will create a tall, steep strato volcano, because it cannot flow far before it cools, while a fluid with low-viscosity called mafic lava will create a wide, shallow- sloped shield volcano. All real fluids (except super fluids) have some resistance to stress and therefore are viscous, but a fluid which has no resistance to shear stress is known as an ideal fluid or inviscid fluid.

1.4.4. Coefficient of viscosity

When a fluid (e.g. Air) flows past a stationary wall (e.g. Tabletop), the fluid right close to the wall does not move. However, away from the wall the flow speed is not zero. So a velocity gradient exists. This is due to the adhesive, cohesive and frictional forces. We find that the magnitude of this gradient (how fast the speed changes with distance) is characteristic of the fluid. This is used to define the coefficient of viscosity \( \eta \) (Greek letter eta).
Fluid in contact with either surface is held to that surface by adhesive forces between the molecules of the fluid and the surface. Therefore, the molecules at the surface of the stationary wall are at rest and the molecules at the surface of the moving plate will be moving with velocity \( v \) [17]. The stationary layer of fluid in contact with the stationary wall will retard the flow of the layer just above it. This layer will retard the layer above and so on. Thus the velocity will vary linearly with distance above the stationary wall. The force required to move the plate at speed \( v \) is

\[
F \propto A \quad \text{where} \quad A = \text{area of either plate}
\]

\[
F \propto (v / L) \quad (v / L) = \text{velocity gradient}
\]

The constant of proportionality for the fluid is called the coefficient of viscosity \( \eta \).

\[
F = \eta \ A \ v / L
\]

The greater the coefficient of viscosity \( \eta \), the greater the force required to move the plate at a velocity \( v \) [18].

This equation does not hold for all fluids. Viscous fluids that obey this equation are called Newtonian fluids and \( \eta = \text{constant independent of the speed of flow} \). When \( \eta \) does depend upon the velocity of flow, the fluids are called non-Newtonian.

Blood is an example of a non-Newtonian mixture because it contains corpuscles and other suspended particles [11].

The corpuscles can deform and become preferentially oriented so that the viscosity decreases to maintain the flow rate. Corn flour and water mixture is another non-Newtonian fluid.

Viscosity \( \eta = (F / A)(L / v) \quad (\text{N.m}^{-2})(\text{m})(\text{m}^{-1}.\text{s}) \equiv \text{Pa.s} \)
SI unit for viscosity is Pa.s

A common unit is the poise P where 1 Pa.s = 10P, 1 mPa.s = 10^-2 P

**Table 1.2-Viscosity of various Fluids**

<table>
<thead>
<tr>
<th>Fluid</th>
<th>η (°C)</th>
<th>(mPa.s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water (0 °C)</td>
<td></td>
<td>1.8</td>
</tr>
<tr>
<td>Water (20 °C)</td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Water (100 °C)</td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>White blood (37 °C)</td>
<td></td>
<td>~4</td>
</tr>
<tr>
<td>Blood plasma (37 °)</td>
<td></td>
<td>~1.5</td>
</tr>
<tr>
<td>Engine oil (AE10)</td>
<td></td>
<td>~200</td>
</tr>
<tr>
<td>Air</td>
<td></td>
<td>0.018</td>
</tr>
</tbody>
</table>

1.4.5. *No-Slip Condition*

The *no-slip condition* for viscous fluids states that at a solid boundary, the fluid will have zero velocity relative to the boundary. The fluid velocity at all fluid–solid boundaries is equal to that of the solid boundary. Conceptually, one can think of the outermost molecules of fluid as stuck to the surfaces on which it flows through [19].

1.4.6. *Newtonian Vs. Non-Newtonian Fluids*

Sir Isaac Newton showed how stress and the rate of strain are very close to linearly related to many familiar fluids, such as water and air. These Newtonian fluids are modeled by a coefficient called viscosity, which depends on the specific fluid.
However, some of the other materials, such as emulsions and slurries and some visco-elastic materials (e.g. Blood, some polymers), have more complicated non-Newtonian stress-strain behaviours. These materials include sticky liquids such as latex, honey, and lubricants which are studied in the sub-discipline of Rheology.

Figure 1.3 Types of Non-Newtonian Behaviour

A non-Newtonian fluid is a fluid whose flow properties differ in any way from those of Newtonian fluids. Most commonly the viscosity (resistance to deformation or other forces) of non-Newtonian fluids is not independent of shear rate or shear rate history. In this study the disease in cardiovascular system has been considered. An introduction about that disease will be helpful to understand the problem [20].
1.5. CARDIAC DISEASES

1.5.1 Atherosclerosis and Arteriosclerosis

Arteriosclerosis refers to several diseases in which the arterial wall thickens and loses its elasticity. Commonly confused with atherosclerosis, which is the formation of plaques consisting of cholesterol and other substances on the arterial walls, arteriosclerosis is the thickening and stiffening of the artery walls from too much pressure. Atherosclerosis can lead to arteriosclerosis, which comes from the Greek for “hardening of the arteries.” A stenosis (plural: Stenoses; from Ancient Greek, “narrowing”) is an abnormal narrowing in a blood vessel or other tubular organ or structure. A catheter is a diagnostic procedure for the diseases in the cardiovascular system.

![Figure 1.4 Atherosclerosis](image)

The formation of plaque on artery walls over time causing the narrowing of the passages and the hardening of the vessel walls is referred to as atherosclerosis [21]. This section will give a brief description of the possible causes of atherosclerosis, the effects of this disease and current available methods of preventing or treating it. The narrowing and any subsequent change of geometry in the artery can produce significant effects on the blood flow, which can in turn influence the artery itself. The blood flow may experience high fluid
stresses as it is forced through the narrow passageway, and this in turn causes the walls to experience a high shear stress. The shapes and severities of the stenoses themselves can result in flow recirculation, which promotes sediment build-up and could possibly result in the growth of the stenosis. The more serious concern arises if the calcified cap over the fatty core is not sufficiently thick to withstand the stresses exerted on its wall. This can result in plaque rupture, which exposes the fatty core to the blood stream. The result of this is that the blood is triggered to coagulate about the rupture, similar to how blood clots to stop bleeding [22]. The blood clot forms a thrombus, which essentially adds a further blockage to the already narrow passageway and is referred to as thrombosis. Should the blockage be sufficiently severe, it can cut off the blood supply along with the oxygen and nutrients needed along that artery.

If this occurs in the coronary artery, the result is a heart attack. If the thrombosis occurs in the cerebral artery, it can trigger a transient ischemic attack or a stroke [23]. A blockage in other non-major arteries can result in pain in the areas of the body deprived of oxygen, which can lead to cell death. It is well known that the first two cases can be potentially fatal and are the leading causes of death in the western world. Because of this, the causes and propagation of atherosclerosis are often the focus of extensive research to determine possible methods of prevention or treatment. The precise causes of atherosclerosis are still unknown, but recent studies have indicated that the cause might be linked to Low-Density Lipoprotein (LDL) cholesterol, which is regarded as “bad” cholesterol and can damage the inside lining of the artery walls [24]. This causes other fatty materials, which are attracted to these
lesions to collect on the walls. Over time, more particles attach to the surface and change the path of the blood flow, which can worsen the situation. The creation of lesions that encourage the growth of plaque is related to the shear stresses induced by the flow and the stresses within the wall itself. These can be made worse by other factors such as age, sex, cigarette smoking, emotional stress and dietary intake. While doctors recommend a healthy diet and exercise to reduce the effects of stenosis, there are currently available several methods to remove the plaque formation on the arterial walls. One of this is a medication, in which the patient ingests either antiplatelets or anticoagulants. Both of these medications seek to prevent the material from clumping together to cause the blockage along the artery. The other methods involve surgery and include balloon angioplasty [25], laser angioplasty or arthrectomy [26]. Balloon angioplasty involves feeding a catheter from a main artery into the coronary artery with a balloon tip, which is inflated at the site of the stenosis. This pushes the stenotic portion into the artery wall and hopefully increases the cross sectional area of the region. A stent, which is a wired mesh, may also be inserted later via the catheter to hold the artery wall in place. Laser angioplasty also relies on having a catheter fed to the coronary artery with a laser tip to destroy the built-up plaque with pulsing bursts of light. The last method, arthrectomy, involves having a drill tip on the catheter and is used where the plaque build-up is too hard to be removed via the other two methods [27]. In the more severe cases, though, it may be necessary to perform a bypass graft, whereby healthy blood vessels are harvested from other parts of the body and sewed onto the coronary arteries to that blood can be routed past the blockage.
This form of open-heart surgery, although risky, is highly effective in restoring blood flow into the heart.

1.5.2. Effect of Stenosis

The term stenosis denotes the narrowing of the artery due to the development of arteriosclerotic plaques or other types of abnormal tissue development. As the growth projects into the lumen (cavity) of the artery, blood flow is obstructed. The obstruction may damage the internal cells of the wall and may lead to further growth of the stenosis. Thus there is a coupling between the growth of a stenosis and the flow of blood in the artery since each affects the other [28].

The stenosis growth usually passes through three stages. In stage I, there is no separation of flow and there is no back flow. In stage II, the flow is laminar, but separation occurs and there is back flow. In stage III, turbulence develops in a certain region downstream. Stage I is called mild stenosis.

The development of stenosis in an artery can have serious consequences and can disrupt the normal functioning of the circulatory system. In particular, it may lead to

(i) Increased resistance to flow, with possible severe reduction in blood flow.

(ii) Increased danger of complete occlusion (obstruction).

(iii) Abnormal cellular growth in the vicinity of stenosis, which increases the intensity of the stenosis and

(iv) Tissue damage leading to post-stenosis dilatation.
1.6 DIAGNOSTIC METHOD

1.6.1 Cardiac Catheterization

Cardiac catheterization (also called heart catheterization) is a diagnostic and occasionally therapeutic procedure that allows a comprehensive examination of the heart and surrounding blood vessels. It enables the physician to take angiograms, record blood flow, calculate cardiac output and vascular resistance perform an end myocardial biopsy, and evaluate the heart's electrical activity [29].

Cardiac catheterization is most commonly performed to examine the coronary arteries, because heart attacks, angina, sudden death, and heart failure most often originate from disease in these arteries. Cardiac catheterization may reveal the presence of other conditions, including enlargement of the left ventricle; ventricular aneurysms (abnormal dilation of a blood vessel); narrowing of the aortic valve; insufficiency of the aortic or mitral valve; and septal defects that allow an abnormal flow of blood from one side of the heart to the other.

Catheters play a vital role in the clinical studies, since they are used to measure different types of flow quantities. Some of the types of catheters used in clinics, their sizes and their usages are mentioned in table 1.3 where $d_i$ is the diameter of the catheter [30].
The study of blood flow through an inserted catheter has been the subject of scientific research for a long time. Its plays an important role in the fundamental understanding, diagnosis and treatment of cardiovascular system. Like most of the problems of nature and life sciences, it is a complex one due to the complicated structure of blood, the circulatory system and their constituent materials. The experimental studies and the theoretical treatment of blood flow phenomena are very useful for the diagnosis of a number of cardiovascular diseases and development of pathological patterns in human or animal physiology and for other clinical purposes and practical applications [31]. Mathematical Modelling of blood flow has been subject to modification in order to account for the new evidence uncovered through the improved initial experimental observation.

Blood is composed of fluid plasma and formed elements. The formed elements of blood are erythrocyte, leukocyte and platelets. The percentage volume of red cells is called the haematocrit and is approximately 40- 45 % for an adult. Red cells may affect the viscosity of whole blood and thus the velocity
distribution depends on concentration of cells. So blood cannot be considered as homogenous fluid. In general, Blood is known to be an incompressible non-Newtonian Fluid.

This property is mainly the result of cell concentration (haemotocrit ratio). However in the course of flow in arteries, the red blood cells in the vicinity of an arterial wall move to the central region of the artery, so that the haematocrit ratio becomes quite low near the arterial wall, which results in lower viscosity in this region. Moreover, due to high shear rate near the arterial wall, the viscosity of blood is further reduced. Hence blood may be treated as a Newtonian fluid with variable viscosity particularly in case of flow through larger vessels [32].

In recent times, with the evaluation of coronary balloon angioplasty, there has been a considerable increase in the use of catheter of various sizes. The insertion of a catheter in an artery will alter the flow field, modify the pressure distribution and increase the resistance. Therefore the pressure gradient recorded by a transducer attached to the catheter will differ from that of uncatheterised artery and it is essential to know that catheter induced error. The use of a catheter is of immense importance and has become a standard tool for diagnosis and treatment in modern medicine [33]. A catheter is made of polyester based thermoplastic polyurethane, medical grade polyvinyl chloride etc. For the purpose of flexible PVC (polyvinyl chloride) materials containing added plasticizers are used in catheters which enable them to move through the branches or curved paths of the circulatory system. Transducers attached to catheters are of large usage in clinical works and the techniques are used for measuring blood pressure or other mechanical properties in arteries [34].
1.7 SCOPE OF THE WORK

Recently there has been a significant amount of research done on stenosed arteries: arteries that have a blockage caused by the disease called atherosclerosis. Atherosclerosis, which literally means the hardening of arteries, is caused by plaque build-up over the artery walls. These are normally smooth to allow for easy transportation of red blood cells, oxygen, white blood cells, nutrients, and other vital substances that the body requires. This plaque build-up tends to cause a hardening of the artery walls as well as a narrowing of the arterial passage. The plaque itself consists of a fatty inner core and a calcified cap. The exact causes of atherosclerosis are still unknown, but recently it has been linked to the dietary intake of a person. Certain cholesterols have been found to promote the formation of plaque on artery walls and over time the build-up affects the blood flow path, which in turn can further complicate the problem. The rupturing of this plaque exposes the fatty core and can lead to the formation of a thrombus, where the blood platelets form a clot about the exposed area. Thrombus formation can block off an entire artery; a potentially fatal condition if the coronary artery or an artery that supplies blood to the brain is blocked off.

The chances of this occurring are further complicated by several factors: whether the plaque contains a thick or thin cap, diseases that affect the property of the blood or arteries are due to age, sex, hypertension and cigarette smoking. It is therefore no wonder that this topic is now of significant concern to humanity and the focus of numerous research efforts. Most of the studies available at present focus on the clinical aspects of the disease. There has
been a great push, however, to understand the physics involved with the disease itself, including the cause and possible methods of treating it. Numerous experiments have been conducted to study the geometry and fluid effects on the condition. These studies have provided valuable data.

There are limitations, however, with these experimental techniques that need to be investigated further using other methods. Numerical methods have extensively studied the relationship between the shape of the stenosis and blood flow, using shapes and physical characteristics derived from medical samples. This study aims to investigate the Newtonian and non-Newtonian nature of the blood through the two fluid model. To achieve this mathematical modelling, analytical solution of newly formed functional equations, Statistical and Artificial Neural Networks analysis have been used. The clinical records of the Atherosclerotic patients, their conditions of artery with the stenosis conditions like mild, moderate and occluded, etc., are taken for this study from the American Heart Association related journals and websites [153 – 155, 157]. A single and two fluid mathematical Casson and Herschel-Bulkley models of catheterized tapered artery have been investigated and the characteristics of the fluid flows have been analyzed in this study. The objective of the analysis is to study the change in flow pattern and estimate the increase in flow resistance in a narrow artery when a catheter is inserted into it.
1.8 THESIS ORGANIZATION

In Chapter I the introduction includes the basic concepts about Blood, basic concepts of fluid flows, and cardiovascular system, characteristics of biological fluids, cardiac diseases and cardiac diagnostic methods, the human circulatory system, arterial properties, atherosclerosis and the physical concepts of blood flow that have been used in the study.

Chapter II defines an in-depth review of the background for this study as well as previous studies conducted in this area of research. This covers early studies into the stenosed arteries. Limitations of the study have been mentioned in this chapter followed by the present proposal of Research oriented investigation.

Chapter III deals with the mathematical functional equations of continuity, Navier-Stokes equations of a viscous incompressible fluid in the cylindrical coordinate system, Newtonian and non-Newtonian flows by mathematical functional equations, and also the characteristic equations for the flow of fluids.

Chapter IV consists of a Single fluid mathematical model of blood flow through catheterized tapered artery with stenosis, the geometry of the model, the constitutive mathematical functional equations and boundary conditions for the model. The analytical expressions for flow rate, Wall shear stress, Plug flow velocity and frictional resistance have been obtained for the single fluid Casson model.

Chapter V consists of a two fluid mathematical model for blood flow through catheterized tapered artery with stenosis, the geometry of the model, the constitutive mathematical functional equations and boundary conditions for
the model. The analytical expressions in the form of mathematical functional equations for Flow rate, Wall shear stress, Plug flow velocity and Frictional resistance have been obtained for the two fluid Casson model.

Chapter VI consists of a Single fluid Herschel-Bulkley model for blood flow through catheterized tapered artery with stenosis, the geometry of the model, the constitutive mathematical functional equations and boundary conditions for the model. The analytical expressions in the form of mathematical functional equations for Flow rate, Wall shear stress, Plug flow velocity and Frictional resistance have been obtained for the single fluid Herschel-Bulkley model [148].

Chapter VII consists of a two fluid Herschel-Bulkley model for blood flow through catheterized tapered artery with stenosis, the geometry of the model, the constitutive mathematical functional equations and boundary conditions for the model. The analytical expressions for flow rate, Wall shear stress, Plug flow velocity and frictional resistance have been obtained for the two fluid Herschel-Bulkley model.

Chapter VIII describes the effects of the characteristics of the steady flow of blood flow through an analytical solution, Numerical Analysis, Artificial Neural Network Algorithm and Statistical method for Data Implementation. The variations of the wall shear stress, plug flow velocity, flow rate and frictional resistance for various pressure gradient, yield stress, catheter radius ratio and angle of tapering have been analyzed for both single and two fluid Casson and Herschel-Bulkley models.
Chapter IX consists of the results and discussions on the results of analytical solutions, Numerical evaluation and the Artificial Neural Network algorithm. The comparative studies have been done for the results of the three methods implemented with Data. The validity of the solutions and stability of the methods have been justified.

Chapter X concludes the findings of the investigations and explains the scope for future research.