Chapter 1

Introduction

1.1 Introduction

Bio-fluid mechanics is the study of a certain class of biological problems from fluid mechanics point of view. For an organism, biomechanics helps us to understand its normal function, predict changes due to alteration, and propose methods of artificial intervention. Thus diagnosis, surgery, and prosthesis are closely associated with biomechanics. Different mathematical models, using the principles of fluid mechanics have been developed with a view to understand the complex phenomena associated with the dynamics of blood flow. These mathematical models are currently being used for (i) diagnosis of various arterial diseases, (ii) appraisal of newly found treatment procedures like drug delivery, and (iii) developing and designing various artificial organs.

So the study of blood flow is very important not only for understanding of blood flow characteristics through the arteries but also for taking preventive measures / curing many diseases which occur in the blood vessels. It is well known that under certain diseased conditions an abnormal and unnatural growth is developed in the arterial wall at various location of the cardiovascular system. This abnormal arterial formation is known as stenosis, which blocks the arteries and disturbs the blood supply to the heart, brain and other important tissues and organs of the human body. This disturbance is the cause of several diseases like, myocardial infarction, angina pictoris, cerebral accident, coronary thrombosis, necrosis, strokes etc. The main factors that play a vital role in the blood flow characteristics are listed by Lighthill (1972). These are (i) unusual range of Reynolds number, (ii) unusual multiplicity of the tube branching, (iii) unusual distensibility properties of containing vessels, (iv) unusual fluid properties, and (v) unusual pulsatility. It is well known that the shapes of the blood vessels are different at different positions of

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the cardiovascular system *viz*. curved, branching, distorted, anisotropic, non-circular, permeable in spots and also elastic in nature. These complex structures are liable to development of such arterial diseases mainly around curvatures, junctions and bifurcations of large and medium size arteries, where the flow patterns are generally complicated in nature. It also noted that at various positions and at various situations blood behaves as a Newtonian or non-Newtonian fluid. At the large blood vessel where the shear rate is high, blood behaves as a Newtonian fluid *viz*. aorta. While at the low shear rate, mainly at the small arteries and micro-vessels, blood behaves as non-Newtonian fluid. Several models have been described by different researchers on the non-Newtonian behavior of blood as Casson fluid model, Herschel-Bulkley fluid model, Bingham plastic model, power law fluid model, viscoelastic fluid model etc. From the above discussion it is clear that there are several parameters which significantly influence the blood flow through cardiovascular system and those are shown in Fig. 1.1. The bold faced are some of the key words that are analysis in the present thesis. Recently several studies have been performed on the biological fluid under the presence of the magnetic field, which is known as biomagnetic fluid dynamics (BFD) in which biological fluid is treated as biomagnetic substance.

1.2 Cardiovascular System

There have been numerous significant contributors to biomechanics research by many physicians, notable among them being William Harvey (1628) who discovered the nature of blood circulation in the cardiovascular system. His unequivocal description of circulation system is considered as the first step on the path to modern cardiovascular physiology. Stephen Hales (1733), investigated the dynamics of circulatory system. Jean Poiseuille (1828) derived the famous Poiseulle law for laminar flow of fluids in tubes on the basis of experiments with the flow of blood serum in glass. Otto Frank (1899) developed the first mathematical model for the propagation of arterial pulse wave in the circulatory system. Their work was recorded in a series of papers during 1899 to 1930 which gave a great impetus to the study of hemodynamics. Several methods have been introduced by Fry (1959) and McDonald (1974) which are applied to determine the pressure gradient. The pressure gradient is also described as a collection of sinusoidal waves of frequencies determined by the harmonic or Fourier series (Womersley, 1955; McDonald, 1955).
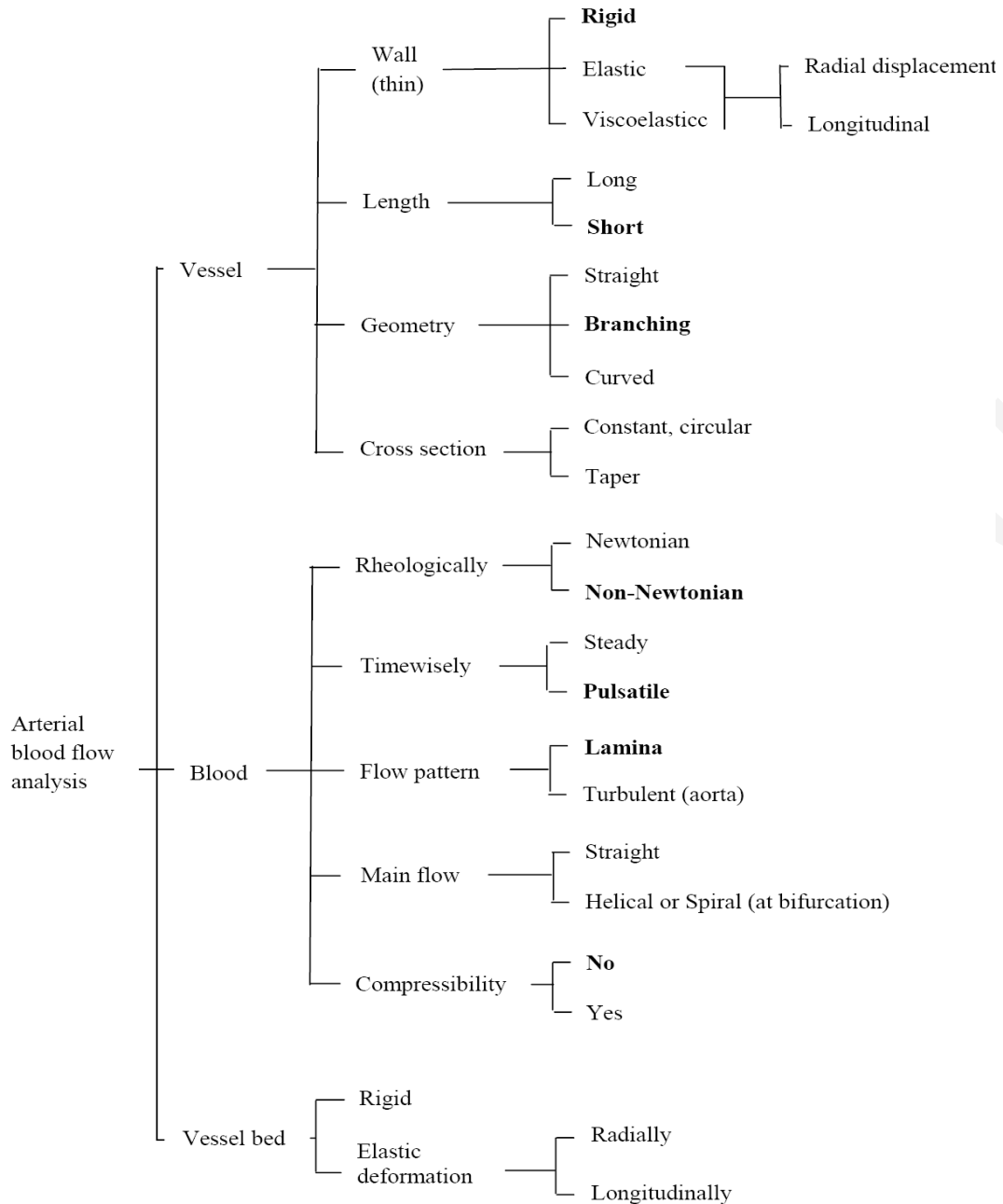
Fig. 1.1: Various constrain on arterial flow analyses (Yang, 1989).

The cardiovacular system primarily functions in nutrient and waste transport through out the body. The circulatory system basically consists of a central pump (the heart) and the peripheral blood vessels (arteries, veins and capillaries). The transport medium, blood, is circulated throughout the body in a network as shown in Fig. 1.2. Rhythemic contraction and relaxation of the heart produces a pressure difference in systole and diastole which in turn

produces a pressure gradient in human system and as a consequence, blood flow through human circulatory system. It can be divided into two main sections : (i) the systematic and (ii) pulmonary circulations. The systematic circulation supplies blood to all the body's tissues except the lungs. The lungs are supplied by the pulmonary circulation, which provides a gas exchange function. Capillaries are mainly involved in the gas exchange function.
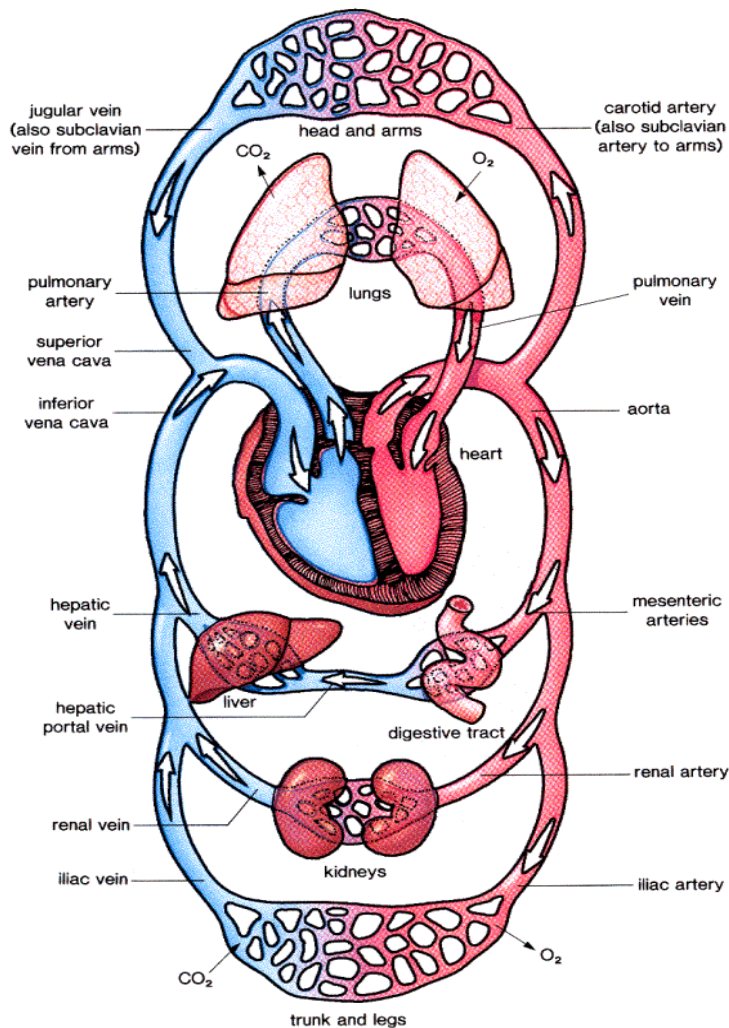

Fig. 1.2: The diagram of the human circulatory system (http://www.tutorvista.com).

1.2.1   The Heart

The circulation system includes a pump, a distributor system, a diffusing system and a collection system. The heart is the pump that propels blood through circulatory system. It is divided into a right heart, which delivers blood to the pulmonary circulation and a left

heart, which supplies blood to the systematic circulation. The schematic diagram of the heart is given in Fig. 1.3. A detailed description about the heart and its functions are given in Guyton (1970) and Fung (1984).
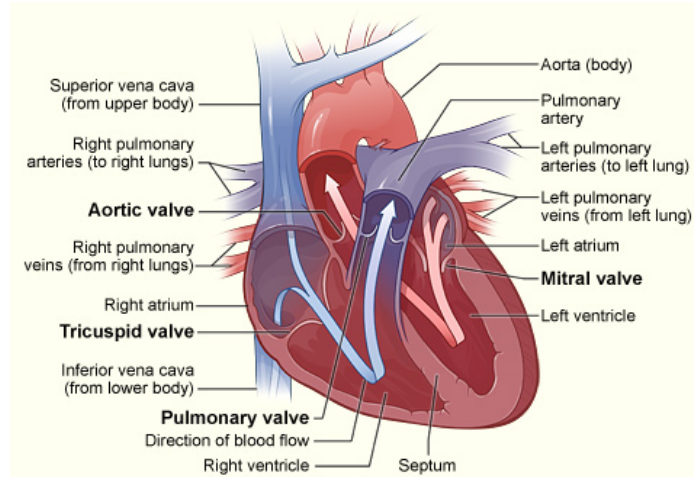

Fig. 1.3: Diagram of the heart (http://www.nhlbi.nih.gov/health)

1.2.2 Blood Vessel

The cardiovascular system is extremely intricate and complex branched networks of tubes which are called blood vessels, can roughly be divided into three parts *viz*. (i) arteries, (ii) capillaries and (iii) veins. The diameter, length, wall thickness and the average velocity at the vessels are listed in Table 1.1.

1.2.3 Abnormality of Blood Vessel

The arterial constriction disturbs the normal flow of blood, and reduces the transport of blood to the regions beyond such constrictions. In order to have a complete understanding of the development of the stenosis from the physiological point of view one need to be fully conversant with the hemodynamics behavior of the streaming blood together with the mechanical properties of the vascular wall material under physiological conditions. Different shapes of the stenosis are taken into account by several researchers and given different geometry of the artery with stenosis shape in their literature. Some of them are as stenosis with different taper angle (Mandal, 2005), Cosine shape stenosis (Ikbal et al., 2009), time variant overlapping stenosis (Chakravarty and Mandal, 1996), asymmetri stenosis (Sankar and Lee, 2009), multi cosine stenosis (Smadi et al., 2006), irregular mild stenosis

(Chakravarty and Sannigrahi, 1994; Anderson et al., 2000) and irregular multistenosis (Mustapha et al., 2009).

Table 1.1: Approximate dimensions of human blood vessel (Mazumdar, 1992).

Vessel	Diameter (m)	Length (m)	Wall Thickness (m)	Avg. Vel (m/s)
Capillaries	8×10^{-6}	0.001	10^{-6}	0.001
Venules	2×10^{-5}	0.002	2×10^{-6}	0.002
Arterioles	5×10^{-5}	0.010	2×10^{-4}	0.050
Arteries	4×10^{-3}	0.500	10^{-3}	0.450
Veins	5×10^{-3}	0.025	5×10^{-4}	0.010
Aorta	2.5×10^{-2}	0.500	2×10^{-3}	0.480
Vena Cava	3×10^{-2}	0.500	1.5×10^{-3}	0.380

1.2.4   Different representations of body-acceleration

In general, during riding a vehicle or flying in a spacecraft, an external acceleration acts on the human body which can cause serious problems in the cardiovascular system leading to the impairment of certain physiological functions. A number of experiments have been conducted on the body acceleration by Arntzenius et al. (1972) and Burton (1966). Sud and Sekhon (1985) have given a mathematical model for the body acceleration as

$$F_b(t) = a_0 \cos(\omega_b t + \phi), \tag{1.1}$$

where a_0 is the amplitude, f_b is the frequency in Hz and ϕ is the phase angle of F_b with respect to the heart action. $\omega_b = 2\pi f_b$ is the angular frequency. Later another mathematical model for the body acceleration has been given by Chakravarty and Mandal (1996). They considered a single cycle of body acceleration $F_b(t)$ is acting along the axial direction. The body acceleration is expressed in terms of unit step functions which are mathematically represented as

$$F_b(t) = a_r(t-t_1)\Psi(t-t_1) - a_r(t-t_2)\Psi(t-t_2) - d_r(t-t_3)\Psi(t-t_3) - d_r(t-t_4)\Psi(t-t_4), \tag{1.2}$$

where a_r and d_r are the respective acceleration and deceleration rates of the body acceleration, t_1 is the time of application of the body acceleration. The time difference

parameters $(t_2 - t_1)$ is the build-up time, $(t_4 - t_3)$ is the climb-down time and t_4 is the moment when the acceleration ceases to apply. $\Psi(t)$ represents the step function. The schematic diagram of the body acceleration with different time period is shown in   Fig. 1.4.
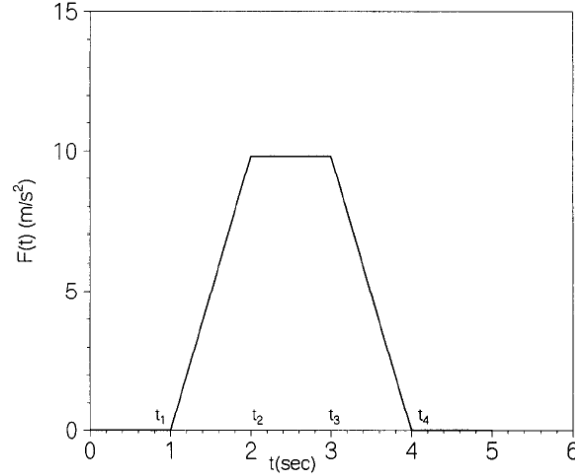

Fig. 1. 4: Schematic representation of body acceleration (Chakravarty and Sannigrahi, 1999).

1.2.5 Blood: A Marvelous Fluid

Whole blood consists of a suspension of red blood cells (erythrocytes), white blood cells (leukocytes) and platelets in an aqueous solution (plasma). The density of the erythrocytes is 1.1 gm/cm^3, while whole blood density is 1.05-1.06 gm/cm^3. The plasma is a transparent, slightly yellowish fluid and its density is about 1.035 gm/ml. The red blood cells are dominant particulate matter in blood with about 40-45 per cent by volume of the whole blood. Sometimes we use the term "hematocrit" to specify the volume percentage of red cells and entrained plasma. Platelets are much smaller than red or white cells, with a diameter of 2-3 μm. Their number is one-tenth of the red cells. Both leukocytes and platelets are not numerous enough to influence significantly the flow characteristics of blood. However, platelets play an important role in the formation of blood clots which may severely interfere with the flow.

1.2.6 Microcirculation

Microcirculation may be defined as the circulation occurring in micro-vessel where the ratio of erythrocytes to vessel size is too large and the blood is considered as a non-homogeneous fluid. The rheology of the blood is non-Newtonian in the mocrovessel. For

human blood, the microvessel diameter is $\leq 1000\,\mu m$. The diameter of capillaries is ≤ 5 μm and these are permeable in nature. The hydraulic conductivity and permeability of the capillaries in different organs is shown in table 1.2. The architecture of the microvasculature and the biophysical behavior of the blood flowing through it strongly influence its capacity for material transport and exchange. It is evident that microcirculatory disorders are one of the major causes of many harmful diseases such as hypertension, sickle cell anemia, diabetes, tissue hypoxia and even organ failure.

Table 1. 2: The hydraulic conductivity of the capillaries L_p for various organs and the corresponding values of the permeability parameter ∏, for radius 10 μm and length 100 μm (Ganong, 2003).

Organ	$L_c \times 10^{-8}$ (m/Pa.s)	∏
Brain	3	0.092
Skin	100	0.536
Skeletal muscle	250	0.848
Lung	340	0.989
Heart	860	1.573
Gastrointestinal tract	13,000	6.118
Glomerulus in Kidney	15,000	6.572

1.3 Equations governing fluid motion

The constitutive equations give better understanding of the flow phenomena and forces that occurs due to the motion of blood through the arteries. The constitutive equations for the Newtonian and different non-Newtonian fluids are presented in this section.

The mathematical expression for the law of conservation of mass is defined as follows

$$In - Out + Source - Sink = Accumulation \, , \tag{1.3}$$

where each term represent a rate for different element of volume.

The continuity equation of fluid free from Source and Sink is written in general form as

$$\frac{D\rho}{Dt} + \rho \nabla . \mathbf{v} = 0 \, , \tag{1.4}$$

where $\dfrac{D}{Dt} = \dfrac{\partial}{\partial t} + \mathbf{v}.\nabla$ with $\nabla = \hat{i}_r \dfrac{\partial}{\partial r} + \hat{i}_\theta \dfrac{1}{r}\dfrac{\partial}{\partial \theta} + \hat{i}_z \dfrac{\partial}{\partial z}$ and $\mathbf{v} = (v_r, v_\theta, v_z)$ is the velocity of the fluid. If the density of the fluid (ρ) is constant (incompressible fluid), Eq. (1.4) reduces to

$$\nabla.\mathbf{v} = 0 . \tag{1.5}$$

The momemtum equation for the incompressible fluid with external force **F** is written as

$$\rho\left(\dfrac{\partial \mathbf{v}}{\partial t} + \mathbf{v}.\nabla \mathbf{v}\right) = -\nabla p + \eta \nabla^2 \mathbf{v} + \mathbf{F}, \tag{1.6}$$

with $\mathbf{v}.\nabla = v_r \dfrac{\partial}{\partial r} + \dfrac{v_\theta}{r}\dfrac{\partial}{\partial \theta} + v_z \dfrac{\partial}{\partial z}$ and $\nabla^2 = \dfrac{1}{r}\dfrac{\partial}{\partial r}\left(r\dfrac{\partial}{\partial r}\right) + \dfrac{1}{r^2}\dfrac{\partial^2}{\partial \theta^2} + \dfrac{\partial^2}{\partial z^2}$. η, p and t are

viscosity of the fluid, pressure and time, respectively. The above momentum equations are known as Navier-Stokes equations (which bears the names of Navier (1823) and Stokes (1845)). The solutions of the above equations are fully determined physically when the boundary and initial conditions are specified. In the case of the viscous fluid, the condition of no-slip on solid boundaries must be satisfied i.e., on the wall both the normal and tangential components of the velocity must vanish.

1.3.1 Governing equations of non-Newtonian Fluid Models

In the small arteries and capillaries, blood behaves as a non-Newtonian fluid and the constitutive equations are discussed below. Haematocrits, antigulants, temperature, viscosity etc. influence strongly the non-Newtonian nature of the blood in different parts of the circulatory system.

I. Time Independent non-Newtonian Fluid

For time independent non-Newtonian fluid, there is a non-linear relation between the stress τ and the rate of strain $\dot{\gamma}$ which can be written as

$$\tau = f(\dot{\gamma}) . \tag{1.7}$$

A Newtonian fluid is a special case of non-Newtonian fluid where the function $f(\dot{\gamma})$ is linear. The power law fluid (Waele, 1929), Bingham fluid (E. C. Bingham, 1916, 1922),

Herschel-Bulkley fluid (Herschel and Bulkley, 1926), Casson fluid (Casson, 1959) and biviscosity fluids are examples of this class. A rheological model of the non-Newtonian fluid is given in Fig. 1.5.
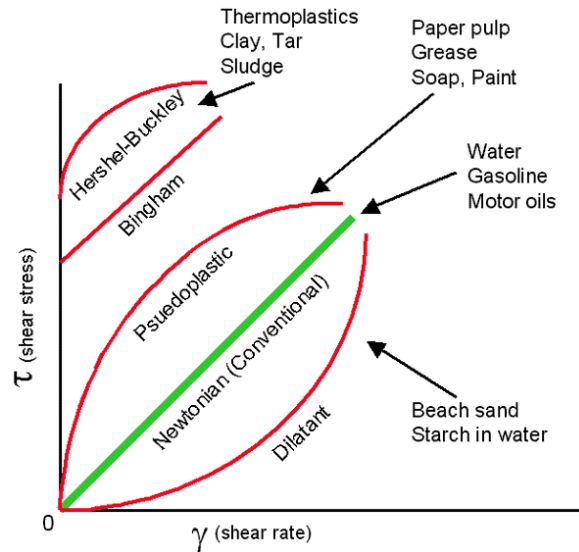

Fig. 1.5: Rheological model of non-Newtonian fluid (http://www.technet.pnl.gov)

II. Time dependent Fluids

The apparent viscosity of some fluids not only depends on the strain rate but also on the time the shear stress has been applied. These are generally classified into two classes as (i) thixotropic fluids and (ii) rheopectic fluids. A thixotropic fluid is a fluid which takes a finite time to attain equilibrium viscosity when introduced a step change in shear rate. Many gels and colloids are thixotropic materials, exhibiting a stable form at rest but becoming fluid when agitated. Some fluids are anti-thixotropic and those are called rheopectic fluid. For this case the shear stress increases with time as the fluid is sheared (Mazumdar, 1992).

III. Viscoelastic Fluids

A viscoelastic material exhibits both elastic and viscous properties. The simplest viscoelastic fluid is one which is Newtonian in viscosity and obeys Hooke's law (Hooke, 1678) for the elastic part and its constitutive equation is given by

$$\dot{\gamma} = \frac{\tau}{\mu} + \frac{\dot{\tau}}{\lambda}, \tag{1.8}$$

where λ is a rigidity modulus. When a viscoelastic fluid flows, certain energy is stored up in the material as strain energy in term of viscous dissipation. From several experimental results (Chmiel et al.,1990; Philips and Deutsch, 1975), it is shown that for the unsteady case, many fluids are not purely viscous, but exhibit significant visco-elastic properties. Second order fluid model (Ericksen and Rivlin, 1955), Walters liquid B (Walters, 1960), Oldroyd B fluid (Oldroyd et al., 1951) etc., are examples of some viscoelastic fluids.

1.3.2 Two-Phase fluid model and Glycocalyx layer

Blood flow in micro-vascular networks (arterioles, capillaries, and venules) show significantly different characteristics from that in the large vessels of the circulatory system due to Fahraeus effect and Fahraeus-Lindqvist effect (Suguhara-Seki and Fu, 2005). This field includes investigation of pressure-flow relationship of apparent effective viscosity of blood, microscopic properties of blood and its formed elements (red blood cells, leukocytes and platelets), and interactions among plasma, cells and blood vessels, in particular blood-vessel wall interactions. Blood is usually delivered through micro-channel networks by pressure gradients. When blood flows through a micro-channel, there will be a peripheral layer of plasma (Newtonian fluid) and a core region of suspension of all the erythrocytes as a non-Newtonian fluid. Power-law model (Qian et al., 2004), Casson fluid model (Srivastava and Saxena, 1995), Herschel-Bulkley fluid model (Sankar, 2008) are considered to represent the non-Newtonian character at core region. It is also shown that in the human blood vessels, the endothelium cells are covered with a gel-like layer of membrane-bound glycoproteins and plasma proteins, named as glycocalyx layer. It mediates the permeability of blood vessels, regulates the interaction between leukocytes and the endothelial surface during inflammation. The layer protects the vasculatures from various vascular diseases such as atherosclerosis. Physically, this layer is highly negatively charged, which interacts with moving plasma phase (treated as electrolyte), induces various interfacial, mechanical and electrochemical phenomena (Fig. 1.6). RBCs normally do not invade this region because of the electrostatic repulsion. It has been experimentally observed that the gycocalyx layer causes additional resistance to microvascular flow and the nature of the glycocalyx layer is highly negatively

charged (Liu and Yang, 2009). Due to the high negative charges at the glycocalyx region, an electric field develops and it may affect the blood flow. The electrical effect of the glycocalyx layer on streaming current, streaming potential and electrophoretic mobility of RBCs is important to investigate. So the electro-viscous or electro-kinetic force may play a vital role in the blood flow through micro-vessel. Its electrochemical characteristics are described by Gouy-Chapman theory (Gouy, 1910; Chapman, 1913).
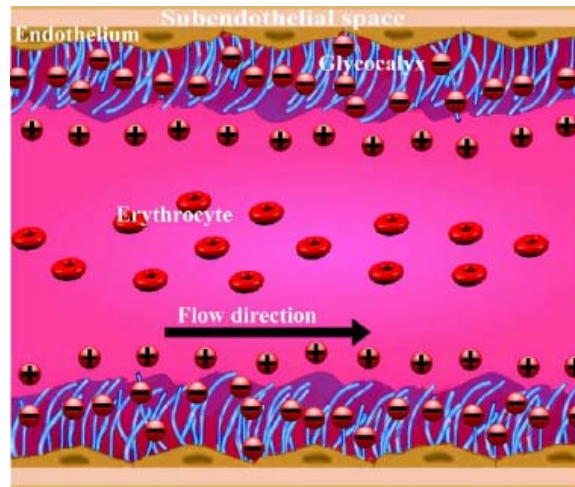

Fig. 1.6: Schematic illustration of blood flow in a micro- vessel. Erythrocytes flow at the core and only plasma at the peripheral layer. Glycocalyx holds negative charges and there are net positive charges in the flow (Liu and Yang, 2009).

1.4 Magnetohydrodynamics

Magnetohydrodynamics (MHD) is the discipline which studies the dynamics of electrically conducting fluid in the presence of magnetic field. During the last few decades, extensive research work has been done on the dynamics of biological fluid in the presence of magnetic field with implications in the bioengineering and medical technology.

1.4.1 Governing Equation of Magnetohydrodynamics

The set of the equations which describe magnetohydrodynamics is the combination of the Navier-Stokes equations and Maxwell's equations of electromagnetism. Let us consider an electrically conducting fluid moving with velocity $\mathbf{v}$ in the presence of an applied magnetic field $\mathbf{B_0}$ which gives an induced electromagnetic field in the normal direction to the direction of both the field and flow. The current $\mathbf{J}$, is made up of two parts, a convection part which is due to the convection charges in the medium and a conduction part that owes

the interaction of the motion and the magnetic field $\sigma[\mathbf{E}+\mathbf{v}\times\mathbf{B}]$ where $\mathbf{E}$ denotes the electric field at any point and σ is electrical conductivity. The current density $\mathbf{J}$ in a moving medium is given by Ohm's law

$$\mathbf{J} = \sigma[\mathbf{E}+\mathbf{v}\times\mathbf{B}]. \tag{1.9}$$

Now one can write the system of MHD equations with a term incorporating the Lorentz force as

$$\frac{\partial\mathbf{v}}{\partial t}+(\mathbf{v}.\nabla)\mathbf{v} = -\frac{\nabla p}{\rho}+\nu\nabla^2\mathbf{v}+\frac{1}{\rho}\mathbf{J}\times\mathbf{B}, \tag{1.10}$$

$$\nabla\times\mathbf{v} = \mathbf{0}. \tag{1.11}$$

Maxwell's equations:

$$\nabla\times\mathbf{E} = -\frac{\partial\mathbf{B}}{\partial t}. \tag{1.12}$$

$$\nabla\times\mathbf{B} = \mathbf{J}. \tag{1.13}$$

It also satisfies the following conditions

$$\nabla.\mathbf{J} = 0 \quad \text{and} \quad \nabla.\mathbf{B} = 0. \tag{1.14}$$

1.4.2 Applications of Magnetohydrodynamics

This area of research has the interest of many researchers in view of its important applications such as plasma studies, petroleum industries, MHD power generators, control of hyper velocity vehicles, cooling of nuclear reactors, boundary layer control in aerodynamics, crystal growth etc. Similarly in medical applications, it is often noted that the prevention and rational therapy of arterial hypertension are closely connected with the mechanism of its origin and development. The flow of blood can be controlled during surgeries by the application of an external magnetic field. It has also important applications in the development of magnetic devices for cell separation, targeted transport of magnetic particles as drug carriers, cancer tumor treatment causing magnetic hyperthermia, provocation of occlusion of the feeding vessels of cancer tumors and the development of magnetic tracers.

1.5 Nanotechnology and Drug Delivery

Nanotechnology is a multidiciplinary scientific field that applies engineering and mulfucturing principles to the design, synthesis, characterization, application of materials and devices on nanoscale. Nanotechnology has applications in several areas which include drug delivery, bioMEMS, tissue engineering, biosensors, microfluidics, microarrays, and bioengineering. The nano-technology based drug delivery system has emarged as mainstream research in advanced medical diagnosis and treatment. Corporate investment on nanotechnology for drug delivery diagnostics increased year by year and nanotechnology based drug delivery has already been commercialized by many reputed companies (Wang et al., 2005).

Nanotechnology-based drug delivery has many advantages and provide the insight for solving problems associated with conventional drug delivery systems. It has control over delivery of drugs to specific sites and to certain cells only, without affecting neighboring normal cells. Different type of carrier particles are used in the targeting of nanotechnology-based drug delivery systems, some of them are pH-sensitive carriers, thermally responsive carriers, photochemically controlled delivery system, magnetic targeted drug delivery of nanocarriers, ultrasound-mediated drug delivery and targeting. In the present analyses we mainly focus on the magnetic drug targeting.

1.5.1 Drug targeting

Drug targeting is the principle by which distribution of drug in the organism is maneuvered in a manner such that its major fraction interacts exclusively with the target tissue at the cellular or subcellular level. Theoretically, selective or targeting drug delivery systems can improve the outcome of chemotherapy by one or more of the following processes

1. By allowing the maximum fraction of the delivered drug molecule to react exclusively with the cancer cells without adverse effects to normal cells.

2. By allowing preferential distribution of drug to the cancer cells.

Fig. 1.7 presents a list of various classifications of drug targeting. A detailed description on this can be found in the article cited below

1.5.2 Magnetic drug targeting

Magnetically induced drug delivery involves encapsulasion of magnetic material, usually magnetite (Fe_3O_4) inside a polymer container that has a drug either tagged or trapped. Magnetic targeting is one of the major drug delivery methods which are used for treatment in different parts of our circulatory system. The therapy is very fruitful because it helps in the development of functional magnetic nanoparticles that are designed to target a specified tissue (Kingsley et al., 2006) and it also reduces the side effects. Magnetic carrier particles with surface-bound drug molecules are injected into the vascular system upstream from the malignant tissue, and are captured at the tumor via a local applied magnetic field. Upon achieving a sufficient concentration, the drug molecules are released from the carriers by changing many physiological conditions such as pH, osmolality, temperature, or different enzymatic activity, which help in releasing the drug molecules from the carrier particle (Molema and Meijer, 2001). Sometimes higher dosage can be applied for more effective treatment as the therapeutic agents are localized to regions of diseased tissue (Speziale, 2008).
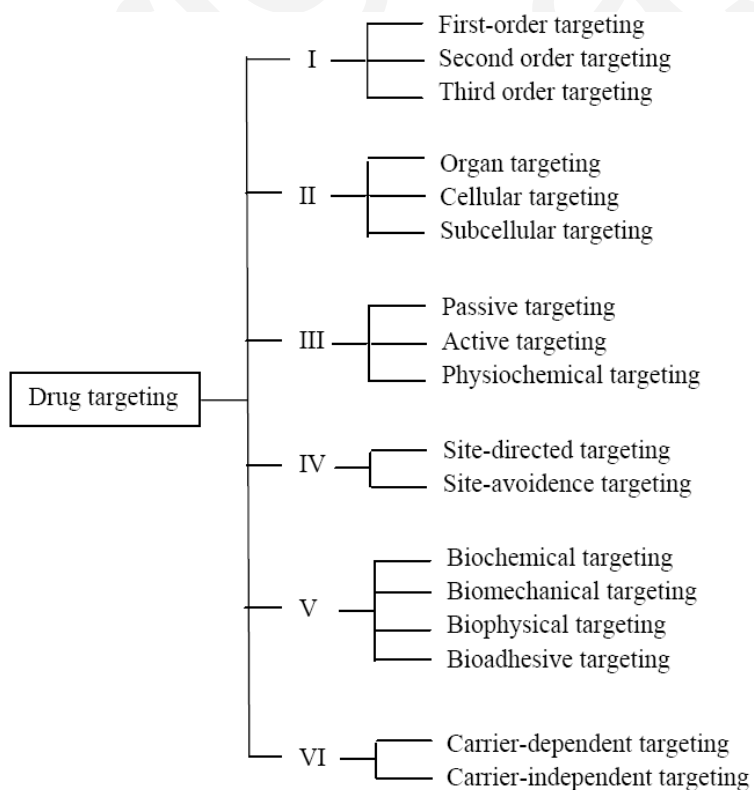

Fig. 1.7: Classification of the drug targeting (Lubbe et al., 1996).

1.6 Literature Review

The geometry of the circulatory system significantly influences the blood flow through cardiovascular system. The geometry of the stenosis also plays a vital role in the blood flow. Quite a good number of theoratical studies related to the presence of a single stenosis have been carried out in the recent past (Young, 1968; Forrester and Young, 1970; Young and Tsai, 1973; Misra and Chakravarty, 1986). All these studies assumed that the flow of the blood as Newtonian. At the low shear stress and at small arteries blood behaves as a non-Newtonian fluid. Scott Blair (1959) has given a mathmatical model for the blood flow through the arteries and fitted Casson's equation with blood nature. Charm and Kurland (1965) suggested that Casson's equation is applicable to the investigation of the viscosity of human blood for shear rates of 0-100,000 per sec . They modified the Casson's equation for different ranges of the shear rates. The nature of the blood at different parts of the cardiovascular system has been analyzed by Whitemore (1967). The effects of the mild stenosis on the resistive impedance and the wall shear stress in an artery have been put forward by Shukla et al. (1980) by considering the flowing blood as non-Newtonian power law and Casson's fluid models. Later Srivastava (2002) has discussed the effect of the hematocrit and the shape of the stenosis on the blood flow through stenotic artery. Effects of multiple stenoses and post-stenotic dilatation on non-Newtonian blood flow in small stenosed coronary arteries have been investigated by Pincombe et al. (1999) by considering the Casson fluid model. Recently, Sankar and Lee (2009) studied the pulsatile blood flow through an asymmetric stenosis treating blood as Herschel-Bulkley fluid. A clinical interest is seen in the study of blood flow in the aortic bifurcation, mainly at the curvature part and at the apex, which also help to genesis and diagnostics of atherosclerosis. A geometry of the bifurcated artery has been developed by Chakravarty and Mandal (1997) by considering a mild stenosis at the lumen. Recently Ro and Ryou (2009) analyzed blood flow in the stenosed bifurcated artery with acceleration of human body in 3-D by taking the rhology of blood as Carreau Viscosity model. In the present study, we investigate the blood flow through a bifurcated artery with a symmetric mild stenosis at the parent artery with Casson fluid and study different flow characteristics at various positions of the parent and daughter artery.

Many external applied forces can effects the blood characteristics and recently many studies are carried out in this direction. Here we mainly discuss the influence of magnetic field on the blood flow. A mathematical model on the effect of a magnetic field on blood flow has been analyzed by Chen (1985) treating blood as an electrically conductive fluid. The influence of a static magentic field on blood viscosity is due to the interaction between the induced magnetic moment on the RBC and the external static magnetic field. The RBC has greater susceptibility along the external magnetic field. It is well known that oxygenated hemoglobin is diamagneic and deoxygenated hemoglobin is paramagnetic in nature (Pauling and Coryell, 1936). The magntic susceptibility of hemoglobin in RBC varies greatly form negative in arteries to positive in veins (Shalygin et al., 1983; Weisskoff and Kiihne, 1992; Sakhnini and Khuzaie, 2001). Sud and Sekhon (1989) studied the blood flow throgh the human arterial system in the presence of a magentic field. Bhargava et al. (2007) have numerically simulated pulsatile flow and mass transfer of an electrically conducting Newtonian biofluid in a channel containing porous medium. MHD flow of a non-Newtonian fluid in a channel of slowly varying cross-section in the presence of a uniform transverse magnetic field was studied by Misra et al. (1998). Haik et al. (2002) developed a mathematical model of the biomagnetic fluid flow with stenosis in a channel and propounded that the presence of the magnetic field influences the flow field considerably. From the recent-most study of Tzirtzilakis (2008), it has been concluded that the flow velocity, the temperature field, the skin friction and the rate of heat transfer are greatly influenced by the magentic field. The effect of imposed strong non-unform magnetic field for different stenosis growth rates has been analyzed by Kenjeres (2008). In the present study, the effect of the magnetic field on the blood flow in the bifurcated artery is investigated considering a non-symmetric mild stenosis at the parent artery.

The biomdical applications of magentic particles can be traced back to the 1950s, when Gilchrist et al. (1957), treated lymphatic nodes and metastases by injecting metallic particles, which were heated using a magnetic field. Lately in 1970s, magnetic micro- and nanoparticles are used as therapeutic drug carriers to target specific sites in the body (Widder

et al., 1978; Senyei er al., 1978; Mosbach and Schroder, 1979, Ito et al., 2005). Among different drug delivery methods, the magnetic targeted drug delivery is one of the most attractive strategies due to its non-invasiveness, high targeting efficiency and minimizing the toxic side effects on healthy cells and tissues. Magnetic drug targeting therapy can be used for the medical tratment of various diseases, especially cancer, and cardiovascular and endovascular diseases, such as stenosis, thrombosis, aneurysm, atherosclerosis, etc (Alexiou et al., 2002; Jurgonset al., 2006; Chen et al., 2005). Once a magnetic carrier is concentrated at the tumor or other target *in vivo*, the therapautic agent is then released from the magnetic carrer, either via enzymatic activity or through changes in physiological conditions such as pH, osmolality, or temperature, leading to increased uptake of the drug by the tumor cells at the target sites (Alexiou et al., 2000). Interest in this therapy is growing due to the recent progress in the development of carrier particles that are designed to target a specific tissue, and effect local chemo-, radio- and genetherapy at the tumor site (Hafeli et al., 1997; Berryl and Curtis, 2003; Pankhurst et al., 2003; Fabrizio and Francois, 2004).

Quantative understanding of the blood flow through arterioles and venules is necessary for assessing the hydrodynamic resistance and its regulation in the microcirculation as well as for analyzing mass transport process. Experimental investigations of Cokelet (1972) and thoretical observations of Haynes (1960) indicate that blood can no longer be treated as a single-phase homogeneous viscous fluid in small size vessels (of diameter $\leq 1000\,\mu$m). Skalak (1972) concluded that in capillary vessels whose diameter (4-10 μm) are equal or smaller than that of diameter of a red blood cell, an accurate description of flow is required. Bugliarello and Sevilla (1970) presented blood in a small diameter tubes by a two-layered model assuming peripheral and core fluids as Newtonian fluids of different viscosities. Seshadri and Jaffrin (1977) modeled the outer layer as cell-depleted, having a lower hematocrit than in the core. Chaturani and Upadhya (1981) addressed the flow of blood in small diameter tubes using the two-layered model of micropolar in the cell free region and couple stress fluid in the core region, respectively. Gupta et al. (1982) divided the outer layer into a cell-free plasma layer and the cell-depleted layer. In both these studies, the

velocity profile in the core was assumed to follow a power law. Chein et al. (1984) reviewed the study on blood flow in narrow tubes. Srivastava and Saxena (1995) modeled blood flow induced by peristalic waves as consisiting of a core of Casson fluid and a peripheral layer of Newtonian fluid. Pries et al. (1996) reviewed biophysical aspects of microvascular blood flow *in vivo* as well as *in vitro*. Damiano (1998) has presented a semi-empirical model for the blood flow in glycocalyx-lined microvessel grater than $20\,\mu$m in diameter. Sharan and Popel (2001) divided the two-layers as immiscible Newtonian fluids, consisting of a cylindrical core surrounded by a less viscous, being discontinous at the interface between the two regions.

1.7 Overview of the Thesis

This thesis consists of eight chapters, the first one is an introductory and chapters 2 to 7 are dealing with main content of the research work done, in chapter 8, concluding remarks are made and future directions of work are indicated.

Chapter 1 is introductory chapter where the research interface has been presented. The motivation for carrying out the research has been outlined and the preliminary concepts used to develop the models have been discussed briefly in this part.

In **chapter 2**, Flow of a pulsatile Casson fluid through a stenosed bifurcated artery has been investigated in this study. The arteries forming bifurcation are assumed to be symmetric and straight cylinders of finite length and undergo wall motion. The governing momentum equation is written in terms of the shear stress, and the resulting equation along with the initial and boundary conditions is solved numerically. The crucial parameters that influence the flow are the radius of the parent artery, length of the stenosis and the curvature at the different sections of the bifurcated tube. Flow variables are computed at various locations in the parent and daughter arteries. It is observed that the wall motion, along with the bifurcation angle, plays a significant role on the fluid flow and the viscous shear stress. The shear stress in the parent and daughter arteries plotted against the axial coordinate clearly indicates that due to the stenosis, there is an increase in the shear stress in the parent artery and its effect is also felt in the daughter arteries. The velocity is derived from the shear stress,

the volumetric flows in both the parent and daughter arteries are computed for various parameters. It is observed in both the femoral and coronary arteries that the variation of axial velocity and the flow rate with yield stress is uniform; the flow rate in the daughter artery shows more oscillations with the Casson fluid model than that with Newtonian one. The effect of blood rheology on the velocity pattern in the daughter artery is greater than in the parent artery. The axial velocity and flow rate are greater in coronary artery than in the femoral artery, and the wall shear stress in the parent artery increases due to the stenosis.

Main focus of **Chapter 3** is to analyze the flow of a pulsatile Casson fluid through a bifurcated artery with asymmetric stenosis in the presence of magnetic field. As in the chapter 2, the arteries forming bifurcation are assumed to be symmetric and straight cylinders of finite length and also it is assumed that the wall of the bifurcated artery undergo wall motion. Here, a family of non-symmetric mild stenoses is considered at the parent artery. Here we have the asymmetric parameter of the stenosis and the Hartmann number (M) as the additional parameters. The velocity and the volumetric flow in both the parent and daughter arteries are computed for various parameters. It is observed that the velocity at the parent artery decreases due to the magnetic field. At the daughter artery the velocity profile changes drastically due to magnetic field. It is evident that the shear stress increases with increase in the height of the stenosis and attains maximum value at the maximum narrowing point of the artery.

In **chapter 4**, a two dimensional unsteady flow of a Casson fluid through an artery with asymmetric stenosis is analyzed under the influence of body acceleration under the influence of an external magnetic field. An explicit finite difference scheme is applied to obtain the flow field. The effect of body acceleration, magnetic field on the axial and radial velocities, flow rate and wall shear stress is analyzed. The wall shear is increasing non-linearly with the yield stress parameter. With the increase in the Hartmann number there is a significant reduction in the volumetric flow rate, and this reduction increases with the increase in the phase of the body acceleration parameter. The axial velocity increases with the axial distance from the pre - to post- stenosis region. It decreased with the non-dimensional radial position in all the regions. It also indicates that there exists a back flow for the case of symmetric stenosis near the pre-stenosis region while this back flow disappears as

the value of the asymmetry parameter ng is increased. This is because of the favorable pressure gradient develops near the wall with the increase in the value of ng.

The development of nanoparticle-based drug delivery system has been the interest of several bio medical researchers now. Drugs can be absorbed onto the particle surface, entrapped inside the polymer / lipid, or dissolved within the particle matrix. Recently, magnetic nanoparticles are used in the magnetic targeting drug delivery system. **Chapter 5** is aimed at understanding the effect of non-Newtonian blood rheology (considering both Casson and Herschel – Bulkley models) on the magnetic targeting of the carrier particles in the micro-vessel of radius $50\,\mu\mathrm{m}$. The dominant fluidic and magnetic forces are used in the momentum equation. Several factors that influence the magnetic targeting of the carrier particles in the microvasculature, such as the size of the carrier particle, the volume fraction of embedded magnetic nanoparticles, and the diameter of the micro-vessel are considered in the present problem. An algorithm is given to solve the system of coupled equations for trajectories of the carrier particle in both non-invasive and invasive cases. It is interesting to note that the volume fraction decreases with the value of non-dimensional parameter ξ_c. The carrier particle needs less volume fraction to be captured by the magnet with increase in ξ_c. The volume of the carrier particle increases with the radius and therefore the magnetic force between the carrier particle and magnet increases. The tendency of the carrier particle to be captured by the magnet increases with the rheology of blood changing from shear-thinning to shear-thickening. It has also been observed that the rheology of the blood is more effective for the invasive case than the non-invasive case.

Chapter 6 deals with finding the trajectories of the drug dosed magnetic carrier particle in a micro vessel which is subjected to the external magnetic field. We consider the physical model that was given in the work of Furlani and Furlani (2007), but deviating by taking non-Newtonian fluid model for the blood and considered the permeability of the micro-vessel. The expression for the fluid velocity in the permeable micro vessel is obtained using the analogy given in Decuzzi et al. (2006) first. Then the expression for the fluidic force for the carrier particle traversing in the non-Newtonian fluid is obtained. The study is focused on analyzing the effect of permeability on the carrier particle trajectories. The

trajectories of the carrier particles are found in both invasive and non-invasive targeting systems. A comparison is made between the trajectories in the Casson and Herschel-Bulkley fluid models and for the permeable and impermeable micro vessels. Also, a prediction of the capture of therapeutic magnetic nanoparticle in the permeable microvasculature is made for different radii and volume fractions in both the invasive and non-invasive cases.

In human blood vessel, the endothelium cells are covered with a gel-like layer of membrane-bound glycol-proteins and plasma proteins, named as the glycocalyx layer. Physically, this layer is highly negatively charged (Potter and Damiano, 2008), which interacts with the moving plasma phase (treated as an electrolyte), induce various interfacial, mechanical and electrochemical phenomena. The endothelial glycocalyx layer on the luminal surface of the blood vessels plays a significant role in regulating blood flow and blood cell movement in micro-vascular network. The **chapter 7** deals with finding the trajectories of the drug dosed magnetic carrier particle in a micro vessel with two phase fluid model which is subjected to the external magnetic field. The micro vessel region is divided into the endothelial glycocalyx layer where in the blood is assumed to obey Newtonian character and a core and plug regions where in the blood obeys the non-Newtonian Herschel Bulkley character. The endothelial glycocalyx layer causes additional resistance to blood flow in small blood vessels. The carrier particles are injected into the vascular system upstream from malignant tissue, and captured at the tumor site using a local magnetic field. The effect of the size of the carrier particle, the volume fraction of embedded magnetic nanoparticles, and the diameter of the micro-vessel are considered in the present problem. It is noticed that the average fluid velocity in the two phase fluid model is more compared to that in single phase model, because of which the number of free particles is observed to be more in the two phase model (present case) compared to those in (Chapter 5) impermeable wall case. From the comparison of the results for the present two phase model and single fluid model, it is evident that the glycocalyx layer of the blood vessel influences significantly the magnetic drug targeting.

Finally, concluding remarks regarding the work presented in Chapter 2 to 7 and the scope of future work related to this is presented in **Chapter 8**.