MASS TRANSPORT OF CHOLESTEROL IN ARTERIES

by

MAGDALENA LUCA

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MAGDALENA LUCA

A Thesis/Practicum submitted to the Faculty of Graduate Studies of the University of Manitoba in partial fulfillment of the requirements for the degree of

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To My Parents

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Magdalena Luca

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ABSTRACT

The thesis consists mainly of two parts. The first part gives a review of the properties of the components involved in blood flow in arteries affected by arteriosclerosis. The blood flow in arteries includes flow through porous medium (deposited cholesterol), as well as flow past porous medium (in the arterial channel). The second part gives a mathematical analysis of the flow in an artery whose cross section is a circle and the porous medium forms an annulus which is a doubly connected region. Analytical expressions are derived for the velocities of the flow, concentrations, and volume flux for both the porous medium and the channel. The results for the velocity components are illustrated by numerical computation for a set of parameters. A new approach to find the rate of growth per unit width per unit time of the cholesterol deposit is also given.

CHAPTER 1

Introduction

1.1 The Problem and the Scope

The radial incorporation of **cholesterol** in an arterial (arteriolar or capillary) wall gives form to deposits which grow inward and restrict blood flow. In time, this produces a disease called **arteriosclerosis**, prevalently found in elderly people and it may lead to cerebral and coronary thrombosis, myocardial infarctions, and others. These ailments are becoming more common throughout the world and much research has gone into elucidating the various factors determining this condition.

Generally speaking, the heart is a muscular pump which contracts about seventy times a minute and is capable of doing so for over eighty years. Like all muscles, it must have a blood supply to carry oxygen and nutriment to it. The blood supply of the heart is carried by three small blood vessels arising from the aorta and known as the **coronary arteries**. The coronary arteries have a smooth inner lining, the **endothelium**, and it is this lining that gradually becomes thicker due to

the progression of arteriosclerosis. This process is largely due to deposition on the endothelium of substances containing **cholesterol**. When the endothelium becomes laden with cholesterol, it seriously impedes the flow of blood to tissue, and in the case of coronary arteriosclerosis, the musculature of the heart begins to suffer the effects of an inadequate blood supply. Ultimately, a coronary artery may even become blocked.

Am important problem related to arteriosclerosis is the rate of accumulation of cholesterol into plaques. As like many other authors, we approach the problem by constructing an idealized model.

Thus, the problems discussed in this thesis have the following objectives:

(a) A biological model of blood flow through and past porous medium will be elaborated.

(b) Cholesterol mass transport in arteries is calculated to further analyze mass transfer and accumulation within the arterial wall. The accumulation of cholesterol is due to diffusion of the blood plasma lipoproteins.

1.2 Brief Description of the Biological Model

The biological problem can be presented mathematically in various levels of generality. To be rigorous, it seems evident that the heart, aorta, arteries, and veins should be represented by a three-dimensional network, and the special geometry and materials of construction of various organs must be described and incorporated in the model. In practice it is useful to consider simplified, unrefined models first, learn the general features, identify the important parameters, and

then add details when feasible, on the assumptions that these important characteristics are retained in the complex system.

To understand the events occurring in the arteries, we consider the following simple model that shows similarities with models studied by other authors: *each artery is treated as an infinite, isolated, circular cylindrical rigid tube; the blood is taken to be a viscous, Newtonian, incompressible, and homogeneous fluid. We approximate the flow to be steady, laminar, and along the axis of the tube.*

The blood flows through and past a porous medium and is driven in both media by the same pressure gradient. The porous medium consists of tissue fluid, lymph, lymphatic vessels, and other cells and particles, including cholesterol, and *it is considered to be homogeneous and isotropic.* As we can see in Figure 1.1, between the interior channel and the porous medium there exists an imaginary wall that we treat as **permeable** to both blood, which constitutes the solvent in a solution containing cholesterol solute, and to solute. The exterior wall of the artery is considered **impermeable**, and thus the tangential component of velocity

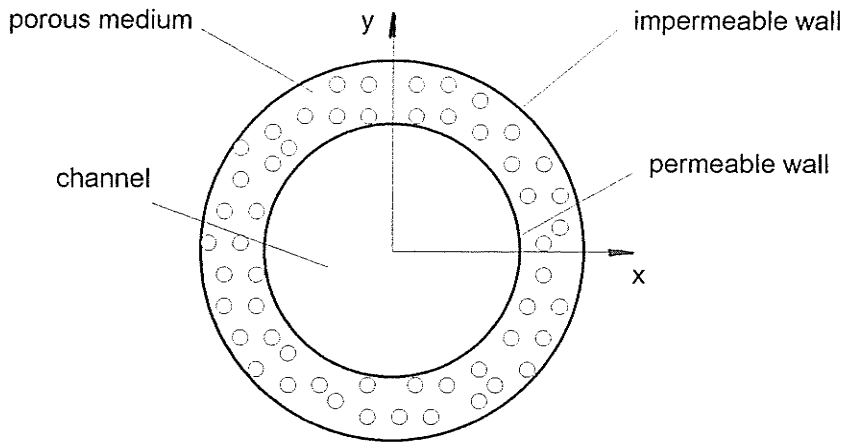

Figure 1.1 Schematic drawing of the idealized model.

will be zero. This property of the impermeable boundary is called a **no-slip condition**.

We assume the velocity of the flow to have only one component along the z-axis which is the longitudinal axis of the two concentric cylinders as shown in Figure 1.2.

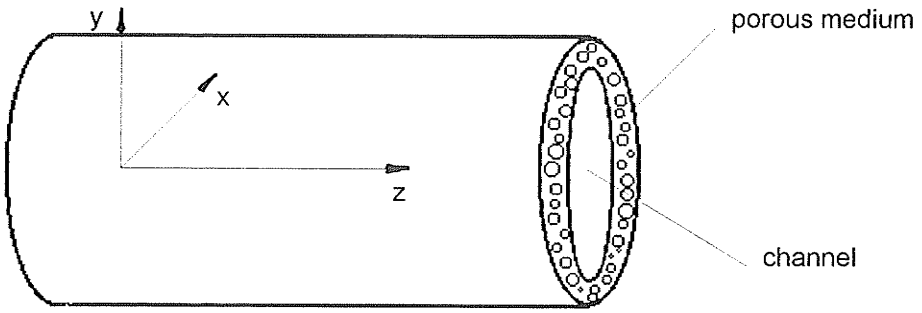

Figure 1.2 System of coordinates for the idealized model.

Such a model represents a biomechanical problem. Consequently, it is important to know the characteristics of the flow through and past porous media. Therefore we will briefly review some features of these types of flow.

1.2.1 Flow Through a Porous Medium

Flow in a porous medium in general is an ordered flow in a disordered geometry. The transport process of flow through a porous medium involves two substances: the fluid and the porous matrix, and therefore it will be characterized by specific properties of these two substances (see Figure 1.3).

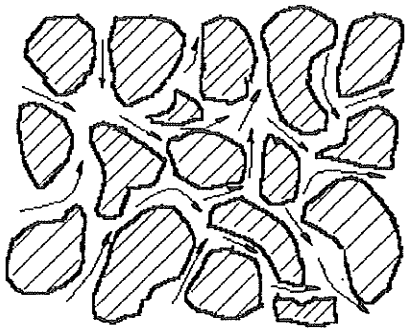

Figure 1.3 Flow in a porous medium (From Ockendon [25]).

A porous medium usually consists of a large number of pores each of which is filled with the fluid. Intuitively, pores are void spaces which must be distributed more or less frequently through the material if it is to be called *porous*. Extremely small voids in a solid are called *molecular interstices*, and very large ones are called *caverns* (see Scheidegger [32]).

The structure of the pores is often highly complicated and differs from medium to medium. Pores are invisible to the naked eye in the majority of porous media. The porous nature of a material is usually established by performing a number of experiments on a sample and observing its behavior.

Appropriate experiments lead to the determination of various *macroscopic* parameters which are often uniquely determined by the pore structure of the sample and do not depend on any other property. The most important macroscopic pore structure parameters are the *porosity*, the *permeability*, the *specific surface area*, the *formation resistivity factor*, and the *reduced breakthrough capillary pressure*, as given by Dullien [11]. For our analysis, following Rudraiah [30], only the permeability parameter will be taken into account.

Permeability is the term used for the conductivity of the porous medium with respect to permeation by a Newtonian fluid. Permeability, used in this general sense, is of limited usefulness since its value in the same porous sample may vary with the properties of the permeating fluid and the mechanism of permeation. It is advantageous to separate out the parameter which measures the contribution of the porous medium to the conductivity and is independent of fluid properties and flow mechanisms. The quantity is the **specific permeability** k, which will be referred to as **permeability**, hereinafter. Its value is uniquely determined by the pore structure (see Dullien [11]).

The *microscopic* pore structure is extremely difficult to analyze due to the great irregularity in pore geometry.

The pores in a porous system may be *interconnected* or *non-interconnected*. Flow of interstitial fluid is possible only if at least part of the pore space is interconnected. According to this description, the following are examples of porous media: towers packed with pebbles, beds formed of sand, granules; porous rocks such as limestone, pumice, dolomite; fibrous aggregates such as cloth, filter paper; catalytic particles containing extremely fine micro-pores.

When a fluid percolates through a porous layer, because of the complexity of microscopic flow in the pores, the actual path of a singular particle cannot be followed analytically. In this case, one has to consider the gross effect of the phenomena represented by a macroscopic view applied to the masses of fluid. In our study case, the porous medium represents the tissue space surrounding the blood vessel. Also, it will be assumed that the porous medium is saturated with fine solid particles uniformly scattered and fixed in space.

1.2.2 Flow Past a Porous Medium

Flow past a porous medium takes place in the channel space described in Figures 1.1 and 1.2. The flow past the porous medium is assumed to be laminar, along the axis of the channel and in steady state. For such a viscous flow, it is important to use appropriate boundary conditions at the permeable wall.

It has been presumed, prior to 1967, that the tangential component of the velocity is zero, i.e. the no-slip condition is valid at the porous interface. In 1967, Beavers and Joseph [2] showed that, in general, the no-slip condition is no longer valid for this type of boundary. They have postulated the existence of a slip at the nominal surface and experimental support was provided. The existence of the slip at the porous bed is due to the transfer of momentum from the free flow in the channel into the porous medium. Since the medium is saturated, as noted in the previous section, this momentum will be converted into drag. Beavers and Joseph have established experimentally that the effects of viscous force in the free flow will penetrate beneath the permeable surface to form a boundary layer region in the porous medium.

The usual boundary condition used at the common boundary of the channel and the porous space is the one that matches the velocities found in each medium. One can employ any of these boundary conditions (and many others) depending on the complexity of the model. There does not seem to be a universally approved type of behavior of the fluids at the interface of the channel flow and the flow in the porous medium.

1.2.3 Method of Description of Fluid Flow

In simple terms, a fluid is a substance which cannot resist a shear force or stress without moving as can a solid. Liquids and gases are classified as fluids. A liquid has intermolecular forces which hold it together so that it possesses volume but no definite shape. Liquids have slight compressibility and the density varies little with temperature or pressure (see Hughes [18]).

The fluid is treated as a *continuous medium*. The continuum theory enables us to use the concept of local velocity of the fluid, and we must consider how the field of flow may be specified as an aggregate of such local velocities. Two distinct specifications are possible. The first one is called the **Eulerian method** and it describes various physical quantities at fixed points in the flow field. The second one, or the **Lagrangian method**, traces the motion of individual fluid particles. The Eulerian method is commonly used in studying fluid flow since standard instruments for measuring pressure or velocity are installed at fixed locations.

1.3 Review of Previous Work

The purpose of this review is to highlight the background literature of the problems discussed in the subsequent chapters. Also, we would like to emphasize that our analysis is a continuation of previous research developed for a different geometry, that is fluid flow through parallel plates.

The previous section presented a model of cholesterol deposition in the arterial wall. Consequently, the two basic aspects of this biological problem are

cholesterol and arteries. Cholesterol is well described in Cook's [8] book "Cholesterol: Chemistry, Biochemistry and Pathology". A representative book about arteries and blood flow through them is McDonald's [21] book "Blood Flow in Arteries". It has elaborate discussions on the structure of arteries and also a detailed mathematical description of the implications of blood flowing through the arteries.

Blood flow in vessels has, for many years, been an interesting and challenging subject, and intensive research has been dedicated to it. Tang and Fung [36] developed in 1975 a model of lung alveolar sheet. The smallest microscopic blood vessels in the human lung are organized into sheet-like networks. These sheets form the walls of the 300 million alveoli in which air flows due to breathing. Each sheet is idealized into a channel bounded by two thin layers of porous media. Blood flow in the channel and water movement in the porous wall were investigated.

Later, in 1985, Rudraiah [31] studied the steady laminar flow in a parallel plate channel bounded below by a porous layer of finite thickness and above by a rigid impermeable plate moving with uniform velocity. He considered the two cases where the porous medium being bounded below: (i) by a static fluid and (ii) by a rigid impermeable stationary wall. He also derived a modified slip condition involving the thickness of the porous medium. This slip condition is related to the slip condition postulated by Beavers and Joseph [2] in 1967. Their experiments showed that the mass outflow of a Poiseuille flow over a naturally permeable block is greatly enhanced over the value it would have if the block were impermeable, indicating the presence of a boundary layer in the block. The velocity presumably changes across this layer from its Darcy value to some slip

value immediately outside the permeable block. This condition was subsequently named the BJ-slip condition.

Complicated models take into consideration blood flow through a channel with varying gap. Guha and Chaudhury [16] studied the fluid mechanical effects of the permeability of the wall of an arteriosclerotic blood vessel by idealizing the tissue space as a porous medium bounding the blood vessel and the arteriosclerotic blood vessel as a constricted axisymmetric tube of slowly but arbitrarily varying cross-section.

Vafai and Thiyagaraja [38] analyzed fluid flow and heat transfer at the interface region of a porous medium. They discussed three general and fundamental classes of problems in porous media: the interface region between two different porous media, the interface region between a fluid region and a porous medium, and the interface region between an impermeable medium and a porous medium. These three types of interface zones constitute a complete investigation of the interface interactions in a saturated porous medium. They derived detailed analytical solutions for the velocity and temperature distributions for all interface conditions.

An important result on the modeling of porous media was obtained in 1985 by Kim and Russel [20]. Part of their research was based on Brinkman's model with an effective viscosity. The use of the Brinkman equation leads to an apparent slip velocity at the boundary of a porous medium. They calculated the bulk stress via volume averaging and thus determined the effective viscosity and the slip coefficient for dilute porous medium. Kim and Russel found that the averaging technique failed since the Brinkman equation itself was no longer valid. They proposed a new form of the Brinkman equation.

In 1986, Shivakumar et al. [33] considered blood flow in arteries idealized into a channel of varying gap bounded by porous layers. They analyzed the problem using the BJ-slip condition. The mathematical results were then applied to a problem of smooth constriction in an artery with stenosis already set in.

Misra and Singh [22] investigated pulsatile flow of blood through arteries by treating blood vessel as a thin-walled anisotropic, non-linearly viscoelastic, incompressible circular cylindrical shell. They also considered nonlinearities of the flow of blood. The displacement components at the vessel wall were obtained from the equations of equilibrium. The influence of the wall deformation on the flow properties of blood was taken into account in their analysis.

A closely related subject to blood flow in arteries is particle diffusion in arteries. An important contributor to this field was Taylor [37] who published a paper on dispersion of particles in a solvent in 1953. His research was based on the fact that when a soluble substance is introduced into a fluid flowing slowly through a small-bore tube it spreads out under the combined action of molecular diffusion and the variation of velocity over the cross section. He showed analytically that the distribution of concentration is centered on a point that moves with the mean speed of flow. He also gave a new method for measuring diffusion coefficients.

Taylor's results have been a major factor in the development of the subject. In 1975, Fung and Tang [13] and [14] extended Taylor's study to the case of flow in a channel bounded by porous layers. Their interest was in longitudinal dispersion of tracer particles in the blood flowing in a pulmonary alveolar sheet. They showed that the mean coefficient of apparent diffusivity is smaller in a channel bounded by porous layers than that in a channel with impermeable walls for the case when the channel walls are permeable to solvent but not to tracer. When

the channel walls are permeable to both solvent and tracer, the mean coefficient of apparent diffusivity is nearly the same as that of a channel with impermeable walls. They also proved that if a tracer is permeable through the membrane that separates the blood from the tissue space, which in turn is limited by an impermeable wall, then, at a steady state, the concentration of that tracer is uniform in both compartments. If a tracer is restricted to the vascular space by a semipermeable membrane, then its concentration is non uniform.

Later, in 1980, Chandrasekhara, Rudraiah and Nagaraj [6] also followed the analysis of Taylor and attempted to construct a deterministic model for the longitudinal dispersion in a porous medium. Their model gives, for the first time in the literature, information about the behavior of the diffusion coefficient with the particle size of a porous medium.

Pal et al. [26] considered, in 1984, longitudinal dispersion of solute in a channel bounded by porous layers using the BJ-slip condition. They found that the effect of slip is significant only in the case when the membrane is permeable to solvent but not to the tracer.

More recently, in 1990, Neumann et al [24] developed a mathematical model of the transient incorporation of cholesterol in the arterial wall. The experimental investigation supported their hypothesis that hemodynamics and the endothelial lining influence wall flux in intact vessels. Exposure to altered hemodynamics was associated with increased incorporation of cholesterol. Based upon measurements of vessel wall forces and endothelial cellular morphology accompanying hemodynamic simulations, the authors suggested that hemodynamically induced alterations to endothelial structures led to the increased permeability, convection and incorporation observed in the study.

Perktold, Thurner and Kenner [28] carried out computer simulations of pulsatile non-Newtonian blood flow in different human carotid artery bifurcation models. Two rigid walled models were analyzed, differing in the bifurcation angle and the bifurcation region, in order to contribute to the study of the geometric factor in atherosclerosis. The results showed a significant difference in the wall shear stress and in the flow separation. Also, flow velocity and wall shear stress distribution were analyzed in a compliant carotid artery bifurcation model. In the mathematical model, the non-Newtonian flow field and the idealized elastic wall displacement were coupled and calculated iteratively at each time step. The investigation demonstrated that the wall distensibility alters the flow field and the wall shear stress during the systolic phase. Comparison with corresponding rigid wall results showed that flow separation and wall shear stress were reduced in the distensible wall model.

To investigate the role of fluid mechanical factors in atherogenesis, Deng, King and Guidoin [10] studied theoretically, using a two dimensional T-junction model, the effect of blood flow on the transfer of low density lipoproteins from flowing blood to the luminal surface. The flow fields in the junction were obtained by solving the Navier-Stokes equations numerically and the concentration distribution of low density lipoproteins at laminar surface was determined using a finite difference analysis. The transfer of low density lipoproteins from flowing blood to the surface of the vessel wall was greatly enhanced in the two regions of this third flow, one in the main vessel, the other in the subsidiary vessel. The authors' mathematical model predicted that locally disturbed blood flows at arterial bifurcations and junctions provided favorable conditions for the

accumulation of atherogenic substances at the luminal surface, thus increasing the potential for lipid infiltration into the vessel wall.

Cavalcanti [5] investigated the hemodynamics in the early stages of the atherosclerotic process. A local, slight increase in the wall thickness of a canine femoral artery was simulated using an original two-dimensional mathematical model of arterial hemodynamics and the effects induced on the velocity field by the simulated mild stenosis were analyzed. The model incorporated: fluid non-linear inertial forces, viscoelastic wall motion, anatomical taper, unsteady flow, pressure propagation and reflections on both the proximal and distal vessel ends. The distribution along the vessel during the cardiac cycle of both the velocity profile and wall shear stress, were shown. The shape of velocity distributions was strongly perturbed by the stenosis and disturbances were clearly evident whatever instant of the cardiac cycle was considered. The reported results provided a coherent explanation of the critical role that hemodynamic factors may play in the early stages of atherogenic process.

1.4 Thesis Outline

The thesis is divided into two main parts. The first part consists of chapters 2 and 3 dealing with the biological aspects of our model. The second part of the thesis contains chapters 4 and 5 which studies the mathematics of the biological model.

In chapter 2, we study blood flow in arteries in general. We review the composition and the rheology of blood. Special attention is given to the viscous

properties of the blood and their implications in the consideration of blood flow. We examine the structure of arteries and their physiological properties.

In chapter 3, we describe the role of cholesterol in arteries. After a brief presentation of the history of cholesterol, we investigate different aspects influencing the physiology of cholesterol, such as diet, race, and age. The significant part is the analysis of the pathological manifestation of cholesterol, in particular, the cholesterol deposition. Dispersion of cholesterol in arteries is then studied and general mathematical description of it is given.

Chapter 4 provides the basic equations of mass, motion and concentration associated with any flow problem. Those equations are then formulated to suit our biological problem. Related boundary conditions are also supplied.

The aim of the thesis is to solve analytically the equations presented in chapter 4 and provide numerical computations and graphs for the velocity components of the flow in both regions for a particular and representative set of numerical values for the parameters involved.

The contribution of the thesis is in chapter 5, where the analytical solutions of the equations governing the flow in the channel and in the porous medium are obtained. The solutions are then used to analyze mass transport in arteries, including the volume flux of blood flowing through arteries and the mass transfer of cholesterol to the wall. In section 5.5, we obtain significant results on cholesterol deposition: the amount of deposited cholesterol and the growth of cholesterol per unit width per unit time.

CHAPTER 2

Arterial Blood Flow

2.1 Composition of Blood

The circulatory blood system that we analyze is complex. Attempting to develop an adequate model of this system and its behavior is almost an impossible task. In order to make any progress, we consider a simplified model.

Under normal conditions, blood flow in the human circulatory system depends upon the pumping action of the heart. Here we concentrate on a small section of this circuit, the relatively straight section following point A in Figure 2.1. We could imagine that blood flow in this part would behave in much the same way as water in a cylindrical tube. However, this is a gross simplification of the situation. To understand this last statement we have to depict some important facts and properties regarding blood flow and arteries.

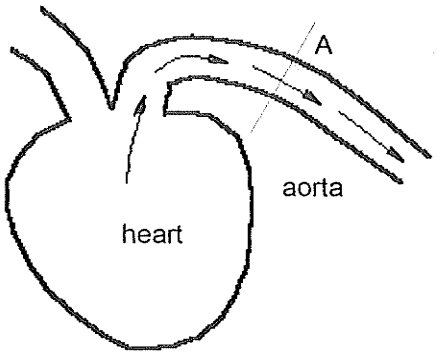

Figure 2.1 Schematic description of an aorta.

When blood is centrifuged in a centrifuge, it separates into a fluid called **plasma** and formed elements: **blood cells** and **platelets** (or **thrombocytes**) . There are two types of blood cells: **red cells** or **erythrocytes** and **white cells** or **leukocytes**. Leukocytes can be either *granulocytes* (and further classified as being of *neutrophil* 65%, *eosinophil* 4%, or *basophil* 1% variety) or *agranulocytes* (and further classified as being *lymphocyte* 25%, or *monocyte* 5%).

Blood plasma is a fluid containing about 90% water by weight, acting as a solvent, and the following solutes:

(a) *plasma protein* 7%. It consists of *albumin* 55%, *globulin* 44.8%, and *fibrinogen* 0.2%. Fibrinogen, for example, is important in blood clotting.

(b) *nitrogenous waste* substances that a carried from their site of production to the kidneys.

(c) *inorganic salts* of sodium, calcium, magnesium, and potassium, the most common being sodium chloride.

(d) *organic nutrients*. The most important are: (i) *blood sugar*, mainly glucose derived from the breakdown of foods. The precise level of blood sugar is critical for maintaining homeostasis[1] and is controlled by a negative feedback

[1]homeostasis = the maintenance by an organism of a constant internal environment.

mechanism in which insulin plays a major part. (ii) *blood lipids* such as fats and **cholesterol**, derived from dietary intake or activity of the liver.

(e) *hormones* manufactured in the endocrine glands.

(f) *dissolved gases* such as nitrogen, small quantities of oxygen, and carbon dioxide.

The **blood cells** mainly consist of **red blood cells**, about 5 million per mm^3 of blood. The erythrocytes occupy approximately 45% of the blood volume. The cell carries carbon dioxide from tissues to lungs, and contains hemoglobin pigment for oxygen transport from lungs to tissues. It is a small cell (7.2 μm in diameter and 2.2 μm thickness), non nucleated, has definite biconcave shape, and a flexible membrane.

The **white blood cells** are unpigmented cells and they make up less than 1 / 600th of the total cellular volume. The leukocyte count is usually about 10,000 cells per mm^3 of blood. This is not the total body count, because leukocytes are found as much in tissues such as spleen, thymus, and kidney as in blood. The cells have a round shape and a short life span, 2 to 14 days. Their primary role is to defend the human body against invading organisms and other foreign material.

Platelets form about 1 / 800th of the total cellular volume. They consist of non nucleated cytoplasmic fragments of large bone-marrow cells 3 μm in diameter, called *megakaryocytes*, that have entered the blood circulatory system. Platelets play an important role in blood clotting.

Rubinow [29] defines the **specific gravity** of a cell as the ratio ρ / ρ_0, where ρ is the mass density of the cell, and ρ_0 is the mass density of water, under normal conditions. Thus, the specific gravity of an erythrocyte is about 1.06, and that of

plasma is 1.03. As a result, if blood stands in a container, the red cells will settle out of suspension.

When plasma was tested in a viscometer it was found to behave like a Newtonian viscous fluid. A **Newtonian liquid** is, by definition, one in which the coefficient of viscosity is constant at all rates of shear. The **non-Newtonian** nature of blood is a direct consequence of the fact that blood is a **suspension**, with plasma the suspending medium, and red cells for the most part being the suspended particles. Therefore, when whole blood was tested in a viscometer, it showed abnormal viscous properties which revealed its non-Newtonian character.

2.2 Rheology[2] of Blood

When analyzing our model, we are concerned with the laws governing the flow of blood in cylindrical tubes. One example might be that of a long straight tube with a constant rate of flow, **steady flow**, along it. In such a system, steady flow can be maintained by applying a constant pressure to the liquid.

Unfortunately, in only a small part of the circulation can the flow be regarded as steady. As described by McDonald [21], the heart pump produces a pressure gradient throughout the arterial and venous network. This pressure gradient consists of two components, one of which is constant or non-fluctuating and the other fluctuating or pulsatile. The flow in large arteries is highly pulsatile, but the flow oscillations are progressively diminished with the ramification of the system. Capillary flow is normally steady. In the arterioles that are close to the capillaries

[2]rheology = the study of the properties and behavior of flowing substances.

significant oscillations of flow are seen. Flow in peripheral veins is regarded as steady, but close to the heart, within the thorax, venous flow becomes very pulsatile.

Steady flow in a cylindrical tube is described by the **Poiseuille** equation:

$$Q = \frac{(P_1 - P_2)\pi R^4}{8\mu L}, \qquad (2.2.1)$$

where Q is volume flow, P_1 - P_2 is the pressure drop, R is the radius of the tube, L is the length of the tube, and μ is the viscosity of the fluid. Poiseuille formula only applies to steady state flow. In arterial channels where the flow is pulsatile this might be thought to be inapplicable. Pulsatile arterial flow, however, has a steady component, say the mean flow, so it is possible, and valid, to apply Poiseuille formula to this mean flow.

McDonald [21] gives details about the experiment of dye injected into liquid flowing in a tube under the above mentioned conditions. It is observed that the liquid in the axis of the pipe is moving much faster than that near the wall. After a short time, the dye takes a parabolic shape. The reason is that the particles of liquid (blood, in our study case) are flowing in layers parallel to the sides of the tube, while the fluid in contact with the wall is stationary (see Figure 2.2). Each layer (or lamina) is slipping against the viscous friction of the layers outside it. The resulting flow motion is called **laminar** (or **streamlined**). If the rate of flow through a tube is continuously increased, the resistance to flow also increases and the Poiseuille law no longer can be applied. When dye is injected in such a flow, it can be seen that the fluid is mixing across the tube and that the particles

of dye are no longer moving regularly in the line of flow but are following more or less random paths over the tube (as in a Brownian motion). The flow is said to

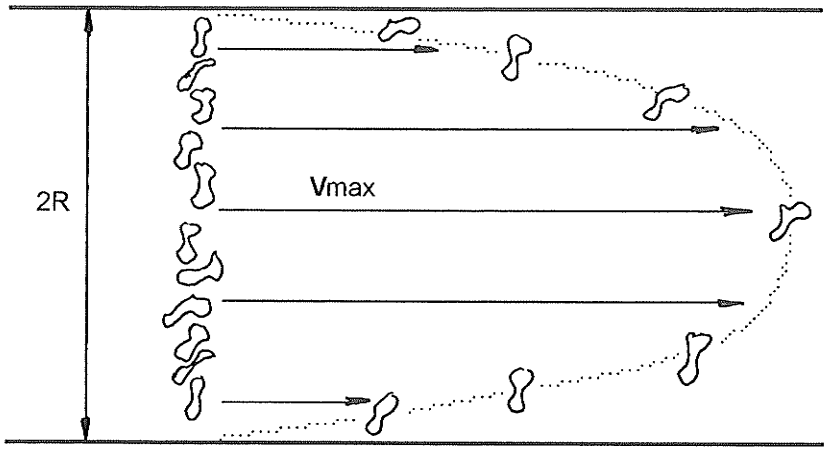

Figure 2.2 Velocity profile in steady laminar flow.

be **turbulent**. The pressure-flow relationships of turbulent flow are not predictable with precision. Thus, when studying any type of flow, we have to precisely determine whether the flow is laminar or turbulent. However, it should be mentioned that this classical difference between the types of flow is only correct for steady flow in rigid tubes and there are intermediate stages of instability in the liquid which become of importance in the irregular flow systems of a living animal.

2.3 Viscous Properties of Blood

Viscosity is a closely related notion to how liquids flow. We can define viscosity in the following way: if a force is applied to a portion of a mass of liquid it will

begin to flow but if the force is removed the movement will be brought to rest (see McDonald [21]). On the other hand, if a similar part of liquid is kept moving, the movement will be transmitted to the rest of the fluid.

Cohesive forces between blood and the blood vessel wall prevent the infinitesimally thin layer of plasma which is in contact with the wall from moving even when the blood farther away is flowing. When liquids come in contact with the walls of a tube, there is **no-slip** at the wall. Burton [4] states that blood behaves in this same way too. It follows that when blood is forced through the blood vessels by the pressure gradient, generated by the action of the heart, there must be a **gradient of velocity** across the vessel, with the highest velocity of flow along the axis of a cylindrical vessel.

The successive cylindrical layers of blood, as we proceed from the axis, move with decreasing velocity, until at the wall the velocity is actually zero. Consequently, the resistance of blood to flow is not due to a friction between blood and the wall of the blood vessel. The resistance is rather attributed to the friction between adjacent laminae of blood, in other words to the **viscosity** of blood.

Newton was the first one to make theoretical remarks on viscosity in his work *Principia Mathematica* in 1706. The hypothesis on which he based his derivation was "that the resistance which arises from the defect of slipperiness of the parts of the liquid, other things being equal, is proportional to the velocity with which the parts of the liquid are separated from one another.". Here, he used the words *defect of slipperiness* for the modern word *viscosity* (or *internal friction*). Newton's hypothesis describes the fact that velocity gradient exists in a direction

perpendicular to the surface. We call this velocity gradient **rate of shear**, and we have the following formula:

$$\tau = \mu \frac{dv}{dr}, \tag{2.3.1}$$

where $\frac{dv}{dr}$ is the rate of shear when r is the distance from the axis, μ is the coefficient of viscosity, and τ is the stress (see Figure 2.3).

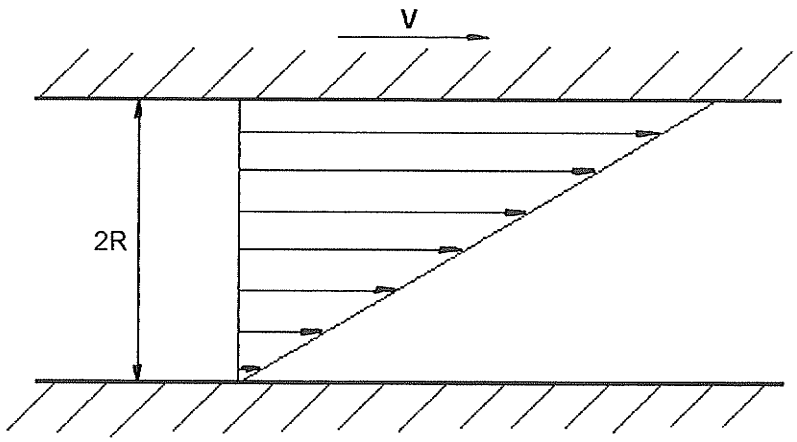

Figure 2.3 Shearing flow.

Newton did not studied this viscosity problem further, and for the next hundred years there were no reports. But his name remains to be used for **Newtonian fluids**.

Poiseuille's law given by equation (2.2.1) is often used to determine the viscosity coefficient of viscous fluids. When blood is investigated in this manner, its coefficient of viscosity is 0.035 P (P = poise), while the coefficient of viscosity of

plasma is 0.012 P, both calculated at the normal physiological temperature of 37°C. Since the effective viscosity coefficient of blood, as determined by means of Poiseuille's law, depends on the radius of the vessel bore in which it is measured suggests that blood is NOT a Newtonian fluid for which μ is a constant. Most **homogeneous liquids**[3] approximate a Newtonian liquid but suspensions of particles (such as blood) show deviations from it. Fluids that have complex molecular structure, and in which the suspended particle size becomes appreciably large in comparison with the dimensions of the channel they are flowing through, are in general non-Newtonian.

2.3.1 Anomalies in the Viscosity of Blood

There are two types of anomalies observed in the viscosity of blood. The first one is called *low shear* and it can be observed at low shear rates when the viscosity increases notably. The second anomaly is the *high shear* effect and it can be detected at high shear rates. In this case, the viscosity is smaller in small tubes than in large tubes. This progressive diminution with tube size begins to be noticeable with tubes of internal diameter less than 1 mm and becomes significant in tubes of the order of 100-200 μ in diameter. These two anomalies are of interest because when studying fluid flow in the circulatory system we have to accurately measure the viscosity of blood.

As already mentioned, plasma has a Newtonian viscosity. Many tests have been made in concentric viscometers and in capillary tubes over a range of shear rates

[3]homogeneous liquids = a liquid for which its properties are independent of position.

from 0.1 to 1,200 sec^{-1} (see McDonald [21]). The reported viscosity for plasma was 1.6 relative to water (the coefficient of viscosity for water is 0.007 P). Other experiments have reported plasma to be non-Newtonian when the measurement apparatus allows plasma-air interfaces to occur. The abnormal results are due to a denatured protein layer at the interface. Since plasma is a colloidal suspension of protein, it is not unusual that it presents deviations from the behavior of a pure liquid. However, deviations of viscosity are not observed until particle size is a much larger fraction of tube diameter. The longest dimension of any of the particles found in plasma is the length of the fibrinogen molecule, that is 50 mμ. Even in a capillary of 5 μ this particle dimension would only be 1% of the lumen[4]. Nevertheless, most studies showed plasma to have a Newtonian viscosity.

If red cells are progressively added to plasma the viscosity increases. Significant non-Newtonian properties become noticeable when the concentration of cells exceeds 10%. The volume concentration of erythrocytes is called **hematocrit**, which in normal physiological circumstances lies in the range 0.41 - 0.44.

When experimental calculations are performed in tubes with an internal radius of about 0.5 mm or larger, and shear rates which are not less than 200 - 300 sec^{-1}, the coefficient of viscosity will be effectively independent of tube size but will vary with the cell concentration (see Figure 2.4). The experimental data show that viscosity varies linearly with cell concentration from 0% (plasma) to a hematocrit of about 45%. In fact, this range covers most clinical conditions. For cell concentrations more than 45%, it was observed that viscosity rises rapidly. Also, in any given tube the apparent viscosity decreases as the shear rate increases;

[4]lumen = any cavity enclosed within a cell or structure.

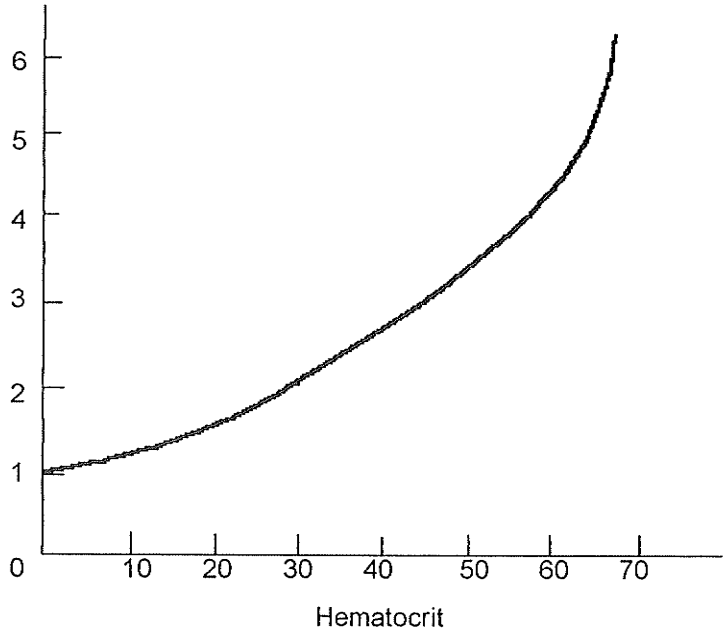

Figure 2.4 The variation of viscosity with hematocrit values (From McDonald [21]).

when the shear rate is greater than some 200-300 sec^{-1}, the viscosity becomes virtually constant, as outlined by McDonald [21].

2.3.2 Why is the Free-Cell Zone Important?

When blood is flowing through a cylindrical tube, the region adjacent to the wall has a low cell concentration that will imply a lowered viscosity, one close to that of plasma. The smaller the tube, the greater the proportion of the whole that would consist of this **cell-free** layer, and thus the lowering of the overall viscosity will be more significant. It is generally accepted that this is not only the simplest,

but also an adequate explanation of the so called **wall-effect**, that is the reduction of the apparent viscosity of blood in small tubes.

This behavior was observed by Fahraeus and Lindquist [21] in 1930, who experimented blood suspensions in tubes of diameter in the range 50-500 μm. In 1971, Barbee and Cokelet [21] extended the experiment and showed that the phenomenon continued at least for tubes of diameter 29 μm (when human blood was used). In 1929, Fahraeus found that when blood of a constant hematocrit is allowed to flow from a large feed reservoir into a small tube, the hematocrit in the tube decreases as the tube diameter decreases. Barbee and Cokelet [21] demonstrated that complete agreement with the experimental calculations can be obtained if the apparent viscosity of blood in a large vessel is measured as a function of the hematocrit, and then the apparent viscosity of the same blood is computed in a smaller tube at the actual hematocrit. This was an important discovery because it extended the usefulness of the apparent viscosity measurements.

The dependence of viscosity on tube diameter occurs not only in blood but in any suspensions and it has been named the *sigma phenomenon*, as noted by McDonald [21]. In regions of flow that are unsheared the existence of particles of finite size will make normal integration of flow in infinitely thin layers to be invalid (Poiseuille's law is deduced by performing an "integration"). Hence, a summation of a series of layers of finite thickness is more appropriate in this case. It should be mentioned that the precise analysis of the causes of the sigma phenomenon is not fully agreed on, but most experimentalists comply that the major cause is due to a low viscosity in the marginal zone of the tube, the cell-free zone. The explanation for the existence of such a cell-free zone has been named the *wall-*

exclusion principle. Assume a liquid suspension of solid particles of finite size, in which the concentration is uniform throughout a large volume of fluid. Mathematically this can be imagined as a distribution of points representing the centers of the particles. By placing a solid wall in this liquid all such points will be excluded up to a distance equal to the mean radius of the particles because they can only be *in contact* with the wall. In 1959, Bayliss [21] has measured that in a tube of 100 μm diameter the cell-free zone was not greater than 2-5 μm wide. We recall that the radius of an erythrocyte is 5 μm. Thus, it can be seen that the radius approximates closely the measured width of the layer found to be deficient in cells.

An important consequence of the cell-free zone near the wall is that more of the cells are in the central region of the tube. This is also the region where flow velocity is higher and hence the cells of blood will traverse at a higher net velocity than the plasma.

2.4 The Significance of Motion and Flexibility of Red Cells

The primary function of the circulation is to transport materials through blood flow to and from tissues. The performance of the circulatory system is determined by the rhythmic contraction of the heart, the capacitative resistance and exchange functions of the vascular system, and the flow condition.

Blood is a suspension of deformable cells (erythrocytes, leukocytes, and platelets) in plasma. The motion, even of a sphere, in a flowing liquid is complicated, and that of a non-spherical deformable particle is even more

complicated. Experiments show that a very small degree of flow of blood results in an overall *orientation of the cells*, specifically where they have room to be oriented. Burton [4] describes such an experiment which was based on a large scale model of blood flow in artery. A fluid full of small rubber discs (to imitate erythrocytes) was pumped down through a transparent tube. The orientation and continual rotation of the discs in the stream was obvious, and when the flow was increased, there was axial accumulation of the rubber discs. In general, it was observed that there was a continuous, but not uniform, rotation of particles in a shear gradient. Although this behavior shows a laminar flow on the macroscopic view, on a smaller scale there is nonlinear "microturbulence" with motion of plasma between the cells in all directions, and motion of the contents of the red cell within its membrane. At normal hematocrits, the blood contains so many cells that their *flexibility* greatly affects the ease of flow. The rheological behavior of erythrocytes varies with flow condition. At low rates of shear, there is insufficient shear stress to cause cell deformation and alignment of deformed cells with flow. Increases in shear stress cause cell deformation.

Chien [7] explains that the remarkable deformational behavior of erythrocytes is due to: (i) the fluidity of the internal hemoglobin-rich fluid; (ii) the favorable geometric relationship between membrane surface area and cell volume, and (iii) the viscoelastic properties of the cell membrane.

The assumption that the red cell consists of a flexible membrane is based on the following observation: when blood flows through capillaries whose diameter is less than that of a red cell, it is obvious that the erythrocyte gets deformed. In narrow capillaries with diameters of 7-10 μm, erythrocytes and leukocytes move in single file. The white cells generally travel more slowly than the red cells,

which consequently accumulate behind the white cell. Downstream of the leukocyte, a region depleted of erythrocytes is formed. Once such a group of blood cells reach a vessel with slightly increased diameter to above 10 μm, the erythrocytes will pass the leukocytes. Hence, the white cell is pressed toward the wall and rolls along it. The interactions between red and white cells have been modeled in large scale experiments on elastic disks (erythrocytes) and rigid spheres (leukocytes) flowing through a straight cylinder. In such a tube, the disks position themselves preferentially edge-on when close to the center and have a higher velocity than the sphere. Whether the disks can pass the sphere depends on their sizes, the tube diameter and the radial positions of these particles. If the diameter of the cylinder is only slightly larger than the sum of the sphere diameter and the disk thickness, the disks rarely can pass the sphere. As a result, several disks gather behind the sphere at close spacing, leaving an empty space downstream, phenomenon which is similar to the condition *in vivo*.

2.5 The Importance of Reynolds Number in Circulation

One of the characteristics of the flow assumed in our model was that the flow is **slow**. More precisely, it is necessary to state what "slow" means by using a reference velocity. Mathematically this is accomplished by introducing the non-dimensional quantity Re called **Reynolds number** given by

$$\mathrm{Re} = \frac{\rho v r}{\mu}, \qquad (2.5.1)$$

where ρ is the fluid density, r is the radius of the particle, μ is the viscosity of the fluid, and v is the mean velocity of the particle. For a large straight tube, Reynolds found that if Re exceeded a value of about 1,000 (if v is the **mean** velocity of the flow) or 2,000 (if v is the **maximal** velocity on the axis, which is twice the mean) the flow changed from **laminar** to **turbulent**. Thus, the property of a flow to be **slow** is directly related to the **laminar** nature of it.

Hagen and Poiseuille observed that the law relating pressure and flow was no longer true when the rate of flow increased. This phenomenon was due to the breakdown of laminar flow and the appearance of turbulent flow. Osborne Reynolds was though the first one to accurately describe in his work in 1883 the transition from laminar to turbulent flow.

A classic experiment performed by Reynolds was to inject a thin lamina of dye in the axis of a long cylindrical tube. The motion of the fluid was smooth and regular until he increased the rate of flow to a critical value when it became turbulent instead. In turbulence, the whole tube was filled with vortex-like eddies (see Burton [4]). The critical point was found to be dependent on the radius of the tube, the mean velocity of the flow, and the density and viscosity of the fluid. Equation (2.5.1) expresses this relationship. The fraction μ / ρ is known as the **kinematic viscosity**, ν. The evaluation of the Reynolds number is not necessarily sufficient to prove the existence of laminar or turbulent flow. The best way to demonstrate turbulence is to calculate the pressure-flow relationship and show that this deviates from that of laminar flow.

2.6 The Structure of Arteries

An **artery** is an elastic tube whose diameter varies with pulsating pressure and, in addition, it propagates pressure and flow waves created by the ejection of blood by the heart, at a certain velocity that is largely determined by the elastic properties of the wall.

The blood arterial wall consists of three zones: the tunicas **intima**, **media** and **adventitia** (see Figure 2.5). The arterial wall encloses a cavity called *lumen*. The demarcation between the intima and media layers is by the *internal elastic lamina*, while the one between the media and the adventitia layers is by the *external elastic lamina*. The internal lamina has a complex structure which

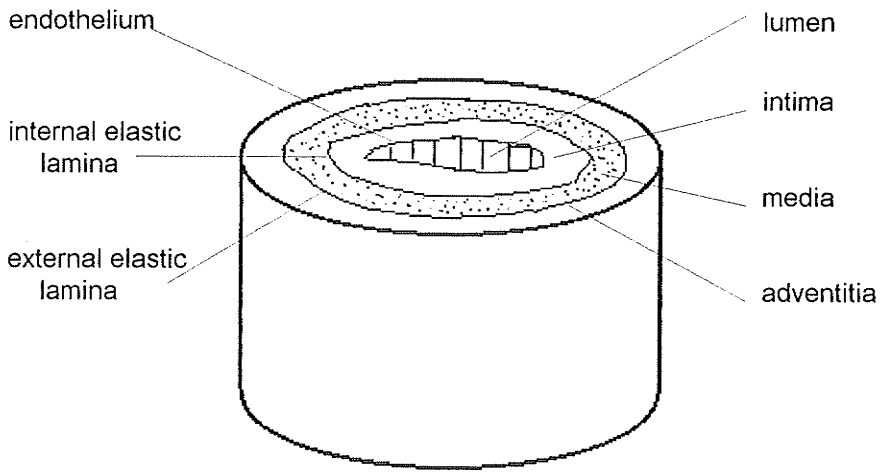

Figure 2.5 Transverse section of an artery.

contains of a fenestrated membrane of elastin lined on the intima border by a coarse fibrous network. The external lamina is a region of collagen and some elastin tissue which joins the surrounding connective tissue and includes the vasa

vasorum - the small vessels which run into and supply the wall of the large arteries with blood, nerves and lymphatics.

McDonald [21] describes the intima as consisting of the vascular **endothelium** which is a single layer of lining cells together with a thin layer of elastin and collagen fibres by which it is coupled to the internal elastic lamina. The lining cells of the endothelium have the important role to provide a smooth wall and to offer a selective permeability to water, sugars, and other substances transferred from the blood stream to the tissues. It would appear that this transport function is most developed in the endothelium of the capillaries, although transfers must occur through the lining of the walls of all vessels. Different vessels have different permeabilities because of the *basement membranes* located behind the endothelial cells, and also in the very much greater surface area of the wall of the capillaries.

The endothelial cells, once they are released from the *cement substance* holding them to the membranes behind them, become spherical. Burton [4] explains that experiments show that the lining cells in small blood vessels, such as arterioles, can enter the lumen and may even close the lumen altogether. This is how complete closure could occur in a very thick-walled vessel. Other experiments performed by Fry in 1968 and later have shown that the endothelium may be easily damaged by shearing stresses that are not much in excess of those normally found in the circulation due to viscous drag.

The tunica media forms the large part of the wall. The intermediate layers have a fibrous structure, the fibres being displayed in circles or in a tight helix. Between these layers lie muscle cells mostly parallel to the elastin found in the external elastic lamina. The structure of the media contains an orderly array of lamellar

units. Elastin and collagen fibres and smooth muscle cells are meticulously oriented and form well defined layers. The function of these two elastic elements (elastin and collagen fibres) in the wall is to maintain a constant tension to hold the wall in equilibrium against the so called **transmural pressure** exerted by the blood in the vessels.

Although the analysis of the arterial wall clearly shows that the artery has an elastic wall, in our biological model we will consider the much simpler situation of a rigid straight artery.

CHAPTER 3

Cholesterol in Arteries

3.1 History of Cholesterol

Cholesterol was discovered as a major component of gallstones in the 18th century. The French chemist Chevreul partly described it in 1816 and called it *cholesterine* from Greek: **chole** = bile, and **steros** = solid. He found cholesterine in 1824 in human and animal bile. In 1938, Lecanu [8] discovered it in human blood, while in 1834 Couerbe found it in human brain.

Cook [8] and Gurr [17] give excellent reviews on the history of cholesterol. In 1846, Gobley wrote a detailed analysis on cholesterol in egg yolk. It was thereafter gradually recognized as a normal component of all animal cells and several secretions, as well as a part of specific pathological deposits.

Later it was shown to be present in alcoholic extracts of blood and in 1859 Berthelot identified it as an alcohol and prepared cholesterol esters[1] by heating the sterol with fatty acids at 200°F.

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[1]ester = a compound formed from an alcohol and an acid.

Cholesterol composition was elucidated by the work of Windaus [8] and his associates. His research was also helped by the ones conducted by Wieland [8] on the chemically related bile acids and by Mauthner and Suida [8] on derivatives of cholesterol. In 1919, Windaus [8] arrived at a tentative chemical formula which was changed in 1932 to the one now accepted.

In early stages experiments on cholesterol were mostly focused on the concentration of cholesterol and its esters in blood and particularly in plasma or serum. This was studied in connection with meals of varying composition with respect to fat and cholesterol and in relation to menstrual cycle, pregnancy, and to diseases such as atherosclerosis, lipidoses, xanthoma[2], and diseases of the liver and thyroid. High interest is showed in research on the presence of cholesterol in lipoproteins[3] in connection to atherosclerosis.

3.2 Physiology[4] of Cholesterol

Cholesterol is a steroid[5] that occurs in the cell membranes of animal cells, but not in plants. Cholesterol is produced in the liver and when in excess is excreted in the bile. Alternatively, if there is excess circulating cholesterol in the blood, it may be deposited on the walls of the blood vessels, obstructing them.

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[2]xanthoma = a skin disease marked by the presence of small yellowish disks formed by the deposit of lipoids.

[3]lipoprotein = a water soluble molecule made up of a protein containing a lipid group.

[4]physiology = the study in animals and plants of internal processes and functions associated with life.

[5]steroid = an important type of lipid, formed of four rings of carbon atoms with various side groups.

The earliest work on the circulating cholesterol was obtained from analysis of extracts of whole blood, but later, in 1937, the distribution of this steroid between cells and plasma was also studied. Experiments showed that cholesterol concentration of plasma was modified by certain factors, while the cholesterol component of the erythrocytes was unaffected. Thus, plasma was the medium choice of experimentalists for further quantitative tests.

The circulating cholesterol is present in two chemically distinct thermostable compounds, namely **free** or **unesterified cholesterol** and **esterified cholesterol**. The proportion of free sterol to sterol ester varies from tissue to tissue, species to species. In the human body, the free cholesterol to ester cholesterol ratio in red blood cells is about 4:1, in white blood cells it is about 3:1.

The plasma cholesterol is synthesized almost exclusively in the liver. This sterol is bound to proteins and discharged into the extracellular fluid. The resultant cholesterol-protein complexes penetrate the arterial and capillary endothelium and circulate through veins and lymphatics back into the blood. This cycle occurs repeatedly for several days until the circulating sterol is removed from the extracellular fluid for utilization or degradation. Hence, changes in the concentration of plasma cholesterol could be attributed to many factors such as an alteration in plasma volume or in capillary permeability, redistribution of existing extracellular fluid for utilization or degradation.

The level of the plasma cholesterol in the normal human is low in infancy (35 mg per 100 ml) and reaches a value of 180-230 mg per 100 ml in normal adult males in Western communities at the fourth decade of life.

There are several factors influencing the physiological level of the plasma cholesterol, such as: race, diet, age, and others.

3.2.1 The Influence of Diet

Diets are affecting plasma cholesterol levels. They may vary in caloric content or be isocaloric with different distributions of calories between protein, fat and carbohydrate[6]. Plasma cholesterol levels are also influenced by the caloric balance between energy intake and energy expenditure.

1. The Effect of Calories

When humans consume food that is in excess of caloric requirements they will always gain weight, and thus their serum cholesterol level will be elevated. Underfeeding implies loss of weight that causes depression of the serum cholesterol concentration. Cook [8] notes that in 1955 Mann has shown that if healthy young men consume twice their normal caloric intake their plasma cholesterol levels remain unchanged as long as they increase their energy expenditure accordingly. When their energy output is restricted while on this regimen their serum cholesterol levels rise significantly.

2. The Effect of Cholesterol

In man the plasma cholesterol is greatly independent of dietary cholesterol. Plasma cholesterol level is slightly influenced by excess cholesterol intake. However, very large amounts of cholesterol, such as 150 g of egg yolk powder (containing 2.5% cholesterol) in 400 ml of milk twice a day for 48 days produce a marked increase in plasma cholesterol in man. In contrast with this phenomenon,

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[6]carbohydrate = a family of organic molecules ranging from simple sugars, such as glucose and fructose, to complex molecules, such as starch and cellulose.

reduction of dietary cholesterol does not induce a significant decrease in plasma cholesterol.

3. The Effect of Fat

Diets rich in fat, but not necessarily in cholesterol, are associated in humans with high levels of plasma cholesterol. Fat has a much higher effect on plasma cholesterol level than any other dietary component. A rice-fruit diet that doesn't contain cholesterol and fat produces a prompt and substantial (35%) fall in the plasma cholesterol of men with normal cholesterol levels. There are two kinds of fats: animal (or **saturated**) and vegetable (or **unsaturated**). Experiments show that saturated fats are associated with high plasma cholesterol levels; lack of unsaturated fats may also result in elevation of the serum cholesterol. Some unsaturated oils have a greater depressant action on the circulating cholesterol than others. For example, corn oil is more effective than sardine oil and sunflower seed oil.

3.2.2 Influence of Age and Sex

Age and sex are also influencing the plasma cholesterol levels. In newborn infants its level is situated at an average of 35 mg per 100 ml, but rises rapidly within the first 10 days to about 130 mg per 100 ml. From the age of 11 year there seems to be no significant increase in plasma cholesterol until puberty, and after that subsequent changes depend on sex.

In men there is a rapid increase in prevalence of elevated total cholesterol from age 18 to 44, whereas in women, the rise is more gradual until age 44 when it increases to exceed the men's rate at age 55. Cholesterol levels in the females are influenced after puberty by the menstrual cycle, pregnancy and menopause. Other factors that influence the plasma cholesterol levels are: seasonal variation, endocrine and chemical substances, and others.

3.3 Pathological Manifestation of Cholesterol

Quantitative cholesterol analysis have produced considerable data on the concentration of cholesterol in the body fluids and tissues of man under physiological and pathological conditions. The total amount of cholesterol in the body is determined by the balance between the rate of increase due to absorption of cholesterol from the diet plus biosynthesis in tissues and the rate of decrease due to metabolic utilization and excretion.

The cholesterol content of blood shows the following anomalies: **hypercholesteremia**, **hypocholesteremia**, and **cholesterol deposition**.

Hypercholesteremia is a metabolic disturbance determined by elevated serum cholesterol levels. In contrast, hypocholesteremia is determined by lowered serum cholesterol levels. Cholesterol deposition is by far the most significant cholesterol content anomaly developed in the circulatory system of the human body.

Cholesterol is deposited in a variety of tissues under diverse pathological conditions. Depending on their site, cholesterol depositions may or may not

disturb the normal functioning of the organism. Cholesterol is deposited in certain types of lesions[7] and lipidoses, and in gallstones.

Atherosclerosis is the most frequent and important pathological alteration of the intima in the arteries. The disease is characterized by the accumulation of cholesterol and other lipid components in the arterial wall. Analysis of lesion material suggests that the majority of this accumulated cholesterol is derived from the blood plasma lipoproteins. As noted by Neumann et al [24], intimal accumulation of lipoproteins beneath the artery's endothelial cellular lining is postulated to result from permeability defects of the resistive endothelial cell layer. The atherosclerotic lesion represents a subgroup of a wider pathological entity defined as **arteriosclerosis**. Such pathological conditions as *medial calcification* and *arteritis obliterans* are often included in the entity of arteriosclerosis.

The atherogenic process is dependent not only on blood lipoprotein levels and endothelial permeability but also on the distribution and removal of these macromolecules within the arterial wall. Experiments show that atherosclerosis has a higher occurrence in conditions associated with abnormally high serum cholesterol levels. On the other hand, abnormally low cholesterol levels are related with a low incidence of atherosclerosis. It is generally believed that low serum lipid levels are connected to the dietary habits of population groups, especially to the low consumption of saturated (animal) fat, although other dietary factors such as low protein and high carbohydrate, and such special conditions as ethnic differences, parasitic infestation, climatic influence, and different social and economic environment are also taken in consideration.

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[7]lesion = a localized area of diseased tissue.

Coronary heart disease, that is reduced blood supply to the heart, is an illness usually due to atherosclerotic lesions. The formation of a **thrombus**, or blot clot, in a major coronary artery, may cause cessation of the blood supply to the heart. This failure of blood supply (**myocardial infarction**) leads either to degeneration of part of the contractile heart tissue and then replacement by non-contractible scar tissue, or else to complete cessation of heart beat (see Gurr [17]).

3.4 Dispersion of Cholesterol in Arteries

When a soluble substance is introduced into a fluid flowing slowly through a small-bore tube it spreads out under the combined action of molecular **diffusion** and the variation of velocity over the cross-section, that is **convection**. This spreading out is referred to as **dispersion**.

Diffusion is a process by which a substance is transported from regions of high concentration to regions of low concentration of that substance, that is down a **concentration gradient**. A solution consists of a fluid called the **solvent** (in our problem, blood), in which some particles has been dissolved, the **solute** (in this case, cholesterol). The composition of the solution is characterized by its mass concentration C, which is the mass of dissolved matter per volume of liquid. Crank [9] defines diffusion as a phenomenon that occurs as a result of the thermal motion of each solute molecules. In a dilute solution each molecule behaves independently of the others, which it seldom meets, and each is constantly undergoing collision with solvent particles, having no preferred

direction of motion towards one or the other. The motion of a single molecule can be described in terms of the mathematical theory of probability as *random walk*. The mathematical theory of diffusion was first developed by Fick.

Let us consider a solution in which simple molecular diffusion is taking place, the fluid being otherwise at rest. The transport of solute is governed by concentration differences. If the solution occupies a three dimensional space, the concentration will be $C=C(t,\ x,\ y,\ z)$ and the equation representing conservation of solute transport is the **equation of continuity**:

$$\frac{\partial C}{\partial t} = D\,\nabla^2 C\ , \tag{3.5.1}$$

where the differential operator ∇^2 is called the **Laplacian** and D is called the **diffusion coefficient** and it is a characteristic of the solute in the fluid. The solvent is considered to be **homogeneous** and **isotropic** so that D is independent of position and is the same in all directions and therefore D is constant. Equation (3.5.1) represents **Fick's second law of diffusion**.

When a solute is in a moving liquid entrained by the flow, the resulting motion of the solute is called **convective transport**. This transport is additional to the diffusive motion described above. Let us examine a small cross-sectional area through which the fluid flows with velocity $\boldsymbol{q}=\boldsymbol{q}(u,\ v,\ w)$. The **equation of convective diffusion** is given by

$$\frac{\partial C}{\partial t} + \boldsymbol{q}\cdot\nabla C = D\,\nabla^2 C\ , \tag{3.5.2}$$

if D is constant and if the fluid is also incompressible, so that $\nabla \cdot \boldsymbol{q} = 0$. Equation (3.5.2) will be used later in order to find the flux of solute molecules (in our case, cholesterol) passing through a unit width of the tube in a unit time.

CHAPTER 4

Mathematical Formulation of the Biological Problem

4.1 Fundamental Equations

The biological problem that we propose to analyze is based on the model presented in section 1.2. In order to develop mathematical equations that fully characterize the model, we give governing equations and conditions.

The phenomena considered within the domain of fluid dynamics are **macroscopic**: any small volume element of the fluid is supposed to be so large that it still contains a very large number of molecules. Hence, the fluid is regarded as a **continuum**.

The basic variables in a three-dimensional space are the velocity components and the thermodynamic properties. Any two of the thermodynamic properties, such as pressure, temperature, density, enthalpy, entropy, etc., suffice to determine the state and all the other properties. The fluid flow is specified by the velocity vector $\boldsymbol{q}$ and by the thermodynamic attributes. For the problem, we have

the **equation of motion**, a **continuity equation** and an **energy equation**. In turbulent flow, additional unknowns appear for the same number of equations, which prevents a complete theoretical formulation of the problem.

For an **incompressible** fluid the energy equation is not needed since density is taken as known and only pressure and velocity need be found to fully describe the fluid flow. The number of unknowns decreases whenever the velocity field is one- or two-dimensional.

The problems discussed here can be grouped in the following broad categories:

1. flow in an infinite circular cylindrical channel bounded by a permeable wall.
2. flow through a porous medium.

The following assumptions regarding the fluid flow are given:

1. the fluid is homogeneous, incompressible, viscous, Newtonian, and flowing under steady condition.
2. the chemical effects are negligible.
3. the porous medium is homogeneous and isotropic on a macroscopic scale and the physical properties like viscosity, permeability etc., are assumed to be constants.
4. the porous layer is completely saturated.
5. the artery is a rigid infinite cylindrical tube of uniform circular cross section.
6. the effects of body force and inertia are neglected.

Under the above assumptions we formulate the fundamental equations for the fluid flow described, namely, conservation of mass, conservation of momentum and conservation of mass flux.

4.1.1 Conservation of Mass

The mass-conservation equation is given by the **continuity equation**

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \boldsymbol{q}) = 0 , \tag{4.1.1}$$

where ρ is the density and $\boldsymbol{q}$ is the velocity of the fluid. For an incompressible fluid, ρ is a constant. The equation of continuity (4.1.1) becomes

$$\nabla \cdot \boldsymbol{q} = 0 . \tag{4.1.2}$$

4.1.2 Conservation of Momentum

The momentum equation gives the basic mathematical relationships of fluid motion. The conservation of momentum has the following form for the fluid flowing **past** the porous medium (see Hughes [18]):

$$\rho \frac{D\boldsymbol{q}}{Dt} = -\nabla p + \mu \nabla^2 \boldsymbol{q} + \rho \boldsymbol{g} , \tag{4.1.3}$$

where p is pressure, $\boldsymbol{q}$ is the velocity of the fluid, ρ and μ are, respectively, the constant density and viscosity of the fluid, and $\boldsymbol{g}$ is the acceleration due to gravity. The term $\rho \boldsymbol{g}$ represents a body force. Equation (4.1.3) is the **Navier-**

Stokes equation for an incompressible Newtonian viscous fluid and it equates the rate of change of momentum and the forces acting on the fluid.

If the fluid is flowing **through** the porous medium, Brinkman [3] models the flow by

$$\rho \frac{D\boldsymbol{q}}{Dt} = -\nabla p + \mu \nabla^2 \boldsymbol{q} + \rho \boldsymbol{g} - \frac{\mu}{k} \boldsymbol{q} , \tag{4.1.4}$$

where k is the permeability of the porous medium.

A basic model of flow of a viscous fluid through a porous medium assumes besides an obvious *microscopic flow scale* defined by the pore size, that there is a much larger *macroscopic scale* over which the problem is to be studied. One can use an intermediate scale which is small compared to the macroscopic scale and yet contains enough pores for an *averaged* velocity $\boldsymbol{q}$ and pressure p to be defined. We can see in Figure 1.3 on page 5 that although the direction of the actual flow has large variations on the pore size scale, the average velocity over a large number of pores will be a flow which goes from left to right. We expect then that on the macroscopic scale both $\boldsymbol{q}$ and p will be smoothly varying functions (see Ockendon [25]). In 1856 Darcy was the first one to verify that the flow through a porous medium obeys the law

$$\boldsymbol{q} = \frac{k}{\mu} (-\nabla p + \rho \boldsymbol{g}) , \tag{4.1.5}$$

where $\boldsymbol{q}$ is the mean filter velocity and k is the permeability of the porous medium, as determined by Muskat [23]. Equation (4.1.5) represents an equilibrium of

forces in the sense that the driving force necessary to move a specific volume of fluid at a certain speed through the porous medium is in equilibrium with the resistance force generated by internal friction between the fluid and the pore structure. The resistance force results from a pressure gradient ∇p and the gravity force $\rho \boldsymbol{g}$.

Equation (4.1.5) may be taken as the dynamical basis for the study of motion of a Newtonian fluid through a porous medium. The flow governed by this law is of potential type rather than a boundary layer type. Also, in 1979, Rudraiah [30] has shown that Darcy's law is valid when k is very large . However, in many practical problems the permeability k is small near the boundary due to the existence of the *cell-free zone*. In 1962, it has been experimentally observed by Benenati and Brosilow [27] that in a bounded porous medium the porosity is not uniform everywhere in the region of the interest but has a maximum value near the wall, due to sparse distribution of particles and has a minimum value at the central regions where the particles at the wall are densely packed. Thus, there exists a boundary layer near the surface. In this boundary layer, viscous effects are very important, even though they are negligible in the main part of the flow. An inviscid fluid does not exert any *stress*, but a viscous fluid (as we have seen in section 2.3) presents a stress component. The viscous effects become important in a boundary layer because the velocity gradients in a boundary layer are much larger than they are in the main part of the flow due to a substantial change in velocity across a very thin layer. Acheson [1] states that in this way the viscous stress becomes significant in a boundary layer, even though the viscosity is small enough for viscous effects to be negligible elsewhere in the flow.

The existence of this boundary layer thickness was experimentally demonstrated by Beavers and Joseph [2] in 1967. Therefore, the form of Darcy's law still needs to be refined in view of many practical applications, especially ones that involve porosity analysis. To completely characterize the flow through porous medium, we have to add a viscous resistance term $\mu \nabla^2 \boldsymbol{q}$ to equation (4.1.5). This aspect was first considered by Brinkman [3] in 1947 and hence is called the **Brinkman model**.

The Brinkman boundary layer type equation has the form

$$\nabla p = \rho \boldsymbol{g} - \frac{\mu}{k} \boldsymbol{q} + \mu \nabla^2 \boldsymbol{q} \, . \tag{4.1.6}$$

The validity of the Brinkman model depends on the magnitude of k / h^2, where h is the vertical thickness of the porous medium. For example, if the porous matrix is made up of small uniform identical spherical particles then the Brinkman model is valid up to the magnitude of k / h^2 of order 10^{-3}. This corresponds to considerably high values of d / h, where d is the diameter of the fillings. It should be noted that for such values of d / h the porous medium may not be homogeneous anymore, as suggested by Rudraiah [30]. If the porosity of the porous medium is close to unity, Darcy's law is not valid. One has to use a non-Darcy equation incorporating the inertia due to the curvature of the curvilinear path through the medium at high speed of flow and the viscous shear due to distortion of velocity. In 1948, Lapwood incorporated the inertial term $(\boldsymbol{q} \cdot \nabla)\boldsymbol{q}$ into the Darcy equation (4.1.5). Whence, whenever the porosity is close to unity we have to use a non-Darcy equation of the form

$$\rho\left[\frac{\partial \boldsymbol{q}}{\partial t} + (\boldsymbol{q} \cdot \nabla)\boldsymbol{q}\right] = -\nabla p + \rho \boldsymbol{g} - \frac{\mu}{k}\boldsymbol{q}\,, \tag{4.1.7}$$

which is known as the Lapwood-Darcy equation. Later, many authors have used this equation to study linear and nonlinear convection in a porous medium. Darcy's law was subsequently generalized because equation (4.1.7) presents the problem of an under-specified system of equations in some cases (see Pal [27]). The inertial acceleration and viscous force terms were added and the resulting equation has the following form:

$$\rho\left[\frac{\partial \boldsymbol{q}}{\partial t} + (\boldsymbol{q} \cdot \nabla)\boldsymbol{q}\right] = -\nabla p + \rho \boldsymbol{g} - \frac{\mu}{k}\boldsymbol{q} + \mu\nabla^2\boldsymbol{q}\,,$$

which is exactly (4.1.4).

4.1.3 Conservation of Mass Flux

The equation of conservation of mass flux or of convective diffusion was described in section 3.5. We consider a model that has two components: the solvent, which is a fluid, and the solute, which is matter dissolved in the solvent. The equation of conservation of mass flux is given by

$$\frac{\partial C}{\partial t} + (\boldsymbol{q} \cdot \nabla)C = D\nabla^2 C\,, \tag{4.1.8}$$

where C is the concentration of solute, $\boldsymbol{q}$ is the velocity of the fluid, and D is a constant coefficient of diffusion. Equation (4.1.8) is true only for an incompressible fluid, so that the divergence of the velocity vector is zero.

4.2 Flow in the Cylinder

The understanding of the flow phenomenon in a cylindrical channel bounded by a porous medium is of considerable physiological importance. In arteries, blood flows through a tube covered by an endothelial wall onto which different particles such as cholesterol deposit.

In their paper, Guha and Chaudhury [16] mentioned the need for a fluid-mechanical study and showed that endothelial wall deterioration and growth is closely related to the shear stress acting on the cells. They initiated such a fluid mechanical study of the blood flow in an arteriosclerotic blood vessel and analyzed the idealized mathematical problem of viscous flow in a circular tube having a local constriction.

Shivakumar et al [33] studied the blood flow in arteries idealized into a channel of varying gap bounded by a porous layer. The motivation for this investigation comes from the study of abnormal flow in the arterial system caused by the presence of occlusion or stenosis. Recently, in 1990, Neumann et al [24] also considered the problem of radial incorporation of cholesterol into the arterial wall using a mathematical model that predicts macromolecular transport in such a biological system.

The physical configuration and the system of coordinates chosen for our problem are shown in Figure 4.1.

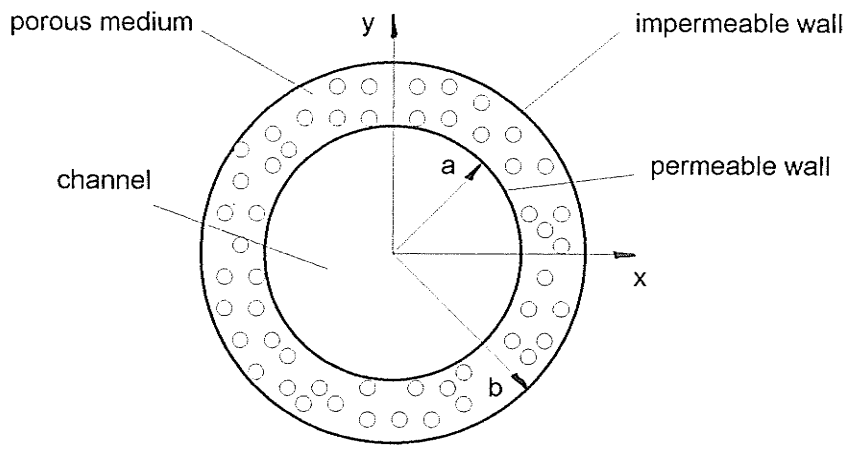

Figure 4.1 Schematic drawing of the biological system.

The viscous fluid in the channel space and in the porous medium space is assumed to be homogeneous, incompressible and Newtonian. The flow in the channel and in the porous medium is driven by common **uniform** and **constant** pressure gradient, such that the pressure p is $p=p(z)$, and it is coupled through boundary conditions. The velocity of the flow is one-dimensional in both spaces. The only non zero component of the velocity vector is along the channel and thus along the z-axis of the system of coordinates. The flow is also steady, so that the velocity does not depend on time.

The two regions form two concentric circles. The radius of the channel space is a, while the thickness of the porous medium is $b - a$. If q_r, q_θ, and q_z are the velocities in the r, θ, and z directions respectively, we have the following

Material derivative: $$\frac{D}{Dt} = \frac{\partial}{\partial t} + q_r \frac{\partial}{\partial r} + q_\theta \frac{1}{r}\frac{\partial}{\partial \theta} + q_z \frac{\partial}{\partial z},$$

Laplacian $$\nabla^2 = \frac{\partial^2}{\partial r^2} + \frac{1}{r}\frac{\partial}{\partial r} + \frac{1}{r^2}\frac{\partial^2}{\partial \theta^2} + \frac{\partial^2}{\partial z^2}, \qquad (4.2.1)$$

Divergence: $$\nabla \cdot \boldsymbol{q} = \frac{1}{r}\frac{\partial}{\partial r}(rq_r) + \frac{1}{r}\frac{\partial q_\theta}{\partial \theta} + \frac{\partial q_z}{\partial z}.$$

The operations $D\ /\ Dt$ and ∇^2 listed above are for operations on a scalar.

For simplicity in notation we denote the channel by region 1 and the porous medium by region 2, so that all the variables related to the channel will carry the subscript "1", while those in the porous medium will carry the subscript "2".

Let us consider that the velocity vector of the flow in the channel is $\boldsymbol{q}_1 = \boldsymbol{q}_1(0,0,u)$, and the one of the flow in the porous medium is $\boldsymbol{q}_2 = \boldsymbol{q}_2(0,0,v)$. The effective viscosity of the fluid in the porous medium, $\overline{\mu}$, is assumed to be different from that of pure viscous fluid, μ, in the channel. We will denote the concentration of the solute in the channel by C_1 and the constant diffusion coefficient by D_1. In the porous medium we will use the notation C_2 for the concentration of solute and D_2 for the constant diffusion coefficient.

4.2.1 Channel Region

Using (4.2.1), the three conservation equations may be rewritten to satisfy the conditions given by our model in the channel.

For an incompressible fluid, applying the divergence formula on the velocity vector $\boldsymbol{q}_1$, we obtain the equation of continuity

$$\frac{\partial u}{\partial z} = 0 \,. \tag{4.2.2}$$

Therefore, $u=u(r)$ due to symmetry in θ. The velocity field $u(r)$ will obey the equation of motion

$$\frac{d^2u}{dr^2} + \frac{1}{r}\frac{du}{dr} = \frac{1}{\mu}\frac{\partial p}{\partial z} \,. \tag{4.2.3}$$

Following the analysis developed by Taylor [37], it will be assumed that the concentration is symmetrical about the axis of the cylindrical tube so that C_1 is a function of r, z, and t only. Thus we obtain the equation of convective diffusion

$$\frac{\partial C_1}{\partial t} + u\frac{\partial C_1}{\partial z} = D_1\left(\frac{\partial^2 C_1}{\partial r^2} + \frac{1}{r}\frac{\partial C_1}{\partial r} + \frac{\partial^2 C_1}{\partial z^2}\right) . \tag{4.2.4}$$

Equations (4.2.2) to (4.2.4) completely describe the model in the channel space. In the next section we will derive equations in the porous medium.

4.2.2 Porous Medium

Since the velocity vector in the porous medium is $\boldsymbol{q}_2 = \boldsymbol{q}_2(0,0,v)$, we obtain a similar equation of continuity as in the channel space, namely

$$\frac{\partial v}{\partial z} = 0 \,. \tag{4.2.5}$$

Thus, $v=v(r)$ due to symmetry in θ. The equation of motion for the flow in the porous medium is based on (4.1.4). Kim [20] proposed a slightly different Brinkman equation in which the effective viscosity $\overline{\mu}$ is considered. Using Kim's procedure, we have the following equation governing the flow in the porous medium

$$\frac{d^2v}{dr^2} + \frac{1}{r}\frac{dv}{dr} - \frac{\mu}{\overline{\mu}k}v = \frac{1}{\overline{\mu}}\frac{\partial p}{\partial z} \,. \tag{4.2.6}$$

We derive a diffusion equation in the porous medium using similar reasoning applied to C_2 and D_2 as in the previous section. C_2 depends on r, z and t, while D_2 is the constant diffusion coefficient. We get

$$\frac{\partial C_2}{\partial t} + v\frac{\partial C_2}{\partial z} = D_2\left(\frac{\partial^2 C_2}{\partial r^2} + \frac{1}{r}\frac{\partial C_2}{\partial r} + \frac{\partial^2 C_2}{\partial z^2}\right) . \tag{4.2.7}$$

Equations (4.2.5) to (4.2.7) fully characterize the system in the porous medium.

4.3 Boundary Conditions for the Biological Problem

4.3.1 Boundary Conditions on Velocities

We will analyze in this section a few classes of boundary conditions for different types of boundaries.

1. Impermeable Boundaries

This kind of boundary is also called a **rigid wall** and it is existent at the exterior of our geometry shown in Figure 4.1 on page 53. It is assumed that such an *insulating* boundary does not allow any substance exchange between the exterior of the wall and the porous medium in our case.

Observations of viscous fluid flow reveal that all the components of fluid velocity at a rigid boundary must be equal to those of the boundary itself. Thus, if the boundary is at rest, $\boldsymbol{q} = 0$ there. For our model this implies

$$v = 0, \qquad \text{at } r = b\,. \tag{4.3.1}$$

The condition on the tangential component of velocity is known as the **no-slip condition**, and it holds for a fluid of any kinematic viscosity $\nu \neq 0$, no matter how small ν may be (see Acheson [1]). In 1985, Rudraiah [31] showed that the no-slip condition is valid only when we invoke the concept of boundary layer which inevitably arises when the Brinkman equation (4.2.7) is used to describe the flow through a porous medium.

2. Permeable Boundaries

Permeable boundaries permit several conditions to be used, depending on the characteristics of the porous medium, especially its thickness.

(a) $u = v$ at $r = a$. (4.3.2)

The velocity u in the channel has to match the velocity v in the porous medium at the permeable wall, i.e. $r = a$.

(b) $$\mu \frac{du}{dr} = \overline{\mu} \frac{dv}{dr} \quad \text{at } r = a \,. \tag{4.3.3}$$

The viscous shear due to the distortion of velocity in the porous layer should be taken into account because the fluid occupies almost all parts of the porous medium. Thus, the fluid and the solid should each receive a shearing stress from the external stream. We assume that the shear produced by the fluid in the channel, i.e. $du \,/\, dr$, must be proportional to that in the porous layer, $dv \,/\, dr$.

(c) $$\frac{du}{dy} = \frac{\alpha}{\sqrt{k}} (u_B - Q) \,, \tag{4.3.4}$$

where α is the slip parameter assumed to be independent of velocity, k is the permeability of the porous medium, u_B is the slip velocity at the nominal surface, u is the velocity of the flow in the channel in the z direction (in Cartesian

coordinates), and Q is the drag velocity or Darcy velocity. In the absence of body forces, Darcy's law is given by

$$Q = -\frac{k}{\mu}\frac{\partial p}{\partial z}. \tag{4.3.5}$$

When a permeable boundary arises in a problem, the no-slip condition is not satisfactory to be utilized. As an alternative to this, Beavers and Joseph [2] were the first ones to postulate and verify experimentally the **slip boundary condition**, also called the **BJ-slip condition**, namely equation (4.3.4). The existence of the slip at the porous bed, due to the transfer of momentum from the free flow in the channel to Darcy flow which sets up the drag, is connected with the presence of a very thin boundary layer of streamwise moving fluid just beneath the nominal surface of the permeable material. The fluid in this layer is pulled along by the flow in the channel.

It should be mentioned that the BJ-slip condition is valid only in a densely packed porous medium or very large thickness so that the variation of velocity in it can be ignored and the flow is governed by Darcy's equation.

(d) $$\frac{du}{dy} = \frac{\sqrt{\lambda}}{\sqrt{k}}\tanh(\delta h)(u_B - \phi\lambda Q), \tag{4.3.6}$$

where λ is the viscosity parameter, ϕ is the porosity, h is the thickness of the porous medium, and $\delta = \sqrt{\lambda k}$.

The BJ-slip condition is valid only when the velocity distribution in the porous medium is governed by the Darcy equation (4.3.5). If the thickness of the porous medium is shallow and the flow is described by the Brinkman equation, Rudraiah [31] has modified the BJ-slip condition to solve the Navier-Stokes equation in the channel and Brinkman equation in the porous medium. The new boundary condition is called the **BJR-slip condition** and is given by (4.3.6). In the limit, when the thickness of the porous layer approaches infinity and if $\alpha = \sqrt{\lambda}$, the BJR-slip condition (4.3.6) tends to the BJ-slip condition (4.3.4).

(e) $$u = \frac{k}{\rho}\left[(p_2 - p_1) - \sigma(\pi_2 - \pi_1)\right], \qquad (4.3.7)$$

where p_1 and p_2 are hydrostatic pressures in the porous space and the channel respectively, π_1 and π_2 are corresponding osmotic pressures, and σ is the reflection coefficient of the wall.

In 1896, Starling [35] proposed a hypothesis to account for the steady state distribution of water between the blood and the tissues. He suggested that the outward filtration of water, resulting from a higher hydrostatic pressure in the capillary lumen than in the extracapillary fluid, is balanced by reabsorption of fluid from the tissues into the blood down a gradient of osmotic pressure[1] resulting from the higher concentration of protein in the interstitial fluid. Equation (4.3.7) is commonly accepted in physiology problems.

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[1]osmotic pressure = a measure of the tendency for water to move into a solution by osmosis. Osmosis is the movement of a solvent through a differentially permeable membrane from a solution with high water concentration and low solute concentration to one with low water concentration and high solute concentration.

4.3.2 Boundary Conditions for Concentrations

The boundary condition which expresses the fact that the exterior wall is impermeable is

$$C_2 = C_0 \qquad \text{at } r = b \,. \tag{4.3.8}$$

At the permeable boundary we will match the two concentrations and thus obtain

$$C_2 = C_1 \qquad \text{at } r = a \,. \tag{4.3.9}$$

Another boundary condition that is considered at the permeable wall is

$$D_1 \frac{\partial C_1}{\partial r} = D_2 \frac{\partial C_2}{\partial r} \quad \text{at } r = a \,. \tag{4.3.10}$$

CHAPTER 5

Solution of the Biological Problem

5.1 Overview

The purpose of this chapter is to solve the equations presented in the previous chapter and to study the longitudinal dispersion of cholesterol in arteries. We evaluate the velocity fields in the channel and the porous medium by matching them through boundary conditions, and use them to calculate the concentration distributions of solute in both regions under stated boundary conditions. The velocity and concentration distributions are then used to find the volume of flow and the mass transport of solute in the channel and the porous medium. We also give an expression for the rate of growth of cholesterol thickness. The results for the velocity components are illustrated by numerical computations and graphs for a particular set of values of the parameters.

5.2 Determination of Velocity Fields

As given in section 4.2.1, the velocity distribution in the channel is, from (4.2.3),

$$\frac{1}{r}\left[\frac{d}{dr}\left(r\,\frac{du}{dr}\right)\right] = P_1\,, \tag{5.2.1}$$

where P_1 is a constant given by

$$P_1 = \frac{1}{\mu}\frac{\partial p}{\partial z}\,,$$

and μ is the coefficient of viscosity of the fluid in the channel.

On integration of (5.2.1), we obtain the solution in the channel in the form

$$u(r) = \frac{P_1}{4}r^2 + c_1 \ln r + c_2\,, \tag{5.2.2}$$

where c_1 and c_2 are constants of integration to be determined.

We first observe that $r = 0$ is in the channel region and since the velocity is finite everywhere, $c_1 = 0$. We let $c_2 = C$ and get

$$u(r) = \frac{P_1}{4}r^2 + C\,, \tag{5.2.3}$$

where C will be determined from the boundary conditions.

For the porous medium we define the constants P_2 and α as

$$P_2 = \frac{1}{\overline{\mu}} \frac{\partial p}{\partial z}, \qquad \alpha^2 = \frac{\mu}{\overline{\mu} k},$$

where $\overline{\mu}$ is the coefficient of viscosity of fluid in the porous medium.

From (4.2.6) the velocity field equation for the porous medium can be written as

$$r^2 \frac{d^2 v}{dr^2} + r \frac{dv}{dr} - \alpha^2 r^2 v = P_2 r^2 . \tag{5.2.4}$$

Equation (5.2.4) is a modified Bessel equation of order zero that has the following general solution

$$v(r) = A I_0(\alpha r) + B K_0(\alpha r) - \frac{P_2}{\alpha^2}, \tag{5.2.5}$$

where $I_0(\alpha r)$ and $K_0(\alpha r)$ are Bessel functions of first and second kind and of order zero, and A and B are constants to be determined from the boundary conditions.

We invoke now the boundary conditions presented in section 4.3. At the exterior impermeable boundary we have

$$v(r) = 0 \qquad \text{at } r = b . \tag{5.2.6}$$

At the permeable interface between the channel and the porous medium we assume

$$u(r) = v(r) \qquad \text{at } r = a\,, \tag{5.2.7}$$

and

$$\mu \frac{du}{dr} = \overline{\mu} \frac{dv}{dr} \qquad \text{at } r = a\,. \tag{5.2.8}$$

From (5.2.6) and (5.2.7) we get

$$AI_0(\alpha b) + BK_0(\alpha b) - \frac{P_2}{\alpha^2} = 0\,. \tag{5.2.9}$$

Using (5.2.3), (5.2.5) and (5.2.7) we obtain

$$AI_0(\alpha a) + BK_0(\alpha a) - \frac{P_2}{\alpha^2} = \frac{P_1}{4} a^2 + C\,, \tag{5.2.10}$$

and using the following identities (see Spiegel [34])

$$I_0'(x) = I_1(x) \tag{5.2.11}$$

and

$$K_0'(x) = -K_1(x)\,, \tag{5.2.12}$$

we obtain from (5.2.8)

$$\mu \frac{P_1}{2} a = \overline{\mu}\left[A\alpha I_1(\alpha a) - B\alpha K_1(\alpha a)\right]. \tag{5.2.13}$$

Solving (5.2.9) and (5.2.13), we get

$$A = \frac{-K_1(\alpha a)\frac{P_2}{\alpha^2} + K_0(\alpha b)\frac{aP_1\mu}{2\alpha\bar{\mu}}}{I_1(\alpha a)K_0(\alpha b) + I_0(\alpha b)K_1(\alpha a)}, \tag{5.2.14}$$

$$B = \frac{I_1(\alpha a)\frac{P_2}{\alpha^2} - I_0(\alpha b)\frac{aP_1\mu}{2\alpha\bar{\mu}}}{I_1(\alpha a)K_0(\alpha b) + I_0(\alpha b)K_1(\alpha a)}. \tag{5.2.15}$$

Substitution of (5.2.14) and (5.2.15) into (5.2.10) gives us the constant C as,

$$C = \frac{\left[I_0(\alpha a)K_1(\alpha a) + K_0(\alpha a)I_1(\alpha a)\right]\frac{P_2}{\alpha^2}}{I_1(\alpha a)K_0(\alpha b) + I_0(\alpha b)K_1(\alpha a)}$$

$$+ \frac{\left[I_0(\alpha a)K_0(\alpha b) - I_0(\alpha b)K_0(\alpha a)\right]\frac{aP_1\mu}{2\alpha\bar{\mu}}}{I_1(\alpha a)K_0(\alpha b) + I_0(\alpha b)K_1(\alpha a)} - \frac{P_2}{\alpha^2} - \frac{P_1}{4}a^2. \tag{5.2.16}$$

Hence, the velocities $u(r)$ (in the channel) and $v(r)$ (in the porous medium) given by equations (5.2.3) and (5.2.5) respectively, are completely determined.

We define the mean velocity in the channel $\bar{u}$ and the mean velocity in the porous medium $\bar{v}$ by

$$\bar{u} = \frac{1}{\pi a^2}\iint_1 u\, dS \tag{5.2.17}$$

and

$$\bar{v} = \frac{1}{\pi\left(b^2 - a^2\right)} \iint_2 v \, dS \, . \tag{5.2.18}$$

By direct substitution of (5.2.3) into (5.2.17), we obtain

$$\bar{u} = \frac{1}{\pi a^2} \int_0^{2\pi} \int_0^{a} \left(\frac{P_1}{4} r^2 + C \right) r \, dr \, d\theta \, ,$$

where C is given by (5.2.16), and yielding

$$\bar{u} = \frac{P_1}{8} a^2 + C \, . \tag{5.2.19}$$

Substituting (5.2.5) into (5.2.18), we get

$$\bar{v} = \frac{1}{\pi\left(b^2 - a^2\right)} \int_0^{2\pi} \int_a^{b} \left[A I_0(\alpha r) + B K_0(\alpha r) - \frac{P_2}{\alpha^2} \right] r \, dr \, d\theta \, ,$$

where A and B are given by (5.2.14) and (5.2.15) respectively.

Using the following formulas given by Erdelyi [12],

$$\int x I_0(x) \, dx = x I_1(x) \tag{5.2.20}$$

and

$$\int xK_0(x)\,dx = -xK_1(x)\,, \tag{5.2.21}$$

we obtain the mean velocity in the porous medium as

$$\bar{v} = \frac{2\{A[bI_1(\alpha b) - aI_1(\alpha a)] + B[aK_1(\alpha a) - bK_1(\alpha b)]\}}{\alpha(b^2 - a^2)} - \frac{P_2}{\alpha^2}\,. \tag{5.2.22}$$

From (5.2.19) and (5.2.22), we can express P_1 in terms of $\bar{u}$ and P_2 in terms of $\bar{v}$ as follows:

$$P_1 = \frac{\bar{u}}{U}\,, \tag{5.2.23}$$

where U is given by

$$U = \frac{a^2}{8} + C'\,, \tag{5.2.24}$$

and

$$P_2 = \frac{\bar{v}}{V}\,, \tag{5.2.25}$$

where V is given by

$$V = \frac{2\{A'[bI_1(\alpha b) - aI_1(\alpha a)] + B'[aK_1(\alpha a) - bK_1(\alpha b)]\}}{\alpha(b^2 - a^2)} - \frac{1}{\alpha^2}\,. \tag{5.2.26}$$

A', B', and C' in (5.2.24) and (5.2.26) are defined by the relations

$$A = P_2 A' , \tag{5.2.27}$$

$$B = P_2 B' , \tag{5.2.28}$$

$$C = P_1 C' . \tag{5.2.29}$$

To illustrate the results of this section, we select a set of assumed numerical values used by other authors to graph representative velocity components of the flow in the channel and in the porous medium. The numerical evaluations of the analytical velocity components in both regions and the graphs were done on *Mathematica*.

We use the following set of values for the parameters involved:

$\mu = 0.04$ dyne·sec/cm^2.

$k = 10^{-7}$.

$b - a = 0.01$cm.

$\frac{\mu}{\overline{\mu}} = 0.1, 1, 10$.

Also, we denote $P = \frac{\partial p}{\partial z}$.

We present velocity graphs for different sets of values of a, b, and $\overline{\mu}$ in Figures 5.1 to 5.8.

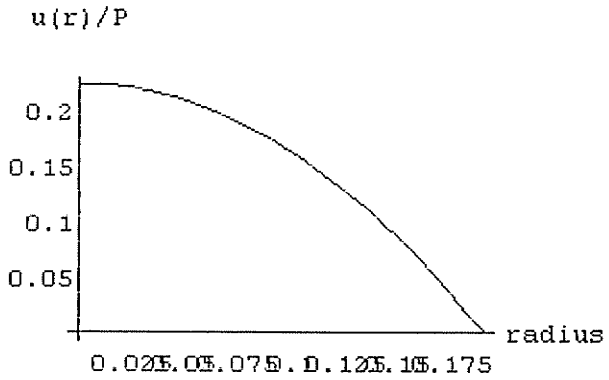

Figure 5.1 Velocity profile in the channel for a = 0.19 and $\overline{\mu}$ = 0.4.

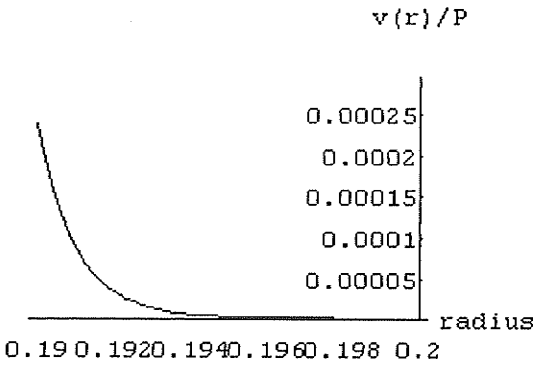

Figure 5.2 Velocity profile in the porous medium for a = 0.19 and $\overline{\mu}$ = 0.4.

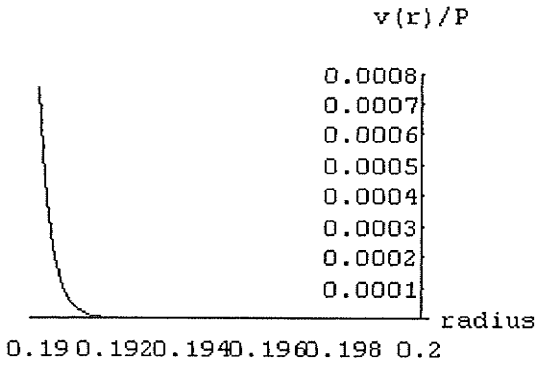

Figure 5.3 Velocity profile in the porous medium for a = 0.19 and $\overline{\mu}$ = 0.04.

For $\overline{\mu}$ = 0.4, the velocity profiles shown in Figures 5.1 and 5.2 match at the point 0.0002393, as we can also see from Table 5.1.

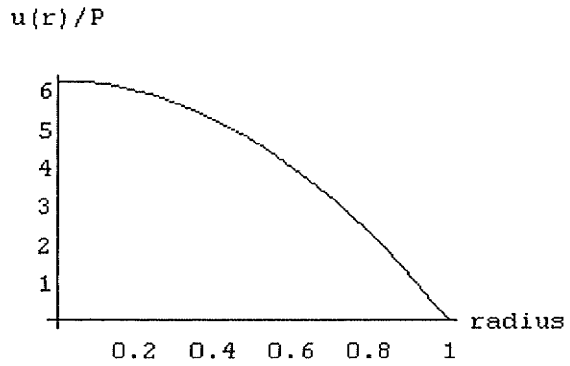

Figure 5.4 Velocity profile in the channel for a = 1.00 and $\overline{\mu}$ = 0.4.

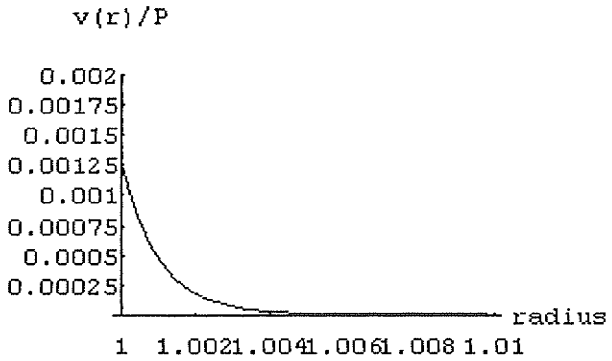

Figure 5.5 Velocity profile in the porous medium for a = 1.00 and $\overline{\mu}$ = 0.4.

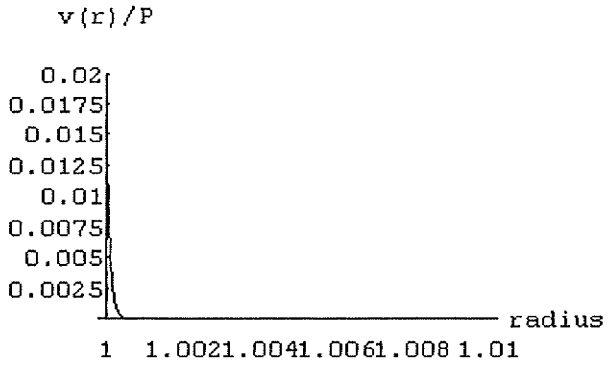

Figure 5.6 Velocity profile in the porous medium for a = 1.00 and $\overline{\mu}$ = 0.004.

In the last three graphs, the velocity profiles in the channel and in the porous medium match at the point 0.0012518.

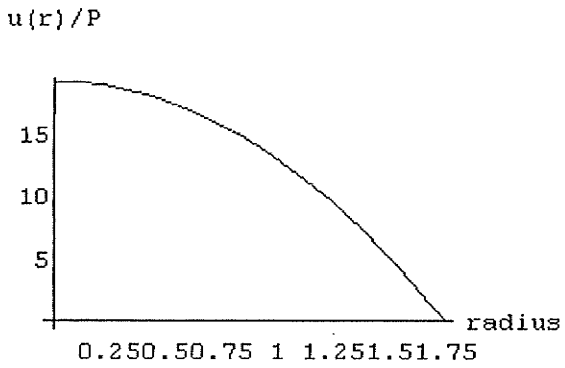

Figure 5.7 Velocity profile in the channel for a = 1.75 and $\overline{\mu}$ = 0.4.

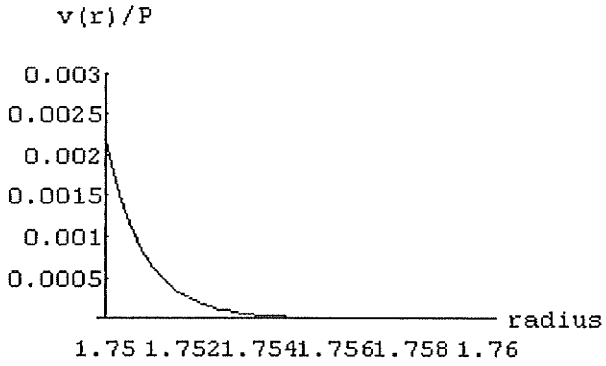

Figure 5.8 Velocity profile in the porous medium for a = 1.75 and $\overline{\mu}$ = 0.4.

In Table 5.1, we give corresponding matching values of $u(r)$ and $v(r)$ at the interface $r = a$.

$\overline{\mu}$ \ d	0.19	0.5	0.75	1.00	1.25	1.75
0.4	2.39377e-04	6.26875e--04	9.39375e-04	1.25183e-03	1.56437e-04	2.18937e-03
0.04	7.52916e-04	1.97829e-03	2.96651e-03	3.95472e-03	4.94293e-04	6.91935e-03
0.004	2.37687e-03	6.25187e-03	9.37687e-03	1.25018e-02	1.56268e-05	2.18768e-02

Table 5.1 Values of $u(r)$ and $v(r)$ at the interface $r = a$.

5.3 Determination of Concentrations

In section 4.2.1 we gave the equation of concentration of solute in the channel in the form

$$\frac{\partial C_1}{\partial t} + u\frac{\partial C_1}{\partial z} = D_1\left(\frac{\partial^2 C_1}{\partial r^2} + \frac{1}{r}\frac{\partial C_1}{\partial r} + \frac{\partial^2 C_1}{\partial z^2}\right), \tag{5.3.1}$$

where $C_1=C_1(r, z, t)$, D_1 is the constant diffusion coefficient and u is given by equation (5.2.3).

In order to solve this equation, we follow Taylor's [37] analysis on dispersion of solute particles. A first assumption that we make is that the longitudinal diffusion is much less than the radial diffusion, that is

$$\frac{\partial^2 C_1}{\partial z^2} << \frac{\partial^2 C_1}{\partial r^2}, \tag{5.3.2}$$

and (5.3.1) is now approximated by

$$\frac{\partial C_1}{\partial t} + u\frac{\partial C_1}{\partial z} = D_1\frac{1}{r}\left[\frac{\partial}{\partial r}\left(r\frac{\partial C_1}{\partial r}\right)\right]. \tag{5.3.3}$$

The combined effect of longitudinal convection (given by the second term in (5.3.3)) and radial diffusion (given by the right hand side of the same relation) is to disperse the solute longitudinally relative to a plane moving at the mean speed

of flow by a mechanism which obeys the same law as ordinary one-dimensional diffusion relative to a fluid at rest (see Rudraiah [31]). Equation (5.3.3) also expresses the fact that the distribution of concentration C_1 of the solute depends on the balance between the convection along the channel due to variation of velocity over the cross section and normal molecular diffusion.

Since we are considering convection across a plane moving with the mean speed of flow, the fluid velocity relative to this plane $w_1(r)$ is given by

$$w_1(r) = u(r) - \bar{u} = \frac{P_1}{8}\left(2r^2 - a^2\right). \tag{5.3.4}$$

Using the following non dimensional quantities

$$\tau_1 = \frac{t}{\bar{t}_1}, \qquad \bar{t}_1 = \frac{L}{\bar{u}}, \qquad \xi_1 = \frac{z - \bar{u}t}{L}, \qquad \eta = \frac{r}{a}, \tag{5.3.5}$$

where L is the characteristic length along the flow direction, (5.3.3) becomes

$$\frac{1}{\bar{t}_1}\frac{\partial C_1}{\partial \tau_1} + \frac{w_1}{L}\frac{\partial C_1}{\partial \xi_1} = \frac{D_1}{a}\frac{1}{\eta}\left[\frac{\partial}{\partial \eta}\left(\eta \frac{\partial C_1}{\partial \eta}\right)\right]. \tag{5.3.6}$$

We will make the following two assumptions. The first one is the Taylor [37] longitudinal condition, namely: if the time of decay (the time in which the concentration degenerates into a uniform concentration) for radial diffusion is much shorter than the time necessary for convection to make an appreciable

change in concentration, time which is of order $L / \bar{u}$, then the approximation that C_1 is a function only of η will be valid. Hence, assuming C_1 is independent of τ_1, we get

$$\frac{1}{\eta}\left[\frac{\partial}{\partial\eta}\left(\eta\frac{\partial C_1}{\partial\eta}\right)\right] = \frac{a^2}{LD_1}\frac{\partial C_1}{\partial\xi_1}w_1(\eta)\ . \tag{5.3.7}$$

The second assumption is that (following Taylor [37]), $\partial C_1 / \partial\xi_1$ is independent of η. Using (5.3.4), we obtain

$$\frac{\partial}{\partial\eta}\left(\eta\frac{\partial C_1}{\partial\eta}\right) = \frac{a^2P_1}{8LD_1}\frac{\partial C_1}{\partial\xi_1}\left(2\eta^3 - \eta\right)\ . \tag{5.3.8}$$

On integration with respect to η, the concentration C_1 in the channel has the form

$$C_1(\eta) = \frac{a^4P_1}{16LD_1}\frac{\partial C_1}{\partial\xi_1}\left(\frac{\eta^4}{4} - \frac{\eta^2}{2}\right) + E\ln\eta + F\ , \tag{5.3.9}$$

where E and F are constants of integration. We observe that $r = 0$ is in the region and for C_1 to be finite we assume $E = 0$. Thus,

$$C_1(\eta) = \frac{a^4P_1}{64LD_1}\frac{\partial C_1}{\partial\xi_1}\left(\eta^4 - 2\eta^2\right) + F\ , \tag{5.3.10}$$

where F will be determined from the boundary conditions.

The distribution of concentration in the porous medium is, from equation 4.2.7, given by

$$\frac{\partial C_2}{\partial t} + v\frac{\partial C_2}{\partial z} = D_2\left(\frac{\partial^2 C_2}{\partial r^2} + \frac{1}{r}\frac{\partial C_2}{\partial r} + \frac{\partial^2 C_2}{\partial z^2}\right), \tag{5.3.11}$$

where $C_2=C_2(r, z, t)$, D_2 is the constant diffusion coefficient in the porous medium, and v is given by equation (5.2.5). Since the equation in C_2 (5.3.11) is similar to the equation in C_1 (5.3.1), a parallel analysis with the non dimensional quantities

$$\tau_2 = \frac{t}{\bar{t}_2}, \qquad \bar{t}_2 = \frac{L}{\bar{v}}, \qquad \xi_2 = \frac{z - \bar{v}t}{L}, \qquad \eta = \frac{r}{a}, \tag{5.3.12}$$

yield

$$\frac{1}{\eta}\left[\frac{\partial}{\partial \eta}\left(\eta\frac{\partial C_2}{\partial \eta}\right)\right] = \frac{a^2}{LD_2}\frac{\partial C_2}{\partial \xi_2}w_2(\eta), \tag{5.3.13}$$

where w_2 is given by

$$w_2(\eta) = v(\eta) - \bar{v}. \tag{5.3.14}$$

In the above relation, $\partial C_2 / \partial \xi_2$ is taken to be independent of η. To find $C_2(\eta)$, it is more convenient to substitute relation (5.3.14) into (5.3.13) and obtain

$$\frac{\partial}{\partial \eta}\left(\eta \frac{\partial C_2}{\partial \eta}\right) = \frac{a^2}{LD_2} \frac{\partial C_2}{\partial \xi_2}\left[A\eta I_0(\alpha a \eta) + B\eta K_0(\alpha a \eta) - \frac{P_2}{\alpha^2}\eta\right]$$

$$- \frac{a^2 \bar{v}}{LD_2} \frac{\partial C_2}{\partial \xi_2} \eta \,. \qquad (5.3.15)$$

Integrating once (5.3.15) and using formulas (5.2.20) and (5.2.21), we get

$$\frac{\partial C_2}{\partial \eta} = \frac{a^2}{LD_2} \frac{\partial C_2}{\partial \xi_2} \frac{1}{\alpha a}\left[AI_1(\alpha a \eta) - BK_1(\alpha a \eta)\right]$$

$$- \frac{a^2}{2LD_2} \frac{\partial C_2}{\partial \xi_2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\eta + \frac{G}{\eta} \,, \qquad (5.3.16)$$

where G is an integration constant to be determined. Integrating (5.3.16) and using relations (5.2.11) and (5.2.12), we obtain the final form of the distribution of concentration in the porous medium

$$C_2(\eta) = \frac{1}{\alpha^2 LD_2} \frac{\partial C_2}{\partial \xi_2}\left[AI_0(\alpha a \eta) + BK_0(\alpha a \eta)\right]$$

$$- \frac{a^2}{4LD_2} \frac{\partial C_2}{\partial \xi_2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\eta^2 + G \ln \eta + H \,, \qquad (5.3.17)$$

where G and H will to be determined from the boundary conditions.

The conditions at the boundaries stated in section 4.3.2 now become

$$C_2(\eta) = C_0 \qquad \text{at } \eta = \frac{b}{a}, \tag{5.3.18}$$

at the impermeable boundary, while at the permeable boundary

$$C_2(\eta) = C_1(\eta) \qquad \text{at } \eta = 1 \tag{5.3.19}$$

and

$$D_2 \frac{\partial C_2}{\partial \eta} = D_1 \frac{\partial C_1}{\partial \eta} \quad \text{at } \eta = 1. \tag{5.3.20}$$

Substituting (5.3.17) into (5.3.18) we obtain

$$\frac{1}{\alpha^2 L D_2} \frac{\partial C_2}{\partial \xi_2} \left[A I_0(\alpha b) + B K_0(\alpha b) \right] - \frac{b^2}{4 L D_2} \frac{\partial C_2}{\partial \xi_2} \left(\frac{P_2}{\alpha^2} + \bar{v} \right)$$

$$+ G \ln \frac{b}{a} + H = C_0 . \tag{5.3.21}$$

Equation (5.3.19) becomes

$$- \frac{a^4 P_1}{64 L D_1} \frac{\partial C_1}{\partial \xi_1} + F = \frac{1}{\alpha^2 L D_2} \frac{\partial C_2}{\partial \xi_2} \left[A I_0(\alpha a) + B K_0(\alpha a) \right]$$

$$- \frac{a^2}{4 L D_2} \frac{\partial C_2}{\partial \xi_2} \left(\frac{P_2}{\alpha^2} + \bar{v} \right) + H , \tag{5.3.22}$$

while the boundary condition (5.3.20) is equivalent to

$$D_2\left\{\frac{a}{\alpha LD_2}\frac{\partial C_2}{\partial \xi_2}\left[AI_1(\alpha a) - BK_1(\alpha a)\right] - \frac{a^2}{2LD_2}\frac{\partial C_2}{\partial \xi_2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right) + G\right\}$$

$$= 0 . \qquad (5.3.23)$$

From (5.3.23) the constant G is determined and is given by

$$G = \frac{a}{LD_2}\frac{\partial C_2}{\partial \xi_2}\left\{\frac{a}{2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right) - \frac{1}{\alpha}\left[AI_1(\alpha a) - BK_1(\alpha a)\right]\right\} . \qquad (5.3.24)$$

The constant H is found by direct substitution of (5.3.24) into equation (5.3.21)

$$H = C_0 - \frac{1}{LD_2}\frac{\partial C_2}{\partial \xi_2}\left\{\frac{1}{\alpha^2}\left[AI_0(\alpha b) + BK_0(\alpha b)\right] + \frac{1}{4}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\right.$$

$$\left.\cdot\left(2a^2 \ln\frac{b}{a} - b^2\right) - \frac{a}{\alpha}\left[AI_1(\alpha a) - BK_1(\alpha a)\right]\ln\frac{b}{a}\right\} . \qquad (5.3.25)$$

Substituting (5.3.25) into (5.3.22) yields

$$F = C_0 + \frac{a^4 P_1}{64LD_1}\frac{\partial C_1}{\partial \xi_1} + \frac{1}{LD_2}\frac{\partial C_2}{\partial \xi_2}\left\{\frac{1}{\alpha^2}\left\{A\left[I_0(\alpha a) - I_0(\alpha b)\right]\right.\right.$$

$$\left.+B\left[K_0(\alpha a) - K_0(\alpha b)\right]\right\} + \frac{1}{4}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\left(b^2 - a^2 - 2a^2 \ln\frac{b}{a}\right)$$

$$\left.+\frac{a}{\alpha}\left[AI_1(\alpha a) - BK_1(\alpha a)\right]\ln\frac{b}{a}\right\} . \qquad (5.3.26)$$

Equations (5.3.10) and (5.3.17) completely determine the concentration distributions in the channel and in the porous medium. We now continue our investigation concerning mass transport in arteries.

5.4 Mass Transport in Arteries

5.4.1 Volume Flux of Blood

The volume flux of blood per unit width per unit time Q_1 in the channel is given by

$$Q_1 = \iint u \, dS = \int_0^{2\pi} \int_0^a u(r) \, r \, dr \, d\theta \, .$$

Using (5.2.3) and integrating, we obtain

$$Q_1 = \pi a^2 \left(\frac{P_1}{8} a^2 + C \right), \tag{5.4.1}$$

where C is given by (5.2.16).

Similarly, the volume of flux of blood per unit width per unit time Q_2 in the porous medium is given by

$$Q_2 = \iint v \, dS = \int_0^{2\pi} \int_a^b v(r) \, r \, dr \, d\theta \, .$$

Using (5.2.5), we get on integration

$$Q_2 = \frac{2\pi}{\alpha^2}\left\{A[\alpha b I_1(\alpha b) - \alpha a I_1(\alpha a)] - B[\alpha b K_1(\alpha b) - \alpha a K_1(\alpha a)] - \frac{P_2}{2}\left(b^2 - a^2\right)\right\}, \tag{5.4.2}$$

where A and B are given by (5.2.14) and (5.2.15) respectively.

5.4.2 Mass Transport of Cholesterol

In section 5.3 we have analyzed and obtained solutions of the concentration distributions in the channel and in the porous medium. The assumptions that we made relative to deriving the forms of C_1 and C_2 are important when dealing with the calculation of the mass transport of solute through arteries. We recall that the derivation of C_1 (and similarly of C_2) was based on the consideration that convection takes place across a plane moving with the mean speed of flow and thus, the flow velocity relative to such a plane was given in the channel by

$$w_1 = u - \bar{u} .$$

Therefore, in the channel, the mass transfer of solute M_1 through a unit width of the tube per unit time is (see Taylor [37] and Chandrasekhara [6])

$$M_1 = \iint C_1 w_1 \, dS \, . \tag{5.4.3}$$

Using polar coordinates, (5.4.3) becomes

$$M_1 = \int_0^{2\pi} \int_0^{a} C_1(r) w_1(r) \, r \, dr \, d\theta \, . \tag{5.4.4}$$

Employing

$$r = a\eta \, , \tag{5.4.5}$$

(5.4.3) becomes

$$M_1 = 2\pi a^2 \int_0^1 C_1(\eta) w_1(\eta) \, \eta \, d\eta \tag{5.4.6}$$

$$= 2\pi a^2 \int_0^1 \left[\frac{a^4 P_1}{64 L D_1} \frac{\partial C_1}{\partial \xi_1} \left(\eta^4 - 2\eta^2 \right) + F \right] \left[\frac{P_1 a^2}{8} \left(2\eta^2 - 1 \right) \right] \eta \, d\eta \, .$$

On integration and evaluation, we get

$$M_1 = - \frac{\pi a^8 P_1^2}{3072 L D_1} \cdot \frac{\partial C_1}{\partial \xi_1} \, . \tag{5.4.7}$$

Following Taylor [37], we assume that the variations of C_1 with η are small compared with those in the longitudinal direction and if $\overline{C_1}$ is the mean

concentration over a section of the channel, $\partial\overline{C_1} / \partial\xi_1$ is indistinguishable from $\partial C_1 / \partial\xi_1$ so that (5.4.7) can be written as

$$M_1 = -\frac{\pi a^8 P_1^2}{3072 L D_1} \cdot \frac{\partial\overline{C_1}}{\partial\xi_1} . \tag{5.4.8}$$

This shows that $\overline{C_1}$ is dispersed relative to a plane which moves with velocity $\overline{u}$ exactly as though it were being diffused by a process which obeys the same law as molecular diffusion but with modified diffusion coefficient, say D_1^*. The continuity equation for $\overline{C_1}$ is given by

$$\frac{\partial M_1}{\partial\xi_1} \quad \pi^{-2} \frac{\partial\overline{C_1}}{\partial\tau_1} , \tag{5.4.9}$$

where $\partial \quad \partial\tau_1$ represents differentiation with respect to time at a point where is constant. Differentiating (5.4.8) with respect to ξ_1, we obtain

$$\frac{\partial M_1}{\partial\xi_1} = -\frac{\pi a^8 P_1^2}{3072 L D_1} \cdot \frac{\partial^2\overline{C_1}}{\partial\xi_1^{\,2}} . \tag{5.4.10}$$

Substituting (5.4.10) into (5.4.9), we get

$$-\frac{\pi a^8 P_1^2}{3072 L D_1} \cdot \frac{\partial^2\overline{C_1}}{\partial\xi_1^{\,2}} = -\pi a^2 \frac{\partial\overline{C_1}}{\partial\tau_1}$$

which is equivalent to

$$\frac{\partial \overline{C}_1}{\partial \tau_1} = \frac{a^6 P_1^2}{3072 L D_1} \cdot \frac{\partial^2 \overline{C}_1}{\partial \xi_1^2} \tag{5.4.11}$$

$$= D_1^* \frac{\partial^2 \overline{C}_1}{\partial \xi_1^2}, \tag{5.4.12}$$

where the diffusion coefficient for the channel is:

$$D_1^* = \frac{a^6 P_1^2}{3072 L D_1}.$$

Using (5.2.23), D_1^* becomes

$$D_1^* = \frac{a^6 \overline{u}^2}{3072 L D_1 U^2}. \tag{5.4.13}$$

Relation (5.4.12) represents Fick's second law of diffusion introduced in section 3.5 and governs the longitudinal dispersion of cholesterol in the channel.

We now calculate M_2, the mass flux of solute through a unit width of the tube per unit time, in the porous medium. Applying the same analysis as in the case of M_1, M_2 can be calculated using the formula

$$M_2 = \iint C_2 w_2 \, dS. \tag{5.4.14}$$

This is equivalent to

$$M_2 = 2\pi \int_a^b C_2(r) w_2(r)\, r\, dr\, d\theta\,, \tag{5.4.15}$$

$$= 2\pi a^2 \int_1^{b/a} C_2(\eta) w_2(\eta)\, \eta\, d\eta\,, \tag{5.4.16}$$

on employing (5.4.5). Using

$$w_2(\eta) = A I_0(\alpha a \eta) + B K_0(\alpha a \eta) - \left(\frac{P_2}{\alpha^2} + \bar{v} \right), \tag{5.4.17}$$

and $C_2(\eta)$ given by (5.3.17), (5.4.16) becomes

$$\begin{aligned} M_2 = 2\pi a^2 \Bigg\{ & \frac{1}{\alpha^2 L D_2} \frac{\partial C_2}{\partial \xi_2} \int_1^{b/a} \left[A^2 \eta I_0^{\,2}(\alpha a \eta) + 2AB\eta I_0(\alpha a \eta) K_0(\alpha a \eta) \right. \\ & \left. + B^2 \eta K_0^{\,2}(\alpha a \eta) \right] d\eta \\ & + \left[H - \frac{1}{\alpha^2 L D_2} \frac{\partial C_2}{\partial \xi_2} \left(\frac{P_2}{\alpha^2} + \bar{v} \right) \right] \int_1^{b/a} \left[A\eta I_0(\alpha a \eta) + B\eta K_0(\alpha a \eta) \right] d\eta \\ & - \frac{a^2}{4 L D_2} \frac{\partial C_2}{\partial \xi_2} \left(\frac{P_2}{\alpha^2} + \bar{v} \right) \int_1^{b/a} \left[A\eta^3 I_0(\alpha a \eta) + B\eta^3 K_0(\alpha a \eta) \right] d\eta \\ & + \frac{a^2}{4 L D_2} \frac{\partial C_2}{\partial \xi_2} \left(\frac{P_2}{\alpha^2} + \bar{v} \right) \int_1^{b/a} \eta^3\, d\eta \\ & + G \int_1^{b/a} \left[A\eta \ln \eta\, I_0(\alpha a \eta) + B\eta \ln \eta\, K_0(\alpha a \eta) \right] d\eta \end{aligned}$$

$$-G\left(\frac{P_2}{\alpha^2}+\bar{v}\right)\int_1^{b/a}\eta\ln\eta\,d\eta$$

$$-H\left(\frac{P_2}{\alpha^2}+\bar{v}\right)\int_1^{b/a}\eta\,d\eta\Bigg\}, \tag{5.4.18}$$

where A, B, C, F, G, and H are given by (5.2.14), (5.2.15), (5.2.16), (5.3.26), (5.3.24), and (5.3.25) respectively.

We give a set of identities involving Bessel functions in the Appendix to enable the evaluation of the integrals in (5.4.18). Identities (1) to (4) were specifically developed for the calculation of M_2. Identities (5) to (7) needed changes from the forms that can be found in Erdelyi [12]. The last two identities, i.e. (8) and (9) are given in Spiegel [34]. Thus, we calculate separately each definite integral in (5.4.18).

$$\int_1^{b/a}\left[A^2\eta {I_0}^2(\alpha a\eta)+2AB\eta I_0(\alpha a\eta)K_0(\alpha a\eta)+B^2\eta {K_0}^2(\alpha a\eta)\right]d\eta$$

$$=\frac{b^2}{2a^2}\left\{\left[AI_0(\alpha b)+BK_0(\alpha b)\right]^2-\left[AI_1(\alpha b)-BK_1(\alpha b)\right]^2\right\}$$

$$-\left\{\left[AI_0(\alpha a)+BK_0(\alpha a)\right]^2-\left[AI_1(\alpha a)-BK_1(\alpha a)\right]^2\right\}, \tag{5.4.19}$$

on using identities (5), (6) and (7) from the Appendix.

$$\int_1^{b/a} \left[A\eta I_0(\alpha a\eta) + B\eta K_0(\alpha a\eta)\right] d\eta$$

$$= \frac{1}{\alpha a^2}\left\{A\left[bI_1(\alpha b) - aI_1(\alpha a)\right] - B\left[bK_1(\alpha b) - aK_1(\alpha a)\right]\right\}, \qquad (5.4.20)$$

on using identities (5.2.20) and (5.2.21).

$$\int_1^{b/a} \left[A\eta^3 I_0(\alpha a\eta) + B\eta^3 K_0(\alpha a\eta)\right] d\eta$$

$$= \frac{1}{\alpha^4 a^4}\left\{\left[(\alpha b)^3 + 4\alpha b\right]\left[AI_1(\alpha b) - BK_1(\alpha b)\right]\right.$$
$$-\left[(\alpha a)^3 + 4\alpha a\right]\left[AI_1(\alpha a) - BK_1(\alpha a)\right] - 2(\alpha b)^2\left[AI_0(\alpha b) + BK_0(\alpha b)\right]$$
$$\left.+2(\alpha a)^2\left[AI_0(\alpha a) + BK_0(\alpha a)\right]\right\}, \qquad (5.4.21)$$

on using identities (1) and (2) from the Appendix.

$$\int_1^{b/a} \eta^3\, d\eta = \frac{1}{4a^4}\left(b^4 - a^4\right). \qquad (5.4.22)$$

$$\int_1^{b/a} \left[A\eta \ln \eta\, I_0(\alpha a\eta) + B\eta \ln \eta\, K_0(\alpha a\eta)\right] d\eta = \frac{b}{\alpha a^2}\left[AI_1(\alpha b) - BK_1(\alpha b)\right] \ln \frac{b}{a}$$

$$- \frac{1}{\alpha^2 a^2}\left\{A\left[I_0(\alpha b) - I_0(\alpha a)\right] + B\left[K_0(\alpha b) - K_0(\alpha a)\right]\right\}, \qquad (5.4.23)$$

on using identities (3) and (4) from the Appendix.

$$\int_1^{b/a} \eta \ln \eta \, d\eta = \frac{1}{2}\left[\frac{b^2}{a^2}\left(\ln \frac{b}{a} - \frac{1}{2}\right) + \frac{1}{2}\right]. \tag{5.4.24}$$

$$\int_1^{b/a} \eta \, d\eta = \frac{1}{2a^2}\left(b^2 - a^2\right). \tag{5.4.25}$$

Putting together all the results, M_2 is

$$M_2 = \frac{2\pi a^2}{LD_2}\frac{\partial C_2}{\partial \xi_2} \cdot S + C_0 \cdot T, \tag{5.4.26}$$

where S is given by

$$\begin{aligned} S = \frac{1}{2\alpha^2}\Bigg\{ & \frac{b^2}{a^2}\Big\{\left[AI_0(\alpha b) + BK_0(\alpha b)\right]^2 - \left[AI_1(\alpha b) - BK_1(\alpha b)\right]^2\Big\} \\ & - \Big\{\left[AI_0(\alpha a) + BK_0(\alpha a)\right]^2 - \left[AI_1(\alpha a) - BK_1(\alpha a)\right]^2\Big\}\Bigg\} \\ & + \frac{1}{\alpha a^2}\left[H' - \frac{1}{\alpha^2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\right]\Big\{A\left[bI_1(\alpha b) - aI_1(\alpha a)\right] - B\left[bK_1(\alpha b) - aK_1(\alpha a)\right]\Big\} \\ & - \frac{1}{4\alpha^4 a^2}\left(\frac{P_2}{\alpha^2} + \bar{v}\right)\Big\{\left[(\alpha b)^3 + 4\alpha b\right]\left[AI_1(\alpha b) - BK_1(\alpha b)\right] - \left[(\alpha a)^3 + 4\alpha a\right] \\ & \cdot\left[AI_1(\alpha a) - BK_1(\alpha a)\right] - 2(\alpha b)^2\left[AI_0(\alpha b) + BK_0(\alpha b)\right] \\ & + 2(\alpha a)^2\left[AI_0(\alpha a) + BK_0(\alpha a)\right]\Big\} \end{aligned}$$

$$+\frac{1}{16a^2}\left(\frac{P_2}{\alpha^2}+\bar{v}\right)^2\left(b^4-a^4\right)$$

$$+G'\left\{\frac{b}{\alpha a^2}\left[AI_1(\alpha b)-BK_1(\alpha b)\right]\ln\frac{b}{a}\right.$$

$$\left.-\frac{1}{\alpha^2a^2}\left\{A\left[I_0(\alpha b)-I_0(\alpha a)\right]+B\left[K_0(\alpha b)-K_0(\alpha a)\right]\right\}\right\}$$

$$-\frac{G'}{2}\left(\frac{P_2}{\alpha^2}+\bar{v}\right)\left[\frac{b^2}{a^2}\left(\ln\frac{b}{a}-\frac{1}{2}\right)+\frac{1}{2}\right]$$

$$+\frac{H'}{2a^2}\left(\frac{P_2}{\alpha^2}+\bar{v}\right)\left(a^2-b^2\right), \tag{5.4.27}$$

and T is given by

$$T=\frac{1}{\alpha a^2}\left\{A\left[bI_1(\alpha b)-aI_1(\alpha a)\right]-B\left[bK_1(\alpha b)-aK_1(\alpha a)\right]\right\}$$

$$\frac{1}{2a^2}\left(\frac{P_2}{\alpha^2}+\bar{v}\right)\left(a^2-b^2\right). \tag{5.4.28}$$

In equation (5.4.27) G' and H' are defined by the following relations:

$$G=\frac{1}{LD_2}\frac{\partial C_2}{\partial \xi_2}\cdot G' \tag{5.4.29}$$

and

$$H=C_0+\frac{1}{LD_2}\frac{\partial C_2}{\partial \xi_2}\cdot H'. \tag{5.4.30}$$

Applying for M_2 the same analysis as for M_1, we consider that if $\overline{C}_2$ is the mean concentration over a section of the porous medium then $\partial\overline{C}_2 / \partial\xi_2$ is indistinguishable from $\partial C_2 / \partial\xi_2$ so that (5.4.26) becomes

$$M_2 = \frac{2\pi a^2}{LD_2}\frac{\partial\overline{C}_2}{\partial\xi_2}\cdot S + C_0 \cdot T \,. \tag{5.4.31}$$

Relation (5.4.31) shows that $\overline{C}_2$ is dispersed relative to a plane which moves with velocity $\overline{v}$ exactly as though it were being diffused by a process which obeys the same law as molecular diffusion but with modified diffusion coefficient, say D_2^*. The continuity equation for $\overline{C}_2$ is given by

$$\frac{\partial M_2}{\partial\xi_2} = -\pi\left(b^2 - a^2\right)\frac{\partial\overline{C}_2}{\partial\tau_2}\,, \tag{5.4.32}$$

where $\partial / \partial\tau_2$ represents differentiation with respect to time at a point where ξ_2 is constant. We differentiate (5.4.31) with respect to ξ_2:

$$\frac{\partial M_2}{\partial\xi_2} = \frac{2\pi a^2 S}{LD_2}\frac{\partial^2\overline{C}_2}{\partial\xi_2^{\,2}}\,. \tag{5.4.33}$$

Equation (5.4.32) becomes

$$\frac{2\pi a^2 S}{LD_2}\frac{\partial^2\overline{C}_2}{\partial\xi_2^{\,2}} = -\pi\left(b^2 - a^2\right)\frac{\partial\overline{C}_2}{\partial\tau_2}\,, \tag{5.4.34}$$

which can be written as

$$\frac{\partial \overline{C}_2}{\partial \tau_2} = -\frac{2a^2 S}{LD_2\left(b^2 - a^2\right)} \frac{\partial^2 \overline{C}_2}{\partial \xi_2^{\,2}} \tag{5.4.35}$$

$$= D_2^{\,*} \frac{\partial^2 \overline{C}_2}{\partial \xi_2^{\,2}}\,, \tag{5.4.36}$$

where the diffusion coefficient for the porous medium is:

$$D_2^{\,*} = -\frac{2a^2 S}{LD_2\left(b^2 - a^2\right)}\,.$$

S can be expressed in the form

$$S = P_2 S'\,,$$

so that using (5.2.25), $D_2^{\,*}$ becomes

$$D_2^{\,*} = -\frac{2a^2 S' \overline{v}}{LD_2 V\left(b^2 - a^2\right)}\,. \tag{5.4.37}$$

Equation (5.4.36) represents Fick's second law of diffusion and it is the equation governing the longitudinal dispersion of cholesterol in the porous medium.

Thus, we have determined the analytical formulas for the mass flux of solute in the channel and in the porous medium. The new quantities that we introduced in this section, D_1^* and D_2^*, are called Taylor's diffusion coefficients.

5.5 Cholesterol Deposition

Using Taylor's diffusion coefficients D_1^* and D_2^* introduced in the previous section, we can calculate the volumetric amount of cholesterol δ deposited at the interface and the rate of growth of cholesterol x per unit width per unit time. We denote by y_1 and y_2 the amount of cholesterol dispersed in the channel and in the porous medium. y_1 and y_2 are given by

$$\frac{D_1^*}{D_1} = 1 + y_1 , \tag{5.5.1}$$

and

$$\frac{D_2^*}{D_2} = 1 + y_2 , \tag{5.5.2}$$

where D_1^* and D_2^* are known from (5.4.13) and (5.4.37), and D_1 and D_2 are given constant diffusion coefficients. We expect $\frac{D_1^*}{D_1} > 1$, $\frac{D_2^*}{D_2} > 1$, and $y_1 > y_2$. Hence, we have the following equation for finding δ:

$$y_1 - y_2 = \delta . \tag{5.5.3}$$

The rate of growth of cholesterol x per unit width per unit time satisfies the relation

$$\delta = \pi a^2 - \pi(a - x)^2 . \tag{5.5.4}$$

Geometrically, the right hand side of equation (5.5.4) can be visualized in Figure 5.9, where a is the radius of the channel, b - a is the thickness of the porous medium, and x is the rate of growth of cholesterol per unit width per unit time.

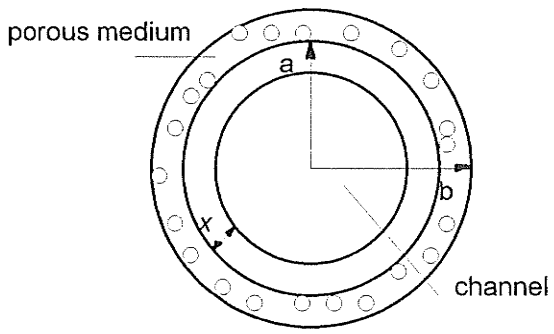

Figure 5.9 Schematic drawing of cholesterol deposition.

Equation (5.5.4) is a quadratic equation that admits two real solutions, namely

$$x = a \pm \sqrt{a^2 - \frac{\delta}{\pi}} , \tag{5.5.5}$$

for $a^2 - \frac{\delta}{\pi} \geq 0$. Since $x \leq a$, then the increase in the radial thickness of the cholesterol deposit is given by

$$x = a - \sqrt{a^2 - \frac{\delta}{\pi}} \, . \tag{5.5.6}$$

5.6 Conclusions

The biological model investigated in this thesis led to analytical solutions of the equations of velocity, concentration, volume flux of blood and mass transfer of cholesterol in the channel and in the porous medium.

For the first time, an expression for the amount of cholesterol deposit and the rate of growth of cholesterol per unit width per unit time is given. The mathematical expressions derived are relevant to the prediction of the development of arteriosclerosis in the human circulatory system. The relevancy would have to be supported by further research showing good agreement with experimental data. Ultimately, by solving this problem, the intend is to give an accurate method for predicting the rate of growth of cholesterol within a time frame.

The analysis of the model is theoretical rather than experimental. Therefore, for numerical evaluations, we need to have experimental values for the parameters, in addition to assumptions on material properties. The topic of porous media is still in the stage of developments with a large variety of views regarding the properties of the porous media itself, as well as the boundary conditions at interfaces. Although we have developed a set of conditions fairly consistent with recent work on the topic, the model does not reach a level of sophistication for which comparison with experimental medical data is suitable.

The biological model can be further developed, making it less restrictive in assumptions. Further work can consist of using more complex conditions like slip boundary conditions, different kinds of diffusion, more complicated structures of the porous medium etc.

APPENDIX

Table of Bessel Integrals

$$\int x^3 I_0(x)\,dx = \left(x^3 + 4x\right)I_1(x) - 2x^2 I_0(x)\,. \tag{1}$$

$$\int x^3 K_0(x)\,dx = -\left(x^3 + 4x\right)K_1(x) - 2x^2 K_0(x)\,. \tag{2}$$

$$\int x I_0(x) \ln x\,dx = x I_1(x) \ln x - I_0(x)\,. \tag{3}$$

$$\int x K_0(x) \ln x\,dx = -x K_1(x) \ln x - K_0(x)\,. \tag{4}$$

$$\int x I_0^2(x)\,dx = \frac{x^2}{2}\left[I_0^2(x) - I_1^2(x)\right]. \tag{5}$$

$$\int x K_0^2(x)\,dx = \frac{x^2}{2}\left[K_0^2(x) - K_1^2(x)\right]. \tag{6}$$

$$\int x I_0(ax)K_0(ax)\,dx = \frac{x^2}{2}\left[I_0(ax)K_0(ax) + I_1(ax)K_1(ax)\right]. \tag{7}$$

$$I_1'(x) = I_0(x) - \frac{1}{x} I_1(x)\,. \tag{8}$$

$$K_1'(x) = -K_0(x) - \frac{1}{x} K_1(x)\,. \tag{9}$$

REFERENCE LIST

[1] Acheson, D. J., 1990. Elementary Fluid Dynamics. Oxford: Clarendon Press.

[2] Beavers, G. S. and D. D. Joseph, 1967. Boundary Conditions at a Naturally Permeable Wall. J. Fluid Mech., Vol. 30, Part 1, 197-207.

[3] Brinkman, H. C., 1947. A Calculation of the Viscous Force Exerted by a Flowing Fluid on a Dense Swarm of Particles. Appl. Sci. Res., Vol. A1, 27-34.

[4] Burton, A. C., 1972. Physiology and Biophysics of the Circulation. Chicago: Year Book Medical Publishers.

[5] Cavalcanti, S., 1995. Hemodynamics of an Artery with Mild Stenosis. J. Biomech., Vol. 28, No. 4, 387-399.

[6] Chandrasekhara, B. C., N. Rudraiah, and S. T. Nagaraj, 1980. Velocity and Dispersion in Porous Media. Int. J. Engng. Sci., Vol. 18, 921-929.

[7] Chien, Shu, 1981. The Rheology of Blood. In The Rheology of Blood, Vessels and Associated Tissues, ed. D. R. Gross and N. H. C. Hwang, 118-136. Rockville, Maryland.

[8] Cook, R. P., 1958. Cholesterol: Chemistry, Biochemistry, and Pathology. New York: Academic Press Publishers.

[9] Crank, J., 1979. The Mathematics of Diffusion. Oxford: Clarendon Press.

[10] Deng, X., M. W. King and R. Guidoin, 1995. Localization of Atherosclerosis in Arterial Junctions. Concentration Distribution of Low Density Lipoproteins at the Luminal Surface in Regions of Disturbed Flow. ASAIO J., Vol. 41, No. 1, 58-67.

[11] Dullien, F. A. L., 1979. Porous Media: Fluid Transport and Pore Structure. New York: Academic Press Publishers.

[12] Erdelyi, A., 1954. Tables of Integral Transforms, Vol. 2. New York: McGraw-Hill Book Company.

[13] Fung, Y. C. and H. T. Tang, 1975. Solute Distribution in the Flow in a Channel Bounded by Porous Layers. J. Appl. Mech.,Vol. 42, No. 3, Trans.ASME, Vol. 97, Series E, September, 531-535.

[14] Fung, Y. C. and H. T. Tang, 1975. Longitudinal Dispersion of Tracer Particles in the Blood Flowing in a Pulmonary Alveolar Sheet. J. Appl. Mech, Vol. 42, No. 3, Trans. ASME, Vol. 97, Series E, September, 536-540.

[15] Fung, Y. C., 1990. Biomechanics: Motion, Flow, Stress, and Growth. New York: Springer-Verlag.

[16] Guha, H. S. and T. K. Chaudhury, 1985. Flow in an Arteriosclerotic Blood Vessel with Rigid Permeable Wall. Bull. Math. Biol., Vol. 47, No. 5, 613-627.

[17] Gurr, M. I. and A. T. James, 1971. Lipid Biochemistry: an Introduction. New York: Cornell University Press.

[18] Hughes, W. F. and J. A. Brighton, 1967. Fluid Dynamics. In Schaum's Outline Series. New York: McGraw-Hill Book Company.

[19] Jones, D. S. and B. D. Sleeman, 1983. Differential Equations and Mathematical Biology. London: George Allen & Unwin Publishers.

[20] Kim, S. and W. B. Russel, 1985. Modelling of Porous Media by Renormalization of the Stokes Equations. J. Fluid Mech.,Vol. 154, 269-286.

[21] McDonald, D. A., 1974. Blood Flow in Arteries. Baltimore: The Williams and Wilkins Company.

[22] Misra, J. C. and S. I. Singh, 1987. A Study on the Non-Linear Flow of Blood Through Arteries. Bull. Math. Biol., Vol. 49, No. 3, 257-277.

[23] Muskat, M., 1946. The Flow of Homogeneous Fluids Through Porous Media. Michigan: Edwards Brothers.

[24] Neumann, S. J., S. A. Berceli, E. M. Sevick, A. M. Lincoff, V. S. Warty, A. M. Brant, I. M. Herman, and H. S. Borovetz, 1990. Experimental Determination and Mathematical Model of the Transient Incorporation of Cholesterol in the Arterial Wall. Bull. Math. Biol., Vol. 52, No. 6, 711-732.

[25] Ockendon, H. and J. R. Ockendon, 1995. Viscous Flow. Cambridge University Press.

[26] Pal, D., R. Veerabhadraiah, P. N. Shivakumar, and N. Rudraiah, 1984. Longitudinal Dispersion of Tracer Particles in a Channel Bounded by Porous Media Using Slip Condition. Int. J. Math. & Math. Sci., Vol. 7, No. 4, 755-764.

[27] Pal, D., 1985, Ph.D. Thesis. Bangalore: Bangalore University, India.

[28] Perktold, K., E. Thurner and T. Kenner, 1994. Flow and Stress Characteristics in Rigid Walled and Compliant Carotid Artery Bifurcation Models. Med. Bio. Engng. Comput., Vol. 32, No. 1, 19-26.

[29] Rubinow, S. I., 1975. Introduction to Mathematical Biology. New York: John Wiley & Sons.

[30] Rudraiah, N., B. C. Chandrasekara, R. Veerabhadraiah, and S. T. Nagaraj, 1979. Some Flow Problems in Porous Media. In PGSAM Series, Vol. 2. Bangalore: Bangalore University, India.

[31] Rudraiah, N., 1985. Coupled Parallel Flows in a Channel and a Bounding Porous Medium of Finite Thickness. J. Fluids Engng., Vol. 107, Trans. ASME, September, 322-330.

[32] Scheidegger, A. E., 1974. The Physics of Flow Through Porous Media. Toronto: University of Toronto Press.

[33] Shivakumar, P. N., S. Nagaraj, R. Veerabhadraiah, and N. Rudraiah, 1986. Fluid Movement in a Channel of Varying Gap with Permeable Walls Covered by Porous Media. Int. J. Engng. Sci., Vol. 24, No. 4, 479-492.

[34] Spiegel, M. R., 1994. Mathematical Handbook of Formulas and Tables. In Schaum's Outline Series. New York: McGraw-Hill Book Company.

[35] Starling, E.M. 1986. On the Absorption of Fluids from the Convective Tissue Spaces. J. Physiology, Vol. 19, 312.

[36] Tang, H. T. and Y. C. Fung, 1975. Fluid Movement in a Channel with Permeable Walls Covered by Porous Media. J. Appl. Mech., Vol. 42, No. 1, Trans. ASME, Vol. 97, Series E, March, 45-50.

[37] Taylor, G. I., 1953. Dispersion of Soluble Matter in Solvent Flowing Slowly Through a Tube. Proc. Royal Soc., Vol. 219, Series A, 186-203.

[38] Vafai, K. and R. Thiyagaraja, 1987. Analysis of Flow and Heat Transfer at the Interface Region of a Porous Medium. Int. J. Heat Mass Transfer, Vol. 30, No. 7, 1391-1405.