Theoretical Predictions of Flow Profiles in Capillary Blood Vessels

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THEORETICAL PREDICTIONS OF FLOW PROFILES IN CAPILLARY BLOOD VESSELS

BY

EILEEN HALLMAN
B.S.E., Florida Technological University, 1971

THESIS

Submitted in partial fulfillment of the requirements for the degree of Master of Science in Engineering in the Graduate Studies Program of Florida Technological University, 1972

Orlando, Florida
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LIST OF SYMBOLS

A  Area

\(d\)  Distance between cells

D  Diameter

h  Gap thickness

L  Length

P  Pressure

Q  Volume flow rate

r, R  Vessel radius

u, U  Velocity (axial direction)

v, V  Velocity (radial direction)

\(\mu\)  Viscosity

\(\bar{\mu}\)  Relative viscosity

\(\rho\)  Density

\(\psi\)  Stream function

\(\tau\)  Shear stress
ABSTRACT

The purpose of this thesis is to illustrate the nature of blood flow within capillaries by using familiar mathematical techniques. Because the circulatory system is so complex, the fluid dynamics of the system is prefaced by a discussion of the circulatory physiology in terms of geometry and physics. The understanding of the basic structures and functions of the circulatory components necessarily precedes the justification of assumptions.

Several mathematical models which attempt to describe the fluid dynamics of blood flow phenomena are presented and discussed. The results of these models are correlated with existing experimental data in order to determine which mathematical models best predict the fluid dynamic behavior within the capillaries. The significance of this behavior is then noted with respect to diffusion within capillaries. It is noted that bolus flow offers the greatest rate of exchange of the models discussed.

Conclusions are discussed and related to further applications and research.
CHAPTER 1

INTRODUCTION

Although the Arabian scholar Ibnul-Nafiess (1208-1288 A.D.) first described accurately the pulmonary circulation (1), William Harvey is given credit for discovering in 1615 the structure and function of the circulatory system. The microscopic capillaries were not actually observed until 1661 by Marcello Malpighi, but Harvey deduced that the circulation must be a closed circuit. In his De Motu Cordis (1628), Harvey wrote (2),

First-blood is incessantly transmitted by the action of the heart from the vena cava to the arteries in such quantity, that it cannot be supplied by the ingesta, and in such wise that the whole mass must very quickly pass through the organ; second—the blood under the influence of the arterial pulse is compelled in a continuous, equable, and incessant stream through every part of the body, in much larger quantity than were necessary for nutrition, or than the whole mass of fluids could supply; third—the veins in like manner return this blood incessantly to the heart from all parts and members of the body. These points proved, I conceive it will be manifest that the blood circulates, revolves, propelled and then returning, from the extremities to the heart, and thus that it performs a kind of circular motion.

Thirty-three years later, after observing the capillaries with the use of a microscope, Malpighi wrote (2),

The power of the eye could not be extended further in the opened living animal, hence I believed that this body of the blood breaks into empty space, and is collected again by a gaping vessel and by the structure of the walls... .But the dried lung of the frog made my belief dubious. This lung had, by chance, preserved the redness of the blood in (what afterwards proved to be) the smallest vessels... .Here it was clear to sense that the blood flows away through the tortuous vessels, that it is not poured into spaces but always works through tubules, and is dispersed by the multiplex winding of the vessels.
Although it has been known since the 17th century that the capillaries are the site of nutrient and waste exchanges between the tissues and the bloodstream, few attempts had been made until more recent times to clarify the fluid dynamics which allow such an efficient exchange. The most significant results of studies in this area were published in 1961 by J. Prothero and A. C. Burton (3), who used a thermal analog to approximate gaseous exchange in the pulmonary capillaries. The thermal simulation was such that the heat transfer between a copper tube and successive water baths represented the gaseous exchange which takes place in the pulmonary circulation. The type of flow Prothero and Burton described is termed "bolus flow". Along with several other models, bolus flow is presented in detail in a later chapter.

Before the dynamics of capillary blood flow are considered, it is necessary that the physiology of the circulation as well as the capillary bed be fully understood.
CHAPTER 2

CIRCULATORY PHYSIOLOGY

The circulatory system is generally thought of as two circuits fed by the heart. The heart consists of four chambers—a left and right atrium and a left and right ventricle. On each side, the atrium is connected to the corresponding ventricle by a valve which permits flow in one direction. The largest arteries, the aorta and the pulmonary artery, arise from the left and right ventricles, respectively. Blood is then returned to the right atrium by the vena cava and to the left atrium by the pulmonary vein. Figure 1 shows schematically the systemic and pulmonary circuits. The systemic circuit carries the blood from the heart to all of the tissues and organs except the lungs, and the pulmonary circuit feeds the lungs. The significant difference in the functions of the separate circuits is in the oxygen transport; the tissues fed by the systemic circuit remove oxygen from the blood and the lungs supply the blood with oxygen in the pulmonary circuit. The circulation is maintained by the pumping action of the heart, which consists of alternate contraction and relaxation phases. During contraction, or systole, blood is forced from the left atrium into the left ventricle, which in turn forces blood into the aorta to begin the systemic circuit. The vessels which carry the bloodstream are the arteries, which branch into smaller arterioles, the microscopic capillaries which branch from arterioles and back to venules, and veins. The systemic circuit is completed when the venous blood is returned by
Fig. 1.--Circulatory system flow schematic
the vena cava to the right atrium during the relaxation phase, or diastole. During the systolic phase, the blood is then ejected into the right ventricle and begins the pulmonary circuit. The pulmonary artery carries the blood from the right ventricle and the pulmonary vein returns the oxygenated blood to the left atrium, from which the systemic circuit is regenerated.

Vessel Differentiation

Since the function of the circulatory system is to supply oxygen, metabolic fuels, vitamins, hormones, and heat to the tissues as well as remove waste products and heat from tissues, it is apparent that there are differences in the tissue structures. These functions are carried out primarily in the capillaries, which differ from other vessels in size, wall composition, and wall thickness. Since nutrient exchange is carried out by diffusion, it is apparent that the composition and thickness of the vessel walls affect the permeability of the walls.

Vessel sizes in adult humans range from approximately three centimeters in the vena cava to six microns in the capillaries (4). The four basic types of tissue found in blood vessels are endothelial cells, elastic fibers, collagen fibers, and smooth muscle. The endothelial or pavement cells are comprised of simple squamous endothelium, which provides all of the vessels with a smooth, highly permeable lining. Although endothelial cells are generally considered as flat, micromanipulation studies indicate that the cells become spherical if released from their cement substances (4). Studies of developing
vessels in tissue culture have also shown that the endothelial cells are free to migrate along the vessel wall (4). The second layer, or elastica intima, is made up of elastin fibers. These highly elastic fibers are thought to be coiled around the vessel so that they resist both extension and compression (1). Folded collagen fibers form networks from within the elastica intima to the outer vessel layer. Collagen fibers are much more highly resistive to extension than elastin fibers, but because of their folded structure, they do not exert an additional tension until they reach their stretched length. Due to this superposition of elastic fibers, the overall elastic modulus for the blood vessel increases with increased vessel length. Thus, together the elastin and collagen fibers exert a steady tension to maintain equilibrium against the transmural pressure due to the vessel blood pressure. The fourth tissue type is vascular smooth muscle, which is arranged circumferentially around the vessel. Although the muscle contracts to produce an active tension and change the diameter of the vessel, it adds little to the total elastic tension.

With the exception of the capillaries and venules, all of the blood vessel walls are composed of all four tissue types. It is important to note that not all vessel walls contain the same quantity of vascular tissues. Hence, arterioles are best equipped to control blood flow by smooth muscle contraction while capillaries and venules, which lack both elastin and collagen, are the sites of the most efficient nutrient exchange. Figure 2 illustrates the differences in size and wall composition and thickness of the various blood vessels. Since
Fig. 2.—Vessel size, wall thickness and composition. The upper figure represents the lumen diameter (i.d.) and the lower figure represents the wall thickness. (From A. C. Burton, Physiology and Biophysics of the Circulation.)
the subject under discussion concerns capillaries, only capillary structure will be considered in detail.

The walls of the capillary vessels are composed of a single layer of endothelial cells which are connected by a cement substance. The elasticity of the vessel is entirely dependent on the elasticity of the individual endothelial cells, but the vessel wall is not responsible for volume changes of the capillary. Studies have shown that the pavement cells blend almost imperceptibly with the tissue matrix; consequently contractions of the host tissue result in the dilation of the capillary vessel, or vasodilation (1). Because of the surface area and wall composition, diffusion is much enhanced in the capillaries. Capillary permeability, though, is not the same for all tissues and organs. Generally, the venous ends of the capillary are more permeable than the arterial ends, and excepting the most extreme situations, the permeability of each individual vessel remains constant even under adverse conditions. Diffusion within the capillary occurs at different sites for different particles; leukocytes or white blood cells migrate through the cement substance, while lipid soluble particles such as water, carbon dioxide, and oxygen, are transferred by pinocytosis through the endothelial cells. In addition, water soluble particles such as glucose and ions are transferred through pores in the vessel wall, and macromolecules pass through "leaks" or large pores in the venules (1). Capillary permeability is never a limiting factor in tissue metabolism as equilibrium in nutrient-metabolite transfer is quickly reached even in maximal flow. Tissue metabolism is influenced
by blood flow rate, flow distribution to the tissues, and the volume of interstitial fluid (5).

**Vascular Bed Geometry**

In reference to the distribution of flow to the tissues and the volume of interstitial fluid, it has been estimated that no cell is more than ten microns from a capillary (4). Considering also that there are over a billion capillaries with an average diameter of eight microns and length of one millimeter, it can easily be shown from the data in Table 1 that the combined capillary and venule surface area available to the tissues is fully 60 percent of the surface area of the entire vascular bed.

Since the rate of circulatory flow is dependent on the individual needs of each cell (6), and most metabolic processes require oxygen, a good indication of blood flow requirements can be obtained from oxygen consumption measurements. The most meaningful units for this type of measurement are \( \text{ml}O_2/\text{min}/100\text{g of tissue} \). Since the oxygen capacity of blood is approximately 20 \( \text{ml}O_2/100\text{ml blood} \) and the blood volume of the body is on the order of 5.5 liters, then the total volume of oxygen available to the tissues is approximately 1.1 liter. But for an average size human at rest, the oxygen consumption is only 20 percent of that available (1). Table 2 lists the estimated distribution of the cardiac output to the organs and tissues and the corresponding oxygen consumption.

At rest, man requires a blood flow rate of approximately five liters/min. The geometrical statistics given for the dog in Table 1
### TABLE 1

**VASCULAR BED GEOMETRY**

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter (mm)</th>
<th>Number</th>
<th>Total Cross-sectional Area (cm²)</th>
<th>Length (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>10</td>
<td>1</td>
<td>0.8</td>
<td>40</td>
</tr>
<tr>
<td>Large Arteries</td>
<td>3</td>
<td>40</td>
<td>3.0</td>
<td>20</td>
</tr>
<tr>
<td>Main Artery Branches</td>
<td>1</td>
<td>600</td>
<td>5.0</td>
<td>10</td>
</tr>
<tr>
<td>Terminal Branches</td>
<td>0.6</td>
<td>1800</td>
<td>5.0</td>
<td>10</td>
</tr>
<tr>
<td>Arterioles</td>
<td>0.02</td>
<td>4.0 x 10⁶</td>
<td>125</td>
<td>0.2</td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.008</td>
<td>1.2 x 10⁹</td>
<td>600</td>
<td>0.1</td>
</tr>
<tr>
<td>Venules</td>
<td>0.03</td>
<td>8.0 x 10⁶</td>
<td>570</td>
<td>0.2</td>
</tr>
<tr>
<td>Terminal Veins</td>
<td>1.5</td>
<td>1800</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Main Venous Branches</td>
<td>2.4</td>
<td>600</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>Large Veins</td>
<td>6.0</td>
<td>40</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Vena Cava</td>
<td>12.5</td>
<td>1</td>
<td>1.2</td>
<td>40</td>
</tr>
</tbody>
</table>

(From the data of F. Mall on the mesentery of the dog, in Burton, A. C.: Physiology and Biophysics of the Circulation [Chicago: Year Book Medical Publishers, Inc., 1948].)
<table>
<thead>
<tr>
<th>Organ</th>
<th>Weight (kg)</th>
<th>Blood Flow (ml/min)</th>
<th>Blood Flow (ml/min/100g)</th>
<th>% Total Cardiac Output</th>
<th>Arteriovenous Difference (ml O₂/100 ml blood)</th>
<th>Oxygen Consumption (ml/min)</th>
<th>Oxygen Consumption (ml/min/100g)</th>
<th>% Total O₂ Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>1.4</td>
<td>750</td>
<td>55</td>
<td>14</td>
<td>6</td>
<td>45</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Heart</td>
<td>0.3</td>
<td>250</td>
<td>80</td>
<td>5</td>
<td>10</td>
<td>25</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Liver</td>
<td>1.5</td>
<td>1300</td>
<td>85</td>
<td>23</td>
<td>6</td>
<td>75</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2.5</td>
<td>1000</td>
<td>40</td>
<td>23</td>
<td>6</td>
<td>75</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.3</td>
<td>1200</td>
<td>400</td>
<td>22</td>
<td>1.3</td>
<td>15</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Muscle</td>
<td>35</td>
<td>1000</td>
<td>3</td>
<td>18</td>
<td>5</td>
<td>50</td>
<td>0.15</td>
<td>20</td>
</tr>
<tr>
<td>Skin</td>
<td>2</td>
<td>200</td>
<td>10</td>
<td>4</td>
<td>2.5</td>
<td>5</td>
<td>0.2</td>
<td>2</td>
</tr>
<tr>
<td>Remainder</td>
<td>27</td>
<td>800</td>
<td>3</td>
<td>14</td>
<td>5</td>
<td>35</td>
<td>0.15</td>
<td>14</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>70</strong></td>
<td><strong>5500</strong></td>
<td><strong>100</strong></td>
<td></td>
<td><strong>250</strong></td>
<td></td>
<td><strong>100</strong></td>
<td></td>
</tr>
</tbody>
</table>

(Values are approximate for an average man at rest, from Folkow, B., and Neil, E.: Circulation [New York: Oxford University Press, 1971].)
can be used to approximate the flow rate within the systemic capillaries if it is assumed that the size ratios are essentially the same for humans. The total capillary cross sectional area is on the order of 800 times that of the aorta. If the velocity of blood in the aorta is known, then the velocity within the capillary bed can be computed from continuity. That is, the product of area and velocity, or volume rate of flow, is constant within the system. Since 1 ml = 1 cc and Q = AV liters/min., then the velocity in the human aorta is given by

\[ V = \frac{5000 \text{ cc/min}}{(\pi)(1 \text{ cm})^2} \]

or \[ V = 26.5 \text{ cm/sec.} \]

Roughly, then, we can say that the velocity in the human aorta is on the order of 30 cm/sec. Then for the capillaries,

\[ (AV)_{\text{aorta}} = (AV)_{\text{cap}} \]

and \[ V_{\text{cap}} = \frac{V_{\text{aorta}}}{800} \]

hence the capillary velocity is on the order of .04 cm or .4 mm per second. This implies that it takes approximately two seconds to travel the length of a capillary.

**Blood Composition**

So far, little attention has been given to the medium which allows the nutrient and waste product transfer across capillary walls. Blood consists of a plasma containing a suspension of cells. By volume, the plasma accounts for approximately 50 percent of the solution. The plasma, by virtue of its composition, maintains a colloidal osmotic
pressure of 25 mm Hg and a pH between 7.3 and 7.4 (7). These normal values are critical for proper diffusion and absorption. Although they comprise only seven percent of the plasma, plasma proteins are primarily responsible for maintaining these levels. The four basic plasma proteins, albumins, globulins, fibrinogen and lipoproteins carry on the separate functions of maintaining the osmotic balance, providing antibodies, forming blood clots, and providing fuel to the cells as well as retaining a nutrition reserve.

The other half of the blood volume consists of cells; platelets, white blood cells or leukocytes, and red blood cells or erythrocytes. The very small platelets assist in clotting and number approximately 250 platelets per ml. The leukocytes numbering about six per ml, act as resistors of bacterial invasion. In comparison with the platelets and leukocytes, the red cells comprise 97 percent of the cell volume with more than 5,000 per ml. The cell count, by volume, is used as a norm in health since the cells can be separated from the plasma by centrifugation. The volume percentage of cells is known as the hematocrit, which varies normally from 44 to 50. The red cells function as oxygen "sinks"; their capacity to carry oxygen is due to the hemoglobin within the cell (3). Normally, the weight of hemoglobin per 100 ml of blood is on the order of 15 grams; this allows an oxygen capacity of 20 ml per 100 ml of blood.

Since the distinguishing factor in capillary blood flow is the relative size of the fluid elements with respect to the vessel, the importance of the erythrocyte geometry can be readily seen. The normal
red blood cell is shaped as a biconcave discoid with a diameter of approximately eight microns, or one capillary diameter. Thus the red cells tend to plug the capillary. The red blood cell membranes are apparently highly flexible; although quantitative data on the elastic properties is not available, red blood cells have been observed to fold to a thimble shape and emerge intact from a capillary three microns in diameter (8).

In normal health, the red cells travel singly, but in disease the cells have been noted to form rouleaux. As an attempt to explain both the tendency to aggregate and the normal discoid shape, it has been suggested that the adsorption of plasma proteins on the red cell membrane causes electrical charges and therefore attractive forces (4).
CHAPTER 3

PHYSICS OF THE BLOODSTREAM

Also pertinent to the circulatory flow rate are the viscosity of the blood, the pressure head within the system, and the Reynolds number effects. These flow parameters are discussed separately in the succeeding paragraphs.

Viscosity

In reference to the laminar flow of fluids, Sir Isaac Newton first described the internal frictional forces as a "lack of slipperiness". For laminar flow in a cylindrical tube, his viscosity law is stated

\[ \tau = \mu \frac{du}{dy}, \quad (4) \]

where \( \tau \) represents the frictional shearing stress, \( \mu \) is the fluid viscosity, and \( \frac{du}{dy} \) is the change in axial velocity with radius. Generally, viscosity is a function of temperature and pressure, but for liquids, the pressure dependence is negligible (9). Homogeneous fluids which possess a viscosity independent of the rate of shear are termed Newtonian fluids. Because blood contains a high volume of cells, it is considered non-Newtonian. That is, as a heterogeneous fluid, it exhibits an increase in viscosity with a decrease in velocity. Additionally, because both the composition of blood and the vessel diameter vary across the vascular bed, the blood viscosity has been observed to increase greatly with increased hematocrit and decrease with decreased
(a) Increase in relative viscosity, $\bar{\mu}$, with increasing hematocrit in a viscometer tube with radius greater than one mm.

(b) Decrease in relative viscosity with decreasing viscometer tube radius.

(From A. C. Burton, *Physiology and Biophysics of the Circulation*.)

Because of these variations in viscosity, blood is considered as having an "anomalous viscosity" (1). As Figure 3 shows, the hematocrit and the vessel radius have been plotted versus the relative viscosity. The relative viscosity is the ratio of blood viscosity to the viscosity of water at a given temperature, and has been used for convenience because it varies only slightly with a change in temperature. Note that both *in vivo* (literally, "in the living") and *in vitro* ("in glass") values have been shown for the changes in viscosity with changing hematocrit, while only *in vitro* values have been
plotted for viscosity versus vessel radius. Because there is a marked difference in the two readings, viscosity measurements in vivo are referred to as apparent viscosities (4). Since the hematocrit and the blood vessel diameter are minima in the capillaries, the apparent viscosity is also a minimum. It should also be noted at this point that the blood plasma is a Newtonian fluid. This does not imply that the viscosity is a function of temperature only; variations in composition result in changes in plasma viscosity (10).

**Pressure**

Since it is by virtue of the pressure head within the circulatory system that blood flow continues, a brief treatment of the nature of the pressure is given. If the circulatory system is considered, as a simplified model, to be a closed resistive circuit containing a Newtonian fluid in steady laminar flow, then it can be assumed that Poiseuille's Law is valid for the model. This fundamental law as applied to flow in cylindrical blood vessels may be stated,

\[ Q = \frac{\pi(P_a - P_v) r^4}{8\mu L} \]  

(5)

where

- \( Q \) = volume flow rate, ml/min
- \( P_a \) = arterial pressure, mm Hg
- \( P_v \) = venous pressure, mm Hg
- \( \mu \) = plasma viscosity, poises (dyne-sec/cm²)
- \( L \) = vessel length, cm
- \( r \) = vessel radius, cm.
This relationship is sometimes expressed as a ratio of pressure to hydraulic resistance (5), or

\[ Q = \frac{P_a - P_v}{R}, \quad (6) \]

where

\[ R = \frac{8\mu L}{\pi r^4}. \quad (7) \]

It should be noted that R, the resistance to flow, is based on the vessel geometry. Therefore, given the various vessel dimensions, the relative resistances can be calculated. By comparison, the most resistive vessels are the arterioles, followed closely by the capillaries, and the veins are the least resistive.

In the systemic circuit, values for arterial and venous pressures are given (1) as

\[ P_{sa} = 90 \text{ to } 110 \text{ mm Hg} \]

\[ P_{sv} = 0, \]

whereas the pulmonary circuit has values of

\[ P_{pa} = 12 \text{ to } 18 \text{ mm Hg} \]

\[ P_{pv} = 3 \text{ to } 5 \text{ mm Hg}. \]

The pressure drop remains fairly constant for both rest and heavy exercise, but the pressure profiles across the vessels vary noticeably. Figure 4 compares the pressure drop profiles during rest, vasodilation, and vasoconstriction.

Although the hydrostatic and osmotic pressures account for the net flow within the capillaries (11), the osmotic pressure does not
significantly alter the hydrostatic pressure, and Poiseuille's Law is valid. From the data in Table 1 and equation 6 it can be seen that the ratio of venous to arterial flow resistance is 1/5, and the mean capillary pressure, $P_c$, can be computed.

$$Q = \frac{P_a - P_c}{R_a} = \frac{P_c - P_v}{R_v}$$

hence,

$$P_c = \frac{P_a (R_v/R_a) + P_v}{1 + R_v/R_a}$$

and

$$P_c \approx 20 \text{ mm Hg}.$$
By definition, Poiseuille's Law is not valid for a non-Newtonian fluid in pulsatile flow, but the mean capillary pressure has value in that it represents a minimum pressure drop for the flow rate (12).

Reynolds Number

So far it has been assumed that blood flow is laminar. Turbulent flow would require a significantly larger pressure difference to force the fluid through a geometrically identical tube. An indication of this characteristic of the flow is given by means of the dimensionless Reynolds number. Based on fluid properties and tube geometry, the Reynolds number, Re, represents the ratio between inertial and viscous forces. Mathematically, the Reynolds number is defined as

\[ Re = \frac{\rho v D}{\mu} \]  

(10)

where

- \( \rho \) = fluid density
- \( v \) = fluid velocity
- \( D \) = tube diameter
- \( \mu \) = fluid viscosity.

Laminar flow is usually considered to occur below a Reynolds number of 2,000, but it is not until it drops below one that inertial forces are considered negligible. Flow below this range is referred to as creep or slug flow and is dealt with in lubrication theory. Primarily as a result of the capillary diameter and the flow velocity, the Reynolds number within the capillaries is on the order of \( 10^{-3} \) to
$10^{-2}$ (13). Since the Reynolds number is so small, there is a direct balance between pressure gradients and viscous forces.

Characteristic of this type of flow within the capillary are the relative insensitivity to vessel geometry, inability of flow separation, and the possibility of reversible motion (14). It has been suggested that the reversibility of flow exists in capillaries arising from two arterioles, and is caused by the phase changes in arteriolar vasomotion cycles (15). In considering the fluid dynamics of the system, reversible motion will not be discussed.
CHAPTER 4

FLUID DYNAMICS

From in vivo observations of blood flow in arteries and veins, researchers have noted that the velocities were so rapid as to obscure the flow patterns of the individual cells. The bloodstream appears as a homogeneous red stream with a lighter colored center and colorless peripheral layers on either side. This phenomenon is termed "axial streaming"; the red cells aggregate toward the vessel axis and leave a cell free zone in contact with the vessel wall. Generally, flow in capillaries is much slower and the hematocrit is considerably reduced so that individual cells can be identified (16).

Because of the geometry and the low Reynolds number for capillary blood flow, the flow is treated from the standpoint of lubrication theory. Mathematical models of blood flow in capillaries consider the red blood cells as solid pellets flowing within a Newtonian fluid. The major discrepancies of this type of model are the absence of the leukocytes and platelets and the approximation of the erythrocyte as being rigid. Despite these differences, the model is a fairly accurate representation of capillary flow (10). The following justifications imply that the model should retain a high degree of accuracy; the combined volume of the white cells and platelets is very small compared to the erythrocyte volume, and the red cells have been observed to resist appreciable deformation until the vessel diameter is smaller than the red cell diameter (10).
Further assumptions for modelling capillary blood flow are that the pellets and the vessel are coaxial, and the flow is axisymmetric and steady. In actuality, pulsatile flow does persist in the capillaries, but it is considerably dampened (17). For convenience in mathematical manipulations, additional assumptions are 1) the capillary vessel is circular in cross section and retains a constant diameter, 2) the plasma is incompressible, 3) a "no-slip" condition exists on the vessel walls and the red blood cell surfaces, and 4) diffusion effects of the red cell membranes and the vessel wall are negligible. With these assumptions, then, the Navier-Stokes equations can be used for the blood plasma.

Consider first the motion of the red blood cell as a function of the gap, $h$, as shown in Figure 5. A stationary cylindrical coordinate system, $(r, \theta, z)$, is assigned to the red cell, and since axial symmetry is assumed, there is no $\theta$-dependence.
Arbitrarily defining a vessel wall velocity of \(-u\), a plasma velocity \(v(r, z)\), a gap thickness \(h(z)\) and a red cell radius \(R(z)\), the Navier-Stokes equations can be applied (18). Assuming creep flow, the Navier-Stokes equations reduce to

\[
\frac{dP}{dz} = \mu \left( \frac{\partial^2 v_z}{\partial r^2} + \frac{1}{r} \frac{\partial v_z}{\partial r} \right),
\]

(11)

where \(P = P(z)\) and \(v_z\) is the plasma velocity in the axial direction. Equation 11 can be rewritten as

\[
\frac{dP}{dz} = \frac{\mu}{r} \frac{\partial}{\partial r} \left( \frac{\partial v_z}{\partial r} \right).
\]

(12)

Integrating twice with respect to \(r\),

\[
v_z = \frac{1}{\mu} \left[ \frac{r^2}{4} \frac{dP}{dz} + C_1 \ln r + C_2 \right].
\]

(13)

The constants of integration are determined by applying the boundary conditions \(v_z = -U\) and \(\frac{v_z}{r} = 0\) at \(r = R + h\). Then

\[
v_z = \frac{1}{4\mu} \frac{dP}{dz} \left[ r^2 - R^2 - \frac{2Rh + \frac{h^2}{2}}{\ln(1 + \frac{h}{R})} \ln \left( \frac{r}{R} \right) \right] - U \frac{\ln(\frac{r}{R})}{\ln(1 + \frac{h}{R})}
\]

(14)

Note that for \(h = 0\) and \(r = R\), the velocity becomes zero, and for \(r = 0\) and \(h = R\), or no cell at all, the velocity relationship reverts to Poiseuille flow,

\[
v_z = - \frac{1}{4\mu} \frac{dP}{dz} R^2.
\]

(15)
Considering now the implications of pressure as a function of gap thickness, the velocity from equation (14) is combined with the continuity equation. From continuity,

\[ \int_{R}^{R+h} V_z r \, dr = -r_o Q, \]  

(16)

where Q represents the backward flux per unit circumferential length, and \( r_o \) is the tube radius. Combining equations (14) and (16),

\[ r_o Q = \frac{1}{4\mu} \frac{dP}{dz} \left[ \frac{2Rh + h^2}{4} \right] \left[ 2R^2 + 2Rh + h^2 - \frac{2Rh + h^2}{\ln(1 + h/R)} \right] \]

\[ + U \left[ \frac{1}{2} (R + h)^2 - \frac{2Rh + h^2}{4\ln(1 + h/R)} \right]. \]  

(17)

Note that as the gap thickness, h, approaches zero and the pellet radius approaches the tube radius, the pressure gradient becomes

\[ \frac{dP}{dz} = \frac{6\mu}{h^2} \left( \frac{2Q}{h} - U \right), \]  

(18)

and for no pellet at all, or \( R = 0 \),

\[ \frac{dP}{dz} = \frac{8\mu}{r_o^2} \left( \frac{2Q}{r_o^2} - U \right). \]  

(19)

It is now possible to examine the theoretical minimum or maximum pressure gradient as a function of the gap thickness. By inspection, it can be seen that for a zero gap thickness, the pressure needed to drive the pellet through the tube is infinite. Realistically, this is not possible. At this point the model assumptions are no longer valid, since the capillary wall will deform to facilitate the passage of the red blood cell.
Preliminary Models

The models of capillary blood flow to be discussed include the Casson model, the shearing core model, the axial train model, and the Prothero and Burton bolus flow model. The first three will be discussed as preliminary models.

The Casson model was first suggested as an explanation of particulate aggregation in suspensions. Applied to blood in capillaries, the Casson model consists of a chain of red cells with a peripheral layer of plasma. Since for extremely low shear rates, the red blood cells do tend to form rouleaux, or little rolls, the Casson model is valid for this instance (19).

The mathematical treatment of the Casson model is based on the assumptions that the flow is unidirectional and the rouleau velocity is constant, as shown in Figure 6. A rectangular coordinate system is chosen to describe the fluid dynamics. A simple Couette flow can be described for the plasma flow between the erythrocyte cylinder and the capillary wall. Isolating the plasma layer for analysis, and arbitrarily assigning a constant velocity of $U_r$ for the rouleau, the governing Navier-Stokes equation is

$$\frac{dP}{dx} = \mu \frac{d^2u}{dy^2} \quad (20)$$

Assuming $P = P(x)$ and integrating twice with respect to $y$, the velocity becomes

$$u = \frac{1}{\mu} \left[ \frac{1}{2} \frac{dP}{dx} y^2 + C_1 y + C_2 \right] , \quad (21)$$
a. Rouleau formation of Casson model.

b. Axial train model

c. Identical flow profile for both Casson and Axial train models.

Fig. 6.—Similarity of Casson and Axial train models.
and applying the boundary conditions \( u = 0 \) at \( y = 0 \) and \( u = U_r \) at \( y = h \), the plasma velocity becomes

\[
    u = \frac{y}{h} \left[ U_r + \frac{h^2}{2\mu} \frac{dP}{dx} \left( \frac{y}{h} - 1 \right) \right].
\]

(22)

The velocity profile is shown in Figure 6.

An identical mathematical treatment is given to the axial train model. The difference in the physical Casson and axial train models is the separation between the coaxial red cells in the axial train model. The entrapped plasma is treated as a constant velocity mass (20), consequently, this model is also an insufficient description of capillary blood flow. Figure 6 compares the Casson and axial train models and illustrates the velocity profile of either system.

The shearing core model is similar to the Casson model in analysis. The physical distinction is that instead of an inner core of coaxial red cells, a core of randomly oriented cells within the plasma is described. The continuous phase plasma sleeve is found in both models and is treated as a Couette model in both cases. The rouleau core, however, is treated as a constant velocity cylinder whereas the dispersed phase core of the shearing core model is treated as a more viscous medium in Poiseuille flow. Although the shearing core model is a more accurate physical representation of the capillary flow system, the mathematical treatment of this model is less than accurate. This is primarily due to the separate analyses of the plasma sleeve and the dispersed phase core. Data taken in tubes from 410 - 2300 \( \mu \) diameters suggests a velocity profile more blunt than parabolic (21). Figure 7 illustrates the geometry and the velocity profile for separate and single analyses of the shearing core model.
It has been suggested that oxygen transport in blood is enhanced by shear, but actual data is not available on diffusion rates from this model (21). Proponents of this model suggest that diffusion enhancement is due to cell rotation.

a. Geometrical representation of the shearing core model.

b. Comparison of shearing core (-----), Poiseuille (----), and suggested actual (→→→) flow profiles.

Fig. 7.—Shearing core model.
Bolus Flow

By expanding the mathematical analysis of the axial train model to include flow between the red blood cells, the possibility of plasma exchange between the train and the peripheral layer can be seen. The original laboratory model by Prothero and Burton was a thermal analog designed to calculate the rate of exchange of gases in the pulmonary capillaries (3). The apparatus consisted of a copper tube and two constant temperature baths. By passing the tube through each bath from higher to lower temperature, the heat transfer was calculated from the final temperature of the fluid within the tube. The results indicated that the heat transfer was up to twice as much as that predicted for Poiseuille flow. A second model was then constructed to simulate the actual passage of red blood cells within a capillary. Air bubbles were rhythmically injected into water in a glass tube. A dye was then injected into each bolus of water. Prothero and Burton were then able to observe that the dye in the center of the bolus travelled at a velocity approximately twice the average velocity of the bolus. As the dye reached the upper interface, it was observed to be carried radially to the wall of the tube. From this point, it adhered to the wall until the next air bubble arrived. Radial components then carried the dye back to the core and the circuit was repeated. The eddy like flow pattern with radial velocity components at the terminal surfaces of the bolus increase the transfer rates of materials from within the bolus and vice versa.

Several mathematical analyses have been carried out for bolus flow, the results of which are very similar. Probably the most
straightforward analysis involving a preliminary Poiseuille flow model for the plasma alone and including a finite difference equation with the superposition of the cells was done by H. K. Huang (22). The geometry of this model is such that a rectangular coordinate system is stationed on the red blood cell.

The method of analysis requires that the Navier-Stokes equations be written in two dimensions. After applying the stream function, the resulting equation is the biharmonic equation,

$$\nabla^4 \psi = 0 . \quad (23)$$

For a square grid, the finite difference equation for

$$\nabla^4 \psi = \frac{\psi_{xxxx}}{4} + 2\frac{\psi_{xxyy}}{4} + \frac{\psi_{yyyy}}{4} = 0 \quad (24)$$

is

$$\psi(x, y) = \frac{2}{5} [\psi(x + 1, y) + \psi(x - 1, y)]$$

$$+ \frac{2}{5} [\psi(x, y + 1) + \psi(x, y - 1)]$$

$$- \frac{1}{20} [\psi(x + 2, y) + \psi(x - 2, y)]$$

$$- \frac{1}{20} [\psi(x, y + 2) + \psi(x, y - 2)]$$

$$- \frac{1}{10} [\psi(x + 1, y + 1) + \psi(x + 1, y - 1)$$

$$+ \psi(x - 1, y + 1) + \psi(x - 1, y - 1)]. \quad (25)$$

For Poiseuille flow with a maximum velocity of $U_0$, the stream function reduces to

$$\psi(x, y) = U_0 \left[ Y - Y^3 R^2 / 3 \right], \quad (26)$$

where $R$ represents the radius of the capillary.
The stream function can be evaluated at the grid points by iterative methods, and the velocity components

\[
\begin{align*}
u(x, y - 1/2) &= \psi(x, y) - \psi(x, y - 1) \\
v(x + 1/2, y) &= \psi(x, y) - \psi(x + 1, y)
\end{align*}
\] (27)

can be evaluated at the half points. The red cells of velocity \(U_r\) can be superposed on the preliminary model, using a coordinate system at the cell center. The boundary conditions for this system are

1) \(u = v = 0\) on the cell surface
2) \(u = -U_r\) and \(v = 0\) on the vessel wall
3) \(u = U_p(x, y) - U_r\) and \(v = 0\) at \(x = \pm \infty\).

\(U_p(x, y)\) is the plasma velocity obtained from the preliminary model.

Applying the boundary conditions to the original stream function and repeating the iterative evaluation gives the streamline results for a red cell flowing in plasma. Numerical experiments by Huang were based on two red cells at a fixed distance apart and travelling at the same velocity. His results are given as a function of cell velocity in Figure 8 and as a function of cell distance with constant velocity in Figure 9.

Although the bolus flow model of blood flow within capillaries is highly idealized, it is the most accurate. By Huang's calculations, the maximum number of red blood cells within a capillary 50 microns long would be six, with five boluses eight to 10 microns in length. This would give a hematocrit of approximately 30. Although this is a considerable reduction from the normal hematocrit, it seems reasonable for capillary flow.
Fig. 8.—Bolus flow streamlines between two red cells 40 microns apart. (From H. K. Huang, Theoretical Analysis of Flow Patterns in Single File Capillaries. Journal of Biomechanics.)

a. $U_r = 20 \mu$/sec

b. $U_r = 30 \mu$/sec

c. $U_r = 40 \mu$/sec

d. $U_r = 50 \mu$/sec
Fig. 9.—Bolus flow streamlines between two red cells at varying distances. $U_r = 50 \mu$/sec. (From H. K. Huang, Theoretical Analysis of Flow Patterns in Single File Capillaries. Journal of Biomechanics.)
CHAPTER 5
CONCLUSION

It is presumed that the bolus flow model allows for the most efficient exchange between the blood plasma and the surrounding tissues because of the greater actual contact with the vessel wall. The thermal analog designed by Prothero and Burton gives an exchange rate approximately double that of Poiseuille flow. Since this model is so highly idealized, the shearing core model is recognized as the most physically realistic. This is because of the random orientation and spacing of the red blood cells. However, the mathematical treatment of the system treats the red blood cells and the plasma together as a Newtonian fluid in laminar flow, hence a Poiseuille profile. A possible improvement to the bolus flow model in the direction of the shearing core model would include a study of the stability of red cells within a bolus from orientations parallel to the vessel axis to the perpendicular position originally given. Other factors which may also affect bolus flow are the possibilities of spinning and variations in shape and permeability of the red cell, and the incidence of disease or local infection. As stated earlier in the text, rouleaux have been observed to form in capillaries during disease. It is not known to what extent they form or the difference in hematocrit within the capillaries, but sufficient boluses of plasma are presumably formed between the rouleaux to allow an efficient exchange between the tissue and the plasma.
LIST OF REFERENCES


