Phase separation in the flow of suspensions through a bifurcation with applications to blood flow in the microcirculation

by Robert Darrell Olson

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE in CHEMICAL ENGINEERING
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Abstract:
Quantitative analysis of blood is complicated by several factors.

One observable phenomenon is plasma skimming. Plasma skimming is the reduction in concentration present in the more slowly flowing branch of a bifurcation.

Due to the problems associated with quantitative measurements on systems the size of vessels in microcirculation, and because of the complex nature of non-Newtonian blood flow in small vessels, plasma skimming was investigated by means of a model using a Newtonian suspension of rigid spheres.

The present research investigated situations of vertical flows through a bifurcation having equal diameter branches. Also considered were horizontal flows through 45° and 90° bifurcations having equal diameter branches and a 90° bifurcation whose side branch was two-thirds the diameter of the main branch. The Reynolds numbers for vertical and horizontal flows, based on flows through the upstream branch and using the physical properties of the suspending media, were 3 x 10^-2 and 160 respectively. Concentration changes were measured using tube and mixing cup concentration ratios.

On the basis of this research, it was concluded that the ratio of relative flow rates in the two branches downstream from the bifurcation and the ratio of the diameters of these branches were important parameters in determining the extent of plasma skimming. The angle of bifurcation and the upstream concentration had little effect for the 45° and 90° bifurcations with equal diameter branches. The 90° bifurcation having the smaller diameter side branch exhibited a dependence on upstream concentration. The degree of plasma skimming being less at the higher concentrations. Of unknown importance is the particle to tube size ratio, the shape and flexibility of the particle, and the density of differences between particles and the fluid. There is also the possibility that inertial effects may be present in the horizontal flows.

The mixing cup and tube concentration ratios are identical for bifurcations having equal diameter downstream branches. For bifurcations having different diameter downstream branches, the mixing cup and tube concentration ratios are not identical.

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Date August 7, 1973

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ABSTRACT

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Due to the problems associated with quantitative measurements on systems the size of vessels in microcirculation, and because of the complex nature of non-Newtonian blood flow in small vessels, plasma skimming was investigated by means of a model using a Newtonian suspension of rigid spheres.

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INTRODUCTION

The smallest vessels of the circulation system are the capillaries. The capillaries form a multiple branched network connecting the arteries and veins. It is in this highly branched network that the transfer of metabolites between the blood stream and adjacent cells occurs. This transfer occurs via passive diffusion and active transport. Because of their basic survival function, the problems of flows through capillaries provides a challenging field of study.

Capillary blood vessels were first discovered by Marcello Malpighi in 1661. One would think that during the 300 years since then, the mechanics of blood flow in the capillaries would be well understood; this is not the case however. The lack of understanding is due in part to the fact that capillaries are very small. Systemic capillaries in humans are about 6×10^{-6} meters (6 microns) in diameter and several hundred microns in length. Also, the mechanical properties of the red blood cells and the cells which compose the capillary are not well defined. It is reasonable to say that the investigation of the mechanics of blood flow in the microcirculation is still exploratory in nature (11).

In 1921, Krogh (18) found that when flow in a small artery branching from a larger vessel was slowed by partial contraction the hematocrit or volume fraction of red blood cells in the artery may be markedly reduced Occasionally to the extent that practically no cells could be seen in the side branch. This phenomenon came to be known as plasma skimming. While posing an interesting fluid dynamics problem, plasma skimming may be of some considerable importance physiologically. It should be noted that blood flow in the microcirculation is under a complex system of vascular controls. These controls operate via three basic mechanisms; 1) basal tone and local control, 2) neurogenic control, and 3) hormonal control. These controls have pronounced effects on blood flows and distributions in the microcirculation(8). These mechanisms of control are by no means completely understood but are presented to give "plasma skimming" perspective. The degree of plasma skimming is the resultant of the effects of the various control mechanisms. By understanding the phenomenon, perhaps a better understanding of its causes will follow.

Few systematic studies of plasma skimming exist. Those that do are of three basic types with special problems and difficulties inherent to each. In vivo or experiments performed on the animal, have special problems of measurements and minimization of unwanted effects. In vitro experiments, invclve exteriorizing the experiment from the animal but uses the same physical set up of animal. Modeling experiments use a convenient scale to perform the experiments. Care must be taken so that the model accurately represents the physical situation which is the basis of the model, known as the prototype.

Svanes and Zweifach (26) observed that by partially occluding capillaries there was a slowing of the flow in the capillary due to the increased resistance and a striking reduction in capillary hematocrit. In situations where the flow in the parent branch was rapid, the capillary hematocrit was reduced to nearly zero. When the flow in the parent branch was slow, the reduction in hematocrit was only slight. There was no significant change in vessel diameter except at the point of compression. While providing some useful information, these data are of purely qualitative nature and do little to quantify the parameters important to the phenomenon.

Johnson, Blaschke, et al, (15) simultaneously measured red cell spacing and red cell velocity in the mesenteric capillaries of the cat and obtained some semi-quantitative data on plasma skimming. Under control conditions, most capillaries exhibited reasonably stable hematocrits, although some showed erratic changes and a few exhibited a well defined periodicity. During reductions in gross flow, capillary hematocrit was generally unchanged though some showed a reproducible increase or decrease. They found that in some cases, capillary hematocrit was affected by vasomotion. Though providing no quantitative information about the important parameters for plasma skimming, Johnson's work did present values of the relative hematocrit change associated with a change in capillary flow. Of importance is the fact that these experiments by their very nature, may have a significant effect upon the degree of plasma skimming. The major weakness of these experiments is that they provide no quantitative values for the relative size of the flows involved.

Gelin (12) perfused blood through channels etched in blocks of polymethyl methacrylate. The two channels crossed to form a perpendicular junction. Investigation of channels of various diameters indicated that plasma skimming would be significant in vessels smaller than 110 microns. It was found that increasing the degree of aggregation of the red blood cells by the addition of high molecular weight dextran, the degree of plasma skimming increased. The usefulness of this information is limited even though it provides the first quantitative data on plasma skimming. The most important objection to the data is that one rarely sees two branches leaving the parent vessel at the same location in the microcirculation. Also, the flows in the three branches were nearly the same and provided no information for other flow situations.

The most comprehensive treatment of the subject is the work of Bugliarello and Hsiao (5). Modeling blood with a suspension of rigid, neutrally buoyant spheres, they investigated the importance of total flow rate, concentration, angle of bifurcation and relative flow rates in the branches, in determining the degree of plasma skimming. The suspension particles were chosen so that the diameter of the tube was ten times the particle diameter, a size ratio in the range where plasma skimming has been observed. Using bifurcations made from Lucite blocks and under situations of vertical flow, the concentration of spheres in the side branch was less than for the main branch for almost all flow conditions. The concentrations measured were the outflow or mixing cup concentrations. The magnitude of the total flow rate had only a minor effect on the degree of plasma skimming. For bifurcations of 45° and 90°, whose side branch is the same diameter as the main branch, the effect of the angle of branching was negligible. Using a bifurcation of 45° whose side branch was one half the diameter of the main branch, it was found that the degree of plasma skimming was less than for the corresponding situation when the branches were of equal diameters. It was found that higher concentrations lessen the effect of plasma skimming, all other factors being equal.

Of unknown importance in attempting to relate observations discussed here is the fact that the concentrations measured or observed are of different types. In the work by Johnson, the concentrations measured were those in the vessel while Gelin and Bugliarello determined the concentration of the outflow, known as the mixing cup concentration. Superficially, this seems to be a relatively minor consideration. However, because of the nature of the Fahraeus effect, significant complications to correlations between the two types of measurements may result. Fahraeus and Lindqvist (7) observed in 1931 that for blood flowing in small capillary tubes, the calculated viscosity of blood decreases as the tube diameter decreases from 500 to 40 microns. This dependence of viscosity upon tube diameter has been explained by assuming a cell free plasma layer at the tube wall and a core of the same concentration as the feed reservoir. This latter assumption is erroneous and results in a calculated plasma layer much too large. Data of Barbee and Cokelet (1) show that the average tube hematocrit is less than the hematocrit for the reservoir feeding the tube. It was also found that for tubes larger than 20-25 microns, the discharge or mixing cup hematocrit was the same as the feed reservoir hematocrit while for tubes smaller than 20-25 microns, the mixing cup hematocrit was less than that for the feed reservoir. Research now indicates that at normal physiological hematocrits, the reduced cell concentrations at the vessel walls is due primarily to physical exclusion of cells and is known as the "smooth-wall" or "Vand" effect (4, 20, 27). It is apparent that extreme caution is required when attempting to correlate data obtained by different techniques, due to the fact the concentration in the vessels is not the same as the concentration of the outflow.

The phenomenon of plasma skimming has been attributed to the nature of the fluid elements deflected into the side branch. Since the fluid at the periphery of the upstream branch moves slower, it is easier to deflect into the side branch. The composition of this fluid will determine the extent to which plasma skimming is observed. In order to understand plasma skimming, it is first necessary to understand to a certain extent, the behavior of suspensions flowing in a straight tube. It would be useful to understand the hydrodynamic aspects of flow division at a bifurcation. Perhaps these concepts can be applied to the more complicated case of suspensions flowing through a bifurcation. With these considerations, a sufficient condition for plasma skimming would be that a radial concentration gradient exist upstream. Specifically, the concentration near the wall must be less than the concentration in the center of the tube. This radial gradient has a theoretical basis which is supported by experimental data. The most substantial evidence for a radial concentration gradient is that single particles and very dilute suspensions exhibit radial migration. The force responsible for this displacement originates in the inertia of the fluid and it is postulated to be akin to the Magnus effect where a transverse force arises from the combination of rotary and translatory motion relative to the undisturbed flow of the fluid. Ségre and Silverberg (23) observed that single spheres migrated radially inward from the wall and outward from the axis until a equilibrium position was reached. The effects of the radial velocity gradient in Poiseuille flow is sufficient to explain inward radial migration but cannot account the outward movement. Inward migration can be evaluated by analogy to the theory of Rubinow and Keller (27) for a rotating sphere.

$\vec{F} = \pi a^3 \rho_f (\vec{\omega} \times \vec{V})$ Where $\vec{F}$ is the force on the sphere; $\vec{V}$ the particle velocity; $\vec{\omega}$ the rotational velocity.

While this equation was not derived for Poiseuille flows, it is reasonable to assume that it yields a force of the correct order of magnitude for such a flow. Repetti and Leonard (21) were able to explain the outward migration by modifying the above equation and by considering that the sphere will influence the fluid to some distance δ past the sphere surface. This modification produces moderately good agreement with experimental data. This was presented only to show that there exists a force which would tend to produce radial concentration gradients for Poiseuille flow. It should be noted that this effect is expected to be much less pronounced at higher concentrations because of particle-particle interactions. At concentrations above 35%, the concentration decrease at the vessel wall can be attributed almost entirely to mechanical exclusion by the wall (16). These higher concentrations produce a velocity profile which is blunted considerably from the normal parabolic. This blunting is found to occur with blood (13). as well as suspensions of rigid spheres (16).

Also since inflow and mixing cup hematocrits are equal even though the tube hematocrits are lower, for blood flow in small straight tubes, there must be a radial red cell concentration gradient. Otherwise, a material balance on the tube could not be closed.

The nature of flows at a bifurcation was studied by Barnett and Cochrane (2) for Newtonian fluids. The limiting streamline, the streamline which just passes by the side branch without entering, was determined for bifurcations of 45° and 90°. It was found that the position of the critical streamline was determined by the relative flow rates, the angle of branching, the viscosity of the fluid, and the diameter of the side branch. The slower the flow in the side branch compared to the flow in the downstream branch, the further the streamline is from the center of the upstream tube. For a given value of relative flow rates, the smaller angle withdraws fluid more toward the center of the upstream branch. This effect is not extreme however. The higher viscosity fluid withdraws more fluid from the center of the upstream branch, all other factors being equal.

It has been demonstrated that the fluid deflected into a branch is the fluid closest to that branch. While the presence of particles in a suspension may have an effect, it is not expected that the basic nature of the flow division would be affected drastically.

In engineering, it is commonplace to evaluate performance characteristics of equipment and units by test procedures using a conveniently sized model. Models are useful whenever the size or expense of the prototype is such that experimentation on it is impractical. Model theory is dependent upon several criteria of similarity. Geometric similarity exists if all the corresponding dimensions of the model and prototype are in the same ratio. Kinematic similarity exists if all the velocities at corresponding positions have a constant ratio. Dynamic similarity is a point-to-point correspondence between inertial, normal, shear, and field forces for the two systems. Geometric similarity is a prerequisite to kinematic and dynamic similarity because of the requirement of corresponding positions (9). If there is complete similarity between systems, all the corresponding dimensionless groups have the same values in the model and prototype. The solutions to the differential equations of flow then will be the same for the two systems.

Dimensional analysis consists of characterizing a dimensionally homogeneous equation by a relationship among a complete set of dimensionless products. Dimensional homogeneity means that each term in an equation has the same dimensions. There are several possible methods of dimensional analysis but the Buckingham Pi Method has the advantages of relative ease of computation and is applicable even when the differential equation of flow describing the situation is unknown (3).

Analysis starts by postulating that some physical process Q is a function of the n dimensional variables $Q_1, Q_2, \cdots Q_n$.

$$Q = f \; (Q_1, Q_2, \cdots Q_n)$$

Since the equation describing the behavoir of the systems must be dimensionally homogeneous, this equation can be reduced to

$$0 = f(\pi_1, \pi_2, \cdots \pi_i)$$

where π_1, π_2, $\cdots\pi_i$ are dimensionless groups.

The number of dimensionless groups i is given by

$$i = n - r$$

where n = number of variables

r = maximum number of these variables which will not form a dimensionless group

The dimensionless groups are expressed by

$$\pi_1 = Q_1^{a1} \quad Q_2^{b1} \cdots Q_j^{j1}$$

$$\pi_2 = Q_1^{a2} \quad Q_2^{b2} \cdots Q_j^{j2}$$

$$\pi_i = Q_1^{ai} \quad Q_2^{bi} \cdots Q_j^{ji}$$

where the exponents are such that the π's are dimensionless.

There are serious limitations to the use of dimensional analysis. Dimensional analysis gives no indication of the fundamental mechanism of the process. Also, the analysis is invalid if any significant parameter is neglected (17).

The primary objective of this research is the quantification of the important parameters of plasma skimming. The first step involved in such an undertaking is the identification of all possible parameters that could possibly have an effect on the phenomenon. From these parameters, dimensionless groups are formed; these will provide the basis of analysis. Through a careful consideration of the fluid dynamic aspects of the flow of suspensions and the relatively complex geometry of the flow situation, the parameters associated with this situation become apparent. Table I presents the parameters considered to have a possible effect on plasma skimming. Also listed are the appropriate symbols and the dimensions for each quantity.

TABLE I. IMPORTANT PARAMETERS

Parameter	Symbol	Dimensions
Upstream Concentration	ϕ	None
Total Flow Rate	V	L^3/T
Relative Flow Rates, Side to Downstream	Vs/Vds	None
Angle of Bifurcation	θ	None
Ratio of particle to upstream tube diam.	Dp/Dt	None
Ratio of the diameter of the side branch to downstream branch	Ds/Dds	None
Diameter of the branch	D	L
Density of the media	ρ	M/L^3
Density of the particle	ρ_p	M/L^3
Orientation relative to gravity		
Shape of the particle	Φ	
Yield Stress	τ_y	F/L^2 or M/LT^2
Flexibility of the particle	E	F/L^2 or M/LT^2
Viscosity of the media	μ	M/LT

F = Force; M = Mass; L = Length; T = Time

Since a number of the parameters are dimensionless, no further characterization is necessary. However, the remaining dimensional quantities must be combined to form dimensionless groups. The result of such an analysis combined with the dimensionless parameters is given in Table II.

TABLE II. DIMENSIONLESS GROUPS

ϕ	Φ	θ
Vs/Vds	$U^2\rho/E$	Orientation relative to gravity
Dp/Dt	E/τ_y	
Ds/Dds	$U\mu/DE$	

Where $U = 4V/\pi D^2$

The orientation relative to gravity may have an effect and will be considered but not included in the analysis of dimensionless groups. A word must be said about the parameters of shape, flexibility and yield stress.

A red blood cell is a biconcave disc and as such, a rather difficult shape to reproduce in quantity on a macroscopic sacle. Also there is the problem of how to characterize the shape. There have been a variety of methods used ranging from determining an equivalent spherical diameter to using ratios of the radii of curvature.

The flexibility of the red cell poses a rather complicated problem for modeling on a macroscopic scale. Values of elastic moduli for the red cell membrane of 10^4 and 10^8 dynes per centimeter squared have been reported (11, 14). These widely different values are explained as the results of measurements of two different stress mechanisms. Apparently the red cell membrane deforms in two different ways. A change in shape with constant membrane area requires only small stresses, while changes in membrane area require large stresses.

A practial definition of yield stress is that critical stress below which fluids plastically deform but do not viscously flow, given a reasonable period of observation. Blood has a yield stress whereas most suspensions do not.

Since these parameters involve quantities which would be difficult if not impossible to model on a macroscopic scale, the model will be simplified by using rigid spherical particles in a suspension having no yield stress.

Eliminating the three parameters discussed leaves the dimensionless groups listed in Table III. Also shown are representative values of these groups based on blood flow in microcirculation along with corresponding values for the model.

TABLE III VALUES FOR THE VARIOUS DIMENSIONLESS GROUPS

Dimensionless Group	Micro-circulation	Vertical Flow	Horizontal Flow
ϕ	<40%	20%	20% - 10%
Vs/Vds	0 - 1.0	.33 - 2.0	.03 - 3.0
θ	$\leq$ 90	45°	45°, 90°
Dp/Dt	> .07	.333	.333
Ds/Dds	<1.0	1.0	1.0, .667
$DU\rho/\mu$	$10^2 - 10$	3.2×10^{-2}	40 - 160
$\rho p/\rho$	1.07	1.08	∿ 1.0

The group identifiable as a type of Reynolds number can be defined in a variety of ways to account for the particles and their size relationship to the tube. As long as the definitions are consistent between cases, no complications result. For simplicity, it will be defined in terms of flow through the upstream branch and the physical properties are those for the suspending media.

EXPERIMENTAL APPARATUS AND PROCEDURES

This research was performed in two parts; in one case the flow was vertically downward, while in the other, the flow was horizontal. The apparatus and experimental methods pertinent for these two situations will be discussed separately.

Vertical Flow

For the vertical flow portion, the suspension consisted of one-eighth inch polystyrene spheres suspended in Dow Corning 200 Fluid. The size tolerance for the spheres is .002 inch and the specific gravity of the polystyrene is in the range of 1.04 - 1.065. The suspending media, a polymer of dimethylsiloxane, was an equal proportion mixture of fluids of two different viscosities. The two base fluids have viscosities of 10 and 100 poise while the resultant mixture has a viscosity of 26.2 poise and a density of 0.975 g/cm^3 at 22°C. Due to the density differences between the particles and the fluid, the spheres had a sedimentation rate of 1.2 centimeters per minute.

The apparatus consisted of a reservoir, a connecting section of Tygon tubing, the tubes associated with the various branches of the bifurcation and the block which forms the junction, as shown in Figure 1. The bifurcation was a Lucite block through which three-eighths inch channels have been drilled such that they formed a junction with each other having an angle of 45°. The transparent acrylic tubes which formed the various branches of the bifurcation, were precision

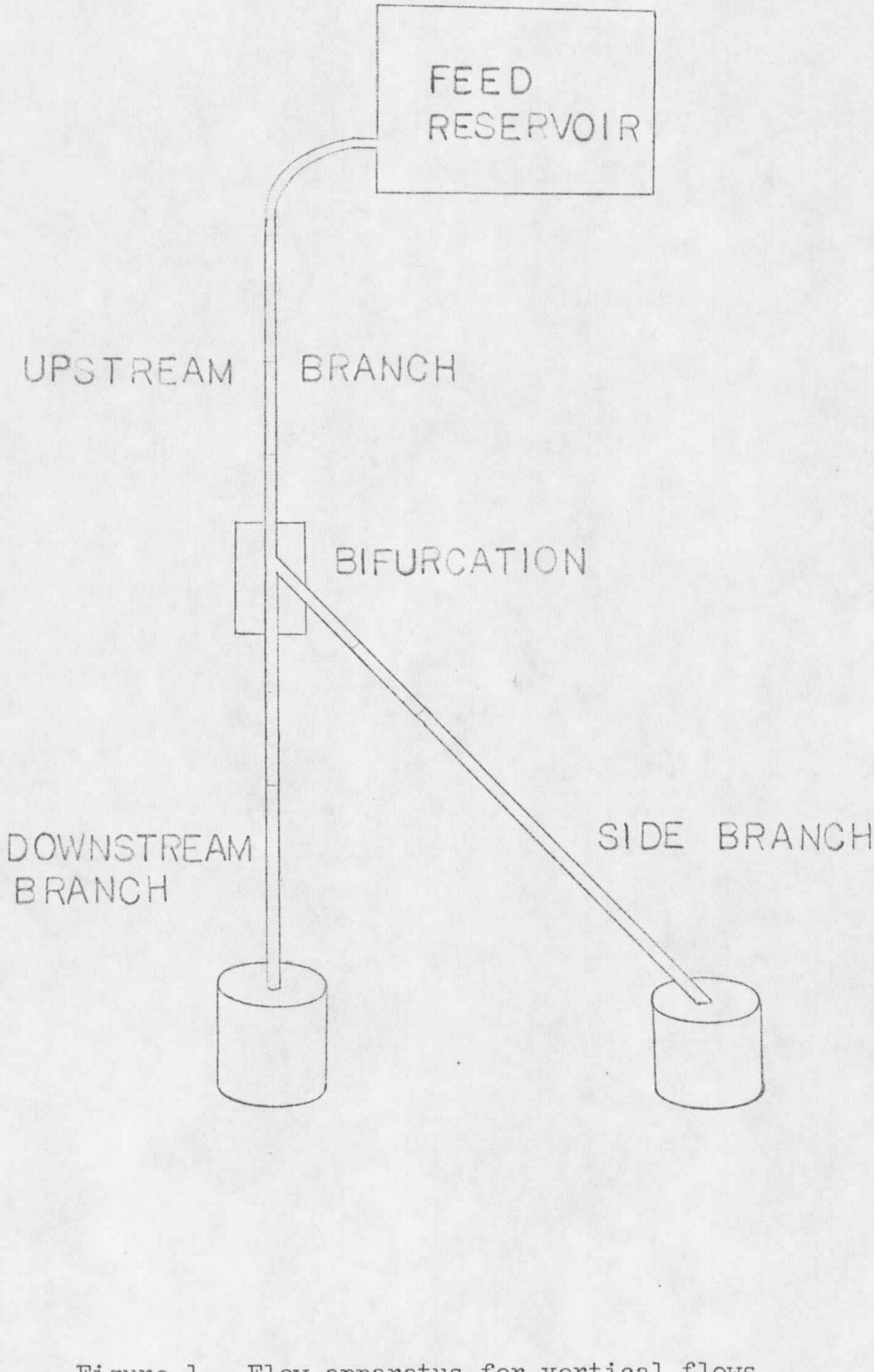

Figure 1. Flow apparatus for vertical flows.

machined. When threaded into the block, the inside of the tube formed a smooth continuous surface with the channels in the block, as shown in Figure 2. Various lengths of tubing were used to alter the flow resistance and hence the relative flow rates in the downstream branches. The suspension flows from the reservoir through the connecting tubing and into the upstream branch of the bifurcation. The flow is divided at the bifurcation and the outflow of the two downstream branches was collected in large beakers. The volume of the reservoir was so large compared to the amount of flow, that the change in pressure head was only one inch in ten feet, and can be neglected.

The procedures involved in gathering of experimental data, began with manually stirring the suspension in the reservoir to resuspend the particles that had settled to the bottom. The stirring was done manually because the high viscosity of the fluid made it impractical to use some automatic method. The system was filled initially with particle free fluid. Flow was initiated and the suspension allowed to fill the system. After the system was completely filled with suspension, the efflux from the side and downstream branches was collected in graduated cylinders and the collection period timed with a stopwatch. Flow was stopped by plugging the ends of the tubes. The number of spheres in several six-inch test sections was determined for each of the three branches. From the average number of spheres in a