A Concentrated Suspension Model for the Couette Rheology of Blood

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A simple "cell" method for concentrated suspensions has been used to construct a model for the rheological behavior of blood. The model includes the physical properties of the suspending medium, red cell membrane and red cell fluid content. Predictions of the gross viscosity of red cell suspensions are found to agree very well with experiment in the cases of hardened red cells (or normal red cells at very low shear rate) and of normal red cells in the asymptotic limit of high shear rates. The behavior at intermediate shear rates requires a knowledge of the viscoplastic properties of the membrane and a number of membrane models are investigated. Of particular interest is a plastic membrane which employs a membrane yield stress obtained from other experiments and whose results are qualitatively in agreement with the viscometric data at these intermediate shear rates.

On a employé une simple méthode dite "de globules" pour les suspensions concentrées, en vue de construire un modèle destiné à déterminer le comportement rhéologique du sang. Le modèle comprend les propriétés physiques du milieu de suspension, une membrane pour globules rouges et la teneur en fluide de ceux-ci. On a constaté que les prévisions de la viscosité brute des suspensions de globules rouges concordaient très bien avec les résultats expérimentaux dans les cas des globules rouges durcis (ou des globules rouges normaux, lorsque la vitesse de cisaillement était très faible) et des globules rouges normaux la limite asymptotique de vitesses élevées de cisaillement. L'étude du comportement du sang à des vitesses intermédiaires de cisaillement exige la connaissance des propriétés viscoplastiques de la membrane; aussi, a-t-on examiné un certain nombre de modèles de membranes. Une membrane qui s'est avérée particulièrement intéressante est une plastique, où l'on emploie l'effort d'affaissement d'une membrane qu'on a obtenu dans d'autres expériences; ses résultats concordent qualitativement avec les données viscosimétriques aux vitesses intermédiaires de cisaillement.

This paper is motivated by a desire to construct a model for the gross rheological behavior of human blood (and red cell suspensions) which includes the physical properties of the constituents of that suspension; namely, the plasma, or exterior fluid viscosity, the mechanical properties of the red cell membrane and the rheological properties of the red cell contents. As Cokelet[1] points out this has been the aim of many recent investigations.

One of the primary difficulties in a physical rather than empirical approach is the fact that blood is essentially a concentrated suspension of red blood cells; that is to say the volumetric concentration, φ, in terms of the ratio of volume of red cells to total volume is outside the range which can be handled by the sophisticated dilute suspensions theories (see Happel and Brenner[2]) derived from the original work of Einstein[3]. The comparative lack of hydrodynamic theory on concentrated as opposed to dilute suspensions can be ascribed to the difficulties in dealing with particle/particle interactions. The precise fluid mechanics of this situation is almost prohibitively complicated especially when the particles thmeselves change their shape in response to the fluid forces, as blood cells do. We are thus forced by necessity to seek some simplified fluid mechanical model which will preserve the essence of the motions while dispensing with features which we might judge to be of lesser importance. Only by comparison with experimental observation can such a model be justified or improved upon.

Of the theories which do exist perhaps the best known and most widely used are the "cell" methods employed by Simha[4], Happel[5], Kynch[6] and others derived from the pioneering works of Taylor[7] and Oldroyd[8,9]. More recently Gal-Or[10] and Yaron and Gal-Or[11] have envisaged "cell" models as representing the ensemble average or typical velocity field surrounding a suspended particle (or red blood cell). This velocity field is comprised of a component due to the mean flow of the suspension plus localized influences due to motions of individual particles. It is assumed that the average hydrodynamic effect on one particle of the presence of all the other particles is equivalent to that of a spherical boundary, radius b, enclosing the particle as depicted in Figure 1. When the total volume of fluid is shared between particles this requires that the volumetric concentration, φ, be given by γ^3 where $\gamma = a/b$ and a is the ensemble average of the particle radii. Various boundary conditions on the outer spherical "cell" have been suggested; we shall follow Simha[4], and Yaron and Gal-Or[11] in assuming zero particle disturbance velocity on $r = b$.

Despite their rather crude nature, "cell" methods have provided surprisingly successful and useful models for predicting the effective characteristic viscosity of concentrated suspensions[2]. Since the "cell" flow can only be considered as qualitatively characteristic of the fluid motions due to individual particles in the real suspension, this success is undoubtedly due in part to the fact that the effective viscosity is computed by integration over the volume of "cell" fluid to obtain the total dissipation; many imperfections may be minimized by such integration.

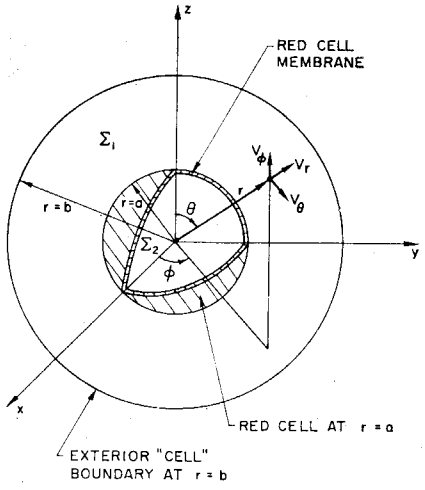


Figure 1 — Schematic of the "cell" method geometry.

It is with this success in mind that this paper attempts to construct a "cell" model for blood flow which incorporates many of the important physical features of the erythrocyte and its contents. Before proceeding it should however be noted that more sophisticated theories are presently being developed for concentrated suspensions by Batchelor[12], Saffman[13], Batchelor and Green[14] and others. The research is presently limited to undeformable spherical particles; however, it is clear from these works that there may be important differences between the characteristics of models which assume that the particles are arranged in a regular array (including "cell" models) and those which assume a random distribution of the particles in the dispersion. Such differences arise when the fluid mechanical results are dominated by two-particle-interactions between close neighbors, a situation which is excluded when a regular array is assumed. In a dispersion, the effect is to alter the functional dependence of the sedimentation rate on concentration[12,13]. In a suspension of neutrally buoyant particles similar effects are indicated for the effective viscosity but occur in higher order terms in concentration[14]. A somewhat different approach was taken by Frankel and Acrivos[15] who restricted their attention to the lubrication films between particles. The neglect of the possibility of such close neighbor interactions in existing "cell" models represents a deficiency which one might hope could be overcome in the near future while still preserving the simplicity of the method.

Contrary to some earlier experimental reports it has now been fairly well estabished that the plasma or exterior fluid in which the red blood cells are suspended is, to all intents and purposes, Newtonian (e.g., Cokelet[16] and Brooks, Goodwin and Seaman[17]). We will concern ourselves with flows in which the typical velocities are much greater than the sedimentation velocity for red blood cells so that the latter can be regarded as effectively neutrally buoyant. The red blood cell or erythrocyte consists of a membrane filled with a solution of hemoglobin and various salts. This interior fluid is also Newtonian and the viscosity as a function of hemoglobin concentration has been fairly well documented (Cokelet and Meiselman[18], Chien, Usami and Bertles[19], Wells and Schmid-Schonbein[20] and Dintenfass[21,22]). This viscosity is commonly some five or ten times that of the exterior fluid.

The nature of the red cell membrane and its deformation stress/strain relationship is much less well established; a recent review article by Gitler[23] on the plasticity of biological membranes indicates the complexity of this general subject. He concludes that recent evidence suggests that biological membranes are quasi-fluid structures in which the constituent molecules are restricted only in an overall bilayer packing arrangement. In the present paper the results of some simple viscoplastic models for the membrane will be compared with experiments. One property of the red-cell membrane on which there is some data is the force required to distort the erythrocyte, and this is used in section 7.

At rest the red blood cell is shaped like a bi-concave discoid which for human blood has a maximum thickness of about 2.4 microns and a diameter of about 8 microns. However in a flow situation this shape is rarely recognizable and the red blood cell is continuously deforming like a flimsy liquid-filled balloon. Such deformations clearly create motion of the interior fluid and the dissipation within this flow must be included in evaluating the effective viscosity. Thus a necessary aspect of the solutions of sections 6 and 7 will be the velocity components creating distortion of the shape of the red blood cell. An exact treatment of such a situation seems algebraically prohibitive; thus in the spirit of the statistical "cell" methods we shall attempt to construct a characteristic solution which is more readily handled. In doing so we shall in fact only solve the flow for a particular instant at which the shape happens to be near-spherical but in which the velocities are such that distortion is taking place. Indeed this would be the potentially exact zeroth order solution for small deformations from a mean spherical shape. However in comparing the results with the experimental measurements on blood flow we will also consider the solution as characteristic of the actual large deformation flows.

Red blood cells in quiescent plasma suspension tend to form aggregates known as rouleaux which may persist in flows at low shear rates with consequent rheological effects. The present paper will not deal with problems of aggregation. Fortunately however aggregates do not form in suspensions of red blood cells in saline. Thus, while valid comparison of theory and experiment at low shear rates is proper for saline suspensions, caution must be exercized in comparing with the plasma suspension. Further comment in this regard is delayed until section 8.

Fluid motions

The basic "cell" model is shown in Figure 1 and the formulation of the fluid motion is similar to those of previous "cell" methods. The red cell membrane is at $r = a$, the fluid "cell" boundary at $r = b$. The flow in the exterior region, Σ_1, will consist of a simple shear flow velocity $\bar{v}^{(0)}$ (shear rate q) plus a particle disturbance velocity $\bar{v}^{(1)}$. The Reynolds numbers of these motions is assumed to be much less than unity so that they are Stokesian; that is they obey the equations of creeping flow and are additive so that the total velocity in Σ_1 is $\bar{v} = \bar{v}^{(0)} + \bar{v}^{(1)}$. The motion in Σ_2 within the red cell is denoted by $\bar{v}^{(2)}$. Defining spherical coordinates (r, θ, Φ) as shown, the components v_r, v_θ, v_Φ of $\bar{v}^{(0)}$ are then

$$v_r^{(0)} = q\, r \cos\Phi \sin\theta \cos\theta \qquad (1$$

$$v_\theta^{(0)} = \tfrac{1}{2} q\, r \cos\Phi\,(\cos^2\theta - \sin^2\theta) \quad \ldots\ldots(2)$$

$$v_\Phi^{(0)} = \tfrac{1}{2} q\, r \sin\Phi \cos\theta \quad \ldots\ldots(3)$$

With these is associated a uniform, constant pressure $p^{(0)}$. The general solution of the incompressible creeping flow equations in terms of spherical harmonics is given by Lamb[24]. However, due to the boundary conditions to be applied at $r = b$ only the harmonics of orders -3 and 2 can have non-zero coefficients so that appropriate general forms for $\bar{v}^{(1)}$ and pressure $p^{(1)}$ are

$$v_r^{(1)} = (6Ar^3 + 2Cr + 6Er^{-2} - 3Gr^{-4}) \cos\Phi \sin\theta \cos\theta \quad \ldots\ldots(4)$$

$$v_\theta^{(1)} = (5Ar^3 + Cr + Gr^{-4}) \cos\Phi\,(\cos^2\theta - \sin^2\theta) \quad \ldots\ldots(5)$$

$$v_\Phi^{(1)} = -(5Ar^3 + Cr + Gr^{-4}) \sin\Phi \cos\theta \quad \ldots\ldots(6)$$

$$p^{(1)} = \mu_1(42Ar^2 + 12Er^{-3}) \cos\Phi \sin\theta \cos\theta \quad \ldots\ldots(7)$$

where μ_1 is the viscosity of the fluid in the exterior region and A, B, C, and D are constants to be determined.

In the interior of the red cell terms corresponding to r^{-2} or r^{-4} cannot be permitted due to their singular behavior at the origin so that the components of the interior flow will be of the form

$$v_r^{(2)} = (6Kr^3 + 2Lr) \cos\Phi \sin\theta \cos\theta \quad \ldots\ldots(8)$$

$$v_\theta^{(2)} = (5Kr^3 + Lr) \cos\Phi\,(\cos^2\theta - \sin^2\theta) \quad \ldots\ldots(9)$$

$$v_\Phi^{(2)} = -(5Kr^3 + Lr) \sin\Phi \cos\theta \quad \ldots\ldots(10)$$

$$p^{(2)} = \mu_2(42\,Kr^2) \cos\Phi \sin\theta \cos\theta + P \quad \ldots\ldots(11)$$

where μ_2 is the viscosity of the contents of the red cell, K, L are constants to be determined and P is a hydrostatic pressure difference which may exist between the interior and exterior of the red cell.

General expressions for the components of the stress dyad, π. acting upon the exterior of a spherical surface in incompressible flow will be required later and these are

$$\pi_{rr} = -p + 2\mu \frac{\partial v_r}{\partial r} \quad \ldots\ldots(12)$$

$$\pi_{r\theta} = \mu \left[\frac{1}{r}\frac{\partial v_r}{\partial \theta} + \frac{\partial v_\theta}{\partial r} - \frac{v_\theta}{r}\right] \quad \ldots\ldots(13)$$

$$\pi_{r\Phi} = \mu \left[\frac{1}{r \sin\theta \sin\Phi}\frac{\partial v_r}{\partial \Phi} + \frac{\partial v_\Phi}{\partial r} - \frac{v_\Phi}{r}\right] \quad \ldots\ldots(14)$$

In all of the cases treated in this paper the conditions taken to apply on the fluid boundary, $r = b$, are those of Simha[4], namely that the disturbance velocities $v_r^{(1)}$, $v_\theta^{(1)}$, $v_\Phi^{(1)}$ are zero. From the Equations (4) , (5) and (6) these lead to

$$Ga^{-5} = -5Aa^2\gamma^{-7} - C\gamma^{-5} \quad \ldots\ldots(15)$$

$$6Ea^{-3} = -21Aa^2\gamma^{-5} - 5C\gamma^{-3} \quad \ldots\ldots(16)$$

so the unknown constants G, E may be eliminated and all further expressions for the exterior flow will contain only the unknowns A and C.

The effective viscosity of the concentrated suspension, μ^*, is obtained from energy considerations as the ratio of energy dissipation within the total "cell" system to the energy dissipated in the simple shear flow which would occur in the absence of any particle or red cell. The energy dissipation of the total "cell" system is most easily obtained from its equality with the rate of work done on the boundary, r = b, and this is found to yield

$$\mu^*/\mu_1 = 1 + 21\gamma^{-2}\, Aa^2/q + 5C/q \quad \ldots\ldots(17)$$

It remains to discuss in detail the conditions on the red cell membrane interface; these conditions will eventually lead to expressions for (Aa^2/q) and (C/q) and therefore to values of the relative viscosity ratio μ^*/μ_1.

Red cell membrane rates

The kinematic condition relating the fluid velocities on the interior and exterior surfaces of the red cell membrane in conjunction with the viscous flow conditions of no-slip requires that

$$(\bar{v}^{(0)} + \bar{v}^{(1)})_{r=a} = (\bar{v}^{(2)})_{r=a} \quad \ldots\ldots(18)$$

Substituting the expressions (1) to (10) for the velocities, one finds that K and L must be given in terms of A and C by

$$4Ka^2 = Aa^2\{4 + 21\gamma^{-5} - 25\gamma^{-7}\} + 5C\{\gamma^{-3} - \gamma^{-5}\} \quad (19)$$

$$4L = 2q - 105Aa^2\,(\gamma^{-5} - \gamma^{-7}) + C(4 - 25\gamma^{-3} + 21\gamma^{-5}) \quad (20)$$

and the membrane velocities may then be written as

$$(v_r)_{r=a} = V_1\, a \cos\Phi \sin\theta \cos\theta \quad \ldots\ldots(21)$$

$$(v_\theta)_{r=a} = V_2\, a \cos\Phi \cos 2\theta \quad \ldots\ldots(22)$$

$$(v_\Phi)_{r=a} = -V_2\, a \sin\Phi \cos\theta \quad \ldots\ldots(23)$$

where

$$V_1 = q + Aa^2\{6 - 21\gamma^{-5} + 15\gamma^{-7}\} + C\{2 - 5\gamma^{-3} + 3\gamma^{-5}\} \quad \ldots\ldots(24)$$

$$V_2 = q/2 + 5Aa^2\{1 - \gamma^{-7}\} + C(1 - \gamma^{-5}) \quad \ldots\ldots(25)$$

In terms of conventional membrane or shell theory (Flügge[25]) it follows that the membrane strain rates $\dot{e}_{\theta\theta}$, $\dot{e}_{\Phi\Phi}$ and $\dot{e}_{\theta\Phi}$ are

$$\dot{e}_{\theta\theta} = \frac{1}{a}\frac{\partial v_\theta}{\partial \theta} + \frac{v_r}{a} = \{V_1 - 4V_2\} \cos\Phi \sin 2\theta/2 \quad \ldots\ldots(26)$$

$$\dot{e}_{\Phi\Phi} = \frac{1}{a \sin\theta}\frac{\partial v_\Phi}{\partial \Phi} + \frac{v_r}{a} + \frac{v_\theta \cot\theta}{a} = \{V_1 - 2V_2\} \cos\Phi \sin 2\theta/2 \quad \ldots\ldots(27)$$

$$\dot{e}_{\theta\Phi} = \frac{1}{2}\left[\frac{\sin\theta}{a}\frac{\partial}{\partial\theta}\left(\frac{v_\Phi}{\sin\theta}\right) + \frac{1}{a \sin\theta}\frac{\partial v_\theta}{\partial \Phi}\right] = V_2 \sin\Phi \sin\theta \quad \ldots\ldots(28)$$

Membrane stresses

To complete the picture, the forces acting upon the membrane are also required; external forces are due to the viscous stresses from both the interior and exterior flows. If Σ_r, Σ_θ, Σ_Φ denote the externally imposed stresses on the membrane in the three directions then their net values are simply

$$\Sigma_r = \pi_{rr}^{(1)} + \pi_{rr}^{(0)} - \pi_{rr}^{(2)} \quad \ldots\ldots(29)$$

$$\Sigma_\theta = \pi_{r\theta}^{(1)} + \pi_{r\theta}^{(0)} - \pi_{r\theta}^{(2)} \quad \ldots\ldots(30)$$

$$\Sigma_\Phi = \pi_{r\Phi}^{(1)} + \pi_{r\Phi}^{(0)} - \pi_{r\Phi}^{(2)} \quad \ldots\ldots(31)$$

The R.H.S. can be evaluated from the equations of the last section to yield

$$\Sigma_r = -P_1 + P_2 \cos\Phi \sin\theta \cos\theta \quad \ldots\ldots(32)$$

$$\Sigma_\theta = P_3 \cos\Phi \cos 2\theta \quad \ldots\ldots(33)$$

$$\Sigma_\Phi = -P_3 \cos\theta \sin\Phi \quad \ldots\ldots(34)$$

where it is found that

$$P_2/\mu_1 = 2q(1-\lambda) + Aa^2[-6+126\gamma^{-5}-120\gamma^{-7}+\lambda(12+273\gamma^{-5}-285\gamma^{-7})/2] + C[4+30\gamma^{-3}-25\gamma^{-5}+\lambda(-8+65\gamma^{-3}-57\gamma^{-5})/2] \quad (35)$$

$$P_3/\mu_1 = q(1-\lambda) + Aa^2[16-21\gamma^{-5}+40\gamma^{-7}-\lambda(32+63\gamma^{-5}-95\gamma^{-7})/2] + C[2-5\gamma^{-3}+8\gamma^{-5}-\lambda(4+15\gamma^{-3}-19\gamma^{-5})/2] \quad (36)$$

the constant λ denoting the ratio of internal to external viscosity, μ_2/μ_1.

The fundamental stress equations for a spherical (or near spherical) membrane or shell can be found in any elementary shell theory text (e.g., Flügge[25]); they relate the internal membrane stresses σ_θ, σ_Φ, and $\tau_{\theta\Phi}$ to the imposed stresses Σ_r, Σ_θ and Σ_Φ as follows

$$-a\Sigma_\theta/t = \frac{\partial\sigma_\theta}{\partial\theta} + \frac{1}{\sin\theta}\frac{\partial\tau_{\theta\Phi}}{\partial\Phi} + \cot\theta(\sigma_\theta - \sigma_\Phi) \quad (37)$$

$$-a\Sigma_\Phi/t = \frac{\partial\tau_{\theta\Phi}}{\partial\theta} + \frac{1}{\sin\theta}\frac{\partial\sigma_\Phi}{\partial\Phi} + 2\tau_{\theta\Phi}\cot\theta \quad (38)$$

$$a\Sigma_r/t = \sigma_\theta + \sigma_\Phi \quad (39)$$

where t is the membrane thickness which is assumed constant throughout.

The solution of these equations given the forms (32)→(34) of Σ_r, Σ_Φ, Σ_r is relatively straightforward; with the restriction that the stresses must be everywhere finite the resulting solution is

$$t\sigma_\theta = -aP_1/2 + a(P_2 - 2P_3)\sin 2\theta\cos\Phi/8 \quad (40)$$

$$t\sigma_\Phi = -aP_1/2 + a(3P_2 + 2P_3)\sin 2\theta\cos\Phi/8 \quad (41)$$

$$t\tau_{\theta\Phi} = a(P_2 + 2P_3)\sin\theta\sin\Phi/4 \quad (42)$$

These then are the shell theory stresses within the red membrane itself where P_2, P_3 are given by 35 and 36.

Limiting cases — hardened red cells

Before proceeding to more complex cases it is of value to examine two simple limiting solutions of particular interest:

(i) the case in which the forces on the membrane are so small or the membrane so strong that it is virtually undeformed during the flow process,

(ii) the case (or cases) in which the forces on the membrane are very large compared with its ability to resist.

It is anticipated that case (1) may occur in blood and red cell suspensions when the shear rate is small or for suspensions of hardened red cells whereas (ii) may be the case when the shear rate is very large.

Case (i) corresponds simply to the problem of solid spherical particles and the result is obtained by setting the strain rates given by (26)→(28) equal to zero. Thus $V_1 = V_2 = 0$ and Equations (24) and (25) yield two equations for the unknowns (Aa^2/q) and (C/q). When these are substituted into (17) the resulting expression for the effective viscosity is, of course, identical with that of Simha[4] for solid spherical particles:

$$\mu^*/\mu_1 = 1 + 10\gamma^3(1-\gamma^7)/(4 - 25\gamma^3 + 42\gamma^5 - 25\gamma^7 + 4\gamma^{10}) \quad (43)$$

For small concentrations, $\varphi = \gamma^3$, this reduces most satisfactorily to Einstein's classical result for very dilute solutions, namely as

$$\gamma^3 \to 0,\ \mu^*/\mu_1 \to 1 + 2.5\varphi. \quad (44)$$

For concentrated solutions the expression (43) has been found by Simha[4], Happel[5] and others to agree surprisingly well with experimental measurements despite the approximations of the "cell" approach.

In Figure 2, the theoretical result (43) is compared with the experimental measurements of Chien, Usami, Dellenback and Gregersen[26] on hardened red cells in water and of Brooks, Goodwin and Seaman[17] on hardened red cells in isotonic saline. The result is very satisfactory although there is some deviation at higher hematocrits or concentrations; this may be due to particle/particle interactions which are not included in the "cell" approach. Cokelet[1] compares the same experimental values with an empirical formula due to Landel[27] of

$$\mu^*/\mu_1 = (1 - \varphi/\varphi_M)^{-5.2}$$

where φ_M is the maximum packing concentration. The degree of agreement is comparable.

It might be expected that suspensions of normal red cells would approach the same relative viscosity as the shear rate became very small. The isotonic saline suspension data of Brooks, Goodwin and Seaman[17] suggests that the shear rates at which this occurs is indeed very small (probably significantly less than 1 sec^{-1}) and may decrease with increasing hematocrit or concentration. The search for this trend must be confined to suspensions in which aggregates do not form at low shear rates; as mentioned in the introduction the presence of rouleaux in plasma sus-

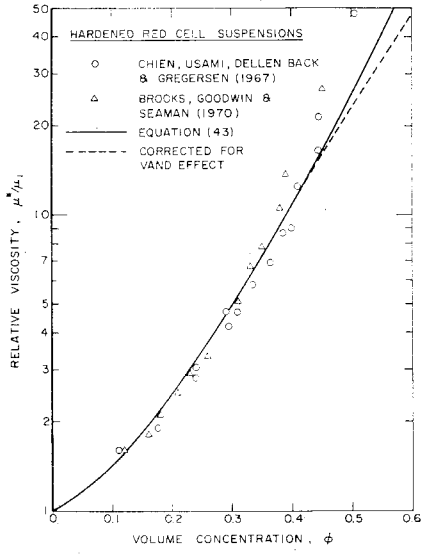


Figure 2 — Comparison of Equation (43) with data for hardened red cell suspensions by Chien, Usami, Dellenback and Gregersen (1967) and Brooks, Goodwin and Seaman (1970).

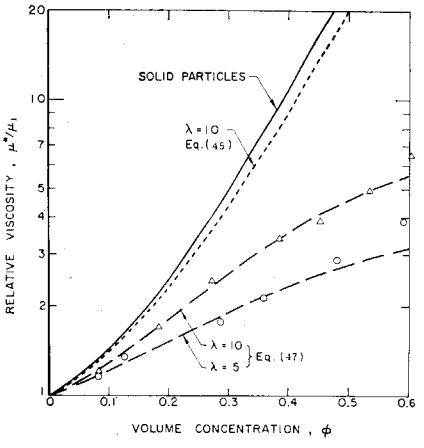


Figure 3 — Normal red cell suspensions at high shear rates. A symptotic data of Brooks, Goodwin and Seaman at high shear rates. (i) in plasma ($\lambda \approx 5$): ⊙ and (ii) in saline ($\lambda \approx 10$): ◬. Theoretical predictions using Equation (47) with $\lambda = 5$ and 10: — —. Also shown are the line for hardened red cells from Figure 2: ——, and a result from Equation (45) for $\lambda = 10$ (- - -).

pensions would invalidate the comparison with the present theory. Thus the asymptotic values which would permit this particular trend to be established have not as yet been documented experimentally.

Liquid droplets

The second limiting case to be examined is that in which the membrane has no resistance to deformation. This however has two subcases both of which are of interest.

The first subcase corresponds to the problem of liquid droplets for which Taylor[7] examined the problem of dilute suspensions. Here the interfacial or surface tension forces are assumed sufficiently large so that the interface does not deviate from its prescribed spherical shape. The first condition is therefore that $(v_r^{(0)} + v_r^{(1)})_{r=a} = 0$ or from (21) that $V_1 = 0$. The second condition is that shear stresses on the interface should balance. that is that $\Sigma_\theta = \Sigma_\Phi = 0$ on $r = a$ or from (33) and (34) that $P_3 = 0$. Then the conditions $V_1 = 0$, $P_3 = 0$ permit solution for (Aa^2/q) and (C/q) and lead to an effective viscosity

$$\frac{\mu^*}{\mu_1} = 1 + \frac{[4 + 10\gamma^7 + 10\lambda(1 - \gamma^7)]\gamma^3}{\left[\begin{array}{l} 4 - 10\gamma^3 + 10\gamma^7 - 4\gamma^{10} \\ +\lambda(4 - 25\gamma^3 + 42\gamma^5 \\ \quad - 25\gamma^7 + 4\gamma^{10}) \end{array}\right]} \quad \ldots\ldots\ldots\ldots (45)$$

where, as before, λ is the ratio of internal to external viscosity or $\lambda = \mu_2/\mu_1$. Note that when λ is large this precisely approaches the Equation (43) for solid particles. Also when the concentration, $\varphi = \gamma^3$, is small it reduces to

$$\mu^*/\mu_1 \to 1 + \gamma^3 (1 + 5\lambda/2)/(1 + \lambda) \ldots\ldots\ldots\ldots (46)$$

which is precisely Taylor's[7] result for a dilute suspension of spherical liquid droplets. Further note that as the concentration or γ approaches unity the expression (45) indicates that μ^*/μ_1 will approach infinity. This might be described as a direct result of not permitting any deviation from the spherical shape; a suspension of particles of *fixed shape* might be expected to have an infinitive viscosity as the concentration approaches its maximum value. In practice such limits are more complex since high concentrates often extract suspending fluid from a nearby source (perhaps a static portion of the suspension) thus reducing the concentration locally, a process termed volumetric dilatancy, and permitting flow in that neighborhood.

When the interior and exterior fluids are considered to be separated by a membrane rather than an interface the stresses in that membrane, given by Equations (40)→(42), become relevant. Then it is clear that in the limiting case when the membrane is infinitely deformable, the appropriate conditions should be those of zero membrane stress or $P_1 = P_2 = P_3 = 0$. The condition $P_1 = 0$ leads no further than the prescription that the hydrostatic pressures of the interior and exterior be identical. However, the condition $P_2 = P_3 = 0$ along with the relations (35) and (36) lead to an effective viscosity

$$\frac{\mu^*}{\mu_1} = 1 + \frac{10(\lambda - 1)[16 + 19\gamma^7 + 19\lambda(1 - \gamma^7)]\gamma^3}{\left(\begin{array}{l} 96 + 400\gamma^3 - 672\gamma^5 + 450\gamma^7 + 76\gamma^{10} \\ +\lambda(178 + 75\gamma^3 - 126\gamma^5 + 25\gamma^7 - 152\gamma^{10}) \\ +\lambda^2(76 - 475\gamma^3 + 798\gamma^5 - 475\gamma^7 + 76\gamma^{10}) \end{array}\right)} \quad \ldots\ldots (47)$$

When the suspension is dilute this reduces to

$$\mu^*/\mu_1 \to 1 + 5\gamma^3 (\lambda - 1)/(3 + 2\lambda) \ldots\ldots\ldots\ldots (48)$$

which, as expected, again reduces to Einsteins formula (4) when λ is large. However, (48) does differ from *Taylor's result; most significantly* when the interior and exterior viscosities are identical ($\lambda = 1$) the suspension viscosity given by (47) takes that same value. This is clearly the correct result since an infinitely deformable membrane was prescribed and the restriction on spherical shape has not been employed. In the case of $\lambda = 1$, the membrane is then merely a material surface in the pure shear flow, q, of an effectively homogeneous medium.

This second sub-case seems more appropriate to the case of blood flow at shear rates which are sufficiently high to completely dominate the resistive ability of the red cell membrane. Indeed there is, as expected, a wide disparity between the results for Equation (45) and for Equation (47) as indicated by the single comparison included in Figure 3.

The results of the theoretical expression (47) will thus be compared with the effective viscosities of red blood cell suspensions in saline and in *ACD* plasma as measured by Brooks, Goodwin and Seaman[17]. They found that at high shear rates of about 500 sec^{-1} the effective viscosities of their suspensions had closely approached asymptotic values and the data clearly suggests that further increase in shear rate would cause little change. These asymptotic values are plotted in Figure 3 (the viscosity of the saline at 25°C is 0.96 cp and that of the plasma was about *1.70 cp (Seaman[28])). It should also be noted that* Brooks, Goodwin and Seaman[17] conclude that rouleaux will not be present to any significant degree at these high shear rates so that direct comparison of theory and experiment should be valid in this respect.

The content of the red cell is primarily a solution of hemoglobin in saline. The Newtonian nature and viscosity of such solutions has been well documented experimentally by Chien, Usami and Bertles[19], by Cokelet and Meiselman[18] and by Wells and Schmid-Schönbein[20]. At normal hemoglobin concentrations of around 32% by weight (Dintenfass[21,22]) the viscosity of the solution is expected from the experimental data to be in the neighborhood of 9 centipoise. But the relevant value of λ for use in Equation (47) will also depend on the viscosity μ_1 of the suspending medium. Thus the appropriate value of λ for the saline suspension is about 10 whereas that for the plasma suspension is about 5. Values from Equation (47) for both λ are shown in Figure 3 and agree most satisfactorily with the experimental measurement. As before the only significant deviation seems to occur at the highest hematocrits and probably for the same reason suggested in section 5.

Erythrocyte suspensions at arbitrary shear rate

Having established some validity for the theory in *the two limiting cases of hardened red cells and red* cells at high shear rates it is of interest to try to complete the analysis in an attempt to predict the properties of red cell suspensions at moderate or transitional shear rates. For this purpose some model of the properties of deformation of the membrane is required. That is to say some constitutive equation which would enable the membrane stresses (Equations (40)→(42)) to be related to the strains and strain rates (Equations (26) to (28)) thus leading to an effective viscosity which would be a function of

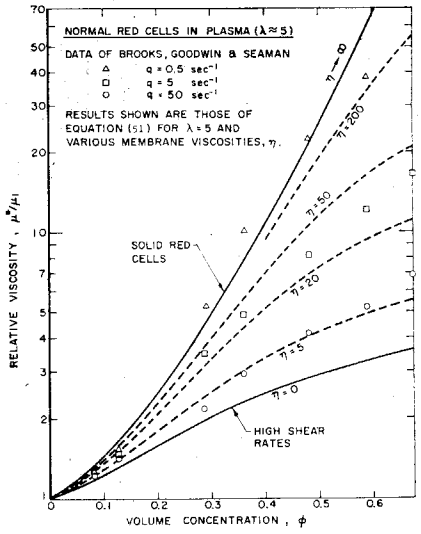
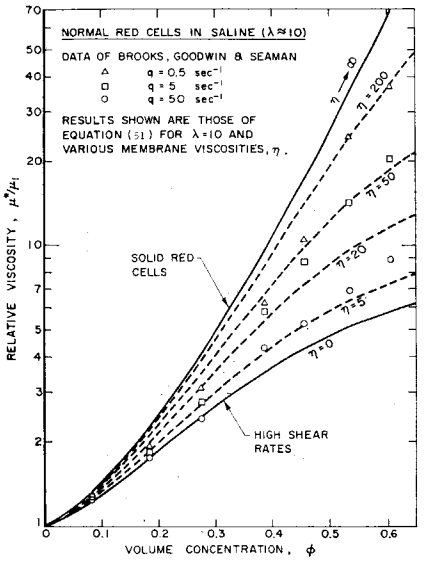


Figure 4 – Comparison of results for "shear viscous membrane" model (- - -) with experimental results for suspensions of normal red cells in plasma ($\lambda \approx 5$) at

Figure 5 – Combarison of results for "shear viscous membrane" model (——) with experimental results for suspensions of normal red cells in saline ($\lambda \approx 10$) at various shear rates.



the constants in that constitutive equation as well as λ and φ.

As mentioned in the introduction there is really insufficient knowledge of the elastic/plastic nature of the red cell membrane to allow such an approach to be implemented directly. Instead we will compare the experimental data at these intermediate shear rates with some admittedly oversimplified membrane models in an attempt to find trends which would suggest not only superior models but also some clues as to the nature of the membrane deformation itself. First it is to be noted that in the context of the present formulation purely elastic deformations of the membrane will yield little energy dissipation and will not therefore contribute to the relative viscosity of the suspension. Thus only visco-plastic membrane deformations will be considered; the analysis and results of some simple models are as follows:

[*A*] *"Viscous Membrane"*. The form of the equation for membrane stress and strain rate are such that the simplest model is to assume that the membrane behaves like a Bingham solid with a negligibly small yield stress (see model [C]) so that

$$\sigma_{ij} = -p\,\delta_{ij} + 2\,\eta^*\,\dot{e}_{ij} + \delta_{ij}\,\xi^*\,\dot{E},\quad i,j = \theta,\varphi$$

where δ_{ij} is the Kronecker delta, η^* is the coefficient of viscosity of the membrane, ξ^* the dilation modulus and $\dot{E}$ the dilation rate, $\dot{e}_{\theta\theta} + \dot{e}_{\varphi\varphi}$. Using the relations for σ_{ij}, $\ddot{e}_{ij}$ this constitutive equation leads to three conditions one of which is redundant so that

$$(P_2 - 2P_3)/\mu_1 = 8\eta\,(V_1 - 4V_2) + 8\xi\,(V_1 - 3V_2) \quad \ldots\ldots(49)$$

$$(P_2 + 2P_3)/\mu_1 = 8\eta\,V_2 \quad \ldots\ldots(50)$$

where $\eta = \eta^* a/t$ and $\xi = \xi^* a/t$. The solution of these equations for (Aa^2/q) and (C/q) given the definitions (24), (25), (35) and (36) enables one to obtain a relative viscosity μ^*/μ_1 as a function of λ, η, ξ and of course $\gamma(=\varphi^{1/3})$. It transpires that the results are to all intents and purposes independent of the dilation modulus ξ; they are altered very little whether ξ is 0 or 10^4. It is for this reason that the results of this model are omitted since they are virtually identical with those of the following model.

[B] *"Shear Viscous Membrane"*. Here it is assumed that as the red cell is distorted a segment of membrane does not change in area; that is to say the dilation E is zero or $V_1 = 3V_2$. If in addition there is viscous resistance, η^*, to its changing shape then this second condition merely repeats Equation (50), namely $(P_2 + 2P_3)/\mu_1 = 8\eta V_2$. The consequent relative viscosity becomes

$$\frac{\mu^*}{\mu_1} = 1 + \frac{10\gamma^3\,[23\lambda(1-\gamma^7) - 16 + 23\gamma^7 + 16\eta(1-\gamma^7)]}{\left\{\begin{array}{l}128 + 400\gamma^3 - 336\gamma^5 - 100\gamma^7 - 92\gamma^{10} \\ +\,\lambda(92 - 575\gamma^3 + 966\gamma^5 - 575\gamma^7 + 92\gamma^{10}) \\ +\,\eta(64 - 400\gamma^3 + 672\gamma^5 - 400\gamma^7 + 64\gamma^{10})\end{array}\right\}} \quad (51)$$

The results of this model (which are virtually identical with those of [*A*] for the reasons given above) are shown in Figures 4 and 5 for $\lambda = 5$ and $\lambda = 10$ respectively and a series of values of the membrane viscosity η. When $\eta \to \infty$ Equation (51) reduces to the case of solid particles (Equation (43)) and when $\eta \to 0$ the numerical result is very close to that of Equation (47). The data of Brooks, Goodwin and Seaman[17] for suspensions of normal red cells in plasma ($\lambda = 5$) and in saline ($\lambda \approx 10$) are also shown in Figures 4 and 5 for shear rates, q, of 0.5, 5 and 50 sec^{-1}.

This model is however not particularly satisfactory since even if the membrane could be characterized by a simple viscosity, Figures 4 and 5 illustrate how that viscosity would have to increase with decreasing shear rate in order to correlate with the experimental data. (The limits of the validity of the comparison in Figure 4 due to aggregation at low shear rates are more conveniently delayed until later). Though such a trend is not beyond the realm of possibility there is insufficient data on the membrane properties to adequately evaluate the results of this model at the present time. It can only be pointed out that the membrane viscosities are the same order of magnitude as the figure of $100 \to 200$ cp quoted by Frye and Edidin[29] for a different biological membrane. For these reasons a somewhat different model based on *known* properties of the red cell membrane but fitting the data rather more crudely is presented below.

[*C*] *"Plastic Membrane"*. Comparison of the model [*B*] with the experimental data indicated (Figures 4 and 5) that the "apparent membrane viscosity" increases with decreasing shear rate. This suggests that a purely plastic membrane model might be worth investigation; this would represent the membrane as

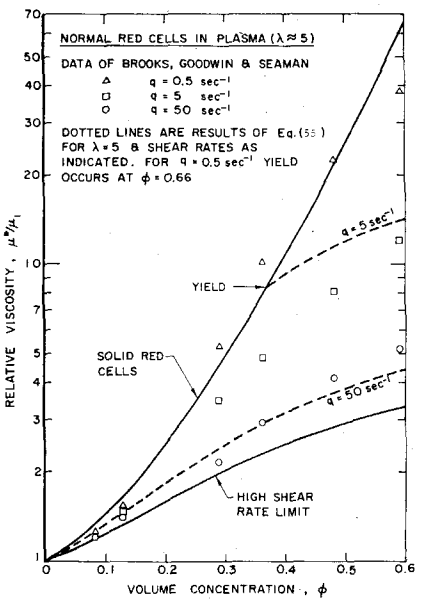


Figure 6 – Comparison of results for the "plastic membrane" model with experimental results for suspensions of normal red cells in plasma ($\lambda \approx 5$) at various shear rates).

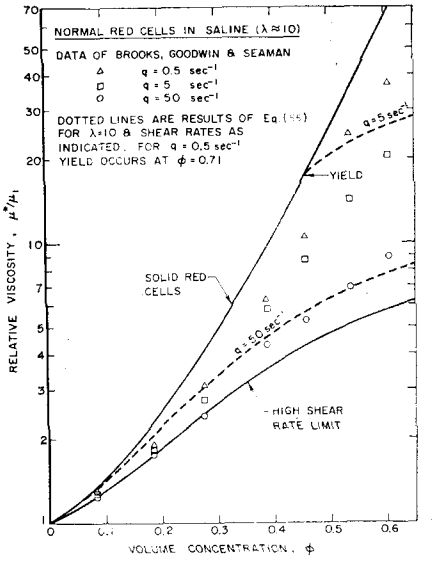


Figure 7 – Comparison of results for the "plastic membrane" model with experimental results for suspensions of normal red cells in saline ($\lambda \approx 10$) at various shear rates.

undeformable up to a certain membrane yield stress and unable to sustain any greater stress. It also happens that there exist experimental observations from which a value for this membrane yield stress can be deduced. It is worth emphasizing, however, that the yield stress referred to is *not* the rupture stress measured by Rand and Burton[30], Leverett et al[31] and others but merely the stress required to initiate deformation of the erythrocyte.

Brooks, Goodwin and Seaman[17] report that the height of a column of sedimented red cells in which deformation is first detected is .042 cms. At this height the force on the bottom layer of cells due to the weight of those above and in terms of an average pressure over the mean cross sectional area of each cell is about 3.8 dynes/cm^2. If this is then equated to a membrane yield stress of k dynes/cm^2 it follows that $2\ kt/a = 3.8$ dynes/cm^2 where a is the average radius of the cross sectional area and t the membrane thickness. The membrane yield stress, $k = 1.9$ a/t dynes/cm^2 will be employed in this membrane model.

The plastic yield criterion which will be used is that of von Mises (Hill[32]); that is to say the membrane stresses at yield will satisfy

$$[\tfrac{1}{4}(\sigma_\theta - \sigma_\varphi)^2 + \tau_{\theta\varphi}^2]_{MAX} = k^2 \quad \ldots\ldots(52)$$

Substituting for $\sigma_\theta, \sigma_\varphi, \tau_{\theta\varphi}$ from equations (40), (41) and (42) this condition becomes

$$|\ P_2 + 2P_3\ | = kt/a \quad \ldots\ldots(53)$$

Then if $P_2 + 2P_3$ is less than kt/a the red cells will act like solid particles and the suspension will conform to Equation (43) of section 5. Using the details of that section to evaluate P_2, P_3 the condition (53) becomes

$$5(8 + 7\gamma^5 + 15\gamma^7)/(4 - 25\gamma^3 + 42\gamma^5 - 25\gamma^7 + 4\gamma^{10}) = 4kt/a\mu_1 q = T, \text{ say} \quad \ldots\ldots(54)$$

Note that this condition also involves μ_1 and the shear rate q. Further assume that once the yield has taen place the maximum membrane stress will remain at the yield value; it follows that Equation (53) is the first condition required for solution. Retaining from model $[B]$ the second condition of zero dilation (or $V_1 = 3\ V_2$) leads to a post-yield relative viscosity of

$$\frac{\mu}{\mu_1} = 1 + \frac{\gamma^3[-80 + 115\gamma^7 + \lambda(115 - 115\gamma^7) + T(96 + 84\gamma^5 - 180\gamma^7)]}{\left[\begin{array}{l}64 + 200\gamma^3 - 168\gamma^5 - 50\gamma^7 \\ - 46\gamma^{10} + \lambda(92 - 575\gamma^3 + 966\gamma^3 \\ - 575\gamma^7 + 92\gamma^{10})/2\end{array}\right]} \quad \ldots\ldots(55)$$

Using the above mentioned value for kt/a, the values of T which correspond to the experimental data of Figure 4 and 5 for shear rates of 0.5, 5.0 and 50 sec^{-1} are respectively 220, 22 and 2.2 for the plasma suspension and 420, 42 and 4.2 for the saline suspension of normal red blood cells. The appropriate results of equation (55) are compared with the experimental results for the plasma and saline suspensions in Figures 6 and 7.

As mentioned previously there is some question concerning the validity of the comparison in Figure 6 (also Figure 4) since aggregates may be present in the plasma suspension at low shear rates. Brooks, Goodwin and Seaman[17] estimate that the force required to disaggregate red cells is less than the force required to initiate deformation of an erythrocyte and may be as little as 1/100 of that value. Thus when the shear rate and hematocrit in the plasma suspension are sufficiently large for red cell deformation to occur (the dashed lines in Figure 6) we would not expect significant numbers of aggregates to be present and comparison with the theoretical model would then be appropriate. But, furthermore, the other portion of the model (solid line, Figure 6) corresponds to essentially solid or undeforming particles the equation for which, (43), is independent of particle size in the first order and would hold equally well for aggregates. Of course, this is overly simplistic but indicates that the effect of rouleaux on the viscosity of blood is not entirely obvious. Indeed comparison of the experimental data in Figure 6 with that of Figure 7 (where aggregation is not a factor) for unyielded flows suggests that if rouleaux is present in the plasma it has a relatively small effect on that relative viscosity. The only substantial difference occurs at the lowest shear rate and with intermediate hematocrits; the reason for this is not clear. We conclude that though Figure 7 (and Figure 5) represent a more reliable comparison of theory and experiment the data of Figure 6 (and Figure 4) are also worth some thought.

It is to be expected that there would be some discrepancy between theory and experiment considering

the oversimplification of the plastic membrane model. No real plastic material has the step-function like behavior assumed here and we would expect that there would be a smoother transition from the state of no deformation to the state of maximum stress as Figures 6 and 7 suggest. With this in mind the quantitative agreement at the higher shear rates and the general qualitative agreement at lower q is most remarkable. It suggests that, aside from the questions of aggregation discussed above, good quantitative agreement at all shear rates may be achieved with better detailed knowledge of the structural properties of the red cell membrane. It is worth stressing that this model [C] has employed only properties of the red cell membrane and contents which are known from other experiments and that no additional factors or properties have been introduced.

Conclusions

The simple cell method approach to concentrated suspensions has been employed in an attempt to construct a model for the rheological properties of blood. Predictions of the gross viscosity of red cell suspensions have been found to agree very well with the experimental data for the case of hardened red cells (or normal red cells at very low shear rates) and the case of normal red cell suspensions in the asymptotic limit of high shear rates. The latter case requires the appropriate value of the ratio of the viscosity of the surrounding medium to that of the red cell content, namely a solution primarily of hemoglobin.

In order to analyze the rheology at intermediate shear rates a knowledge of the stress/strain relationship for the membrane is required. A number of simple membrane models are investigated. Most significantly the model based on a membrane yield stress whose value is known from other experiments leads to results which are compatible with the experimental observations at intermediate shear rates. The significance of these results lies in the fact that the model incorporates properties of the red cell membrane and red cell contents which are known from other sources and that no additional factors or unknown properties are incorporated.

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Nomenclature

a = volumetric radius of red cell
A, C, E, G, K, L = constants
b = "cell" radius
$\dot{e}$ = membrane strain rates
$\dot{E}$ = membrane dilation rate
k = membrane yield stress
p, P = pressure
$P_1\ P_2, P_3$ = stress component magnitudes
q = shear rate
r, θ, Φ = spherical coordinate system
t = membrane thickness
$\underline{T}$ = $kt/a\mu_1 q$
$\overline{v}$ = velocity vector
V_1, V_2 = velocity component magnitudes
γ = a/b
δ_{ij} = Kronecker delta
η = $\eta^* a/t$
η^* = membrane viscosity
λ = μ_2/μ_1
μ_1 = exterior fluid viscosity
μ_2 = interior fluid viscosity
μ^* = suspension viscosity
ξ = $\xi^* a/t$
ξ^* = membrane dilation modulus
π = fluid stress dyadic
σ, τ = internal membrane stresses
Σ = external stresses on membrane
φ = volume concentration, γ^3

Superscripts

$^{(0)}$ = exterior shear flow
$^{(1)}$ = particle generated exterior flow
$^{(2)}$ = interior flow

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