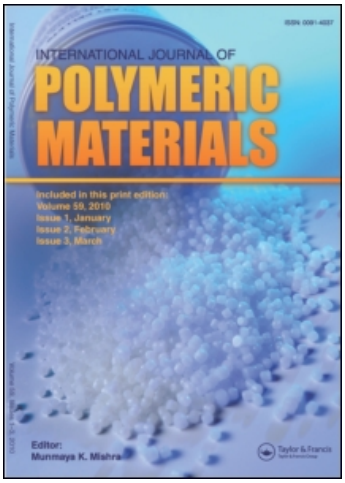

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Theory of Blood Rheology Based on a Statistical Mechanics Treatment of Rouleaux, and Comparisons with Data

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Theory of Blood Rheology Based on a Statistical Mechanics Treatment of Rouleaux, and Comparisons with Data

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A constitutive equation for the rheology of blood is obtained from the view of blood as a suspension of rouleaux (erythrocyte aggregates), with the rouleaux idealized as *elastic* cylinders. Properties depend on the distribution of rouleaux lengths, which is related to the state of cell aggregation and characterized by a structural distribution function. A kinetic equation is developed to describe the balance of aggregation/disaggregation phenomena. The result is a structure-dependent Maxwell model for the stress tensor, with viscosity and relaxation time linearly related to a structure parameter. Comparisons with data are shown and discussed.

KEY WORDS Blood rheology, blood viscosity, erythrocytes, aggregation, disaggregation.

INTRODUCTION

Blood flowing at shear rates above $10\ s^{-1}$ is usually Newtonian, with a low viscosity associated with complete dispersal of erythrocytes. At lower shear rates, cell aggregates (rouleaux) can survive and lead to enhanced viscosity with non-Newtonian and thixotropic behaviour.[1–3] Thus, blood is a "structured fluid" and its rheological modeling must incorporate some characterization of its structure and how the structure changes.

In this work, we address the problem of relating macrorheological response to the existing microstructure, and also describe the structure in a precise and realistic fashion. Previous attempts to interrelate rheology to structure have generally employed abstract structure parameters with no tangible significance[4,5]; one such

model for blood[5] led to unrealistic artifacts in predictions. Blood viscoelasticity has also been represented by a superposition of Maxwell models,[6] though connection of parameters to microstructure was absent. Here, we define the microstructure in terms of the rouleaux length distribution and develop a kinetic equation to describe its evolution. The stress tensor is then represented in terms of this distribution, so rheological properties embody the rouleau structure in a fundamental way.

ROULEAUX DISTRIBUTION FUNCTION

The three-dimensional branched structures of red cell aggregates observed at rest are too complex to accommodate exactly. However, these are usually very unstable in flow and decompose into a basic linear structure of cylindrical geometry (with the cells stacked face-to-face in the cylinder). Each rouleau cylinder can be characterized by the number of cells it contains (n), so the state of aggregation is related to cylinder length. The cylinder end-to-end vector $\mathbf{q}$ thus has a length proportional to nw, where w is cell thickness. Also important to the rheology is the cylinder orientation, given by the spatial direction of $\mathbf{q}$. We therefore require a distribution function, ψ_q, that characterizes the assembly of all the rouleaux lengths and orientations. In general, $\psi_q = \psi_q(\mathbf{q}, \mathbf{r}_q, t)$ where t is time and $\mathbf{r}_q$ is the position in space of a rouleau described by $\mathbf{q}$.

MICROSTRUCTURAL KINETICS

Using methods similar to those of Wiegel,[7] and restricting attention to incompressible fluids in a homogeneous flow, one can derive a continuity equation for ψ_q:

$$\frac{\partial \psi_q}{\partial t} = -\frac{\partial}{\partial \mathbf{q}} \cdot [(\nabla \mathbf{v} \cdot \mathbf{q})\psi_q] + K_q - L_q \tag{1}$$

when K_q and L_q characterize the mechanisms by which ψ_q is increased or decreased, respectively, by mechanical phenomena. The variable $\mathbf{r}_q$ vanishes in a homogeneous flow, so $\psi_q = \psi_q(\mathbf{q}, t)$ only.

Rouleaux reformation kinetics have been treated in a fashion similar to addition polymerization kinetics,[8] showing that K_q is complex in general. However, for conditions not far from equilibrium, where all rouleaux are still very long, one can show that an approximate expression is valid[9]:

$$K_q \cong k' N_0(\psi_q^e - \psi_q) = k(\psi_q^e - \psi_q) \tag{2}$$

Here, ψ_q^e = equilibrium value of ψ_q and N_0 = number of cell faces/vol in the system, a factor proportional to hematocrit (H). This expression has a driving force $(\psi_q^e - \psi_q)$ similar to those used by other workers dealing with structure build-up,[10,11] and independent data[12] suggest that Equation (2) is a reasonable low-order description.

Rouleaux break-up kinetics in flow depend on the concentration of each $\mathbf{q}$-

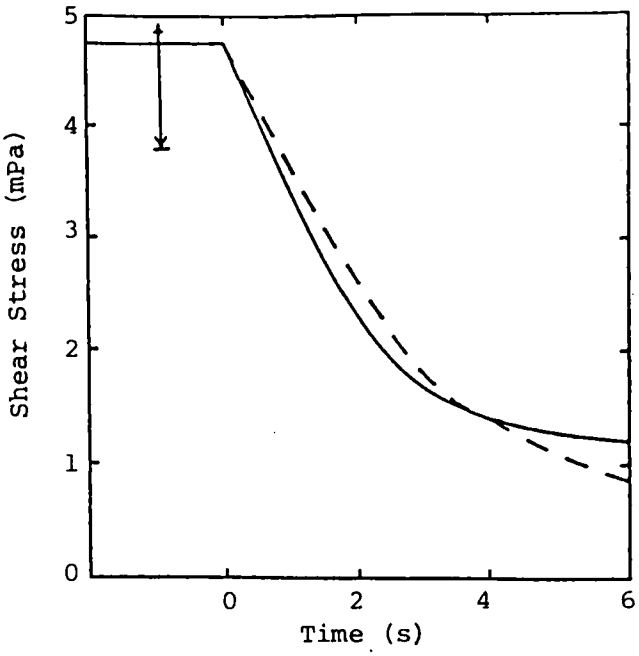

FIGURE 1 Stress decay after steady shear at $\dot{\gamma} = 0.05\ s^{-1}$. Model (– –) and data (—).

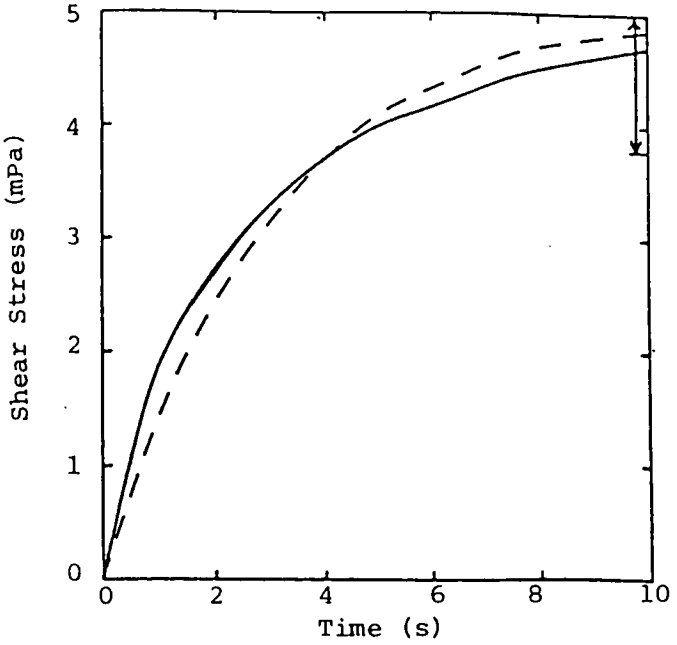

FIGURE 2 Stress growth, after rest, following start of steady shear at $\dot{\gamma} = 0.05\ s^{-1}$. Model (– –) and data (—).

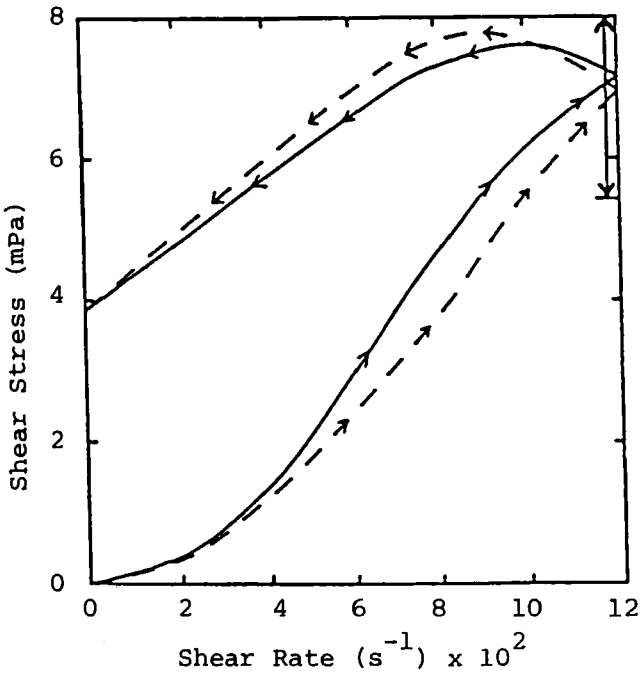

FIGURE 3 Stress hysteresis, during linear increase of $\dot{\gamma}$ from 0 to 0.12 s^{-1} during 6.5 s, followed by a similar decrease. Model (– –) and data (—).

rouleau, the local hydrodynamics, and the critical tensile force (F_c) at which the adhering cell faces can be separated. Arguments based upon mechanical time scales and (again) the long-rouleaux approximation lead to the simplified form[9]

$$L_q \cong \frac{\alpha'}{F_c} |\dot{\gamma}| \psi_q = \alpha |\dot{\gamma}| \psi_q \tag{3}$$

where $\dot{\gamma}$ = shear rate and α = dimensionless empirical coefficient that can be evaluated from steady state flow data. The linear $\dot{\gamma}$-dependence in L_q leads to viscosity predictions that agree well with experiments.[13] Because most effects of cell surface chemistry and membrane elasticity are embedded in α, we see how pathological conditions that lead to abnormal aggregation are reflected in the rheology. In this way, rheological measurements can be interpreted for clinical diagnostic purposes.

Combination of Equations (1–3) produces the dynamical equation for $\psi_q(\mathbf{q}, t)$ evolution. That equation can be integrated over configuration space ($\int$ (---) **dq**, term-by-term) to give a kinetic equation for N, the total number of aggregated cell faces/vol. This is transformed to

$$dP/dt = k(1 - P) - \alpha |\dot{\gamma}| P \tag{4}$$

where $P = N(t)/N_0$ is the structure factor in this theory. All rheological properties depend on $P(t)$.

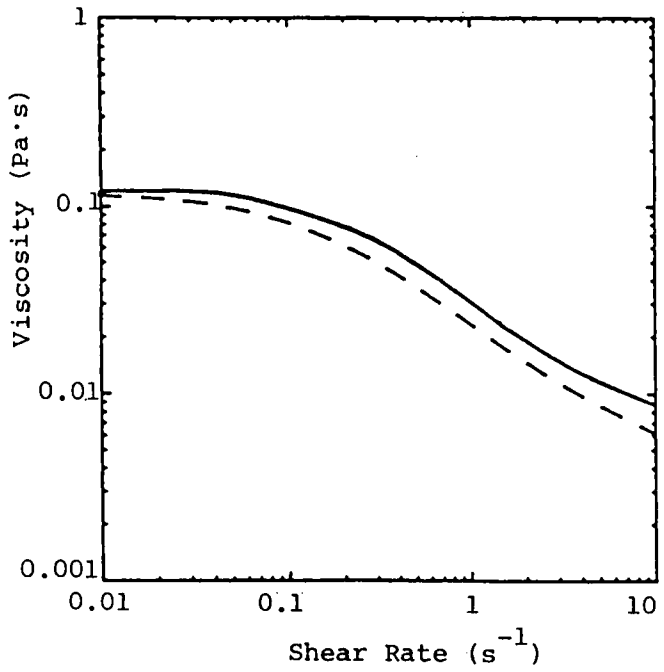

FIGURE 4 Non-Newtonian viscosity in steady shear. Model (– –) and data (—) on a different blood.

STRESS TENSOR

The stress τ can be viewed as having three components: $\tau = \tau_{pl} + \tau_{cell} + \tau_{st}$. Here, τ_{pl} represents the plasma contribution, τ_{cell} arises from the presence of free cells, and τ_{st} is the structural (aggregated cells) contribution. At high $\dot{\gamma}$, $\tau = \tau_{pl} + \tau_{cell}$ because the cells are fully dispersed, but this case is not considered further. Instead, we address the low-to-moderate $\dot{\gamma}$ regime where structure is dominant and few isolated cells exist: $\tau = \tau_{pl} + \tau_{st} \cong \tau_{st}$. This is consistent with our earlier use of the long-rouleaux case.

Using a relationship derived originally for elastic polymer molecules,[14] we express the stress contribution of one elastic rouleau cylinder as proportional to $\mathbf{f}_q\mathbf{q}$, where $\mathbf{f}_q$ is the tensile force. For the entire collection of rouleaux, $\tau_{st} = \rho_R\langle\mathbf{f}_q\mathbf{q}\rangle$ where ρ_R = number of rouleaux/volume and $\langle\ \rangle$ denotes the average with respect to ψ_q. Furthermore, we assume that rouleaux deform like linear springs: $\mathbf{f}_q = \Omega(\mathbf{q} - \mathbf{q}_e)$, where $\mathbf{q}_e$ is the equilibrium value (actually, the value measured at $\dot{\gamma} = 0$). Finally, it can be shown that $\rho R = wN_0/2\langle q_e\rangle$. Various manipulations[9] then lead to the *deviatoric* measurable stress,

$$\tau'_{st} = \frac{wN_0}{2\langle q_e\rangle}\,\Omega\,[\langle\mathbf{qq}\rangle - \langle\mathbf{qq}\rangle^e] \tag{5}$$

The factor containing $\langle\ \rangle$ is evaluated directly from the evolution equation for ψ_q, by multiplying each term by $\mathbf{qq}$ and integrating $\int$ (---) $\mathbf{dq}$. The result can be ex-

pressed in terms of the Oldroyd upper convected derivative, $\boldsymbol{\delta/\delta t}$, as $[\langle \mathbf{qq} \rangle - \langle \mathbf{qq} \rangle^e] = (P/k)\boldsymbol{\delta}\langle \mathbf{qq} \rangle/\boldsymbol{\delta t}$. When this is used in Equation (5), together with the relation $\langle \mathbf{qq} \rangle^e = (\langle q_e^2 \rangle/3)\mathbf{I}$ and the identity $\boldsymbol{\delta I/\delta t} = -\dot{\boldsymbol{\gamma}}$, the result can be rearranged as

$$\boldsymbol{\tau}'_{st} + \theta \frac{\boldsymbol{\delta} \boldsymbol{\tau}'_{st}}{\boldsymbol{\delta t}} = \eta_{st} \dot{\boldsymbol{\gamma}} \tag{6}$$

This is simply a structured nonlinear Maxwell model with structural viscosity η_{st} and relaxation time θ given by

$$\eta_{st} = \left(\frac{\langle \mathbf{q}_e^2 \rangle w N_0 \Omega}{6 \langle q_e \rangle k} \right) P = \eta_{st}^0 P, \qquad \theta = \left(\frac{1}{k} \right) P = \theta^0 P \tag{7}$$

Both parameters are largest at rest ($P = 1$) and vanish when cells are fully dispersed ($P = 0$).

APPLICATIONS

For each type of shearing program $\dot{\gamma}(t)$, model predictions of stress are obtained by simultaneous solution of Equation (4) for $P(\dot{\gamma}, t)$ and Equation (6) for the τ_{st} components of interest. For comparisons with viscosity data, it is useful to write $\eta = \eta_{st} + \eta^\infty$ where η^∞ is the high-$\dot{\gamma}$ limit that includes both plasma and dispersed-cell contributions. Experiments on steady and transient stress can be described using $\alpha = 1.2$, $k = 0.25\ \mathrm{s}^{-1}$, $\eta_0 = 0.12\ \mathrm{Pa \cdot s}$, $\eta^\infty = 0.004\ \mathrm{Pa \cdot s}$. Direct studies of cell aggregation kinetics[15] also give $k = 0.25\ \mathrm{s}^{-1}$. From these, and from other independent evidence, we estimate $\Omega = 7 \times 10^{-8}\ \mathrm{N/m}$; direct measurements have not yet been reported. Normal stresses are predicted to be very small, as is indeed observed.

The capability of the model for curve-fitting complex data, such as nonlinear transient stresses, should be quite good. A model developed for entangled polymer liquids[10,16] had a similar mathematical structure, and it was very successful at such tasks. Curve-fitting examples for transients at low $\dot{\gamma}$ are given in Figure 1 (stress decay), Figure 2 (stress growth), and Figure 3 (hysteresis). Data[17] are shown as solid lines, representing the average of tests on several human bloods. The dashed lines show model predictions made with α, k, η_0, and η^∞ values cited above, as well as $P_0 = 0.806$ to initiate the decay after cessation of shear and $P_0 = 0.98$ to initiate the growth upon beginning shear. The curve-fits are reasonably successful at low $\dot{\gamma}$, but deficiencies are expected at high $\dot{\gamma}$, because the long-rouleaux approximation is then less valid.

The steady-state non-Newtonian prediction is shown in Figure 4 (dashed line), using the same parameters as in Figures 1–3. A comparison is also displayed there with data on an entirely different blood, obtained by different workers.[13]

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