A literature research into the rheology of whole human blood

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Summary

This literature study has been done in the context of the study of the rheology of viscoelastic dispersions. From the interest of the research in the inter-university project "Atherosclerosis", a cooperation of the Eindhoven University of Technology and the University of Limburg (the Netherlands), literature dealing with the most important aspects of the rheology of human blood has been reviewed.

Blood is found to be a non-Newtonian shear thinning, thixotropic and viscoelastic fluid; no measurable normal stress differences have been found. The rheology of blood is mainly determined by the red blood cells, that can form structures called rouleaux by aggregation at low deformation rates. These rouleaux can form a three dimensional network at very low shear rates. With increasing deformation rates disaggregation takes place, and the non-Newtonian behaviour of blood is primary determined by the deformation and orientation of the dispersed red blood cells.

The constitutive models used in literature to describe the rheological behaviour of blood are mainly generalized non-Newtonian models, that only model the shear thinning behaviour of blood; only a few viscoelastic models have been found. In two dimensional numerical flow studies in artery models only non-viscoelastic models have been used (generalized Newtonian models, micropolar model). In flows with accelerating and decelerating material elements, which can also be the case in a steady two-dimensional flow, these models may not be appropriate. The viscoelastic models found are used at the most to describe the shear rate dependent viscosity, complex viscosity, and transient response in shear flows. All these models are based on the assumption that there is a structure buildup - breakdown process taking place. A modified Bird-Carreau model as reported by Bernadin e.a. [1986] was found to be a serious candidate to be used in future calculations. However, because the numerical calculations will be done using the finite element software package SEPRAN in which this Bird-Carreau model has not been implemented yet, its use at a short term is precluded. The other visco-elastic models (named Charara model, Rosenblatt model and Reher-Vogel model) all consist of a Maxwell type equation together with a separate kinetic structure equation. There is too little data available yet to judge their adequacy. Of the models already available in SEPRAN a KBKZ-type model and a Phan-Thien-Tanner model may be good candidates too.

Non-Newtonian flow studies with real human blood are for several reasons not appealing and very difficult: it is unstable, can carry diseases, is opaque to light, and difficult to obtain in large volumes. Therefore a number of non-Newtonian rheological analog fluids for blood have been proposed in literature. However, none is completely satisfactory. In general with both fluids and constitutive models comparisons with blood are made using steady, oscillatory, and transient

shearing measurements. One should be careful making conclusions based on these experiments alone. Some additional testproblems should be used, especially a test with an elongating flow. This flow situation is however very difficult to realize experimentally, for a low viscosity fluid such as blood even impossible. As an alternative, mixed shear/elongating flows can be used. For example, Armstrong e.a. [1985] use the flow between two excentric cilinders to evaluate different constitutive equations. Possibly, this flow situation can be used for blood too.

Contents

Introduction

This report is the result of a literature research into the rheology of whole human blood The expression "whole human blood" is used instead of simply "blood" to make clear what kind of blood is studied. This biofluid is being studied from several research areas, and consequently with very different interests and aims. Examples are the clinical hemorheology[†] (see for example Persijn e.a. [1990], Chmiel e.a. [1990]), the study of biocompatible blood substitutes, biology, blood flow in small arteries, and blood flow in the microcirculation. Our reason for studying the rheology of blood is the question into the importance of the non-Newtonian character of whole human blood when it flows in the human carotid artery bifurcation. This flow situation is the subject of study in the research project "Atherosclerosis". In most previous flow studies, blood has been assumed to behave as a Newtonian fluid (for example Rindt e.a. [1988], Rindt [1989], v.d.Vosse e.a. [1990]), which is a valid assumption in large straight tubes where only very high shear rates occur. From oscillatory shearing experiments, it has been found that blood can behave viscoelastic (for example, it has a non-zero elastic component of the complex viscosity for a wide range of frequencies (10^{-1} Hz < f < 10^{1} Hz) at low shear rates ($\dot{\gamma} < 1\ s^{-1}$) (Thurston [1979])). When bends and bifurcations are present, with low shear rate areas and relatively sharp corners, the non-Newtonian viscoelastic character of blood may influence the flow patterns significantly. Although many authors (for example Perktold [1989], Liepsch [1990]) acknowledge that the study of the flow of blood in such cases should incorporate the shear thinning and viscoelastic character of blood, no such numerical study has been found in literature yet. Shear thinning models do have been used (e.g. Rodkiewicz [1990], Perktold [1990], Baaijens [1991]); the results showed on the one hand that the general flow structure is not altered, but on the other hand that significant differences in stress or pressure were found too. No viscoelastic (or thixotropic) flow calculations were found; although it is unsure what the effect of this behaviour in physiological flow situations is. The lack of these calculations has probably partly been caused by the numerical problems associated with the use of viscoelastic constitutive models in complex flows that have existed. Recently important progress has been made in this research subject (Hulsen [1988], [1990], Hoitinga [1990], Baaijens [1991a]). Some experimental studies on the viscoelastic flow of blood exist (Liepsch [1987], Liepsch e.a. [1991], Mann and Tarbell [1990]), but because of the short-

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† This science studies blood rheology and its clinical and pathophysiological implications. On the one hand by measuring the rheological properties of blood certain diseases can be diagnosed. On the other hand, by altering these properties certain diseases can be treated.

comings of the used blood rheological analog fluids, no definite conclusions can be made yet. This makes clear the need of this study.

The literature search was focused on papers discussing constitutive models and rheological analog fluids used for blood; for sake of completeness, only a short description of the composition of blood and its rheological characteristics are given in the first sections of chapter 1. The characteristics of physiological blood flow are discussed at the end of this chapter.

Both experimental and numerical research on the problem of the non-Newtonian behaviour of blood have only been very basically until today. This is discussed in chapter 2 and 3. In chapter 2 the emphasis is on the constitutive models for blood as used in literature; some papers of major interest are reviewed. The numerical calculations will be performed using the finite element software package SEPRAN. For that reason, constitutive models that are implemented in SEPRAN are discussed. Finally the choice of a constitutive model for blood is discussed.

In chapter 3, the non-Newtonian rheological analog fluids for human blood, as described in literature, are described. These fluids are purposed to be used in experimental flow situations and have to simulate the rheological behaviour of blood. Such a fluid enables experimental validation of numerical calculations.

This report ends with a summary of the major conclusions and recommendations in chapter 4.

1 Rheology of blood†

1.1 Introduction

According to Carrig and Schneck [1986] it was Hess [1980] who discovered in 1915 that blood exhibited non Newtonian behaviour. He found that its viscosity is shear rate dependent. Numerous researches (e.g. Thurston [1979], Charara [1986], Huang e.a [1975]) have shown that blood also exhibits viscoelastic and thixotropic behaviour. This complicated material behaviour is caused by the microstructure of blood, that is determined by the chemical and physical properties of its constituents. In the following, first the composition of blood is elucidated in section 1.2, and then the characteristics of the red blood cells are discussed in section 1.3. (These two sections are based on Caro e.a. [1978] who provide a more detailed discussion of the subject). Section 1.4 deals with the non-Newtonian shear thinning, viscoelastic and thixotropic behaviour of blood. When characterizing the physiological flow situation, as it is the subject of this study, several dimensionless parameters are important. These are discussed in section 1.5. Finally, in section 1.6 the relation between the non-Newtonian behaviour of blood and its microstructure, depending on the flow situation, is discussed tentatively.

1.2 Composition of blood

Blood is a suspension of blood cells and liquid particles (the chyomicrons) in the plasma. It has a specific mass of $1.050\ 10^3$ kg/m^3. If all the particles are removed from the blood and it is anticoagulated, then the plasma rests. This an aqueous solution, with several low-molecular weight particles of anorganic and organic material in low concentrations. It consists for about 7% of proteins (Caro e.a [1978]). It appears from experiments (Caro e.a [1978]) that plasma is a Newtonian fluid; at 37°C it has a viscosity $\eta_{plasma} = 1.2\ 10^{-3}$ Ns/m^2.

The chyomicrons, which play a role in the fat transport mechanism of blood, are 0.2 - 0.5 μm long and have such a small concentration that they do not influence the macroscopic rheological properties of blood. The blood cells can be divided in red and white blood cells and blood platelets. The white blood cells (leukocytes) and platelets have such a low concentration relative to the red blood cells (erythrocytes), see table 1.1, that they are not important when considering the rheological behaviour of blood. The composition of blood is depicted in table 1.1.

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† This chapter is partly based on the work of Van Steenhoven [1984].

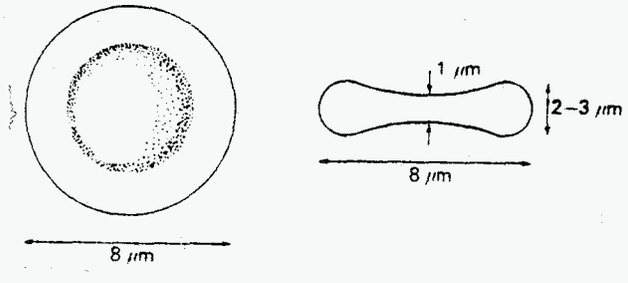
Table 1.1 Cells in blood (From Caro e.a. [1978]).

Cells in blood

Cell	Number per mm^3	Unstressed shape and dimensions (μm)	Volume concentration (%) in blood
Erythrocyte	$4–6\times10^6$	Biconcave disc $8\times1–3$	45
Leucocytes			
Total	$4–11\times10^3$		
Granulocytes			
Neutrophils	$1{\cdot}5–7{\cdot}5\times10^3$	Roughly spherical 7–22	1
Eosinophil	$0–4\times10^2$		
Basophil	$0–2\times10^2$		
Lymphocytes	$1–4{\cdot}5\times10^3$		
Monocytes	$0–8\times10^2$		
Platelets	$250–500\times10^3$	Rounded or oval 2–4	

1.3 Characteristics of red blood cells

Thus the red blood cells (RBC) determine the rheology of blood. They have a concentration, also called the hematocrit (HTC), of 45 %. The red blood cells contain hemoglobine, which gives blood a red color and it carries the oxygen. When the cell is not deformed, it has a concave shape (see figure 1.1), and a specific mass of 1.08 10^3 kg/m^3 (slightly larger then the whole blood). The cell consists of a thin membrane containing a fluid. The cell has no nucleus. The viscosity of the interior fluid is about 6 10^{-3} Ns/m^2, about 5 times the plasma viscosity.



Composition of the red cell

	Percentage of mass
Water	65
Membrane components (protein, phospholipid, cholesterol)	3
Haemoglobin	32
Inorganic:	
Potassium	0·420 g per 100 ml
Sodium	0·025 g per 100 ml
Magnesium	0·006 g per 100 ml
Calcium	small amount

Figure 1.1 *The red blood cell. (From Caro e.a. [1978]).*

The RBC has two important characteristics that influence the flow of blood. First, the cell is strongly deformable (it has a Young's modulus of order 10^5 Nm^{-2} (Bernadin [1986]), compare rubber: 10^6 Nm^{-2}), with high shear stresses it is stretched. The deformation of the red cells becomes significant for shear rates greater then 1 s^{-1}, it reaches a maximal value for $\dot{\gamma} \approx 100$ s^{-1} (Bernadin [1986]). Secondly, at low shear rates ($\dot{\gamma} < 10$ s^{-1}, see for example figure 1.2) the red blood cells aggregate. This is called rouleaux formation. At very low shear rates ($\dot{\gamma} << 1$ s^{-1},

Bernadin [1986]) a three dimensional network can be formed. With increasing shear rate the network is broken down, and the rouleaux are dispersed into individual cells (see also section 1.4). In this regime there exists a structural kinetic process of competing structure breakdown and build-up. For $\dot{\gamma} > 10\ s^{-1}$ no rouleaux exist in steady shear. Figure 1.2 illustrates both effects. Depending on the shear stress, aggregates of undeformed cells are formed, or no aggregates are formed and the cells are undeformed, or the cells are deformed. The formation of aggregates depends on several factors: the surface charges on the cell surface, the concentrations of fibrinogen and globulines (both important for the stopping of a bleeding), and the shape of the cells (only undeformed cells can aggregate).

Summarizing: blood can be considered as a suspension consisting of a Newtonian fluid (plasma) in which deformable non-symmetric particles (the red blood cells) are dissolved that aggregate at low shear rates can form rouleaux; at very low shear rates ($\dot{\gamma} \approx 0\ s^{-1}$) a three dimensional network of rouleaux can be formed.

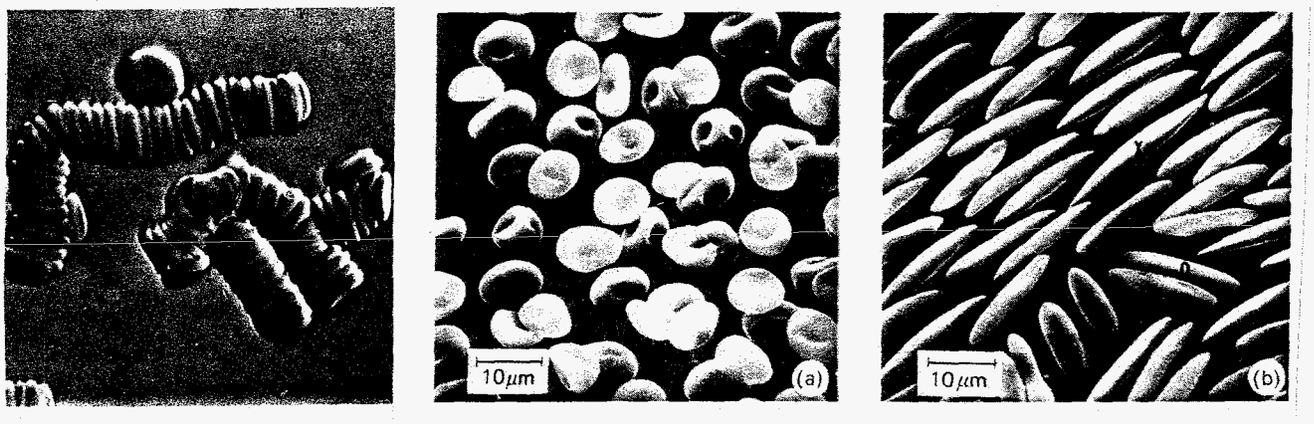


Figure 1.2 *Three states in which the RBC can exist with increasing shear rate: (a) undeformed, aggregated (τ = 0 N/m^2), (b) undeformed, unaggregated (τ = 10 N/m^2), (c) deformed, unaggregated (τ = 300 N/m^2). (From Caro e.a. [1978]).*

1.4 The non-Newtonian behaviour of blood and its microstructural explanation

Shear thinning

In steady shear, blood shows shear thinning behaviour (see figure 1.3). This can be explained as follows. At very low shear rates ($\dot{\gamma} << 1\ s^{-1}$) aggregation of formed rouleaux to a three dimensional network causes relatively high shear stresses. With increasing shear rates, first the network is deformed and broken down; at shear rates $0.1 < \dot{\gamma} < 1\ s^{-1}$ the bending and orientation of the rouleaux result in a further decrease of the viscosity. At higher shear rates ($\dot{\gamma} > 1\ s^{-1}$) the rouleaux are broken down, while for $\dot{\gamma} > 10\ s^{-1}$ no rouleaux exist and with increasing shear rate

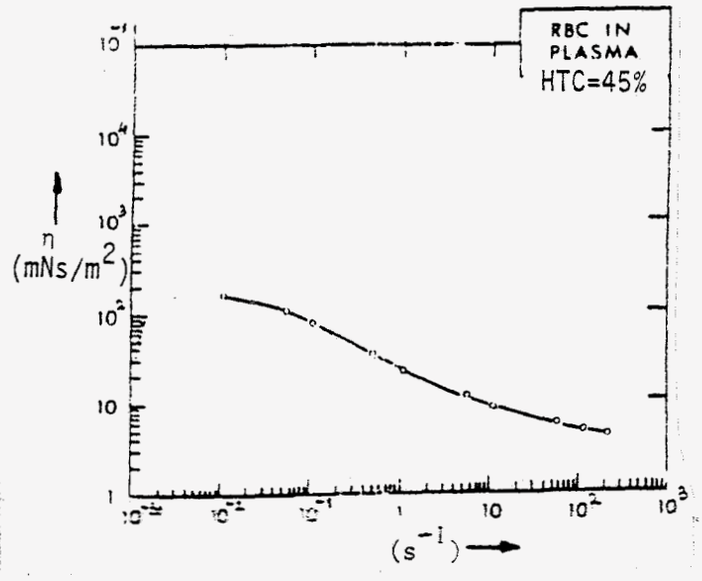


Figure 1.3 *The shear viscosity as a function of shear rate for whole human blood (HTC = 45 %, T = ? °C). (From Chien [1979]).*

the viscosity decreases as a result of the orientation and deformation of the individual red blood cells. For high shear rates ($\dot{\gamma} > 100\ s^{-1}$) the viscosity gets a constant, Newtonian value. The separate influences of the deformation and aggregation on the shear viscosity of blood is illustrated in figure 1.4. The shear rate dependence of the viscosity of blood is often described by a power-law or Casson relation:

power-law: $$\eta = C\,\dot{\gamma}^{n-1} \qquad (1.1)$$

Casson: $$\eta = (\tau_y + 2\tau_y^{\frac{1}{2}}(\eta_c\dot{\gamma})^{\frac{1}{2}} + (\eta_c\dot{\gamma}))/\dot{\gamma} \qquad (1.2)$$

with η the viscosity, C the power-law constant, n the power-law index, $\dot{\gamma}$ the shear rate, τ_y the

yield stress, η_c the Casson viscosity. The Casson model contains a yield stress, this is discussed in the next section. Typical parameter values for human blood are (Baaijens [1991]): C = 0.028, n = 0.63, $\tau_y = 4.8\ 10^{-3}$ N s m^{-2}, $\eta_c = 2.8\ 10^{-3}$ N s^2 m^{-2}.

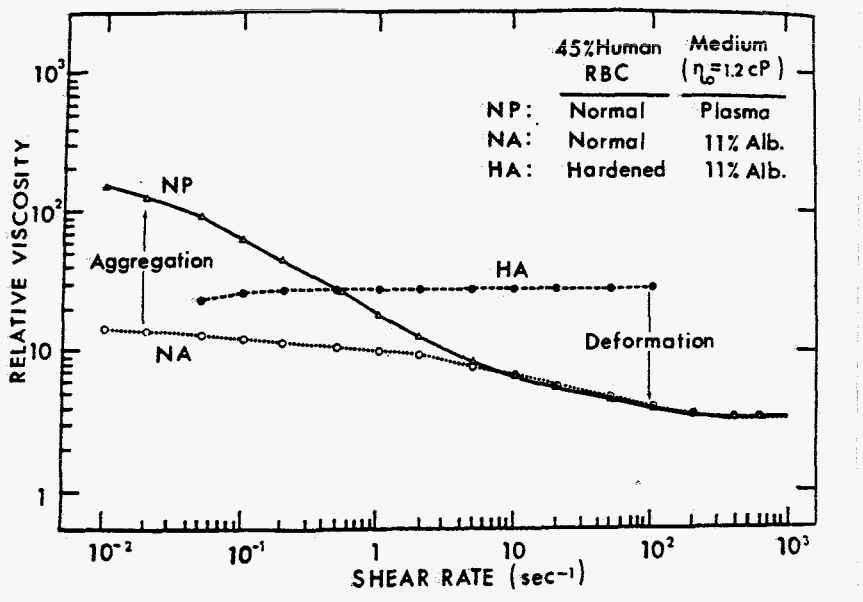


Figure 1.4 *The relative shear viscosity (η/η_0; η_0 = viscosity of the plasma = 1.2 mPas) of whole human blood (HTC = 45 %, T = ? °C) as a function of shear rate; the contribution of deformability and aggregation is indicated. (NP = normal red cells in plasma, NA = normal red cells in isotonic saline containing 11 % albumin (to make suspending medium viscosity the same as plasma viscosity); HA = hardened discoid red cells in the same saline). (From Chien [1970]).*

The influence of the HTC on the shear viscosity is illustrated in figure 1.5.

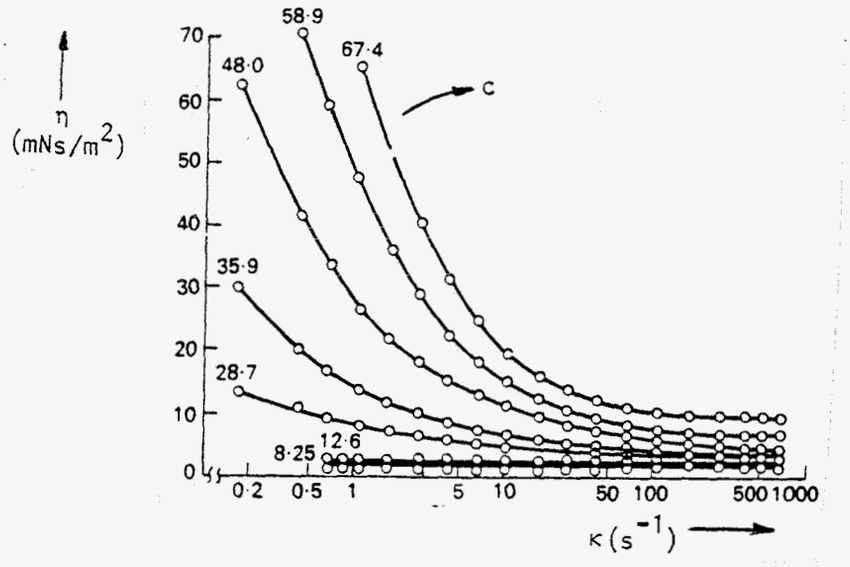


Figure 1.5 *The influence of the HTC on the shear rate dependent viscosity at T = 25 °C. (From Caro e.a. [1978]).*

Yield stress

The property that blood has a yield stress still is a point of discussion. According to Caro e.a. [1978] the yield stress has a magnitude of 1.5 - 5 mN/m^2. However, as discussed for example by Walburn and Schneck [1976], the yield stress was measured only under static loading conditions. They doubt if the yields stress is at all manifest in a dynamic situation (see section 1.3).

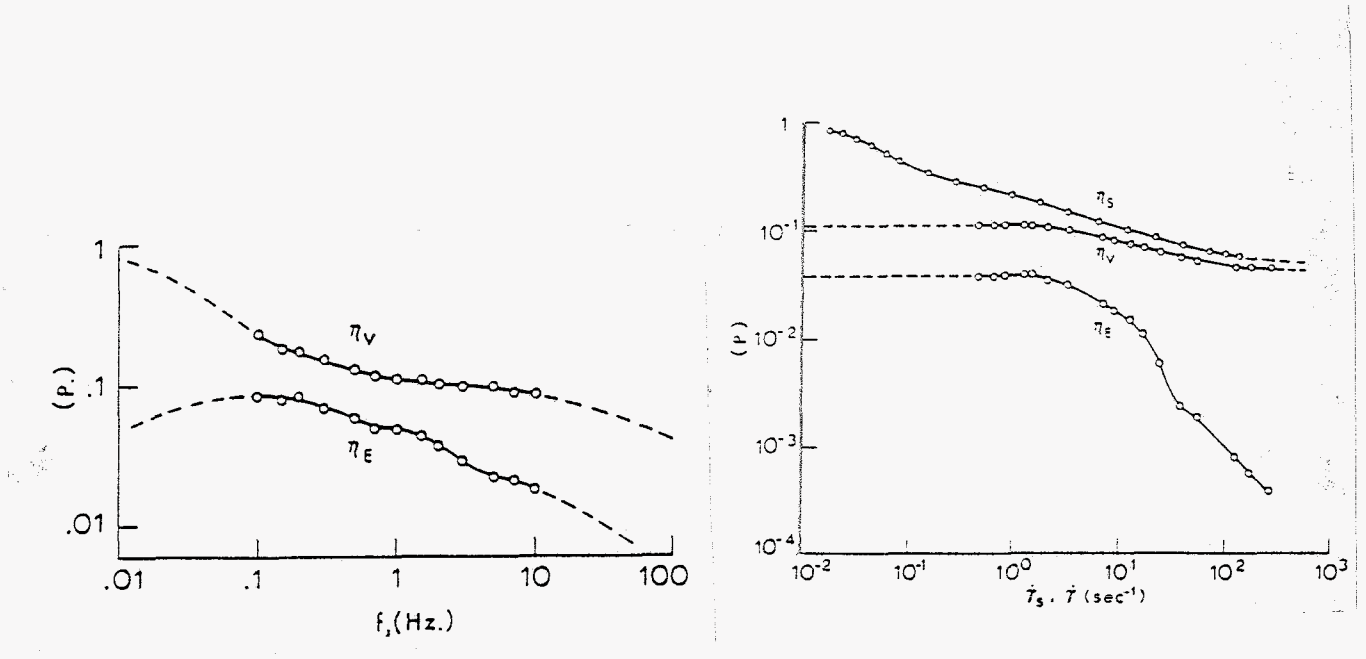
Viscoelasticity

The deformability and capacity of forming aggregates of red blood cells provide a means of storing energy during flow: by deformation of the cell membrane, and by aggregation of the individual blood cells. So blood, in principle, is viscoelastic. Standard measurements quantifying the viscoelastic behaviour are viscometric measurements of the dynamic complex viscosity or its elastic and viscous components (figure 1.6). From this last picture it is evident that blood shows viscoelastic behaviour.

The relation between the complex viscosity of blood and its microstructure is elucidated by the study of Huang e.a. [1975]. They found that blood (40% HTC) for $\dot{\gamma}_0 < 1$ s^{-1} at low oscillation frequency large rouleaux exist, that deform elastically. This leads to a substantial elastic component of the complex viscosity. They also found that with increasing frequency above 0.1 Hz the rouleaux size decreases as well as the value of η_e, probably because of the cyclic deformation. At frequencies of 1 Hz or larger hardly no rouleaux exist in the suspension. Only the deformation and orientation of the individual red blood cells contribute to the elastic component

η''. This is confirmed by figure 1.7 in which the complex viscosity in a RBC suspension in plasma is compared with a RBC in Albumin-ringer. In this latter solution no aggregation can take place; it has a constant η'' that is about 5 times smaller compared with the suspension in plasma. The difference becomes smaller when the frequency increases, as a result of the disaggregation process.

In the same way, the shear rate dependence of the complex viscosity at 2 Hz in figure 1.6b can be explained: at low shear rate amplitudes the cyclic deformation of the rouleaux results in a contribution to the elastic component of the complex viscosity. With increasing amplitude of the shear rate the rouleaux will disaggregate and the deformability of the individual red blood cells results in a lower η''.



a b

Figure 1.6 *a)The elastic and viscous components of the complex viscosity of whole human blood (HTC = 43 %, T = ? °C) as a function of frequency; b) the shear rate dependence of steady flow viscosity, η_s, and viscous and elastic components of the complex viscosity, measured at 2 Hz for the same blood as in a) (From Thurston [1976]).*

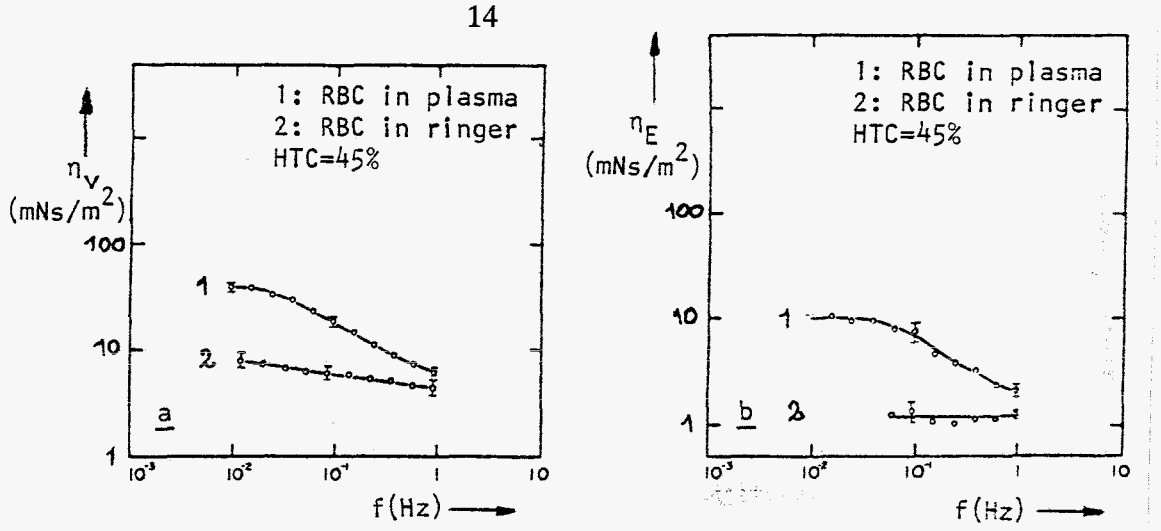


Figure 1.7 *The components of the complex viscosity as a function of frequency in plasma and in a Ringer solution (in which the red cells cannot aggregate); a) η', b) η''. (From Chien [1979]).*

Thixotropy

A third aspect of non-Newtonian behaviour is thixotropy. Thixotropy is the time- dependent behaviour of blood caused by the kinetic structure processes of aggregation and disaggregation during which the blood is in a rheological non-equilibrium state. This phenomenon is studied using transient flow experiments. A sudden step in the steady shear rate is imposed and the shear stress, or the viscosity (time-dependent viscosity) is measured as a function of time. Typical results are presented in figure 1.8. At $\dot{\gamma} = 0.1\ s^{-1}$ a typical phenomenon is visible: a peak value in the shear stress ("overshoot") is measured. For shear steps $\dot{\gamma} < 1\ s^{-1}$ the shear stress decreases after a peak value is reached, with a relaxation time that varies with the shear rate; for $\dot{\gamma} = 1\ s^{-1}$ it is 30-60 s. At higher $\dot{\gamma}$ no stress relaxation is measured. Also measurements are presented of the complex viscosity after a sudden step in the amplitude of the oscillatory shear rate (figure 1.9). In Reher and Vogel [1988] thixotropy is defined as the effect that, when the shearing stress increases with time, the aggregates are dispersed to increasingly smaller aggregates down to the individual cells, whereas with decreasing shearing stress the sizes of the aggregates increase up to the formation of networks. According to Bernadin [1986] the thixotropic behaviour of blood attenuates for $\dot{\gamma} > 10\ s^{-1}$; for shear rates larger than $\pm 25\ s^{-1}$ blood shows no longer thixotropy.

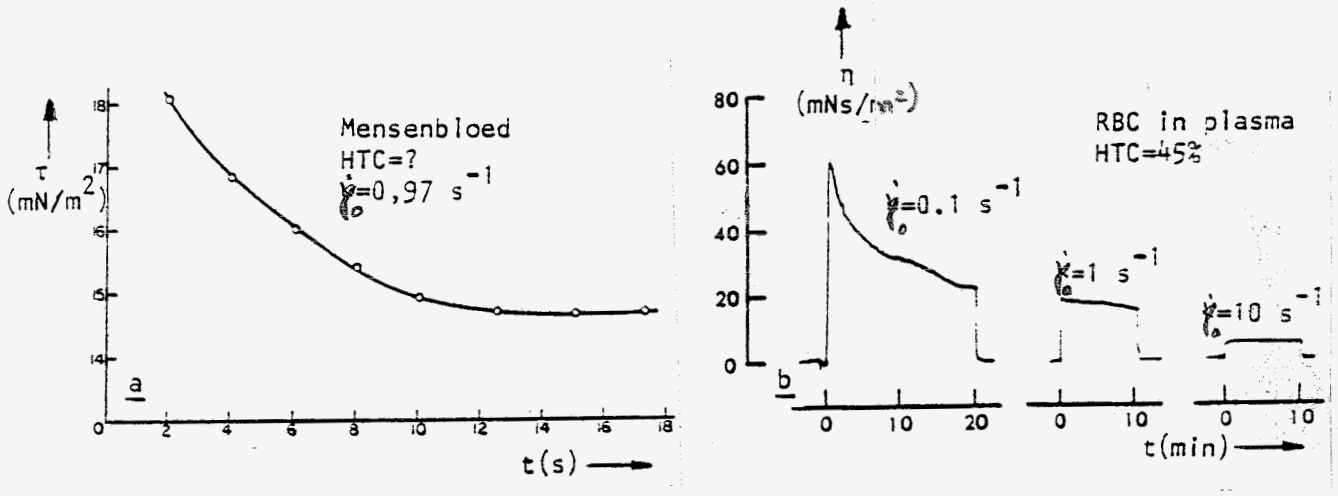


Figure 1.8 *a) Time-dependent shear-stress after a sudden step (from $\dot{\gamma}$ = 0 s^{-1} to $\dot{\gamma}$ = 0.97 s^{-1} in the steady shear rate is imposed for whole human blood (HTC ? %, T = ? °C) (from Huang e.a. [1975]); b) time-dependent viscosity after three different step shears from 0 to $\dot{\gamma}$ = 0.1 s^{-1}, 1 s^{-1} and 10 s^{-1} (HTC = 45 %, T = ? °C) (from Chien [1975]).*

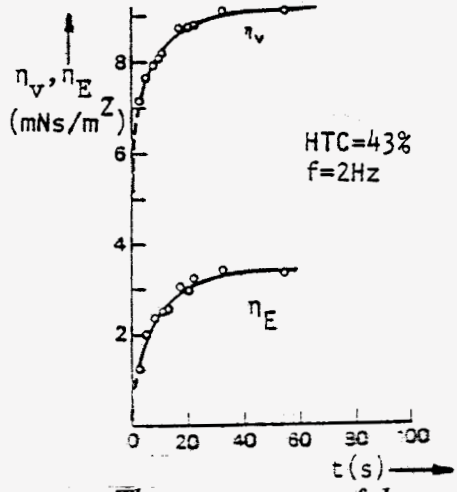


Figure 1.9 *The components of the complex viscosity measured after a sudden step in the shear rate amplitude from $\dot{\gamma}$ = 75 s^{-1} to 25 s^{-1} during an oscillatory flow with f = 2 Hz for whole human blood (HTC = 45 %, T = ? °C). (From Thurston [1979]).*

Normal stress differences

To the best of the author's knowledge, no reliable measurements of first or second normal stress differences for blood exist in literature. Although there have been developed several measurement devices (Whorlow [1980]) , normal stress differences above the measurement accuracy limit of 100 10^{-3} mN/m^2 could not be measured (Copley and King [1975]).

1.5 Non-Newtonian flow and dimensionless numbers

In traditional Newtonian fluid mechanics the definition of the Reynolds number is well known. Because in general a non-Newtonian fluid has no constant viscosity, an alternative definition must be used. Additional to the Reynolds number in non-Newtonian fluid mechanics a Weissenberg number and a Deborah number are defined to characterize the flow. In this section the definitions for the Reynolds number and Deborah number as used in this study in case of the non-Newtonian flow are given.

The Reynolds number definition as used by Hulsen [1990] and Hoitinga [1990] is based on the description of viscoelastic fluids using the Maxwell model (see chapter 2). This model contains a number of, in general, N modes, each having a viscosity η_k. Then a zero-shear viscosity η_0 is defined as:

$$\eta_0 = \eta_s + \sum_{k=1}^{K} \eta_k \qquad (1.3)$$

With this, the Reynolds number is then defined as:

$$Re = \rho\, V\, D/\eta_0 \qquad (1.4)$$

In this definition the Reynolds number is the ratio of inertia stresses (ρV^2) and linear viscous stresses ($\eta_0 V/D$).

Hulsen [1988, 1990] and Hoitinga [1990] define the Deborah number as:

$$De = \text{natural time of fluid/observation time of observer} = t_n/t_o \qquad (1.5)$$

This definition uses the concept of "observation time of observer", which origins from the name "Deborah" that was derived from a bible citate: "The mountains melted from before the Lord", prophetess Deborah, Judges 5:5. The time t_n is defined as:

$$t_n = \lim_{\dot{\gamma} \to 0} N_1/2\dot{\gamma}\tau \qquad (1.6)$$

with $\dot{\gamma}$: shear rate, τ: shear stress. Using the Maxwell model, this results in:

$$t_n = \text{averaged relaxation time} = \lambda_n = \sum_{i=1}^{N} G_i \lambda i^2 / \sum_{i=1}^{N} G_i \lambda i \qquad (1.7)$$

with G_i, λi the elasticity modulus and relaxation time of mode i of the Maxwell model. The observation time of observer t_0 is defined as:

$$t_0 = D/V \qquad (1.8)$$

With this the Deborah number becomes:

$$De = \lambda_n V/D \qquad (1.9)$$

According to Schowalter [1978], *the Deborah number is an inverse measure of time for which the liquid has been tending toward the "fluid like" behaviour of the viscometric flow.*
Schowalter [1978] defines the Weissenberg number as:

$$We = \text{first normal stress difference/shear stress} \qquad (1.10)$$

and:

$$We = \theta V/D \qquad (1.11)$$

with:

$$\theta = \int_0^\infty \dot{\gamma} N_1 \, d\dot{\gamma} / \int_0^\infty N_1 \, d\dot{\gamma} \qquad (1.12)$$

This definition is interpreted by Schowalter as: *the Weissenberg number is a measure of the relative importance of elastic (represented by θ) and viscous forces (represented by V/D).* If one chooses $\theta = \lambda$, then We = De. Thus, although the Deborah number number originally was meant to be a measure for the extent of which the viscous behaviour of the fluid is manifest, and the Weissenberg number a measure for the extent to which the elastic behaviour of the fluid was manifest relatively to the viscous behaviour, in many cases the working definitions are equivalent. In literature different authors do not make a distinction between those two numbers (see appendix), and usually the above interpretation of the Weissenberg number is meant. A low Weissenberg number means: the elastic behaviour of the fluid is not manifest, the viscous properties dominate;

a high Weissenberg number means that the elastic behaviour is dominating.

1.6 Characteristics of the physiological flow situation

In this study the physiological flow geometry is a two dimensional model of the carotid artery bifurcation, see figure 1.8. This geometry, as determined by Bharadvaj [1982]

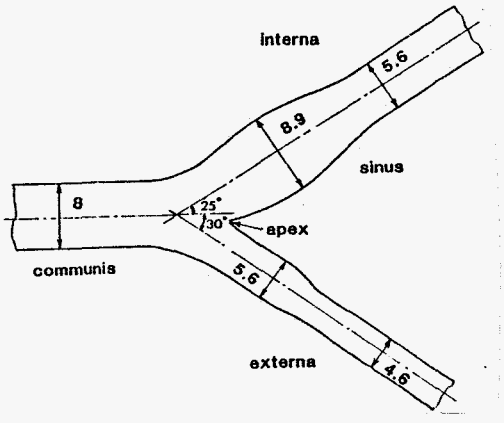


Figure 1.10 *The two dimensional model of the carotid artery bifurcation as determined by Bharadvaj. (From Bharadvaj [1982]).*

from 100 angiograms, is a simplification of the real three dimensional geometry. However, because of the stage of the research on this subject and the available numerical algorithms, the two dimensional model will be used. The physiological flow is an unsteady pulse cycle. As presented by Rindt [1989] during this cycle the Reynolds number varies between 200 and 800 as is shown in figure 1.11. The time averaged mean value of this Reynolds number is 300. Rindt assumed blood to behave as a Newtonian fluid, thus the Reynolds number was defined using the high shear rate constant viscosity, equation (4). From (1.4) with η/ρ = 3.4 10^{-6} m^2/s and D = 0.008 m (the communis carotid diameter) it follows that the average fluid velocity in the communis is 0.13 ms^{-1}. Using the data of Bernadin e.a. [1987] who fitted a modified Bird-Carreau model to blood data (see chapter 2) a characteristic relaxation time of blood is λ = 5 s. With this the Deborah number, that is associated with the viscoelastic character of blood, has a value of about 68 in this situation. This is a high Deborah number: in viscoelastic flow literature values up to 10 are usual, and until developments made recently (values up to 300 are found by Hoitinga [1990] for example) this flow situation would have been impossible to calculate numerically. This will be discussed later in chapter 2.

Anticipating the constitutive models for blood as will be discussed in section 2.4, an important question is: what kind of structure has blood in the physiological flow situation of interest?

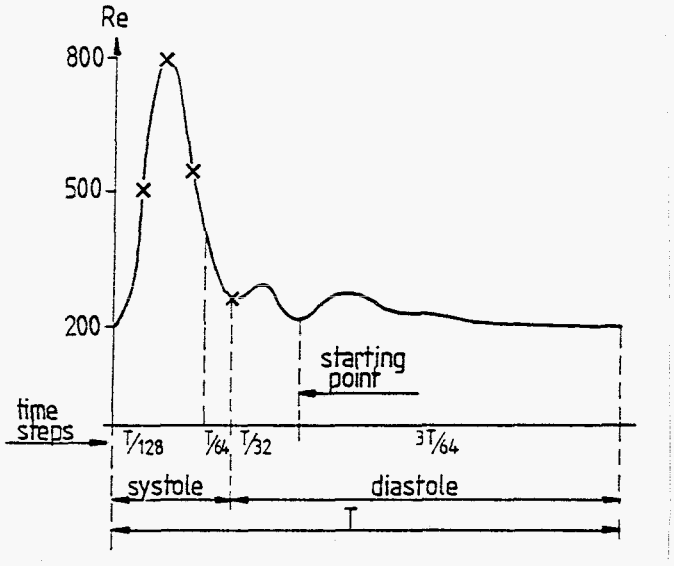


Figure 1.11 *The Reynolds number during one physiological pulse cycle according to Rindt. (From Rindt [1989]).*

Does the aggregation - disaggregation process take place in the human carotid artery bifurcation, or do only dispersed blood cells exist? According to Bernadin [1987] deformation of the 3D network influences the rheological behaviour of blood in particular at low shear rates. Rosenblatt e.a. [1986] state that the rouleaux can be considered as cilindrical, without branches; branches get loose at very low shear rates, as they state. From the considerations in section 1.2 the rouleaux do not exist when $\dot{\gamma} > 10\ s^{-1}$, and in oscillatory shear flow with a shear rate $\dot{\gamma} < 1\ s^{-1}$ they are increasingly broken down for frequencies above 0.1 Hz, and are completely dispersed at 1 Hz.
In the following, to get an idea of the actual shear rates in a large artery, some results of Newtonian flow studies in models of the carotid artery bifurcation as found in literature will be discussed with the attention focused on the appearing shear stresses. First the results of Ku and Giddens [1987] are of interest. They presented measurements of Laser Doppler Anemometer measurements of steady and pulsatile flow in a three dimensional model carotid bifurcation. The Reynolds number definition used was $Re = 2Q/R\nu$, where Q is the volume rate, R is the tube radius, and ν is the blood kinematic viscosity, giving values 300 for the mean and 800 for the peak Reynolds number. The unsteadiness Womersley parameter α ($= R(\omega/\nu)^{\frac{1}{2}}$ was 4.0 ($\omega = 5.84$ rad s^{-1}). It appeared that the mean wall shear rates during a cycle are mostly of order $10^2\ s^{-1}$, the peak values even of of order $10^3\ s^{-1}$. One should realize that the presented mean values are time averaged mean values of $\dot{\gamma}$, while in case of the rouleaux formation mean values of $|\dot{\gamma}|$ are of interest in which case much larger values would have been found. These results are confirmed by the results of v.d Vosse e.a. [1990]; they found in a two dimensional numerical analyses of unsteady flow in the carotid artery bifurcation wall shear stresses with a magnitude of order $10^2\ s^{-1}$ - $10^3\ s^{-1}$. There is no data of the variation of the shear rate in a two or three dimensional

model of the carotid bifurcation along a particle trajectory in steady or unsteady flow. The wall shear stresses are in general much larger then those in the internal of the geometry. However no such data is available. Rodkiewicz e.a. [1990], who considered the pulsatile flow of blood in a conduit, showed that the actual shear rates in a femoral artery are predominantly low ($\dot{\gamma} < 100$ s^{-1}). High shear rates occur only during a relatively short part of the cycle period, and mainly close to the wall (this is illustrated in table 1.2). They conclude that blood behaves predominantly as a non-Newtonian fluid.

On the ground of the above it is very reasonable to assume that in the physiological flow case no rouleaux exist; only individual blood cells will be present. Although low shear rates ($\dot{\gamma} < 10$ s^{-1}) may exist during a certain period of the physiological pulse cycle, for example in the recirculation area, there is probably not enough time for the aggregation proces to take place (in steady flow the characteristic process time for rouleaux formation at $\dot{\gamma} = 1$ s^{-1} is about 30 - 60 s^{-1}, see figure 1.8b).

In the steady flow case at Re = 300 there may rouleaux be present locally. The absence of high pulse shear rates with $\dot{\gamma} >> 100$ s^{-1} and the steady character of the flow may provide the opportunity of rouleaux to survive.

Table 1.2 The shear rates measured in the femoral artery during the cycle of a physiological pulsatile pressure gradient (HTC = 45 %, T = ? °C). (From Rodkiewicz [1990]).

Shear rates for Newtonian fluid

r \ t	0	π/8	π/4	3π/8	π/2	5π/8	3π/4	7π/8	π	9π/8	5π/4	11π/8	3π/2	13π/8	7π/4	15π/8	2π
0.9375	132.59	466.86	1179.29	1176.83	817.14	97.30	253.21	350.80	208.43	142.87	158.93	48.69	46.02	41.25	21.57	117.61	132.58
0.8750	112.50	325.87	933.89	1030.79	642.49	203.66	129.43	283.76	189.11	137.70	144.94	63.34	19.55	29.79	19.05	86.08	112.50
0.8125	94.16	230.52	738.05	890.32	634.18	274.96	30.57	185.19	161.90	127.74	131.39	71.23	0.47	18.68	15.37	63.19	94.15
0.7500	78.03	161.74	577.61	759.51	603.30	317.49	45.26	117.03	131.20	114.32	117.90	74.13	14.97	8.73	11.17	46.72	78.02
0.6875	64.20	112.31	451.43	641.05	558.24	337.08	100.47	80.21	100.22	98.85	104.42	73.39	24.85	0.38	6.93	34.99	64.20
0.6250	52.56	77.00	351.41	535.92	506.17	338.90	137.73	14.82	71.24	82.62	91.11	70.04	30.96	5.19	3.03	26.68	52.55
0.5625	42.86	51.97	272.41	444.00	448.50	327.37	159.73	19.58	45.72	66.69	78.19	64.89	34.02	10.98	0.31	20.79	42.86
0.5000	34.82	34.39	210.19	364.48	391.23	306.08	169.05	43.81	24.51	51.90	65.91	58.58	34.89	14.09	2.94	16.56	34.82
0.4375	28.16	22.19	161.24	296.10	335.29	277.83	168.01	58.92	6.00	38.82	54.49	51.60	33.52	15.70	4.79	13.44	28.16
0.3750	22.60	13.86	122.71	237.50	281.77	245.16	158.70	66.08	3.83	27.78	44.09	44.30	30.95	15.99	5.89	11.03	22.59
0.3125	17.89	8.29	92.25	187.20	231.17	209.37	142.89	66.46	11.24	18.91	34.79	36.94	27.35	15.18	6.26	9.03	17.89
0.2500	13.83	4.69	67.95	143.71	183.52	171.72	122.06	61.23	14.70	12.15	26.56	29.67	23.02	13.47	5.99	7.25	13.83
0.1875	10.24	2.47	48.23	105.55	138.47	132.91	97.41	51.49	14.77	7.29	19.36	22.57	18.15	11.05	5.17	5.57	10.24
0.1250	6.96	1.18	31.69	71.20	95.26	93.17	69.77	38.19	12.12	4.00	12.94	15.61	12.89	8.06	3.90	3.90	6.96
0.0625	3.80	0.47	16.91	38.63	52.35	51.79	38.30	21.96	7.36	1.83	6.97	8.60	7.22	4.59	2.26	2.17	3.80
.0000	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Thus: non-Newtonian aspects of the flow of blood in large arteries are expected to be primary determined by the deformation and orientation of the individual red blood cells. Under unsteady physiological conditions no rouleaux will exist, while in the steady case they may exist in local areas.

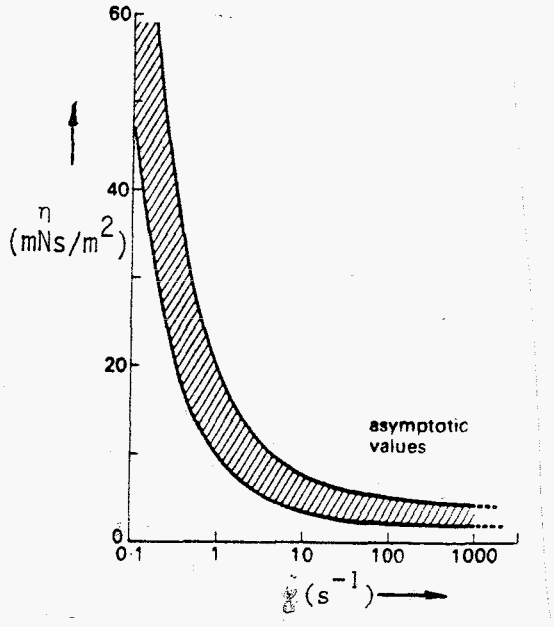


Figure 1.10 *Spread in steady shear viscosity in blood from different human beings. (From Caro e.a. [1978]).*

Another factor in studying the flow of blood is the spread in the value of the viscometric functions among blood from different human beings. This spread determines the degree of accuracy of the modelparameters and thus the meaningful accuracy of the models and experiments that will be done. However, at this point no good information is yet found, except for the steady shear viscosity data presented in figure 1.10 (the viscosity values differ from 20% at $\dot{\gamma} < 1\ s^{-1}$ to 70% at $\dot{\gamma} > 100\ s^{-1}$, and the data of Rosenblatt e.a. [1986], fig. 2.11 - 2.14). Here, the error bars for the peak values of the stresses are about 20 % - 40 % large.

1.7 Summary

Blood can be considered as a suspension consisting of a Newtonian fluid (plasma) in which deformable non-symmetric particles (the red blood cells) are solved that aggregate in the unloaded situation. From experiments it was found that blood exhibits non-Newtonian behaviour: *shear-thinning*, usually described by a power-law or Casson model; *yield stress*, although this is very small or not existing, especially in a dynamic situation; *viscoelasticity*, as it appears from the existence of an elastic component of the complex viscosity; *thixotropy*, the time dependent behaviour of blood caused by the kinetic structure processes of aggregation and disaggregation which is manifest at low shear rates ($\dot{\gamma} < 10\ s^{-1}$); *normal stress differences* are to small to be measured. Non-Newtonian flow can be characterized by a Reynolds number, a Deborah (Weissenberg) number, and a Womersley parameter. In case of a physiological flow situation, i.e. the carotid artery bifurcation, during one physiological pulse cycle the Reynolds number varies

between 200 and 800, with an time averaged mean value of 300. From this averaged Reynolds number and additional parameters, the Deborah number was found to be about 68, which is very high and thus the problem is rather complicated. In this study a two dimensional model of the bifurcation will be used. Non-Newtonian aspects of blood flow in large arteries are probably primary determined by the deformation, orientation and collision of individual red blood cells. Under physiological conditions no rouleaux exist, in the steady case they do may exist. There is a spread in the values of the viscosity among different blood donors of 20% at low shear rates to 70% at high shear rates, which limits the meaningful accuracy of calculations or experiments.

2 Constitutive models for blood

2.1 Introduction

In this chapter a survey is given of the constitutive models that have been presented in literature being used or proposed to describe the flow behaviour of blood. Many constitutive models are proposed to describe blood rheological behaviour, varying from very simple to very complex models. This will be outlined in section 3.2. Our main interest is to apply such a model in order to describe the flow of blood in large arteries, especially those with bends and bifurcations. One of the reasons that merely simple models have been used with the description of non-Newtonian blood flow in more complex situations, i.e. complex geometry and/or time-dependent flow, is the fact that numerical problems are associated with complex rheological models. However, recent developments in the viscoelastic flow theory have lead to new algorithms that in testproblems have given very promising results (see section 2.4). An other reason for using simple constitutive models is the argument that in case of blood flow in large arteries (diameter > 500 μm) high shear rates ($\dot{\gamma}$ > 1000 s^{-1}) occur, and therefore the Newtonian assumption is valid. However, in case of bends and bifurcations flow recirculation and separation occurs with low shear stress areas which may give rise to significant differences with the Newtonian case. Basic numerical non-Newtonian results of Hogan and Henriksen [1990], Rodkiewicz e.a. [1990] and Baaijens [1991] show significant differences with the Newtonian case. In section 2.3 some results of calculations with time-independent models are discussed; in section 2.4 the major interesting papers dealing with viscoelastic constitutive models proposed for blood are reviewed more detailed. In rheology, especially in case of the polymer rheology, many models exist that may provide a good description of the flow of blood. Because of the intention to use the finite element software package SEPRAN [1984] for numerical calculations, all available models in this package will be discussed in section 2.5. Fortunately these models include almost all models that are of importance in viscoelastic flow theory, or the implementation can be extended in a rather simple way to include missing ones. Finally, a discussion in section 2.6 will point out which constitutive models are most suitable for our purpose.

2.2 Survey of constitutive models for blood

The models are divided into two groups:

a) time-independent models,

b) time-dependent models.

The first group of models are models that model only the shear-thinning behaviour, but no memory effects (i.e. the history of deformation does not influence the present stresses). These models are only accurate in situations that are dominated by a shear rate dependent viscosity. In

flows with accelerating and slowing down of material elements, as can also be the case in a time-independent two dimensional flow with sharp corners in the geometry or with flow reversal areas, these models may not be adequate to describe non-Newtonian flow behaviour. The shear stress-shear strain relations can be extended to three dimensional tensor relations between the Cauchy stress tensor and the rate of deformation tensor (an exception in table 2.1 is the micropolar continuum model, that is not a simple shear stress - shear strain relation, see next section 2.3 for a review of this model). Especially the Casson model has been used very frequently for describing blood flow. In section 2.3 some results of calculations of flows with shear thinning models will be discussed.

The second group of models include memory effects, and have more or less a microstructural basis (not all theories are as solid on this point; for example the parameters of the Maxwell model have no clear physical interpretation).

In table 2.2 a list of all the mathematical expressions of the time-independent models listed above are presented. Easthope [1980] has compared eleven different time-independent constitutive equations, with all a hematocrit dependence (the models originally without a HTC dependence, were extended with that), some of them are present in the list above. The Walburn and Schneck model was found by Easthope [1980] to fit the experimental data best. The Quemada equation was also satisfactory, it has the advantage that its parameters have some physical meaning.

In table 2.2, a list with time-dependent constitutive models is given, but no mathematical expressions. These will be presented in section 2.2 for the major interesting cases. In table 2.3 all the models from table 2.1 and 2.2 are listed and some additional information (references, flow studies†) to clarify the way and extent the models have been used for describing blood. As is clear from table 2.3, the number of flow studies is limited, and only non-viscoelastic models have been used, mostly a generalized Newtonian model (Casson, Bingham, power-law, Walburn and Schneck).

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† With "flow study" is meant here: a study of a complex two-dimensional time-independent flow field, for example the flow in a two-dimensional artery; thus not a viscometric flow nor transient response such as stress growth or stress relaxation.

Table 2.1 Time-independent constitutive models for blood

MODEL	EQUATION
Power-law:	$\tau = \eta\, \dot{\gamma}^n$
Casson:	$\lvert\tau\rvert^{\frac{1}{2}} = \tau_y^{\frac{1}{2}} + (\eta_c\dot{\gamma})^{\frac{1}{2}}$
Bingham:	$\tau = \tau_y - \eta_b\dot{\gamma}$
Walburn-Schneck:	$\tau = C_1\exp(C_2H)\exp(C_4(TPMA/H^2)](\dot{\gamma})^{1-C_3H}$
Quemada	$\tau = x_4[(1 + (x_1\lvert\dot{\gamma}\rvert)^{-\frac{1}{2}})/(1-x_2\,H + (1-x_2\,x_3\,H)(x_1\lvert\dot{\gamma}\rvert)^{-\frac{1}{2}})]^2\dot{\gamma}$
biviscosity	$\tau = 2(\mu^B + p_y/(2\pi)^{\frac{1}{2}})\dot{\gamma},\ \pi > \pi_c,\ \tau = 2(\mu^B + p_y/(2\pi_c)^{\frac{1}{2}})\dot{\gamma},\ \pi < \pi_c$
Phillips-Deutsch	$\tau = x_1\exp(x_4)[(1+ x_2\dot{\gamma}^2)/(1+ x_3\dot{\gamma}^2)]\dot{\gamma}$
Herschel-Bulkley	$\tau = (-K\dot{\gamma})^{\frac{1}{n}} + \tau^h,\ \tau \geq \tau^h;\ \tau = \tau^h,\ \tau \leq \tau^h$
Huang-Fabisiak	$\tau = \eta_{plasma}\,\dot{\gamma} - cA\dot{\gamma}^n\exp(-c\dot{\gamma}^n t_0)$
micropolar continuum theory	

Table 2.2 Time-dependent constitutive models for blood

MODEL	PAGE
Charara	
Rosenblatt	
Maxwell	
Four constant Oldroyd	not discussed, see Phillips and Deutsch [1977]
Reher-Vogel	
modified Bird-Carreau	

Table 2.3 Survey of constitutive models used for blood and their applications

MODEL	FLOW STUDY	OTHER REFERENCES
Non-viscoelastic models:		
Power-law	Chaturani and Palanisamy [1990] Baaijens [1991], Perktold e.a. [1989]	
Casson	Baaijens e.a. [1991], Perktold e.a. [1989], Oka and Nakai [1989], Wang e.a. [1989], Chaturani and Palanisamy [1990]	
Bingham	Rodkiewicz e.a. [1990]	
Walburn-Schneck	Rodkiewicz e.a. [1990]	Easthope and Brooks [1980], Walburn and Schneck [1976]
Quemada biviscosity	Wang e.a. [1989]	
Phillips-Deutsch		Cokelet [1981]
Herschel-Bulkley	Chaturani and Sami [1985]	
Huang-Fabisiak	-	Easthope and Brooks [1980]
micropolar	Hogan and Henriksen [1990]	Skalak and Tözeren [1981]
couple stress	Sinha and Singh [1984] Srivastava [1985]	

Table 2.3 continued:

Viscoelastic models:		
Charara	--	Charara e.a. [1985]
Rosenblatt	--	Rosenblatt [1986]
Maxwell model	--	Thurston [1979]
Oldroyd model	--	Phillips-Deutsch [1977]
Reher-Vogel	--	Reher and Vogel [1988]
modified		
Bird-Carreau	--	Bernadin e.a. [1987]

2.3 Some results of calculations with time-independent shear thinning constitutive models

In this section attention is paid to the results of numerical calculations with constitutive models that only model the shear-thinning behaviour of blood. But first, the the background of the Walburn and Schneck model is discussed.

Walburn and Schneck [1976]

The aim of this study was to develop a constitutive equation that includes parameters that represent significant blood properties. As a starting point a power-law $\tau = k\ \dot{\gamma}^n$ was chosen. Discussing the validity of this equation, Walburn and Schneck argue that although a yield stress has been observed for blood, this was only under static loading conditions. They doubted that the yield stress is at all manifest in a dynamic situation, because, as they state further, though fluid velocities and velocity gradients pas routinely through zero in an oscillatory flow situation, there is probably not enough time for static phenomena to appear. These statements seem very reasonable, however no experimental data to support them is provided. The parameters k and n were assumed to be constant for a given hematocrit level and a given chemical composition. The parameters investigated in this study were hematocrit, the total lipids, albumin, and total protein minus albumin (TPMA). TPMA is composed of fibrinogen and the globulines. These chemical variables were chosen because they are composed of long chain asymmetric molecules which exist in blood in large numbers and interact more than symmetric particles do. Therefore, according to Walburn and Schneck, it was expected that they contribute most to the rheological properties of the fluid. Analyzing the viscometric data of shear stress - shear rate measurements they considered the four parameters mentioned above together with the shear rate to be the

independent variable and the apparent viscosity was considered to be the dependent variable. In reality this assumption may not be true, because "in the cardiovascular system of man blood is constantly changing in chemical composition and shear rate and the interrelations are many and complex" as Walburn and Schneck state. However, to them the assumption seemed to be reasonable as a first approximation. Using a multiple regression computer procedure, the variables of greatest significance were determined. The eventually resulting constitutive equation, that fitted the experimental data the best, is called the Walburn and Schneck model, and is given by:

$$\tau = C_1 \exp(C_2 H) \exp[C_4(TPMA/H^2)](\dot{\gamma})^{1-C_3 H} \text{ dyne/cm}^2 \qquad (2.1)$$

with: $C_1 = 0.00797$, $C_2 = 0.0608$, $C_3 = 0.00499$, $C_4 = 145.85$ dl/g, H = hematocrit, TPMA = total protein minus albumin.

Hogan and Henriksen [1990]

Hogan and Henriksen [1990] have used a micropolar constitutive model to describe the rheological behaviour of blood. The micropolar theory is essentially a modification of the classical continuum mechanics: each particle in the suspension can have a rotation independent of the classical rotation of the surrounding fluid. The theory is applied to the flow through a blood vessel with a stenosis, not only because of its clinical relevance, but also because of the relatively large velocity gradients existing near the stenoses that in principle amplify the micropolar effects.In the calculations (using the Finite Element Method (FEM)), blood has been treated as a Newtonian fluid and a micropolar fluid. It seems that this model is only appropriate in case of arteries with a diameter from about 0.3 mm to 0.5 mm; in arteries with larger diameters it seems to be equivalent with the Newtonian model. From the results of the numerical calculations it is concluded that micropolar fluids exhibit greater resistance to flow than do classical fluids of equivalent shear velocity. This increased flow resistance is a consequence of the relative rotation between microspin and vorticity. The calculations further showed that there is no essential difference between the Newtonian model and the micropolar model in case of the streamline picture. However, the question of whether a micropolar fluid is a more accurate model for whole blood (in case of the mentioned artery size) is not yet answered for several reasons. First, because there are no experimental data of measurements of the wall shear stresses in a vessel with a stenosis with blood as the working fluid. Second, in this article no calculations were presented of standard tests of constitutive theories: the dynamic loss and rigidity moduli, and the steady shear viscosity. Finally, this study was restricted to the steady flow situation.

Rodkiewicz, Sinha, Kennedy [1990]

In this recent article four constitutive models for blood are used: the Newtonian model, Casson, Bingham, and Walburn and Schneck model. These models are applicated to the pulsatile laminar flow of a fluid through a very long tube of radius R. The flow was assumed to be axial symmetric and fully developed, the fluid was incompressible, gravitational forces were negligible, and the temperature was uniform. Using in the pulsatile flow situation the models mentioned above being valid only for the steady state case in principle means that the assumption is made that blood belongs to the category of suspensions in which the particle rearrangement is achieved very rapidly. In case of the steady state flow situation, analytical solutions for all models were obtained. Significant, but small (< 5 %) differences between the different models were found.

Solutions for the pulsatile flow situation in all cases were calculated by the finite difference method. Now very remarkable differences were found as is evident from the figures 2.1 and 2.2. In these plots several dimensionless parameters are used: dimensionless time $t^+ = 2\pi t/T = \omega t$ (T: time period, ω = frequency), dimensionless velocity $w^+ = w/(\nu_a/R)$ (ν_a: apparent kinematic velocity) with maximal value w^+_{max}, dimensionless radial coordinate $r^+ = r/R$ (R: tube radius). All the results are obtained for a pressure gradient pulse which is representative of the actual pulse that exists in an artery. They are a function of the flow rate Q, the frequency parameter α $(=R(\omega/\nu_a)^{\frac{1}{2}})$ and the pressure gradient. The results for the Casson and Bingham model depend on an additional parameter, the yield stress, whereas the results for the Walburn and Schneck model are functions of the hematocrit concentration and TPMA. The following data were used: radius of the femoral artery = 0.003 m, blood viscosity = 7.97 10^{-3} Pa s, blood density = 1133 kg/m^3, pulse frequency = 1.2 Hz, flow rate = 1140 ml/min, average hematocrit = 40 - 45 percent, average TPMA = 30-40 g/l. Figure 2.1 describes the manner in which the velocity pulse would travel during part of a cycle, it shows the velocity as it alters from a diastole to systole. Note the large differences between the Newtonian, Bingham, and Casson model on the one hand and the Walburn and Schneck model on the other. Negative velocity ratios indicate a flow reversal at the start or end of each pressure gradient pulse. Large differences between the two groups of models also exist at $t^+ = 0, 3\pi/8, 3\pi/4$ (not shown here).

The shear stress at the wall also shows remarkable differences, the Walburn and Schneck model gives much lower shear stresses then the other models, see figure 2.2.

Rodkiewicz e.a. mention some experimental results which confirm their calculations. However one must be careful interpreting the results, because the Walburn and Schneck model is developed using experimental data acquired at low shear rates. Thus at locations where high shear rates appear, the present solutions might not be valid. Also, the assumption the Walburn and Schneck model being valid in case of the time dependent flow situation may cause differences with the actual situation. No explanation for the remarkable difference between the Walburn and Schneck

model on the one hand and the Newtonian model, Bingham and Casson model on the other hand is given.The authors conclude that experiments are needed to validate their results.

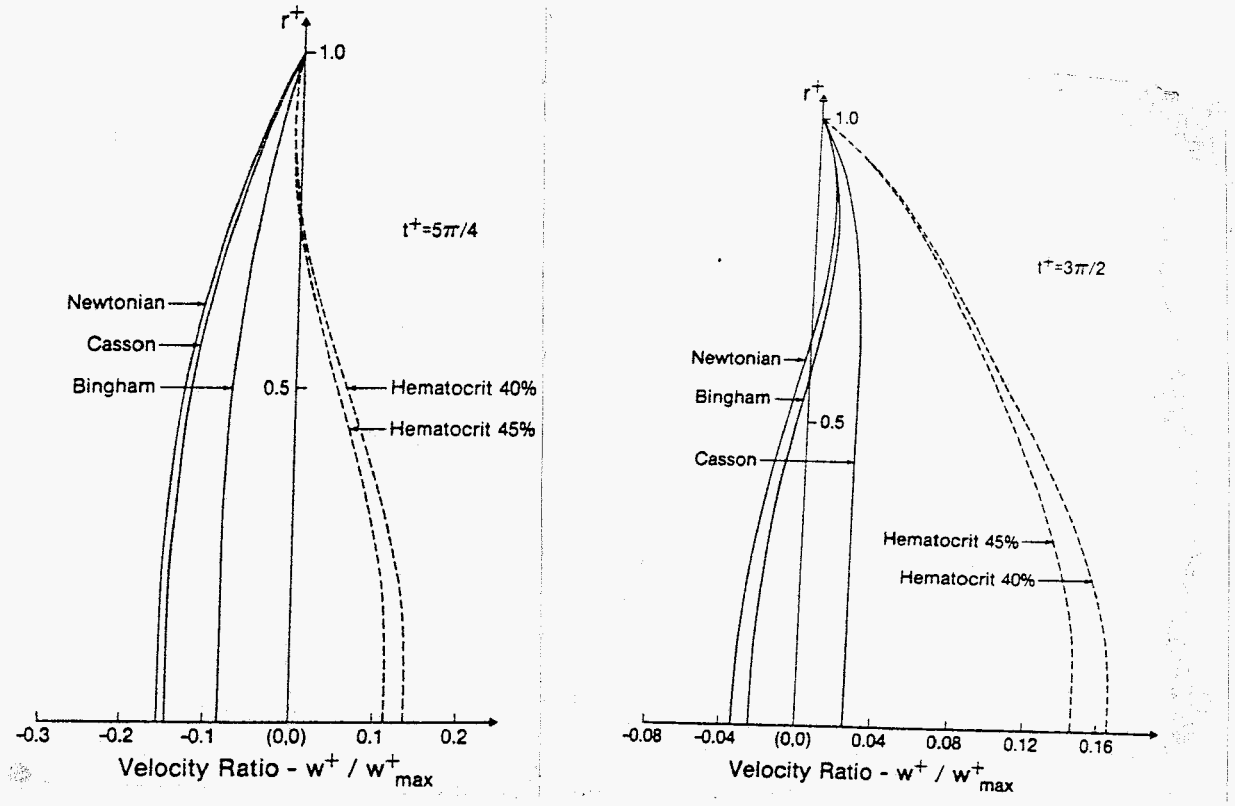

Figure 2.1 *The velocity ratio's as a function of the radius at t^+ = (a) $5\pi/4$, (b) $3\pi/2$ (from Rodkiewicz e.a. [1990]).*

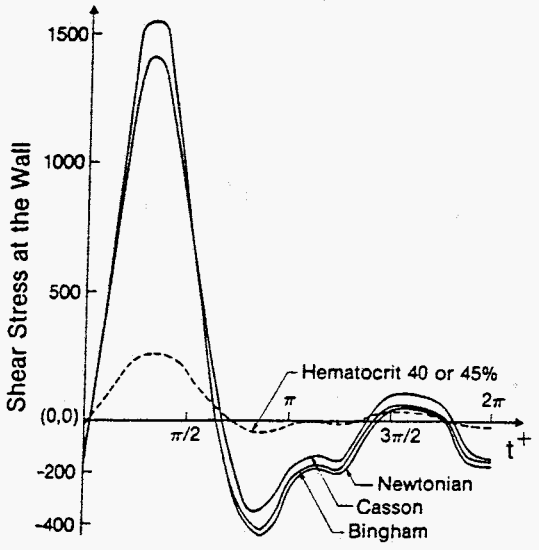

Figure 2.2 *The shear stress at the wall for the four models as a function of time during one cycle of the pulsatile pressure gradient. (From Rodkiewicz e.a. [1990]).*

Perktold e.a. [1990]

Perktold e.a. calculated using a finite element method the pulsatile flow of blood through a two dimensional bifurcation with an aneurysm, see figure 2.3.

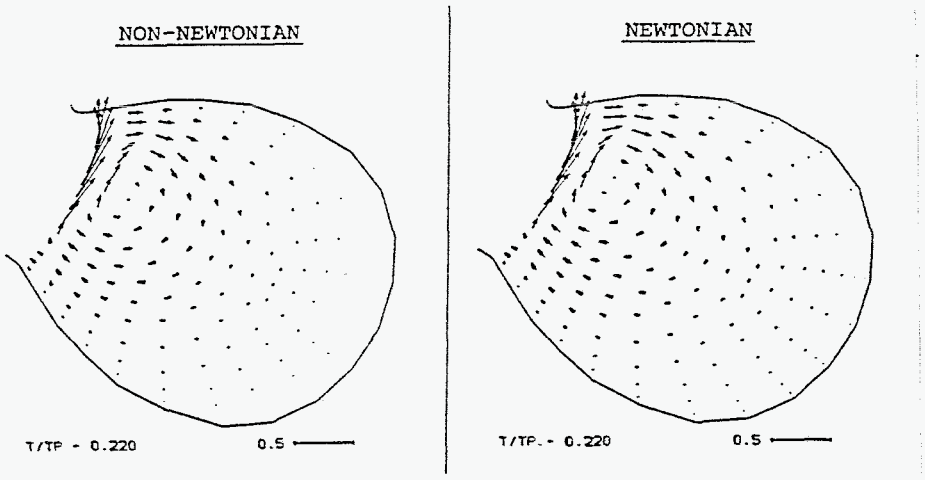

Figure 2.3 *Comparison of calculated pulsatile velocities in the two dimensional bifurcation with an aneurysm, in the aneurism, using the non-Newtonian Casson model and the Newtonian model at Re = 150 at maximum flow rate. (From Perktold e.a. [1990]).*

They used a Casson equation to describe the shear thinning behaviour of blood. Typical results are displayed in figure 2.3 for Re = 150.It is clear from the above figure that the differences between the two used models are minimal.

Baaijens e.a. [1991]

Baaijens e.a. studied numerically (FEM) the steady flow of blood in a two dimensional model of the carotid artery bifurcation with Re = 300, using a Newtonian model, a power-law model and a Casson model. Typical results are displayed in figure 2.4. It is clear that only minor differences (< 5 - 10 %) in the axial velocities are found using a generalized Newtonian (shear thinning) model and a Newtonian model. Wall shear stresses and pressure values can locally differ up to 40 % and 25 % respectively. But in general the flow structure is not altered by using a generalized Newtonian model.

Summarizing: In general the generalized Newtonian models (Casson, Bingham, power-law), give no essential differences in the flow structures in bifurcations and large arteries compared with the Newtonian model, in both steady and unsteady flow. Local, significant differences in velocity, pressure and wall shear stresses can exist. The micropolar model has only been used in a steady flow, but it gives the same kind of results; it seems to appropriate only in case of arteries with a diameter of 0.3 to 0.5 mm. The most remarkable result is that the Walburn and Schneck model

does give essential differences in pulsatile flow through a straight tube compared with the Newtonian model; no explanation is given for this.

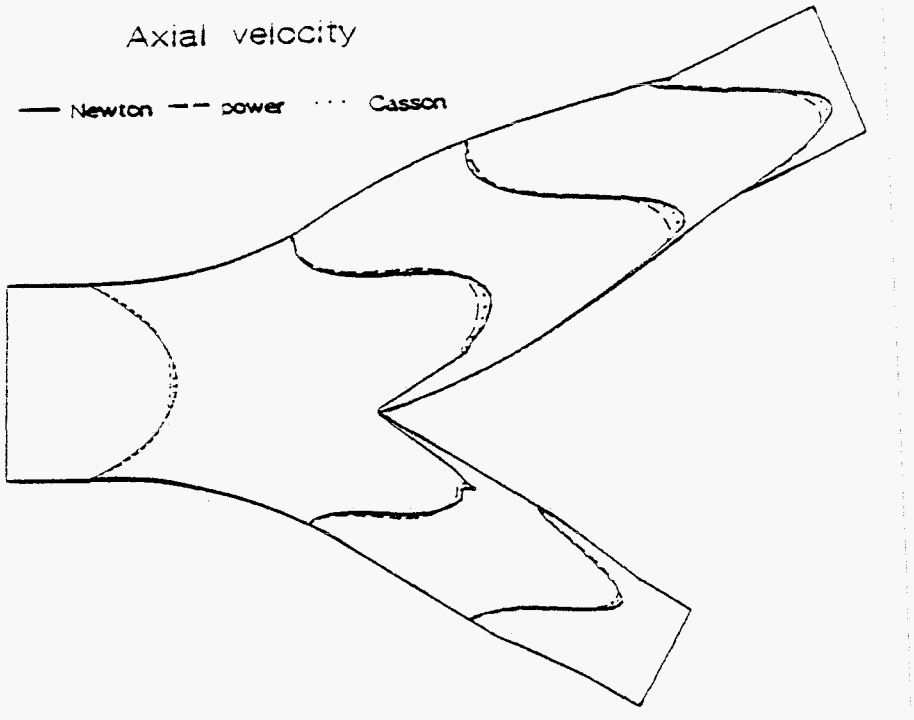

Figure 2.4 *Some results of the numerical calculations of Baaijens e.a. in case of the steady flow at Re = 300 in a two dimensional model of the carotid artery bifurcation, with two generalized Newtonian models (power-law, Casson) and the Newtonian model. (From Baaijens e.a. [1991]).*

2.4 Review of major interesting papers dealing with viscoelastic constitutive models for blood.

Thurston [1979]

Thurston used a six mode Maxwell model to describe the viscoelastic viscosity of human blood. In the one dimensional case of the simple shear flow, in differential form the multimode model is for each mode p described by :

$$\dot{\tau}_p + \lambda_p \tau_p = 2\eta_p \dot{\gamma} \qquad (2.2)$$

and the total extra stress is the summation of all partial stresses of the modes, given by:

$$\tau = \sum_{p=1}^{N} \tau_p \qquad (2.3)$$

This model is illustrated in figure 2.5.

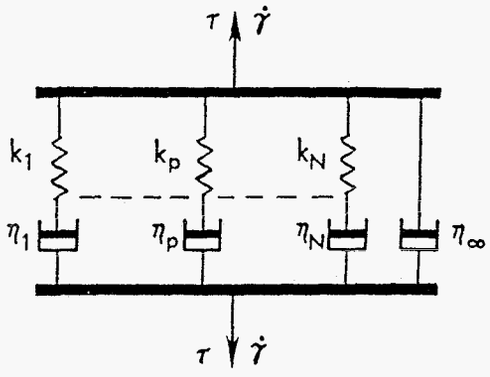

Figure 2.5 *The generalized Maxwell model. (From Thurston [1979]).*

In order to distinguish between the viscoelastic and thixotropic behaviour of blood, he uses the concept of "state of rheological equilibrium" ; only in this state the above model, that is intended to describe the viscoelastic (not the thixotropic behaviour of blood) is valid. He defines the rheological equilibrium as "the condition under which the aspects of the blood which control the rheological properties are not changing with time". The non-equilibrium condition is defined as "that existing while the internal structure and consequential rheological properties are in the process of change"; this concept is used describing thixotropic behaviour. The ground state is that equilibrium state that exists at very low shear rates.
The complex viscosity in a small strain sinusoïdal shear flow is described by the equations:

$$\eta_p^* = \eta_p/(1+i\omega T_p) \tag{2.4}$$

$$\eta^* = \eta^\infty + \sum_{p=1}^{6} \eta_p^* \tag{2.5}$$

The steady flow viscosity is given by:

$$\eta_s = \eta^\infty + \sum_{p=1}^{6} \eta_p \tag{2.6}$$

In the ground state of equilibrium (thus $\omega \rightarrow 0$, $\dot{\gamma} \rightarrow 0$) the model gives:

$$\eta_0 = \eta^\infty + \sum_{p=1}^{6} \eta_{0,p} \tag{2.7}$$

with $\eta_{0,p}$ being the ground state value of η_p; K_p, η_p :spring constant, viscosity of mode p; T_p relaxation time (= η_p/K_p) of mode p. For this ground state the modelparameters were fitted, they

are listed in table 2.4.

The frequency dependence of the viscous and elastic components of the complex viscosity as calculated by this model are presented in figure 2.6 together with the data for human blood. A good agreement between numerical and experimental values is found. Thurston has also adapted this model in order to describe the thixotropic behaviour of blood.

Table 2.4 Parameters of the Maxwell model fitted for human blood as used by Thurston [1979].

TABLE I

Model parameters for the ground state of equilibrium for .43 H human blood.
N = 6, η_o = 1.1 P, η_∞ = .04 P

p	$\eta_{o,p}$ (P)	T_p (sec)	$K_{o,p}$ (dy/cm^2)
1	.93	25.	.037
2	.033	1.	.033
3	.050	.3	.017
4	.032	.1	.32
5	.016	.01	1.6
6	.007	.001	7.

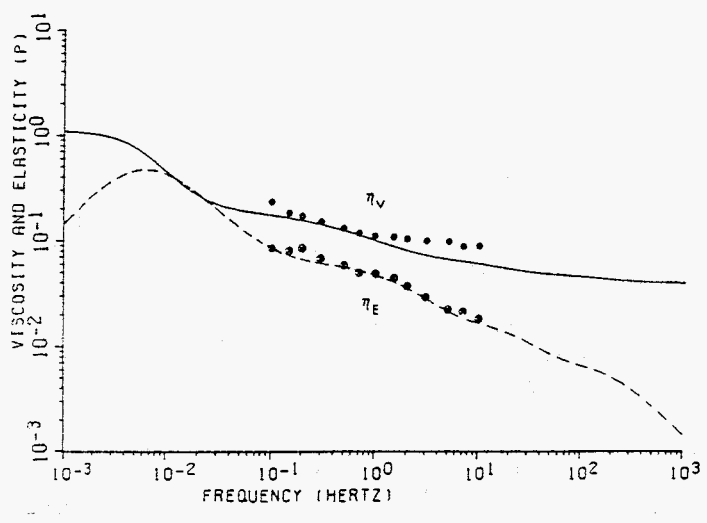

Figure 2.7 *Frequency dependence of the elastic and viscous components of the complex viscosity of the six mode Maxwell model together with human blood data. (From Thurston [1979]).*

Charara, Aurengo, Lelievre, Lacombe [1985]

In this article, first a review is given considering the constitutive models that have been used in literature to describe blood. The authors state that none of those models was satisfactory, and therefore they present there new model, being derived from a previous model proposed by them. The results of their study are outlined briefly in the following.

Referring to a study of Aurengo e.a. [1983], it is assumed that the shear thinning, viscoelasticity and thixotropy of blood can be modeled by a Maxwell like system. In this system, three functions of the shear rate are used: the viscosity η, elasticity modulus G, and kinetic parameter K (this parameter will be explained below). In stationary flow, $\eta_s(\dot{\gamma})$, $G_s(\dot{\gamma})$, $K_s(\dot{\gamma})$ are the steady state functions. In transient flow, $\eta(t)$, G(t) and K(t) are defined as the instantaneous viscosity, elasticity modulus and kinetic parameter. The structure of blood is represented by a single parameter having the dimension of shear rate. This parameter is called the structure shear rate $\omega(t)$, and it is a major parameter in this theory. It is assumed that $\eta(t)$, G(t), and K(t) are functions of the structure shear rate ω, which is time dependent: $\omega = \omega(t)$, with the relations: $\eta(t) = \eta_s(\omega(t))$, $G(t) = G_s(\omega(t))$, $K(t) = K_s(\omega(t))$. The kinetic structure varying parameter K accounts for the fact that the structure shear rate is determined by disaggregation processes (which increase ω) and aggregation processes (which decrease ω), both processes being determined by K.

With these definitions, using the results of Aurengo e.a. [1983] and some additional derivations, the following is proposed as the rheological model for blood:

$$d\tau/dt = (\dot{\gamma} - \tau/\eta_s)G_s + \tau/G_s \, dG_s/dt \qquad (2.8)$$

$$d\omega/dt = K_s(\omega)\omega[\eta_s(\omega) - \eta_s(\dot{\gamma})]^{P(\omega)} \qquad (2.9)$$

with $P(\omega)$ the order of kinetic aggregation - disaggregation. In these two equations several functions are unknown: $\eta_s(\dot{\gamma})$ (has to be measured), $\eta_s(\omega)$ (has the same form as $\eta_s(\dot{\gamma})$ with ω instead of $\dot{\gamma}$), $P(\omega)$, $G_s(\omega)$ and $K_s(\omega)$. The last three parameters are described by the same empirical relation, in general form:

$$F(\omega) = F(\infty) + (F(0) - F(\infty))\exp(-F_c\omega) \qquad (2.10)$$

with $F(\infty)$ and $F(0)$ experimental determined limit values, and F_c an empirical fit constant.

The two differential equations (2.8) - (2.9) comprise five unknowns: $\tau = \tau(\omega(t),t)$, $\omega = \omega(t)$, $P_c G_c K_c$. The parameter identification is performed using an iterative hybrid numerical-experimental method, as shown in figure 2.8. The rheological model is simulated by a Kutta-Merson method, and parameter identification is obtained using a Gauss-Marquardt

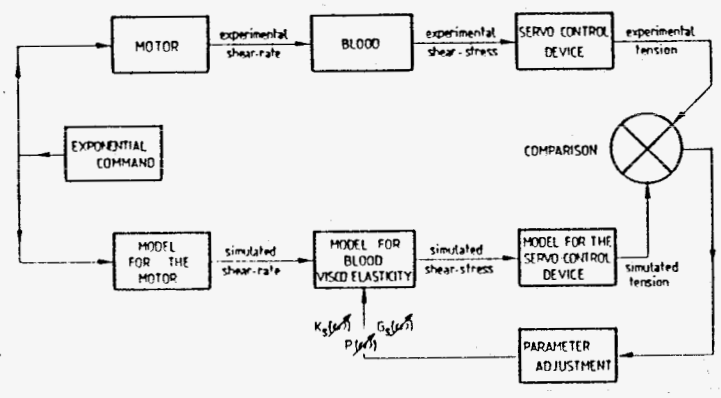

Figure 2.8 *Hybrid experimental-numerical set-up to determine the modelparameters in case of the "Charara" model. (From Charara e.a. [1985]).*

algorithm, that minimizes the quadratic distance between the measured shear stress and computer simulation. The viscometric measurements were done with a Couette viscometer; both motor and servo control characteristics were taken into account in the simulation. In this way the model was fitted to the transient response when a sudden increase in shear rate was applied in steady flow. The results were very satisfactory. Some of them are presented in figure 2.9 and 2.10. Figure 2.9 shows the measured shear stress as a function of time with the fitted model curves, for different shear steps. Figure 2.10 shows the normalized structure shear rate ω versus normalized apparent shear rate $\dot{\gamma}$, also for different steps in shear rate.

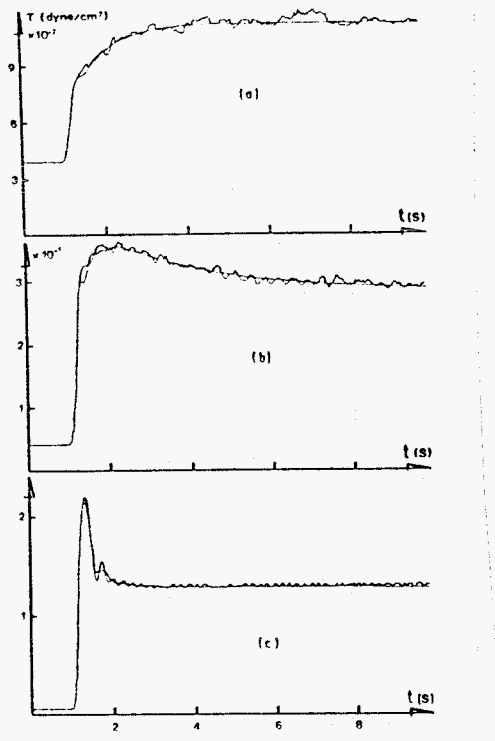

Figure 2.9 *Data fitting of the experimental shear stress τ versus time t. Initial shear rate $\dot{\gamma}_1 = 0.05\ s^{-1}$, final shear rate $\dot{\gamma}_2 = 0.2\ s^{-1}$ (a), $\dot{\gamma}_2 = 1\ s^{-1}$(b), $\dot{\gamma}_2$=10 s^{-1}. (From Charara e.a. [1985]).*

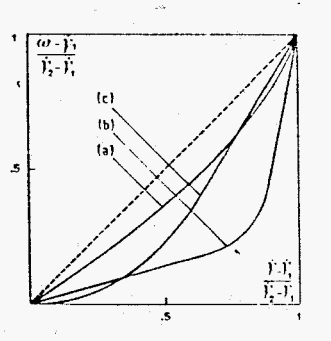

Figure 2.10 *Normalized structure shear rate ω as a function of the normalized apparent shear rate $\dot{\gamma}$. The dotted line represents the Newtonian case with $\omega = \dot{\gamma}$ at each time. Initial shear rate $\dot{\gamma}_1 = 0.05\ s^{-1}$, final shear rate $\dot{\gamma}_2 = 0.2\ s^{-1}$ (a), $\dot{\gamma}_2 = 1\ s^{-1}$ (b), $\dot{\gamma}_2 = 10\ s^{-1}$. (From* Charara *e.a. [1985]).*

Rosenblatt, Soong, Williams [1986]

Rosenblatt, Soong and Williams present a constitutive model that describes the non-Newtonian transient behaviour of human blood, being derived from the view of blood as a structured fluid. This very readable paper contains a comprehensive derivation; here it will be outlined only briefly. Rosenblatt e.a. [1986] consider blood as a solution of elastic dumbbell molecules (the rouleaux) and have derived the following expressions for this fluid:

$$dP/dt = k(1-P) - \alpha\, |\boldsymbol{D}|\, P \qquad (2.11)$$

$$\boldsymbol{T}_{st}' + \lambda_{st}\, \delta/\delta t(\boldsymbol{T}_{st}') = \eta_{st}\, \boldsymbol{D} \qquad (2.12)$$

with $\delta/\delta t$: a contravariant Oldroyd or upper-convected time derivative, α: a dimensionless empirical constant, k: an inverse time-constant; P: a structure factor, defined as the fraction of cell sides in the system which are aggregated; $\boldsymbol{T}_{st}'$: the structure dependent (indicated by "$_{st}$"), extra-stress tensor (indicated by " ' "), $\boldsymbol{D}$: rate of deformation tensor, $|\boldsymbol{D}| = (II_D)^{\frac{1}{2}} = \dot{\gamma}$ in a simple shear flow. This is a differential constitutive model, (2.12) being a structure-dependent Maxwell model, with the structure-dependent viscosity and relaxation time given by:

$$\eta_{st} = (\langle q_e^2 \rangle CP)/3k \qquad (2.13)$$

$$\lambda_{st} = P/k \qquad (2.14)$$

$$\text{with } C = w\, N_0\, \Omega/2\langle q_e \rangle \qquad (2.15)$$

with w: the thickness of a red blood cell, N_0: total number of cell sides per volume, Ω: spring constant in an elastic dumbbell (Hooke's law), $\langle q_e \rangle$: average rouleaux length at equilibrium (zero shear). N_0, w and $\langle q_e \rangle$ are measured by observations under a microscope. Ω is computed from equation (2.16), that is found after rearranging equation (2.13) and (2.15):

$$\Omega = 6\, k\eta_{st}^0 / w q_e N_0 \qquad (2.16)$$

Here $k = 1/\theta^0$ is used, which is the limit value at low shear rate when P = 1. From low-$\dot{\gamma}$ stress growth experiments found in literature they obtained a value for θ^0 of 4 s, thus k = 0.25 s^{-1}. Further, $\eta_{st}^0 = \eta^0 - \eta^\infty$. From limiting low-$\dot{\gamma}$ data found in literature a value of 0.12 Ns/m^2 was found; from high-shear data a value of 0.004 Ns/m^2 for η^∞ was found. Other values are: w = 2.0 μm, N_0 = 0.012 (sides/μm^3) when HTC = 45 %, $\langle q_e \rangle$ = 172 μm (= 50 · w). These values lead to

Ω = 7.2 . 10^{-5} dynes/cm. The value of α is found from fitting the model's non-Newtonian steady-state viscosity given by:

$$\eta = \eta_{st} + \eta^{\infty} = [\eta^0 - \eta^{\infty}]\, k/(k+\alpha|\dot{\gamma}|) + \eta^{\infty} \qquad (2.17)$$

which yielded a value of 0.71 for α.
As usually, the deviatoric stress tensor is given by:

$$\boldsymbol{T}_{st}' = \boldsymbol{T}_{st} - p\boldsymbol{I} \qquad (2.18)$$

For computing the total measurable stress, equation (2.11) and (2.12) must be solved simultaneously using equations (2.13) - (2.15). The model contains four independent parameters k, η_0, η^{∞}, and α. In general, model predictions fitted data better at low shear rates then at high shear rates. Some results are shown in figures 2.11 - 2.12.

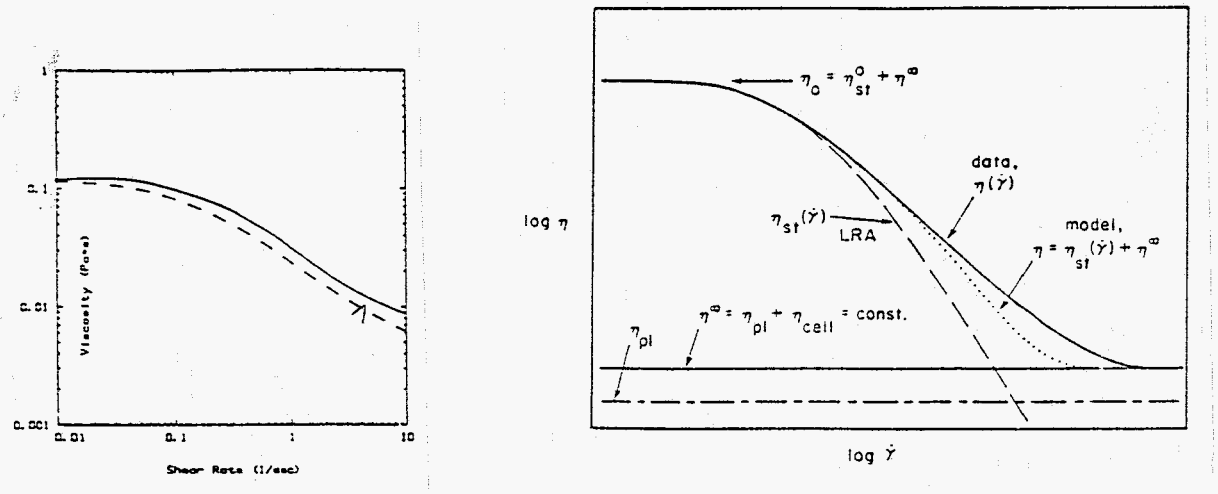

Figure 2.11 *Steady shear viscosity, a) numerical fit, b) analytical curve. (From Rosenblatt e.a. [1986]).*

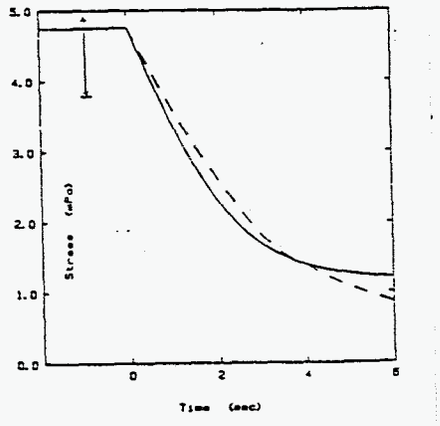

Figure 2.12 *Stress relaxation after a steady-state shear rate of $\dot{\gamma}_0 = 0.05\ s^{-1}$ suddenly was stopped. (From Rosenblatt e.a. [1986]).*

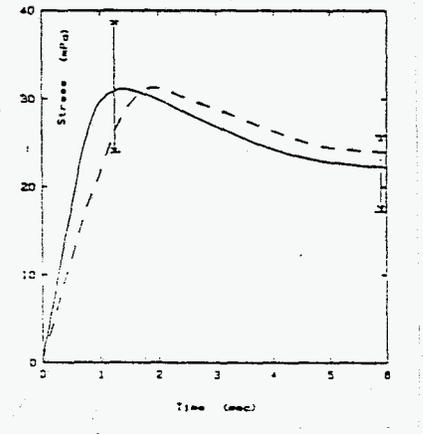

Figure 2.13 *Stress growth after the blood was suddenly sheared from rest to $\dot{\gamma}_0 = 1\ s^{-1}$. (From Rosenblatt e.a. [1986]).*

Finally, it is noted that fluid stresses arising from structure are dependent on cell shape and rigidity. Rosenblatt e.a. [1986], from there view of interest, therefore suggest that with more sophisticated models of cell adhesion, more clinical useful information about blood chemistry can be obtained.

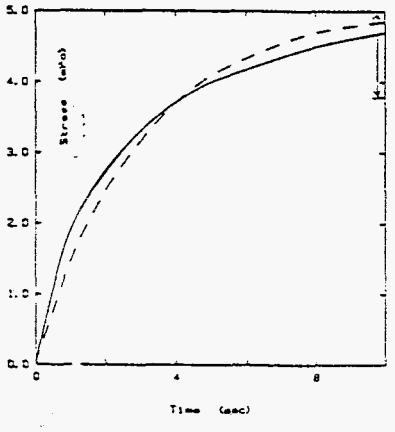

Figure 2.14 *Stress growth after the blood was suddenly sheared from rest to $\dot{\gamma}_0 = 0.05$ s^{-1}. (From Rosenblatt e.a. [1986]).*

Bernadin, Sero-Guillaume, Lucius [1987]

Bernadin, Sero-Guillaume and Lucius [1987] propose a modified Bird-Carreau model as a constitutive model for whole human blood. From a previous study they had found that the Bird-Carreau was not satisfying because it did not account for the fact that blood consists of two media: the blood cells and the plasma. The first are viscoelastic, the second Newtonian. In the modified model both the characteristics of the plasma, and the interaction between both components of the mixture are taken into account. Deriving this new model, they used the theory of mixtures as described by Bowen, Green and Naghdi, Müller and Truesdell. Neglecting the influence of diffusion of blood cells (thus assuming that no density gradients exist), the eventually obtained stress tensor of the mixture is the sum of partial stress tensors of the components. This theory is the molecular approach of a network theory (compare the Rouse theory, the Carreau-B model, the Lodge network theory, the Yamamoto network theory). It considers blood analogous to a concentrated polymer solution formed by dissolved polymer molecules that have a strong interaction and in which intermolecular junctions are constantly being formed and broken.
A comprehensive derivation is presented in Bernadin [1986] and Bernadin e.a. [1987]. Here only the results will be given and discussed. The final obtained constitutive equation is described by:

$$\boldsymbol{T} = -p\boldsymbol{I} + h \overset{0}{\underset{s=-\infty}{\mathrm{F}}} (\boldsymbol{U}^2(x,t-s)) + 2\eta_\infty(h)\boldsymbol{D}(x,t) \qquad (2.19)$$

with h: the hematocrit (HTC), $\boldsymbol{U}^2(x,t-s)$: the right Cauchy-Green strain tensor , $\boldsymbol{D}(x,t)$: rate of deformation tensor, and the functional F given by:

$$\overset{0}{\underset{s=-\infty}{\mathbf{F}}}(U^2(x,t-s))=$$

$$-\int_{-\infty}^{t} \mathbf{M}(t,\tau,\ \underset{\tau\le u\le t}{II(u)})[(1+\tfrac{1}{2}\varepsilon)C^{-1}(x,t)-\tfrac{1}{2}\varepsilon C(x,t)]d\tau \qquad (2.20)$$

with C^{-1} the Finger strain tensor, and $\mathbf{M}$ a memory functional depending on II(u), the second invariant of the rate of deformation tensor D:

$$\mathbf{M}(t,\tau,\ \underset{\tau\le u\le t}{II(u)})=\sum_{p\ge 1}(\eta_p/\lambda_p^2)f_p(II(\tau))\exp[-\int_{\tau}^{t}du/(\lambda_p g_p(II(u)))] \qquad (2.21)$$

and ε an empirical constant:

$$\tfrac{1}{2}\varepsilon = N_2/N_1 \qquad (2.22)$$

with N_1,N_2 the first and second normal stress differences. The functions f_p and g_p depend on the second invariant $II(\tau)$, α, λ,s,r,and on p:

$$f_p(II(\tau)) = \frac{1 + ((2^{\alpha}\lambda')^2 II(\tau)\ 2)^S/(p+1)^{2\alpha}}{(1 + \lambda^2\ II(\tau)\ 2)^{2r}} \qquad (2.23)$$

$$f_p(II(\tau))\ g_p(II(\tau)) = (1 + \lambda^2 II(\tau)\ 2)^{-r} \qquad (2.24)$$

with: (2.25)

$$\eta_p = \eta_0\ \lambda_p/\sum_{k\ge 1}\lambda_k \qquad (2.26)$$

$$\lambda_p = 2^{\alpha}\lambda/(p+1)^{\alpha} \qquad (2.27)$$

It is worth noting that the extra term $2\eta_{\infty}(h)D(x,t)$ in (2.19) is a consequence of the assumption that blood is a mixture of a purely viscous and a visco-elastic fluid.

The model has been tested in case of a simple shear flow. The stress tensor as described by (2.19) then has one component of interest, T_{12}, given by:

$$T_{12} = [-\eta_0/(2^{\alpha}\lambda(Z(\alpha)-1))] \sum_{p\geq 1} \int_{-\infty}^{t} (f_p/\lambda_p)\exp(-\int_{\tau}^{t} du/\lambda_p g_p)a(t,\tau)d\tau + \eta_{\infty}\dot{\gamma} \tag{2.28}$$

with

$$a(t,\tau) = \int_{\tau}^{t} \dot{\gamma}(u)du \tag{2.29}$$

and $\dot{\gamma}$ is the shear rate.The parameters λ_p is given by (2.27), and $Z(\alpha)$ by:

$$Z(\alpha) = \sum_{p\geq 1} 1/p^{\alpha} \tag{2.30}$$

The model contains 6 parameters: the viscosity at very low shear rates η_0, the longest relaxation time λ, a dimensionless parameter α characterizing the rouleaux structure, and three complementary parameters r, s, λ'. The choice of η^{∞} is not free, but it is determined experimentally. The parameter γ^{∞} ($\dot{\gamma} = d\gamma/dt$) is the maximal shear; the instantaneous viscosity is then defined by:

$$\eta(\dot{\gamma}^{\infty},t) = T_{12}(t)/\dot{\gamma}^{\infty} \tag{2.31}$$

and the apparent viscosity by:

$$\eta(\dot{\gamma}^{\infty}) = \lim_{t\to\infty} \eta(\dot{\gamma}^{\infty},t) \tag{2.32}$$

The parameters were fitted using the results of stress growth experiments, i.e. measuring the stress after a stepwise increase in the steady shear rate, see figure 2.16. Their values for whole human blood (HTC = 45%) at 25° C are: η_0 = 89 cp, λ = 5s, α = 3, r = 0.42, s= 1.1, λ' = 6s, η^{∞} = 6 cp. In figure 2.15 the apparent viscosity as a function of shear rate is shown.

As a test, two kinds of additional experiments were performed: stress relaxation (figure 2.17 and forced oscillations (figure 2.18, 2.19). In general there is a good agreement between the experimental values and the numerical values calculated with the modified model for these flows. The differences with the (normal) Bird-Carreau model are clear.

Only in case of η'' there is no good agreement between theory and experiment, although here also

the modified model yields better results than the Bird-Carreau model. Bernadin e.a. suggest that the non-diffusion hypothesis is not valid for very low shear rates in particular. In that case there exist deforming rouleaux, with the fluid flowing in between, and possibly the diffusion velocity is no longer negligible.

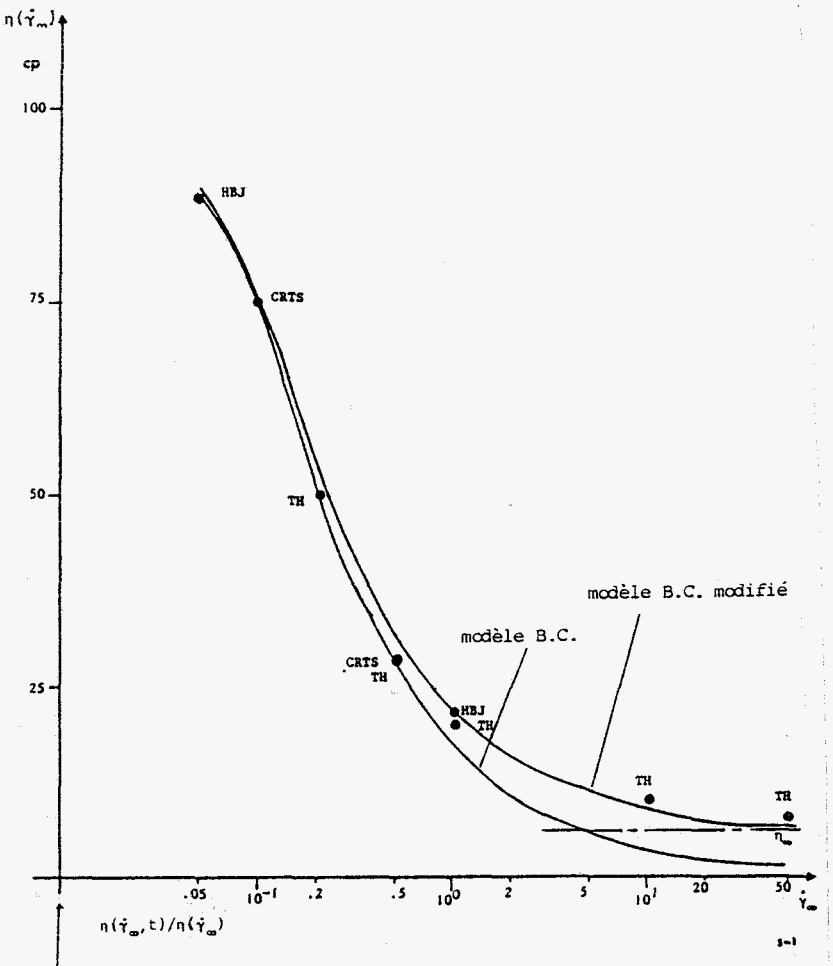

Figure 2.15 Apparent viscosity as a function of shear rate (from Bernadin e.a. [1987]).

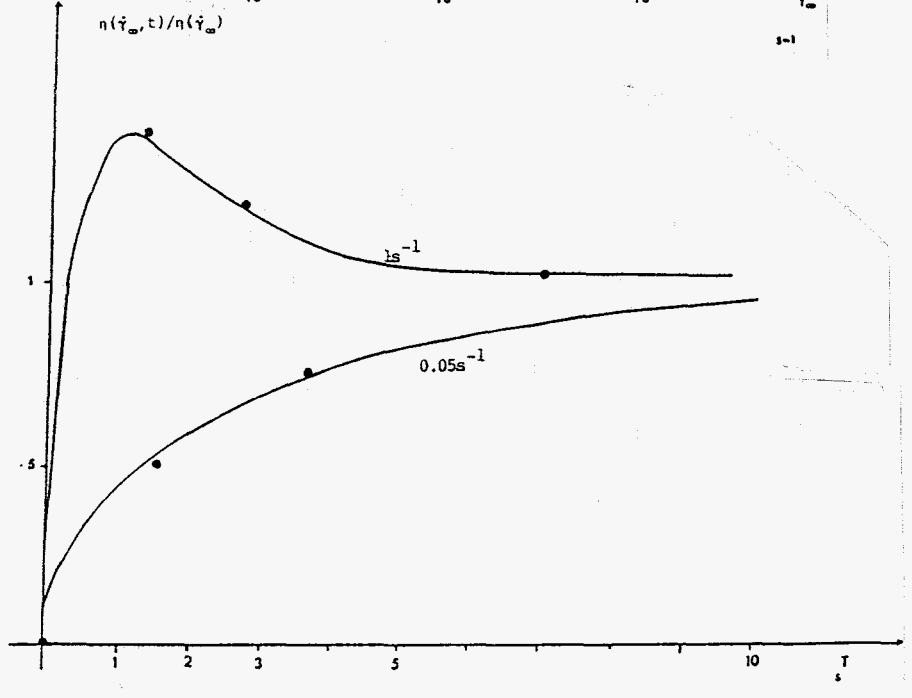

Figure 2.16 Stress growth as a function of time after a step shear from 0 s^{-1} to 0.05 s^{-1} and to 1 s^{-1} (from Bernadin e.a. [1987]).

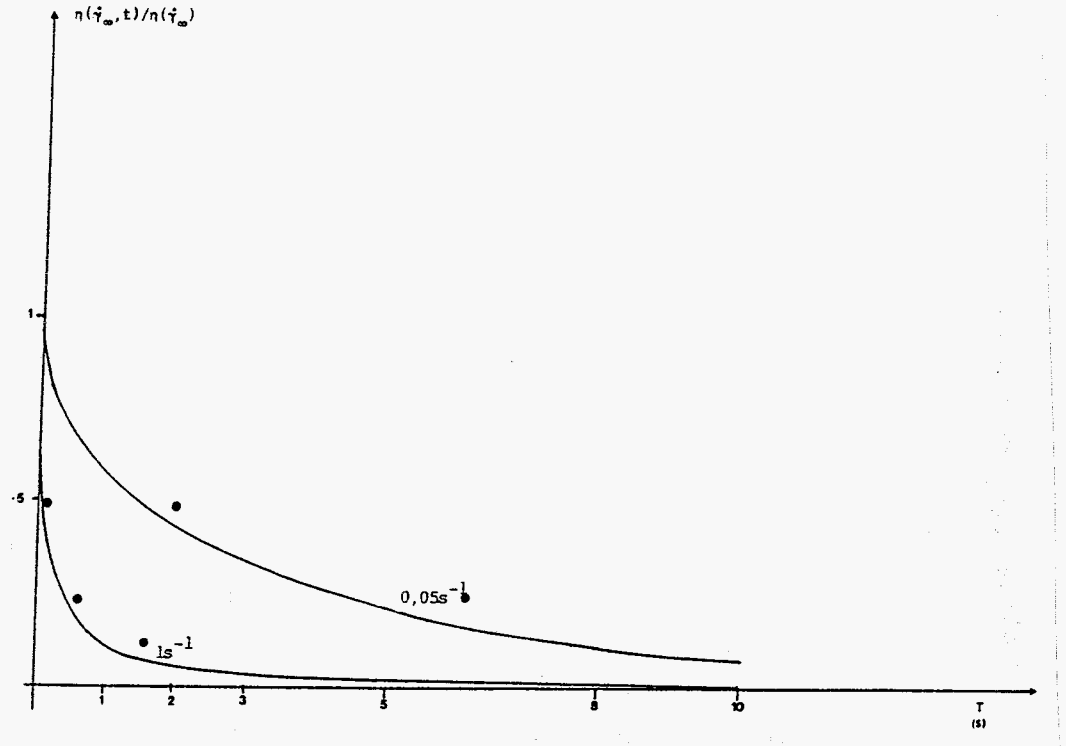

Figure 2.17 *Stress relaxation after a shear step from 0.05 s^{-1} and 1 s^{-1} to 0.0 s^{-1} as a function of time (Bernadin e.a. [1987])*

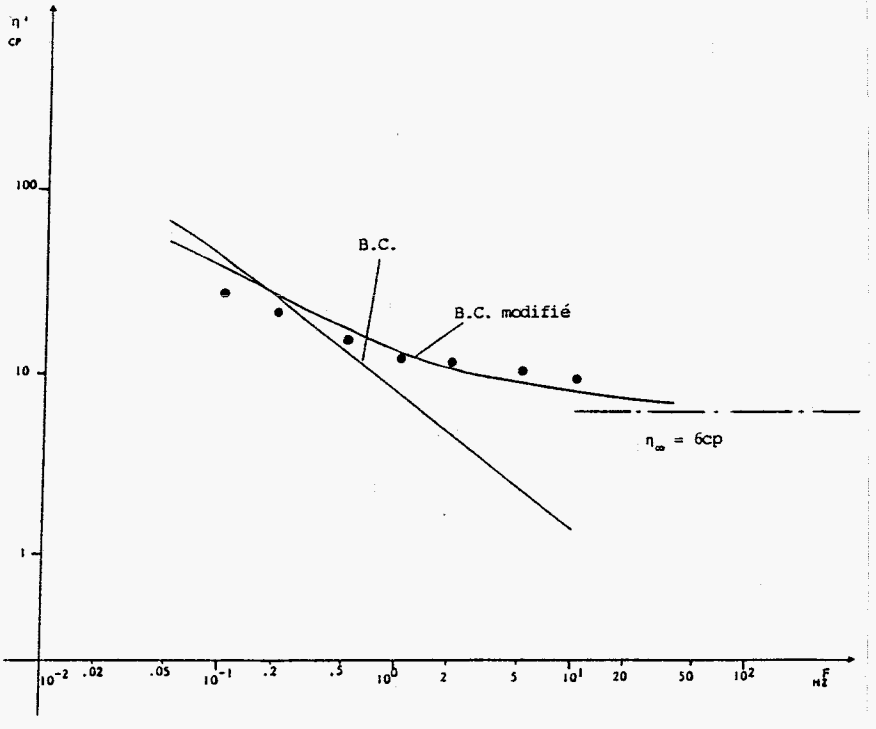

Figure 2.18 *Viscous component of the complex viscosity as a function of frequency (from Bernadin e.a. [1987]).*

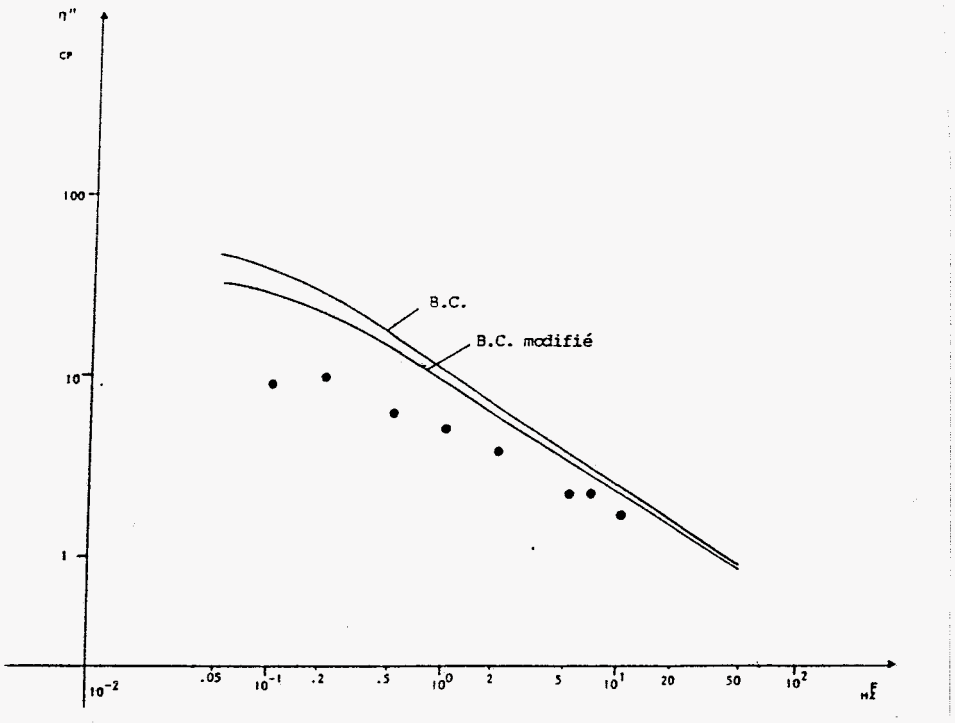

Figure 2.19 *Elastic component of the complex viscosity as a function of frequency (from Bernadin e.a. [1987]).*

Reher and Vogel [1988]

Reher and Vogel present a rheological model that is intended to describe the coupled thixotropic-viscoelastic behaviour of a class of fluids consisting of a suspension of particles in a Newtonian suspending fluid, where the particles are able to form aggregates. They state that the structural kinetic behaviour is caused by the degradation or formation of the aggregates at varying shearing loads. The deformation of the three dimensional network or the aggregates causes the viscoelastic behaviour. In this model, the deformation of the dispersed particles, their rotation in the shearing flow and the geometry of the particles is not taken into account. Although the starting point of the derivation is more basic, here it is started by presenting the main equation of this model, a modified Maxwell model for the extra stress tensor T:

$$T + \lambda \overset{\cdot}{T} = (\eta(I_2(t),t)-\eta^{\infty})\, D \tag{2.33}$$

with

$$\lambda = \lambda(\eta_e(I_2(t))) = (\eta_e(I_2(t)) - \eta^{\infty})/G \tag{2.34}$$

for $\eta_e > \eta^\infty$ (η_e = dynamical equilibrium viscosity).
It is assumed that the viscosity is a function of $I_2(t)$ and t. The parameter $I_2(t)$, the second invariant of the rate of deformation tensor, is a measure for the intensity of the shearing load. A second differential equation is presented to find $\eta(I_2(t),t)$, being the effective viscosity due to the aggregation of the colloïdal components of the suspension. Reher and Vogel state that "from a phenomenological point of view structure kinetic changes of viscosity in case of unsteady shearing loads exhibit a behaviour analogous to the change of shear stress in viscoelastic fluids. Differences exist only in the initial conditions". They however do not show any experimental evidence to validate this statement. Based on this, the differential equation for $\eta(I_2(t),t)$ has the same form as equation (2.33), and they propose:

$$(\eta(I_2(t),t)-\eta^\infty)+\varphi(I_2(t'),I_2(t))\partial/\partial t(\eta(I_2(t),t)-\eta^\infty) = \eta_e(I_2(t)) \qquad (2.35)$$

The parameter $\varphi(I_2(t'),I_2(t))$ is determined by the following assumed relationship:

$$\varphi = \begin{cases} \rho(I_2(t)), & |I_2(t')| > |I_2(t)| \\ 0 & |I_2(t')| = |I_2(t)| \\ \delta(I_2(t)), & |I_2(t')| < |I_2(t)| \end{cases} \qquad (2.36)$$

with $t' < t$, and ρ the characteristic time for formation and δ for degradation. A few parameters have still to be determined. If $\xi = |I_2(t)|^{\frac{1}{2}}$, so that $\xi = |\dot{\gamma}|$ in a simple shear flow, on experimental basis it was found that power-law relations were suitable:

$$\lambda = \alpha_1\xi^{-\alpha_2},\ \delta = \beta_1\xi^{-\beta_2},\ \rho = \varepsilon_1\xi^{-\varepsilon_2} \qquad (2.37)$$

From these equations (2.37) and using equation (2.34), equation (2.38) was derived:

$$d\eta_e(\xi)/d\xi = -\beta_2(\eta_e(\xi)-\eta^\infty)/\xi \qquad (2.38)$$

Furthermore, as usually, $\boldsymbol{D}$ was computed using:

$$\boldsymbol{D} = -\partial/\partial t'(\boldsymbol{C}^{-1}) \qquad (2.39)$$

with $\boldsymbol{C}^{-1}$ the Finger strain tensor. Reher and Vogel present analytical integrals of equations (2.33) and (2.36) - (2.39), and finally find one integral constitutive equation that relates $\boldsymbol{T}$ to $\boldsymbol{D}$. From

rheometrical investigations, the following model parameter set, for whole human blood (HTC = 45 %, ? ° C) was determined: η_0 = 136 mPa s, η^{∞} = 2.97 mPa s, ε (?) = 18.46 mPa s, α_1 = 1.43, α_2 = 0.506, β_1 = 0.66, β_2 = 0.95, ε_1 = 0.076, ε_2 = 2.273; 9 parameters in total. Unfortunately, no application of this model to any flow situation is presented.

Discussion

In table 2.4 a comprehensive overview of the mathematical expressions of the models discussed above is shown. Table 2.5 gives a survey of the results of those models in some shear flows compared with blood data. As is evident from these tables, the Maxwell type of equations have been used very frequently to describe the rheological behaviour of blood. Although this type of equation has been very popular in rheology, it is criticized to a large extent. The classical Maxwell model as used by Thurston [1979] is more an illustrating example then an useful model. The main criticism is that it is not objective, i.e. it is not invariant under transformation to another coordinate system (Larson [1988]). Further it has proven to be insufficient to describe the flow of real viscoelastic fluids. In case of blood, it is important to realize that shear thinning is not described by a (normal) Maxwell model, and that it predicts significant non-zero normal stress differences (Larson [1988]). The upper-convected Maxwell model (UCM) satisfies the objectivity principle, but also predicts significant non-zero normal stresses and no shear thinning (Larson [1988]). In this context the research of Hulsen [1988] is of interest. His research was on the numerical analyses of viscoelastic fluid flow and he divided the models he studied in quasi-linear models on the one hand and Leonov and Giesekus models on the other. The UCM model belongs to the class of quasi-linear models. Those models have only physical significance for small deformation rates. Hulsen concluded that the agreement of quasi-linear models with experiments in various viscometric flows of polymeric liquids is only moderately good (this is confirmed for the Maxwell equations by Tanner [1985], p.222). For these models the stress tensor can become singular in plane steady flow, which is expected to lead to numerical difficulties. The quasi-linear models show an unstable behaviour in elongation dominated flow; according to Tanner [1985] the Maxwell equations describe elongating flows poorly (p. 222). For these reasons Hulsen concludes that quasi-linear models should not be used in numerical simulations.

In general, flows are mixtures of elongation and shear; this is also true in case of the flow in the carotid artery bifurcation. With the above considerations in mind, one should be careful applying the Rosenblatt model, although it has a sophisticated microstructural basis, to describe complex flow of blood because it is based on an UCM equation. Further, considering the relation of the Rosenblatt model with other models it is found that the Rosenblatt model shows a strong similarity with standard models in rheology. The balance equation is equivalent to the Yamamoto's network time-evolution equation (Larson [1988], p. 168). The structural kinetics

equation Rosenblatt e.a have derived is similar to the structural model of Liu, Soong and Williams (Larson [1988], p.177) with a structural viscosity $\dot{\gamma}$ incorporated:

$$dP/dt = (k_1/b)(1-P) - k_1 |\dot{\gamma}|^m P \qquad (2.40)$$

with $k = k_1/b$, $\alpha = k_1$, and $m = 1$. Larson states that this equation together with the UCM equation is not adequate in extensional flows. There is, however, no experimental information about the behaviour of blood in elongating flow. Fortunately, it is expected that in the flow situation of interest in this study the flow is dominated by shear (see section 1.4). Thus the possibly poor behaviour of the Rosenblatt model in elongating flow is not a decisive factor.

The Charara and Reher-Vogel models have such a level of empiricism that their molecular or structural foundations should not be taken too seriously. The Charara model was developed to describe the rheological behaviour of blood in transient flow after a step in the shear rate was imposed. In case of the Reher-Vogel model no comparison with experimental data is available. Both models are based on an ordinary (not convected) Maxwell model; for that reason, in this form the models are not useful in complex flow situations.

The Charara, Reher-Vogel and Rosenblatt model are very similar models: they all consist mainly of a Maxwell type of differential equation together with a structural kinetics equation. This latter equation is based upon the consideration that in blood the structural kinetics proces of aggregation and disaggregation is taking place. As discussed in section 1.4 this proces is very probably not important or non-existing in the physiological flow of blood through a bifurcation. In case of the steady equivalent of this flow it might be of importance.

The original Bird-Carreau equation is for polymers according to Larson [1988] and Schowalter [1978] only accurate in steady flow, not in transient flow. Further Larson [1988, p. 180] describes that, because in the Bird-Carreau model the modulus dependson the instantaneous strain rate, it shows departures from linear viscoelasticity at arbitrarily small strain amplitudes in oscillatory shear if the strain rate is high enough. This is in contradiction with the viscoelastic "simple fluid" theory and experimental evidence (of polymers), that shows such a departure only after a critical strain amplitude is exceeded, no matter what high the strain rate is. There is however no experimental information for blood available at this point. Further Larson states that this equation "may be useful in describing thixotropic (or structured) fluids for which the structure depends on the instantaneous strain rate" (Larson [1988], p. 179). From the table above it is evident that in a range of different test situations for blood very satisfactory results were obtained with the modified model as used by Bernadin e.a.. For that reason it is a serious candidate to describe the flow of blood in complex flows. However, this model considers blood as a structured fluid in which a network of rouleaux with junctions (or entanglements) is present. As discussed in section

Table 2.4 Basic mathematical expressions of some viscoelastic constitutive models proposed for blood

	Equation number:
CHARARA [1985]	
"Maxwell":	
$d\tau/dt = (\dot{\gamma} - \tau/\eta_s)G_s + \tau/G_s\, dG_s/dt$	(2.8)
"Structure kinetics":	
$d\omega/dt = K_s(\omega)\omega[\eta_s(\omega) - \eta_s(\dot{\gamma})]^{P(\omega)}$	(2.9)
ROSENBLATT [1986]	
"Maxwell":	
$\boldsymbol{T}_{st}' + \lambda_{st}\, \delta/\delta t(\boldsymbol{T}_{st}') = \eta_{st}\, \boldsymbol{D}$	(2.12)
"Structure kinetics":	
$dP/dt = k(1-P) - \alpha\, \lvert\dot{\gamma}\rvert\, P$	(2.11)
REHER-VOGEL [1988]	
"Maxwell":	
$\boldsymbol{T} + \lambda \overset{\cdot}{\boldsymbol{T}} = (\eta(I_2(t),t)-\eta^{\infty})\, \boldsymbol{D}$	(2.33)
"Structure kinetics":	
$(\eta(I_2(t),t)-\eta^{\infty})+\varphi(I_2(t'),I_2(t))\,\partial/\partial t(\eta(I_2(t),t)-\eta^{\infty}) = \eta_e(I_2(t))$	(2.35)
MODIFIED BIRD-CARREAU [1986]:	
$\boldsymbol{T} = -pI + h \overset{0}{\underset{s=-\infty}{F}} (\boldsymbol{U}^2(x,t-s)) + 2\eta_{\infty}(h)\boldsymbol{D}(x,t)$	(2.19)
$\overset{0}{\underset{s=-\infty}{F}} (\boldsymbol{U}^2(x,t-s)) =$	
$-\int_{-\infty}^{t} \underset{\tau\le u\le t}{M}(t,\tau;\ II(u))[(1+\tfrac{1}{2}\varepsilon)\boldsymbol{C}^{-1}(x,t)-\tfrac{1}{2}\varepsilon\boldsymbol{C}(x,t)]d\tau$	(2.20)

Table 2.4 continued:

$$\mathbf{M}(t,\tau;\ \underset{\tau\le u\le t}{II(u)}) = \sum_{p\ge 1} (\eta_p/\lambda_p^2) f_p(II(\tau)) \exp\left[-\int_\tau^t du/(\lambda_p g_p(II(u)))\right] \qquad (2.21)$$

$$\tfrac{1}{2}\varepsilon = N_2/N_1 \qquad (2.22)$$

important or non-existing in the physiological flow of blood through a bifurcation. In case of the steady equivalent of this flow it might be of importance.

The original Bird-Carreau equation is for polymers according to Larson [1988] and Schowalter [1978] only accurate in steady flow, not in transient flow. Further Larson [1988, p. 180] describes that, because in the Bird-Carreau model the modulus dependson the instantaneous strain rate, it shows departures from linear viscoelasticity at arbitrarily small strain amplitudes in oscillatory shear if the strain rate is high enough. This is in contradiction with the viscoelastic "simple fluid" theory and experimental evidence (of polymers), that shows such a departure only after a critical strain amplitude is exceeded, no matter what high the strain rate is. There is however no experimental information for blood available at this point. Further Larson states that this equation "may be useful in describing thixotropic (or structured) fluids for which the structure depends on the instantaneous strain rate" (Larson [1988], p. 179). From the table above it is evident that in a range of different test situations for blood very satisfactory results were obtained with the modified model as used by Bernadin e.a.. For that reason it is a serious candidate to describe the flow of blood in complex flows. However, this model considers blood as a structured fluid in which a network of rouleaux with junctions (or entanglements) is present. As discussed in section 1.4, this network only exists at very low shear rates ($\dot{\gamma} < 0.1\ s^{-1}$). Another problem is that the Bird-Carreau model, an integral type of model without a differential equivalent, is not yet implemented in SEPRAN, thus applications will be limited in the first instance. Comparison with more experimental data of blood is needed to make a good judgment of this model.

From the above, it is evident that the (micro-)structural ideas on which the models are based loose their meaning in the physiological flow situation. In that case there is no reasons to prefer them compared with other models that will be discussed in the next section.

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Comparison with more experimental data of blood is needed to make a good judgment of this model.

From the above, it is evident that the (micro-)structural ideas on which the models are based have possibly little meaning in the unsteady physiological flow situation. In that case there is no reasons to prefer them compared with other models that will be discussed in the next section.

Table 2.5 Survey of viscoelastic constitutive models used for blood.

Author name	Type of model	η_s	η'	η''	stress growth	stress relax.
Thurston	6-mode Maxwell	U	E	M	-	-
Roosen-blatt e.a.	UCM eq. with a structure kinetics eq.	M	-	-	M	M
Reher and Vogel	Maxwell eq. with a structure dependent viscosity eq.	-	-	-	-	-
Bernadin e.a	modified Bird-Carreau model	E	G	M	E	E
Charara e.a.	Maxwell type eq. with a structure kinetics eq.	-	-	-	E	-

E = excellent (within a few percent), G = good (within 10 - 20 %), M = moderate (within 20 - 50 %), P = poor (error > 50 %), U = unsuitable or useless result.

2.5 Constitutive models in SEPRAN

In rheology numerous constitutive models exist; especially polymer rheology provides many models. The similarity between the flow of polymers and of blood is already perceived by Bernadin e.a. [1987], as discussed in the previous section. The rouleaux can be considered as long chain molecules, that at low shear rates are able to form networks that with increasing rates of deformation are broken down again. The viscoelastic characteristics of blood have been presented in chapter 1.

A large group of constitutive models for describing viscoelastic flow are implemented recently in the finite element software package SEPRAN (Segal [1984]). These models have their origin in polymer rheology (compare Larson [1988], Tanner [1985]). In future, numerical calculations of the viscoelastic flow of blood will be carried out using this package SEPRAN. For that reason it is useful to investigate the implemented models. A survey of them is presented in table 2.6; all implementations are for the steady two
dimensional or axisymmetric case. Hulsen [1988, 1990] has implemented differential models, Hoitinga [1990] an integral type of model. The main difference between the two publications of Hulsen is the numerical algorithm used (the streamlines are integrated quadratic in an element in Hulsen [1990] instead of linearly in Hulsen [1988]). The implementations are made in a very general way and can easily been extended to certain other models not mentioned in table 2.6. For more detailed information about numerical algorithms used and other mathematical or numerical aspects it is referred to the literature.

Table 2.6 Survey of viscoelastic constitutive models available in SEPRAN

Hulsen [1988]
Differential models
Quasi-linear models
UCM
Oldroyd-B
LCM
Johnson-Segalman (JS)
Leonov and Giesekus models

Table 2.6 Continued

Hulsen [1990]
Differential models
JS
Larson
Giesekus
Phan-Thien Tanner
Leonov
Hoitinga [1990]
Integral models
Papanastasiou (KBKZ type)
Baaijens [1991a]
Differential models
Phan-Thien Tanner
Leonov

2.6 Concluding discussion: which model to use for blood?

In this section the chapter is ended with (a preliminary) search for an answer on the crucial question: which constitutive model should be used to describe the viscoelastic behaviour of blood in steady complex flows?

Following Larson [1988, p.189-190], several factors influence the choice of a constitutive equation: the type of flow (shear/elongating, steady/transient), the type of material ((polymer) melt or concentrated solution/dilute solution, molecules with/without long side branches), the numerical scheme employed, and the kind of phenomena that should be predicted.

In a complex flow with complex phenomena, such as the steady flow in the carotid artery bifurcation, where a recirculation area exists and that is characterized by a relatively high Reynolds and Deborah number (see section 1.6), it is impossible to decide a priori which constitutive equation should be used. However, some remarks can be made. Larson uses two concepts to divide general flows into different categories. The first concept is "flow strength": a flow can be a strong flow or a weak flow. A flow is weak when some material lines grow at most linearly in time, e.g. a shear flow. A flow is strong when some material lines grow exponentially in time, e.g. an elongating flow. The second concept is "alignment strength"; a flow can be strongly aligning (e.g. an uniaxial elongating flow, it strongly aligns molecules along a single axis because stretching occurs in one direction), neutrally aligning (e.g. a shear flow) and weakly

because stretching occurs in one direction), neutrally aligning (e.g. a shear flow) and weakly aligning (e.g. a biaxial extensional flow, stretching takes place equally in two directions). Larson shows that this second concept can be quantified by the difference of the first (I_1) and second (I_2) invariants of the Finger strain tensor. This is shown in figure 26. The use of these concepts becomes practical, when it is realized that both different constitutive models as materials show different sensitivity to flow strength and alignment strength. For example Larson states that materials with long side branches need to be described with a model that is sensitive to alignment strength.

With these general considerations in mind the candidate models will be discussed. From the discussion in section 2.3, the modified Bird-Carreau model proved to be tested the most seriously in a range of flow situations. The results were very satisfactory, it indicates that it is an adequate model to describe the flow of blood. However, with this model, no complex flow situations have been presented in literature yet. For that reason the model should be tested first in more severe test problems and compared with experimental blood data. Of all the implemented models in SEPRAN the quasi-linear models are of secondary interest for reasons discussed in section 2.4. This is probably also true for all models in table 2.4, except the modified Bird-Carreau model, because those models are based on a Maxwell model. There is only one aspect that possibly makes a difference: all these models include a separate structural kinetics equation. It is unsure whether this alleviates the problems that exist with the ordinary Maxwell or with the UCM model.

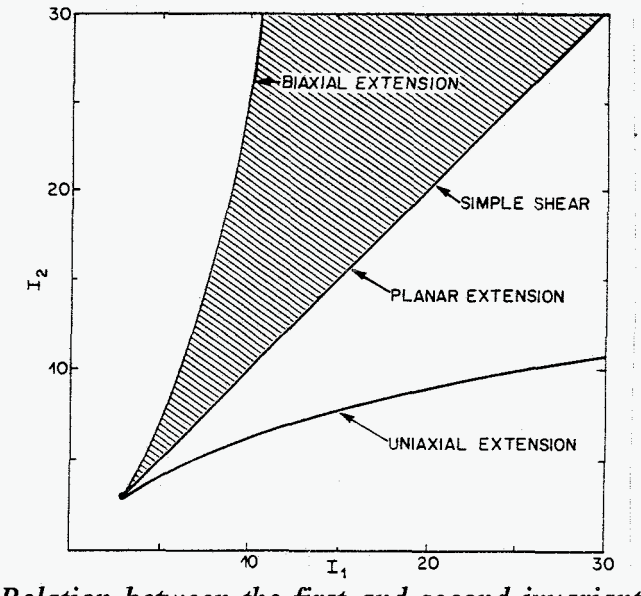


Figure 2.13 *Relation between the first and second invariant of the Finger strain tensor (I_1 and I_2 respectively) for particular types of strain histories. (From Larson [1988]).*

In the unsteady physiological flow situation the aggregation-disaggregation proces is not existing

In the unsteady physiological flow situation the aggregation-disaggregation proces is not existing (see discussion section 1.4 and 2.3). Therefore, in the unsteady physiological flow situation all models in table 2.4 probably loose their original physical interpretation. Further, realizing that in case of blood the rouleaux have no long side branches (see for example the discussion in Rosenblatt [1986], p. 5), it means that the constitutive model should not be sensitive to alignment strength. Thus the stresses it predicts should not be different because of a difference in alignment strength of the flow. Considering the models as known from polymer rheology, according to Larson [1988], the Phan-Thien Tanner (PTT) model and Larson model are not sensitive to alignment strength. These two model show different sensitivity to flow strength: the PTT model produces in a strong flow higher stresses than in a weak flow; the Larson model is not as much flow strength dependent. No experimental data for blood is available at this point yet.
The integral model of Papanastasiou as used by Hoitinga [1990] is strongly criticized by Larson [1988, p.213 - 214]. Contrary to Tanner [1985] he concludes that it does not belong to the class of KBKZ equations.
Tanner [1985] showed in a comparative study of constitutive model predictions of various viscometric and test flows of polymer melts and experimental data that a KBKZ model showed very satisfactory results. This type of model can be a good candidate, but is not yet implemented in SEPRAN. From Hoitinga [1990] it appears that it can relatively easily be achieved.
In order to make a good judgment of the accuracy (both qualitatively as quantitatively) of the discussed models above, more comparisons of model predictions with experimental data of blood is needed very much. This can possibly be achieved by using a few test problems, that are relatively easy to be performed in experiments. Larson [1988, p. 199] uses, three different test flows: relaxation after step shear, stress growth in start up of steady elongation and relaxation after a step biaxial extension in order to have a broad range of deformation types. Unfortunately, the elongating test flows can not experimentally be performed with such a low viscosity fluid as blood. As an alternative, another attempt to use a relatively simple test geometry to evaluate different constitutive models is proposed by Armstrong e.a. [1985]. They have used a geometry with two excentric cilinders, the outer one standing still, the inner one rotating. This geometry results in a flow that is a mixture of a shear flow and an extensional flow. Armstrong e.a. show that it can be useful to evaluate the validity of different constitutive models. The practical aspects of carrying out these experiments need to be investigated.

2.7 Summary

Of all the constitutive models applied to blood as found in literature, only the Bird-Carreau model seems to be a serious candidate for describing the flow situation of interest (i.e. the carotid artery bifurcation). This is concluded on the ground of the available comparative model data with blood

based on a Maxwell equation (mostly UCM) together with a structural kinetics equation. There is a lack of data to judge the adequacy of these models. In principle, the Maxwell type of models are not preferred to be used in modern rheology. Of all models only data is available for shear flows, no elongating flows, nor mixed ones. It is crucial to have data for flows that have elongating deformation in order to judge the different constitutive models. All models for blood as found in literature are based on considerations of the aggregation-disaggregation process. This is probably not appropriate in the physiological flow case. Because of the similarity between the rheology of blood and of polymers, constitutive models used for polymers are of interest. Some of them are implemented in SEPRAN; of all implemented models, the Phan-Thien Tanner model and Larson model are expected to be the most useful. Additionally, a KBKZ model, not yet implemented completely, has proved to be a very good model for describing the viscoelastic flow of polymers. For that reason the use of this model should be investigated more detailed. There is a strong need to have more experimental data of blood in order to make a good judgment of the accuracy of the different models.

3 Non-Newtonian blood rheological analog fluids

3.1 Introduction

There are several reasons in case of a non-Newtonian flow study to use a blood rheological analog fluid instead of blood it self:

- blood is unstable, tending to separate into a cell phase and a plasma phase;
- it is opaque to light (problematic in case of LDA measurements and flow visualization study)
- it may carry disease;
- it is difficult to obtain in large volumes.

In the next section different fluids which are used as non-Newtonian rheological analog fluids for blood will be discussed.

3.2 Non-Newtonian blood rheological analog fluids

In table 7 the non-Newtonian blood rheological analog fluids as found in literature are listed with the references and their composition given.

Table 3.1 Non-Newtonian blood rheological analog fluids

NAME	COMPOSITION	REFERENCES
Separan	0.05 % AP30:0.04% AP45 = 3 :1 + 4% isopropanol + 0.01 % $MgCl_2$	Liepsch [1991]
Milling Yellow	a commercial dye ("alphanol echtgelb",Hoechst)	Schmitz [1983], [1984] Liepsch [1987]
Polystyrene microspheres	12 % by weight 1μm polystyrene particles in distilled water + 10 mMol $CaCl_2$ + 5% Dextran.	Fukada e.a. [1989]

Table 3.1 Continued

Xanthan gum	500 ppm in distilled water	Thurston [1989]
Xanthan gum gel	50 % by volume in glycerol	Thurston [1989]
Ghost cells	washed red blood cells prepared according to "Dodge" (see reference)"	Liepsch e.a. [1991]
Biconcave disc shaped particle solution	16 % BASF particles + 2% Dextran (see reference)	Liepsch e.a. [1991]
AP30	0.05 % AP30 + 4% isopropanol + 0.01 % $MgCl_2$	Liepsch e.a. [1991]
AP45	0.04 % AP45 + 4% isopropanol + 0.01 % $MgCl_2$	Liepsch e.a. [1991]
Vanadium-pentoxid sol	see reference	Liepsch [1987]

3.2 Experimental results

Several papers contribute to the problem of finding a non-Newtonian blood rheological analog fluid. In the following the most recent and important papers are reviewed in chronological order.

Fukada, Seaman, Liepsch, Lee, Friis-Baastad [1989]

This study concerns a blood rheological analog fluid with non-Newtonian properties, that consists of an aqueous suspension of uniform polystyrene microspheres, a polystyrene latex. Even though the particles are solid and nondeformable, a model fluid is proposed. The latex consists of

polystyrene microspheres with a diameter of 1.07 μm ± 2 % suspended in distilled water. There is an electrostatic repulsive force between the particles, caused by the sulphate end groups on the surface of microspheres which have a negative charge. On the other hand, most of the surface area of the particles is hydrophobic, and they are attracted to one another by long range van der Waals forces., The short term stability of such a colloïdal system is usually determined by a balance equation:

$$V^T = V^R + V^A + V^S \qquad (3.1)$$

V^T the total potential energy of interaction; with V^R the repulsive potential energy; V^A the attractive potential energy; V^S the solvation or entropic energy. Aggregation between particles can only occur when $V^A > V^R$.

Sodium chloride and calcium chloride were used to modify the surface charge and thus V^R between the particles. V^A was also modified by means of the ionic strength of the suspending medium, the distilled water. Dextran, an organic molecule, producing interparticle bridges, was used for increasing the attractive forces between particles. In the following the major interesting results are discussed.

In figure 3.1 the steady flow viscosity η for a 32 % by weight 1 μm polystyrene suspension in H_2O with different amounts of $CaCl_2$ is presented. For the same suspension the dynamic viscosity (a), dynamic elastic (b), and loss moduli (c) are presented in figure 3.2. In all figures data for human blood are given for comparison. From these pictures it is concluded that blood is mimiced by this suspension fairly well in a qualitative sense, but not yet in a quantitative sense. The 20 mM $CaCl_2$ solution gives results most closely to blood, however values are about a factor 1.5 - 2 too small.

Fukada e.a. argue that the 32 % concentration of the microspheres is about equivalent in influence to blood with a hematocrit of 45 %. On the other hand, in figure 3.3 the effect of adding 10 mM Calcium chloride and 5 % dextran each separately causes no aggregation, while together a suspension with only 12 % polystyrene microspheres produces clearly a non-Newtonian steady flow viscosity that is very close to blood. No dynamic measurements are reported.

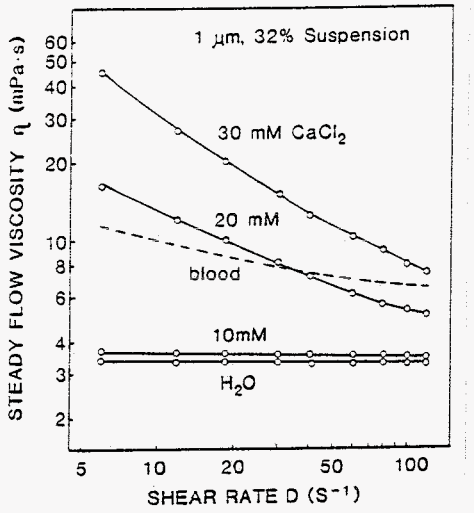


Figure 3.1 *The steady flow viscosity η for a 32 % 1 μm polystyrene suspension in H_2O with different amounts of $CaCl_2$ at T = 25°C. (From Fukada e.a. [1989]).*

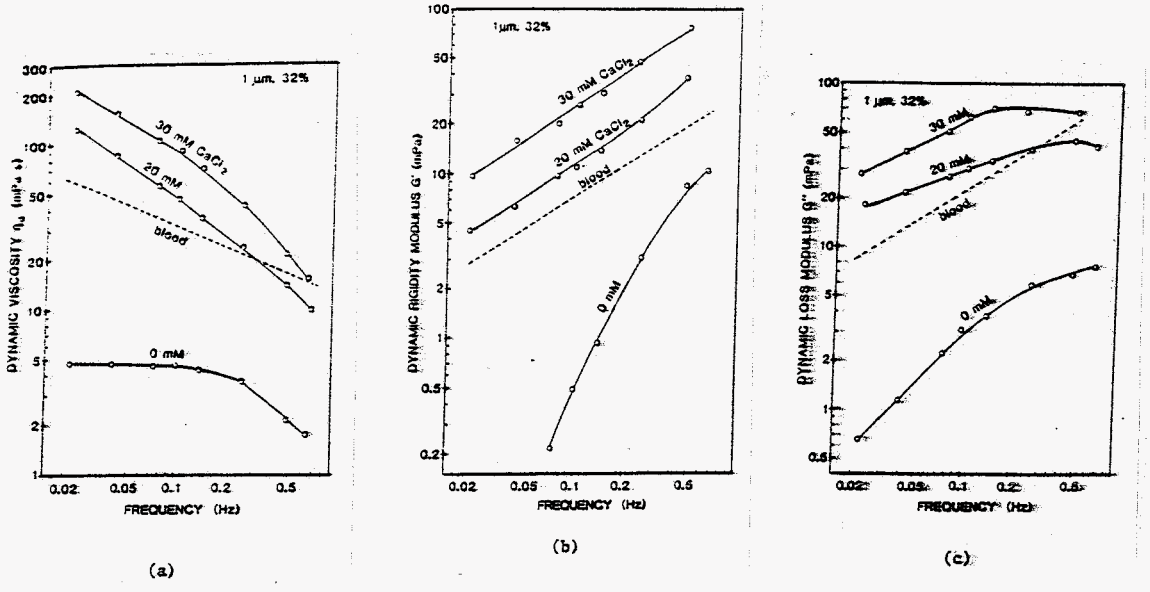


Figure 3.2 *The dynamic viscosity (a), rigidity modulus (b), and dynamic loss moduli (c) for the same solution as in figure 27. (From Fukada e.a. [1989]).*

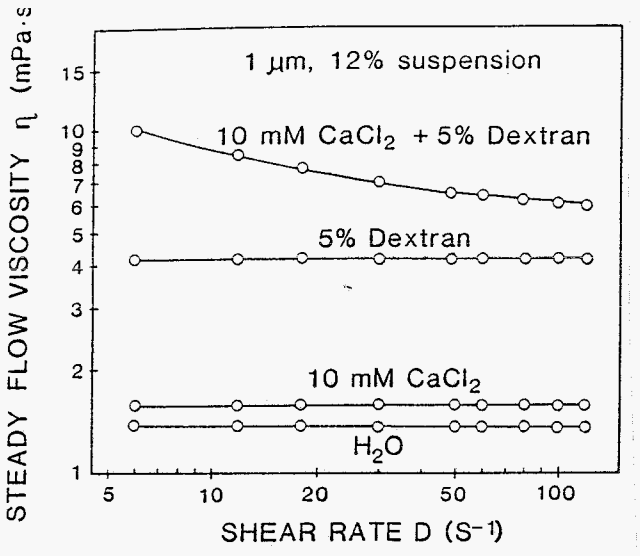


Figure 3.3 *The effect on the non-Newtonian steady flow viscosity of adding 10 mM Calcium chloride and 5 % dextran each separately to a suspension of 12 % polystyrene microspheres (that causes no aggregation), or together (that causes a steady flow viscosity very close to blood (compare figure 3.1). (From Fukada e.a. [1989]).*

Thurston [1989]

Thurston presents measurements of the steady shear viscosity and of the components of the complex viscosity for human blood and three non-Newtonian blood rheological analog fluids: a hydrolyzed polyacrylamide ("Flopaam 2000") of molecular weight ≈ 12 million dispersed in distilled water at a concentration of 300 ppm, Xanthan gum (a high molecular weight polysaccharide, a rod-like macromolecule produced by a strain of Xanthomonas compestris organism), and Xantan gum gel fragments. In figure 3.4 the steady shear viscosity and the oscillatory shear rate amplitude (rms value) dependence of the viscoelasticity of normal blood measured at 2Hz and 22°C is shown. In figure 3.5 the same measurements are presented for the polyacrylamide solution at 23°C, in figure 3.6 for the Xanthan gum (macromolecular concentration 500 ppm) at 22°C and in figure 3.7 for the Xanthan gum gel solution in 50% (by volume) glycerol at 22°C. From these figures (3.4 - 3.7) it is evident that the three analog fluids all provide rheological properties that are to a certain extent similar to normal human blood. There are however important differences that will be discussed below.

The steady flow viscosity in case of the polyacrylamide solution is for the shear rate values below unit strain to high compared with the blood data (50 - 300%), for higher values a good agreement is found. The viscous component of the complex viscosity as a function of shear rate at 2Hz is in good agreement with blood for $1\ s^{-1} < \gamma < 50\ s^{-1}$ (within 20 %); for larger values the

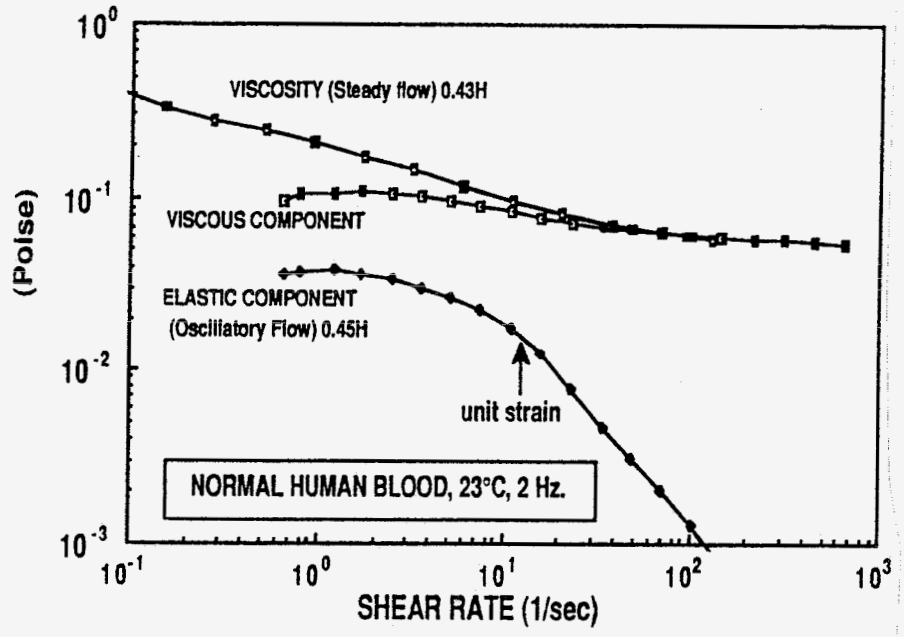


Figure 3.4 *The steady shear viscosity and the oscillatory shear rate amplitude (rms value) dependence of the viscoelasticity of normal blood measured at 2Hz and 22°C. (From Thurston [1989])*

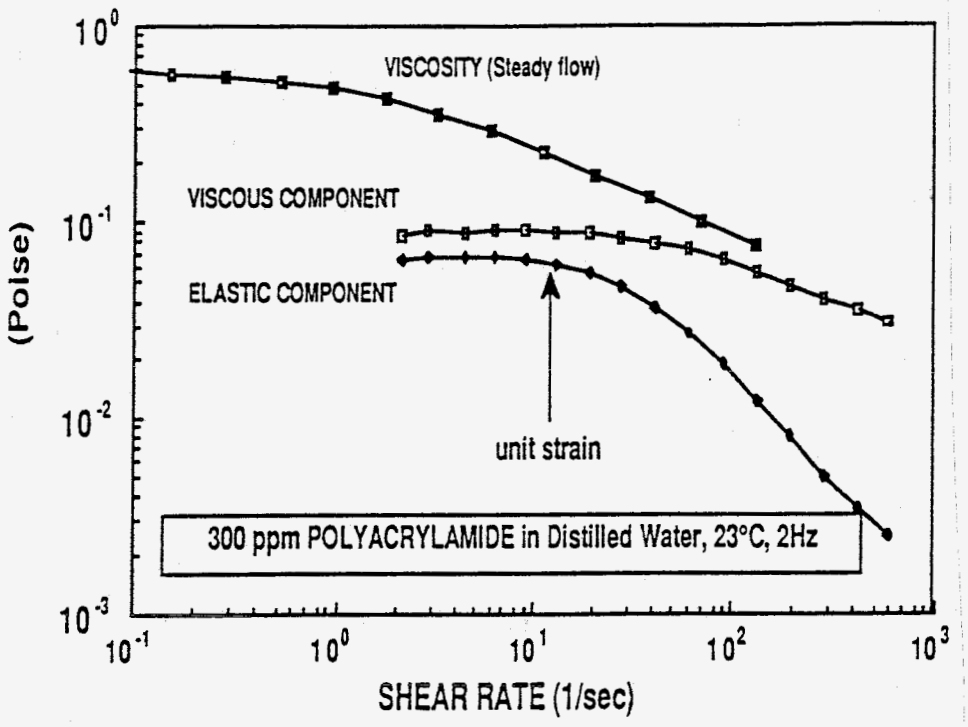


Figure 3.5 *The steady shear viscosity and the oscillatory shear rate amplitude (rms value) dependence of the viscoelasticity of the polyacrylamide solution measured at 2Hz and 23°C. (From Thurston [1989]).*

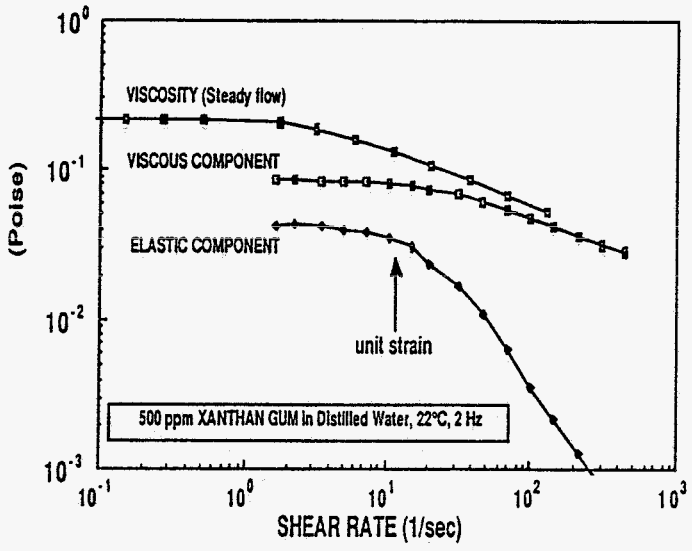


Figure 3.6 *The steady shear viscosity and the oscillatory shear rate amplitude (rms value) dependence of the viscoelasticity of the Xanthan gum solution measured at 2Hz and 22°C. (From Thurston [1989]).*

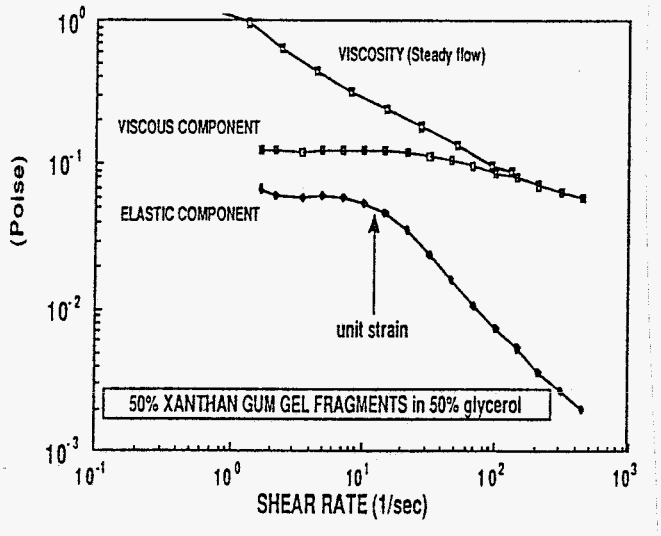


Figure 3.7 *The steady shear viscosity and the oscillatory shear rate amplitude (rms value) dependence of the viscoelasticity of the Xanthan gum gel solution measured at 2Hz and 22°C. (From Thurston [1989]).*

polyacrylamide values are to low (20 - 50 %). For polyacrylamide the elastic component is too high compared with blood (200%). The constant value of the viscous and elastic components of the complex viscosity as a function of the shear rate at 2Hz below unit strain (η' = 0.09 Poise, and η'' = 0.07 Poise) and the increase of the steady flow viscosity toward a constant value at low

shear rates (η_s = 0.6 Poise) suggest that this solution has a stable, time-independent internal structure at low rates of deformation ($\gamma < 4\pi$ s^{-1}; 1 unit of strain γ). This is in contradiction with the time-dependent formation of red cell aggregates in human blood, that are broken up at low shear rate amplitudes ($\gamma > 2$ s^{-1}) in oscillatory flow.

For the Xanthan gum solution the steady flow viscosity is about 200% too high at very low shear rates ($\gamma \approx 0.1$ s^{-1}). The difference decreases till at intermediate and higher values of the shear rate ($\gamma \approx 20$ s^{-1}) the differences are within 10%. As with the polyacrylamide solution the constant value of the viscosity at low shear rates ($\gamma < 1$ s^{-1}) is a remarkable difference compared with blood, where no such constant level is measured. The viscous component of the complex viscosity agrees within 10% with the values of human blood for shear rates up to 200 s^{-1}. With increasing γ the Xanthan gum values decrease too fast, the difference increasing up to 50% with normal blood at $\gamma = 400$ s^{-1}. The elastic component at low shear rates ($\gamma < 5$ s^{-1}) is about 50% too high, the difference increasing up to 400% at higher shear rates ($\gamma \approx 200$ s^{-1}). Remarkable is the relatively constant level of the elastic component at low shear rates ($\gamma < 10$ s^{-1}), that does not exist for human blood. This suggests that no large groups of macromolecules, which would be analogous to large red cell aggregates, are formed.

The third fluid, the Xanthan gum gel solution is expected to simulate the rheological behaviour of blood more closely then the two previous discussed fluids. This is because the microstructure of this gel is more similar to blood: elastic particles (~ erythrocytes) suspended in a viscous fluid (~ plasma), which interact (~ aggregation). The results in figure 3.7 show that below $\gamma = 4$ s^{-1} the steady flow viscosity of the gel increases too fast with decreasing γ, the difference being 200% at $\gamma = 1$ s^{-1}. For $\gamma > 4$ s^{-1}, the values of the gel solution are in a fairly well agreement with blood; they are no more than 10% too high compared with blood. The viscous component of the complex viscosity is in a very good agreement with the value of blood (within a few percent). The elastic component however is much too high compared with blood; at $\gamma = 10$ s^{-1} the values of the gel are about 300% too high, for smaller values of γ, the difference increases to 800% too high values at $\gamma = 200$ s^{-1}. Further , the elastic component is nearly constant below unit strain. This indicates together with the too high value of the steady flow viscosity at low shear rates, that in the gel a stronger interparticle binding exists compared with blood.

Concluding: the three analog fluids all simulate the rheological behaviour of blood,as described by the steady shear viscosity and the complex viscosity (as a function of shear rate at 2 Hz or frequency ω) only in a qualitative way; the Xanthan gel exhibits the most similar behaviour. However, even this fluid is not satisfactory, as it seems to have too strong interparticle binding compared with blood.

Mann, Tarbell [1990]

Mann and Tarbell report viscometric and flow studies of three non-Newtonian blood analog fluids in rigid curved and straight artery models. The three fluids are polyacrylamide (Separan), Xhantan gum gel and glycerin. They were compared with bovine blood.

The steady flow viscosities η for all four fluids were all well correlated by a power-law model ($\eta = k\,\dot{\gamma}^{n-1}$) over the entire shear rate range of the measurement, see table 3.2.

Table 3.2 Power-law constants for the steady shear viscosity for blood rheological analog fluids (T = 23 - 28 °C) as used by Mann and Tarbell [1990].

Viscosity Power Law Constants for Blood Analog Fluids at Room Temperature (23°C - 28°C).

Fluid	m (dynes sec^n/cm^2)	n	r
0.0375% Xanthan gum + 0.02% NaCl	0.118	0.732	0.990
0.020% Separan AP30 + 0.02% NaCl	0.123	0.753	0.999
Bovine Blood (H = 30%)	0.04 - 0.07	0.86 - 0.92	0.999
Human Blood† (H=43.2%, T=37°C)	0.135	0.784	---

(m,n) are the constants in the correlation $\mu = mS^{n-1}$; r is the correlation coefficient. † from (23).

Normal stress τ_N data for the Xanthan gum and Separan solutions were well correlated by a power-law model ($\tau = a\,S^b$), see table 3.2. For Separan normal stresses were measured that are about three times higher than for the Xanthan gum solution. The only measurements of τ_N for human blood known to the authors are those of Copley and King, who were unable to detect appreciable τ_N in the shear rate range of 5 - 1000 s^{-1}.

Measurements of complex viscosity in oscillatory shear experiments are reported for human blood as well as for the analog fluids (figure 35). The viscous (figure 35 a) and elastic (figure 35b) components of the complex viscosity were measured as a function of the shear rate. For human blood Mann and Tarbell present the data of Thurston [1979].

From these figures, it appears that the viscous components for the three fluids are quite close to each other in the shear rate range 20 $s^{-1} < \dot{\gamma} < 100\ s^{-1}$, but the elastic components are significantly different in the same shear rate range. Although elasticity measurements are not available for bovine blood, we expect bovine blood to be less elastic than human blood because it

Table 3.3 Power-law constants for the normal stress for blood rheological analog fluids (T = 23-28 °C) as used by Mann and Tarbell [1990].

Normal Stress Power Law Constants for Blood Analog Fluids at Room Temperature.

Fluid	a (dynes sec^b/cm^2)	b	r
0.0375% Xanthan gum + 0.02% NaCl	0.0002	2.050	0.991
0.020% Separan AP30 +0.02% NaCl	0.00041	2.135	0.943

(a,b) are the constants in the correlation $\tau_N = aS^b$; r is the correlation coefficient.

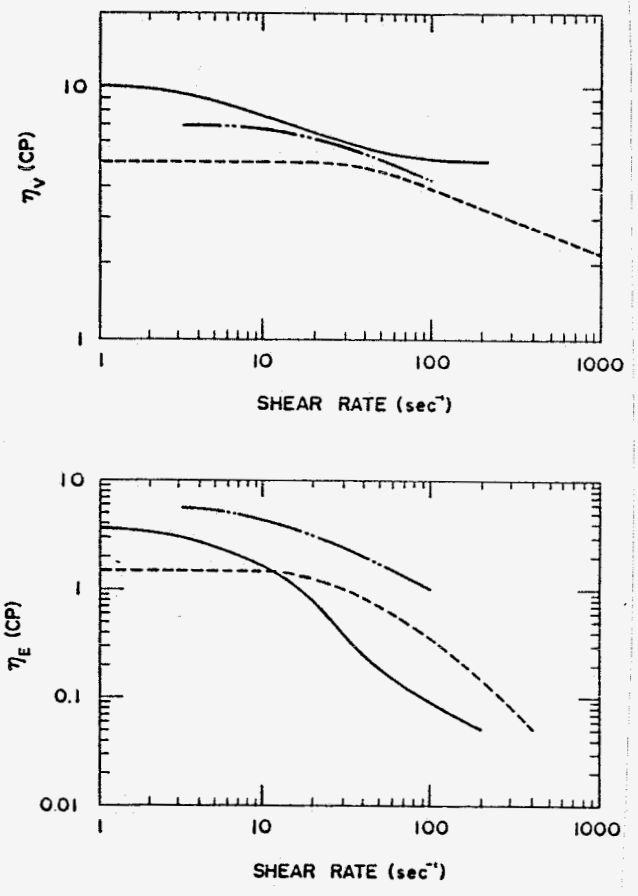


Figure 3.8 *The shear rate dependence of the a) viscous and b) elastic components of the complex viscosity at 2 Hz for 0.015 % Polyacrylamide ——— — — ——— (Moravec and Liepsch 1983); 0.0375 % Xanthan gum - - - (Thurston and Pope (1981)); human blood (HTC = 43 %) ——— (Thurston 1979). (From Mann and Tarbell [1990]).*

nearly does not aggregate. The viscous properties (both steady and oscillatory), as the authors conclude, of the polymer solutions simulate human blood fairly well. They fail however to simulate the elastic properties accurately.

From both normal stress measurements and oscillatory viscometry, it is concluded that Separan solutions are significantly more elastic than Xhanthan gum solutions, which in turn are more elastic than human blood. The effect of these differences on the flow behaviour of these fluids under physiological conditions is the question to be addressed to next. For that reason, measurements of wall shear rates have been done in a curved tube, in both stationary and oscillatory flow, using a flush-mounted hot film anemometer probe. Figure 3.9 illustrates the experimental set-up used. The aspect ratio (= internal radius/ curvature radius) of the curved tube was 11.9, the internal diameter was 2.54 cm. All shear rate data have been normalized by a factor:

$$S_{pl} = ((3n+1)/4n)\ (4Q/\pi R^3) \qquad (3.2)$$

with Q the flow rate in case of steady flow, or the time averaged flow rate in case of sinusoïdal flow, n the powerlaw index of the fluid, R the tube radius, S_{pl} the theoretical
value of the wall shear rate for a power-law fluid in fully developed steady flow through a straight tube. Also, a modified Dean number D_n (= $Re_{pl}/\sqrt{\lambda}$), based on a generalized Reynolds number for a power-law fluid:

$$Re_{pl} = 1/((3n+1/4n)^n\ 8^{n-1})\ [(2R)^n \underline{V}^{2-n}\ \rho\ m^{-1}] \qquad (3.3)$$

with m power-law coefficient, $\underline{V}$ sectional mean velocity. Some results are shown in figures 3.10 to 3.12. For each fluid, four steady flows and three sinusoïdal flows were investigated (with different flow rates between 2 and 9 l/min) with a Dean number up to 650. For comparison, a typical Dean number for mean flow in the aortic arch has a value of 300 - 500, and in a coronary artery this value would be 50 - 100. The fundamental frequency of the oscillatory flow was 0.7 Hz, thus the Womersley parameter $\alpha = \nu\rho/\omega = 14$ in the Newtonian case. The data points represent the mean values obtained in replicated experiments. The standard deviation divided by the mean averaged 10.6 % for all experiments reported. The wall shear rate was measured at three locations: $\theta = 0^\circ$ (outer wall), $\theta = 180^\circ$ (inner wall), $\theta = 180^\circ$ (outer wall). In figure 3.10 the normalized wall shear rate as a function of Dean number in steady flow at the entrance of the curved tube, $\theta = 0^\circ$, is shown. The data for non-Newtonian fluids are not significantly different from one another and are parallel to the data for the Newtonian fluid. Between those two groups, a difference of 35 % exists.

In figure 3.11 the normalized wall shear rate data along the outer curvature at $\theta = 180^{\circ}$ are displayed. Polyacrylamide and Xanthan gum give data that are very close, differences being maximal 12%. The deviation between those two fluids and the Newtonian fluid are smaller than 35%. The bovine blood, and the Newtonian fluid give very similar results for $D_n < 300$; above this value the differences are significant, up to 20 %. For higher values ($D_n > 300$) all analog fluids give too high data compared with blood.

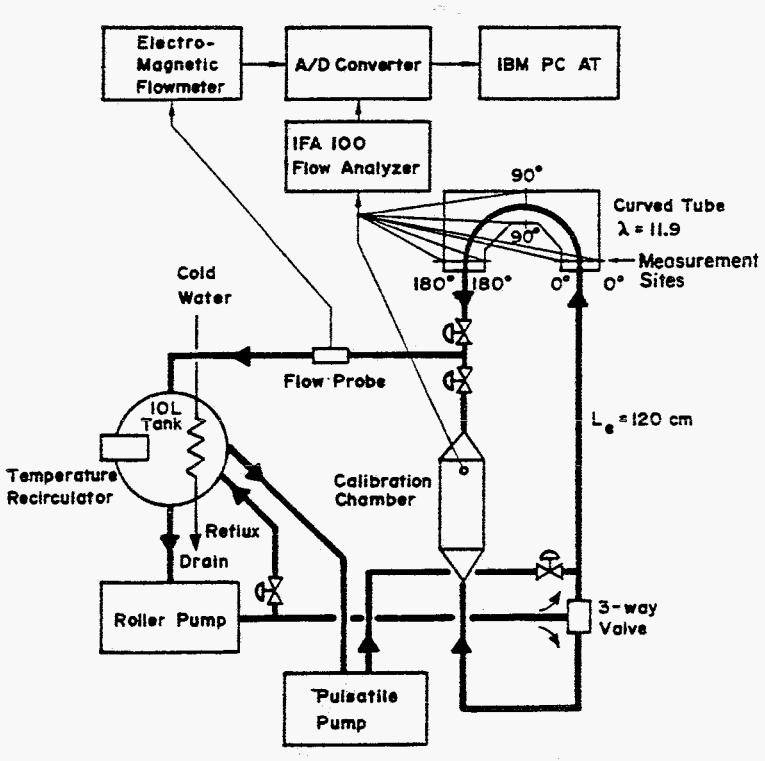


Figure 3.9 *Experimental set-up as used by Mann and Tarbell. (From Mann and Tarbell [1990]).*

The normalized wall shear rate data along the inner curvature at $\theta = 180^{\circ}$ is given in figure 3.12. Again polyacrylamide and Xanthan gum display almost identical values over the entire Dean number range which are not significantly different from the Newtonian fluid values. The values of bovine blood are significantly different from the values for the analog fluids, that are about 50 % lower over the entire Dean number range. Since both fluids have negligible normal stress differences, the viscous properties of bovine blood as measured in a capillary viscometer with parallel flow streamlines seem to be altered by the strong secondary flows in the curved tube sections ($\theta = 180°$). As a possible explanation it is suggested by Mann and Tarbell that a disruption or reorganization of the cell layers takes place, as recently described by Thurston [1990].

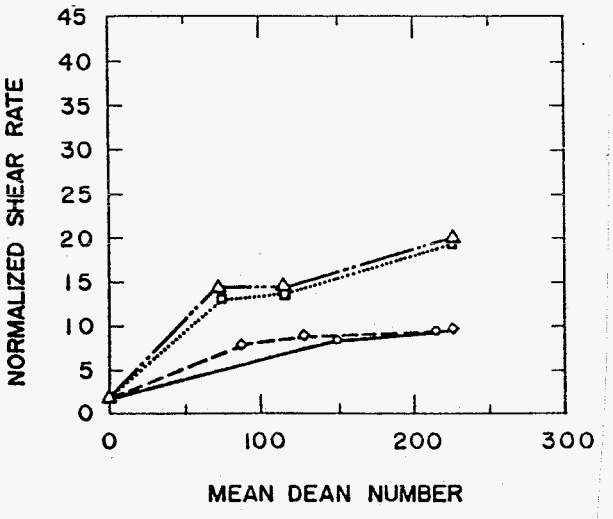


Figure 3.10 *Normalized wall shear rate a function of Dean number in steady flow at the entrance to the curved tube (θ = 0 °) along the outer curvature. o = Glycerin; Δ = Xanthan gum; □ = Polyacrylamide; ◊ = bovine blood. (From Mann and Tarbell [1990]).*

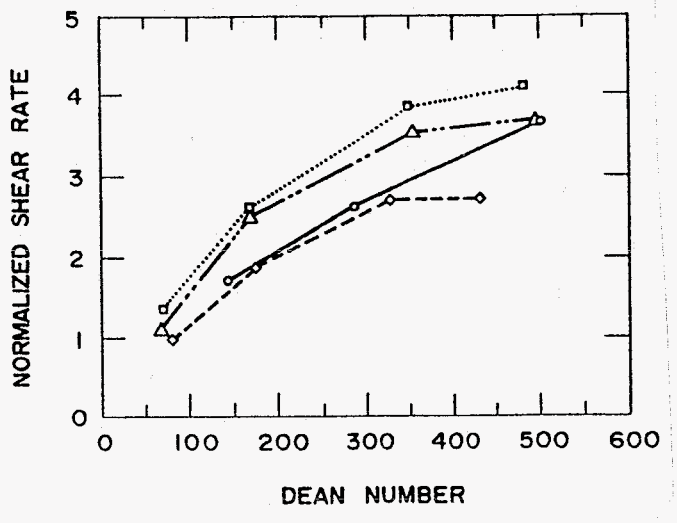


Figure 3.11 *Normalized wall shear rate as a function of Dean number in steady flow at the exit of the curved tube (θ = 180°) along the outer curvature. o = Glycerin; Δ = Xanthan gum; □ = Polyacrylamide; ◊ = bovine blood. (From Mann and Tarbell 1990).*

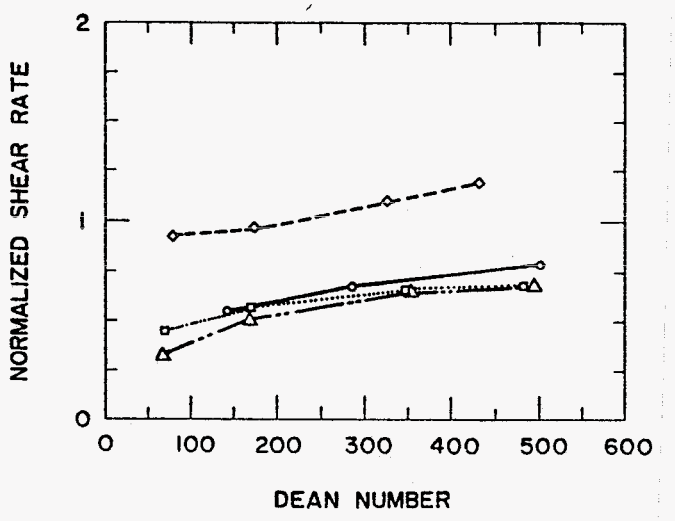


Figure 3.12 *Normalized wall shear rate as a function of Dean number in steady flow at the exit of the curved tube (θ = 180°) along the inner curvature. o = Glycerin; Δ = Xanthan gum; □ = Polyacrylamide; ◊ = bovine blood. (From Mann and Tarbell 1990).*

In all experiments described above, almost no difference in shear rates for polyacrylamide and Xanthan gum can be distinguished. There is little difference between those two fluids and the Newtonian fluid, at any of the locations investigated. The differences in elastic properties (i.e. normal stresses) of these fluids are not manifest in this flow situation, despite the existence of secondary flow. On the other hand, the bovine blood resulted in somewhat larger deviations from the data for the Newtonian fluid.

In oscillatory flow (a sinusoïdal waveform with the flow rate varying between 0 and 6.5 l/min) significant differences in flow behaviour are found between the different fluids. On the one hand at $\theta = 0^{\circ}$ a good agreement exists between the wall shear rates of the Xantan gum solution and the bovine blood: the peak values differ 16% (figure 3.13). On the other hand, the glycerin and polyacrylamide produce very similar wall shear rates, the peak values differ about 10 %. Those two groups are however very different. The bovine blood and Xanthan gum have a factor two larger values compared with the glycerin and polyacrylamide during the entire cycle. The secondary peak in the wave form is associated with wall shear reversal, as is confirmed by numerical results of Chang and Tarbell [1985].

At $\theta = 180^{\circ}$ along the outer curvature, a completely different picture of the different fluid behaviors exists, see figure 3.14. Now, the Newtonian glycerin fluid provides the best simulation of bovine blood, the peak values agree within 7%. The Xanthan gum solution has a rather different waveform, the maximum difference is a factor two too high. The polyacrylamide and the

Xanthan gum give fairly similar results, the polyacrylamide gives the most different wave form compared with the bovine blood. No secondary peak exists at the wave form, meaning that no wall shear reversal occurs at this location. This is confirmed by numerical simulations reported in literature.

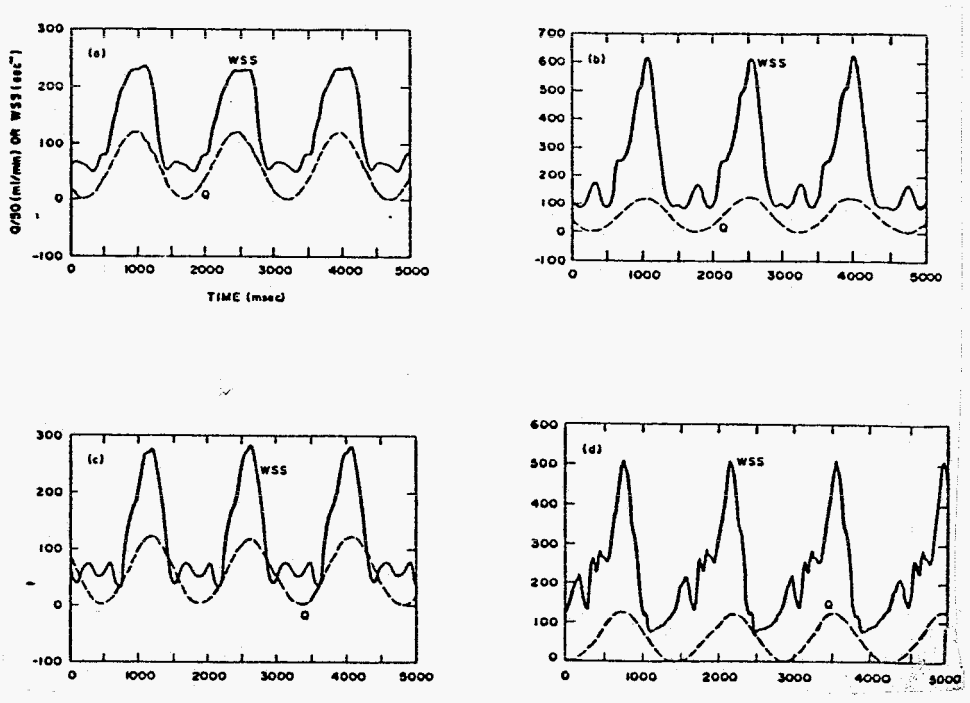


Figure 3.13 *Wall shear rate (WSS) and flow (Q) waveforms at the entrance to the curved tube (θ = 0 °) along the outer curvature (a) glycerin, (b) Xanthan gum, (c) Polyacrylamide (d) bovine blood. (From Mann and Tarbell [1990]).*

The wall shear rates at the third location, $\theta = 180^{\circ}$ along the inner curvature are presented in figure 3.15. The Newtonian, Xanthan gum and bovine blood waveforms do have a strong secondary wall shear peak, associated with the existence of wall shear rate reversal. In case of the Newtonian fluid, this is confirmed by previous numerical work (Chang and Tarbell [1985]). These three fluids qualitatively exhibit at this location very similar flow behaviour. Compared with the blood, the Xanthan gum has about 35% higher values and a phase shift that results in a delay of 300 ms.

Conclusions: in oscillatory flow the fluids exhibit more different behaviour then in steady flow; it is believed that in part this is caused by the higher shear rates (and thus higher normal stresses, that increase with the square of the shear rate). This means that oscillatory flow is a good test to discriminate between different fluids. *In general none of the blood analog fluids tested provides a completely satisfactory model of bovine blood in a curved tube, not in steady flow nor in*

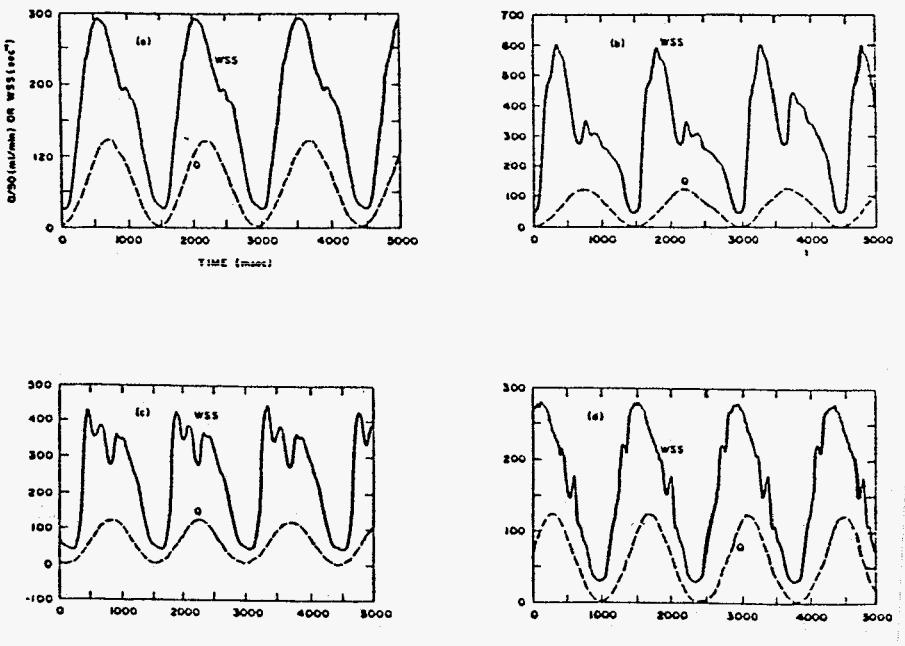


Figure 3.14 *Wall shear rate (WSS) and flow (Q) waveforms at the entrance to the curved tube (θ = 180 °) along the outer curvature (a) glycerin, (b) Xanthan gum, (c) Polyacrylamide (d) bovine blood (from Mann and Tarbell [1990]).*

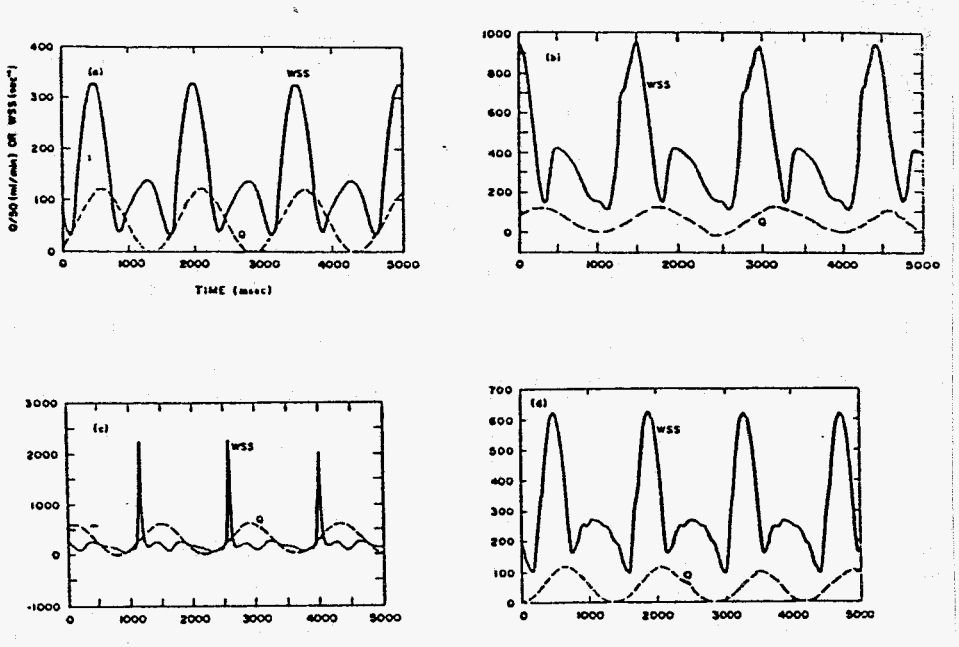


Figure 3.15 *Wall shear rate (WSS) and flow (Q) waveforms at the entrance to the curved tube (θ = 180 °) along the inner curvature (a) glycerin, (b) Xanthan gum, (c) Polyacrylamide (d) bovine blood (from Mann and Tarbell [1990]).*

oscillatory flow.
From their results, Mann and Tarbell conclude that polyacrylamide is completely inadequate. Xanthan gum and the Newtonian fluid give qualitatively better results, the Newtonian fluid especially in the steady case. However, significant quantitative differences exist (a factor two). The cellular nature of blood is probably an important missing factor in the fluid models used.

Liepsch, Thurston, Lee [1991]
In this study six non-Newtonian blood rheological analog fluids were investigated. First the viscous and viscoelastic properties of these fluids were compared with human blood samples in steady flow, transient flow and in oscillatory flow. The fluids were Separan polyacrylamide suspensions, with 4% isopropanol and 0.01 % MgCl added, of 1) aqueous 0.05 % Separan AP30 , 2) 0.04 % aqueous AP 45, 3) a mixture of fluids 1) and 2) in a proportion 3:1; 4) a 2 % aqueous Dextran suspension with a 16 % weight fraction biconcave disc-shaped particles; 5) 40 % ghost cells prepared according to Dodge in tri(hydroxymethyl)aminomethane; 6) a suspension of 5% Dextran (70000) with 12 % polystyrene particles (1μm) and 10 mM $CaCl_2$.
For several different concentrations for Separan AP 30 (figure 3.16) and AP 45 (figure 3.17) solutions separately the steady state shear viscosity was determined and compared with the blood data. The 0.05 % AP 30 solution gave a good agreement with the blood data for shear rates of 4 s^{-1} and higher. In this range the maximum difference is about 14 %, but in the interval 10 $s^{-1} < \dot{\gamma} < 100\ s^{-1}$, a very good agreement is found (within 6%). For shear rates below 4 s^{-1} significant lower values for AP 30 were found. From figure 3.17, the 0.04 % AP 45 solution yielded the best results. In the range $4\ s^{-1} < \dot{\gamma} < 400\ s^{-1}$ a good agreement was found (within 8 %). Just as with the AP 30 solution lower values were found for the AP 45 solution at shear rates below 4 s^{-1}. For the 0.05 % AP 30 and 0.04% AP 45 solutions, the viscous and elastic components versus shear at a frequency of 2 Hz were measured (figure 3.18 and 3.19 respectively); these can be compared with blood data (for example figure 3.4). The viscous components agree the best with the blood data; for Separan AP 30 the differences are maximal 2 %, thus a very good agreement. For Separan AP 45 larger differences are found of about 4 % but still a good agreement compared with the blood data. The elastic components of the Separan solutions are qualitatively similar to the blood data but differ dramatically quantitatively. The AP 30 solution data values are a factor 1.6 too high compared with the blood data; for the AP 45 solution values that are a factor 1.2 - 1.5 higher were found. This is rather good compared with the other analog fluids.

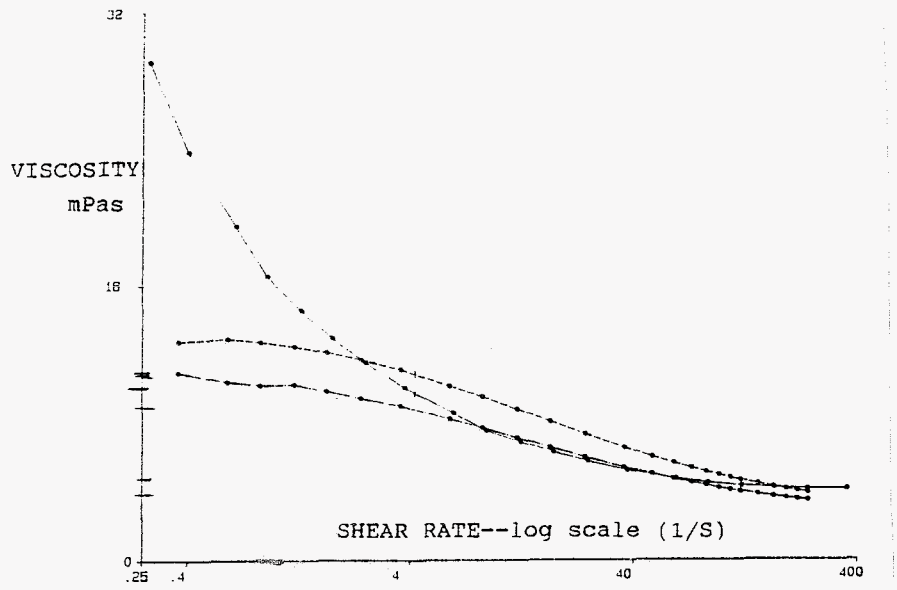


Figure 3.16 *Viscosity versus shear rate for an 0.07 % (- - -) and 0.05 % (- · -) aqueous polyacrylamide solution (Separan AP 30) with 4% isopropanol and 0.01% $MgCl_2$ compared to human blood, HCT = 46 % at 37 °C. (From Liepsch e.a. [1991]).*

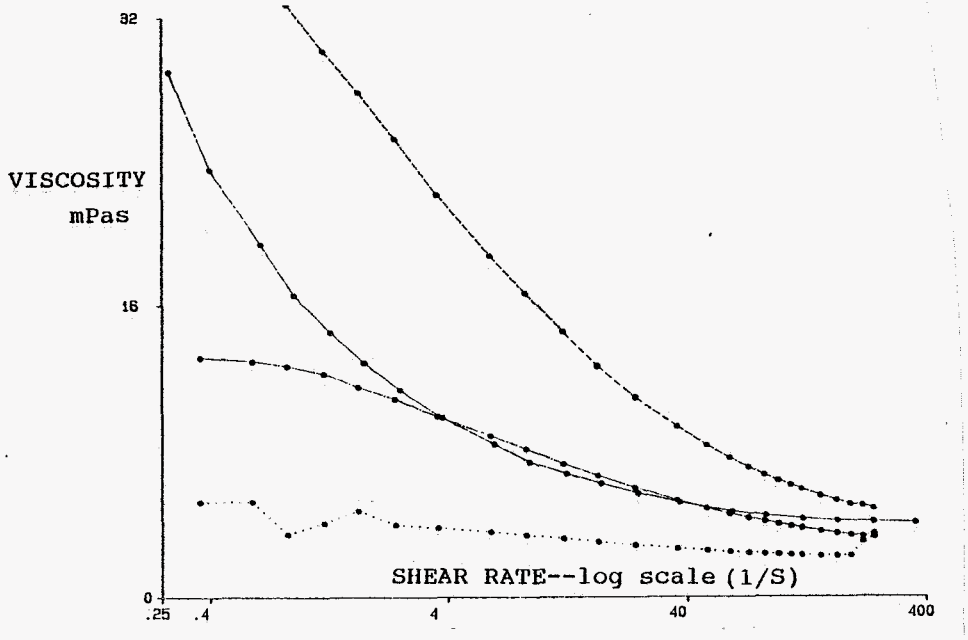


Figure 3.17 *Viscosity versus shear rate for an 0.06 % (- - -), 0.04 % (- · -), and 0.02 % (· · ·) aqueous polyacrylamide solution (Separan AP 45) with 4% isopropanol and 0.01% $MgCl_2$ compared to human blood, HCT = 46 % at 37 °C.(From Liepsch e.a. [1991]).*

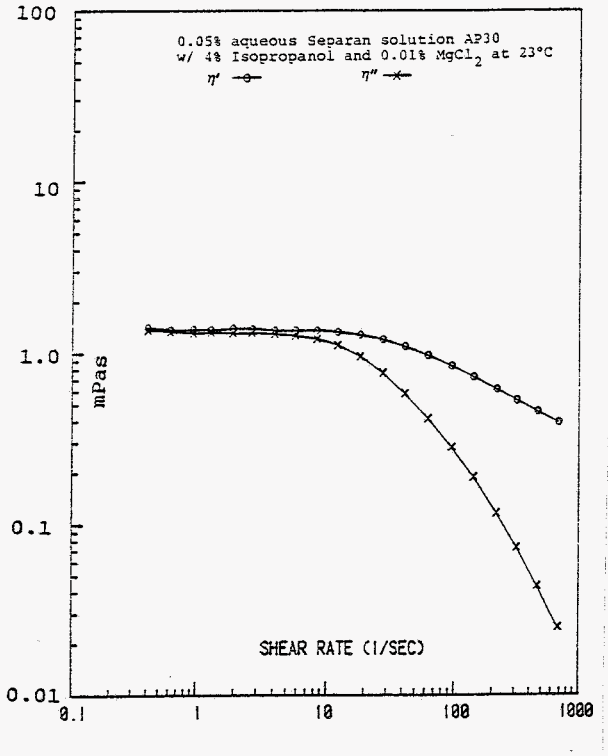


Figure 3.18 *Viscous and elastic component versus shear rate for a 0.05% aqueous Separan (AP30) solution with 4% isopropanol and 0.01% $MgCl_2$ at 23°C. (From Liepsch e.a. [1991]).*

The steady flow viscosity for the aqueous Separan mixture (fluid 3)) at 37 °C is compared to blood (HTC 46 %) at 37 °C (figure 3.20); this was also done at 23 °C. At 23 °C the Separan and blood data agree within 8 - 14 % over the entire shear range 0.4 s^{-1} - 400 s^{-1}. At 37 °C for shear rates larger than 10 s^{-1} the Separan values are about 12 - 17 % lower then the measured blood data. No complex viscosity is presented.

The Dextran solution with BASF bi-concave disc-shaped particles is discussed next. The steady shear viscosity is presented in figure 3.21a). For shear rates higher than 10 s^{-1} the Dextran/BASF particle solution gave values that were maximal 25 % too high; below $\dot{\gamma}$ = 10 s^{-1} the Dextran solution gave too low values compared with blood. The differences increase with decreasing shear rates to a maximum of about 30 % at $\dot{\gamma}$ = 10 s^{-1}. The rigidity modulus G' and elasticity modulus G'' are presented in figure 3.21b) and compared with blood.

The Dextran/BASF particles values G' differ significantly from the blood data , the maximum difference is about 30 %, the blood data having higher values. The Dextran/BASF particles solution values for G'' are about a factor 3 lower compared with blood. No viscometric measurements at all have been reported in this paper for the ghost cell solution.

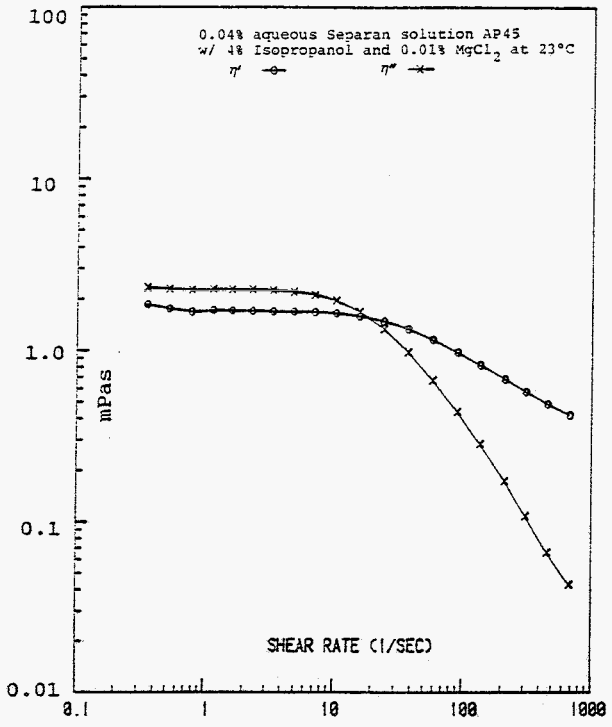


Figure 3.19 *Viscous and elastic component versus shear rate for a 0.04 % aqueous Separan (AP 45) solution with 4% isopropanol and 0.01 % $MgCl_2$ at 23°C. (From Liepsch e.a. [1991]).*

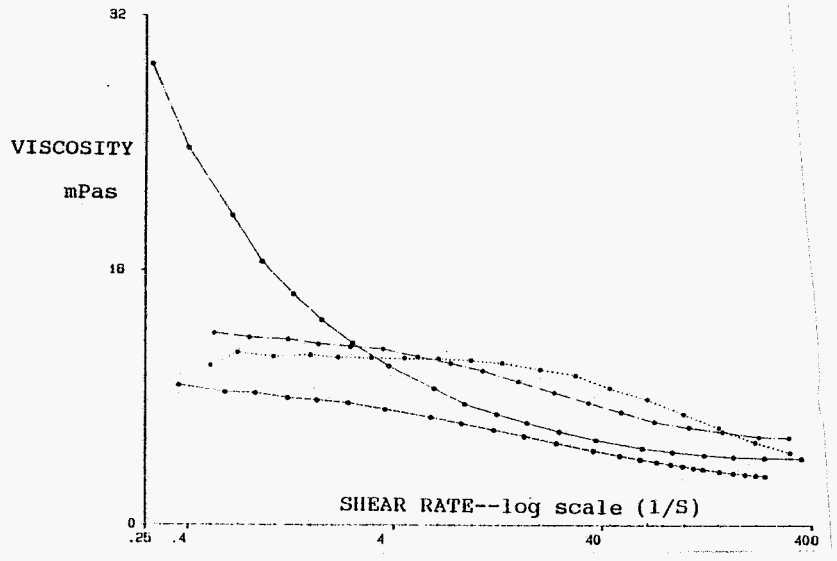


Figure 3.20 *Steady shear viscosity of a Separan mixture (fluid 3), see text) (---) compared with blood (HTC = 46%) (————) measured in a Couette viscometer at 37°C; the same Separan solution (....) compared with human blood (HTC = 44%) (-·-) at 23°C measured in an oscillatory capillary viscometer.*

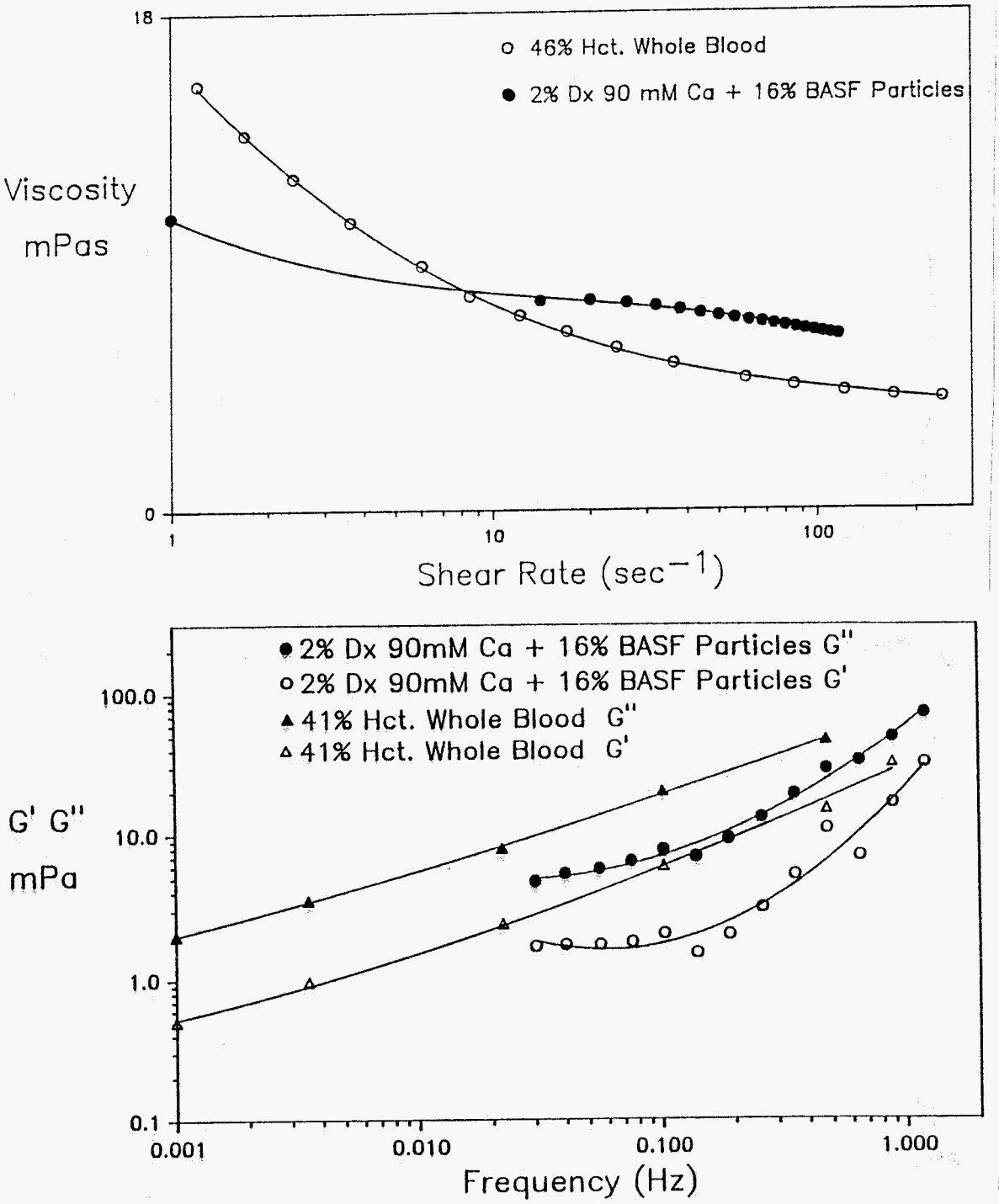


Figure 3.21 *a)The steady shear viscosity of a suspension of 2% Dextran (Dx) with 90 mMol Ca and 16% BASF particles and b) the rigidity modulus G' and elasticity modulus G'' for the same solution, compared with blood data. (From Liepsch e.a. [1991]).*

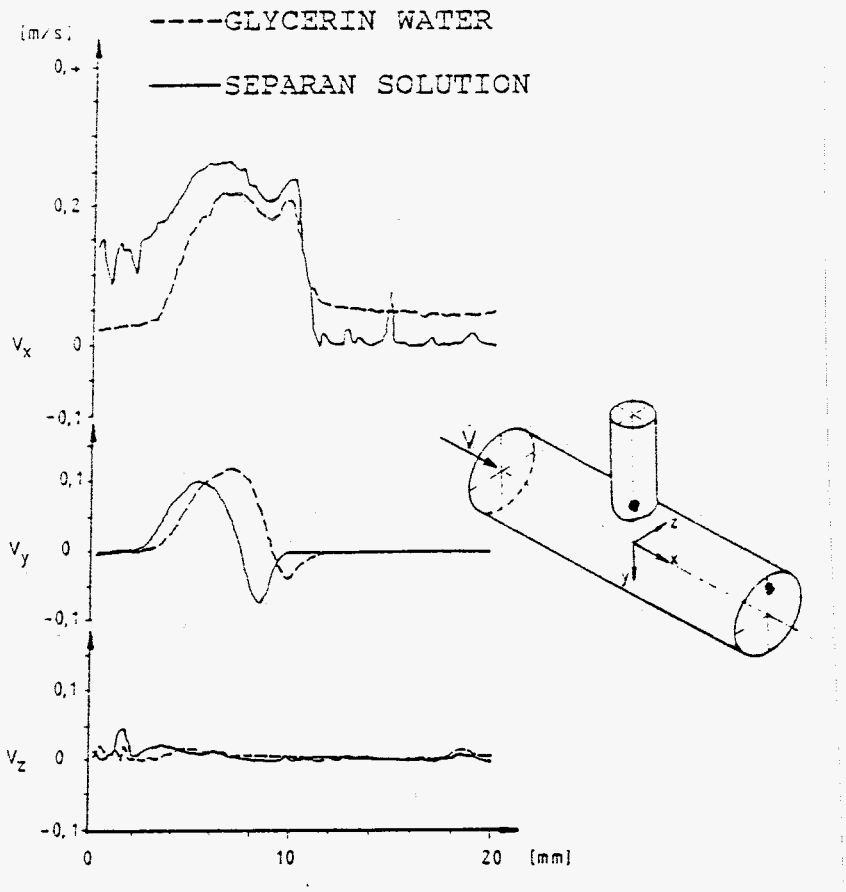


Figure 3.22 *Measured velocity profiles using 3D LDA measurements with the Separan mixture and the aqueous glycerin solution in a branched tube in case of the steady flow situation.(From Liepsch e.a. [1991]).*

To end, some flow studies using 3D LDA measurements were done with the Separan mixture and the aqueous glycerin solution in a branched tube in case of the steady flow situation with Re = 265 (defined in the entrance branch) at T = 20°C. The measured velocity profiles showed remarkable differences, as is clear from figure 3.23. This is, according to Liepsch e.a., in agreement with data presented by Liepsch [1986] and Ku and Liepsch [1983]; these data however is not presented here. A Tri-suspension with 40% ghost cells was also used in a LDA flow study with Re = 165 . The velocity profiles gave also similar results as presented by Liepsch [1986]; these data is however not given for comparison.

Concluding: the steady shear viscosity data in case of the Separan fluids 1) - 3) are in good agreement with the blood data (maximum difference 14 %); the viscous components of the complex viscosities of these fluids are in good agreement with the blood data (maximum difference 4%); the elastic components for these fluids are qualitatively but not quantitatively in

good agreement (differences about 20 - 60 %). For fluid 4 (BASF particles) the steady shear viscosity is not in good agreement with the blood data (differences about 25 %). In this case the G' and G" differ significantly from the blood data, the maximum difference being 30% and 300 % respectively. No viscometric data for fluid 5) (ghost cell solution) is presented, nor for fluid 6) (microspheres) (in Fukada e.a. [1990] some measurements of the steady shear viscosity of this latter fluid are presented). It is impossible to draw right conclusions about the importance of the non-Newtonian behaviour of blood on the steady flow phenomena in a bifurcation based on the experiments as described in this paper. Differences between the Newtonian model fluid and the non-Newtonian model fluids used (fluids 3) and 5)) do not have to be representative for the non-Newtonian behaviour of blood.

Schmitz [1984], Liepsch [1987]

Schmitz and Liepsch discuss "Milling Yellow", an aqueous colloidal suspension containing 1 or 2 % by weight of the Milling Yellow, a dye, and has been used in flow birefringent studies, not only to mimic blood but mainly because it has very satisfactory characteristics for the birefringent technique (see for example Schmitz [1983]). The shear rate dependent viscosity function is shown in figure 3.23; only a qualitative agreement exists here. By adjusting the temperature and concentration a broad range of viscosity functions can be established. No other viscometric measurements nor any dynamic or flow studies have yet been found.

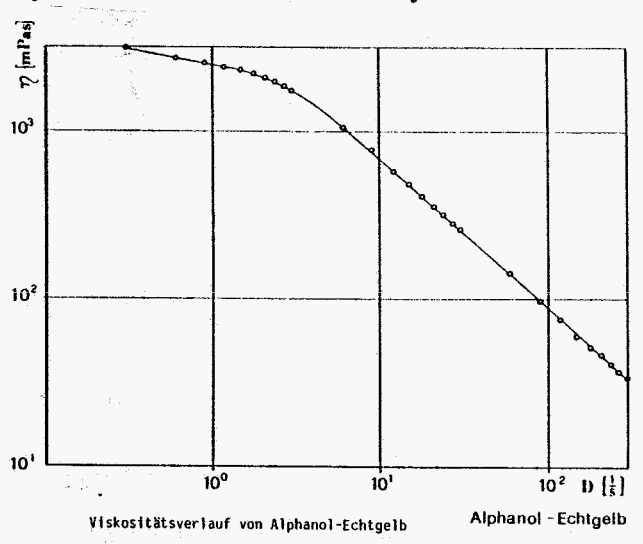
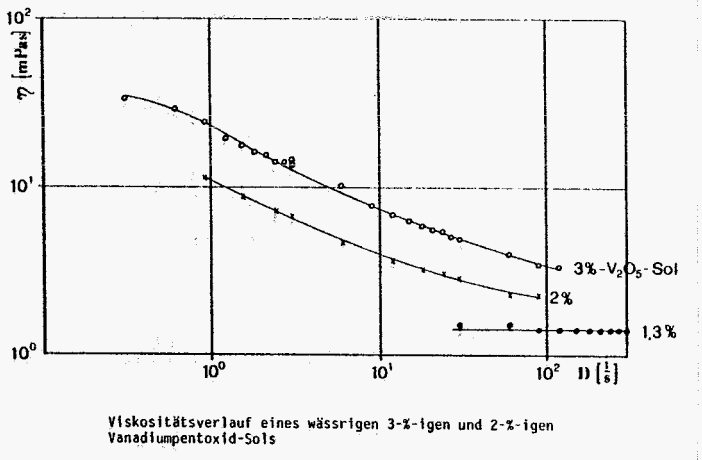


Figure 3.23 *The shear rate dependent viscosity for Milling Yellow. (From Liepsch [1987]).*

Liepsch [1987]

Another birefringent solution is a Vanadiumpentoxid sol, as used by Liepsch. Its shear rate dependent viscosity is given in figure 3.24. Only a qualitative agreement is found.

The major disadvantage of this fluid is its unstableness.



Viskositätsverlauf eines wässrigen 3-%-igen und 2-%-igen Vanadiumpentoxid-Sols

Figure 3.24 *The shear rate dependence of the Vanadium pentoxid sol. (From Liepsch [1987])*

3.4 Summary

None of the non-Newtonian blood rheological analog fluids undoubtedly mimics blood in all aspects and all situations. There is contradiction between the opinion of Liepsch e.a. [1990] and Mann and Tarbell [1990] about the adequacy of the frequently used Separan fluid to simulate the rheological behaviour of blood. From experiments of mann and Tarbell [1990] it follows that it is considerably too elastic compared with blood data. There is also a lack of experimental data of basic viscometric functions in case of the ghost cell solution and the polystyrene microsphere solution as used by Liepsch e.a. [1990]. The BASF particles solution as mentioned by Liepsch e.a. [1990] does not match the oscillatory blood data well. Xanthan gum and Xanthum gel mimic blood better then the already mentioned fluids, but are not completely satisfactory. Of the birefringent fluids, Milling Yellow dye and a Vanadiumpentoxid-sol, only the shear rate dependent viscosity has been found; in both cases only a qualitative agreement exists. As with the constitutive models, to test a model fluid there is, besides the standard viscometric functions and complex viscosity, a need for more additional experimental data in other flow types compared with human blood data. From the results of Mann and Tarbell [1990], it is found that sinusoïdal flow in a curved tube is a good discriminating flow situation. Because of their results in the oscillatory flow case in a curved tube, it seems to be important to incorporate in the analog fluid the cellular nature of blood.

4 Conclusions and recommendations

From viscometric and oscillatory experiments it is found that blood behaves as a non-Newtonian shear thinning, viscoelastic and thixotropic fluid; no measurable normal stress differences have been found. The red blood cells (RBC) determine the rheological behaviour of blood. In steady shear, at relatively low shear rates ($\dot{\gamma} < 10\ s^{-1}$) the RBC can aggregate to form cilindrical rouleaux; at low shear rates deformation of these structures results in the viscoelastic behaviour of blood. At very low shear rates ($\dot{\gamma} << 1\ s^{-1}$), the rouleaux can form a three dimensional network. With increasing shear rates, first these three dimensional structures are deformed and broken down again; then the rouleaux are deformed, oriented in the flow direction and broken up into the individual cells. With increasing shear rates, the viscosity is only determined by the deformation and orientation of the individual red blood cells. This all together results in the shear thinning, viscoelastic and thixotropic behaviour of blood. In oscillatory flow with $\dot{\gamma} < 1\ s^{-1}$ and f = 1 Hz, no rouleaux exist. The rouleaux formation has a characteristic proces time of 30 - 60 s. This also a function of the shear rate amplitude. At high shear rates blood behaves as a Newtonian fluid. Based on these results, in the unsteady physiological flow situation no rouleaux are expected to exist; non-Newtonian effects if present will be primary determined by the deformation and orientation of the dispersed red blood cells. In case of the steady variant (Re = 300) of this flow, a contribition of the rouleaux to the rheological behaviour of blood may exist because areas are present that have continuously low shear rates. The physiological flow is characterized by a mean Reynolds number of 300, and an estimate Deborah number of about 70.

The non-Newtonian models used in literature to calculate the flow of blood in large arteries model only the shear thinning behaviour of blood, and no viscoelastic effects. These models result in a flow field that in general is not altered compared with the Newtonian case. Significant local differences in stress or pressure can exist, however. Several viscoelastic models have been proposed for blood; some have been tested too, but only in simple shear flows. Of all constitutive models used to describe the rheological behaviour of blood as found in literature, the modified Bird-Carreau model, originating from polymer rheology, as described by Bernadin e.a. [1986] is a serious candidate to be used in a complex flow, especially in steady flow. This conclusion is based on the fact that it has shown to give good results in comparison with blood for different types of shear flows (steady shear viscosity, complex viscosity, low shear stress growth and stress relaxation). However, the model is not yet implemented in the software package SEPRAN that is to be used; this should be investigated in more detail. All viscoelastic models for blood found are based on considerations of the microstructure: the existence of the structural kinetic process of aggregation and disaggregation. As conclude above, in the unsteady physiological situation these ideas may not be appropriate. However, there is too little data available to judge the adequacy of

the Reher-Vogel, Charara and Rosenblatt models. Blood shows similar rheological behaviour as many polymers. Possible useful models from polymer rheology that have been implemented in SEPRAN are the differential Phan-Thien Tanner and Larson models. The KBKZ class of integral models, because of its success in describing the viscoelastic flow of polymers, can provide a good model too; it can possibly be implemented rather easily.

None of the non-Newtonian blood rheological analog fluids used as found in literature mimics undoubtedly the rheological behaviour of blood adequately in a complex flow situation. The very frequently used Separan solution does simulate the shear thinning behaviour of blood, but is far too elastic as is evident from the measurements of Mann and Tarbell [1990] in a curved tube, especially in the oscillatory flow case. There is a great lack of experimental information on all other fluids described. On the ground of the results of Mann and Tarbell [1990]. it seems to be important that the fluid incorporates the cellular nature of blood.

With both constitutive models and analog fluids, in order to judge their adequacy, it is essentially to have more experimental data of blood. Viscometric functions or the complex viscosity are indicating, but not sufficient parameters. It is of major importance to have more information of the rheological behaviour predicted by constitutive models, analog fluids and blood, especially in flows with elongating deformation. For that the test problem as described by Armstrong e.a. [1985] may be useful: the flow between two excentric cilinders, or the oscillating flow in a curved tube as described by Mann and Tarbell [1990]. As long as there is no reliable analog fluid for blood the experimental validation of the numerical calculations will be of doubtful value.

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