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Volume 8

Editors: T. K. Ghose, A. Fiechter,
N. Blakebrough

Mass Transfer in Biotechnology

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Technical Aspects of the Rheological Properties of Microbial Cultures

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Summary

The rheological properties of culture fluids have a profound effect on the course of a fermentation, the response and reliability of sensors, and on the difficulty of recovery processes. In addition, the rheological properties can be sensitive indicators of the state of a fermentation and can be useful for

purposes of control and monitoring. In this paper the fundamentals and important nomenclature of rheology are introduced, the merits of various experimental methods for measuring rheological properties are discussed, critical evaluations are presented of past studies of the rheological properties of culture fluids and the effects of these properties, and suggestions are made for further investigation and development.

1. Introduction

The rheological characteristics of a culture fluid affect directly bulk mixing behavior, all forms of mass transfer, and heat transfer and therefore can have a profound influence not only on the course and outcome of a microbial reaction but also on the response of sensors used for monitoring and control. In addition, the rheological properties of the final culture fluid play a large part in determining the ease or difficulty of recovery and purification operations. Accurate measurement and meaningful correlation of culture fluid rheological properties with the various transport phenomena are of critical importance in the

- (1) interpretation and control of basic experiments,
- (2) development of rational scale-up procedures,
- (3) design and utilization of monitoring and control systems,
- (4) interpretation of sensor responses,
- (5) control of plant-scale bioprocesses,
- (6) development of methods to increase yield and/or productivity,
- (7) design and operation of recovery equipment.

It is also important to note that in most cases where rheological properties are controlling factors they are also sensitive indicators of the state of the process and should be considered for purposes of monitoring and control.

Usually, pre-inoculation media exhibit simple water-like rheological behaviour but as the fermentation proceeds the rheological characteristics tend to become more complex and usually more adverse. These changes are caused by increased cell mass and/or the accumulation of appreciable quantities of high molecular weight products such as extracellular polysaccharides. Effects of cell mass are usually most pronounced for mycelial cultures in which the mycelia tend to "structure" the fluid. Thus, a given fungus will cause more troublesome rheological conditions when growing in a mycelial habit than when growing in pellet form. Most bacteria and yeasts at concentrations normally encountered do not have very great effects on rheological conditions.

Insofar as extracellular products are concerned, only polysaccharides exert a strong effect on rheological properties. As opposed to mycelial broths, the rheological properties of polysaccharide-containing culture fluids are determined by the nature of the continuous phase. This difference is significant as will be seen later. Other macromolecules such as proteins do influence rheological properties, particularly in the presence of finely dispersed gas bubbles [1], but such rheological effects are usually negligible in bioprocesses.

Finally, there are cases in which the initial medium itself exhibits complex rheological behavior which is generally associated with moderate to high concentrations of starch, etc. In such cases the hydrolytic action of extracellular enzymes usually decreases the average molecular weight of these nutrients thereby decreasing viscosity quite rapidly during the early reaction stages of the fermentation. Subsequent changes are governed by factors already noted.

Few careful and systematic studies of the rheological properties of culture fluids have been reported and little has been done to explore carefully and to correlate the effects of rheological behavior on reactor performance. Part of the reason for this is the complex nature of the problem which requires simultaneous consideration of rheological, microbiological, mixing and mass and heat transfer effects. In most cases only the microbiological aspect is considered and this frequently results in misinterpretation or in conclusions of highly limited applicability. It is the purpose of this paper to discuss, in a general fashion, the importance of the "mechanical" effects and to describe how they are related to rheological properties. Since the rheology of non-Newtonian fluids and the techniques required to study it are not discussed widely in the biotechnology literature, we begin with a concise review of this topic.

2. Rheology: Principles and Methods

2.1. Basic Concepts and Definitions; Newtonian Fluids and Laminar Flow

The movement of solid surfaces (e.g., an impeller) in contact with a fluid causes the fluid to move in some characteristic pattern which results in the development of internal stresses and the application, on the solid surfaces, of characteristic forces which must be continuously counterbalanced (e.g., by a drive motor) in order to sustain the fluid motion. The nature of the flow pattern and the magnitudes of internal stresses and applied forces depend primarily on the geometry of the system, the rate of fluid motion, and the intrinsic rheological (flow) properties of the fluid. A very simple example illustrating these phenomena is given in Fig. 1. Here a liquid is confined between two coaxial cylinders of large enough radii that curvature is negligible and exerts no influence; the surfaces approximate parallel flat planes. From experience we know that if we rotate the inner cylinder the fluid will move and a torque will have to be applied to the outer cylinder to keep it stationary. Clearly, then, the fluid exerts a tangential force on the outer cylinder while the inner cylinder exerts such a force on the fluid in contact with it and this force is transmitted through the fluid from one layer to the next. At any point in the fluid, the tangential force divided by the surface area on which it acts is defined as the *shear stress*. Experience teaches that for a given fluid the magnitude of this shear stress varies with the rate of fluid motion (which is determined in part by the speed of the driven cylinder). Furthermore, if the rate of rotation is not too high the only macroscopic component of fluid velocity will be in the direction of bulk flow; as shown in Fig. 1 the velocity component in both the r or θ directions will

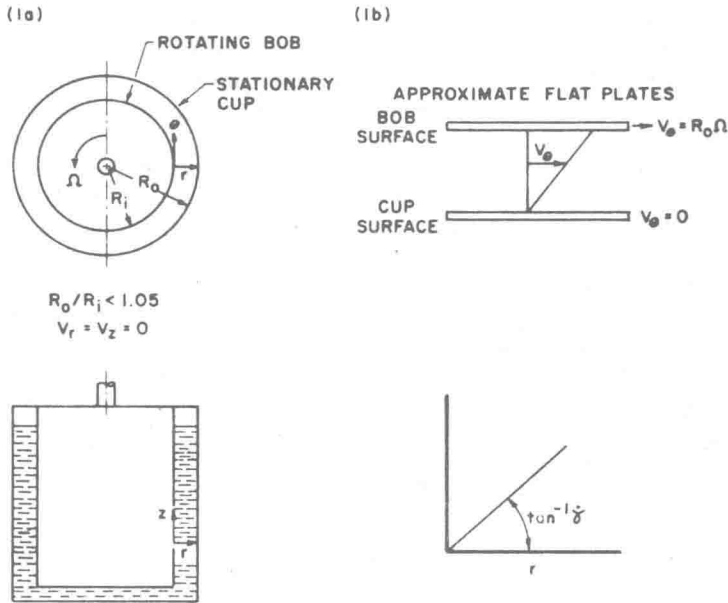


Fig. 1. (a) Laminar flow between concentric cylinders having negligible curvature. (b) Velocity profile; flat plate approximation

be zero. This type of fluid motion is called *laminar flow*: A dye stream injected at any point will move in a straight line and the only dispersion will be that due to **random** (thermal) molecular motion.

Analysis of the fundamental equations [2] of fluid dynamics reveals that for **laminar flow of the type illustrated in Fig. 1**, the shear stress will be constant throughout the fluid and the fluid velocity will vary linearly from zero at the fixed surface to $R_o\Omega$ at the rotating surface. To further describe the nature of the flow field we define, for laminar flow, the shear rate, $\dot{\gamma}$, as

$$\dot{\gamma} = \frac{du}{dn} \quad (1)$$

where n represents the direction perpendicular to the direction of the fluid motion at a point and u is the fluid velocity. Shear rate is usually reported in units of s^{-1} . (More generalized definitions are discussed in various works on fluid mechanics and rheology [2, 3].) For the case under consideration

$$\dot{\gamma} = \frac{du}{dx} = \frac{\Delta y}{\Delta x} = \frac{u_i}{\Delta x} \quad (2)$$

where u_i is the velocity of the inner cylinder and Δx is the thickness of the liquid layer. It must be emphasized that Eq. (2) is valid only for the flow illustrated in Fig. 1 (for example, it is not valid for coaxial cylinders for which curvature does effect the flow pattern).

For a variety of fluids (e.g., water, sugar solutions) it is found that the relationship between shear stress, τ , and shear rate (the constitutive equation) for laminar flow is given by

$$\tau = -\eta \dot{\gamma} \quad (3)$$

where η is a constant called the fluid viscosity and is generally reported in units of centipoises (1 centipoise = $\frac{1 \text{ g}}{\text{cm} \cdot \text{s}}$). [The minus sign in Eq. (3) is a convention.] Such fluids are called *Newtonian* fluids.

Except for special cases which need not concern us here, Eq. (3) is valid for all simple laminar flows of Newtonian fluids. However, it must be recognized that the expression for shear rate, $\dot{\gamma}$, is not always as simple as that for flow between parallel flat plates because the velocity profile (flow pattern) will not always vary in a simple linear fashion. For example, it can be shown [2] that when a Newtonian fluid flows in laminar fashion through a round tube, the velocity varies parabolically from zero at the wall to a maximum at the center of the tube;

$$u_z = u_m \left[1 - \frac{r^2}{R^2} \right] \quad (4)$$

where

$$\begin{aligned} u_z &= \text{fluid velocity at radial position } r \\ u_m &= \text{maximum fluid velocity at } r = 0 \\ R &= \text{tube radius} \end{aligned}$$

We can use Eq. (4) to calculate the fluid shear rate;

$$\dot{\gamma} = \frac{du}{dn} = \frac{du_z}{dr} = -\frac{2u_m}{R} \left(\frac{r}{R} \right) \quad (5)$$

The shear stress is then

$$\tau = -\eta \dot{\gamma} = \frac{2u_m}{R} \eta \left(\frac{r}{R} \right) \quad (6)$$

Thus, both the shear rate and shear stress vary linearly from zero at the center of the tube to maximum values at the tube wall. As will be discussed in Sect. 2.4.1., both shear rate and shear stress at the tube wall are easily calculated (for Newtonian fluids) from measurements of flow rate and pressure drop and therefore tube or capillary flow provides a convenient means for determining Newtonian viscosity in many cases.

For coaxial cylinders which do not approximate parallel flat plates it can be shown that for Newtonian fluids in laminar flow, the shear rate is [4]

$$\dot{\gamma} = -r \frac{d\omega}{dr} = -\frac{2\Omega}{r^2} \frac{R_i^2 R_o^2}{R_o^2 - R_i^2} \quad (7)$$

and the shear stress is [5]

$$\tau = \frac{M}{2\pi r^2 h} \quad (8)$$

where

$$\begin{aligned} \omega &= \text{angular velocity} \\ \Omega &= \text{angular velocity of inner cylinder} \\ R_i &= \text{radius of inner cylinder} \\ R_o &= \text{radius of outer cylinder} \\ M &= \text{torque} \\ h &= \text{liquid height.} \end{aligned} \quad (9)$$

The coaxial system can therefore be used in a simple fashion to determine the viscosity of Newtonian fluids since

$$\eta = \frac{\tau}{\dot{\gamma}} = \frac{M_o}{4\pi h \Omega} \left(\frac{1}{R_o^2} - \frac{1}{R_i^2} \right) \quad (10)$$

(For further discussion of the coaxial cylinder viscometer, including various correction factors, see Skelland [6], Middleman [7] and the series of articles by Krieger and Maron [8, 9, 10]).

2.2. Non-Newtonian Fluids

2.2.1. Pseudoplasticity

Many fluids, including various culture broths, do not exhibit Newtonian behavior. Among the more common non-Newtonian characteristics is *pseudoplasticity*. A typical flow curve (shear stress vs shear rate) of a pseudoplastic fluid is illustrated in Fig. 2a. The ratio of shear stress to shear rate in a well-defined laminar flow field is called the *apparent viscosity*, η_a , and decreases with increasing shear rate as shown in Fig. 2b:

$$\eta_a = \frac{\tau}{\dot{\gamma}} \quad (11)$$

The apparent viscosity is, in a sense, an equivalent Newtonian viscosity but generally is not equal to the slope of the flow curve. Usually, pseudoplastic fluids exhibit "New-

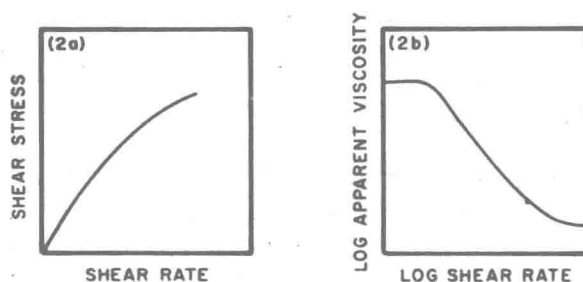


Fig. 2. Pseudoplastic fluid (a) flow curve and (b) viscosity characteristics

tonian" behavior at very low shear rates (zero shear viscosity) and at very high shear rates (infinite shear viscosity). In any event, it should be clear it is meaningless to specify the viscosity of a pseudoplastic fluid without noting the shear rate at which it was measured. It must be emphasized that the above definition of viscosity (which is accepted by rheologists) requires measurement with an apparatus that provides laminar flow and permits unambiguous calculation of both shear rate and shear stress. It should be noted also that expressions for shear rate and shear stress are much more complex for pseudoplastic fluids than for Newtonian fluids even for simple geometries. This complicates the measurement of viscosity and will be discussed at greater length in Sect. 2.4.2.1.

Pseudoplastic behavior results in flow characteristics which depart significantly from those of Newtonian fluids. Characteristics of laminar flows through round tubes are illustrated in Fig. 3. In comparison to Newtonian flow, the pseudoplastic flow is typified by a relatively flat velocity profile with significant gradients only near the wall and hence shear rates which are rather high near the wall and very low elsewhere. As a result viscosity is relatively low near the wall and relatively high elsewhere. Clearly, this has a significant effect on both mass and heat transfer. Similar behavior is observed in stirred

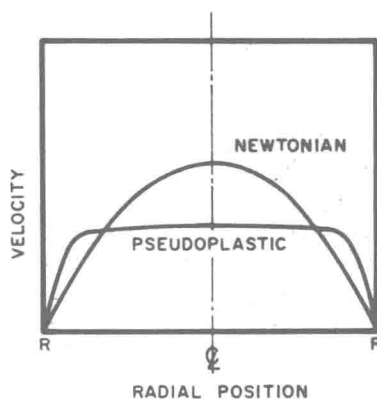


Fig. 3. Velocity profiles for Newtonian and pseudoplastic fluids in laminar flow through a round tube

tanks; shear rates are usually high very near the impeller and low elsewhere and hence fluid viscosity is low near the impeller but high at even relatively short distances from it [11]. This behavior of pseudoplastic fluids is illustrated in Fig. 4 [11]. Again, the effects on mass and heat transfer are quite important.

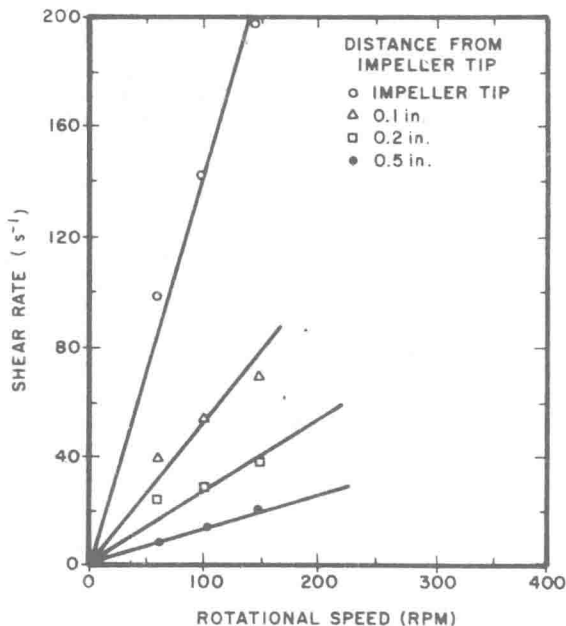


Fig. 4. Shear rate vs. rotational speed at various distances from the tip of a turbine impeller [11]

A variety of mathematical expressions has been developed to correlate viscosity data for pseudoplastic fluids. None is completely satisfactory for all fluids nor for the entire range of shear rates for any given fluid. The *Power Law* model is probably the most widely used because of its simplicity:

$$\eta = K\dot{\gamma}^{m-1} \quad (12)$$

Where K is the *consistency index* (given in pseudopoise) and m is the *power law index*. In general m and K are constant only over limited ranges of shear rate. For pseudoplastic fluids m is less than 1; the smaller m the more rapid is the decline of viscosity with increasing shear rate and the more pronounced are the effects of pseudoplasticity on flow and other transport phenomena. K is a direct measure of viscosity at a given rate of shear; the larger K , the greater the viscosity at a given rate of shear. However, it must be recognized that, in general, particular values of K and m are valid only for some particular range of shear rates. Furthermore, the value of K is obtained by extrapolation of viscosity data to 1 s^{-1} and may not have real physical significance at that rate of shear.

Some of the other mathematical models for pseudoplastic fluids which have been used widely are [12]

(a) Eyring

$$\tau = \frac{\dot{\gamma}}{C_1} + C_2 \sin(\tau/C_3). \quad (13)$$

(b) Powell-Eyring

$$\tau = C_1 \dot{\gamma} + C_2 \sinh^{-1}(C_3 \dot{\gamma}). \quad (14)$$

(c) Prandtl

$$\tau = C_1 \sin^{-1}(\dot{\gamma}/C_2). \quad (15)$$

(d) Williamson

$$\tau = \frac{C_1 \dot{\gamma}}{C_2 + \dot{\gamma}} + C_3 \dot{\gamma}. \quad (16)$$

These are usually more difficult to apply than the power law model and have not been found useful for culture broths. More extensive discussions of these and other models along with more generalized discussions of mathematical descriptions of shear rate can be found in a variety of works on fluid mechanics and rheology [13–16].

Finally, fluids whose viscosities increase with increasing shear rate are called *dilatant*. Such behavior has not been reported for culture broths.

2.2.2. Yield Stress

Some fluids will not flow until some minimum shear stress (*yield stress*) is exceeded. Fluids which exhibit Newtonian-like behavior once flow is initiated (i.e., once the yield stress is exceeded) are called *Bingham plastics* (see Fig. 5). Bingham plastic behavior can be expressed mathematically as [17]

$$\tau - \tau_y = \eta_p \dot{\gamma} \quad \tau > \tau_y, \quad (17)$$

where τ_y is the *yield stress* and η_p is the *plastic viscosity* or *rigidity*.

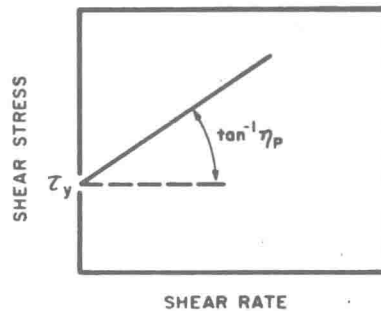


Fig. 5. Bingham plastic flow curve

A number of culture fluids exhibit yield stress but not all behave as Bingham plastics. Most of the reported cases involve fungal cultures in which yield stresses are associated with the structure imposed by the mycelial mat and the breakdown of this structure upon application of a stress greater than the yield stress. Experimental data for such systems will be presented in Sect. 3.1. but it is worth noting here that Roels *et al.* [18] have developed a rheological model which incorporates explicitly mycelial structure and which is based on the Casson viscosity equation:

$$(\tau)^{1/2} = (\tau_y)^{1/2} + K_c(\dot{\gamma})^{1/2}. \quad (18)$$

These authors found that the Casson equation, which incorporates features of the power law and the Bingham plastic equations, is superior to either in correlating experimental viscosity data for two different strains of *P. chrysogenum*.

The effects of yield stress on flow are somewhat similar to those of pseudoplasticity but are much more pronounced. For example, when a Bingham plastic flows through a round tube (laminar flow) it is quite possible for a "solid" plug of fluid to exist from the center of the tube to a point where the shear stress is just exceeded. This is illustrated in Fig. 6 [17]. Similar effects can occur in agitated vessels.

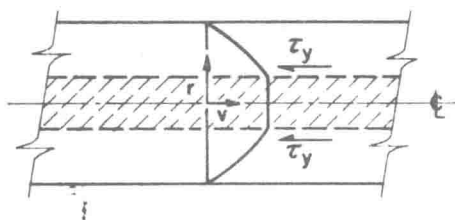


Fig. 6. Velocity profile for a Bingham plastic in laminar flow through a round tube [17]

2.2.3. Time Dependent Viscosity

Fluids whose viscosities increase or decrease with time of shearing are called *rheopectic* and *thixotropic* respectively [19]. Thixotropic behavior is illustrated in Fig. 7a [19]. When thixotropic (or rheopectic) fluids are subjected to varying shear rate they exhibit

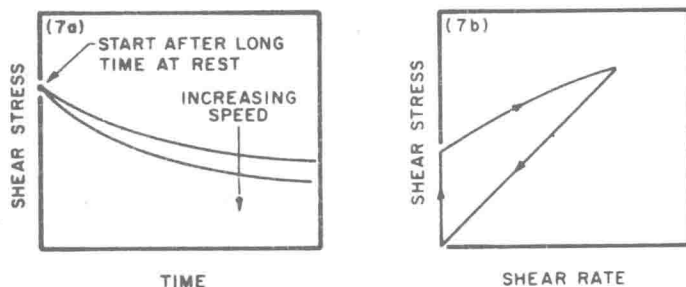


Fig. 7. Thixotropic fluid (a) time-dependent shear thinning, (b) hysteresis [19]

hysteresis as illustrated in Fig. 7b. Thixotropic behavior appears to be associated with reversible structure effects and could be important in mixing cultures containing fungal mycelia or extracellular microbial polysaccharides. As already noted, (Sect. 2.2.1.) a culture fluid is exposed to various shear rates as it moves about the reactor and might therefore exhibit viscosity hysteresis. The importance of this effect will depend on the time scale of the structure effects compared to the time scale of mixing and on the importance of thixotropy in comparison to other phenomena such as pseudoplasticity. To the author's knowledge there have been no reports of any significant efforts to determine the importance of thixotropy (or rheopecty) in culture broths. Finally, it should be noted that even if thixotropic properties are not important during the reaction *per se*, they can influence the outcome of an experiment designed to study power consumption [20, 21]. When performing such experiments the investigator should always keep in mind that (1) at a given impeller speed power uptake may vary with time and (2) the power consumption at a given speed may depend on whether the preceding speed was higher or lower and on the time scale of the experiment.

2.2.4. Viscoelasticity

Many fluids, particularly solutions of high polymers such as microbial polysaccharides [20], exhibit elastic response superimposed on a characteristic viscous behavior and are therefore called *viscoelastic*. If the fluid contained in the simple rheometer illustrated in Fig. 1 is non-elastic and we uncouple the driven cylinder from its drive shaft we will find that motion continues in the original sense for the short time required to dissipate the kinetic energy of the system. However, if the fluid is viscoelastic, the driven cylinder will reverse its direction. This is caused by elastic stresses developed during the steady state flow period. These rather complex stresses are responsible for a variety of phenomena including the well-known Weissenberg effect illustrated in Fig. 8. Most viscoelastic fluids are pseudoplastic and may exhibit other rheological characteristics such

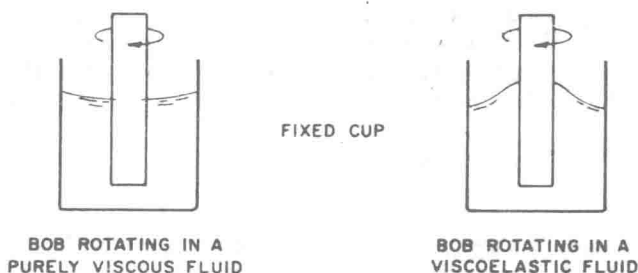


Fig. 8. Rod-climbing (Weissenberg) effect

as yield stress. Therefore, mathematical expressions for viscoelastic behavior are generally very complex and are not suitable for use in analysis of complex systems such as bioreactors. (A comprehensive treatment of viscoelastic behavior has been given by Fredrickson [15].) Finally, viscoelasticity has been shown to affect flow patterns in agitated vessels [22] but the importance of this effect during cultivation has not been studied.

Before concluding this section it should be re-emphasized that non-Newtonian behavior results in flow patterns (some of which were described above) which depart markedly from those exhibited by Newtonian fluids and that the nature and magnitude of such departures are influenced profoundly by system geometry and operating conditions. In turn, these effects on flow pattern affect all of the transport phenomena and therefore must be considered not only for the reaction *per se* but also for subsequent recovery operation^s.

2.3. Turbulent and Other Complex Flows

Thus far we have made a point of confining our attention to laminar flow. This has been done to insure an unambiguous definition of viscosity. When the flow becomes rapid enough or the fluid is subjected to accelerations (e.g., rapid change of direction) severe enough to establish components of velocity perpendicular to the main flow then a turbulent flow regime is established and a precise definition of shear rate becomes quite difficult. In addition, the magnitude of the shear stress is no longer simply related to shear rate and viscosity (a result of momentum transfer via turbulent eddies). Viscosity calculated on the basis of turbulent flow measurement varies with flow conditions even for Newtonian fluids and hence such measured values can not be thought of as intrinsic fluid properties. Indeed, the development of reliable theoretical expressions for such simple calculations as pressure drop vs. flow rate for turbulent flow of a Newtonian fluid through a round pipe is quite difficult and as a result the accepted practice in designing for turbulent flow has been to employ empirical methods based on dimensionless parameters of proven value in providing reasonably reliable scale-up correlations. (The same approach is often used for laminar flow in complex geometries such as agitated vessels.)

One of the most important of these dimensionless parameters is the *Reynolds number*, N_{Re} , which, in essence, represents the ratio of inertial forces (attributed to fluid momentum) to viscous forces. It is useful not only for purposes of correlation and scale-up but also for delineating laminar and turbulent flow regimes. The most useful form of the N_{Re} depends on the system geometry. Thus, for round tubes,

$$N_{Re} = \frac{D\bar{u}\rho}{\eta}, \quad (19)$$

where D is the tube diameter, \bar{u} is the average fluid velocity, ρ the fluid density and η the fluid viscosity, while for agitated vessels

$$N_{Re} = \frac{d_i^2 N \rho}{\eta} \quad (20)$$

where N is the rotational speed of the impeller and d_i is the impeller diameter. Application of these definitions is simple and straightforward for Newtonian fluids but somewhat involved for non-Newtonian fluids: In particular, it is not clear immediately