

Complex and biofluids / Fluides complexes et biologiques
Complex and biofluids: From Maxwell to nowadays

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Abstract

Complex fluids are the rule in biology and in many industrial applications. Typical examples are blood, cartilage, and polymer solutions. Unlike water (as well as domestic oils, soft clear drinks, and so on), the law(s) describing the behavior of complex fluids are not yet fully established. The complexity arises from strong coupling between microscopic scales (like the motion of a red blood cell in the case of blood, or a polymer molecule for a polymer solution) and the global scale of the flow (say at the scale of a blood artery, or a channel in laboratory experiments). In this issue entitled *Complex and Biofluids* a large panel of experimental and theoretical problems of complex fluids is exposed. The topics range from dilute polymer solutions, food products, to biology (blood flow, cell and tissue mechanics). One of the earliest model put forward as an attempt to describe a complex fluid was suggested a long time ago by James Clerk Maxwell (in 1867). Other famous scientists, like Einstein (in 1906), and Taylor (in 1932) have made important contributions to the field, but the topic of complex fluids still continues to pose a formidable challenge to science. This field has known during the past decade an unbelievable upsurge of interest in many branches of science (physics, mechanics, chemistry, biology, medical science, mathematics, and so on). Understanding complex fluids is viewed as one of the biggest challenge of the present century. This synthesis will provide a simple introduction to the topic, summarize the main contribution of this issue, and list major open questions in this field. **To cite this article: C. Misbah, C. R. Physique 10 (2009).**

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Résumé

Fluides complexes et biologiques : De Maxwell à nos jours. Les fluides complexes constituent la règle en biologie et dans de nombreuses applications industrielles. Le sang, le cartilage, et les solutions de polymères constituent des exemples typiques. A la différence de l'eau (ainsi que plusieurs huiles usuelles, des boissons douces, etc.) les lois décrivant le comportement des fluides complexes ne sont pas encore bien établies. La complexité provient d'un couplage fort entre les entités microscopiques (comme un globule rouge dans le cas du sang, ou une molécule de polymère dans le cas d'une solution de polymères) et l'écoulement à l'échelle globale (disons à l'échelle d'une artère sanguine, ou d'un canal dans une expérience de laboratoire). Dans ce numéro thématique intitulé *Fluides complexes et biologiques* on présente un éventail assez large de problématiques expérimentales et théoriques sur les fluides complexes. Les sujets vont de solutions diluées de polymères, en passant par les produits alimentaires, jusqu'à la biologie (le sang, et la mécanique des cellules et tissus). Un des premiers modèles mis en avant dans le but de décrire les fluides complexes est dû à James Clerk Maxwell (en 1867). D'autres scientifiques célèbres comme Einstein (en 1906) et Taylor (en 1932) ont apporté une contribution importante au domaine, mais néanmoins le thème des fluides complexes continue encore à poser un grand défi à la science. Ce sujet a connu durant la dernière décennie un sursaut incroyable d'intérêt dans différentes branches scientifiques (physique, mécanique, chimie, biologie, sciences médicales, mathématiques, etc.). La compréhension des fluides complexes est vue comme un des défis scientifiques majeurs de ce siècle. La présente synthèse présente une introduction simple du domaine, les principales contributions de ce numéro, et les défis majeurs. **Pour citer cet article : C. Misbah, C. R. Physique 10 (2009).**

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1. Introduction

1.1. What is a simple fluid?

Water is the most usual fluid in everyday life. Water (like, for example, domestic oils, and soft drinks) is called a simple fluid. The law describing a simple fluid is well established, since the work of the French scientist Navier (1785–1836) and the British one Stokes (1819–1903). The corresponding equations of motion are referred to in text books as the Navier–Stokes equations. One of the important feature that makes water a simple fluid is that the water molecules (being about a nanometer size) make extremely fast motions (rotation, translation before collisions, and vibration), on time scales of less than a nanosecond. When studying flow of water we are interested in macroscopic time scales (say a second, a minute, a day, and so on). During a second water molecules undergo about 10^{10} different kind of cycles (e.g. rotation). We then say that the microscopic time scale of the motion of the molecules is decoupled from the macroscopic time scales, or in other words during a second the molecules have performed a huge number of cycles, that the microscopic details of the water molecule motion scale out (or they are averaged out).

When water flows out of a tap, for example, the flow is not affected by the microscopic details of the conformation of a such or a such molecule. The microscopic conformation of the molecules only fixes the two following macroscopic physical quantities: the mass density ρ (which is 1 g/cm^3 for water) and the fluid viscosity η (which is equal to 10^{-2} Poise for water – the unit Poise can be explicitly written in terms of fundamental units as $\text{g}/(\text{cm s})$). If the flow properties of water are determined, then those of any other simple fluid are deduced by just substituting the density and viscosity of water by those of the simple fluid under consideration. From this point of view the Navier–Stokes equations may be called *universal equations*, in the sense that they apply to any simple fluid.

1.2. What is a complex fluid?

The situation is quite different with a complex fluid. Perhaps, the simplest introduction of a complex fluid may follow from consideration of a dilute polymer solution. A polymer molecule is a long chain made of small molecules (called monomers). Its total length may attain several tens of microns. Polymers are abundant in several industrial applications (textiles, plastic industry, etc.). Long molecular chains are also frequent in biology (DNA, proteins, and so on), and are sometimes called biopolymers. A polymer molecule in water may be viewed either as a *coil* or as *spaghetti* (Fig. 1), but intermediate configurations are also possible. When the solvent (say water) is at rest, the polymer molecule configuration may be as a coil, or spaghetti, or an intermediate stage. In the first case one says that the liquid in which the molecule is suspended is a bad solvent (since the molecule is more or less closed on itself, avoiding thus as much as possible contact with the liquid). In the third case one talks about a good solvent, since the molecule tries as much as possible to stay in contact with the liquid. The coil or spaghetti configuration depends on the nature of the polymer, its specific interaction with the solvent, the temperature, and so on. This is a whole old topic of thermodynamical equilibrium physics of polymer science which has known a tremendous progress during the past century. This problem is now fairly well understood.

On the other hand, under non-equilibrium conditions (e.g. under flow) the understanding of the flow properties of an aqueous solution of even a dilute suspension of polymers continues to pose a formidable challenge to the scientific community. Why is this fluid called complex? Suppose that at rest the polymer molecule is in a coil state. Under flow (say under a simple shear flow, or elongational flow) the molecule will be stretched, unfolded, will tumble, and so on. Nowadays it is quite possible to visualize (by fluorescent optical techniques) a single molecule under flow and to follow its change of conformation in time (see Fig. 2). The key point for understanding the notion of a complex fluid is that this polymer motion (we can speak of a conformation change) is quite *slow*; it may take place in a typical time range of a second (for example the frequency of tumbling motion is close to the applied shear rate), more or less. Thus, the time scale of the motion of the suspended molecule is of the order of the time scale of the imposed macroscopic flow. A separation of the microscopic and the macroscopic time scales of the fluid motion is not legitimate. In addition,

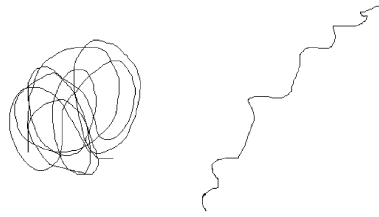


Fig. 1. Left: a schematic view of a polymer molecule in the coil state. Right: the molecule in the stretched, or spaghetti-like state.

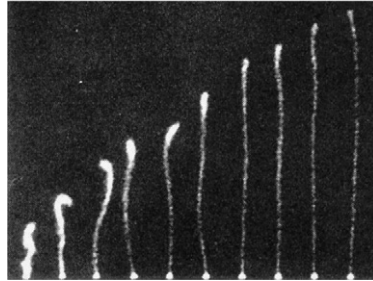


Fig. 2. Image of a fluorescently DNA molecule tethered at one end to a latex sphere and subject to a uniform velocity field with increasing intensity from left to right. Extracted from Perkins et al. [1].

the polymer molecule tries, from time to time, to go back to its coil configuration. Indeed, the molecule can be viewed as a spring that is stretched by the flow, and if at some time, in some orientation, the elongational part of the flow is not large enough, then the stretched molecule will suddenly attempt to go back to its unstretched state, as would a spring do if the applied force were lowered. By doing so the molecule will restore part of its strain to the fluid, a fact which results in a modification of the flow properties of the fluid, which in turn will react back on the molecule, and so on. There is thus an intimate micro/macro coupling in a complex fluid. The restitution of the chain elastic stress to the fluid makes the fluid acquire a *visco-elastic* character. In some complex fluids, like a cross-linked networks of molecules (say the case of the actin gel found in the cytoplasm of biological cells; see review by Verdier et al. [2]) the bonds may break and reform, and the deformation of the network is permanent, or plastic. Similar phenomena occur, for example, with blood where the red blood cells may form rouleaux which then may be destroyed upon shearing and reform again, and so on. In general, complex fluids have a visco-elasto-plastic behavior.

The constitutive law (or the precise equations of motion) for the motion of a complex fluid should in principle emerge from the knowledge of the precise configurations of the suspended entities, which depends on the precise flow properties, which are in turn determined by the motion of the suspended entity. In addition, in principle, a molecule like a polymer, may have a large number of configurations (it can have several types of folding, at different scales, several orientations, . . .). That is to say it has a large number of degrees of freedom, to each is associated a typical time scale. Thus, a polymer molecule has a broad temporal spectrum that can be exhibited at the macroscopic scale. This example gives a simple picture on how complex the problem is, a fact which still prevents us from having a complete understanding of complex fluids. Nevertheless, some progress has been made, as will be seen in this issue, but major challenges are still present, as we will describe briefly at the end of this synthesis.

Complex fluids are abundant in nature. They are found in several domains: (i) in food products (mayonnaise, ketchup, and so on, see review in this issue by Fischer et al. [3]), (ii) in the polymer science (see the review by Lindner and Wagner [4] and that of Steinberg [5] in this issue) and industry (textiles, plastic materials, and so on), in (iii) biology (blood flow – see review by Guido et al. [6] and by Vlahovska et al. [7] –, in cell tissue mechanics – see Verdier et al. [2] in this issue –, in cartilage etc.), and many more. Several famous scientists, like Maxwell [8], Einstein [9] and Taylor [10], have addressed questions related to complex fluids, but this topic is still challenging, and knows a high level of activity in different disciplines.

2. Spectacular effects in complex fluids

We would like in this section to briefly describe some apparent macroscopic effects that obviously show a distinction with usual fluids.

2.1. Drag reduction

A complex fluid exhibits much astonishing and spectacular behavior. Perhaps, the most dramatic effect is the so-called drag reduction. A minute addition of polymers to water (say with a concentration of 10 to 100 milligrams of polymers in a liter of water) may reduce up to 80% the resistance to flow in a turbulent regime. This is called the Toms effect (see review of Steinberg in this issue [5]), or drag reduction (exhibited as a reduction of the pressure drop between the entry and exit of the channel). This effect results from a subtle interplay between the turbulent solvent (simple fluid) and the suspended molecules. The precise understanding of this phenomenon is still an ongoing point of contention in the literature.

2.2. Non-Newtonian viscosity

An important feature of complex fluids is that they have a *shear-dependent* viscosity, also called *non-Newtonian* viscosity. For this reason complex fluids are also often called *non-Newtonian fluids*. The decrease in viscosity with increasing shear rate is referred to as *shear thinning*, and the fluid is said to be *shear-thinning* or *pseudoplastic*. This effect can be quite dramatic, with the viscosity decreasing by a factor by as much as 10^3 and 10^4 (a typical example is a polymer solution with polyacrylamide in water and glycerin). Blood can exhibit in our body a decline of its viscosity as a function of the shear rate which may attain a factor larger than a decade.

For some other fluids the opposite behavior is observed: the viscosity increases with shear rate. This behavior is referred to as *shear thickening*. A fluid belonging to this category is said to be *shear thickening* or *dilatant*. This behavior is often exhibited by fairly concentrated suspensions of small particles; see review by Fischer et al. [3].

2.3. Normal stress effects

If a simple fluid is subject to a shear flow (say by moving the two plates delimiting the fluid relative to each other by a constant velocity in the x -direction), then the fluid will exert only a friction force (called the drag force) in the opposite x -direction. Let us call σ_{xy} the shear stress (a force – or a stress – which is directed in the x -direction and acting on the y -plate – the plate is perpendicular to y). In a simple fluid under shear flow $\sigma_{yy} = \sigma_{xx} = \sigma_{zz} = 0$. In a complex fluid these quantities are nonzero in general. The two normal stress differences are defined as $N_1 \equiv \sigma_{xx} - \sigma_{yy}$ and $N_2 \equiv \sigma_{yy} - \sigma_{zz}$ (and are both zero for a simple fluid). A complex fluid exhibits generally nonzero values for both N_1 and N_2 . For example, a nonzero N_1 means that if we follow a fluid particle (a small portion of the fluid) having a cubic shape, then that fluid particle will experience a stretching (or compression) of its square section in the x – y plane, and will become a rectangle (of course the total volume is conserved due to incompressibility). The presence of normal stress differences are responsible for several effects, like the so-called rod-climbing and die-swell effects discussed below.

2.4. Rod climbing effect

Let us insert two rotating rods into two beakers, one containing a simple fluid and the other a polymer solution. In the first case a dip is formed near the rod due to centrifugal forces that push the fluid outwards. In the second case the fluid moves in the opposite direction and the fluid climbs up the rod (Fig. 3). This striking effect may be interpreted as follows. The rotating rod causes elongation of the polymer molecules along circular lines surrounding the rod, since the rotation induces streamlines which are closed circles. This causes a stretching of molecules along these circles that “strangulate” the fluid and force it inward (try to stretch a circular elastic rubber, you will clearly feel a centripetal force). This centripetal force may be so large that it dominates again the centrifugal force (in this experiment the inertial effect is quite small resulting in a small centrifugal force). The fluid climbs up to a height where the elastic force is balanced by the potential gravitational energy (Fig. 3). This rod climbing effect can be described in terms of the normal stress differences.

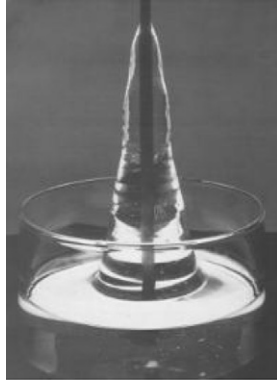


Fig. 3. A complex fluid climbing up a rotating rod. Extracted from the web site: <http://www.mie.utoronto.ca/labs/rheology/>.

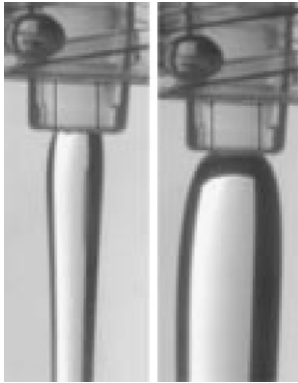


Fig. 4. Left: a simple fluid exiting a hole, with a diameter very close to that of the hole. Right: a complex fluid exiting the hole and forming a jet which is much larger than that of the hole. This is the illustration of the so-called die swell. Extracted from the web site: <http://web.mit.edu/nmf/research/phenomena/>.

2.5. Die swell effect

We describe here a last example, known as a die-swell effect. Consider a fluid that exits from a capillary of diameter D forming a jet in air of diameter D_e . If the fluid is simple (Fig. 4, left), then D_e is about 13% larger or smaller depending on whether the flow is slow (small Reynolds number) or fast (large Reynolds number, albeit the flow is still laminar). In other words the fluid leaves the capillary without any significant modification of diameter. For a complex fluid the exit of the fluid may exhibit dramatic swelling. For a polymeric complex fluid the jet may extrude with a diameter D_e that may be 300% larger than D (Fig. 4, right). This phenomenon is referred to as *die-swell* or sometimes *extrudate swell*. The origin of this swelling can be explained by reference to the normal stress differences.

Many other phenomena are revealed by complex fluids; see Refs. [11,12] for extensive discussions.

3. Motivations and organization of the thematic issue *Complex and biofluids*

This thematic issue focuses on a very active part of research on complex fluids. We have tried to make a balance between traditional complex fluids and biological ones. The various contributions are ordered as follows.

3.1. “Viscoelastic surface instabilities” by Lindner and Wagner [4]

In this review the authors describe three types of surface instabilities. The first example is the Rayleigh–Plateau (RP) instability. If you open normally a water tap at home the water jet is cylindrical. If now you try to lower the flow rate by slowly turning off the tap, the jet becomes thinner and thinner, until a stage where the continuous jet pinches

off into small droplets. This is the RP instability. The surface tension is the driving mechanism for this instability: if the jet is thin enough then the total area of the jet is lowered when the radius undergoes a modulation (the initial stage of the instability). The second instability is the Saffmann–Taylor (ST) one. When a fluid pushes another more viscous fluid (say air pushes oil) in the Hele–Shaw geometry (i.e. between two large plates separated by a thin gap), the initial planar interface becomes unstable, and ultimately form a finger (called the ST finger) that fills half of the channel width. The third instability is the Faraday instability: when a sample having a free liquid/air surface is shaken vertically the planar surface undergoes an instability (known also as a parametric instability) for an adequately chosen vibration frequency. This is a gravity wave-like instability. Performed on complex fluids the authors show that the manifestation of these instabilities are entirely different from those seen in simple fluids.

The study of these instabilities on complex fluids provides simple probes for understanding complex fluids. For example, the necking of the jet due to the pinch-off in a complex fluid is dramatically different in a complex fluid: instead of an algebraic temporal law for the decay to zero of the neck in simple fluids, the law becomes exponential. In addition, this type of experiment provides an interesting “rheometer” for measuring the so-called *elongational viscosity* η_e (the analogue of shear viscosity in an elongational flow). In a simple fluid, $\eta_e = 3\eta$, where η is the usual shear viscosity. In a complex fluid η_e may be (even in a dilute enough polymer solution) five orders of magnitude larger.

For the ST problem with a complex shear-thinning fluid (while the fluid exhibits negligible normal stress differences) the finger can be much narrower than with a simple fluid. If, on the contrary, the complex fluid has normal stress differences (but negligible shear thinning), the situation is reversed: there is a finger widening as compared to a simple fluid. These observations highlight the nontrivial character of complex fluid properties, which carry information on the microscales (the various complex fluids used in these experiments differ by the microscopic nature – e.g. the flexibility – of the suspended molecules).

The Faraday instability is subharmonic (the optimal excitation of the surface gravity wave occurs when the surface natural frequency ω_0 is equal to half of the perturbation frequency). This subharmonic instability is generic in systems which are parametrically excited. A classical example is a pendulum whose suspension point (which is immobile in the elementary theory of oscillators) oscillates vertically in time (it modulates the parameter ‘gravity’ and thus acquires the name ‘parametric oscillator’). A complex fluid may run contrary to this rule: the first optimal excitation may become harmonic (instead of subharmonic). This feature is a consequence of the fact that the elastic relaxation time of the suspended macromolecules becomes comparable to the inverse of the excitation frequency.

3.2. “Elastic stresses in random flow of dilute polymer solution and turbulent drag reduction problem” by Steinberg [5]

The basic question regards how a polymer behaves in a turbulent flow. In turbulence the smallest dissipation scale remains larger than the polymer length. Thus, a polymer sees, so to speak, a spatially smooth flow field which is chaotic in time only. A polymer molecule may be stretched by local spatial gradients of the flow. This may, in principle, trigger a coil–stretch transition of the polymer. The inverse of the gradient of the velocity field provides a natural time scale λ_{turb} that has to be compared to the elastic relaxation time (actually the longest relaxation time associated with the end-to-end length of the polymer) λ . It was suggested by Lumley in 1972 [13] that a coil–stretch transition should occur if $\lambda/\lambda_{\text{turb}} > 1$. This suggestion seems to have some experimental support. A corollary of the Lumley theory would be that due to stretching of the polymer the viscosity would significantly increase in a buffer layer, very much like what happens in an elongational flow (see the last section and the review by Lindner and Wagner [4]). This would then “kill” turbulence below a certain scale, leading thus to drag reduction.

However, as discussed in this review, several points of contention still persist in literature. For example, it does not seem clear whether or not a coil–stretch transition is essential to explain drag reduction. It has been suggested by de Gennes (in 1986) [14] that the polymer should not undergo a coil–stretch transition in a random velocity field, but only a partial stretching of the polymer would be needed to explain drag reduction. The essential idea is that turbulence would be terminated at some scale larger than the dissipation scale, provided that the elastic energy (associated with the polymer) is sufficiently large. Suppression of turbulence above the smallest inertial scale would cause a drag reduction, as would do the increase of viscosity in the Lumley view. This review points out that measurements and characterization of polymer stretching and elastic stresses in a turbulent flow are the key issues to solve the turbulent drag reduction problem. Thanks to the progresses made during the past decade both experimentally and numerically

some key ingredients are beginning to emerge, but at the same time new questions have been raised. For example, while some facts would support a possibility for a coil–stretch transition, it does not seem clear that only small scales, below the dissipation scale, are decisive for polymer dynamics.

Finally, this review states that the discovery of the so-called elastic turbulence (made in 2000 by Steinberg and co-workers, following a prediction about elastic instability in 1990 by Larson et al. [15]) may provide new perspectives in the understanding of the drag reduction phenomenon.

Elastic turbulence occurs at very small Reynolds number (theoretically at zero Reynolds number). In a dilute polymer solution under flow there is an interplay between the stretching (even partial) of the polymer by the flow gradient and elastic relaxation of the polymer that induces dissipation. When inertia is absent, the stretching of the polymer by the velocity gradient provides the source of nonlinearities that may promote a rather complex dynamics. If the elastic stretching is large enough to overcome dissipation due to relaxation of the polymer, then an instability of the basic flow (typically a Couette flow between rotating cylinders) occurs. The primary basic flow becomes unstable, the leading mode of instability is caused by the elastic stress, which in turn induces a different flow field from the Couette one. Upon increasing the driving force (say by increasing the velocity gradient, or the cylinder rotation speed) the type of flow and elastic stresses may become more and more complex, until dynamics become chaotic both in time and in space. The analysis of the flow field revealed that the dynamics is turbulent (with a cascade of energy transfer that is reminiscent to that of inertial turbulence, albeit with some noticeable differences). Elastic turbulence indeed shows a flow field which is smooth in space but random in time, unlike inertial turbulence above the dissipation scale.

Recall that polymer dynamics is basically (but not necessarily entirely, as discussed in this review) determined by small scales in inertial turbulence where the flow field is also smooth but random in time. In other words, this is the same type of field that is induced in elastic turbulence. From this observation it is tempting to conjecture that a further understanding of elastic turbulence, and more generally the behavior of a polymer in a temporally random field, would constitute a new angle of attack towards understanding of drag reduction.

3.3. “Rheology of food systems” by Fischer et al. [3]

The two reviews discussed above are concerned with basic understanding of complex fluids by selecting canonical systems on which it is hoped to make progress regarding elementary processes of complex fluids. Complex fluids found in foods, consumer products and cosmetics, for example, are quite complex in that they present several features of complex fluids that can not easily be split into elementary processes. It has seemed to us essential to address in this issue questions which have a direct link with industrial applications. A special focus in this review is paid to food systems. Characterizing and, ideally, understanding the rheology of food materials is essential for numerous aspects of food science and technology, such as the standardized characterization of raw materials and innovative products, or for optimized conservation and industrial processing.

Unlike the fluids discussed above, foods are generally made of a mixture of a variety of microstructures (particulate suspensions, emulsions, foams, gels, biopolymer mixtures, phase separated aggregates, etc.). In other words, a piece of food is a multi-scale material composed of materials that have distinguishable rheological properties themselves. In addition, the interaction between sub-materials makes the task even more complex. Thus food rheology rather belonged, for a long while, to “engineering” science. Despite the inherent complexity, food materials may lend themselves to several rheological measurements (such as the effective viscosity as a function of shear rate).

Experimental results of model systems are presented and reference to phenomenological laws are made; the most frequent ones are power law behaviors relating the viscosity to shear rate. This type of law is injected into the Navier–Stokes equations (the resulting model is sometimes called a “generalized Newtonian model” in the sense that one keeps the usual form of a simple fluid and only replaces the viscosity by a shear-dependent one extracted from experiments). Then numerical simulations on the generalized model are performed to guide further development (to design and to scale processing equipment). Several flow behaviors of food materials (like chocolate and some biopolymer solutions) are shown and discussed in the light of phenomenological equations. The review emphasizes the clear distinction between the non-colloidal properties (that are determined by large enough aggregates where Brownian motion can be disregarded) and colloidal ones (which are decisive at smaller scales), although both features may be exhibited within the same food material, depending on the length scales we are interested in. For example, the non-colloidal approach provides information on the role of different ingredients on length scale relevant for processing, while the colloidal approach addresses the interaction of individual ingredients to eventually provide a full picture of the aggregation in

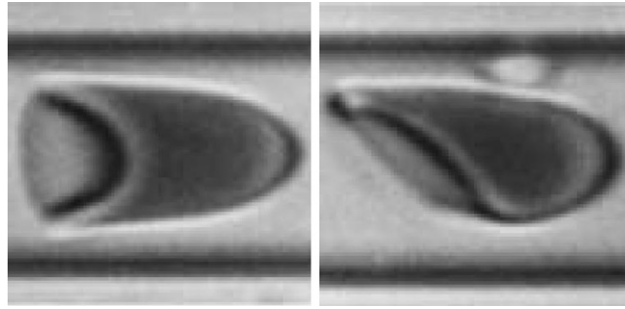


Fig. 5. A symmetric shape (parachute) and a non-symmetric shape (slipper) of a flowing RBC in a capillary.

complex food material compositions: Knowing the influence of specific ingredients on the flow behavior of complex fluids enables the design of manufacturing processes for materials with tailored properties. This review sheds light on rheology of foods and their relative complexity, but at the same time it shows that there is a hope for a future fundamental contribution in this field.

3.4. Blood and biomimetic systems

We may regroup three reviews under this item:

- “Microconfined flow behavior of red blood cells in vitro” by Guido and Tomaiuolo [6],
- “Capsule motion in flow: deformation and membrane buckling” by Barthès-Biesel [16],
- “Vesicles and red blood cells in flow: from individual dynamics to rheology” by Vlahovska, Podgorski and Misbah [7].

These three reviews have in common the ultimate objective of understanding blood flow from the analysis of elementary processes of suspended entities.

After nearly a century of research on blood, our understanding of the basic blood flow mechanisms at the cellular level (at the scale of red blood cells, platelets, etc.) is still an open issue. Blood is a complex fluid. To date, blood flow has been described by means of phenomenological continuum models that require many assumptions which are difficult both to justify and to validate [17]. Furthermore, the modern view of complex fluids [12] has highlighted the intimate coupling between the dynamics of the microscopic suspended entities (RBCs in the example of blood) and the flow at the global scale. Blood is primarily composed of red blood cells (RBCs), which occupy (in a healthy human body) about 45% of the blood volume. The rest consists of plasma, while the other blood elements (white blood cells, platelets, etc.) take up less than 1% of the total blood volume. Thus, an understanding of blood flow needs a precise knowledge of dynamics of RBCs.

In the first review a systematic analysis of red blood cells microcirculation is analyzed. Studies in capillaries, in rectangular microfluidic channels (obtained from soft lithographic techniques) and in blood vessels are reviewed. The main focus is to understand the link between deformation of RBCs, the geometry, and flow properties. The RBCs may flow by keeping a symmetric shape (called parachute; Fig. 5) or they may adopt a non-symmetric shape, called a *slipper*, Fig. 5 [18]. Understanding why red blood cells (RBCs) move with an asymmetric shape (*slipper*-like shape) in small blood vessels is a longstanding puzzle in blood circulatory research. While this thematic issue was being finalized, a theory on how and why a slipper shape should form at all has been given, but this will not be addressed in this issue, albeit a brief mention will be given in the review by Vlahovska et al. [7]

Another important feature discussed in the review by Guido et al. [6] is the fact that the flow resistance in small blood vessels *in vivo* is about twice larger than that in a glass tube of the same size. The internal wall of blood vessels is covered by layer of cells, called the endothelial layer, which is protected on top by a brush of polymers which is about 0.5 μm thick. This layer is called the *glycocalyx*. The increased flow resistance of blood is attributed to the glycocalyx. Collective dynamics of RBCs show also various features, the most noticeable is a transition from single to multi-file (zipper) flow upon increasing the tube diameter.

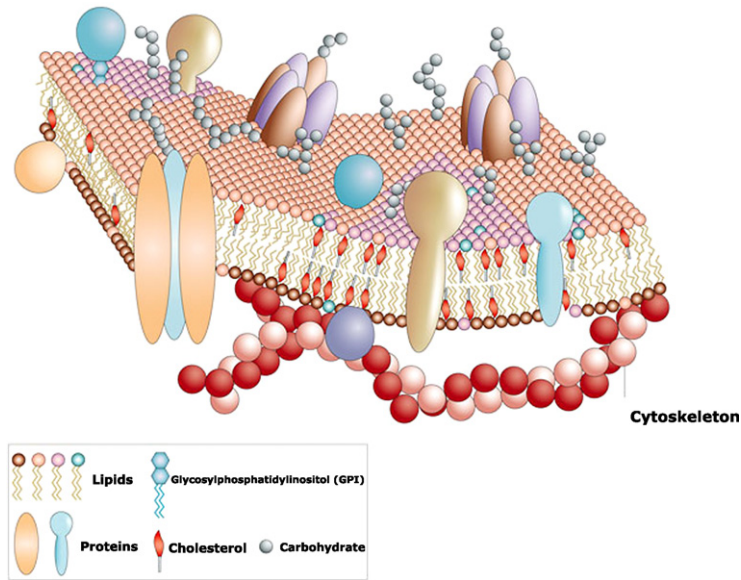


Fig. 6. A cartoon of a red blood cell membrane showing the phospholipid bi-layer and the cytoskeleton.

The accumulated knowledge on microcirculation may also serve to conceive of new diagnosis tools for the analysis of abnormal cells. This point is an active field of research in the lab-on-chip technologies. Several scientists try to compare the microelectronic revolution with that of the lab-on-chip.

The second review by Barthès-Biesel [16] focuses on dynamics of capsules. One of the early motivations for studying capsules was to design artificial RBCs. A second motivation was to use them as carriers for a specific drug delivery in the organism. Capsules have some mechanical properties that are close to those of RBCs (like the shear elasticity). RBCs are made of a phospholipid bilayer (as vesicles, see review by Vlahovska et al. [7]) and in addition they are endowed with a cytoskeleton, a cross-linked network of proteins (see Fig. 6).

Artificial capsules can be obtained through interfacial polymerization of a liquid droplet. The process thus leads to approximately spherical particles enclosed by a thin polymerized membrane with mechanical properties that depend on the fabrication procedure. Capsules mechanical properties are discussed. Unlike vesicles (see review by Vlahovska et al. [7]) capsules have a finite stretching modulus, and have a shear elasticity, mimicking the cytoskeleton of a RBC. Elasticity is of nonlinear nature. A nontrivial question is the treatment of a pre-stressed situation under flow. Material points belonging to the capsule membrane move under flow and keep memory on their previous pre-stressed state, which may be taken to be the reference configuration. These notions are often the sources of mistakes in literature, and the review by Barthès-Biesel [16] sheds a nice light on this challenging problem. Both the analytical treatment (based on a small deformation of the shape close to a sphere) and numerical methods (based on boundary integral formulation) are presented. Capsules are deformed under flow, and they may exhibit wrinkling (or buckling) instability. The experimental results may be used in order to extract mechanical properties (and thus the elastic constitutive laws) via an inverse problem. Hydrodynamic interaction among capsules, which is briefly mentioned, is also an interesting topic, that constitutes a first step towards understanding dynamics and rheology of a model system that may serve to ultimately build a sound basis for rheology of a suspension of capsules.

The third review focuses on vesicles (closed phospholipid bilayer membranes) and on some results on RBCs under shear flow. Vesicle have a pure phospholipid membrane. They share with the RBCs the fact they are both inextensible (unlike capsules), but they are not endowed with a cytoskeleton, thus missing the notion of membrane shear elasticity. They may thus be viewed as a simplistic model for RBCs, allowing to identify whether or not the cytoskeleton is decisive in a such or a such situation.

The topic of vesicles under flow continues to gather increasing interest in different disciplines ranging from biology to mathematics. The vesicles that are the focus of this review are usually called “giant vesicles,” and have a typical size in the 10–100 μm range (the word “giant” is used in reference to vesicles in the cytoplasm which are in the 100 nanometers range). The review briefly recalls the various equilibrium shapes exhibited by vesicles; among them

we find the bi-concave one known for healthy RBCs. Most of the review is then dedicated to dynamics under flow and to rheology. Despite their simple structure, vesicles have revealed a considerable amount of dynamics. Under a linear shear flow they may exhibit: (i) tank-treading (TT): the vesicle assumes a steady inclination angle with respect to the flow direction, while its membrane undergoes a tank-treading motion; (ii) tumbling (TB); and (iii) vacillating-breathing (VB) – aka swinging, trembling –: the vesicle main axis oscillates about the flow direction, whereas the overall shape undergoes a breathing-like motion, and so on. It is discussed that these dynamics impact on the overall rheology (there is a clear link between these individual dynamics and the macroscopic rheology, like in the behavior of the effective viscosity). An interesting result is that the behavior of rheology of a dilute suspension of vesicles is quite distinct from that of emulsions.

Under a Poiseuille flow, vesicles migrate towards the center, they may exhibit coexistence of shapes. The most striking fact is the occurrence of slipper-like shape (Fig. 5), known for RBCs. This study opens the way towards a basic understanding of a bottom-up approach of blood flow, but also towards applications in a lab-on-chip technology regarding transport, cross streamline migration, and sorting out of cells in microfluidic devices.

3.5. “Rheological properties of biological materials” by Verdier et al. [2]

Biological cells (like RBCs and white blood cells) have complex structures that impact on their mechanical properties. They behave often as visco-elasto-plastic materials, in that they are complex fluids (or solids). The individual mechanical cellular behavior impact also on the scale of a collection of cells, like suspensions. The ultimate limit of a suspension is the situations where the cells are closely connected to each other, like in a biological tissue. Modeling and experimental studies on tissues are also the focus of this review.

Individual cell mechanics are analyzed experimentally by various local probes, like optical tweezers, micropipettes, Atomic Force Microscopy, particle tracking microrheology, and so on. The advantages and drawback of each method is discussed, along with the type of information that can be extracted. The use of local probes has known a huge number of studies during the past two decades and extractions and interpretations of various nontrivial mechanical properties have been made. Models for cell rheology are discussed, and some of them are reminiscent of those referred too in other review articles of this thematic issue.

A systematic extraction of rheological laws from microscopic considerations is a formidable task, and the philosophy remains, in general, rather phenomenological. Some rheological features known in glassy materials (Soft Glassy Rheology) seem to be similar to what biological cells exhibit. As noted by Verdier et al. [2] (their Fig. 1), it was known since a long time that the behavior of the response properties (the so-called storage modulus – carrying information on elastic properties – and the loss modulus – carrying information on viscous effects –) as functions of the frequency (in an oscillating cone-plate rheometer) exhibit a complex feature and contains a part of the spectrum which is shared with the soft glassy rheology. This results is comforting since it tells us that some generic behavior may even be present also within complex biological materials.

Biological suspensions and tissues along with cartilage-like systems are discussed. A brief presentation on blood flow is also given and some model suspensions systems are mentioned. Some constitutive laws put forward for tissues share some similarity with those used at the cellular level (like capsules and RBCs, see Review by Barthès-Biesel [16]). Anisotropy in tissues is accounted for by analogy with dilute fiber suspension models, or liquid-crystal like theories.

Several complex fluids in biology may be called *active*: for example, tissues are growing and remodeling, because the cells forming them duplicate and die, the extracellular matrix is continuously remodeled and even in the absence of growth the cells undergo an internal re-organization in response to strain. This is a formidable task, and the review shows how ideas allowing one to tackle these questions are beginning to emerge. The proposed models were partially successful in interpreting experimental data, but, in general, great challenges are still present.

4. Open issues

We would like to list our personal point of view regarding major open issues:

- Complex fluids do not seem to lend themselves to a universal description. Depending on the materials, the range of frequency, etc., the models evoked to interpret experiments are often different. Is there an ultimate theory that

would allow us to write a universal constitutive law into a concise form? This is probably very difficult to imagine at present.

- Some simplified models for complex fluids have been successful in describing various properties, like in the case of dilute polymer solutions (reviews 1 and 2). Nevertheless, still several questions remain unanswered. Drag reduction is still a matter for debate. In the necking instability (review 2) when the neck radius is small, it is not clear whether or not a simplified model (Oldroyd B model) continues to make sense, due to the local accumulation and strong stretching of the polymers.
- In food materials, as well as in biological tissues and cells, the general task is quite complex due to the composite nature of the materials and the imbrications of many features and phenomena within the same material. Despite this complexity, the field knows a considerable activity both experimentally and theoretically. Theories are rather phenomenological, and the emergence of a simple theory based on microscopic considerations is still difficult to imagine.
- In blood and biomimetic systems (capsules and vesicles), considerable progress has been achieved on individual dynamics theoretically and experimentally. Numerical studies from microscopic considerations are beginning to emerge, and it is clear that major impact may be expected in the next coming decade, especially in the field of blood rheology.

In conclusion, we believe that this field will continue to see a higher and higher level of activity.

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