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Living fluids/Fluides vivants

Living fluids

Fluides vivants

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ABSTRACT

One of the major emerging fields of research of the beginning of this century concerns living fluids. By "living fluids", we mean two major categories of complex fluids: (i) fluids which are essential to life, like blood, and (ii) active fluids made of particles that are able to propel themselves in the suspending fluid by converting a form of their energy into mechanical motion. Studies on active fluids have known a considerable interest since the last decade. Blood might be viewed as an old topic, but the progresses in experimental techniques, analytical concepts and numerics, have contributed nowadays to a dramatic renewal of the interest in this field, with a great potential towards understanding physical and mechanical factors in cardiovascular diseases. These fields have considerably strengthened interdisciplinary research. The series of reviews of this dossier focus on the tremendous recent progress achieved in research on living fluids both from the experimental and theoretical points of views. These reviews present also the major open issues, making of this dossier a unique guide for future research in these fields. This project grew up thanks to the international summer school that we organized on the topic "living fluids" at the IES (Institut d'études scientifiques) of Cargèse (Corsica) in 2012.

RÉSUMÉ

Un des thèmes de recherche émergents du début de ce siècle concerne les fluides vivants. Par « fluides vivants », nous entendons deux catégories majeures de fluides : (i) les fluides essentiels à la vie, comme le sang, et (ii) les fluides actifs constitués de particules capables de se s'auto-propulser dans le fluide au sein duquel elles baignent, et ce en convertissant une forme de leur énergie en mouvement mécanique. Les études sur les fluides actifs ont connu un véritable engouement depuis la dernière décennie. Le sang peut être vu comme un vieux sujet, mais les progrès des techniques expérimentales et les nouveaux concepts analytiques et numériques contribuent actuellement à un regain d'intérêt extraordinaire pour celui-ci, avec un potentiel énorme en vue d'élucider des mécanismes physiques et mécaniques de base impliqués dans les maladies cardiovasculaires. Ces thèmes de recherche ont été à l'origine d'une grande percée interdisciplinaire. La série de revues de ce dossier met l'accent sur les progrès réalisés au cours de ces dernières années sur les fluides vivants sur les plans tant expérimental que théorique. Ces revues présentent également les défis majeurs, en faisant un guide précieux pour les recherches futures dans ces domaines. Ce dossier est arrivé à maturation grâce à l'école internationale que nous avons organisé

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à l'IES (Institut d'études scientifiques) de Cargèse (Corse) en 2012, sur le thème « fluides vivants ».

1. Introduction

The past decade has known a considerable upsurge of interest in the field of living fluids. Blood flow is certainly an old topic, since the first comprehensive study is traced back to Poiseuille (in the 1830s) [1,2], who reported that most of the blood flow dissipation occurs in the microvasculature. He also pointed out that close to the blood vessel walls, there is a cell-free layer, a fact that was subsequently identified by Fahraeus and Lindqvist (in 1931) [3] (see also [4]) to considerably affect blood viscosity: the apparent blood viscosity decreases upon decreasing the channel diameter D, until a typical value of D of about a few micrometers; in other words, the more the blood is squeezed, the easier it flows! The advent of microfluidic and optical techniques together with the increase of computer powers, not forgetting the societal need for cardiovascular therapies (cardiovascular diseases constitute the major cause of mortality in western countries), have played an important role in the huge renewal of interest in this field. The field of active fluids is, in turn, a more recent field of research, which has known a rapid development in the past decade. Active fluids generically refer to suspensions of particles that have the ability to propel themselves within the suspending medium. The word "active" means a motion that arises from conversion of energy from one form, say chemical, to a mechanical propulsion energy. This entirely differs from the passive mechanical responses of the microstructure to thermodynamic fluctuations or to flow forcing (e.g., shearing). Examples of active fluids are diverse, and they range from artificial self-propelling colloids based on a catalytic reaction, over motor and filament-suspensions to microswimmers from which the most studied ones are (without being exhaustive) (i) bacteria suspensions (e.g., *Escherichia coli* or *Bacillus subtilis*), (ii) spermatozoa, (iii) microalgae suspensions (e.g., *Chlamydomonas reinhardtii*). Active fluids raise important fundamental and practical questions. From the fundamental point of view, active fluids belong to a class of systems where traditional equilibrium statistical physics is difficult to apply, and the expected constitutive law of the fluid should drastically differ from those of non-active fluids (like polymer solutions, emulsions, etc.). From the practical point, it is evident that these fluids are biologically relevant. For example, particles transport, mixing and diffusion, have possible consequences for nutrient uptake and the spreading of bacterial infections. Furthermore, sensitivity of microorganisms (like microalgea) to external fields (like light) may lead to their spontaneous agglomeration having potential applications in the fields of biofuel algal production and the improvement of pollutant biodetector technology [5].

2. Organization of the reviews

2.1. Blood flow

Blood is a complex fluid that 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.

The descriptions of blood flow properties escape the traditional laws for simple fluids. The complex character results from an intimate coupling between the shape of RBCs and the ambient plasma, which leads to a rich set of RBC morphologies in the blood circulatory system. Understanding the selection of shapes and dynamics among a large manifold of possibilities, the collective effects, the spatiotemporal organizations, is a challenging problem. The plasma proteins (e.g., fibrinogen) cause RBCs to form aggregates, called rouleaux. The rouleaux can be destroyed under large enough shear rates, but how they do behave in the microvasculature (e.g. in capillaries) is still a controversial issue.

In addition, the RBCs move in the vascular networks and they constantly interact with blood vessels. Blood vessels are lined up with a layer of cells, called endothelium, and protected on top by a brush of biopolymer (about 0.5 μm thick), called glycocalyx. This layer plays important roles in hemodynamics (it affects strongly the flow rate), but it also has several essential functions: it prevents undesirable cell adhesion and lipid transmigration, controls tissue hydration, prevents edema formation and affects mechanotransduction (biological answers to variations of blood-flow-induced stresses). This first part is organized in the following way: it starts from basic questions such as the behavior of individual RBC (and its biomimetic counterpart), discusses the rouleaux formation and the behavior of viscosity and hematocrit in the microvasculature all the way up to endothelial dysfunctions. This thematic review has attempted to cover a wide range of these questions, but does not pretend to be exhaustive.

- **Review 1** by Vlahovska, Barthès-Biesel and Misbah ("Individual and collective behavior of red blood cells and their biomimetic counterparts"). This review is motivated by a bottom-up approach (i.e. describing blood flow by taking explicitly into account the corpuscular nature of blood, which is predominantly represented by RBCs). The first step is to elucidate the behavior of a single (or a few tens) entity under flows. The entities are either RBCs or their biomimetic counterpart (vesicles and capsules). Understanding of even a single entity under flow is not yet completely achieved.

This review will expose the progresses achieved experimentally and theoretically during the past few years. Questions related to collective effects, like clustering, will also be reported. The review presents also contradictory results and ongoing debates in the literature which will surely incite further future studies. Perhaps one of the main open issues is how to adequately model the RBC cytoskeleton.

– **Review 2** by Wagner, Steffen and Svetina ("Aggregation of red blood cells: From rouleaux to clot formation"). This review focuses on the problem of rouleaux formation of RBCs and their contribution to blood clots. RBCs aggregate reversibly thanks to plasma proteins to aggregates called rouleaux, but clot formation is an irreversible process. The latter aggregation mechanism is an essential factor in stopping bleeding after an injury. However, this aggregation can be fatal if it occurs inside the vascular networks (initiated by platelet activation), leading to thrombus formation, the major cause of death in western countries. The review discusses in great detail the rouleaux formation process and the intervention of different molecular factors. The review discusses the current state of affairs in experimental and theoretical description. The review, like the previous one, emphasizes the role of the cytoskeleton controlling RBCs deformation.
– **Review 3** by Secomb and Pries ("Blood viscosity in microvessels: experiments and theory"). One of the most interesting features in blood flow in vivo is the appearance of a cell-free layer near the blood vessels, a fact reported first by Poiseuille in the 1830s. This effect leads to the observation that the apparent blood viscosity decreases upon decreasing the channel diameter D, until a typical value of D of about few micrometers; in other words, the more the blood is squeezed, the easier it flows! This is the famous Fahraeus–Lindqvist effect (reported in 1931) [3] (see also [4]). Despite the old history of this phenomenon, a complete understanding is still lacking. This review discusses the experimental reports both in vivo and in vitro and focuses on the theoretical understanding of this effect and its far-reaching consequences.
– **Review 4** by Barakat ("Blood flow and arterial endothelial dysfunction, mechanisms and implications"). The flow properties of blood are known to considerably affect vascular functions (such as remodeling) and dysfunctions (such as endothelial dysfunction), which can in turn lead to a cascade of chemical and biological reactions that dictate the overall cardiovascular response and correlations with diseases. For example, blood recirculation (occurring often at vascular bifurcations) is often correlated with atherosclerosis. How are the flow properties sensed by the endothelium and transmitted to the cell cytoplasms, and what type of feedback is implicated, is a fascinating area of research known under the name of *mechanotransduction*. This review presents the current state-of-the-art in this highly interdisciplinary field of research.

2.2. Active fluids

The last decade has known a quite rapid upsurge of interest in the field of active fluids made of a suspension of active, or out-of-equilibrium, particles that propel themselves in a suspending fluid by converting a part of some energy (like chemical energy) into mechanical motion, or by interaction with external fields. These fluids escape *par excellence* the traditional frame of statistical mechanics since, in the present case, notions like the fluctuation–dissipation theorem are difficult to apply. These fluids have opened a new field of research in physics, mechanics, applied mathematics, engineering, and so on. While few pioneering early articles appeared several decades ago in the literature (such as that of Taylor in 1951 [6] and that of Purcell in 1977 [7] – with which the famous scallop theorem is associated), we can say that study on active fluids knows now its high glory days. Several microorganisms use flagella, cilia, or even a global shape ! adaptation to swim. Synthetic chemists and colloidal physicists have also become more and more adept at creating microscopic synthetic particles that can propel themselves, in some instances autonomously, such as through catalytic chemical reactions at their surfaces, or in a more directed fashion, say through interactions with externally imposed magnetic fields. Two contributions are presented in this thematic issue.

– **Review 5** by Aranson ("Collective behavior in out-of-equilibrium colloidal suspensions"). This review focuses on colloidal suspensions that can be maintained out of thermodynamic equilibrium by external electric or magnetic fields, light, chemical reactions, or hydrodynamic shear flow. One of the fascinating points is the ability of these suspensions to self-assemble into complex architectures. Several nontrivial beautiful patterns emerge as a result of the interaction of the suspension with external fields (e.g., electric or magnetic field). By tuning the fields, series of spatial and temporal events are exhibited and interpreted with elegance and pedagogy. It is discussed that these suspensions may exhibit novel material properties, e.g., reduced viscosity, enhanced self-diffusivity, etc.
– **Review 6** by Saintillain and Shelley ("Active suspensions and their nonlinear models"). This review presents the state-of-the-art in modeling active suspensions with kinetic theories and discusses several important consequences. The swimmer is modeled as a rod-like particle that propels itself in a suspending fluid (with a free-force and free-torque); the propulsion occurs by assuming that the posterior of the particle behaves differently than the anterior does (symmetry-breaking is needed for propulsion). Other types of modeling are evoked, in particular those using the notion of phantom flagella, which creates, in the vicinity of the swimmer, a direct force on the fluid that is equal and opposite to the drag experienced by the particle. A distinction is made between two types of swimmers: (i) the so-called pushers, such as the bacteria *Escherichia coli* and *Bacillus subtilis*, which push their cell body (the anterior) forward through the fluid thanks to the turning of their flagellar bundle (located on the posterior end), and (ii) the pullers, such as the microalga

Chlamydomonas reinhardtii, where the situation is reversed, with the motive stress exerted on the anterior half of the rod and a no-slip condition on the posterior. An illuminating explanation is given to the difference in behavior between these two types of swimmers, such as why is the intrinsic viscosity of pushers negative while that of pullers is positive. The review presents nice pattern formation due to collective effects, patterns that seem to be a particular specificity of pusher suspensions only.

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References

[1] J. Poiseuille, Recherches sur la force du coeur aortique, Dissertation, Didot le jeune, Paris, 1828.
[2] J. Poiseuille, Recherches sur les causes du mouvement du sang dans les veines, J. Physiol. Exp. Pathol. 10 (1830) 277–295.
[3] R. Fahraeus, T. Lindqvist, The viscosity of the blood in narrow capillary tubes, Am. J. Physiol. 96 (1931) 562–568.
[4] A. Pries, N. Neuhaus, P. Gaehtgens, Blood viscosity in tube flow: dependence on diameter and hematocrit, Am. J. Physiol. 20 (1992) H1770–H1778.
[5] X. Garcia, S. Rafaï, P. Peyla, Light control of the flow of phototactic microswimmer suspensions, Phys. Rev. Lett. 110 (2013) 138106–138110.
[6] G. Taylor, Analysis of the swimming of microscopic organisms, Proc. R. Soc. Lond. A 209 (1951) 447–461.
[7] E. Purcell, Life at low Reynolds number, Am. J. Physiol. 45 (1977) 3–11.