Realistic Simulation of Hemodynamics and Hemorheology in the Microcirculation

Aims and Background: Modelling the flow of blood as it is transported via a complex network of blood vessels back and forth between the heart and peripheral organs in a physiological system, is an intense area of research across the world. This is due to the importance of understanding healthy and pathological behaviours of the system, in order to develop and optimize techniques to treat disorders in the system. Typically, blood flow in small vessels, such as arterioles, venules, and capillaries is referred to as *microcirculation*, while flow in larger arteries is referred to as *macrocirculation*. From a fluid mechanical viewpoint, the distinction between the micro and macrocirculation is generally based on the Reynolds number, *Re*; the microcirculation corresponds to flows where *Re* is small, and inertial forces can be neglected, while the macrocirculation corresponds to flows where inertial forces are significant. Although the blood flow in micro and macrocirculation has a fundamental common feature, namely, the interaction between blood and vessel walls, there are still significant differences that require a completely different approach to model each of them. Given the prevalence of cardiovascular diseases and their role as major contributors to morbidity and mortality in modern society, it is perhaps not surprising that much of the current research effort is focussed on the macrocirculation—to which the cardiovascular system belongs. It is also perhaps not unexpected that preliminary modelling efforts have been directed at understanding flow features in the macrocirculation, since, as will be elaborated below, modelling the microcirculation presents additional and formidable challenges. The aim of the present proposal is to initiate a systematic research effort aimed at developing flexible, modular and efficient numerical tools that can be used to model blood flow in the microcirculation.

Blood is a concentrated suspension of multiple components, with a complex rheological behaviour, that interacts with vessel walls chemically and mechanically giving rise to an intricate fluid-structure interaction. Consequently, obtaining a quantitative description of blood circulation requires not only understanding the blood rheology, but also understanding how the flow depends on architectural and mechanical properties of the vascular system. In both these aspects, differences arise in micro and macrocirculation. In the medium to large arteries of the macrocirculation, it has been well accepted that blood can be modelled as a viscous, incompressible, Newtonian fluid, and that the Navier-Stokes equations are a good model for the blood flow. Further, the relatively small thickness of the vessel wall in comparison to the vessel diameter, justifies the use of two-dimensional shell models for the mechanics of the arterial wall. By adopting a coupled approach centred on two interacting models, one for the fluid based on the Navier-Stokes equations, and the other for the structure based on shell models (with suitable matching conditions playing the role of boundary conditions), significant progress in the mathematical and computational modelling the macrocirculation has been made in recent years [1,2].

Our capacity to model blood flow in the microcirculation, on the other hand, is still in its infancy. The particulate nature of blood, which is a suspension of red blood cells, white blood cells and platelets in plasma, leads to a non-Newtonian behaviour at low shear rates, and in small vessels [3]. Furthermore, a fact of considerable importance is that blood flow in the microcirculation is regulated largely by diameter change, i.e. by vasodilation or vasoconstriction [4]. Most of these diameter changes occur in arterioles and small arteries. Particularly relevant is the fact that the relatively large ratio of the wall thickness to lumen diameter in the small arteries and arterioles is crucial for enabling blood flow regulation by diameter change. This implies that the simplifying assumption of small vessel that allowed the adoption of shell theory for the arterial wall mechanics in the macrocirculation cannot be realistically invoked for modelling blood flow in the microcirculation. To date, there are no models for blood flow in the literature that simultaneously account for the compliant nature of a thick vessel wall and the non-Newtonian character of blood. The aim of this research is to develop computational models that explicitly account for the interaction between internal flow and wall deformation in the microcirculation.

Methodology, research plan and timetable: The blood flow in a compliant artery can be classified as a *free-boundary* problem since the artery wall is free to deform in response to the forces exerted on it by the flowing blood. The numerical solution of free boundary flows is a very challenging task. This is due mainly to two reasons: (1) In free boundary flows one has to solve not only for the fluid velocity and pressure, but simultaneously also for the location of the interface and its time evolution. (2) The interface deformation is coupled to the fluid flow both kinematically (continuity of the velocities) and dynamically (balance of stresses), and the coupling is nonlinear. In recent years, although there has been significant progress on addressing these challenges, they have been dealt with individually by researchers working in a variety of different areas. For instance: (1) The methodology to compute the free-surface flow of non-Newtonian fluids using a continuum description has been developed by Pasquali and Scriven [5]. Here, two of the above mentioned challenges were successfully tackled, namely, the development of a technique to compute the interface location, and the solution of the constitutive equations for a non-Newtonian fluid. However, the authors considered a free-surface flow between two fluids, and therefore no fluid-structure interaction was involved. (2) While several different stable algorithms have been developed to describe fluid-structure interactions [1], we mention here in particular the recent development of one such algorithm because of its relevance to this proposal. In a seminal recent work Carvalho and Scriven [6] have developed an algorithm to describe roll coating flows in which one of the two rolls that make up the forward-roll coating gap is covered by a layer of deformable elastomer. Since the liquid carried into the gap develops high enough pressure to deform the resilient roll cover, a complete description of the problem necessitates a solution of the shape of the deformable roll cover. The big advance achieved in the algorithm developed by Carvalho and Scriven is its ability to account for the *finite thickness* of the roll cover, with a plane-strain elastic and viscoelastic model of the roll cover deformation. Their algorithm, however, couples the finite thickness roll cover equations with the Navier–Stokes equations for a viscous incompressible fluid, and is hence not applicable to the description of non-Newtonian fluids. The aim of this research is to extend the algorithm of Carvalho and Scriven by accounting for the presence of a non-Newtonian fluid, using the techniques initiated by Pasquali and Scriven, and apply it to the problem of blood flow in a deformable artery. The significance and innovation of this research lies in the development for the first time of a robust free-boundary flow algorithm that is capable of describing the flow of a non-Newtonian fluid in a deformable artery with finite thickness.

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