Modelling the transport behaviour of platelets in intracranial aneurysms

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Introduction

Intracranial aneurysms are developed as localized abnormal deformations of brain vessels and their possible rupture can be lethal to patients. The natural self-repair mechanism is the formation of a thrombus inside the cavity, which significantly lowers the risk of rupture [1, 2]. This thrombus formation can also be induced by positioning a stent in the orifice of the aneurysm.

An important factor for the initiation and the formation of a thrombus is the local concentration of platelets and special attention has to be given to the transport properties of these cells. It is widely known that the concentration profiles of platelets exhibit excess in the concentration near the vessel walls [17]. This lateral position of platelets is considered to be due to the complex motion of red blood cells. This proximity of platelets to the vessel wall ensures a more effective response to tissue damages.

Several methods have been proposed and used to describe platelet transport in blood flow. A simple approach for the transport model is by using the advection diffusion equation. This model was used in several studies on thrombosis [6, 18]. Eckstein and Belgacem [5] extended this approach by adding a drift term to the convection diffusion equation and suggested that the diffusion coefficient can depend on the local hematocrit and the local shear rate.

Fully resolved red blood cells and platelets suspensions are generally avoided due to the computational cost of simulating tens or hundreds of thousands of particles, but smaller scale studies of blood flow have been performed. Crowl and Fogelson [3, 4] simulated the lateral motion of platelets in a two-dimensional straight channel under a variety of flow conditions, using the Lattice Boltzmann method coupled with the immersed boundary method. Mori et al. [10] and Pivkin et al. [12] modeled the adhesion of platelets using rigid spheres as RBCs and they both suggested that the presence of RBCs is necessary when investigating the mechanisms of platelet adhesion and aggregation. Fogelson and Guy [7] used only platelets in their thrombosis model and added a random step to the motion of platelets during each time step to model the RBC induced platelet motion.

The research to date mainly focused on the transport of platelets in straight channel flows providing adequate results, but little has been done for more complex geometries where most of them may lack in confidence [9].

This contribution will focus on the transport behavior of platelets in aneurysm geometries by explicitly simulating platelet-sized and *deformable membraneous* RBC-shaped particles in realistic dimensions. The aim of the fully resolved simulation is to obtain a detailed view on the platelet transport by explicitly considering the enhancing effect of the presence of RBCs. The results from the fully resolved blood flow can be used to obtain scaling and coefficients used in computationally less expensive advection-diffusion models.

Materials and Methods

The current work involved simulations of fully resolved blood flow, deformable RBCs and platelets immersed in plasma, for a channel and two cases of aneurysms, with and without stent.

The Lattice Boltzmann method [13] was employed as a fluid solver and was coupled to a discrete-element representation of deformable RBC's and platelets using the immersed-boundary method [11]. The coupled LBM-IBM approach has been widely used in modeling red blood cells [14, 4, 3].

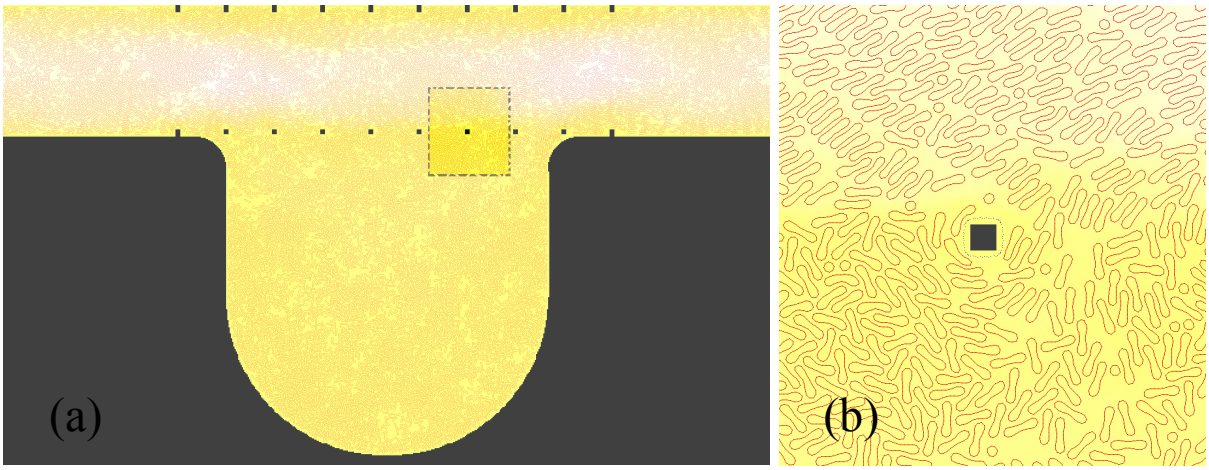

Figure 1: (a) Snapshot of a simulation with a stented aneurysm. (b) Magnification of the area marked in (a)

The mechanical model of the RBC's has been validated through simulations of single RBC's in shear flow and full blood in channel flow. Results obtained from the simulations, e.g. the density profiles in (fig 2), are in good agreement with those found in the literature.

The parameters of the simulations and the aneurysm geometries were chosen according to *Hirabayashi et al.* [8] in order to have a quantitative view on the differences of the velocity fields found for a non-stented aneurysm and a stented one. A hematocrit of 42% was chosen to mirror physiological conditions, along with a parent vessel diameter of 0.2mm. The aspect ratio of the aneurysm, neck to diameter, is AR = 1.0. The setup for the aneurysms contained more than 5.000 RBCs and platelets together. A snapshot of the simulation of a stented aneurysm is shown in figure 1a and in a magnification in figure 1b revealing the deformability of the particles representing RBC .

Results and Discussion

Three different approaches were considered: a) fully resolved RBC and platelet simulations b) fully resolved platelet-only simulations and c) convection diffusion simulations for the platelets. Some of the results obtained for the computationally intensive approach (a) are discussed here.

The distribution profiles of platelets and RBCs for the straight channel case are shown in figure 2. The clearly visible RBC-free layer (CFL) is a major factor that contributes to the Fåhræus–Lindqvist effect [15] and its width depends on the hematocrit and the vessel diameter.

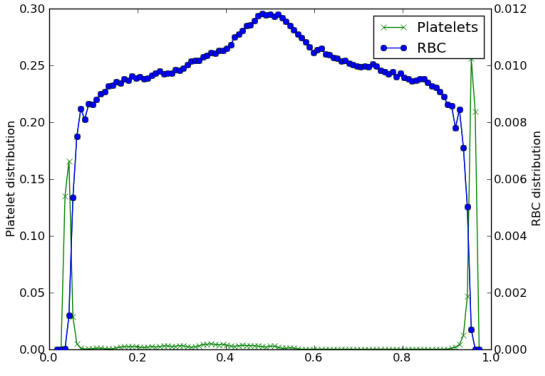

Figure 2: Radial distribution profiles of RBCs and platelets for a straight channel

The peak of the RBC concentration shown in Fig. 2 is observed in suspension flows [16] and is a result of the symmetry of the channel while in an experimental environment a higher mixing is observed faster.

The effect of RBCs in the transport of platelets is obvious in Fig. 2. A near wall excess of platelets is observed, while in the absence of RBCs, platelets exhibit what is called the “tubular pinch” effect in which particles crowd at 0.6 x tube radius [17].

In the case of the aneurysm (fig 3c.) three zones can be distinguished: a) the zone of parent vessel with a part entering the aneurysm b) the circulation zone in the middle of the aneurysm and c) the stagnation zone on the top of the aneurysm. The density of RBCs is shown in fig. 3b where the three zones are also distinguishable.

The lateral motion of platelets is present in the aneurysm case as well, where platelets flow close to the wall of the parent vessel. The concentration of platelets is higher at the left side of the vessel wall in comparison to the right side (fig. 3a), where platelets flow inside the aneurysm and can be caught in the circulation zone of the aneurysm and be transferred in any of the other two zones, or deeper into

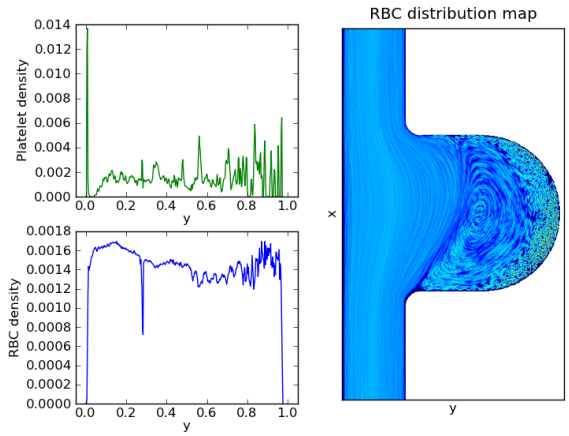

Figure 3: (a) Platelet density along the y axis of the aneurysm geometry (b) RBC distribution along the y axis of the aneurysm geometry (c) Distribution map of RBCs for an aneurysm.

the circulation zone. A peak in the platelet density is observed at the center of the vortex. These are preliminary results and further equilibrated profiles will be presented.

Conclusions

By explicitly modeling RBCs and platelets in complex geometries, a better level of detail can be obtained on the transport of platelets. The rich behavior of platelets in complex geometries can give insights on the thrombus formation inside intracranial aneurysms. This way the accuracy of coarser methods can be assessed and in case these simpler models are sufficient, coefficients for the less computationally expensive advection-diffusion models can be provided.

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