Towards numerical prediction of red blood cells dynamics within a cytometer

E. Gibaud*†, J. Siguenza, S. Mendez† and F. Nicoud†

† I3M. UMR CNRS 5149, CC 051. Place Eugène Bataillon, 34095 Montpellier, France

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1. Introduction

Recently, numerical simulations of deformable particles, including red blood cells (RBCs), have been a highly active and developing field. Researches on flows of RBCs have been mostly related to *in vivo* micro-circulation. Aside from physiological flows, it would be of great interest to study RBCs flowing through medical devices, such as blood pumps, cytometers, dialyzers, etc. Indeed, the understanding of RBCs flowing in these instruments is needed to improve their design and performances while avoiding undesired effects like thrombosis (blood coagulation) or hemolysis (blood damage). Moreover, computational fluid dynamics can provide detailed local quantities in complex geometries, which are generally difficult to reproduce in experiments.

When simulating RBCs in flows, difficulties arise from the complex coupling between mechanics of the RBC membrane and the flow of inner and outer fluids. The membrane of the RBCs is known to resist area change, shear and curvature. These properties have to accounted for when modeling the RBC membrane, in order to accurately predict their deformations in flows. Numerical simulation of RBCs under flow has seen remarkable progresses over the last decade, but is often limited to simple geometries and Stokes flows.

There are two major obstacles concerning the computation of the dynamics of RBCs in medical devices flows. First, the geometry of the device can be complex. Then, high flow velocity can be reached, leading to large values of the Reynolds number, even in sub-millimetric devices, as in blood analyzers.

In the present study, we aim at developing a numerical method to handle any complex flows with RBCs, including non-physiological ones. An extensive validation of its accuracy is performed through numerous test cases. While most existing solvers are dedicated either to vesicles (Seifert et al., 1997) (inextensible particles resisting to curvature, but not shear) or elastic capsules (Walter et al., 2010) (neglecting the curvature resistance, but authorizing variations of the membrane area), one needs to gather validation test cases used for both vesicles and capsules to validate a flow solver dedicated to RBCs.

2. Methods

The numerical method is based on the combination of front-tracking and immersed boundary methods (FT-IBM) also used by Bagchi et al. (Bagchi and Kalluri 2011, for instance) to study the deformation of particles over Cartesian regular grids. The cyto-plasm and the external fluid are represented by a unique incompressible fluid of variable properties.

The membrane of a RBC is supposed to be an infinitely thin hyperelastic surface. Such a model accounts for shear and area dilatation resistance. Bending resistance is modeled by the force derived from the Helfrich energy. The infinitely thin membrane is triangulated, each vertex of the membrane mesh being seen as a material point, whose evolution is computed by solving the fluid-structure interaction problem.

The membrane presence is taken into account by adding a source term to the Navier-Stokes equations, which mimics the force exerted by the membrane on the fluid. Incompressible Navier-Stokes equations are solved over a fixed Eulerian unstructured grid, using a finite-volume flow solver. Regularization of the membrane force over the fluid grid and interpolation of the fluid velocity at the membrane vertices is then done using the numerical strategy by Pinelli et al. (2010), based on Reproducing Kernel Particle Methods, which extends the IBM to unstructured grids.

3. Results and Discussion

Existing tests cases from the literature for isolated deformable particles confirm the ability of the method to reproduce existing analytical, experimental, and numerical results. Test cases include, in two and three dimensions: static pressurized particles (Walter et al., 2010), relaxation of elastic particles (Cottet et al., 2008), relaxation of vesicles to equilibrium state due to bending resistance (Seifert et al., 1997), evolution of particles in simple shear flow (Breyiannis et al., 2000) and mechanical deformation by optical tweezers (Dao et al., 2003).

***Corresponding author. Email: etienne.gibaud@univ-montp2.fr**

Deformation of a 2-D circular capsule in shear flow is studied as a function of Ca= $\mu ka/E$, often called the capillary number, defined from the initial capsule radius a, the membrane elastic modulus E, the shear rate associated with the flow k and the dynamic viscosity of the fluid μ. After stabilization, the capsule tank-treads and undergoes a deformation that depends on Ca. The Taylor deformation parameter at equilibrium $D=(A-B)/(A+B)$, where A and B are the maximum and minimum capsule dimensions, is reported in Table 1. Excellent agreement is shown with the results obtained by Breyiannis et al. (2000) with a boundary integral method.

Ca	0.003125	0.0125	0.05	0.125
Present results : *D*	0.1595	0.2492	0.3820	0.4930
Breyiannis et al. (2000) : *D*	0.1596	0.2491	0.3819	0.4938

Table 1 Asymptotic Taylor deformation parameter D of 2-D capsules in linear shear flow for different values of Ca.

Figure 1 shows the deformation of a RBC by optical tweezers, as a function of the force applied. The RBC membrane is modelled as a neo-Hookean hyperelastic surface, as in Dao et al. (2003). The present results, using the FT-IBM formalism, are in excellent agreement with the numerical data from Dao et al. (2003) and are close to the experimental measurements. More sophisticated membrane models are expected to yield better comparisons with the experiment.

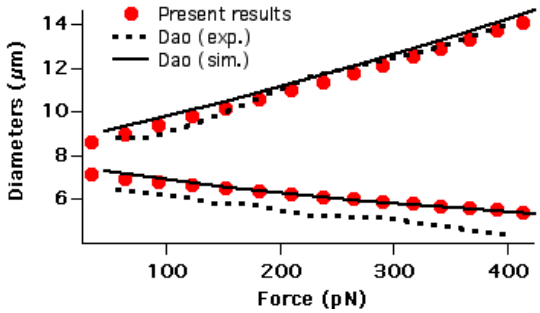

Figure 1 Axial and transverse diameters of RBCs deformed by optical tweezers. Comparison with experimental and numerical data (Dao et al. 2003)

Validation of the solver in simple cases authorizes its application to more complex configurations, related to cytometers. Cytometers are complex medical devices, in which samples of diluted blood are injected to measure the hematocrit and the RBCs volume. In cytometers, RBCs flow through a micro-orifice and perturb an electrical field. Such a perturbation depends on the shape and orientation of cells in the micro-orifice. In order to demonstrate the ability of the present method to face such situations, the entry of a 2-D capsule is computed. Figure 2 shows the carrying velocity field (the reference velocity ub=4.4 m/s and the Reynolds number is 220) and a sequence of shapes of the capsule. The capsule is first elongated (labels a to b) then undergoes compression at the entry of the contraction (c). Inside the contraction, lateral migration is observed (c to d).

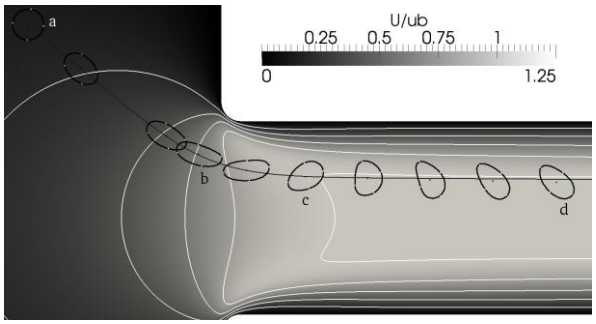

Figure 2 Entry of a capsule in a contraction (sequence of membrane shapes at different times). Non-dimensional horizontal velocity field and iso-lines (from 0.25 to 1.25 every 0.25). The black line is the streamline issued from the initial capsule center.

4. Conclusions

A numerical method able to compute deformable particles in flows at large Reynolds number is shown and validated against existing numerical and experimental data. The numerical tool developed is able to simulate the behaviour of capsules and cells and is applied to a configuration of sudden contraction, typical of cytometers.

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