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INERTIAL MICROFLUIDICS FOR BLOOD PARTICLE SORTING IN SPIRAL MICRODEVICES

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SUMMARY

With the aim of providing an accurate investigation of the physical mechanism of blood particle transport within curved microchannels in inertial microfluidics regimes, we present a parametric study that exploits fluid- and particle-resolved simulations. The numerical framework is based on a lattice-Boltzmann method for incompressible flows, coupled with a Finite Element model for soft particles with different mechanical properties by means of an Immersed-Boundary technique. The study is performed in spiral microchannels spanning the geometrical, flow and structure parameters in order to evaluate their effects on the resulting particle sorting.

Key words: *inertial microfluidics, particle sorting, lattice Boltzmann, fluid-structure interaction*

1 INTRODUCTION

In the last decades, significant advancements in the field of microfluidics allowed the development of diagnostic or therapeutic devices to sort multiple blood cell populations. Several sorting techniques have been developed for separating platelets, red blood cells and other blood cells from each other, e.g. [1, 2]. In this context, inertial microfluidics has become a very attractive separation method because the desired particle focusing can be achieved without the need for external forces acting on the system. When the channel Reynolds number is in the range 10÷100, particles moving in such configurations migrate laterally to different equilibrium positions due to the counteraction of two inertial effects: the shear gradient lift force due to the curvature of the fluid velocity profile, and the wall lift force as result of the interaction with the adjacent walls. Secondary flow can also appear in curved channels, where the pressure gradient in the radial direction can generate two counter-rotating Dean vortices. The combination of inertial forces, centripetal forces and viscous forces lead to different flow regimes and different strength of Dean vortices; these effects are described by the Dean number, whose definition includes the Reynolds number and the curvature ratio. Hence, the equilibrium position of the particles depends on the ratio of the net lift force to the secondary flow resistance, thus differential particle size-dependent focusing can be obtained. Additionally, deformability-induced forces have an impact on the equilibrium position of soft particles in inertial flows, leading to particle deformability-dependent focusing—an interesting review of the inertial microfluidics and its effects is provided by Zhang et al. [3].

Recently, the authors developed a fluid-structure interaction (FSI) framework based on a lattice-Boltzmann (LB) method coupled with a Finite Element (FE) model for structure dynamics by means of an Immersed-Boundary (IB) technique for particle-resolved simulations [4]. The framework handles FSI applications of particle transport in both Stokes flow and inertial microfluidics regimes. In particular, the authors investigated capsule transport in inertial microfluidics regimes within straight and curved microchannels and the sensitivity of the equilibrium position of the capsules to the characteristic flow and structure parameters.

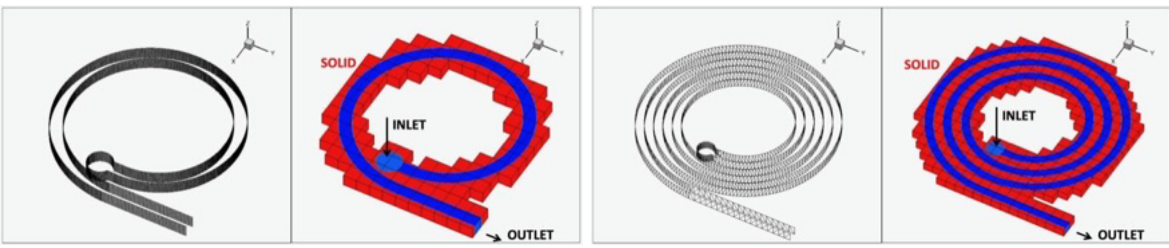
With the goal of providing an accurate investigation of blood particle transport in inertial flow regimes to design microfluidic particle-sorting devices, the numerical framework is here used for particle focusing applications in curved microchannels with spiral geometries. The idea of using spiral geometry for focusing applications is already established in literature although its range of usage is limited by the smallest size of cross-section obtainable by manufacturing techniques [5]. Several simulations are performed spanning the geometrical, flow and structure parameters in order to evaluate their effects on the equilibrium positions and particle focusing achievable as a consequence of the balance of the involved forces.

2 METHODOLOGY

The FSI framework based on a fully-incompressible LB method coupled with a FE model for structure dynamics by means of an IB technique is described hereafter.
Owing to the length scales of flows within microfluidic devices, there may be a significant pressure difference between the device input and output, hence using a traditional LB flow solver would not guarantee the incompressibility condition. The derivation of the incompressible form of the Navier–Stokes equations from LB equations including also a forcing term [6] to account for the presence of moving structures is permitted by the alternative version of the LB method [7]. Particles are considered as a collection of Lagrangian markers immersed in the Eulerian fluid lattice. The in-plane elastic response of the particles is evaluated by using the FE model developed for large deformations and unstructured triangular meshes [8]. The versatility of FE model allows to derive the Piola–Kirchhoff stress tensor starting from a given strain energy function (e.g. neo-Hookean law, Skalak law) and include the Helfrich model of the membrane bending elasticity and the Standard-Linear-Solid model to account for the membrane viscoelasticity, so that microparticles with different rheological properties can be investigated. An IB treatment [9] is used to impose the dynamic and kinematic continuity at the fluid-structure interface, and the time advancement of the FSI solution is performed following an explicit procedure. Finally, the fixed channel geometry is immersed in the Eulerian lattice and no-slip conditions [10] are imposed to account for the curved walls; on the lattice boundaries, pressure, velocity, and no-slip conditions are imposed following the procedure of Zou and He [11] adapted for the fully-incompressible LB derivation. The mathematical derivation of the FSI solver is reported in [4].

3 RESULTS AND CONCLUSIONS

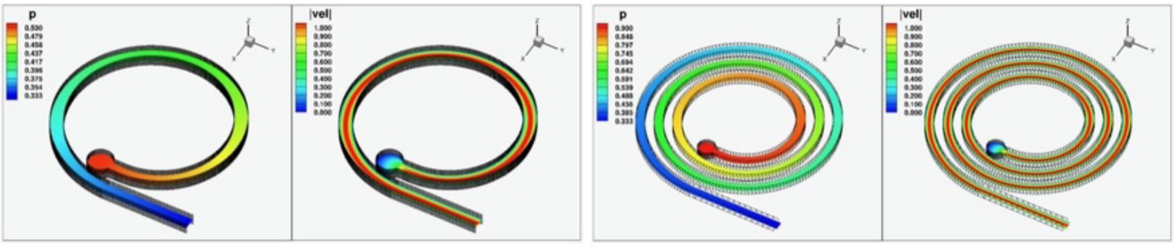
The numerical framework is used to investigate the physical mechanism of inertial particle focusing in curved microchannels with spiral geometries.
At the beginning of each simulation, a tagging procedure is employed to determine the nature of each lattice node with respect to channel walls of fixed position. The nodes in the lattice can be classified into three different types: solid, fluid, and interface nodes. Solid nodes are those outside the channel, fluid nodes are those inside the channel, and interface nodes are defined as fluid nodes that have at least one solid node nearby. The algorithm detects inner (fluid, interface) and outer (solid) nodes regardless of the geometrical complexity as shown in Figure 1. Flow solver applied only onto the inner (fluid, interface) nodes. A velocity inlet boundary condition was prescribed according to Poiseuilles theory, a reference pressure was imposed at the outlet, and no-slip wall condition was used elsewhere. Due to the presence of curved walls, no-slip conditions [10] have been used.



(a) (b)

Figure 1: Results of the tagging procedure for simulations performed with one-loop (a) and three-loops (b) spiral microchannels. Outer (solid) nodes are indicated in red, inner (fluid, interface) nodes in blue.

For the sake of brevity, here we present only simulations within one-loop and three-loops spiral microchannels with rectangular cross-section (hydraulic diameter D_h = 80), performed on a grid of dimensions (N_x, N_y, N_z) = (1280, 1200, 80) and (N_x, N_y, N_z) = (1900, 1800, 80), respectively. The Reynolds number is defined as $Re = U_{max} D_h/\nu_f$ and the Dean number as $De = Re\sqrt{D_h/(2R_c)}$, being ν_f the kynematic viscosity of the fluid and R_c the radius of curvature of the path of the channel. Pressure and velocity flow fields obtained for $Re = 50$ without any transported structure are shown in Figure 2.

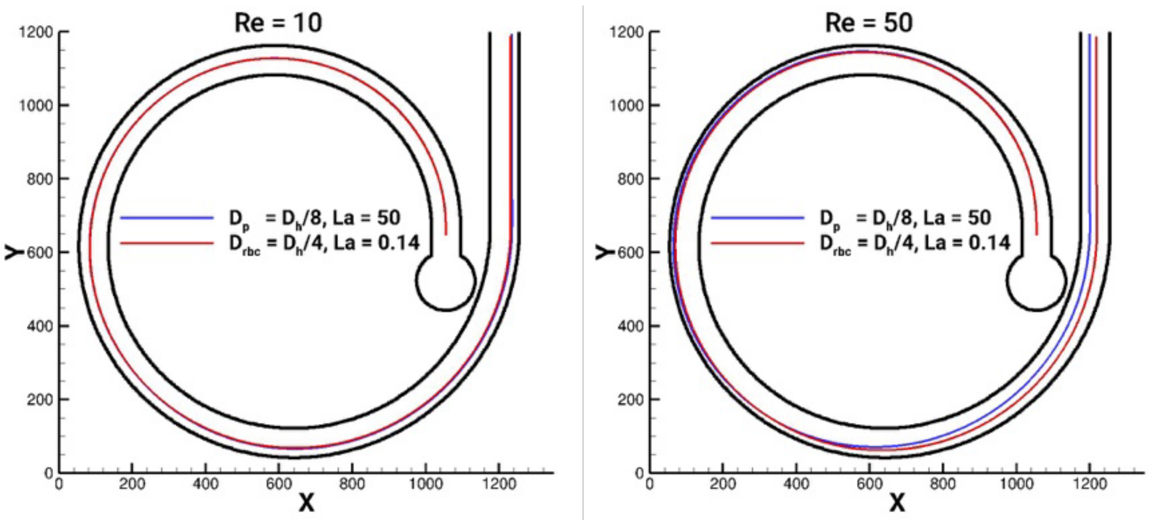


(a) (b)

Figure 2: Pressure and velocity fields obtained in the one-loop (a) and three-loops (b) spiral microchannels.

Deformable, viscoelastic, and neutrally-buoyant particles containing a fluid with the same viscosity as the surrounding medium are placed inside the microchannel. Being k_s the constant shear modulus, the Laplace number computed as $La = k_s(D_p/2)/(\rho_f \nu^2)$ is adopted to describe the deformability of the particle. The deformation mechanics of particles with different rheological properties has been investigated. FSI computations are initialized with the solution obtained without any transported structure.

First, mechanical properties of a red blood cell in physiological conditions are reproduced using the Skalak law assigning an appropriate value to the Laplace number $\approx 0.05 \div 0.15$ and to the elastic dilatational modulus $k_\alpha = 50k_s$; in addition, bending modulus is defined as $k_b = 0.00263\ k_s\ (D_{rbc}/2)^2$ and membrane viscosity as $\mu_m = 33.889\ \mu_f\ D_{rbc}$. Moreover, in the present investigations platelets have been modeled as spherical particles following the neo-Hookean law for the in-plane elastic response. The Laplace number is assumed equal to 50 in order to ensure high physiological stiffness; bending modulus is defined as $k_b = 0.000263\ k_s\ (D_p/2)^2$. In the simulations presented here the red blood cell and the platelet have an initial diameter $D_{rbc} = D_h/4$ and $D_p = D_h/8$, respectively. Figure 3a and Figure 3b show particle trajectories of a red blood cell and a platelet travelling in the spiral microfluidic device at $Re = 10$ and $Re = 50$, respectively.



(a) (b)

Figure 3: Trajectories of a single platelet and a single red blood cell for $Re = 10$ (a) and $Re = 50$ (b) in the one-loop spiral microchannel.

Increasing the influence of the curvature effects from $Re = 10$ ($De \approx 2.5$) to $Re = 50$ ($De \approx 12.5$) allows differential particle size- and deformability-dependent focusing although the confinement ratio D_h/D_{rbc} is only equal to 4.
Preliminary investigations on spiral microfluidic devices confirmed that the developed FSI framework reliably predict the flow field in inertial microfluidics regimes and the deformation of soft particles, thus is suitable for the inertial transport of blood particles in microfluidic devices.
Starting from the results obtained for the one-loop spiral geometry, further investigations have been carried out increasing the confinement ratio and the number of loops to amplify the differential focusing. In conclusion, the numerical framework is appropriate for the investigation of inertial microfluidic phenomena that gears towards the design of microfluidic devices for particle-sorting applications.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the results of this study.

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