Computational Fluid Dynamics Models for the Rational Design of Magnetic Microseparators – In Memory of Dr. Ed Furlani

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ABSTRACT

In this work, we report a numerical flow-focused study of bead magnetophoresis inside a continuous-flow microchannel in order to provide a detailed analysis of bead motion and its effect on fluid flow. Different Computational Fluid Dynamics (CFD) models are introduced and a screening process is carried out. All the models involve a Lagrangian approach and predicts the bead separation from blood and their collection into a flowing buffer by the application of a magnetic field generated by a permanent magnet. The following scenarios are modelled: i) one-way coupling wherein momentum is transferred from the fluid to beads, which are treated as point particles, ii) two-way coupling wherein the beads are treated as point particles and momentum is transferred from the bead to the fluid and vice versa, and iii) two-way coupling taking into account the effects of bead volume in fluid displacement. The results indicate that although there is little difference in the bead trajectories for the three scenarios, there is significant variation in the flow fields, especially when high magnetic forces are applied on the beads. Therefore, an accurate full flow-focused model that takes into account the effects of the bead motion and volume on the flow field should be solved when high magnetic forces are employed. Nonetheless, when the beads are subjected to medium or low magnetic forces, computationally inexpensive models can be safely employed to model magnetophoresis. The model that provided the best trade-off between computational cost and accuracy was experimentally validated via application to a prototype device employing human whole blood. The impact of a wide range of flow rates on bead recovery was theoretically and experimentally quantified. The performance of the prototype device was characterized using fluorescence microscopy and the experimental results are found to match theoretical predictions within an absolute error of 10%. Overall, it is concluded that the modeling effort presented in this contribution enables understanding of the fundamental physical phenomena involved in magnetophoresis, while offering an ideal parametric analysis and optimization platform. Finally, I would like to express my most sincere gratitude to Dr. Ed Furlani for his invaluable contributions to this work, to whom I will be eternally grateful.

Keywords: magnetic particle separation, fluid-bead coupling, CFD modeling, magnetophoresis, microfluidics, blood detoxification.

1. INTRODUCTION

In recent years, there has been a proliferation of applications of superparamagnetic beads in a diverse range of fields [1,2]. For most of these applications, the precise control of the particle magnetic manipulation is of paramount importance. Magnetophoretic continuous-flow microfluidic devices provide an especially good platform for magnetic particle manipulations because of their advantages in comparison to other separators, e.g. controlled laminar flow, small required volumes, integration with multiple functionalities, continuous operation mode, etc. However, these devices must be properly designed to achieve complete magnetic particle separation while minimizing the effects of the bead motion in the fluid flow. While previous research has shown that micron-sized particles can be manipulated with simple permanent magnets, there has been relatively little work specifically focused on the effect of bead motion on fluid flow, which may be due to the complexity of the mathematical description.

Therefore, in this work we provide a detailed analysis of bead motion and its effect on fluid flow inside a continuous-flow magnetophoretic device where the beads are magnetically separated from a flowing biological fluid (blood) and recovered into an aqueous buffer solution. Our numerical model describes the particle separation due to the presence of a magnetic field provided by a permanent magnet. Three model scenarios are employed for describing particle-fluid interactions: i) one-way coupling between the beads and the fluid wherein the fluid flow affects bead motion but the bead motion does not perturb the fluid flow, ii) two-way coupling wherein there is a two-way momentum transfer between the beads and the fluid, i.e. the bead motion perturbs the fluid flow, and iii) two-way coupling including fluid displacement dependent on the bead volume. We provide useful guidelines about the model to be chosen depending on the magnetic conditions inside the channel, in order to optimize the simulation runtimes without sacrificing results accuracy. Furthermore, the most accurate model (taking into account the computational cost) is experimentally validated and used to predict the particle recovery under a high range of flow and magnetic conditions. This approach can be employed for parametric analysis and optimization, facilitating the development of novel microfluidic systems for many other biomedical applications that involve two or more confined liquid phases.

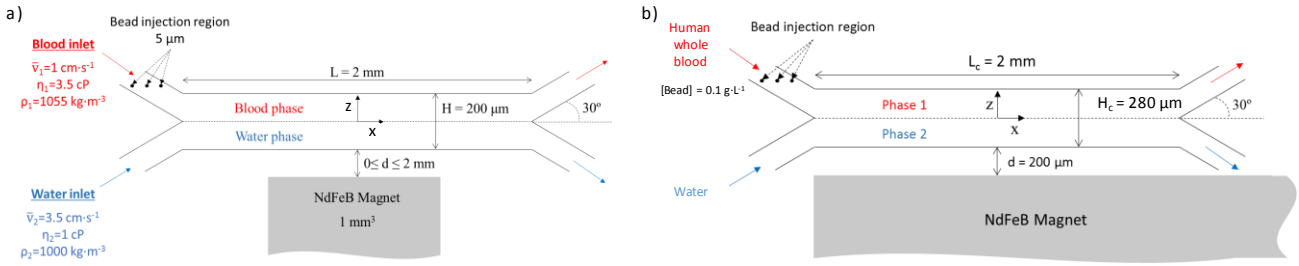

Figure 1. Schematic view of the design of the continuous-flow magnetophoretic separator that was employed for : a) Model screening process between the three different model scenarios; b) Magnet-channel system employed for the experimental validation of the model that reported the best results during the screening process.

2. NUMERICAL MODELS AND EXPERIMENTAL VALIDATION

The computational models used in this work involve an Eulerian-Lagrangian approach to predict the magnetophoretic bead transport inside the microseparator schematized in Fig. 1 a). The Computational Fluid Dynamic (CFD) analysis not only includes the major forces driving the separation, which are the magnetic and the fluidic forces, but also the effect of the particle motion on the fluid flow through three different scenarios. According to the aforementioned approaches, beads are considered discrete elements and their trajectories are estimated as follows:

$$m_p \frac{d\mathbf{v_p}}{dt} = \sum \mathbf{F_{ext}} \quad (1)$$

where m_p and $\mathbf{v_p}$ are the mass and velocity of the particle and $\mathbf{F_{ext}}$ represents all external force vectors exerted on the particle, which are the magnetic and the hydrodynamic drag forces. Expressions for these forces can be found in our published works [3].

The fluid velocity field was predicted using the Navier Stokes and continuity equations, to which certain modifications were applied in order to precisely describe the bead-fluid interactions. In the scenario 1, we did not take into account the effects of the bead motion or bead volume in the fluid flow field, but only the effect of the fluid motion on the magnetophoresis process. Thus, the fluid velocity field is estimated by Navier-Stokes and continuity equations [3]. In the second scenario, we account for a two-way coupling, i.e. two-way momentum transfer between the moving particles and the fluid. However, the beads were considered as point particles. Two-way coupling is taken into account by including the particle accelerations into the momentum equation, as follows [2]:

$$\frac{d(\rho\mathbf{v})}{dt} = -\nabla P + \mathrm{div}(\boldsymbol{\tau}) + \frac{1}{V}\mathbf{F_P} \quad (2)$$

where ρ and $\mathbf{v}$ are the density and velocity of the fluid, P is pressure and div(τ) term represents the contribution of shear stress on the fluid velocity. The last term in equation (2) represents particle induced fluid accelerations, where V is the volume of fluid in the cell. A precise formulation of $\mathbf{F_p}$ can be found in our previous work [4]. For the third case, we take into account two-way coupling and the effects of the liquid being displaced by the bead volume. Thus, the continuity equation is altered to account for solid objects in the computational cells as follows [5]:

$$\frac{\partial}{\partial t}(\rho V_f) + \nabla(\rho \mathbf{v}\mathbf{A}) = S_m \quad (3)$$

where Vf and $\mathbf{A}$ represent the fractional volume and fractional area open to flow for each mesh cell and Sm is a physical mass source term of fluid which may be present in the cell.

Multiple simulations were run by keeping the average drag force at a constant value (same velocities at the inlets) and adjusting the magnet distance from the lower wall of the channel (Fig. 1 a), which in turn, affects the magnitude of the magnetic force acting on them. The different models were solved using the commercial CFD software ***FLOW-3D*** (versions 11.1 and 11.2, Flow Science, Inc.). For scenarios 1 and 2, we used a Lagrangian particle model and a specific mass flowrate of beads was introduced into the upper inlet (500 particles/s). However, for scenario 3, explicit modeling of moving objects was used and only the motion of three beads was modelled. A uniform grid was employed for all the simulations. For scenarios 1 and 2, the mesh was composed by 75,000 cells (2D simulations), whereas this number was increased up to 1,200,000 cells for scenario 3 (in order to accurately account for the bead volume).

For the experimental validation of the CFD models, we used a NdFeB magnet for generating the magnetic field with dimensions of 10x5x3 mm^3. Human whole blood (containing fluorescent magnetic beads of 4.9 µm in diameter at a constant concentration of 0.1 g·L^{-1}) and aqueous buffer solutions were employed as fluid phases, as presented in Fig. 1 b). A glass microchannel was employed with a U-shaped cross-section of 280 µm × 60 µm (Fig. 1 b). The glass chip was mounted into an aluminum holder and connected to the pumps with fused silica capillaries. Two syringe pumps were used to control the flow.

Table 1. Analysis of particle recovery and fluid perturbation as a function of the magnetic conditions applied inside the device for scenarios 2 and 3.

Magnet distance (mm)	Magnetic force (nN)	Bead separation		Fluid perturbation	
		Scenario 2	Scenario 3	Scenario 2	Scenario 3
0	6.71	100%	Complete	Medium	High
1.00	0.59	100%	Complete	None	Medium
1.15	0.36	95.7%	Complete	None	Low
1.25	0.24	70.4%	Incomplete	None	Low
1.50	0.10	34.7%	Incomplete	None	None
2.00	0.02	15.5%	None	None	None

3. RESULTS AND DISCUSSION

3.1 Numerical model screening

The recovery of the particles, as they move from the biological fluid to the buffer solution, as a function of the distance of the magnet to the channel wall are shown in Table 1. In this case, only the results for scenarios 2 and 3 are presented, since the difference in bead recovery from scenarios 1 and 2 was negligible. It can be seen that, when the distance "d" between the magnet and the channel is 1 mm or less, all the beads are recovered from blood to the buffer stream. However, larger distances resulted in the incomplete separation, which is in agreement with our previous calculations [5]. It should be noted that the magnetic field is very high when the magnet is place next to the wall (d=0), reaching magnetic forces of around 7 nN. However, the field decays rapidly with d, being practically negligible for d≥2 mm. This field variation with d causes a decrease of the average magnetic force experienced by the beads, as seen in Table 1. Also it can be seen that the recovery rates for the scenarios 2 and 3 are nearly identical, which suggests that the particle recovery is not affected by the inclusion of a two-way momentum transfer into the momentum equation or the bead volume into the continuity equation.

However, there exist a difference between the three scenarios in the fluid perturbation as the bead crosses the blood to the buffer. By comparing scenarios 1 and 2, we observed that this change of the momentum equation appears to affect the fluid flow only at high magnetic field conditions, due to the acceleration of the beads. However, under low magnetic forces, the fluid perturbation is negligible. Nevertheless, when the volume of the beads is taken into account in the flow field equations (scenario 3), the liquid displacement due to each bead as it moves from the blood stream to the buffer solution has a significant effect on the fluid flow, especially under high magnetic forces, as seen in Table 1.

Based on these results, we conclude that when relatively high magnetic force fields are applied for the recovery of magnetic beads, an accurate full flow-focused model should be solved since there is a risk of neglecting the effects that the motion and volume of the magnetic beads have on the flow field. However, this model is computationally expensive and takes substantially more time to run (in our case 2-3 weeks). When medium or low magnetic force fields are employed (in comparison to the average fluidic forces), the bead-fluid interactions could be omitted as they are negligible for these cases. Moreover, since the bead accelerations are not desirable for continuous-flow devices because of the flow alterations, the best alternative is to employ medium to low magnetic forces to carry out the magnetophoresis. And, under these desirable circumstances, less accurate and computationally inexpensive models could be safely employed (either scenarios 1 or 2, which took only a couple of hours to run on a modern multicore workstation). Thus, we considered that the model that provides the best accuracy at a reasonable computational cost is the developed for scenario 2, which is next experimentally validated.

3.2 Experimental validation

The experimental validation of the model was carried out with human whole blood co-flowing with an aqueous buffer solution in a Y-Y shaped microchannel. In Fig. 2, the separation of the beads as a function of the applied flow rate is presented. As expected, the separation of these beads decreases as the applied flow rate increases from 0.01 to 0.1 $\mu L \cdot s^{-1}$ due to an increased in the drag force exerted on the beads. Nevertheless, the simulated and experimental results follow the same trend with an error less than 10%, showing the capability of our model to accurately describe magnetophoresis from complex fluids as blood.

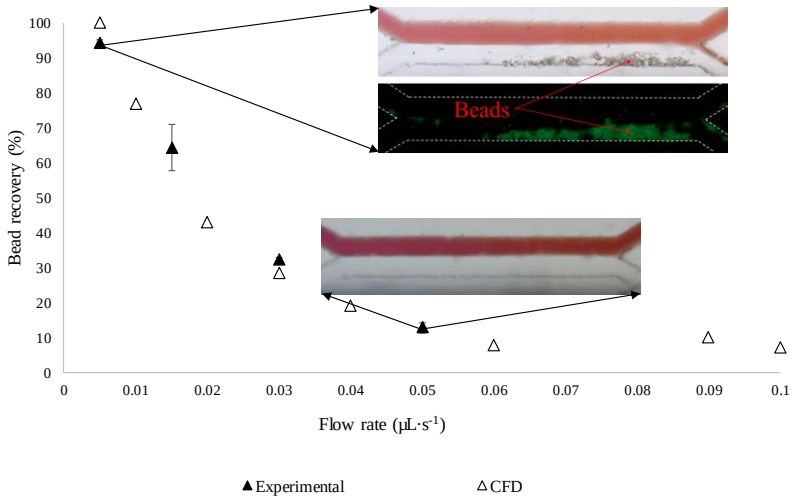

Figure 2. Experimental validation of the CFD model developed for Scenario 2 showing the influence of the flow rate on the particle recovery, as well as experimental microscope images of the device when the magnetophoresis process is being carried out.

4. CONCLUSIONS

In this work, we have performed a flow-focused study of the magnetophoresis of micron-sized magnetic beads inside a continuous flow microfluidic device in order to provide a detailed analysis of the bead motion and its effect on the fluid flow. Different fluid perturbation scenarios were modelled: i) one-way coupling between the beads and the fluid, ii) two-way coupling, modeling the beads as point particles, and iii) two-way coupling in which the volume of the beads was taken into account to include the corresponding fluid displacement. Our results suggest that the second model (two-way coupling model scenario neglecting the effect of the bead volume) reports the best results in terms of accuracy and computational cost, and that this model can be safely employed to model magnetophoresis when the hydrodynamic and magnetic forces remain in the same order of magnitude. Finally, we have validated this model via the analysis of a prototype device and have used fluorescence microscopy to characterize key performance metrics: flow patterns and bead separation. The experimental data are consistent with the theoretical predictions within an absolute error of 10%. Therefore, we conclude that the computational model enables understanding of the fundamental underlying mechanisms of device performance and is useful for the development of novel magnetophoretic applications.

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