Optimization of continuous-flow magnetic bioseparators through CFD numerical models

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ABSTRACT

Continuous flow magnetic bioseparators integrating magnetic bead technology are gaining increased attention due to their ability to selectively remove dangerous pathogens from biofluids. Specifically, the unique properties of magnetic particles and microfluidic devices allow these devices to be employed for blood detoxification in a continuous process. However, the optimization of the magnetic particle recovery after the capture of the toxins is performed, remains less explored. Indeed, obtaining high recovery rates while operating at high throughputs, is still a scientific challenge. Moreover, the geometrical characteristics of the devices with an emphasis on the available chip fabrication methods and their limitations has never been taken into account for studying particle magnetophoresis. In order to address these challenges, we introduced a Computational Fluid Dynamics (CFD)-based Eulerian-Lagrangian approach using the commercial software FLOW-3D, to accurately describe bead magnetophoresis in a two-phase microdevice, where the particles are continuously deflected from blood and collected into a coflowing buffer. The model results were experimentally validated through fluorescence microscopy for two of the chip designs under study. Both experimental and computational results suggest that the shape of the cross section has a tremendous effect on the velocity profile developed within the channel, and thus, in the flow rates that can be used to achieve maximum recoveries. Thereby, when considering U-shaped cross sections, as the ones typically obtained by conventional photolithography and wet etching fabrication techniques, the velocities for obtaining recoveries higher than 95% are one order of magnitude lower than when rectangular cross sections are employed. Also, by increasing 5 times the chip length, the separation efficacy increases as much as 68% for all the devices allowing the use of higher flow rates and thus enhancing the system throughput. Overall, the theoretical and experimental methodology developed in this work provide insight into the rational design of magnetophoretic-microfluidic devices for biomolecule separations and can be applied to a broad range of magnetically-enabled microfluidic applications.

Keywords: magnetophoresis, chip design, microfluidics, bioseparator, detoxification,

1. INTRODUCTION

Magnetophoretic-based capture of harmful molecules in microfluidic devices has been considered to be a promising alternative for the extracorporeal removal of toxic substances from blood. In this process, known as blood detoxification, magnetic beads selectively bind to the target poisoning substances, and subsequently, the resulting complex particle-toxin can be magnetically-isolated, leading to a clean blood solution that preserves its original properties. [1,2] The design of such microfluidic-magnetophoretic devices has attracted outstanding attention and numerous continuous flow separators for the recovery of magnetic particles from biofluids have been proposed. [3] However, the feasible application of these devices requires the treatment of high volumes (high system throughput) while delivering both maximum bead recovery and impaired blood quality, which remains a technological challenge due to the channel dimensions and the limitations of the current chip fabrication methods that greatly influence the cross-sectional channel shape and the materials to be employed. Hence, the non-symmetrical, U-shaped sections derived from wet etching techniques highly impacts the system performance when compared to channels with the strictly rectangular section shape that arise from lithography techniques. [4,5]

In this work, we address the optimization of multiphase continuous-flow Y-Y shaped microfluidic devices by assessing the effect of both channel length and cross-sectional shapes in the system performance. For that purpose, we introduce a fluidic analysis coupled to a magnetic model to accurately describe bead trajectories under different flow rate conditions. Besides, dimensionless parameters are introduced to gain insight into the design of magnetophoretic microdevices. This study provides a powerful guideline for the optimization of magnetophoretic microchannels, regarding the necessity of apply different microchannel fabrication techniques, that can be exploited not only for biofluid detoxification applications but also for any magnetically-driven separations.

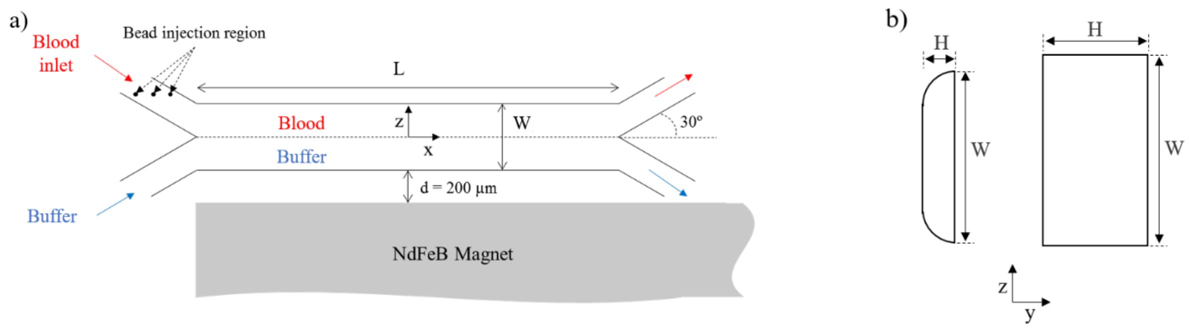

Figure 1. a) Schematic view the continuous-flow magnetophoretic separator; b) Generic cross-section of the microchannels.

2. THEORY

The model was developed by customizing a commercial multiphysics CFD software program, ***FLOW-3D*** from Flow Science Inc. (ver11.2, www.flow3d.com) and is based on an Eulerian-Lagrangian approach. The Lagrangian framework is used for describing the bead motion whereas the Eulerian approach is used to model the fluid transport.

In this model, only the dominant forces acting on the particles (i.e. magnetic and fludic drag forces) have been considered. Hence, according to the Lagrangian approach, particles are modelled as discrete units and their trajectories are predicted by applying the classical Newtonian dynamics:

$$m_p \frac{d\mathbf{v_p}}{dt} = \sum F_m + F_d \qquad (1)$$

where m_p and $\mathbf{v_p}$ are the mass and velocity of the particle and $\mathbf{F_m}$ and $\mathbf{F_d}$ represents the magnetic and drag external force vectors exerted on the particle respectively. Expressions for the magnetic and drag forces acting on a particle can be found in our published work. [2]

The following assumptions have been considered to develop this model: (a) all fluids are Newtonian and incompressible (Newtonian rheology of blood has been demonstrated when the shear rate exceeds about 100 s^{-1}) [2], (b) the magnetization of the particle are a linear function of the applied magnetic field up to a saturation value, (c) interparticle magnetic dipole-dipole coupling is negligible because of a low particle concentration (common values of detoxification applications), (d) the field sources are ideal 3D rare-earth permanent magnets, and (e) there are no other magnetic materials present in the computational domain that would otherwise perturb the magnetic field.

3. METHODOLOGY

In order to assess the influence of the microchannel geometry on the system performance, both computational and experimental analysis were carried out. For all of the systems under study, a 0.1 g/L suspension of 4.9 um magnetic particles in blood were injected through the upper inlet of a Y-Y shaped microdevice (Fig. 1). The application of a magnetic field by a permanent magnet with dimensions 10x5x3 mm^3, allows the collection of the beads in the co-flowing stream (deionized water). Channels with rectangular and U-shape cross sections, as well as three different lengths (L = 2, 5 and10mm) were considered. In Table 1 the dimensions of the microchannels under study are listed.

Two dimensionless parameters were introduced to elucidate the effect of channel geometry in the system performance and to efficiently compare across the spectrum of geometries. The first one, J, relates the magnetic and the drag forces that are exerted on the beads in z and x directions, respectively. Thereby, the fluidic and magnetic variables and parameters that influence the beads trajectory in the microdevice (particle volume, magnetization, magnetic field strength and gradient inside the channel viscosity of the fluids and inlet mean velocities) are considered. The J number can be described as:

$$J = \frac{\overline{F_{m,z}}}{\overline{F_{d,x}}} \qquad (2)$$

On the other hand, the parameter θ balances both the residence time of the particles in the microdevice (t_{res}), and the time they require to travel from the blood to the buffer solution, considering that they move completely perpendicular to the flow direction (t_m). Apart from the variables and parameters considered in J, the width and the length of the channel are included. Hence, this design parameter can be written as:

$$\theta = \frac{t_{res}}{t_m} = \frac{L}{W} \cdot J \qquad (3)$$

Table 1. Dimensions and geometric features of the microchannels under study.

	Rectangular-shaped			U-shaped		
Volume (mm^3)	0.12	0.3	0.6	0.03	0.08	0.15
L/D_h	8	21	42	21	51	103
L (mm)	2	5	10	2	5	10
D_h* (µm)	240	240	240	97.1	97.1	97.1
W (µm)	300	300	300	280	280	280
H (µm)	200	200	200	60	60	60

*D_h represents the hydraulic diameter of the microchannels.

4. RESULTS AND DISCUSSION

4.1 Influence of cross-sectional shape

Cross-sectional shape entails a tremendous effect in the flow patterns developed inside the microfluidic device, and thus, in the range of flow rates that can be safely employed to obtain complete recoveries. In Fig. 2, the velocity distribution for the same average velocity (0.0033 m/s) is presented for both cross sectional shapes under consideration (i.e. U-shaped and rectangular channels).. It can be seen that in U-shaped channels the maximum velocity takes a significant area of the cross section although the magnitude is lower than in the rectangular ones, where the maximum velocity is located in the middle of the section. Thereby, in U-shaped channels, particles are subjected to the maximum velocity to a higher extent than what they experience in rectangular microdevices. Therefore, the drag force is lower for rectangular chips, resulting in a higher particle recovery due to the higher J values obtained in these devices when the same magnetic field force is employed. Thus, in order to obtain the complete particle recovery, velocities one order of magnitude lower must be considered when using the U-shape channels, resulting in an undesirable decrease of the system throughput. Hence, the optimization of the geometrical features (i.e. channel length) of the devices is of paramount importance.

4.2 Influence of channel length

Lengthening of channels affects the residence time of the beads in the microdevice. Thereby, a five-fold increase of the channel length involves an improvement of 41% and 55% of the particle recovery for U-shape and rectangular cross-section channels respectively.

In Fig. 3.a), the percentage of bead recovery as a function of the θ para meter has been represented. We found that independently of the channel length, rectangular channels allow to achieve high particle recoveries with a faster rate than U-shaped ones. Besides, for each type of cross section, the increase of the L/D_h ratio when increasing L is compensated with the decrease in the J number, due to the higher velocities that can be used to obtain the same particle recovery.

The effect of the fluid velocity in the bead recovery in clearly shown in Fig 3. b). The 10 mm rectangular cross-section channel delivers the best performance since allows to obtain complete particle recovery by using velocities one or two orders of magnitude higher than the other geometries. For sharing the same trend, L/D_h ratios of U-shape channels must be one order of magnitude higher than for rectangular ones, according to Table 1. The low volume of 2mm U-shaped channel explains its deficiently performance.

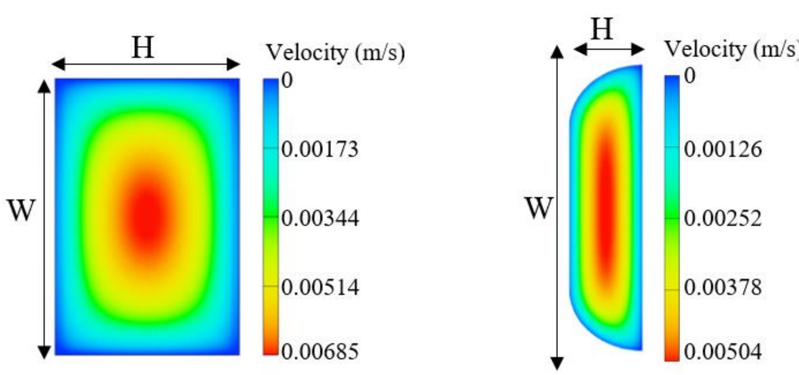

Figure 2. Velocity distribution in a section perpendicular to flow direction for rectangular (left) and U-shaped (right)channels.

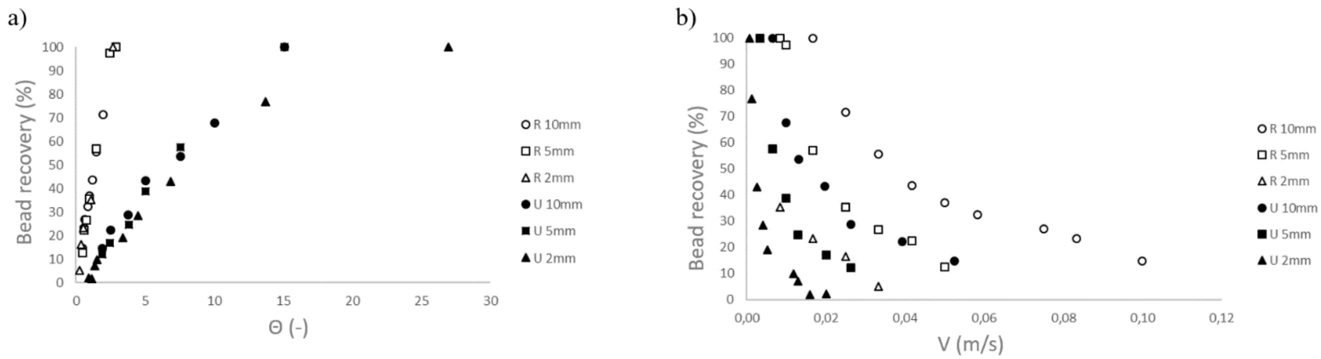

Figure 3. a) Influence of cross-sectional areas in bead recovery and b) Influence of fluid velocity in the system performance for rectangular (R) and U-shaped (U) channels.

5. CONCLUSIONS

We have introduced a methodological guide for the rational design of multiphase continuous flow microfluidic-magnetophoretic separators. In this regard, the effect cross sectional shape, which derives from the chip fabrication methods, and the increase of channel length has been carefully studied by using the J ratio and the design parameters θ and L/D_h ratio. Thus, the range of velocities that gives complete particle recovery has been defined for all of the geometries, specifying the best one that delivers high particle recovery with the highest system throughput. Besides, the experimental validation of two of the geometries under study fitted the simulated results with an absolute error of 15%. This analysis gives insights into the optimization of microfluidic channels that can be spread to a wide range of magnetophoretic based applications such as purification, enrichment and isolation.

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