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CAPTURE OF MAGNETIC MICROSPHERES IN ELECTROKINETIC FLOW FOR APPLICATION IN LAB-ON-CHIP DEVICES

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ABSTRACT

Isolation of bio-molecules, cells and pathogens for immunoassays is a critical component in micro total analysis systems (µTAS). Magnetophoretic technique is often used for separation of such target species, where magnetic beads tagged with specific antibodies against cell surface epitopes, are captured in the microfluidic device. In this study, a numerical model is developed for capture of beads under an external magnetic field in electrokinetically driven flow. The results indicate an increase in the number of beads captured when the magnetic field is higher and the flow is driven by lower electric fields.

INTRODUCTION

Micro total analysis systems (µTAS) provide high speed sorting of target cells in a portable device, while consuming a very small volume of reagents. Magnetophoretic separation is among the most popular separation technique in which magnetic beads, conjugated with antibodies against specific cell surface epitopes, are used to tag cells of interest [1]. Cell separation is achieved by applying a magnetic field gradient to impart magnetophoretic mobility to the tagged cells. These beads can be functionalized with a large variety of antibodies.

Flow in microfluidic devices can be either pressure driven or electrokinetically driven. Electrokinetically driven flow such as electroosmotic flow (EOF) has advantages due to the absence of mechanical pumps, which are sometimes inefficient and difficult to build at small scales [2]. To ensure efficient cell separation, it is essential to ensure efficient capture of magnetic beads so that the target cells can form conjugates with the beads. The performance of such a microfluidic device would depend upon particle capture efficiency (CE) which is the ratio of number of particles captured to the number of particles injected into the channel. Studies indicate that many beads escape the magnetic field because the viscous drag force overcomes the magnetic force [3,4]. As a result, these beads are discharged though the device's outlet and remain unused. To ensure optimum capture of these beads, electric and magnetic fields need to be optimized. It is necessary to ensure that beads flow in a region where the magnetic force can overcome the viscous drag force. Accordingly, the goal of this study is to develop a numerical model using commercial finite volume software package (CFD-ACE+, Huntsville, AL, USA) to demonstrate the CE of magnetic beads under the influence of variable electric and magnetic fields.

METHODOLOGY

The 2D model used in the simulation is shown in Fig. 1. The beads are injected into the domain from the inlet, and the beads that are uncaptured are discharged through the outlet. The channel is 100 µm high and 1 mm long. The governing equations for EOF are given in Eqs. 1-5:

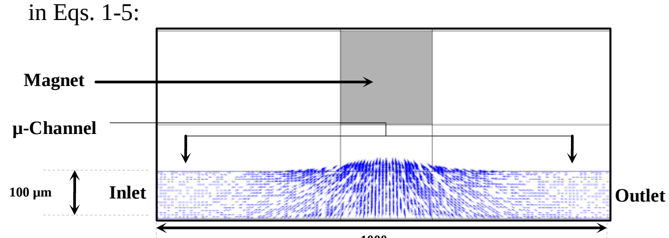

Figure 1: 2D model of microchannel with magnetic field vectors

Conservation of mass: $$\nabla \boldsymbol{V} = 0 \qquad (1)$$

Conservation of momentum: $$\rho \frac{D\boldsymbol{V}}{Dt} = -\nabla \boldsymbol{p} + \mu \nabla^2 \boldsymbol{V} + f_e \qquad (2)$$

Coulomb force: $$f_e = \rho_e E = 0 \qquad (3)$$

Poisson's equation: $$\nabla^2\boldsymbol{\phi} = 0 \quad (4)$$

Helmholtz- Smoluchowski eq.: $$U_e = \varepsilon\zeta E/\mu \quad (5)$$

The term f_e in Eq. 2, which is the Coulomb force arising due to the external electric field, is zero since the bulk charge density, ρ_e is zero. The pressure drop term is zero in Eq. 2 as constant pressure is maintained using EOF. The Poisson's equation (Eq. 4) is coupled with the momentum through Helmholtz-Smoluchowski equation (Eq. 5) which provides the EOF velocity U_e corresponding to the applied potential, Φ, in V. The governing equations for velocity of the beads and magnetic force due to finite gradient of magnetic field are given in Eqs. 6-10:

Magneto-static equation: $$\boldsymbol{M} = \frac{\boldsymbol{B}}{\mu_o\mu_r}(\mu_r - 1) \quad (6)$$

Magnetic force on beads: $$\boldsymbol{F_m} = \frac{1}{2\mu_o}\chi\left(\frac{4}{3}\pi r_b{}^3\right)(\mathbf{B}\nabla)\cdot\mathbf{B} \quad (7)$$

Drag force on beads: $$\boldsymbol{F_d} = 6\pi r_b\mu(\boldsymbol{V} - \boldsymbol{v_b}) \quad (8)$$

Newton's Second Law: $$\frac{4}{3}\pi r_b{}^3\rho_b\frac{d\boldsymbol{v_b}}{dt} = F_m + F_d + F_g + F_t \quad (9)$$

Velocity of bead: $$\boldsymbol{v_b} = \boldsymbol{V} + \frac{\boldsymbol{F_m}}{6\pi r_b\mu} \quad (10)$$

For beads with radius, r_b> 40 nm, Brownian force, F_t and gravitational force, F_g can be ignored. For the properties of the beads used, the time constant is very small. Thus, the time varying term in Eq. 9 can be ignored. Hence, F_m= -F_d. Using Eqs. 7 and 8, velocity of bead, v_b is computed (Eq. 10). Permanent magnet (NdFeB) is modeled to generate the magnetic field within the channel.

In the numerical model, one-way coupling of beads and fluid is assumed i.e. the velocity of the fluid, $\boldsymbol{V}$ affects the velocity of beads, $\boldsymbol{v_b}$ and not vice versa. The solver then computes $\boldsymbol{v_b}$ based on $\boldsymbol{V}$ and $\boldsymbol{F_m}$.

Table 1: List of the properties used in the numerical calculations.

Parameter	Value	Parameter	Value
Buffer density (ρ)	997 kg/m^3	Electric fields	250-1500 V/cm
Dynamic viscosity (μ)	0.00086 Ns m^{-2}	Magnetic fields	2-7 x10^4 A/m
Relative permittivity (ε_r)	78.8	Radius of bead (r_b)	1.42 µm
Zeta potential (ζ)	-0.1 V	Density of bead (ρ_b)	1800 kg/m^3
Debye-layer (λ_D)	0.1 µm	Susceptibility (χ)	1.42

RESULTS AND DISCUSSION

The trajectories of the beads are shown in Fig. 2 when E = 250 V/cm and M = 40000 A/m. Initially when the beads flow, most evade capture. This is due to the plug profile of EOF, where velocity close to the wall is higher compared to pressure driven flow for the same maximum channel velocity. As a result, particles experience a larger viscous drag force that overcomes the magnetic force and are swept downstream.

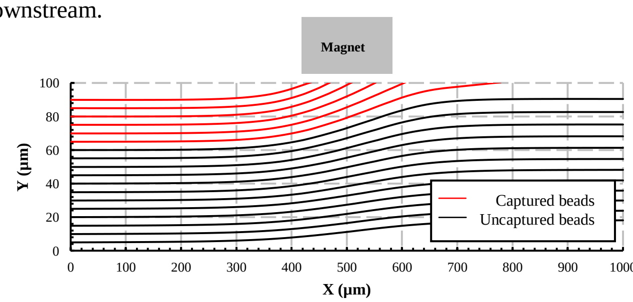

Figure 2: Trajectories of the beads at E=250 V/cm, M = 40000 A/m

As seen in Fig. 3, CE is higher for lower electric fields. This is because at lower electric fields the fluid velocity is lower (from Eq. 5, $U_e \propto E$). Consequently, the magnetic force overcomes the drag force for most of the particles. A maximum CE of 37% is obtained at E = 250 V/cm.

The effect of magnetic field on the CE is more significant (Fig. 4). The increase in CE with magnetic field is due to the increase in magnetic force which eventually overcomes the viscous drag force. A maximum CE of 75% is obtained at M = 7 x10^4 A/m.

To ensure higher CE, the magnetic field can be increased and electric field can be decreased. However, due to certain limitations in the electric and magnetic field parameters, the magnetic field cannot be increased and electric field cannot be decreased beyond a certain value. Also, to ensure higher throughput of the lab-on-chip device, the electric field has to be increased. It is, therefore, necessary to optimize the electric and magnetic fields to ensure optimum capture of beads for the specific application in a lab-on-chip device. The current numerical model presented can help in designing a device with optimized electric and magnetic fields with desired CE.

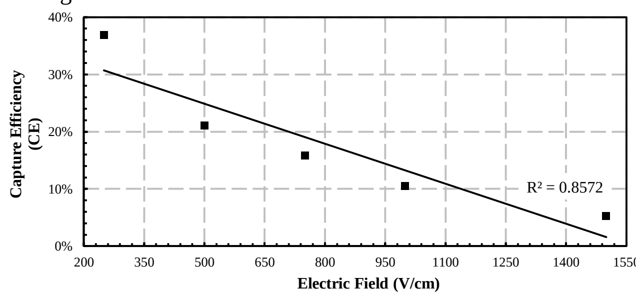

Figure 3: CE at different electric fields, M = 40000 A/m

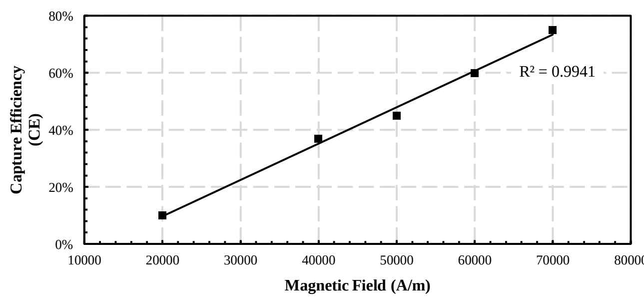

Figure 4: CE at different magnetic fields, E = 250 V/cm

CONCLUSIONS

In this study, a numerical model is developed to demonstrate capture of magnetic microspheres driven by EOF in an external magnetic field. The results indicate that the CE increases at higher magnetic fields and lower electric fields. Based on the preliminary results, a microfluidic chip can be designed to capture magnetic beads at optimized electric and magnetic fields. During future investigations, numerical results would be validated with experimental data in our lab.

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