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Scalability analysis of magnetic bead separation in a microchannel with an array of soft magnetic elements in a uniform magnetic field

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The scalability of magnetic bead separation and capture efficiency are studied for a flow through microfluidic system with integrated magnetic functionality. The system consists of a microchannel on a substrate that contains a planner array of embedded soft-magnetic elements. The elements become magnetized in the presence of an applied field and produce a local magnetic force that separates the beads from the flow. The Particle and fluid transport for this system are predicted using a discrete particle model (DPM) that employs a combined Lagrangian–Eulerian computational fluid dynamic (CFD) approach. The model is used to predict the bead separation dynamics and capture efficiency for different configurations of the magnetic elements. Both the total (system level) and local (per-element) capture efficiency are analyzed as a function of the number of magnetic elements, their volume, aspect ratio and spacing. The analysis shows that both the total and local capture efficiency increase as the volume of the elements increases for a fixed element aspect ratio and spacing. The total capture efficiency increases as the element aspect ratio increases or alternatively, as the inter-element spacing decreases. A key finding is that the total capture efficiency increases with the addition of the first few elements to the array, but then remains essentially constant as more elements are added. This implies that scale up for high throughput separation can best be realized by parallelizing the process, i.e. by replacing a single channel with a large number of magnetic elements with a parallel arrangement of shorter channels having fewer elements. These findings provide insight into the capture dynamics and define metrics for optimizing system performance.

1. Introduction

Magnetic beads are finding increasing use in microfluidic systems to separate and sort small samples of target biomaterials for biological, biomedical and clinical diagnostic applications. These beads are micron-sized and typically consist of a number of magnetic nanoparticles embedded in a host organic or inorganic matrix material. The nanoparticles provide magnetic functionality that enables the beads to be manipulated by a magnetic field. A key advantage of such beads is that they can be functionalized to selectively bind to (label) a wide variety of biomaterials, e.g. proteins, enzymes, nucleic acids and whole cells, and once labeled the biomaterials can be efficiently separated or sorted using an external field. The integration of magnetic functionality with microfluidics is an emerging field. Relatively few devices for bead manipulation have been demonstrated [1–6] and these typically use some form of magnetic elements integrated in proximity to a flow channel to provide the magnetic force needed to separate labeled biomaterial under flow. Both passive elements in the form of soft- or hard-magnetic microstructures, and active voltage-driven elements (e.g. coils) have been demonstrated [7–18]. A system with soft-magnet magnetic (e.g. nickel-based) elements is shown (partially) in Fig. 1. Once magnetized, these elements produce a localized nonuniform field distribution that permeates the microchannel. This, in turn, gives rise to a force on the beads that acts to separate them from the flow, downwards towards the elements. Once the external field is removed, the elements revert back to an unmagnetized state and the force is effectively turned off [15,16]. Thus, by applying and removing a bias field, a target biomaterial can be captured, held and released in the microchannel on demand. This level of manipulation can also be achieved with active elements, but these consume energy and provide a relatively weak force [8,9,18].

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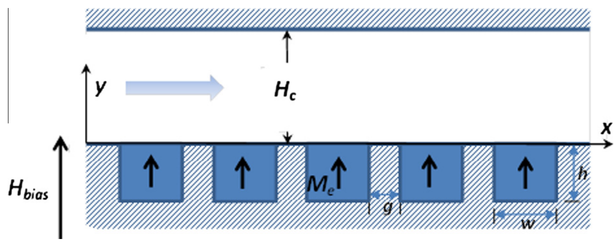

Fig. 1. A microfluidic system (snapshot) with planner embedded soft-magnetic elements at the lower sidewall.

In this paper, we use a computational model to study the dynamics of bead separation and capture efficiency for the microsystem shown in Fig. 1. Both the total (system level) and local (per-element) capture efficiency are analyzed as a function of various parameters including the number of magnetic elements in the array, their volume, aspect ratio and spacing. A key goal of this study is to quantify the scalability of the capture efficiency with respect to the number of elements used. It is reasonable to expect that the efficiency will scale with the number of elements and that a relatively large number is needed to achieve a high and useful degree of bead separation. However, our study clearly shows that the capture scalability is limited to only the first few elements, after which additional capture, if any, can be attributed to nonmagnetic effects such as gravitational sedimentation. This is a significant result as it implies that a practical system of this design can be realized without the costly integration of a relatively large number of magnetic elements and high throughputs can best be achieved using a parallel arrangement of shorter microchannels with fewer magnetic elements. With regards to the impact of the magnetic array parameters, our analysis shows that the total and local capture efficiency increase with the volume of the elements given a fixed aspect ratio and spacing. We also find that the total capture efficiency increases as the element aspect ratio increases or the inter-element spacing decreases. These results provide insight into the capture dynamics and metrics for optimizing system performance when the embedded magnetic elements are magnetized by a homogeneous external field. They are less-relevant to systems that utilize soft-magnetic elements in a nonhomogeneous external field to provide a multi-scale magnetophoretic force [19,20].

2. The computational model

We use a computational model to analyze the dynamics of magnetic bead separation and capture efficiency in the microsystem shown in Fig. 1. The model takes into account the magnetic and fluidic forces on the beads and predicts their motion through the flow cell. We use numerical CFD analysis to predict the bead-fluid transport and analytical analysis to predict the magnetic force that governs bead capture. The CFD analysis involves a Lagrangian–Eulerian formulation, wherein bead motion is predicted using Lagrangian dynamics and the fluid transport is computed by solving the Navier–Stokes equations within an Eulerian framework [21,22]. This approach differs from the full Eulerian approach in which the bead transport is predicted by virtue of a concentration equation [23–25]. We briefly describe the approach here, details of the model can be found in reference [22].

The Lagrangian equation of motion for a bead can be presented as,

$$m_b \frac{d\mathbf{u}_b}{dt} = 6\pi\eta a(\mathbf{u} - \mathbf{u}_b) + V_b(\rho_b - \rho)\mathbf{g} + \mathbf{F}_m \tag{1}$$

where m_b, ρ_b, a, V_b and $\mathbf{u}_b$ are, respectively, the mass, density, radius, volume and the velocity field of the bead. In this equation, ρ, η and $\mathbf{u}$ are, the density, viscosity and velocity vector of the fluid, respectively. $\mathbf{g}$ is the gravity vector. The terms on the right hand side of Eq. (1) include Stokes' drag, buoyancy and the magnetic force vector $\boldsymbol{F_m}$. The magnetic force on the bead can be expressed as [21,22,26,27],

$$\mathbf{F}_m = \mu_0(\mathbf{m}_{b,\mathrm{eff}} \cdot \nabla)\mathbf{H}_a \tag{2}$$

where μ_0 is the free-space permeability. The vectors $\mathbf{m}_{b,\mathrm{eff}}$ and $\mathbf{H_a}$ represent the "effective" dipole moment of the bead and the applied magnetic field intensity at the center of the bead, respectively. An expression for $\mathbf{m}_{b,\mathrm{eff}}$ that takes into account magnetic saturation of the bead M_s is $m_{b,\mathrm{eff}} = V_b f(H_a)\mathbf{H}_a$ where,

$$f(H_a) = \begin{cases} \chi_{b,e} & H_a < M_s/\chi_{b,e} \\ M_s/H_a & H_a \geqslant M_s/\chi_{b,e} \end{cases} \tag{3}$$

and $\chi_{b,e}$ is the effective magnetic susceptibility of the bead, and $H_a = |\mathbf{H}_a|$.

A closed-form expression for the field $\mathbf{H_a}$ due to an array of soft-magnetic elements in a homogeneous magnetic field can be found in the literature [22]. Analytical field solutions for other common geometries are also known [28–32]. Using the expression for $\mathbf{m}_{b,\mathrm{eff}}$ the equation of motion Eq. (1) can be rewritten as,

$$\frac{d\mathbf{u}_b}{dt} = \frac{(\mathbf{u} - \mathbf{u}_b)}{6m_b\pi\eta a} + \frac{V_b(\rho_b - \rho)\mathbf{g} + \mu_f V_b f(H_a)\mathbf{H}_a \cdot \nabla\mathbf{H}_a}{m_b} \tag{4}$$

The trajectory of a bead $\mathbf{x}_b(t)$ can be predicted by integrating the velocity,

$$\frac{d\mathbf{x}_b}{dt} = \mathbf{u}_b. \tag{5}$$

In this paper we consider the dynamics of micron-sized beads in a dilute concentration and ignore the impact of the bead motion on the flow. Thus, the fluid flow can be predicted using Navier–Stokes equations for an incompressible Newtonian fluid,

$$\rho\left(\frac{\partial\mathbf{u}}{\partial t} + \mathbf{u}\nabla\mathbf{u}\right) = -\nabla P + \nabla\cdot(\eta\nabla\mathbf{u}), \tag{6}$$

$$\nabla\cdot\mathbf{u} = 0. \tag{7}$$

The computational model defined by Eqs. (4)–(7) was implemented using ANSYS FLUENT (http://www.ANSYS.com). The Lagrangian discrete phase model (DPM), and the Eulerian finite-volume-based solver, available in ANSYS FLUENT, were used to track the bead motion (Eqs. (4) and (5)) and solve for the flow (Eqs. (6) and (7)), respectively. The details of this approach can be found in the literature [21,22]. Other similar models have also been reported [33,34].

3. Results

We use the model to investigate the capture efficiency of a microfluidic system as shown in Fig. 1. The flow cell is taken to be 200 m in height (H_c) and 10 mm in length (L_c). The width (W_c) is assumed to be sufficiently large so that a 2D analysis can be used to determine the flow, i.e. $W_c/H_c > 10$. An array of soft-magnetic elements are embedded immediately beneath the bottom wall of the flow cell. These are assumed to be permalloy (78% Ni 22% Fe, $M_{es} = 8.6 \times 10^5$ A/m). Fully developed laminar flow enters the inlet with an average velocity denoted u_{ave} and a zero gauge pressure is set at the outlet. The carrier fluid is water ($\eta = 0.001$ N s/m^2, $\rho = 1000$ kg/m^3 and $\chi_f = 0$) and all materials in the system, except for the beads, are assumed to be nonmagnetic. We model the behavior of MyOne magnetic beads (Dynal Biotech), which have the following properties: radius $a = 0.5$ m, $\rho_p = 1800$ kg/m^3, $\mathbf{M_s} = 4.3 \times 10^4$ A/m and $\chi_{p,e} = 1.4$.