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Three-dimensional mathematical modelling of magnetic bead interactions within a magnetic separation system

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ABSTRACT

Magnetic separation relates to the ability to separate particles based on their magnetic mobilities. This is often limited by the formation of bead agglomerates. Bead agglomerates are formed as a result of attractive magnetic induced interactions among magnetic beads suspended in fluid. A three-dimensional model of the interactions among three equal sized super-paramagnetic beads suspended in a static fluid within a uniform magnetic field is presented here. The beads' trajectories were recorded on video while the relative axial displacement of the bead was obtained using the recorded off-focus images. A good agreement was obtained by comparing the beads' simulated trajectories with the video data. Therefore, the model is able to predict the behaviour of magnetic beads in immunoassays as well as magnetic separation system.

1. Introduction

Super-paramagnetic beads are made of a core which consists of nano-particles (magnetic iron oxide) embedded within a spherical matrix [1,2]. The large surface to volume ratio of super-paramagnetic beads (or particles) allow for easy attachment to specific biomolecules (e.g. amino acid, carboxyl group etc.) through specific binding sites on the beads [1–3] while the chemical modification of their surfaces through coating allows for specificity and high selectivity when used as tagging agents [4,5]. The inherent magnetic properties and physical characteristics of these beads enable easy manipulation when functionalized with bio-molecules within a magnetic field [1,5]. This magnetic manipulation is facilitated by the low relative permeability (μ_r) of the fluid which enables strong interaction between the magnetic field and the magnetic-tagged complex [6]. Furthermore, these beads have physical dimensions comparable to some biological entities e.g. Escherichia coli (2 µm), red blood cell (6–8 µm), the malaria parasite (1–1.2 µm), etc. and they are widely available in different sizes from different manufacturers [3,6]. These numerous benefits have promoted their usage in biomedical applications such as immunoassays [1,5], drug delivery [1,4,5], magnetic separation [2,3,6], cell transport [2,6], hyperthermia [1,5], etc.

Amongst such biomedical applications includes continuous flow magnetic separation, which involves binding biomolecules to magnetic beads and their continuous separation from a mixture using a magnetic device within microfluidic channels. This concept has been applied to continuously separate magnetic particles from a mixture of magnetic and non-magnetic particles [7,8], leukocytes from whole blood [9], microphages and tumour cells [10], E. coli bacteria from red blood cell [11], etc.

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Magnetic separation is often limited by the formation of magnetic bead agglomerates. Bead agglomerates refer to a cluster of magnetic beads bound by attractive magnetic forces when suspended in fluid. Existing literature has shown that bead agglomerates lead to the blockage of magnetic columns [12], channel clogging and surface adhesion [13], alter the magnetic field properties [11,14], reduce surface–volume ratio [13] and make it difficult to visualize the attached bio-molecules when viewed under an optical detector [11,15].

A knowledge of the trajectory pattern of magnetic beads alongside their interaction with neighbouring beads within the magnetic field would aid the manipulation of these beads (or magnetic tagged complexes) within a magnetic separation system which would help to reduce agglomerate formation. Furthermore, the trajectory knowledge is also useful in predicting the behaviour of magnetic beads in diagnostic assays where bead agglomerates are used in detecting bio-molecules such as proteins, virus [16,17] and for in vivo applications (e.g. the micro-magnetic manipulation of magnetic beads to measure the visco-elastic response inside the cytoplasm of a living cell [18,19], the elastic behaviour of a single DNA molecule [20,21]).

Herein lies a three dimensional numerical model which predicts the trajectory pattern and interaction among three super-paramagnetic beads suspended in a static fluid placed in a uniform magnetic field. The magnetic interactions among the beads builds upon a similar method introduced earlier in [22,23] which accounts for the induced magnetization and perturbed field due to the presence of neighbouring beads within a uniform magnetic field. The hydrodynamic interactions was derived using the method of reflection in a vector form (with the lubrication approximation [22,24,25]) to account for the change in velocity field within the fluid due to the movement of suspended beads [22,26,27].

In this paper, interaction among magnetic beads was observed within a static fluid in the presence of a uniform magnetic field. The uniform magnetic field and static fluid conditions serve as an approximation to the environment within a magnetophoretic system because when magnetic beads are separated within very small separation (on the order of microns), it is possible that they would experience the same magnitude and gradient of magnetic field, then the differences in magnetic drift velocity can be neglected; Also, the velocities of the beads within a static fluid are equivalent to the relative velocities of the beads, if suspended in a moving fluid, due to the laminar flow conditions.

Magnetic bead pair interaction within a magnetophoretic system has been studied by these authors [22,28] while interaction among chains of magnetic beads have been previously presented in [29,30]. This study predicts the trajectories of three super-paramagnetic beads within a magnetic separation system which allows for a better understanding of the agglomeration process. The developed model can predict the build-up of agglomerates from single particles in diagnostic assays requiring a medium bead density ($1–10 \times 10^6$ beads/ml).

2. Theoretical model

When three super-paramagnetic beads are suspended in fluid and placed within a uniform magnetic field, interaction exist among the beads mediated by both the fluid and the magnetic environment, called hydrodynamic interaction and magnetic interaction respectively. The force-equation for the beads is expressed as,

$$\sum \mathbf{F} = 0, \tag{1}$$

where $\mathbf{F}$ is the force in N. Here, the bold letter indicates a vector. All forces will be considered within a three-dimensional region.

2.1. Magnetic force

There is a translational force which causes a magnetic bead to move in the direction of the magnetic field gradient [22,23]. Due to the assumption of fast relaxation time of the bead's induced dipole, any rotation of the bead is neglected in this model.

The magnetic force interaction on a bead (e.g. bead 1) due to another bead (e.g. bead p, where $p=2$ or 3) within an external magnetic field is expressed as,

$$\mathbf{F}_{\mathrm{m1p}} = \int \mu_o((\mathbf{M}_1 + \Delta\mathbf{M}_{\mathrm{p}}).\nabla)(\mathbf{H}_{\mathrm{ext}}(\mathbf{r}_1) + \Delta\mathbf{H}_{\mathrm{p}})\ dV, \tag{2}$$

where μ_o is vacuum permeability, $\mathbf{M}_1$ is the magnetization of bead 1 in the absence of other beads in A/m, $\Delta\mathbf{M}_{\mathrm{p}}$ is the induced magnetization due to the presence of bead p in A/m, $\mathbf{H}_{\mathrm{ext}}$ is the external field in A/m, $\Delta\mathbf{H}_{\mathrm{p}}$ is the perturbed external field due to the presence of bead p in A/m, V is the volume of bead 1 in m^3 and $\mathbf{r}_1$ is the position vector of bead 1 with respect to the origin [22,23].

The principle of super-position is used to evaluate the total interaction force on a single bead due to the presence of other beads within the magnetic field (see Appendix A).

2.2. Hydrodynamic interaction

Assume bead 1 moves within fluid, the movement generates a velocity field which is transmitted through the fluid. The transmitted velocity field is assumed to be reflected by the pth bead (where $p=2$ or 3) taking into consideration their local velocity fields. The reflected velocity field in turn affects the movement of bead 1 [22,26,27].