# Numerical Analysis of Fully-Coupled Particle-Fluid Transport and Free-Flow Magnetophoretic Sorting in Microfluidic Systems

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## ABSTRACT

Magnetic particles are increasingly used in microfluidic systems to selectively separate and sort biomaterial for biomedical and clinical diagnostic applications. In this presentation we introduce a computational model that can be used for the rational design of systems for such applications. The model takes into account dominant mechanisms that govern particle transport including magnetic and hydrodynamic forces, fully-coupled particle-fluid interactions and magnetic dipole-dipole interactions that induce self-assembly of the particles. We demonstrate the model via application to a continuous flow separation system and microfluidic mixing based on rotating self-assembled particle chains.

**Keywords**: magnetic bioseparation, magnetic field-directed transport, particle-fluid coupling, magnetophoretic sorting, free-flow magnetophoreis.

## 1 INTRODUCTION

Magnetic particles are widely used for applications in biomedical science and technology where they serve as carrier particles for biomaterials such as proteins, enzymes, nucleic acids and whole cells etc. Magnetic particles are well suited for such applications because they can be designed to selectively target a given biomaterial and they enable controlled transport and separation of a labeled biomaterial using a noninvasive (external) magnetic field. In this presentation we introduce a computational model that can be used to predict the field-directed transport, continuous sorting, capture and self-assembly of magnet particles and the manipulation of self-assembled particle microstructures in microfluidic systems. The model involves the use of closed-form magnetic analysis combined with computational fluid dynamics (CFD) to predict coupled particle-fluid transport in microfluidic environments in the presence of an applied field. The modeling approach is based on fully-coupled 3D calculation and described below. We demonstrate the model via application to two experimental systems. In the first system, magnetic particles are introduced into a flow cell that has an array of magnetic beads embedded in the base of the microchannel. Free flowing magnetic particles form chains in response to an applied field and the chains become anchored to the beads embedded in the base of the channel. We predict the self-assembly of particle chains and the separation of individual chains as they become anchored to the embedded beads. In the second system, magnetic particles are dispersed within a carrier fluid in a capillary tube where they self-assemble into chains in the presence of a static applied field. A time-varying field is then applied that causes the chains to rotate, which in turn produces a mixing of the fluid.

## 2 NUMERICAL MODEL

We predict fully-coupled particle-fluid transport using a hybrid numerical/closed-form modeling approach that combines numerical transport analysis with closed-form field analysis. The model employs a coupled Lagrangian-Eulerian CFD-based numerical scheme wherein Lagrangian analysis is used to track the motion of individual particles while an Eulerian-based CFD analysis is used to solve the Navier Stokes momentum equations. We have adapted a commercial CFD program FLOW-3D (www.flow3d.com) for this analysis. Specifically we have integrated magnetic force and dipole-dipole interaction functionality into the FLOW-3D Volume-of Fluid (VOF)-based CFD solver. At each time step, our custom algorithms predict the induced dipole moment of each particle, the magnetic force on the particle due to the applied field and interparticle forces due to dipole-dipole interactions. The latter gives rise to self-assembly of the particles. The ability to predict two-way particle-fluid coupling and self-assembly is an important feature of the model that distinguishes it from most other models in this field, which typically ignore one or both of these effects.

In our model the translational and rotational motion of a particle are predicted using the following set of equations

$$m_p \frac{d\vec{V}_G}{dt} = 6\pi\eta R_p \left(\vec{u} - \vec{V}_G\right) + \vec{F}_m + \vec{F}_{dd} \quad (1)$$

$$[\mathrm{J}] \cdot \frac{d\vec{\omega}}{dt} + \omega \times ([\mathrm{J}] \cdot \vec{\omega}) = \vec{T}_G \quad (2)$$

$$\vec{V}_P = \vec{V}_G + \vec{\omega} \times \vec{r}_{P/G} \quad (3)$$

where $m_p$ and $R_p$ are the mass and radius of the particle, $\vec{F}_m$ and $\vec{F}_{dd}$ are the magnetic and dipole-dipole forces on the particle, $\vec{T}_G$ the total torque about its center of mass G, $\vec{V}_G$ and $\vec{\omega}$ are the linear and angular velocity of the center of mass and [J] is the inertia tensor about G in the body system [1]. Also, $\vec{r}_{P/G}$ is the distance vector from a point *P* on the object to its mass center, $\vec{V}_P$ is velocity of that point and η is the viscosity of the fluid. The particle transport alters the fluid velocity $\vec{u}$ within the flow channel. The general form of the fluidic continuity equation in an Eulerian computational cell can be written as:

$$\frac{\partial}{\partial t}\left(\rho V_F\right) + \nabla \cdot \left(\rho \vec{u} A\right) = S_m \quad (4)$$

where $S_m$ is the physical mass source term of fluid and $V_F$ and $A$ are the fluid volume and area fractions in the cell, which vary as a particle moves through the cell. For incompressible flow, which we assume, this reduces to:

$$\nabla \cdot \left(\vec{u} A\right) = -\frac{\partial V_F}{\partial t} + \frac{S_m}{\rho} \quad (5)$$

AI is difficult to calculate $-\frac{\partial V_f}{\partial t}$ for different particles with different shapes. An alternate equation that can be used is

$$-\frac{\partial V_f}{\partial t} = \frac{S_{obj}}{V_{cell}} \cdot \vec{V}_{obj} \cdot \vec{n} \quad (6)$$

where $V_{cell}$ is the total volume of the computational cell and $S_{obj}$, $\vec{n}$ and $\vec{V}_{obj}$ are the area, unit normal and velocity of the boundary of the moving object in the cell. The variables $\vec{n}$ and $\vec{V}_{obj}$ are relatively easy to obtain and $-\frac{\partial V_f}{\partial t}$ can be determined using Eq. (6). The fluid velocity $\vec{u}$ is obtained by substituting Eq. (6) into Eq. (5), which is shown in Eq. (7)

$$\nabla \cdot \left(\vec{u} A\right) = \frac{S_{obj}}{V_{cell}} \cdot \vec{V}_{obj} \cdot \vec{n} + \frac{S_m}{\rho} \quad (7)$$

The magnetic force on a particle is predicted using an effective dipole moment approach in which the particle is treated as an equivalent point dipole $m_{eff}$. The magnetic force is given by [2, 3]

$$\vec{F}_m = \mu_f \left(\vec{m}_{eff} \cdot \nabla\right) \vec{H}_a \quad (8)$$

where $\mu_f$ is the permeability of the carrier fluid and $H_a$ is the applied magnetic field intensity at the center of the particle. The moment is given by $m_{eff} = V_p M_p$ where $V_p$ and $M_p$ are the volume and magnetization of the particle, respectively. It can be determined using a magnetization model that takes into account self-demagnetization and magnetic [4,5].

In the presence of an applied field, the magnetic core of the particles becomes magnetized and aquire an effective moment $\boldsymbol{m}_{eff}$ as described above. The potential energy for two dipoles is given by

$$U_{dd,ij} = -\frac{\mu_f}{4\pi}\left(3\frac{\left(m_{i,eff} \cdot r_{ij}\right)\left(m_{j,eff} \cdot r_{ij}\right)}{r_{ij}^5} - \frac{m_{i,eff} \cdot m_{j,eff}}{r_{ij}^3}\right) \quad (9)$$

where $m_{i,eff}$ and $m_{j,eff}$ are the moments of i'th and j'th particle, respectively, and $\boldsymbol{r}_{ij}$ is the displacement vector between them. The dipole-dipole force in Eq. (9) is obtained as the gradient of the potential,

$$F_{dd,ij} = -\nabla U_{dd,ij} \quad (10)$$

Finally, Eqs. (1) to (10) form a closed system that can be solved during each time step for the coupled particle fluid transport.

## 3 CONTINUOUS FLOW SEPARATION

We apply the computational model to study magnetic separation for the system illustrated in Figs. 1 and 2. Magnetic beads are preassembled in a 2D staggered array pattern and embedded in a substrate that forms the floor of a microchannel. The system is inserted in a coil that creates a uniform magnetic field that magnetizes the embedded beads. Magnetic particles are introduced into the flow channel and self-assemble into individual chains under the influence of the applied field. Once formed the chains are attracted to the embedded beads and become anchored [6, 7].

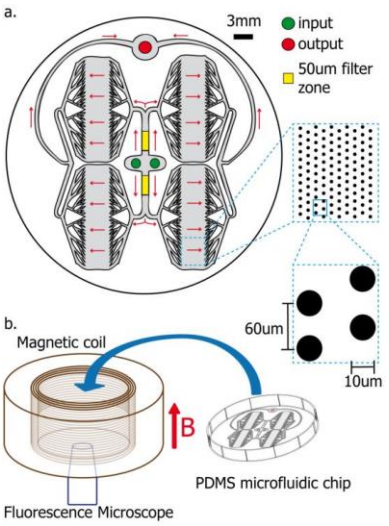


Figure 1: a. Microfluidic design with a 2D staggered array of magnetic beads (black dots) embedded in the substrate beneath a flow channel, red arrows indicate direction of flow. b. system inserted in a coil that provides a uniform bias field that magnetizes the embedded beads to enable capture of flowing beads.

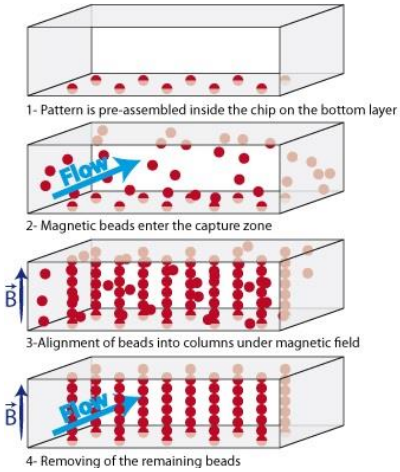


Figure 2: Illustration of field-induced self-assembly and capture of particle chains that become anchored to the beads embedded in the substrate.

Figure 3 illustrates a computed time-lapsed sequence of the self-assembly of pairs of free flowing magnetic particles and the subsequent anchoring of two particle chains to the immobilized floor-embedded beads. Figure 4 shows a more general case of the same process where multi-particle chains form and become anchored. Labeled particles can also be rereleased once the applied field is withdrawn.

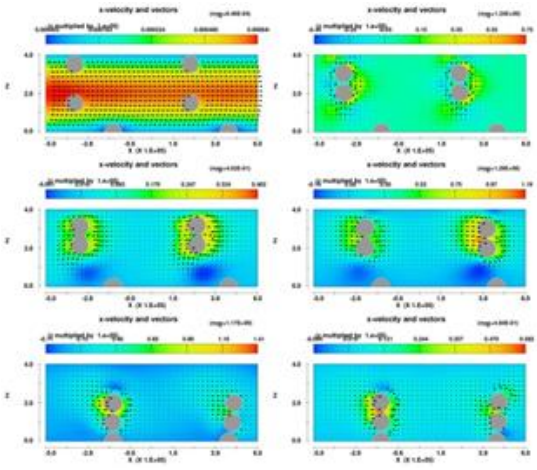

Figure 3: Cross-sectional view of a 3D analysis of the self -assembly of two particle chains and the attraction of the chains to magnetic beads embedded in the base of the flow channel.

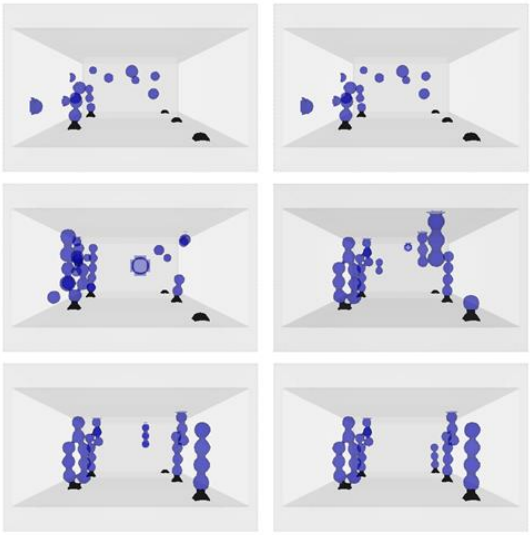

Figure 4: 3D view of self-assembled multi-particle chains magnetically attached to magnetic beads embedded in the base of the flow channel.

## 4 SELF-ASSEBLY AND MIXING

Next we use the model to study microfluidic mixing based on rotating chains of magnetic particles. The particles are initially randomly dispersed in a capillary tube, which is placed between permanent magnets so that the magnetic field is perpendicular to the axis of the tube. In the original experiment, the capillary tube is subjected to steady rotation with angular velocity ω [8] as shown in Figure 5. However in our model, the capillary tube is held stationary and a rotating magnetic field is applied. The particles are introduced into the capillary tube and self-assemble into a chain

due to the magnetic moments that they acquire in bias field. Once the chain is formed and stabilized a rotating field is applied. Figure 6 shows the predicted time-lapsed dynamics of the rotating particle chain and the induced mixing of two different (red and blue) concentrations of molecules.

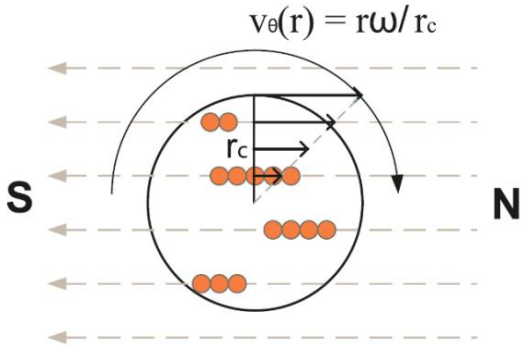


Figure 5: Magnetic particles self-assemble into chains in a capillary tube under uniform magnetic field.

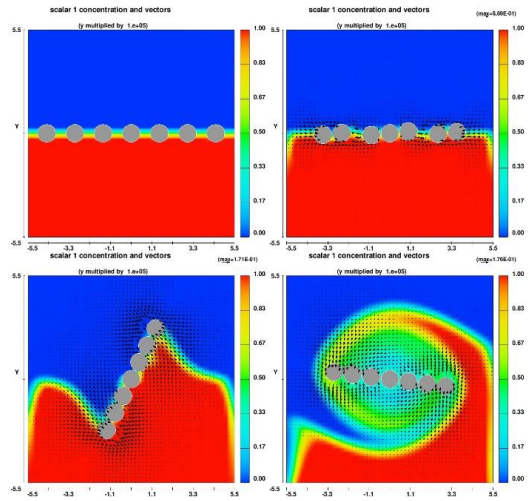


Figure 6: Magnetic nanoparticle chaining and rotating following an external filed and causing the mixing of two different molecular concentrations.

## 5 CONCLUSIONS

The integration of magnetism with microfluidics is in its infancy and growing rapidly due to a proliferation of novel devices and applications. Many of these device are highly versatile, fully-automated and highly reproducible. Magnetically-functional microfluidic systems can be used to selectively separate, sort and assemble magnetic particles and magnetically labeled biomaterials that range in size from biomolecules to whole cells. We have developed a unique computational model that enables the rational design of microfluidic systems for a broad range of magnetic particle applications. The model predicts the transport of individual particles and the self-assembly and dynamics of multi-particle chains. It takes into account fully-coupled particle fluid interactions and dipole-dipole effects, which are neglected in most other models. It should prove useful for the development of novel magnetophoretic microsystems.

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