

MODEL OF AN APPROACH TO TARGETED DRUG DELIVERY BASED ON UNIFORM MAGNETIC FIELDS

Z. G. Forbes¹, B. B. Yellen², K. A. Barbee¹, G. Friedman^{1,2}

Drexel University, Philadelphia, PA 19104

(1) Department of Biomedical Engineering and Sciences

(2) Department of Electrical and Computer Engineering

INTRODUCTION

The ability of superparamagnetic colloidal particles to induce phase transformation in the presence of external magnetic fields has been harnessed in many biomedical applications, including prosthetics [1], targeted drug delivery [2] and anti-angiogenesis strategies [3,4]. Previous attempts to use magnetic particles in these applications, however, have not enjoyed marked success because they have relied on high gradient external magnetic fields, which apply relatively small and insufficiently local forces on micron-sized particles.

We investigate a method for inducing highly localized phase transformations at defined locations in the vascular system by applying uniform magnetic fields to an injected superparamagnetic colloidal fluid. The proposed design involves seeding magnetic particles onto blood vessel walls at designated sites through specific receptor-ligand recognition, followed by the use of the anchored particles as magnetic traps for the injected magnetic colloid. The image shown in Figure 1 is a motivation for what we are trying to achieve. A simplified model of the trapping process will be presented, which predicts the stability of a single chain of magnetic particles anchored perpendicular to flow in a fluidic channel.

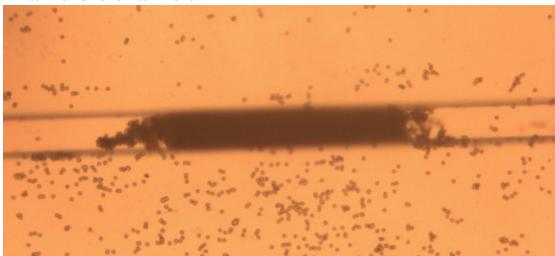


FIG 1: Optical image of a PDMS microchannel with 50- μm square cross-section that is blocked by a mass of 4.5- μm superparamagnetic beads pumped through the channel. Embedded in the channel walls are additional 4.5- μm beads which are intended to serve as magnetic traps for beads flowing through the channel

A diagram of the theoretical situation considered in this paper is shown in Figure 2. A chain of superparamagnetic beads is aligned by external uniform magnetic field across a fluidic channel.

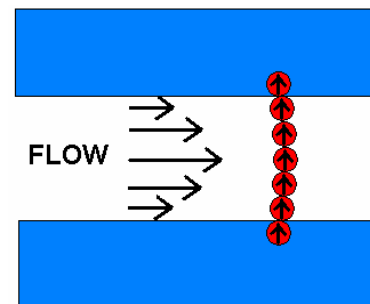


FIG 2: A chain of superparamagnetic beads is aligned across the channel, and the equilibrium chain conformation is determined for varying flow conditions.

The beads at each end of the chain are embedded in the channel walls, serving as magnetic anchors for the chain under conditions when fluid is flowing through the channel. The goal of this analysis is to determine the equilibrium chain conformation and estimate the magnitude of flow required to break the chain.

COMPUTATIONAL METHODS

Several assumptions have been made to simplify calculations. One is that the beads are uniformly magnetized. Another is that the beads are magnetized to saturation. With these assumptions, the force on the n^{th} particle can be determined according to:

$$\vec{F}_n = \mu_0 (\vec{m}_n \cdot \nabla) \vec{H}_n \quad (1)$$

The horizontal drag force on each particle is assumed to be that of an isolated particle and is given as a function by:

$$\vec{D}(z_n) = 6\pi\eta a v(z) \quad (2)$$

where α is the radius of the bead, $v(z)$ is the flow velocity at the bead center, and η is the viscosity of the liquid.

The equilibrium positions of the beads can be obtained using Eq. (1-2) in conjunction with the following equation:

$$\vec{r}_{j,n} = \vec{r}_{j-1,n} - \sigma \left(\vec{D}(z_n) - \vec{F}(\vec{r}_{j-1,n}) \right) \quad (3)$$

where the relaxation constant σ was selected for fastest convergence.

RESULTS

Beads with 5- μm diameter were assumed to reach saturation at around 600 Oe, while the channel gap was taken to be 100- μm . The viscosity of the liquid was taken to be consistent with that of blood, which is three times the viscosity of water.

The maximum flow velocity in the channel was varied between 1 and 20 mm/s, and the equilibrium positions of the beads in the chain were computed under each condition. The graphical illustration in Figure 3 depicts the equilibrium bead positions under varying flow conditions. It is clear from Figure 3 that the chain can withstand flow conditions under 5 mm/s, but at larger flow conditions the chain will break.

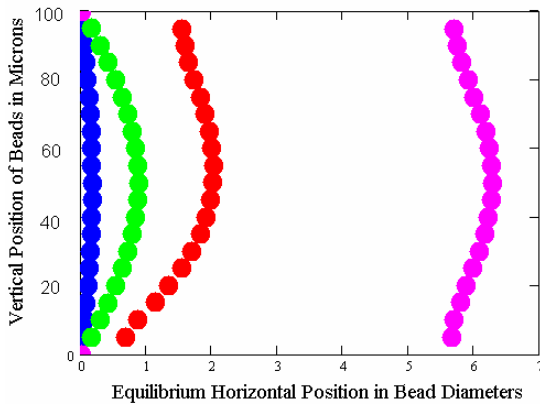


FIG 3: Graphical illustration of equilibrium positions of 20 beads in terms of bead diameter under maximum flow conditions of 1 mm/s (blue), 5 mm/s (green), 10 mm/s (red), and 20 mm/s (magenta).

CONCLUSIONS

While this model predicts that the chain will break above 5 mm/s flow conditions, it cannot predict the equilibrium positions after breaking because the model only takes into account static situations. Many experiments are underway for studying this phenomena in a physical scenario. 100 micron PDMS micro-channels with side-embedded magnetic particles are being used for the purpose of flowing magnetic particles in solution at a range of flow rates through, in the presence of magnetic fields. Chain formation, attachment, and flow occlusion of these channels has been obtained on numerous occasions. It is the intent of the authors to provide additional experimental data and analysis along side of the computational model by commencement of the 2003 Summer Bioengineering Conference in Key Biscayne, Florida.

REFERENCES

1. H. Herr. *Journal of Rehabilitation Research and Development*. **39**(3): 11 (2002).
2. S. Goodwin. *JMMM*, **194**:132-9 (1999).
3. J. Liu, G. Flores, R. Sheng. *JMMM*. **225**: 209-217 (2001).
4. R. Sheng, G. Flores, J. Liu. *JMMM*. **194**:167-175 (1999).