Nanoscale Manipulation of Biological Entities

using Magnetic Fluids and Fields

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The interaction of proteins, DNA and cells with external fields has long been of interest to biologists and chemical and biological engineers. Such fields can affect cell regulation and other biological function, and can be used to probe fundamental interactions and forces in biological systems. They also provide a convenient method for the separation of biological compounds on the basis of size, density and charge. While light and electric fields have often been used in such studies and applications, scant attention has been paid to the use of magnetic fields as most biological components have little or no intrinsic magnetic susceptibility, and what few studies are available have provided conflicting results. When these biological entities are immersed in a magnetic fluid having high magnetic susceptibilities, however, their behavior can be modified readily by the application of external magnetic fields.

We are exploring the use of magnetic fields for the nanoscale manipulation of biological entities such as cells, vesicles, viruses, nucleic acids and inclusion bodies immersed in magnetic fluids [1]. Two new Lab-on-Chip techniques are being developed for the rapid separation of biological molecules: ratched magnetophoresis and nanoparticle post arrays.

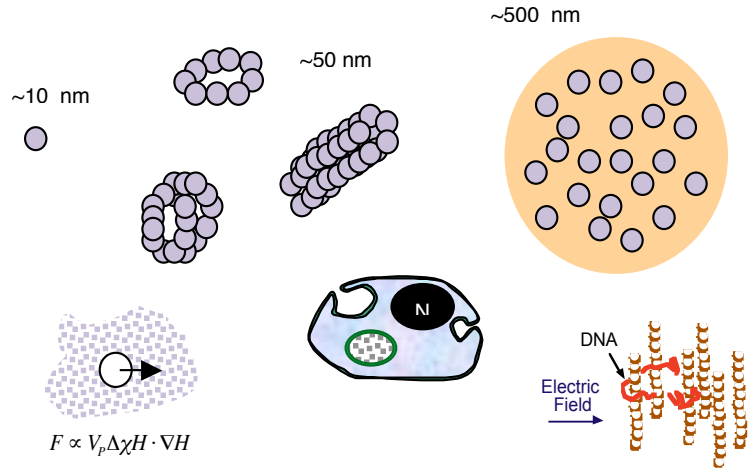

Figure 1: Schematic summarizing the scope of the project. Magnetic nanoparticles are synthesized and then assembled to have a range of morphologies (rods, cages, rings, etc.). These particles are then used in magnetophoresis of non-magnetic entities, applying local forces on cells and separations of DNA in magnetic arrays.

Magnetophoresis: Nonmagnetic, submicrometer particles were trapped according to size at specific locations along a fluid channel in a miniaturized magnetic separation device (chip) [2]. The chip was fabricated using standard micromachining techniques, including physical vapor deposition, photolithography, electroplating, and poly(dimethylsiloxane) (PDMS) bonding. Ferromagnetic (Ni) core elements on the chip produced a "sawtooth" magnetic field along a microfluidic channel when magnetized by external permanent magnets. The sawtooth field contained peaks of successively increasing magnetophoretic intensity ($M_f \nabla H$), forming trapping points between peaks. Particles were trapped against pressure-driven flow when the magnetophoretic force overcame the drag force, i.e., when $F_{mag} = -\mu_0 M_f V_p \nabla H = 6\pi\eta a v = F_{drag}$. The particles of interest were 840 nm and 510 nm fluorescently-tagged polystyrene beads, suspended with equal concentrations in a water-based magnetic fluid (ferrofluid). The concentration profiles of both particle sizes were observed via optical fluorescence intensity measurements. Experiments demonstrated size-based trapping, where 840 nm beads were trapped near the beginning of the channel, while 510 nm beads were trapped further down. Moreover, the location at which particles of a given size were trapped was shown to be a function of flow rate. The magnetophoretic trapping demonstrated in this work could form the basis of high-resolution, size-based separation methods for DNA, cellular organelles, viruses, and other like-sized biological particles.

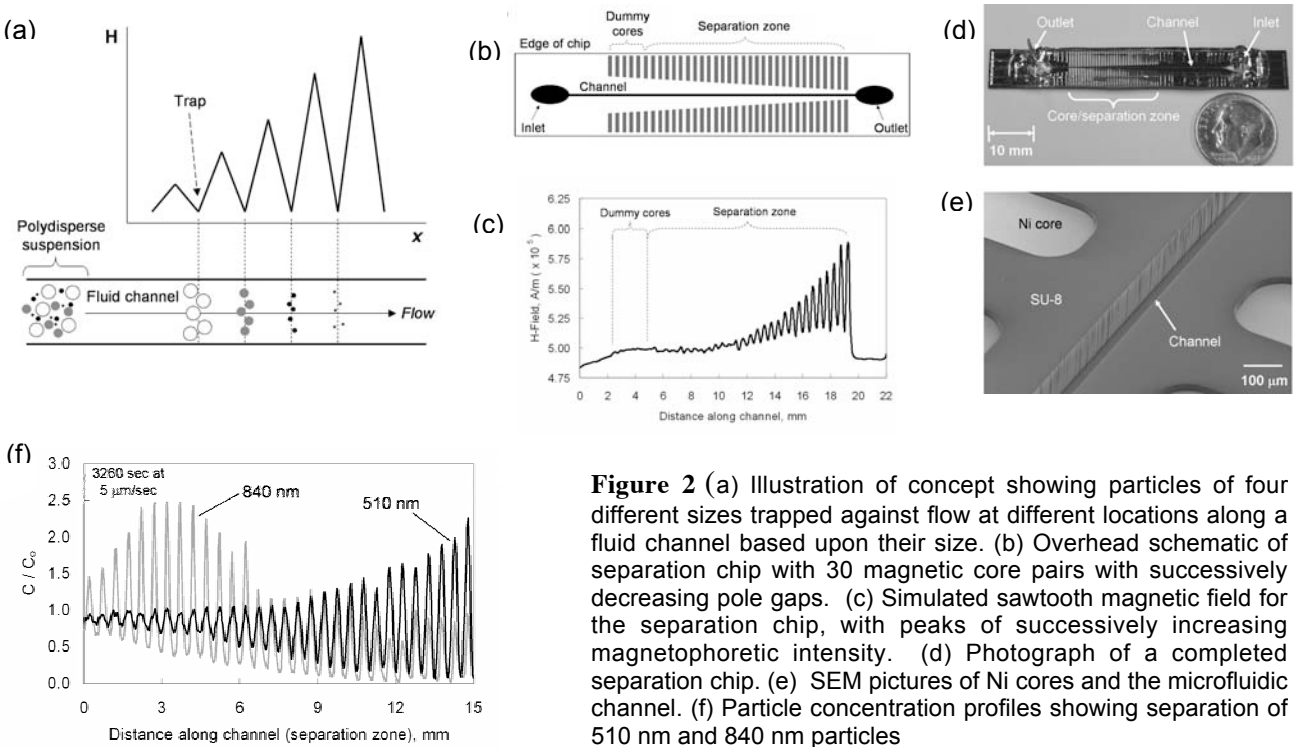

Figure 2 (a) Illustration of concept showing particles of four different sizes trapped against flow at different locations along a fluid channel based upon their size. (b) Overhead schematic of separation chip with 30 magnetic core pairs with successively decreasing pole gaps. (c) Simulated sawtooth magnetic field for the separation chip, with peaks of successively increasing magnetophoretic intensity. (d) Photograph of a completed separation chip. (e) SEM pictures of Ni cores and the microfluidic channel. (f) Particle concentration profiles showing separation of 510 nm and 840 nm particles

Nanoparticle post arrays: Upon application of a homogeneous magnetic field a superparamagnetic suspension of nanoparticles will self-assemble into a fixed array [3] (c.f. figure 3a). This self-assembled structure is being used as *sieving matrix* for electrophoretic separations of DNA, organelles and cells in a lab-on-a-chip device [4]. The advantage of this technique is that it makes use of self-assembly to quickly and inexpensively create fine-scale features in a microchannel. Rectangular microchannels have been fabricated in silicone (PDMS) and initial studies of the self-assembly of the nanoparticles has begun. We have focused initial efforts on the separation of large double-stranded DNA molecules. A set-up has been put in place that allows for direct observation and tracking of single DNA molecules as they move through this array (c.f. figure 3c-d). Future studies will be focused on quantifying the nanoparticle structure and correlating this to the resolving power of the separation device.

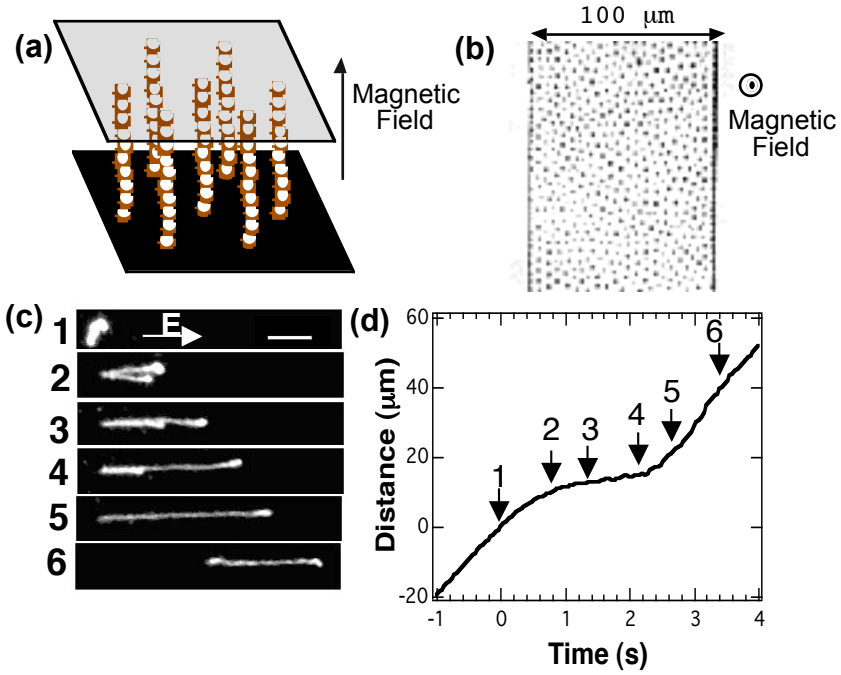

Figure 3: (a) Schematic of a magnetic nanoparticle array in a magnetic field. (b) Experimental images of a microchannel filled with magnetic nanoparticles (~700 nm diameter) under application of a magnetic field. (c) Fluorescence microscopy images of a single DNA colliding with a nanoparticle post. Scale bar is 10 microns. (d) Trajectory of the DNA molecule shown in (c).

References

[1] For further information about this project email **pdoyle@mit.edu**

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