TRAPPING AND FOCUSING OF PARTICLES AND CELLS BASED ON MAGNETIC ATTRACTION AND DIAMAGNETIC REPULSION

Mark D. Tarn, Sally A. Peyman, Angeles I. Rodríguez-Villareal, Aden Swinley and Nicole Pamme*

Department of Chemistry, University of Hull, Cottingham Road, Hull HU6 7RX, UK

ABSTRACT

We are exploring the use of magnetic attraction and diamagnetic repulsion forces for the handling of microparticles and cells in microchannels. Here, we report on the application of both of these types of forces to allow simultaneous trapping of magnetic and diamagnetic particles via a single set of magnets, and demonstrate the ability to perform assays on one type of particle while the other acts as a control. Additionally, we show how the setup can be adjusted to enable the continuous flow focusing of diamagnetic particles in a paramagnetic medium.

KEYWORDS: Diamagnetic repulsion, Flow focusing, Magnetic particles, Magnetism, Microparticles, Trapping

INTRODUCTION

It is intuitive that magnetic particles or magnetically labeled cells are attracted to magnetic fields [1], but it is less commonly known that diamagnetic materials, such as polymer particles and cells, are repelled from magnetic fields [2]. This repulsive effect can also be greatly enhanced by suspending the particles in a paramagnetic medium containing Gd^{3+} or Mn^{2+} ions. We have previously reported basic proof-of-principle experiments for the trapping and focusing of diamagnetic polystyrene particles [3-4] between simple, inexpensive permanent magnets. Here, we significantly extend this work by demonstrating, for the first time, the simultaneous trapping of magnetic particles and diamagnetic polystyrene particles into two separate plugs with one pair of magnets (Fig. 1a), and apply this to an assay with a negative control. Additionally, we include previously unpublished data for the diamagnetic focusing of polystyrene particles in continuous flow (Fig. 1b).

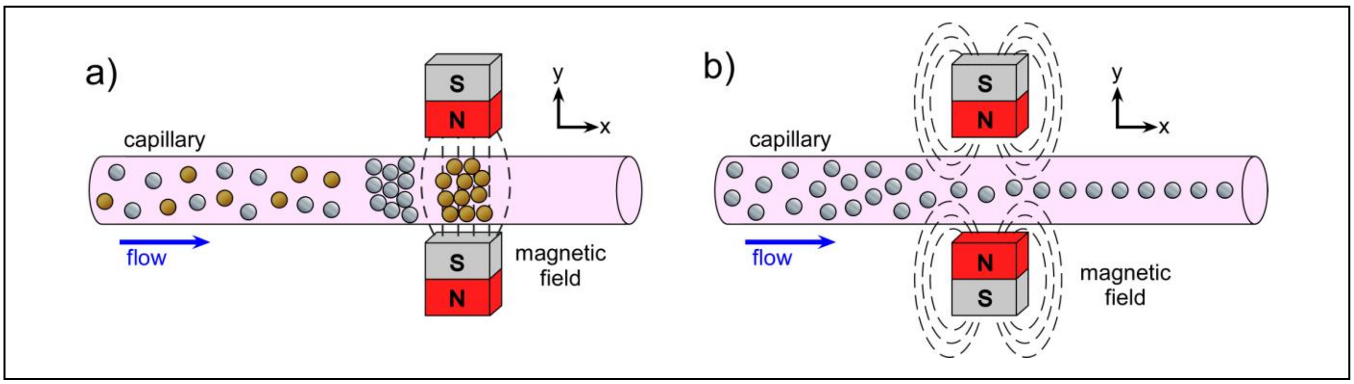

Figure 1: (a) Exploiting magnetic attraction and diamagnetic repulsion for the simultaneous trapping of magnetic (brown) and polymer (grey) particles into two separate plugs between a pair of magnets with their opposite poles facing. (b) Focusing of polymer particles into the centre of a microchannel via their diamagnetic repulsion from two magnets with their like poles facing.

THEORY

A magnetic force, $\mathbf{F}_{\mathbf{mag}}$, can be applied to both magnetic and diamagnetic particles. The extent of that force is shown in Eqn. (1), and depends on the volume of the material affected by the magnetic field (V), the difference in magnetic susceptibility between the particle (χ_p) and the medium (χ_m), the magnetic flux density ($\mathbf{B}$) and its gradient ($\nabla\mathbf{B}$), and the permeability of free space (μ_0).

$$\mathbf{F}_{\mathbf{mag}} = \frac{(\chi_p - \chi_m)\ V\ (\mathbf{B}\cdot\nabla)\mathbf{B}}{\mu_0} \tag{1}$$

Whether a particle will migrate towards or away from a magnetic field depends on the difference between χ_p and χ_m, i.e. $\Delta\chi$. If a superparamagnetic particle ($\chi_p > 0$) is suspended in a diamagnetic medium ($\chi_m < 0$), then $\Delta\chi$ will be positive, meaning that the particle will be attracted towards a magnetic field. However, if a diamagnetic particle ($\chi_p < 0$) is suspended in a paramagnetic solution ($\chi_m > 0$), then $\Delta\chi$ is negative, and the particle will be repelled from the field. Thus, to achieve the required repulsion of the diamagnetic polystyrene particles used in these experiments, they were suspended in aqueous solutions of paramagnetic manganese (II) chloride or gadolinium (III) chloride. Additionally, when superparamagnetic particles were suspended in the paramagnetic medium, the magnetic susceptibility of the former was still larger than the latter, hence the particles were attracted towards the field despite being in a solution of paramagnetic ions.

EXPERIMENTAL

Simultaneous trapping of magnetic and diamagnetic particles: 10 μm polystyrene particles (χ_p = -8.21 x 10^{-6}) and 8 μm magnetic particles ($\chi_p > \chi_m$) were suspended in 0.79 M $MnCl_2$ solution (χ_m = 1.46 x 10^{-4}), and pumped through a 100 μm i.d. fused silica capillary at a flow rate of 8 - 10 μL h^{-1}. Permanent neodymium-iron-boron (NdFeB) magnets were situated around the capillary with their opposite poles facing, thus creating a region of high magnetic field between them.

Focusing of diamagnetic particles: Polystyrene particles, suspended in $GdCl_3$, were pumped through a 150 μm i.d. fused silica capillary between a pair of NdFeB magnets with their like poles facing. This created regions of low magnetic field in the centre of the capillary, with regions of high field at the surfaces of the magnets.

RESULTS AND DISCUSSION

Simultaneous trapping of magnetic and diamagnetic particles: As the two particle populations were pumped through the capillary, they became trapped at different positions with respect to the magnetic field; the magnetic particles became trapped between the poles where the field was strongest, while the diamagnetic particles were repelled from this same region and formed a plug further upstream (Fig. 2a). Thus, two plugs of particles were formed using only one pair of magnets. By employing polystyrene particles that were functionalized with streptavidin, whilst leaving the magnetic particles with a plain surface, an assay was performed by flushing fluorescently labeled biotin over the two plugs, before washing with $MnCl_2$ solution. This yielded a marked increase in fluorescence of the functionalized polystyrene plug that indicated successful binding of the reagent to the particles (Fig. 2b), whilst the magnetic particle plug remained non-fluorescent, essentially acting as a simultaneous negative control during the assay procedure. Furthermore, the trapping of six particle plugs was performed in one capillary via the application of three magnetic fields (Fig. 2c), with fluorescently labeled magnetic particles used to demonstrate the trapping of each plug without any contamination of particles from one plug to the next. Such a setup illustrates the potential for forming multiple plugs in a capillary in less time and with far less tedium than when using only magnetic or diamagnetic particles by themselves. The ability to generate two plugs with one magnetic field could also be applied to the separation of particle mixtures, as well as particle-based extraction and analysis.

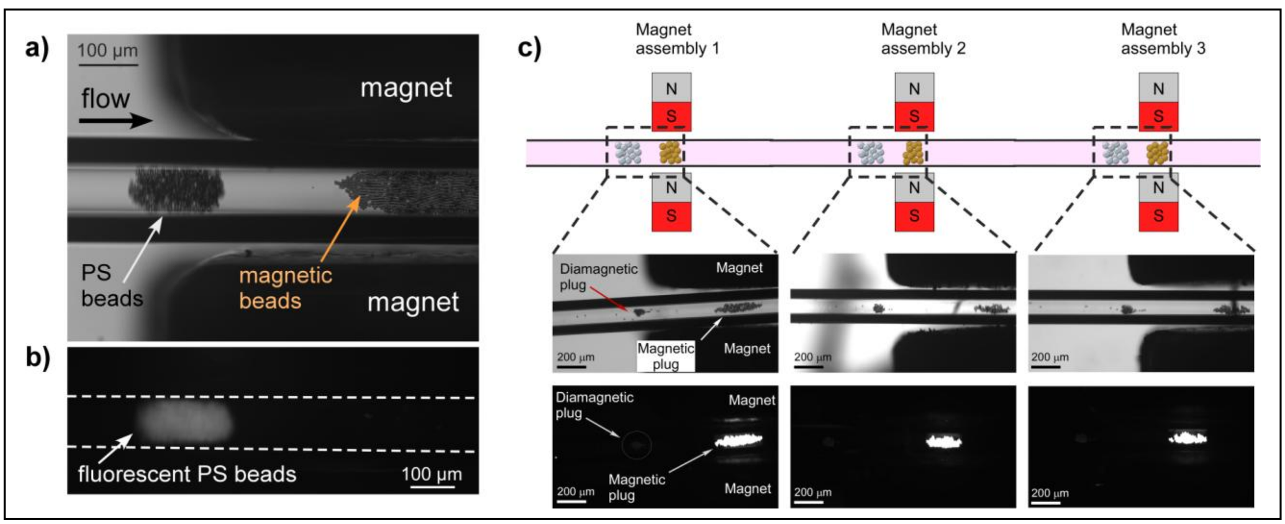

Figure 2: (a) Simultaneous trapping of a mixture of 10 μm streptavidin coated polystyrene particles and 8 μm plain magnetic particles into two separate plugs. (b) Fluorescence of the polystyrene particles observed after flushing with fluorescently labeled biotin, with the magnetic particles exhibiting no increase in fluorescence intensity. (c) Six plugs of particles formed along a microchannel using three magnetic fields. Fluorescently labeled magnetic particles were trapped between the magnetic poles, whereas the non-fluorescent polymer particles became trapped upstream from the magnets.

Focusing of diamagnetic particles: When polystyrene particles were pumped through the capillary between two magnets with their like poles facing, they were repelled from the regions of high field near the magnet surfaces and into the region of low field in the centre of the capillary. The effect of the applied flow rate on the extent of focusing was investigated by suspending 10 μm particles in 0.56 M $GdCl_3$, and pumping them through the capillary at flow rates of 20, 40 and 60 μL h^{-1} (Fig.

3a). Here, it was observed that at higher flow rates, fewer particles were focused into the centre of the channel than at lower flow rates, indicating that an increased residence time between the magnets is required for better focusing. A further parameter that was studied was that of the volume of the particles, hence 5, 10 and 20 μm particles were pumped through the microchannel, whereupon it was found that the extent of focusing increased with increasing particle volume (V), as expected by the theory according to Eqn. (1). We also found that higher concentrations of paramagnetic salt yielded greater $\Delta\chi$ values that resulted in enhanced focusing effects, and established that suspending the particles in $MnCl_2$ yielded worse deflection behavior than $GdCl_3$ solutions, due to lower values of χ_m for the Mn^{2+} ions [4]. Furthermore, we found that it is feasible to focus viable HaCaT skin keratinocyte cells when they are suspended in biologically benign Gd-DTPA (gadolinium (III) diethylenetriaminepentaacetic acid) solution [4], showing great promise for the focusing of a variety of cell types for diamagnetic repulsion-based cytometry.

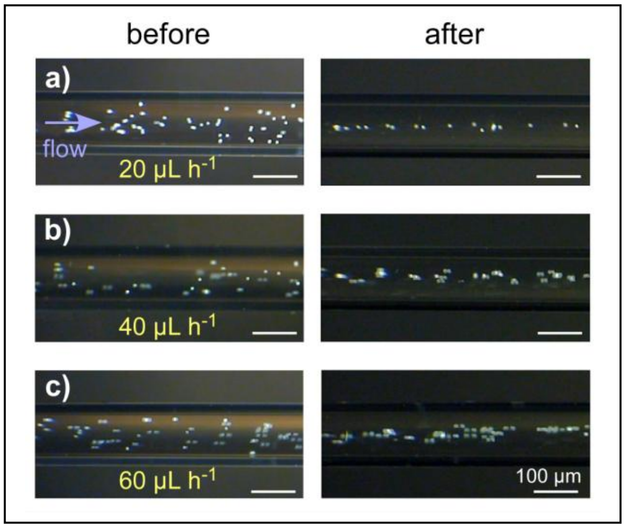

Figure 3: Focusing of 10 μm polystyrene particles suspended in 0.56 M $GdCl_3$ solution at flow rates of (a) 20 $\mu L\ h^{-1}$, (b) 40 $\mu L\ h^{-1}$, and (c) 60 $\mu L\ h^{-1}$. Slower flow rates yielded a more pronounced focusing effect due to the increased residence time in the magnetic field.

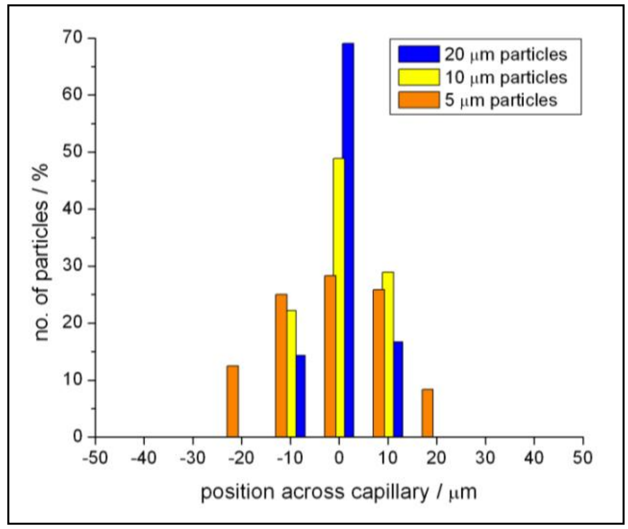

Figure 4: Focusing as a function of particle size for 5 μm, 10 μm, and 20 μm polystyrene particles suspended in 0.79 M $GdCl_3$ solution at a flow rate of 25 $\mu L\ h^{-1}$. Larger particles exhibited greater focusing than the smaller particles due to the increase in volume.

CONCLUSION

The results shown here demonstrate the versatility of magnetic forces, which can not only be exploited for attraction of magnetic particles and magnetically labeled cells, but also for the repulsion of "non-magnetic" particles and cells. We have utilized both of these attractive and repulsive forces to form simultaneous plugs of magnetic and diamagnetic particles with one magnetic field, and have performed an assay on the trapped particles. We have also applied repulsive forces to the flow focusing of polystyrene particles and cells, based entirely upon their intrinsic properties, and have exemplified the ease with which these forces can be generated and employed.

REFERENCES

[1] S. Bronzeau and N. Pamme, Simultaneous bioassays in a microfluidic channel on plugs of different magnetic particles, *Anal. Chim. Acta*, 609, pp. 105-112, (2008).

[2] A. Winkleman, R. Perez-Castillejos, K.L. Gudiksen, S.T. Phillips, M. Prentiss and G.M. Whitesides, Density-based diamagnetic separation: Devices for detecting binding events and for collecting unlabeled diamagnetic particles in paramagnetic solutions, *Anal. Chem.*, 79, pp. 6542-6550, (2007).

[3] S.A. Peyman, E.Y. Kwan, O. Margarson, A. Iles and N. Pamme, Diamagnetic repulsion – A versatile tool for on-chip label-free particle handling, *J. Chromatogr. A.*, 1219, pp. 9055-9062, (2009).

[4] A.I. Rodrígues-Villareal, M.D. Tarn, L.A. Madden, J.B. Lutz, J. Greenman, J. Samitier and N. Pamme, Flow focussing of particles and cells based on their intrinsic properties using a simple diamagnetic repulsion setup, *Lab Chip*, 11, pp. 1240-1248, (2011).

CONTACT

*Nicole Pamme, tel: +44 (0) 1482 465027; n.pamme@hull.ac.uk.