THREE-DIMENSIONAL HYDRO-MAGNETIC FOCUSING OF SUPERPARAMAGNETIC BEADS

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ABSTRACT

We present magneto-microfluidic three-dimensional focusing of magnetic microparticles from a dense plug into a single streamline with longitudinal inter-particle spacing. Plug formation is induced by a high-gradient magnetic field generated at the sidewall of a microchannel by a micromachined magnetic tip that is connected to an electromagnet. Controlled release of the microparticles is achieved using an exponential damping protocol of the magnetic retention force in the presence of an applied flow. Adding subsequently a lateral sheath flow microchannel focuses the microparticles into a single stream situated within ± 5 μm from the channel center axis.

KEYWORDS: Magnetophoresis, microfludic, focusing, magnetic beads

INTRODUCTION

Magnetic beads are versatile mobile carriers in microfluidics. The possibility to combine magnetic and fluidic forces for bead manipulation in small liquid volumes, for the extraction of target molecules from complex sample matrixes and for bead separation according to their size opens the way to innovative concepts with previously unmatched performance [1-3]. For accurate bead discrimination and counting, it is particularly attractive to implement on-chip an approach based on individual bead analysis, similar to cytometric techniques. Flow cytometry, however, requires 3-dimensional (3D) focusing of the particle suspension for reliable detection. Particles should pass one-by-one in-line and with a constant passage time through the illumination spot of the laser light coupled into the microchannel or precisely in front of an integrated detector [4-6]. The requirement of a very narrow focused particle stream is particular important for detecting small cells or micrometer-size beads. 3D hydrodynamic focusing in a microfluidic device may be realized in a variety of ways, as was summarized in a recent review [7].

We propose a microfluidic system with a magnetic microtip that is positioned close to one microchannel sidewall. Our system permits bead retention and controlled release near the channel wall, by controlled decrease of the local magnetic force in the presence of an applied flow. Combining subsequently the bead-containing flow with a lateral sheath flow from a joining secondary channel focuses the beads along a single central line downstream in the main microchannel.

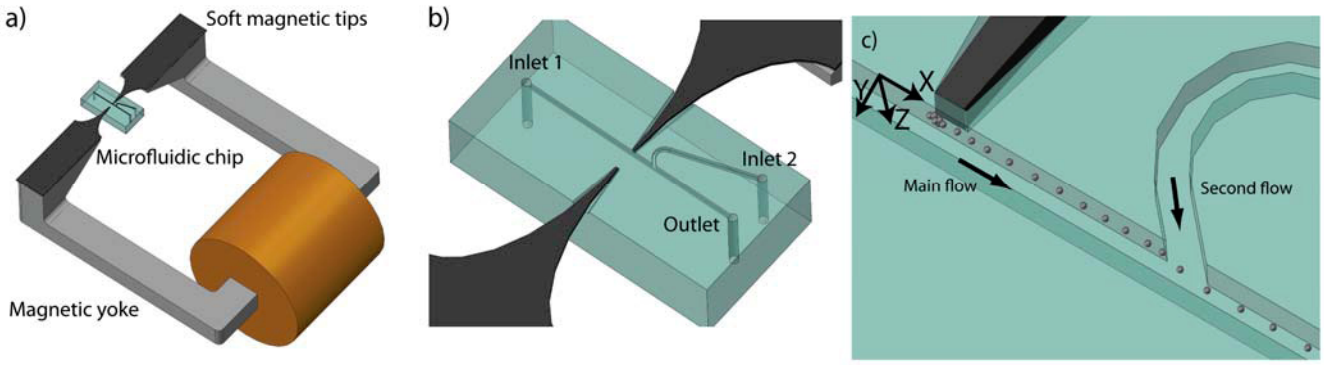

Figure 1: a) Magnetic bead actuation system including an electromagnet comprising a coil, a magnetic yoke and a pair of soft-magnetic tips interfacing with the microfluidic chip; b) Zoom on the microchip comprising a first microfluidic channel (inlet 1), a secondary channel (inlet 2), the main channel (outlet) and the asymmetric arrangement of two magnetic poles; c) Enlarged view of the zone of interest on the chip, showing schematically the release of a magnetic bead plug and the deviation of a 3D focused stream of individual beads towards the middle of the main channel

THEORY

We use magnetophoresis to attract particles towards a magnetic tip prior to controlled release in a fluid flow. For the design of our system, the magnetic force $\vec{F}_{mag}$ on the beads in a magnetic field B was calculated by

$$\vec{F}_{mag} = \frac{1}{2\mu_0}\Delta\chi V_m \nabla \vec{B}^2$$

where $\Delta\chi$ is the magnetic susceptibility of the particle relative to the suspending medium, μ_0 is the vacuum permeability and V_m is the magnetically active volume of the particle. This expression holds for unsaturated particles and is a good approximation for the present experiments.

EXPERIMENTAL

The magneto-microfluidic set-up comprising the chip and the magnetic circuit is schematically shown in Fig. 1a, The magnetic part of the system consists of an external coil, a magnetic yoke and a pair of soft magnetic tips (50 µm width). Fig. 1b shows a zoom on the microfluidic chip. The chip has a principal straight microfluidic channel (10 mm long, 200 µm wide, 100 µm high), and a secondary microchannel (200 µm wide, 100 µm high). The fluidic junction is located 0.5 mm downstream the magnetic tip location (Fig. 1b). Fig. 1c is an enlarged schematic view of the region of interest, illustrating the release of a magnetically retained bead plug into a 3D-focused stream. Only a single precision syringe pump is connected simultaneously to both fluidic inlets of the chip for fluidic control. As both channel portions before the fluidic junction have equal hydraulic resistance, the flow rates in both sections are equal. Consequently, the secondary flow focuses the released magnetic bead stream exactly towards the middle of the main channel.

Fig. 2 shows a two-dimensional (2D) Finite Element Method (FEM) simulation of the magnetic field lines and the magnetic force field close to the tip that is adjacent to the microchannel (COMSOL MULTIPHYSICS 3.4). The resulting force field is asymmetric with respect to the channel middle axis. Beads will therefore be attracted only towards this tip and form a single plug on one channel side wall.

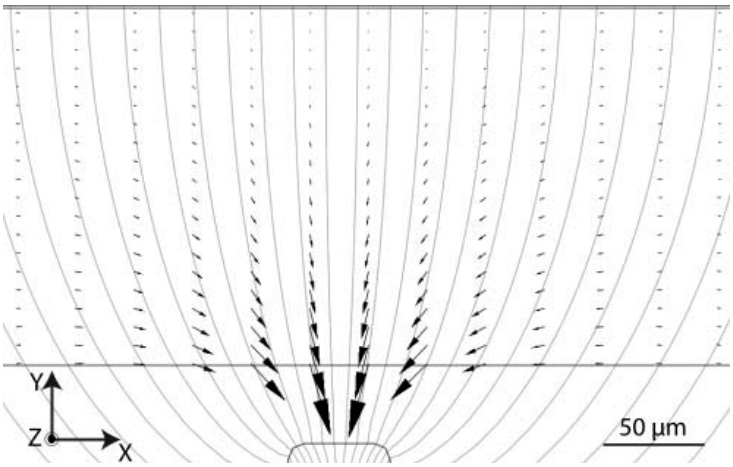

Figure 2: 2D FEM simulation of the magnetic field lines in the main channel close to the tip. The relative variation of the resulting magnetic force (equation (1)) exerted on a magnetic particle field is represented by arrows of different size. Significant field concentration, thus attractive force, is observed only on one channel side wall. The force field distribution has the same symmetry in the channel plane (x-y plane) and the channel cross section plane (y-z plane).

RESULTS AND DISCUSSION

Observation of the particle trajectories is done using an inverted optical microscope (Zeiss Axiovert S100) equipped with a fast monochrome digital camera (PixeLINK PL-B741) and using video recording software (StreamPixTM) and image processing for particle counting (ImageJ, open source).

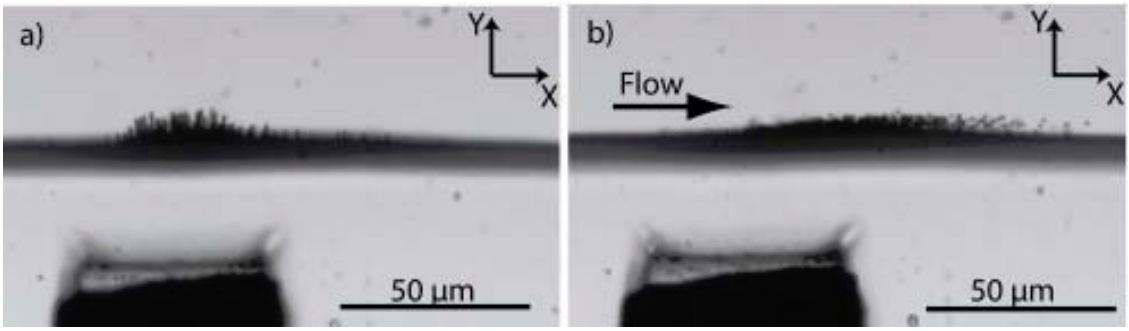

Figure 3: a) Top view photograph of a magnetic plug immobilized on the sidewall of microchannel under the effect of the applied magnetic field (about 400 beads of diameter 1 µm are retained, t=0 s); b) After t≈1 s, beads are progressively released from the plug into the flow by controlled attenuation of the sinusoidal coil current.

Bead capture and plug formation near the magnetic tip on the channel wall, as well as subsequent release is demonstrated in the images shown in Fig. 3a and Fig. 3b. In the present case, parameters have been chosen to form a plug that contains 400±20 beads of 1 µm diameter [8], superparamagnetic beads progressively lose their magnetic moment during exponential attenuation of the magnetic field (Fig. 3b). The hydrodynamic shear force progressively overrules the decreasing magnetic retention force and tears off the beads from the plug. The released particles are confined in a narrow stream close to the channel wall.

At the fluidic junction, the released magnetic bead stream is deviated towards the center of the main channel where the flow rate and the maximum flow velocity are twice as high as in the upstream channel sections. Furthermore, beads are pushed from a region with very low flow velocity close to the channel wall towards the center of the parabolic flow profile. Particles in the released stream are therefore strongly accelerated (Fig. 4).

Figure 4: a) Photograph of the focusing 1 µm bead stream at the channel junction. The final bead velocity is 0.6 mm/s

CONCLUSION

We presented a new magneto-microfluidic method for 3D focusing The particles are aligned one-by-one in a stream with a maximum deviation of ±5 µm from the center position in the channel. Focusing in the vertical direction is achieved by taking advantage of the strongly focused magnetic field generated by a soft-magnetic microtip that is integrated on-chip. Accuracy and stability of focusing is suitable for combination with on-chip particle counting applications.. In addition to 3D focusing, our set-up allows precise dosing, i.e. retention of a very accurate and small amount of beads in the sample flow. Moreover, it enables dynamic actuation of the beads in the flow [9], useful for antigen capture. The demonstrated in-flow separation may simplify and optimize detection protocols and, in particular, this method takes full advantage of 3D focusing. We think that the present device may play a future role in an integrated versatile platform for performing several magnetic manipulation steps on-chip, like required for magnetic bead-based bio-assays.

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