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# A NOVEL DEVICE FOR CONTINUOUS FLOW MAGNETIC TRAPPING AND SORTING OF HUMAN CELLS USING FLAT MICRO-PATTERNED NdFeB FILMS

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## ABSTRACT

The manipulation of magnetically labeled bio-objects of nano or micrometer sizes is now realizable by combining the magnetic forces with microfluidics. This paper reports a novel method for manipulating, trapping and sorting magnetic beads and magnetically labeled cells under continuous flow. This method uses a microfluidic device with integrated flat micro-patterned hard magnetic films which generate high magnetic field gradients.

**KEYWORDS:** Magnetism, Cell separation, Microfluidic

## INTRODUCTION

Magnetic field applications at the microscale are of growing interest in biology [1], as magnetic field sources can now be integrated directly into microchips [2-3]. Due to the recent progress in the synthesis of nano and micro-superparamagnetic particles which bound to biological objects, a large number of biotechnological devices based on magnetophoresis have been developed. Nevertheless, the generation of magnetic fields and field gradients strong enough to manipulate magnetic micro objects remains a challenge. Several papers report the use of micro-electromagnets or the combination of soft materials and external magnetic field to create magnetic field gradients for manipulating biological objects [4]. The use of permanent-magnet-based microstructures is very attractive since Joule heating is avoided while no energy source is required.

## RESULTS AND DISCUSSION

In our experiments, we used flat chessboard micro-magnet arrays (figure “1”) obtained by thermo-magnetic patterning of hard magnetic neodymium iron boron (NdFeB) thick film [5].

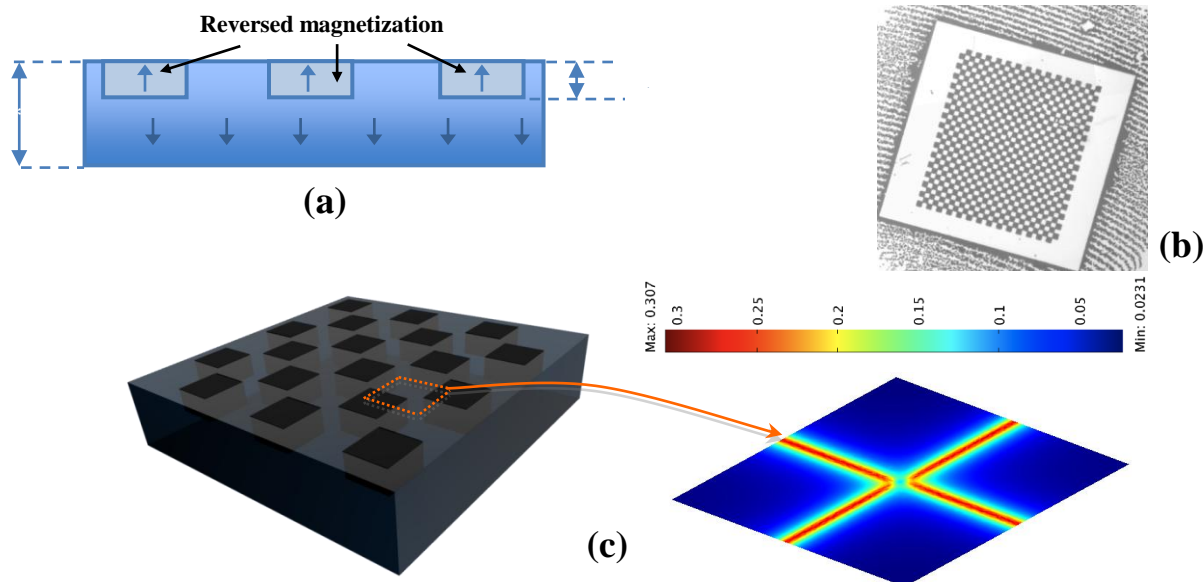


Figure 1: (a) Structure of the thermomagnetically patterned micromagnet array - (b) Magneto-optic image (Faraday effect) of a MOIF placed on top of a patterned NdFeB films - (c) Norm of the magnetic flux density in a plane situated at the magnetic film surface

Such patterned films have already been used to trap liposomes containing superparamagnetic nanoparticles [6]. Figure “2” shows HEK 293 cells, which have endocytosed 100 nm-magnetic nanoparticles, attracted towards the regions of maximum magnetic field gradient (edges of the squares).

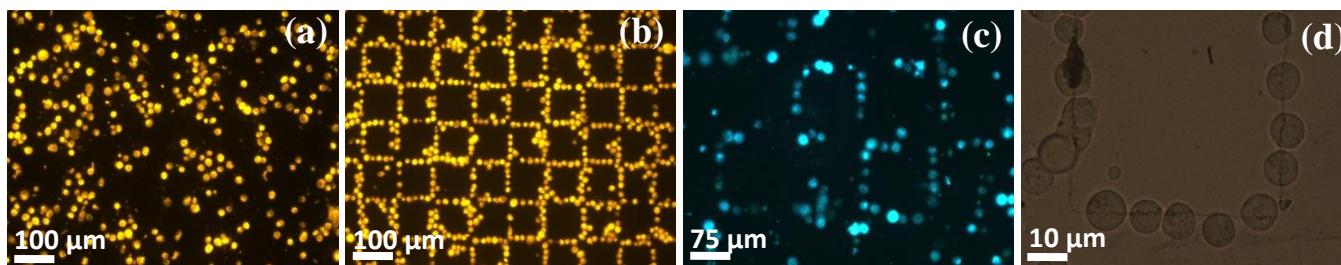


Figure 2: Attraction of HEK 293 towards magnetic field gradient maxima. (a) unlabeled cells. (b) Magnetically labeled cells. (c) Magnetically and fluorescently labeled cells. (d) zoom on a group of attracted cells.

This result reveals the applicability of micro-magnets for trapping biological cell and for potential applications in medical diagnostics based on cell endocytic ability. We also demonstrated the efficient trapping of Jurkat cells labeled via the binding of cell antigens with antibody-coated magnetic particles of 1  $\mu\text{m}$  (figure “3”).

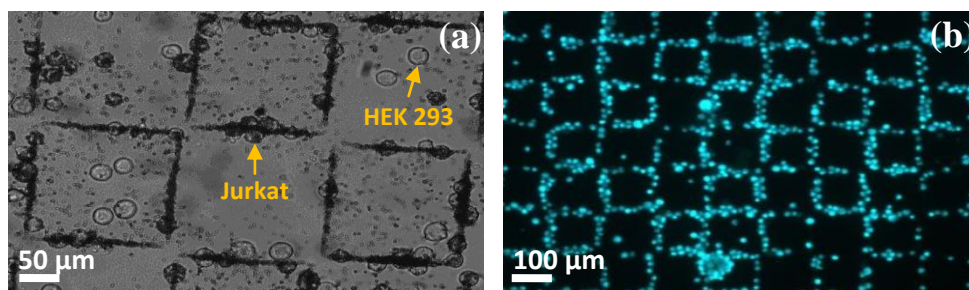


Figure 3: Attraction of magnetically (a) and fluorescently (b) labeled Jurkat cells towards magnetic field gradient maxima. HEK 293 (unlabeled cells) remained untrapped.

Due to the flatness of the micro-magnet array, this type of autonomous micro magnetic field source can be easily integrated into a microchannel. The micro-magnet array was first covered with a thin layer of PolyDiMethylSiloxane (PDMS) obtained by spin-coating, the thickness (2 to 12  $\mu\text{m}$ ) being controlled by mixing PDMS with heptane to decrease its viscosity and by varying the ratio between both. A PDMS microchannel was sealed onto the PDMS layer using an  $\text{O}_2$  plasma (figure “4”).

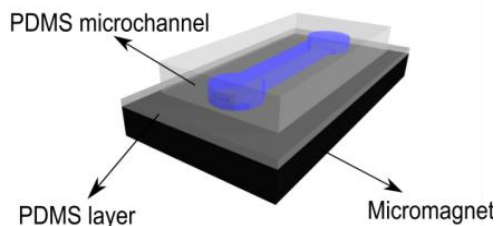


Figure 4: schematic view of the microfluidic device.

The PDMS layer serves to protect the micro-magnet array from degradation due to contact with liquid and offers a bio-compatible interface with the manipulated bio-objects. Moreover, by adjusting the thickness of the PDMS layer, the magnetic force exerted on the particles can be varied. To demonstrate the trapping efficiency of our microfluidic magnetic device, two types of 1  $\mu\text{m}$ -fluorescent beads (magnetic and non-magnetic) were injected. Figure “5” shows magnetic beads trapped at the regions of maximum field gradient while non-magnetic beads moved freely.

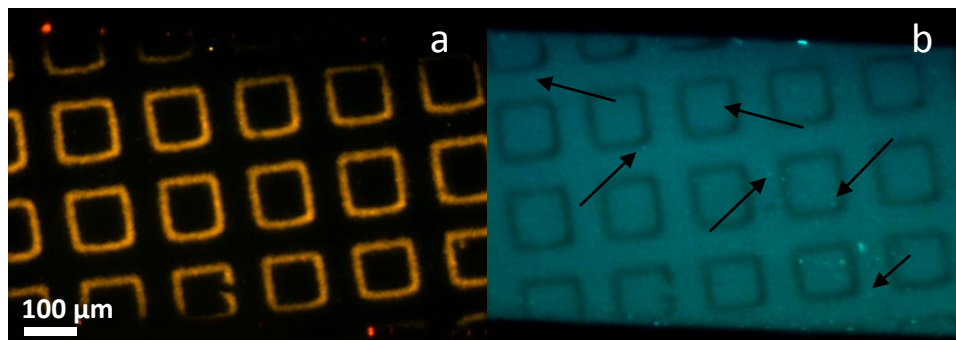


Figure 5: (a) Fluorescence image of magnetic beads trapped at the maximum of the gradient field. (b) Fluorescence image of the non-magnetic particles (bright spots indicated by arrows), moving freely in the microchannel.

## CONCLUSION

The lab on chip combination of micro-patterned magnetic films and microfluidic is convenient for trapping and sorting bio-objects. As the microscale patterning of the hard magnetic films generates strong magnetic field gradients (up to  $10^6$  T/m), cells can be efficiently trapped with reduced magnetic loads. Future experiments will be directed towards comparing our device with commercial kits (eg. *Dynabeads*<sup>®</sup> FlowComp<sup>™</sup>) enabling selective isolation of labeled cells using macro-magnets. As a first step, we succeeded in trapping cells labeled with 30 nm-magnetic nanoparticles using micro-patterned hard magnetic films (figure “6”). Note that due to their very small size, such nanoparticles cannot be attracted using macro-magnets.

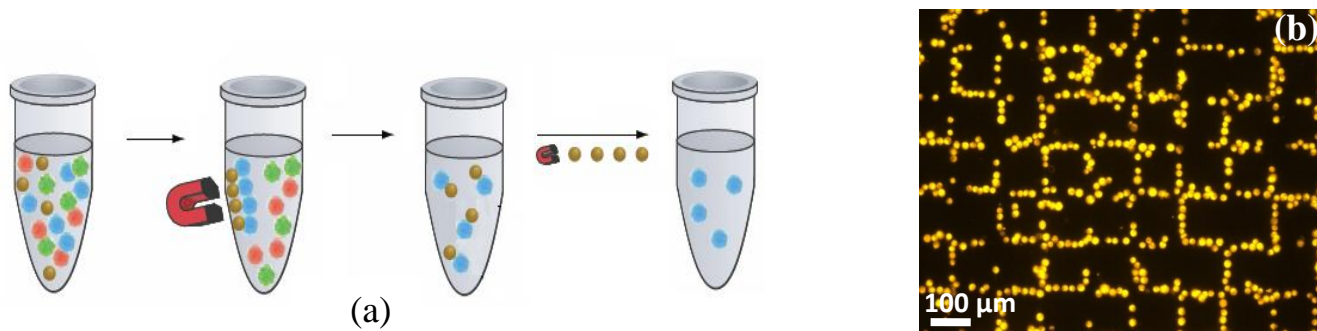


Figure 6: (a) Overview of the *Dynabeads*<sup>®</sup> FlowComp<sup>™</sup> isolation procedure. (b) Attraction of HEK 293 cells labeled with 30 nm-nanoparticles toward magnetic field gradient maxima.

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