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ELECTROMAGNETIC TRAPPING OF CANCER CELLS ON AN ARRAY OF THIN-FILM PERMALLOY MICROFEATURES FOR SINGLE CELL ANALYSIS

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ABSTRACT

Isolation of individual cells from a bulk sample is vital in cell based diagnostics. Previous work has established the ability to arrange target cells into ordered arrays, using physical barriers such as micropillars and cups [1]. We here present a magnetic separation device that allows the tagged cells of interest to align into a highly ordered array where they are selected based on both immuno-markers and size. But, unlike the physical barrier methods, our device is able to trap the cells using an only 160-nm thin film of permalloy (80% Nickel, 20% Iron) micropatterned on the base of the chamber (Fig. 1). Maxima of the magnetic field arise in the vicinity of the sharp edges of these localized micro-spots (Fig. 2), thereby creating potential wells to localize paramagnetic bioparticles such as tagged cells or beads during analysis or successive washing steps (Fig. 3). Compared to a complex network of physical barriers, the trapped cells can simply be released by turning off the external magnet, allowing for further downstream analysis or removal to waste.

PRINCIPLE OF OPERATION

Magnetic cell isolation has become widespread, with the majority of systems using bulk magnetic forces [2,3]. The novelty in our system is the arrayed trapping of the magnetically tagged cells where they can be individually studied and undergo media change or fluorescent staining. The thin-film nature of these traps avoids inevitable divergence of flow lines around 3D-obstacles, thus enhancing capture efficiency and subsequent exposure to media reagents, also ensuring that cells are uniformly exposed to media. Following on-array retention, the cells can be released with very high recovery rates into a capture chamber by removing the magnetic field. Our technology also suppresses clogging inherent to common arrays of 3-D obstacles.

MATERIALS AND METHODS

The permalloy features are deposited on the floor of the chip by sputter-coating a UV-lithographically patterned AZ-photoresist which was spin-coated on glass slides. A PMMA lid was cut by a CO_2 laser and bonded to the glass via a pressure sensitive adhesive featuring an 86-µm high microchannel for the passage of the cells. The MCF7 cancer cells were incubated with 4.5-µm magnetic anti-EpCAM beads before being introduced to the system.

RESULTS AND DISCUSSION

This chip enables the separation of target bioparticles from an abundant background into array of magnetic traps with single occupancy distribution. We have measured a capture efficiency of over 99% for magnetic beads and a purity of 98.5%, with a non-magnetic particle purity of over 99.9% in the waste chamber (Fig. 4). We have also shown a capture efficiency of 100% for magnetically tagged MCF7 cells in a background of whole blood; over 99% of the background blood cells are routed to the waste chamber. We have also demonstrated media exchange without disturbing the retention of the cells and successfully released them for downstream analysis. We have also shown size separation by the variation of micro-dot geometry. Overall, this new and reversible magnetic alignment method of individual cells could easily be adapted to various types of bioassays.

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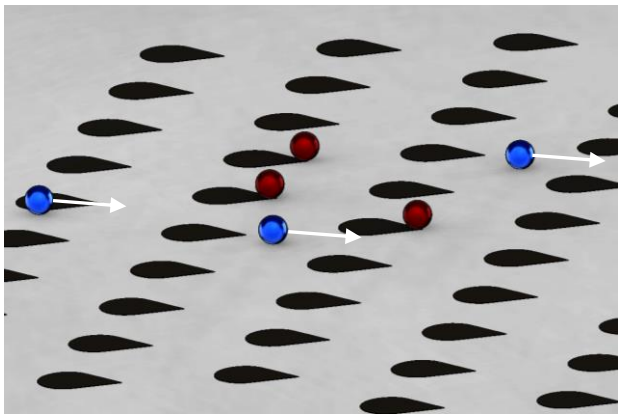

Figure 1: Magnetic bioparticles such as beads or tagged cells (red) are held down on the tip of the teardrop-shaped magnetic dots (black), where the local field is strongest, while the non-magnetic particles (blue) continue to flow past, unperturbed by the magnetic field.

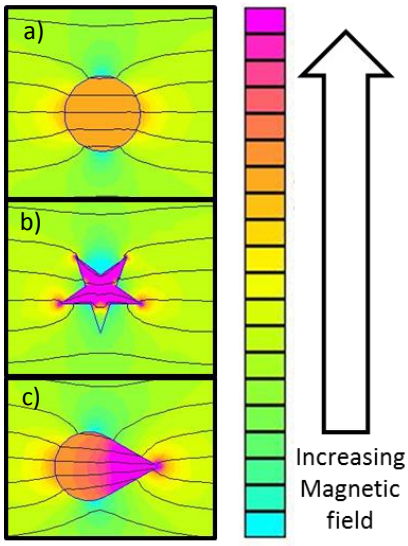

Figure 2: Local magnetic field simulations for different shapes of a patterned permalloy film. a) The round dot delivers a rather even distribution of magnetic field. b) The star-shaped structure provides a larger value but it has a number of maxima. c) The teardrop shape focusses the magnetic field in into a single maximum which turned out to be optimal for capture of individual bioparticles at high spatial definition.

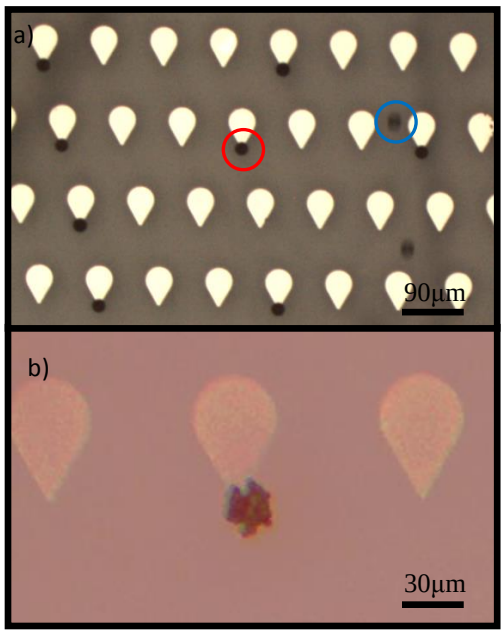

Figure 3: a) Microscope image of 20-µm magnetic beads (red circle) trapped by the local magnetic field maximum at the tips of the magnetic permalloy teardrops while the trajectory of non-magnetic beads (blue circle) remains unperturbed. The magnetic beads were captured with a sensitivity of 99.6% and a purity of 98.5%. 99.95% of the non-magnetic beads were routed to the waste chamber. b) Magnetically tagged MCF7 cancer cells are also trapped on the magnetic permalloy teardrops.

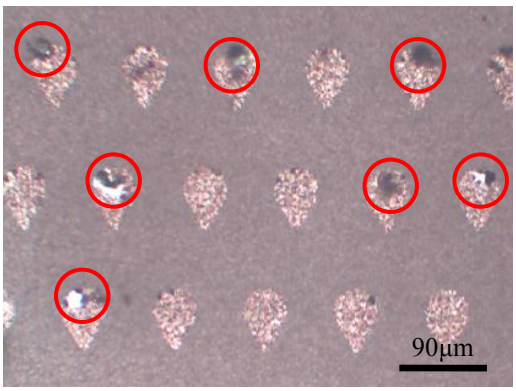

Figure 4. Capture of tagged MCF7 cells (circled in red) in a background of whole blood, which is flowing past. The MCF7 cells were captured with a sensitivity of 100%, while over 99% of the blood cells were routed to the waste chamber.

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