HIGHLY EFFICIENT SINGLE CELL CAPTURING UNDER STAGNANT FLOW CONDITIONS ON A CENTRIFUGAL MICROFLUIDIC PLATFORM

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ABSTRACT

In this work we present a novel design for highly efficient cell capturing on a centrifugal lab-on-a-chip platform. The cells sediment under stagnant flow conditions due to the influence of the centrifugally induced artificial gravity field. They are then captured in an array of designated geometrical traps. The absence of flow of the suspending liquid appreciably increases the capture efficiency to up to 98%, which compares to less than 20% in typical pressure-driven systems

KEYWORDS: cell capture, centrifugal microfluidics, cell screening, cell trap

INTRODUCTION

Lab-on-a-chip systems offer unique experimental approaches to cell research and cellular based drug screening [1]. One advantage of microfluidic systems compared to traditional cell culturing techniques is the possibility to investigate the behaviour of single cells. This allows to monitor the response of individual cells to factors such as drugs rather than a average response that is measured in cell cultures cultivated in conventional Petri dishes. Several groups have presented single cell capturing chips in the past, using physical obstacles and pressure driven flow [2], spiral channels with pockets to capture cells [3] or negative DEP traps [4]. Our novel capturing structure overcomes the low capture efficiency of pressure driven systems and is much easier to fabricate than DEP devices.

THEORY

Previously presented pressure driven single cell capturing chips are constitute of an array of C- or V-shaped retention structures scale-matching the size of a cell [2]. The presence of a flow field in these devices implies that cells are dragged along the continuous flow lines and thus tend to follow the continuous flow lines around the capturing elements. This has been partly compensated by introducing small slits between the capturing elements and lid. However, simulations show that the capturing efficiency of these devices is only approximately 20% (Fig. 1a). The setup presented here comprises of a dead-end chamber with an array of capturing elements that are arranged to avoid straight paths between sample inlet and bottom of the chamber that do not cross a capturing element. The device is mounted on a rotable disk substrate and the chamber is filled with liquid. Due to the fact that there is no flow in the chamber during rotation, cells sediment in straight trajectories along the radially directed centrifugal field and are eventually captured in the geometrical re-

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tention structures. The size of the capturing elements is chosen such that only one cell can be held per element. Subsequently arriving cells are thus diverted to the next capturing line. Therefore our system achieves a theoretical capture efficiency of 100 % (Fig. 1b). Due to the stagnant flow conditions the capturing scheme presented here does not need gaps in the capturing elements, which significantly facilitates fabrication.

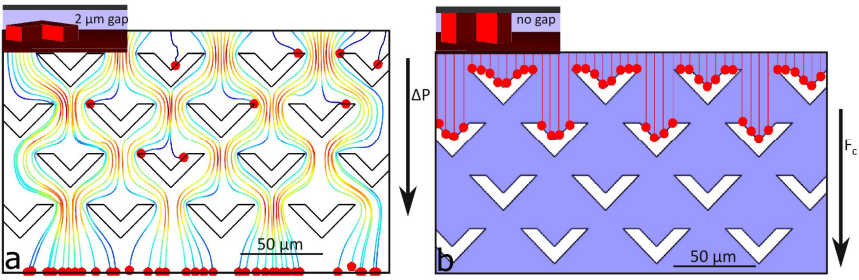

Figure 1. Comparison of pressure driven capturing scheme with 2 µm gaps between capturing elements and cover, as in [2] (a) and stagnant flow capturing (b).

EXPERIMENTAL

All chips used in this work have been fabricated in PDMS. Moulds for PDMS casting have been produced in SU-8 with a thickness of 25 µm, using standard photo lithography processes. After replication the PDMS is bonded to a glass microscopy slide and placed on a disk shaped substrate to perform the experiments. Prior to priming the chamber, the PDMS device has been placed in a desiccator for at least 30 min. This procedure allows the filling of dead-end structures and has been described in detail elsewhere [5]. Experiments have been performed at a rotation speed of 20 Hz (1200 rpm). Capturing experiments have been performed with 10-µm silica beads of (Kisker, Germany). Figure 2 displays the experimental setup.

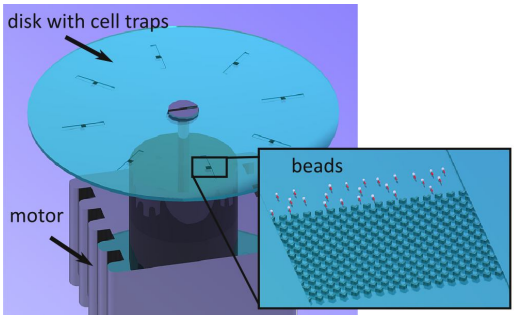

Figure 2: Experimental setup, consisting of motor and disk with cell traps.

RESULTS AND DISCUSSION

In our experiments between 85 to 98 % of all beads could be trapped, thus proving the high capturing efficiency of our novel structure. An image of trapped silica

beads is shown in Figure 3. This figure also shows the bead population in each capturing row at different times.

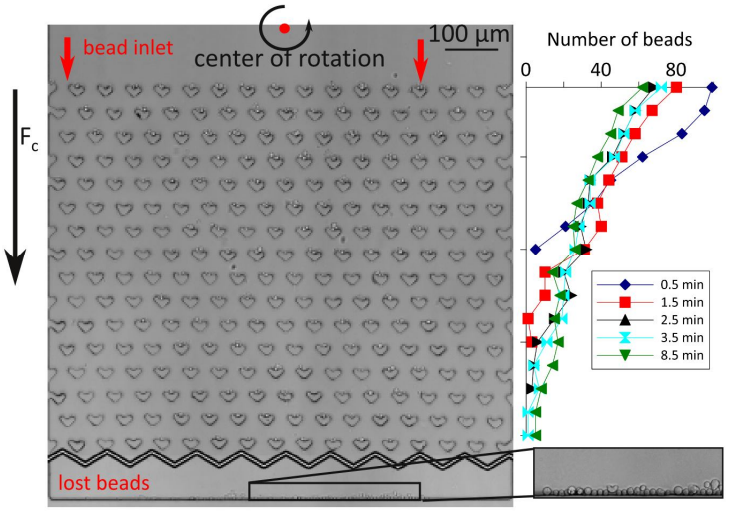

Figure 3: Image of cell capturing chip with 16 capturing lines. In the experiment shown here, a capture efficiency of 85 % was achieved. Other experiments showed capture efficiencies up to 98 %. The graph on the right shows the population of beads in each capturing row over time.

CONCLUSIONS

We presented a novel, simple and highly efficient device for capturing cells on a centrifugal microfluidic platform. Future work will focus on increasing homogeneity of cell distribution, improved single-cell capturing and performing biological experiments such as drug screening on single cell level.

ACKNOWLEDGEMENT

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