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Electromagnetic microfluidic cell labeling device using on-chip microelectromagnet and multi-layered channels

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ABSTRACT

We present a new design for a microfluidic cell sorting system in which microelectromagnets are implemented and the Joule heating energy is dissipated to maintain a biocompatible temperature. The microfluidic channel has a multi-layered structure for rapid separation in a high gradient magnetic field. The top and bottom layers of our device both contribute to separate the magnetically labeled bio-particles, such as animal cells and bacteria, in the vertical direction. Joule heat was exploited to supply the thermal energy to an active area of cell sample channels, and the channel temperature was maintained in the biocompatible range (37 °C) using cooling channels embedded in the top channel layer.

We numerically analyzed heat transfer for an on-chip electromagnet and solved the Joule heat problem of the device. Experimentally, we demonstrated the separation of a T-cell leukemia line, human Jurkat cells, utilizing immune-magnetophoresis. Magnetic beads with a characteristic polymer surface for coupling with CD3 T-cells made it possible to sort the human Jurkat cells with a labeling efficiency of greater than 95%. According to the cell viability test, the number of dead cells did not exceed 10% of the total, indicating that our cell sorting system did not cause any heat damage to the cells, despite utilizing electromagnets.

1. Introduction

Novel lab-on-a-chip (LOC) devices are becoming very important in the biological and medical sciences. Specifically, manipulation of magnetically activated cells in a microfluidic environment is used for trapping, sorting, and separating specific cells from a mixed cell population [1–4].

The magnetically activated cell sorting (MACS) system utilizes magnetic particles with antibodies specifically targeted to the cells of interest. A high magnetic field gradient mobilizes target cells to the sorting direction, because the target cells are tightly bound to magnetic particles. Several studies including the new creative continuous magnetic separator have reported methods for cell separation [5–7], with other groups studying bead–cell binding and immobilization using microelectromagnetic conductors on the fluidic channel surface [8]. Further advances led to the design of an on-chip magnetic bead sorting system with fully integrated microelectromagnet and microfluidic systems [9,10]. There are studies that focus on various designs of a microcoil pattern for magnetic particle separation [11].

In general, microelectromagnets generate a relatively weak magnetic field compared with permanent magnets, thus they may require a stronger current. In microelectromagnet systems, a strong current is applied to the electromagnet to generate a large magnetic field and consequently exert a great trapping force on the magnetic particles. However, the application of a high input current results in the generation of a large amount of heat within the micro-sized device [12]. The increased temperature of the device could denature proteins and irrevocably damage or destroy the cells being sorted and analyzed, rendering the device unusable for medical testing. Also, heat shock response was associated with the synthesis of heat shock proteins which was strictly regulated by heat shock transcription factors (HSFs). HSFs regulate heat induced cell death. A cell failed to synthesize heat shock proteins when subjected to typical heat shock conditions. The lack of heat shock proteins synthesis in cells was due to a failure in HSF1 DNA binding activity [13]. So cell sorting experimental time was limited in order to prevent cellular heat shock that would occur with longer high heat exposures. For these reasons, our group has previously developed magnetophoretic cell sorter utilizing a permanent magnet [14,15] and spin-valve sensor to count magnetically labeled cells in real-time [16,17]. Recently, we have demonstrated that a cooling system should be integrated onto microelectromagnets to ensure that the biological components being measured remain in their active form [18].

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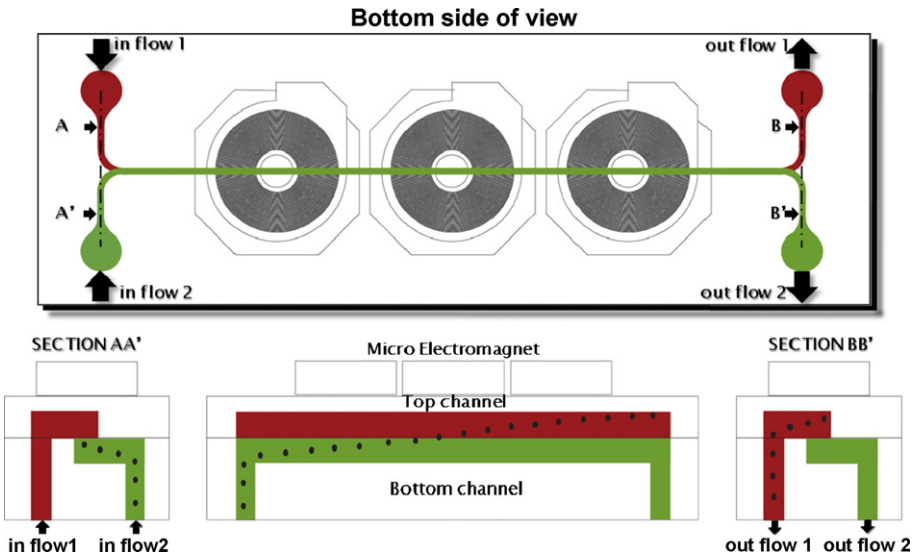

Fig. 1. Schematic diagram of magnetic labeled cell separation using on-chip microelectromagnet in multi-layer structured microfluidic channel: (i) without magnetic field: magnetic beads go through the bottom channel only (inflow2 → outflow2); and (ii) with magnetic field: magnetic beads change the path from bottom to top channel (inflow2 → outflow1).

In this paper, our newly designed microfluidic separation system is presented using an on-chip microelectromagnet. Our system has top and bottom layers of channels and aims for rapid separation in the vertical direction. The device is easily integrated with on-chip microelectromagnets and can be useful for high throughput screenings. The high gradient of the magnetic field may give rise to a mixing effect of immune affinity binding process of Jurkat cells and Dynabead® M45 CD3. Furthermore, the new system overcomes a weakness of existing Joule heating electromagnets; a cooling system was embedded in the multi-layer structured microfluidic channel to keep the internal temperatures of channel biocompatible. The integrated cooling system resides in the active area and controls the temperature of the device by using part of the Joule heat to maintain the temperature at 37 °C. The remainder of the Joule heat is dissipated. With these adaptations, our new microfluidic separation system can be used widely in biomedical applications.

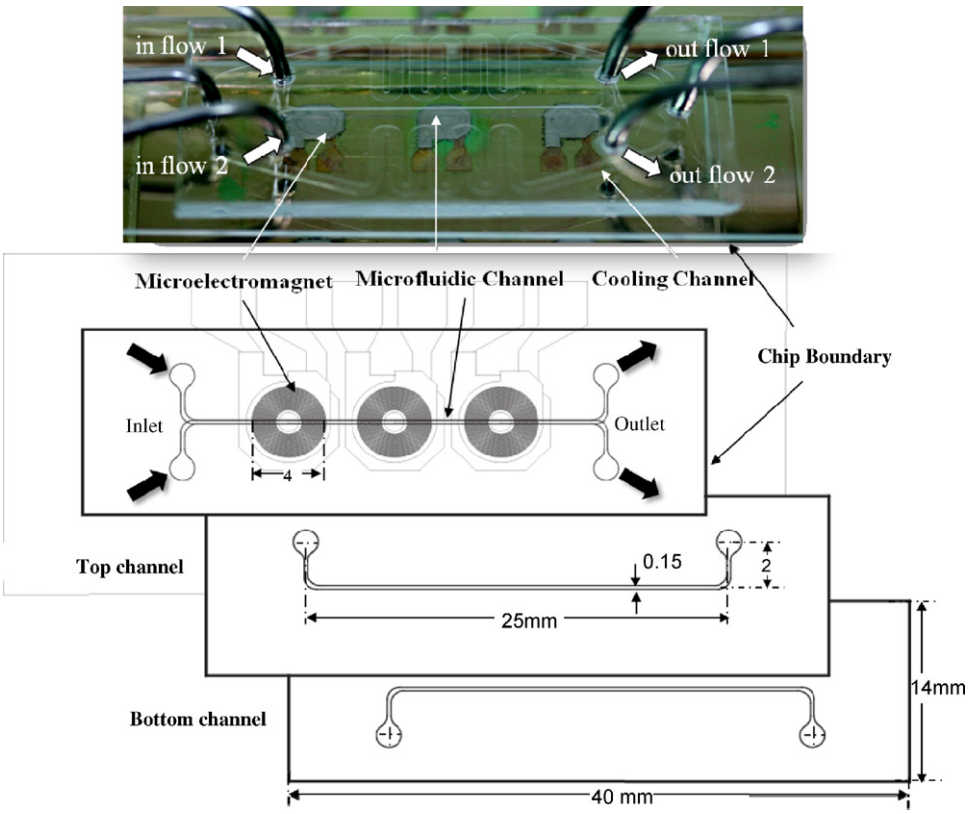

Fig. 2. Multi-layered structure channels with on-chip microelectromagnet.