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Novel application of Joule heating to maintain biocompatible temperatures in a fully integrated electromagnetic cell sorting system

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ABSTRACT

Manipulation of magnetically labeled cells in a microfluidic channel is becoming a very important technique in the field of biomedical science. A microfabricated electromagnet produces a large magnetic field gradient in a cell sorting system. The microfabricated electromagnet generates Joule heating so it causes unnecessary heat-up in the device, which has been problematic for the development of a Lab-On-a-Chip (LOC). In this paper, we present a new application of Joule heating to supply thermal energy to an active area of a microfluidic device to increase the internal temperature of the device from ambient to a biocompatible temperature, e.g. 37 °C. The temperature is maintained in conjunction with coolant. We analyzed the temperature distribution of the device numerically and the results were in good agreement with the experimental data. Our approach will facilitate development of cell chips such as a micro-mammalian cell culture or electromagnetic micro-cell sorter.

1. Introduction

The manipulation of a cell within a microfluidic device is becoming one of the most important techniques in the fields of biological and medical science. Specifically, the development of novel Lab-On-a-Chip (LOC) device is based on the trapping and sorting of magnetic bead-labeled cells via the use of a magnetic field in the microfluidic device [1–3]. Previous works on cell separation techniques have demonstrated the feasibility of using external permanent magnets [4,5], instead of embedded electromagnets. Recent advances in this field have led to the design of an on-chip magnetic bead sorting system with a fully integrated microelectromagnet and microfluidic system [6,7].

In these micro 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 beads. The typical trapping force created by the microelectromagnets is in the order of 100 pN resulting from strong magnetic fields ($B \sim 0.1\,\mathrm{T}$) and field gradients ($VB \sim 10\,\mathrm{T/m}$) [8]. However, the application of high input current results in the generation of a large amount of heat within the microdevice [9]. An increased temperature of the device, such as a cell sorter, would denature proteins and irrevocably damage or destroy the cells being sorted and analyzed, rendering the device unusable for medical testing. Also, the time of experiment was limited, only 3–5 min, because we should prevent the cell from having a heat shock under the undesired circumstance [10]. Due to this issue, a cooling system must be integrated to ensure that the biological components being measured remain in their active form. In this study, we used Joule heat emitted from the electromagnet to increase the temperature of the device from ambient temperature. So in new device design, it is important to identify and manage the heat source of device in order to maintain biocompatible temperatures, 37 °C.

In order to create this temperature controlled microdevice, an on-chip microelectromagnet and an integrated microfluidic cooling system was fabricated to maintain internal temperatures. While a conventional cooling system is located away from the device, our new integrated cooling system resides in the active area and controls the temperature of device by using a part of the Joule heat to maintain 37 °C. The rest of the Joule heat was dissipated. A multi-layered thermal chip model was also developed to analyze the temperature distribution of the device for the purpose of verifying the experimental data.

2. Material and methods

2.1. Design

The novel design of our on-chip microelectromagnetic and microfluidic system for magnetophoretic separation of biological samples is illustrated in Fig. 1 This system is composed of three regions according to different compositions along the z-direction, those being: a polydimethylsiloxane (PDMS) microfluidic channel,

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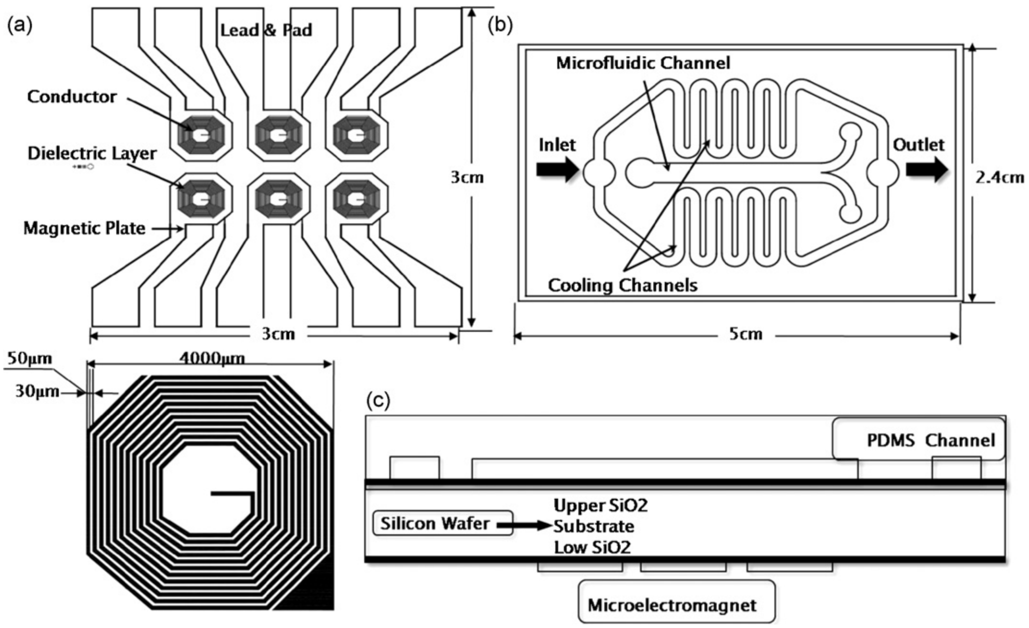


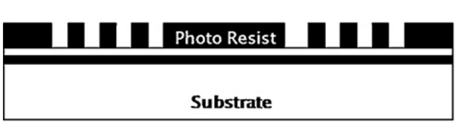
Fig. 1. Schematic illustration of the on-chip microelectromagnet/microfluidic system; (a) on-chip microelectromaget, (b) microfluidic system, (c) front view of system.

a silicon wafer, and a microelectromagnet. The microfluidic system is made up of two fluidic channels, one used for magnetophoretic cell separation and the other used to dissipate a portion of the Joule heat from the electromagnet. The silicon wafer consists of an upper silicon oxide (SiO_2) layer, a substrate layer, and a lower silicon oxide layer. The on-chip microelectromagnet is composed of six electromagnets, which are built onto the backside of the silicon wafer. The thermal conductivity of silicon is high enough to transfer thermal energy easily from the electromagnets to the active area of the microfluidic device.

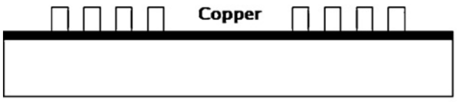
2.2. Fabrication

The microelectromagnet was fabricated using MEMS technology [11,12]. The fabrication process for on-chip microelectromagnet is illustrated in Fig. 2 as follows: (a) SiO_2 was deposited 1 μm on a double-side-polished Si wafer by furnace and the microconductor was patterned using UV-lithography; (b) a copper microcoil, as a conductor for the microelectromagnet, was manufactured by 25 μm thick electroplating with a photoresistor mold [13]. For the electrical insulation, the dielectric layer based on polymer material (AZ4620, Clariant, Korea) was deposited between the microcoil and the magnetic plate; (c) The polymer, as a dielectric layer, was encapsulated on the microcoil and was hard-baked; (d) The seed layer, Ti/Ni 500/3000 Å, was deposited onto the dielectric layer for electroplating of the nickel plate; (e) the nickel, as a magnetic plate, was electroplated 25 μm thick and (f) the PDMS microfluidic channel system was integrated [14].

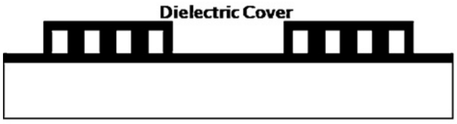
The design parameters for the electromagnet are described by the following specifications: (a) the size of the electromagnet is 4 mm × 4 mm; (b) the width of the microcoil is 50 μm; (c) the height of the microcoil is 25 μm; (d) the gap between microcoils is 30 μm;



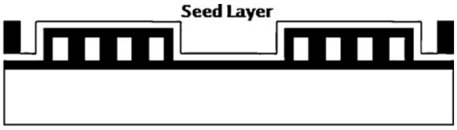
(a) Micro conductor Patterning



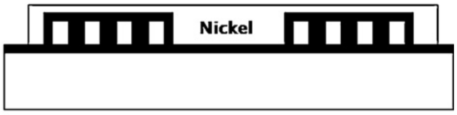
(b) Copper Electroplating



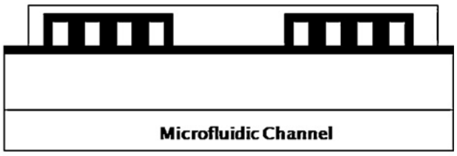
(C) Resist Coating and Hard bake



(d) Magnetic Plate Patterning



(e) Nickel Electroplating



(f) Integrated Microfluidic System

Fig. 2. Fabrication processes of the microelectromagnet and microfluidic system.