Thermally Actuated Microfluidic System for Polymerase Chain Reaction Applications

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1 Introduction

Lab-on-Chip (LOC) systems, in which functionalities as handling, treatment, and detection of biological solutions are downsized and integrated, represent one of the most attractive device for biomolecular and chemical analysis [1–4]. In particular, implementation of the polymerase chain reaction (PCR) in LOC devices has received a lot of attention [5–7] for applications such as DNA finger printing, genomic cloning, and genotyping for disease diagnosis. Indeed, its miniaturization results in reduced consumption of samples/reagents, shorter analysis times, and higher sensitivity and portability. Different solutions in terms of materials for the substrate and for the microfluidics have been proposed.

In this paper the authors present the design, fabrication, and characterization of a LOC system for DNA amplification based on a PolyDiMethylSiloxane (PDMS) microfluidic structure with integrated thermo-actuated valves and indium tin oxide (ITO) heaters. The use of these materials coupled with their deposition on a microscope glass presents features of easy fabrication, low cost, transparency, and biocompatibility.

2 LOC Design

The structure of the proposed LOC system (see Fig. 1) comprises:

1. A microfluidic network, made in PDMS, that includes a rectangular channel for inlet and outlet, a chamber for the PCR, and two thermo-actuated valves.

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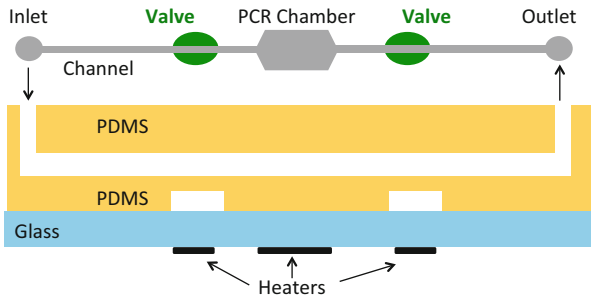

Fig. 1 Top view and cross section of the proposed LOC system

2. Three thin film heaters. Two of them, located at the inlet and outlet positions of the chamber, actuate the valves and allow the chamber isolation, while the last one, positioned below the chamber, is dedicated to the PCR thermal cycle.
3. A glass substrate hosting the microfluidic network on one side and the heaters on the opposite side.

The solution to be amplified is injected in the microfluidic channel through the inlet. As the channel and the PCR chamber are filled, the two heaters below the valves are actuated to avoid sample losses, due to the pressure developed in the reaction chamber during the thermal cycles. Indeed, applying power to the heaters, the air contained in the valve reservoir (rectangular white spaces over the heaters in Fig. 1) heats up and increases its volume creating a pressure that pushes up the PDMS membrane into the channel. As the valves are closed, the PCR cycle may begin by turning on the heater below the PCR chamber.

3 PCR Chamber Design

As reported in Fig. 1, the shape of the PCR chamber is rhomboidal-like in order to avoid air bubble formation [6] during chamber filling. The chamber size is $8 \times 4 \times 0.05$ mm^3 providing 1.6 µl solution volume for DNA amplification.

4 Heater Design

In order to achieve a uniform temperature distribution inside the PCR chamber, the geometry of the PCR chamber heater and the distance between the three heaters have been optimized using the software COMSOL Multiphysics. We found that selecting a chirp geometry for the PCR chamber heater [8], a serpentine geometry for the valve heaters, and 6 mm distance between the valve heaters and the PCR

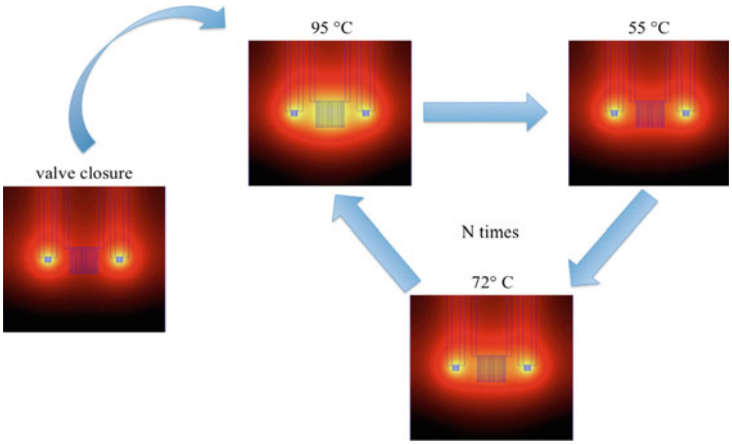

Fig. 2 Temperature distribution over the heaters during the simulated PCR cycles

chamber, the temperature uniformity in the PCR chamber is better than 3 % for the three temperature steps, satisfying the PCR technique requirements. A simulated temperature distribution during a PCR cycle along the microfluidic network is reported in Fig. 2.

5 Valve Design

The valves have a cylindrical shape with diameter and height equal to 500 µm and 50 µm, respectively. These sizes have been chosen, as a result of finite element simulations, to ensure that the deformation of the valve membranes closes the microfluidic channel when the heaters are turned on.

6 LOC Fabrication and Testing

Device fabrication begins with the deposition of the ITO thin film heaters by magnetron sputtering on one side of a $5 \times 5 cm^2$ ultrasonically cleaned glass substrate. The film thickness is 200 nm, the same utilized in the simulations.

The PDMS structure was obtained by using soft lithography techniques. Two 50-µm-thick SU-8 molds were fabricated and patterned by photolithography: the first for the thermo-actuated valves and the second one for the microfluidic channel and the PCR chamber. PDMS was spun on the first mold in order to obtain a 100-µm-thick layer and a 50-µm-thick PDMS membrane over the SU-8 cylinders. PDMS was also poured onto the second mold to achieve a 3-mm-thick structure. The two PDMS structures were merged using the partial curing method [9], and

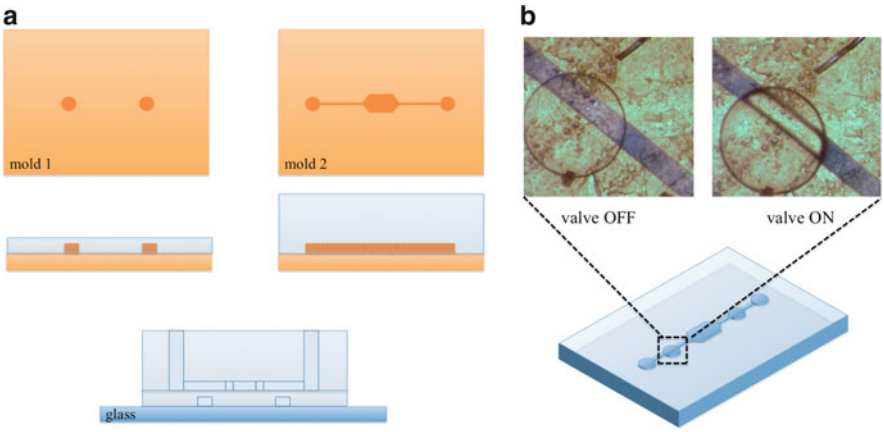

Fig. 3 (**a**) Schematic representation SU-8 molds and PDMS device fabrication (channel cross section: 500 μm×50 μm, PCR chamber volume: 1 μl); (**b**) demonstration of thermal valve actuation

subsequently the overall microfluidic device was bonded to the heaters on the glass substrate by oxygen plasma (Fig. 3a).

The PDMS microfluidic channel was filled with a mix of water and a blue dye in order to easily monitor the fluid position during the experiment. The valve-heater temperature has been raised slowly, and the behavior of the valve has been monitored under the microscope. Valves activation began around 60 °C, and complete closure was observed around to 100 °C as shown in Fig. 3b, without any loss of liquid from the chamber.

7 Conclusions

This paper has presented the design and fabrication of a microfluidic network integrated with thin film heaters for implementation of the PCR technique in Lab-on-Chip systems. The heaters have been designed to achieve temperature uniformity inside the PCR chamber better than 3 % at each temperature of the DNA amplification cycle. The microfluidic network, made in PDMS, includes two thermally actuated valves, whose successful operation in avoiding loss of samples from the PDMS chamber has been demonstrated.

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