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A Self-contained Microfluidic Platform Combining Pumps and Valves for Biochemical Applications

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Abstract

The novelty of this study lies in the fabrication of an all-polymer-based, self-contained, integrated microfluidic platform comprising a microvalve, a micropump, channels, chambers, heaters, and sensing electrodes for bioanalytical applications. A cyclo-olefin copolymer (COC) top substrate molded by hot embossing and a COC bottom substrate fabricated by polymer injection molding are bonded using an ultrasonic bonder and hermetically sealed. A polyimide substrate with an embedded microheater is then bonded with UV-curable epoxy. Thermally actuated paraffin-based microvalves and a micropump powered by chemically produced carbon dioxide gas were integrated on the chip to provide fluidic movements. The device is self-contained; external pressure sources, fluid storage, mechanical pumps, and valves are not necessary for fluid manipulation, which eliminates any chance of sample contamination and makes device operation simple. The platform can provide cost-effective biochemical analysis and has great potential for point-of-care testing, environmental testing, and biological analysis with integrated microfluidic control.

Keywords: Polymer devices, Integrated microfluidic platform, Self-contained, Microfluidic pump and valves

Introduction

Developments in production protocols for polymer-based microdevices have been in the limelight[1-3]. With the advancement of microelectromechanical system (MEMS), silicon has been widely used as a base material for microdevices. However, owing to the high costs of material and fabrication, silicon is no longer competitive compared with polymers for single-use biochemical microdevices. With the speedy market expansion for microfluidics-based biochips, including protein and DNA chips, many researchers have sought cost-effective materials and fabrication methods. Currently, cyclo-olefin copolymer (COC) is of interest owing to its good chemical and optical properties. Microfluidic components, including micropumps and microvalves, are generally required to control fluid flow in microelectromechanical systems and furthermore, for integration on a single substrate[4,5]. Integrated biochips have been reported for performing functions that include sample preparation, mixing, chemical reactions, and detection in a miniature fluidic device for genomic analysis[6-8], glucose sensing[9], immunoreaction[10,11], and cell-based biochemical analysis[12,13]. However, most systems require complex components, high-cost fabrication, and compatibility with other instruments. Most fabrication processes are not compatible with integrated circuit mass-production technologies.

A simple, low-cost, precise-control microfluidic platform can meet the requirements of point-of-care diagnostics or in-field environmental testing[14]. For this purpose, many passive microfluidic components, including capillary pumps and diffuse valves, have been reported because of their simplicity and cost-effectiveness[15,16], but there are still problems concerning reliability, leakage, and pumping power. Polymer-based active microfluidic components using simple embedded heaters or chemical reactions can achieve the desired functions with a simple structure, low fabrication cost, and high reliability.

In this paper, we report on a novel self-contained, integrated COC/polyimide polymer-based microfluidic platform applicable to portable point-of-care diagnostics and biochemical analysis. The platform comprises a microvalve, a micropump, channels, chambers, heaters, and electrodes for sensors. The design, fabrication, and functional characterization of the microfluidic platform device are demonstrated.

Results and Discussion

The microfluidic chip consists of a COC top sub-

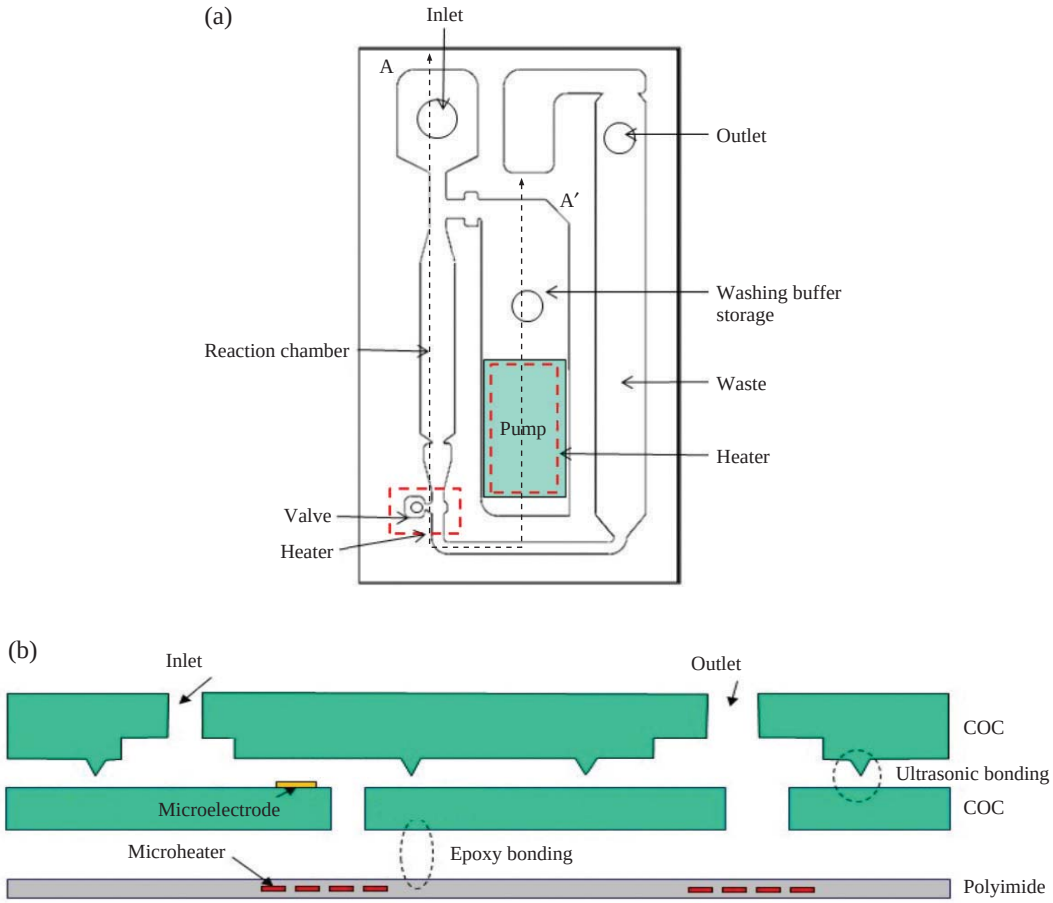

Figure 1. (a) Schematic diagram of the polymer microfluidic device. The reaction chamber is filled with a sample mixture by capillary force and the chemically-driven pump is used to wash the reaction chamber. (b) The cross-sectional view (A-A′) of the integrated polymer microfluidic device.

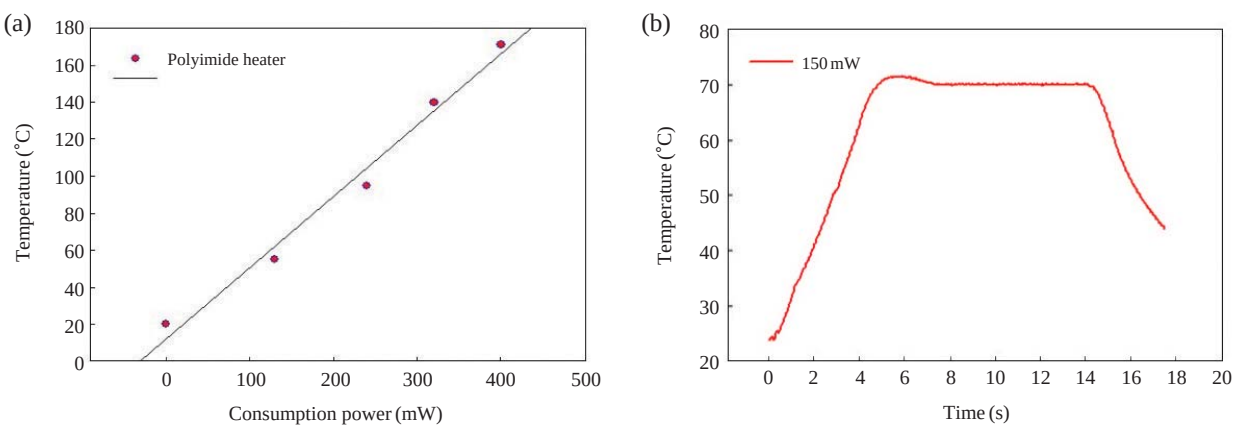

Figure 2. (a) Temperature versus consumption power response curve and (b) thermal response as a function of time for the polyimide-chip microheater.

strate comprising microfluidic channels, chambers, inlets, and outlets, a COC middle substrate with Au electrodes for sensing, and a polyimide bottom substrate comprising a microheater, a temperature sensor,

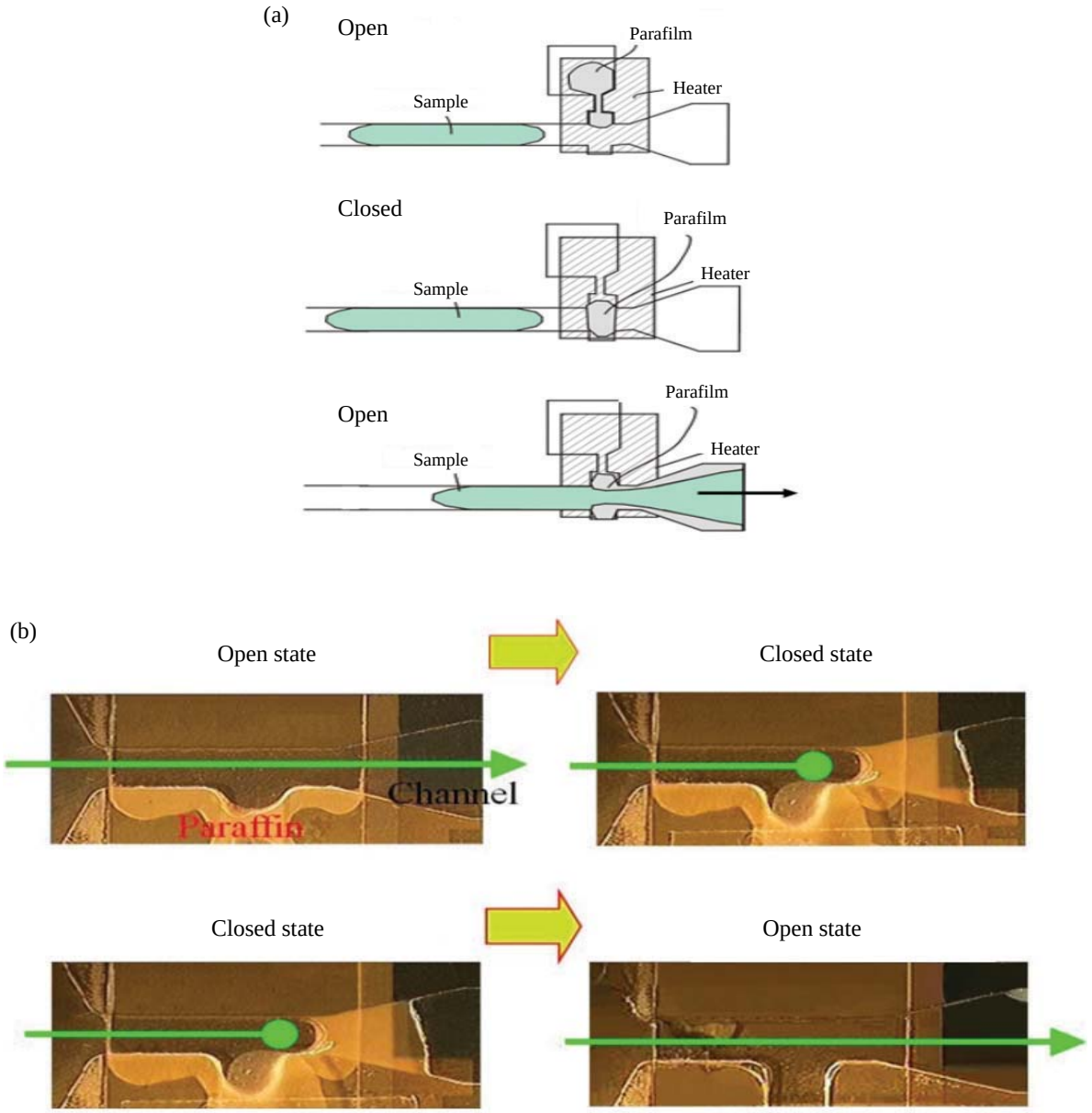

Figure 3. (a) Working schematics of the COC-based microvalve and (b) images showing the working of the fabricated microvalve.

and control circuitry. A schematic view of the integrated microfluidic device is shown in Figure 1(a).

The operation of the microdevice is as follows. A biological sample mixture is loaded through an inlet hole into a chamber. Washing buffer solution is loaded in the other storage chambers. The microfluidic device is then inserted into an instrument that provides electrical power. The sample mixture is pumped by capillary force from the inlet hole into the reaction chamber, where target biochemical reactions take place. After the reaction chamber is filled with the sample mixture, the microvalve closes. The microvalve remains closed through the biochemical reaction/detection. After the process, the washing buffer is pumped by the pressure of chemically-produced gas through the reaction chamber to remove the undesired remaining chemicals. Electrochemical or optical signals corresponding to the biochemical reaction/detection are detected on the chip and recorded by the instrument. In this study, an electrode array for electrochemical sensing is fabricated. The cross-sectional view of the microfluidic platform containing microelectrode is shown in Figure 1(b). The alternating current voltammetry techniques for obtaining electrochemical signals corresponding

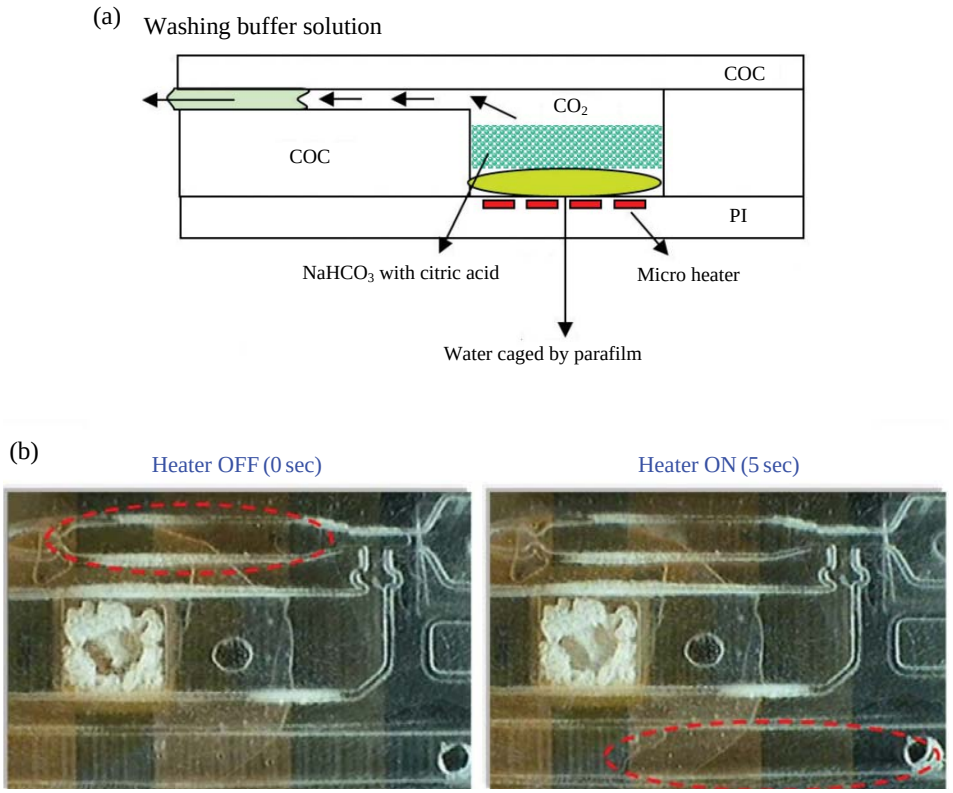

Figure 4. (a) Working principle of the COC-based micropump and (b) images showing the fluid movement by the fabricated micropump.

to enzyme reaction have been described in detail in the literature[17].

To observe the performance of the fabricated microfluidic chip, the thermal properties of the heating elements on the polyimide-based film device, including the temperature-consumption power and the time response curve, were investigated. Two copper resistive lines were used as a heater and resistive temperature sensor. The resistance linearly increased over the temperature range 20-120˚C and the approximate temperature coefficient of resistance was 3,000 ppm/K, which fits the Callendar-Van Dusen equation. The microheaters were used to melt the paraffin wax for valving and the Parafilm for pumping. With the simple resistive heating and passive cooling of the heaters, consumption power less than 250 mW was needed to heat to 100˚C as shown in Figure 2(a). This means that the technology can be applied to a battery-powered handheld system. Even though a polymer substrate had very low thermal conductivity of 0.12 W/(mK), the much reduced thermal mass of the microfabricated polymer heating film facilitated fast heating (~10˚C/s) and cooling (~8˚C/s) during the pumping and valving of the fluidic chip, as shown in Figure 2(b).

Figure 3(a) shows images of the working of the microvalve on COC substrate using paraffin wax and the polyimide microheater. The microvalve was open for the filling of the chamber, and then closed via the melting of Parafilm by the embedded microheater. After the biochemical reaction/detection, the valve opened via heating by the microheater to above the melting temperature. To obtain the melting temperature of ~70˚C, power consumption of 150 mW was required. Figure 3(b) shows enlarged images of the opening and closing of the microvalve. Liu *et al.* reported a paraffin microvalve fabricated on a printed circuit board with a thickness greater than one milimeter[6]. In that case, the thermal response, with the heater on, was very slow and power consumption large. However, the microfluidic device in this study, which was microfabricated on a flexible printed circuit board with a thickness of 70 μm, has less thermal mass, resulting in a very fast thermal response (~10˚C/s) and low power consumption. It took about 5 seconds of heating to melt the paraffin wax to work the valve. A silicon-based microheater with very fast thermal response and very low power consumption has been reported[18]; however, it has very complex fabrication steps and consumes high fabrication cost. In addition, it is fragile to outside shock. However, the polyimide heater is fabricated easily with thin film thickness using the flexible printed circuit board (FPCB) protocols, which are one of the most popular processes in microfabrication technology.

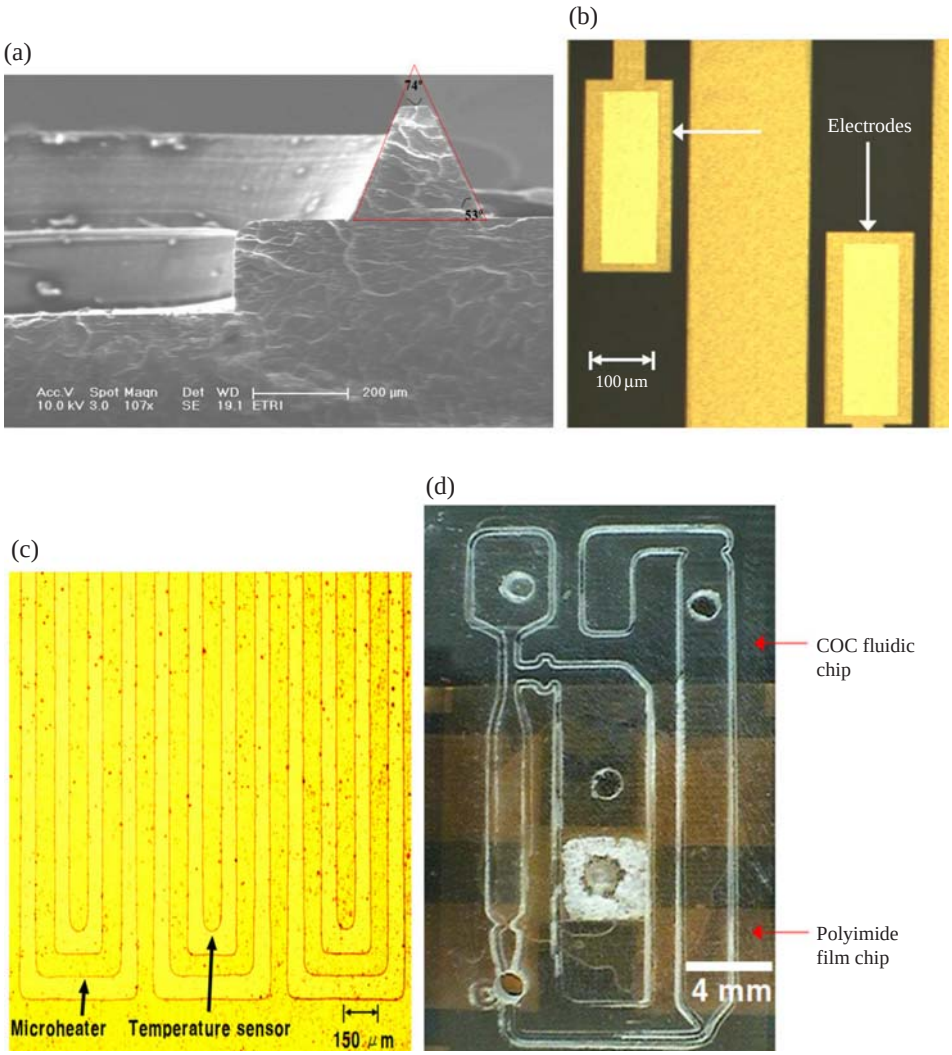

Figure 5. Images of (a) the microfabricated microfluidic COC lid (first layer), (b) the micropatterned electrodes on COC (second layer), (c) the micropatterned heater on polyimide (third layer), and (d) the final microfluidic device composed of the three laminated layers for biochemical analysis.

Figure 4(a) shows the working schematics of the polymer micropump using a water drop encapsulated in Parafilm and $NaHCO_3$ with citric acid. When the microheater produces the melting temperature (~70°C), the Parafilm melts and the caged fluid starts to react according to reaction (1).

$$2NaHCO_3(s)+HOC(COOH)(CH_2COOH)_2(s) \rightarrow HOC(COOH)(CH_2COONa)_2(s)+2H_2O(l)+2CO_2(g) \quad (1)$$

The initial thickness of Parafilm was about 100 μm, and the film was thinned to about 20 μm. The thinned Parafilm could be simply melted. As a result, CO_2 gas generated abruptly and it could strongly push the reaction solutions from the reaction chamber to the waste chamber. Figure 4(b) shows images of the movement of solution in the 10 μL volume reaction chamber when electric power was applied to the microheater.

The micropump using the chemical reaction has a simple structure but is powerful in moving the solution in the microchannels. Hong *et al.* reported a chemical micropump that uses nitrogen gas as the pumping source[19]. Azobis-isobutyronitrile for the production of nitrogen gas was decomposed using a microheater. That pump requires continuous activation, whereas ours requires only single ignition using a microheater. Therefore, we believe that the CO_2 micropump is a powerful and versatile tool for biochemical applications, including the transportation of solutions. Finally, the proposed micropump exhibited a fluid flow rate of about 4 mm/s for a 3 μL volume.

The integrated microfluidic platform with functionalities of capillary filling, paraffin wax-based valving, electrochemical detection, and chemically reacting fluidic motion on the same substrate demonstrates potential for applications to integrated, self-contained, and disposable biochemical lab chips.

Conclusions

We have designed, fabricated, and characterized an all-polymer-based, self-contained, integrated microfluidic platform. It comprises a microvalve and micropump, channels, chambers, heaters, and electrodes for sensors, all polymer-based, and can be used for biochemical analysis. The structure is a COC top microfluidic component, a COC middle microelectrode component, and a polyimide bottom microheater component, all of which are simple and cost-effective. The pumping and valving are performed by the simple heating of paraffin barriers to enable fluid flow or chemical reaction. Wash buffer solution and chemicals for pumping and valving are contained in the microfluidic platform. The valve based on paraffin wax and a microheater embedded in the polyimide film has fast thermal response (~10˚C/s) and low power consumption (150 mW). The polymer micropump based on the chemical production of carbon dioxide gas using a polyimide microheater is integrated on the chip to provide a buffer solution. The micropump has a fluid flow rate of about 4 mm/s for a 3 μL volume. The resulting device is self-contained; pressure sources, fluid storage, chemical pumps, and valves used for fluid manipulation are all internal, so the device eliminates sample contamination and makes for simple operation. This platform would provide a cost-effective device for mass production.

Materials and Methods

A COC top substrate is fabricated by hot embossing and a COC microfluidic substrate is molded by polymer injection to make a 5-inch wafer. These two parts are bonded with an ultrasonic bonding machine and hermetically sealed. Using photolithographic protocols, the Au/Cr electrodes are micropatterned on the COC middle substrate[17]. A polyimide bottom film substrate including a microheater and a micro-resistance temperature detector is fabricated using FPCB protocols. It is further bonded to the middle COC substrate with a UV-curable epoxy. A high-resolution computerized numerical control machine is used as a metal master for the microfluidic substrate, and the surface is chemo-mechanically polished. The microfluidic components are hot-embossed. Two inlet ports and an air vent are made by drilling through the COC top component. After filling the chambers with the sample mixture and wash buffer solutions, the holes are sealed with adhesive tape. Fabrication of the paraffin-based microvalves in the microfluidic chip begins with instantly heating the plastic chip above the melting temperature of the paraffin (70˚C) using a soldering iron. Solid paraffin (~3 mg) is put into the paraffin access holes on the chip. The melted paraffin is driven into the channels by capillary force. By removing the soldering iron, the paraffin solidifies on the polyimide film with heat from the microheater and forms a microvalve in the chip. The paraffin access hole is sealed with adhesive tape. For fluidic transport of washing buffer solutions, chemically generated CO_2 gas is employed. A water drop of diameter 2-3 mm encapsulated in Parafilm, $NaHCO_3$ powder (~2 mg), and citric acid powder (~1 mg) are placed together in the chamber. The mixture access hole is sealed with an adhesive tape. A scanning electron microscopy image of the top component microstructure is shown in Figure 5(a). An image of the middle component, bottom heater component, and final microfluidic platform fabricated using the protocols are shown in Figure 5(b)-(d). The polymer chip measures 20 mm × 30 mm × 2 mm and has channels and chambers that range from 200 μm to 1.2 mm in depth and 0.5 to 3 mm in width.

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