A PRINTED CIRCUIT BOARD BASED MICROFLUIDIC SYSTEM FOR POINT-OF-CARE DIAGNOSTICS APPLICATIONS

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ABSTRACT

We propose an alternative approach for fabricating microfluidic devices by using printed circuit board (PCB) as a substrate to produce high precision, highly integrated microfluidic systems. Driven by consumer electronics industry, the PCB manufacturing has reached a high level of maturity and precision, enabling the production of sophisticated electronic substrates at high-resolution and low cost. Lacking the integration capability in current microfluidic technology, PCB makes an ideal platform for producing microfluidics for lab-on-a-chip applications. We report the development of new techniques to integrate microfluidics with PCBs. Isotachophoresis was performed as a demonstration to employ such devices for point-of-care applications.

KEYWORDS: PCB, Integrated microfluidics, Diagnostics

INTRODUCTION

Microfluidic systems promise benefits of bio-chemical analysis with high performance, versatility, small sample, portability and rapid processing. However, these advantages can only be realized if multiple components and functions can be integrated onto a single platform. This has been a significant challenge for microfluidic chip fabrication. Typical methods for fabricating lab-on-a-chip platforms involve embossing, etching, or soft-lithography in polymers and glass [1]. Current manufacturing techniques do not readily allow the integration of functional electronics onto a single device. A microfluidic device containing integrated functions must include components designed from scratch and integrated monolithically during manufacture. This is highly inefficient and requires each chip designer to design a unique masterpiece, significantly hindering standardization and commercialization.

THEORY

We report on an alternative approach to microfluidic manufacturing by fabricating and building microfluidic devices onto printed circuit boards (PCB) for integrated on-chip electronic control and cost reduction. PCBs are manufactured in large quantities at high precision and low cost, readily integrated with functional components [2-3], making this an attractive platform for integrated microfluidics. In the PCB model, the designer can choose from hundreds of standardized specialty components that have been optimized for a function, and standardized for use on a printed circuit board.

Microfluidics devices are typically characterized by structures having small feature sizes but only in limited regions of a large surface area substrate (usually "chips" are cards several centimeters in size). Furthermore, most microfluidic devices require many different technologies and materials that are not readily fabricated in a monolithic process. For example, an integrated microfluidic device may require electrodes, valves, pumps, heaters, sensors, and optics, all of which may require different manufacturing techniques. Thus the monolithic, small footprint paradigm of the semiconductor chip is a woefully inadequate manufacturing model for microfluidics. However, the heterogeneous manufacturing paradigm of the modern printed circuit board gracefully demonstrates how one can integrate multiple high precision components on to a single low cost substrate.

Isotachophoresis (ITP) is a capillary-based separation technique that uses multiple buffers of different mobilities produce a discontinuous electrical field, thus creating sharp boundaries between sample constituents and focusing the sample analyte [4]. Without the need for pinch injection, ITP is a powerful electrophoresis technique for simultaneous extraction, purification and preconcentration from sub-microliters of biological samples such as blood and urine which then identifies the target infection in a matter of minutes. This separation technique is traditionally performed in glass capillaries, but it can also be performed in polymers such as epoxy or polyurethane, which we currently use for PCB-based microfluidics.

EXPERIMENTAL

To demonstrate the feasibility of employing such systems for point of care diagnostics applications, e.g., malaria detection in developing countries, we fabricated a portable PCB-based microfluidic system to perform lysis and ITP. Figure 1a shows the side-view schematic of the device including a surface mount on-chip thermal component (figure 1c) in sample reservoirs for sample lysing and mixing via thermal convection. The two sample reservoirs are connected to a microchannel (figure 1b), which after lysis, ITP-based extraction is performed to separate the target nucleic acid from the lysate using on-board platinum electrodes.

The key steps to our fabrication include the application of a lithographically definable planarizing polymer layer [5], which provides a flat, biocompatible surface for microfluidics, yet also enables optional fluidic connections to the electronics layer below. This dry negative photosensitive polymer, 1002F, can be applied by hot press, allowing multiple fluidics layers to be integrated onto PCB at different stages of manufacturing. The detailed fabrication step of using 1002F dry resist on PCB is shown in figure 2, which includes surface mounting electronics on PCB, 1002F planarization and encapsulation, 1002F fluidic layer patterning and sealing. With this technique, we were able to achieve high aspect ratio structures over 1 mm in height, which would be extremely difficult using traditional lithography method.

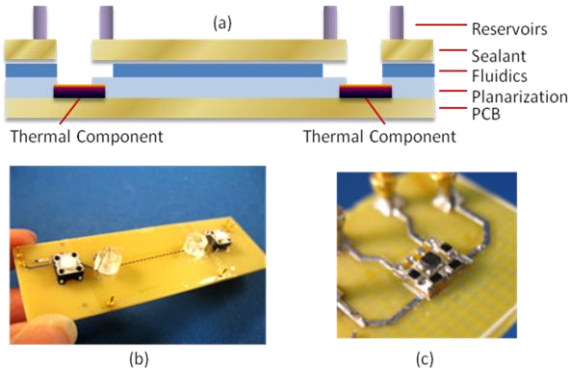

Figure 1: (a) Schematic showing full device in side view, indicating major features of the unit. (b) Prototype of the ITP device on PCB with integrated thermal component/electrodes in reservoirs connected to the microchannel (3 cm x 70 µm x 50 µm, indicated by dotted line). (c) Prototype of the thermal component consisting of four resistive heaters and a temperature sensor packaged together as a surface mount component (3 mm x 3 mm x 900 µm), which can be simply picked and placed onto the main PCB as shown in (b).

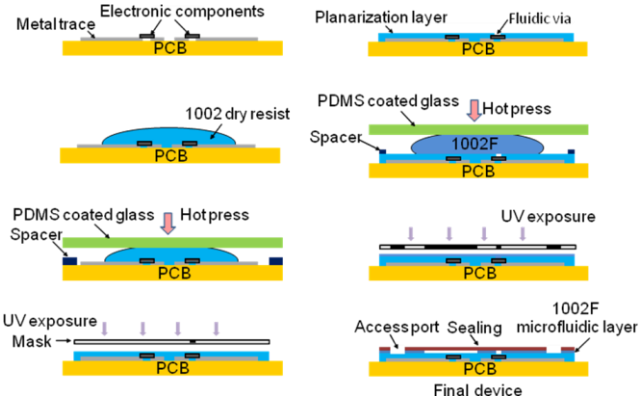

Figure 2. Detailed 1002F fabrication process on PCB using hot pressing and lithography. The steps include surface mounting electronic components on PCB, 1002F planarization, encapsulation and patterning, 1002F microchannel patterning, and finally sealing. The process enables immense flexibility in type and number of surface mounted components (e.g., resistors, LEDs, sensors, and photodiodes) embedded beneath the microfluidic device channels.

RESULTS AND DISCUSSION

To mimic the lysing of the cells in sample reservoirs, we performed heating and mixing using the integrated thermal component. Temperature response and on-chip thermal convection studies were conducted to characterize the component. We applied 0.25A at 4V to the thermal component in the reservoir and recorded a temperature response curve for 50 µL of deionized water (figure 3a). Lysing temperature (85^{o}C) was reached within one minute. Thermal convection induced mixing was readily observed by seeding the solution with 6 µm fluorescence beads. The microbeads produced rapid movement upon the application of current shown as streaks in figure 3a, with moving direction indicated by red arrows.

ITP extraction on PCB microfluidics was achieved by running a standard Alexa-Fluor assay. The microchannel was initially loaded with a leading electrolyte buffer and a terminating electrolyte buffer containing the Alexa-Fluor 488 fluorescent dye. As shown in figure 3b, immediate separation and focusing were observed upon application of 100 V/cm using on-chip platinum electrodes. We then performed thermal lysis and ITP extraction using Malaria-infected human blood. The sample reservoir was

loaded directly with untreated blood containing malaria parasite P. falciparum, which was thermally lysed at 85°C for 10 minutes releasing the target nucleic acids. Due to the auto fluorescence of the PCB substrate material (epoxy resin FR-4), we imaged the ITP extraction in a glass microchannel after lysis, using SYBR Gold DNA-selective dye as shown in figure 3c. In the future, we will modify the fabrication technique by laminating low or none auto-fluorescent materials on PCB before integration of microfluidics or providing an access window on board for imaging.

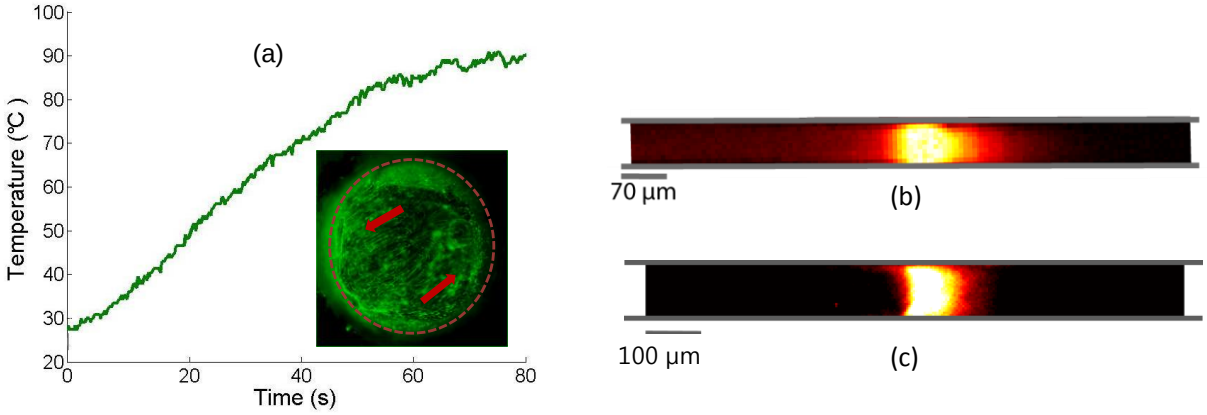

Figure 3. (a) Plot showing the temperature response curve of 50µL of DI water in sample reservoir, with applied power at 0.25A and 4V. The required lysis temperature was achieved within one minute. Image of thermal convection/mixing during heating is shown by seeding 6 µm fluorescence beads into the flow and imaging under UV light. Particle streaks demonstrate strong thermal convection and vigorous mixing. (b) Alexa Fluor 488 focused on PCB channel, using leading electrolyte, 50 mM Tris HCl, and terminating electrolyte, 25 mM Tris Hepes. (c) Malaria-infected blood is thermally lysed on PCB, extracted, and focused in a glass microchannel (for imaging purpose).

CONCLUSION

We present a PCB-based approach to integrate microfluidics. This alternative method can be used for real-world applications by fabricating and demonstrating a point of care device, with on-chip heating, mixing, and ITP successfully. With its excellent manufacturability and high degree of integration, PCB-based microfluidics presents a potential opportunity and feasible solution for multi-functional microfluidic devices in biochemical applications.

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