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A stand-alone pressure-driven 3D microfluidic chemical sensing analytic device

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ABSTRACT

This study introduces a new stand-alone pressure-driven 3D microfluidic chemical sensing analytic device (PD-PAD), fabricated by enclosing a cover substrate and inserting a void-channeled substrate on a conventional capillary-driven microfluidic paper-based analytical device (CD-PAD). Adhesive cold-laminating film and filter paper were used as a substrate. The flow rates of 3D PD- and CD-PAD platforms were compared through five different character-shaped microfluidic channels. A single 60-μL drop of fluid inducing 0.4 mbar of pressure showed that the PD-PAD was roughly 300-fold faster than the CD-PAD. The more input pressure in the PD-PAD increased, the more flow increased. The structures with the curved channels less than 90° led to a decreased flow rate in the CD-PAD, but did not affect the PD-PAD. The superior flow rate in the PD-PAD was likely due to the concurrence of the pressure-driven and capillary-driven flows. The glucose and albumin concentrations with a clinically relevant range and pH levels were successfully detected. Therefore, a stand-alone 3D microfluidic PD-PAD platform has great potential for assessing for the presence of diseases in very urgent situations such as the operating room or for use in low-cost and fast point-of-care applications.

1. Introduction

The microfluidic paper-based analytical device (PAD) is functionalized as a platform for performing rapid diagnostic tests requiring biochemical and analytical sensing [1,2]. The capillary-driven microfluidic PAD (CD-PAD) offers a portable and miniaturized platform at a low-cost, with very low minimum volume requirements and no need for external power, and is a highly value-added business [3–5]. The microfluidic PAD contains hydrophilic channels that are delimited by hydrophobic barriers on the paper. Its patterning provides quantitative control of the bio-fluids on the chromatography and filter papers using pure capillary force without external switches and valves. In particular, various hydrophobic patterning techniques have been suggested for the fabrication of paper-based point-of-care (POC) diagnostic devices, including photolithography [6,7], silane and UV/O_3 patterning [8], PDMS printing [9], inkjet printing [10–12], plasma treatment [13], flexographic printing [14], wax printing [15–23], wax dipping [24], computer-controlled knife shaping [25], and CO_2 laser cutting [26]. The wax printing technique with a non-toxic reagent is considered to be one of the best methods for the laboratory-scale fabrication of POC platforms. However, this method cannot fabricate precise nano-scale channels. Also, since the wax impregnation could lead to the deformation of channels, it is very important to develop portable bio-sensing platforms with well-controlled patterning for applying the proper capillary force and acquiring the proper flow rate.

The conventional microfluidic PAD is made up of an open channel exposed to the environment. Although it has a fast and simple fabrication process and good sensing ability, the open channel results in some limitations such as a loss of samples and the ease of contamination. In particular, evaporation-driven fluid loss leads to a low efficiency of sample delivery and limits the travel of fluids. Several attempts to overcome the disadvantages of open channels have been reported. There are two categories of open channels: a channel enclosed by other materials or a hollow channel with void space. Jahanshahi-Anbuhi et al. [18] fabricated sandwiched channels by two flexible polyster films. The film-based sandwiching channels were ten-fold faster than open channels. Schilling et al.

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[19] invented fully enclosed channels by printing the black toner on the top and bottom faces of the microfluidic PAD. The toner-enclosed channels showed 32–40% increases in flow rate compared to open channels. However, this result was only possible under 53% relative humidity, and the toner printing resulted in a <10% degradation of enzyme activity. Glavan et al. [27] designed omniphobic hollow channels by the gas-phase infusion of a fluoroalkyl silane on engraved thick cardstock paper. This channel showed a fast, laminar flow; however since it required the injection of fluids by a syringe pump, it was not appropriate for POC applications. Renault et al. [20,21] suggested a microfluidic PAD with hollowed channels by cutting out the hydrophilic channels that were delimited by hydrophobic barriers on the paper. This proposal resulted in interesting platforms, but required external transparent supporting devices such as acrylic plastic and was also not appropriate for POC applications. Therefore, we propose a new stand-alone 3D microfluidic chemical sensing analytic device with hydrophobic film-fabricated void channels for POC applications, called the pressure-driven microfluidic PAD (PD-PAD). Two platforms with the pressure-driven flow (PD-PAD) and capillary-driven flow (CD-PAD) were characterized and compared through five microfluidic channels designated **T**, **X**, **Y**, **Y2**, and **Z**. Although this analytic device did not require an additional pumping or supportive device, it led to fast-flow response characteristics. Therefore, this stand-alone 3D microfluidic PD-PAD is likely to be useful for chemical sensing application as a low-cost and faster POC diagnostic device.

2. Experimental setup

2.1. Materials and chemicals

Tetrabromophenol blue (TBPB; Sigma–Aldrich, St. Louis, MO, USA), pH 1.8 citrate buffer (Samchun Pure Chemical, Seoul, Korea), and bovine serum albumin (EMD Millipore, Darmstadt, Germany) for the albumin assay, potassium iodide (Sigma–Aldrich), glucose oxidase (Sigma–Aldrich), horseradish peroxidase (Sigma– Aldrich), and D-glucose (Sigma–Aldrich) for the glucose assay, universal indicator solution pH (Sigma–Aldrich) and acetic acid (Sigma–Aldrich) for the pH assay, hand-coating film (Copierland, Seoul, Korea) and Whatman grade 1 chromatography paper (Sigma–Aldrich) for substrate, PDMS (Dow-Corning, Cortland, NY, USA) for adjusting the pressure drop, methylene blue water-soluble dye (Samchun Pure Chemical, Seoul, Korea) for blue coloring and congo red water-soluble dye (Samchun Pure Chemical) for red coloring, a Xerox ColorQube 8570 N printer (Fuji Xerox, Tokyo, Japan) for wax printing, a BF-150C drying oven (DAIHAN Scientific, Seoul, Korea) for wax impregnating, a Silhouette CAMEO electronic cutting system (Silhouette America, Inc., Orem, UT, USA) for film cutting, a spatula (Silhouette America, inc.) for peeling the protective layer from the film substrate, a Digital-3500plus (Hyundai Office Co., Daejeon, Korea) for cold laminating, a handheld digital microscope AD7013MZT Dino-Lite Premier (AnMo Electronics, New Taipei City, Taiwan) for obtaining the experimental pictures and movies.

2.2. Device design

Two microfluidic chemical sensing analytic devices based on a 3D structure configuration were designed. The rapid flow 3D microfluidic PD-PAD (Fig. 1Ba) consisted of four layers, including a top film substrate with an inlet for loading the samples, a middle film substrate for void channels, a paper substrate for the capillary-driven microfluidic channel, and a bottom film substrate for preventing the spread of samples and for supporting the platform, while the conventional 3D microfluidic CD-PAD (Fig. 1Bb) consisted of two layers, including a paper substrate and a bottom film substrate. The size of each substrate was $22 \times 30\,mm^2$. The thickness of the fabricated microfluidic devices and the height of fluid channel were 480 and 280 μm for the PD-PAD, and 280 and 180 μm for the CD-PAD. Five character-shaped microfluidic channels designated **T**, **X**, **Y**, **Y2**, and **Z** were fabricated for various POC applications (Fig. 1C, Table S3).

2.3. Device fabrication

Hydrophobic barriers designed by AutoCAD (Autodesk, San Rafael, CA, USA) were printed using a Xerox ColorQube 8570 N printer. A 0.18-mm-thick chromatography paper with a linear flow rate of 72.22 μm/s was used as the microfluidic PAD substrate. Uniform impregnation of wax on the paper was performed in a BF-150C drying oven at 120 °C for 45 s. A 100-μm-thick hand-coating film was used as the top, middle, and bottom substrates through a Silhouette CAMEO electronic cutting machine. With the spatula, the protective layer of each film substrate was peeled away revealing the adhesive surface and the peeled substrates were attached to the paper substrate in the same order (Fig. 1). Since the hand-coating film had an adhesive surface, it could easily be applied to other substrates. The assembled 3D microfluidic analytic devices were pressed using a Digital-3500plus cold laminating machine.

2.4. Flow rate measurement

The flow rate of two 3D microfluidic analytic devices was measured by the experimental setup (Fig. 2). Water-soluble solutions of 0.05% methylene blue and congo red in water were injected into the inlet reservoir. The pressure drop (P) was controlled by adjusting the height difference (Δh, PDMS thickness) of the solution between the inlet and outlet reservoirs. The PDMS was prepared with a curing agent-PDMS ratio of 1:10. The value of P was calculated by

$$P = h \times \rho \times g \quad (1)$$

where ρ denotes the density of water at 22 °C and g is the gravitational acceleration (Table S4). All experiments were recorded by the handheld digital microscope AD7013MZT Dino-Lite Premier. This test value was presented as an average of the six replicates. For each assay, the travel time was limited to a maximum of 1.5 h.

2.5. Colorimetric bioassays

Colorimetric albumin, glucose, and pH bioassays [23] were selected to evaluate the stand-alone 3D microfluidic PD-PAD platform. Each priming and reagent solution was spotted on the detection zone using a micropipette and allowed to dry for 2 min in ambient conditions. For the albumin bioassay, a 0.3-μL 250-mM citrate buffer (pH 1.8) solution and 0.3 μL of 9 mM TBPB were preloaded sequentially. For the glucose bioassay, a 0.3-μL 0.6-M potassium iodide solution and 0.3 μL glucose oxidase and horseradish peroxidase solution (120 units of glucose oxidase enzyme activity and 30 units horseradish peroxidase enzyme activity per mL of solution) [6] were preloaded sequentially. For the pH assay, a 0.3-μL pH indicator solution from pH 3 (dark pink) to pH 10 (light pink) was preloaded.

2.6. Statistics

Quantitative data are expressed as the mean ± standard deviation. Statistical analyses were performed using a two-tailed Student's t-test to compare the mean values obtained from the two groups. Statistical significance was defined as P-values < 0.05.