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Paper capillary force driven hollow channel as a platform for multiphase flows bioassays

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ABSTRACT

This paper develops a simple, inexpensive, and portable diagnostic assays that may be useful in remote settings, and in particular, in less industrialized countries where simple assays are becoming increasingly important for detecting disease and monitoring health. In this assays, the paper capillary force is first used to transport complex fluids such as whole blood or colloidal suspensions that contain particulates in a new type channel - paper capillary driven hollow channel, which offset the disadvantages of current paper microfluidic technologies. To demonstrate the various applications of the paper capillary force driven hollow channel, several devices are design and made to complete the purpose of exhibiting laminar flow in a T-junction microchannel, sheath a core stream in a three-inlet channel and transportation whole blood.

1. Introduction

The original reports of two-dimensional (2D) and three dimensional (3D) PADs by the Whitesides group [1,2] in 2007 and 2008, respectively, stimulated research in the field of highly functional paper-based sensors. Due to their lower cost, minimal required infrastructure, ease of fabrication, speed of fabrication, ease of use, potential to be used remotely, and ability to provide semi-quantitative results in a point-of-care fashion, those devices provide an alternative to elastomer (Polydimethylsiloxane, PDMS) and rigid polymer based, open-channel microfluidic systems [3]. Despite their advantages, current paper microfluidic technologies share some common disadvantages [4–6]. For example flows of complex fluids, such as whole blood or colloidal suspensions that contain particulates, are generally incompatible with wicking flow. Due to sample retention in the porous cellulose matrix, the volume that reaches the detection zones is usually less than 50% of the total volume within the device [7]. The groups of Website and Richard M. Crooks have developed hollow-channel paper analytical devices to overcome these disadvantages [8–10]. Those channels will allow micrometer-sized objects, such as bacteria or microbeads, to flow freely. However, an external force is needed to force the liquid into the channel, such as pressure arising from pumping or hydraulic pressure. In this paper we describe a simple well defined millimeter-sized channels, in which multiphase fluidics are transported without external force.

In the hollow channels, the capillary force is used to transport multiphase fluidics, such as whole blood or colloidal suspensions that contains particulates. We believe that this type of channels will become the basis for low-cost, portable, and technically simple multiphase flows. We demonstrate this capability by the simultaneous transportation of colloidal suspensions that contain particulates and whole flood. The channel system is small, disposable, easy to use (and carry), and requires no external equipment, reagents, or power sources. We believe this kind of system is attractive for use in less industrialized countries, in the field, or as an inexpensive alternative to more-advanced technologies already used in clinical settings [11–14].

2. Materials and methods

We believe that channel may be one of the least expensive platforms available for multiphase fluidics assays. We made assay device combining the hollow-channel and paper channel. The hollow-channel provides spatial control of biological fluid and the paper provides force to transport multiphase flows owing to capillary action in the millimeter-sized channels produced. Hollow channel makes it feasible to transport multiphase fluidics and run multiphase fluidics diagnostic assay. Paper channel makes it feasible to transport multiphase flow without external force. In a fully developed technology, a platform suits for diagnostic assay will be developed by combining the paper channel and the hollow channel.

We combined hollow channel and paper channel as shown in Fig. 1. First we paste transparent adhesive tape on the top of glass slide layer by layer. Then we used a laser craft cutter (Han's laser marking machine DP-H50L) to carve micro-channels into multilayer transparent adhesive tape. Finally we put a strip chromatography paper on the top of the micro-channel and sealed with transparent adhesive tape to form the device (Fig. 1).

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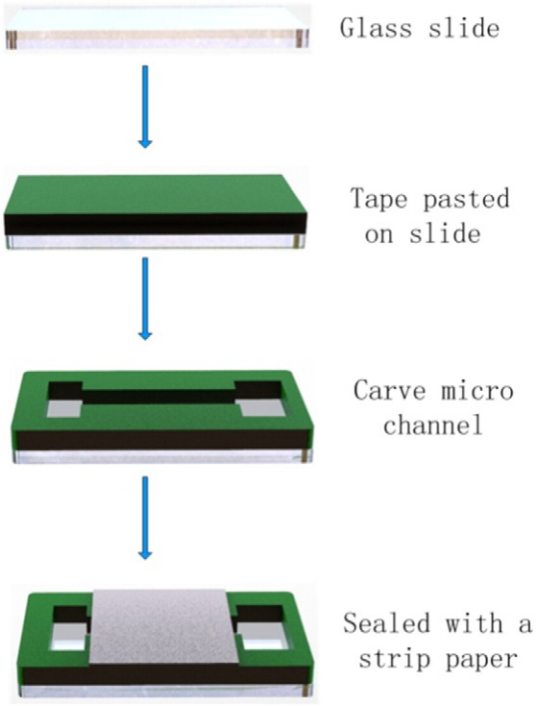

Fig. 1. Diagram depicting the manufacturing operation of paper capillary force driven hollow channel.

3. Results and discussion

3.1. The velocity of the fluidic in paper capillary force driven hollow channel

The first part of the study focuses on the flow of fluidic in a capillary force driven hollow channel. Fig. 2a is the Schematic plot of the channel equipment. First, 100 μL solutions are put on the buffer by the pipette. When the solutions contacted the paper, a capillary force imposed on the solution. The solution flowed in the channel under the impact of the capillary force. The flow process was imaged by the observation equipment (for example a mirror, a mobile phone or an inverted microscope) under the channel. Although the width of paper cannot be same everywhere, the area of the paper exposed to the hollow channel is always determined by the channel. We hypothesize that capillary force, arising from paper wick, is constant when the width of the channel is defined. So the velocity of the fluidic depends on the resistance of water surface tension and the friction force between the fluid and the walls. We design two groups of channels to measure the velocity of the fluidic. The flow process of Rhodamine B solution is recorded by the mobile phone camera and the velocity of fluidic can be calculated by images processing using the software of MATLAB. Rhodamine B solutions (0.1 mmol/L) were prepared in the carbonate buffer and filtered before use with a syringe filter (0.2 μm pore size). The width of the first group channels is 1 mm and the heights of the channels are 165 μm, 275 μm, 385 μm, 495 μm, with the layers of tape 3, 5, 7, 9 layers. The height of the second group channels is 275 μm, with 5 layers of tape and the widths of the channels are 0.5 mm, 1 mm, 1.5 mm, 2 mm. The velocities of the fluidic in the two group channels can be seen from Fig. 2b and c. The width of the first group channels is defined. When the height is short enough, the surface tension dominates the resistance and when the height is high enough, the friction force dominates the resistance. There exists a height with the minimum resistance. So the velocity curve in Fig. 2b is a parabola. The height of the second group channels is defined. When the width is small enough, the surface tension dominates the resistance. With the increase of the width, the surface tension decreases, however the friction force and capillary force increase. So the velocity can approach a maximum velocity, as Fig. 2c.

3.2. Laminar flow in the paper capillary force driven hollow channel

To demonstrate the various applications of the paper capillary force driven hollow channel, a T-junction microchannel was design and made (see Fig. 3a). We put 100 μL deionized water, on inlet 1, and 100 μL miscible aqueous phase, labeled with a water-soluble dye (0.05% solutions of Methylene Blue), on inlet 2. Then the paper strips contact two

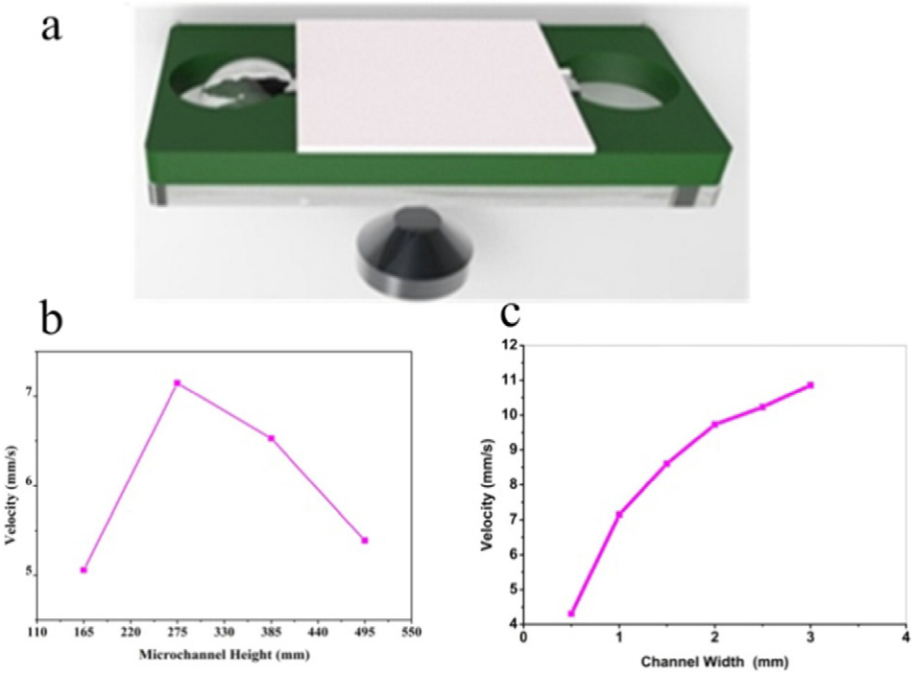

Fig. 2. The velocity of the fluidic in paper capillary force driven hollow channel. (a) Schematic drawing of experiment device. (b) The velocity of the fluidic as the function of the channel height. The width of this group channel is 1 mm and the height of the channel is 165 μm, 275 μm, 385 μm, 495 μm, with the layers of tape 3, 5, 7, 9 layers. (c) The velocity of the fluidic as the function of the channel width. The height of this group channel is 275 μm, and the width of the channel is 0.5 mm, 1 mm, 1.5 mm, 2 mm.

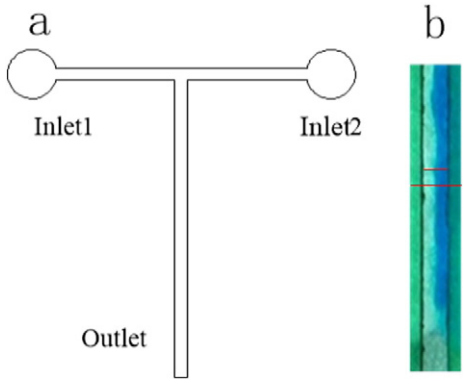

Fig. 3. Laminar flow in the paper capillary force driven hollow channel devices. Schematic drawing of (a) T-shaped microfluidic channel. (b) T-shaped microfluidic channel (1000 μm wide, 275 μm deep) exhibits laminar flow with diffusion-limited mixing of two aqueous solutions of dye. The short red line showed the width of the channel, and the long red line showed the width of the paper strip.

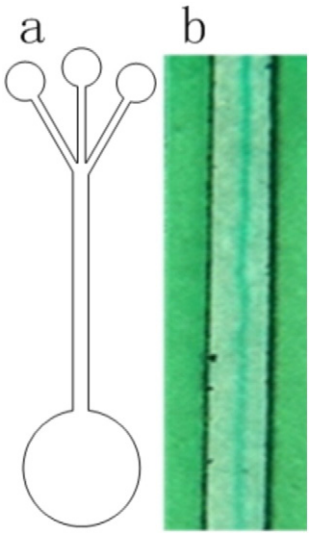

Fig. 4. Sheath flow in the paper capillary force driven hollow channel devices. Schematic drawing of (a) three inlet hollow channel. (b) The three inlet channel exhibits sheath flow with diffusion-limited mixing of three aqueous solutions of dye.

droplets. Two miscible aqueous phases flowed under the driving of the paper capillary force, and formed laminar flow. Fig. 3b shows a paper capillary force driven hollow channel exhibiting laminar flow: two miscible aqueous phases were driven through a T-junction. A phone under the channel imaged the two parallel streams within the 1000- and 275-μm-high channel. These observations confirm that these devices can reproduce the classical diffusion-limited co-flows reported in open-channel microfluidic devices fabricated in materials such as PDMS [15]. In this study, the paper strip was clipped with hand-cut, so the width of paper strip exceeded the width of the channel. In Fig. 3b, the short line showed the width of the channel, and the long line showed the width of the paper strip. The extra paper not only absorbed water but also disturbed the laminar flow. By introducing the printing technique, more precise channels (the width of the paper in accordance with the width of the channel) and more complex channels (for example serpentine channels) could be designed and made. In the future, the paper capillary force driven hollow channel could be widely applied in point-of-care test and bioassay, by combining with techniques such as magnetic, optic, dielectrophoretic, etc.

3.3. Sheath flow in the paper capillary force driven hollow channel

Microscopic flows almost always occur at low Reynolds number (*Re*), and are laminar and stable. Therefore, particles and molecules injected into them follow well defined streamlines. This allows efficient hydrodynamic focusing-a stream carrying the particles is squeezed by other streams into a narrow tube of flow with a uniform velocity [16]. The focusing stream is called sheath flow. This sheath flow device has been used to fabricate nano-structure fibers, align particles and cells [17,18]. Unlike other microfluidic sheath-flow devices that employ multiple sheath inlets to focus the sample stream and are complicated to fabricate [17–19], our sheath-flow device uses the paper capillary force to sheath a core stream in a three-inlet hollow channel (show as Fig. 4). First, 100 μL deionized water is put on the buffer of two sheath flow inlets. Dragging by the paper capillary force, water flows in the channel. Then water with dye (0.05% solutions of Methylene Blue in water) is put on the buffer of the core stream inlet. For the end of the paper on the core stream channel is triangular (Fig. 4c), there is only a little Methylene Blue solution can flow in the channel. Finally, the core stream can be confined in a narrow flow (Fig. 4b). The three-inlet channel is fabricated by the laser craft cutter. The height of the channel is 275 μm. The width of the channel is 1 mm and the width of the inlet is 500 μm.

3.4. Human blood fluidic in paper capillary force driven hollow channel

Microfluidics has been utilized to miniaturize analytical systems [20] in order to reduce sample volumes and analysis time and to increase versatility of procedures. Several blood related applications of microfluidics have been reported for separation and analysis of cells and plasma [21–23]. For point-of-care and self-monitoring applications, simplicity of the device is important both in terms of product cost and its operation. In this article, the paper capillary force driven hollow channel can meet the requirement of the point-of-care. The channel is used to transport whole blood. Fresh human blood was obtained using a needle lancet, and was used immediately. Fig. 5 showed the flow of human blood in channel. Fig. 5a showed the flow of human flood, recorded by the phone. For the driving force, arises from the paper capillary forces, is uniform across the channel, the contour line in the front of the flow is almost a straight line perpendicular to the channel wall. When the flood flows through the channel, it dyes the paper strip red as shown in Fig. 5b. The results show that the capillary force driven hollow channel is suitable for multiphase flows without external force. However the multiphase flows could only reach the end of the paper. Fig. 5c shows the human cells recorded by the inverted microscope (Nikon ECLIPSE TS100/TS100-F) with enlargement factor of 100, when the blood keeps still in the channel. In order to maintain the fluidics flow, another driving force is needed. In this study, we put paper on the end of the channel. The paper offered the driving force of fluidic flow, when the fluidic reached the end of paper strip. So the flow could continue. Fig. 5d shows the blood cells recorded by the inverted microscope (Nikon ECLIPSE TS100/TS100-F) with enlargement factor of 100, when the blood flows through the channel.

This capillary force driven hollow channel is suitable for multiphase flows without external force. By combining the capillary force driven hollow channel as transportation component and paper channel as reactor, the system will develop the paper based bioassays device to suit for almost all of application. Finally, the capillary force driven hollow channel can easily realize the aim of automatic control by controlling the driving component of paper. These methods suggest a path for the development of simple, inexpensive, and portable diagnostic assays that may be useful in remote settings, and in particular, in less industrialized countries where simple assays are becoming increasingly important for detecting disease and monitoring health.

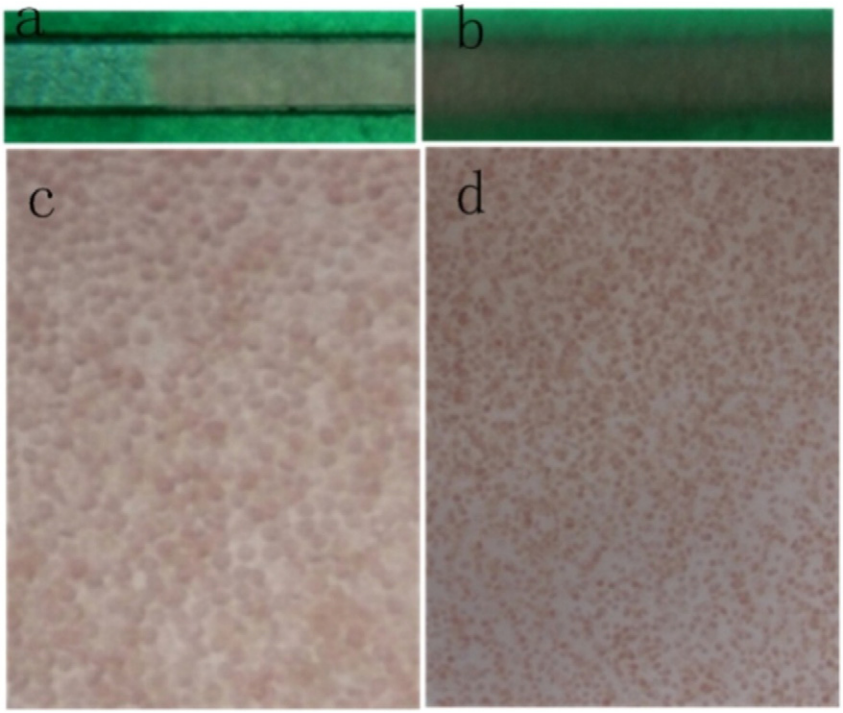

Fig. 5. Human blood fluidic in paper capillary force driven hollow channel. Fresh human blood flow in paper capillary force driven hollow channel, (a) imaged by the phone under the glass substrate; (b) imaged by the phone on the paper strip. Fresh human blood flow in paper capillary force driven hollow channel, imaged by the inverted microscope with enlargement factor of 100, (c) when fluid is still; (d) when fluid is flowing in the channel.

4. Conclusions

In a summary, we have shown that the paper capillary force driven hollow channel can be used to transport multiphase fluidics without the external force, by combining the paper and the hollow channel. In this paper, variety channels with different structures have been manufactured to form laminar flow, mix two fluid streams at low Reynolds number, create sheath flow and transport whole blood. Due to the merit of the ability to transport complex fluid without external force, in the future the channel can be widely used in point-of-care, as a supplement of the paper-based microfluidics. Further, the channel can be easily integrated with other techniques, such as magnetic, optic, dielectrophoretic, etc. So it can act as a power unit of the fluid in the intelligent portable test instrument. We believe that the channel will be widely used in the multiphase flows bioassays.

Acknowledgments

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