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Besides Detection: Other Usage of Paper-Based Devices

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Abstract: Fabricated paper-based microfluidic setups and devices were widely utilized in the field of low-cost and onsite detection, such as disease diagnosis, food safety analysis, and environmental pollution monitoring. The results could be determined with bared eyes. Those setups could also serve as a tool for quantitative and semi-quantitative measurements, with the aid of a small result reading device. It is easy to distabpose those used devices by burning, without risk to cause environmental pollution. Besides analytical tools, those paper-based microfluidic setups were also designed for other purpose, including timer, cell culture, touchpads, etc. Though research in those field were far less than the detection platforms, they were very interesting and open-minded. In this paper, I'll briefly introduce paper-based microfluidic devices, following by reviewing those interesting studies. Hope some significant researches could be inspired by those meaningful studies.

1. Introduction

Patterned paper-based microfluidic devices were introduced by Whitesides group [1], in order to perform an inexpensive onsite detection assay. Unlike conventional production of paper-based microfluidics which uses dip stick devices, these devices were fabricated with chemicals (wax, carbon ink, silver ink, polymers) or nanoparticles, which could serve for high-through put generation of the devices. Many fabrication methods were reported, including lithography, wax printing, wax dipping, inkjet printing, flexographic printing, stamping, plasma treatment, screen printing and drawing [2-7], etc. All of those fabrication methods were low-cost, and some of them can serve for high-throughput generation of the paper-based devices [8]. Therefore, studies about paper-based microfluidic devices were mostly reported for analytical purpose, in the field of disease diagnosis, food safety, environmental pollution [9], etc. Interestingly, some groups have successfully applied the fabricated paper-based device to other fields (see Table 1 in Section 2). Paper-based microfluidic devices for analytical detection were summarized plenteously15. Here, we reviewed literatures about paper-based microfluidic devices for other purposes. Hope more fascinating studies could be inspired by those interesting researches.

Table 1: Utility of paper-based microfluidic devices

Utility	References
Analytical Devices	[9]
Timers	[10-12]
Thermal hydrogels	[13]
Hydrogel templates	[14]
Cell culture	[15,16]
Cantilevers	[17]
Touchpads	[18]
Catalysts	[2]
Batteries	[19-21]

2. Purposes Other Than Analytical Detection

2.1. Timers

The Phillips group made a timer with a wax printed paper-based microfluidic device [10]. It is composed of several layers of cellulose paper attached with double-sided tape. The top layers are for solution separation, followed by a meter layer. After passing through the dye-loading layer, the solution that reached the bottom layer could be visually measured by the color of the dissolving dye. The meter was paraffin wax dissolved in hexane. By adding larger concentrations of paraffin wax, the time for solution to pass is prolonged and results in the delayed arrival of dye to the bottom layer. They also tested the repeating assembly of the meter layer, which prolongs the retention time required for the solution to pass through the entire device.

Another study from the same group further incorporated this paraffin wax timer onto a paper-based microfluidic device for glucose detection [11]. This device was assembled with different layers and four vertical channels. Paraffin wax was loaded on one of the channels as a timer, while the others were reserved for glucose detection. The result of this assay would decay after reacting for a period of time, which required a timer. Besides elimination of an external timer, this paper-based microfluidic device would not be affected by changes in humidity, because of its all-in-one design.

Using the same principle, the Phillips group developed a microfluidic device for hydrogen peroxide detection [12]. The whole setup was composed of several patterned paper layers attached with double-sided tape. Buffer, reagent and dye were pre-loaded onto the layers. The green color from dye served as an indicator for the samples that flow through. For the detection of hydrogen peroxide, they utilized a compound which would change from a hydrophobic to hydrophilic form upon reacting with hydrogen peroxide. After the change to the hydrophilic form, the sample could pass through the device. The time for the sample to pass correlated with concentration of hydrogen peroxide.

2.2. Thermal Hydrogels

The Whitesides group fabricated paper with a heat sensitive dye covered on one side, and metal wires deposited on the other side [13]. By applying current to the metal wire, the dye which is black at ambient room temperature would become transparent due to the heat generated, making the paper visible under heat. They further utilized this method to generate textual and image indicator, and also displayed in 3-dimensions by folding the fabricated paper.

2.3. Hydrogels and Cell Culture

The Whitesides group also fabricated different shapes of hydrogels with the patterned paper as a template [14]. Furthermore, they cultured cells in hydrogels loaded into a wax-printed 96-well microzone plate, which they named "Cells-in-gels-in-paper" [15]. By stacking several layers of the cell-contained microzone plate, they generated a three-dimensional cell culture platform. This device was used to characterize spatial cell growth and cell migration under different conditions, including oxygen, nutrition signalling molecules, and to other environmental factors (temperature, mechanical stress, etc.). Instead of the average behavior of the cells in conventional plate cell culture, this method could analyze cells under different conditions in each well by simply separating the paper layers. Therefore, this method could be used for high-throughput detection. Also, the recovery was studied after de-stacking the three-dimensional cell-culture into single layers. This method provides a simple approach to study cells under different conditions, and a convenient solution for moving cells and tissues.

The Juvonen group grew two dimensional cell cultures using a flexographic-printed paper [16]. The group printed a 24-well plate with polydimethylsiloxane (PDMS), a cell-repellent material, to separate the cell culture zone. This design is only a substitution for traditional cell culture plate, whereas the previously mentioned paper-based cell-culture method can also be studied in the z-axis.

2.4. Cantilevers

The Whitesides group utilized Whatman® 3MM chromatography paper (340 μm thick) as the material for a force-sensing cantilever through the combination of screen-printing of high-resistant graphite ink and low-resistant silver ink [17]. The stiffness of the cantilever was 2.0 ± 0.16 mN/mm, which changes within 4% after bending it 1000 times.

2.5. Touchpads

The Whitesides group also developed a touchpad with a polymer coated metallized paper layer (which consisted of layers of a cellulose support bottom, evaporated aluminum, and a polymer protection coating on the top), and a cellulose paper layer [18]. The system was completed with two electrodes which was an active electrode (coupled with external impedance upon finger touch) and a ground electrode (no finger touch). They tried with both layered and adjacent electrodes, and designed buttons with those electrodes to form a touchpad or keypad. The buttons was tested by pressing over 2000 times, resulting in good reproducibility.

2.6. Catalysts

The Whitesides group generated a precipitated palladium ring using a stamping method, which provides oxygen bubbles when positioned in a hydrogen peroxide solution that could serve as cylindrical cage trapped plastic floats [2]. Due to the porous structure of cellulose paper, the precipitate was generated not only on the surface of the paper, but also in the pores. Thus, the catalyst stamped by this method has more surface area.

2.7. Batteries

The Hu group studied lithium storage in paper functionalized with carbon nanotubes (CNT) and V_2O_5 nanoparticles [19]. The resulted V_2O_5/CNT/cellulose cathode performed a high charge/discharge rate, because of the combined contribution from CNTs (high electronic conductivity), V_2O_5 nanoparticles (short Li^+ diffusion length), and cellulose paper (porous structure for easy transportation of Li).

The Crooks group included a battery in detection device as the indicator for oxidation/reduction reaction [20]. The electron transfer can be seen with unaided eyes by the using an electrochromic dye, whose oxidized state shows a different color than its reduced form. The Phillips group assembled fluidic batteries with several layers of wax-fabricated paper pre-loaded salt bridge, electrolytes, and electrodes in the hydrophilic area with tape [21]. In order to generate more energy, they incorporated two, four, sixteen, and even twenty-four cells into one battery. They found the increased salt bridge volume stabilized the current, but decreased the maximum current a cell could generate. Meanwhile, larger electrodes would generate higher current to some extent. They also tried different arrangement of several cells for one battery device.

2.8. Combination with Other Materials

Paper, as a brittle material, can be folded or shaped easily. However, it cannot be compressed or extruded. While plastic materials, such as hydrogels and polymers, have the characteristic of plastic deformation, the combination of the two kinds of materials could inherit the two characteristics. The Whitesides group utilized a highly stretchable silicon elastomer with an easily bendable paper to generate different materials that could be used in a variety of actuation demand [22]. Though no direct application of this composite was reported, it introduced another possibility for the utilization of paper.

3. Conclusions

Paper-based microfluidic devices were initiated with easy and fast patterning methods, such as wax-printing and photolithography. Because of the characteristics of paper, which include its low cost, easy fabrication, and disposable, it is an ideal platform for analysis. However, some groups have demonstrated the potential capabilities of paper-based microfluidics for other application, such as timer, cell culture, batteries, and touchpads. The possibility and application of paper is still expanding by introducing different properties to paper through the integration of other materials.

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