Paper Based Sensors

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Since its inception in the early 21st century, paper based sensors have evolved as good alternative for analytical, bioanalytical and point-of-care testing over traditional analytical instruments because they are easy to use, portable, require small volumes of reagents and samples, provide rapid analysis and are inexpensive and disposable. Paper based sensors have a simple architecture where hydrophobic channels, created using polydimethylsiloxane (PDMS) wax or varnish, are patterned onto a hydrophilic paper substrate. The hydrophobic channels constrain the flow of the solution via capillary action while preventing overflows.

Different types of papers have been employed as the substrate, based on the application and the fabrication method. The most commonly used papers in developing paper based sensors have been Whatmann brand filter paper which are differentiated with respect to porosity, particle retention and flow rate. Another popular paper type used in the sensor is the chromatographic paper. Both these papers were selected mainly due to its good wicking ability. Other types of paper have also been explored due to compatibility issues. Such an alternative is the nitrocellulose membrane, that have been widely used due to its nonspecific binding ability towards the biomolecules. Glossy paper, a flexible substrate made of cellulose fiber blended with an inorganic filler, is another alternate substrate that has been used due to its non-degradable nature and flexibility.[1,2,3]

In paper based sensors, the fluid flow is retained in a microfluidic channel that is patterned on to the paper substrate by way of creating a hydrophobic barrier. While the hydrophilic nature of the paper allows the flow of solvent, its direction and amount can be controlled via the hydrophobic barrier. Substances such as wax, varnish and PDMS have been patterned on the paper using different fabrication techniques.

Fabrication techniques

Microfluidic devices are patterned onto the paper by a variety of physical and chemical methods which are shown schematically in Figure 1. Photolithography, plasma treatment, and inkjet printing are some of the chemical methods used in creating hydrophobic barriers in the paper. All chemical fabrication methods have the advantage of creating high resolution microfluidic channels. In photolithography, a photoresist is applied on to the surface of the paper. Then the photoresist is allowed to dry. A mask with the pattern of microfluidic channels / devices is placed on top of the photoresist and is exposed to UV light. Afterwards the non-polymerized photoresist that is not exposed via the mask is removed by a washing step creating the channels. The photolithography

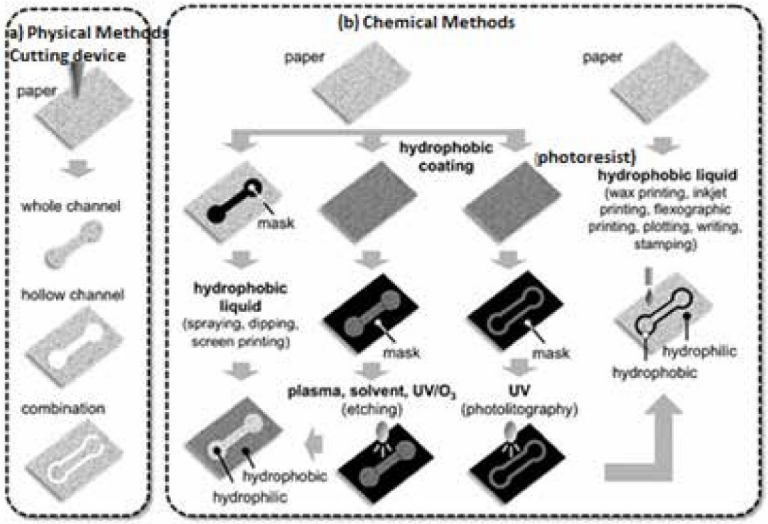

Figure 1: Schematic of a) physical b) chemical methods used in the fabrication of channels in the paper based sensor. Figure source: www.elveflow.com

process is time consuming as a mask is required and is expensive due to the price of the photoresist. Similar to photolithography, plasma treatment too requires a mask for the pattering. Designing of the mask is accompanied by a long wait-time making the method more expensive. Inkjet printing does not require a mask; however, designing of suitable ink requires more research.

The most common physical patterning methods are wax patterning, plotting, paper cutting and shaping and screen printing. Although these physical methods do not require expensive chemicals, some methods such as screen printing require masks. Plotting, paper cutting and shaping require precision printers making the methods expensive. Wax patterning, consisting of wax printing, wax dipping and wax screen printing is the most economical when considering other methods. However, all these methods require an oven or a hot plate to melt the wax. Moreover, when melting, the wax spread is hard to control creating channels of low resolution.[1,2]

Analyte Detection[1,3]

Analyte detection in paper based sensors have been mainly done via optical and electrochemical techniques. Colourimetric detection has been used in paper based sensors for qualitative analysis where appearance or disappearance of a colour gives an "yes or no" answer for the availability of a specific analyte and for quantitative analysis. As visible in Figure 2, in quantitative analysis, the visible colour change is measured using a camera phone or a scanner and the pixel value is analysed and correlated to the concentration using computer software. Colourimetric methods have been successfully used to detect enzyme-substrate complexes which produce a colour change. Glucose has been detected qualitatively, in the presence of glucose oxidase enzyme. During this process gluconic acid and H_2O_2 are produced and the colour change is given by the reduction of H_2O_2 while oxidizing iodide to iodine. ELISA based immunoassay too has been carried out successfully using colourimetric detection.

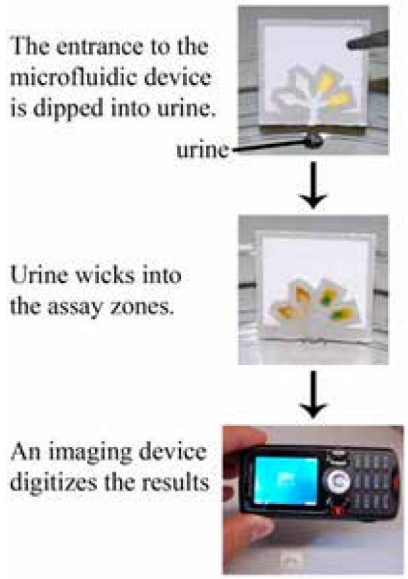

Figure 2: Colourimetric quantitative detection of analytes (glucose & protein) in urine[4]

Chemiluminescent quantitative detection of uric acid was performed via an enzymatic reaction that produced hydrogen peroxide as a by-product while decomposing the substrate. Luminescence was analyzed using a computerized detector, producing a signal with the peak height representing its concentration.

In electrochemical detection, the analyte is detected

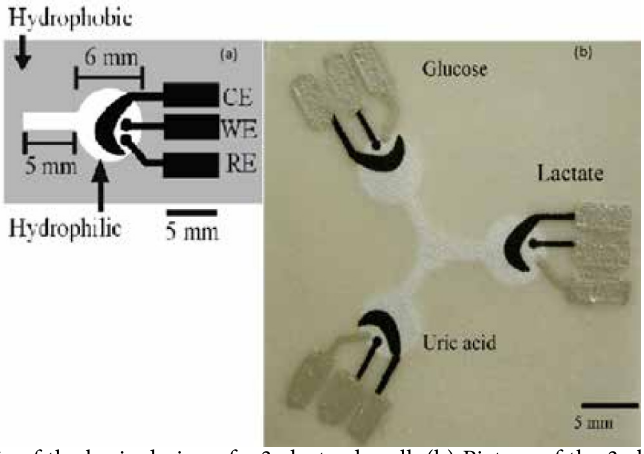

Figure 3: (a) Schematic of the basic design of a 3 electrode cell; (b) Picture of the 3 electrode design on a paper based sensor[5]

by either a three electrode; working electrode (WE), counter electrode (CE) and reference electrode (RE) as depicted in Figure 3, or a two electrode (WE and RE) system. The electrodes are patterned on the hydrophilic area of the sensor. Electrodes could be constructed using a conductive paste of carbon, gold, platinum and silver. The most commonly used RE material has been Ag/AgCl ink while the WE material will depend on the analyte of interest. Quantity of the analyte is measured via amperometry, cyclic voltammetry and potentiometry.

Biomedical detection of analytes such as glucose, uric acid and ascorbic acid, detection of alkaline, alkaline-earth , heavy metal ions, and simple anions in environmental samples and food analysis in the detection of nitrites, ethanol, caffeine and hydrogen peroxide are some areas where electrochemical detection is used.

The use of conductivity measurements, in spite of its inherent simplicity, has not been utilized much as a detection method in paper based devices.

Over the past decade, paper based devices have evolved considerably as analytical devices which are sensitive and accurate; however, improvements are still being introduced in areas such as power consumption and portability. With such improvements, paper based sensors are bound to spread over numerous application areas in the future.

References

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