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POINT OF VIEW

Paper-based microfluidics: What can we expect?

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In the last three decades, the scientific community has observed exponential growth in the development of microfluidic platforms and their use for applications in different fields. The noticeable advances are attributed to the advantages provided by miniaturization.[1] In summary, the downscaling of analytical devices has offered attractive features, including reduced consumption of samples and reagents, short analysis time, and minimal waste generation. In addition, the possibility to perform multiplexed assays in portable devices without bulky instrumentation is another attractive feature that boosted the investigation of miniaturized devices with the capability to be tested directly in the point-of-care (POC). Due to the sample volume required to proceed with a chemical analysis on a microscale (typically in the µL range), a complete understanding of the fluid control and handle on channels defined in micrometric dimensions was necessary, giving rise to the science known as microfluidics.[2] Many platforms including rigid and flexible materials can be explored for manufacturing microfluidic networks. Among all the substrates reported in the literature, the “paper” is by far the simplest and cheapest material currently employed for the development of microfluidic devices dedicated to analytical, bioanalytical, biomedical, environmental, food, and forensics applications.[3] For many readers, the first question is why paper is used instead of other materials such as glass. Well, glass is a rigid material, and microchannel engraving requires cleanroom facilities, photolithographic patterning, developing steps, and thermal sealing. This standard protocol makes use of sophisticated instrumentation, and it is not readily available to most researchers. In this way, paper emerges as a simple and alternative material to be used for microfluidics.

One of the major benefits of microfluidics refers to the sample-in-answer-out capability, which requires a fully automated fluid control to allow sample preparation, analytical separation, and detection stages. The fluid-controlled handling inside microchannels opens the possibility to integrate multiple analytical tasks in parallel into a high-throughput device. Considering these possibilities, it is worthwhile reflecting on how paper can be used to transport and handle a fluid.

Paper is currently one of the most widely used raw materials in research laboratories. Its use has been explored for over a century. In 1949, a paper containing barriers made of paraffin was exploited to successfully demonstrate the elution of pigments within a channel based on the sample diffusion process.[4] In 2007, paper was reinvented by the Whitesides group as a globally affordable substrate material for the development of miniaturized analytical platforms.[5] Since this period, paper has become an increasingly popular platform for multipurpose applications. Probably, its broad use is associated with advantages over other conventional substrates, as well as the fabrication technologies and the concept of “do-it-yourself microfluidics”.[6] In comparison with other conventional materials, like glass and silicon, paper is relatively inexpensive, globally affordable, lightweight, bioactive, and easy to transport and store. Furthermore, paper-based products can be easily found as kitchen towels, coffee filters, blood separation paper, filter paper, office paper, and others.

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How does one create an analytical device on paper? This question is a common inquiry of undergraduate and graduate students when starting to study microfluidics. Initially, it is important to emphasize that paper substrates have a porous structure, which facilitates the spontaneous transport of fluid by capillarity. The wicking speed of liquid on a microchannel defined on paper depends on pore size and paper thickness. Microfluidic networks can be created on paper using hydrophobic barriers or defined by cutting approaches, which make it possible to obtain single paper strips or more complex designs containing interconnected microchannels for multiplexed assays.[3] In this regard, lithography-based fabrication methods were first employed to demonstrate the potential of paper substrates for developing microfluidic structures. However, due to the contradictory view in terms of cost, many other alternative approaches were developed to make affordable and popular the concept and potential of paper-based microfluidics. Thanks to the researchers´ creativity and paper versatility, the fabrication of microfluidic paper-based analytical devices is feasible through direct printing using wax, inkjet, or laser printing processes or even by manual protocols (freehand drawing or spraying) involving pens, pencils, stamps, scissors, scholar's glue, or lacquer resins.

Paper-based microfluidic devices, including examples of simple spot test arrays, chemosensors, biosensors, electrochemical sensors, wearable devices, and lateral flow assays, have been found in the main scientific Journals associated with analytical and bioanalytical chemistry.[7-10] In the academy, most of the advances seen in the recent literature have demonstrated improvements in terms of durability, shelf life, reproducibility, robustness, and analytical reliability, making paper-based microfluidic devices promising and emerging candidates to gain space in the market as alternatives to other materials. In this way, entrepreneurship and innovation deserve to be highlighted and emerge as the focus of many researchers interested in opening their businesses or company. The bridge between the academy and the productive sector depends on investment and engagement to overcome administrative and legal bureaucracies not only to open a company but also to maintain it in full operating mode.

The commercialization of microfluidic devices has been constantly growing. In the last three years, for example, many companies located in different countries have shipped over five hundred million units/year, clearly demonstrating the potential of microfluidic devices for different application areas including drug delivery, flow chemistry, analytical devices, pharmaceutical and life science, point-of-care diagnostics and clinical and veterinary settings.[11]

Considering the advantages of paper-based materials, what can we expect in the coming years? Commercially available products with sample-in-answer-out capabilities are highly desirable to be found more and more in the market. Due to the global affordability of paper as well as its attractive features to create microfluidic and sensor prototypes, it is possible to see a real niche full of possibilities for success. In this view, it is time to try our best and make commercially available paper-based products like wearable sensors or lateral flow devices to monitor clinically relevant compounds in different biological fluids like blood, urine, serum, sweat, saliva, and tears. This may be accelerated by spin-offs or startups independently or in partnership with well-established companies. In other words, it is time to innovate and transform an idea into a commercial product with a societal impact. The interface between rapid tests and immediate responses directly by the end user are highly desirable features in the market and risk analysis.

The SARS-CoV-2 worldwide outbreak is the most recent example that science can offer the possibility to obtain clinical diagnostics in a matter of minutes, allowing one to decide on the ideal treatment or, in this case, social isolation to prevent the virus transmission. Tens of self-diagnostics kits based on paper strips for SARS-CoV-2 are already commercially available for society in drug shops, hospitals, or healthcare clinics. Similar strategies may be seen shortly for Monkeypox or other global outbreaks.

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