REAL-TIME FLOW MEASUREMENT IN PAPER-BASED MICROFLUIDICS
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ABSTRACT
Recently the field of paper-based microfluidics has garnered significant interest due to the desire to develop very low cost diagnostic devices [1]. Critical to the development of the field is the availability of tools to monitor, or measure, liquid flow in paper, a porous and opaque material. Despite recent efforts to monitor flow in paper, there is yet a technique that is both easy to use and provides detailed flow information in real-time. To address this critical need, we demonstrate a real-time, non-optical technique, based on electrochemical velocimetry, to monitor liquid flow in paper samples.

KEYWORDS: Paper-based microfluidics, paper velocity, electrochemical velocimetry, amperometric, electrochemistry
INTRODUCTION
Paper, a very low cost material with the intrinsic ability to pump fluids, is rapidly gaining interest in the Lab-on-a-Chip community because of the desire to make inexpensive point-of-care (POC) diagnostic devices that are self-powered [1]. The several advantages associated with paper make it an ideal technology for POC diagnostics, particularly in resource limited environments. While the field has impressively grown over recent years, there is a clear need for techniques to monitor liquid flow in paper. With tools to monitor flow in paper, device designs can be evaluated to identify the best configuration to optimize the diagnostic performance and designs can be validated in an effort to confirm theory. Monitoring flow in paper is still difficult as it is a non-transparent and porous material, rendering it unsuitable for use in traditional, optically-based, flow velocimetry techniques such as micro particle image velocimetry (μPIV). In order to offer the field a quantitative method to monitor flow in paper, a technique, based on changing the optical properties of a dye (either by light or electrochemically) to mark flow profiles in an actively wicking paper, has been recently offered by Kauffman et al.[2]. In the work by Kauffman et al., the migration of the flow lines in the paper were optically recorded and sequential images were analyzed off-line to determine flow behavior. Despite this effort to monitor flow in paper, there is yet a velocimetry technique for paper that is both easy to use and provides detailed flow information in real-time. To address this critical need, we demonstrate a real-time non-optical technique, based on electrochemical velocimetry, to monitor liquid flow in paper strips. It will be demonstrated in this report that with our innovative technique, information related to the flow behavior, flow duration, and the identity of the paper can be rapidly determined.

THEORY
Our technique is fundamentally based on electrochemical velocimetry (E.V.), a method in which an electrochemical sensor is embedded within a fluid-filled channel and acts as flow sensor. When flow is present in a channel, containing an electrode parallel to the direction of flow, flow brings more electroactive species to the working electrode’s surface, resulting in an increase in current. The limiting current, $i$, measured by the electrode in the channel is related to the average volumetric flow rate, $v$, in the channel as:

$$i = 1.47 n F C (\frac{D A}{B})^{2/3} v^{1/3}$$  (1)

where $n$ is the number of electrons, $F$ is Faraday’s constant, $C$ is the concentration of the analyte, $D$ is the diffusion coefficient, $A$ is the area of the electrode, and $B$ is the channel height [3]. Therefore, the current, $i$, measured by the working electrode can be converted to the average volumetric flow rate, $v$, by Eq. (1). This general technique has been applied before in microfluidics to measure hydrodynamic conditions in a straightforward PDMS-based channel [4], but has never before been adapted to measure fluid flow in porous materials, such as paper. We applied the phenomenon of E.V. to build a straightforward device to indirectly measure flow in porous materials, like paper. More specifically, we fabricated the device presented in Figure 1 which essentially consists of two large liquid reservoirs that are connected by a channel containing an electrochemical sensor. When a material that exhibits capillary-driven flow, e.g., paper, is partially inserted into the outlet reservoir of this device it induces flow within the channel in which there is an electrochemical sensor. Therefore, our devices is based on the assumption that if there is flow in the paper, then there is flow in the channel.
EXPERIMENTAL

Experimental procedure is summarized as follows. First, an electrolyte solution (10 mM Fe(CN)$_6^{4-}$ with 250 mM KCl) was loaded into our novel device (Figure 1) which is comprised of two large reservoirs connected by a channel that has an embedded electrochemical sensor (screen printed carbon electrodes with an Ag/AgCl reference). Each reservoir of the device has a volume of 1.5 mL and the connecting channel has a geometry of 2 mm wide, 1.5 mm high, and 20 mm long. The electrodes of the fluidic device were connected to a potentiostat (Model: VSP, BioLogic, France) and electrochemical recordings were performed using its proprietary software (EC-Lab Software v.10.02 BioLogic, France). Once the loaded electrolyte solution came to rest in the device, chronoamperometric measurements were taken on the stagnant solution to obtain a baseline measurement to measure the current when there is no flow in the system. Subsequently, paper strip samples were vertically inserted into the outlet reservoir of the device (Figure 1(b)) such that they wicked solution out of the device, inducing flow in the channel. While the paper sample wicked the solution out of the device, chronoamperometric measurements were also taken until the point at which the paper became saturated with solution. All experiments were performed in triplicate. Finally, using Equation (1), recorded currents were converted to theoretical flow rates.

RESULTS AND DISCUSSION

A typical experimental result from our device is presented in Figure 2 which is a plot of the flow rate (µL/min) vs. time (s) for a single paper strip sample (Pall Corporation (USA) Products: Absorbent Pad 133). The flow rates of Figure 2, and all other graphs in this report, were calculated from the experimentally measured current using Equation (1) with the following constants based on our setup: $n = 1$, $F = 96,485.3365$ C/mol, $C = 10$ mM, $A = 4$ mm$^2$, $D_{Fe(CN)_6^{4-}} = 0.65 \times 10^{-5}$ cm$^2$/s, and $B = 1.5$ mm. Upon inspection of Figure 2, it is clear that there are several identifiable phases to the flow which are: (1) insertion of the paper sample into the device outlet, (2) wetting out in the paper upon initial contact with the liquid, (3) fully wetted flow in the paper – a state of quasi-steady state flow, and (4) saturation. Furthermore, from Figure 2, it is possible to determine the duration of flow. For example, the flow rate during the fully wetted flow phase in Figure 2 is ~16 µL/min, which lasts for ~ 60 s, and the total duration of flow in the paper is ~ 150 s.

Figure 1: Conceptual design of device for monitoring flow in paper. (a) Schematic of the microfluidic device containing an input and output reservoir connected by a channel with embedded miniaturized electrochemical sensors. (b) Longitudinal cross-sectional view of the mechanism of operation. Electrolyte solution is first loaded into both reservoirs of the device. Then, paper is partially dipped into the device to induce flow that is recorded by the electrochemical sensors present in the channel.

Figure 2: A recording of flow rate (µL/min) vs. time (s) for a single strip of paper determined by our novel technique. Flow rates were calculated from theoretically expected values (Eqn.1) based on the measured current.
Using our technique, it was also possible to measure the flow rate in paper strips from the same source (i.e., the same paper product) but with different geometries (3-mm, 6-mm, and 12-mm wide and 5 cm long) (Figure 3(a)). As expected from the theory (i.e., Darcy’s Law), the cross-section of the paper was proportional to the flow rate generated. More specifically, the 12-mm wide paper produced the highest flow rates (~55 µL/min) of the three samples, and the 3-mm wide paper produced the lowest flow rates (~15 µL/min) of the three samples. Our technique was also utilized to distinguish different paper products, Figure 3(b). Specifically, in Figure 3(b) the paper products labeled as Product #1 and #2 were Pall Corporation (USA) Products: Absorbent Pad 133 and Pad 111, respectively. Product #3 was Whatman filter paper No.4. It is clear from Figure 3(b) that different paper products generate unique flow behaviors that can be recorded using our device.

**Figure 3:** (a) Comparing different geometries (3, 6, and 12 mm wide) of paper strips from the same source. (b) Comparing different paper products with the same geometry (3mm wide by 5cm long).

**CONCLUSION**

Overall, we present a novel, straightforward, and real-time tool to monitor flow in paper-based microfluidic devices. This is a much needed technology for the field because there is currently a lack of techniques to accurately monitor flow in paper or other porous materials. Using our technique, it is not only possible to record the different phases of flow in the paper (i.e., wetting out, fully wetted flow, and saturation), but it is also possible to determine the duration of the flow and the geometry of the paper. Furthermore, as different paper products have unique flow behaviors, our technique can be utilized to rapidly identify unknown paper samples or be used as a quality control (QC) tool. The techniques presented in this report will aid the development process of paper-based devices and, therefore, help to move the field forward to produce more advance diagnostic devices. Future work involves calibrating the data, evaluating a wider range of paper samples, and optimizing the fluidic device to better control for experimental variables.

**ACKNOWLEDGEMENTS**

The authors wish to thank the Basic Science Research Program (2012-0005090) for their financial support

**REFERENCES**


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