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An electrochemical-sensor system for real-time flow measurements in porous materials

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ABSTRACT

Flow monitoring in porous materials is critical for the engineering of paper-based microfluidic bioassays. Here, we present an electrochemical-sensor system that monitors the liquid flow in porous materials without affecting the real flow in paper-strip samples. The developed microfluidic sensor records an amperometric signal created by the solution movement mediated by paper wicking. This approach allows the *in situ* monitoring of the different hydrodynamic conditions of a specific paper geometry or composition. In addition, the method proposed in this work was employed to characterise the fluid flow of different nitrocellulose paper strips after oxygen-plasma treatment or dextran coating. The dextran fluid-flow modifiers were further used on the paper strip-based assays as means of signal enhancement. The proposed electrochemical-sensing method offers a valuable alternative to existing optical-based monitoring techniques for flow measurement in paper-based microfluidic systems.

1. Introduction

While its foundations date back to the 1940s, the field of paper-based microfluidics has recently regained interest largely because paper is a very low cost material that has the intrinsic ability to pump fluids by capillary forces (Cheng et al., 2010; Dungchai et al., 2009; Fu et al., 2012; Hwang et al., 2011; Lewis et al., 2012; Martinez et al., 2010; Muller and Clegg, 1949; Nie et al., 2010). The ultimate goal of a paper-based microfluidic device is to offer point-of-care diagnostics at an unprecedented low price ($\ll$ \$1 per device) to achieve a widespread use in medicine. The resurgence of paper-based diagnostics can also be attributed to the fact that the basic tools required to fabricate such devices are relatively inexpensive (Carrilho et al., 2009). Therefore, a wide variety of new paper-based devices has been proposed during this current renaissance of the field.

Critical to the development of any microfluidic platform is the availability of tools to monitor/measure the liquid flow within the device. With tools to monitor the flow, microfluidic designs can be experimentally validated in an effort to confirm theory or to identify the best configuration for the microfluidic components. For optically clear microfluidic devices, well-established flow-monitoring techniques already exist, such as microparticle image velocimetry (μPIV), which can provide detailed information about the flow profile (Sinton, 2004). Although an impressive number of paper-based devices have been reported in a relatively short period of time, methods to measure or quantify liquid flow in paper-based devices are scant.

To monitor the flow in a paper is not trivial, as it is a non-transparent, porous, dense material; these properties prevent its application in traditional flow-velocimetry techniques. Although techniques to monitor and measure the flow in paper have been recently proposed (Fu et al., 2011; Kauffman et al., 2010), there is yet to be a velocimetry technique for paper-based devices that is both easy to use and that provides detailed flow information in real-time. To address this critical need, we developed a non-optical technique, based on electrochemical velocimetry, to monitor the liquid flow in porous-material samples. Our data clearly demonstrated that our innovative technique can rapidly and accurately provide relevant information related to the geometry, flow duration, volume absorption capacity, and type of paper strips. Finally, the potency of fluid paper strips embedded flow modifiers was characterised using the proposed technique.

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2. Material and methods

The microfluidic sensor presented in Fig. 1 was designed using a solid modelling CAD software and fabricated using standard top-down fabrication techniques. The device is made of polycarbonate (PC) parts that are held together by double-sided pressure sensitive adhesive (DFM 200 clear 150 POLY H-9V-95, FLEXcon, USA). Each reservoir has a volume of 1.5 mL and the connecting channel is 2 mm wide, 1.5 mm high, and 19 mm long. The embedded electrochemical sensor was fabricated with screen-printing carbon paste (Product: C2000802P2, Gwent Group, UK) and Ag/AgCl ink (Product: 011464, ALS, Japan) onto a PC substrate (SI-1).

Paper samples were obtained from Pall Corporation (Absorbent Pad Pall 111 &133, Vivid 170 Nitrocellulose (NC), USA) and Whatman TM (Filter paper 4, UK). The samples were cut to a desired size with a paper-cutter (Smart cutter A445; Rexel, UK). The dimensions of the paper were verified by a digital calliper, *i.e.,* all paper samples had a tolerance of ±0.1 mm.

Electrolyte solutions of 10 mM $[Fe(CN)_6]^{4-}$ (Sigma-Aldrich) with 250 mM KCl (Junsei Chemical Co., Ltd., Japan) in DI water were prepared and used within 1 h of preparation to avoid excessive oxidation. The electrodes of the fluidic device were connected to a potentiostat (Model: VSP, Biologic, France); chronoamperometric recordings were performed using its proprietary software (EC-Lab Software v.10.02 Biologic, France). In addition to the theoretical calculation of the flow rate from the measured current, experimental recordings were calibrated as follows: While chronoamperometric measurements were performed, a syringe pump was connected to the outlet reservoir in order to induce a known range of suction flow rates in the device to mimic the capillary effect of the paper strips.

To minimise the effects of humidity on the measurements, experiments were performed in an enclosure with a water source. Furthermore, paper strips were vertically suspended into the output reservoir of the microfluidic device and were dipped to a depth of 5 mm into the liquid reservoir.

NC was modified either with an oxygen plasma treatment or dextran (DEX) solution. An oxygen-plasma treatment was performed on the NC strips using a *vacuum* plasma system (Model: Cute-MP, FEMTO Science, South Korea). Solutions of DEX were prepared separately by addition of 8% w/v, 12% w/v, and 20% w/v DEX T500 (MW: 500,000, Pharmascosmos, Denmark) to separate buffer solutions. The different DEX solutions were applied on the NC strips *via* a fine brush and allowed to dry at ambient temperature for 10 min prior to the experiment.

The potency of the DEX valves was tested on a prostate-specific antigen (PSA) immunochromatographic assay (Product: SD Bioline PSA Prostate specific Antigen Test, Standard Diagnostic Inc., South Korea). The strip sensor was separated from the plastic body part and decorated with a 2-mm thick band of a DEX solution at a median location from the test line and the control line. The assay was reassembled and tested with 100 ng/mL PSA in a phosphate-buffered saline (PBS) solution. Images of the test-area strip sensors were taken at fixed intervals with a camera (EOS 500D Canon) equipped with an EF 24–70 mm f/2.8 USM Canon zoom lens. The mean grayscale intensity of each sample was measured and analysed with the software Image J.

3. Results and discussion

3.1. Device calibration

Our technique is based on electrochemical velocimetry—a method in which an electrochemical sensor is embedded within a fluid-filled channel and acts as a flow sensor (Abi-Samra et al., 2013). When present in the channel, flow brings more electroactive species to the working electrode's surface, resulting in an increase in the current (Cottrell, 1903; Kjeang et al., 2007; Ranz, 1958). The limiting current, *i*, measured by the electrodes relates to the average volumetric flow rate, *v*, as follows:

$$i = 1.47nFC\left(\frac{DA}{B}\right)^{2/3} v^{1/3} \tag{1}$$

where *n* is the number of electrons, *F* is the Faraday 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 (Bard and Faulkner, 2001).

We developed a device (Fig. 1A) based on electrochemical velocimetry, which measures flow in porous materials. This device consists of two large liquid reservoirs that are connected by a channel containing an electrochemical sensor. An electroactive solution is loaded into the device and is allowed to come to rest (*i.e.*, stagnant). Next, amperometric measurements are performed on the stagnant solution to obtain a baseline current measurement (Fig. 1B). Subsequently, a material that exhibits capillary driven flow is partially inserted into the outlet reservoir *via* a dimensioned slit to induce flow within the device. Insertion of the porous material is operated *via* a mechanic arm to avoid any discrepancy in the capillary driven flow conditions (SI-2). The vertical positioning of the porous sample is preferred for monitoring convenience and do not modify the wicking process, since gravity is negligible in capillary based wicking process of porous material with these dimensions (Gillespie, 1959; Marmur and Cohen, 1997). Finally, the current measured during these processes is converted to an average volumetric flow rate *via* Eq. (1).

The electrolytes transport across the microfluidic channel results in a chronoamperometric signal that is proportional to the magnitude of the fluid flow. Proximity of the sensing apparatus to the wicking region of the paper provides real-time information of

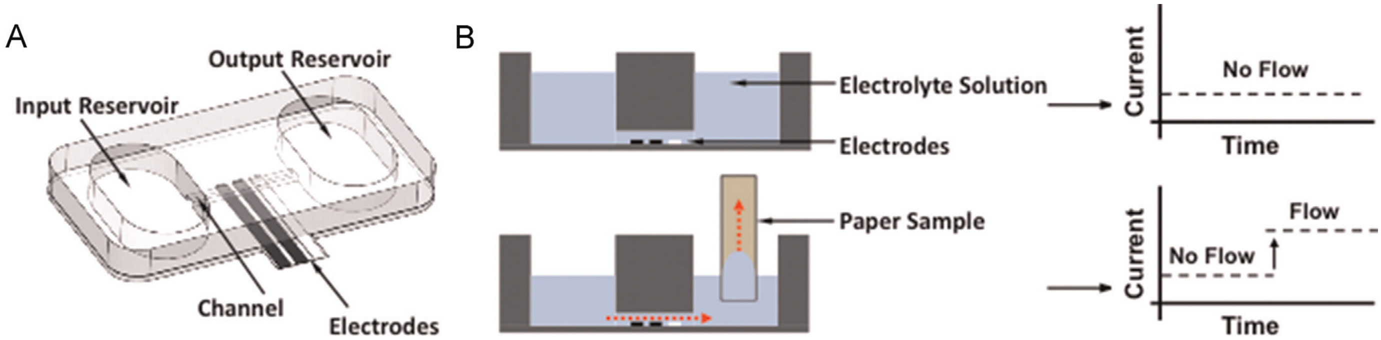

Fig. 1. (A) Illustration of the microfluidic sensor device. (B) Device operation with/without flow induced by introducing a paper strip sample to the outlet reservoir of the sensing device with corresponding electrochemical velocimetry measurements.