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DOI

[10.1109/SENSORS52175.2022.9967281](https://doi.org/10.1109/SENSORS52175.2022.9967281)

Publication date

2022

Document Version

Final published version

Published in

Proceedings of the 2022 IEEE Sensors

Citation (APA)

Motreuil-Ragot, P., Turcan, G., Wagenaar, B. D., Hunt, A., Sarro, P. M., & Mastrangeli, M. (2022). Ionic polymer metal composite-based microfluidic flow sensor for bio-MEMS applications. In *Proceedings of the 2022 IEEE Sensors* (pp. 1-4). (Proceedings of IEEE Sensors; Vol. 2022-October). IEEE.
<https://doi.org/10.1109/SENSORS52175.2022.9967281>

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Ionic polymer metal composite-based microfluidic flow sensor for bio-MEMS applications

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Abstract—Sensing flow rates in structured microenvironments like lab-on-chip (LOC) and organ-on-chip (OoC) is crucial to assess important parameters such as transport of media and molecules of interest. So far, these micro-electromechanical systems for biology (bio-MEMS) mostly rely on flow sensing systems based on thermal sensors. However, thermal flow sensing has limitations, since the measurement principle, which is based on generation of heat, can negatively affect the biological system by increasing the fluid temperature above physiological conditions. To overcome this issue, we propose a novel electro-mechanical flow sensor centered around the deformation of a cantilever made of a thin and biocompatible ionic electroactive polymer. The polymer, called ionic polymer metal composite (IPMC), is doped with ions naturally present in most cell media for LOC and OoC devices. Unlike already existing cantilever-based systems which rely on piezo sensitive materials, our IPMC-based flow sensor shows durability in wet environment. We were able to successfully measure pulsatile flow induced by pipetting with flowrate gradually increasing from $10\mu\text{L/s}$ to $40\mu\text{L/s}$. The proposed flow sensor shows good sensing capabilities ($4.78\text{ mV}/(\mu\text{L/s})$) with a linear behavior in the studied range. This work sets a milestone for using flexible, electroactive materials for sensing applications in delicate biological microenvironments.

Index Terms—Flow sensor, Ionic polymer metal composites, microfluidics, stereolithography

I. INTRODUCTION

An organ-on-chip (OoC) is an engineered microphysiological system that aims to recapitulate the smallest functional unit of an organ in order to perform in-vitro realistic drug analysis or disease modeling. A lab-on-chip (LOC) is a MEMS device that aims at analyzing chemical components in order to study disease and biomolecular species e.g. DNA, RNA, proteins, drugs. OoC and LOC can be both defined as biological micro-electromechanical systems (bio-MEMS). Since the very beginning of bio-MEMS, microfluidics has been a cornerstone to control precisely the microenvironment and mechanical clues in OoC or delivery of molecules of interest in LOC [1]. Therefore, monitoring flow inside microfluidic devices

is a crucial need. To date, widely used systems for flow sensing rely on thermal flow sensors [2]. In these sensors the difference in fluid temperature between a heating element and a temperature probe provides a measure of flow rate. This measurement technique presents certain drawbacks. For instance, the heat transfer might deteriorate the biological molecules of interest and disturb cell phenotype. Other sensing techniques exist, such as Coriolis flow measurement [3] or acoustic flow measurement [4]. However both techniques cannot record backflow easily which is essential for vasculature modeling in OoC [5]. In addition acoustic flow measurement and Coriolis flow measurement are complex, costly, bulky, and might be hampered by the presence of circulating cells in an OoC. Alternatively, cantilever-based approaches have been proposed in order to precisely measure flow rate. The displacement of beams can either be recorded optically or through a piezoresistive system [6], [7]. However, the optical approach is not integrated in the microfluidics device, while the piezo material characteristics get altered overtime by temperature and liquid exposure [2].

Recently, electrically conductive polymers have been studied for biological applications because of their inherent properties such as high flexibility and conductivity [8]. Among potential candidates, ionic polymer metal composite (IPMC) has recently emerged as it additionally features low voltage, robustness, biocompatibility and affinity with ionic medium [9]. Moreover IPMC is water compatible and doped with cations (Na^+) naturally present in most of the cell media used for LOC and OoC. IPMC, often addressed as artificial muscles [10], was first reported in 1992 by Oguro *et al.* [11] and extended by Shahinpoor *et al.* [10]. IPMCs are typically made of a perfluorinated sulfonic acid (PFSA) ion-conductive polymer known under the brand name of Nafion and chemically coated with platinum. The PFSA is composed of a chemically-stable fluoropolymer-copolymer covalently bonded with anions (sulfonate). The material is water permeable and absorbs cations,

which can freely move in the polymer backbone. In the sensing mode of IPMC, the induced deformation of the IPMC triggers displacement of the cations, leading to a voltage drop across the electrodes that can be used as a readout signal (Fig 1). Researchers already used IPMC for sensing flow [12] [13]. However Zhong *et al.* and Yang *et al.* used standard IPMC, 180 μm -thick for macro-scale application, not flexible enough for microscale applications such as microfluidic flow sensing. To the best of the authors' knowledge, thin IPMC has never been used for microfluidics sensing.

In this paper, we report the first IPMC-based microfluidic flow sensor based on a 50 μm -thick IPMC that can sense pulsatile flow in a microfluidic channel. We experimentally characterise the sensing performance of the system in saline solution commonly used in cell biology. We validate the viability of the concept by pipetting volumes ranging from 10 μl to 40 μl , and calculate the sensitivity of the sensor in the studied range.

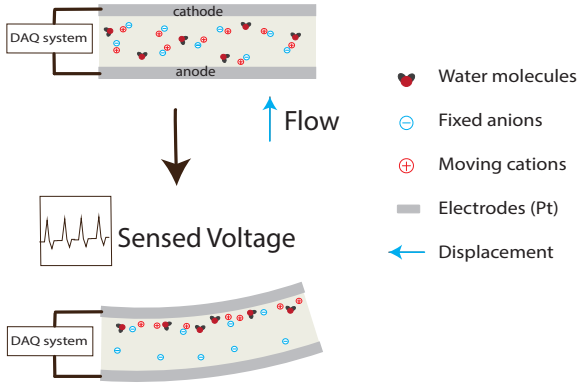


Fig. 1. IPMC sensing principle. The displacement of the ionic electroactive material (top) triggers cations migration, causing a charge imbalance, measurable as a voltage difference output across the electrodes (bottom)

II. MATERIALS AND METHODS

A. Flow sensor platform

The proposed platform is represented in Fig. 2. The platform is composed of the microfluidics structure in which the IPMC cantilever, working as flow sensor, is embedded and an electronic board connected to a PC.

The microfluidic structure hosting the flow sensor has been designed using computer-aided design software (Solidworks). The structure is made of 2 parts printed through high-resolution stereolithography (Asiga MAX X27 UV, Mojin Tech clear resin) (Fig 3). The microfluidic circuit is 0.5 mm high and 1 mm wide. In the center of the structure a 4 mm-wide chamber host the IPMC cantilever. The IPMC cantilever has been laser cut (Optec) with the dimensions of 2.5 mm x 7.5 mm and clamped in between 2 laser-cut gold electrodes. The bottom and top part of the flow sensor

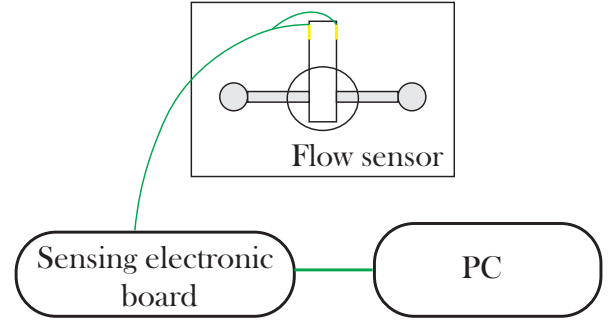


Fig. 2. Schematic of the sensing platform, IPMC is connected to the electronics board through gold electrodes

have been bonded using laser-cut pressure sensitive adhesive (PSA 81 μm -thick, Adhesive research). The IPMC has been manufactured as previously described by Motreuil Ragot *et al.* [14], the electrodeless deposition recipe has been optimized for thin Nafion (Nafion 212, 50 μm -thick Alfa Aesar).

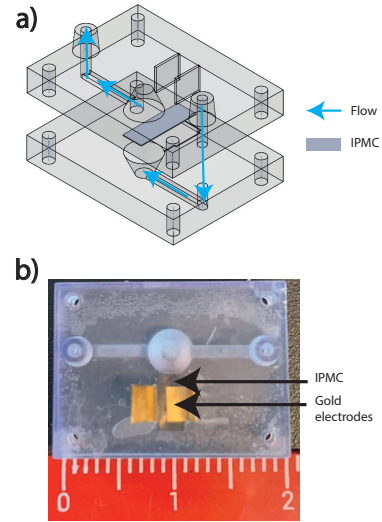


Fig. 3. a) CAD view of the flow sensor with the IPMC cantilever embedded in the center and direction of the flow. b) Close view of the flow sensor, gold electrodes can be seen.

We have developed an electronic board for sensing the charge produced on the IPMC electrodes [15] (Fig 4). IPMC electrodes are connected to the board input. The first stage of the board is made of a charge amplifier circuit with gain $G=100$. The signal is sent to an instrument amplifier ($G=1$), then a second-order passive low-pass filter with cut-off frequency of 1125 Hz is used to filter out high-frequency noise. Data are saved in real-time on a memory card.

B. Flow sensor characterization

To characterize the flow sensor, phosphate buffered saline solution (PBS) has been used. PBS is a commonly used saline solution, employed to keep osmotic pressure in cells medium and wash biological samples. PBS was injected using a micro pipette (Gilson), and pipette tips have been connected to the input and output of the flow sensor. Manual pipetting

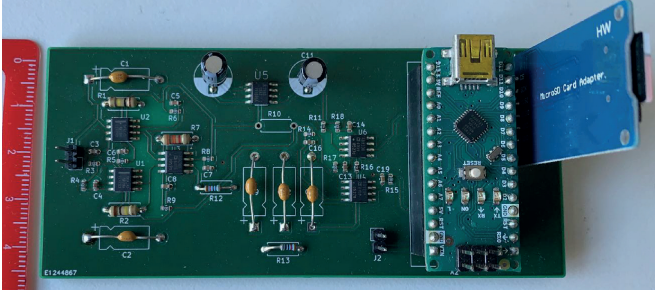


Fig. 4. Close view of the charge-based electronics board.

with a cadence of 1 s has been performed with volumes increasing from 10 μL to 40 μL . The recorded data have been processed using Python 3.6. The signal has been filtered using Savitzky–Golay filter method. For each pipetted volume, 12 flow peaks have been detected and used to calculate the flow rate (Fig. 5 a). Mean and standard deviation of the volumetric flowrate has been calculated using the pipetted volume divided by time recorded between each peak. The voltage measured against volumetric flowrate was used to obtain the responsivity curve (Fig. 5 b). Fitting with a 1st-order polynomial has been performed using least mean-squares method in Python 3.6 for the linear part of the responsivity curve.

III. RESULTS AND DISCUSSION

Flowrate measurement data for 3 different volumes show a good fit ($R^2 = 0.998$) with a first-order polynomial in the linear range ($4.78x + 116.92$). The sensitivity extracted from the slope of the first-order polymer is 4.78 mV/($\mu\text{L/s}$).

Values can be compared to the flow measured with standard IPMC or cantilever-based design. Mohammadamini *et al.*, who used an optical cantilever-based flow sensor, were able to obtain a sensitivity of 0.126 $\mu\text{m}/(\mu\text{L}/\text{min})$ in the range of measured flow rates (0-100 $\mu\text{L}/\text{min}$) [6]. Lei *et al.* who used a thick IPMC sensor (254 μm thick) could detect flow velocity in the cm/s range in the vicinity of their IPMC sensor for flow detection in an open environment [16]. In addition we can compare the sensing performance to the work of Zhang *et al.* who achieved to sense flow in 0–0.23 m/s range with a cantilever-based piezo sensor [7]. Unlike IPMC, the performance of piezoresistive material can be influenced by temperature and humidity overtime. Thus, aging of the materials used for piezo sensitive flow sensor have adverse effects on sensor performance, limiting its use in wet, warm environment such as in bio-MEMS.

We noticed output signal saturation starting at high flowrate (Fig 5). We hypothesize that the saturation of our sensor comes from the relative dimension of the ionic-electroactive cantilever and the chamber where it is inserted. A bigger chamber and longer cantilever could achieve detection in a wider range of flowrates. In addition, longer microfluidic circuit would allow to use higher liquid volumes. Performing further experiments under wider flow range, and calibration with precise thermal flow sensor to further quantify the sensor

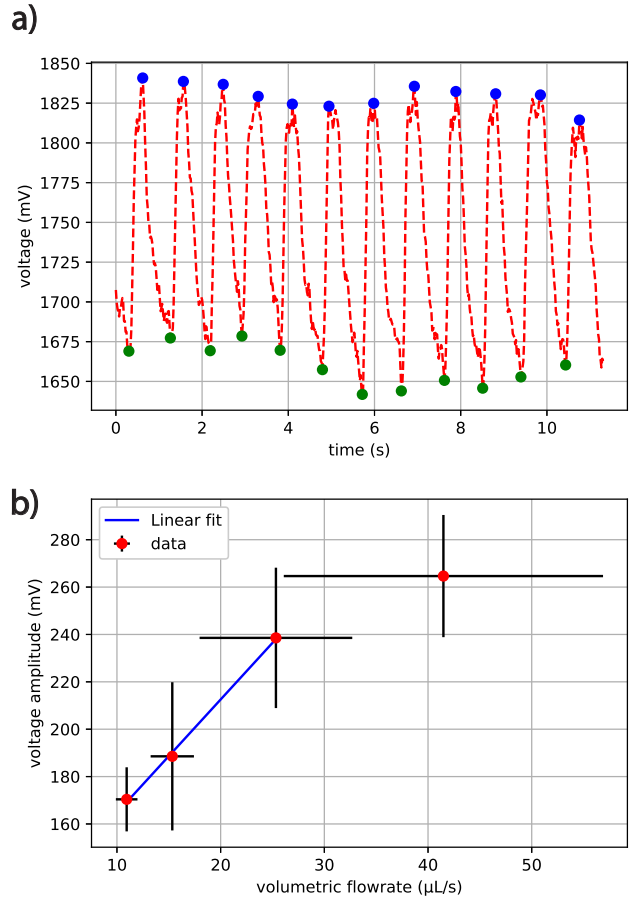


Fig. 5. a) Peaks detected for 10 μL pipetting. Blue, top of the peak used to calculate the voltage amplitude. Green, points used to estimate time for each peak. b) Responsivity plot. Linear fit used to calculate the sensitivity (blue), $R^2 = 0.998$. Sensitivity is 4.78 mV/($\mu\text{L/s}$).

sensitivity, are reserved for future work. One might also consider to characterize the sensor with fluids of different viscosity (e.g., blood).

IV. CONCLUSION

We have presented a novel, simple, inexpensive and easy-to-use flow sensor device that could be used for bio-MEMS applications. The inherent properties of the ionic electroactive polymer make the device a good candidate to monitor flow in sensitive microenvironments such as LOC and OoC devices. This sensor could compete with already existing systems such as other cantilever-based sensors and thermal sensors. The proposed thin ionic polymer-based flow sensor allows to measure pulsatile flowrate in a range from 0 to 40 $\mu\text{L/s}$ with a sensitivity of 4.78 mV/($\mu\text{L/s}$). Future improvements and characterization will aim at increasing the range of detection and calibrating the measurement for further comparison. The proposed device could be easily tailored to many other uses such as Point-of-care (POT) and micro total analysis system (μTAS) applications. The present IPMC-based device anticipates a potentially significant impact of smart materials in the development of bio-MEMS.

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