A NEW MICROFLUIDIC MONITORING METHOD USING INFRARED SENSOR UNIT

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ABSTRACT

A new microfluidic flow monitoring method has been developed using infrared sensors, and then fully implemented and characterized over an immunoassay lab-on-a-chip (LOC) which needs precise monitoring and control for a sequential flow of reagents. This new microfluidic monitoring method can be applied for the development of a functional microfluidic tracker for counting and characterizing droplets in a microfluidic droplet generator and digital PCR, cells in a cell counter, or reagent columns in an immunoassay LOC.

KEYWORDS: Infrared fluidic control sensor, microfluidic monitoring method, immunoassay lab-on-a-chip

INTRODUCTION

There has been a large demand for the development of new methods for monitoring microfluidic flow of reagents, cells, droplets flowing through microchannels or microchambers which can improve the performance of point-of-care testing (POCT) [1, 2]. DiFilippo et al. reported an active control of fluid using a charge couple device (CCD) imager to keep track of fluid to provide more degree of control [3], but CCD elements are costly to implement. Our lab reported sequential flow of pre-loaded reagents on immunoassay LOC with a time-based pump control [4], which was simple but lacked precision in fluid control. In this work, we have developed a novel microfluidic flow monitoring method using an infrared sensor unit (ISU). The infrared sensing method was fully characterized over an immunoassay LOC which needs precise monitoring and control for sequential flow of reagents.

EXPERIMENTAL

The infrared sensor unit (ISU) consists of an infrared (IR) LED emitting 1,550 nm wavelength (LED1550L, ThorLabs) through a microchannel and an InGaAs IR-photodiode (FGA01, ThorLabs) detecting the IR intensity from the other side of the microchannel as shown in Figure 1(a). The output voltage with air filled inside the microchannel is considered as the baseline signal. Since most reagents contain biological molecules in aqueous solution, the molecules in the reagent absorb a considerable amount of IR signal emitted from the LED which causes a significant reduction in the output voltage from the baseline. Hence, the level of output voltage of the photodiode can be used to indicate the presence of different molecules or fluids filled inside the microchannel.

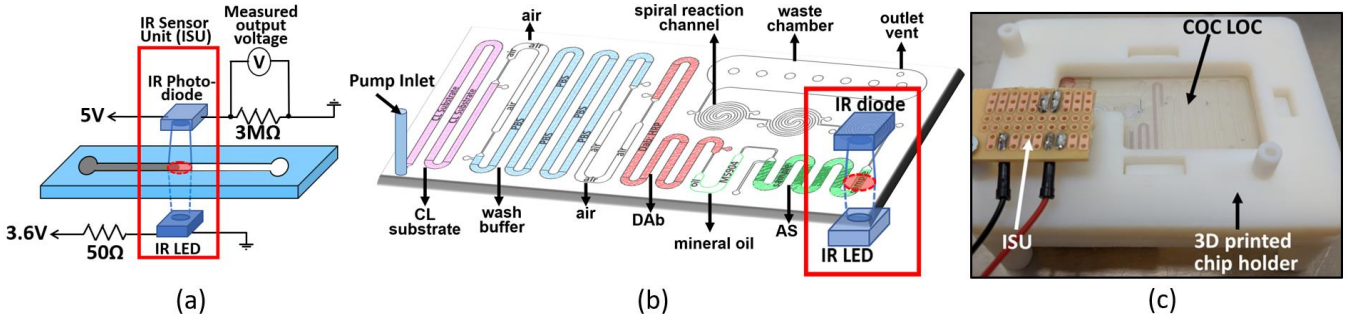

Figure 1: (a) Schematic of IR Sensor Unit (ISU), (b) Schematic of LOC with ISU located at the end of sample chamber, (c) Picture of COC chip (reagents are added with food dye for better photographic visual), and (d) Picture of 3D printed prototype.

The ISU was positioned on the both sides of a Cyclic Olefin Copolymer (COC) immunoassay LOC as shown in Figure 1(a). The ISU was implemented at the end of the sample chamber of the LOC, as illustrated in Figure 1(b), to keep track of fluid flowing through the three spiral reaction channels. A 3-D printed structure was built to align the ISU and LOC as shown in Figure 1(c). Assay reagents were flowed sequentially through the spiral reaction channels in the following sequence: antigen spiked artificial serum (AS), horseradish-peroxide (HRP) conjugated

detection antibody (DAb), washing buffer (PBS), and chemiluminescent (CL) substrate [4]. Each reagent is separated with an airgap, whereas the gap between AS and HRP-DAb is filled with mineral oil M5904.

RESULTS AND DISCUSSION

As shown in Figure 2(a), the signal response of ISU to different fluids in the sample chamber was recorded for air, reagents, and mineral oil M5904 through microchannels. The measured results show that the ISU can identify whether the fluid inside the microchannel was air, oil, or water-based reagents, even though the ISU might not be sensitive enough to differentiate different types of water-based reagents. Figure 2(b) shows the output voltages from the ISU when a full immunoassay for the LOC shown in Figure 1(b) was performed. Measured output voltages of reagent, oil and air were 2.7, 4.2 and 3.9 V, respectively. The detection and control of different fluid phases can be achieved for the optimized immunoassay of POCT. By using the time span with a given flow rate, the ISU can also be used as a volume-measuring sensor to measure the volume of each fluid loaded into the reaction zone.

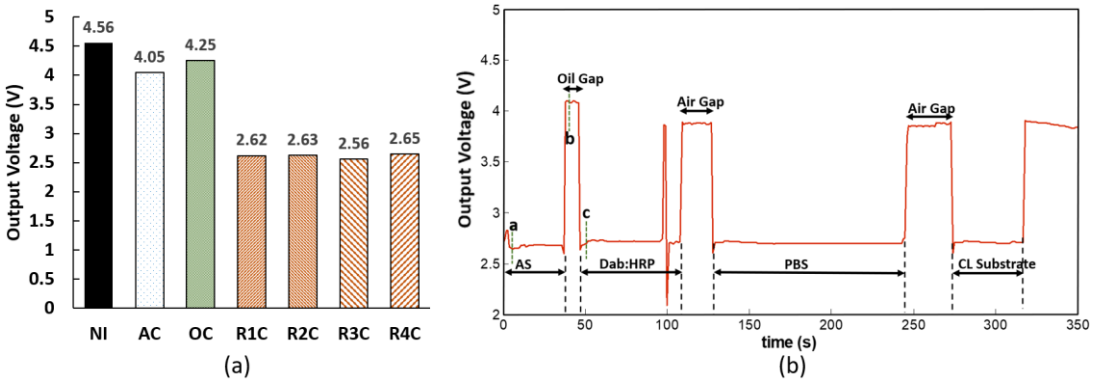

*Figure 2: (a) Static output signal of ISU (NI: no interference; AC: air in chip; OC: oil in chip; R1C: reagent diluent in chip; R2C: serum in chip, R3C: PBS in chip; R4C: CL substrate in chip) and (b) Dynamic output signal of ISU for continuous moving fluid on chip (*a - *timestamp when sample is entering spiral chambers;* b - *timestamp when sample is fully loaded into all spiral chambers; and* c - *timestamp when DAb-HRP is entering spiral chambers).*

CONCLUSION

In this work, an active microfluidic tracker using infrared sensor unit (ISU) has been developed and fully characterized for precisely tracking reagents flowing through polymer microchannels. This new microfluidic monitoring method can be used for the development of a functional microfluidic tracker for monitoring and characterizing droplets in microfluidic droplet generators [5], cells in cell counters, as well as liquid columns in immunoassay LOCs. The simple, low-cost ISU based microfluidic tracker can be easily integrated with any lab-on-a-chips, cell-on-a-chips or POCTs which require precision control of moving cells or fluid columns.

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