ABSTRACT
This paper reports a novel silicon based lateral flow device for DNA hybridization detection. The device applies microfabricated micropillar array to generate capillary flow with controllable capillary flow rates. A rapid DNA hybridization detection was demonstrated within 1 min with extremely low sample consumption.

KEYWORDS: Lateral flow device (LFD), Micropillars, DNA biosensor

INTRODUCTION
The concept of point-of-care testing (POCT) came into the spotlight for human healthcare. Capillary flow devices (also referred to as lateral flow devices, LFD) have received increasing interests over other microfluidic actuations (e.g., pressure driven) for POCT applications [1]. Paper-based test strips (e.g., pregnancy test strip) are successful products for POCT utilizing such a technology. However, with the drawback of simple unidirectional fluidic movement of current strips, it is difficult to precisely control the capillary flow and thus, their application remains very limited. In this abstract, a silicon based LFD (Si-LFD) was fabricated, which provided greater capillary flow control capability and showed the potential to implement more complicated assays. As a first test, a rapid DNA hybridization detection using the Si-LFD with extremely low sample consumption was demonstrated.

WORKING PRINCIPLE
The strategy for implementing the concept of capillary DNA sensor is illustrated in Figure 1. A micropillar array with high aspect ratio inside a microfluidic channel was designed. DNA probe spots are pre-spotted on the detection region and sample droplets is introduced into the device by capillary force. The sample containing excess analyte is drawn by the capillary force, which largely determines the flow rate and total sample volume used for the DNA hybridization. A few minutes after the introduction of the sample into the chip, most of the DNA complements has either hybridized to the DNA probe spots, or been transported through the capillary pump. The fluorescence signal during the hybridization can be monitored using an external fluorescence microscope.

EXPERIMENTAL
The device was fabricated using standard lithography and deep reactive ion etch (DRIE) of Si wafer. Afterwards, a SiO$_2$ layer was thermally grown on the device to obtain a hydrophilic surface. Three different pillar diameters (PDs) of 5 µm, 2.5 µm and 2 µm with inter-pillar distances (IPDs) half of the PDs were prepared. Between the sample loading port and the cylindrical micropillar array, there are well-designed distributor region to enable a low-dispersion transition.

To characterize the capillary flow behavior, one-dimensional liquid propagation was studied. As shown in Figure 3a, the device was positioned vertically over a water reservoir and was partially submerged in the water reservoir. The water rise was recorded and the wicking capability was assessed.

To test the capability for biomolecule detection, fluorescently labeled DNA hybridization detection was demonstrated on the device. The single steps are depicted in Figure 1: (1) the Si-LFD was functionalized with a self-assembly monolayer of azide silane [3]. (2) 1 µM alkyne DNA probe was spotted on the micropillar array with 100 nL DNA sample for each spot. (3) The device was incubated in 90% humidity for 30 min, rinsed with DI-water and dried with N$_2$.

Figure 1: Schematic of Si lateral flow device (Si-LFD) for rapid DNA hybridization detection.

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a 20 µL droplet of Cy3 labeled complementary DNA (100 nM) was added into the sample loading port and the sample penetration in the device and DNA hybridization dynamics were recorded with a fluorescence microscope.

RESULTS AND DISCUSSION

Figure 2 shows representative SEM images of the Si-LFD with 5 m PD and 25 m height. The device shows highly ordered cylindrical micropillars with 5 m PD and perfect vertical pillar walls. The static contact angle with water on a flat surface of the Si-LFD is 39°. Figure 3a shows an image taken during the capillary rise of water in vertically-oriented, partially immersed Si-LFDs. It is observed that the pillar array with 5 m PD has the fastest capillary flow while the pillars with 2 m PD have the lowest. Figure 3b shows the averaged flow rates for each centimeter along the devices for the three different Si-LFDs during the capillary rise. The maximum rise height is about 5 cm for the 2.5 m and 2 m PD devices, while the liquid penetrates the entire length (8 cm) of the 5 m PD Si-LFD.

Figure 2: SEM images of fabricated Si-LFD: (a) top view of the distributor and micropillars (b) side view of the 5 m PD micropillars (c) cross-sectional view of the 5 m PD micropillars.

Figure 3: Image of liquid penetration during the capillary rise of water; (b) averaged capillary flow rates for three Si-LFDs with different PDs/IPDs

Figure 4 shows series of images from the DNA hybridization experiment. In Figure 4a, the micropillar didn’t show fluorescent signal before the Cy3 labeled complements approach the detection region. After about 20 s, a clear liquid front could be observed when the complements penetrated into the detection region, as shown in Figure 4b. Once the complements reached the area of the DNA probe spot, a higher signal with a profile of the spot could be observed, and after 35 s of sample addition, the fluorescence signal due to DNA hybridization was readily observed in the area of the spotted probe DNA (Figure 4d). In Figure 5, after thoroughly rinsing the device with PBS to remove the bulk complementary DNA, a bright fluorescence signal from the spot was still easily discernable with each pillar fluorescently.
We also should mentioned that for this DNA hybridization detection on the developed Si-LFD, only 100 nL DNA probes were used for each spot and 20 µL DNA complements for the hybridization.

CONCLUSION
We designed and fabricated a compact Si-LFD, which allowed generating capillary flow and developing lateral flow assay. The capillary flow behavior was characterized and it was found that the 5 µm micropillar array provided a capillary force to fill in the entire device with highest flow rate, compared to 2.5 µm and 2 µm micropillar arrays. A rapid DNA hybridization detection was successfully demonstrated within 35 s with extremely low sample consumption. The proposed Si-LFD and DNA detection method represent an alternative for conventional LFD technique to overcome its shortcomings [1].

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