DIGITAL MICROFLUIDIC CHIP WITH BLADE STRUCTURES FOR PRECISE DROPLET SPLITTING

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ABSTRACT

We present here the first attempt to fabricate micro 3D structures on DMF chips for precise droplet splitting to achieve one drop multiple analysis. The structures were constructed by fabricating SU8 blades of different height on the dielectric layer. The droplet splitting is more consistent and controllable compared with the current 3-electrode splitting methods. With this new method, DNA multiplex detection was successfully performed in parallel with a single fluorescence channel. All these together had confirmed its potential for a wide range of multi-step biochemical applications including post-PCR molecular detection for point-of-care disease diagnostics.

KEYWORDS: Digital Microfluidic, Splitting, Electrowetting, Micro Structures, Multiplex Detection

INTRODUCTION

Digital microfluidics (DMF) is a technology that allows the manipulation of discrete micro droplets on electrode arrays by applying actuation forces such as electro-wetting on dielectric (EWOD) force, magnetic forces or opto-electrowetting force. It has been successfully utilized in biochemical assays for cell analysis, DNA amplification or immunoassays etc. For multiple on-chip quantitative analyses, a uniform on-chip droplet splitting is highly recommendable. Reported research shows that three consecutive electrodes can be coordinately charged to split a mother droplet into two daughter droplets, with a volume variation of the latter in the order of 7%[1] and the success of splitting depending on the sizes of the droplet and the electrode, the actuation voltage and the gap between the bottom plate and the top plate of the DMF device.[2] All of those characteristics of the current splitting practices prevents the use of DMF applications on precise multiple analyses of one single drop. To address this issue, we introduce here a new approach for accurate droplet splitting by constructing 3D micro structures, designated as blades on DMF chips, as shown in Fig.1(a).

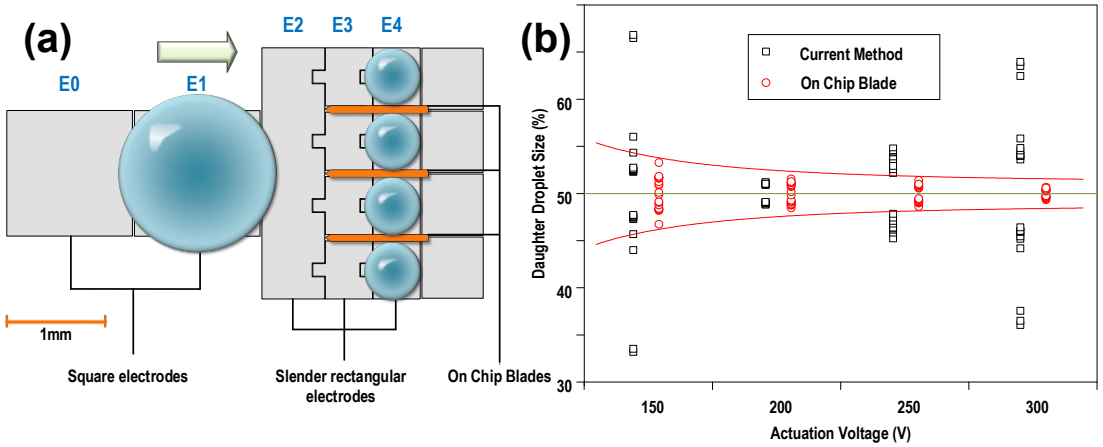

Figure 1: (a) Top view of an on chip blade system that split one droplet into 4 daughter droplets. (b) Volume in Percentage of two daughter droplets. The droplet splitting, with or without blade, was repeated 10 times for each of the 4 different actuation voltages respectively.

RESULTS AND DISCUSSION

When compared with the currently accepted method, the splitting performance of the proposed scheme is more consistent and independent of the original volume or the initial position of the mother

droplet against the electrodes. We observe less than 2% dividing variation of the daughter droplets volume when applying this method to generate two equal size daughter droplets on various kinds of fluids. As Fig.1(b) depicts, the volume error of the proposed method, when compared with the existing three consecutive electrodes splitting, was smaller and can be further narrowed by increasing the actuation voltage. Moreover, as shown in Fig. 2(a-d), we can accurately achieve uneven daughter droplets with different volumes, from 20% to 80%, by adjusting the blade position. We have also fabricated multiple blades on one electrode to accomplish one-step multiple daughter droplets generation with a volume error lower than 3% by charging only one electrode, which significantly saved on-chip electrode space and control. The shape, height, and length of the blade and their effects on the success rate of the droplet splitting were also investigated, demonstrating that the splitting was robust as long as the height of the blade was more than 2/3 of the height of the droplet while the length and shape of the blade did not affect the splitting accuracy. We took septicemia as a model system for multiple potential microbial pathogens detection. One single mother droplet with different combinations of pathogen DNA mixture was successfully split into four and mixed with individual DNA molecular beacon probes for different pathogen targets, as illustrated in Fig.2(e).

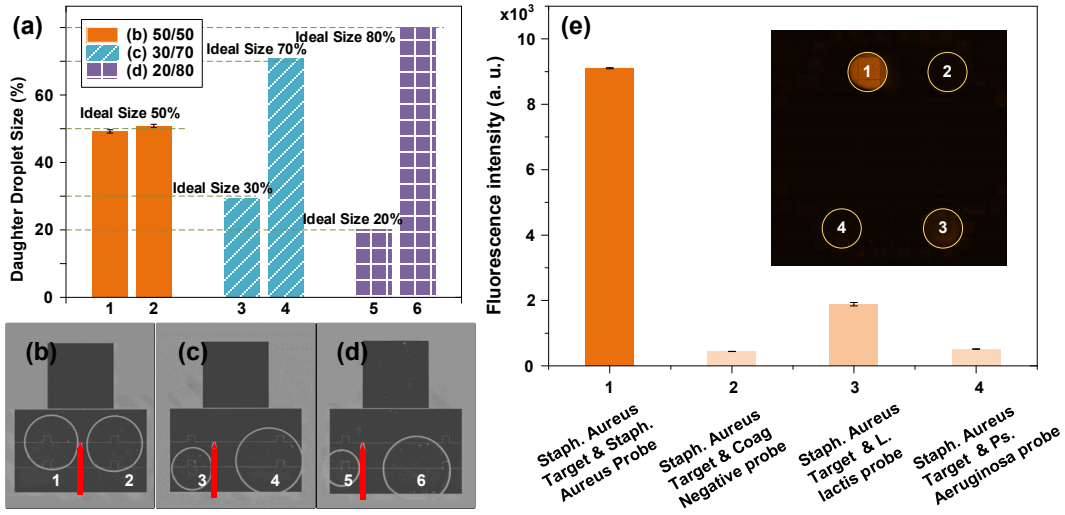

Figure 2: (a) Average volume and standard deviation (%) of 10 splitting from each of 3 different blade locations. (b) The result of the multiplex molecular diagnostic assay for the detection of different DNA segments of microbial pathogens associated with septicaemia.

CONCLUSION

In this paper, a novel simple, robust and accurate droplet splitting method allowing us to analyze one droplet for multiple assays was introduced. In the assay, DNA molecular beacon probes were labeled with the same fluorophore, significantly simplifying the detection system, impossible to be achieved in conventional off-chip detection assays.

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