On-chip Pico-pipette: A Method for Precise Delivery in a DMF system

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Digital microfluidics (DMF) experienced a substantial technical development in recent years, as a kind of microfluidic system that can realize automatic precise operation. This paper reports a novel method with a jetting electrode design for precise and controllable sample dispense.

Different chip designs have been developed for sample delivery and mixing on-chip. For the channel based microfluidic platform, passive and active micromixer were presented [1, 2]. For the electronic-based digital microfluidic (DMF) platform, droplets were normally merged with similar amount of size to realize sample mixing [3, 4]. Electronics control of the DMF device make the droplets manipulation automatic and accurate. However, volume increase imposes difficult mobility because it implies surpassing the limit of the single electrode. Moreover, it requires complex merging and splitting operation for multi-step reactions due to the change in concentration. On the other hand, a totally different protocol intimidates biochemical researchers of trying a microfluidic platform because of the necessary training for using an off-chip micropipette.

In this work, we use a phenomenon designated by "jetting" for sample transfer. When we supply the bar-shaped jetting electrode with high AC voltage, groups of tiny droplets would be ejected from the mother droplet and picked up by the droplet that needs to be added.

Figure 1 illustrates the design of the system. We designed a bar-shaped electrode for jetting. The control electronics generated the driving AC voltage to the DMF chip. Figure 2 shows the operation of the sample transfer. We used a periodic peak high AC voltage amplified from a square wave signal for jetting and the lower AC sinusoidal signal for movement.

We tested the effect of bar width, time, voltage and frequency on jetting volume to allow a controllable volume transfer. We loaded a 100μM DNA probe with fluorescence onto the chip as the sample to be transferred and a 10mM tris-HCl buffer (~0.5uL) as the pick-up drop. The jetting volume could be calculated by measuring the fluorescence intensity change of the pick-up drop.

As Figure 3 shows, with the increase of the pipetting times, the addition of the DNA probe increased with a good linear relationship. Moreover, increasing the voltage and frequency of the supplied signal resulted in a larger jetting volume.

The proposed designed implemented a PH change test. The sample of the NaOH solution was transferred to the droplet containing indicator (Thymol Blue). With the increase of PH value, the colour of the indicator droplet became blue.

We tested our pico-pipette for DNA identification on chip. When the drop containing specific DNA probe was transferred to the drop containing the corresponding DNA target, fluorescence would be detected. Figure 5 shows the results.

This simple, low-cost and controllable on-chip pipetting method for sample transfer reveals a significant potential to improve the efficiency of sample transfer on DMF chips and reduce the complexity of the operation. We expect that with such advantages this method can be easily accepted by biochemists and thus become a bridge to realize "lab-on-a-chip".

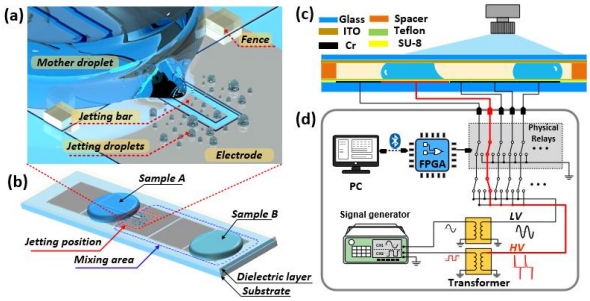

Figure 1: Device design of pico-pipette. (a)Detail of the jetting position. (b) Pico-pipette chip design. (c) Section of the DMF chip. (d) Control electronics of the DMF system. ***[Enlarged Figure]***

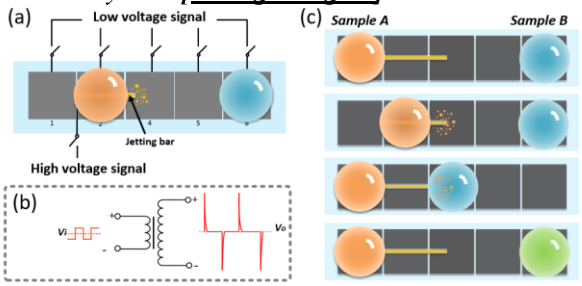

Figure 2: Pipetting operation. (a) Low voltage AC signal used for movement, and high voltage AC signal used for jetting. (b) The square wave was transferred to a high peak voltage signal by a transformer. (c) The pipetting operation process.

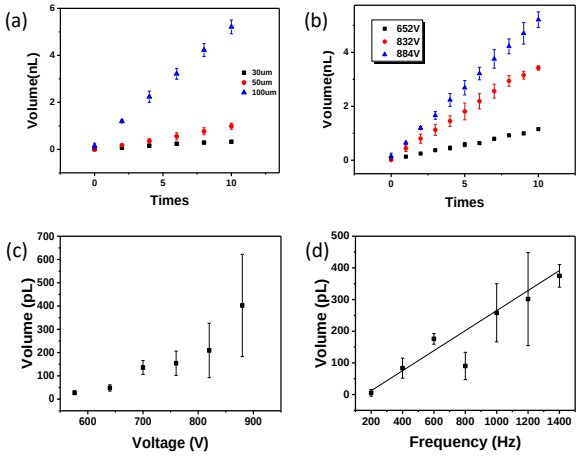

Figure 3: The effect of bar width, time, voltage and frequency on jetting volume.

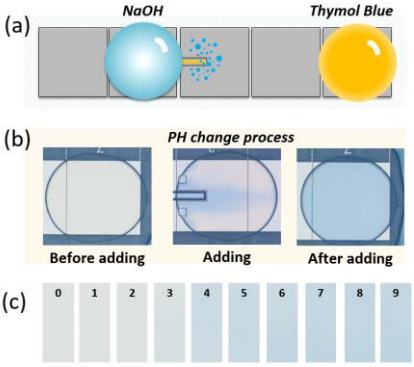

Figure 4: PH change test. (a) Samples containing NaOH used as jetting drop, and the drop containing Thymol Blue loaded as pick-up drop. (b) The process of PH change test. (c) Color change with increasing number of pipettes.

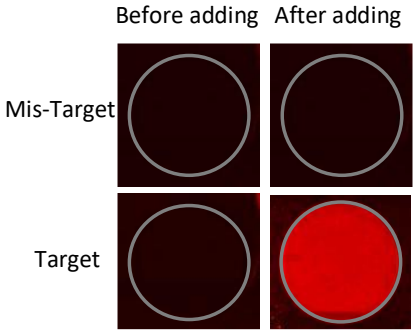

Figure 5: DNA detection. When the probe was transferred to the Mis-target, there was no fluorescence detected, however, when the right target was added with the probe, the drop lighted up.

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