GRAVITY-DRIVEN PULSATILE MICROMIXER WITHOUT USING DYNAMIC OFF-CHIP CONTROLLERS

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ABSTRACT

This paper reports a pulsatile micromixer without using any dynamic off-chip controllers and only relies on constant water-head pressure. This significantly differs from other pulsatile micromixers that use expansive, bulky controllers including high-voltage power supplies and function generators. The device is composed of self-actuated oscillator and mixer units, both of which include microfluidic valves and flexible membranes, With a constant input of water-head pressure, the oscillator unit generates pulsatile pressure to drive the mixer unit, thereby producing narrow periodic fluidic bands of two solutions for rapid mixing. The micromixer achieves up to 95% mixing efficiency in the flow rate and flow switching frequency of 2–20 μL/min and 14–20 Hz, respectively.

INTRODUCTION

Microfluidic mixer is widely used to implement the chemical and biological reactions. Such reactions include polymerization and crystallization in chemistry [1–4] and DNA fording and enzyme assay in biology [5–8]. So far, numerous passive and active micromixers have been presented [9–12]. The passive micromixers, however, normally require a long mixing distance of up to several centimeters [9, 10] and have limited ranges of operational flow rate. On the other hand, while the active micromixers present efficient and rapid mixing within a short distance, they need dynamic off-chip controllers for their actuation [11, 12]. This makes their experimental setups complex and sometimes incompatible with the microfluidic system integration.

Among the active micromixers, pulsatile flow mixers require several external controllers, such as high-voltage supplies and function generators. If pulsatile mixing can be formed without any external off-chip controllers, it can greatly simplify the active micromixer system. We have recently developed an oscillator that can generate pulsatile pressure driven by the constant water-head pressure, without the need for external controllers [13]. However, the valve switching frequency and flow velocity affect to each other and flow velocity increases with the increasing valve switching frequency. Under that condition, long periodic bands are produced and effective micromixing is not possible.

Here, we develop a pulsatile micromixer driven by constant water-head pressure without using any dynamic off-chip controllers and achieves efficient mixing of 95%. The system composed of oscillator and mixer unit. The oscillator unit affects the switching frequency and mixer unit can control the flow rate. It means that the frequency and flow rate can be separately controlled, rather than interacting with each other. First, we explain the structure of the micromixer system and its working principle. Then we analyze the mixing efficiency at 14–20 Hz switching frequency and 2–20 μL/min flow rate.

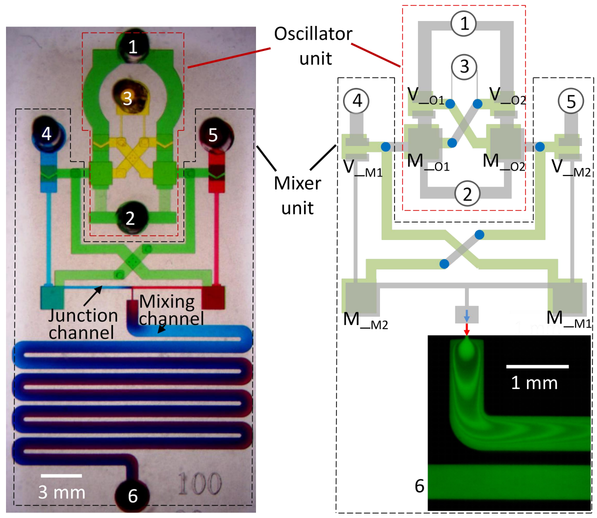

Figure 1: Photograph (left) and schematic (right) of the micromixer system. The valves of oscillator (mixer) unit are V_{O1} and V_{O2} (V_{M1} and V_{M2}). The flexible membranes of oscillator (mixer) unit are M_{O1} and M_{O2} (M_{M1} and M_{M2}). Applied pressures are noted in the schematic (right).

MATERIALS AND METHOD

Device and structure

The micromixer system consisting of three layers (Top and bottom channels and middle layer membrane) includes oscillator and mixer units (Figure 1). Each unit has two microfluidic valves and two flexible membranes. In the oscillator unit, two valves (V_{O1} and V_{O2}) and two flexible membranes (M_{O1} and M_{O2}) are automatically operated to generate pulsatile pressure by the preprogrammed interaction of each component under the constant water-head input pressure. In the mixer unit (Fig. 1), two valves (V_{M1} and V_{M2}) and two flexible membranes (M_{M1} and M_{M2}) are controlled by the pressure pulses of the oscillator unit.

Device fabrication

The device was fabricated by multilayer soft lithography. Top and bottom channels were made by polydimethylsiloxane (PDMS). Master mold was fabricated with Si wafer and SU-8 (Model 2025 and 2075, MicroChem). Middle flexible membrane was made through the spin coating of PDMS and curing at 120 °C. Three layers were bonded by a plasma oxidizer (Model Cute-1MP, FemtoScience) for 30 s. We put stamps on valve sheet and membrane sides during plasma treatment and prevented the bonding of the area of the valve seat.

Experiment setup

In the oscillator unit, input and output were 5.5–7.5 kPa and -9 kPa. We varied the input pressure to get 14–20 Hz frequency. In the mixer unit, two input pressures commonly maintained 3.5 kPa and the output pressure was varied with -0.5–3.4 kPa to get the required flow rate. In order to quantify the mixing efficiency, we used fluorescent solution (Model Fluorescein, Sigma-Aldrich) and captured images with a digital camera (Model u-Nova20C, Novitec) and a microscope (Model Ti-U, Nikon).

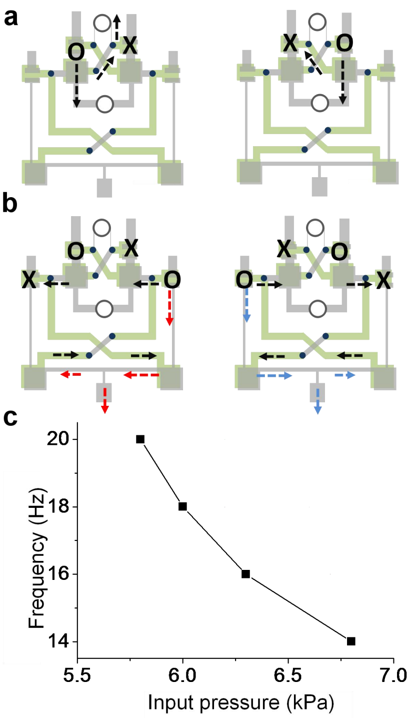

Figure 2: Self-generation of pulsatile flow. O and X show the valve open and close state. The arrows show the fluidic directions of working solutions. (a): Self-regulation of opening and closing of valves in the oscillator unit. The state variation of the valve generates periodic pressure pulses. (b): Generation of periodic flow pulses in the mixer unit. This process is controlled by the oscillator unit. (c): Change of the fluidic switching frequency by water-head input pressure.

RESULTS AND DISCUSSION

Mixing process with gravity driven oscillator

The micromixer system composed of oscillator and mixer unit (Figure 1). Each unit has two microfluidic valves and two flexible membranes. The oscillator unit is driven by constant pressure and its valves and membranes interact with each other. Opening (or closing) the valves (V_{O1} and V_{O2}) increases (or decreases) the pressures of the top and bottom sides of the membranes (M_{O1} and M_{O2}). (Figure 2a). Because this process repeats by the autonomous interaction of the device components, the oscillator unit generates pulsatile pressure at the membranes. With the pulsatile pressure, the mixer unit can drive its valves and membranes and generates alternation of two solutions at its outlet (Figure 2b). Because of the fast alternation, narrow fluidic bands are generated, thereby decreasing the diffusion length between the bands. Figure 2c shows the fluidic switching frequency by the input pressure.

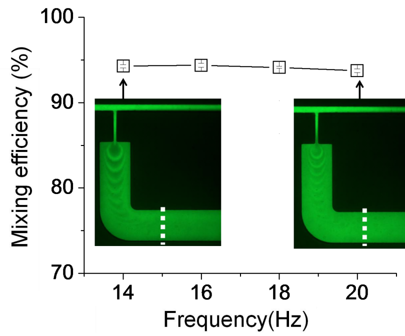

Figure 3: The influence of valve switching frequency on the mixing efficiency at a flow rate of 2 μL/min.

The effect of switching frequency on mixing efficiency

We have changed switching frequency and analyzed its effect on the mixing efficiency. To change the frequency, input pressure of oscillator unit was varied. The mixing efficiency was measured at the line marked in the inset of Fig. 3. Although the frequency changed from 14 to 20 Hz, mixing efficiency remained nearly constant at ~ 93%. We explain this result with the Strouhal number $St = Lf/V_O$, which is the ratio of switching frequency (f) and steady flow velocity (V_O). Here L is the hydraulic diameter. In the experiment, St is at a high level and varies in the narrow range of 11.4–16.3 (a 43.0% variation). As a result, the mixing efficiency is high and nearly constant even with the change of switching frequency.

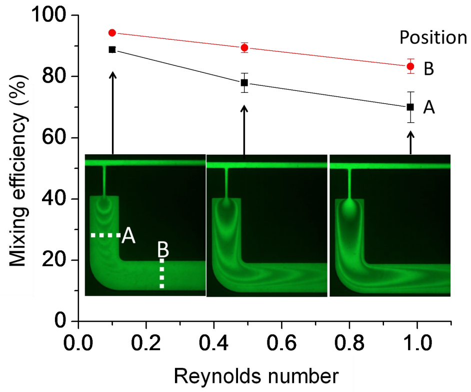

Figure 4: The influence of Reynolds number on the mixing efficiency at the valve switching frequency of 14Hz.

The effect of flow rate on mixing efficiency

Figure 4 shows the mixing efficiency under various Reynolds number (*Re)* at 14 Hz switching frequency. To obtain several Reynolds number (*Re),* we controlled pressure of mixer unit. The images indicate that increasing *Re* directly increases the size of fluidic bands and the mixing efficiency decreases accordingly. Note that *St* varies in the broad range of 1.1–11.4 (a 936.3% variation). However, as fluid stream moves from point A to B, diffusion occurs within the fluidic bands and the mixing efficiency increases to ~ 90 %.

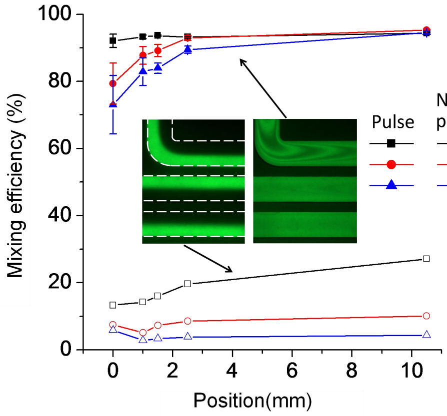

Figure 5: Change of mixing efficiency with and without pulsatile micromixing at different positions. The valve switching frequency is 18 Hz. The mixing efficiency measured at different positions with different Reynolds numbers (Re). The insets were photographs at Re =1.

Mixing efficiency with and without pulsatile mixing

Finally, the effect of pulsatile flow on the mixing efficiency was studied. Figure 5 compares mixing efficiency with and without pulsatile mixing. Without any pulse, the two stream have laminar flow and their interface was very clear without any mixing. In this case, mixing efficiency was < 30% even at the channel length of 1 cm. In contrast, with the pulsatile micromixing, the two solutions were rapidly mixed within a short distance. The interface between the two solutions was already blurred at the entrance of the channel because of the short diffusion length. Consequently, the efficiency of the pulsatile flow was significantly better than that of the laminar flow. This result demonstrates the advantage of proposed mixer system .

CONCLUSION

We developed a gravity-driven pulsatile microfluidic mixer. The system was driven by constant pressure to produce pulsatile flow. This process depended on the interaction of valves, flexible membranes, and channels, and it did not require any complex external controllers. The pulsatile micromixer could separately control the valve switching frequency and the flow rate in the range of 14 to 20 Hz and 2 to 20 μL/min, respectively. Our micromixer system is simple and compatible incompatible with the microfluidic system integration, and would be suitable for more complex biology and chemistry experiments.

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