DEVELOPMENT OF AN ACTIVE MICROMIXER USING AN EXTERNAL MECHANICAL ACTUATOR ARRAY

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ABSTRACT

We present an active continuous-flow micromixer based on channel-wall deflection in a polydimethylsiloxane (PDMS) chip using Braille display pins. The chip design comprises a main micro-channel connected to a series of side channels with dead ends aligned on the Braille pins. Computer-controlled deflection of the side-channel walls induces chaotic advection in the main-channel, which substantially accelerates mixing in low-Reynolds number flow. Several influencing parameters such as the number of cross-channels, actuation frequency, side-channel width, actuation sequence, and flow rate velocities have been investigated. Sufficient mixing of fluids could be achieved within seconds (~500 ms). Finally, continuous dilution of yeast cell sample by a ratio down to 1:10 is successfully demonstrated.

KEYWORDS

Active micro-mixer, mixing index, chaotic advection, channel wall deflection, PDMS chip, and cell sample dilution.

INTRODUCTION

Mixing of fluids in micro-channels is challenging due to stable laminar flow. The speed of mixing is limited by molecular diffusion, and is inversely proportional to the size of the fluid molecule or particle to be mixed [1]. Typically, for relatively large biomolecules such as cells, mixing can take as long as hours in microchannels. An efficient method for mixing enhancement in microchannels is needed for biomedical applications such as cell counting, enzyme assays, screening assays, cell lysis, protein folding, and biological analytical assay [2].

One method for efficient microscale mixing is chaotic advection [3], which involves local stretching and folding of the fluid streams and the resulting significant reduction in the effective diffusion length. The key to effective mixing lies in producing strong stretching and folding [4].

Active mixers generally provide efficient mixing with enhanced control over the process and independence of flow conditions [5]. Several active mixers based on chaotic advection have been reported where efficient mixing was observed in subseconds [3-5]. Tabeling *et. al.* [3] reported a cross-channel micromixer which exploit chaotic motion in the main channel due to the pressure perturbation at side channels. Such structures with robust and compact pressure-perturbation sources can be used for rapid mixing in microscale continuous flow.

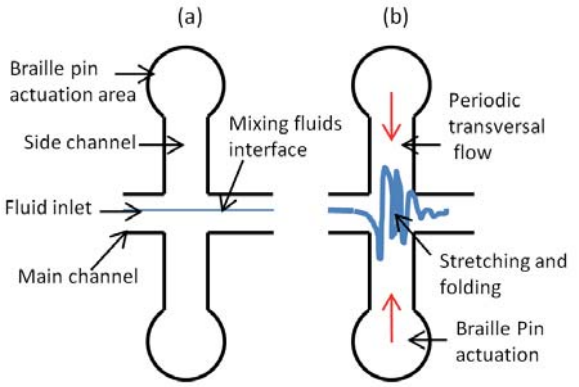

Fig. 1: Schematic of a cross-channel mixer and principle of pressure perturbation. (a) At no actuation, flow in main channel is laminar. (b) After pin actuation stretching and folding of fluid interface occur in main channel.

In this work we present a PDMS active micromixer that creates chaotic advection in cross-channel structures. The main microchannel is connected to a series of side channels with dead ends that are aligned to Braille display pins. The side channel walls deform as the Braille pins underneath deflect, creating transverse flow at the mixing fluid interface in the main channel. By operating the Braille pins in a periodic sequence, the fluid undergoes local stretching and folding, which leads to rapid fluid mixing. Fig. 1 depicts the principle of chaotic advection in the main channel due to pressure perturbation in the side channels.

MATERIALS AND METHODS

Chip Fabrication

The microfluidic chip is composed of poly-dimethylsiloxane (PDMS) fabricated using standard soft lithography procedures [6]. Fig. 2 shows the schematic of the chip fabrication process. The master mould structure was fabricated on a 4-inch silicon wafer patterning multilayered photoresist (AZ9260, Microchemicals GmbH). The patterned 100-µm thick

structures were reflowed at 120 °C for 2 hours to obtain round channel cross sections. The PDMS channel structures were made by pouring Sylgard 184 (Dow Corning Corp., mixture ratio of curing agent to prepolymer 1:10) onto the mould and baking in an oven at 70 °C for 2 hours. A 100 µm thick PDMS membrane was spun on another silicon wafer and cured in the same oven to form the deformable wall. The two PDMS layers were permanently bonded after surface activation in oxygen plasma. Fig. 3a shows the PDMS chip after fabrication. The microfluidic channel width is 200 µm, and the dead-end chambers for Braille-pin actuation has a diameter of 1.5 mm.

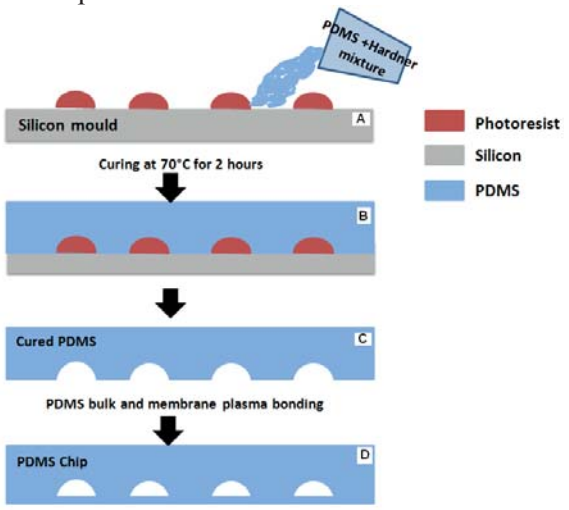

Fig. 2: PDMS chip fabrication steps

Braille Pin Actuator

The commercial Braille display (KGS Corp.) used in the current study provided an 8 × 8 array of 1.3-mm diameter pins that are each connected to piezoelectric bimorphs. These pins each deliver a force of 0.1 N for membrane deflection of up to 700 µm. The force corresponds to approx. 280 kPa pressure at the PDMS chambers when the chip is aligned and clamped on the Brialle display (Fig. 3b). The resonance frequency of each piezoelectric element is 10 Hz. The pin actuation is controlled by an in-house developed computer program connected through an electronic interface circuit.

Experimental Setup

The schematic of experimental setup is illustrated in Fig. 4. The PDMS chip is placed over the grid of the Braille disply pin, in such a way that the lower PDMS membrane is in direct contact with the Braille display pins. To pump the fluid through the chip at a predetermined flow rate, a neMESYS syringe pump (Cetoni GmbH) was used. A high-speed camera (pco. 1200, PCO AG) was used to acquire instantaneous images of the fluid mixing inside the fluid channels. A 12x objective lens (Navitar Inc.) was attached to the high-speed camera to magnify the image.

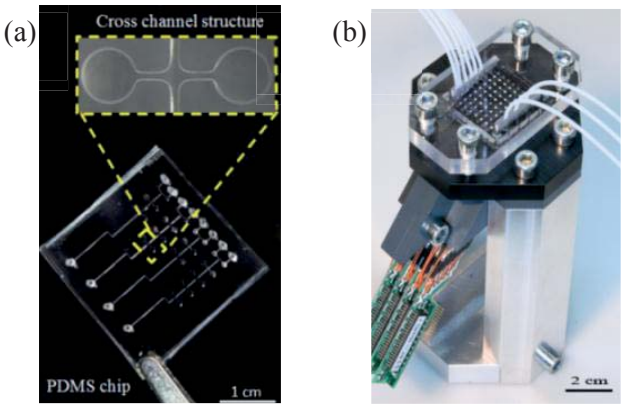

Fig. 3: (a) Cross-channel structures in the PDMS chip. Braille pins deflect the membrane at the circular areas of the cross-channel. (b) PDMS chip with integrated cross channel on a commercially available Braille pin actuator.

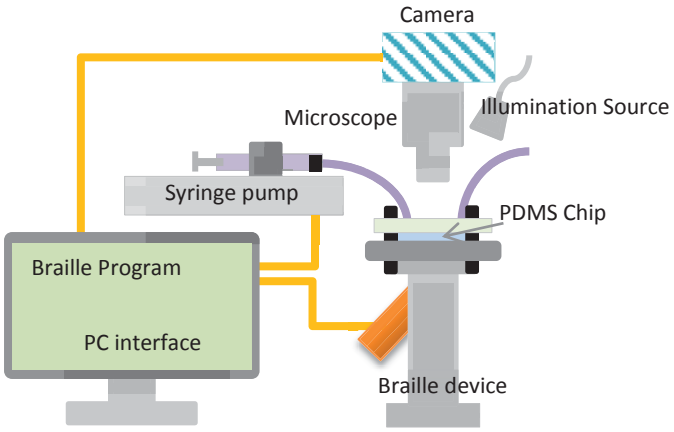

Fig. 4: Schematic of complete experimental setup

Mixing quantification

The efficiency of the Braille-actuated micromixer is evaluated by image analysis of instantaneous images of two water streams, one of which is colored with ink. The performance is quantified using a mixing index (MI) defined as the standard deviation of the pixel intensity values of an instantaneous image from a reference image at time t. In the current study, the reference is defined as the image where the fluid is homogenized or completely mixed [5]. The expression for MI is given in eq. 1.

$$MI = \sqrt{\frac{1}{N}\sum_{n=1}^{N}\left(\frac{I(t,n) - I_{avg}}{I_{avg}}\right)^2} \qquad (1)$$

Where N is number of pixels and I is the optical intensity. Mixing index value of 1 and 0 indicates laminar flow and completely mixed state, respectively. Many of the literature considered 0.1 mixing index as an arbitrary value to define well mixed fluids [5]. Mixing time is therefore defined as the time to reach mixing index value of 0.1.

RESULT AND DISCUSSION

Qualitative Analysis

The snapshots of fluid interface at the cross channel indicates the stretching and folding behavior of the fluid interface in the main channel during pin actuation are shown in Fig. 5. This image sequence indicates that the Braille-actuated micromixer induces chaotic advection and consequently enhances fluid mixing. The Braille pin displaces 3 µl of fluid during each actuation step.

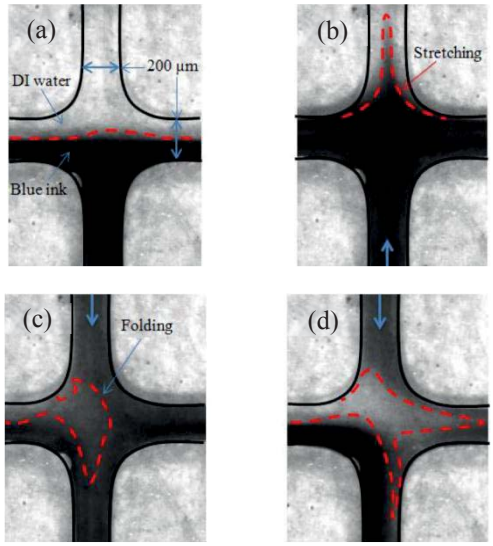

Fig. 5: Snapshots of the cross-channel structure (Top view) during Braille actuation at an interval of 200 ms. (a) Before actuation. (b) Lower Braille pin is actuated and induces transversal flow causing stretching of the fluid interface. (c), (d) Upper pin is actuated, causing the folding of the stretched interface. The stretching and folding of the interface is a key fluidic behaviour in chaotic advection (Total flow rate in channel is 0.4 µL/s).

Quantitative Analysis

Fig. 6 illustrates the effect of pin-actuation frequency on the mixing efficiency. At lower frequencies (<1 Hz) mixing is not efficient due to weak perturbation; in this case the actuation time is more than the residence time of the fluid element in the mixing structure. At higher frequencies (> 10 Hz) mixing efficiency is low due to unstable actuation (practical limitations). Therefore the optimal for mixing performance is observed at 10 Hz.

Fig. 7 depicts the dependency of mixing efficiency on the total flow rate of fluids inside the main channel. The mixing efficiency decreases as flow rate increases due to the fact that the residence time of the fluid in the channel is decreased and fluid elements undergo less perturbation before they leave the mixing chamber. Although the Reynolds number at 2 µl/s is relatively high (~20), it is not high enough to enhance mixing by turbulence. Thus for velocities higher than 0.4 µl/s, higher number of Braille pins (>4) are required for efficient mixing.

Fig. 8 depicts the effect of fluid viscosity on the mixing index. Fluids with different viscosities were prepared by diluting glycerol at different percentages in DI water. The mixing index increases (decreasing mixing efficiency) with the increase in the fluid viscosity, which is natural since viscosity is inversely proportional to the diffusion constant. Still, for wide range of viscosities (up to 50 mPa·s), the mixing index is within the sufficient range.

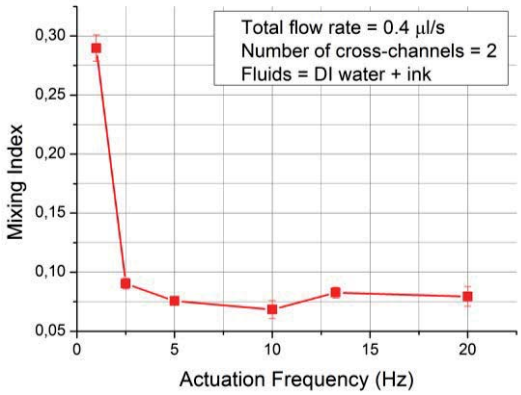

Fig. 6: Mixing index response of cross-channel mixer for different actuation frequencies.

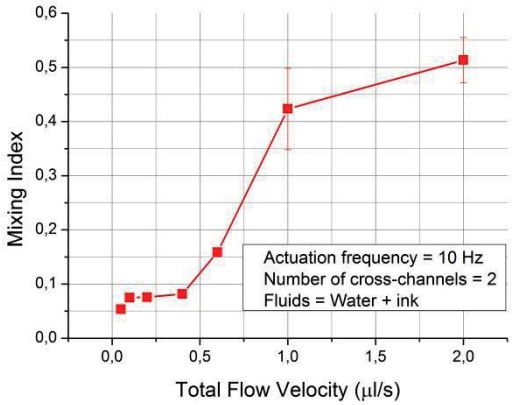

Fig. 7: Mixing index response at different fluid velocities at the chip inlet.

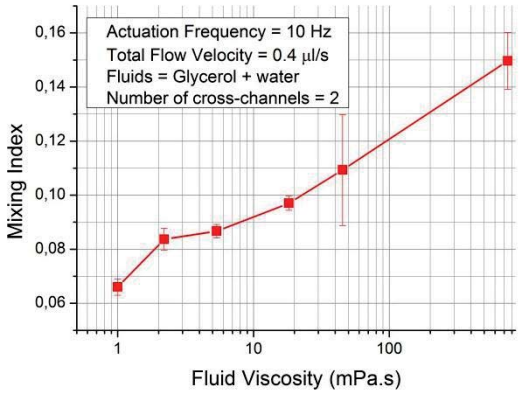

Fig. 8: Effect of fluid viscosity on the mixing index of the cross-channel mixer

The transient response of the mixing index at optimal conditions defined through the above-mentioned parameter studies is shown in Fig. 9. Here the mixing time is on the order of 100 ms, and homogeneous mixing is sustained for as long as the experiment was conducted.

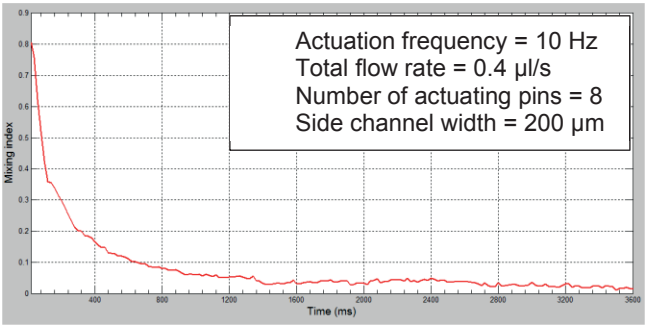

Fig. 9: Transient response of the mixing index for optimal process and design parameters.

Finally, dilution experiments of continuous-flow cell samples was performed. The cell sample was of wild yeast type (S. cerevisiae) in a buffer solution YNB medium. The photographs of cell dilution near the outlet channel over the Braille pin is given in Fig. 10. The total flow rate is 0.4 µl/s, and the flow rate ratio is 1:10 (cell sample : DI water). Initially at t = 0 no mixing is observed and all cells flow in the lower part of the channel in the image. After 2 s the cells are dispersed throughout the width of the channel and diluted. The shear stress in the cross-channel due to the main channel and the induced side flow is roughly calculated to be on the order of ~102 Pa. In this range, shear-stress does not affect the viability of yeast cells [7].

CONCLUSION

We demonstrated a novel approach for mixing enhancement by membrane actuation using mechanical actuator array. It is shown that rapid mixing of cell/particle flow can be achieved across a wide range of flow parameters using a cost-effective configuration with easily replaceable PDMS microfluidic chips.

Chaotic advection in the main channel is demonstrated by the generation of periodic stretching and folding. Development of strong stretching and folding trajectories is decisive in efficient mixing. Sufficient mixing of continuously flowing fluids was achieved within half a second. Several influencing parameters of the mixing setup have been studied. It is found that parameters like flow rate ratio and fluid viscosity have no significant effect on mixing for a wide range. The successful demonstration of cell sample dilution proved the feasibility of Braille display as a mechanical actuator in biomedical analysis. This micromixer setup can be implemented in automated processes for high-throughput biomedical analysis.

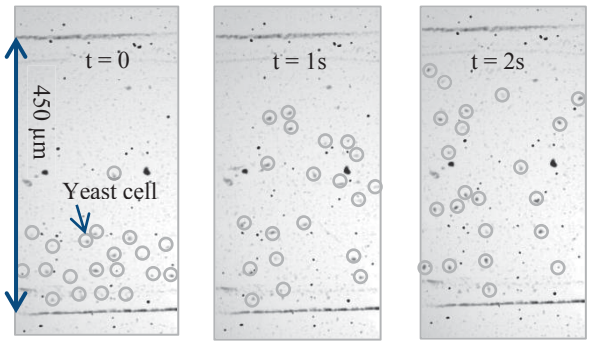

Fig. 10: Snapshots of the yeast cell sample at the downstream of the cross-channel after the onset of Braille actuation. Original flow rate ratio of yeast sample and DI water is 1:10 (total flow rate = 0.4 µL/s).

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