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Experimental investigation of passive micromixers conceptual design using the layout optimization method

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Abstract
This paper presents an experimental investigation of the novel efficient passive micromixers conceptual design using the flexible layout optimization method. Utilizing the layout optimization method when designing passive micromixers results in decreased reliance on the experience and intuition of designers. The detailed layout of passive micromixers is obtained by solving a variational optimization problem, in which the manufacturability and periodicity of passive micromixers can be considered by adding the corresponding design constraints. The obtained micromixers are fabricated by using polydimethylsiloxane soft photolithography techniques. The mixing performance is evaluated by stereoscopic and confocal microscopes. The effectiveness of the layout optimization method is confirmed by a comparison of the numerical and experimental results.

1. Introduction

The micromixer is a key component for mixing fluids in a microfluidic system. Micromixer technologies can be applied in chemical and biological applications, as well as in the detection/analysis of chemical or biochemical content [1]. In principle, the mixing of two or more different fluids depends on convection and diffusion. Mixing within microfluidic devices with laminar flow is heavily dependent on the diffusion process. Fundamentally, mixing is a diffusion process. At boundaries of fluid impurities, the concentration gradient is large and materials flow until the concentration gradient vanishes. Therefore, diffusion alone is inefficient in this case. Moving fluids can greatly enhance mixing through chaotic advection. The region containing the impurity is strongly deformed, and the length of the boundary of the impurity grows exponentially. Therefore, the diffusion process becomes efficient [2]. Diffusion and fluid convection are factors influencing the mixing effect of micromixers. The relative significance of these two factors can be measured by the dimensionless Peclet number (*Pe*) and the Reynolds number (*Re*). Fluid convection is considered the main factor when the Peclet number satisfies $Pe \gg 1$; otherwise, diffusion is considered the main factor. The convection strength of the flow in a micromixer can be measured by the Reynolds number *Re*. When $Re \gg 1$, convection dominates the flow; otherwise, viscosity dominates the flow [3].

Micromixers can be categorized into active and passive types [1, 3, 4]. The active micromixer requires external actuation elements, which increase the difficulty or complexity of manufacturing and integration. In contrast, the passive micromixer implements the mixing of reagents by using the layout of the microchannel. The reasonable layout of the microchannel in a micromixer strengthens the convection of the steady flow and enhances the mixing effect. The mixing effect of the micromixer is strongly dependent on the shape and arrangement of blocks in the microchannel. Blocks are achieved by using grooves manufactured at the microchannel

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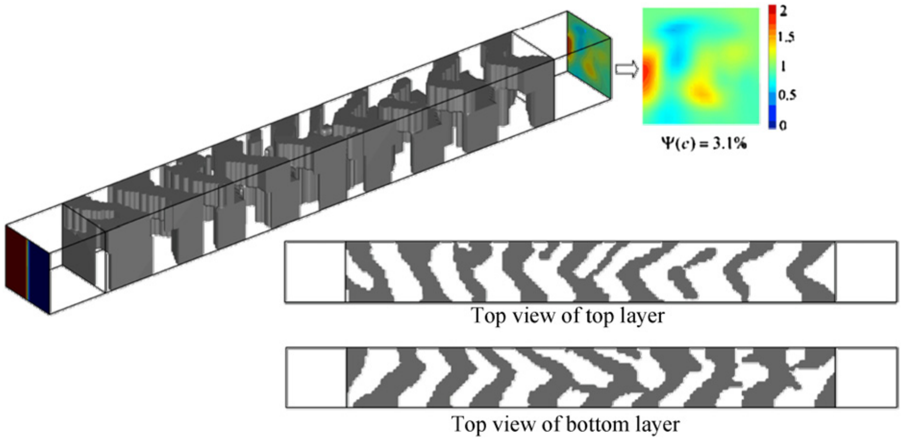


Figure 1. Layout of the micromixer with design domain divided into two layers. The length and height of the bottom layer are 3.2 mm and 240 μm, respectively. The value of the mixing measurement corresponding to the optimized design is 0.031.

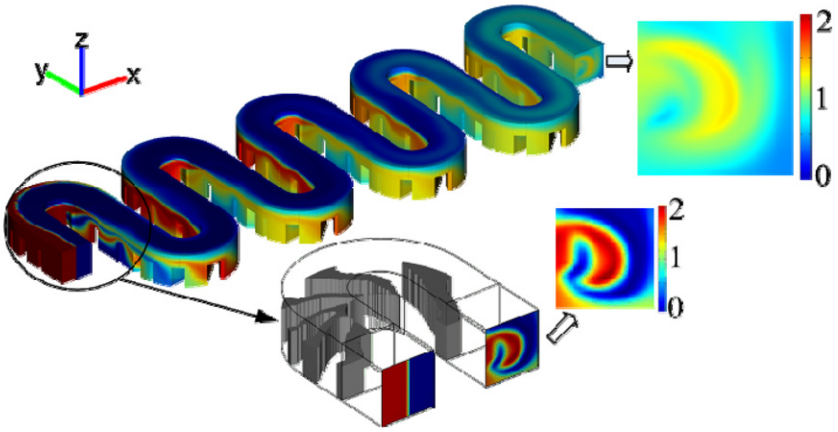


Figure 2. Series-wound extension of the bending cells obtained by the layout optimization method. The corresponding value of the mixing measurement is 0.045.

walls to strengthen the chaotic advection in most passive micromixers. Stroock *et al* arranged grooves periodically on the bottom of a microchannel to produce vortex flows inside the channels [5]. To enhance the mixing performance, Kim *et al* periodically arranged the barriers and slanted grooves at the top and bottom walls of a microchannel to induce a periodic lateral motion of fluids [6]. Howell *et al* arranged multiple grooves flexibly on both the top and bottom of a microchannel. They found that different groove features could be combined to achieve a desired fluid advection in the microchannel [7]. These mixing structures have regular shapes designed based on the intuition of the designer. The regular shapes are arranged periodically to improve mixing performance. Several optimization methods for the blocks of passive micromixers have been implemented using the shape optimization method [8–10] and the mapping method [7, 11, 12]. Given that the shape optimization method cannot change the topology of a micromixer, the extent to which the method can improve the mixing efficiency is limited by the initial choice of microchannel topology. The mapping method is used to optimize the arrangement of regular blocks. Although regular blocks are convenient for designing micromixers, a reasonable irregular design is more useful for the enhancement of the mixing performance. The layout optimization method obtains a suitable design for the passive micromixer through the optimization of the layout or distribution of materials, which in turn enables the simultaneous determination of the shape and arrangement of the blocks in the micromixer. Therefore, the layout optimization method can improve the mixing efficiency of the passive micromixer. The layout optimization method of the passive micromixers has been researched numerically in [13], and several design disciplines have been presented. However, limited experimental investigation was conducted on the designed micromixers. Therefore, this paper focuses on the experimental investigation and validation of the mixing performance of passive micromixers designed using the layout optimization method.

The remainder of this paper is organized as follows. The theory of the layout optimization method is provided in section 2. Several passive micromixers are designed numerically by using the layout optimization method presented in section 3. The experimental investigation of the design of the passive micromixers is presented in section 4. The paper is concluded in section 5.

2. Theory of the layout optimization method

In this study, we consider the mixing of two fluid streams with different solute concentrations. The concentration of

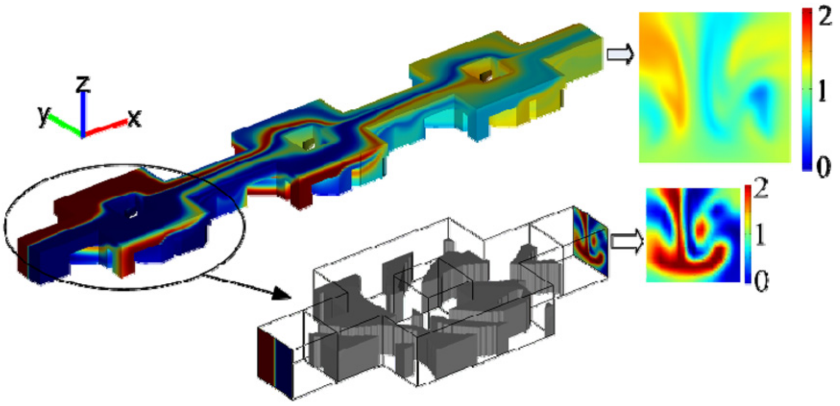
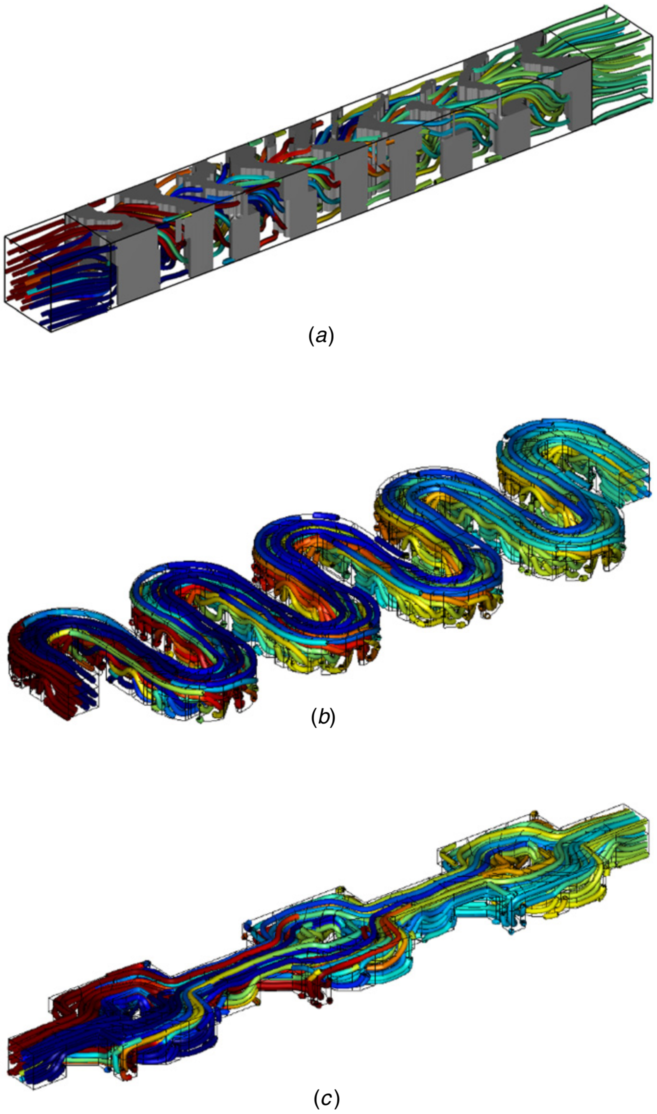


Figure 3. Series-wound extension of the split-combination cells obtained by the layout optimization method. The corresponding value of the mixing measurement is 0.040.



(*a*)

(*b*)

(*c*)

Figure 4. Streamline distribution corresponding to the designed passive micromixers shown in figures 1–3.

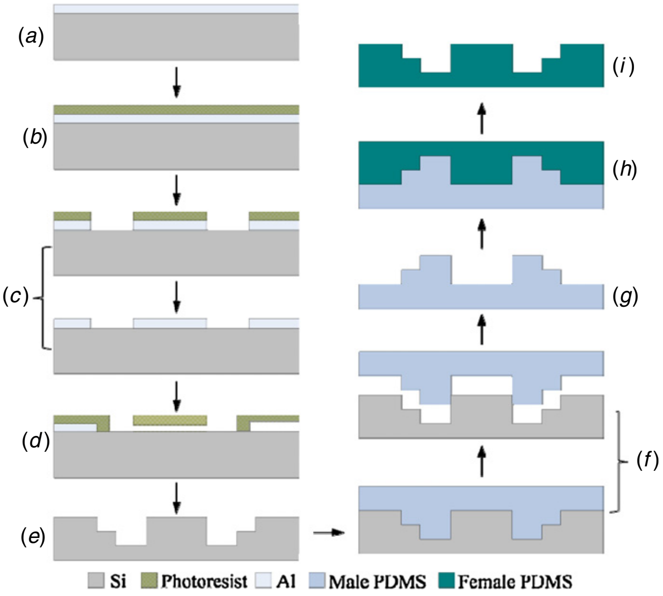


Figure 5. Flowchart of the fabrication process for passive miromixers designed using the layout optimization method.

the two solutes in the liquid is set to be the dimensionless values 2 and 0. The solute at the outlet has an anticipated concentration distribution of $c_a = 1$, in which two flows have equal flux at the micromixer inlets. The mixing performance of a micromixer can be measured by the mixing measurement defined as [14, 15]

$$\Psi(c) = \int_{\Gamma_o} (c - c_a)^2 \, \mathrm{d}\Gamma \Big/ \int_{\Gamma_i} (c_r - c_a)^2 \, \mathrm{d}\Gamma \qquad (1)$$

where c_r is the reference distribution of the solute concentration at the inlet Γ_i, and Γ_o is the outlet of the micromixer. A lower $\psi(c)$ value corresponds to better mixing performance. Therefore, the task for the micromixer design is to identify a reasonable micromixer layout that has the lowest mixing measurement $\psi(c)$ value. A variational problem with the mixing measurement $\psi(c)$ as an objective function can be constructed for the layout design of passive micromixers. The constraints of the variational problem are the Navier–Stokes equations and the convection–diffusion equation:

$$\rho(\mathbf{u} \cdot \nabla)\mathbf{u} = \nabla \cdot [-p\mathbf{I} + \eta(\nabla\mathbf{u} + \nabla\mathbf{u}^{\mathrm{T}})] + \mathbf{f} - \nabla \cdot \mathbf{u} = 0 \qquad (2)$$

$$\nabla \cdot (-D\nabla c) + \mathbf{u} \cdot \nabla c = 0 \qquad (3)$$

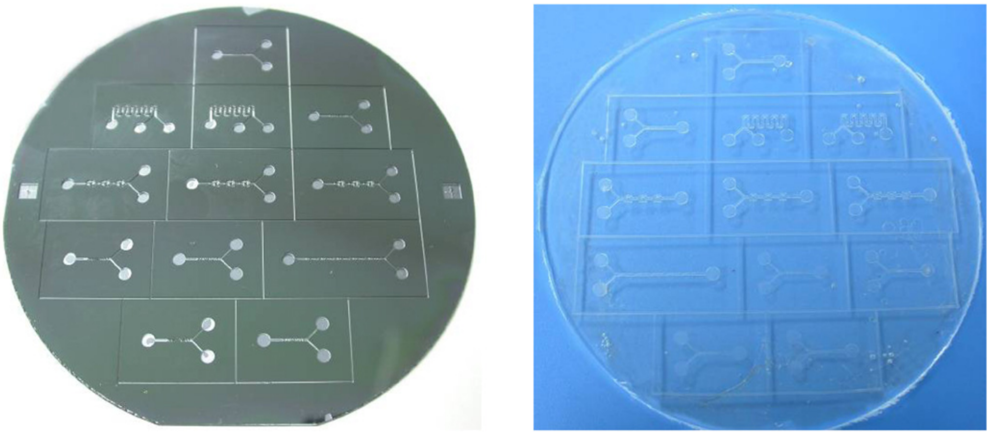

(*a*) (*b*)

Figure 6. The Si mold (*a*) and the male PDMS mold (*b*) of the designed passive micromixers.

where ρ is the fluid density; η is the fluid viscosity; D is the diffusion constant; $\mathbf{u}$ and p indicate velocity and pressure, respectively; c is the concentration of the solute; $\mathbf{f}$ is the body force. The parabolic velocity distribution at the inlet, the zero pressure condition at the outlet, and the no-slip boundary condition at the wall are the boundary conditions for the Navier–Stokes equations. The concentration distribution at the inlet and the zero normal diffusion at the wall are the outlet boundary conditions for the convection–diffusion equation. In the topology optimization method for fluid flow, the body force in the Navier–Stokes equation is set as the artificial Darcy force $\mathbf{f} = -\alpha\mathbf{u}$, where α is the artificial impermeability of the porous medium filled in the design domain [16, 17]. Impermeability is interpolated by the design variable [16]:

$$\alpha = \alpha_{\max} q \frac{1-\gamma}{q+\gamma} \tag{4}$$

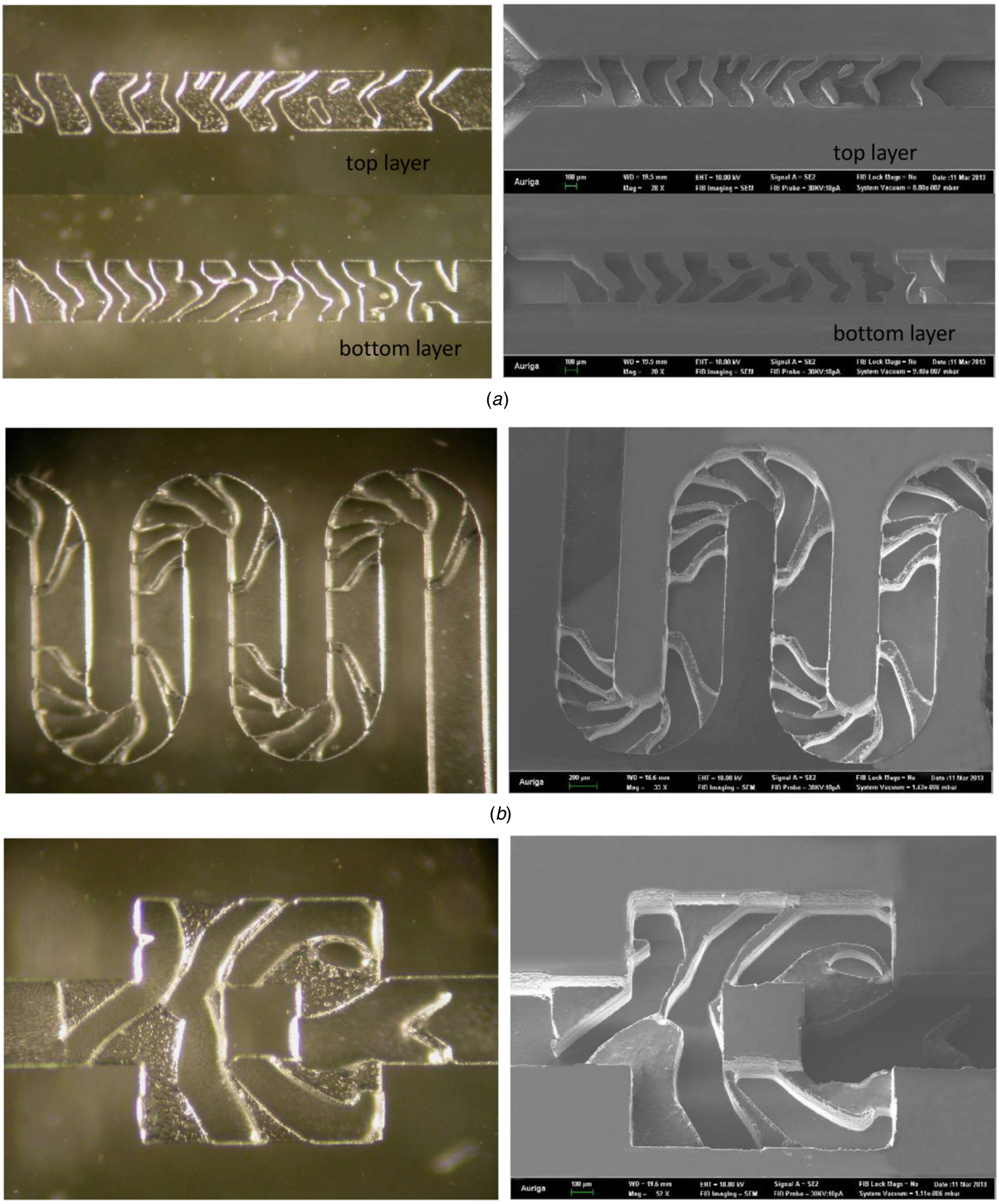
where γ is the design variable used to represent the layout of the passive micromixer; $\alpha_{\max}$ is the artificial impermeability of the solid; q is a positive parameter used to tune the convex property of equation (4). $\alpha_{\max}$ and q are set to be 1×10^7 and 1, respectively. These values are determined based on numerical experiments. The design variable is bounded in the interval 0 to 1; these values correspond to the solid and liquid phases, respectively. The variational problem can be solved by using the gradient-based iterative approach, and the design variable can be evolved by using the optimization algorithm [13]. The quasi-Newton method, together with the inverse Hessian updated via the L-BFGS formulation, is adopted in this paper [18]. As the iterative procedure converges, the optimized layout of the passive micromixer in the specified design domain can be obtained.

During the calculation of the variational optimization problem for the layout of micromixers, the gradient of the variational problem is analyzed by using the adjoint method [19]; the Navier–Stokes and convection–diffusion equations are solved by the finite element method using the commercial software COMSOL Multiphysics (version 3.5) with linear elements. The Navier–Stokes and convection–diffusion equations are stabilized via the Galerkin least squares and the streamline-upwind/Petrov-Galerkin technologies, respectively [20]. The design variable is updated by using the method of moving asymptotes [21]. The design iterative procedure is stopped when the 1-norm of the step length of the iteration is less than 1×10^{-3} or when the iteration number reaches 3×10^3.

3. Passive micromixers designed using the layout optimization method

In passive micromixers, the inconsistent cross-sections along the flow direction results in chaotic advection and distortion of the streamlines, which indicate the interplay among inertial, centrifugal and viscous effects of fluid flow [22]. Chaotic advection, which results in the manifold of the streamline, increases the mixing length and area of the interface between two mixing flows. Therefore, the layout design of a micromixer should be performed in three dimensions. Manufacturability can be ensured by adding a corresponding manufacturing constraint into the variational problem. In this study, the size of the cross-section of the design domain is set to 400 μm × 400 μm; the density and dynamic viscosity of the fluid are set to 1×10^3 kg m^{-3} and 1×10^{-3} Pa s, respectively; the Peclet and Reynolds numbers are set to 2500 and 2.5, respectively.

Microfluidic designs should be compatible with the planar, layer-by-layer geometries imposed by current, lithography-based techniques of microfabrication [5]. Therefore, micromixer designs should have layer-by-layer geometries to ensure manufacturability. Manufacturability requires that each layer of the layout can be extruded from a two-dimensional graphic, i.e., the design variable has a consistent value in the depth direction of every layer of the design domain. Manufacturing designs increases in difficulty with increasing design layers. Therefore, this paper focuses on the case in which the micromixers have two layers. The design domain is set to be the layered straight channel, in which the length and height of the bottom layer are 3.2 mm and 240 μm, respectively. The variational problem with manufacturing constraint is solved, and the micromixer (figure 1) is obtained. The corresponding value of the mixing measurement is 0.031,



(*a*)

(*b*)

(*c*)

Figure 7. Female PDMS molds of the passive micromixers designed using the layout optimization method. (*a*)–(*c*) The micromixers corresponding to the layouts shown in figures 1–3, respectively.

which is less than the mixing threshold level (0.050). Mixing is assumed sufficient when the value of the mixing measurement is less than 0.050 [14].

The periodic layout is a typical choice for the design of passive micromixers [5, 8–10, 12, 23–29]. Although the periodic design of micromixers based on the series-wound method is the suboptimal choice, the series-wound method is a widely used strategy for simplifying the periodic design of a micromixer in a long design domain. Two different mixing cells and their corresponding series-wound extensions are obtained based on the layout optimization method (figures 2 and 3), in which the values of the mixing measurement are both less than the mixing threshold level (0.050) after sequentially connecting nine and three cells, respectively. These two micromixers with series-wound cells occupy the same spatial distance in the x-axis direction (7.6 mm). Figure 4 shows the distribution of the streamline of the passive micromixers designed using the layout optimization method, in which the

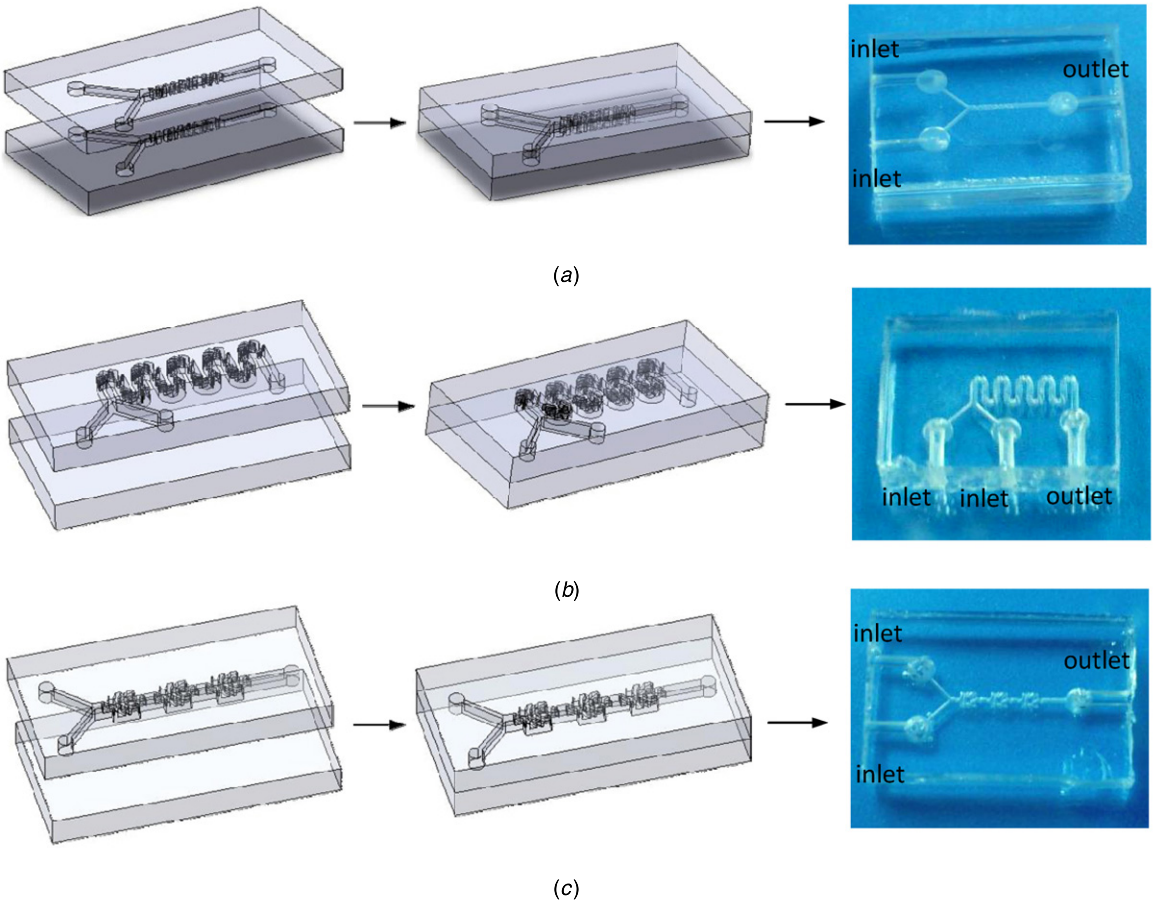


Figure 8. Assembling of the passive micromixers designed using the layout optimization method. (*a*)–(*c*). The assembled micromixers corresponding to the layouts shown in figures 1–3, respectively.

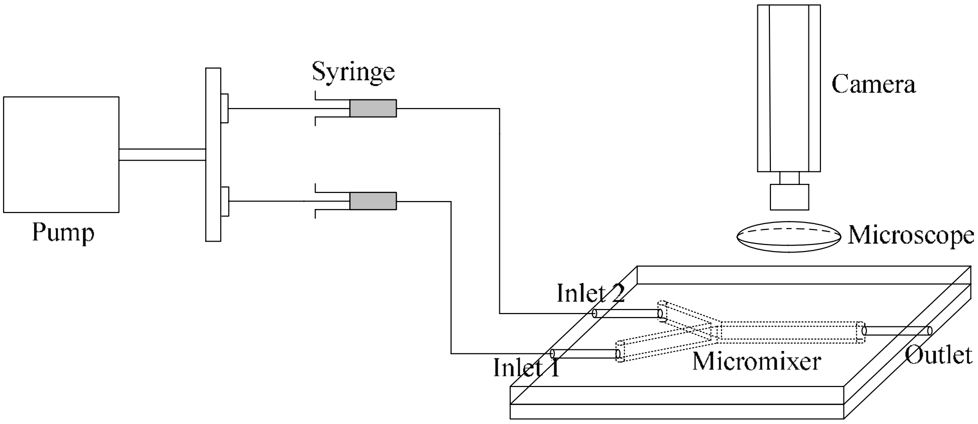


Figure 9. Schematic for the experimental instrument used in the experiments of the designed passive micromixers.

streamline is distorted impetuously by the designed blocks and arrangements.

4. Experimental investigation

To validate the effectiveness of the layout optimization method for designing passive micromixers, the passive micromixers with layouts shown in figures 1–3 are fabricated and tested as follows. The photomask film used in the lithography is obtained based on the computer data translated by using our Matlab codes, which can translate the mixing structures designed by the computer into AutoCAD files in PDF format. The photomask film can be generated by importing CAD files into a photoplotter (EIE RP224+SXT). Figure 5 shows the fabrication procedure of the designed micromixers: (a) an Al layer with thickness equal to 500 nm is deposited on a silicon substrate; (b) the Al layer is coated with photoresist (AZ 4620); (c) after standard lithography (KarSuss MA6/BA6 photo-etching machine), the photoresist is developed to obtain an Al mask, in which the wet etching process is used to pattern

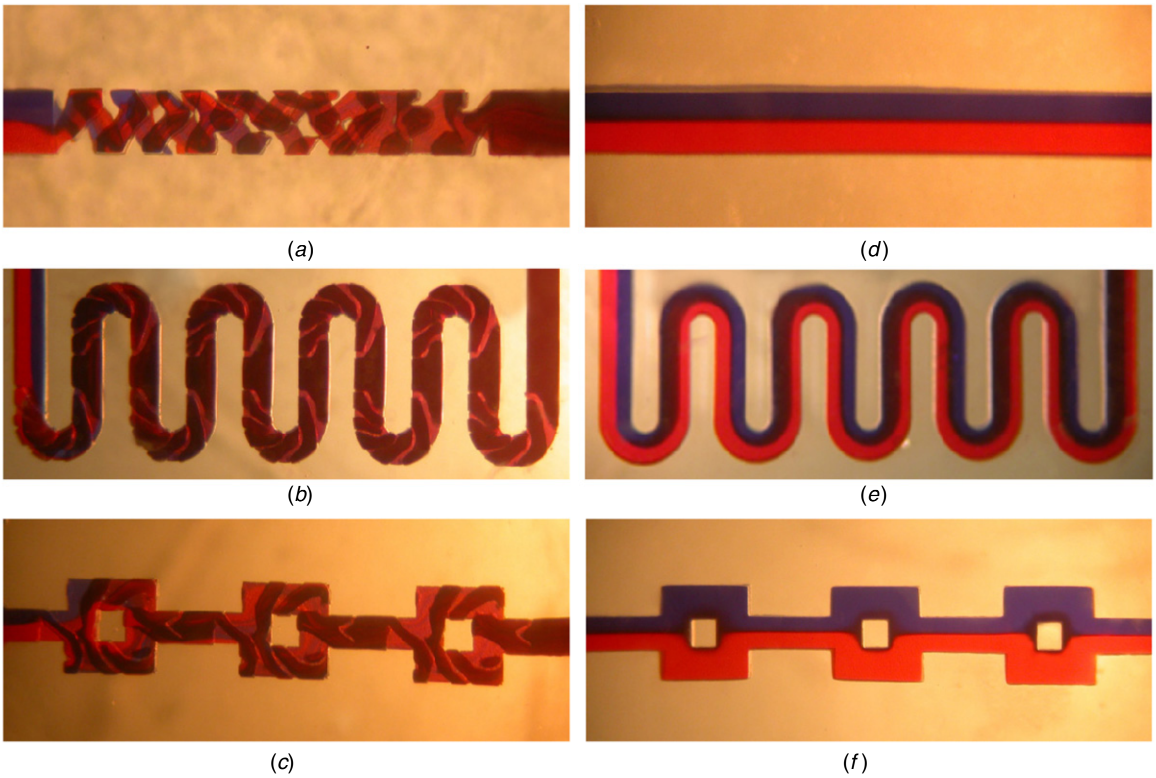
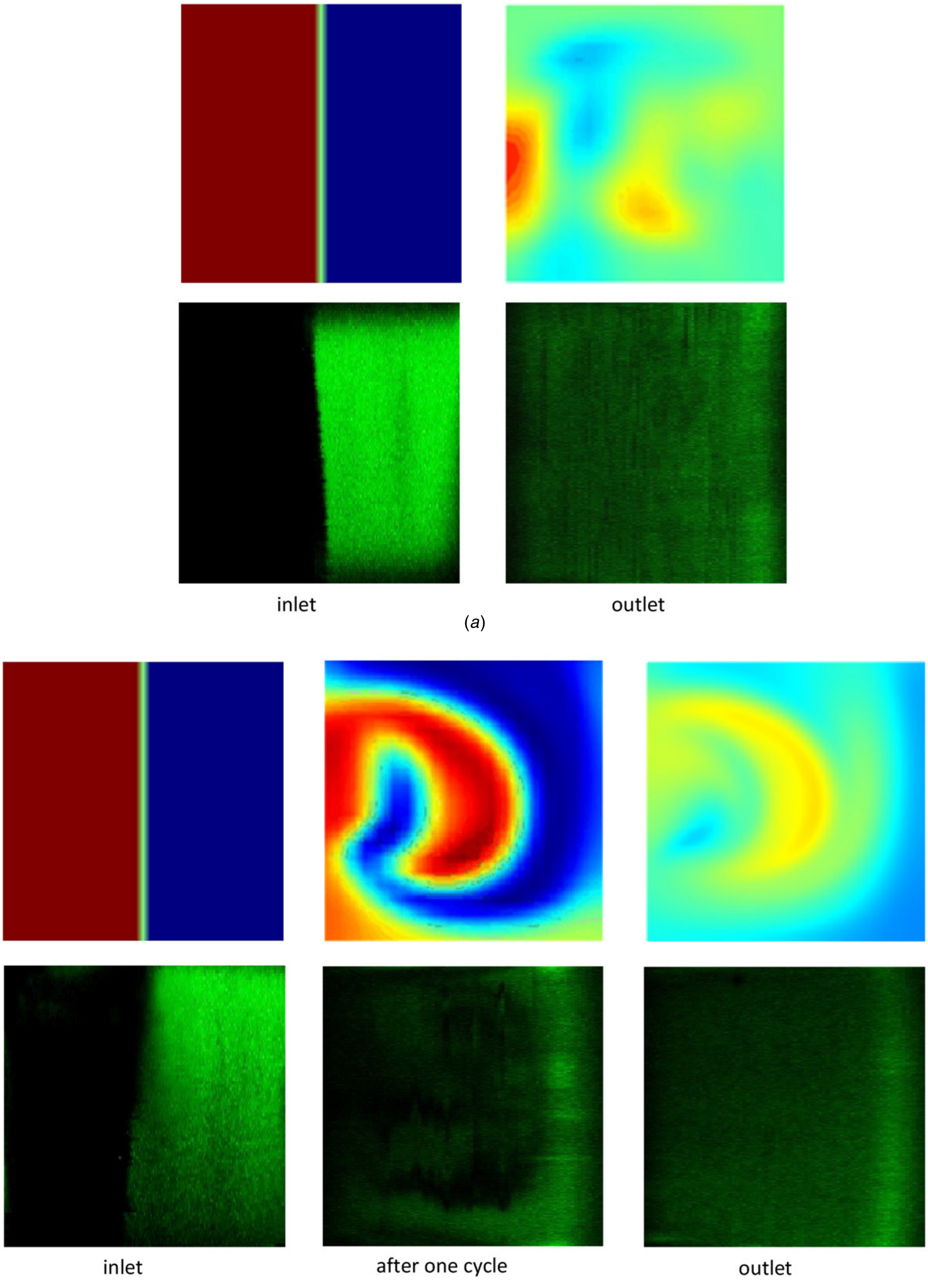


Figure 10. Concentration distribution on the horizontal top-plane of the micromixers. (*a*)–(*c*) The micromixers corresponding to the layouts in figures 1–3, respectively. (*d*)–(*f*) The microchannels corresponding to the micromixers in (*a*)–(*c*), where the blocks are removed from the micromixers.

the Al layer; (d) another layer of photoresist is patterned for the two-step Si etching; (e) the Si substrate is etched by inductively coupled plasma (ICP) dry etching process (Alcatel 601E ICP); the silicon mold is obtained, in which the Si substrate is first etched to a depth of 240 μm and the secondary etching (160 μm) is performed after the photoresist is removed (figures 6(*a*)); (*f*) after the curing agent and the polydimethylsiloxane (PDMS) prepolymer with weight ratio of 1:10 are mixed, the PDMS mixture is degassed with a mechanical vacuum pump to remove air bubbles. The PDMS mixture is poured onto the silicon mold and then heated at 80 °C to cure for 10 min; (g) the male PDMS mold with inverse microstructures is formed and peeled off from the Si mold (figures 6(*b*)); (*h*) the mixed PDMS is poured onto the male PDMS mold and then heated at 80 °C to cure for another 10 min; (i) the female PDMS mold is peeled off from the male PDMS mold, as shown in figure 7 (these images are obtained by the CCD camera and scanning electron microscope, respectively). The female PDMS mold can be bonded after oxygen plasma treatment (PVA TePla GIGAbatch 310M plasma system) to obtain the passive micromixers. The micromixer shown in figure 8(*a*) is assembled by two layers of PDMS, in which each layer contains microstructures. The micromixer shown in figures 8(*b*) and (*c*) is assembled by bonding one layer of PDMS with another layer of polycarbonate plate (0.8 mm thickness).

In the experiments, two aqueous solutions with different colors are injected into the micromixers to evaluate the mixing performance of the micromixers. Figure 9 shows the schematic of the experimental instrument. During the experiment, the flux provided by the pump is set to 1.8 $\mu\mathrm{l\,s^{-1}}$ to ensure that appropriate Reynolds and Peclet numbers of the microflow are used in the numerical computation (section 3). The experimental results are recorded by a MEIJI EMZ-TR stereoscopic microscope and a Nikon Coolpix 4500 CCD camera. Figures 10(*a*)–(*c*) show the concentration distributions on the horizontal plane of the micromixers corresponding to the layouts illustrated in figures 1–3. To demonstrate the mixing performance of the passive micromixers designed using the proposed layout design method, the mixing performance of the microchannels without blocks are also tested (figures 10(*d*)–(*f*)). Figure 10 demonstrates that the layout of the blocks designed using the layout optimization method can effectively improve the mixing performance of the passive micromixers.

The scanning laser confocal microscope (LSM 700, Carl Zeiss) with a 10 × /0.25 objective is used to record the mixing performance of the designed passive micromixers. Fluorescein solution and water are introduced into the mixer by a syringe pump with 1.8 $\mu\mathrm{l\,s^{-1}}$ flux. The total stack height is 400 μm. Stacks of each confocal x–y scan of 512 × 512 pixels are collected with a step of 4 μm in the z-direction. Cross-sectional images are recorded at different positions along the mixing length direction of the micromixers during the mixing of fluorescein and water (figure 11). The mixing efficiency of the experimental results shown in figure 11 are measured by ratio of the variances of the grayscale value of the recorded concentration distribution at the inlet and outlet of



(*a*)

(*b*)

Figure 11. Comparison of numerical and experimental results. (*a*)–(*c*) The micromixers corresponding to the layouts shown in figures 1–3, respectively.

the micromixer. And the variances of the grayscale value are computed using Matlab. Then the effectiveness of the mixing effect of the micromixers can be confirmed by comparing the numerical and experimental concentration distributions in the micromixer cross-section. However, several aberrations exist between the numerical and experimental results, as shown in

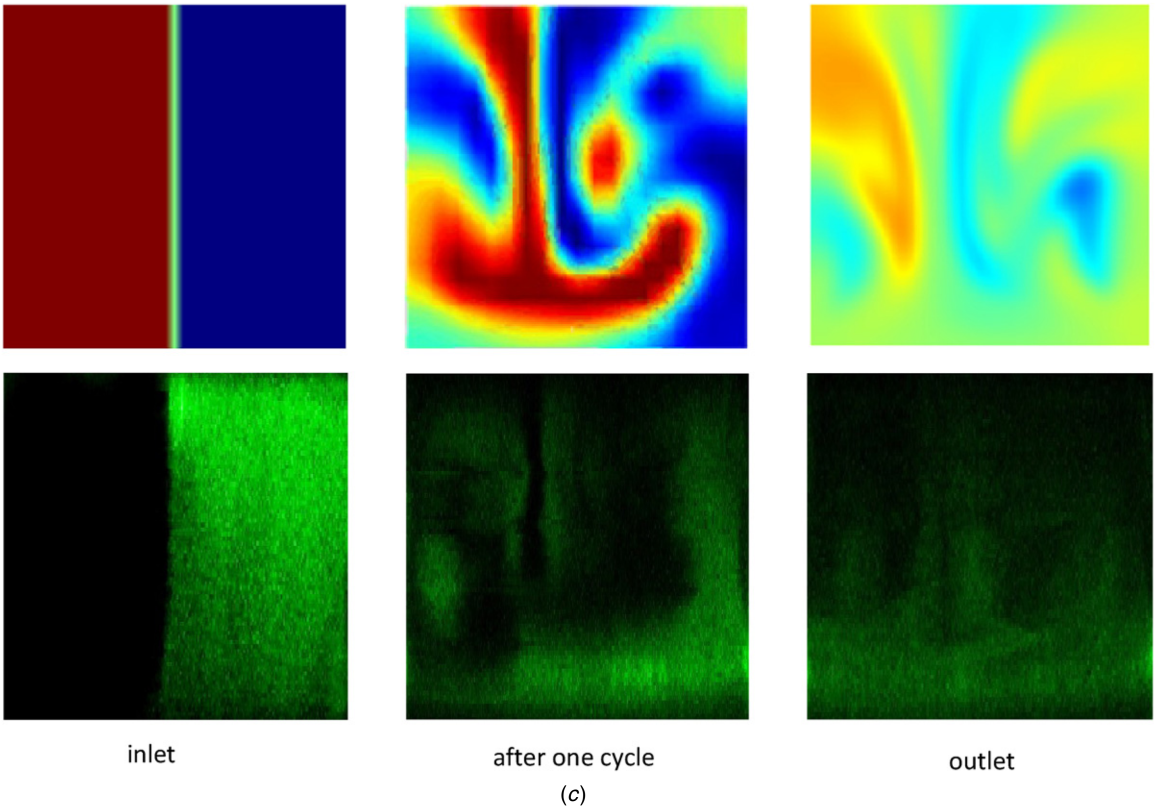


Figure 11. (Continued.)

figure 11. On the basis of our analysis, these aberrations are caused by microfabrication errors, e.g., the surface roughness of the micromixer walls, as well as the inevitable fabrication errors of lithography, etching and PDMS demolding.

The streamline distribution of the numerical results (figure 4) and concentration distribution of experimental results (figure 10) indicate that the streamlines are distorted impetuously and that the vortexes arise along with the distortion of the streamlines in the micromixers. The distortion of the streamline and induced vortexes along the flow direction clearly indicates the occurrence of chaotic advection due to interplay between centrifugal, inertial and viscous forces. The chaotic advection strongly deforms the interface between fluids. The area of the interface grows exponentially, and diffusion becomes efficient. Therefore, the passive micromixers obtained using the layout design method can achieve effective micromixing.

5. Conclusion

The effectiveness of the layout optimization method for conceptual design passive micromixers has been demonstrated experimentally. Our studies have demonstrated that the layout of a passive micromixer can be obtained by solving a variational problem, in which the irregular shape and arrangement of blocks can be determined simultaneously. In addition, this method is flexible in considering the manufacturing feasibility and periodic layout of passive micromixers. By comparing the mixing performance of micromixers with layouts obtained using the layout optimization method and that of micromixers without blocks, we can verify the effectiveness of the layout optimization method in improving the mixing performance of micromixers. In the conceptual design of passive micromixers, pressure loss, material weight and nonuniformity are ignored in this paper. Pressure loss and material weight can be considered by adding the corresponding constraints into the design optimization problem. If nonuniformity is presented in the obtained layout, then the projection techniques can be employed to ensure the clarity of the implicit boundary between fluid and solid phases. In the obtained layout of the passive micromixer, the closely spaced blocks can result in the trapping of fluid and can affect the mixing throughput. This problem can be solved by applying filtering techniques for topology optimization to ensure the minimum size of blocks. The layout optimization method can be extended for the design of more general micromixers, such as active micromixers. These topics require further investigation.

Acknowledgments

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