#### **ORIGINAL ARTICLE**



# **Comparison and Analysis of Mixing Efficiency in Various Micromixer Designs**

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#### **Abstract**

In this paper, we evaluate the influence of various micromixer designs on the mixing efficiency of passive micromixers. We analyze the designs of various passive micromixers to identify the most efficient micromixer. Among them, the toroidal micromixer and 3D zig-zag micromixer demonstrated the highest mixing efficiency. We investigated the key factors infuencing mixing in the toroidal and 3D zig-zag micromixer, identifying and confrming optimal designs. Ultimately, when comparing the mixing efficiency of the two micromixers, the 3D zig-zag micromixer achieved full mixing in a very short time of 0.8 ms. Through this research, it is anticipated that a benchmark will be provided for micromixer design in microfuidic devices when manufacturing micromixers of various forms.

Keywords Microfluidic system · Passive micromixer · Laminar flow · Enhancing mixing efficiency · Microchannel design

## **Introduction**

Microfluidic systems play an important role in various application felds. In impacted on industries, such as environmental science, drug delivery, and biochemistry [[1](#page-8-0)[–8](#page-8-1)]. Recently, with the global pandemic of COVID-19, there has been active development of mRNA vaccines. Notably, the utilization of lipid nanoparticles (LNPs) in RNA delivery technology has a crucial role in the application of mRNA vaccines [[9–](#page-8-2)[11](#page-8-3)]. Macroscale LNP formation technologies are commonly used for convenience. However, achieving precise control over the size and polydispersity of liposomes poses inherent challenges for these techniques [\[12](#page-8-4)]. On the other hand, within microfuidic devices, the formation of LNPs using micromixers efficiently utilizes the surface and structure of microchannels for efective mixing, resulting in LNPs with an exceptional particle-size distribution. This methodology has attracted considerable attention from the

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biomedical industry and the fundamental biology and chemistry research area felds [[13,](#page-8-5) [14\]](#page-8-6).

In microfuidic systems, the microchannels exhibit a high surface area-to-volume ratio, leading to enhanced mass density and heat transfer and faster reaction rates. Furthermore, the handling of small fuid volumes provides the advantage of reduced reagents and energy consumption [\[15](#page-8-7), [16\]](#page-8-8). The rapid and uniform mixing of two or more samples within these microchannels is crucially utilized in various applications, including biomedical analysis and synthesis [[17\]](#page-8-9).

To investigate the transient events occurring during chemical/biological processes on a microscale or to achieve optimal synthesizing results, rapid mixing within milliseconds before the reaction proceeds is essential [[18](#page-8-10)]. However, the fuid fow in microchannels typically cannot generate turbulent fow and exhibits a laminar fow, resulting in a low Reynolds number (*Re*) [[19\]](#page-8-11). *Re* is defned as

$$
Re = \frac{\rho V D}{\mu},
$$

where  $\rho$  is the density of the fluid, *V* is the velocity of the fluid, *D* is the characteristic length, and  $\mu$  is the fluid dynamic viscosity.

In microfuidic device, the characteristic length (*D*) and the fuid velocity (*V*) are relatively small. Consequently, mixing in microfuidic devices occurs through molecular difusion based on concentration gradients. This leads to an increased mixing

time and increases the microchannels length [\[20](#page-8-12)]. Therefore, in numerous studies, various designs of micromixers have been developed to enhance the mixing efficiency in a short mixing channel [[21\]](#page-8-13). In general, micromixers can be classifed into active and passive, depending on the application of external forces. Active micromixers utilize external energy sources, such as electric force, magnetic force, and acoustic waves, to enhance mixing efficiency  $[22-26]$  $[22-26]$ . In microfluidic system, external energy sources are employed to control fuid fow and facilitate mixing, achieving faster mixing rates and increased efficiency. However, active micromixers, requiring connection to an external energy source, exhibit a relatively intricate structure. The device fabrication process is complex and involves high costs [[27\]](#page-9-1). In contrast, passive micromixers utilize the inherent properties of fuid fow at the microscale for mixing without the need for external energy inputs. This is achieved by extending fuid interfaces with low-pressure drops and short mixing lengths or inducing chaotic fow, attracting significant interest  $[28-32]$  $[28-32]$  $[28-32]$ . Passive micromixers offer the advantages of simplicity in structure, ease of device fabrication, and independence from external energy sources. These mixers are typically designed in both 2-dimensional (2D) and 3-dimensional (3D) structures.

However, previous studies on passive micromixers focused on the improving mixing efficiency through unique geometric confgurations, surface treatment, or the integration of obstacles within the fuidic pathways [\[33–](#page-9-4)[37](#page-9-5)]. Thus, a notable gap persists in previous studies, and it is difficult to find a comprehensive comparison of these various designs under standardized conditions to determine the most efective approach for passive mixing in microfuidic devices. This lack of comparative analysis makes it difficult for researchers to select the optimal design for their specifc applications, thereby impeding progress in the development and application of microfuidic technologies.

In this paper, we perform a systematic investigation into the mixing efficiency of various micromixers. By employing a consistent set of experimental conditions across all designs tested, this study is to provide a clear and objective comparison of their performance, thereby ofering valuable into the most efective design principles for passive mixing in microfuidic device. This study not only contributes to the advancement of microfuidic technology but also aids in the optimization of its applications.

# **Materials and Methods**

#### **Device Fabrication**

In this experiment, various micromixers were designed using AutoCAD (Autodesk). Subsequently, the designs were fabricated through photolithography and soft lithography techniques. Through photolithography, we create a master mold with a design pattern on a silicon wafer, allowing for continuous and repeated use in subsequent experiments. To obtain a microfuidic device from master molds, soft lithography technology is applied using polydimethylsiloxane (PDMS). An elastomer (Sylgard 184, Dow Corning) and curing agent were mixed at a ratio of 10:1 (w/w) to make PDMS. After pouring PDMS onto the fabricated master mold, a thermal curing process was conducted on a hot plate at 65 °C for over 4 h. To fabricate the 2-dimensional microfuidic device, the cured PDMS was then separated from the master mold and bonded to a bare PDMS substrate through oxygen plasma treatment. We construct all four sides of the channel using PDMS, so we utilized PDMS to form the bottom part of the microchannel. The PDMS substrate was formed by curing PDMS in a petri dish, and it was subsequently peeled off for use. In contrast, the 3-dimensional microfuidic device is confgured by stacking 2D structures to create layers. During the photolithography process, two separate 2D structures are produced. Subsequently, for the fabrication of the 3-dimensional device, PDMS is demolded from each silicon wafer, and after oxygen plasma treatment, the PDMS structures are aligned and bonded at the junctions.

#### **Experiment in Mixing**

To conduct comparative experiments, we utilized Alexa Flour 568 and Deionized water. Alexa flour 568 was dissolved in deionized water to create a 1 μM solution. For injecting solutions into the microfuidic device, we used a syringe pump (Harvard Apparatus PHD-2000 Advance Syringe pump) to inject fuid at a rate of 1 mL/min into each inlet. Fluorescence images for mixing efficiency analysis were captured using an optical microscope (Nikon ECLIPSE TE200-U) and a CCD camera (CoolSNAP™ cf Monochrome). We obtained fuorescent images of each microchannel. Furthermore, cross-sectional mixing images were acquired using a confocal microscope (Nikon A1 confocal, Japan) to observe fuid mixing patterns within the microchannels when interacting solutions into the 3D zigzag micromixer.

#### **Analysis of Mixing Efficiency**

The analysis of mixing efficiency aimed to utilize the average fuorescence intensity and standard deviation obtained from analyzing the region of interest (ROI) in each micromixer. To quantitatively assess the mixing efficiency within our passive micromixer designs, we employed a fuorescencebased the equation [[38](#page-9-6)]

$$
M = \left(1 - \frac{\sigma}{\bar{l}}\right) \times 100\%;
$$

 $\overline{I}$  represents the average fluorescence intensity measured in the region of interest (ROI), and  $\sigma$  is the standard deviation value of fuorescence intensity measured in the ROI.

Furthermore, to provide a more accurate representation of mixing performance, we normalize the mixing efficiency using the equation [[39\]](#page-9-7)

$$
M_n = \frac{M_k - M_{min}}{M_{max} - M_{min}}.
$$

In this formula,  $M_n$  represents the normalized mixing efficiency,  $M_k$  is the calculated mixing efficiency,  $M_{max}$  is the maximum observed mixing efficiencies, and  $M_{min}$  is the minimum observed mixing efficiencies, respectively. By normalizing the mixing efficiency, we effectively scale the values, such that 0 indicates no mixing, and 1 indicates complete mixing, facilitating a clearer comparison between diferent micromixer designs.

# **Results and Discussion**

#### **Design of Passive Micromixers**

In previous studies, various passive micromixers have been proposed. In this study, to determine which design among passive micromixers achieves the most efficient mixing, we designed a total of 5 passive micromixers with diferent channel geometries (Table [1\)](#page-2-0).

For passive micromixers with a 2D structure, we developed designs for straight, serpentine, herringbone [\[40](#page-9-8)], and toroidal [\[41\]](#page-9-9) micromixers. For the 3D structure, we designed a 3D zig-zag micromixer [\[42,](#page-9-10) [43\]](#page-9-11). Additionally, we compared the  $M_n$  values for each micromixer design. The inlet and outlet of each micromixer were designed to be identical. To compare the  $M_n$  based on the structure of the micromixer, we designed them with variations only in the mixing region. Figure [1](#page-3-0) shows the detailed structure of the designed micromixers. After designing each micromixer, we injected fuid with the same Reynolds number into each micromixer and compared the  $M_n$  at the same time.

## **Comparison and Analysis of Mixing Efficiency in Various Micromixers**

In this study, we aimed to identify the most efficient design among micromixers with diferent designs. Figure [2](#page-3-1) illustrates the  $M_n$  results of the five micromixers. To assess the  $M<sub>n</sub>$  value in each micromixer, we measured the distance from the point where the two fuids meet to the ROI within the

<span id="page-2-0"></span>**Table 1** Types of micromixer designs



\*The measurement points marked by closed triangles

\*\*The open triangle represents the msec missing point in the serpentine micromixer

micromixer. This distance was then converted into time units for comparative analysis. In Fig. [2,](#page-3-1) the 3D zig-zag micromixer reached an  $M_n$  value of 1.0 at around 1.3 ms mixing time. In contrast, other micromixer designs did not reach within the same time. Even upon reaching the endpoint at 1.6 ms, the  $M_n$  did not attain a high value. This demonstrates that the  $M_n$  value is influenced by the microchannel design of each micromixer.

The straight micromixer relies on molecular difusion at the fuid interface due to the absence of structural elements. However, this process is generally slow; the  $M_n$  value is observed to be low, around 0.01 [[44](#page-9-12)]. The herringbone micromixer difers from the straight micromixer in that it features an asymmetric herringbone structure repeated on the bottom surface of the microchannel.

The herringbone structure consists of two connected channels of diferent lengths, one relatively long and the other short, designed asymmetrically. This herringbone structure indicates a helical fow pattern of the fuid within the microchannel, facilitating efective mixing [\[45](#page-9-13), [46\]](#page-9-14). As a result, the  $M_n$  at the endpoint increased to around 0.54, indicating improved mixing performance compared to a straight micromixer. However, the  $M<sub>n</sub>$  value did not reach or come close, even at the endpoint.

In the serpentine micromixer, as the two injected fuids traverse through a curved channel, secondary fow driven by centrifugal forces induces a dean fow pattern, causing the fluid to move from the inner side of the channel



<span id="page-3-0"></span>**Fig. 1** The schematic drawing of each micromixer. **a** Straight micromixer. The channel height (H) and width (W) are 100 μm. The total length of the channel is 28 mm. **b** Serpentine micromixer. Both the height and width are 100 μm. The total length of the channel is 22 mm, and the number of repeat units is 4. **c** Herringbone micromixer. The channel has a height of 77 μm and a width of 100 μm. In the herringbone structure, height (h) is 23 μm, and the width **d** is 50 μm.

toward the outer wall [[47](#page-9-15)]. During this process, the fuids experience an increased interfacial area due to the curved geometry, leading to enhanced mixing efficiency. This results in more efficient mixing compared to the previous micromixer, with a confirmed  $M<sub>n</sub>$  value of approximately 0.81 at the termination point. However, the  $M_n$  value exhibits a monotonic increase toward the later part of the microchannel due to the absence of obstacle within the microchannel, evenly saturating.

In the toroidal micromixer, fuid undergoes splitting induced by the toroidal shape, followed by recombination at the neck, resulting in asymmetric collisions that promote efective mixing [[48\]](#page-9-16). Additionally, the toroidal micromixer, characterized by its repetitive pattern of spit and recombining, exhibits a substantial increase in the interfacial area where the fuids come into contact. This unique structure contributes to more effective mixing, resulting in an efficiency of approximately 0.88 at the outlet. Based on these results, the toroidal micromixer has

The total length of the channel is 28 mm, and the number of repeat units is 8. **d** 3D zig-zag micromixer. Both the height and width are 100 μm. The total length of the channel is 23 mm, and the number of repeat units is 7. **e** Toroidal micromixer. Height (H) is 90 μm and width (W) is 110 μm. The inner circle of the toroidal micromixer (**a**) has a 330 μm, while the outer circle (**b**) has a 550 μm. The total length of the channel is 25 mm, and the number of repeat units is 8



<span id="page-3-1"></span>Fig. 2 Comparison of normalized mixing efficiency in various micromixer designs. The dashed line at the point where the normalized mixing efficiency value is 1.0 represents the criteria for the perfect mixing. The flow rates are fixed for all experiments with  $Re = 332$ 



<span id="page-4-0"></span>**Fig. 3** Design of toroidal micromixer

<span id="page-4-1"></span>**Table 2** The design parameters of toroidal micromixer

Neck angle $(\theta)$	$90^\circ$	120°	$140^\circ$	$160^\circ$	$180^\circ$
Width ratio (W1/W2)	1.0	2.0		3.0	4.0

been confirmed to exhibit the most efficient mixing among the micromixers with a two-dimensional structure.

Finally, the 3D zig-zag micromixer features a threedimensional structure in contrast to the previous micromixers. The 3D structure induces also primary flow in the  $x$ –*y* plane and secondary flow in the vertical *z*-axis. This secondary flow enhances mixing by increasing the contact surface of the fuids. With this improved mixing, the 3D zig-zag micromixer achieves a  $M<sub>n</sub>$  of approximately 0.98 at 1.3 ms, earlier than the endpoint at 1.6 ms.

Therefore, this paper, we aimed to modify the design parameters affecting  $M_n$  in the toroidal and 3D zig-zag micromixers. We optimized the design of toroidal and 3D zig-zag micromixer designs to confirm the most efficient one.

## **Experimental Assessment of Mixing in the Toroidal Micromixer with Various Designs**

We anticipated that the neck angle  $(\theta)$  and width ratio  $(W_1)$  $W_2$ ) in the toroidal micromixer would influence  $M_n$ , as illustrated in Fig. [3.](#page-4-0) Consequently, we modifed each parameter to investigate the correlation with the parameters and  $M_n$ . Ultimately, we aimed to design the most efficient micromixer within the toroidal micromixer. As shown in Table [2,](#page-4-1) to investigate the influence of neck angle on  $M_n$ , we designed different neck angles  $(90^{\circ}-180^{\circ})$ , and we fixed the width ratio at 1.0. In designs with various width ratios, we fxed the neck angle at 120° and adjusted the width ratio (1.0–4.0).

To analyze  $M_n$ , we defined each section of the neck in the toroidal micromixer as a Region of Interest (ROI) and captured fluorescent images. The  $M_n$  was calculated using the average fuorescence intensity and standard deviation within the designated ROI.

First, the  $M_n$  of each micromixer with different neck angle was compared. Comparing the  $M_n$  values when the mixing

time reached 1.4 ms, we observed respective values of 0.89, 0.78, 0.65, 0.5, and 0.25, respectively. At the endpoint  $(2.6 \text{ ms})$ , the M<sub>n</sub> values were calculated as 0.95, 0.95, 0.91, 0.83, and 0.5 for each design, respectively. Through these results, it was observed that as the neck angle approached 90°, the graph of  $M<sub>n</sub>$  exhibited a rapid increase in values within a short time, saturating quickly (Fig. [4](#page-5-0)a). At the endpoint, a comparison of  $M_n$  at the smallest neck angle of 90 $^{\circ}$  and the largest angle of 180 $^{\circ}$  revealed that the  $M_n$  at a neck angle of 90 $^{\circ}$  was approximately 90% higher than at 180°. In addition, as shown in Fig. [4b](#page-5-0), an increase in the neck angle leads to a more distinct boundary between the two fuids. When fuid is injected into the toroidal micromixer, it undergoes split and recombination due to the structure of the microchannel. This process results in imbalanced collision and mixing. This is attributed to the fuid recombining at the neck section and causing collisions, which become more imbalanced when the neck angle approaches 90° compared to grades closer to 180°. Therefore, chaotic fow occurs at the neck section, increasing interfacial area and facilitating mixing. It suggests that the diference in neck angles infuences *Mn*.

To investigate the correlation between  $M_n$  and the width ratio of the microchannel, we conducted mixing experiments and compared the  $M<sub>n</sub>$  in toroidal micromixers with varying width ratios. In the toroidal micromixer with width ratios of 3.0 and 4.0,  $M<sub>n</sub>$  values achieving 0.99 were observed at approximately 2.0 ms. However, mixing was not complete in the toroidal micromixers with width ratios of 1.0 and 2.0, with  $M_n$  values of 0.89 and 0.96, respectively. For both designs, even at the endpoint, the  $M_n$  values were not reached 1.0 (Fig. [4](#page-5-0)c). In particular, with a width ratio of 4.0, the mixing of the two fuids was confrmed at 1.4 ms, while the ratio of 1.0 did not mix, and the boundary between the two fuids was visible (Fig. [4](#page-5-0)d). This indicates that, as the width ratio increases, the  $M<sub>n</sub>$  reaches 1.0 within a short time. In the toroidal micromixer, when the width ratio is varied, one fuid enters the wider side of the channel with the other fuid, increasing the contact area between the fuids. This leads to enhanced mixing as the interface area increases, and there is an increase in imbalanced collisions at the recombination neck section, resulting in improved  $M_n$ . In contrast, when the width ratio of the channel is the same, the two fuids symmetrically enter the channel, leading to reduced imbalanced collisions and limiting the  $M_n$  [\[45,](#page-9-13) [49](#page-9-17)].

As a result, we confrmed that in the design of the toroidal micromixer, lower neck angles and larger width ratios lead to improved  $M_n$ . Among the toroidal designs, we identified the micromixer with a neck angle of 90° and a width ratio 4.0 as the most efficient design.



<span id="page-5-0"></span>**Fig. 4** Investigation of various designs to evaluate the infuence of neck angle and width ratio on a toroidal micromixer. **a** Comparison of normalized mixing efficiency in toroidal micromixer with different neck angle. **b** Fluorescence images illustrating variations in mixing across diferent toroidal mixers with diferent two neck angles. (i) and (iii) are the fuorescence images at 1.4 ms. (ii) and (iv) are the fuorescence images at 2.6 ms. **c** Comparison of normalized mixing

# **Comparison of Mixing Efficiency in 3D Zig-Zag Micromixer with and Without Junction**

In Fig. [2,](#page-3-1) we confrmed that the 3D zig-zag micromixer is the most efficient. However, we observed a significantly lower

efficiency in toroidal micromixer with different width ratio. d Fluorescence images showing variations in mixing across diferent toroidal mixers with diferent width ratios. (v) and (vii) are the fuorescence images at 1.4 ms. (vi) and (viii) are the fuorescence images at 2.6 ms. **e** Schematic diagram of the measurement points in toroidal micromixer. The closed triangles represent 1.4 ms, while the open triangles indicate 2.6 ms (scale bar size =  $100 \mu m$ )

 $M_n$  at 0.4 ms than other micromixers. We anticipated this due to the absence of junctions when entering the mixing region from the inlet in the 3D zig-zag structure. Therefore, we compared the 3D zig-zag micromixer with and without a junction at the inlet (Fig. [5](#page-6-0)a).

<span id="page-6-0"></span>

To evaluate the  $M_n$ , we obtained fluorescence images by designating the middle of each channel in the 3D mixer as an ROI. Then, we calculated the average fuorescence intensity and standard deviation from the fuorescence images.

In both designs, with and without a junction at the inlet, the  $M_n$  value increases sharply at the initial junction. However, the design with a junction was observed to mix more rapidly (Fig. [5b](#page-6-0)).

When compared the  $M_n$  value at 0.4 ms between the designs with and without a junction, the design without a junction exhibited approximately 0.27, while the design with a junction improved to approximately 0.75. This indicates that the design with a junction at the inlet achieved enhanced  $M<sub>n</sub>$  value at the same time.

In addition, the design without a junction required approximately 1.3 ms to reach the  $M<sub>n</sub>$  value of 1.0, while the design with a junction reached it at approximately 0.8 ms. The mixing time can be reached about 0.5 ms faster than the design without a junction, resulting in an improvement of approximately 38%. This demonstrates that the additional junction induced secondary flow, allowing for more efficient mixing. In conclusion, in the design of the 3D zig-zag micromixer, the confguration with an additional junction at the inlet proved to be the most efficient design.

# **Comparative Analysis of Mixing Efficiency in Toroidal and 3D Zig‑Zag Micromixers**

Ultimately, we compared the  $M<sub>n</sub>$  of the toroidal micromixer and 3D zig-zag micromixer to identify the most efficient micromixer design (Fig.  $6$ ). The comparison of  $M_n$  between the two micromixers revealed that the 3D zig-zag micromixer is a more efficient design. The toroidal micromixer achieved a  $M_n$  value of 1.0 within about 2 ms. However, using the 3D zig-zag micromixer achieving an  $M_n$  value 1.0 in a short time of 0.8 ms. This indicates that the 3D zig-zag



<span id="page-6-1"></span>Fig. 6 Graph of normalized mixing efficiency between the final design of 3D zig-zag and toroidal micromixers

micromixer exhibited a signifcant improvement of about 60% compared to the toroidal micromixer, demonstrating superior mixing performance.

The difference in  $M_n$  is attributed to the toroidal micromixer having two-dimensional structure, while the 3D zig-zag micromixer has three-dimensional structure. In the case of the toroidal structure, mixing is confned to the x–y plane, whereas in the 3D zig-zag structure, in addition to the primary fow in the *x*–*y* plane, secondary fow occurs along the *z*-axis. This multi-dimensional fuid motion contributes to increased interfacial area, resulting in enhanced *Mn* compared to the toroidal micromixer.

Based on these results, we compare the  $M_n$  value of the 3D zig-zag micromixer with that of other micromixers. Table [3](#page-7-0) presents a comparison of the  $M_n$  among five different micromixers. The toroidal micromixer features a design with a neck angle of 90° and a width ratio of 1.0, while the

Micromixer Straight Herring- design	bone	Serpentine Toroidal 3D zig-zag		
Normalized 0.02 mixing index	0.48	0.72	0.91	0.99

<span id="page-7-0"></span>Table 3 Normalized mixing efficiency values at 1.0 ms for various micromixers

3D zig-zag micromixer incorporates a design with junctions. When compared at a mixing tine of 1.0 ms, other micromixers, excluding the 3D zig-zag micromixer, did not reach the fully mixed value of 1.0. These results indicate that the comparison of  $M_n$  among different micromixers revealed that the mixing in the 3D zig-zag micromixer is the most efficient. And this attains an  $M_n$  value of 1.0 within a short time of 0.8 ms.

## **Estimation of Mixing in 3D Zig‑Zag Micromixer with Diferent Reynolds Number**

We investigated the  $M_n$  in the 3D zig-zag micromixer at different Reynolds numbers. Furthermore, we visualized the fluid flow along each junction using a confocal laser scanning microscope to observe the extent of fuid mixing.

Figure [7](#page-7-1)a shows the comparing normalized  $M_n$  in the 3D zig-zag micromixer at diferent Reynolds numbers. All

variables except for the fow rate were fxed, and as a result, the Reynolds number increased with the fow velocity within the micromixer.

The results showed that as the Reynolds number decreased, the  $M_n$  also reduced. Conversely, an increase in the Reynolds number correlates with an upward trend in  $M_n$ . This indicates that at low Reynolds numbers, the mixing of fluids in the micromixer occurs slowly, decreasing in M<sub>n</sub>. In contrast, as the Reynolds number increases, turbulence is induced in the fluid, resulting in an upward trend in  $M_n$ . As shown in the fgure, except the case of *Re* = 17, we observed that the  $M_n$  value reached 1.0 at all other Reynolds numbers. Particularly, at  $Re = 332$  and  $Re = 449$ , the  $M<sub>n</sub>$ value reached 1.0 at 2.7 mm. These results imply the impact of fow velocity on Reynolds number.

Additionally, we visualized the mixing at the middle of each channel in a 3D zig-zag micromixer, and the fuid velocity fixed at  $Re = 332$  (Fig. [7b](#page-7-1)). In the first crosssection (1.2 ms), we observed that the fluids remained unmixed. However, starting from the second crosssection (2.2 ms), mixing occurred, resulting in a uniform mixture.

In conclusion, in the 3D zig-zag micromixer, there was a trend of rapid increase of  $M<sub>n</sub>$  at higher Reynolds numbers. When examining the cross-sectional area, it was confrmed that the two fuids are uniformly mixed.



<span id="page-7-1"></span>Fig. 7 Effect of Reynolds numbers on mixing efficiency. a Comparison of normalized mixing efficiency in 3D zig-zag micromixer at different Reynolds numbers. **b** 3D confocal fuorescence images for vis-

ualizing cross-sections of a 3D zig-zag micromixer (*Re* = 332). Scale  $bar size=100 \text{ µm}$ 

#### **Conclusions**

Efficiently achieving high mixing efficiency within a short time in microfuidic devices is a critical technology in chemistry and biological reactions. To address this challenge, numerous researchers have proposed various designs for micromixers. In this paper, we compare various passive micromixer designs and propose a micromixer design that efectively achieves rapid mixing quickly. To confirm the most efficient design in a passive micromixer, designs for straight, serpentine, herringbone, toroidal and 3D zig-zag micromixers were developed and compared for  $M_n$ . As a result, it was confirmed that toroidal and 3D zigzag micromixer achieved more efficient mixing compared to other micromixers. Additionally, we identified the parameters influencing the  $M_n$  of the toroidal and 3D zig-zag micromixer. The most efective designs for each micromixer were determined, and the  $M<sub>n</sub>$  was compared among the final designs of each micromixer.

Ultimately, the 3D zig-zag micromixer was identifed for exhibiting the highest  $M_n$ , with secondary mixing flows occurring along the *z*-axis. This result demonstrates the capability of achieving efective mixing in a short time, approximately 0.8 ms. Through this study, the proposed 3D zig-zag micromixer is expected to fnd valuable applications, particularly in efficiently conducting chemical reactions with small amounts of reagents or promoting reactions by mixing reagents in medical diagnostics and testing. Especially for the mRNA-LNP vaccines, aimed at relieving the world from a tragic global pandemic, where the uniform formation of nanoparticles and nanostructures is crucial, a rapid mixing process is essential. The 3D zig-zag micromixer introduced in this paper is expected to be highly beneficial, as it can achieve a high  $M_n$  quickly, making it suitable for various applications.

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