

Electronic Supporting Information

Thermoformed fluoropolymer tubing for in-line mixing

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1. Details of micromixer fabrication

Aluminum modes with surface patterns were fabricated by CNC (Computerized Numerical Control) milling in Proto Labs Inc., USA. The structures of the patterns on the modes are given in Fig. S1. The surfaces of the modes were blasted by light glass beads after milling to protect aluminum from oxidization. The fluoropolymer tube was sandwiched between the two models before heating. During the heat treatment, the oven was heated up from room temperature to the set temperature in about 15 min. This time was included in the total thermoforming time of 60 min. After the heat treatment, the modes and the tube were cooled down in air naturally. The melting points and highest heat treated temperatures of the fluoropolymers employed in this study are obtained from the website of Chemours (Fluoroplastic Comparison – Typical Properties).¹ The thermoforming temperature of 240°C for FEP connectors could also stick the micromixer and the FEP connector, but we found the connector was easily blocked. Therefore, the Y-connectors and the screw-tube mixers used in the dye tracing experiments, were bonded by epoxy resin glue.

Table S1 Temperature parameters for fluoropolymer tubes¹

	Melting points(°C)	Thermoforming T for tubular mixers (°C)	Thermoforming T for connectors(°C)
PFA	306	260	-
FEP	260	200	240
ETFE (Tefzel®)	267	160	-

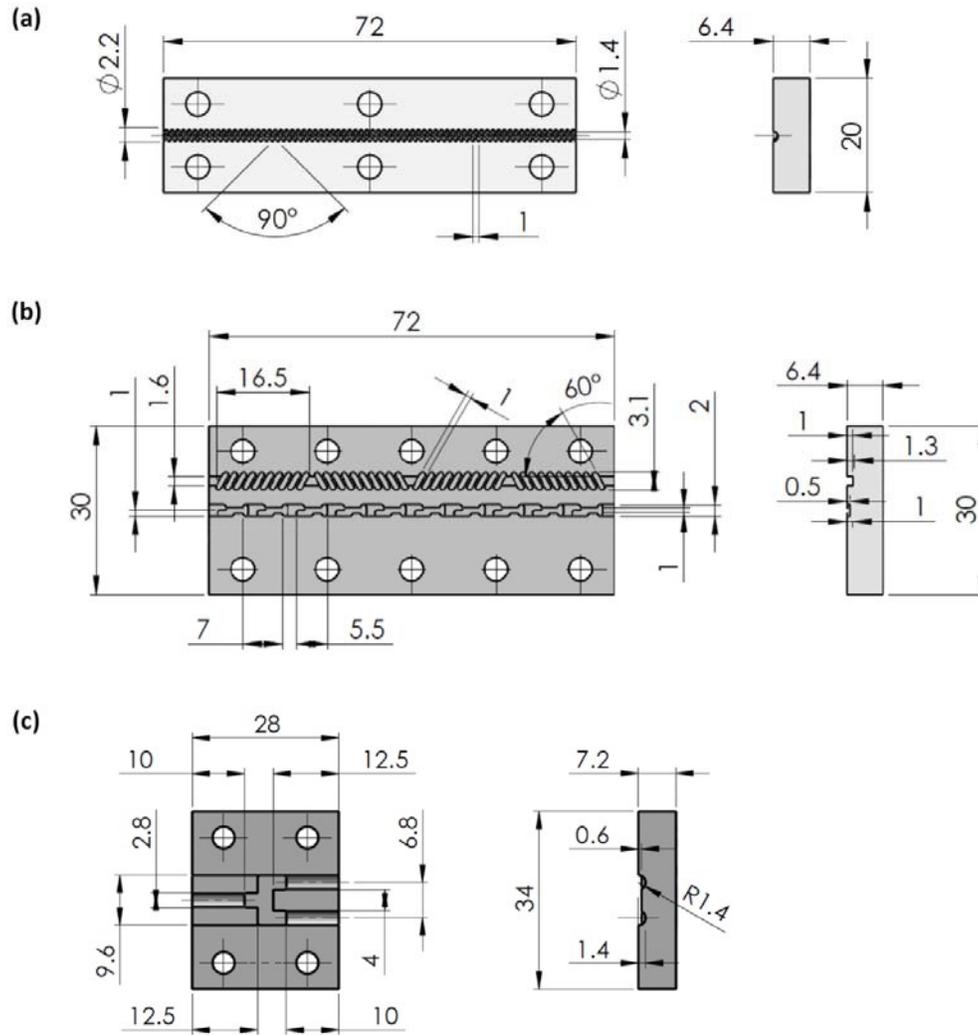


Fig. S1 Structure parameters on the aluminum modes. (a) Screw pattern, (b) Slant grooved tunnel and split-recombined tunnel. (c) Pattern for the Y-connector. The length unit is mm.

In order to make longer tubular micromixers, which are able to enhance mixing in low Re regime, the tube needs to be heat treated part by part. However, the oven would potentially destroy the formed patterns on the tube surface; therefore, we improved the heating source using heating rods, sensors and temperature controllers to ramp up the modes temperature. A picture for the whole apparatus is shown in Fig. S2, and we found this heating method did not influence the patterns on the surface of mixer. Using this method, the tubular mixers can be fabricated as long as possible.

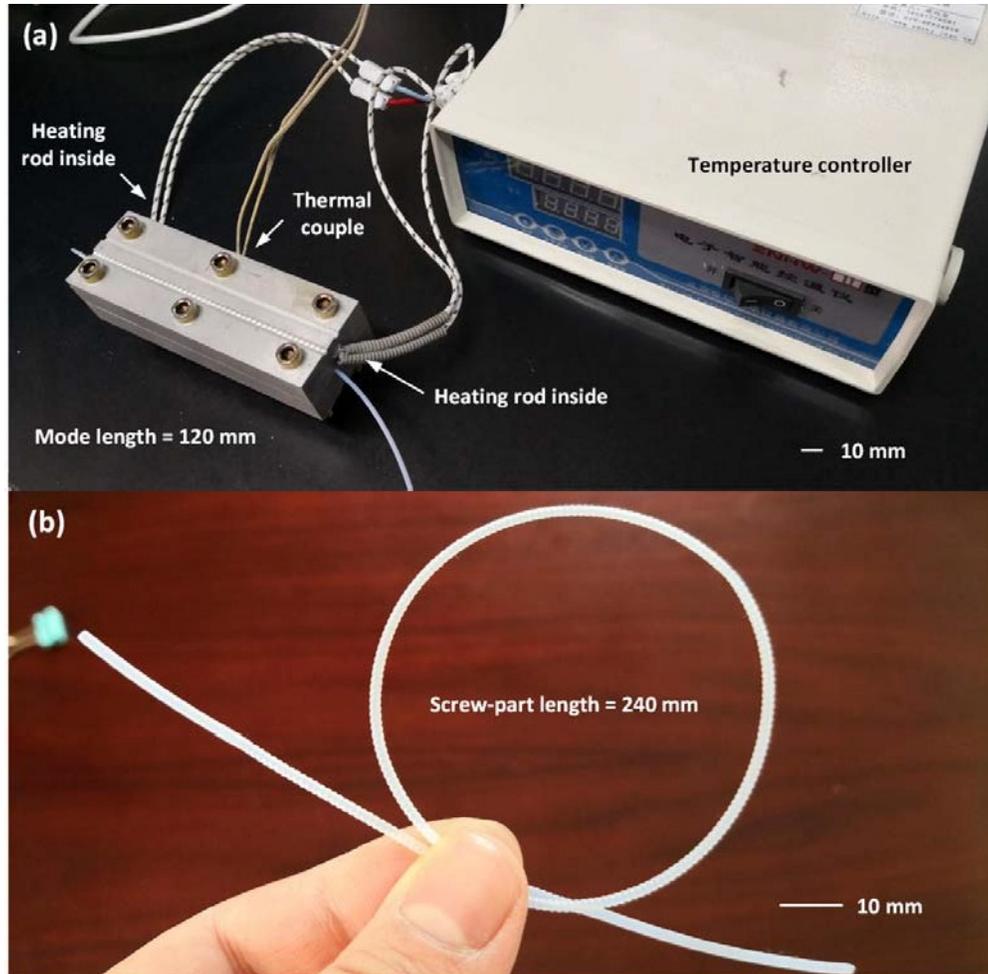


Fig. S2 Pictures for the improved heating system and longer fabricated tubes.

2. Dye tracing experiments

In order to show fluid mixing in micromixers, dye tracing experiments were implemented with two aqueous solutions that contained 0.062 wt% erioglaucine (blue, Sigma-Aldrich) and 0.10 wt% Rhodamine B (red, Sigma-Aldrich), respectively. Those solutions were fed by syringe pumps (PHD Ultra 2000, Harvard Apparatus) into the tubular mixers through the Y-connector. Limited by the intrinsic view field of the microscope, an image joint method was used to visualize the whole mixer in Figs. 2(b), 2(c) and S3, for the steady-state flow patterns in the systems. To illustrate the mixing process more accurately, videos of the mixers were recorded with moving cameras and attached in the paper.

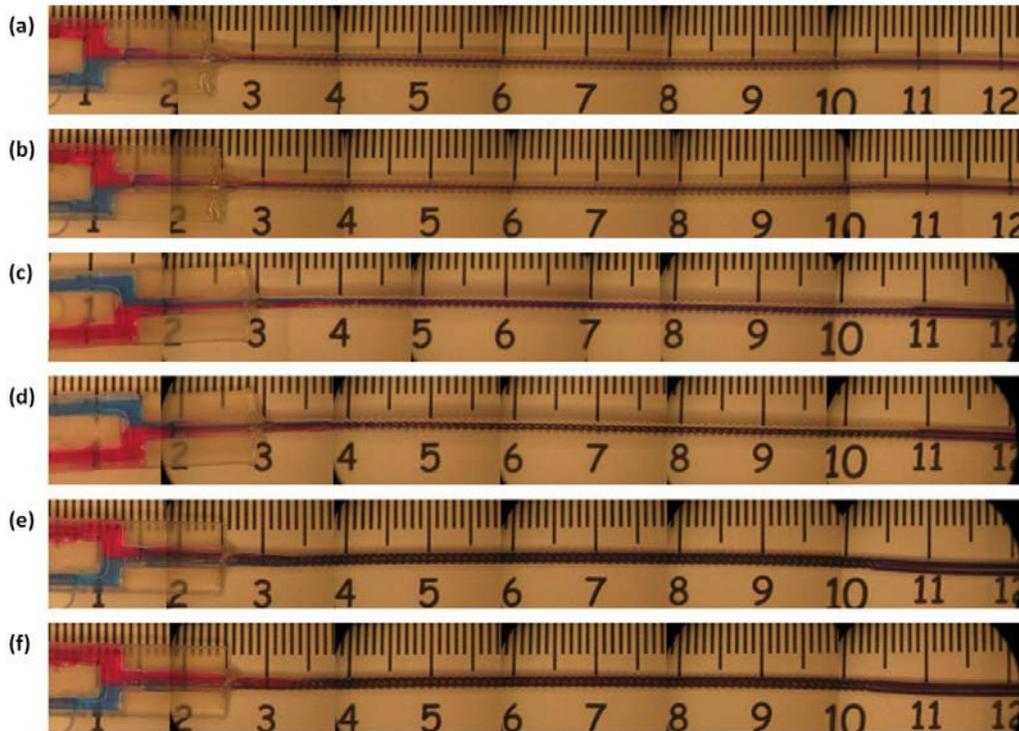


Fig. S3 Pictures of typical dye tracing experiments. (a) Original tube ID (inner diameter) = 0.5 mm, $Q_{\text{blue}} = 0.4$ mL/min, $Q_{\text{red}} = 0.8$ mL/min. (b) Original tube ID = 0.5 mm, $Q_{\text{blue}} = 0.2$ mL/min, $Q_{\text{red}} = 1.0$ mL/min. (c) Original tube ID = 0.75 mm, $Q_{\text{blue}} = 1.0$ mL/min, $Q_{\text{red}} = 2.0$ mL/min. (d) Original tube ID = 0.75 mm, $Q_{\text{blue}} = 0.8$ mL/min, $Q_{\text{red}} = 4.0$ mL/min. (e) Original tube ID = 1.0 mm, $Q_{\text{blue}} = 2.0$ mL/min, $Q_{\text{red}} = 4.0$ mL/min. (f) Original tube ID = 1.0 mm, $Q_{\text{blue}} = 0.4$ mL/min, $Q_{\text{red}} = 2.0$ mL/min.

Experimental movie 1: Screw-tube mixer, original ID = 1.0 mm, $Q_{\text{blue}} = Q_{\text{red}} = 0.5$ mL/min.

Experimental movie 2: Screw-tube mixer, original ID = 0.75 mm, $Q_{\text{blue}} = Q_{\text{red}} = 0.5$ mL/min.

Control group movie 1: Straight tube, original ID = 1.0 mm, $Q_{\text{blue}} = Q_{\text{red}} = 0.5$ mL/min.

Control group movie 2: Straight tube, original ID = 0.75 mm, $Q_{\text{blue}} = Q_{\text{red}} = 0.5$ mL/min.

3. CFD (computational fluid dynamics) simulations

The working mechanism of the screw-tube mixer is to force the fluids rotate along the axial direction of the tube, which is similar to the stirrers in vessels. This mechanism can be clearly illustrated by the CFD simulations of flow field in a 10 mm long screw-tube mixer (Fig. S4(a)).

Laminar models for incompressible fluids, including the continuity equation, the Navier-Stokes equation and the diffusion-convection equation (Eqn. S1 to S3) were solved, and all the Re for the simulation tests were below 100.

$$\nabla \cdot \mathbf{u} = 0 \quad (S1)$$

$$\rho \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \mu \nabla^2 \mathbf{u} \quad (S2)$$

$$\mathbf{u} \cdot \nabla C = \nabla \cdot (D \nabla C) \quad (S3)$$

Here, \mathbf{u} is the velocity vector, ρ is the density (0.998 g/mL), μ is the dynamic viscosity (1 mPa·s), p is the pressure, C is the dye concentration, and D is the diffusion coefficient (D was set to $1 \times 10^{-9} \text{ m}^2/\text{s}$ in this study). The geometry of the screw-tube mixer shown in Fig. S4 with 0.8 mm major diameter and 0.5 mm minor diameter was generated by SOLIDWORKS. This geometry had a little difference from the inner structure of the thermoformed screw tube with 0.75 mm original ID (Table 1) to avoid the errors in building calculation cells in the CFD simulation. The geometry was then imported into COMSOL Multiphysics 5.3a and about 7 million tetrahedron grid cells with 0.0415 mm maximum grid length were used in the calculation as shown in Fig. S4(b). The left end surface was set to the fluid inlet with a constant flow rate ($Q_{in} = 1.0 \text{ mL/min}$) and the right end was set to the outlet with atmosphere pressure. A step function was used to set the top half of the inlet to a dye concentration of 10 mol/m^3 and the bottom half to 0 mol/m^3 . The calculation took about 3 hrs in a Thinkpad P50 Workstation with Intel Core i7-6820HQ CPU @ 2.70 GHz, and 64 GB memory. We have proved that the mesh size was small enough for accurate results, and the effect of numerical diffusion could be neglected based on a mesh independent study shown in Fig. S4(c).

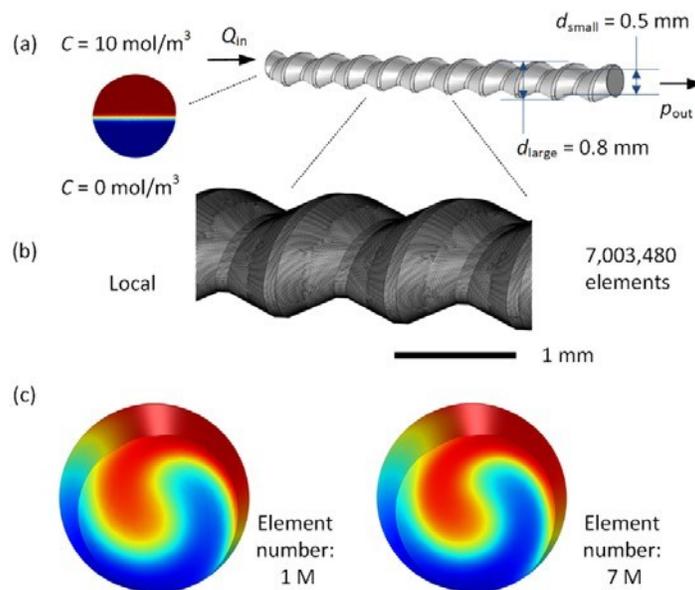


Fig. S4 Structure details of the simulation and mesh independent study. (a) Size parameters of the screw-tube mixer and the settings of inlet and outlet. (b) Local mesh in the simulation. (c) Mesh independent study of the reactor outlet surface. The 1 million mesh elements were range from 0.0112 to 0.0594 mm and the 7 million mesh had a size range from 0.00448 to 0.0415 mm.

The simulations were further extended to the whole mixer as shown in Fig. S5. A T-connector was employed as the inlets of fluids with different flow rates (Q_{dye} and Q_{blank}). At the outlet the pressure used the atmosphere value. A no-slip boundary condition was implemented at the wall. This model has comparable grid density to the 10 mm screw-tube mixer simulation. A typical result of the flow direction in the screw-tube mixer is given in Fig S5(b). We can see periodic flow directions in the mixer, in combinations of forward and rotating flows. Fig. S5(c) shows the dye concentration in the mixer in different operation conditions. In the screw-tube mixer, the rotating flow pattern makes substance blend very quickly as the uniformed color shown on the tube cross-section. Fig. S5(d) displays the pressure drop along the mixer. It is clear that the pressure drop is severer in the screwed part, but the total pressure drop is only as high as 0.353 kPa at total flow rate of 1 mL/min.

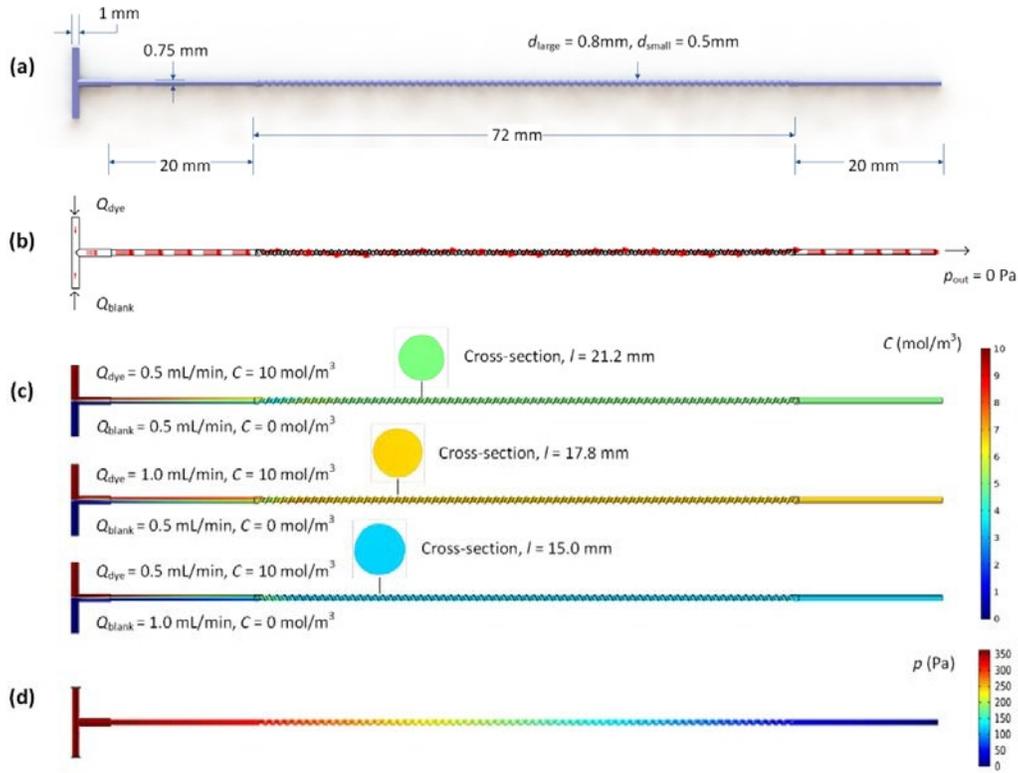
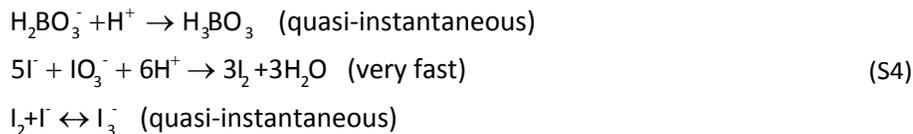


Fig. S5 CFD simulations for the fluid flow and concentration profiles in the screw-tube mixer. (a) The geometry of the screw-tube mixer connected to a T-connector. (b) Flow directions of the fluids. $Q_{dye} = Q_{blank} = 0.5\text{ mL/min}$. (c) Dye concentration profiles at different flow rates. (d) Pressure drop in the mixer. Flow rates are $Q_{dye} = Q_{blank} = 0.5\text{ mL/min}$.

4. Villermaux-Dushman reaction experiments

The mixing performance in the screw-tube mixer was quantified by using the Villermaux–Dushman reaction (also known as the iodide–iodate method), which is commonly employed for characterizing micromixers.^{4, 5} The principle of this method is based on the rate competition of a quasi-instantaneous reaction of acid and base (H^+ and H_2BO_3^-), and a fast reaction between I^- , IO_3^- , and H^+ , which is relatively slower.



The reaction rate constant of the second reaction $r_2 = k_2[\text{I}^-]^2[\text{IO}_3^-][\text{H}^+]^2$ is a function of ionic strength I , as $\log k_2 = 9.28 - 3.66I^{1/2}$, at $I < 0.16\text{ mol/L}$, and $\log k_2 = 8.38 - 1.51I^{1/2} + 0.23I$, at $I > 0.16$

mol/L, which is about $10^8 \text{ m}^{12}/(\text{mol}^4\text{s})$ in this experiment. The reaction rate constants of the third reversible reaction $r_3 = k_3[\text{I}^-][\text{I}_2] - k_3'[\text{I}_3^-]$ are $k_3 = 5.6 \times 10^6 \text{ m}^3/(\text{mol} \cdot \text{s})$ and $k_3' = 7.5 \times 10^6 \text{ 1/s}$, according to the literature reported by Fournier et al.⁶ When the molar amount of H^+ is smaller than the amount of H_2BO_3^- , the yield of $\text{I}_2 + \text{I}_3^-$ is mixing sensitive. Therefore, the segmented index, X_s ,^{4,7}, which ranges from 0 to 1, is introduced to quantify the relative yield of $\text{I}_2 + \text{I}_3^-$ to its highest value in theory. X_s is calculated as follows:

$$X_s = \frac{Y}{Y_{ST}} = \frac{2(n_{\text{I}_2} + n_{\text{I}_3^-})/n_{\text{H}^+,0} (C_{\text{I}_2} + C_{\text{I}_3^-})Q_T}{6C_{\text{IO}_3^-,0} (6C_{\text{IO}_3^-,0} + C_{\text{H}_2\text{BO}_3^-,0})} = \frac{(C_{\text{I}_2} + C_{\text{I}_3^-})Q_T}{n_{\text{H}^+,0}} \cdot \frac{C_{\text{IO}_3^-,0} + C_{\text{H}_2\text{BO}_3^-,0}}{3C_{\text{IO}_3^-,0}} \quad (\text{S5})$$

where Y is the yield of $\text{I}_2 + \text{I}_3^-$ in experiment; Y_{ST} is the yield in infinitely slow mixing conditions; n is the molar flow rate; C is the concentration; Q_T is the total flow rate of the mixture; and subscript 0 represents the original reactant solutions.

Fig. S6 shows schematics of the experimental apparatus. T-connectors were used to blend the solutions, then reactions occurred in the following tubes. The ID of the T-connector was 1 mm. The original tube IDs of the screw-tube mixers were chosen from 0.5, 0.75 and 1.0 mm in different experiments, and 0.75 ID coiled and straight tubes were tested as control experiment. An inline UV-vis spectrometer (Ocean Optics 2000+) with a self-assembled quartz flow cell (ID = 0.6 mm) was used to measure the concentration of $\text{I}_2 + \text{I}_3^-$ at 286 nm, and X_s was subsequently calculated. I^- is usually in excess to keep the ionic strength of the solution and facilitate as much as I_2 to convert to I_3^- for UV-vis analysis. The equilibrium constant $K = [\text{I}_3^-]/[\text{I}^-][\text{I}_2]$ is 736 L/mol at 25°C.⁸ All the lengths of the screwed parts in the tubular mixers were 72 mm. A 120 mm long tube with the same original ID of the mixer connected the micromixer and the flow cell. The coiled tube shown in Fig. 6S(b) has 2 circles and the loop diameter was 32 mm, smaller than which the tube became flat. The total length of the coiled and straight connection tube are 400 mm. Fig. S6(c) shows the control group experiment using a straight tube, which is also 400 mm in length. H_2SO_4 aqueous solution was used as the acid, which is labeled to Solution A in Fig. S6. This solution contained 0.02 mol/L H^+ . Solution B was a mixture of KH_2BO_3 , KI and KIO_3 , whose concentrations were 0.041, 0.02 and 0.0027 mol/L, respectively. All water used to prepare the solutions had been degassed by at least 2 hours N_2 bubbling in a stirred vessel to remove O_2 . The chemicals were from Sigma-Aldrich.

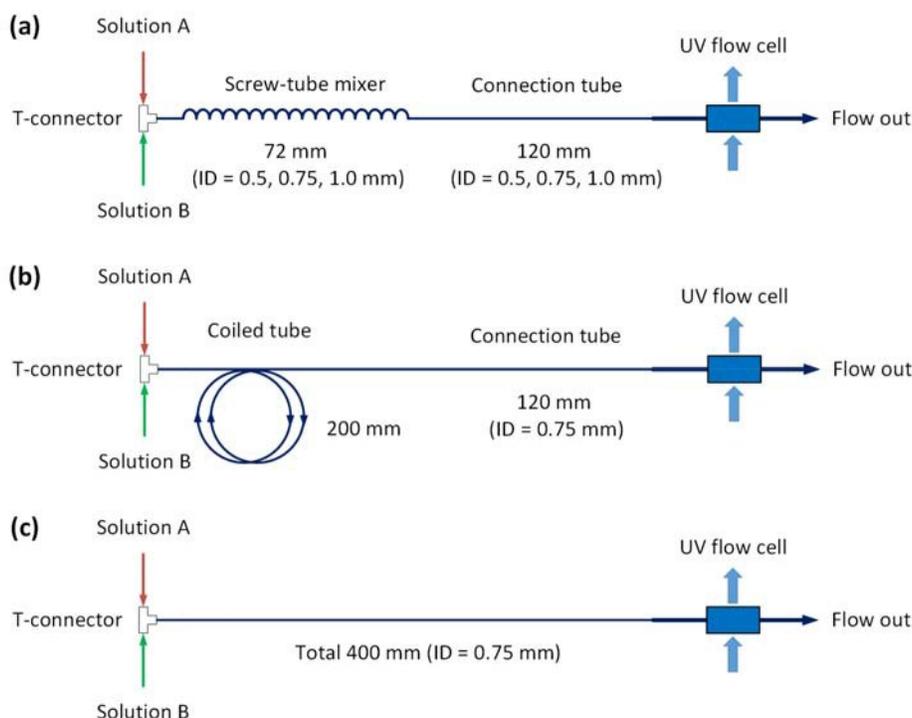


Fig. S6 Schematics of the Villermaux-Dushman reaction platforms. (a) The screw-tube mixer, (b) the coiled tube, and (c) the straight tube.

5. Residence time distribution (RTD) experiments

The RTD experiments were implemented in a platform shown in Fig. S7, with water as a testing solution. In order to determine the RTD solely from the screw-tube micromixer, a bypass test, shown in Fig. S7(b), was carried out to exclude the influence of tracer injection and detection. A 6-way check valve (Idex Health & Science) is used to inject the tracer, a 0.1 wt% erioglaucine aqueous solution. The quantified tube on the 6-way check valve has a 0.5 mm ID and 10 or 30 cm length (longer tube was used at $Q > 1$ mL/min). The flow rate is controlled by a syringe pump (PHD Ultra 2000, Harvard Apparatus). The mixer locates after the check valve, and is connected to the flow cell of the UV-vis spectrometer with a 0.75 mm ID connecting tube. Different from Villermaux–Dushman reaction experiment, the flow cell was an FEP tube with 0.75 mm ID in this study, and a connecting tube was also used between the micromixer and the flow cell. The 6-way valve and the UV-vis spectrometer were synchronously controlled by a homemade LabVIEW program (National Instruments).

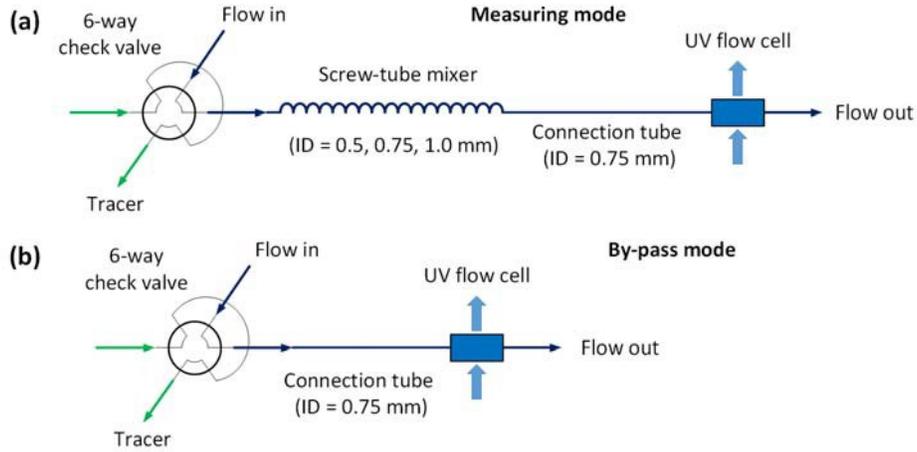


Fig. S7 Schematics of RTD experimental platforms. (a) The entire platform for measuring RTD in the screw-tube mixer. (b) The platform to obtain by-pass RTD.

After recording the tracer concentration function $C(t)$, the time distribution function $E(t)$, and the mean residence time \bar{t} , were calculated by Eqn. S6 and S7 using a MATLAB program.

$$E(t) = \frac{C(t)}{\int_0^{\infty} C(t) dt} \quad (S6)$$

$$\bar{t} = \frac{\int_0^{\infty} t \cdot C(t) dt}{\int_0^{\infty} C(t) dt} = \frac{V}{Q} \quad (S7)$$

Here, V is the volume of the tested tube and Q is the flow rate. Based on the by-pass and total experiments, the time distribution functions in the screw-tube mixers are regressed by a convolution of E , $C_{\text{by-pass}}$ and C_{total} .

$$C_{\text{total}} = E(t) * C_{\text{by-pass}} \quad (S8)$$

A dimensionless dispersion model with “open-open” boundary conditions, as shown in Eqns. S9 to S11, is employed in Eqn. S8.⁹

$$E(\theta) = \frac{1}{\sqrt{4\pi(D_{\text{screw}}/uL)}} \left[\frac{\exp\left(\frac{(1-\theta)^2}{4\theta(D_{\text{screw}}/uL)}\right)}{4\theta(D_{\text{screw}}/uL)} \right] \quad (S9)$$

$$E(\theta) = \bar{t}E(t) \quad (S10)$$

$$\theta = t/\bar{t} \quad (S11)$$

where θ is the dimensionless time variable, D_{screw} is the longitudinal dispersion coefficient of the micromixer; u is the mean velocity; L is the length of mixer. The D_{screw} was regressed using a MATLAB program. The time distribution functions $E(t)$ from experiment and the calculated results are compared. Typical results are given in Fig. S8, corresponding to 3 different original IDs.

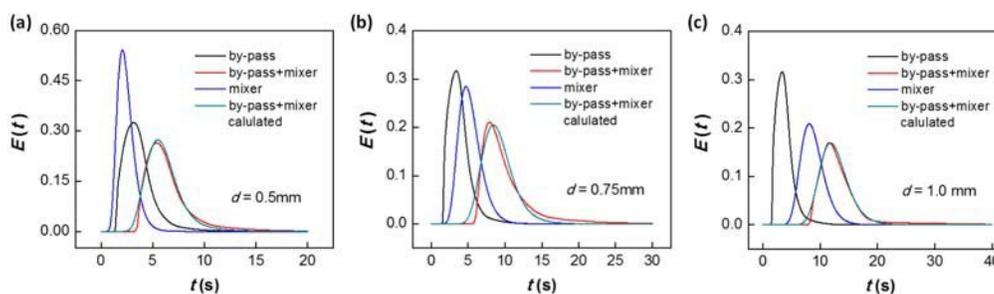


Fig. S8 Comparisons of $E(t)$ from experiments and calculation for three mixers with different original IDs. $Q = 1$ mL/min. The blue lines named mixer are correlated $E(t)$ with Eq. S9 to S11. The green lines named calculated “by-pass+mixer” are from the correlated $E(t)$ and Eq. S8. (a) Original tube ID = 0.5 mm, (b) = 0.75 mm, and (c) = 1.0 mm, labelled with d in the figures.

6. Gold nanoparticle (Au-NP) synthesis experiment

The Au-NPs were prepared from HAuCl_4 and NaBH_4 with tetradecyltrimethylammonium bromide (TTAB) as ligands.¹⁰ The reaction was implemented in the platform shown in Fig. S9. During the reaction, one aqueous solution containing 0.5 mmol/L HAuCl_4 and 10.2 mmol/L TTAB was used as one reactant solution, and a 1.5 mmol/L NaBH_4 aqueous solution was used as the second reactant solution. These solutions were blended through a T-connector, then flowed into the screw-tube mixer as shown in Fig. S9(a) with identical flow rates at 0.4 mL/min. The reaction proceeded in the following PFA tube with a length of 2.4 m and an ID of 1.0 mm. The ID of the T-connector (Idex Health & Science) was 0.5 mm, and the original IDs of screw-tube mixers were 0.5 and 0.75 mm, respectively. The reaction was carried out at 25°C and the solutions were injected by syringe pumps (PHD Ultra 2000, Harvard Apparatus). A control group experiment without mixer was also implemented as shown in Fig. S9(b). All chemicals used for this experiment were purchased from Sigma-Aldrich.



Fig. S9 Schematics of Au-NPs synthesis experimental platform.

In this system, NaBH_4 can also react with H_2O as a competitive side reaction; therefore, the molar ratio between NaBH_4 and HAuCl_4 was higher than the stoichiometric ratio. The NaBH_4 solution was used freshly after preparation. The yields of Au-NPs were characterized UV-Vis spectroscopy (Shimadzu 3101PC).¹¹ The particle sizes are determined from the TEM (JEOL 2010) images with at least 300 particle analyzed.

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