Electronic Supplementary Material (ESI) for Lab on a Chip.

Electronic supplementary information (ESI) for

A Microfluidic Tubing Method and Its Application to Controlled Synthesis of Polymeric Nanoparticles

Jidong Wang,[‡a] Wenwen Chen,[‡a] Jiashu Sun,[*a] Chao Liu,[b] Qifang Yin,[b] Lu Zhang,[a] Yunlei Xianyu,[a] Xinghua Shi,[b] Guoqing Hu,[*b] and Xingyu Jiang[*a]

[a] Beijing Engineering Research Center for BioNanotechnology & Key Lab for Biological Effects of Nanomaterials and Nanosafety, Beijing 100190, China.

E-mail: *xingyujiang@nanoctr.cn; sunjs@nanoctr.cn*

[b] LNM, Institute of Mechanics, Chinese Academy of Sciences, 100190, China.

E-mail: *guoqing.hu@imech.ac.cn*

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‡ These authors contributed equally to this work.

Nanoparticle synthesis

To prepare nanoparticles, PLGA (lactide to glycolide ~ 75:25, Evonik Industries) is first dissolved in dimethylformamide (DMF) and tetrafluoroethylene (TFE, DMF to TFE ~ 1.3) to yield a 2% PLGA solution. We use syringe pumps (PHD Ultra, Harvard Apparatus) to introduce the 2% PLGA solution and two water sheaths into the semicircular microchannel (300 µm × 50 µm cross-section) through the middle inlet and two side inlets (three inlets are identical) (Fig. S4). For high-flow-rate synthesis, the flow rate of PLGA stream ranges from 10 to 38 mL/hr, and that of each water stream is between 186 and 200 mL/hr to maintain a total flow rate of 410 mL/hr. The flow in each inlet channel is precisely controlled by a syringe pump, and the flow rate ratio (FR, the inlet flow rate of two side channels to that of the middle channel) is from 10 to 40. For low-flow-rate synthesis, the flow rate of middle stream increases from 1 to 4 mL/hr, and that of each side stream is 20 mL/hr. The FR ranges from 10 to 40.

Nanoparticle characterization

PLGA nanoparticles were characterized using dynamic light scattering (DLS, Zetasizer 3000HS, Malvern Instruments Ltd.) and transmission electron microscopy (TEM, FEI Tecnai T20). To visualize the mixing inside the semicircular microchannel, we use fluorescein aqueous solution (Sigma-Aldrich) instead of 2% PLGA, and record the images at different flow rates by a Zeiss LSM 710 confocal microscope (Carl Zeiss).

Numerical simulation

Numerical simulation is performed to investigate the mixing process in the semicircular microchannel at both low and high flow rates. The flow field and species transportation is solved by commercial CFD software Fluent 6.4 (Ansys Inc.). Hexahedral grids are generated using Gambit (Fluent 6.4, Ansys Inc.) All walls are set as non-slip boundary conditions. Mass flow boundary condition is applied at the three inlets and outflow condition is applied at the outlet.

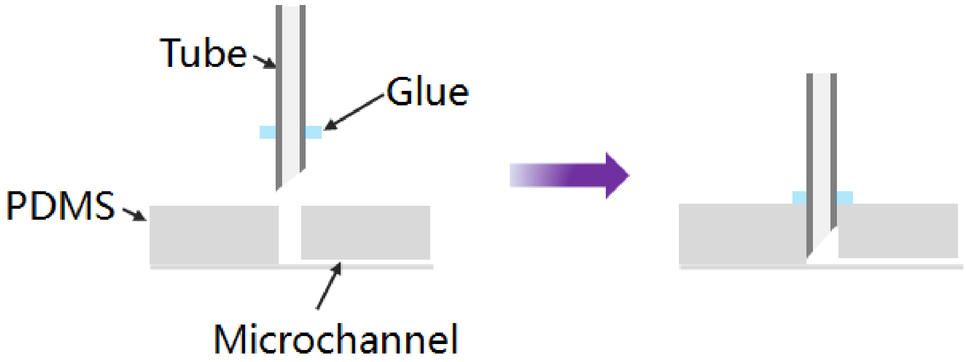

Fig. S1 The illustration of the plastic tube smeared with adhesive before and after inserting into the PDMS port.

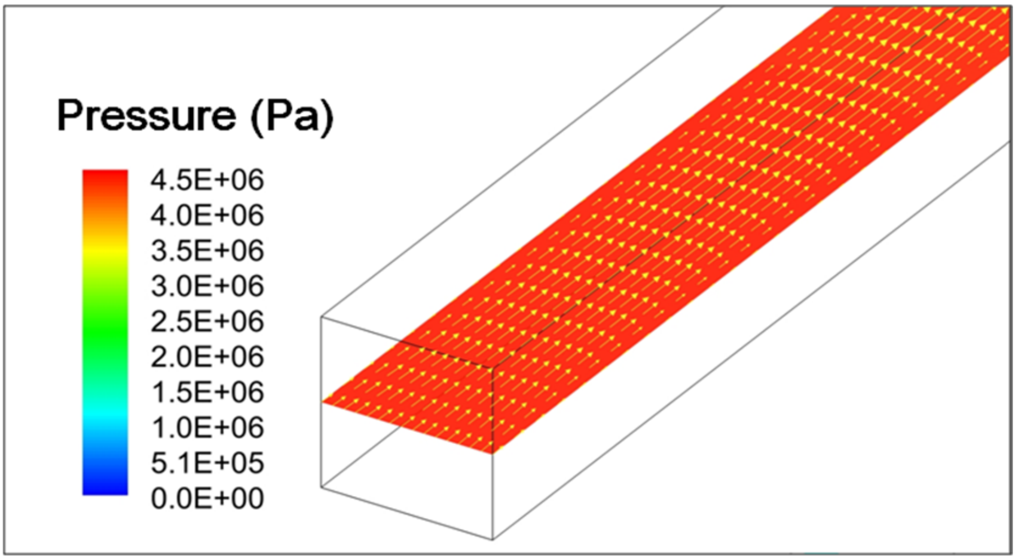

Fig. S2 Simulation result of inlet pressure (4.5 MPa) at 60 mL/hr (Re = 333). The small yellow arrows indicate the flow velocity.

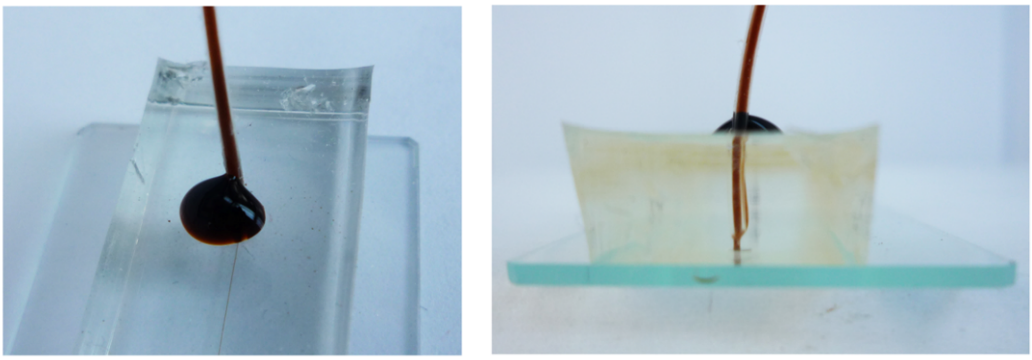

Fig. S3 Photography of the glued tubing interconnection without the second layer of PDMS. The interconnection leaks colored water from the gap between plastic tube and the PDMS port at 10 mL/hr. The microfluidic channel is 50 μm wide × 50 μm high × 6 cm long.

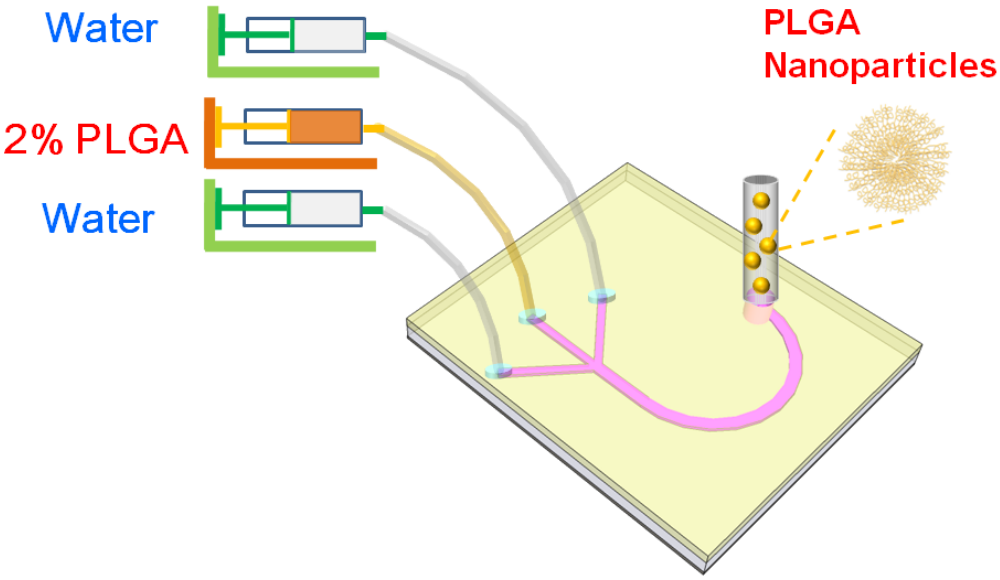

Fig. S4 Illustration of the experimental set-up for precipitating PLGA nanoparticles in the semicircular microchannel (300 µm × 50 µm cross-section).

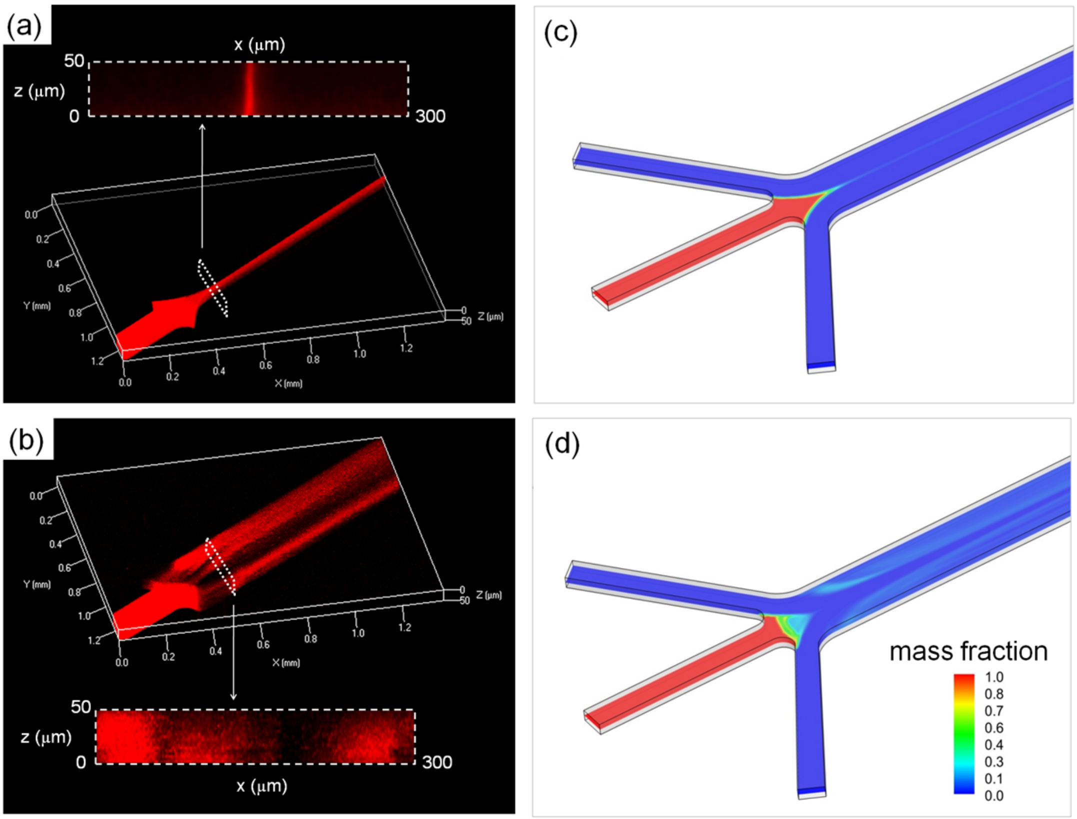

Fig. S5 3D Confocal fluorescent microscopic image of mixing. (a) diffusion mixing at a total flow rate of 41 mL/hr (middle fluorescein solution: 1 mL/hr, each side water: 20 mL/hr), and FR of 40. (b) convective mixing at 410 mL/hr (middle fluorescein solution: 10 mL/hr, each side water: 200 mL/hr), and FR of 40. (c) and (d) are simulating prediction of mixing at (a) and (b).

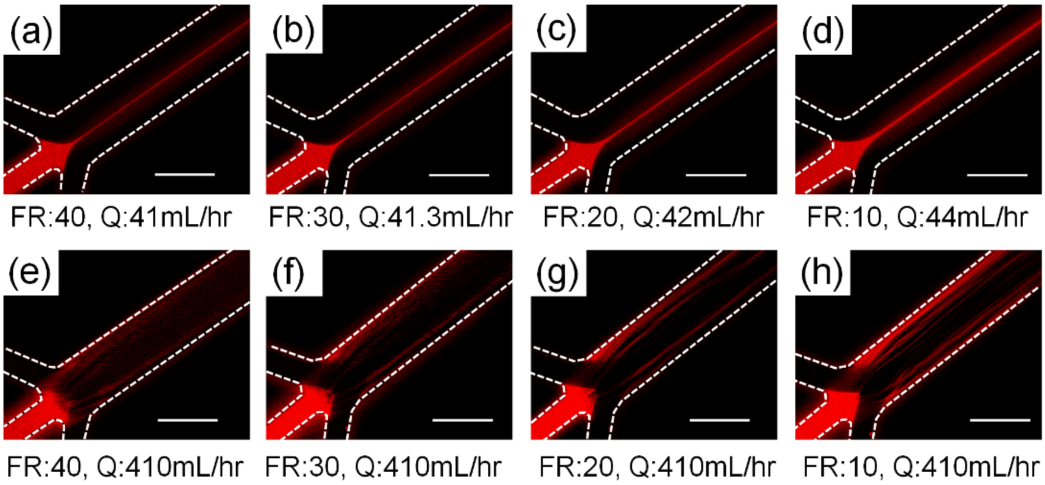

Fig. S6 Confocal fluorescent microscopic images of mixing at low and high flow rates with different FRs. (a) middle channel: 1 mL/hr, each side channel: 20 mL/hr, and FR: 40. (b) middle channel: 1.33 mL/hr, each side channel: 20 mL/hr, and FR: 30. (c) middle channel: 2 mL/hr, each side channel: 20 mL/hr, and FR: 20. (d) middle channel: 4 mL/hr, each side channel: 20 mL/hr, and FR: 10. (e) middle channel: 10 mL/hr, each side channel: 200 mL/hr, and FR: 40. (f) middle channel: 13 mL/hr, each side channel: 198.5 mL/hr, and FR: 30. (g) middle channel: 20 mL/hr, each side channel: 195 mL/hr, and FR: 20. (h) middle channel: 38 mL/hr, each side channel: 186 mL/hr, and FR: 10. The scale bar is 300 μm.

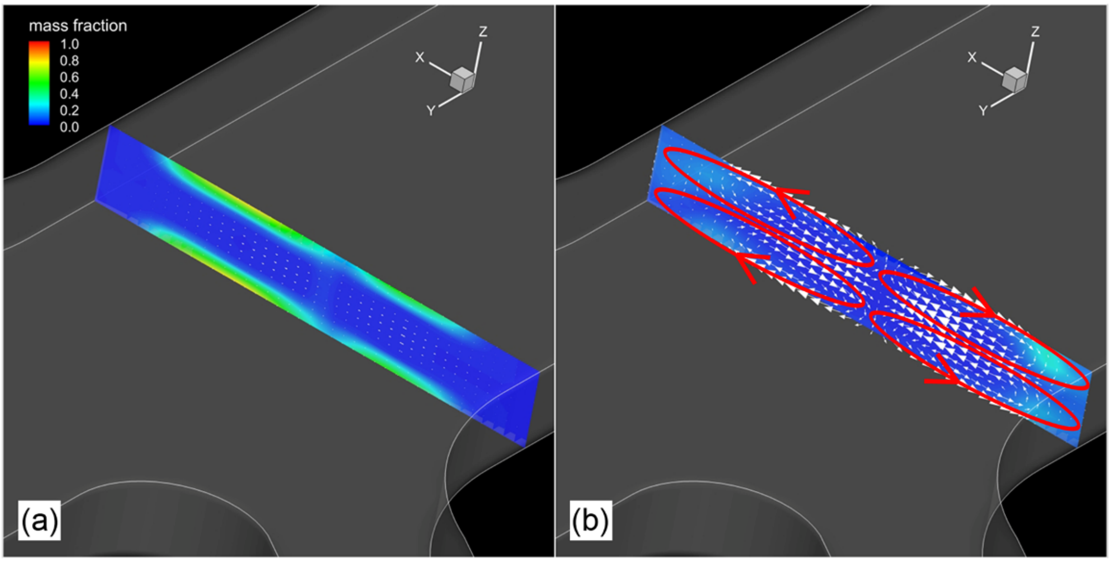

Fig. S7 Simulating prediction of mixing at the channel inlet with FR of 40. (a) middle channel: 1 mL/hr, each side channel: 20 mL/hr. (b) middle channel: 10 mL/hr, each side channel: 200 mL/hr. white arrows represent the velocity vector projected onto the cross-section. Four vortices are highlighted by ellipses in red.