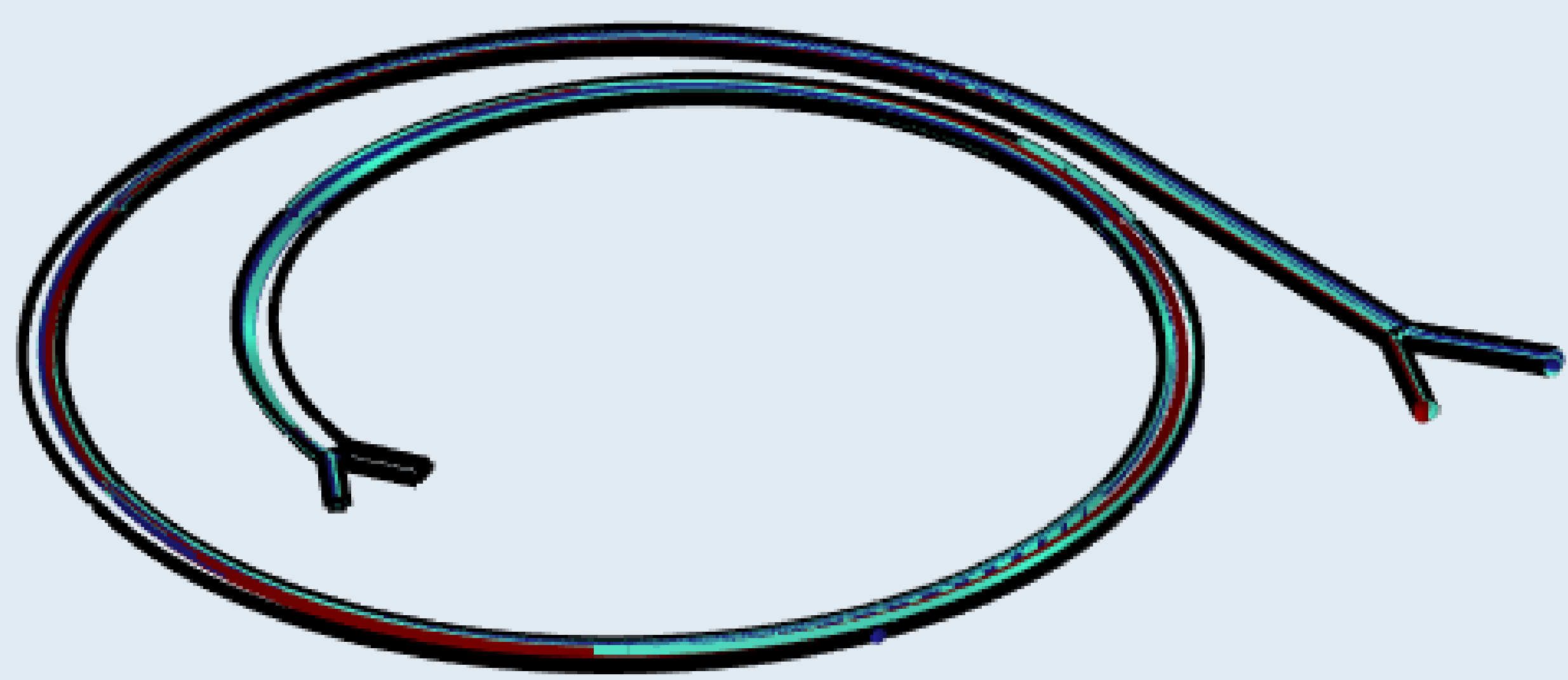




High-Throughput Submicron Particle Separation With Cascaded Spiral Microfluidics

Inertial microfluidics offers much higher flow rates and high throughput, though a single-stage device struggles to separate submicron particles. Two spiral devices in series extend the working range into the submicron.

F. Demann, B. Choudhury, L. Batarilo, F. M. Guerra, O. Hayden, S. Pandey
Heinz Nixdorf Chair of Biomedical Electronics, School of Computation, Information and Technology, Technical University of Munich, TranslaTUM, Munich, Germany

Abstract

Extracellular vesicles serve as promising biomarkers and therapeutic carriers; however, no isolation protocol currently achieves both high recovery rates and high specificity. Inertial microfluidics offers significantly higher throughput than alternative methods, although the focusing capability diminishes for particles smaller than approximately 1 μm . In this study, we introduce a cascaded spiral platform comprising two serially arranged devices designed to resolve a broader size range than a single device could achieve independently. Both stages were modeled using COMSOL Multiphysics®, where the velocity field within the spiral microchannel was calculated assuming

stationary laminar flow, followed by a time-dependent simulation tracing particles ranging from 10 μm to 100 nm. The first stage, featuring a cross-sectional area of $250 \times 50 \mu\text{m}$, effectively removes 10 μm particles, whereas the second stage, with an 8 μm height, separates 1 μm particles from 100 nm particles. The initial stage was fabricated accordingly, and experimental validation using fluorescent polystyrene beads confirmed the predicted separation: 10 μm polystyrene beads exited through the inner outlet, and 1 μm polystyrene beads through the outer outlet.

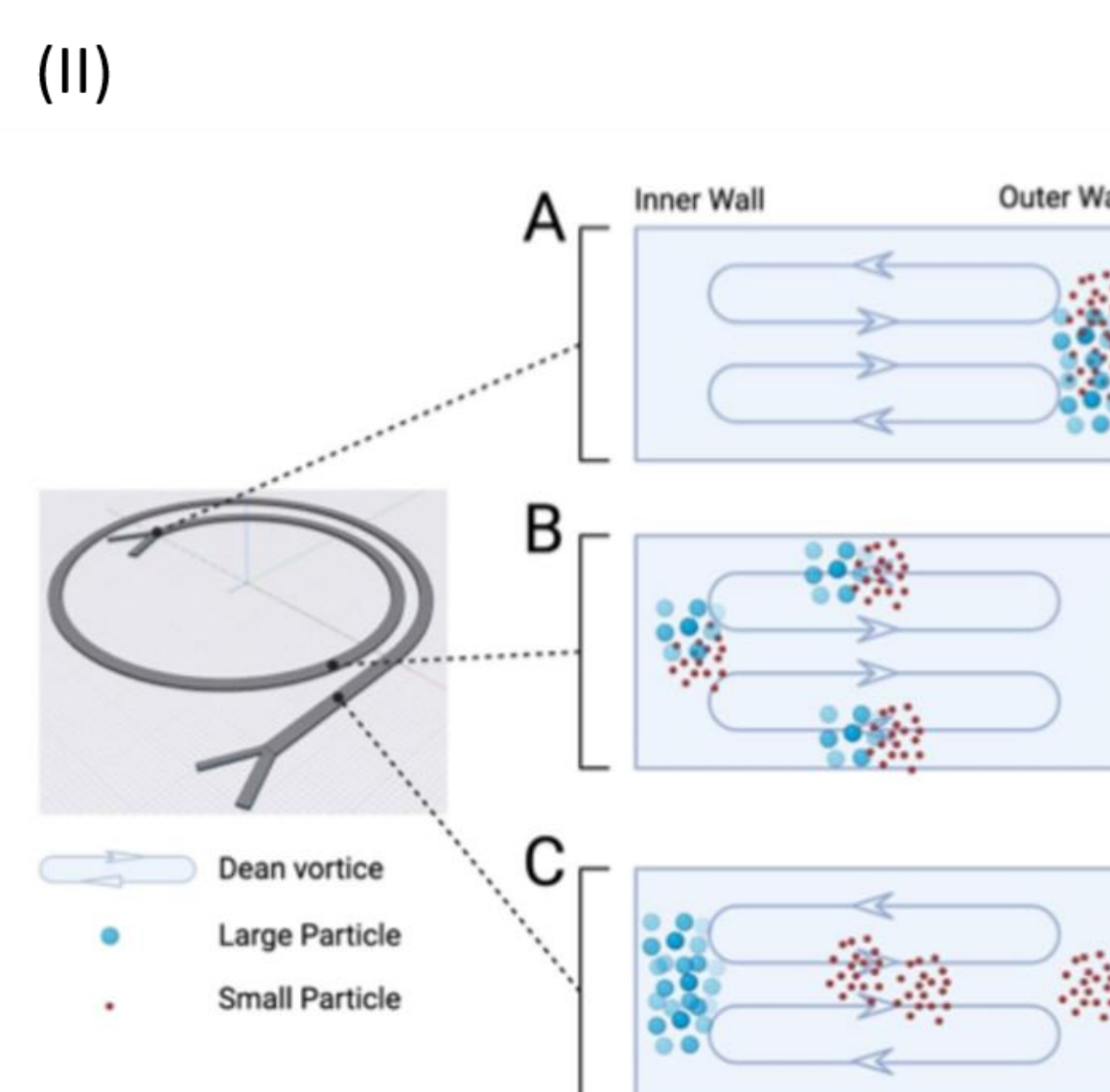
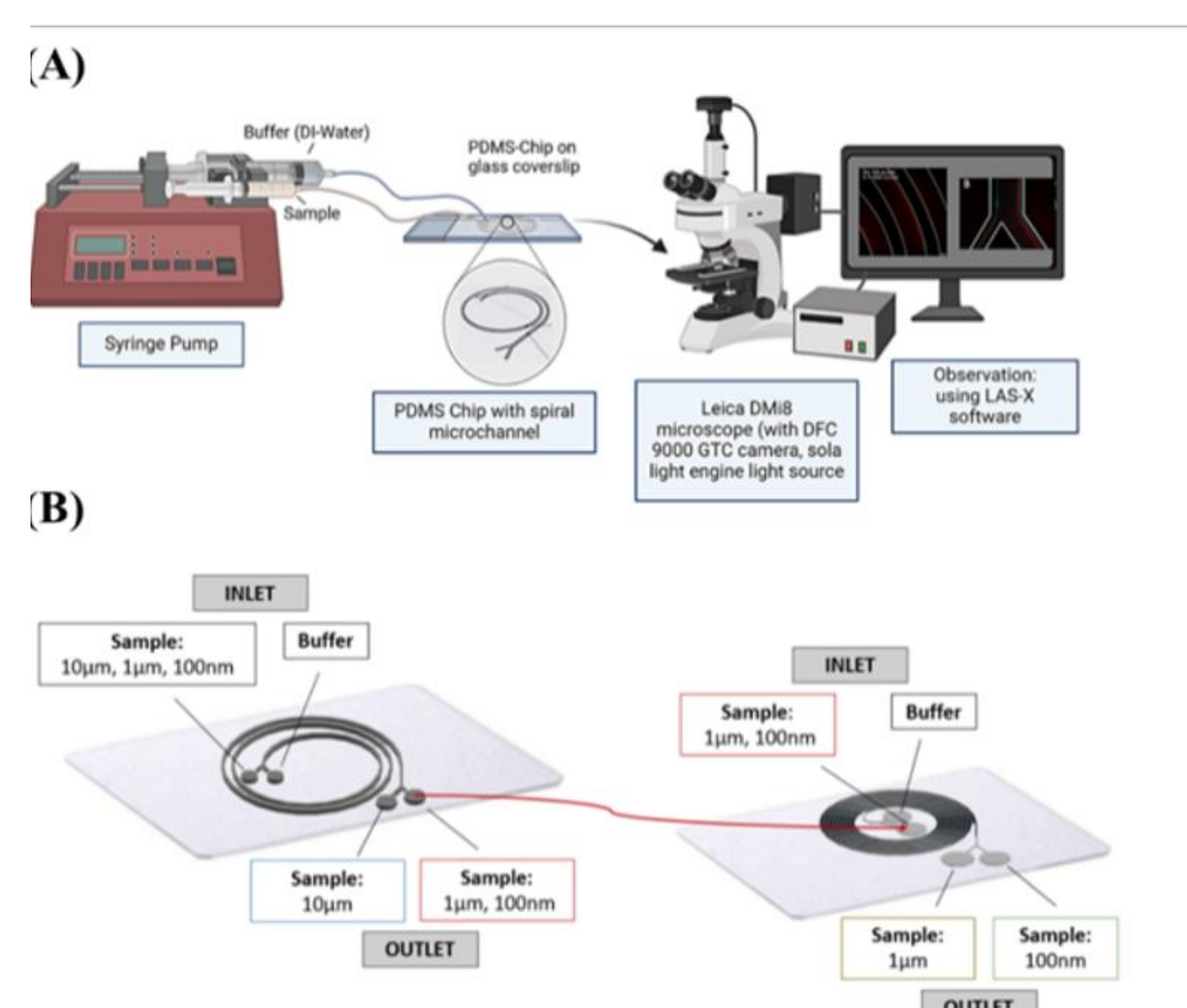


FIGURE 1. (I) Particle positions across the channel cross-section at three points along a spiral, marked on the device at left. In each panel the inner wall is at the left and the outer wall at the right. Blue circles denote large particles, dark red dots small particles, and the looped arrows the counter-rotating Dean vortices. (A) At the inlet. (B) Partway along the spiral. (C) At the outlet. [Created with BioRender.com]. (II) Dean flow and particle migration. Sketched particle positions in the channel cross-section, inner wall at left. (A) Inlet. (B) Partway along the spiral. (C) Outlet.

Results

The first stage separates 10 μm particles from everything smaller. Simulations set the cross-section at $250 \times 50 \mu\text{m}$, and a fabricated device reproduced the separation with 10 μm and 1 μm fluorescent beads. The second stage resolves 1 μm particles from 100 nm ones, which requires a channel about 8 μm high. Figure 2 follows that separation: Particles enter together at the inner wall, and by the end of the spiral they have formed two distinct streams, 1 μm at the inner wall and 100 nm at the outer. Simulations of both stages support the cascaded spiral as a route to submicron separation.

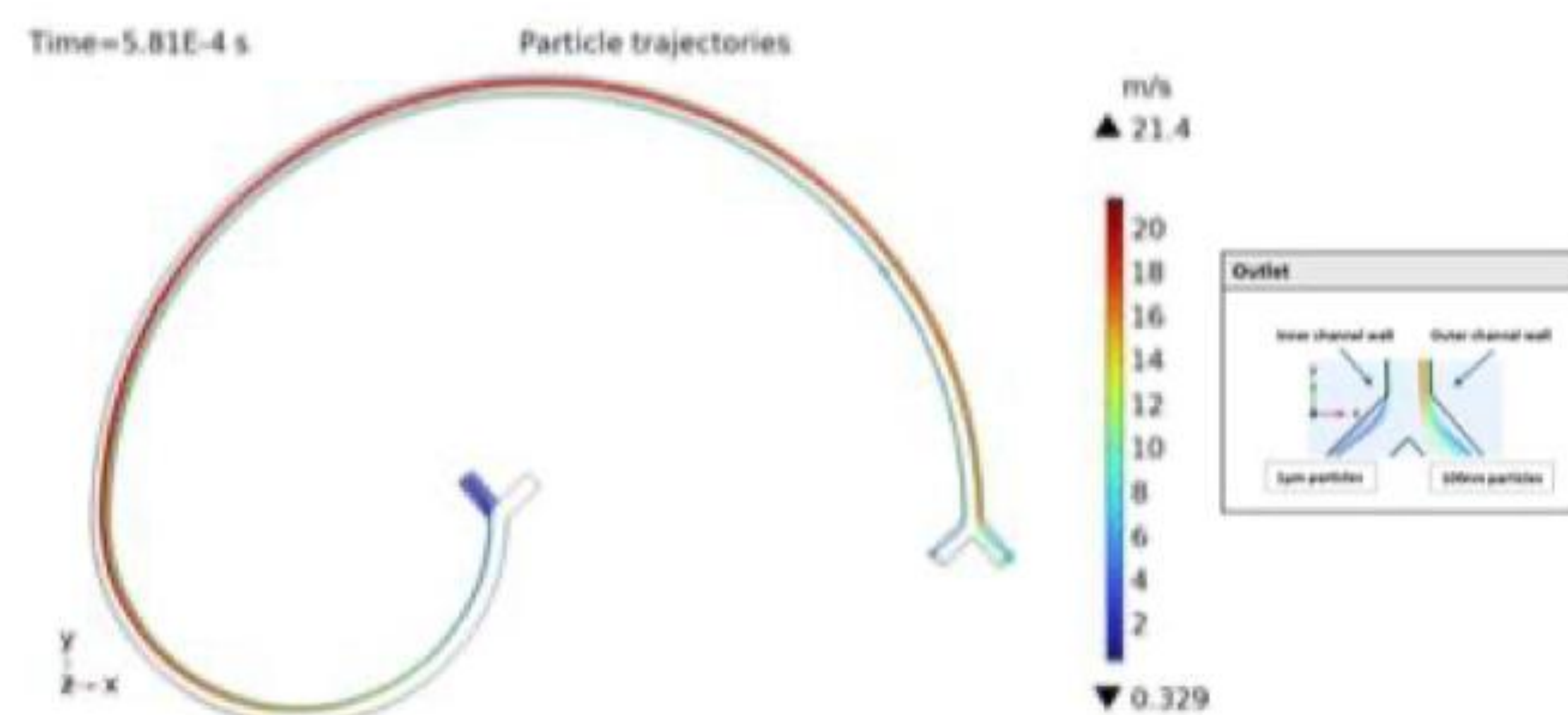


FIGURE 2. Simulated trajectories in a $30 \times 8 \mu\text{m}$ second-stage channel, colored by flow velocity. The inset enlarges the outlet, where 1 μm and 100 nm particles separate.

REFERENCES

1. C. Théry et al., "Minimal information for studies of extracellular vesicles 2018 (MISEV2018)", J Extracell Vesicles, vol. 7, art. no. 1535750, 2018.
2. S. Hassanpour Tamrin et al., "Label-free isolation of exosomes using microfluidic technologies", ACS Nano, vol. 15, pp. 17047–17079, 2021.
3. D. Di Carlo et al., "Continuous inertial focusing, ordering, and separation of particles in microchannels", PNAS, vol. 104, pp. 18892–18897, 2007.

