Electronic Supplementary Material (ESI) for Nanoscale.

Supplementary information

Viscoelastic microfluidics for enhanced separation resolution of submicron particles and extracellular vesicles

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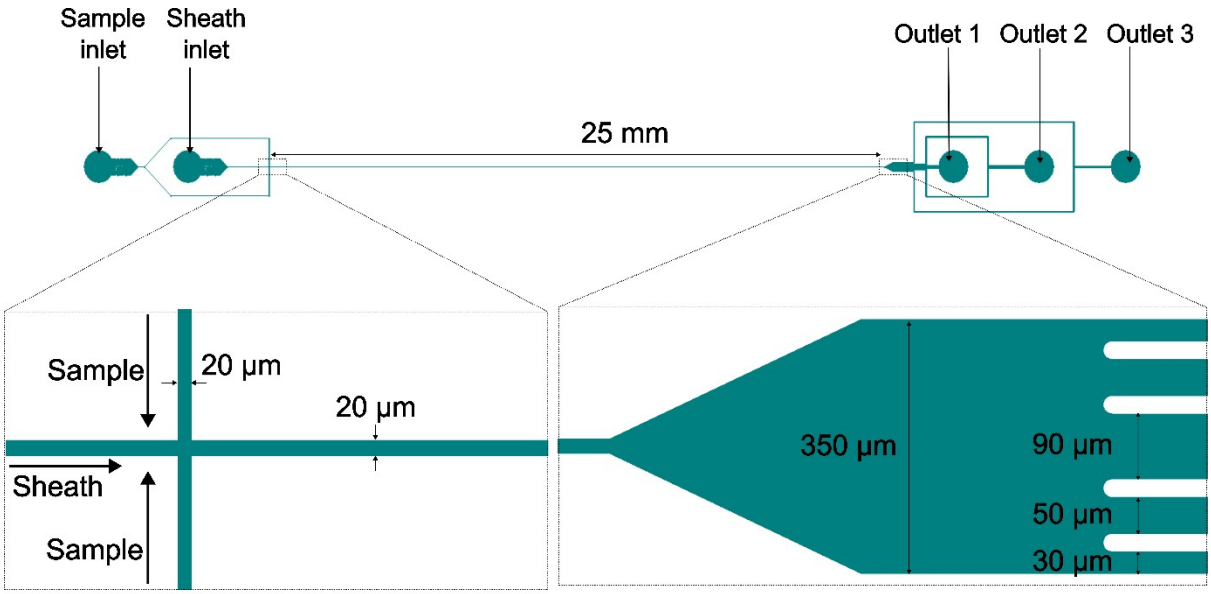

Fig. S1. CAD design of the co-flow microfluidic device.

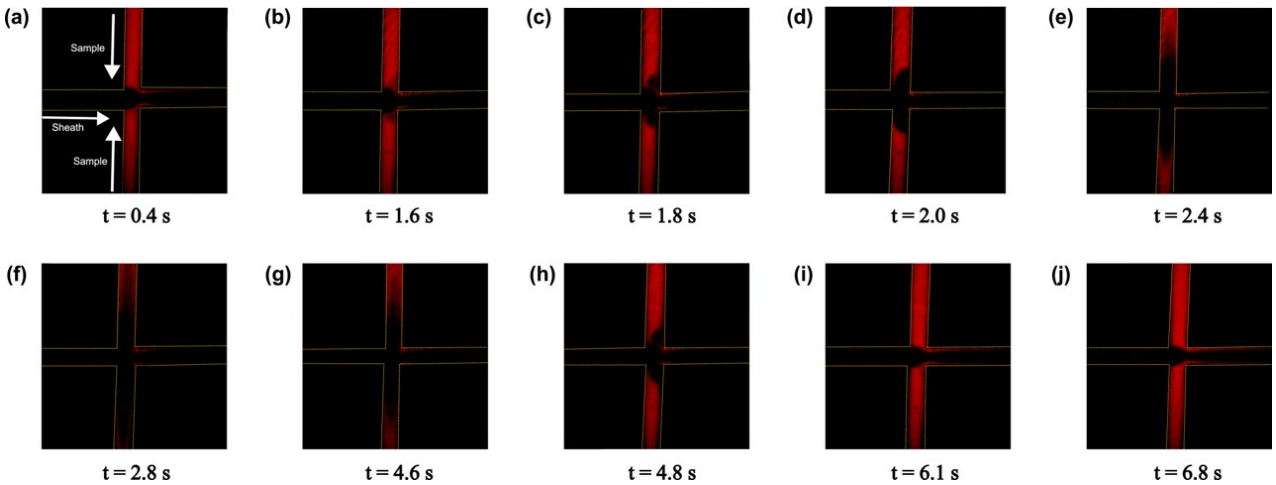

Fig S2. Time-lapse images of the flow oscillation in 5,000 ppm PEO concentration for 100 nm particles (pseudo-coloured red) at the cross junction of the microfluidic device. (a) The particles from the side channels flow into the main straight channel at t = 0.4 s. (b)-(e) Gradually sheath flow from the middle becomes dominant and pushes the particle flow towards the inlet from t = 1.6 s to t = 2.4 s. (f) Particles are completely pushed beyond the boundary of the microscopic focusing area at t = 2.8 s. (g)-(i) Sample flow overcomes the resistance of the sheath flow and gradually flows towards the straight section of the microfluidic device through the coss junction from t = 4.6 s to t = 6 s. (j) The particles from the side channels flow into the main straight channel as usual at t = 6.8 s.

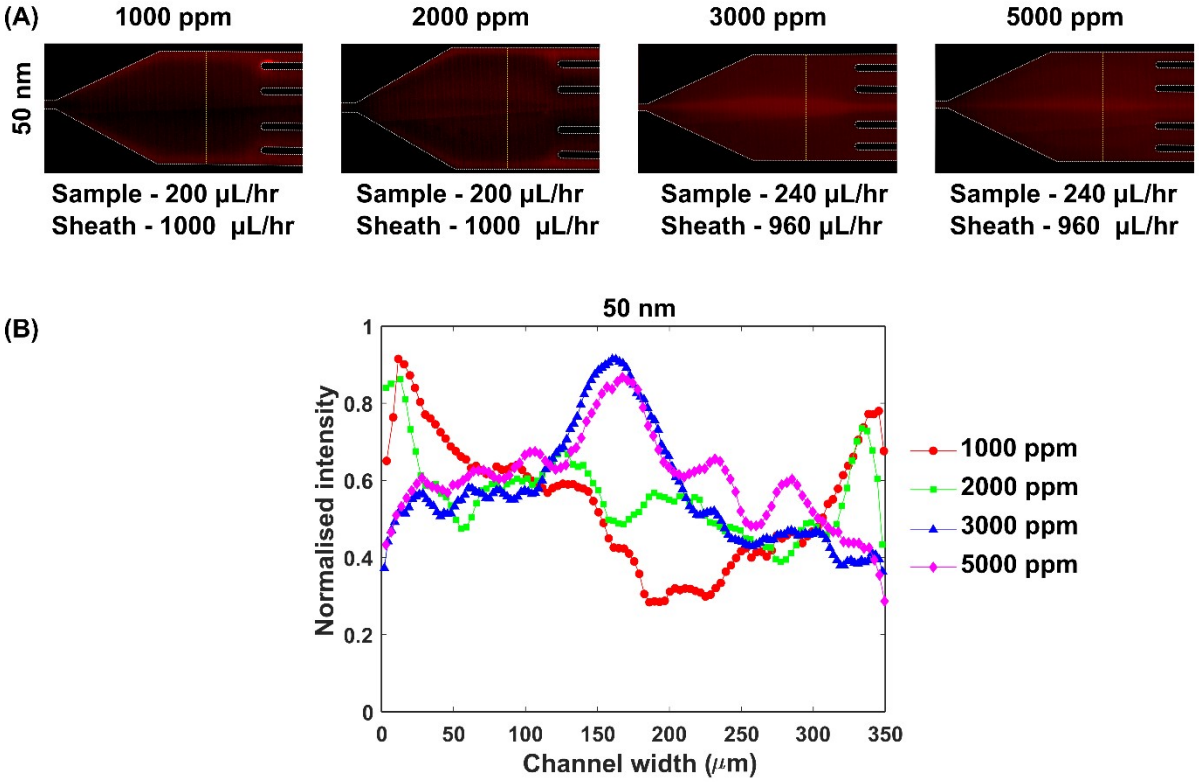

Fig. S3(A) Fluorescent trajectories of 50-nm (pseudo-coloured red) polystyrene particles at the expansion region of the co-flow microfluidic device under different PEO concentrations. When increasing the PEO concentration to 3,000 ppm or above, we observed 50-nm particles migrated from the channel side walls toward the channel centre. Due to the flow oscillations at PEO concentrations of 3,000 ppm and 5,000 ppm, we used a flow rate ratio of 4:1 for those PEO concentrations to ensure the flow is stable. (B) Normalised fluorescence intensity of particle distribution across the yellow dotted line.

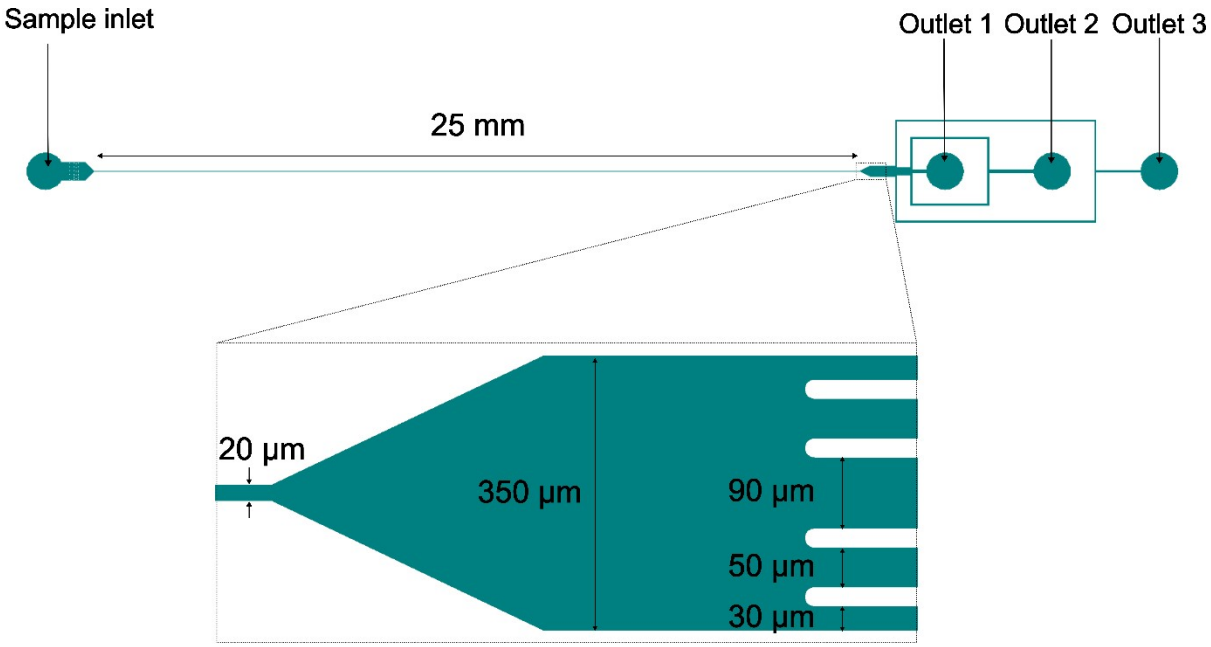

Fig. S4. CAD design of the sheathless microfluidic device used for high concentration PEO concentration experiments to investigate the focusing of nanoparticles.

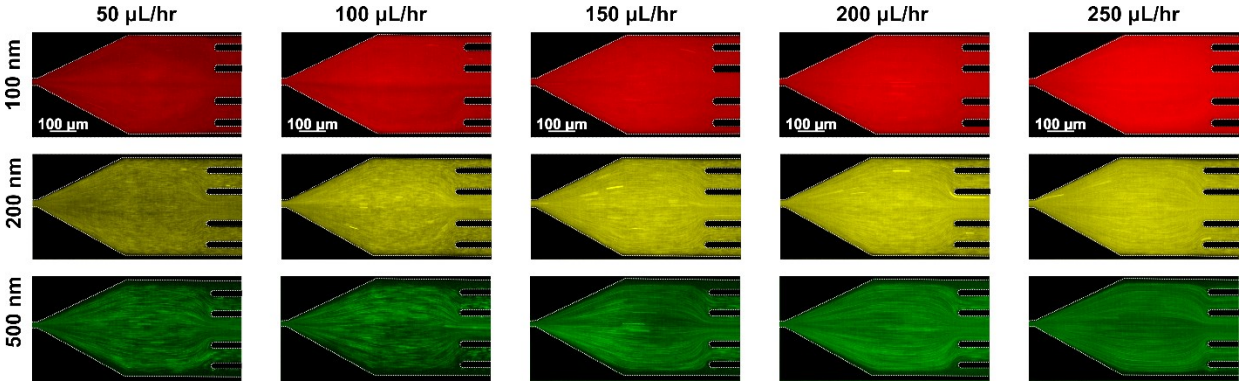

Fig. S5. Fluorescent trajectories of 100-nm (pseudo-coloured red), 200-nm (pseudo-coloured yellow) and 500-nm (pseudo-coloured green) polystyrene particles at the expansion region of the sheathless microfluidic device for 5,000 ppm PEO aqueous solution.

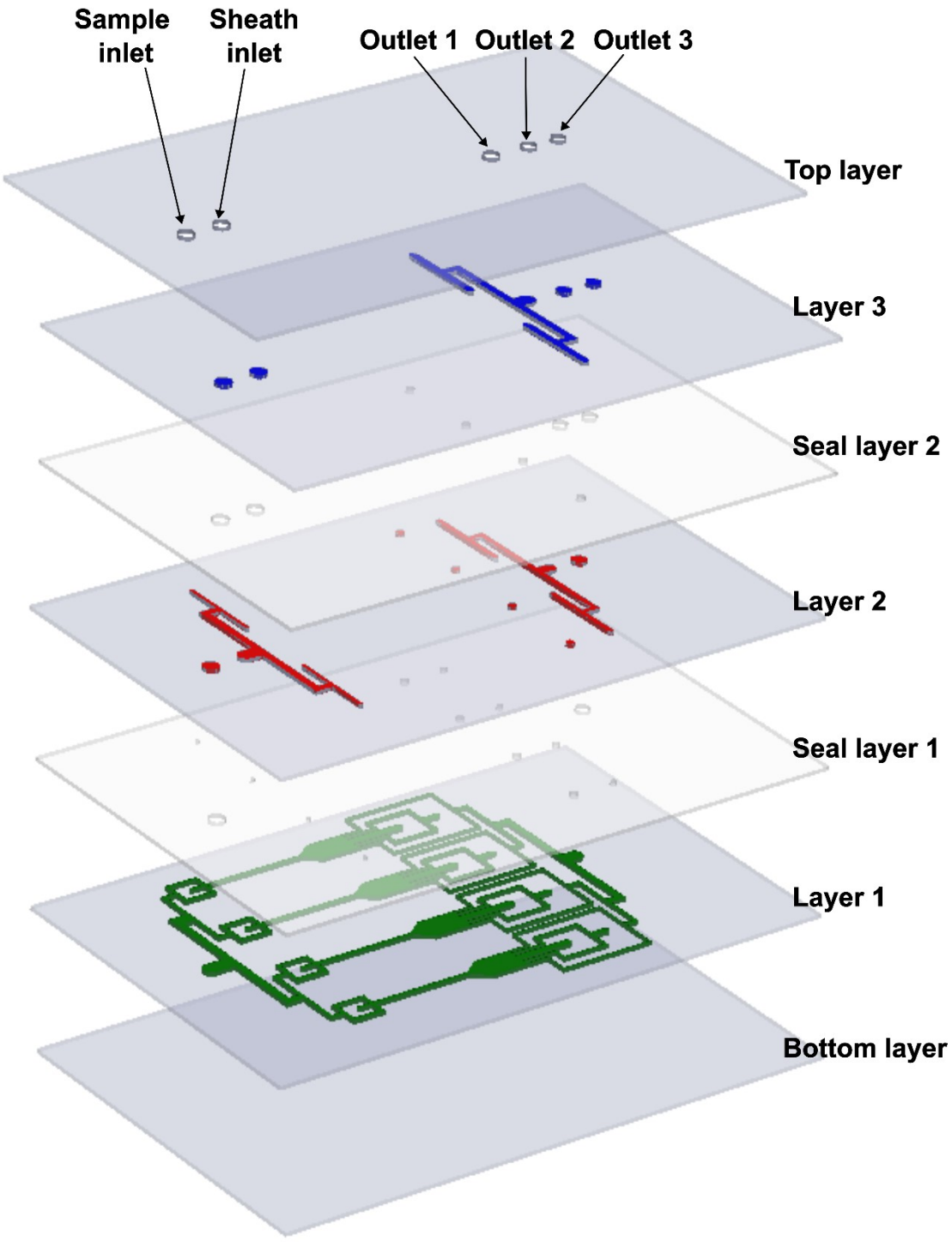

Fig. S6. Design of a parallelised microfluidic device with straight channels to enhance the throughput.

Table S1 Summary of submicron and nanoparticle separation techniques

Separation mechanism	Particle sizes	Separation resolution	Biological particles	Separation purity	Separation efficiency	Throughput	References
Ultracentrifugation	50–200 nm	100-150 nm	Exosomes, EVs	N/A	23% - 70%	53 μL/min	[1–3]
Ultrafiltration	50-250 nm	150 nm	Exosomes, natural organic matters	91.5%	70% - 82%	16 mL/min	[4–6]
Size exclusion chromatography	50–200 nm	120-150 nm	Exosomes	N/A	80%-90%	0.5 mL/min	[7–9]
Acoustophoresis	100–900 nm	230 nm	EVs	98%	> 90%	4–80 μL/min	[10]
Electrophoresis	100-1,000 nm	400 nm	Exosomes	N/A	65% - 98%	1 μL/min	[11]
Magnetophoresis	5 nm-200 nm	800 nm	EVs	80%	80% - 90%	2.5 μL/min	[12]
Inertial microfluidics	200 nm–2 μm	800 nm	EVs	N/A	15% - 97%	80 μL/min	[13,14]
Deterministic lateral displacement	51 nm-1.5 μm	150 nm	EVs	98%	39%	0.05 μL/min	[15,16]
Microfluidic filtration	30–200 nm	150 nm	Exosomes	N/A	74%	40 μL/min	[17]
Pinched flow fractionation	30 nm–2 μm	400 nm	EVs	N/A	70% - 90%	20 μL/min	[18]
Viscoelastic microfluidics	100 nm– 2 μm	400 nm	Exosomes, EVs	96%	93%	3 μL/min	[19,20]
Viscoelastic microfluidics	**100–500 nm**	**100 nm**	**EVs**	**40% - 90 %**	**50% - 86%**	**3 μL/min**	**This study**

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