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


# Supporting Information (SI) for: Exosome trapping and enrichment using a Sound Wave Activated Nano-Sieve (SWANS)†

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**Table S1:** *Basic parameters of all FEM models that were simulated in this work based on Ref. 1 methodology. Material data were obtained from COMSOL material library otherwise stated.*

| Parameter | Symbol | Unit | Value |
|---|---|---|---|
| **Fluid Domain** | | | |
| **Water** | | | |
| Density | $\rho_f$ | kg m$^{-3}$ | 1000 |
| Speed of sound | $c_f$ | m s$^{-1}$ | 1500 |
| | | | |
| Domain height | L | µm | 100 |
| Domain width | W | µm | 50 |
| | | | |
| Frequency | $f$ | MHz | see Table 2 |
| Wavelength | $\lambda$ | µm | $c_f/f$ |
| Wavenumber | k | µm | $2\pi/\lambda$ |
| Acoustic pressure amp. | $P_0$ | kPa | 100 |
| Max. mesh size | $e_f$ | nm | 400-600 |
| Curvature factor | | - | 0.15 |
| Max. mesh growth rate | | - | 1.05 |
| | | | |
| **Solid Domain (NP)** | | | |
| **Material** | | | Polystyrene |
| Density[2] | $\rho_{ps}$ | kg m$^{-3}$ | 1050 |
| Modulus of elasticity[a] | $E_{ps}$ | GPa | 3.60 |
| Poisson ratio[3] | $\nu_{ps}$ | - | 0.35 |
| | | | |
| Domain dimensions: | | | |
| Nanoparticle diameter | $d_{NP}$ | µm | 0.5 |
| Max. mesh size range | $e_s$ | nm | 60∼100 |
| Curvature factor | | - | 0.15 |
| Max. mesh growth rate | | - | 1.05 |
| | | | |
| **Fluid-Solid interface** | | | |
| Mesh size range | $e_1$ | nm | 7∼20 |
| Curvature factor | | - | 0.15 |
| Max. mesh growth rate | | - | 1.05 |

[a] Calculated from Bulk Modulus ($K_{ps}$) as $E_{ps} = 3K_{ps}(1 - 2\nu_{ps})$ from ref. 3 and 4.

**Table S2:** *Specific parameters of each FEM model that were simulated in this work to study the effect of size or material of microparticles (MPs) in the packed bed. Material data are obtained from COMSOL material library otherwise stated.*

| Parameter | Symbol | Unit | **7-PS** | **10-PS** | **15-PS** | **10-PMMA** | **10-SG** |
|---|---|---|---|---|---|---|---|
| **Fluid Domain** | | | | | | | |
| **Water** | | | | | | | |
| Frequency | $f$ | MHz | 20 - 215 | 15 - 150 | 10 - 100 | 15 - 150 | 15 - 150 |
| **Solid Domain (MP)** | | | | | | | |
| **Material** | | | PS | PS | PS | PMMA | Silia Glass |
| Microparticle diameter | $D_{MP}$ | μm | 7 | 10 | 15 | 10 | 10 |
| Density | $\rho_{ps}$ | kg m$^{-3}$ | 1050[2] | 1050[2] | 1050[2] | 1190 | 2203 |
| Modulus of elasticity | $E_{ps}$ | GPa | 3.60[a] | 3.60[a] | 3.60[a] | 3.0 | 73.1 |
| Poisson ratio | $\nu_{ps}$ | - | 0.35[3] | 0.35[3] | 0.35[3] | 0.4 | 0.17 |
| **Fluid-Solid interface** | | | | | | | |
| Gap between MP and NP | Gap | nm | 300 | 500 | 900 | 500 | 500 |

[a] Calculated from Bulk Modulus ($K_{ps}$) as $E_{ps} = 3K_{ps}(1 - 2\nu_{ps})$ from ref. 3 and 4.

## References


[1] R. Habibi, C. Devendran and A. Neild, *Lab Chip*, 2017, **17**, 3279–3290.

[2] P. B. Muller, R. Barnkob, M. J. H. Jensen and H. Bruus, *Lab Chip*, 2012, **12**, 4617–4627.

[3] P. Mott, J. Dorgan and C. Roland, *Journal of Sound and Vibration*, 2008, **312**, 572 – 575.

[4] R. Kono, *Journal of the Physical Society of Japan*, 1960, **15**, 718–725.

[5] R. Habibi and A. Neild, *Lab Chip*, 2019, **19**, 3032–3044.

**Table S3:** *Summary of peak frequencies and their corresponding attraction Force on the 500 nm nanoparticle for each simulated pair of nanoparticle and microparticle.*

| **PS 7 μm** | $f_1^*$ | $\mathbf{F}_{att}$ (fN) | $f_2^*$ | $\mathbf{F}_{att}$ (fN) | $f_3^*$ | $\mathbf{F}_{att}$ (fN) |
|---|---|---|---|---|---|---|
| SW | 94 | 13.71 | 123 | 18.01 | 174 | 19.31 |
| TW + | 80 | 31.87 | 132 | 136.78 | - | - |
| TW – | 84 | 36.24 | 134 | 23.11 | - | - |

| **PS 10 μm** | $f_1^*$ | $\mathbf{F}_{att}$ (fN) | $f_2^*$ | $\mathbf{F}_{att}$ (fN) | $f_3^*$ | $\mathbf{F}_{att}$ (fN) |
|---|---|---|---|---|---|---|
| SW | 66 | 26.03 | 87 | 35.29 | 122 | 39.09 |
| TW + | 55 | 18.27 | 95 | 28.07 | - | - |
| TW – | 56 | 19.18 | - | - | - | - |

| **PS 15 μm** | $f_1^*$ | $\mathbf{F}_{att}$ (fN) | $f_2^*$ | $\mathbf{F}_{att}$ (fN) | $f_3^*$ | $\mathbf{F}_{att}$ (fN) |
|---|---|---|---|---|---|---|
| SW | 44 | 52.38 | 58 | 75.27 | 81 | 86.43 |
| TW + | 36 | 10.66 | 63 | 14.05 | - | - |
| TW – | 36 | 10.29 | - | - | - | - |

| **PMMA 10 μm** | $f_1^*$ | $\mathbf{F}_{att}$ (fN) | $f_2^*$ | $\mathbf{F}_{att}$ (fN) | $f_3^*$ | $\mathbf{F}_{att}$ (fN) |
|---|---|---|---|---|---|---|
| SW | 60 | 43.74 | 85 | 47.23 | 115 | 39.92 |
| TW + | 53 | 20.86 | 85 | 26.68 | 113 | 40.53 |
| TW – | 56 | 19.18 | - | - | - | - |

| **SG 10 μm** | $f_1^*$ | $\mathbf{F}_{att}$ (fN) | $f_2^*$ | $\mathbf{F}_{att}$ (fN) | $f_3^*$ | $\mathbf{F}_{att}$ (fN) |
|---|---|---|---|---|---|---|
| SW | 69 | 9.87 | - | - | - | - |
| TW + | 73 | 7.66 | - | - | - | - |
| TW – | 69 | 8.28 | 97 | 33.11 | - | - |

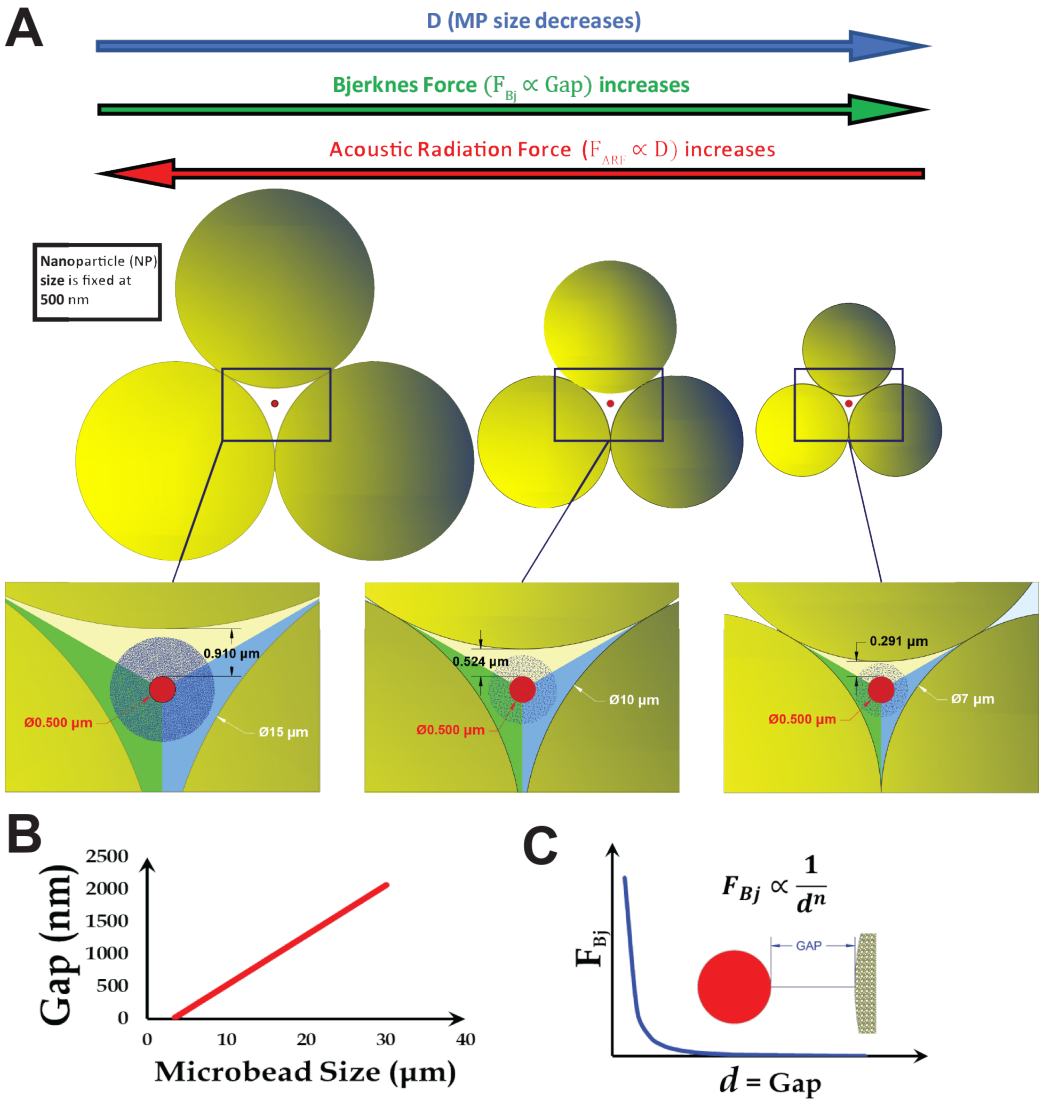


**Fig. S1:** *(A) Interplay between the size of the microbeads in the packed bed and the attraction force (secondary Bjerknes force) induced on nanoparticles: By increasing the MP size, the gap between the beads and the nanoparticle decreases (linearly as shown in (B) so enhances the Bjerknes force between the MP and NP as the Bjerknes force scales to the inverse of gap squared or even higher powers(C). On the other hand, although increasing the size of the beads increases the gap, but with the same acoustically normalised size (d/λ), larger particle generates higher amplitude scattering so higher radiation forces (both primary and secondary). At a fixed gap distance, larger particle normally generates higher attraction forces.*

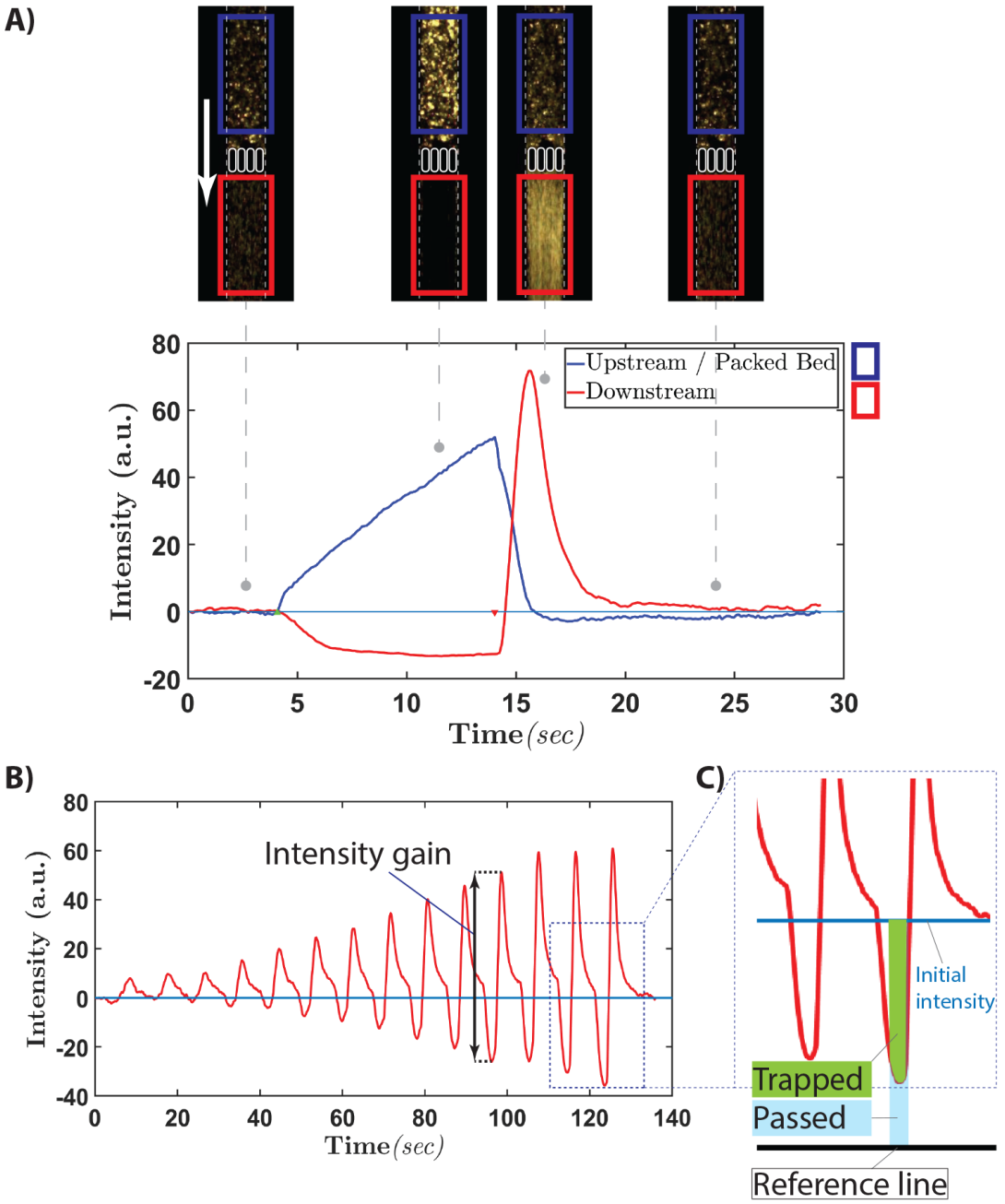


**Fig. S2:** *(A) Measuring the fluorescent intensity level indicates successful trapping of particles in the packed bed and also capturing efficiency when measured at the downstream of the pillars. Here, intensity change is demonstrated when the packed bed is excited at one fixed frequency. Captions are reproduced from Fig. 1B. The intensity level is set to zero at initial level (before SAW activation). (B) A typical frequency response of fluorescent intensity level change as an indication of nanoparticle collection/release, measured here at the packed bed downstream; Measurement of the intensity is calculated at different locations (upstream or downstream) to find the mean value of intensity gain at each frequency. The intensity gain at each frequency is then normalised versus highest and lowest values. Similarly, intensity measurement and normalisation is discussed in more detail in Ref. 5. (C) The efficiency of nanoparticle capturing is measured by investigating the change of the intensity at the downstream while ultrasound is activated (SAW is on). If all particles are trapped at the upstream the intensity level drops to the lowest level (indicated as reference line). So the efficiency is calculated as the ratio of the trapped particles to the total (sum of trapped and passed particles).*

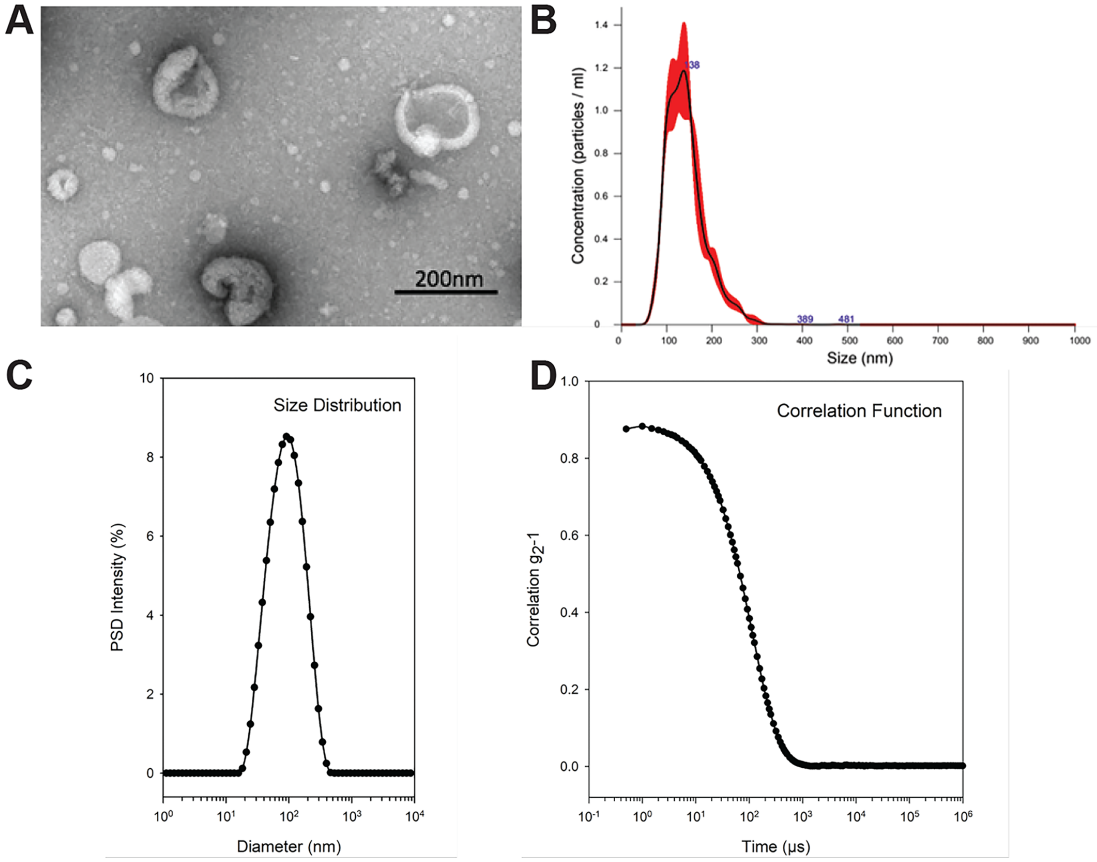


**Fig. S3:** *A) TEM image of the original exosome sample: the EVs used for this project are of typical exosome shape, bearing a distinct cup-shaped morphology. B) The particle concentration of the EV sample was* $4.5 \times 10^{10}$ *per mL. The particle size distribution was D10 67 nm, D50 109 nm and D90 300.5 nm with mean size of 167.3 nm. C) and D) Dynamic light scattering (DLS) results of liposome size distribution. The mean diameter of liposomes measured at 75.75 nm (peak at 107 nm) with PDI of 0.25 and mean count rate of 325.2.*

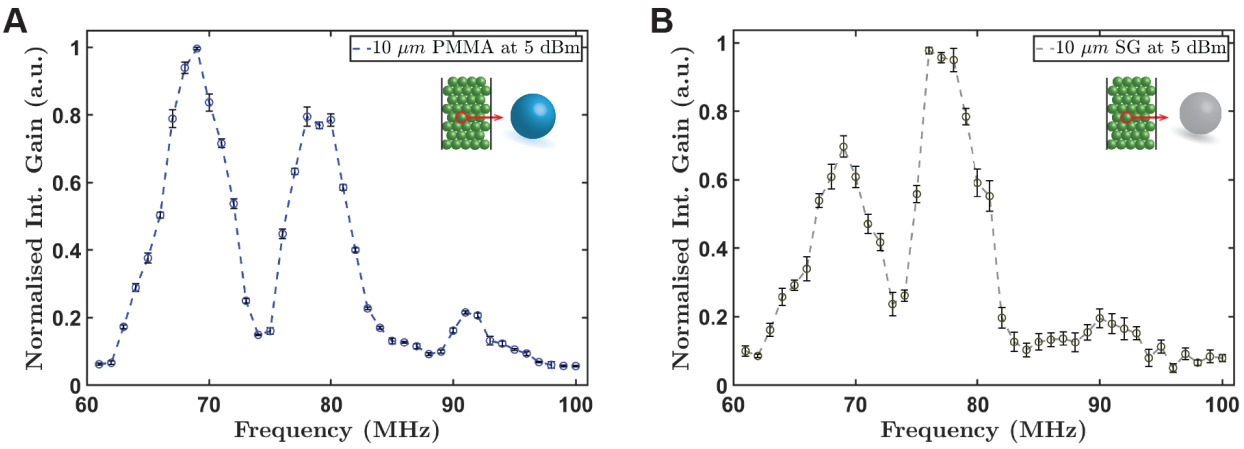


**Fig. S4:** *Experimental results for intensity change (as an indication of fluorescent 500 nm NPs collection) for packed bed made of (A) 10 μm PMMA that shows two major peaks at frequencies around 70 MHz and 80 MHz and (B) 10 μm SG with two major peaks around 70 and 79 MHz.*

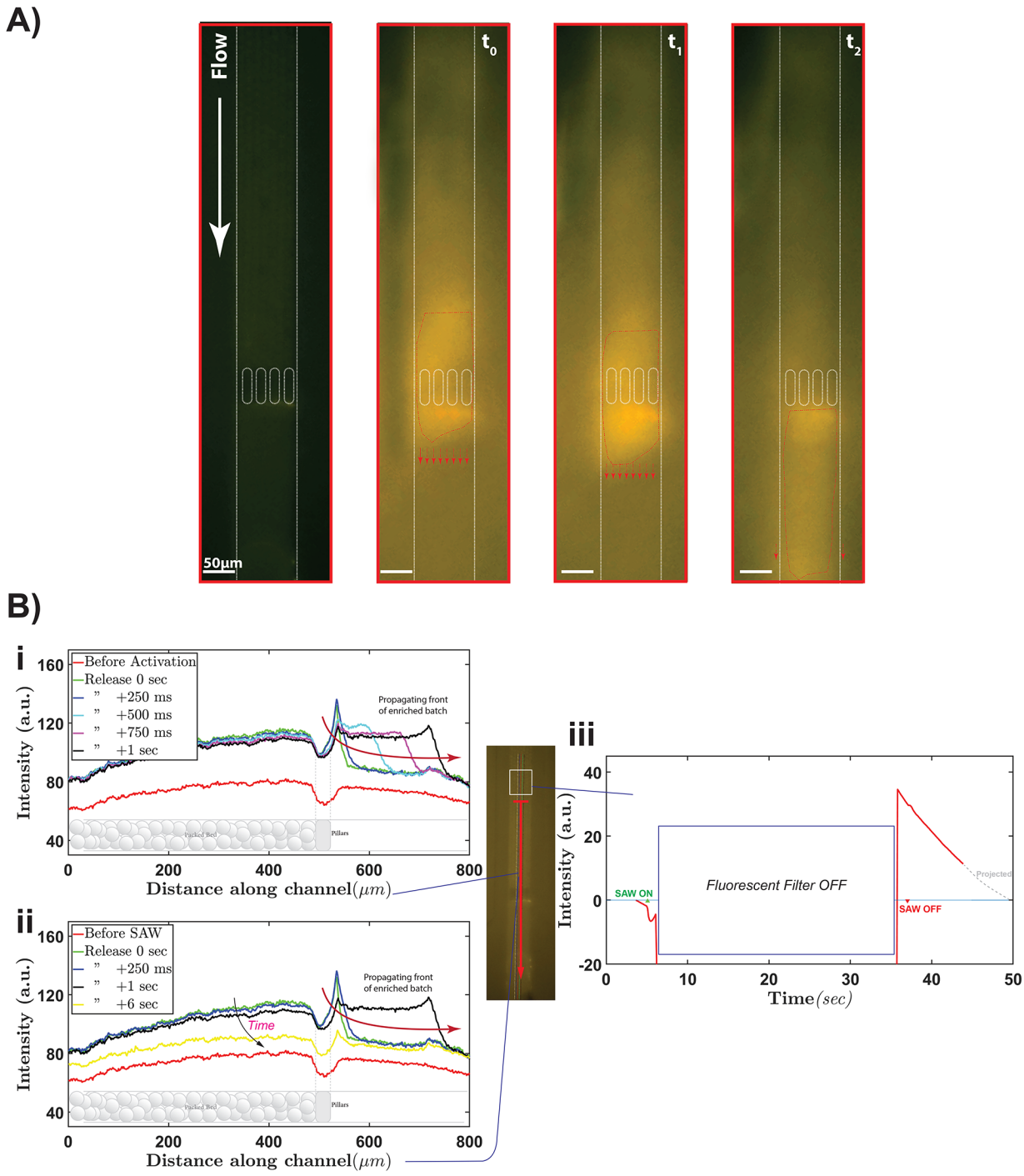


**Fig. S5:** *(A) Another experimental demonstration of capturing, enriching and releasing of high concentrated exosome batch to the downstream, where the left caption shows the channel before SAW excitation. Further captions show the release and propogation of high concentrated batch toward the downstream at $t_0$ = After SAW OFF, $t_1 = t_0 + 100$ ms and then $t_2 = t_0 + 3$ sec when the front of the batch left the image borders. (B) The spatial profile of intensity along the channel length at different times shows the release of high concentrated batch of exosomes when SAW is turned off. The front propagates and leaves the frame area(i); intensity level eventually will revert to initial level (ii). Temporal variation of intensity before and after SAW activation (iii).*

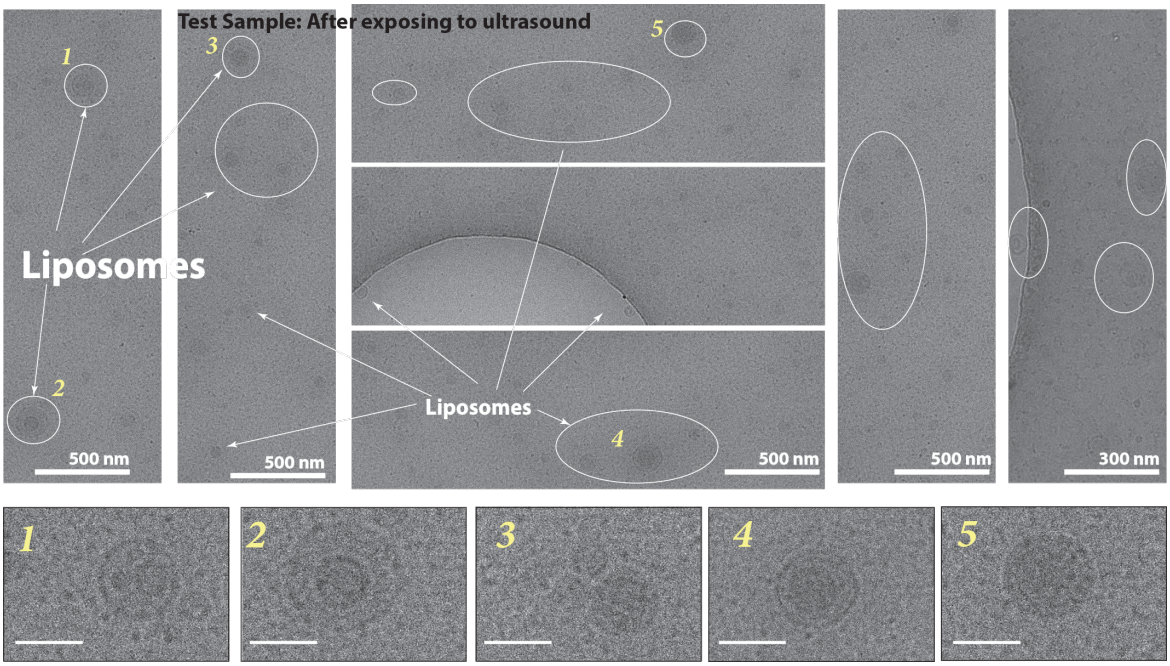


**Fig. S6:** *Multiple Transmission electron microscopy (TEM) images of liposome particles (with 100 nm mean size) show that the particles retain their morphology and bilayer lipid membrane after being exposed to ultrasound wave (SAW 70 MHz at 13 dBm source power level), collected and released by the activated packed bed. The sample collected after 1 hour continuous collection and release cycles. Insets 1 to 5 shows examples of liposome particles after ultrasound exposure for more clarity. All scale bars are 100 nm unless specified.*