Supporting Information

Low Intensity Focused Ultrasound-Responsive Microcapsules for Non-ablative Intracellularly Ultrafast Release of Small Molecules

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Materials

Tetraethyl orthosilicate (TEOS, Si-$(OC_2H_5)_4$), ammonium hydroxide solution (NH_4OH, 28.0–30.0 % NH_3 basis), poly(allylamine hydrochloride) (PAH, Mw = 56 kDa), poly(sodium 4-styrenesulfonate) (PSS, Mw = 70 kDa), rhodamine B (Rh-B, Mw = 479), ethylenediaminetetraacetic acid disodium salt (EDTA), polyethyleneimine (PEI), 2-hydroxyethylagarose, NaCl and other salts were purchased from Sigma-Aldrich. Materials used for cell culture and live/dead assay including Dulbecco's modified eagles media (DMEM), fetal bovine serum (FBS), phosphate buffer solution (PBS), penicillin, streptomycin and trypsin were also supplied by Sigma.

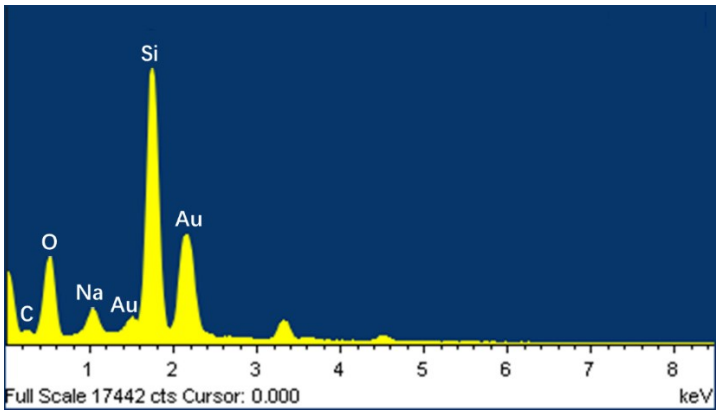

Figure S1. EDX spectra of capsules after silica incorporation.

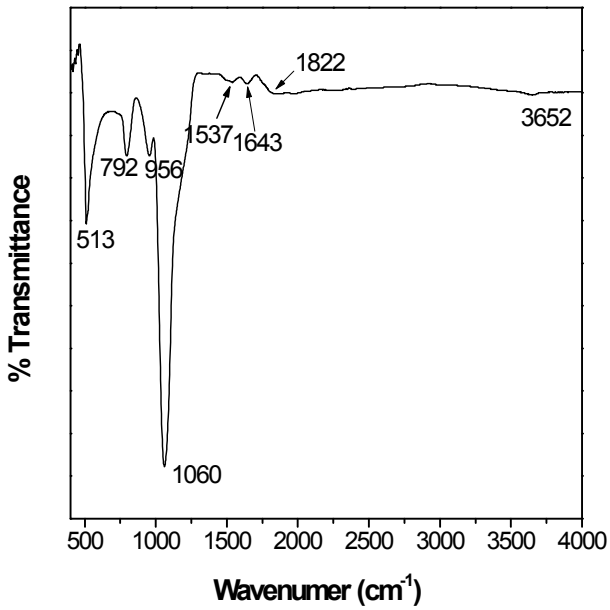

Figure S2. FTIR spectra of capsules after silica incorporation.

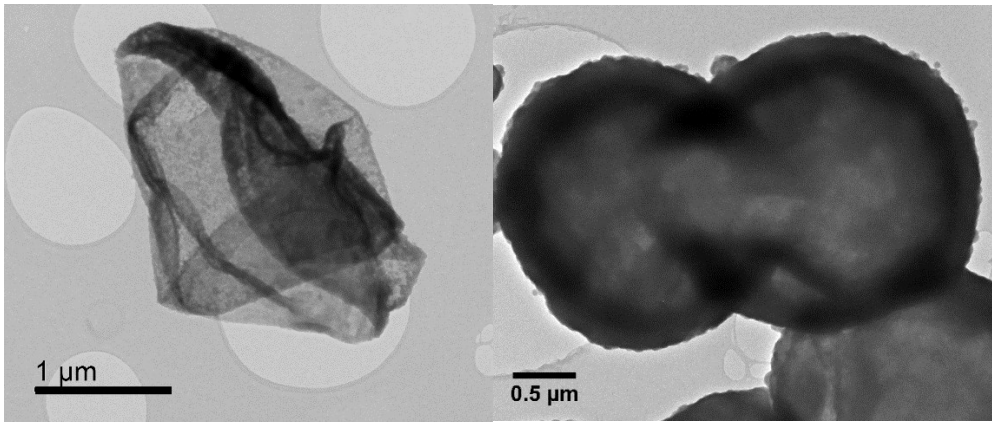

Figure S3 TEM images of $(PAH/PSS)_4$ capsules before (A) and after (B) silica coating.

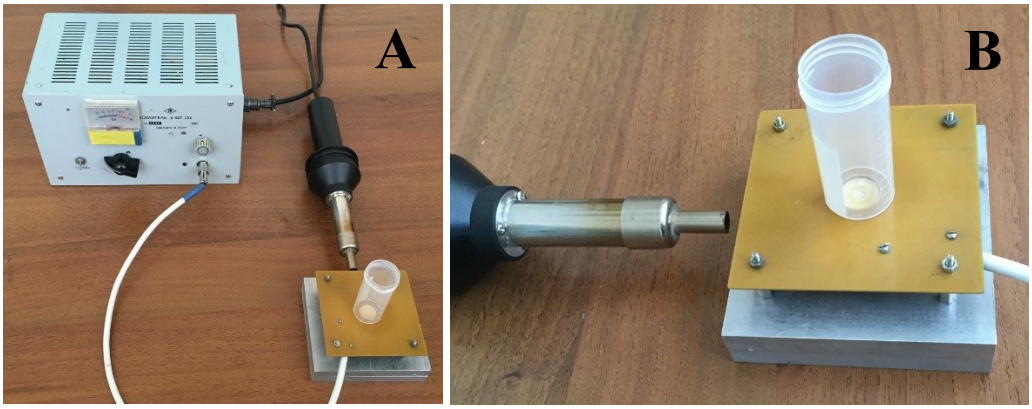

Figure S4 (A) Hand-made laboratory set-up for FU processing and (B) Cooling system.

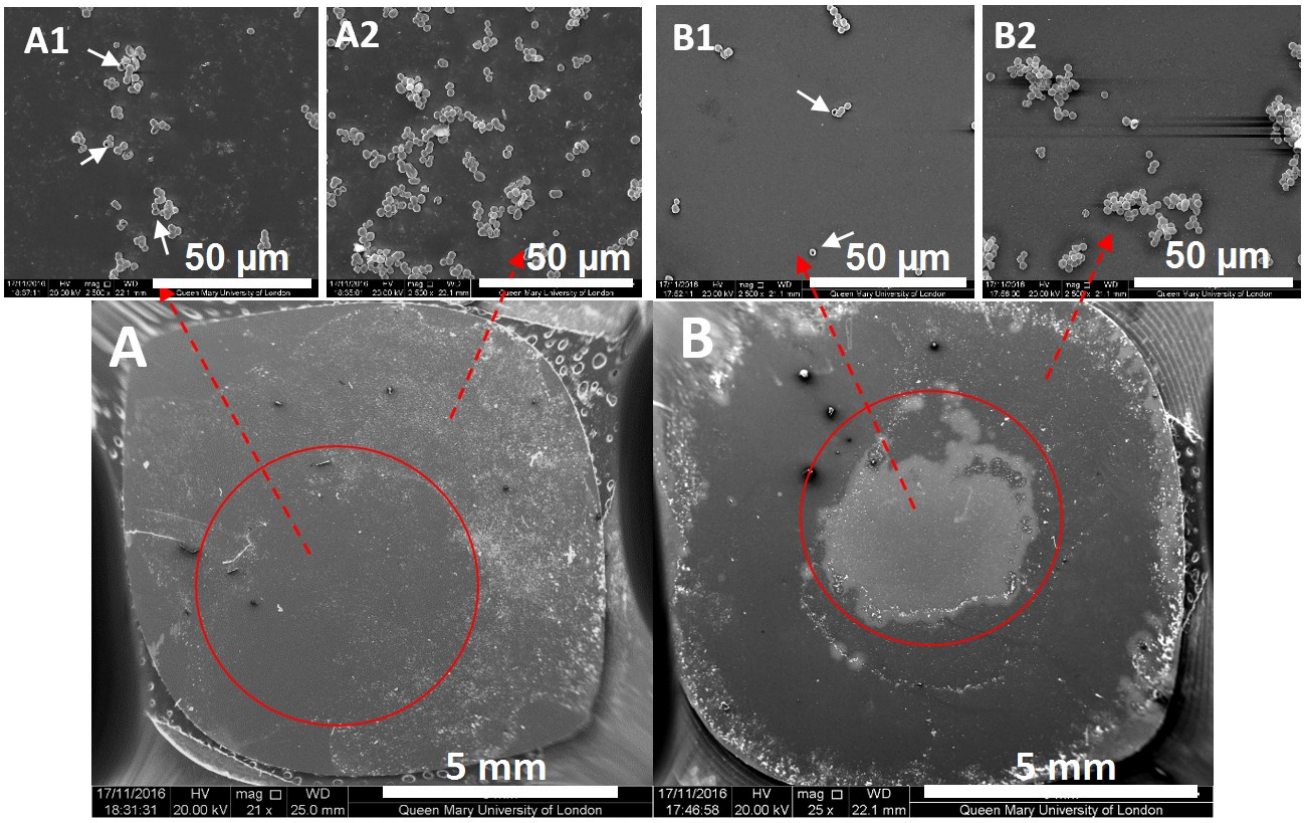

Figure S5. SEM images (low magnification) of PEI fixed capsules treated by LIFU for (A) 30s and (B) 120s.

Upon LIFU treatment. Capsules located in the focal area will be effectively affected. The SEM images in Figure S5 (Supporting Information) show higher particle density in the peripheral area than that in the central area, indicating that LIFU is mainly focused on the central area. The enlarged SEM images in the top line further confirm this points. In addition, more broken composite capsules can be found in the central area.

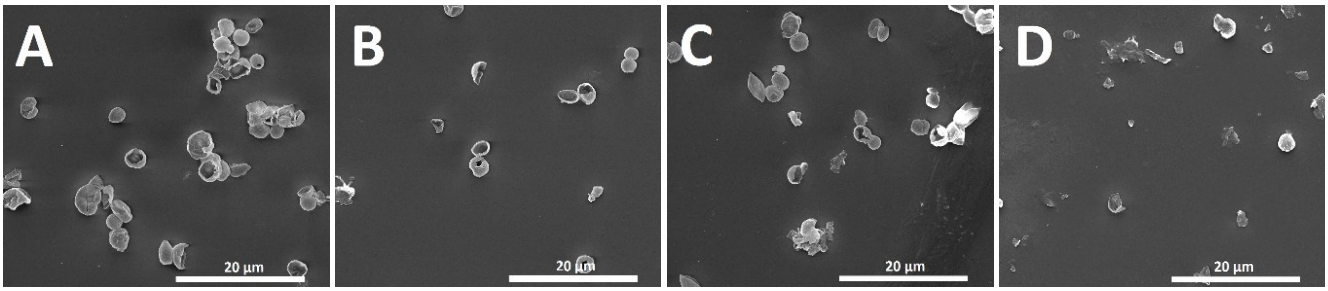

Figure S6. SEM images of the precipitate collected from the water bath after LIFU treatment for (A)10 s, (B)30 s, (C) 60 s, and (D) 120 s. (PEI fixed)

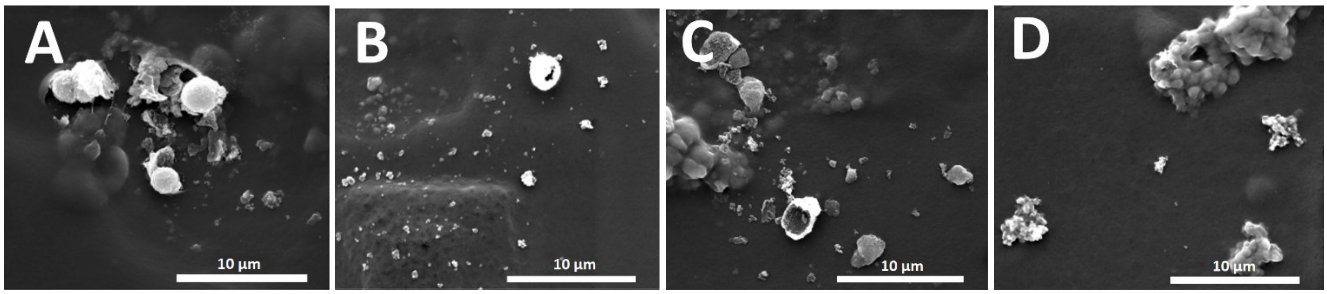

Figure S7. PAH/PSS/SiO_2 microcapsules fixed by hydrogel and treated by LIFU for different time: (A) 30 s, (B) 60 s, (C) 90 s, and (D) 120 s.

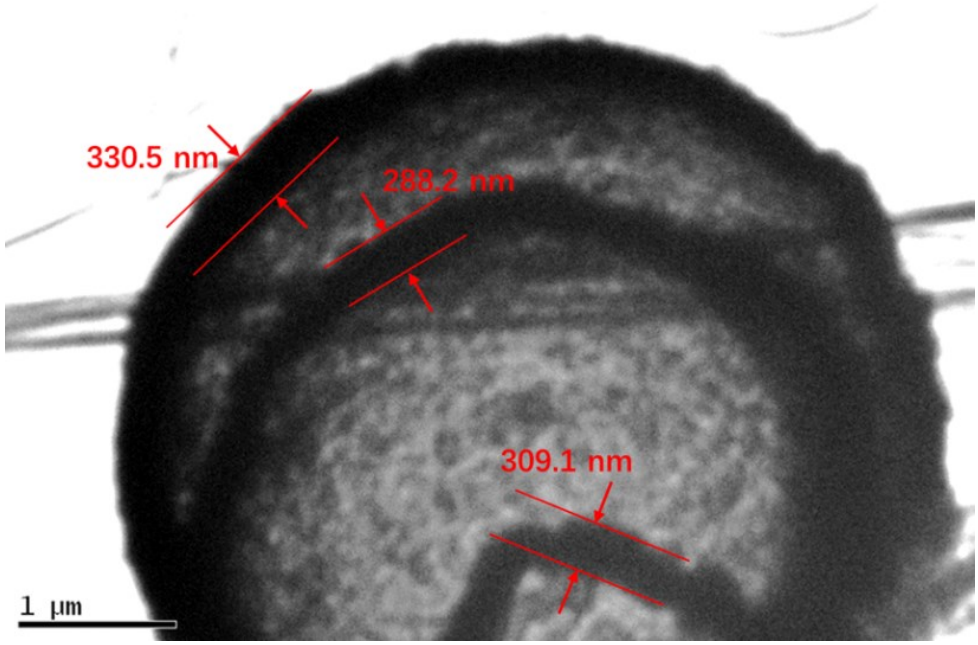

Figure S8 TEM images of $(PAH/PSS)_4$ capsules with silica coating.The red arrow denotes the thickness of composite capsule shell.

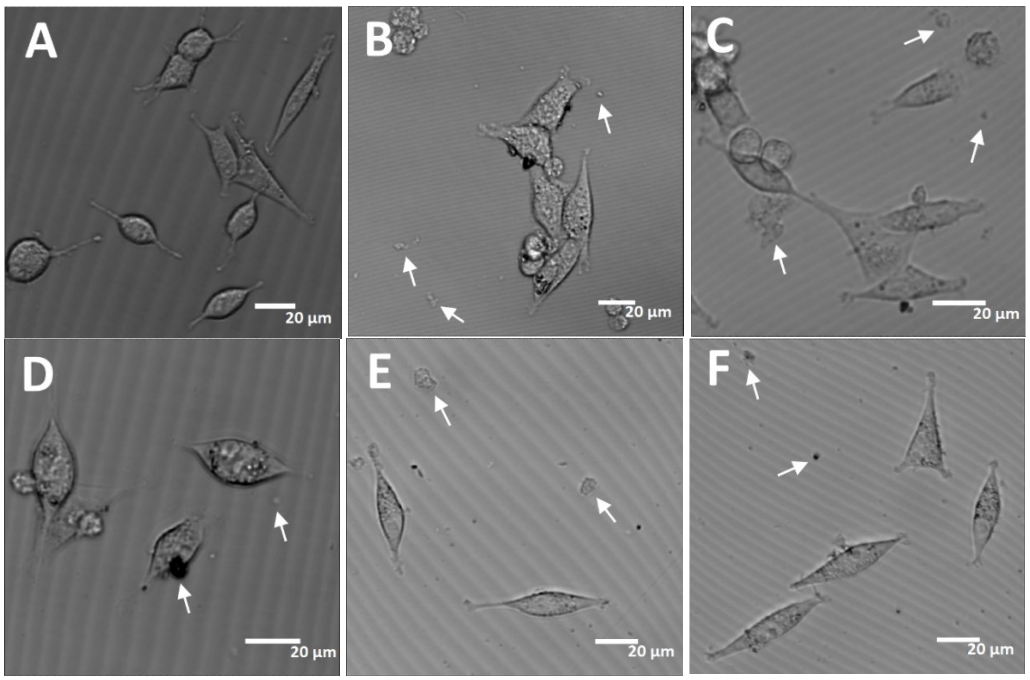

Figure S9. Optical microscope images of B50 cells treated by LIFU for different time: (A) 0 s, (B) 10 s, (C) 30 s, (D) 60 s, (E) 90 s, (F) 120 s, and then cultured for 24 h. The image of 0 s was obtained from the initial cells sited on glass slide.

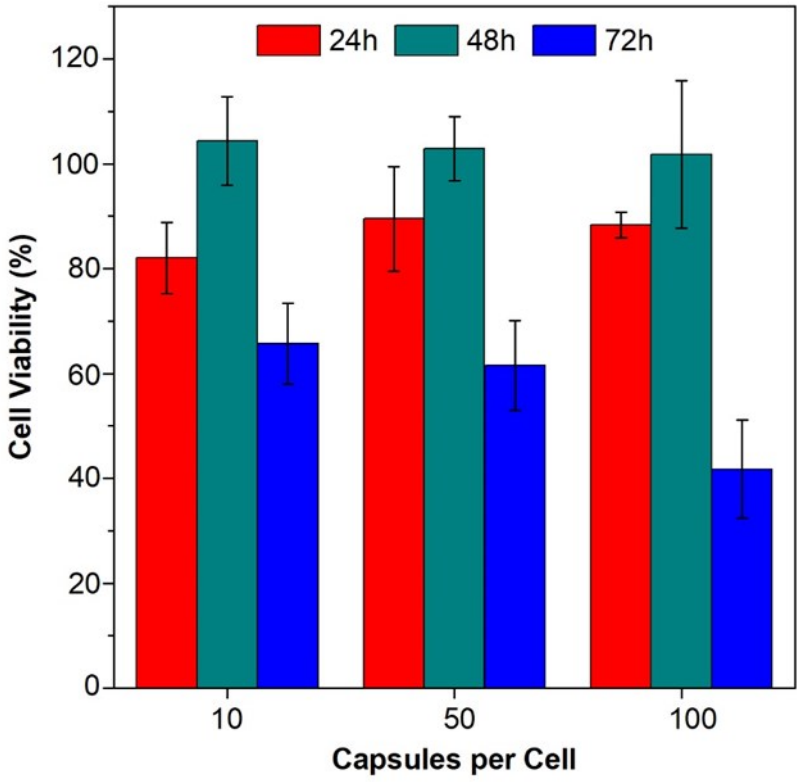

Figure S10. Cell viability of B50 cells cocultured with different concentrations of PAH/PSS/SiO_2 composite microcapsules for 24 h, 48 h and 72 h at 37 ^{o}C, as measured by an MTT colorimetric assay compared with the control. The error bars show the standard deviations.