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Supporting Information

Stimuli-Responsive Attachment for Enabling the Targeted Release of Carriers

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Methods and Materials

Materials. 10x Phosphate buffered saline (PBS) (ultra-pure grade) was purchased from Vivantis Technologies Sdn. Bhd, Malaysia. Hydrochloric acid (HCl, 37%) was purchased from Merck. Ammonia solution (NH_3, 25% for analysis), acetic acid, and sodium hydroxide were bought from EMSURE®. Polydimethylsiloxane (PDMS) was purchased from Dow Corning Corporation, Midland. Chloroform was purchased from Beijing chemical works (China). Rhodamine B was purchased from Sigma Life Science. Adhesive was purchased from 3M. Super merah (red dye) was purchased from Ng Chee Lee (Pte) Ltd. *N, N'*-Methylenebisacrylamide (BIS) was purchased from Alfa Aesar. Ammonium persulfate (APS), *N,N,N',N'*-tetramethyl-ethylenediamine (TEMED), calcium chloride, glutaraldehyde solution (GA), *N*-isopropylacrylamide (NIPAM), tannic acid, sodium alginate, acrylic acid (AA), 2-hydroxyethyl methacrylate (HEMA), ethylene glycol dimethacrylate (EGDM), fluorescein sodium salt, L-*α*-phosphatidylcholine, polystyrene (pellets, average molecular weight ~28,000 by GPC), and all other materials were purchased from Sigma-Aldrich.

Preparation of Liposomes. Liposomes were prepared using the thin film hydration method. 75 mg of L-*α*-phosphatidylcholine was dissolved in 5 mL of chloroform in a round bottom flask. The chloroform was then removed by evaporation at 50 ºC for 1.15 h under reduced pressure in a rotary evaporator. The lipid film formed at the bottom of the flask was hydrated with 10 mL of 100 mM fluorescein sodium salt solution and sonicated for 60 min in ice water bath before being vortexed for 20 min at room temperature. The crude liposomes were then extruded through 100 nm polycarbonate membrane filter using a nitrogen extruder 5 times. The resulting dispersion of liposomes was analysed for size by dynamic light scattering (DLS)

Zetasizer ZS90 (Malvern instrument). This analysis showed that the liposomes had an average diameter of 132 nm (Figure S1).

Preparation of the temperature-responsive attachment with liposomes. Liposomes embedded in poly(*N*-isopropylacrylamide) (PNIPAM) hydrogels were synthesized by first preparing (at 22 ^{o}C) a 1.5 mL aqueous solution that consisted of 0.10 g of NIPAM, 0.0050 g of BIS, and 0.5 mL solution containing the liposomes (5 mg/mL). 50 μL of APS (5 % w/v) and 30 μL of TEMED were then added into the solution. The solution containing the suspended liposomes was vigorously mixed with a vortex mixer for 10 s, poured in excess into a PDMS mold with cylindrical cavities (as illustrated in Figure 2b of the main text), and placed in a vacuum chamber for 30 min. The hydrogel polymerized in the PDMS mold with time. It was then washed with ultra-pure water and then extracted from the PDMS mold. Because the monomeric solution was poured in excess into the mold, the polymerized hydrogel had a flat base (30 mm × 30 mm) with cylindrical protrusions (diameter: 1 mm and height: 1 mm) in a 14 ×14 array on the base.

Coating the temperature-responsive attachment with liposomes with tannic acid. 5 mg/mL of tannic acid was dissolved in a 10 mM PBS buffer (pH 7.4) solution. The temperature-responsive hydrogels with the liposomes embedded in their matrices were then immersed into the buffer solution with tannic acid at 37 ^{o}C for 8 h. With a high temperature, the temperature-responsive hydrogel contracted. The coating was thus performed on the contracted hydrogel. After coating, the surface was rinsed extensively with ultrapure water, and dried under a stream of nitrogen. The cylindrical protrusions were cut away from its flat

base. The cylindrical pieces of the partially coated temperature-responsive hydrogel with liposomes embedded in its matrix had dimensions of 500 μm – 800 μm in diameter and height. The hydrogel was coated on all sides except the surface that was cut away from the flat base.

Preparation of the pH-responsive attachment with liposomes. An aqueous solution that consisted of 5 wt% of APS dissolved in deionized water was first prepared in a tube. The tube was wrapped with aluminum foil to prevent the molecules from exposure to light. The solution was then mixed using a vortex mixer. In a separate step, 0.41 g AA, 2.96 g HEMA, 0.0351 g EGDM, and 1.0447 g of the solution containing the liposomes were mixed in a vial by a vortex mixer. 0.08 mL of the APS solution was then added to 2 mL of the mixture. Nitrogen gas was bubbled into the mixture for 3 min. The mixture was poured into the PDMS mold (i.e., with the cylindrical cavities as illustrated in Figure 2b in the main text) and placed in a vacuum chamber for 30 min for removing any air bubbles. 0.05 mL of TEMED was then added to the mixture. The liquid mixture was placed with a lid covering it in an oven operated at 80°C for 5 min. After removing the polymerized hydrogel in the PDMS mold from the oven, it was left to cool at room temperature for at least 2 h. The hydrogel was then extracted from the PDMS mold gently while ensuring that the cylindrical protrusions were intact. The hydrogel was subsequently dried at room temperature for 24 h. Because the monomeric solution was poured in excess into the mold, the polymerized hydrogel had a flat rectangular base (30 mm × 30 mm) with cylindrical protrusions (diameter: 1 mm and height: 1 mm) in a 14 ×14 array on one surface of the base.

Coating the pH-responsive attachment with liposomes with adhesives. By polymerizing the pH-responsive hydrogel loaded with the liposomes in the PDMS mold, the resultant material consisted of a rectangular base with many cylindrical protrusions on one surface of the base. The hydrogel was first dried in an open atmosphere at room temperature for more than 1 h. After drying, this whole slab of hydrogel was coated with adhesive evenly throughout, including the cylindrical protrusions. The adhesive was allowed to dry completely for at least 30 min. Thereafter, the hydrogel was coated with another layer of adhesive to ensure that the surface of the hydrogel was completely coated. The adhesive was allowed to dry completely for another 30 min. After coating, the cylindrical protrusions were cut away from its flat base. The cylindrical (500 μm – 800 μm in diameter and height) pieces of the partially coated pH-responsive hydrogel with liposomes embedded in its matrix were thus obtained. The hydrogel was coated on all sides except the surface that was cut away from the flat base.

Preparation of the highly crosslinked particles. Two types of aqueous solutions were prepared. The first solution consisted of 0.3 g sodium alginate and a minimal amount of rhodamine B dissolved in 20 mL ultrapure water. The second solution consisted of 0.10 g low molecular weight chitosan and 1.00 g calcium chloride dissolved in 20 mL of an aqueous solution that contained 3 wt% of acetic acid. An aqueous solution with 0.2 g/mL sodium hydroxide was used to adjust the pH of the second solution to 5.5. The first solution was then added dropwise by a syringe (0.60 mm × 38 mm; TERUMO) into the second solution (i.e., the needle of the syringe was ~5 cm above the surface of the second solution). Due to the relatively high viscosity of the first solution, the droplet submerged into the second solution as a whole drop. The droplet was allowed to remain submerged in the second solution for ~1

h. During this process, the calcium ions diffused into the droplet and crosslinked the alginate; thus, the liquid droplet became a hydrogel. At the same time, the chitosan molecules also diffused into the droplet that turned into the hydrogel. The red colored (due to the dye) hydrogel particles (~50 in each batch) were washed by immersing the particles in separate vials of 30 mL of ultrapure water for 3 times (i.e., each time for 10 min). This step washed the red colored dye away from the surface of the particles. After washing, the particles were submerged in a 10 mL aqueous solution that contained 90% vol of glutaraldehyde (GA) for 10 min. This process allowed the GA to crosslink with the chitosan on the surface of the hydrogel particles, thus forming the highly crosslinked shell. Hence, the core-shell particles (~16 μL) obtained had a core that consisted of the alginate hydrogel filled with the aqueous solution (i.e., containing the dye and any unreacted chitosan molecules), and a shell that consisted of the highly crosslinked chitosan with GA. When cut into half, the particle was indeed observed to be consisted of a fairly rigid shell together with a soft highly porous sponge-like core filled the aqueous solution.

Preparation of the temperature-responsive attachment with the highly crosslinked particles. 10 mL of an aqueous solution that consisted of 5 wt% APS dissolved in deionized water was prepared in a bottle. The bottle was wrapped with aluminum foil to prevent the molecules from exposure to light and was stored in a 4 ℃ fridge. In a separate step, 0.1 g of *N*-isopropylacrylamide (NIPAM), 0.0050 g of BIS, and 1.5 mL of ultrapure water were mixed together. 0.05 mL of the aqueous APS solution was added to this mixture. Nitrogen gas was bubbled into the mixture for 3 min. 0.03 mL of TEMED was then added to the mixture and mixed for 10 s. 0.2 mL of the viscous liquid mixture was pipetted into the well of a 96 well plate (polystyrene; diameter was 6.94 mm and height was 10.65 mm for each well). The

highly crosslinked particle was placed carefully in the center of the viscous liquid mixture. Due to its high viscosity, the highly crosslinked particle was able to stay in the center of the well. The temperature-responsive hydrogel polymerized at room temperature after 30 min. After polymerization, the temperature-responsive hydrogel with the highly crosslinked particle embedded within its matrix was extracted from the well carefully. It was then immersed in water at 37 ℃ for contracting the temperature-responsive hydrogel completely and dried at room temperature for 24 h. The dried surface of the temperature-responsive hydrogel was coated with adhesive evenly throughout except the top and bottom sides. The adhesive was allowed to dry completely for at least 30 min. Thereafter, the hydrogel was coated with another layer of adhesive to ensure that the surface of the hydrogel was completely coated. The adhesive was allowed to dry completely for another 30 min. After coating, the temperature-responsive hydrogel with the highly crosslinked particle embedded in the center with its sides coated (~0.5 mm) except the top and bottom surfaces was obtained. The SRDDC obtained was cylindrical with a height of 5 mm and a diameter of 8 mm.

Preparation of the pH-responsive attachment with highly crosslinked particle. 10 mL of an aqueous solution that consisted of 5 wt% APS dissolved in deionized water was prepared in a bottle. The bottle was wrapped with aluminum foil to prevent the molecules from exposure to light and was stored in a 4 ℃ fridge. 0.41 g AA, 2.96 g HEMA, 0.03511 g EGDM, and 1.0447 g ultrapure water were mixed in a vial. 0.05 mL of the aqueous APS solution was then added into the mixture. Nitrogen gas was bubbled into the solution for 3 min. 0.03 mL of TEMED was added to the mixture and mixed for 10 s. 0.2 mL of the mixture was pipetted into the well of a 96 well plate (polystyrene; diameter was 6.94 mm and height was 10.65 mm for each well). The liquid mixture was placed in an oven at 120 ℃ for 3 min for polymerizing

the liquid into the pH-responsive hydrogel. Immediately after taking the mixture out of the oven (i.e., after 3 min), the highly crosslinked particle was placed in the center of the well in the viscous liquid mixture. Due to its high viscosity, the highly crosslinked particle particle was able to stay in the center of the well. The viscous liquid was cooled at room temperature for at least 120 min. After polymerization, the pH-responsive hydrogel with the highly crosslinked particle particle embedded within its matrix was extracted from the well carefully. It was then contracted in an acidic solution (pH 2) and dried at room temperature for 24 h. The dried surface of the pH-responsive hydrogel was coated with adhesive evenly throughout except the top and bottom sides. The adhesive was allowed to dry completely for at least 30 min. Thereafter, the hydrogel was coated with another layer of adhesive to ensure that the surface of the hydrogel was completely coated. The adhesive was allowed to dry completely for another 30 min. After coating, the pH-responsive hydrogel with the highly crosslinked particle particle embedded in the center with its sides coated (~0.5 mm) except the top and bottom surfaces was obtained. The SRDDC obtained was cylindrical with a height of 5 mm and a diameter of 8 mm.

Preparation of the polystyrene core-shell particles. A PDMS mold with cylindrical cavities (diameter: 1 mm and depth: 1 mm) was first fabricated. Solid polystyrene pellets (average molecular weight of ~28,000) was dissolved in toluene to form a 10 wt% polymeric solution. This solution was poured into the cavities of the PDMS mold, and allowed to dry at room temperature overnight. After drying, the inner surface of the cavities of the PDMS mold was coated with a layer of polystyrene. A red dye solution (super merah) was added into the cavities until they were completely filled; any excess amount of red dye solution (i.e., outside the cavities) was removed carefully. Subsequently, the 10 wt% polymeric solution was again

poured into the cavities so that it covered the top of the cavities and over the red dye solution. The excess amount of the polymeric solution outside of the cavities was removed. The polymeric solution was dried completely at room temperature for several hours. After drying the polymer, the cylindrical core-shell particle (diameter: 1 mm and depth: 1 mm) was extracted from the PDMS mold carefully. The particle consisted of a polystyrene shell and a core with the red dye solution.

Preparation of the pH-responsive attachment with the polystyrene core-shell particle. 10 mL of an aqueous solution that consisted of 5 wt% APS dissolved in deionized water was prepared in a bottle. The bottle was wrapped with aluminum foil to prevent the molecules from exposure to light and was stored in a 4 ℃ fridge. In a separate step, 0.41 g AA, 2.96 g HEMA, 0.03511 g EGDM, and 1.0447 g ultrapure water were mixed in a vial. 0.05 mL of the aqueous solution containing APS was then added into the mixture. Nitrogen gas was bubbled into the resultant solution for 3 min. 0.03 mL TEMED was subsequently added to the mixture and mixed for 10 s. This monomeric solution was cast in a PDMS mold. The PDMS mold had a square cavity with lateral dimensions of 3 mm × 3 mm and 1 mm in depth. A rod (1 mm in diameter) was placed standing vertically in the middle of the cavity. The monomeric solution was poured into the cavity with the rod fixed vertically in the middle of the cavity. The PDMS mold and the solution were placed in an oven at 120 ℃ for 3 min for polymerizing the liquid into the pH-responsive hydrogel, and then allowed to cool down at room temperature for at least 120 min. After polymerization, the rod was removed and the hydrogel was extracted from the cavity. The pH-responsive hydrogel obtained was cylindrical with dimensions of 3 mm × 3 mm × 1 mm and a hole of 1 mm in diameter in the middle due to the rod in the mold. The particle that consisted of a polystyrene shell and a core with the red dye solution as

prepared by the procedure described in the previous section was placed in the hole in the middle of the pH-responsive hydrogel carefully. The pH-responsive hydrogel loaded with the core-shell particle was then contracted in an acidic solution (pH 2) and dried at room temperature for 24 h. The dried surface of the pH-responsive hydrogel was coated with adhesive evenly throughout except the top and bottom sides. The adhesive was allowed to dry completely for at least 30 min. Thereafter, the hydrogel was coated with another layer of adhesive to ensure that the surface of the hydrogel was completely coated. The adhesive was allowed to dry completely for another 30 min. After coating, the cylindrical pH-responsive hydrogel with the core-shell particle embedded in the center with its sides coated (~0.5 mm) except the top and bottom surfaces was obtained. The SRDDC had an overall diameter of 4 mm and height of 1 mm.

SEM imaging of the liposomes in the hydrogel. The partially coated cylindrical temperature-responsive hydrogels with liposomes embedded in the bulk matrix were first frozen by liquid nitrogen. After all the liquid nitrogen evaporated, the samples were placed in bottles and freeze-dried in a freeze dryer (Alpha 1-4 LSC plus, Martin Christ) for over 4 h. To observe the liposomes embedded in the temperature-responsive hydrogel, the freeze-dried samples were cut to expose the cross-sectional areas of the bulk of the hydrogel. The exposed cross-sectional areas were observed by JEOL JSM-6700F microscope operated at 5 kV.

Studying the controlled release of the SRDDCs. Liposomes that was loaded with the fluorescein sodium salt were embedded in the bulk of a stimuli-responsive hydrogel as described previously. The controlled release of the fluorescein sodium salt from this SRDDC

was studied. First, the case of the SRDDC that consisted of the temperature-responsive hydrogel was discussed. This temperature-responsive SRDDC was originally immersed in deionized water at a high temperature of 37 °C for keeping the temperature-responsive hydrogel contracted. At time $t = 0$, the SRDDC was immersed in 10 mL deionized water at room temperature (i.e., 25 ℃) for expanding the temperature-responsive hydrogel. Samples (each with a volume of 0.08 mL) were collected from the medium at regular time intervals. The fluorescent intensities of the samples were determined by a fluorescence analyzer (microplate reader Infinite® 200 PRO, TECAN). The excitation and emission wavelengths were set at 495 and 517 nm respectively. After extracting each sample, a same volume (i.e., 0.08 mL) of deionized water was added back to the medium to ensure that the total amount of medium remained the same throughout time. The fluorescent intensity of the sample taken at $t = 0$ is denoted as I_0. The fluorescent intensity of the ith sample taken from the medium is denoted as I_i. In a separate experiment, the total amount of fluorescein dye released was determined by immersing the temperature-responsive SRDDC in a 10 mL aqueous solution that contained 2 v/v% of the surfactant, Triton-X100, for 2 days. The surfactant could break the bilayer phospholipid membrane of the liposomes, thus allowing all the fluorescein dye to be released into the medium. The fluorescent intensity of the sample taken after treating SRDDC with the Triton-X100 for 2 days was denoted as I_{max} (i.e., the maximum intensity possible after releasing all the dye).

The initial intensity (I_0), the intensity of the ith sample (I_i), and the maximum intensity (I_{max}) allowed us to calculate the relative concentration of the fluorescent dye in the ith sample, R_i, as indicated in Equation S1.

$$R_i = C_i / C_{max} = (I_i - I_0)/(I_{max} - I_0) \quad \text{(S1)}$$

C_i represents the concentration of the ith sample and C_{max} represents the maximum concentration of the sample after treating the SRDDC with the surfactant for 2 days. We used this relative concentration for calculating the percentage of fluorescent dye released at the specific time, t. For this calculation, we took into consideration the same amount of deionized water replaced in the medium each time after a sample was taken. We first calculated the total (or cumulative) amount of dye released into the solution, Q_i, by summing all the amounts of dye present in the solution at time t when the ith sample was taken and in all the samples that were taken (Equation S2).

$$Q_i = C_iV_0+(C_1+C_2+\ldots+C_{i-1})V \quad \text{(S2)}$$

V_0 is the volume of the sample solution (i.e., 10 mL in our case). This volume included all the deionized water added to replace the sample taken away for analysis. V is the volume of the sample taken (i.e., 0.08 mL). The percentage of fluorescent dye released at the specific time, t, was the total amount of dye released into the solution, Q_i, divided by the maximum amount of the dye in the SRDDC (Equation S3).

$$\text{Release (\%)} = Q_i/C_{max}V_0 \times 100 \quad \text{(S3)}$$

By substituting Equation S2 into Equation S3, we obtained Equation S4.

$$\text{Release (\%)} = [R_i+(R_1+R_2+\ldots+R_{i-1})V/V_0\,]\times 100 \quad \text{(S4)}$$

Based on the intensities that we determined by the fluorescence analyzer, we were able to obtain all the relative concentrations, R_i, (i.e., via Equation S1); hence, we were able to determine the percentage of fluorescent dye released at the specific time, t.

Two control experiments were conducted as follows. The first control experiment involved repeating the same experiment except that instead of immersing the SRDDC in cool

deionized water at room temperature, the SRDDC was immersed in deionized water at a higher temperature of 37 °C. This high temperature kept the temperature-responsive hydrogel of the SRDDC in the contracted state. The second control experiment involved repeating the same experiment except that the SRDDC was not coated with tannic acid (i.e., the SRDDC was immersed in deionized water at room temperature).

The whole set of experiments was subsequently repeated for the SRDDC that consisted of the pH-responsive hydrogel with liposomes embedded in the bulk of the hydrogel. The SRDDC was originally immersed in an acidic solution (i.e., pH 2 hydrochloric acid solution) for keeping the pH-responsive hydrogel contracted. At time $t = 0$, the SRDDC was immersed in a 10 mL basic solution (i.e., pH 12 NaOH solution) for expanding the pH-responsive hydrogel. The samples were taken at regular time intervals and were analyzed as described in previous paragraphs. For the first control experiment, the SRDDC was immersed in an acidic solution (i.e., pH 2 hydrochloric acid solution); thus, the pH-responsive hydrogel of the SRDDC remained in the contracted state. The second control experiment involved the piece of pH-responsive hydrogel embedded with the liposomes but without the rigid adhesive coating. It was immersed in 10 mL basic solution (i.e., pH 12 NaOH solution) for expanding the pH-responsive hydrogel.

Subsequently, we repeated the experiment for the SRDDC that consisted of the stimuli-responsive hydrogel and the highly crosslinked particle loaded with rhodamine B. Both the temperature-responsive and pH-responsive SRDDCs were immersed in the same types of liquid media as described in the previous paragraphs. For analyzing the release of the dye rhodamine B, 0.3 mL of sample was taken at regular time intervals. The samples were analyzed by a fluorescence spectrometry (Cary Eclipse Fluorescence Spectrophotometer, Agilent Technologies). The excitation and emission wavelengths were set at 540 and 625 nm,

respectively. After extracting the sample, an equal amount of 0.3 mL deionized water was added back to the medium to ensure that the total amount of medium remained the same throughout time. For determining I_{max}, a separate batch of the SRDDCs that consisted of the stimuli-responsive hydrogel and the highly crosslinked particle were prepared in the same way except that the shells of highly crosslinked particles were not crosslinked. These SRDDCs were similarly placed in the liquid media that allowed the stimuli-responsive hydrogels to be expanded. Without the crosslinking of the shells of the particles, the rhodamine B released readily. The release of the rhodamine B was determined to be completed after 30 h. The fluorescent intensity of the sample taken from the liquid medium after the release completed at 30 h was I_{max}. The procedure for the calculation of the percentage release of the dye was the same as described in the previous paragraphs.

The two control experiments for both the temperature-responsive and the pH-responsive SRDDCs were also performed in the same way (i.e., as the SRDDCs that consisted of the stimuli-responsive hydrogels with liposomes embedded in the bulk of the hydrogels).

Finally, we repeated the experiment for the SRDDC that consisted of the pH-responsive hydrogel and the hydrophobic polystyrene core-shell particle loaded with a red dye (super merah). The SRDDC was originally immersed in an acidic solution (i.e., pH 2 hydrochloric acid solution) for keeping the pH-responsive hydrogel contracted. At time $t = 0$, the SRDDC was immersed in a 10 mL basic solution (i.e., pH 12 NaOH solution) for expanding the pH-responsive hydrogel. Photographs of the liquid medium were taken at regular time intervals. As the red dye released from the SRDDC into the liquid medium, the liquid turned red gradually. This color intensity was determined quantitatively by analyzing the red component of each pixel of the photograph by a software (i.e., Photoshop, Adobe). For determining I_{max}, the hydrophobic polystyrene core-shell particle embedded within the

hydrogel was ruptured manually, thus allowing all the dye loaded in the particle to be released.

The two control experiments for the pH-responsive SRDDC were also performed in the same way (i.e., as the SRDDC that consisted of the pH-responsive hydrogel with liposomes embedded in the bulk of the hydrogel).

Measuring the force needed to rupture the highly crosslinked particle. The highly crosslinked particle loaded with rhodamine B was first prepared as described in a previous section. The particle was then placed on a piece of filter paper that rested on an electronic balance. A force was applied onto the particle manually via pressing a metallic surface onto the particle for 2 s. At the same time, the force was measured directly by the electronic balance. The amount of dye released by applying the force on the particle was estimated by measuring the area of paper that was stained with the dye. Specifically, this area was determined by first taking a photograph of the paper and then analyzing the area by Photoshop.

Another experiment was performing in which the SRDDC consisted of the highly crosslinked particle that did not have the crosslinked shell. This SRDDC was simply placed on a piece of filter paper without any force applied to it. Without the crosslinked shell, the dye released from the SRDDC and onto the paper gradually and spontaneously.

Observing the highly crosslinked particle embedded within the SRDDC. A highly crosslinked particle that consisted of the hydrogel (i.e., alginate) core loaded with a dye (i.e., rhodamine B) and the highly cross-linked polymeric shell (i.e., chitosan) was first fabricated.

Separately, a 200 μL of the solution used to make the pH-responsive hydrogel was poured into the cylindrical wells (polystyrene) with dimensions of 6.94 mm in diameter and 10.65 mm in height), and polymerized. In the course of polymerization when the solution became viscous, the core-shell bead was placed in the center of the well. After the pH-responsive hydrogel fully polymerized, 200 μL of pH 10.0 solution was placed on top of the hydrogel with the core-shell bead embedded in it. The pH-responsive hydrogel expanded and exerted pressure on the core-shell bead. The changes in size of the highly crosslinked particle were recorded by a camera.

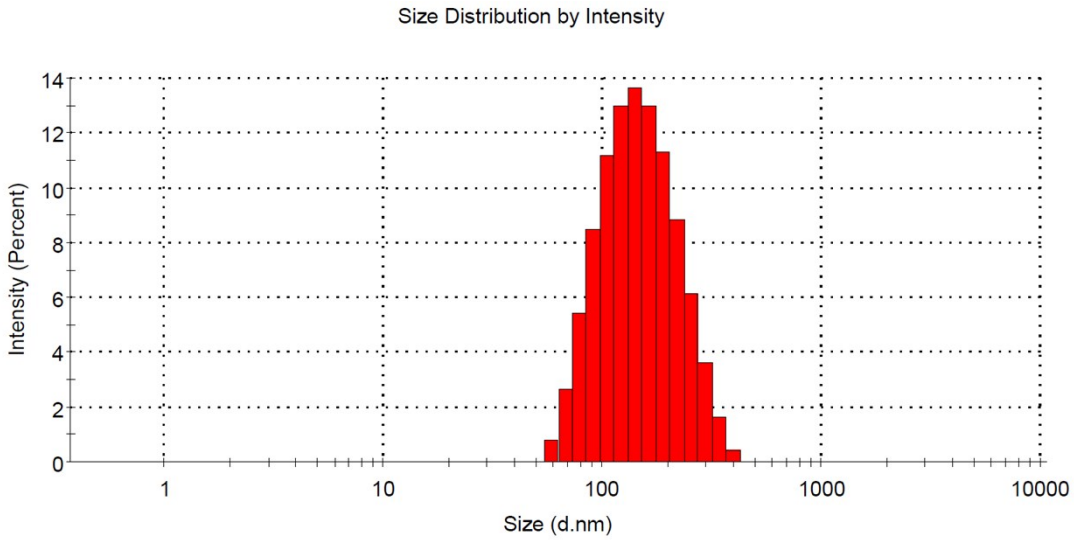

Figure S1. Size distribution of the liposomes analyzed by dynamic light scattering (DLS).