

Supporting Information

Trigger-Responsive Poly(β -amino ester) Hydrogels

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Experimental section

Materials

2-Hydroxy-4'-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959, I-2959), triethylamine (TEA), bis(2-hydroxyethyl) disulphide, acryloyl chloride, hexanediol-diacrylate (HDA), albumin–fluorescein isothiocyanate conjugate bovine (BSA-Fluo), acrylamide, dithiothreitol (DTT), and other reagents and solvents were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used as received, unless otherwise specified. Disulfanediybis(ethane-2,1-diyl) diacrylate (SSDA),¹ ((propane-2,2-diylbis(oxy)) bis(ethane-2,1-diyl) diacrylate (KTDA),² and 3,6,9-trioxadecylamine (mOEG-NH₂)³ were prepared according to the previously reported procedures.

Instrumentation

NMR spectra were recorded on a Varian UI400 (400 MHz), a UI500NB (500 MHz), or a VXR-500 (500 MHz) spectrometer. Tandem gel permeation chromatography (GPC) was performed on a system equipped with an isocratic pump (Model 1100, Agilent Technologies, Santa Clara, CA, USA), a DAWN HELEOS 18-angle laser light scattering detector (also known as multi-angle laser light scattering detector; Wyatt Technology, Santa Barbara, CA, USA), and an Optilab rEX refractive index detector (Wyatt Technology). The detection wavelength of the HELEOS was set at 658 nm. Separations were performed on serially connected size exclusion columns (100 Å, 500 Å, 10³ Å and 10⁵ Å Phenogel columns, 5 µm, 300 × 7.8 mm, Phenomenex, Torrance, CA, USA) at 60°C with DMF containing 0.1 M LiBr as the mobile phase. The HELEOS detector was calibrated with pure toluene without the need for external polymer standards and was used for the determination of the absolute molecular weights. The molecular weight of each polymer was determined from the dn/dc value calculated offline by means of the internal calibration system processed by the ASTRA V software (ver. 5.1.7.3, Wyatt Technology). Measurement of fluorescence spectra of compounds was carried out on a LS55 fluorescence spectrometer (Perkin Elmer, Santa Clara, CA, USA).

Synthesis of PBAE-CT, PBAE-SS or PBAE-KT

mOEG-NH₂ was mixed with HDA, SSDA or KTDA at 5:4 molar ratio and stirred at 60°C for 24 h to yield the corresponding macromer (PBAE-CT, PBAE-SS, or PBAE-KT) that were used di-

rectly without further purification.

Acid triggered cleavage of PBAE-KT analyzed by ^1H NMR

PBAE-KT (10 mg) was added into a small vial containing 1 mL of D_2O . The solution was tuned to pH 2 by addition of DCl. The solution was incubated at rt for 4 h and analyzed by ^1H NMR. The control NMR study was similarly set up except that the solution pH was tuned to pH 8 by NaOD.

UV-Vis Transmittance Measurement

The transmittances of the solutions of PBAE-KT, PBAE-SS or PBAE-CT in PBS buffer (pH 7.4) were measured at 600 nm using a thermostatically controlled cuvette. The concentrations of polymers were fixed at 5 mg/mL.

Synthesis of BSA-Fluo encapsulated hydrogel

In a 7 mL vial, PBAE (4 mg), acrylamide (20 mg, 0.28 mmol) and I-2959 (0.2 mg, 0.9 μmol) were dissolved in PBS (pH 7.4, 380 μL), to which BSA-Fluo solution (1 mg BSA-Fluo in 20 μL PBS) was added. The solution was degassed by nitrogen for 2 min, placed in a photoreactor (365 nm, 10 mW/cm^2) and irradiated for 10 min to yield BSA-Fluo encapsulated hydrogels.

Typical BSA-Fluo release study from PBAE-KT hydrogels at different pH

PBS buffer solutions with different pH values (5 mL) were prepared and added into vials containing BSA-Fluo/PAA hydrogel. The mixture was placed on a shaker and incubated at 37 $^\circ\text{C}$. After a designated time interval, an aliquot of the solution (0.2 mL) was taken from the mixture and diluted with pH 7.4 PBS to 2 mL. Its fluorescence intensity was determined ($\lambda_{\text{ex}} = 494$ nm; $\lambda_{\text{em}} = 522$ nm). The concentration of the released BSA-Fluo was determined by comparing the fluorescence intensity against a standard curve separately prepared.

Typical BSA-Fluo release study from the PBAE-SS hydrogel under redox conditions

A PBS buffer solution (5 mL) containing 20 mM DTT was added to a vial containing BSA-Fluo/PAA hydrogel. The mixture was incubated at 37 $^\circ\text{C}$. After a designated time interval, an aliquot of the solution (0.2 mL) was taken from the mixture and diluted with pH 7.4 PBS to 2

mL. Its fluorescence intensity was determined ($\lambda_{\text{ex}} = 494 \text{ nm}$; $\lambda_{\text{em}} = 522 \text{ nm}$). The concentration of the released BSA-Fluo was determined by comparing the fluorescence intensity against a standard curve separately prepared.

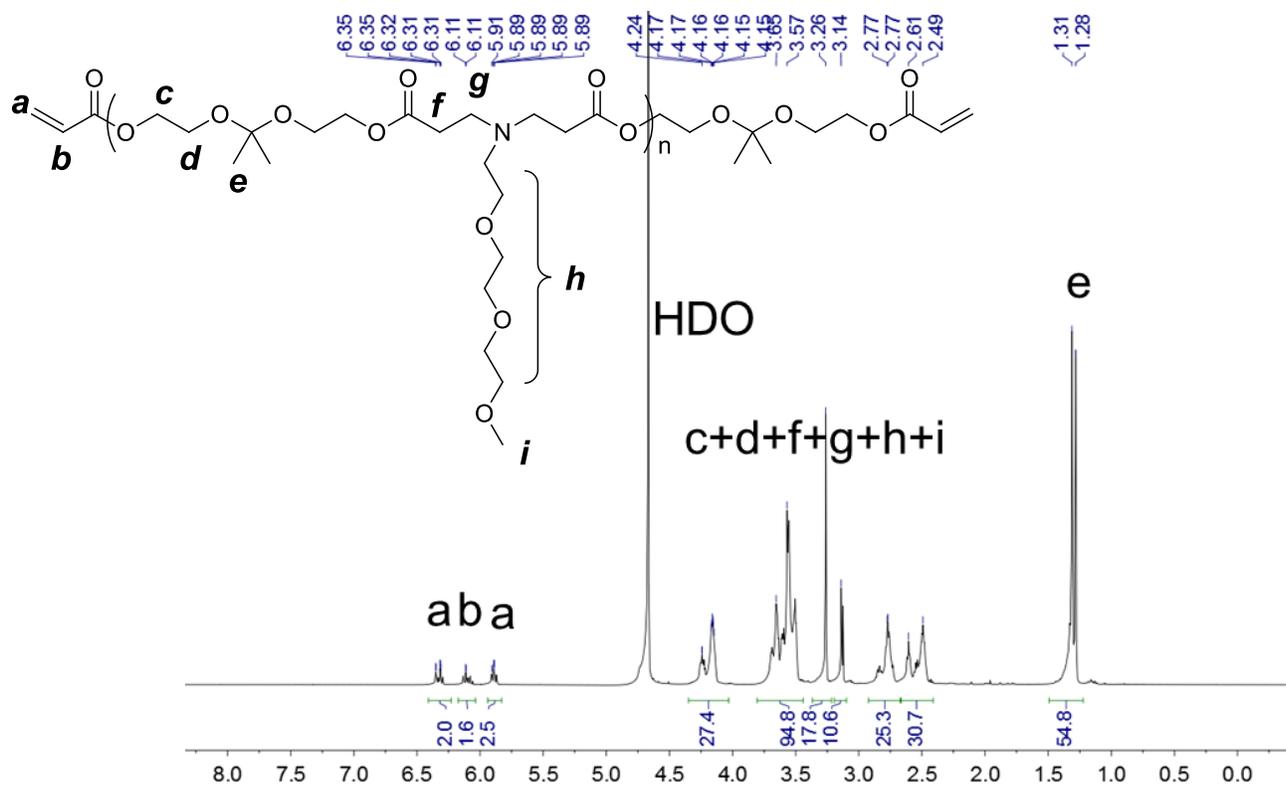


Figure S1. ^1H NMR of PBAE-KT in D_2O

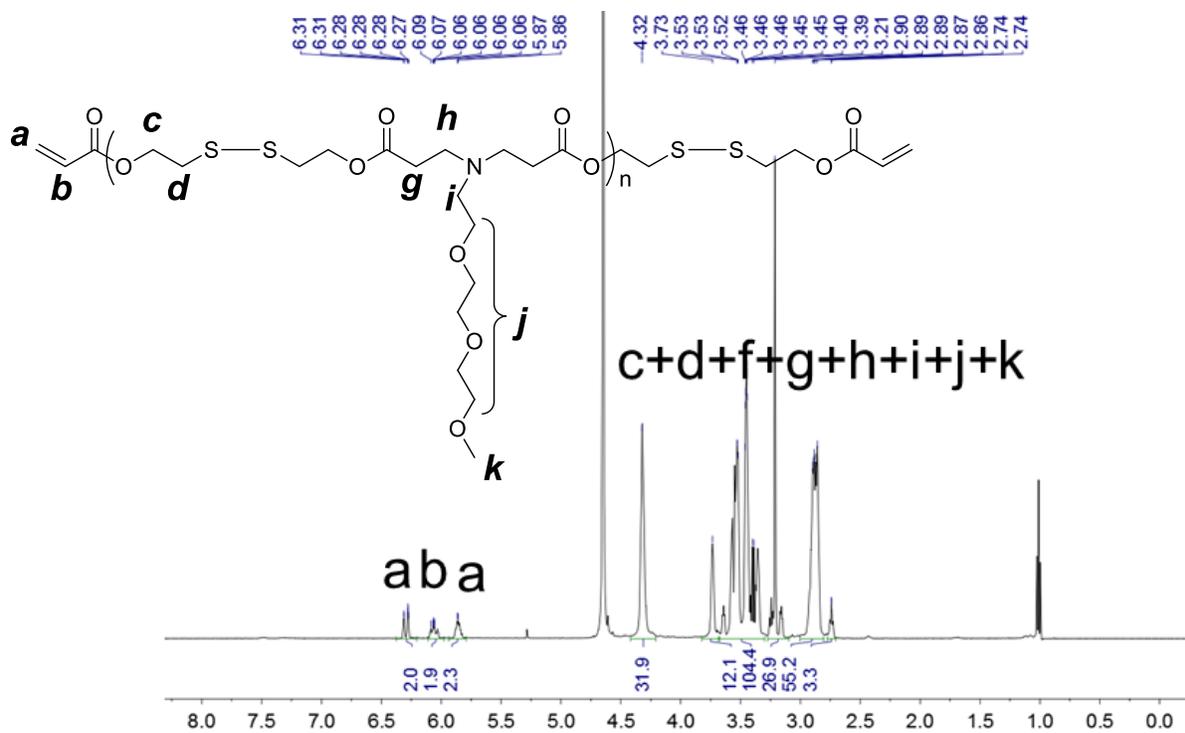


Figure S2. ¹H NMR of PBAE-SS in D₂O

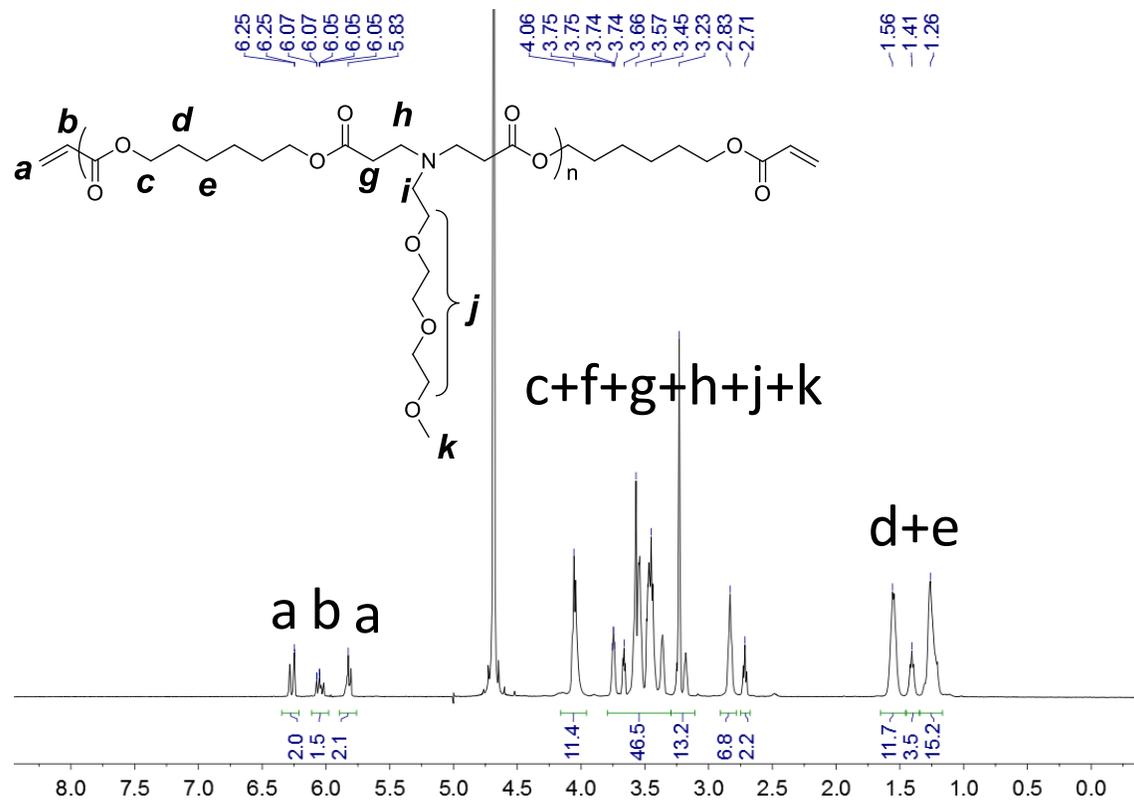


Figure S3. ^1H NMR of PBAE-CT in D_2O

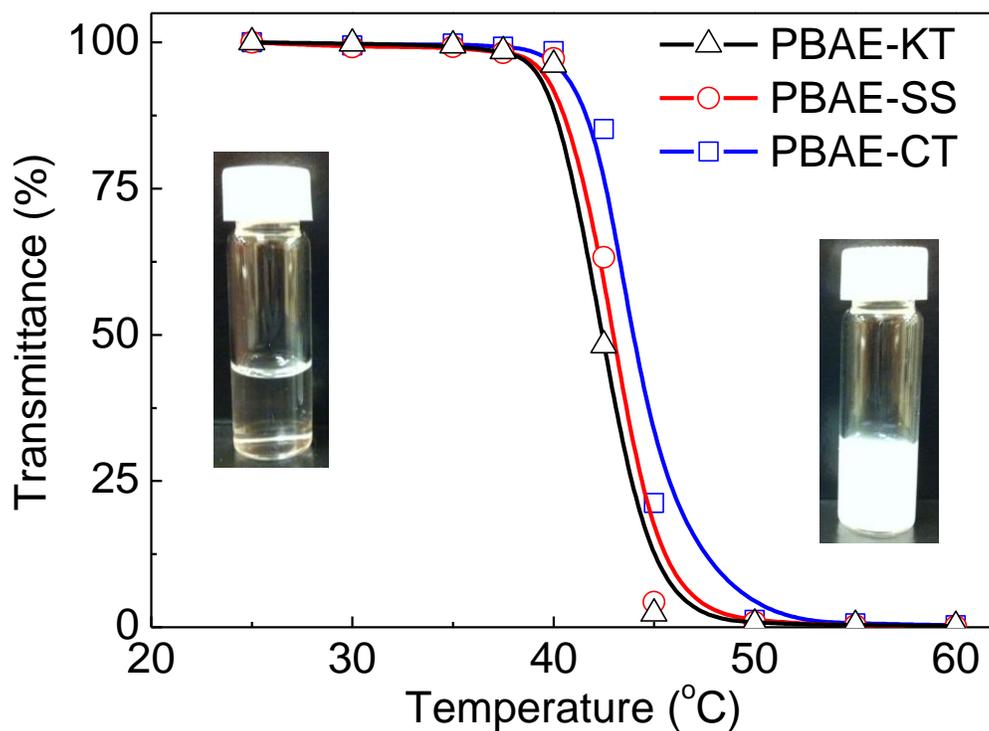


Figure S4. Temperature dependence of the transmittances of the solution of PBAE-KT, PBAE-SS and PBAE-CT in PBS (pH 7.4). The concentration of polymers was set at 5 mg/mL. The images shown here were PBAE-KT in PBS buffer (pH 7.4) at 25 °C (left) and 50 °C (right).

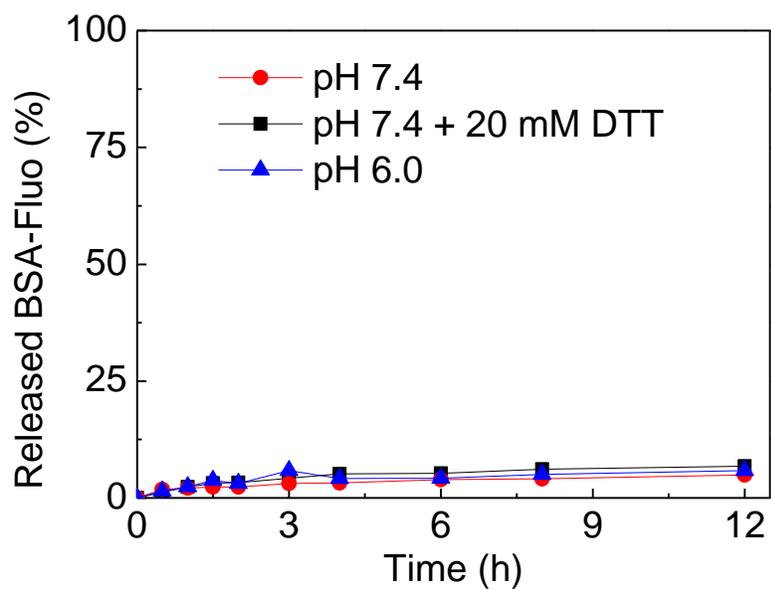


Figure S5. Release profiles of BSA-Fluo from PBAE-CT/PAA hydrogels at different pH in the absence or presence of 20 mM DTT.

Reference:

- (1) Gao, H. F.; Tsarevsky, N. V.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 5995.
- (2) Cohen, J. A.; Beaudette, T. T.; Cohen, J. L.; Brooders, K. E.; Bachelder, E. M.; Frechet, J. M. J. *Adv Mater* **2010**, *22*, 3593.
- (3) Dombi, K. L.; Griesang, N.; Richert, C. *Synthesis-Stuttgart* **2002**, 816.