

Supporting Information

‘Schizophrenic’ Micellization Associated with Coil-to-Helix Transitions Based on Polypeptide Hybrid Double Hydrophilic Rod-Coil Diblock Copolymer

Jingyi Rao, Zhaofeng Luo, Zhishen Ge, Hao Liu, and Shiyong Liu*

*Department of Polymer Science and Engineering, School of Life Science, Hefei
National Laboratory for Physical Sciences at the Microscale, University of Science
and Technology of China, Hefei, Anhui 230026, China*

* To whom correspondence should be addressed. E-mail: sliu@ustc.edu.cn

Sample Preparation. *Synthesis of γ -Benzyl-L-Glutamate N-Carboxyanhydride.*

N-Carboxyanhydride of γ -benzyl-L-glutamate (BLG) was prepared according to literature procedures with slight modification.^{1,2} Briefly, 50 mL triphosgene/THF solution (0.07 g/mL) was added to the suspension of BLG (7.0 g, 29.5 mmol) in 250 mL of anhydrous THF at 50 °C. After stirring for ~2 h, a clear solution was obtained. The reaction mixture was evaporated to dryness under reduced pressure to remove HCl and residual triphosgene. The resulting dry solids were re-dissolved in 80 mL anhydrous THF and then precipitated into an excess of anhydrous petroleum ether. This purification cycle was repeated for three times, yielding white crystals of BLG-NCA (~92% yield). ¹H NMR in CDCl₃, δ (ppm): 2.10-2.50 (m, 2H, CH₂), 2.74 (t, 2H, CH₂), 4.46 (t, 1H, CH), 5.25 (s, 2H, OCH₂), 6.35 (s, 1H, NH), 7.48 (m, 5H, C₆H₅).

Synthesis of PNIPAM₆₅-b-PBLG₁₁₀.^{3,4} Mono-amino-terminated PNIPAM (1 g, 0.14 mmol) was dissolved in ~30 mL anhydrous CH₂Cl₂ in a 250 mL baked flask. BLG-NCA (4.7 g, 18 mmol) was dissolved in 25 mL anhydrous CH₂Cl₂ in a separate 100 mL flask. The BLG-NCA/CH₂Cl₂ mixture was then cannulated into the PNIPAM₆₅-NH₂/CH₂Cl₂ solution via a double-tipped stainless needle. The reaction mixture was allowed to stir for 3 d at room temperature under dry N₂ atmosphere. After partially removing the solvents, the reaction mixture was precipitated into an excess of anhydrous diethyl ether. This purification cycle was repeated for 3 times. The obtained white solids were dried in a vacuum oven overnight at room temperature. The molecular weight and molecular weight distribution of PNIPAM-*b*-PBLG were determined by GPC using THF as the eluent: $M_n = 35,100$, $M_w/M_n = 1.29$. The actual degree of polymerization (DP) of PBLG block was determined to be 110 by ¹H NMR analysis in CDCl₃ (containing ~10 v/v% TFA). The obtained diblock copolymer was denoted as PNIPAM₆₅-*b*-PBLG₁₁₀.

Synthesis of PNIPAM₆₅-b-PLGA₁₁₀. The removal of protecting benzyl groups was carried out as follows. PNIPAM₆₅-*b*-PBLG₁₁₀ diblock copolymer (1.0 g, 0.03 mmol) was dissolved in 40 mL THF, aqueous NaOH solution (1.0 mL, 25 wt%) was then added. After stirring for 12 h at room temperature, the solvents were removed under reduced pressure. The obtained solids were redispersed in water and the solution pH

was adjusted to 3 with the addition of HCl. The aqueous solution was then dialyzed against deionized water for 12 h using semipermeable membranes with a cutoff molar mass of 3,500 g/mol. The obtained PNIPAM₆₅-*b*-PLGA₁₁₀ was dried in a vacuum oven overnight at room temperature. The complete removal of benzyl protecting groups was further confirmed by ¹H NMR and FT-IR analysis.

References

- (1) Wang, L. Y.; Wang, S. G.; Bei, J. Z. *Polym. Adv. Technol.* **2004**, *15*, 617-621.
- (2) Daly, W. H.; Poche, D. *Tetrahedron Lett.* **1988**, *29*, 5859-5862.
- (3) Cheon, J. B.; Jeong, Y. I.; Cho, C. S. *Polymer* **1999**, *40*, 2041-2050.
- (4) Cho, C. S.; Cheon, J. B.; Jeong, Y. I.; Kim, I. S.; Kim, S. H.; Akaike, T. *Macromol. Rapid Commun.* **1997**, *18*, 361-369.

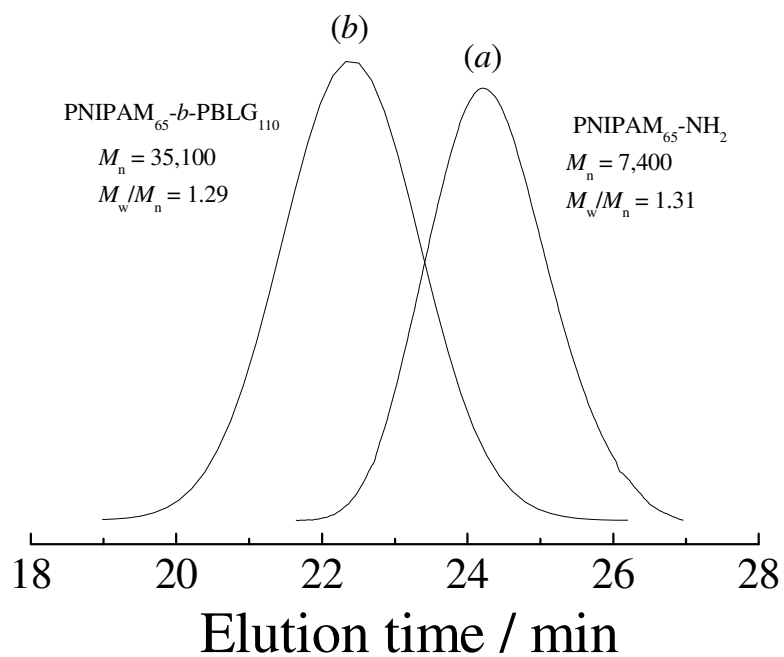


Figure S1. GPC traces of mono-amino-terminated PNIPAM precursor and $\text{PNIPAM}_{65}\text{-}b\text{-PBLG}_{110}$ diblock copolymer.

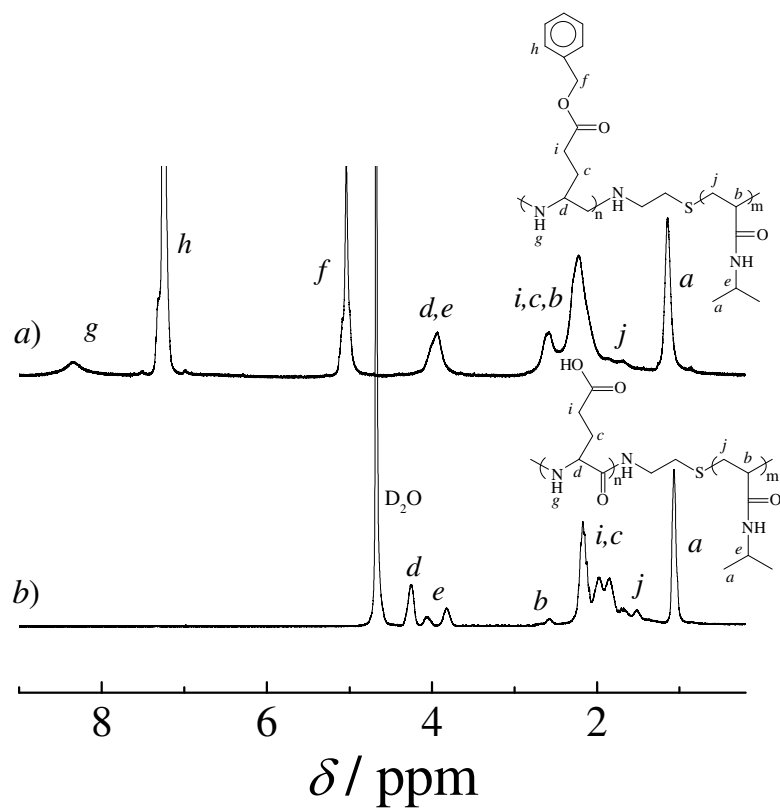


Figure S2. ^1H NMR spectra of (a) $\text{PNIPAM}_{65}\text{-}b\text{-PBLG}_{110}$ in CDCl_3/TFA mixture, and (b) $\text{PNIPAM}_{65}\text{-}b\text{-PLGA}_{110}$ in D_2O at pH 10.

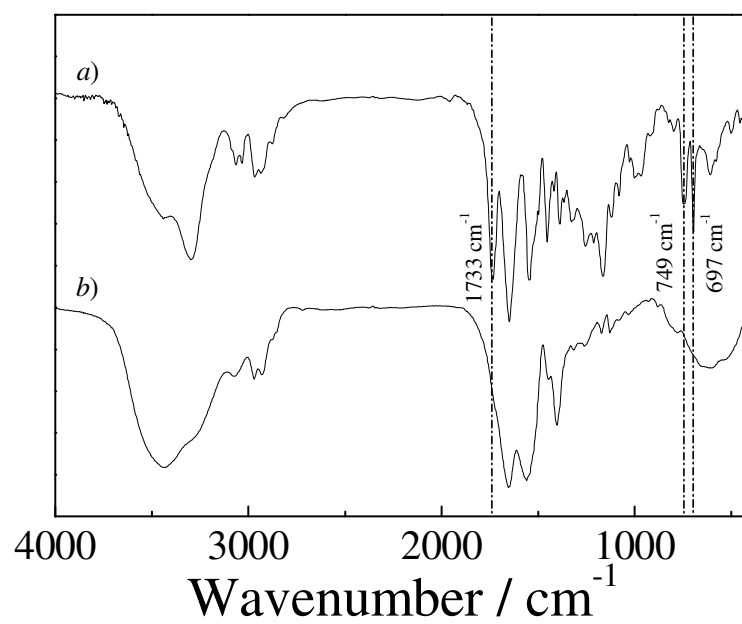


Figure S3. FT-IR spectra of (a) PNIPAM₆₅-*b*-PBLG₁₁₀ and (b) the hydrolyzed product, PNIPAM₆₅-*b*-PLGA₁₁₀.

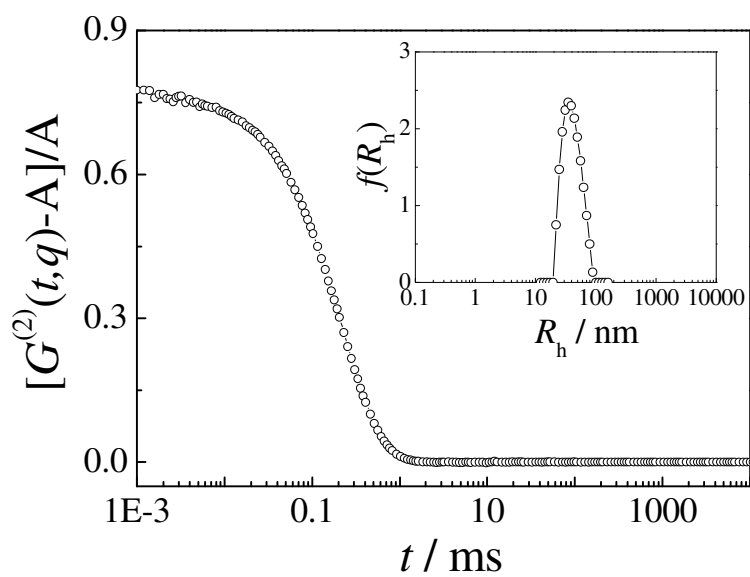


Figure S4. Typical intensity-intensity time correlation function $G^{(2)}(t,q)$ obtained for 1.0 g/L aqueous solution of PNIPAM₆₅-*b*-PLGA₁₁₀ at pH 10 and 35 °C. The inset shows typical hydrodynamic radius distribution, $f(R_h)$.