Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Zwitterionic Polypeptides Bearing Carboxybetaine and Sulfobetaine: Synthesis, Self-Assembly, and Their Interactions with Proteins

Yu-Lin Tsai,[1] Yu-Chao Tseng, [1] Yan-Miao Chen,[2] Tain-Ching Wen, [1] and Jeng-Shiung Jan[*,1]*

[1] Department of Chemical Engineering, National Cheng Kung University, Tainan City 70101, Taiwan

[2] Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung City 80708, Taiwan

Experimental Section

Protein interactions. For zwitterionic homopolypeptides, the polypeptide solutions (1 mg/mL) were prepared and the protein solutions (10 mg/mL) with a designated volume were added to the solutions. The resultant solutions were mixed well and measured by a Scinco S-3100 spectrophotometer.

Results and Discussion

Interactions of helical, zwitterionic homopolypeptides and proteins

The interactions between the helical, zwitterionic homopolypeptides (**3a** and **3b**) and proteins were investigated in order to evaluate the zwitterionic nature of these helical polypeptides. The three proteins, BSA, Mb, and LYZ, were selected as model protein due to their difference in the isoelectric point (pI) values. It is well known that the pI values for BSA, Mb, and LYZ were pH 4.7, 7.2, and 11.35, respectively. Hence, BSA and LYZ would be negatively and positively charged at neutral condition, respectively. Rather, Mb would carry little charge at neutral condition. The transmittance spectra of the resultant solution at the wavelength of 300-800 nm were shown in Figure S9. As expected, the helical, zwitterionic homopolypeptides exhibit no apparent interactions with BSA, evidenced by the little change in the transmittance. In the case of Mb, the percentage of transmittance decreased linearly with the increase of protein concentration, which was mainly due to the UV-vis absorption of Mb. It revealed that the helical, zwitterionic homopolypeptides exhibited no apparent interactions with Mb. In the case of LYZ, **3a** exhibit low interactions with LYZ, evidenced by the percentage of transmittance higher than 70%. However, **3b** strongly interacted with LYZ, evidenced by the drastic decrease in the percentage of transmittance upon increasing the protein concentration. The relatively low interactions between **3a** and LYZ can be mainly attributed that **3a** carried less charge than **3b** at neutral condition because the pI

value of **3a** (i.e., pH 7.1) was close to neutral condition. **3b** would instead carry negative charge at neutral condition because the pI value of **3b** was away from the neutral condition.

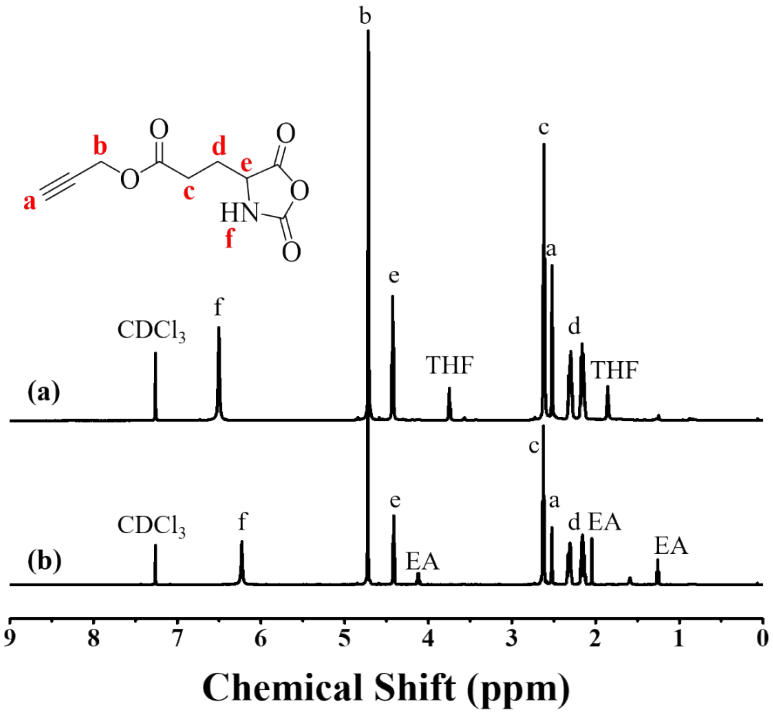

Fig. S1. ^{1}H NMR spectra of PLG NCA (a) before and (b) after purification in $CDCl_3$.

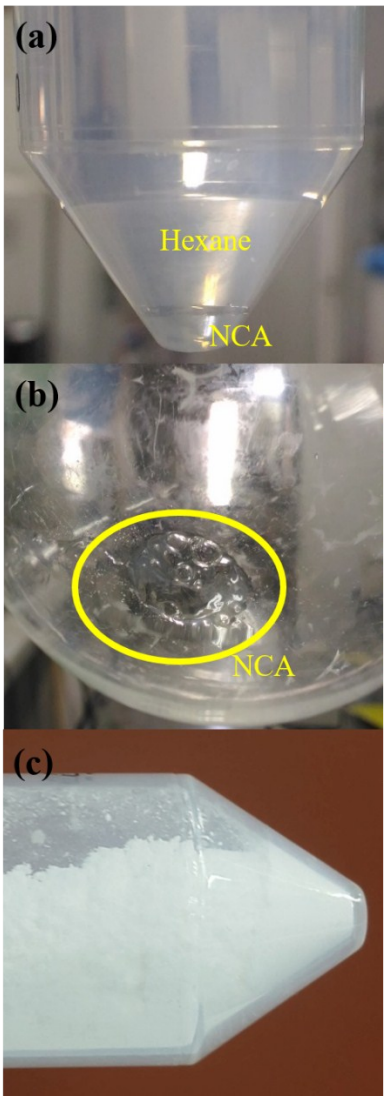

Fig. S2. Optical photograph images of (a, b) PLG NCA (colorless oil) and (b) $PPLG_{20}$ (white powder).

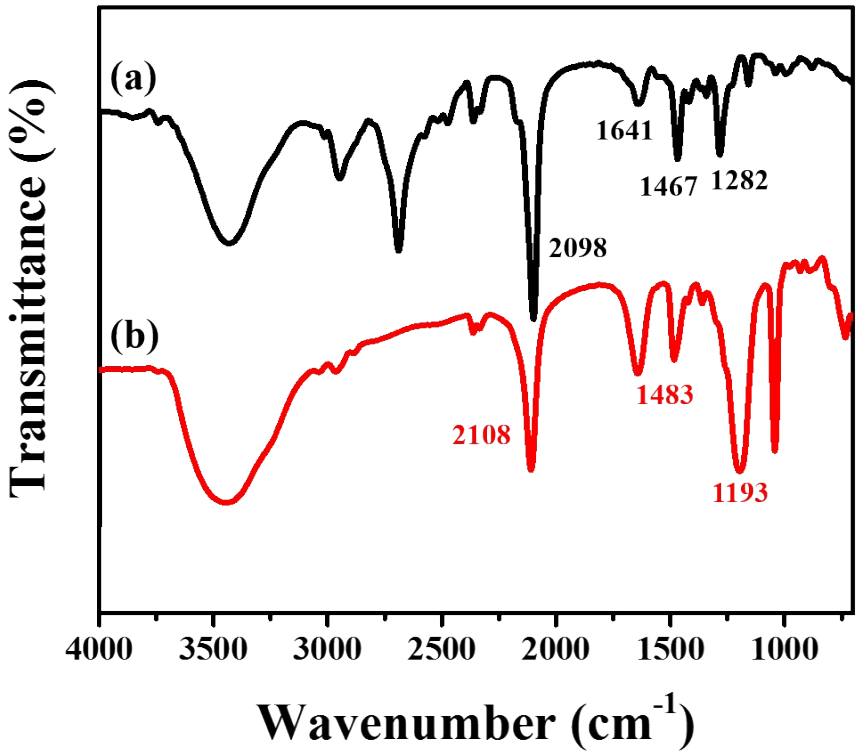

Figure S3. FTIR spectra of (a) N_3CB (**1a**) and (b) N_3SB (**1b**) monomers in the solid state.

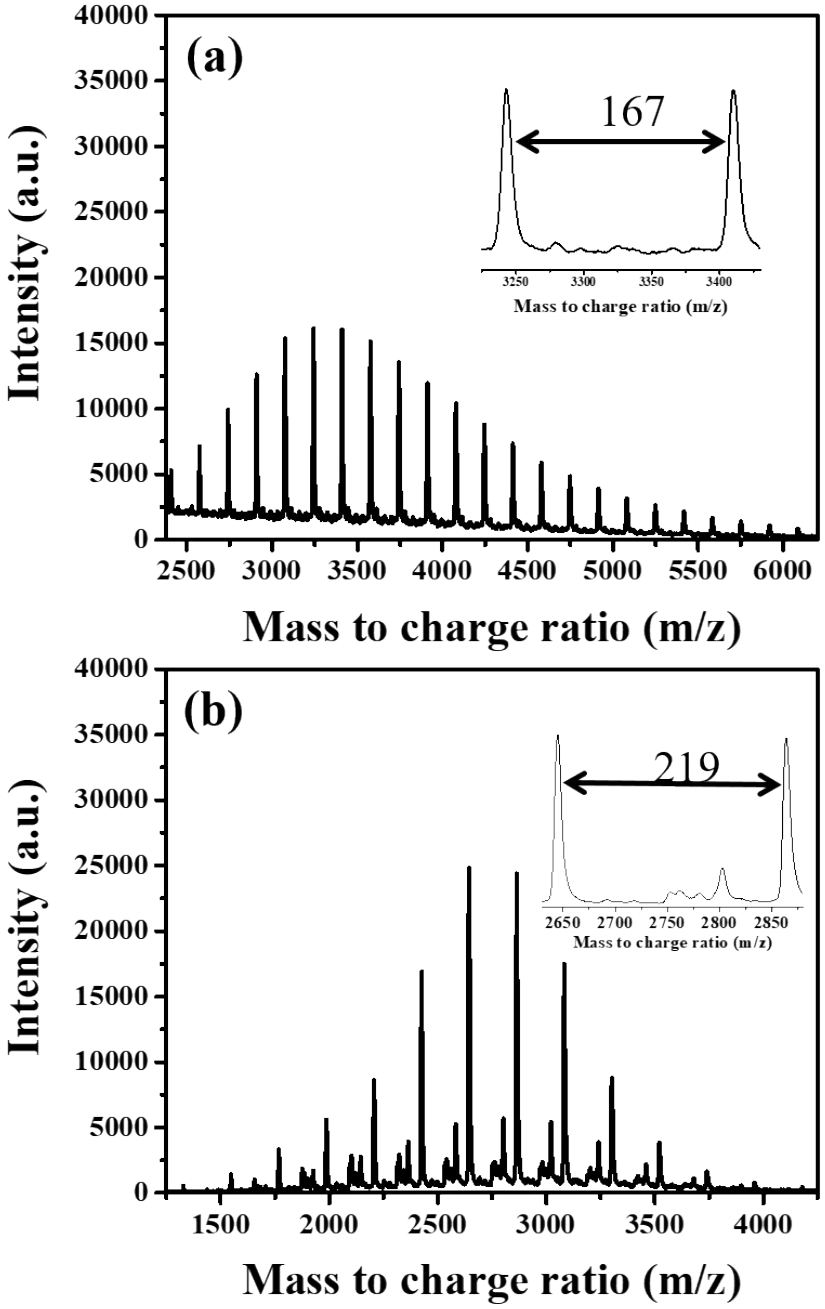

Fig. S4. MALDI-TOF spectra of (a) $PPLG_{20}$ and (b) $PBLG_{13}$.

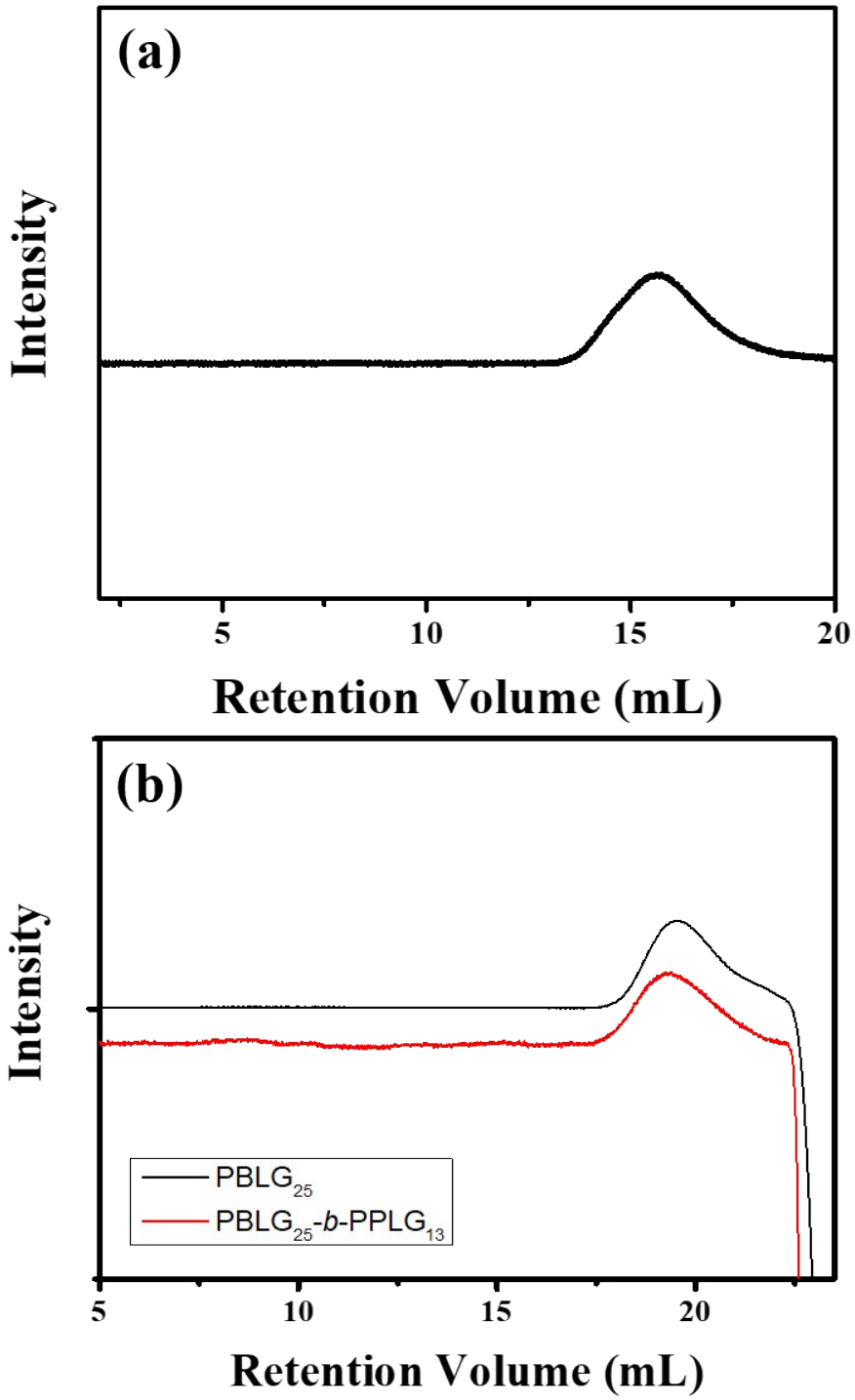

Fig. S5. GPC chromatograms of (a) $PPLG_{60}$ and, (b) $PBLG_{25}$ and $PBLG_{25}$-*b*-$PPLG_{13}$.

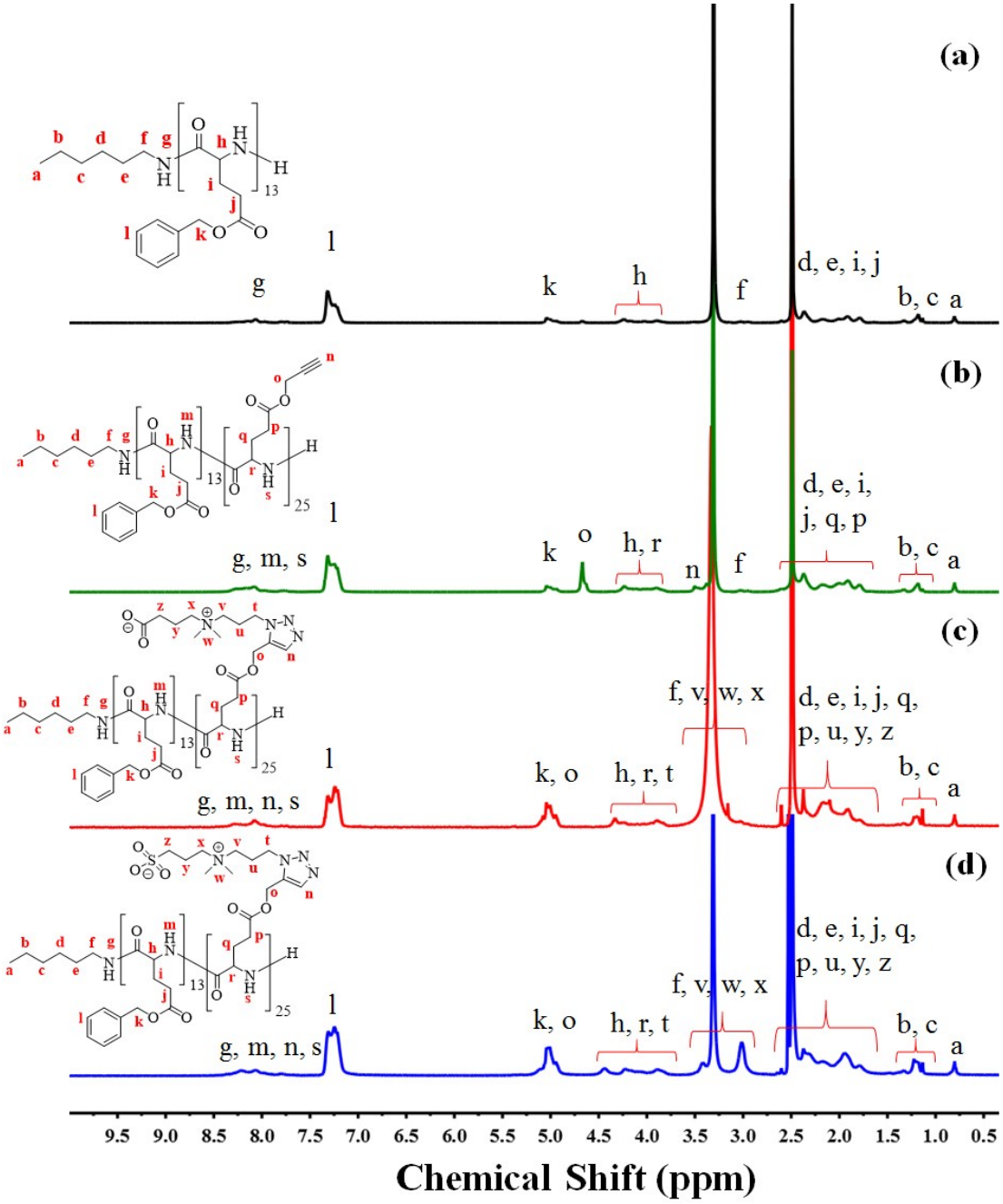

Figure S6. ^{1}HNMR spectra of (a) $PBLG_{13}$, (b) $PBLG_{13}$-*b*-$PPLG_{25}$ (**5**), (c) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-CB) (**5a**), and (d) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-SB) (**5b**) in DMSO-d_6.

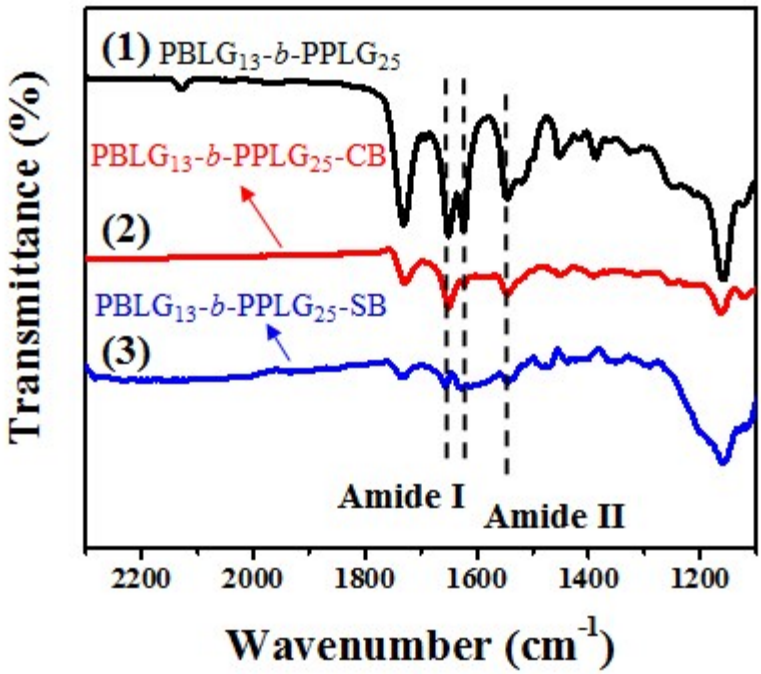

Figure S7. FTIR spectra of (1) $PBLG_{13}$-*b*-$PPLG_{25}$ (**5**), (2) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-CB) (**5a**), and (3) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-SB) (**5b**) in the solid state.

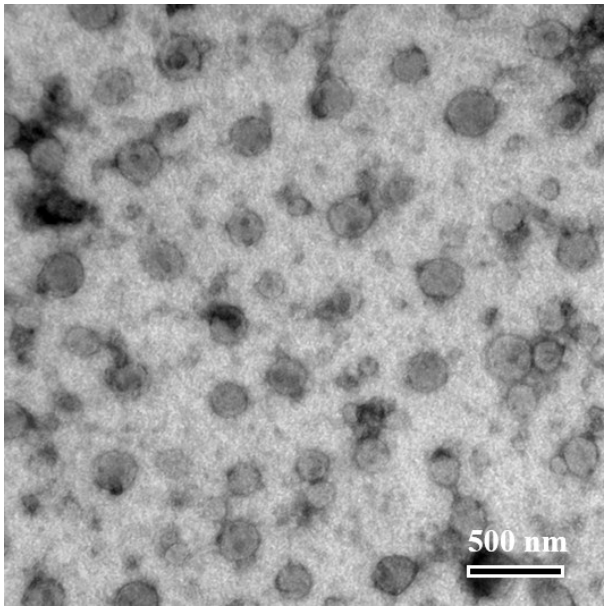

Figure S8. TEM image of the assemblies formed by $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-SB) (**5b**) zwitterionic polypeptide. The sample was stained by RuO_4.

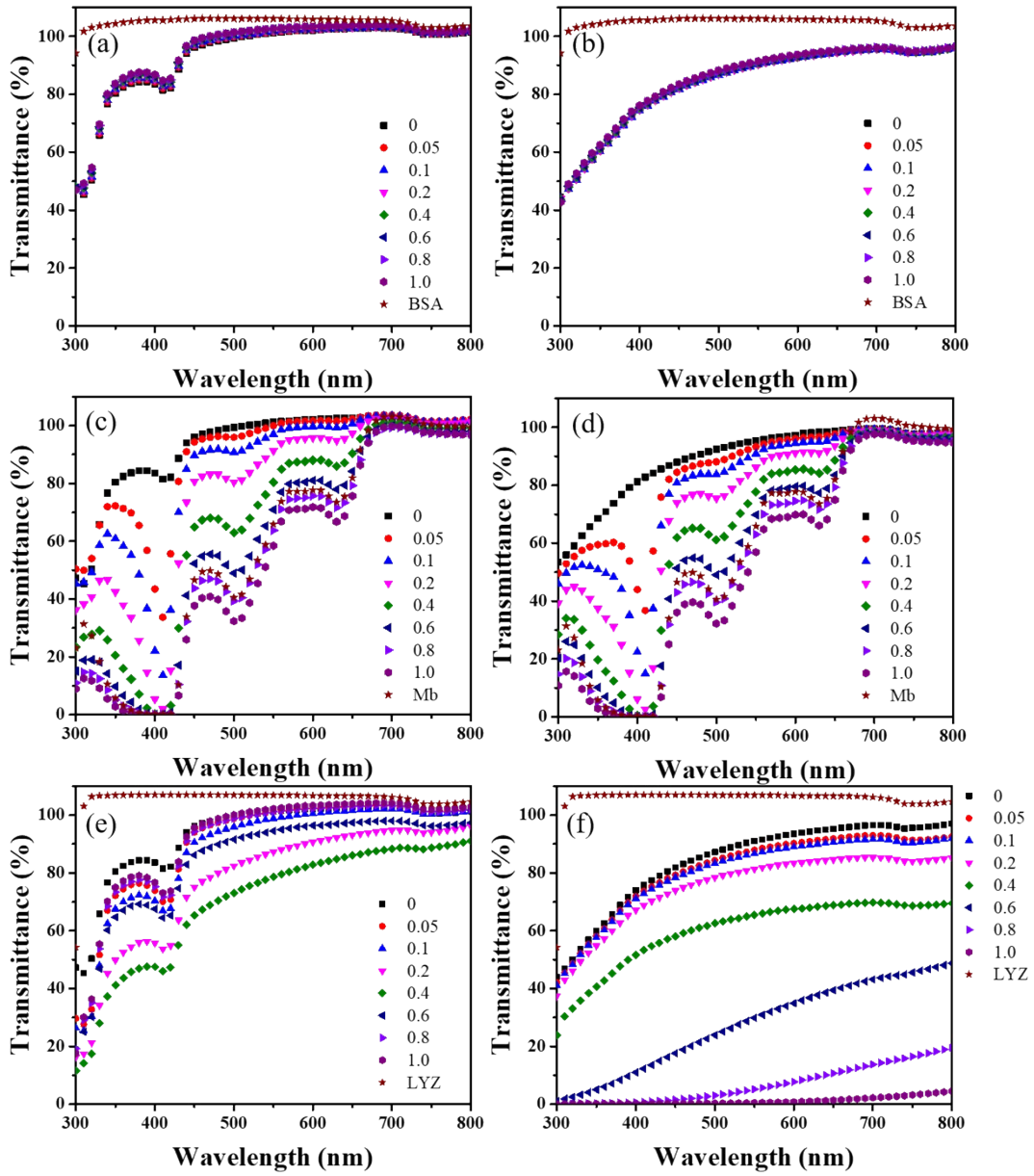

Figure S9. Transmittance spectra of (a, c, e) $PPLG_{60}$-*g*-CB (**3a**) and (b, d, f) $PPLG_{60}$-*g*-SB (**3b**) zwitterionic polypeptides in the presence of (a, b) BSA, (c, d) Mb, and (e, f) LYZ as a function of protein concentration. The polypeptide concentration was 1 mg/mL.

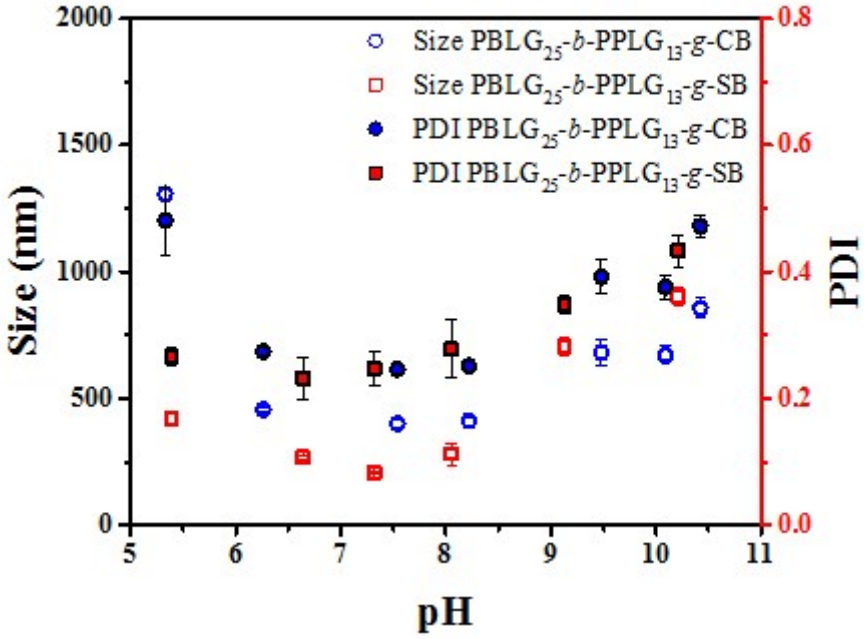

Figure S10. Hydrodynamic diameter (size) and polydispersity index (PDI) of $PBLG_{25}$-*b*-($PPLG_{13}$-*g*-CB) (**4a**) and $PBLG_{25}$-*b*-($PPLG_{13}$-*g*-SB) (**4b**) zwitterionic assemblies at different solution pH.

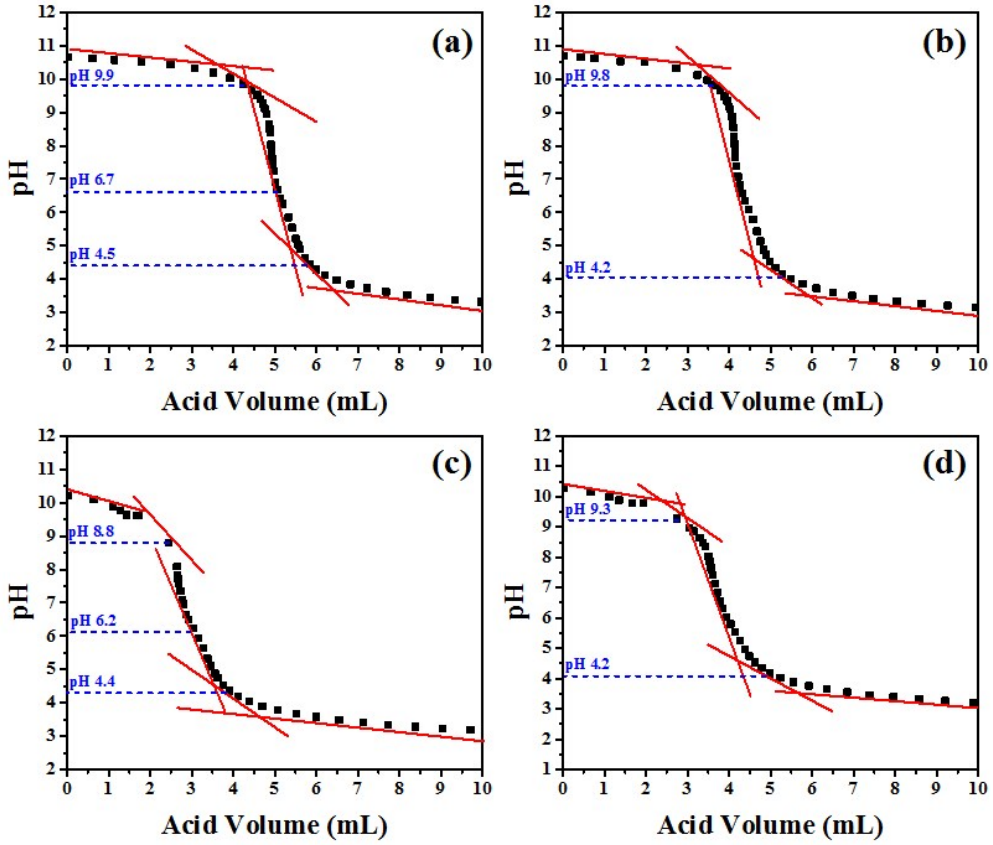

Figure S11. Titration curve of (a) $PBLG_{25}$-*b*-($PPLG_{13}$-*g*-CB) (**4a**), (b) $PBLG_{25}$-*b*-($PPLG_{13}$-*g*-SB) (**4b**), (c) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-CB) (**5a**), and (d) $PBLG_{13}$-*b*-($PPLG_{25}$-*g*-SB) (**5b**) zwitterionic copolypeptides in DI water.