Supplementary Information

Biocompatible Acid-Labile Polymersomes from PEO-*b*-PVA Derived Amphiphilic Block Copolymers.

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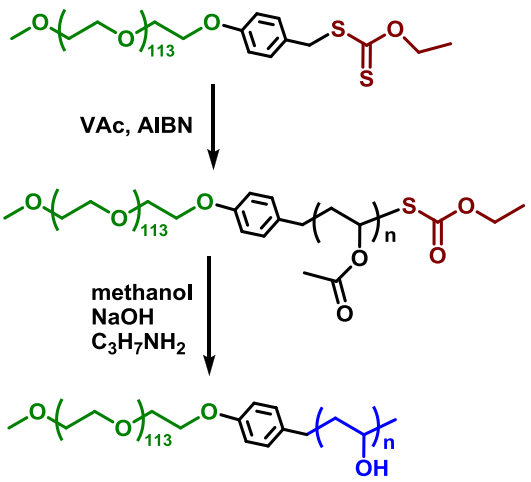
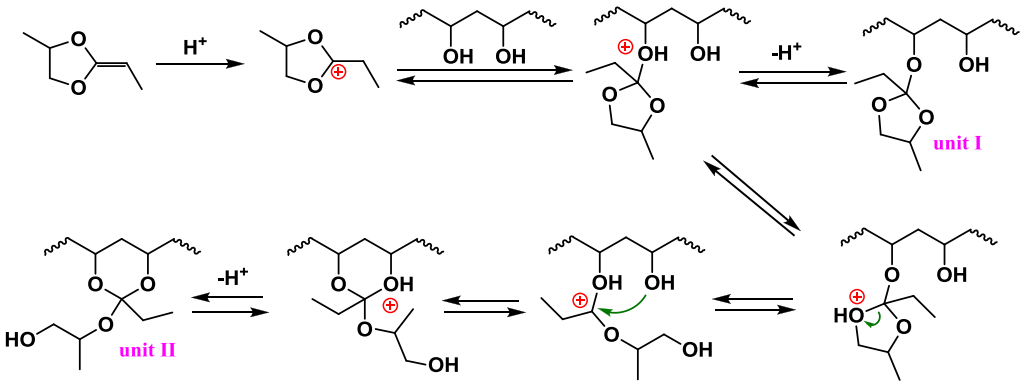
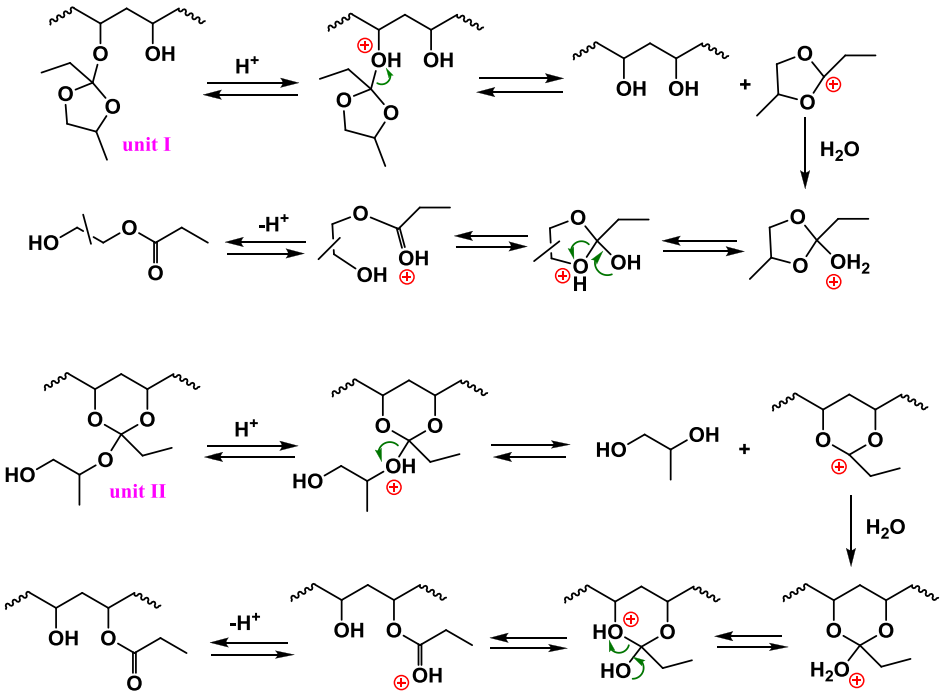


Scheme S1. Synthetic route of block copolymer PEO_{114}-*b*-PVA_{240}.



Scheme S2. The mechanism of PVA modification by EMD.



Scheme S3. The mechanism of acid-catalyzed hydrolysis of the cyclic ortho ester groups. The exocyclic C-O bond breaks first during acid-catalyzed hydrolysis of the cyclic ortho esters. Therefore, hydrolysis of unit II generates the propanoic ester as a pendent moiety in the PVA chain.

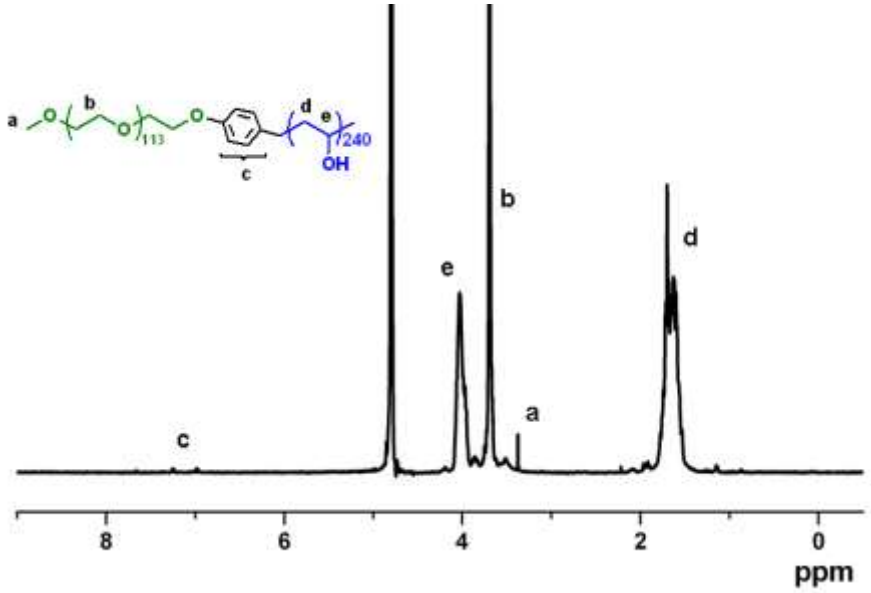


Figure S1. ^{1}H NMR spectrum of block copolymer PEO_{114}-*b*-PVA_{240} in D_2O. The polymerization degree of PVA block is calculated by comparing the intensity of peak "d" and peak "a". After fully acetylation, the block copolymer PEO_{114}-*b*-$PVAc_{240}$ is soluble in THF. The polydispersity index as characterized by GPC is 1.44.

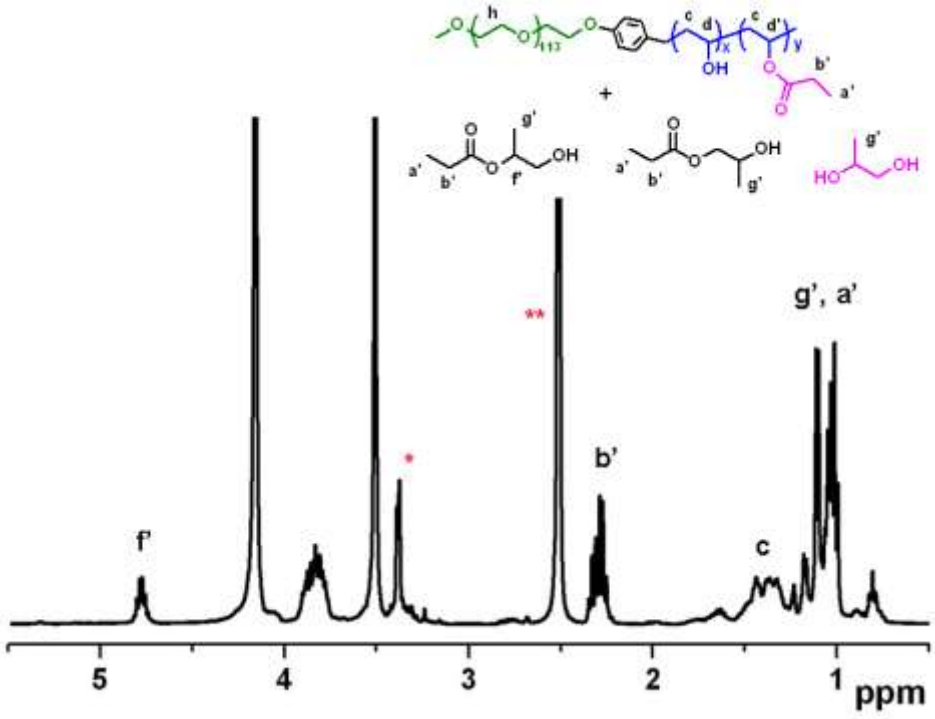


Figure S2. ^{1}H NMR spectrum of the *in situ* hydrolyzed copolymer **P1** in d^{6}-DMSO.

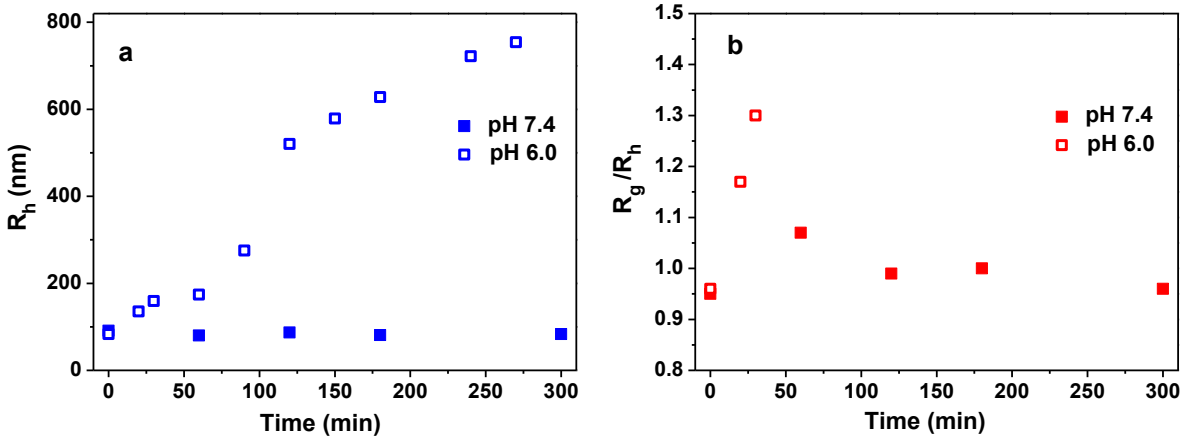
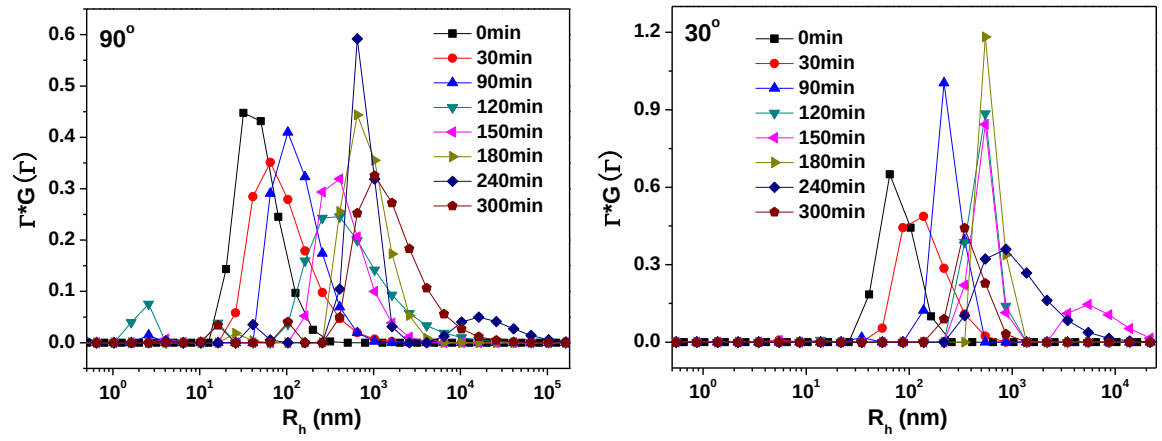


Figure S3. Incubation time-dependent change of (a) R_h and (b) R_g/R_h of **P1** polymersomes at different pH. Buffer concentration: 50 mM; polymer concentration: 0. 2 mg/mL; 37 °C.

(a)



(b)

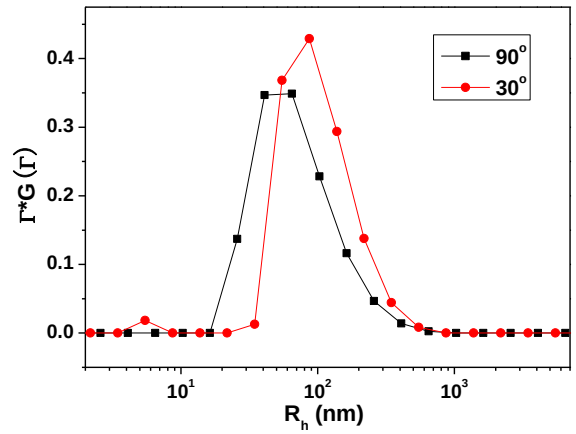


Figure S4. CONTIN analysis of (a) **P1** polymersomes at selected time points during the incubation at pH 6.0; (b) CONTIN analysis of **P1** polymersomes after 30 min of incubation at pH 5.0. Polymer concentration: 0.2 mg/mL; temperature: 37 °C.

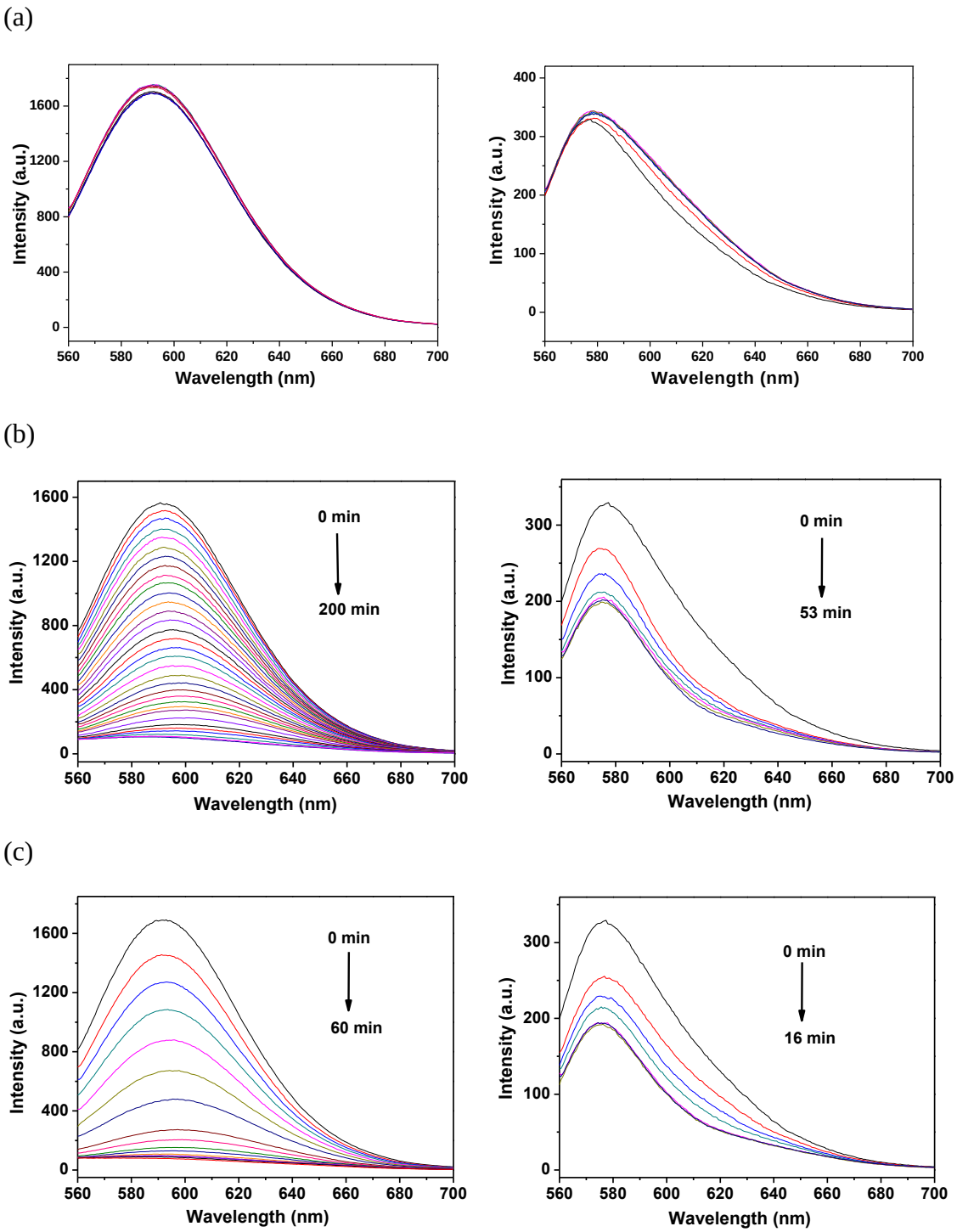


Figure S5. Fluorescence spectra of NR in **P1** polymersome (left) and **P4** nanoparticle (right) aqueous dispersions at pH (a) 7.4 (0-200 min), (b) 6.0, and (c) 5.0. λ_{ex} = 545 nm; 37 ^{o}C; polymer concentration: 0.5 mg/mL; NR concentration: 1.0 x 10^{-6} M.