Supramolecular Crosslinks Enable PIC Micelles with Tuneable Salt Stability and Diverse Properties

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Experimental section

Materials

The diblock copolymer, poly(N-methyl-2-vinyl-pyridinium iodide)-b-poly(ethylene oxide) ($P2MVP_{128}$-b-PEO_{477}), was obtained by quaternization of poly(2-vinylpyridine)-b-poly(ethylene oxide) ($P2MVP_{128}$-*b*-PEO_{477}) (Polymer Source, Mw/Mn= 1.10, Mn= 34.5 k) following a procedure described elsewhere.[1] The quaternary ammonia ratio is about 90%. The bis-ligand compound 1,11-bis(2,6-dicarboxypyridin-4-yloxy)-3,6,9-trioxaundecane (L_2) and tris-ligand compound 1,3,5-tris(2,6-dicarboxypyridin-4-yloxymethyl)benzene (L_3) was synthesized according to literature.[2,3] Zinc(Ⅱ) nitrate hexahydrate $Zn(NO_3)_3 \cdot 6H_2O$, Europium(Ⅲ) nitrate hexahydrate $Eu(NO_3)_3 \cdot 6H_2O$, terbium nitrate $Tb(NO_3)_3.6H_2O$ and Gadolinium chloride $GdCl_3.6H_2O$, MES salt $C_6H_{13}NO_4S$ were purchased from Sigma-Aldrich and used without further purification. Nile red $C_{20}H_{18}N_2O_2$ were purchased from J&K Scientific and used without further purification. The deionized water was applied as solvent and all samples were prepared in 20 mM MES buffer at pH 6.

Preparation and salt titration of PIC micelles

All stock solutions were prepared by dissolving an appropriate amount of block copolymer, $Zn(NO_3)_3 \cdot 6H_2O$, $Eu(NO_3)_3 \cdot 6H_2O$, $Tb(NO_3)_3.6H_2O$, $GdCl_3.6H_2O$ and the ligand in deionized water. PIC micelles were prepared by mixing the designed components under the coordination and charge stoichiometry in in 20mM MES buffer at pH 6. For preparing Zn-Ln-L_2 micelles, the bis-lingadd and diblock copolymer concentrations are fixed, and the metal concentration, for Zn(II) is 1 mM, corresponding to 0.67 mM of Ln(III). For Zn-L_2-L_3 micelles, the Zn(II) concentration is fixed at 0.3 mM due to the limited solubility of the L_3 ligand. Mixing all the components hardly change the solution pH, and the ionic strength because of that the counter ions from all the building blocks are only around few mM, which gives only limited change to the ionic strength due to the 20 mM of the buffer salt. Salt-persistent stability were investigated by titrating 5M NaCl to the micellar solution, and followed by the recording of the light scattering intensity and hydrodynamic radius after each titration step.

Light Scattering.

The light scattering at a 90° angle is carried out with an ALV light scattering device, which is equipped with a 22mW argon ion laser with a working wavelength of 632.8nm. All samples were tested at room temperature. The light scattering intensity is expressed as the excess Rayleigh ratio R_θ divided by the total polymer concentration. R_θ is obtained as

$$R_\theta = \frac{I_{sample} - I_{solvent}}{I_{toluene}} \times R_{toluene} \times \frac{n^2_{solvent}}{n^2_{toluene}} \tag{1}$$

where I_{sample} is the scattering intensity of the micellar solution and $I_{solvent}$ is the intensity of the solvent. $I_{toluene}$ is the scattering intensity of toluene, $R_{toluene}$ is the known Rayleigh ratio of toluene ($2.1 \cdot 10^{-2}$ m^{-1}) and n is the refractive of solvent (1.333) and toluene (1.497). The CUMULANT method[4] was used to analyze the mean apparent hydrodynamic radius (R_h) and the polydispersity index (PDI). R_h is calculated from the average decay rate Γ and the PDI from the second moment μ_2, according to the following formulas:

$$R_h = kTq^2 / 6\pi\eta\Gamma \tag{2}$$

$$PDI = \mu_2 / \Gamma^2 \tag{3}$$

where q is the scattering vector, k is the Boltzman constant, T is the absolute temperature, η is the viscosity of the solvent. The CONTIN method[5,6] was used to analyze the distribution of particle radii.

For angular-dependent LS, six correlation functions $g_2(t)$ were recorded at 6 angles θ, from 50° to 150° at intervals of 20°. And the diffusion coefficient D of the micelles is plotted as a function of the scattering vector q, which is

$$q = \left(\frac{4\pi n}{\lambda}\right) \sin\left(\frac{\theta}{2}\right)$$

Fluorescence spectroscopy

Micelles solution was put in 1.0 cm quartz cells for steady state measurements on a Cary-4000 spectrometer. The slit was set at 10 nm and the spectra were corrected for the instrumental function. The excitation is set at 277 and 395 nm, and the emission spectra was recorded in the range of 550–720 nm. The concentration of Ln(III) was fixed at 0.1 mM in all samples.

Methanol solution of Nile Red was added dropwise to the prepared micelles solution, and the final Nile Red concentration was 1 μg/ml. Sample was put in 1.0 cm quartz cells for steady state on a Cary Eclipse Fluorescence Spectrophotometer. The excitation and emission slit were set at 10 nm. The excitation was set at 545 nm, and the emission spectra was recorded in range of 580-800 nm.

Transmission Electronic Microscopy (TEM)

TEM was performed on a JEM-1400 electron microscope operating at 100 kV. 230-mesh copper grids were coated with formvar support film followed by subsequent coating with carbon. 10 μL of the sample solution was placed on the copper grids, and the excess solution was absorbed by lens paper, and the copper grids were dried at room temperature.

MRI relaxation and imaging test

The MRI testing and T_1 relaxation time measurements were tested at a 0.47 T NMRI20-Analyst NMR Analyzing and Imaging system (Niumai Corporation, Shanghai, China).

Figure S1

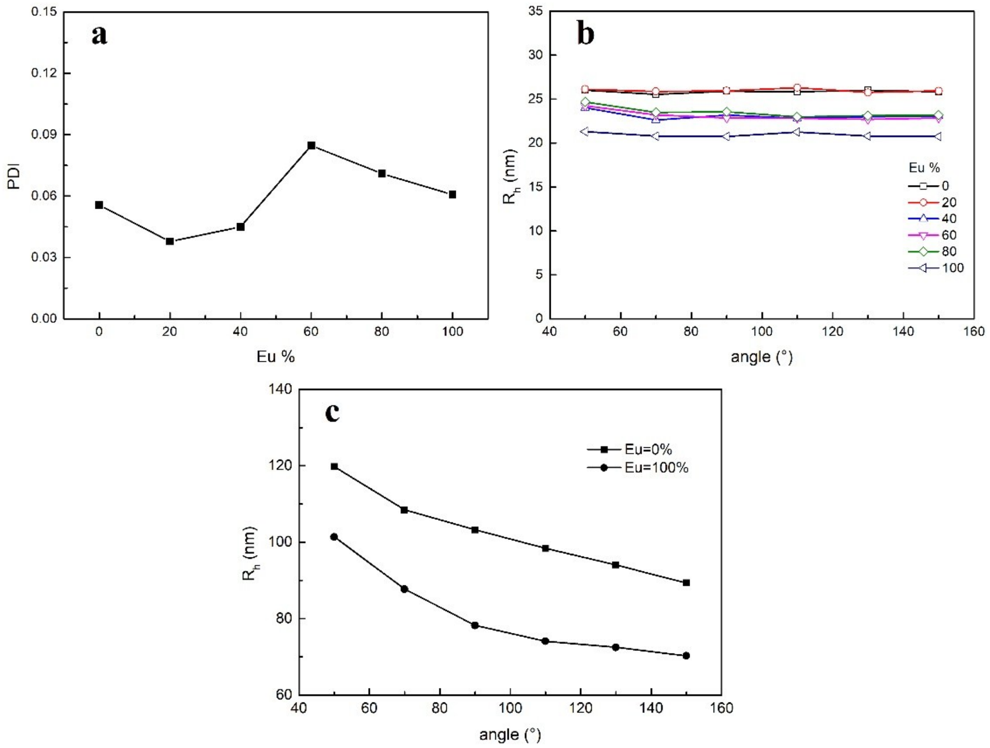

Figure S1. a) Polydispersity index (PDI) of Zn-Eu-L_2 micelles as a function of Eu%. b) Size of Zn-Eu-L_2 micelles at different light scattering detect angles. c) Angular dependent of Zn-Eu-L_2 micelles at salt concentration under which the intensity jumps due to the morphology transition.

Figure S2

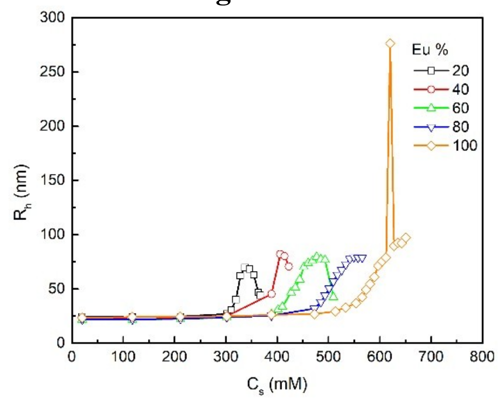

Figure S2. Variations of hydrodynamic radius upon adding NaCl into Zn-Eu-L_2 micelles solution.

Figure S3

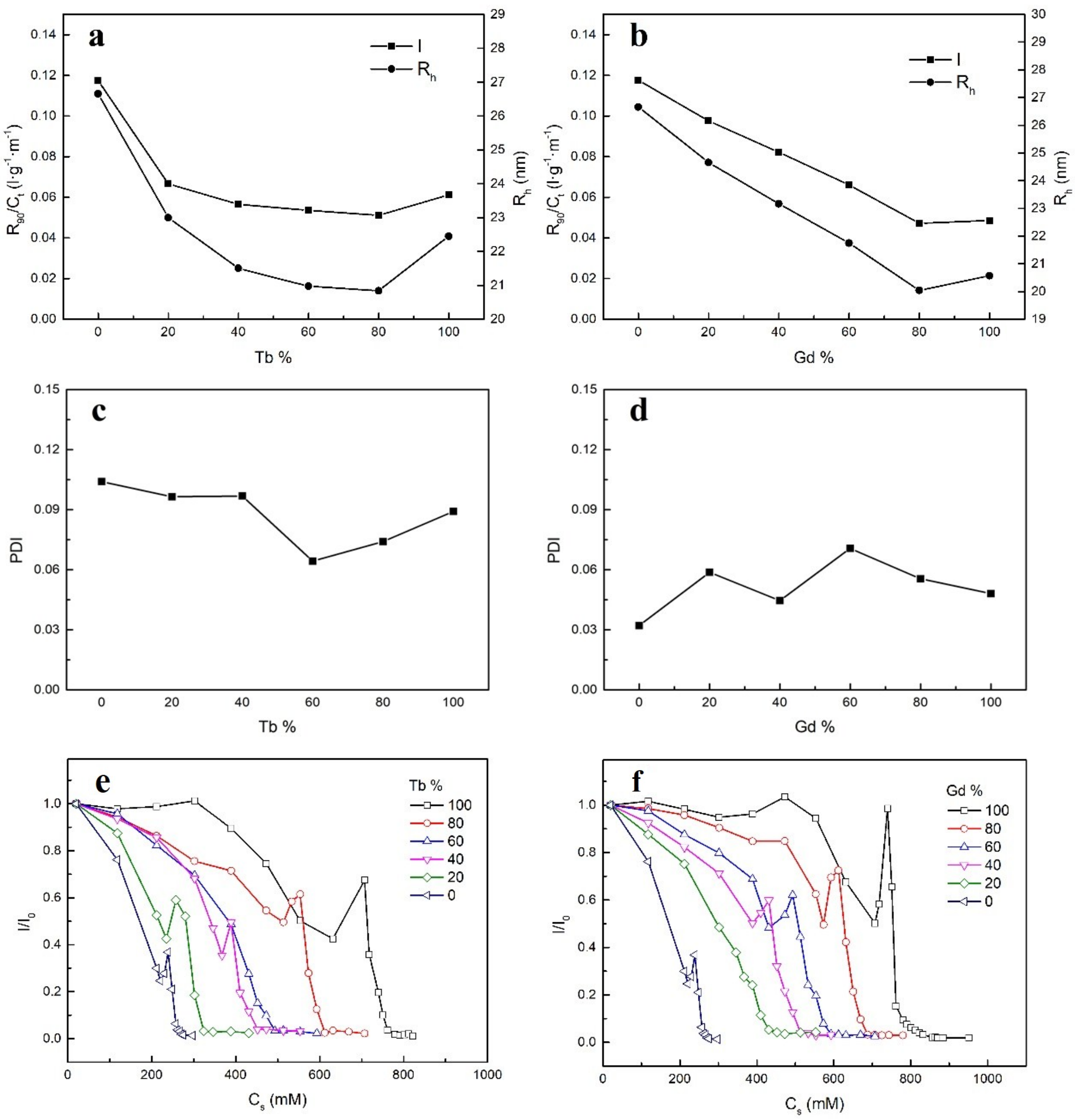

Figure S3. a) Light-scattering intensity and hydrodynamic radius of micelles at different Gd/Zn ratio. b) Light-scattering intensity and hydrodynamic radius of micelles at different Tb/Zn ratio. c) Polydispersity index (PDI) of Zn-Tb-L_2 micelles as a function of Tb%. d) PDI of Zn-Gd-L_2 micelles as a function of Gd%. e) Light-scattering intensity for Zn-Gd-L_2 micelles at different Gd/Zn ratio with increasing salt concentration. f) Light-scattering intensity for Zn-Tb-L_2 micelles at different Tb/Zn ratio with increasing salt concentration.

Figure S4

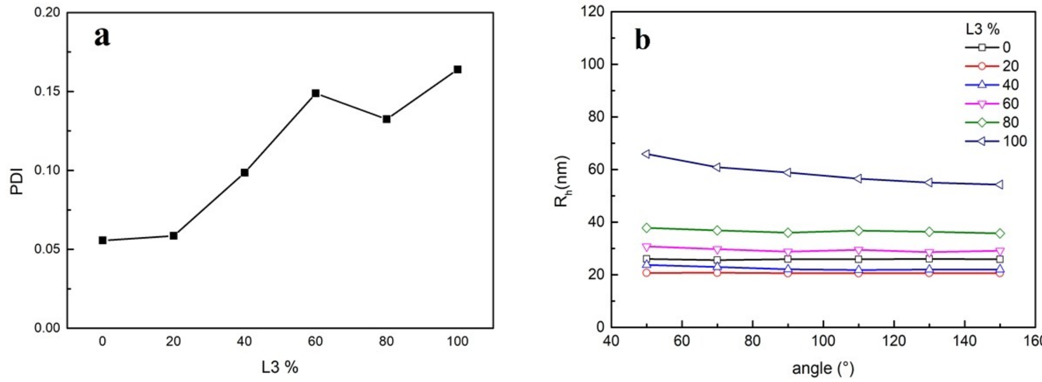

Figure S4. a) Polydispersity index (PDI) of Zn-L_2-L_3 micelles as a function of L_3%. b) Hydrodynamic radius of Zn-L_2-L_3 micelles at different light scattering detect angels.

Figure S5

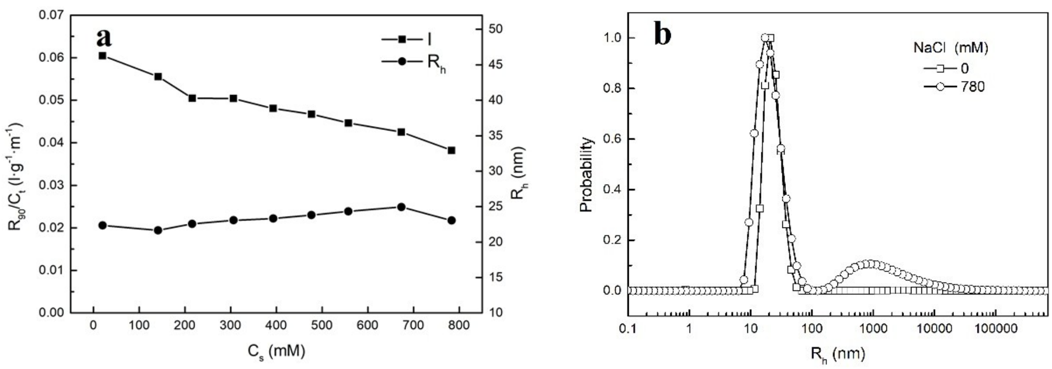

Figure S5. a) Changes in scattering intensity and hydrodynamic radius upon adding NaCl into Zn-L_2-L_3 micelles solution (40% of L_3); b) CONTIN analysis of Zn-L_2-L_3 micelles at different salt concentration.

Figure S6

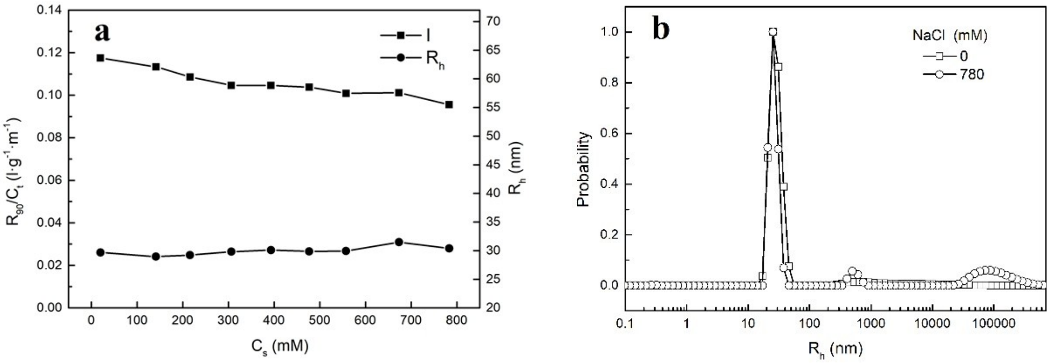

Figure S6. a) Changes in scattering intensity and hydrodynamic radius upon adding NaCl into Zn-L_2-L_3 micelles solution (60% of L_3); b) CONTIN analysis of Zn-L_2-L_3 micelles at different salt concentration.

Figure S7

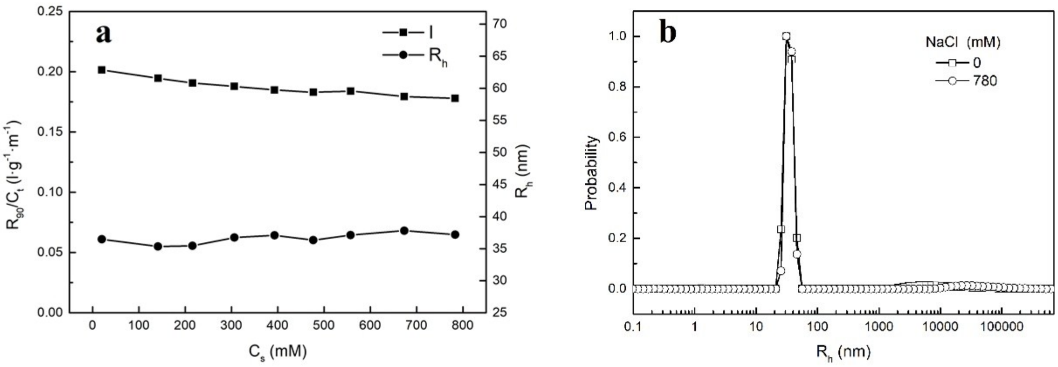

Figure S7. a) Changes in scattering intensity and hydrodynamic radius upon adding NaCl into Zn-L_2-L_3 micelles solution (80% of L_3); b) CONTIN analysis of Zn-L_2-L_3 micelles at different salt concentration.

Figure S8

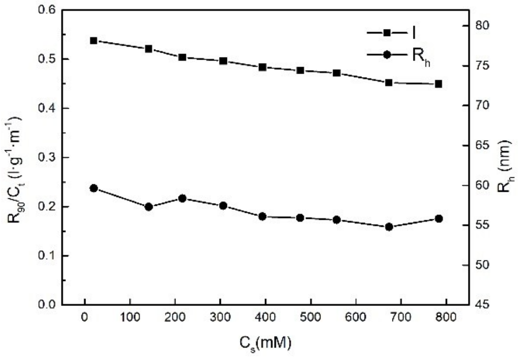

Figure S8. Changes in scattering intensity and hydrodynamic radius upon adding NaCl into Zn-L_3 micelles solution (100% of L_3).

Reference:

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