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Voltage-responsive reversible self-assembly and controlled drug release of ferrocene-containing polymeric superamphiphile †

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A new type of voltage-responsive comb-like superamphiphilic block polymer **PEG_{113}-*b*-PAA_{30}/FTMA** was prepared by the electrostatic interactions of ionic ferrocenyl surfactant (**FTMA**) and oppositely charged double-hydrophilic block polyelectrolyte poly-(ethylene glycol)-*b*-poly(acrylic acid) (**PEG_{113}-*b*-PAA_{30}**) in aqueous solution. An in-situ electrochemical redox system was designed to research its electrochemical activity in aqueous solution. The polymeric superamphiphilie **PEG_{113}-*b*-PAA_{30}/FTMA** could reversibly aggregate to form spherical micelles of 20-30 nm diameter in aqueous solution, and also disaggregate into irregular fragments by electrochemical redox reaction when its concentration is in the range of the critical aggregation concentration (cac_{red}) of the reduction state to its cac_{ox} of the oxidation state. Interestingly, above the cac_{ox}, the superamphiphile can aggregate into spherical micelles of 20-30 nm diameter, which can be transformed into larger spherical micelles of 40-120 nm diameter after electrochemical oxidation and reversibly recovered initial sizes after electrochemical reduction. Moreover, this reversible self-assembly process can be electrochemically controlled just by changing its electrochemical redox extent without adding any other chemical reagent. Further, rhodamine 6G (**R6G**)-loaded polymeric superamphiphile aggregates have been successfully used for the voltage-controlled release of loaded molecules based on their voltage-responsive self-assembly, and the release rate of **R6G** could be mediated by changing electrochemical redox potentials and the concentrations of polymeric superamphiphile. Our observations witness a new strategy to construct an voltage-responsive reversible self-assembly system.

Introduction

Amphiphilic block polymers can self-assemble into nano-sized spheres, vesicles, rods, lamella, tubes, toroid, or more ordered and complex micro-nano structures under different conditions.[1-5] On the other hand, the feature of block polymer amphiphiles with stimuli-responsive functional groups can be changed in response to external stimuli so that their self-assembled nanostructures in solutions and material macronature can be tuned in a controllable manner, which have been widely used as gene or drug delivery systems, catalyst supports, template synthesis and other research fields.[6-8] However, most conventional block polymer amphiphiles need complicated synthesis and purification processes. Moreover, the self-assembly of these amphiphilic block polymers in aqueous solution usually need complicated preparation processes and organic solvents as cosolvents.[5, 9]

In recent years, a new concept of superamphiphiles has been well established and received substantial attention in chemist community due to their facile preparation and interesting self-assembly behaviour.[10, 11] These so-called superamphiphiles are usually made of non-amphiphilic molecules, or non-amphiphilic molecules and amphiphilic small molecules by noncovalent interactions or dynamic covalent bonds in aqueous solution, such as hydrogen-bonding, electrostatic interaction, metal-coordination bonding, π-stacking, and host–guest interaction.[12-17] For example, Yan et al reported that two homopolymers, poly(styrene)-*β*-cyclodextrin (PS-*β*-CD) and poly(ethylene oxide)-ferrocene (PEO-Fc), can construct a polymeric superamphiphile (PS-*β*-CD/PEO-Fc) in aqueous solutions based on the terminal host-guest interactions, which can further form voltage-responsive supramolecular vesicles.[18] That provides new way to build complex and functional micro-nano structures.[19] However, a simple and facile method to prepare the polymeric superamphiphiles is based on electrostatic interactions.[10] As previously reported, water-soluble double-hydrophilic block copolymers with ionic and nonionic hydrophilic segments and oppositely charged surfactants could form a polymeric superamphiphile after simple mixing in aqueous solution drived by electrostatic interactions.[15, 20] As a result, the linear double-hydrophilic block copolymers are spontaneously transferred to non-covalent comb-like polymeric superamphiphiles consisting in nonionic hydrophilic block and hydrophobic block with non-covalently linked linear surfactant side chains. The polymeric superamphiphiles can self-assemble to form micelle or vesicle in

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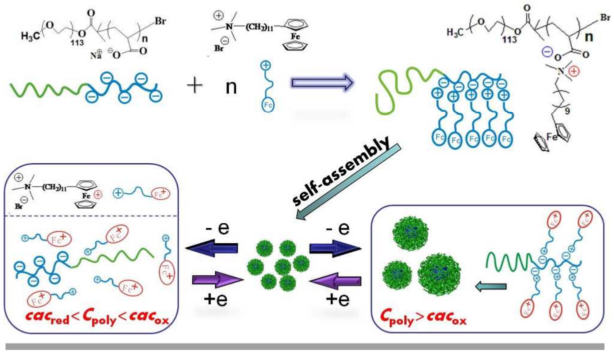
† Electronic Supplementary Information (ESI) available: The synthesis and characterization of block copolymer **PEG_{113}-*b*-PAA_{30}**, the effect of voltage on the electrochemical redox rate of polymeric superamphiphile, the absorption intensity of **FTMA** and **R6G** in different concentrations of aqueous solutions. See DOI: 10.1039/x0xx00000x

Scheme 1. Schematic illustration of the voltage-responsive reversible aggregation behavior of the polymeric superamphiphile **PEG_{113}-*b*-PAA_{30}/FTMA**.



aqueous solution, which provides new way to build complex and functional micro-nano structures.[20, 21] It is therefore desired that by introducing stimuli-responsive functional surfactants, block polymer superamphiphiles may form stimuli-responsive controllable self-assembly systems in aqueous solution, which make promising devices in catalyst supports, pharmaceutics, drug and gene delivery systems.[20-23] For example, Zhang's group reported that the block polymer superamphiphileionic made of a double-hydrophilic block poly (ethylene glycol)-b-poly(acrylic acid) (PEG_{43}-*b*-PAA_{153}) and an azobenzene surfactant (AzoC10) form vesicle-like aggregates in aqueous solution and the vesicles can self-assembly and disassembly by photoisomerization of azobenzene moieties.[21]

It is well known that the ferrocenyl amphiphiles are particularly of interest for supramolecular chemistry and voltage-responsive materials due to their synthetic convenience, reversible change in hydrophilicity and outstanding electrochemical activity.[24-26] When a redox raction takes place, ferrocenyl groups (**Fc**) are oxidized to yield ferrocenium cations (**Fc**$^+$), and **Fc**$^+$ can be reversibly reduced to give **Fc** again, leading to a remarkable change in the hydrophilic–lipophilic balance.[27-29] Therefore, ferrocenyl amphiphiles can reversibly aggregate and disaggregate in aqueous solution by means of alternative redox reaction due to their different critical micelle concentration (*cmc*) of the reduction state (**Fc**) and oxidation state (**Fc**$^+$).[30, 31] This clearly shows that ferrocenyl amphiphiles have a great potential for stimuli-responsive controllable self-assembly systems.

In this work, we describe a new voltage-responsive block polymeric superamphiphile made of the cationic ferrocenyl surfactant ((11-ferrocenylundecyl) trimethyl ammonium bromide, **FTMA**) and oppositely charged double-hydrophilic block copolymer poly-(ethylene glycol)-*b*-poly(acrylic acid) (**PEG_{113}-*b*-PAA_{30}**) drived by electrostatic and hydrophobic interactions, as shown in Scheme 1. Firstly, we report that this kind of polymeric superamphiphile could form voltage-responsive micelles that undergo reversible self-assembly and disassembly controlled by the electrochemical redox in terms of the critical micelle concentration (*cmc)* difference between oxidation and reduction state **FTMA**.[31] Moreover, according to Yuan's researches that the electrochemical redox rate of ferrocene-containing supramolecular polymers could be adjust by redox voltage,[18, 22, 32] we find that the self-assembly process of polymeric superamphiphile can be reversibly controlled just by its electrochemical redox degree without adding any other chemical reagent. Finally, we will demonstrate that such polymeric superamphiphile micelles can be used as nanocontainers for encapsulation and release of guest molecules controlled under mild redox potential.

Experimental

Materials

(11-Ferrocenylundecyl) trimethylammonium bromide (**FTMA**) was synthesized according to the method reported by Saji and co-workers.[33] The block copolymers **PEG_{113}-*b*-PAA_{30}** were synthesized by atom transfer radical polymerization (ATRP)[34, 35] and were detailed in the supporting Information (Figure S1 and S2, Table S1, ESI†). Poly(ethylene glycol) methyl ethers (PEG, Flakes, average M_n=5000) were used as received. All chemicals were analytical reagents and purified according to the standard procedures. Water used in all experiments was deionized and filtered with a Millipore purification apparatus with a resistivity of more than 18.0 M cm.

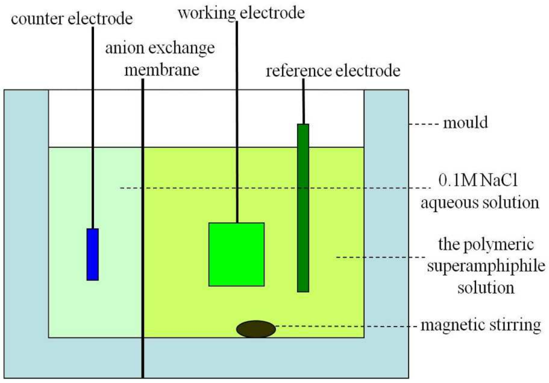
Instruments

UV-vis absorption spectra were recorded with a HITACHI U-3010 UV/vis spectrophotometer. The size distribution of the aggregates was determined with a Malvern Nano-ZS 90 Zetasizer using a monochromatic coherent He-Ne laser (633 nm), and analyzed by dynamic light scattering (DLS) at 25 ˚C. Surface tensions were determined with a Dataphysics OCA20 surface tension meter (Germany) at 25 ˚C. Transmission electron microscopy (TEM) images were obtained by a JEM-2100HR Microscope with an accelerating voltage of 200 kV, and the solution samples were sprayed on cellulose-coated copper grids through the homemade atomizer,[36] and then negative stained by 2.0 wt% uranyl acetate before observation.

Preparation of polymeric superamphiphile micelles

The block copolymer **PEG_{113}-*b*-PAA_{30}** was dissolved in 0.10 M NaCl aqueous solution at pH=10 in which the molar concentration of carboxylate group is 4.2 mM. **FTMA** was dissolved in 0.10 M NaCl aqueous solution with a concentration of 4.2 mM. To prepare the

Scheme 2. Schematic illustration of the homemade two electrolytic cells system



polymeric superamphiphiles micelles, 10 mL of **FTMA** solution was added to 10 mL of **PEG$_{113}$-*b*-PAA$_{30}$** solution, and the charge-molar ratio of the **FTMA** to carboxylate groups of **PEG$_{113}$-*b*-PAA$_{30}$** (Z = [FTMA]/[COO-]) is 1:1. The final concentration of polymeric superamphiphile was 1.54 mg/mL, in which the molar concentrations of both **FTMA** and carboxylate groups were 2.1 mM. The obtained polymeric superamphiphile solution could be diluted into different concentrations for further experiments.

Electrochemical response of polymeric superamphiphile

Electrochemical response of the polymeric superamphiphile was studied by potentiostatic method in homemade two electrolytic cells system (Scheme 2) with anion exchange membrane (Shandong Tianwei Membrane Technology Co., Ltd.). Cyclic voltammograms (CV) and amperometric *i-t* curves were obtained on a CHI 660C electrochemical workstation (CH Instruments, Shanghai) at room temperature under argon atmosphere using a three-electrode system. And platinum plate electrode (2.0 cm×2.0 cm) was selected as the working electrode, platinum plate electrode (0.2 cm×1.0 cm) was selected as the counter electrode, and saturated calomel electrode (SCE) as the reference electrode.

Loading of rhodamine 6G

To prepare Rhodamine 6G (**R6G**) loaded micelles, 20.0 mg of polymeric superamphiphile micelles and 3.0 mg of R6G were stirred at room temperature for 12 h. The superamphiphile solution was dialyzed against 0.10 M NaCl aqueous solution for 24 h (cutoff membrane: 1000 g mol^{-1}) to remove excess of R6G until the solution outside the dialysis tube exhibited negligible R6G.

Results and discussion

Formation of polymeric superamphiphile micelles.

The formation mechanism of ferrocene-containing polymeric superamphiphile micelles is illustrated in Scheme 1. Because of good water solubility of the two segments, the double-hydrophilic block copolymer **PEG$_{113}$-*b*-PAA$_{30}$**, used herein as its sodium salt, cannot form aggregates in water. When anionic **PEG$_{113}$-*b*-PAA$_{30}$** and cationic surfactants **FTMA** were mixed together, the hydrophobic segment **PAA/ FTMA** would be formed based on the electrostatic interaction, which led to the formation of the polymeric superamphiphile due to the charge neutralization and the reduce of hydrophilicity.

As is well known, amphiphiles can form different aggregates in aqueous solution above their critical micelle concentration (*cmc*).[37-39] To study the self-assembly behaviour of ferrocene-containing polymeric superamphiphile, the critical aggregation concentration (*cac*) of the superamphiphile **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** with reduction and oxidation state in 0.10 M NaCl solution (Z=1:1, 25 °C) were determined through the surface tension method. As shown in Figure 1, the cac_{ox} of the oxidation state superamphiphile is higher than cac_{red} of the corresponding reduction state one, which is agreement with the corresponding *cmc* of **FTMA** in aqueous solution[37]. The cac_{red} and cac_{ox} values of polymeric superamphiphile are about 0.06 mg/mL and 0.30 mg/mL, respectively, in which the concentrations of **FTMA** are 0.08 mM and 0.40 mM, respectively. However, in 0.10 M Li_2SO_4 aqueous solution, the cmc_{red} value of **FTMA** was 0.1 mM, and the cmc_{ox} value of **FTMA** was more than 10 mM.[37] This indicated that the **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** aggregates were formed in aqueous solution, rather than the self-assembly of **FTMA** alone.

Therefore, the formation and destruction of the **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** aggregates in aqueous solution may be alternatively achieved by electrochemical redox reaction taking advantage of the different *cac* values of the oxidation and reduction state superamphiphiles, when the concentration of superamphiphiles is between its cac_{red} and cac_{ox} values. Furthermore, the **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** may form two different aggregates respectively by electrochemical redox reaction when the concentration of

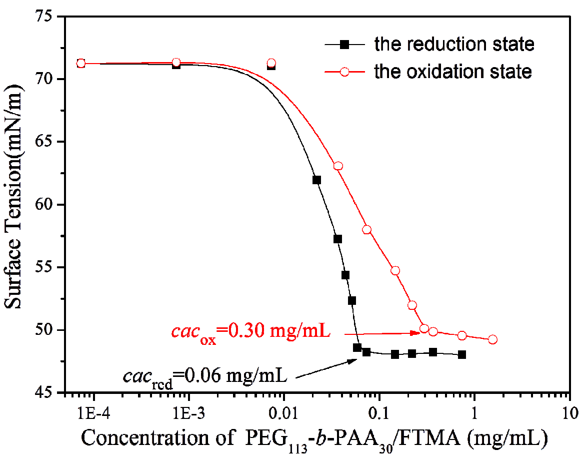


Figure 1. Plots of surface tensions against the concentrations of the **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** at the reduction and oxidation state in 0.10 M NaCl solution, respectively. The Z value [**FTMA**]/[**COO-**] is 1:1.

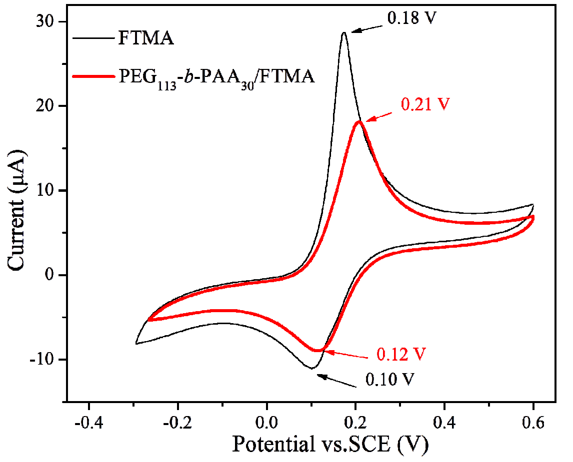


Figure 2. Cyclic voltammograms (25 °C, 10 mV/s) for **FTMA** (black curve) and the **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** (red curve) in 0.10 M NaCl aqueous solution. The concentration of polymeric superamphiphile (Z=1:1) is 1.54 mg/mL.

superamphiphiles is above its cac_{ox} value. These results suggest that an electrochemically reversible self-assembly process of polymeric superamphiphile in 0.10 M NaCl solution would be established by electrochemical redox reaction, if only the concentration of polymeric superamphiphile is above its cac_{red} value.

Electrochemical activity of polymeric superamphiphile

As previously described, ferrocenyl groups can be transformed to the ferrocenium salt and undergo reversible redox reactions.[18, 25] However, the reversible self-assembly and disassembly of ferrocene derivatives was basically implemented by adding redox reagents,[40, 41] which inevitably introduced impurities to the systems. Therefore, in this work, an in-situ electrochemical redox system was designed to research the electrochemical redox activity of the polymeric superamphiphile (Scheme 2). The electrochemical responsivity and reversibility of the **PEG_{113}-*b*-PAA_{30}/FTMA** in solution were performed by cyclic voltammetry (CV) (Figure 2). The CV results show that the oxidation peak potential (E_{pa}) and the anodic peak current (i_{pa}) of ferrocenyl surfactant **FTMA** were 0.18 V and 28.8 μA, respectively (Figure 2, block curve), and for the **PEG_{113}-*b*-PAA_{30}/FTMA**, the E_{pa} increased to 0.23 V, and the i_{pa} dropped to 18.1 μA (Figure 2, red curve). The reason is that the electrostatic interactions between **FTMA** and **PEG_{113}-*b*-PAA_{30}** limit the free motion of non-covalent linked **FTMA** side groups. However, both polymeric superamphiphile and free **FTMA** in solution have almost the same potential difference ΔE_p (~0.08 V), which shows that the polymeric superamphiphile has a reversible electrochemical redox activity in 0.10 M NaCl aqueous solution.

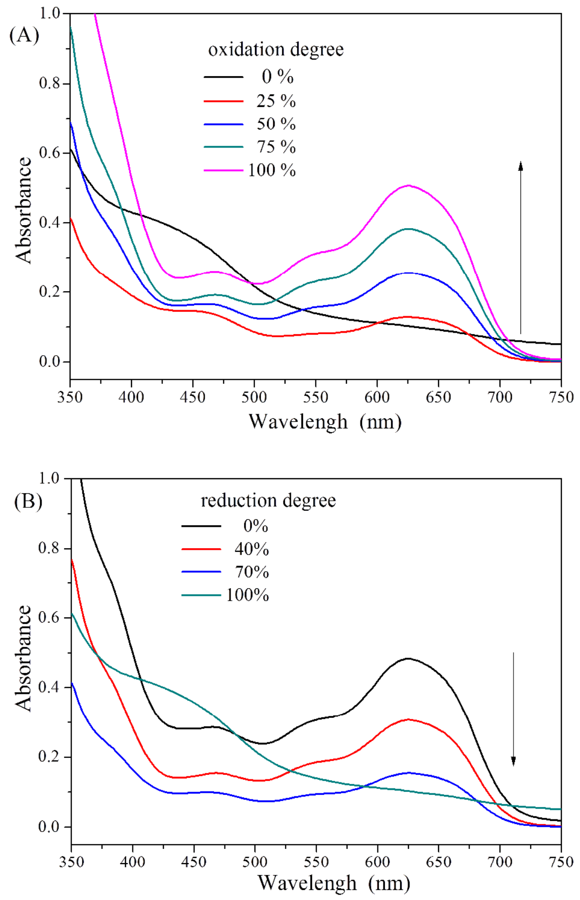


Fig. 3 UV-vis absorption spectra of the **PEG_{113}-*b*-PAA_{30}/FTMA** at different redox degree in aqueous solution. The concentration of polymeric superamphiphile (Z=1:1) is 1.54 mg/mL.

According to the principle of ferrocene redox reactions,[42] the electrochemical redox reactions of the **PEG_{113}-*b*-PAA_{30}/FTMA** are attributed to the gain or loss of electronics for ferrocenyl groups on the electrode surface. The potential of the working electrode is a determinant factor influencing the electrochemical reaction happened or not on the electrode surface. Yuan's group found that increase of redox potential can enhance the electrochemical reaction rate of ferrocene inclusion complexes.[18, 32] Hence, we select +0.50 V and +0.00 V as the oxidation voltage and reduction voltage respectively to obtain faster electrochemical redox rates of polymeric superamphiphile (Figure S3, ESI†).

The redox degree of ferrocenyl groups can be observed through UV-vis absorption spectra as well,[30, 41] and thus the electrochemical redox process of the polymeric superamphiphile was traced by a UV-vis spectrophotometer (Figure 3). The maximum absorption intensity of **FTMA** in the oxidation state at 627 nm in 0.10 M NaCl aqueous solution is proportional to its concentration (Figure S4, ESI†), and therefore the absorbance is calculated as the redox degree of the superamphiphile from the working curve. In a word, the UV-vis absorption spectra of polymeric superamphiphile solution can track the process of its reversible electrochemical redox reaction.

Voltage-responsive reversible aggregation behavior of polymeric superamphiphile in aqueous solution

The voltage-responsive reversible aggregation behaviour of superamphiphilic **PEG_{113}-*b*-PAA_{30}/FTMA** in aqueous solution was

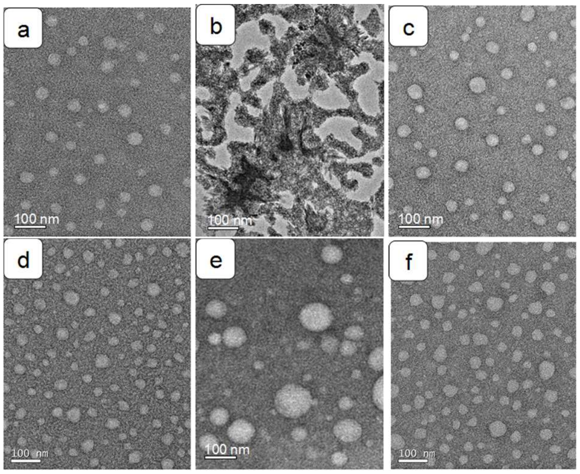


Fig. 4 TEM images of the **PEG_{113}-*b*-PAA_{30}/FTMA** micelles (a), irregular fragments (b) oxidized at the oxidative potential (+0.50 V) and (c) reduced at the reduction potential (+0.00 V) when the concentration (Z=1:1) is 0.25 mg/mL. TEM images of the **PEG_{113}-*b*-PAA_{30}/FTMA** micelles (d), and aggregates (e) oxidized at the oxidative potential (+0.50 V) and (f) reduced at the reduction potential (+0.00 V) when the concentration (Z=1:1) is 1.54 mg/mL.

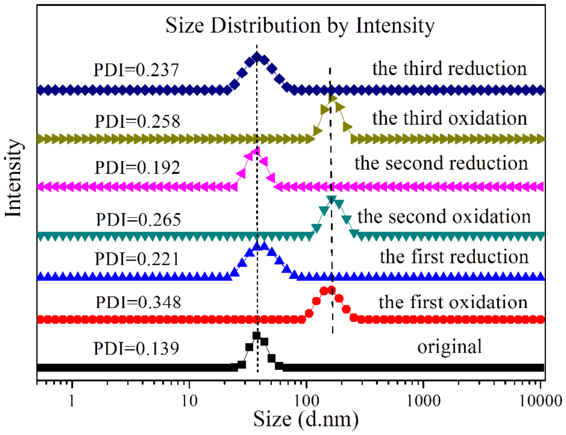


Fig. 5 Reversible changes of the **PEG_{113}-*b*-PAA_{30}/FTMA** micelle size (determined by DLS) followed by electrochemical redox reactions. The polydispersity indexs (PDI) of micelle sizes are obtained by Malvern analysis software. The concentration of polymeric superamphiphile (Z=1:1) is 1.54 mg/mL.

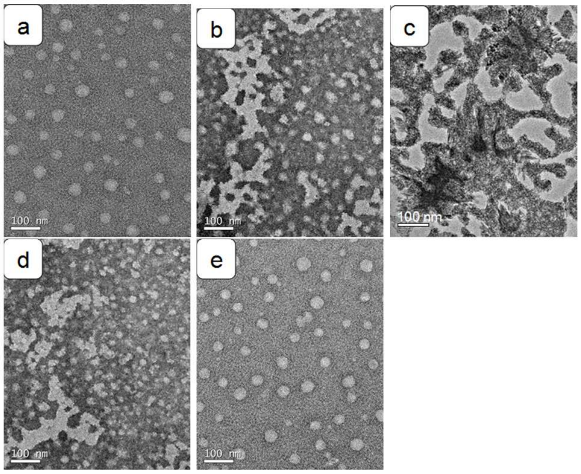


Fig. 6 TEM images of the **PEG_{113}-*b*-PAA_{30}/FTMA** micelles (a), and aggregates after oxidized for 0.6 h (b) and 1.3 h (C) at the oxidative potential (+0.50 V), and after reduced for 0.3 h (d) and 1.3 h (e) at the reduction potential (+0.00 V). The concentration of polymeric superamphiphile (Z=1:1) is 0.25 mg/mL.

respectively investigated by TEM and DLS. As reported, the polymeric superamphiphile can aggregate to form spherical micelles in solution through hydrophobic and electrostatic interactions.[20, 21] When the concentration of superamphiphile is above its cac_{red} value (Fig. 4a and 4d), only spherical micelles are observed, and their sizes are about 20-30 nm in diameter. When the concentration of superamphiphile is in the range of cac_{red} to cac_{ox}, as expected, the spherical micelles are disassembled into irregular fragments after electrochemical oxidation (Fig. 4b) and reversibly recovered initial micellar sizes after electrochemical reduction (Fig. 4c). Interestingly, when the concentration is above its cac_{ox} value, the size of spherical micelles is increased to 40-120 nm in diameter after electrochemical oxidation (Fig. 4e), and reversibly recovered initial micelles of 20-30 nm after electrochemical reduction (Fig. 4f). It is worth noting that this redox process can be cycled at least 3 times by electrochemical redox reactions (Figure 5), indicating that electrochemical redox-controlled reversible self-assembly of the superamphiphile aggregates is successfully achieved by electrochemical method.

As previously described, the redox degree of the **PEG_{113}-*b*-PAA_{30}/FTMA** could be tuned by its electrochemical redox times (Figure S3, ESI†). Therefore the reversible aggregation behaviour of the polymeric superamphiphile could be controlled by its electrochemical redox times (Fig. 6). When the superamphiphile solution (0.25 mg/mL, Z=1:1) is electrochemically oxidized for 0.6 h at the oxidative potential (+0.50 V), the redox degree of the polymeric superamphiphile reaches 50%, and about half of spherical micelles disassemble, but the other half of spherical micelles keep their original size (Figure 6b). This indicates that the disassembly of polymeric superamphiphile micelles is a controlled and gradually developed process. When ferrocenyl groups in micelles are oxidized to a certain extent, the hydrophilicity and charge density of polymeric superamphiphile increase, which cause spherical micelles to be disassembled into free **FTMA** and **PEG_{113}-*b*-PAA_{30}**. Those free surfactants **FTMA** would be preferential oxidized due to their higher electrochemical activity, however, the other micelles would maintain their original state due to weaker electrochemical activity. Moreover, when the polymeric superamphiphile is oxidized for 1.3 h, ferrocenyl groups are fully oxidized and no spherical micelles appear, as shown in Figure 6c. In addition, half of spherical micelles appear again after 0.3 h electrochemical reduction, and only spherical micelles are observed after 1.3 h electrochemical reduction (Figure 6e). This phenomenon is in agreement with the results observed in the redox-controlled reversible assembly and disassembly of side-chain selenium-containing amphiphilic block copolymers.[43] In a word, the reversible aggregation behavior of the **PEG_{113}-*b*-PAA_{30}/FTMA** could be controlled by its electrochemical redox times.

In order to further illustrate the two reversible self-assembly behaviours of the **PEG_{113}-*b*-PAA_{30}/FTMA** at different concentrations, a schematic illustration is given in Scheme 1. When the concentration of polymeric superamphiphile is above its cac_{red} value, the polymeric superamphiphile can aggregate to form spherical micelles in solution through hydrophobic and electrostatic interactions，which is in agreement with the Zhang's research results of polymeric superamphiphiles.[20, 21] When the concentration of superamphiphile is in the range of cac_{red} to cac_{ox}, spherical micelles of reduction state polymeric superamphiphiles are disassembled into free **PEG_{113}-*b*-PAA_{30}** and oxidized state **FTMA** after electrochemical oxidation, because the cac_{ox} of the oxidation state superamphiphile is higher than cac_{red} of the reduction state one (Figure 1) accompanied by a conversion of hydrophobic **Fc** to less hydrophobic **Fc^+**. But when the concentration of superamphiphile is above its cac_{ox} value, both oxidation state and reduction state superamphiphiles can aggregate in solution. After electrochemical oxidation, the initial neutral micellar cores of hydrophobic block with non-covalently linked ferrocenyl side groups will transfer into the charged cores due to a conversion of **Fc** to **Fc^+**. Accordingly, the original micelles will rearrange to re-form larger micelles in the oxidation state superamphiphile solution due

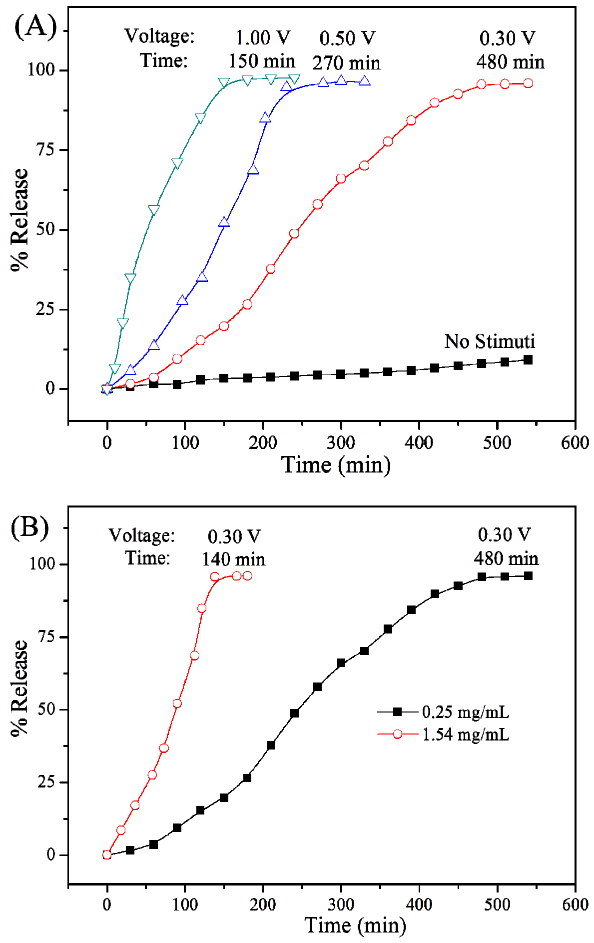


Fig. 7 Cumulative release (A) of R6G-loaded polymeric superamphiphile solutions (1.54 mg/mL, Z=1:1) upon various voltage stimuli. Cumulative release (B) of R6G-loaded polymeric superamphiphile solution with different concentrations at the oxidative potential (+0.30 V).

to stronger electrostatic repulsions between **Fc**$^+$ side groups and the decrease of hydrophobicity of micellar cores (Scheme 1). In addition, these aggregation structures could recover initial sizes when **Fc**$^+$ is reduced to **Fc**, which is driven by the minimization of the interfacial energy and qualitatively follows the theory of Israelachvili et al.[44, 45]

From above results, we can draw one conclusion that the polymeric superamphiphile **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** can reversibly self-assemble into different sizes of the spherical micelles, and also disassemble into irregular fragments in aqueous solution by electrochemical redox reaction when changing its concentration. Particularly, the self-assembly process can be reversibly controlled by its electrochemical redox times without adding other chemical reagents. Thus, this kind of electrochemical redox-controlled reversible self-assembly and disassembly systems has a great potential application in drug delivery systems, catalyst supports and other research fields.

Voltage - controlled release of R6G from polymeric superamphiphile micelles

As aforementioned, the voltage-responsive polymeric superamphiphile **PEG$_{113}$-*b*-PAA$_{30}$/FTMA** can self-assemble into micelles and disassemble after electrochemical oxidation when the concentration of superamphiphile is between its *cac*$_{red}$ and *cac*$_{ox}$ values; it will be turned into larger micelles after oxidation when the concentration is above its *cac*$_{ox}$ value. If drug molecules are loaded into the micelles, they will quickly release when micelles disaggregate after oxidation at lower concentrations; drug molecules also will be solubilized in large micelles, and slowly release after electrochemical oxidized at higher concentration with the change of aggregates. In this work, **R6G** is used as a model drug molecule, and **R6G**-loaded polymeric superamphiphile micelles were prepared to perform voltage-controlled release experiments. **R6G**-loaded micelles solution, platinum plate electrode (2.0 cm×2.0 cm, as the working electrode) and SCE (as the reference electrode) were added in a dialysis tube (cutoff membrane: 1000 g mol^{-1}), and platinum plate electrode (0.2 cm×1.0 cm) was kept outside the dialysis tube as the counter electrode. Then exerted to an oxidation potential, the release rate of **R6G** was monitored by the UV-Vis absorption of the solution outside the tube, because the UV-Vis absorption intensity of **R6G** at 527 nm in the water was proportional to its concentration (Figure S5, ESI†). Therefore, the cumulative release (W_i) of **R6G** from polymeric superamphiphiles micelles could be calculated according to equation 1.

$$W_i = \frac{C_i V_i}{C_0 V_0} \times 100\% \qquad (1)$$

where C_i was the concentration of R6G in the solution outside the dialysis tube, which was calculated by working curve (Fig. S5, ESI†). C_0 was the initial concentration of **R6G** loaded in the polymeric superamphiphile micelles. V_i was the volume of the solution outside the dialysis tube, and V_0 refer to the initial volume of **R6G**-loaded superamphiphile solution in the dialysis tube.

Figure 7A shows the release rate of **R6G** can be adjusted by changing electrochemical redox voltages. When no stimulus was applied, the **R6G**-loaded polymeric superamphiphile micelles released less than 10 % of R6G after 9.0 h, indicative of good storage properties. When oxidative potential (+0.30 V) was applied, about 95 % of **R6G** was released within 480 min. Interestingly, **R6G**-loaded superamphiphile micelles showed a faster release rate (270 min) upon higher voltage stimuli (0.50 V), and the fastest release rate (150 min) at the highest voltage (1.00 V). This phenomenon should be caused by the different electrochemical oxidative rates upon different oxidative potentials. Thus, the conclusion can be drawn that the change of the oxidative potentials could effectively control the release rate of **R6G** from the **R6G**-loaded polymeric superamphiphile solution. In addition, when the concentration of polymeric superamphiphile was below its *cac*$_{ox}$, the release rate of R6G sped up due to the disassembly of micelles in solution after oxidization, as seen from Figure 7B. The release rate of R6G can also be mediated by the concentrations of polymeric superamphiphile.

Conclusions

A new type of voltage-responsive polymeric superamphiphile **PEG_{113}-*b*-PAA_{30}/FTMA** was obtained by electrostatic and hydrophobic interactions of ferrocenyl surfactant **FTMA** with oppositely charged double-hydrophilic block polyelectrolyte **PEG_{113}-*b*-PAA_{30}** in aqueous solution. An in-situ electrochemical redox system was successfully designed to research the electrochemical activity of the polymeric superamphiphile. It is observed that polymeric superamphiphile **PEG_{113}-*b*-PAA_{30}/FTMA** at oxidation state has higher cac_{ox} than the corresponding reduction state (cac_{red}) in aqueous solution. Interestingly, the polymeric superamphiphile could reversibly aggregate to form spherical micelles of different nanoscales in solution, and also disassemble into irregular fragments by electrochemical redox reaction depending on the concentration range of **FTMA**. And the redox rate of the polymeric superamphiphiles can be adjusted by its redox potentials. Particularly, the aggregation structures and self-assembly process of the polymeric superamphiphile can be reversibly controlled by its electrochemical redox degree without adding other chemical reagents. Further, **R6G**-loaded polymeric superamphiphile aggregates have been successfully used for the voltage-controlled release of loaded molecules based on their voltage-responsive controlled self-assembly behavior, and the release rate of **R6G** could be mediated by changing electrochemical redox potentials and the concentrations of polymeric superamphiphile. This work offers tremendous possibilities for the fundamental science of controlled self-assemblies and drug release.

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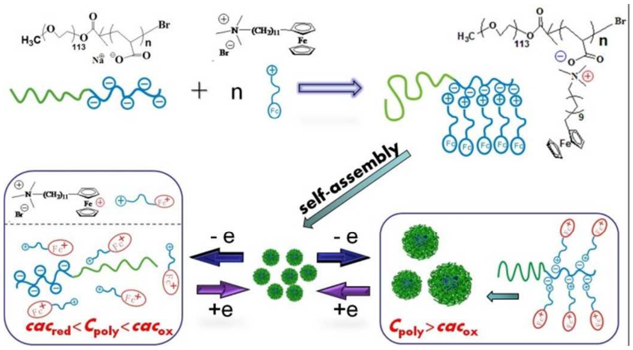
self-assembly
- e
+e
- e
+e
$cac_{red} < C_{poly} < cac_{ox}$
$C_{poly} > cac_{ox}$
n
Fc