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Effects of Interaction between Polycation and Nonionic Polymer on Cross-assemble into Mixed Micelles

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1. Polymerization of PEGMEMA and PQAs

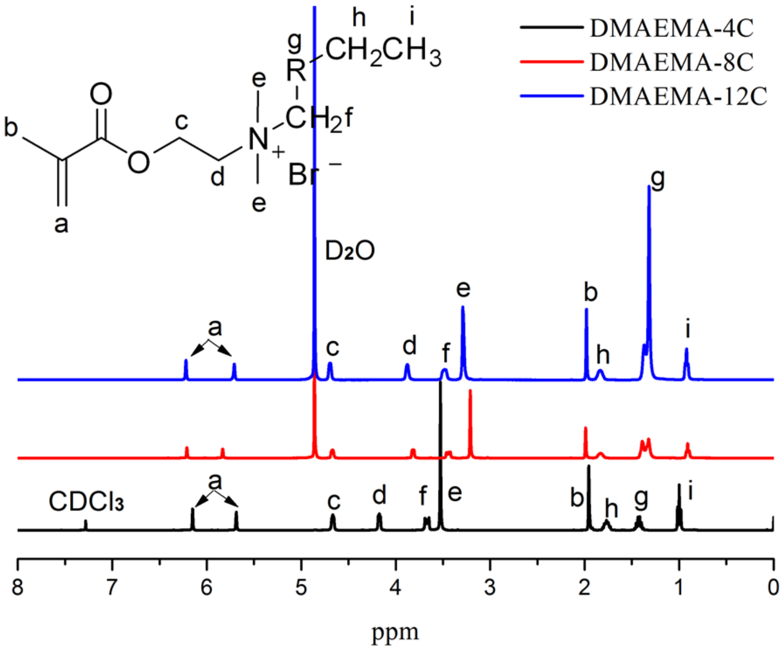
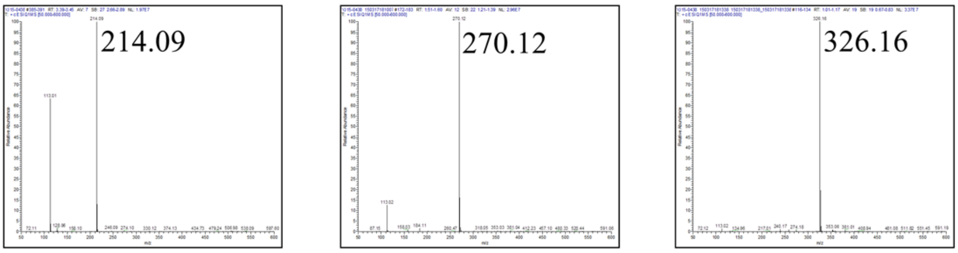


Fig. S1. ^{1}H NMR spectra of DMAEMA-4C in $CDCl_3$ and DMAEMA-8C, DMAEMA-12 in D_2O.



DMAEMA-4C DMAEMA-8C DMAEMA-12C

Fig. S2. Mass spectra of DMAEMA-4C, DMAEMA-8C, and DMAEMA-12C

The molecular weights of quaternary ammonium salts monomers were carried out by mass spectroscopy (MS) (TSQ QUANTUM ULTRA). The detailed experimental conditions of MS are: ESI source and positive ion mode; spray voltage, 4000V; capillary temperature, 350 °C; full scan and scan range 50-600 m/z.

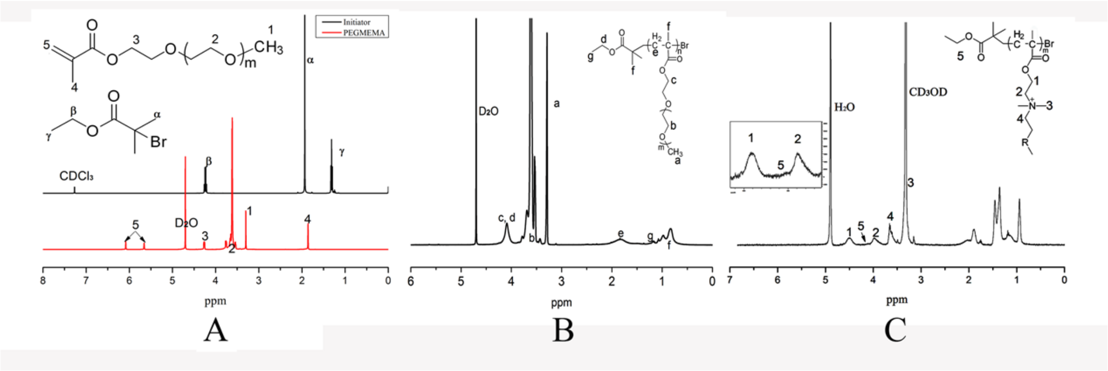


Fig. S3. ^{1}H NMR spectra of initiator (A) in $CDCl_3$, PEGMEMA (A), PPEG (B) in D_2O and PQA8c (C) in CD_3OD.

Fig. S3 shows the ^{1}H NMR spectra of initiator ethyl 2-bromoisobutyrate, PEGMEMA, PPEG and PQA8c (as an example of these quaternary ammonium salt polymers). Comparing Fig. S3B with Fig. S3A, the peaks of the double bond protons in the PEGMEMA monomer disappear and the peak at 1.83 ppm is assigned to the $-CH_2-$ of the backbone chain. The peaks at 3.29 ppm (a), 3.61 ppm (b), and 4.08 ppm (c) belong to the three protons of the terminal $-OCH_3$, the four protons of $-CH_2CH_2O-$, and the two protons of $-COOCH_2-$ of the PEG side chains, respectively. The peaks at approximately 0.8~1.0 ppm are attributed to the three protons of the $-CH_3$ in the polymer. And the peaks of the initiator can be found in the picture of PPEG. These similar results were reported by Gu L. et al.,[1] indicating that PPEG was synthesized successfully.

Fig. S3C shows the ^{1}H NMR spectrum of PQA8c. Compared with Fig. S1, we can find the double bond protons in the PQA monomer disappear. The protons of the methyl group (3) that connect to the N^+ observed at $\delta = 3.33$ ppm are hidden by the peak of the solvent, while the protons adjacent to CH_2, numbered 1, 2, and 4, are observed at $\delta = 4.5$, 3.99, and 3.67 ppm, respectively. The peak “5” (4.12 ppm) belongs to the $-CH_2-$ of the initiator. Clearly, PQA8c has been successfully synthesized.

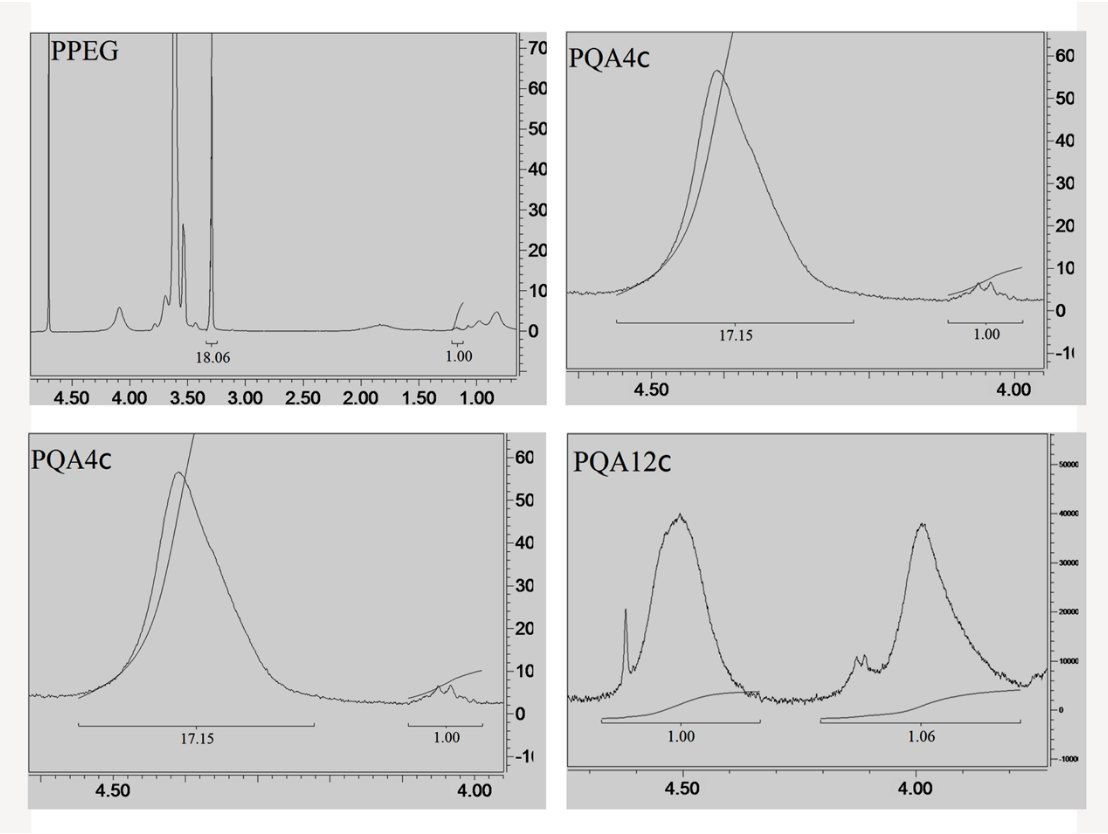
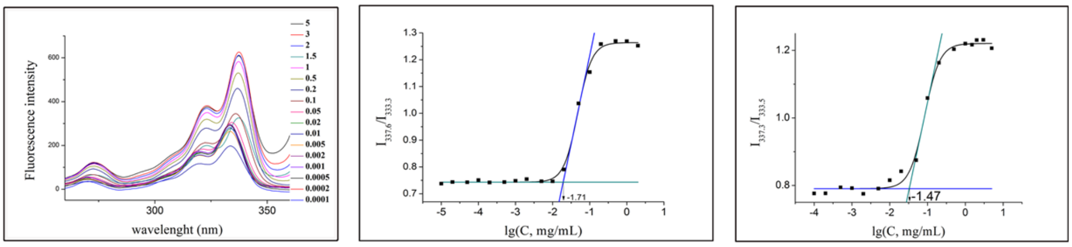


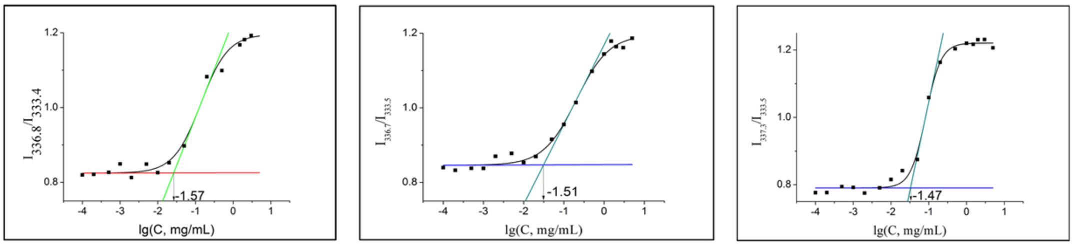
Fig. S4. The calculation of the degree of polymerization of PPEG and PQAs.

The DP values of the polymers were calculated from ^{1}H NMR spectra. For PPEG, we can calculate from the ratio of the area of the peak of terminal -OCH$_3$ in PEG and the area of the peak of terminal -CH$_3$ in initiator. And the DP is 18. For PQA4c, the DP is equal to the values of S$_1$/S$_5$, and the value of S$_1$ and S$_5$ is shown in Fig. S4. We can easy know that the DP of PQA4c is 17. Here we should point out that the peak “5” is not substantive, and the area of peak “1” and “2” is equivalent. Thus, we can obtain S$_5$ from the difference value between S$_1$ and (S$_1$+S$_5$) which were shown in Fig. S1. And the DP is 16 for PQA8c and 16 for PQA12c.

2. Cross-assembly of PPEG/PQA



A PQA12c PPEG



PPEG/PQA4c PPEG/PQA8c PPEG/PQA12c

Fig. S5. The typical fluorescence excitation spectra (λ_{em}= 373 nm) (A) and calculation of CMC for PQA12c, PPEG, PPEG/PQA4c, PPEG/PQA8c, and PPEG/PQA12c

In Fig. S5A, with an increase of micelles' concentration in an aqueous solution of pyrene, the total fluorescent intensity increased, and the absorption band shifted of pyrene translate from around 334 to around 337 which suggest that pyrene molecules transfer from the water environment to a microenvironment within the micelles. This is the evidence of formation of micelles. The CMCs are obtained from the intersection of the two tangent lines (Fig. S5).

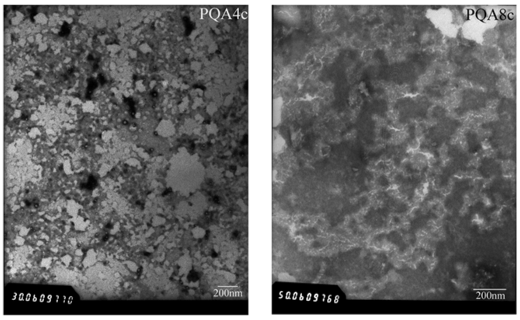


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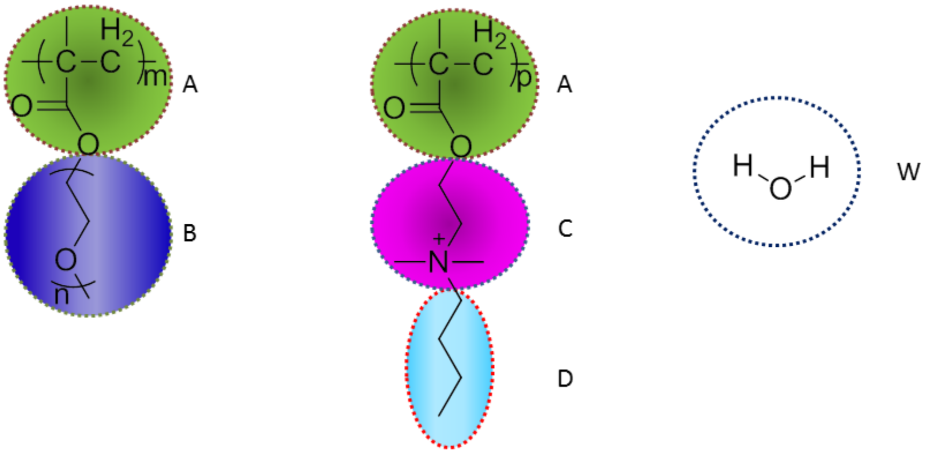
Fig. S6. TEM images of PQA4c and PQA8c micelles

Fig. S6 shows that PQA4c and PQA8c did not self-assemble into micelles. We can only observe unordered polymer aggregations but no spherical, rod, worm or other form micelles.

3. DPD simulation

Mesoscale simulation requires the definition of beads by coarse-graining the component of the polymer. The coarse-grained models are shown in Scheme S1. For the PPEGMEMA, The backbone was defined as A, and the repeating unit of PEG was designated as B. For the PQAs, the backbone was defined as A, the hydrophilic quaternary ammonium salt was marked as C, and the hydrophobic carbon chain (-$(CH_2)_4$-) was defined as D. W represented water molecule.



Scheme S1. Molecular structures and coarse-grained models of PPEG, PQAs, and water.

Bead -bead interactions were entered as DPD repulsion units (α_{ij}). α_{ij} depends on the atomistic interactions and has the relation with Flory – Huggins parameter χ_{ij} (eq. 1): [2]

$$\alpha_{ij} = \alpha_{ii} + 3.27\chi_{ij} \qquad (1)$$

Where α_{ii} is the repulsion parameter between beads that have the same type. The value of α_{ii} can be obtained from $\alpha_{ii}=75k_BT/\rho$, where the bead density $\rho=3$ and the cut off radius is $r_C= k_BT=1$.

Therefore, it is important to determine χ_{ij} to calculate α_{ij}. χ_{ij} can be calculated from solubility parameters by eq. 2:

$$\chi_{ij} = \frac{(\delta_i - \delta_j)^2 V_{ref}}{RT} \qquad (2)$$

Where δ_i and δ_j are the solubility parameters of the interacting beads i and j, V_{ref} is the average molar volume of the beads i and j, R is the universal gas constant and T is the temperature.

All the α_{ij} values were calculated from eq.1 and eq. 2 except the repulsion parameter between bead B and bead W. PEG is miscible in water over a wide range of concentration and molecular weight, according to the large amount of hydrogen bond between PEG and water. Therefore, Flory-Huggins parameter $\chi_{Eo\text{-}W}$ was used as 0.3 by the reference of Groot. et al.[3,4].and then $a_{Eo\text{-}W}$=25.9.

All computational modeling was performed using the Materials Studio 4.0 software program (Accelrys Software Inc, San Diego, CA, USA).Molecular dynamic was used to calculate the Flory-Huggins parameters for the molecular components. And all the components were calculated by the COMPASS force field.[5] Each system was constructed by the Amorphous Cell module with the density of 0.5g/cc. 10000 steps of energy minimization were used to eliminate unfavorable contacts of the initial configurations with Steepest Descent, Conjugate Gradient and Newton method by Discover module. The van der waals interactions were calculated by atom based method. Moreover, the Ewald method was used to calculate the Coulombic interactions. After minimization, 5 configurations with the lowest energy were chosen. Thermal annealing from 500 to 298 K was conducted, followed by 10 ns molecular dynamics (MD) at isothermal and isobaric (NPT) conditions to obtain accurate density. The Andersen thermostat was used to maintain the temperature at 298 K and the pressure was maintained at 0.1 GPa by Berendsen method. Another 5ns MD at isothermal and isochoric (NVT) was conducted to collect data.

In this study, DPD simulation was used to investigate the micellization of PPEGMEMA, PQA4c, PQA8c, PQA12c, PPEG/PQA4c, PPEG/PQA8c and PPEG/PQA12c. The degree of polymerization is 20 for all of polymers. The simulation system contained polymers and water in a cubic 20 ×20 × 20 with a period boundary condition. The density of bead was 3.0 and the grid spacing was 1.0, corresponding to 24000 beads. The default values of dissipation parameter were 4.5 and the spring constant was chosen as 4.0. The time step was 0.05ns and

1×10^6 steps were used to get a stable system. No dihedral angle constrain was considered during the whole simulation.

The computational studies provided useful information to further understand the cross-assembly behavior of mixture micelles. Table S1 shows the calculated α_{ij} values which are used to investigate the micellization of PPEG/PQA.

Table S1. Interaction parameters a_{ij} in PPEG/PQA system used by DPD simulations

	W	A	B	C	D
W	25.0				
A	84.6	25.0			
B	25.9	25.6	25.0		
C	36.6	222.6	246.9	25.0	
D	94.1	25.2	25.6	248.0	25.0

Fig. S7 illustrates the equilibrious morphologies and slice views of three kinds of PQA/PPEG at the molar concentration 3%. For PPEG/PQA4c, a rodlike micelle which is consistent with TEM observation is observed. In detail, PQAs and PPEG assemble together respectively and combine together through hydrophobic chain. Interestingly, the two constituents are not covered by each other. This result provides theoretical support for the ^{1}H NMR of PPEG/PQA4c that N_1 nearly equal to N_2. Apparently, the loose structure reflects that the interaction between PQAs and PPEG is weak and easily be destroyed, as a result that PPEG/PQA4c is not stable. In contrast, PPEG/PQA8c and PPEG/PQA12c can form regular spherical micelles, which are consistent with TEM results. The hydrophilic PEG locates on the surface of the micelle, indicating that N_2 is smaller than N_1 and the hydrophilic N^+ is exposed to the water which maintains the antibacterial activity. So as to this structure, the mixture micelles can kill E. coil and S. aureus well with unobvious cell toxicity

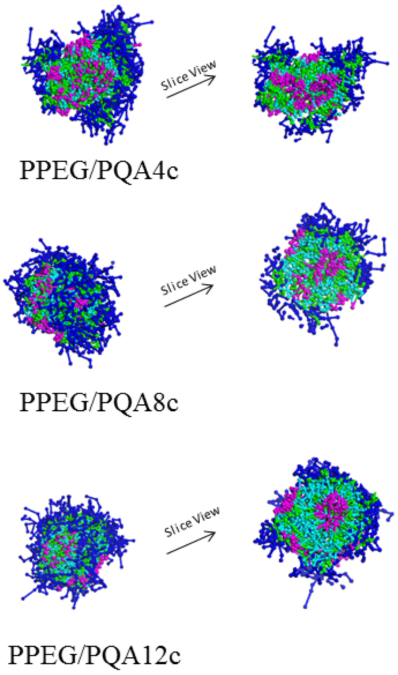


Fig. S7. The equilibrious morphologies and slice views of PPEG/PQA4c, PPEG/PQA8c and PPEG/PQA12c. Water is not shown for clarity. A, B, C, D beads are denoted in green, blue, pink, and azure, respectively.

References

1. L. Gu, Z. Shen, S. Zhang, G. Lu, X. Zhang and X. Huang, *Macromolecules,* 2007, 40, 4486-4493.

2. R. D. Groot and P. B. Warren, *J. Chem. Phys.*, 1997, **107**, 4423-4435.

3. R. D. Groot and K. Rabone, *Biophys. J.*, 2001, **81**, 725-736.

4. S. Saeki, N. Kuwahara, M. Nakata and M. Kaneko, *Polymer*, 1976, **17**, 685-689.

5. H. Sun, P. Ren and J. Fried, Comput. Theor. *Polym. Sci.*, 1998, **8**, 229-246.