

Case Study to Bridge the Gap between Chemistry and Chemical Product Engineering: From Molecules to Products Based on Brush Copolymers Having Different Backbone Composition Profiles

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S Supporting Information

ABSTRACT: This paper first achieved a triplet "backbone molecular structure– Ca^{2+} responsivity–synthesis methodology" multiscale study in the field of chemistry through preparing a series of poly(acrylic acid) (PAA) based pH-responsive brush copolymers (i.e., poly(methyl methacrylate (MMA)-*co*-2-(2-bromoisobutyryloxy)ethyl methacrylate (BIEM)-*graft*-acrylic acid (AA)) with three backbone composition profiles (random, gradient, and block) and investigating the effect of backbone composition profile on their Ca^{2+} responsivity. And then, a chemical product engineering perspective was introduced to develop these PAA-based pH-responsive brush copolymers into new chemical products which may be used in water softening. The preceding triplet backbone molecular structure– Ca^{2+} responsivity–synthesis methodology multiscale study was closely related to the completing of chemical product pyramid in chemical product engineering field. The whole study can be seen as a case study of manufacturing a useful product with desired function from individual molecules based on a chemical polymerization method and chemical product engineering.

1. INTRODUCTION

Traditional chemical process industries have made great contributions for our society through producing necessities, including the petroleum, fine chemicals, pharmaceuticals, cosmetics, and so on. However, in order to face challenges from dynamic and demanding markets, these process industries should adopt more systematic approaches to remain competitive. As a consequence, the ongoing paradigm of chemical engineering begins to shift from an emphasis on process design to one on product design. And chemical product engineering, as a well-established branch of chemical engineering, according to the demand requires switching product design from empirical work to scientific research.¹⁻⁵ This new, broader engineering is evolutionary rather than revolutionary. $\overset{\circ-9}{}$ It will reemphasize the research on molecular structure-property relationships in the chemistry field including organic, inorganic, and biochemistry. Chemical engineers should do some contribution to bridge the gap between chemistry and chemical product engineering.³

pH stimuli-responsive brush copolymers have attracted extensive attention over recent years. Researchers have found that their increasing complexities and defined three-dimensional morphologies may better mimic some features of biomacromolecules compared to the linear copolymer counterparts.^{10–12} In the chemical product engineering field, this foundation is very useful to design excellent chemical products with certain functions, such as hydrogels, micelles, and bioconjugates, which can be potentially used in drug delivery, biotechnology, chromatography, and sensors.^{13–15} As a typical

candidate for pH-responsive systems, the chain conformation of weak polyelectrolyte poly(acrylic acid) (PAA) can be changed through the alternating ionic strength causing by the protonation-deprotonation equilibrium of carboxylate groups in aqueous medium.¹⁶ Therefore, micelles formed in aqueous solutions by PAA-based pH-responsive brush copolymers should also exhibit responsive features with respect to variation in ionic strength of the solution by adding salt influences.¹⁷ The complexation between cationic metal ions and polyelectrolyte chains can be used in water treatment systems.¹⁸ For example, in view of the rapid and unique cationic ions responsivity of the charged macromolecules, they could be used as a new polymeric sensor for water pollution by cationic ions. On the other hand, hard water containing excessive Ca²⁺ and Mg²⁺ ions will cause boilers, cooling towers, and other industrial settings breakdown.^{19,20} Systematic investigation about the complexation between Ca²⁺ or Mg²⁺ ions and charged macromolecules is helpful to realize their application in water softening.

The interactions between side chains usually exhibit a dramatic influence on the chemical properties of brush copolymers through causing their conformational changes.²¹ Previous reports have confirmed that the steric repulsion of neighboring side chains can be tuned via varying the solvent quality, side chain length, and grafting density.^{22–24} Adjusting

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the grafting density directly through different backbone composition profiles could establish the corresponding relationship between backbone structure and physicochemical behavior of brush copolymers.^{25,26} Based on the chemical product engineering viewpoint, it is very useful to design excellent chemical products with certain functions. Therefore, we prepared a series of PAA-based brush copolymers with random, gradient, and block backbone composition profiles respectively (poly(MMA-co-BIEM-graft-AA)).^{26,27} Their random, gradient, and block backbone copolymers were prepared using different approaches, and the relationship between synthesis methodology and molecular structure was established. On the other hand, the relationship between backbone structure and Ca²⁺ responsivity of brush copolymers was confirmed through investigating their Ca²⁺ responsive micelle behaviors in aqueous medium using transmission electron microscopy (TEM), light transmittance, and dynamic light scattering (DLS).

Especially, the chemical product engineering perspective will be introduced to help develop these PAA-based pH-responsive brush copolymers into new chemical products which can be used in water softening. That is to say, our present study is aiming to achieve a triplet "backbone molecular structure– Ca^{2+} responsivity–synthesis methodology" multiscale correlation, and guide for manufacturing a useful product with desired function from individual molecules in chemical product engineering field. The theme of this contribution illustrated in Scheme 1 connects the microscopic and macroscopic world and bridges the gap between chemistry and chemical product engineering.

Scheme 1. Schematic Relationship between Chemistry and Chemical Product Engineering



2. PREPARATION OF POLY(MMA-CO-BIEM-GRAFT-AA): BACKBONE MOLECULAR STRUCTURE-SYNTHESIS METHODOLOGY RELATION

Generally, liner copolymers involving random, block, and gradient composition distributions along chains can be achieved through different synthesis methodology. Typically, random copolymers with statistical average composition can be synthesized by the one-pot copolymerization of monomer pairs. Block copolymers with abrupt composition change at a joint location of two different monomers can be synthesized by sequential homopolymerization.²⁸ Additionally, gradient copolymers with gradual composition change can be easily prepared by semibatch operation.²⁹

Recently, atom transfer radical polymerization (ATRP) as one of controlled/"living" radical polymerization techniques was thought as a convenient tool for preparing well-defined (co)polymers due to its well-controlled copolymerization of monomer pairs and, thus, was usually chosen to synthesize random, block, and gradient copolymers.^{30–41} Simultaneously the controlled preparation of macromolecular brushes by "grafting from" a macroinitiator via ATRP has been extensively studied.^{42,43} This method can be used to prepare brushes with a high grafting density without being affected by steric hindrance. And the products can be easily purified through removing the low molecular weight monomer.

The detailed brush copolymers preparation process in this work is described as follows (see Scheme 2).

2.1. Synthesis of poly(MMA-co-HEMA-TMS) with Three Backbone Composition Profiles. Random copolymer was prepared via batch ATRcoP. Diblock copolymer was synthesized via sequential batch ATRP using PMMA-Br as macroinitiator which was also prepared by ATRP. The typical batch ATRP procedure is as follow: toluene, monomer, and catalyst system were first added into a flask, after deoxygenization, the initiator Eib-Br was added under N2, and finally the reaction was carried out at 90 °C for 7 h. The gradient copolymer was synthesized through semibatch ATRP. Toluene, MMA, and the catalyst system were first added into a flask. After deoxygenization, the initiator Eib-Br was added under N₂. Synchronously, the second mixture (catalyst system and HEMA-TMS) was continuously added into the first one at a model optimized rate corresponding to targeted composition.²⁷ The reaction was also carried out at 90 °C for 7 h.

The poly(MMA-*co*-HEMA-TMS) with random, block, and gradient composition profiles were obtained after removing copper complex via passing the polymer solutions through a neutral alumina column and precipitating in methanol.

2.2. Synthesis of Poly(MMA-co-BIEM) with Three Composition Profiles. First, dissolving each kind of poly-(MMA-co-HEMA-TMS) in appropriate dry THF, adding KF and TBAF, and stirring the solution for 24 h at room temperature. And then, slowly adding triethylamine and 2-bromoisobutyl bromide to the polymer solution at 0 °C and stirring it for another 24 h. Finally, the macroinitiator poly(MMA-co-BIEM) was obtained through precipitating the polymer solution into methanol. (Mn_{radom} = 15 100 g/mol, $(M_w/M_n)_{random} = 1.34$; Mn_{gradient} = 14 200 g/mol, $(M_w/M_n)_{block} = 1.22$).

2.3. Synthesis of poly(MMA-*co*-BIEM-*graft*-AA) with Three Backbone Composition Profiles. The brush copolymers with different backbone composition profiles were synthesized via batch ATRP using poly(MMA-*co*-BIEM) as macroinitiator. The reaction was carried out at 70 °C for 8 h. The polymerization was terminated via exposure to air and dilution with THF. After similar purification, the brushes poly(MMA-*co*-BIEM-*graft*-*t*BA) were obtained through precipitating the polymer solution into the mixed solvent of methanol and water (v/v, 1:1). $Mn_{radom} = 117\ 800\ g/mol$, $(M_w/M_n)_{random} = 1.42$; $Mn_{gradient} = 112\ 500\ g/mol$, $(M_w/M_n)_{gradient} = 1.44$; $Mn_{block} = 116\ 100\ g/mol$, $(M_w/M_n)_{block} = 1.45$. More characterization of the polymers (i.e., gel permeation Scheme 2. Synthesis Route of PAA-Based Brush Copolymers Poly(MMA-co-BIEM-graft-AA) with Different Backbone Structure



chromatography (GPC) and thermal gravimetric analysis (TGA)) is given in the Supporting Information.)

Subsequently, the dried brush poly(MMA-co-BIEM-grafttBA) was dissolved in dry dichloromethane. A 5-fold molar excess of CF₃COOH was added to the polymer solution, and it was stirred at room temperature. Eventually, PAA-based pHresponsive brush copolymer poly(MMA-co-BIEM-graft-AA) was obtained through precipitating the polymer solution into petroleum ether (60–90 °C).

The experimental materials, measurement methods, detailed recipes for the experimental studies, and the characterization of products can be found in our previous paper.²⁶

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The complexation between cationic metal ions and polyelectrolyte chains can be used in water treatment system.¹⁸ The brush copolymers poly(MMA-co-BIEM-graft-AA) based on random, gradient, and block backbone structure will have different properties according to their different structure. A better understanding of their backbone molecular structure— Ca^{2+} responsivity relation at the molecular level is helpful to realize their application in water softening.

3.1. Preparation of poly(MMA-*co***-BIEM**-*graft***-AA) Solution.** The copolymer aqueous solution was prepared as follows. Twenty milligrams of copolymer sample was first dissolved in a mixed solvent of dioxane and water (v/v, 95/5) overnight. Then the polymer solution was diluted by slow adding distilled water and stirred some time for equilibration. After that, a desired content CaCl₂ solution (4.0 mg/mL) was dripped to adjust the Ca²⁺ concentration of the copolymer solution. Finally, the copolymer content was adjusted to 0.1 mg/mL by adding excessive amount of water.

3.2. Measurements. Transmission electron microscopy (TEM) observation was made by a JEM1400 microscope at an acceleration voltage of 100 kV. The light transmittance through 0.1 mg/mL brush copolymer solution was determined using an Ultrospec2550 pro UV/vis spectrophotometer at $\lambda = 275$ nm through a 1.0 cm quartz sample cell. Dynamic light scattering (DLS) measurements were made on a Malvern light scattering instrument equipped with a 400 mW argon ion laser at 25 °C. The Wavelength was 532 nm, and scattering angle was 90°.

3.3. Results and Discussion. PAA-based pH sensitive brush copolymers poly(MMA-*co*-BIEM-*graft*-AA) with three different backbone structures (random, gradient, and block) but approximately the same average chemical composition ($F_{\text{BIEM}} \approx 0.3$) were successfully synthesized via the "grafting from" method.²⁶ In order to demonstrate the effects of the backbone molecular structure on the Ca²⁺ responsivity of the investigated brush copolymers, TEM was introduced to study the micelle's morphology formed in polymer solutions with different Ca²⁺ concentration and the results are shown in Figures 1–3.

Sphere micelles can be formed in the solution of random, gradient, and block brush copolymers without Ca²⁺. Their diameters are approximately 20-25 (Figure 1A), 30-40 (Figure 2A), and 40-50 nm (Figure 3A), respectively. Micelle aggregation happens eventually in all brush copolymer solutions with the increase of the Ca²⁺ concentration; however, the detailed aggregation processes of the three brush copolymers are different (Figure 1-3). For the random brush, the size of micelles decreases first when a small amount of Ca²⁺ is added into the solution and begin to increase when the Ca²⁺ concentration continue to increase, the above dimension varies within a small range (Figure 1B and C). With further increase of Ca²⁺ concentration, intermicelle complexation starts to occur and a loosely connected micelle cluster is obtained ultimately (Figure 1D). The sphere micelles formed in the solution of gradient brush also shrink by introducing Ca²⁺ (Figure 2B). However, with the increase of Ca²⁺ concentration the dimension of the contracted micelles does not increase and distinguishable micelle aggregates appear (Figure 2C). The aggregates become more and more denser with further increase of Ca^{2+} concentration (Figure 2D).

Figure 1. TEM images of the representative micelle morphologies formed in random brush copolymer poly(MMA-*rand*-BIEM-*graft*-AA) solutions at different Ca^{2+}/COO^{-} values: $Ca^{2+}/COO^{-} = (A) 0.0$, (B) 1.0, (C) 2.0, (D) 3.0.



Figure 2. TEM images of the representative micelle morphologies formed in gradient brush copolymer poly(MMA-*grad*-BIEM-*graft*-AA) solutions at different Ca^{2+}/COO^{-} values: $Ca^{2+}/COO^{-} = (A) 0.0$, (B) 1.0, (C) 2.0, (D) 3.0.

Compared with the other two brush copolymers, the average diameter of sphere micelles formed by the block brush copolymer is larger and the shrinkage of micelles is more apparent when Ca^{2+} is added into the solution (Figure 3B). Then, micelles come together to form large spherical aggregates and the second aggregation happens with the increase of the amount of Ca^{2+} (Figure 3C and D).



Figure 3. TEM images of the representative micelle morphologies formed in block brush copolymer poly(MMA-*block*-BIEM-*graft*-AA) solutions at different Ca^{2+}/COO^{-} values: $Ca^{2+}/COO^{-} = (A) 0.0$, (B) 1.0, (C) 2.0, (D) 3.0.

DLS data was recorded to confirm the results mentioned above. The size of micelles formed by random copolymer first decreases and then increases in a small range when Ca²⁺ is added into the solution (Figure 4B and C). The size distribution turns wider at $Ca^{2+}/COO^{-} = 2.0$ due to the existence of a small amount of micelle aggregates which can be seen in Figure 4C. The corresponding TEM image of these few micelle aggregates is given in the Supporting Information. When the Ca^{2+} concentration continues to increase, the size of micelles increases significantly because almost all micelles gather to form aggregates; only few scattered micelles still stay in the solution, which correspond to the two peaks in Figure 4D. For the gradient brush copolymer, the size of micelles also decreases to a small extent first (Figure 5B). Then, the size of micelles increases significantly and the size distribution turns wider due to the coexistence of a large amount of micelle aggregates and few scattered micelles (Figure 5C). The corresponding TEM image of these few scattered micelles is given in the Supporting Information. The size of micelles keeps increasing while the Ca²⁺ concentration continues to increase (Figure 5D). To the block brush copolymer, the size of micelles experiences little decrease (Figure 6B) and twice obvious increase (Figures 6C and D) with the increase of Ca²⁺ concentration. The micelles measured by DLS are with water-swollen corona, while the samples measured by TEM under high vacuum are nearly dry. Meanwhile, the polyelectrolyte effect will increase the micelle size artificially. Therefore, the size of micelles obtained via DLS is much larger.

Our previous studies²⁶ have demonstrated that random, gradient and block brush copolymers (poly(MMA-*co*-BIEM-*graft*-AA)) based on PAA as side chains exhibited different pH-induced conformational transitions due to the different spatial arrangement of side chains formed by their different backbone structure. Similarly, micelles formed by these amphiphilic ionic brush copolymers should exhibit different micelle aggregation

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Figure 4. DLS results of random brush copolymer poly(MMA-*rand*-BIEM-*graft*-AA) solutions at different Ca^{2+}/COO^- values: Ca^{2+}/COO^- = (A) 0.0, (B) 1.0, (C) 2.0, (D) 3.0.

behaviors with respect to variation in Ca^{2+} concentration. According to the analysis obtained from TEM and DLS results, the proposed different aggregation behaviors of micelles formed by three brush copolymers with different side chain distributions are schematically illustrated in Scheme 3.

Our previous studies²⁶ have demonstrated that grafting density remains constant along the random copolymer backbone and almost all AA groups distribute on the periphery of micelles. If a balance is attained between the electrostatic repulsion of the side chains and hydrophobic interactions of the backbone chains, micelles will exist stably in solution. When a small amount of Ca²⁺ is added into the solution, complexation between Ca²⁺and COO⁻ occurs within the micelle, screening of electrostatic interactions between ionized acrylic acid units by Ca²⁺ becomes a dominant effect, which induces progressive shrinkage of the corona and decrease in the size of micelles. As a result of weakened intermolecular electrostatic repulsion, the aggregation number is expected to increase and the sizes of the micelles increase. When the Ca²⁺ concentration continues to increase, intermicelle complexation between Ca²⁺ and COO⁻ groups starts to occur and, ultimately, a loosely connected micelle cluster is obtained. With further increase of Ca2+ concentration, an increasing number of micelles connect through intermicelle complexation (the schematic illustration of Ca²⁺ resulted micelle aggregation behaviors of random brush copolymer is shown in Scheme 3A).

For gradient brush, a loosely grafted molecule formed on the one end and a densely grafted molecule formed on the other end. Loosely grafted molecule ends are easy to insert in micelles because of their higher hydrophobicity. On the contrary, densely grafted molecule ends are more inclined to distribute



Figure 5. DLS results of gradient brush copolymer poly(MMA-grad-BIEM-graft-AA) solutions at different Ca^{2+}/COO^- values: $Ca^{2+}/COO^- = (A) 0.0$, (B) 1.0, (C) 2.0, (D) 3.0.

on the periphery of micelles, resulting in a higher AA density on the surface of micelles when compared with micelles formed by random brush.²⁶ The addition of Ca²⁺ will also cause screening effects on electrostatic interactions between ionized acrylic acid units. And then the corona will shrink and the hydrodynamic radius of the micelles will decrease. However, the aggregation number does not increase after the hydrodynamic radius of the micelles decreases because inside the micelles formed by gradient brush copolymer, hydrophobic interactions between the methyl groups are stronger and the aggregation number is larger compared with the random brush. Intermicelle complexation occurs much earlier at a lower Ca²⁺ concentration. Moreover, a higher AA density on the surface of micelles will provide more binding sites, and micelle aggregates formed through intermicelle complexation between Ca2+ and COOare more denser. When the Ca²⁺ concentration continues to increase, more and more micelles connect to form aggregates with network structure (the schematic illustration of Ca²⁺ resulted micelle aggregation behaviors of gradient brush copolymer is shown in Scheme 3B).

Due to the absence of steric hindrance from grafted side chains, the hydrophobic blocks PMMA of block brush copolymer are more likely to aggregate with each other and hydrophobic interactions between them are very strong.²⁶ Sphere micelles formed, by block brush, with larger size and more aggregation number compared to the other two brush copolymers. Simultaneously, the other block with high grafted density makes the shrinkage of micelles more apparent when Ca²⁺ is added into the solution. The aggregation number of the

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Figure 6. DLS results of block brush copolymer poly(MMA-*block*-BIEM-*graft*-AA) solutions at different Ca^{2+}/COO^{-} values: $Ca^{2+}/COO^{-} = (A) 0.0$, (B) 1.0, (C) 2.0, (D) 3.0.

micelles is extremely hard to change. In order to maintain micelles in equilibrium the neighboring micelles become connected through the complexation of Ca^{2+} and COO^- to form sphere aggregates with the increase of Ca^{2+} concentration. With the further increase of Ca^{2+} concentration, the second aggregation occurs between sphere aggregates. Consequently, the micelles formed by block brush copolymer undergo twice aggregation obviously (the schematic illustration of Ca^{2+} resulted micelle aggregation behaviors of block brush copolymer is shown in Scheme 3C).

In order to confirm above analyses, the micelle aggregation behaviors of three different brush copolymers induced by changing Ca²⁺ concentration were also monitored by light transmittance measurement (Figure 7) and DLS (Figure 8). From Figure 7, the light transmittance of random, gradient and block brush copolymer solutions depends on the Ca²⁺ concentration. For the random brush, when $Ca^{2+}/COO^{-} <$ 2.25, the complexation of Ca^{2+} and COO^{-} mainly occurs in the micelle, the light transmittance of the solution first increases as the shrinkage of hydrophilic shell and then decreases with the increase of the aggregation number, and these dimensions vary within a small range. When $Ca^{2+}/COO^{-} = 2.25$, the complexation of Ca2+ and COO- occurs among micelles and there is a sharp decrease for the light transmittance because of the intermicelle complexation. For the gradient brush, intramicelle complexation of Ca²⁺ and COO⁻ can also cause the shrinkage of the hydrophilic shell. However, after a small range increase, the transmittance of solution dramatically reduces to <15% (Ca^{2+}/COO^{-} = 1.75), indicating the formation of micelle aggregates. The transmittance curve of the block brush solution follows the same trend of the gradient brush: the light transmittance of the solution increases first and then sharply decreases. However, the abrupt decrease for the light transmittance occurs in a lower Ca^{2+} concentration ($Ca^{2+}/COO^- = 1.5$) and this process can be divided into two stages.

Figure 8 illustrates that the average hydrodynamic radius $(R_{\rm h})$ of aggregates in random, gradient, and block brush copolymer solutions depends on the Ca²⁺ concentration. For all the three copolymers, the micelles shrink or stretch in a small range with the increase of the Ca²⁺ concentration in solution, and then the average hydrodynamic radius of micelles increases significantly with the continuous increase of the Ca²⁺ concentration behaviors eventually occur in all brush copolymer solutions. However, the Ca²⁺ concentration for the onset aggregation increases according to the order block brush, gradient brush, and random brush, and the degree of aggregation increases in the reverse order. The micelles formed by block brush copolymer obviously undergo aggregation twice.

In summary, the above results demonstrate that the micelle aggregation behaviors in three brush copolymer solutions induced by Ca^{2+} are different due to their different backbone structure. There is a corresponding relationship between the backbone molecular structure and Ca^{2+} responsivity of PAA-based pH-responsive brush copolymers.

4. CHEMICAL PRODUCT ENGINEERING PERSPECTIVE

Generally, customers judge the value of chemical product on the basis of functionality and performance, such as hearing, smelling, and handling properties, rather than technical specifications. Compared to commodity, the structure of chemical product has a predominant impact on end-use properties. Therefore, the design and manufacture of chemical products not only requires traditional chemical industry enterprises to have a set of novel skills but also to meet the requirements of customers about end-use properties of products.

One aspect of chemical product engineering as a branch of chemical engineering is to cope with the ever-changing demands of the current industrial environment.^{1,44} And thus, well-established scientific research of chemical product engineering has been an irresistible trend in this context, where a scientific and systematized process in chemical products design is sought rather than trial-and-error procedures.⁴⁴

The objective of the preceding triplet backbone molecular structure-Ca²⁺ responsivity-synthesis methodology multiscale study about PAA-based pH-responsivity brush copolymers is to try to complete a pyramid of chemical products aiming to realize product customization. As discussed in section 2, the backbone molecular structure is an important variable in the synthesis methodology. The obtained results in section 3 illustrated that backbone composition profile will affect the Ca²⁺ responsivity of poly(MMA-co-BIEM-graft-AA) directly. Take water softening as the target chemical product, optimal water softening needs a trade-off between the backbone molecular structure, Ca²⁺ responsivity, and synthesis methodology. Consequently, the trade-off can be effectively established through combining a defined property function with respect to the product performance and backbone structure and a defined process function relating backbone structure to preparation conditions. As a whole, the complexity of the case study in this Scheme 3. Schematic Illustrations of Ca²⁺/COO⁻ Complexation-Induced Micelle Aggregation of Brush Copolymers with Different Backbone Composition Profiles



paper has been effectively managed by employing chemical product engineering concepts, which involve chemical industry, innovative chemical products, and water treatment.

Compared with the traditional product used in water softening, the alternative products in this study can be tailored previously according to the hardness of water, realized the specificity of product. The product then can be fixed in a device, removing water hardness similar to using an ion exchange membrane, or also can be used as a water softner, adding it to the water which should be softened and later removing it by filtration. However, it is inevitable that any product needs a long way to go to be available to the market. For example, it took ten years for DuPont to achieve from a polymer produced in the lab the nylon stockings sold in the market. The productization of taxol took 30 years from its discovery in the bark of pacific yew having antitumor activity to a commercially available product. Both examples tell us that chemical product engineering covers diverse areas, which require engineers to make efforts in discovery, design, manufacturing, recycling, and marketing. The case in our study still stays in the product design stage. More study should be undertaken before its commercial manufacture.

5. CONCLUSIONS

This paper first prepared a series of PAA-based brush copolymers with three backbone composition profiles (random, gradient, and block) to establish the relationship between the synthesis methodology and their backbone molecular structure. And then the effect of backbone composition profile on their Ca^{2+} responsivity was systematically investigated. TEM, light



Figure 7. Ca²⁺ concentration dependence of the light transmittance through 0.1 mg/mL poly(MMA-*co*-BIEM-*graft*-AA) solutions.



Figure 8. Ca^{2+} concentration dependence of average hydrodynamic radius (R_h) of aggregates formed in 0.1 mg/mL poly(MMA-*co*-BIEM-*graft*-AA) solutions.

transmittance, and DLS results indicate that Ca^{2+} induced micelle aggregation behaviors in three brush copolymer solutions are different due to their different backbone structure and there is a corresponding relationship between their backbone molecule structure and Ca^{2+} responsivity. The triplet backbone molecular structure– Ca^{2+} responsivity–synthesis methodology multiscale study was therefore completed in the field of chemistry. Finally, chemical product engineering perspective was introduced to successfully develop these PAA-based pH-responsive brush copolymers into new chemical products which can be used as water treatment agent.

In conclusion, the whole study can be seen as a case study of creating a useful product with desired function from individual molecules based on chemical polymerization methods and a chemical product engineering perspective. It connects the microscopic and macroscopic worlds and bridges the gap between chemistry and chemical product engineering.

ASSOCIATED CONTENT

S Supporting Information

More characterization of the polymers (i.e., GPC and TGA figures) and TEM images of micelles. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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