This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
A series of pH-responsive amphiphilic conetworks were synthesized through cross-linking of well-defined amphiphilic pentablock copolymers via atom transfer radical polymerization.
PH Sensitive Amphiphilic Conetworks Based on End-Group Cross-linking of Polydimethylsiloxane Pentablock Copolymer and Polymethylhydrosiloxane

Ming Qiu,a Xin-Zheng Zhao,a Da-Peng Liu,a and Chun-Ju Hea*

ABSTRACT: A series of pH-responsive amphiphilic conetworks (APCNs) were synthesized through cross-linking of well-defined amphiphilic pentablock copolymers via atom transfer radical polymerization (ATRP). A new ditelechelic polydimethylsiloxane macroinitiator was synthesized to initiate the polymerization of N, N-dimethylaminoethyl methacrylate. The resulting triblock copolymers show well-defined molecular weight with narrow polydisperisty, which are used as macroinitiator to incorporate allyl methacrylate to get the pentablock copolymers with allyl pendant groups. Then pentablock copolymers are fully cross-linked with polyhydrosiloxanes through hydrosilylation. The so-prepared APCNs exhibit unique properties of microphase separation of hydrophilic (HI) and hydrophobic (HO) phases with small channel size, a variable swelling capacity in media with different pH and polarity, a good mechanical property (1.3 ± 0.2 MPa) and outstanding oxygen permeability (300 ± 120 barrers). The properties of APCNs depend on the ratio of HI-HO, which can be regulated via precise synthesis of the triblock copolymers. The APCNs show well-controlled drug release to Rhodamine 6G upon varying the pH. Meanwhile, the controlled manner is also attributed to the well-defined molecular structure and tunable HI/HO composition of the APCNs.
Introduction

As the rapidly emerging novel materials that consist of covalently interconnected hydrophilic and hydrophobic polymer chains,^1^-^4^ amphiphilic conetworks (APCNs) have many unique properties, such as swelling dependence on solvent, microphase separation structure and biocompatibility, which make them promising for applications in a wide variety of areas.\textsuperscript{5}-\textsuperscript{15}

The APCNs prepared from polydimethylsiloxane (PDMS)\textsuperscript{16,17} have received great attention due to its own characteristics, i.e. excellent biocompatibility, high elasticity, heat resistance, low surface free energy, biological inertness as well as the highest oxygen permeability among all polymers, which shows a wide range of potential applications in intelligent polymer materials, soft contact lenses, biomedical materials, antifouling surfaces and biochemical sensors.\textsuperscript{18,19} Poly(N, N-dimethylaminoethyl methacrylate) (PDMAEMA), one of well-investigated hydrophilic polymers with thermo and pH sensitivity,\textsuperscript{20-24} have potential applications in drug delivery and release,\textsuperscript{25,26} gene carrier,\textsuperscript{27,28} and antibacterial surface.\textsuperscript{29,30} Patrickios group\textsuperscript{31-36} has prepared PDMAEMA-based APCNs with different architecture and studied their swelling property, degradation characteristics, storage and delivery of DNA. Therefore, an APCN consisting of PDMAEMA and PDMS segments is of great interest due to the distinguished characteristics of segment, its microphase separation, physiological inertness and biocompatible properties. However, there is no report about the synthesis of such a conetwork.

Most APCNs reported are synthesized by uncontrollable free radical
polymerization,\textsuperscript{37-39} which inevitably leads to bad conformation regularity, structure defect or even loss of performance. To minimize the defects, more recently APCNs have been prepared by cross-linking polymer chains of well-defined length using controlled methods, such as quasiliiving carbocationic polymerization (QLCCP), group transfer polymerization (GTP), reversible addition fragmentation chain transfer (RAFT) polymerization and atom transfer polymerization (ATRP).\textsuperscript{35,40-43} Among these methods, ATRP has shown outstanding capability to prepare hydrogels and APCNs with well-defined molecular structure and good mechanical properties,\textsuperscript{42,44} and the use of macroinitiator has received much attention because it simplifies the synthesis step and has a high tolerance for functional groups and impurities.\textsuperscript{45} In this study, polydimethylsiloxane di-2-bromoisobutyrate (Br-PDMS-Br) initiate the ATRP of DMAEMA (Scheme 1), and the resulting well-defined PDMAEMA-b-PDMS-b-PDMAEMA triblock copolymers is used as the macroinitiator for the ATRP of allyl methacrylate due to the preservation of active alkyl halide chain end. The introduction of poly (allyl methacrylate ) (PAMA) units in the resulting pentablock copolymers guarantees the full cross-linking of the resulting APCN since the allyl pendant groups act as crosslinking sites with polymethylhydrosiloxane. The good water swelling property as a function of pH, excellent mechanical properties and interesting drug release profile of prepared APCN suggest a promising excellent carrier for controlled release.

\textbf{Experimental Part}

\textbf{Materials.} N, N-dimethylaminoethyl methacrylate (DMAEMA) and allyl
methacrylate (AMA) were purchased from Energy Chemical Co. and purified by passing through a babic silica column to remove the inhibitor. Hydroxypropyl polydimethylsiloxane (PDMS, $M_n=4000$ g/mol, PDI=1.41), polymethylhydrosiloxane (PMHS, $M_n=6000$ g/mol, PDI=1.40) and Karstedt’s catalyst (3% Pt(0) in xylene) were purchased from Gelest and were used as received. Copper(I) bromide was purchased from Shanghai Chemical Reagent Plant and was purified according to a standard procedure.\(^{46}\) *N,N,N',N',N''-pentamethyldiethylenetriamine* (PMDETA), anhydrous magnesium sulfate (MgSO\(_4\)), Rhodamine 6G and 2-bromoiodobutyl bromide were purchased from Aldrich and used as received.

**Synthesis of Macroinitiator Br-PDMS-Br.** Hydroxypropyl polydimethylsiloxane (30 g, 7.5 mmol) and triethylamine (1.59 g, 15.8 mmol) were dissolved in 200 mL dry THF in a three-neck round bottomed flask. 2-bromoiodobutyrate (3.45 g, 15.0 mmol) was added dropwise to the stirred solution at 0 °C for 1 h. The reaction was stopped after stirring at room temperature for 16 h, filtered to remove the triethylamine hydrobromide byproduct, and evaporated under vacuum. The resulting liquid was redissolved in hexane and washed with a saturated aqueous sodium hydrogen carbonate solution three times. The organic layer was dried by anhydrous magnesium sulfate. The final PDMS macroinitiator (Br-PDMS-Br) was obtained as a slightly yellow liquid with a yield of 95%. \(^1\)H NMR (400 MHz, CDCl\(_3\), Me\(_4\)Si, $\delta$): 0.00 (m, 6H), 0.079 (s, 6H, Si(CH\(_3\))\(_2\)), 0.87 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)), 1.6 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)), 4.33 (m, 2H, SiCH\(_2\)CH\(_2\)H\(_2\)), 1.96 (s, 6H, BrC(CH\(_3\))\(_2\)).

**Synthesis of PDMAEMA-b-PDMS-b-PDMAEMA Triblock Copolymers.** A series
of triblock copolymers were synthesized by ATRP. In a typical experiment, Br-PDMS-Br macroinitiator (1.00 g, 0.25 mmol), PMDETA (0.865 g, 0.5 mmol) and CuBr (0.072 g, 0.5 mmol) were added to a Schlenk flask (100 mL) equipped with a magnetic stirring bar and degassed three times. DMAEMA (7.85 g, 50 mmol) and isopropanol (15 mL) were then injected into the reaction flask. The flask was placed in a thermostated bath at 60 °C for 12 h. The mixture was then diluted in THF and passed through a basic alumina column to remove the copper residue and evaporated until dry. The crude product was redissolved in THF and precipitated in cold hexane twice, prior to being dried for 24 h in a vacuum oven. \(^1\)H NMR (400 MHz, CDCl\(_3\), Me\(_4\)Si, \(\delta\)): 0.00 (m, 6H), 0.079 (s, 6H, Si(CH\(_3\))\(_2\)), 1.1-0.94 (3H, m, CH\(_2\)C(CH\(_3\))CO), 1.9-2.0 (m, 2H, CH\(_2\)C(CH\(_3\))CO), 2.35 (m, 6H, N(CH\(_3\))\(_2\)), 2.75 (m, 2H, COCH\(_2\)CH\(_2\)N(CH\(_3\))\(_2\)), 4.13 (m, 2H, COCH\(_2\)CH\(_2\)N(CH\(_3\))\(_2\))

**Synthesis of PDMS-Based Pentablock Copolymers.** The pentablock copolymers were synthesized using a molar feed ratio [AMA (0.6 g)]:[CuBr]:[PMDETA] of 50:1:1 in 8 mL isopropanol at 60 °C involved of 2 g triblock polymers for 18 h. The operations were used the same procedures as described above. \(^1\)H NMR (400 MHz, CDCl\(_3\), Me\(_4\)Si, \(\delta\)): 0.00 (m, 6H), 0.079 (s, 6H, Si(CH\(_3\))\(_2\)), 1.1-0.94 (3H, m, CH\(_2\)C(CH\(_3\))CO), 1.9-2.0 (m, 2H, CH\(_2\)C(CH\(_3\))CO), 2.35 (m, 6H, N(CH\(_3\))\(_2\)), 2.75 (m, 2H, COCH\(_2\)CH\(_2\)N(CH\(_3\))\(_2\)), 4.13 (m, 2H, COCH\(_2\)CH\(_2\)N(CH\(_3\))\(_2\)), 4.46 (m, 2H, OCH\(_2\)CHCH\(_2\)), 5.30 (m, 1H, CH\(_2\)CHCH\(_2\)), allyl), 5.9 (m, 2H, CH\(_2\)CHCH\(_2\), allyl).

**Synthesis of Amphiphilic Conetworks.** PAMA-b-PDMAEMA-b-PDMS-b-PDMAEMA-b-PAMA (1 g), PMHS (0.1 g) and Karstedt’s catalyst (50 uL) was
dissolved in 20 mL toluene and the mixture was stirred at room temperature for 12 h. Then the homogeneous solution was poured into a Teflon mold (3×3cm) and placed in an oven at 60 °C for 24 h. After crosslinking, the formed film was extracted by THF, and dried in vacuo at room temperature.

Scheme 1  Schematic diagram illustrating the preparation of pentablock copolymer via ATRP and crosslinking APCNs with PMHS.

Characterization Techniques

Proton Nuclear Magnetic Resonance Spectroscopy. $^1$H NMR spectra was performed at room temperature on a Bruker Avance 400 instrument using CDCl$_3$
solutions with tetramethylsilane (TMS) as an internal standard.

**Fourier Transform Infrared Spectroscopy.** FT-IR spectra were obtained with a Nicolet Instrument Nicolet 8700 spectrometer. The sample was dispersed in a KBr disk.

**Gel Permeation Chromatography.** GPC was performed on a BI-MwA Gel Permeation Chromatography (Waters, Milford, MA), equipped with a light scattering instrument (Brookhaven, Holtsville, NY) at room temperature, using THF as the eluent at a flow rate of 0.8 mL/min with a polystyrene standard as the reference.

**Determination of the Sol Fraction.** The sol fraction was determined by extracting a freshly synthesized APCN with THF for 72 h. The sol fraction was calculated as the ratio of the mass of the extractable mixture divided by the mass of virgin conetwork.

\[
Sol = \frac{m_0 - m_q}{m_0} \times 100\%
\]

Where \( m_q \) is the dry mass of the extracted samples and \( m_0 \) is the dry mass of the virgin sample.

**Measurement of the Swelling Ratio.** Swelling experiments were carried out at room temperature by immersing a pre-weighed sample in an excess of distilled water, THF, hexane and aqueous solutions of various pHs, respectively. The extent of swelling was determined by periodically taking the samples from the solvent, removing the solvent adsorbed to the surfaces by blotting with tissue paper, and weighing equilibrium swelling ratio \( (S_w) \) was recorded when the weight of the swollen samples remained unchanged for 48 h. The swelling ratio was calculated as following equation:
\[ S_\text{w} = \frac{m_t - m_0}{m_0} \times 100\% \]

Where \( m_t \) is the mass of the swollen samples and \( m_0 \) is the mass of the dry sample.

**Measurement of the Degree of Ionization.** The degree of ionization of APCN was calculated as the ratio of added HCl equivalents divided by the number of DMAEMA unit equivalents (calculated from the conetwork dry mass and conetwork composition) present in the sample. The acid titration curves were obtained by plotting the calculated degrees of ionization against the measured solution pH.

**Tensile Strength and Elongation at Break.** The tensile strength and elongation at a break of APCN were measured by Universal Testing Machine (KEXIN, WDW3020, China) in water-swollen state. The samples were formed into rectangles (6×2 cm) and the tensile speed was set at 10 mm/min. Each sample was measured three times, respectively, and the average value was obtained. The error is less than 5%.

**Oxygen Permeability.** Apparent oxygen permeability of APCN was determined at 35 °C. The instrument used together with specifications and the operational principle were described in detail.\(^4\) To obtain comparable results with different compositions, the membranes were of the same dimensions (4 cm × 4 cm × 0.2 mm) and measurements were carried out under the same conditions.

**Atomic Force Microscopy.** AFM images were recorded with a Veeco Dimension Icon Scanning Probe Microscope (Veeco Instruments) in tapping mode using silicon cantilevers from Mikromasch USA with resonance frequencies of about 160 kHz, spring constants of 10.0 N/m.

**Loading and in vitro release of drug.** The dried APCNs were immersed in 30 mL
aqueous solution of Rhodamine 6G (20 mg/mL) at room temperature for 72 h. Then the samples swollen to equilibrium were taken out and washed with water to remove the drug residued on the surface. The APCNs loaded with drugs were dried under vacuum for 2 days. These samples were available for drug release experiments without any further treatment. The amounts of drug loading in the conetworks were estimated in an indirect way. Rhodamine 6G in the conetworks exhibited the same molar absorption coefficient (530 nm) in the UV spectra as the free drugs. The amount of drug loading and encapsulation efficiency were calculated as following equation.

\[
\text{drug loading (ug/g)} = \frac{(C_0 - C_t)V}{M}
\]

\[
\text{encapsulation efficiency (\%)} = \frac{(C_0 - C_t)V}{m}
\]

Where \(C_0\) and \(C_t\) are concentrations at different time (ug/mL), \(V\) is the volume of solution (mL), \(M\) is the weight of the conetwork (g), \(m\) is the weight of drug in feed (ug).

In vitro release studies were performed in water. The samples loaded with the drug were immersed in 50 mL water at pH 7.4 and 5.2, respectively. 3 mL of the solution was withdrawn from the release medium at intervals and replaced with 3 mL fresh water. The cumulative percentage of drug release was calculated as the average of three determinations and the standard deviations did not exceed 3%.

**Results and Discussion**

Scheme 1 illustrates the synthetic strategy for a novel family of APCNs. The first step is the synthesis of PDMS macroinitiator by coupling commercially available
hydroxypropyl polydimethylsiloxane with 2-bromoisobutyryl bromide. As far as PDMS-based copolymer is concerned there are few reports of controlled synthesis of amphiphilic block copolymers. Thus Meier et al. reported the synthesis of PDMS-based amphiphilic block copolymers via ATRP using PDMS-based macroinitiator. Haddleton and co-workers reported the control synthesis of PDMS-based triblock copolymers. Here, a triblock copolymer PDMAEMA-b-PDMS-b-PDMAEMA was synthesized via ATRP of DMAEMA using Br-PDMS-Br macroinitiators and CuBr/PMDETA catalyst system. The synthesis of pentable block copolymer with allyl groups on ends is the key for preparation of well-defined amphiphilic conetworks, therefor, the incorporation of AMA segment through ATRP using PDMAEMA-b-PDMS-b-PDMAEMA macroinitiator produced pentablock copolymer with well-defined molecular weight and narrow molecular weight distribution. AMA has a conjugated methacrylic and an unconjugated allylic group. The former group has higher reactivity to form copolymers with allyl pendant groups. The present research concerns the synthesis of APCNs by combining amphiphilic pentablock copolymers with the polymethylhydrosiloxane (PMHS) through hydrosilylation. There exists an average of 100 Si-H pendant bonds per PMHS chain available for hydrosilylation, which means that the PDMAEMA-b-PDMS-b-PDMAEMA acts as cross-linker for the PMHS chains. Therefore, the important difference between the conetworks obtained by free radical copolymerization of functional macromonomers and the present work is the specific average chain length and relatively narrow molecular weight distribution of the PAMA-b-PDMAEMA-b-PDMS-b-PDMAEMA-b-PAMA
chains in comparison with the broad distribution of the cross-linked chains in the conetworks prepared by conventional free radical copolymerization of telechelic macromonomers with low molecular weight monomers.

**Polymer Synthesis**

Well-defined PDMAEMA-b-PDMS-b-PDMAEMA triblock copolymers and PAMA-b-PDMAEMA-b-PDMS-b-PDMEMA-b-PAMA pentablock copolymers are summarized in Table 1. The triblock copolymers with different block lengths of PDMAEMA were synthesized by varying the reaction time. As the reaction time is increased from 12 to 24 h, $M_n$ of the copolymer is increased from 13400 to 31000. The PDI of the triblock copolymers is increased only slightly from 1.18 to 1.24 and their GPC traces are all symmetrical monomodal (Figure 1), which indicates that no side-reactions occurred during the polymerizations. The relative wide PDI of PDMS macroinitiator, i.e.1.41, does not influence the low PDI of the resulting copolymer, which narrows down with increasing PDMAEMA chain length, indicating that the polymerization of DMAEMA proceeds in a controlled manner. As ATRP process occurs at a rate balance between activation ($K_{act}$) and deactivation ($K_{deact}$), the rate of reaction is not as high as radical polymerization reaction. When the conversion reaches a high level, the rate of propagation is slowed down considerably, the rate of any side reaction increases, leading to an increasing PDI of the final polymer. Pentablock copolymers were synthesized by ATRP using triblock copolymers as the macroinitiators. However, the chain length of triblock copolymers influences the activity of alkyl halide chain ends, the larger molecular weight of triblock copolymer
is, and the lower activity of alkyl halide is. Therefore, the number of AMA repeat units in the pentablock copolymers decreases with increasing PDMAEMA chain length, i.e. 40, 34 and 26, respectively. The PDI of the pentablock copolymers remain almost the same as the triblock copolymers, indicating the polymerization is controllable.

Table 1 Characterization of the PDMAEMA-b-PDMS-b-PDMAEMA triblock copolymers and PAMA-b-PDMAEMA-b-PDMS-b-PDMAEMA-b-PAMA pentablock copolymers synthesized by ATRP.

<table>
<thead>
<tr>
<th>polymer structure</th>
<th>reaction Time</th>
<th>( M_{\text{n,cal}}^b )</th>
<th>( M_{\text{n,NMR}}^c )</th>
<th>( M_{\text{n,GPC}}^d )</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>( D_{30})-b-P_{54}-b-D_{10} )</td>
<td>12</td>
<td>14.0</td>
<td>13.4</td>
<td>17.8</td>
<td>1.20</td>
</tr>
<tr>
<td>( D_{61})-b-P_{54}-b-D_{61} )</td>
<td>18</td>
<td>18.8</td>
<td>23.2</td>
<td>23.4</td>
<td>1.18</td>
</tr>
<tr>
<td>( D_{86})-b-P_{54}-b-D_{86} )</td>
<td>24</td>
<td>30.7</td>
<td>31.0</td>
<td>35.8</td>
<td>1.24</td>
</tr>
<tr>
<td>( A_{20})-b-D_{30})-b-P_{54}-b-D_{30})-b-A_{20} )</td>
<td>18</td>
<td>17.2</td>
<td>18.5</td>
<td>20.8</td>
<td>1.26</td>
</tr>
<tr>
<td>( A_{17})-b-D_{61})-b-P_{54}-b-D_{61})-b-A_{17} )</td>
<td>18</td>
<td>25.3</td>
<td>27.5</td>
<td>31.5</td>
<td>1.21</td>
</tr>
<tr>
<td>( A_{13})-b-D_{86})-b-P_{54}-b-D_{86})-b-A_{13} )</td>
<td>18</td>
<td>32.8</td>
<td>34.3</td>
<td>37.9</td>
<td>1.33</td>
</tr>
</tbody>
</table>

\( ^a D, \text{DMAEMA}; P, \text{PDMS}; A, \text{AMA}. \) The subscript means the number of the unit, calculated from the NMR.

\( ^b \)Calculated from \(^1\)H NMR based on PDMS unit (6H at 0.09 ppm) , DMAEMA unit (2H at 4.1 ppm) , AMA unit (2H at 4.5 ppm).

\( ^c \)Determined by GPC measurement using polystyrene standards.

\( ^d \)Theoretical \( M_n = [\text{monomer}]/[\text{initiator}] \times (\text{monomer conversion}) \times (\text{monomer molecular weight}) + \) (initiator molecular weight).
Figure 1. GPC traces of D₄₋b-P₅₄₋b-D₄ triblock copolymers and A₁₃₋b-D₇₆₋b-P₅₄₋b-D₇₆₋b-A₁₃ pentablock copolymer. D, P and A are further abbreviations for DMAEMA, PDMS and AMA, respectively. The subscript means the number of repeat units.

The compositions of the copolymers were first determined by ¹H NMR. Figure 2 (a) shows the ¹H NMR spectrum of the Br-PDMS-Br macroinitiator. The chemical shift at 1.92 ppm is assigned to the protons (d, BrC(CH₃)₂) of the 2-bromo-isobutyryl groups. The chemical shift at 4.12 ppm is attributed to the protons adjacent to the oxygen moiety (e, OCH₂). From the area ratio of peak d and peak e, the extent of halogenation in the Br-PDMS-Br macroinitiator is determined to be 90.8%. Figure 2 (b) and (c) shows the ¹H NMR spectra of PDMAEMA₃₀₋b-PDMS₅₄₋b-PDMAEMA₃₀ and PAMA₂₀₋b-PDMAEMA₃₀₋b-PDMS₅₄₋b-PDMAEMA₃₀₋b-PAMA₂₀, respectively. The signals at 2.35, 2.63 and 4.12 ppm are mainly assigned to the methylene (d, NCH₂) and methyl (e, N(CH₃)₂) and methylene (f, COOCH₂) protons of the DMAEMA units. The chemical shifts at 4.50, 5.32 and 5.89 ppm correspond to the protons in allyl group of the AMA units, indicating the successful incorporation of
AMA. To further confirm the structure of copolymer, FT-IR measurement is utilized to characterize the block copolymer. Figure 3 shows the FT-IR spectra of D$_{30}$-b-P$_{54}$-b-D$_{30}$ and A$_{20}$-b-D$_{30}$-b-P$_{54}$-b-D$_{30}$-b-A$_{20}$, respectively, where the three strong tertiary amide absorption bands at about 2825 cm$^{-1}$, 2764 cm$^{-1}$, 1266 cm$^{-1}$ are associated with the DMAEMA block. The intensities of peak at about 1736 cm$^{-1}$ increased significantly with the incorporation of AMA. The characteristic band of the AMA component at about 1640 cm$^{-1}$ is observed in the FT-IR spectra of the A$_{20}$-b-D$_{30}$-b-P$_{54}$-b-D$_{30}$-b-A$_{20}$.
Figure 2. The $^1$H NMR spectra of the (a) Br-PDMS-Br; (b) D$_{61}$-b-P$_{54}$-b-D$_{61}$; (c) A$_{17}$-b-D$_{61}$-b-P$_{54}$-b-D$_{61}$-b-A$_{17}$ in CCl$_3$D.
Characterization of the APCNS

Sol Fraction of the Conetworks. Table 2 shows the compositions of APCNs and the sol fraction extracted from each conetwork. In all cases the sol fraction was relatively low, with the lowest value being as low as 4.5% and the highest 8.5%, indicating essentially complete crosslinking and control over the conetwork structure.

Table 2 Fabrication composition of conetworks and corresponding sol fraction percentage and thickness.

<table>
<thead>
<tr>
<th>sample</th>
<th>block used (g)</th>
<th>PMHS crosslinker (g)</th>
<th>total DMAEMA (w %)</th>
<th>sol fraction (w/w %)</th>
<th>thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APCN-1</td>
<td>0.56</td>
<td>0.30</td>
<td>33.2</td>
<td>4.5</td>
<td>0.20 ± 0.02</td>
</tr>
<tr>
<td>APCN-2</td>
<td>0.80</td>
<td>0.30</td>
<td>50.7</td>
<td>6.3</td>
<td>0.19 ± 0.03</td>
</tr>
<tr>
<td>APCN-3</td>
<td>0.97</td>
<td>0.30</td>
<td>60.1</td>
<td>8.5</td>
<td>0.20 ± 0.04</td>
</tr>
</tbody>
</table>

Characterization of the Degree of Swelling of the APCNs. One of the most attractive characteristics of APCN is its property in different solvents due to the
existence of both HO and HI phases in conetworks. Figure 4 shows the $S_w$ of APCN-3 in THF, neutral water and hexane. THF is a good solvent for both PDMS and DMAEMA, which APCN can fully swell. In contrast to THF, pure water is a good solvent for DMAEMA but poor for PDMS and AMA units, leading to lower $S_w$ in neutral water than in THF. Figure 4(c) shows the swelling ratios of APCNs in hexane, which is a good solvent for PDMS and AMA but poor for DMAEMA. The $S_w$ value of APCN-3 in hexane is smaller than that in neutral water as APCN-3 has more hydrophilic phase than hydrophobic phase.

Figure 5 shows both the degree of swelling and the calculated degree of ionization of APCN-3 against the solution pH. The $S_w$ increased as the pH decreased. Because the DMAEMA units become protonated at low pH, which resulted in the establishment of an osmotic pressure within the conetwork from the counterions to the charged DMAEMA units and creation of electrostatic repulsions between the polymer chains.\textsuperscript{31} The degrees of swelling and the calculated degrees of ionization of APCN-1 and APCN-2 have the same changing trend as the APCN-3. And the APCNs do not start to swell at the same pH, which influenced by their composition.
Effective pKₐs of the conetworks. The effective pKₐ values of the DMAEMA units in the conetworks were taken from Figure 5 and presented in Table 3. The pKₐ of PDMAEMA is approximately 8, while the effective pKₐ values of the DMAEMA units in all conetworks were significantly lower, at a range from 5.2 to 5.8, which is attributed to the polyelectrolyte effect, Donnan equilibrium and the reduction of the
Conetwork dielectric constant induced by the presence of the hydrophobic units.\textsuperscript{31} This phenomenon shows similar tendency with other conetwork studies.\textsuperscript{31, 36}

**Table 3** $pK_a$s of the DMAEMA Monomer Repeating Units in the End-Linked Conetworks

<table>
<thead>
<tr>
<th>Sample</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>APCN-1</td>
<td>5.2</td>
</tr>
<tr>
<td>APCN-2</td>
<td>5.7</td>
</tr>
<tr>
<td>APCN-3</td>
<td>5.8</td>
</tr>
</tbody>
</table>

**Mechanical Properties of the Conetworks.** As shown in Figure 6, the tensile strengths of all the APCNs exceed 1 MPa at water-swollen state, which are 3 times to other conetwork that contained DMAEMA and ε-caprolactone (CL) through ATRP reported in the literature, i.e., 0.37 MPa.\textsuperscript{50} This phenomenon is mainly contributed to the existence of PDMS phase, which reinforced the hydrophilic PDMAEMA phase. Meanwhile, ATRP avoids the formation of inhomogeneity throughout the conetwork structure as usually encountered with an uncontrolled polymerization. Figure 6 shows a decrease in tensile strength and an increase in elongation ratio with increasing PDMAEMA block length into APCN.
Oxygen Permeability. High oxygen permeability is a key requirement for a biological device and we focus on this requirement when constructing the APCN. Figure 7 shows the apparent oxygen permeability of water-swollen PDMAEMA$_x$-$b$-PDMS$_{54}$-$b$-PDMEMA$_y$/PMHS membranes as a function of PDMAEMA segment chain length. The data are collected by using 0.2 mm thick membranes and the boundary layer effect is not taken into account. Therefore, the true permeability is slightly higher than those test values.

As shown in Figure 7, oxygen permeability is decreased from 420 to 181 barrers by increasing the PDMAEMA content from 33 to 61%. This trend is not surprising in view of the high gas permeability of PDMS and low oxygen permeability of hydrogels. It is noteworthy that the oxygen permeability of the present APCN, even those containing relatively large amounts of PDMAEMA, are similar to the best commercial extended-wear soft contact lenses, i.e. 195±4 barrers. Therefore, the resulting APCNs exhibit very high oxygen permeability.
Figure 7. Oxygen permeability of APCNs as a function of PDMAEMA content (1barrer = $10^{-11}$ (cm²/s)(mL of O₂ (STP))/(mL mmHg)).

**Atomic Force Microscopy.** Atomic force microscopy (AFM) was used to visually investigate the morphology of the APCNs. Figure 8 displays the AFM images (phase mode) of the surface of the conetworks, which depicting the nanoscale phase separation. The soft PDMS appears darker. Brighter structures are related to the brittle PDMAEMA. It is obviously that APCN-3 has larger brighter domain than the APCN-1, which is in agreement with the fact that APCN-3 has a higher HI content.

Figure 8. AFM phase mode images on surface of APCN-1 and APCN-3. In the
tapping mode, PDMS shows dark and DMAEMA show light.

**In Vitro Drug release Studies.** The DMAEMA-based hydrogels and APCNs have been widely explored as a drug carrier.\textsuperscript{25,26,52} Herein, a highly water-soluble dye, Rhodamine 6G was used for loading and in vitro release from the prepared APCNs. Table 4 shows the amount of drug loading and encapsulation efficiency of the APCNs. The results shows a similar drug loading levels of APCNs, indicating that the drug loading levels is dominated by the swelling ratio ($S_w$) of the APCNs rather than the hydrophilic (HI) / hydrophobic (HO) composition. The larger $S_w$ of APCNs allows more Rhodamine 6G solution encapsulation, and thus a higher drug loading levels.

**Table 4** Drug loading levels and encapsulation efficiency of APCNs

<table>
<thead>
<tr>
<th>sample</th>
<th>weight of samples (g)</th>
<th>drug loading (%)</th>
<th>encapsulation efficiency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APCN-1</td>
<td>0.33</td>
<td>2.2</td>
<td>1.2</td>
</tr>
<tr>
<td>APCN-2</td>
<td>0.55</td>
<td>5.3</td>
<td>4.8</td>
</tr>
<tr>
<td>APCN-3</td>
<td>0.54</td>
<td>7.1</td>
<td>6.4</td>
</tr>
</tbody>
</table>
**Figure 9.** Release kinetics of Rhodamine 6G from loaded APCNs

Figure 9 present the dissolution profile of pure Rhodamine 6G with a concentration of 0.2 g/L and Rhodamine 6G in vitro release profiles from contworks with different pHs. It can be clearly seen that the pure drug is completely released in water in 10 minutes, which accounts for the dissolution procedure of the drugs. But all three contworks are able to control the Rhodamine 6G release. APCN-3 exhibits a relatively faster drug release rate than APCN-1 and APCN-2 in water (pH=7.4). Rhodamine 6G release is facilitated by the swelling behavior of conetworks with the diffusion as the driving force. APCN-3 has a high HI content, high Sw in water, which presents a fast drug release profile. And APCN-3 has less cross-linking point than APCN-1 and APCN-2, which also increases the drug release efficiency.

APCN-3 was chosen for a pH-triggered release study. Figure 9 shows the pH-sensitive drug release behavior of APCN-3 in pH 7.4 and pH 5.2 respectively, where APCN-3 in acid buffer (pH=5.2) has a faster drug release profile, which is 15 percent more than in the neutral buffer (pH=7.4). At low pH, the DMAEMA units become protonated, leading to an increase in hydrophilicity of polymer chains, which facilitated drug escape from conetworks. Overall, the result shows that these conetworks respond to pH stimuli to control drug release.

**Conclusions**

Conclusively, we have described the synthesis of PDMAEMA-involved amphiphilic conetworks through cross-linking of amphiphilic pentablock copolymers via ATRP with well-defined molecular weight and narrow polydispersity. The APCNs
exhibit unique pH-responsive swelling behavior, excellent mechanical properties, outstanding oxygen permeability and phase separation, which can be regulated via precise control of molecular structure and tunable HI/HO composition. The APCNs are suitable for controlled release of Rhodamine 6G, where the release rate can be regulated by varying the HI composition, cross-linking density and the pH of media. The ability of these APCNs to adsorb and desorb solutes in a controlled manner upon triggering the pH in aqueous media, may allow for their potential application as a carrier for controlled release.

**Acknowledgments**

This work was financially supported by National Science Foundation (NSF51103019, NSF21174027) and National High technology Research and Development Projects (863, 2012AA03A605). Program for New Centure Excellent Talents in University (12X10623).

**Notes and References**

a State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, College of Materials Science and Engineering, Donghua University, 2999 North Renmin Road, songjiang District,Shanghai, 201620, P. R. China.

E-mail: chunjuhe@dhu.edu.cn


8 J. Kang, G. Erdodi, J. P. Kennedy, H. Chou, L. Lu and S. Grundfest-Broniatowski,


14 S. Meskath, G. Urban and J. Heinze, A New Optochemical Chlorine Gas Sensor Based on the Application of Amphiphilic Co-networks as Matrices, *Sensors and


20 A. S. Lee, A. P. Gast, V. Bultulin and S. P. Armes, Characterizing the Structure of


27 Y. L. Lo, G. J. Chen, T. H. Feng, M. H. Lia and L. F. Wang, Synthesis and


40 A. I. Triftaridou, D. Kafouris, M. Vamvakaki, T. K. Georgiou, T. C. Krasia, E.


