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A Clean Synthesis Approach to Biocompatible Amphiphilic Conetworks via Reversible Addition-Fragmentation Chain Transfer Polymerization and Thiol-ene Chemistry

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Abstract

A series of amphiphilic block copolymers containing hydrophobic polydimethylsiloxane (PDMS) segments and hydrophilic poly(N,N-dimethylacrylamide) (PDMAAm) segments have been synthesized by reversible addition-fragmentation chain transfer (RAFT) polymerization, which were then crosslinked into well-defined amphiphilic conetworks (APCNs) via ultraviolet (UV) induced thiol-ene click chemistry. Briefly, PDMS-based RAFT agent was synthesized from esterification between trithiocarbonate and bis(hydroxyethyloxypropyl) PDMS, which was applied to control the RAFT polymerization of monomer DMAAm and allyl methyacrylate (AMA) to form amphiphilic copolymers with well-defined molecular mass and narrow dispersity. The amphiphilic copolymers were then crosslinking via UV induced thiol-ene click chemistry into APCNs, which showed unique amphiphilic characters as well as good mechanical properties, making them potential candidates in biomaterials. Transmission electron microscope (TEM) and atomic force microscope (AFM) inferred that the resultant APCN exhibited the behavior of microphase separation with small channel size and uniform phase domain. Therefore, this kind of APCN possessed excellent comprehensive properties, i.e. well-defined and co-continuous microstructure, high water uptake property with homogeneous hydrophilic channel, low cytotoxicity, high mechanical strength (2.1±0.7 MPa) and elongation ratio (173±17%), suggesting a promising biomaterial candidate in contact lenses, drug controlled systems, biomedical scaffolds for tissue engineering and supports for biocatalysts.

Keywords: polydimethylsiloxane, amphiphilic conetworks, thiol-ene, reversible addition-fragmentation chain transfer polymerization

Introduction

Amphiphilic polymer conetworks (APCNs)[1-41], as a fairly class of emerging polymeric materials, consisting of covalently interconnected hydrophiphilic and hydrophobic units with continuous morphology result in orthogonal properties, such as amphiphilic structure, nano-phase separated morphology, and semi-permeability,[3,4] which can swell both in water and organic solvents and exhibit a large tendency for micro-phase separation due to thermally incompatible hydrophilic and hydrophobic segments.[5-10] The diversely functional behavior of APCNs makes them

good candidates for various applications, including contact lenses[11], drug controlled release[12,13], enzyme immobilization[14], separation membranes[15,16], tissue engineering[17]and other biomaterials.[18,19]

Recently, polydimethylsiloxane (PDMS) has received great attention in APCN fabrication due to its unique characteristics as low surface free energy, high elasticity, heat resistance, biological inertness, excellent biocompatibility as well as the highest oxygen permeability among other polymers,[20-22] which has been widely associated with other units into block and graft copolymers.[22-24] A wide variety of hydrophilic units, such as poly(ethylene glycol)[22,24], polyvinylpyrrolidone[25], and (meth)acrylamides and functional (meth)acrylates[26-31] have been used. Poly(N,N-dimethylacrylamide) (PDMAAm), as one of the acrylamides, a commonly used hydrolytic stable, physiologically inert and biocompatible polymer, is deemed to be suitable for the biomaterial applications.[32-34] Kennedy's group has prepared APCN containing PDMAAm segments and studied its insulin permeability for semi-permeable artificial pancreas application,[35] which draws great attention to fabricate APCN containing PDMS and PDMAAm.[32,36]

Conventionally, most reported APCNs have been prepared via free radical polymerization between macromonomer and monomer,[33,34,37.38] where macro phase separation will occur originated from thermodynamic incompatibility of different segments and thermodynamic aggregative of same segments, which inevitably leads to poor conformation regularity, structure defect or even loss of performance[2,39]. Although another optional method is to choose multifunctional polymers with defined molecular mass,[3,4,16,24,40,41] the random crosslinking between hydrophilic polymers and hydrophobic polymers often leads to some structure defects in the resulting APCNs. Besides, the limited types of polymers with multifunctional groups restrict its extensive application in APCN fabrication. To minimize these defects, many efforts have been made to seek effective approaches for the preparation of polymeric networks by cross-linking well-defined amphiphilic polymer chains via controlled methods.[9,10,36] Reversible addition-fragmentation chain transfer (RAFT) polymerization as one of the most powerful methods in the field of reversible deactivation radical polymerization,[42,43] has been widely used for the preparation of polymers with well-defined molecular mass and narrow dispersity. In addition, RAFT polymerization has been proved to be a functional group tolerant method to control the polymerization process without any heavy metal ion residual, which has been extensively applied for the synthesis of various kinds of topological structure copolymers with functional groups.[43-46] Meanwhile, the functional groups in well-defined copolymer have explored their possible combination with click chemistry as a highly effective approach for the preparation of well-defined polymer co-networks due to its reaction specificity, high efficiency and functional group tolerance.[47-49] The newly emerging thiol-ene click chemistry induced by thermal or photochemical process, without any heavy ions residual as encountered by azide-alkyne click reaction, exhibits a more attractive application for biomaterials fabrication, where low toxicity and high efficiency are required especially in oral rehabilitation areas.[47-51] Thus, the combination of RAFT polymerization and thiol-ene click chemistry has been extensively used for the preparation of functional polymers materials with well-defined molecular structure and high efficiency, which provides an convenient approach in the areas of new material fabrication.[52-54] Therefore, it is of great interest to fabricate an APCN containing PDMS/PDMAAm segments via RAFT polymerization and crosslinked by thiol-ene click chemistry.

In this work, a straightforward method has been investigated to fabricate PDMS based APCN by combining RAFT polymerization with thiol-ene click chemistry in a clean way with high efficiency. Briefly, a new

PDMS-based macro-RAFT agent was synthesized to control the polymerization of N,N-dimethylacrylamide to obtain a triblock copolymer, which further controlled the polymerization of allyl methacrylate and was then modified to remove bio-toxic thiocarbonylthio groups. The allyl groups in the resulting copolymer were crosslinked with pentaerythritol tetra(3-mercaptopropionate) into APCN via thiol-ene click chemistry induced by ultraviolet light. The resulting APCN with well-defined molecular structure exhibits distinguished properties, i.e. unique swelling properties, low cytotoxicity, high mechanical properties as well as microphase-separated morphology with small channel size and uniform phase domain, suggesting a promising biomaterial in contact lenses, drug controlled systems, biomedical scaffolds for tissue engineering, supports for biocatalysts and especially semi-permeability materials for bioartificial pancreas fabrication.

Experimental

Materials

Azobisisbutyronitrile (AIBN) was recrystallized from methanol before use. N,N-dimethylacrylamide (DMAAm) and allyl methacrylate (AMA) were purified by passing over a column of basic alumina to remove inhibitor. Tris (2-carboxyethyl) phosphine (TCEP, 98%), phosphate buffer solution (PBS, pH=7.4), tert-butyl acrylate (t-BA, 99%) and n-hexamine were supplied by Aladdin Industrial Inc. without further purification. N,N-Dicyclohexylcarbodiimide (DCC, 99%), 4-dimethylaminopyridine (DMAP, 99%), and 2,2-dimethoxy-2-phenylacetophenone (DMPA, 98%) were purchased from J&K Scientific Ltd. Bis(hydroxyethyloxypropyl) polydimethylsiloxane (HO-PDMS-OH, DMS-C21, M_n=4000 g.mol^{-1}, D=1.12) was purchased from Gelest. Pentaerythritol tetra(3-mercaptopropionate) (PETMP, 90%) was purchased from Tokyo Chemical Industry Co., Ltd. BHK-21 cells were purchased from Shanghai Institute of Biochemistry Cell Biology. Anhydrous dichloromethane and tetrahydrofuran were distilled over calcium hydride before use. All reagents unless otherwise stated were purchased from Sinopharm Chemical Reagent Co., Ltd. and used as received without further purification.

Characterization

Gel Permeation Chromatography. GPC was performed on a BI-MwA Gel Permeation Chromatography (Waters, USA), equipped with a light scattering instrument (Brookhaven, USA) at room temperature, using THF as the eluent at a flow rate of 1mL/min with a polystyrene standard as the reference.

Proton Nuclear Magnetic Resonance. ^{1}H NMR spectroscopy was performed on a Bruker Avance 400 instrument with $CDCl_3$ containing 1% TMS as internal reference.

Ultraviolet Irradiation. Intelli-Ray 400 (Uvitron, USA) was applied to induce the thiol-ene reaction in light intensity of 50%-100% for 0.5 h (λ=365 nm).

Atomic Force Microscopy. AFM (E-SWEEP, Seiko, Japan) was applied for imaging the micro-phase separation of APCN surfaces in tapping mode. The surfaces of the dried samples were microtomed at room temperature with a demand knife from Diatome and a Microtom ULTRACUTUCT (Leica), removing about 300 nm from the surface.

Transmission Electron Microscope. TEM was performed on a JEOL JEM-2010 high-resolution transmission electron microscope at an acceleration voltage of 120 kV. Sections of samples with 200-300 nm were trimmed using an ultrathin microtome machine before testing.

Scanning Electron Microscopy. SEM was performed on a JEOL JSM5600 scanning electron microscope using an accelerating voltage of 15 kV. The samples were then mounted on aluminium specimen stubs and sputter coated with gold before being examined.

Differential Scan Calorimeter. DSC thermographs were performed on a DSC 204 F1 (Phoenix, Germany) instrument. The samples were quickly heated to 150 ℃ to eliminate theirs heat history and then quickly cooled to -150 ℃ with liquid nitrogen. After preparation process, DCS curves were recorded during the reheating process from -150 ℃ - 150 ℃ at a heating rate of 10 ℃ $\cdot$min^{-1} under nitrogen flow.

Tensile Strength and Elongation at Break. Tensile strength and elongation at break were measured by Universal Testing Machine (KEXIN, WDW3020, P. R. China). Samples were made into rectangle (6×2 cm^2) and tensile speed was set at 10 mm/min. Each sample was measured three times and the average value was obtained. The error was less than 5%.

Cell Culture. BHK-21 cells were cultured in a culture flask in RPMI-1640 medium filled with 1% L-glutamine, 1% penicillin/streptomycin and 10% fetal bovine serum, which then grew at 37 ℃ with 5% CO_2 for 3 days. Prior to cell culture, all samples (15×15×2 mm^3) were placed in a 12-well plate and washed with PBS.

Synthesis of PDMS-based Macro-RAFT

Chain transfer agent (CTA) S-1-Dodecyl-S'-(α, α'-dimethyl-α''-dimethyl-α''-acetic acid) trithiocarbonate was synthesized according to the literature[45] with some modification. PDMS based macro-RAFT was prepared by the esterification of CTA and HO-PDMS-OH in the presence of DCC/DMAP.[55] Procedures were performed as follows: CTA (2.2 g , 6.0 mmol) and DMAP (0.18 g, 1.5 mmol) were dissolved in 30 mL of anhydrous methylene chloride, then the mixture was stirred for 5 min before 4.0 g of HO-PDMS-OH (1 mmol) and 0.45 g of DCC (2.2 mmol) were added. The solution was stirred at room temperature for over 24 h, filtered through a Buchner funnel and passed through a silica gel column. The solution was concentrated on a rotary evaporator, re-filtered and washed several times to remove the 1, 3-dicyclohexylurea (DCU) and unreacted CTA, and then dried under vacuum overnight to yield transparent yellow oil. Yield: 3.91 g (63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.27 (t, 4H, $CH_2C\boldsymbol{H}_2OC{=}O$), 3.64 (t, 4H, $CH_2C\boldsymbol{H}_2O$), 3.43 (m, 4H, $OCH_2C\boldsymbol{H}_2$), 3.29 (t, 4H, $SC\boldsymbol{H}_2(CH_2)_8$), 1.73 (s, 12H, $C(C\boldsymbol{H}_3)_2$), 1.57 (m, $SiCH_2C\boldsymbol{H}_2$), 1.28 (m, $CH_2(C\boldsymbol{H}_2)_8CH_3$), 0.9 (t, 6H, $C\boldsymbol{H}_3CH_2$), 0.55 (m, 4H, $SiC\boldsymbol{H}_2CH_2$), 0.1 (s, 6H, $Si(C\boldsymbol{H}_3)_2$). $M_{n,GPC}$=6800 g mol^{-1}, $M_{n,NMR}$=4700 g mol^{-1}, D=1.18.

Synthesis of Triblock Copolymer Polydimethylacrylamide-polydimethylsiloxane-polydimethylacrylamide (PDMAAm-PDMS-PDMAAm)

A mixure of the macro-RAFT (1.46 g, 0.31 mmol**)**, AIBN (6 mg, 0.037 mmol), and DMAAm (3.22 g, 25 mmol**)** in THF (20 mL) was placed in a round-bottom flask, deoxygenated by bubbling nitrogen for 30 min at room temperature and then immerged in a preheated oil bath. The polymerization proceeded at 65 ℃ for 6 h under constant magnetic stirring. The reaction mixture was quenched after being exposed to air. The polymer was precipitated into n-hexane three times to get a bright yellow solid, which was then removed to a vacuum oven and

dried at 65 ℃ overnight. Yield: 3.83 g (82%). ^{1}H NMR (400 MHz, $CDCl_3$):δ 3.64 (t, 4H, CH_2CH_2O), 3.43 (m, OCH_2CH_2), 3.16 (t, 2H, CH_2CH(CON)S), 3.08 (s, 1H, SCH_2CH_2), 3.05-2.80 (m, 6H, $N(CH_3)_2$), 2.66 (s, 2H, CH_2CH(CON)S), 1.73 (s, 6H, $C(CH_3)_2$), 1.62 (m, 2H, $SCH_2CH_2CH_2$), 1.28 (m, $CH_2(CH_2)_8CH_3$), 0.92-0.86 (t, 5H, CH_3CH_2), 0.1 (s, 6H, $Si(CH_3)_2$). $M_{n,GPC}$ =2.88×10^4 g mol^{-1}, $M_{n,NMR}$=3.08×10^4 g mol^{-1}, D=1.30.

Synthesis of Pentablock Copolymer Polyallylmethacrylate-polydimethylacrylamide-polydimethylsiloxane-polydimethylacrylamide-polyallylmethacrylate (PAMA-PDMAAm- PDMS-PDMAAm-PAMA)

A mixture of triblock copolymer PDMAAm-PDMS-PDMAAm (6.16 g, 0.2 mmol), AMA (0.256 g, 2 mmol), AIBN (4 mg, 0.022 mmol), and THF (20 mL) was placed in a 100 mL round-bottom flask, deoxygenated by bubbling nitrogen for 30 min at room temperature and then immerged in a preheated oil bath. The polymerization proceeded at 65 ℃ for 11 h under constant magnetic stirring. The reaction mixture was quenched after being exposing to air. The polymer was precipitated into n-hexane three times to obtain a light yellow solid, which was dried under vacuum at 65 ℃ overnight. Yield: 5.61 g (87%). ^{1}H NMR (400 MHz, $CDCl_3$):δ 5.98 (s, 1H, $CH_2CH=CH_2$), 5.34 (d, 2H, $CH=CH_2$) 4.49 (s, 2H, $CH_2CH=CH_2$), 4.14 (m, $CH_2CH_2OC=O$), 3.16 (t, 2H, CH_2CH(CO)S), 3.08 (s, 1H, SCH_2CH_2), 3.05-2.80 (m, 6H, $N(CH_3)_2$), 2.66 (s, 2H, CH_2CH(CON)S), 1.80 (s, 3H, CH_2C(COO)(CH_3)S), 1.73 (s, 6H, $C(CH_3)_2$), 1.62 (m, 2H, $SCH_2CH_2CH_2$), 1.28 (m,$CH_2(CH_2)_8CH_3$), 1.07 (s, 3H, $CH_2CH(CH_3)$), 0.92-0.86 (t, 6H, CH_3CH_2), 0.49-0.58 (m, $SiCH_2CH_2$), 0.1 (s, 6H, $Si(CH_3)_2$). $M_{n,GPC}$ =3.16×10^4 g mol^{-1}, $M_{n,NMR}$= 3.19×10^4 g mol^{-1}, D=1.33.

Post Modification of PAMA-PDMAAm-PDMS-PDMAAm-PAMA

Pentablock copolymer PAMA-PDMAAm-PDMS-PDMAAm-PAMA (6.90 g, 0.2 mmol), n-butylamine (0.07 g, 1 mmol), and trace amount of the reducing agent, TCEP, were dissolved in THF (20 mL). The solution was stirred for 1 h at room temperature under a nitrogen atmosphere, which was changed from originally yellow to colorless. An access of tert-butyl acrylate (0.256 g, 2 mmol) was added and the reaction was left to proceed at room temperature for another 10 h. Afterwards, the solution was precipitated into n-hexane 3 times to get a colorless solid, which was then removed to a vacuum oven and dried at 65 ℃ overnight. Yield: 6.58 g (91%). ^{1}H NMR (400 MHz, $CDCl_3$):δ 5.98 (s, 1H, $CH_2CH=CH_2$), 5.34 (d, 2H, $CH=CH_2$) 4.49 (s, 2H, $CH_2CH=CH_2$), 4.14 (m, $CH_2CH_2OC=O$), 3.16 (t, 2H, SCH_2CH_2), 3.05-2.8 (m, 6H, $N(CH_3)_2$), 2.66 (s, 2H, CH_2CH(CON)S), 1.80 (s, 3H, CH_2C(COO)(CH_3)S), 1.73 (s, 6H, $C(CH_3)_2$), 1.37 (s, 9H, $COO(CH_3)_3$), 1.28 (m,$CH_2(CH_2)_8CH_3$), 1.07 (s, 3H, $CH_2CH(CH_3)$), 0.49-0.58 (m, $SiCH_2CH_2$), 0.1 (s, 6H, Si ($CH_3)_2$). $M_{n,GPC}$ =3.08×10^4 g mol^{-1}, $M_{n,NMR}$=3.40×10^4 g mol^{-1}, D=1.35.

Preparation of APCNs via Thiol-Ene Click Chemistry crosslinking

Post modified PAMA-PDMAAm-PDMS-PDMAAm-PAMA (1.0 g, 0.1 mmol), pentaerythritol tetra (3-mercaptopropionate) (0.326 g, 0.67 mmol) and DMPA (6 mg, 0.022 mmol) were dissolved in 2 mL dichloromethane. The solution was moved into Intelli-Ray 400 machine and kept in 90% light intensity at the light wavelength of 365 nm for 10 min. A colorless APCN membrane was obtained until the solvent evaporated.

Swelling Measurement

The soluble content (Sol) in APCN was recorded at room temperature when the weight of APCN membranes remained unchanged after extracting with $CHCl_3$ for several times. The following equation was used to express the data:[56,57]

$$\text{Sol} = \frac{m_{dry} - m_{ex}}{m_{dry}} * 100\% \quad (1)$$

where m_{ex} is the mass of dry APCN membranes after extracting in $CHCl_3$ and m_{dry} is the original mass of the dry APCN membranes.

Swelling measurements were performed at room temperature by immersing preweighed samples in excessive distilled water (or hexane). The swelling extent was measured by periodically moving samples from water (or hexane), removing the water (or hexane) absorbed to the surface by blotting with tissue paper and weighing. When the weight of the swollen samples remained unchanged for 40 h, the equilibrium swelling of APCNs (S_w) was recorded. Following equation was used:

$$S_W = \frac{m_{sw} - m_{dry}}{m_{dry}} \quad (2)$$

where m_{sw} is the mass of swollen APCN membranes and m_{dry} is the mass of dry APCN membranes after extraction.

Results and discussion

The synthesis strategy for the target APCN has been shown in Figure 1. Commercially available bis(hydroxyethyloxypropyl) polydimethylsiloxane is end-functionalized with S-1-Dodecyl-S'-(α,α'-dimethyl-α''-dimethyl-α''-acetic acid) trithiocarbonate to form a PDMS-based macro-RAFT agent, which initiates the RAFT polymerization of N,N-dimethylacrylamide. The resulting triblock copolymer polydimethylacrylamide-polydimethylsiloxane- polydimethylacrylamide (PDMAAm-PDMS-PDMAAm) induces the RAFT polymerization of several AMA units to form the pentablock copolymer polyallylmethacrylate-polydimethylacrylamide-polydimethylsiloxane-polydimethylacrylamide-polyallylmethacrylate (PAMA-PDMAAm-PDMS-PDMAAm-PAMA). The bio-toxic trithiocarbonate groups in the resulting pentablock copolymer have been removed by reductive elimination in the presence of excessive n-butylamine, while the existing pendant AMA units provide the crosslinking points, where the terminal allyl groups can further react with tetra-mercapto compounds to ensure fully crosslinking of the resulting APCN. RAFT polymerization guarantees the well-defined structure of the copolymers, which provide the prerequisite of well-defined APCN. Therefore, the difference between the present work and the conetworks synthesized by free radical copolymerzation of functional macromolecular is the narrow molecular mass distribution and specific crosslinking points in comparison with the broad distribution and random crosslinking points in the conetworks synthesized by conventional free radical copolymerization.

In contrast to previous work by Kennedy, who crosslinks allyl-telechelic amphiphilic pentablock copolymer (PAMA-*b*-PDMAAm-*b*-PDMS-*b*-PDMAAm-*b*-PAMA) via hydrosilation with pentamethylcyclopentasiloxane (D_5H) in the presence of Karstedt' catalyst, we adopt the UV light induced thiol-ene click reaction between the pentablock copolymer and pentaerythritol tetra(3-mercaptopropionate) under mild conditions, which also proves to be a rapid and efficient crosslinking method.[58]

Polymer Synthesis

PDMS-based macro-RAFT agent is synthesized by coupling the commercially available precursor HO-PDMS-OH with trithiocarbonate CTA in the presence of DCC/DMAP. The ^{1}H NMR spectrum of macro-RAFT agent in Figure 2(B) shows a new chemical shift at 4.26 ppm assigned to the -CH_2-O-C=O- newly formed during the esterification reaction and the absence of resonance at 3.74 ppm associating with -CH_2-OH group in HO-PDMS-OH, indicating the successful conversion of HO-PDMS-OH to macro-RAFT agent. Besides, the remaining shift at 0.90 ppm assigned to trithiocarbonate groups suggests no loss of trithiocarbonate groups after the esterification reaction. The obtained macro-RAFT agent is brightly yellow oil after post purification, indicating the trithiocarbonate groups were successfully transferred to the end of PDMS chain.

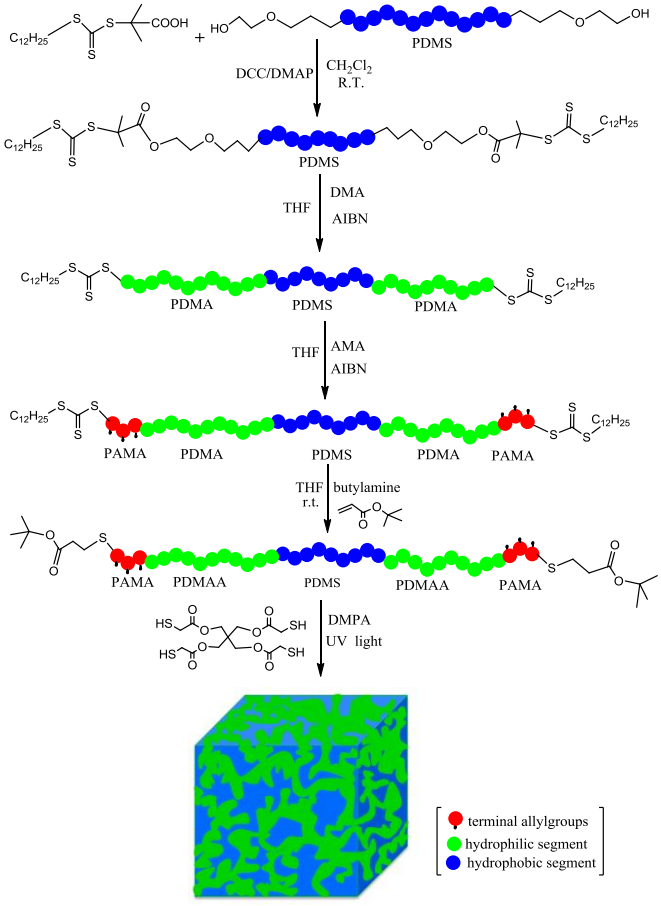
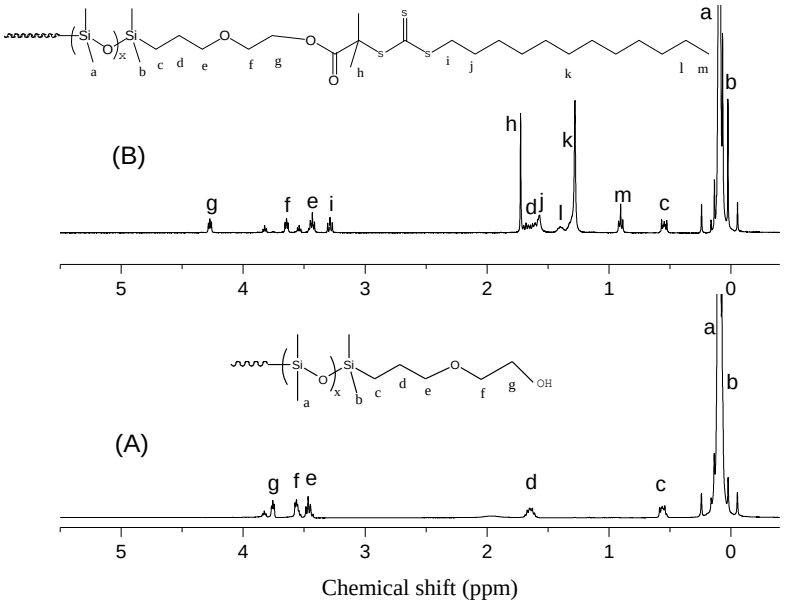
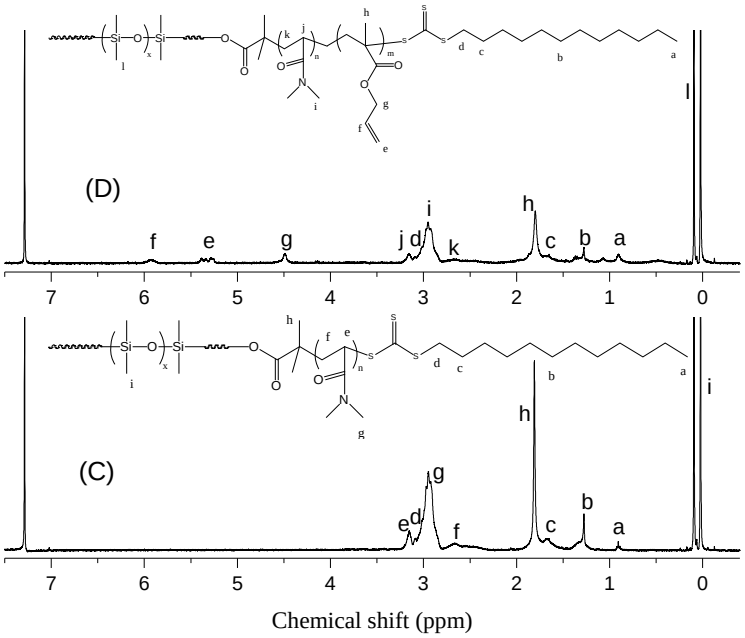


Figure 1. Synthesis strategy of APCN.





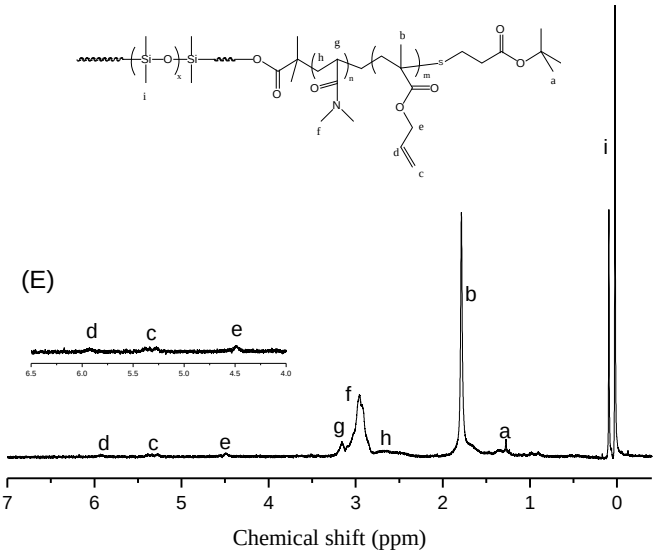


Figure 2. ^{1}H NMR spectra of intermediates: (A) HO-PDMS-OH, (B) PDMS-based macro-RAFT, (C) triblock copolymer PDMAAm-PDMS-PDMAAm, (D) pentablock copolymer PAMA-PDMAAm-PDMS-PDMAAm-PAMA and (E) modified PAMA-PDMAAm-PDMS-PDMAAm-PAMA.

^{1}H NMR spectroscopy in Figure 2(C) gives further proof of the successful synthesis of triblock copolymer PDMAAm-PDMS-PDMAAm, where the resonances at δ 3.2-2.8, 3.16 and 2.66 ppm are assigned to the methyl protons of the amide function -$N(CH_3)_2$, copolymer backbone methane protons and methylene protons, respectively. Additional resonance can be found at δ 0.1 and 0.49-0.58 ppm respectively, assigned to the methylene protons and siloxnae methyl groups in the PDMS segments. The polymerizations of DMAAm in the presence of PDMS-based macro-RAFT are performed at variable temperature to get an optimal polymerization condition for PDMAAm-PDMS-PDMAAm synthesis. As shown in Table 1, the molar mass and *D* of the copolymer go up with increasing temperature from 60 ℃ to 75 ℃ due to the increase of propagation radical concentration, leading to a faster polymerization rate and higher probability of bimolecular termination. The temperature is eventually set at 65 ℃ to obtain copolymer with narrow molecular mass distribution (D<1.3) as well as high average molar mass (M_n~30 kDa). The typical GPC trace of the copolymer is symmetrically monomodal (Figure 3) and the *D* is less than 1.5 (Table 1), indicating that the polymerizations of DMA proceeds in a controlled manner. As RAFT polymerization occurs at a rate balance between activation (K_{act}) and transfer (K_{trans}), the rate of the polymerization is not as high as conventional radical polymerization, which intensively relies on the transfer activity of chain transfer agents. When the conversion reaches a high level, the rate of transfer reaction slows down and the rate of any side reaction increases, leading to a higher *D* of the product. The M_n and *D* of triblock copolymers go up accordingly with prolonged reaction time as more DMA units coupling into the polymer chains lower the chain transfer activity, increase prolonging chain termination and broaden the molecular mass distribution.

Table 1. Effect of different temperature and time on RAFT polymerization: $[M]_0$/[macro-RAFT]/AIBN=320:1:0.2.

NO.	Temperature ℃	Reaction Time (h)	$M_{n,\,NMR}$ [a] ×10^{-4}	$M_{n,\,GPC}$ [b] ×10^{-4}	*D*	Polymer structure [c]
1	60	8	1.25	1.06	1.19	$PDMAAm_{40}$-$PDMS_{54}$- $PDMAAm_{40}$
2	65	8	3.08	2.88	1.30	$PDMAAm_{132}$-$PDMS_{54}$- $PDMAAm_{132}$
3	70	8	3.52	3.06	1.39	$PDMAAm_{154}$-$PDMS_{54}$- $PDMAAm_{154}$
4	75	8	3.67	3.29	1.50	$PDMAAm_{163}$-$PDMS_{54}$- $PDMAAm_{163}$
5	65	4	1.75	2.18	1.17	$PDMAAm_{65}$-$PDMS_{54}$- $PDMAAm_{65}$
6	65	6	2.52	2.32	1.25	$PDMAAm_{103}$-$PDMS_{54}$- $PDMAAm_{103}$
7	65	8	3.08	2.88	1.30	$PDMAAm_{132}$-$PDMS_{54}$- $PDMAAm_{132}$
8	65	10	3.35	3.09	1.38	$PDMAAm_{145}$-$PDMS_{54}$- $PDMAAm_{145}$

[a] Calculated from ^{1}H NMR based PDMS unit (6H at 0.1 ppm) and DMAAm unit (6H at 3.0 ppm).

[b] Determined by GPC measurement using polystyrene standards.

[c] For triblock copolymer $PDMAAm_x$-$PDMS_y$-$PDMAAm_x$, the subscript means the number of the unit, calculated

from the ^{1}H NMR.

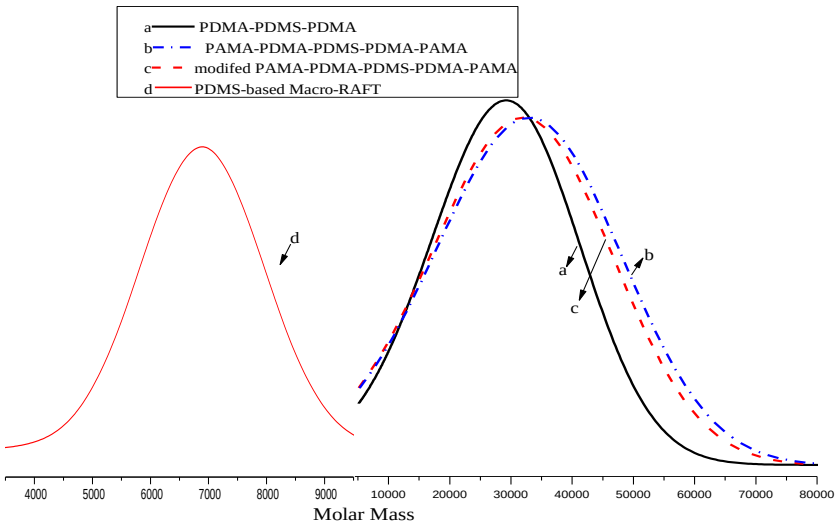


Figure 3. GPC traces of block polymers: (a) PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$ (*D*=1.30), (b) PAMA$_4$-PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$-PAMA$_4$ (*D*=1.33), (c) modified PAMA$_4$-PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$-PAMA$_4$ (*D*=1.35) and (d) PDMS-based macro-RAFT agent (*D*=1.18).

Allyl methacrylate (AMA), an asymmetrical divinyl monomer, has been copolymerized with triblock copolymer via RAFT polymerization to obtain the amphiphilic pentablock copolymer with multiple reactive pendant allyl groups along the copolymer, which are readily crosslinked by thiol-ene click chemistry.

Successful synthesis of the key pentablock copolymer PAMA-PDMAAm-PDMS-PDMAAm-PAMA has been identified by ^{1}H NMR spectroscopy. (Figure 2(D)), where the resonance at δ 5.98, 5.34, and 4.49 ppm is originating from pendant ally ester group (CH_2=CH-CH_2-O-C=O-). The spectrum also shows signals of the DMAAm units and PDMS segment at 2.96 and 0.1 ppm, which are ascribed to the proton resonance of the -N(CH_3)$_2$ groups and -Si(CH_3)$_2$-O- groups, respectively.

Moreover, the GPC traces of the intermediates have been characterized and symmetrical monomodal GPC traces have been obtained as shown in Figure 3. The narrow peak of PDMS-based macro-RAFT agent indicates its narrow molecular mass dispersity (*D*=1.18) as shown in Figure 3(d). The molecular mass distribution of PAMA$_4$-PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$-PAMA$_4$ (*D*=1.33) also shows a narrow peak almost the same as that of PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$ (*D*=1.30) in GPC traces as shown Figure 3(b) and 3(a), respectively, indicating the polymerization of both DMAAm and AMA in a controlled manner.

Apart from GPC traces, DSC traces has also been employed to confirm the block structure of the resulting copolymers. The triblock and pentablock copolymers were treated at the heating rates of 10 ℃ min^{-1} from -150 ℃ to 150 °C after quickly cooling down from 150 °C to eliminate the effect of samples' heat history during the characterization, then the samples were reheated and the heating curves were collected to identify the glass transition temperature (T_g). As shown in Figure 4, both triblock copolymer PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$ and pentablock copolymer PAMA$_4$-PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$-PAMA$_4$ show two T_g, indicating the existence of two phases in triblock and pentablock polymer chains, respectively,. Glass transition temperature of the PDMAAm segment in triblock copolymer PDMAAm$_{132}$-PDMS$_{54}$-PDMAAm$_{132}$ is around 102.10 ℃, which is

less than that of DMAAm homopolymer (113.00 ℃) due to the plasticization effect of the PDMS segment (–118.26 ℃).[59] Compared with the triblock copolymer $PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$, the T_g of $PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$ is shifted from -118.26 ℃ to -112.35 ℃ for PDMS segment and from 102.10 ℃ to 108.50 ℃ for PDMAAm segment respectively, since the introduction of several AMA units leads to the thermal de-reactive movement by slight elongation of PAMA segment. Additionally, the exothermic peaks at around -80 ℃ and -90 ℃ in the DSC curves are cold crystallization effects originated from the PDMS chains moving from disordered state to ordered state, resulting in energy release and exhibiting exothermic peaks in DSC curves.

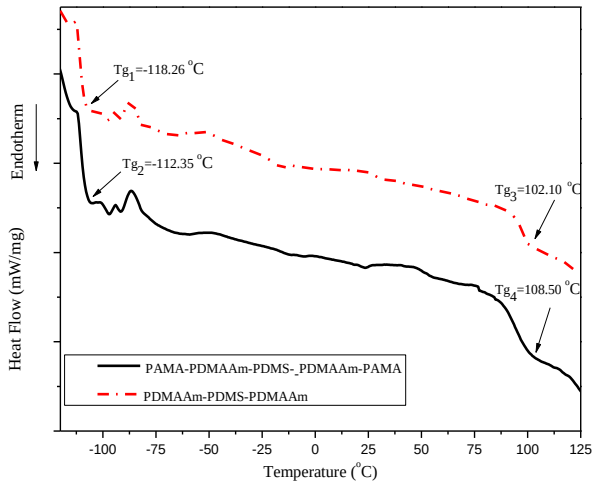


Figure 4. DSC traces of $PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$ and $PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$ pentablock copolymers.

As the thiocarbonylthio group has been deemed to be bio-poisonous in the field of biomaterials applications[60], the thiocarbonylthio end group in pentablock copolymer PAMA-PDMAAm-PDMS-PDMAAm-PAMA has been removed by reductive elimination with n-butylamine. The successful modification has been confirmed by the ^1H NMR spectrum in Figure 2(E), which shows resonances at 4.49, 5.34 and 5.98 ppm ascribed to the pendant ally groups, while the resonance at 0.9 ppm associated with thiolcarbonylthio group disappears. Besides, the absence of yellow color of the final product indicates the successful removal of thiocarbonylthio group. Therefore, the pentablock copolymer shows no resonances associated with thiocarbonylthio groups after butylamine aminolysis, suggesting the successful modification of pentablock copolymer.

GPC traces of the modified pentablock copolymer in Figure 3(c) shows little *D* difference with original pentablock copolymer, illustrating the successful conversion.

UV Light Induced Crosslinking

The remaining pendant allyl groups are crosslinked with proper amount of PETMP (mercapto groups 1.2-fold stoichiometric equal to allyl groups) by thiol-ene click chemistry under the UV light irradiation. After solvent evaporation and being extracted with DMF at room temperature for 24 h, an optically clear APCN membrane has been obtained. The low Sol content (<5%) indicates the efficient crosslinking, which demonstrates that the UV-induced thiol-ene crosslinking goes through a thorough conversion.

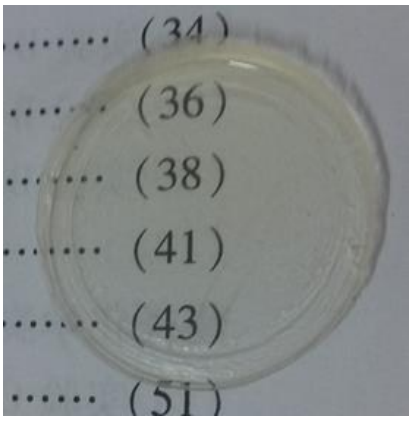


Figure 5. Appearance of optically clear APCN membrane ($PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$) in dry state.

Swelling

The swelling data is good predictor to evaluate the permeability of APCN since nutrients diffusion and swelling ratio of the APCN (S_w) are proportional to the volume fraction of the hydrophilic domain in the conetworks.[61,62] As shown in Figure 6, the overall water S_w of APCN membranes goes up with increasing PDMAAm content due to the excellent hydrophilicity of PDMAAm segments, which even goes up to 700% with increasing PDMAAm unit. For even APCN membrane consisted of $PDMAAm_{65}$-$PDMS_{54}$-$PDMAAm_{65}$, the water swelling even reaches 150% after 40 h, while the corresponding hexane swelling reaches a balance of 50%. This swelling behavior was also consistent with previous works by Patrickios and Tiller.[26,27] Therefore, the swelling behavior of APCN varies with its composition and swelling medium, which confirms the amphiphilicility and co-continuous characteristic of resulting APCN membranes.

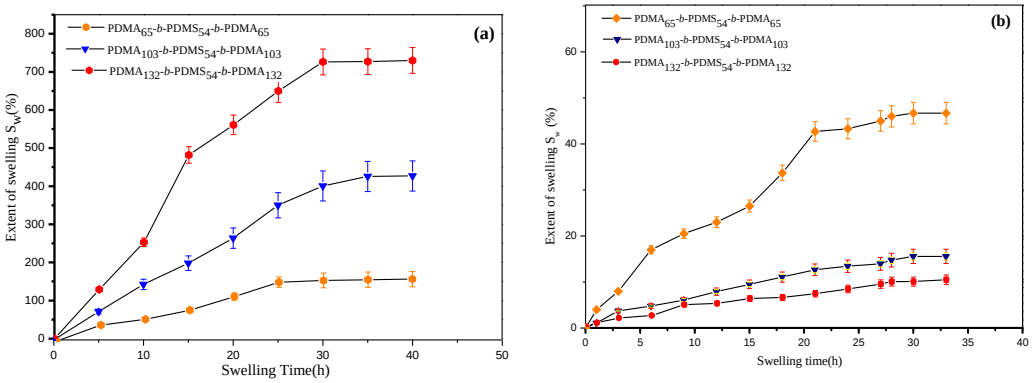


Figure 6. Effect of hydrophilic segment length on the degre of swelling of conetworks in water (a) and hexane (b).

Mechanical Properties

As human body is a water environment, the excellent mechanical strength for swollen membranes will guarantee their application in the area of bio-supporting and bio-filtration areas.[32] In order to investigate the mechanical properties, a series of APCN membranes with different PDMAAm amount (wt.%) have been synthesized, whose tensile strength and elongation ratio have been tested. As shown in Figure 7, with the increasing PDMAAm

content from 50% to 65%, the corresponding tensile strength of swollen APCN membranes is decreased sharply from 2.80 MPa to 1.39 Mpa and the corresponding elongation ratio gets a slight decrease from 190% to 156%. Considering the relatively fine mechanical properties among other swollen APCN membranes reported by J. Kang and coworkers (1.30-1.80 MPa, 45-60% elongation, 30-60% hydrophilic PDMAAm weight percentage)[63], the prepared PCN is a good candidate material in biomaterial areas.

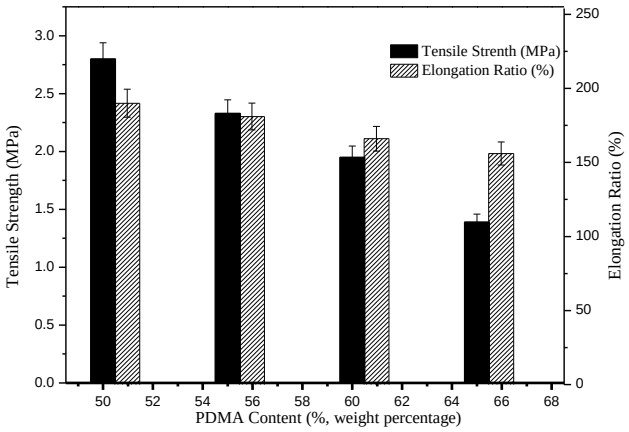


Figure 7. Mechanical properties of APCN membranes with different PDMAAm content. Membrane properties: thickness, 150 ± 10 μm; swollen state.

AFM Morphology

The APCN is designed to be the semi-permeability membrane in bioartificial pancreas fabrication. As we know, hydrophilic segments in APCN provide channels,[63] where nutrients diffuse to reach the pancreas cell, while the wastes can be sent out. On the other hand, hydrophobic PDMS segments provide channels for gas exchanging channels, where oxygen can be taken in while the waste gases can be taken out. Therefore, a uniform channel size is important to guarantee permeation of the nutrients and oxygen for each transplanting cell to grow well.

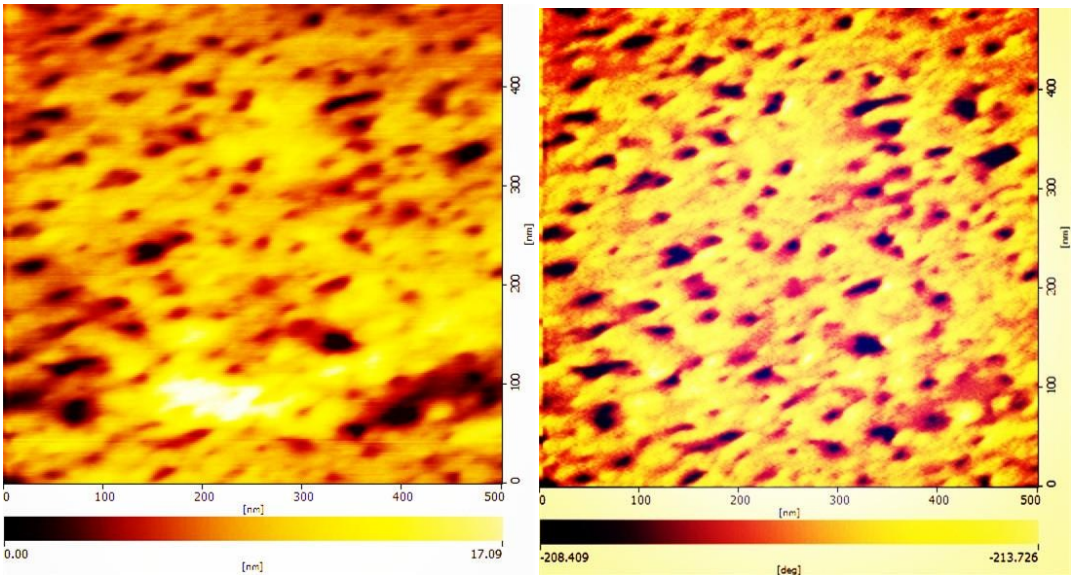


Figure 8. AFM images of APCN consisted of $PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$ copolymer. Left, Height; Right, Phase. Scan rate 1 nm/s; Scan box, 500×500 nm^2.

Mirco-phase separation morphology of APCN membranes has been characterized by atomic force microscope (AFM). According to the report of Bryan B. Sauer,[64] phase topology is intensively correlated with the segments properties, which can be sorted as hydrophilic and hydrophobic. As shown in Figure 8, there appear obvious dark areas and bright areas in APCN membrane during the AFM phase-mode scanning, which is related to the hydrophobic PDMS segments and hydrophilic segments, respectively. The dark areas assigned to the PDMS segments (around 10 nm) are much smaller than the bright ones (around 60 nm) assigned to the PDMAAm segments. This phase separated phenomenon was in accordance with the previous reports by Tiller and Patrickios.[27,30,65,66] A reasonable explanation is that the prolonged hydrophilic segment lengths is six times longer than the hydrophobic segments in designed molecular ($PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$), which further confirms the well-defined triblock copolymer. The obviously phase separated morphology and well controlled hydrophilic segments indicate that the resulting APCN may provide well biocompatibility and uniform channels for substances exchange in the bioartificial pancreas fabrications.

TEM Morphology

Apart from the AFM scanning, the uniform micro-structure of the APCN has also been characterized by transmission electron microscope (TEM) as shown in Figure 9. The dark areas assigned to PDMS segments are surrounded by the light areas assigned to PDMAAm segments, forming a uniform "sea-island" structure with relatively uniform size of dark "island", which is originated from the well-defined structure of the block copolymers The significant difference between the AFM and TEM images is the much smaller light domain sizes in the TEM images than that in the AFM images, which is originating from the scanning methods.[47] Both AFM and TEM methods confirm the uniform structure in the present APCN, which provides uniform channels in semi-permeability membranes fabrication. Therefore the combination of RAFT polymerization with thiol-ene is an effective method to fabricate APCN membranes with almost precisely controlled microstructure.

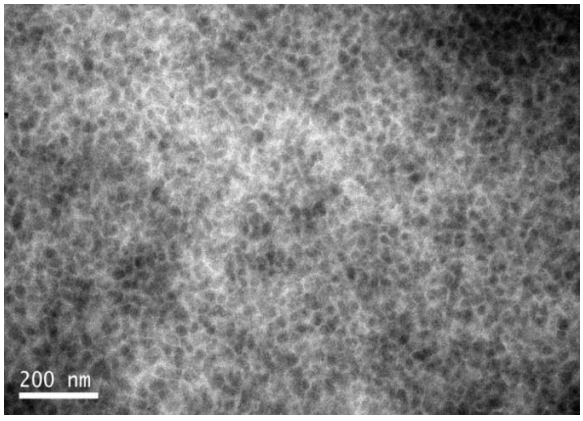


Figure 9. TEM image of swollen APCN consisted of $PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$ copolymer.

Cell Culture

As this APCN has been designed to be applied in biomaterial areas, its cell toxicity is necessary for its biomedical safety. As shown in Figure 10, BHK-21 cells reproduce well on the APCN materials and the survival rate of cells on APCN sample is over 95% after two weeks as compared with the controlled one, which infers its relatively low

toxicity to the cultured cells. The well biocompatibility of these materials indicates the accessibility to fabricate biomedical materials by this method.

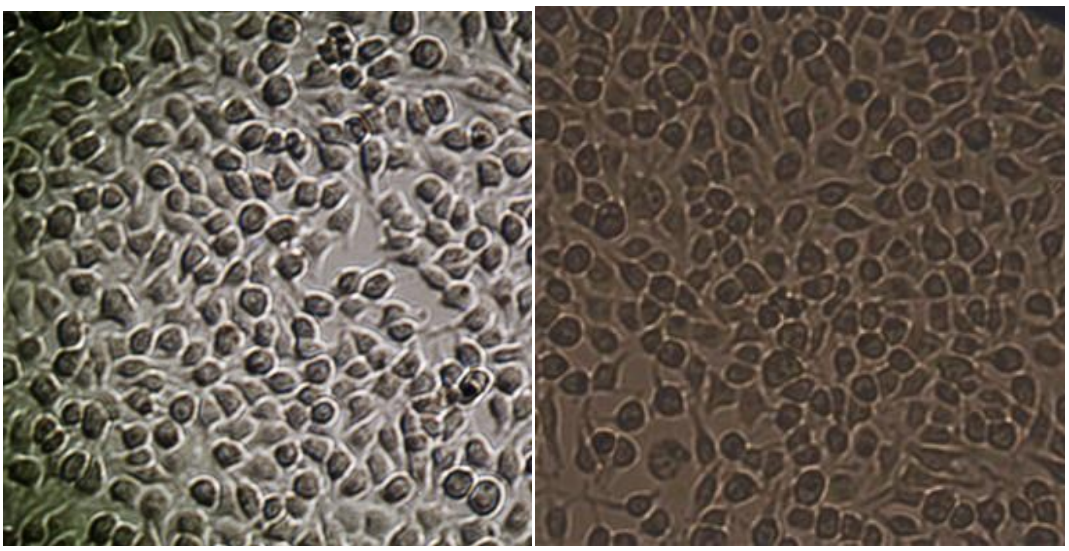


Figure 10. Left, cell colony morphology after immersing APCN membranes in cell-culture medium. (×1000, Sample); Right, cells colony morphology in cell-culture medium (×1000, Control). APCN consisted of $PAMA_4$-$PDMAAm_{132}$-$PDMS_{54}$-$PDMAAm_{132}$-$PAMA_4$ copolymer, cell colony morphologies were taken by SEM.

Conclusions

Novel amphiphilic conetworks contained PDMAAm and PDMS segments are fabricated through thiol-ene click end-crosslinking with well-defined allyl terminated amphiphilic pentablock copolymers via RAFT polymerizations. The resulting APCN exhibits unique amphiphilic characters, i.e. controllable swelling behavior, microphase separated morphology and excellent mechanical properties. Moreover, cell culture test indicates the target APCN possesses low cytotoxicity and well biocompatibility. Therefore, this work provides an accessible method to fabricate a series of APCNs with controlled structure and low cytotoxicity by the combination of RAFT polymerization with non-Cu^{2+} click chemistry, whose diverse excellent properties are suitable for potential biomaterial applications.

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Notes and references

1 G. Erdodi and J. P. Kennedy, *Prog. Polym. Sci*., 2006, **31**, 1.

2 C. S. Patrickios and T. K. Georgiou, *Curr. Opin. Colloid Interface Sci.*, 2003, **8**, 76.

3 C. Fodor, G. Kali and B. Iván, *Macromolecules*, 2011, **44**, 4496.

4 C. Fodor, J. Bozi, M. Blazsó and B, Iván, *RSC Adv.*, 2015, **5**, 17413.

5 J. Scherble, R. Thomann, B. Iván and R. Mülhaupt, *J. Polym. Sci. Part B: Polym. Phys.*, 2001, **39**, 1429.

6 B. Iván, K. Almdal, K. Mortensen, I Johannsen and J. Kops, *Macromolecules*, 2001, **34**, 1579.

7 A. Domján, G. Erdodi, M. Wilhelm, M. Neidhöfer, K. Landfester, B. Iván and H. W. Spiess, *Macromolecules*, 2003, **36**, 9107.

8 B. Iván, M. Haraszti, G. Erdodi, J. Scherble, R. Thomann and R. Mulhaupt, *Macromol. Symp.*, 2005, **227**, 265.

9 N. Bruns, J. Scherble, L. Hartmann, R. Thomann, B. Iván, R. Mülhaupt and J. C. Tiller, *Macromolecules*, 2005, **38**, 2431.

10 G. Kali, T. K. Georgiou, B. Iván and C. S. Patrickios, *J. Polym. Sci. Part A: Polym. Chem.*, 2009, **47**, 4289.

11 J. Xu, X. Li and F. Sun, *Drug Deliv*., 2011, **18**, 150.

12 N. Ghasdian, E. Church, A. P. Cottam, K. Hornsby, M. Y. Leung and T. K. Georgiou, *RSC Adv.*, 2013, **3**, 19070.

13 C. Lin and I. Gitsov, *Macromolecules*, 2010, **43**, 10017.

14 N. Bruns and J. C. Tiller, *Nano Lett*., 2005, **5**, 45.

15 J. Tobis, L. Boch, Y. Thomann and J. C. Tiller, *J. Membr. Sci*., 2011, **372**, 219.

16 S. K. Jewrajka, G. Erdodi, J. P. Kennedy, D. Ely, G. Dunphy, S. Boehme and F. Popescu, *J. Biomed. Mater. Res., Part A*, 2008, **87**, 69.

17 Y. Sun, J. Collett, N. J. Fullwood, S. M. Neil and S. Rimmer, *Biomaterials*, 2007, **28**, 661.

18 S. Meskath, G. Urban and J. Heinze, *Sensor Actuat. B: Chem*., 2013, **186**, 367.

19 Y.Wang, J. A. Finlay, D. E. Betts, T. J. Merkel, J. C. Luft, M. E. Callow, J. A. Callow and J. M. DeSimone, *Langmuir*, 2011, **27**, 10365.

20 R. Wang, Y. L. Yang, M. Qin, L. K.Wang, L. Yu, B. Shao, M. Q. Qiao, C. Wang and X. Z. Feng, *Chem. Mater.*, 2007, **19**, 3227.

21 A. L. Cordeiro, S. Zschoche, A. Janke, M. Nitschke and C. Werner, *Langmuir*, 2009, **25**, 1509.

22 G. Lin, X. Zhang, S. R. Kumar and J. E. Mark, *Silicon*, 2009, **1**, 173.

23 E. Pouget, J. Tonnar, P. Lucas, P. Lacroix-Desmazes, F. Ganachaud and B. Boutevin, *Chem. Rev.*, 2009, **110**, 1233.

24 G. Erdodi and J. P. Kennedy, *J. Polym. Sci. Part A: Polym. Chem.*, 2005, **43**, 4953.

25 V.P. Torchilina, T.S. Levchenkoa, K.R. Whitemana, A.A .Yaroslavovb, A.M. Tsatsakisc, A.K. Rizosb, E.V. Michailovad and M.I. Shtilmand, *Biomaterials*, 2001, **22**, 3035.

26 D. S Achilleos, T. K. Georgiou and C. S. Patrickios. *Biomacromolecules*, 2006, **7**, 3396.

27 G. Kali, T. K. Georgiou, B. Ivan, C. S. Patrickios, E. Loizou, Y. Thomann and J.C. Tiller, *Langmuir*, 2007, **23**, 10746.

28 T. K. Georgiou, C. S. Patrickios, P. W. Groh and B. Ivan, *Macromolecules*, 2007, **40**, 2335.

29 G. Kali, T. K. Georgiou, B. Iván and C. S. Patrickios, *J. Polym. Sci. Part A: Polym. Chem.*, 2009, **47**, 4289.

30 G. Kali, T. K. Georgiou, B. Iván, C. S. Patrickios, E. Loizou, Y. Thomann and J. C. Tiller, *Macromolecules*, 2007, **40**, 2192.

31 M. Achilleos, T. Krasia-Christoforou and C. S. Patrickios, *Macromolecules*, 2007, **40**, 5575.

32 J. Kang, G. Erdodi, J. P. Kennedy, H. Chou, L. Lu and S. Grundfest-Broniatowski, *Macromol. Biosci.*, 2010, **10**, 369.

33 B. Ivan, J. P. Kennedy and P. W. Mackey, *ACS Symp. Ser.*, 1991, **469**, 194.

34 B. Ivan, J. P. Kennedy and P. W. Mackey, Amphiphilic Networks, *US Patent*, 5,073,381, (Dec. 17, 1991)

35 J. P. Kennedy, G. Fenyvesi, S. Na, B. Keszler and K. S. Rosenthal, *Des. Monomers Polym.*, 2000, **3**, 113.

36 R. Karunakaran and J. P. Kennedy, *J. Polym. Sci. Part A: Polym. Chem.*, 2007, **45**, 4284.

37 J. Scherble, B. Ivan and R. Mulhaupt, *Macromol. Chem. Phys*., 2002, **203**, 1866.

38 M. Haraszti, E. Tóth and B. Ivan, *Chem. Mater*., 2006, **18**, 4952.

39 G. Kali, S. Vavra, K. László and B. Ivan, *Macromolecules*, 2013, **46**, 5337.

40 G. Erdodi and B. Ivan, *Chem. Mater.*, 2004, **16**, 959.

41 W. H. Binder, L. Petraru, T. Roth, P. W. Groh, V. Pálfi, S. Keki and B. Ivan, *Adv. Funct. Mater.*, 2007, **17**, 1317.

42 A. D. Jenkins, R. G. Jones and G. Moad, *Pure Appl. Chem*., 2009, **82**, 483.

43 G. Moad, E. Rizzardo and S. H. Thang, *Aust. J. Chem.*, 2012, **65**, 985.

44 J. Chiefari, Y. K. Chong, F. Ercole, J. Krstina, J. Jeffery, T. P. T. Le, R. T. A. Mayadunne, G. F. Meijs, C. L. Moad, G. Moad, E. Rizzardo and S. H. Tang, *Macromolecules* 1998, **31**, 5559.

45 J. T. Lai, D. Filla and R. Shea, *Macromolecules*, 2002, **35**, 6754.

46 M. R. Hill, R. N. Carmean and B. S. Sumerlin, *Macromolecules*, 2015, **48**, 5459.

47 A. B. Lowe, *Polym. Chem.*, 2010, **1**, 17.

48 S. P. S. Koo, M. M. Stamenović, R. A. Prasath, A. J. Inglis, F. E. Du Prez, C. Barner-Kowollik, W. V. Camp and T. Junkers, *J. Polym. Sci. Part A: Polym. Chem.*, 2010, **48**, 1699.

49 C. N. Walker, K. C. Bryson, R. C. Hayward and G. N. Tew, *ACS Nano*, 2014, **8**, 12376.

50 C. E. Hoyle and C. N. Bowman, *Angew. Chem. Int. Ed.*, 2010, **49**, 1540.

51 L. M. Campos, K. L. Killops, R. Sakai, J. M. J. Paulusse, D. Damiron, E. Drockenmuller, B. W. Messmore and C. J. Hawker, *Macromolecules*, 2008, **41**, 7063.

52 C. Boyer, A. Granville, T. P. Davis and V. Bulmus, *J. Polym. Sci. Part A: Polym. Chem.*, 2009, **47**, 3773.

53 J. W. Chan, B. Yu C. E. Hoyle and A. B. Lowe, *Chem. Commun.*, 2008, **40**, 4959.

54 C. Boyer and T. P. Davis, *Chem. Commun.*, 2009, **40**, 6029.

55 M. L. Wadley and K. A. Cavicchi, *J. Appl. Polym. Sci*., 2010, **115,** 635.

56 J. P. Kennedy, K. S. Rosenthal and B. Kashibhatla, *Des. Monomers Polym.*, 2004, **7**, 485.

57 G. Erdodi and J. P. Kennedy, *J. Polym. Sci. Part A: Polym. Chem.*, 2007, **45,** 295.

58 R. Karunakaran and J. P. Kennedy, *J. Polym. Sci. Part A: Polym. Chem.*, 2008, **46**, 4254.

59 D. Pavlović, J. G. Linhardt, J. F. Künzler and D. A. Shipp, *J. Polym. Sci. Part A: Polym. Chem.*, 2008, **46**, 7033.

60 C. Boyer, V. Bulmus, T. P. Davis, V. Ladmiral, J. Liu and S. Perrier, *Chem. Rev.*, 2009, **109**, 5402.

61 T. Canal and N. A. Peppas, *J. Biomed. Mater. Res.*, 1989, **23**, 1183.

62 S. R. Lustig and N. A. Peppas, *J. Appl. Polym. Sci*., 1988, **36**, 735.

63 J. Kang, G. Erdodi and J. P. Kennedy, *J. Polym. Sci. Part A: Polym. Chem.*, 2007, **45**, 4276.

64 B. B. Sauer, R. S. McLean and R. R. Thomas, *Langmuir*, 1998, **14**, 3045.

65 N. Bruns and J. C. Tiller, *Nano Lett*., 2005, **5**, 45.

66 J. Tobis, Y. Thomann and J. C. Tiller, *Polymer*, 2010, **51**, 35.

GRAPHICAL ABSTRACT

A series of APCNs from the amphiphilic clickable pentablock copolymers with narrow polydispersity synthesized via RAFT polymerization. The resulting APCN exhibits unique amphiphilic characters, i.e. controllable swelling behavior, microphase separated morphology and excellent mechanical properties as well as low cytotoxicity, which can be potentially employed in the desirable range for some biomaterial applications.