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Cationic Amphiphilic Model Networks Based on Symmetrical ABCBA Pentablock Terpolymers: Synthesis, Characterization, and Modeling

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Eight isomeric networks based on equimolar terpolymers were synthesized using group transfer polymerization (GTP) and were characterized in terms of their swelling properties. Two hydrophilic monomers, the nonionic methoxy hexa(ethylene glycol) methacrylate (HEGMA) and the ionizable 2-(dimethylamino)ethyl methacrylate (DMAEMA), and a hydrophobic (nonionic) monomer, methyl methacrylate (MMA), were employed for the syntheses. 1,4-Bis(methoxytrimethylsiloxymethylene)cyclohexane (MTSMC) was used as the bifunctional GTP initiator, while ethylene glycol dimethacrylate (EGDMA) served as the cross-linker. Seven of the networks were model networks, six of which were based on the symmetrical pentablock terpolymers ABCBA, ACBCA, BACAB, BCACB, CBABC, and CABAC, whereas the seventh model network was based on the statistical terpolymer. The eighth network was a randomly cross-linked network based on the statistical terpolymer, prepared by the simultaneous quaterpolymerization of the three monomers and the cross-linker. The molecular weights and molecular weight distributions of the linear pentablock terpolymer precursors, as well as those of their homopolymer and ABA triblock copolymer precursors, were characterized by gel permeation chromatography (GPC) in tetrahydrofuran. The sol fraction of each network was measured and found to be relatively low. The aqueous degrees of swelling of all networks were found to increase at acidic pH due to the ionization of the DMAEMA tertiary amine units. The acidic degrees of swelling of the pentablock terpolymer networks were lower than those of their statistical counterparts due to microphase separation in the former type of networks, also confirmed by thermodynamic calculations and small-angle neutron scattering experiments.

Introduction

Amphiphilic polymer networks[1] represent an emerging class of biomaterials, combining the properties of linear amphiphilic block copolymers[2] and hydrogels.[3] These properties are the aqueous self-assembly and microstructure formation of the former and the stimulus-regulated absorption of water of the latter. Amphiphilic hydrogels usually exist in a microphase-separated state, with their hydrophilic component conveying to the biomaterial a friendly aqueous environment in one microphase, and with the hydrophobic component rendering the other microphase apolar. Depending on the chemical nature of the hydrophobic component, special properties can also be obtained, such as oxygen permeability, degradability, or improved mechanical strength. Thus, these materials are considered for various applications, including drug release systems,[4] scaffolds for tissue engineering,[5] supports for enzymes,[6] templates for the synthesis of mesoporous silica,[7] hosts for the growth of CdS semiconducting nanocrystals,[8] soft contact lenses,[9] pervaporation membranes,[10] extractants of organic solvents from water,[11] and temperature-activated actuators.[11]

Another novel type of polymeric material with a growing interest is that of linear amphiphilic ABC triblock terpolymers,[12,13] consisting of three chemically different components, each one conferring to the polymer one different function. Thus, these materials have a richer response behavior than their diblock counterparts. To date, the following combinations of functions have been reported in ABC triblock terpolymers: positively charged−negatively charged−neutral-hydrophobic,[14−19] neutral-hydrophilic−temperature-sensitive-hydrophilic−neutral-hydrophobic,[20,21] hydrophilic−two-incompatible-hydrophobic,[22] and hydrophilic−hydrophobic−cross-linkable.[23−25] In addition to molecular weight and composition, block sequence is another parameter that is offered for macromolecular engineering in these novel materials. In the limited number of studies exploring this parameter, block sequence was found to affect the solution properties of ABC terpolymers.[12−16,20,21]

The present work aims at combining the linear ABC triblock terpolymer structure with the amphiphilic polymer network structure. Thus, linear, amphiphilic, symmetrical ABCBA pentablock terpolymers were synthesized and cross-linked to result in novel terpolymer networks (which might be called “ternetworks” rather than “conetworks”[1b] to reflect their constitution of three rather than two components). The synthesis was performed using a “living” polymerization technique,[26] group transfer polymerization (GTP),[27−31] by sequential methacrylate monomer and dimethacrylate cross-linker additions. The use of a bifunctional GTP initiator ensured the symmetrical growth on both polymer sides. The similar reactivities of methacrylate monomers toward GTP allowed the efficient synthesis of all six block sequence isomers for the linear pentablock terpolymer precursors, ABCBA, ACBCA, BACAB, BCACB, CABAC, and CBABC, from which the corresponding six isomeric networks were prepared. Two more network

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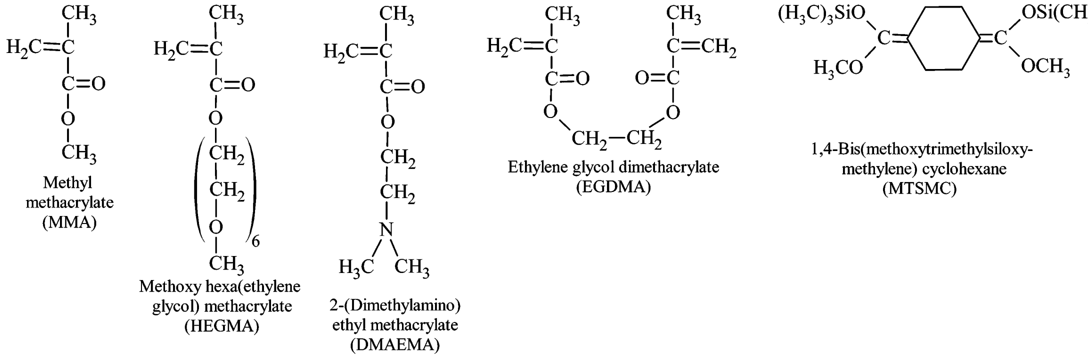

Figure 1. Chemical structures and names of the three monomers, the cross-linker, and the initiator used for the preparation of the terpolymer networks.

structures were also prepared, in the first of which the three monomers were randomly distributed, and in the second the three monomers and cross-linker were randomly distributed. A neutral-hydrophilic monomer, a positively ionizable hydrophilic monomer, and a neutral-hydrophobic monomer were combined, resulting in networks with water compatibility, pH sensitivity, and microphase separation capability. Another goal of this work was the investigation of the swelling behavior in water and in an organic solvent of all eight networks, which was to be compared to each other and to that of two-component networks.

Experimental Section

Materials and Methods. The chemical structures and names of the three monomers, methyl methacrylate (MMA, neutral-hydrophobic), methoxy hexa(ethylene glycol) methacrylate (HEGMA, neutral-hydrophilic), and 2-(dimethylamino)ethyl methacrylate (DMAEMA, ionizable-hydrophilic), the ethylene glycol dimethacrylate (EGDMA) cross-linker, and the bifunctional GTP initiator, 1,4-bis(methoxytrimethylsiloxymethylene)cyclohexane (MTSMC), are shown in Figure 1. MMA, DMAEMA, and EGDMA were purchased from Aldrich, Germany. HEGMA was kindly donated by Cognis Performance Chemicals, U.K. MTSMC was in-house synthesized by the silylation of dimethyl 1,4-cyclohexanedicarboxylate.[32] All monomers and the cross-linker were passed through basic alumina columns to remove the polymerization inhibitor and protic impurities. Because of the high viscosity of the neat monomer, a 50% v/v solution in freshly distilled tetrahydrofuran (THF) of the HEGMA monomer was used for the processing with basic alumina. The HEGMA monomer solution was passed twice through basic alumina columns, whereas DMAEMA, MMA, and EGDMA were passed only once due to the higher initial purity of these materials. Subsequently, DMAEMA, MMA, and EGDMA were stirred over calcium hydride (to remove the last traces of moisture and protic impurities) overnight in the presence of a free-radical inhibitor, 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH), and were vacuum-distilled just prior to use. The HEGMA solution was stirred over calcium hydride (without DPPH) and filtered through a 0.45 μm PTFE syringe filter directly into the polymerization flask. The MTSMC initiator was distilled 1 day before the polymerization. The polymerization solvent, THF, was refluxed over a potassium/sodium alloy for 3 days and was freshly distilled prior to use. The polymerization catalyst, tetrabutylammonium bibenzoate (TBABB), was prepared according to the literature[29] and kept under vacuum until use.

Network Synthesis. All the networks of this study were prepared by GTP at room temperature and were equimolar in the three monomers. The number of moles of the cross-linker used was 8 times the number of moles of the MTSMC initiator to optimize interchain connection and network formation, according to a previous study.[33] Isomeric networks with different monomer/cross-linker distribution were prepared by varying the order of monomer/cross-linker addition. The synthetic routes followed for the preparation of the eight different sequence isomers are given in Figure 2. A typical polymerization procedure yielding the network with block sequence DMAEMA-HEGMA-MMA-HEGMA-DMAEMA with 10 units of each monomer type is detailed below. To a 60 mL cylindrical glass vial containing a small amount (~10 mg) of TBABB was syringed 20 mL of freshly distilled THF and 0.2 mL (0.24 g, 0.70 mmol) of MTSMC initiator, in this order. A volume of 0.75 mL (0.70 g, 7.0 mmol) of MMA was slowly added under stirring. The polymerization exotherm (25.5−31.9 °C) abated within 5 min, a sample for GPC was extracted, and 4.6 mL (2.4 g of neat monomer, 7.0 mmol) of a 50% v/v solution of HEGMA in THF was added, which produced an exotherm (29.5−32.4 °C). After extraction of a sample for GPC of the HEGMA-MMA-HEGMA triblock copolymer, 1.2 mL (1.12 g, 7.1 mmol) of DMAEMA was added to the solution, generating an exotherm, (30.9−34.2 °C), and a sample for GPC of the DMAEMA-HEGMA-MMA-HEGMA-DMAEMA pentablock terpolymer was extracted. Finally, 1 mL (1.05 g, 5.3 mmol) of the EGDMA cross-linker was added (31.1−35.7 °C) and led to the gelation of the solution within seconds.

Characterization by GPC. Linear homopolymer, ABA triblock copolymer, and ABCBA pentablock terpolymer samples were obtained before cross-linking and were characterized in terms of their molecular weight (MW) using GPC. GPC was performed on a Polymer Laboratories system equipped with a PL-LC1120 isocratic pump, an ERC-7515A refractive index detector, and a PL Mixed “E” column. The eluent was THF, pumped at 1 mL min^{-1}. The MW calibration was based on six narrow MW (630, 1400, 4250, 7600, 13 000, and 28 900 g mol^{-1}) PMMA standards also supplied by Polymer Laboratories.

Characterization by ^{1}H NMR. The compositions of the linear terpolymer (pentablock and statistical) precursors to the networks were determined by ^{1}H NMR using a 300 MHz Avance Bruker NMR spectrometer equipped with an Ultrashield magnet. The solvent was $CDCl_3$, containing traces of tetramethylsilane (TMS), which was used as an internal reference.

Recovery and Characterization of Extractables. The networks were first taken out of the polymerization vials which were incised using a diamond knife and broken by the application of a hot glass rod. Subsequently, the gels were placed in excess THF and left there for 1 month to extract the polymer not incorporated in the network. The THF solution of the extracted material was dried in a rotary evaporator, and the mass of that polymer was determined. Samples of the extractables were characterized by GPC in THF using the equipment as described above.

Measurement of the Degree of Swelling and the p*K*. The degrees of swelling (DSs) of the networks were measured in THF, water, and in aqueous solutions covering the pH range between 2 and 12. After the equilibration in excess THF and the removal of the extractables (described in the preceding paragraph), 10 pieces were cut from each network. Each piece was weighed and subsequently dried in a vacuum oven at room temperature (to avoid oxidation of the HEGMA units)

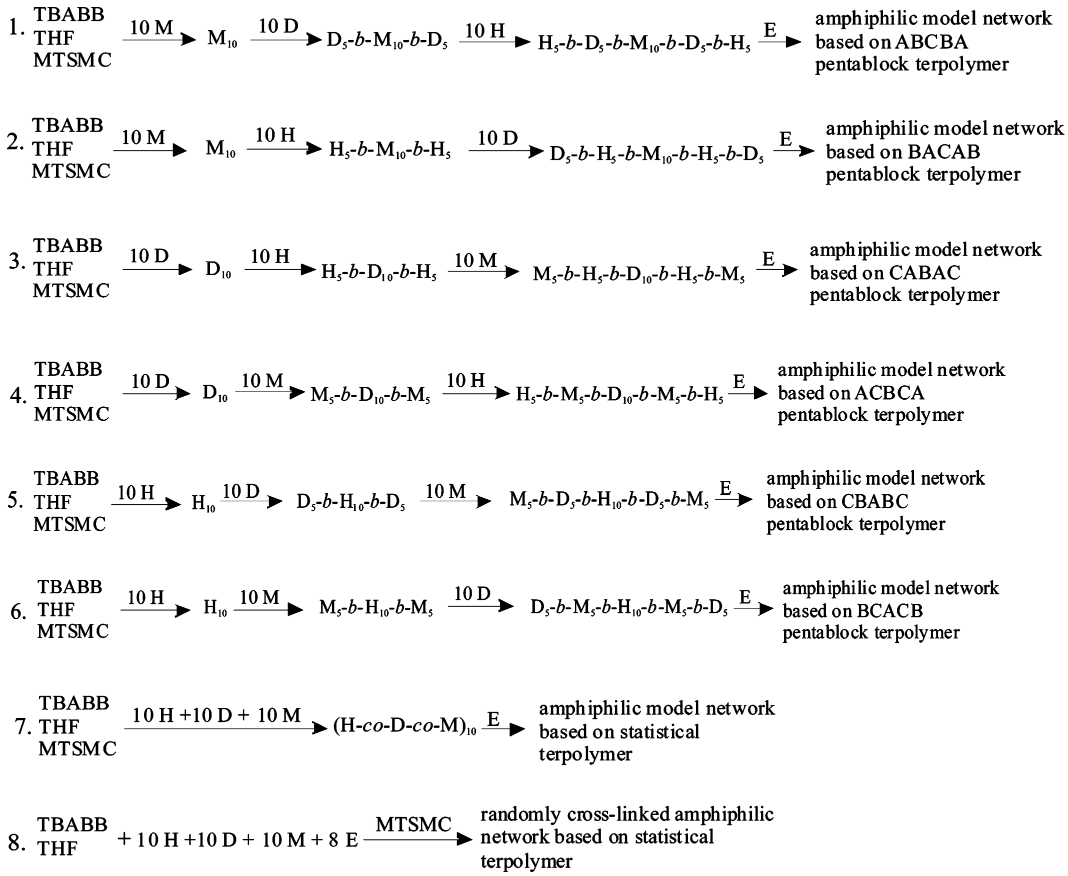

Figure 2. Synthetic routes followed for the preparation of the eight isomeric terpolymer networks. M, D, H, and E are further abbreviations for MMA, DMAEMA, HEGMA, and EGDMA.

for 14 days and weighed again. The DSs in THF were calculated as the ratio of the swollen divided by the dry mass, and their values were averaged over the 10 samples of each network. In order to measure the DSs in aqueous media at different pH values, 5 mL of deionized water was added to each sample of the dried networks, followed by the addition of the appropriate number of drops of 0.5 M HCl solution to adjust the pH within the range between 2 and 8, corresponding to degrees of ionization between 100% and 0% (eight samples used). The required number of moles of HCl in each case was calculated as the product of the desired degree of ionization times the number of moles of DMAEMA units present in the sample. Small amounts of 0.5 M NaOH solution were added to the two remaining samples of each gel to cover the pH range from 8 to 12. The DSs were measured four times, and the average values are presented, along with the 95% confidence intervals. The effective p*K*'s of the DMAEMA repeating units in the networks were estimated as the pH at 50% ionization.

Small-Angle Neutron Scattering (SANS). Two of the terpolymer model networks were characterized using small-angle neutron scattering (SANS). These were the pentablock terpolymer network with $\mathrm{MMA_5}$-*b*-$\mathrm{DMAEMA_5}$-*b*-$\mathrm{HEGMA_{10}}$-*b*-$\mathrm{DMAEMA_5}$-*b*-$\mathrm{MMA_5}$ elastic chains and the statistical terpolymer network based on (HEGMA-*co*-DMAEMA-*co*-MMA)$_{10}$ elastic chains. Both network samples were neutral (uncharged state), prepared for SANS by first being dried from water and subsequently being equilibrated in D_2O for 10 days. The SANS experiments were performed on the 30 m NG3 instrument at the Center for Neutron Research of the National Institute of Standards and Technology (NIST) in the United States with incident neutron beam wavelength $\lambda = 6$ Å. Each one of the samples was loaded in 1 mm gap thickness quartz cells. Three sample-to-detector distances were employed, 1.35, 4.5, and 13.1 m, and the *q*-range used ($q = 4\pi/\lambda \sin(\theta)/2$) covered 0.004 Å^{-1} < q < 0.44 Å^{-1}. The data were averaged and corrected for empty cell and background, whereas the measured counts were azimuthally averaged.

Thermodynamic Modeling of Network Swelling Behavior

The DSs of the two triblock terpolymer model networks with hydrophobic MMA end-blocks and those of the statistical terpolymer model network were predicted theoretically using a thermodynamic model developed recently by our group.[34,35] The total Gibbs free energy was calculated from its four main components. These were the elastic and electrostatic free energies, the free energy of mixing, and the interfacial free energy. The elastic free energy comprised a Gaussian component and a non-Gaussian component, which did not allow the chains to erroneously stretch beyond their fully extended length. The electrostatic free energy was approximated by the osmotic pressure due to the translational entropy of the counterions. The mixing free energy was composed of the enthalpic terms describing the interaction of each block with water via the appropriate Flory−Huggins χ parameters and the term due to the translational entropy of water, ignoring the translational entropy of the polymer, following the approach of Flory.[36] The interfacial free energy was considered only for the ordered systems. The total Gibbs free energy was minimized with respect to the polymer volume fraction with the aid of a numerical code, incorporating the Newton method, written in GWBASIC. The DSs at equilibrium were calculated as the inverse of the polymer volume fraction at the free energy minimum.

The following inputs to the code were required. First was the polymer volume fraction upon cross-linking, which was equal to 0.2 in all cases, consistent with the network synthesis procedure. Second was the number of arms per cross-link, which was taken equal to 20, based on the number of arms in star polymers prepared by GTP and using the same cross-linker.[37−39]

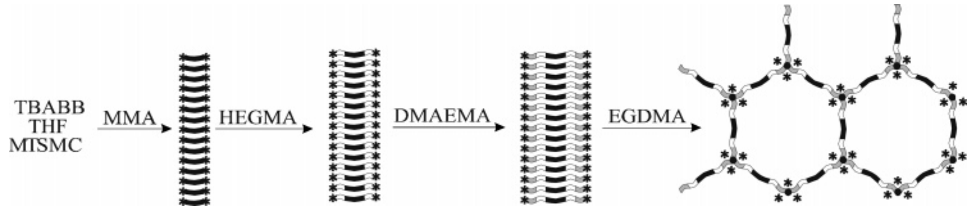

Figure 3. Schematic representation of the synthetic procedure followed for the preparation of the model network based on the pentablock terpolymer DMAEMA$_5$-*b*-HEGMA$_5$-*b*-MMA$_{10}$-*b*-HEGMA$_5$-*b*-DMAEMA$_5$. The DMAEMA units are shown in gray, the HEGMA units in white, and the MMA units are in black. The "$*$" symbols indicate the "living" sites of the polymerization. The number of arms at the cross-links is not three, as indicated in the figure, but between 15 and 25.

Third was the number of backbone carbon atoms in each block, taken as twice the corresponding degree of polymerization, i.e., 10 for each block. Fourth were the Flory−Huggins interaction parameters χ between the solvent and each of the three monomer repeating units. For the DSs in THF, χ values of 0.3 were used for each monomer unit−THF pair to reflect the good solvency of all three units in THF. For the DSs in water, three different χ values were used for the three monomer unit−water pairs. For the water−DMAEMA pair, a χ value of 0.45 was assigned to reflect the marginal water solubility of the DMAEMA homopolymer known to precipitate in water at ∼35 °C.[40] This choice was also consistent with experimentally determined χ values for similar oxygen-and-nitrogen-containing acrylic monomers in hydrogels.[41] The lower χ value of 0.30 was assigned to the water−HEGMA pair to reflect the higher hydrophilicity of HEGMA, whose homopolymers do not precipitate in aqueous solution even after heating up to 90 °C.[20] This was also in agreement with the χ value of around 0.3 used for PEG in the literature,[42,43] which was based on activity measurements for the system PEG−water.[44] For the water−hydrophobe (MMA) pair, a χ value of 2.0 was employed, which is typical for the value of the water−propylene oxide pair.[42] And, the final input was the degree of ionization of the ionizable block, which was examined at the values of 0% and 100%.

Results and Discussion

Three-Component Model Networks. The materials in the present study are, to the best of our knowledge, the first three-component hydrogels with controlled structure, and, in particular, well-defined length of the elastic chains. The few examples in the literature of three-component networks do not have a model network structure. In their pioneering work, Kurian and Kennedy prepared three-component segmented networks based on α,*ω*-diallyl polyisobutylene (PIB, hydrophobic, rubbery, prepared by "quasiliving" carbocationic polymerization), α,*ω*-diallyl poly(ethylene glycol) (PEG, hydrophilic, prepared by anionic polymerization), and pentamethylcyclopentasiloxane (hydrophobic, oxygen-permeable) in which the PIB and PEG macro-cross-linkers were placed in random positions.[45] The same nonideality was also present in the networks prepared by these investigators, and in which the α,*ω*-diallyl PIB was substituted for α,*ω*-divinyl poly(dimethylsiloxane).[46] The novel three-component networks of Bromberg and co-workers[47] prepared by the simultaneous grafting with acrylic acid (AA, hydrophilic, ionizable) and cross-linking with EGDMA of amphiphilic nonionic PEG-*b*-poly(propylene glycol)-*b*-PEGs (PEG-*b*-PPG-*b*-PEGs) (commercially available ABA triblock copolymers known as Pluronics) had PAA grafts of uncontrolled lengths emanating from random positions on the PEG-*b*-PPG-*b*-PEG chain. In contrast, the three components of the present materials were placed in a highly ordered manner: they were composed of the five blocks of symmetrical ABCBA pentablock terpolymers, which were uniformly cross-linked at the chain ends.

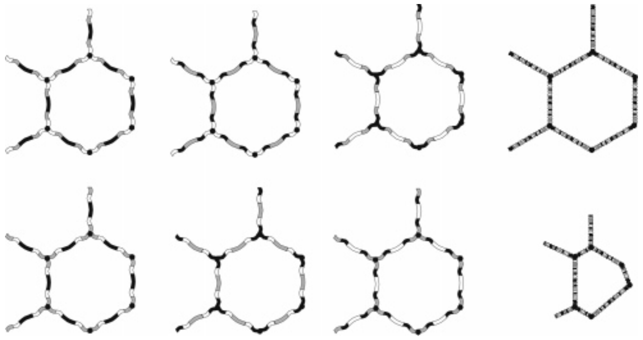

Figure 4. Schematic representation of the structures of the eight terpolymer networks of this study. The color coding is the same as that in Figure 3.

Polymerization Methodology. The synthetic procedure for the preparation of the model networks is presented schematically in Figure 3, where the synthesis of the network based on the DMAEMA$_5$-*b*-HEGMA$_5$-*b*-MMA$_{10}$-*b*-HEGMA$_5$-*b*-DMAEMA$_5$ pentablock terpolymer is shown. The synthesis involved sequential monomer and cross-linker additions. The first step in Figure 3 resulted in the preparation of linear MMA homopolymers active at both ends (indicated by asterisks) due to the use of the bifunctional initiator. The second step led to the synthesis of the HEGMA-MMA-HEGMA triblock copolymer with two active ends. The third step was the addition of DMAEMA, which provided the pentablock terpolymer. The synthesis was completed by the addition of the EGDMA cross-linker, which effected the interconnection of the polymer active ends, providing a three-dimensional network. The number of arms at the cross-links was not three, as indicated in the figure, but higher, between 15 and 25, similar to the number of arms in star polymers also prepared by GTP and characterized by static light scattering.[37−39]

All eight network structures prepared are illustrated schematically in Figure 4. The first six network structures on the left were those of the model networks based on the six possible block sequence isomeric linear precursors, ABCBA, ACBCA, BACAB, BCACB, CABAC, and CBABC, while the last two structures on the right were those of the statistical terpolymer model network and of the randomly cross-linked statistical terpolymer network.

Molecular Weights. Table 1 shows the MWs of the linear precursors to the networks as measured by GPC. The number-average molecular weights, M_n's, were systematically higher than the theoretically predicted MWs, probably due to partial deactivation of the initiator (samples 1a and 1b) or/and hydrodynamic differences between PHEGMA and PDMAEMA and the PMMA MW calibration standards. Molecular weight

Table 1. Molecular Weights of the Linear Precursors and p*K*'s of the DMAEMA Units in the Terpolymer Networks

				GPC results[c]			
no.		polymer formula[a]	theoretical MW[b]	M_n	M_w/M_n	H/D molar ratio[d]	effective pK
1	a	M_{10}	1196	1880	1.17		5.2
	b	D_5-*b*-M_{10}-*b*-D_5	2748	3900	1.14		
	c	H_5-*b*-D_5-*b*-M_{10}-*b*-D_5-*b*-H_5	6248	8780	1.13	1.12	
2	a	M_{10}	1196	1650	1.18		5.3
	b	H_5-*b*-M_{10}-*b*-H_5	4676	7200	1.12		
	c	D_5-*b*-H_5-*b*-M_{10}-*b*-H_5-*b*-D_5	6248	8740	1.13	0.85	
3	a	D_{10}	1748	2610	1.18		5.6
	b	H_5-*b*-D_{10}-*b*-H_5	5248	8570	1.13		
	c	M_5-*b*-H_5-*b*-D_{10}-*b*-H_5-*b*-M_5	6248	9650	1.13	0.90	
4	a	D_{10}	1748	2300	1.15		5.3
	b	M_5-*b*-D_{10}-*b*-M_5	2748	4020	1.14		
	c	H_5-*b*-M_5-*b*-D_{10}-*b*-M_5-*b*-H_5	6248	9490	1.12	1.29	
5	a	H_{10}	3676	6000	1.11		5.3
	b	D_5-*b*-H_{10}-*b*-D_5	5248	7300	1.09		
	c	M_5-*b*-D_5-*b*-H_{10}-*b*-D_5-*b*-M_5	6248	8500	1.10	1.18	
6	a	H_{10}	3676	5910	1.11		5.4
	b	M_5-*b*-H_{10}-*b*-M_5	4676	7040	1.10		
	c	D_5-*b*-M_5-*b*-H_{10}-*b*-M_5-*b*-D_5	6248	8800	1.10	0.86	
7	a	(H-*co*-D-*co*-M)$_{10}$	6248	9910	1.12	1.27	5.2
8	a	(H-*co*-D-*co*-M)$_{10}$-*co*-E_8					5.6

[a] H, HEGMA; D, DMAEMA; M, MMA; E, EGDMA. [b] Contribution from the initiator fragment of 196 g mol^{-1} included. [c] Based on a calibration using PMMA standards of narrow MWD. [d] By ^{1}H NMR in $CDCl_3$.

distributions (MWDs) were found to be narrow, and the polydispersity indices (PDIs, M_w/M_n) were calculated to be lower than 1.2 in all cases. This confirms the homogeneity of the lengths of the segments between cross-links in the networks.

Composition. The composition of the elastic chains of the networks was characterized by ^{1}H NMR. However, due to the overlap of the MMA characteristic peak (methoxy protons at 3.6 ppm) with that of HEGMA (oxyethylene protons at the same shift), the calculation of the MMA content by subtraction involved a large error due to the dominance of the HEGMA protons at 3.6 ppm. Thus, ^{1}H NMR could provide an accurate measurement only for the HEGMA/DMAEMA molar ratios (each contribution determined using an independent peak), which are also shown in Table 1. These molar ratios were close to 1 (within the NMR error, ~10 to 15%), as expected. However, we are confident that the compositions in all three monomer repeating units had the expected values because the GPC traces contained no unreacted monomers, indicating full conversions of the monomers fed.

Extractables. The results of the characterization of the extractables are listed in Table 2, including their percentage, M_n, and PDI. The percentage of the extractables (sol fraction) was found to be relatively low, below 12% in all cases, confirming the well-defined structure of the networks. It is noteworthy that the statistical terpolymer-based model network (sample no. 7) had the lowest percentage of extractables (6.2%), whereas the statistical terpolymer-based randomly cross-linked network (sample no. 8) had one of the highest percentages (10.0%), indicating a difference in the level of perfection between these two network structures.

Table 2. Characteristics of the Extractables from the Terpolymer Networks

			GPC results[b]	
no.	polymer formula[a]	% w/w extractables	M_n	M_w/M_n
1	H_5-*b*-D_5-*b*-M_{10}-*b*-D_5-*b*-H_5	7.7	5700	1.24
2	D_5-*b*-H_5-*b*-M_{10}-*b*-H_5-*b*-D_5	8.2	5600	1.11
3	M_5-*b*-H_5-*b*-D_{10}-*b*-H_5-*b*-M_5	10.7	7140	1.19
4	H_5-*b*-M_5-*b*-D_{10}-*b*-M_5-*b*-H_5	9.8	7060	1.09
5	M_5-*b*-D_5-*b*-H_{10}-*b*-D_5-*b*-M_5	9.1	7100	1.12
6	D_5-*b*-M_5-*b*-H_{10}-*b*-M_5-*b*-D_5	11.3	7070	1.13
7	(H-*co*-D-*co*-M)$_{10}$	6.2	7870	1.15
8	(H-*co*-D-*co*-M)$_{10}$-*co*-E_8	10.0	16500	1.36

[a] H, HEGMA; D, DMAEMA; M, MMA; E, EGDMA. [b] Based on a calibration using PMMA standards of narrow MWD.

The M_n's of the extractables, also listed in Table 2, were lower than those of the corresponding linear precursors. This was as expected because the extractables contained early terminated polymers (homopolymers and ABA triblock copolymers) as well as living ABCBA pentablock terpolymers which could not approach the cross-link due to steric hindrances. The PDIs of the extractables are also shown in Table 2. These, in most cases, were higher than the PDIs of the corresponding linear terpolymer precursors listed in Table 1. This was in accord with the expectation for an increased size heterogeneity of the extractables, and in (qualitative) agreement with Poisson distribution,[48] dictating higher PDIs for polymers with lower M_n's, as was the case with the extractables.

Although the synthetic procedure (and rapid cross-linking) precluded sampling for GPC characterization of the precursor to the randomly cross-linked network, GPC characterization of the extractables from this network was straightforward. The determination of the M_n and PDI of the extractables from the randomly cross-linked network was very important because these quantities would be the only (approximate) indicators for the MW characteristics of this network. The M_n of the extractables of the randomly cross-linked network was more than twice the M_n of the extractables from the other networks. This was consistent with a branched structure of the extractables

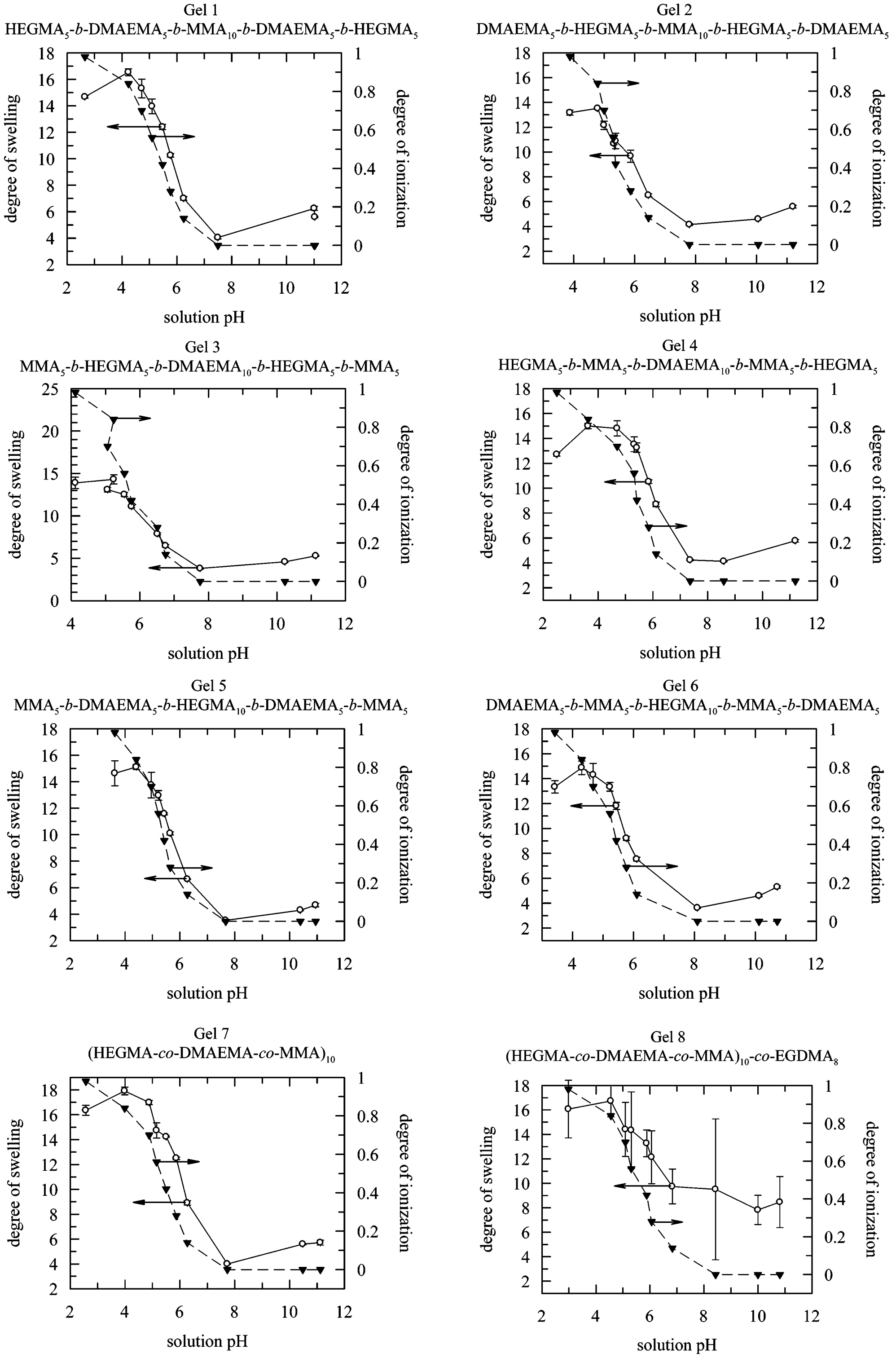

Figure 5. Degrees of swelling and degrees of ionization as a function of pH for all the terpolymer networks of this study.

from the randomly cross-linked network, originating from the simultaneous copolymerization of the monomers and the cross-linker during the synthesis of this network. Despite their high M_n value, the PDI of the extractables from the randomly cross-linked network was the highest of all networks, 1.36, indicating the increased heterogeneity of this material, due to branching. However, the value of PDI of 1.36 is still acceptably low, reflecting the "livingness" of the synthetic method.

pH Dependence of the Aqueous Degrees of Swelling. The experimentally measured DSs and degrees of ionization of all the networks are plotted against pH in Figure 5. The structure of each network is indicated above each plot. The effective p*K*'s of the DMAEMA units in the networks, also presented in Table 1, were read out from the degree of ionization curves as the pH at 50% ionization. All networks were found to have similar p*K*'s which, however, span a range of values, from 5.2 to 5.6. These values are to be compared with the p*K* value of DMAEMA homopolymer which is around 7.[49] The discrepancy is probably due to the measurement of the pH in the supernatant liquid rather than inside the mass of the networks and the lower pH of the supernatant than the network. This is dictated by Donnan

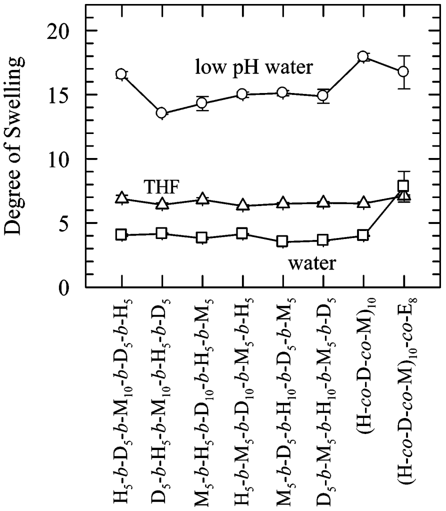

Figure 6. Degrees of swelling of the terpolymer networks in THF, water, and acidic water.

equilibrium[50] according to which a semiprotonated network would electrostatically repel to the supernatant further incoming protons.

The networks began to swell at pH 6 or lower because of the presence of DMAEMA, a tertiary amine becoming ionized in that pH range. Ionization of the DMAEMA repeating units resulted in electrostatic repulsions between them and in the buildup of an osmotic pressure created by the counterions to the charges in the network.[51] The DS and degree of ionization curves followed each other, confirming the importance of the electrostatic interactions in swelling. DSs dropped again at very low pH due to charge screening arising from the relatively high ionic strength imparted by the high acid concentration.

Degrees of Swelling in Water and THF. The DSs of the neutral networks in water (pH ~ 8) and of fully ionized networks in acidified water at maximum swelling (pH ~ 3.5−4.5) were extracted from Figure 5 for all networks and are plotted in Figure 6 along with the corresponding DSs in THF (neutral networks). With the exception of the randomly cross-linked network, which is structurally less perfect, the DSs of all other networks increased in the following order: water < THF < acidic water, with values of approximately 4, 7, and 14, respectively. THF is a nonselective solvent, in which all three monomer repeating units of the networks swelled to a good extent. In contrast, water is a selective solvent for HEGMA and DMAEMA, and a precipitant for MMA. Thus, the equilibration of the terpolymer networks in water led to their microphase separation with collapsed MMA cores. The collapse of the MMA units in water explains the lower swelling of the terpolymer networks in this solvent than in THF. The acidified water was still a nonsolvent for MMA, but it caused the ionization of the DMAEMA units, which led to extensive swelling, resulting in the highest DSs in this solvent compared to those in the other two.

It is interesting to compare the average DSs in neutral and acidified water of the terpolymer networks of the present study with those of two-component conetworks prepared by the same method. In particular, ABA triblock copolymer-based model conetworks of DMAEMA and MMA (amphiphilic)[52,53] exhibited DSs in neutral and acidic water of 2 and 5, respectively, while DMAEMA and HEGMA (double-hydrophilic) conetworks[54] presented corresponding DS values of 8 and 20. Thus, the corresponding DSs of the terpolymer networks of the present study of 4 and 14 had values intermediate and between those of the two above-mentioned two-component conetworks, reflecting the hydrophobic character of MMA and the hydrophilic character of HEGMA. However, in addition to the numerical differences between the DSs of the terpolymer and the copolymer networks, there were substantial structural differences. In particular, unlike the DMAEMA-MMA conetworks, these terpolymer networks were not fully collapsed in their neutral state, underlining the role of the second type of hydrophilic units, HEGMA. Moreover, unlike the DMAEMA-HEGMA conetworks, the present terpolymer networks were microphase separated (partially collapsed) in their ionized state, emphasizing the role of the hydrophobic MMA.

By examining Figure 6 more carefully, we can see that, in a given solvent, the various isomers did not present large differences in their DSs, possibly reflecting the low degrees of polymerization of their blocks. Indeed, the DSs in THF (nonselective solvent) of all terpolymer networks were the same, with the less perfect randomly cross-linked terpolymer network exhibiting a slight upward deviation. Also, in water, the DSs of most networks were similar, with the randomly cross-linked network again presenting some deviation to higher values. In acidic conditions, in which all terpolymer networks swelled much more, the statistical terpolymer model network differentiated itself from the others for the first time, presenting the highest DS, reflecting highly extended chains due to the random distribution of the MMA units which precluded microphase separation. In contrast, the segregation of the MMA units in blocks in the case of the pentablock networks promoted microphase separation which reduced the effective chain length, resulting in a decrease in the DS. In ionized DMAEMA-MMA networks, the DSs of the block isomers were also lower than those of the statistical counterparts. These differences in the DSs between block and statistical networks were reproduced by the thermodynamic model discussed below.

Predicted Degrees of Swelling of the Terpolymer Model Networks. Table 3 lists the predictions of the thermodynamic model for the DSs in water, both in the neutral and in the fully ionized state, and in THF (only in the neutral state) for the statistical terpolymer model network and the two terpolymer model networks with MMA end-blocks. For comparison, the same table also shows the corresponding experimental results of Figure 6.

The table shows that the theoretical DSs were more extreme than the corresponding experimental DSs. In particular, for the collapsed networks the theoretically predicted DSs were lower than the experimental, while for the highly swollen networks the theoretically predicted DSs were higher than the experimental. The former difference can be attributed to the increased DSs in the experimental system resulting from cycle and dangling chains formation (at the expense of elastic chain) and from the retention of extra water within the pores of the networks, whereas the latter may be due to the extensive catenation (mechanical interlinking) between the polymer elastic chains in the experimental system, which severely restricted chain extension,[55] and was more intensely manifested for higher DSs.

Despite the discrepancies between the theoretical and the experimental values of the DSs, the theoretically predicted DSs reproduced correctly the trends observed experimentally. First, for all three terpolymer networks modeled, the predicted DSs increased in the order water < THF < acidic water, just like in the experimental system. Moreover, the theoretical DSs in acidic water were higher for the statistical than the pentablock terpolymer networks, in accord with the experimental observations.

Table 3. Comparison between the Theoretically Predicted and the Experimentally Determined Degrees of Swelling in Various Solvents of the Terpolymer Networks

network[a]	M_5-*b*-D_5-*b*-H_{10}-*b*-D_5-*b*-M_5			M_5-*b*-H_5-*b*-D_{10}-*b*-H_5-*b*-M_5			(H-*co*-D-*co*-M)$_{10}$		
	neutral	THF	ionized	neutral	THF	ionized	neutral	THF	ionized
theoretical	2.89	9.22	31.5	2.89	9.22	31.5	1.65	9.22	48.1
experimental	3.5	6.5	15.1	3.8	6.8	14.3	4.0	6.5	17.9

[a] H, HEGMA; D, DMAEMA; M, MMA; E, EGDMA.

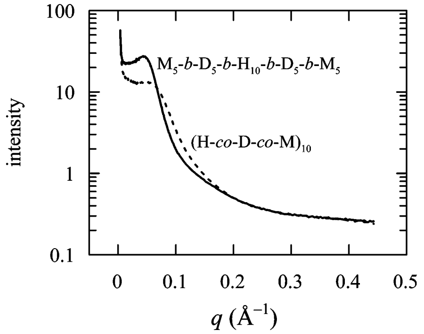

Figure 7. SANS profiles of a pentablock terpolymer network and the statistical terpolymer network in the neutral state in D_2O.

Structure of the Networks in Water. Figure 7 depicts the SANS profiles of one pentablock and the statistical terpolymer model networks in the neutral state in deuterated water. It is noteworthy that these experiments provide the first published example of SANS characterization of segmented conetworks in a selective solvent, as a previous relevant report involved SANS work on bulk conetworks.[56] The scattering profile of the pentablock network exhibited an intensity maximum, indicating the presence of relatively large scattering centers. In this network, these centers should consist of the hydrophobic PMMA end-blocks surrounding the also hydrophobic EGDMA cores. This suggests the structuring of this material in water and is consistent with the microphase separation discussed earlier. In contrast, the scattering profile of the statistical network did not exhibit a clear maximum, but a broad shoulder, due to the scattering of the EGDMA cores alone. In this network, the hydrophobic MMA units are randomly distributed along the elastic chains and, therefore, cannot easily assemble around the core to enhance the scattering.

From the position of the intensity maximum of the pentablock network on the q-axis, the average distance between the scattering centers can be estimated as $2\pi/q_{\max}$.[57] This gives a distance of 14.4 nm, which could be compared with the distance calculated based on the molecular structure of the network elastic chains and the experimentally measured DS in water. Using the GPC M_n of the elastic chains (8500 g mol^{-1}) and adding to it the contribution from the EGDMA cross-linker units leads to an overall equivalent chain M_n of 10 655 g mol^{-1}. Assuming 20 chains per cross-link, this provides a total M_n of 213 099 g mol^{-1} for the dry unit cell. Multiplying this figure by the DS in water of 3.5 results in the M_n of the swollen unit cell of 745 845 g mol^{-1}. With the use of a density of 1 g cm^{-3}, the molecular volume of this cell can be calculated to be 1238 nm^3. Assuming a cubic unit cell, the cube root of this volume provides the average distance between adjacent cores as 10.7 nm, which is to be compared with the distance of 14.4 nm that resulted from the SANS experiment. The agreement is very satisfactory, given the various assumptions made in the calculations.

Conclusions

GTP was used to synthesize novel biomaterials based on model networks composed of three different monomer repeating units placed symmetrically in five blocks. All six possible block sequence isomers were prepared, plus the statistical terpolymer network. The randomly cross-linked terpolymer network was also synthesized. The following three functional monomer repeating units were employed: one hydrophobic (MMA), one hydrophilic (HEGMA), and one pH-responsive (DMAEMA), conferring to the networks a very rich swelling behavior. Thus, in water, the pentablock networks had a trend for microphase separation and presented a pH-dependent swelling behavior without completely collapsing in their neutral state. The isomeric networks presented similar swelling behavior under most conditions, with the exception of the statistical terpolymer model network which exhibited a higher DS, manifesting its inability to microphase separate in water. The inability of the statistical network for microphase separation was confirmed by SANS measurements in water, which also suggested microphase separation in the pentablock networks. All experimental trends in the swelling of the terpolymer networks were qualitatively reproduced by a thermodynamic model.

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