

Supplementary Information for Manuscript Entitled:

Model Dynamic Covalent Thermoresponsive Amphiphilic Polymer Conetworks Based on Acylhydrazone End-linked Tetronic T904 Star Block Copolymers

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Submitted for publication in *Polymer Chemistry* October 2022; revised November 2022.

Experimental Section

Syntheses

End-functionalizations of Tetronic T904. The amphiphilic star block copolymer Tetronic T904, a kind gift from BASF SE, in Ludwigshafen am Rhein, Germany, was end-functionalized with either benzaldehyde or benzaacylhydrazide groups, following our strategy reported in our previous work on four-armed star poly(ethylene glycol)s (tetraPEG stars) [1]. Briefly, the four hydroxyl end-groups of this star copolymer were first activated *via* mesylation, followed by substitution of the mesyl group either with 4-hydroxybenzaldehyde or benzaldehyde-protected 4-hydroxybenzhydrazide, succeeded by removal of most of the excess low-molar-mass reagents *via* extraction from dichloromethane using alkaline water. However, unlike the benzaldehyde-derivatized tetraPEG, the benzaldehyde-derivatized Tetronic T904 (T904-Bz) which could not be precipitated in cold diethyl ether required column chromatography (90% v/v dichloromethane - 10% v/v methanol) for the complete removal of the last traces of excess 4-hydroxybenzaldehyde. After column chromatography, this end-functionalized product was dried under vacuum at 50 °C and stored. The other end-functionalized (intermediate) product, *i.e.*, the one derivatized with benzaldehyde-protected 4-hydroxybenzhydrazide, was hydrazinolyzed at room temperature, to yield the benzaacylhydrazide-derivatized Tetronic T904 (T904-Hz), which was subsequently purified by dialysis against water, and finally lyophilized.

End-functionalizations of PEG-OH 550. The monohydroxy-functionalized linear PEG methyl ether of molar mass of 550 g mol^{-1} (PEG-OH 550), purchased from Merck-Sigma-Aldrich, Germany, was also end-functionalized with either benzaldehyde or benzaacylhydrazide groups, following a similar, but not identical, strategy to that followed for Tetronic T904 described above. The difference involved only the end-functionalization with the benzaacylhydrazide group, which followed the original recipe by Deng *et al.* [2], where mesylation of the PEG-OH 550 was followed by displacement of the mesyl group using methyl 4-hydroxybenzoate, and completed by hydrazinolysis of the methyl group in the ester to yield the desired benzaacylhydrazide derivative. Details of these end-functionalizations follow.

Synthesis of mono-methanesulfonyl-poly(ethylene glycol) methyl ether (PEG-MS). First, mono-hydroxyl poly(ethylene glycol) methyl ether (10.0 g, 18.2 mmol) was transferred into a round-bottomed flask, dissolved in the minimum volume of anhydrous 1,4-dioxane, and, then, lyophilized to remove any traces of water. Subsequently, the lyophilized mono-hydroxyl-poly(ethylene glycol) methyl ether was dissolved in freshly distilled dichloromethane (DCM) (50 mL), followed by the addition of freshly distilled triethylamine (3.7 g, 5.0 mL, 36.4 mmol, 2-fold molar excess with respect to the hydroxyl end-group). After that, methanesulfonyl (“mesyl”) chloride (2.4 mL, 3.5 g, 30.9 mmol, 170% molar excess with respect to the hydroxyl end-group) was added dropwise into the polymer solution, while the temperature of the system was kept constant at $0 \text{ }^{\circ}\text{C}$. After 30 min, the mixture was allowed to warm up to room temperature, and it was stirred for another 48 h. Thereupon, the reaction mixture was diluted with DCM, washed with 300 mL of a 10% w/v aqueous solution of NaHCO_3 (twelve times, 25 mL each time), washed with 50 mL of water (twice, 25 mL each time), dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness to obtain a viscous yellowish liquid (11.2 g, 17.8 mmol, 98% yield).

Synthesis of mono-methyl benzoate-poly(ethylene glycol) methyl ether (PEG-PRHz). First, mono-methanesulfonyl-poly(ethylene glycol) methyl ether (5.62 g, 8.9 mmol), methyl 4-hydroxybenzoate (2.3 g, 15.2 mmol, 170% molar excess with respect to the methanesulfonyl end-group), potassium carbonate (2.5 g, 17.9 mmol, 2-fold molar excess with respect to the methanesulfonyl end-group), and DMF (70 mL) were transferred into a round-bottomed flask. Then, the mixture was refluxed at $80 \text{ }^{\circ}\text{C}$ for 24 h. After that, the reaction mixture was diluted with DCM, washed with 200 mL of an aqueous solution of 1 M NaOH (eight times, 25 mL each time), washed with 50 mL of water (twice, 25 mL each time), dried over anhydrous magnesium sulfate, and filtered. Subsequently, the mono-methyl benzoate-poly(ethylene glycol) methyl ether was obtained as a viscous yellowish liquid using column chromatography (at 19 : 1 volume ratio of a DCM : methanol mixture) (4.5 g, 6.6 mmol, 74% yield).

Synthesis of mono-benzaacylhydrazide-poly(ethylene glycol) methyl ether (PEG-Hz). First, mono-methyl benzoate-poly(ethylene glycol) methyl ether (2.5 g, 3.67 mmol), hydrazine hydrate (80% w/w in water, 11 mL, 0.25 mol, 70-fold molar excess with respect to the methyl benzoate end-group) and DMSO (15 mL) were transferred into a round-bottomed flask. Then, the mixture was refluxed at $90 \text{ }^{\circ}\text{C}$ for 24 h. Afterward, the solvents and the excess of hydrazine hydrate were removed under reduced pressure. The resulting viscous liquid was dissolved in 100 mL of 1 M aqueous solution of NaOH and the mono-benzaacylhydrazide-poly(ethylene glycol) methyl ether was extracted with 400 mL DCM (ten times, 40 mL each time). The organic layers were combined, washed with 50 mL water (twice, 25 mL each time), dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness to obtain a viscous transparent liquid (1.9 g, 2.8 mmol, 76% yield).

Synthesis of mono-benzaldehyde-poly(ethylene glycol) methyl ether (PEG-Bz). First, mono-methanesulfonyl-poly(ethylene glycol) methyl ether (5.6 g, 8.9 mmol), potassium carbonate (2.5 g, 17.9 mmol, 2-fold molar excess with respect to the methanesulfonyl end-group), 4-hydroxybenzaldehyde (1.9 g, 15.1 mmol, 170% molar excess with respect to the methanesulfonyl end-group), and DMF (20 mL) were transferred into a round-bottomed flask. After that, the mixture was refluxed for 24 h at 80 °C. Then, the reaction mixture was diluted with DCM, washed with 200 mL of an aqueous solution of 1 M NaOH (eight times, 25 mL each time), washed with 50 mL of water (twice, 25 mL each time), dried over anhydrous magnesium sulfate, and filtered. Subsequently, the mono-benzaldehyde-poly(ethylene glycol) methyl ether was obtained as a viscous yellowish liquid using column chromatography (employing again as eluent a solvent mixture composed of DCM : methanol at a 19 : 1 volume ratio) (4.7 g, 7.19 mmol, 81% yield).

Gel Formation. The dynamic covalent amphiphilic polymer conetworks (APCNs) were formed by mixing equimolar aqueous solutions of the two above-prepared end-functionalized Tetric T904 amphiphilic star block copolymers, the T904-Bz and T904-Hz, each typically at 15% w/v, adjusted to values of pH between 1.5 and 5.5 using either a 200 mM phosphoric acid buffer (pH range from 1.5 to 2.0) or a 200 mM sodium acetate / acetic acid buffer (pH range from 3.5 to 5.5).

Gel and Linear Acylhydrazone Model Compound Cycling. For the dissociation and re-association cycles of the gel, the same star block copolymer concentration of 15% w/v was employed as in *Gel Formation* above, but neat water or neat D₂O was used instead of buffer, so as to facilitate gel dissolution and reformation upon the additions of HCl (or DCl) and triethylamine, respectively. Similarly, neat D₂O was also used for the cycling of the linear acylhydrazone model compound.

Characterization

NMR Spectroscopy. Proton nuclear magnetic resonance (¹H NMR) spectroscopy was performed on 500 MHz Avance Bruker NMR spectrometer equipped with an ultrashield magnet, and used to verify the quantitative end-functionalization, structure and purity of the Tetric T904 derivatives in CDCl₃ or *d*₆-DMSO, and to determine the percentage conversion to acylhydrazone bonds in both the gel and solution states during the conetwork reversibility experiments performed in D₂O.

Gel permeation chromatography. Gel permeation chromatography (GPC) was used to record the molar mass distributions, and from those to calculate the average molar masses, of Tetric T904 and all of its derivatives. GPC was performed on an Agilent gel permeation chromatograph, equipped with a single “mixed D” column (and appropriate guard pre-column) from Polymer Laboratories, calibrated against low molar mass dispersity linear poly(methyl methacrylate) standards, and employing tetrahydrofuran as the mobile phase delivered at a flow rate of 1 mL min⁻¹.

Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) was also employed to obtain the molar mass distributions (and estimated average molar masses) of the starting Tetric T904 and its derivatives. MALDI-TOF was performed on a Bruker UltraFlex III MALDI tandem time-of-flight (TOF/TOF) mass spectrometer equipped with a Nd:YAG laser emitting at 355 nm [3]. Dithranol (DIT) served as the matrix, whereas sodium trifluoroacetate (NaTFA) was employed as the cationization salt. Both DIT and NaTFA were dissolved in THF at concentrations of 20 and 10 mg mL⁻¹, respectively. The polymer polymer sample was dissolved in THF at a concentration of 10 mg mL⁻¹. Solutions at matrix : sample : salt ratios equal to 10 : 2 : 1 were prepared and spotted onto the MALDI target.

Attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR spectroscopy). ATR-FTIR spectra of the two end-functionalized derivatives (in dry form) of the Tetronic T904 amphiphilic star block copolymer, T904-Bz and T904-Hz, and the conetwork prepared from the two, also after drying, were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with a Pike Miracle Ge ATR accessory.

Rheology. Rheology was performed on a Discovery HR2 rheometer from Thermal Analysis Instruments (TA), operated in oscillation time mode using parallel plate geometry, with 10% angular frequency and 1% strain. The top plate had a 20 mm diameter, while the bottom one was also a Peltier element, thermostatically controlling the system at 25 °C. The rheometer was used to determine both the gel formation times (operation at a constant oscillation frequency of 1 Hz) and the characteristic relaxation times of the dynamic covalent cross-links (operation within the angular frequency range from 10^{-2} to 10^2 rad s^{-1}).

Small-Angle Neutron Scattering. Small-angle neutron scattering (SANS) experiments were performed on the V4 instrument at the Helmholtz Zentrum Berlin (HZB), Germany [4]. Samples were kept in quartz cuvettes (Hellma) of 1 or 2 mm path length in a thermostated sample changer. Measurements were performed at three configurations with sample-to-detector distances of 1, 4, and 15.75 m and collimation lengths of 2, 4, and 16 m, respectively. The wavelength λ was always kept at 6 Å (FWHM 11%). This covers a q -range from 0.03 to 5.10 nm^{-1} , where q is the magnitude of the scattering vector, $q = 4\pi/\lambda \cdot \sin(\theta/2)$, with θ being the scattering angle. Spectra were recorded on a 2-dimensional He^3 gas detector of 128×128 pixels of 5×5 mm^2 . Raw data were corrected for the scattering of the empty cell, sample transmission, and thickness. The pixel efficiency and solid angle variation were taken into account by using pure water in a 1 mm cuvette as reference. The background noise was accounted for by measurements with Cadmium, the absolute scale was determined by using the transmission and scattering intensity of the 1 mm water sample. The reduced data were azimuthally averaged and merged, using a scaling factor of 200 for the low q range, since no water correction was possible here. All data reduction steps were carried out with the software BerSANS [5]. The presented SANS curves still contain the incoherent background scattering of the solvent and the sample.

Tensile and Compressive Testing. An Instron (Instron, Norwood, MA) 5944 mechanical testing system was used to characterize, at room temperature (~ 25 °C), the **compressive** mechanical properties of the Tetronic T904 dynamic covalent APCNs both in the original state prepared at a final polymer concentration of 15% w/v in water with the addition of a small volume of glacial acetic acid (~ 2 μL), and at the recycled state (dissolved with the addition of a small volume of HCl 5 M, and reformed by the addition of an equivalent amount of neat triethylamine). An Instron 5565 mechanical testing system, equipped with an environmental chamber, filled with paraffin oil, allowing a precise control of the temperature was used to characterize, at a strain rate of 0.06 s^{-1} and at 25, 40 and °C, the **tensile** mechanical properties of the Tetronic T904 dynamic covalent APCNs in their original state prepared at a final polymer concentration of 15% w/v and in a 200 mM sodium acetate / acetic acid aqueous buffer.

Results and Discussion

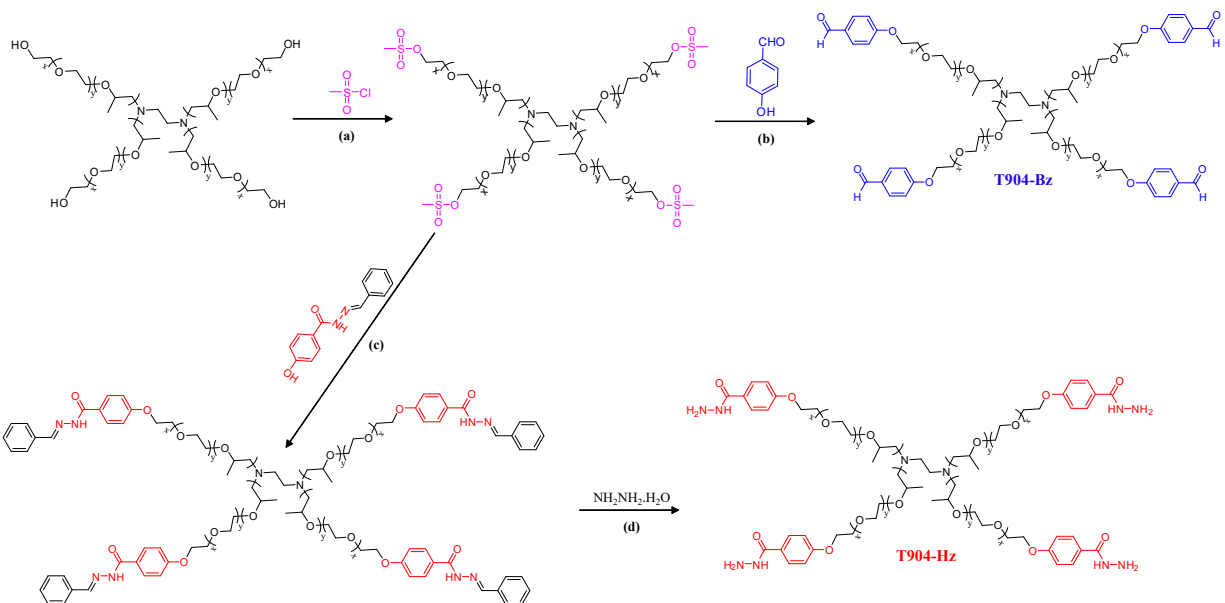


Figure S1. Chemical reaction schemes for the preparation of the T904-Bz, and T904-Hz star copolymers. (a) Triethylamine (Et_3N), dichloromethane (DCM), 0°C , 72 h, (b) *N,N*-dimethylformamide (DMF), K_2CO_3 , 80°C , 24 h, (c) DMF, K_2CO_3 , 80°C , 17 h, and (d) dimethylsulfoxide (DMSO), 24 h, room temperature.

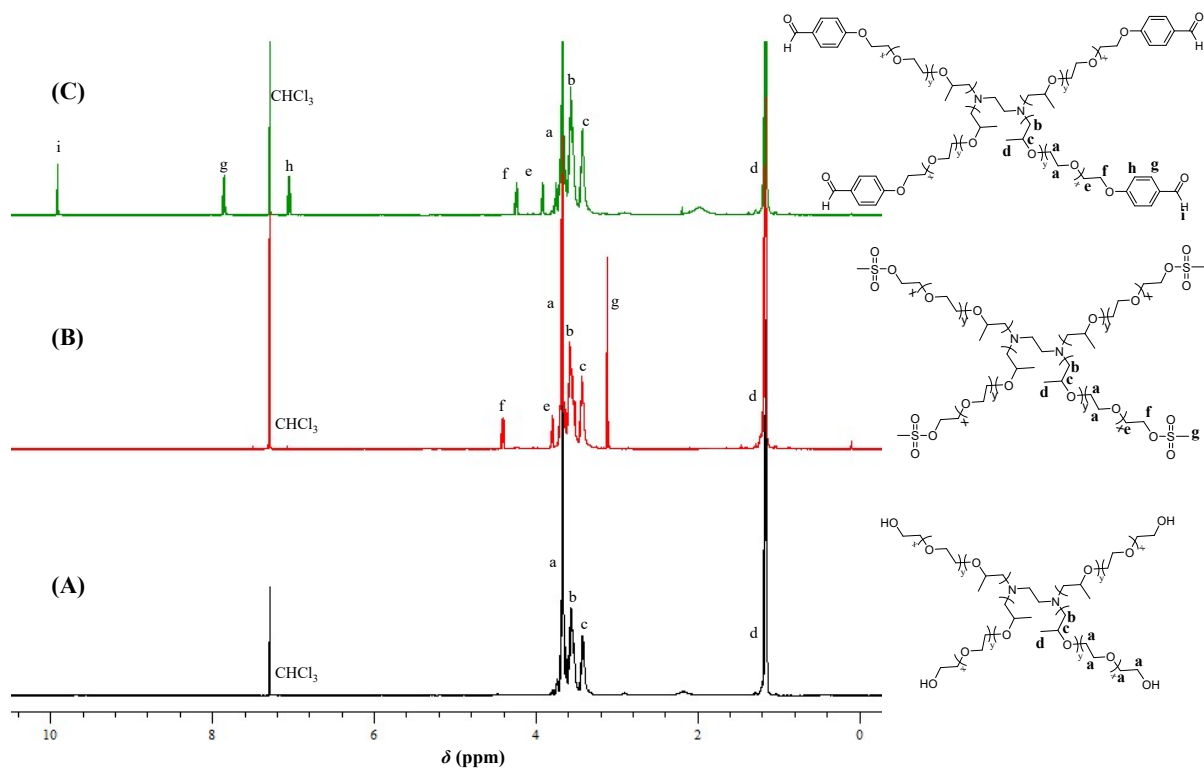


Figure S2. ^1H NMR spectra of (A) T904-OH, (B) T904-MS and (C) T904-Bz star copolymers in CDCl_3 .

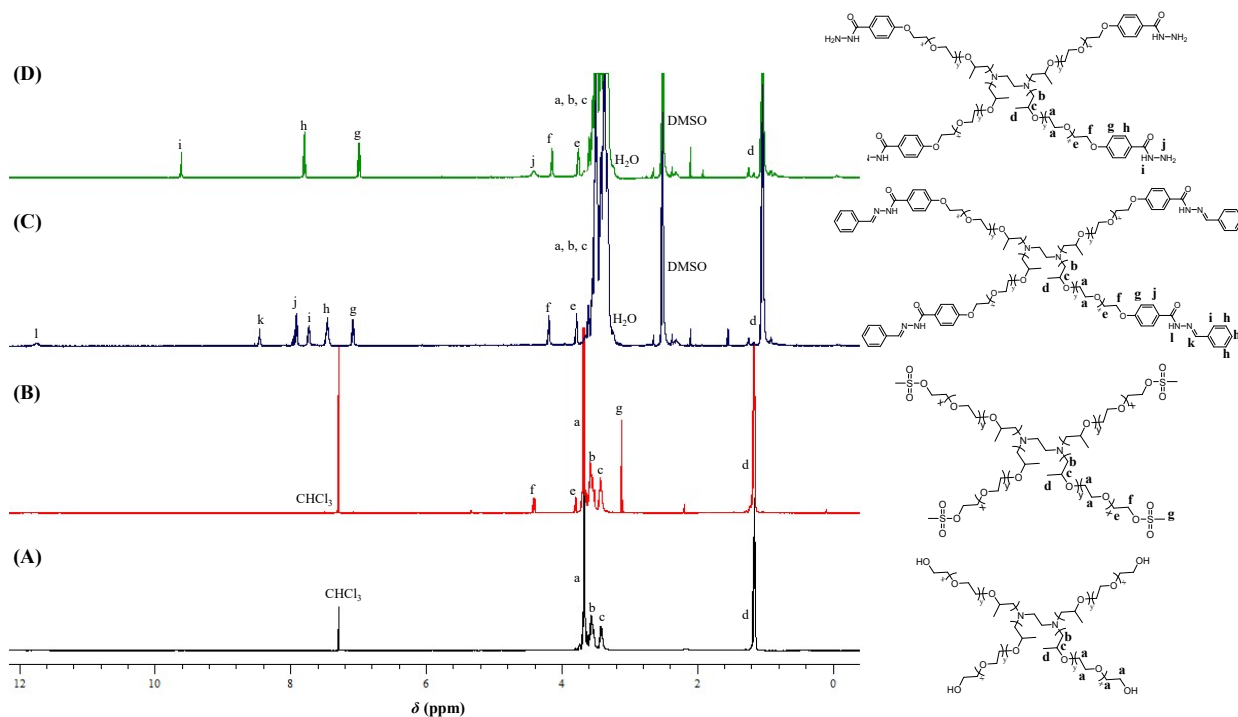


Figure S3. ^1H NMR spectra of (A) T904-OH and (B) T904-MS star copolymers in CDCl_3 , and (C) T904-PRHz and (D) T904-Hz star copolymers in d_6 -DMSO.

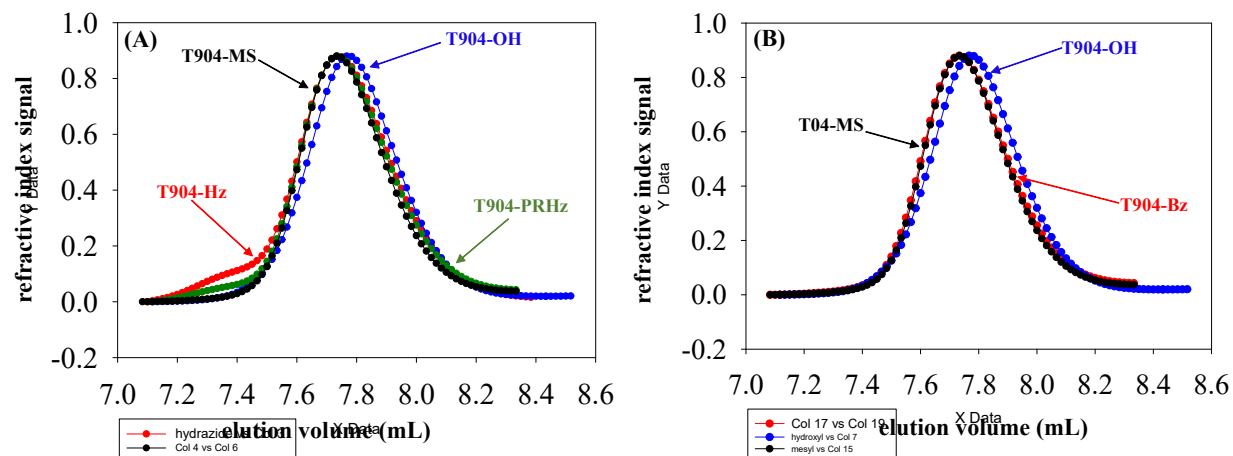


Figure S4. (A) GPC traces of the T904-OH, T904-MS, T904-PRHz and T904-Hz star copolymers. (B) GPC traces of the T904-OH, T904-MS and T904-Bz star copolymers.

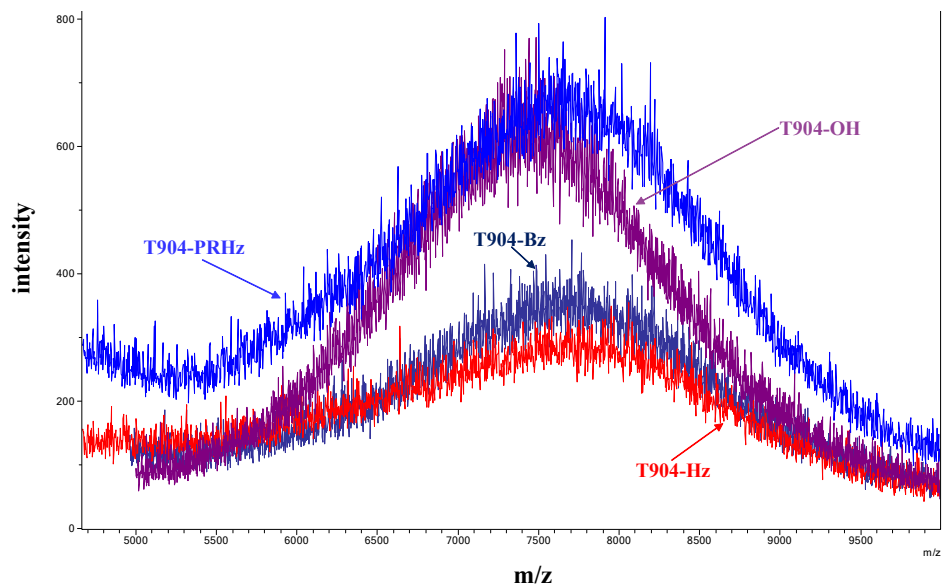


Figure S5. MALDI-TOF mass spectra of the T904-OH, T904-PRHz, T904-Hz and T904-Bz star copolymers.

Table S1. Molar mass characteristics of the starting T904-OH and the modified T904 star copolymers.

no.	Star Copolymer	Molar Mass (g mol^{-1})			\bar{D} from GPC
		Theory	MALDI-TOF	GPC (M_n)	
1	T904-OH	6700	7400	9200	1.10
2	T904-Hz	7236	7800	9790	1.16
3	T904-PRHz	7588	7650	9620	1.11
4	T904-MS	7012	-----	9650	1.09
5	T904-Bz	7116	7750	9610	1.09

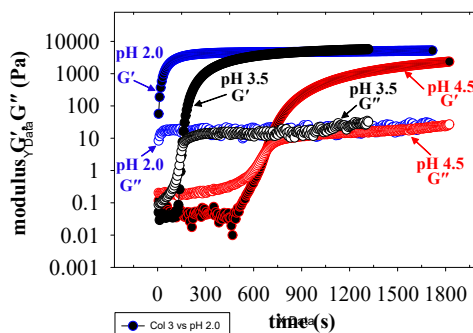


Figure S6. Temporal evolution of the shear elastic modulus, G' , and shear loss modulus, G'' , upon mixing the complementarily end-functionalized T904-Hz and T904-Bz amphiphilic star block copolymers in aqueous 0.2 M phosphate buffer solutions of pH 2.0, 3.5, and 4.5.

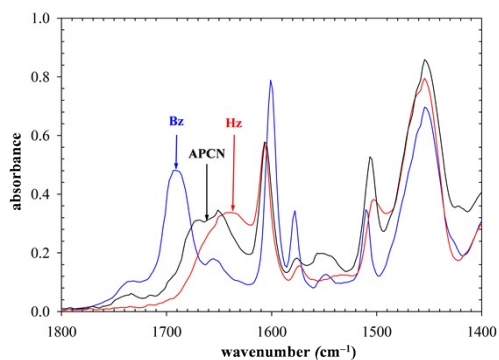


Figure S7. ATR-FTIR spectrum of the dried T904 APCN, overlaid together with the spectra of its two dry constituents, T904-Bz (Bz) and T904-Hz (Hz). The intensity in the APCN spectrum at 1690 cm^{-1} (benzaldehyde C=O stretching) is very low, consistent with a high ($\sim 90\%$) conversion to acylhydrazone.

Table S2 lists the compressive mechanical properties of original (top part of table) and corresponding reformed (lower part) APCN gels, so as to assess the efficiency in gel reformation from the mechanical property perspective. The measured mechanical properties were the compressive Young’s modulus and the stress and strain at break. The steps involved in this test are schematically illustrated in Figure 2(d) in the main text. In particular, an as-prepared original (“virgin”) APCN was subjected to compression until (compressive) fracture in a testing machine to determine its compressive mechanical properties. This was followed by APCN reconstitution *via* the dissolution of the fractured pieces in minimum volume of concentrated (5 M) HCl which was consequently neutralized by the addition of an equivalent amount of Et_3N , leading to gel reformation (“recycled gel”). The thus-recycled gel was subjected to evaluation of its mechanical properties in compression using again the testing machine. The compressive mechanical properties, especially modulus of the recycled and virgin gels, were found identical, within the experimental error (standard deviation) calculated for five virgin and the corresponding five recycled gels, thereby manifesting efficient gel reformation.

Table S2. Mechanical properties of original (“virgin”) and recycled (“reformed”) gels over five repeats.

T904 gel state	Elastic modulus (MPa)	stress at break (MPa)	strain at break (%)
original	0.0185	5.98	91
original	0.0216	2.48	86
original	0.0160	4.61	90
original	0.0153	4.62	90
original	0.0280	7.37	93
Average	0.020 ± 0.005	5.0 ± 1.8	90.0 ± 2.5
T904 gel state	Elastic modulus (MPa)	stress at break (MPa)	strain at break (%)
recycled	0.028	6.68	91
recycled	0.033	3.59	88
recycled	0.025	5.60	90
recycled	0.020	5.60	91
recycled	0.031	4.88	90
Average	0.027 ± 0.005	5.3 ± 1.1	90.0 ± 1.2

Parts (a) and (b) of Figure S8 plot the oscillation frequency (ω) dependence of the shear elastic, G' , and loss, G'' , moduli of APCNs prepared in 200 mM aqueous buffers of pH 1.5 and 2.0, respectively. In part (a) of the figure (also plotted in the main text as Figure 2(e)), the two moduli cross at a frequency of $\omega_{\text{crossing}} = 0.0116 \text{ rad s}^{-1}$, corresponding to a bond lifetime of 9 min ($= 540 \text{ s} = 2\pi/\omega_{\text{crossing}}$), suggesting that each acylhydrazone cross-link “opens up” with a characteristic timescale of 9 min, providing to it the chance of exchanging with neighboring cross-links which also happen to be “open” at the same time. The frequency sweep plot for the APCN prepared at pH 2.0 displayed in Figure S8(b) did not exhibit crossing of the two moduli, as the modulus crossing apparently occurred at frequencies lower than the ones employed in the experiment. However, using superposition (extrapolation using as template the plot at pH = 1.5), shown in part (c) of Figure S8, the acylhydrazone cross-link lifetime at this pH was found to be 39 min (from $\omega_{\text{crossing}} = 0.00268 \text{ rad s}^{-1}$), expectedly longer than the one at pH = 1.5.

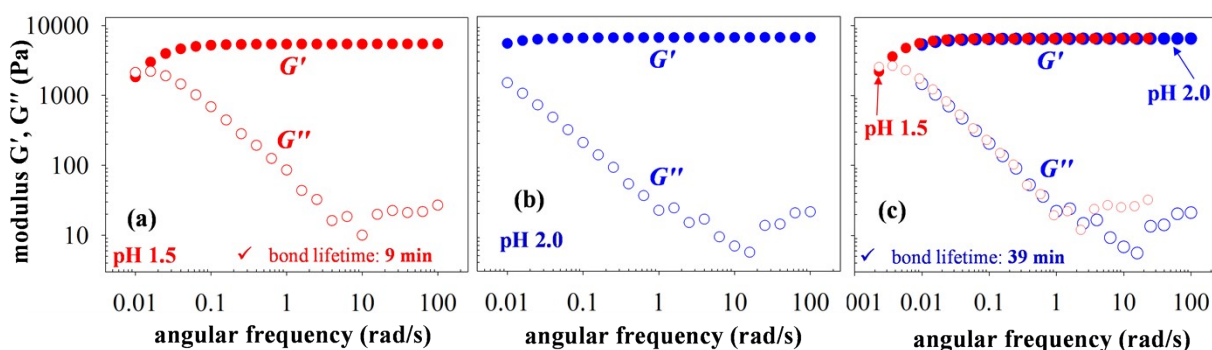


Figure S8. Frequency sweep rheological experiments on the dynamic covalent APCNs in order to determine the acylhydrazone cross-link lifetime. (a) APCN prepared at pH = 1.5. (b) APCN prepared at pH = 2.0. (c) Superposition (overlay) of the rheology profiles in (b) with that in (a) in order to extrapolate and determine the frequency of intersection of the shear elastic and loss moduli at pH 2.0.

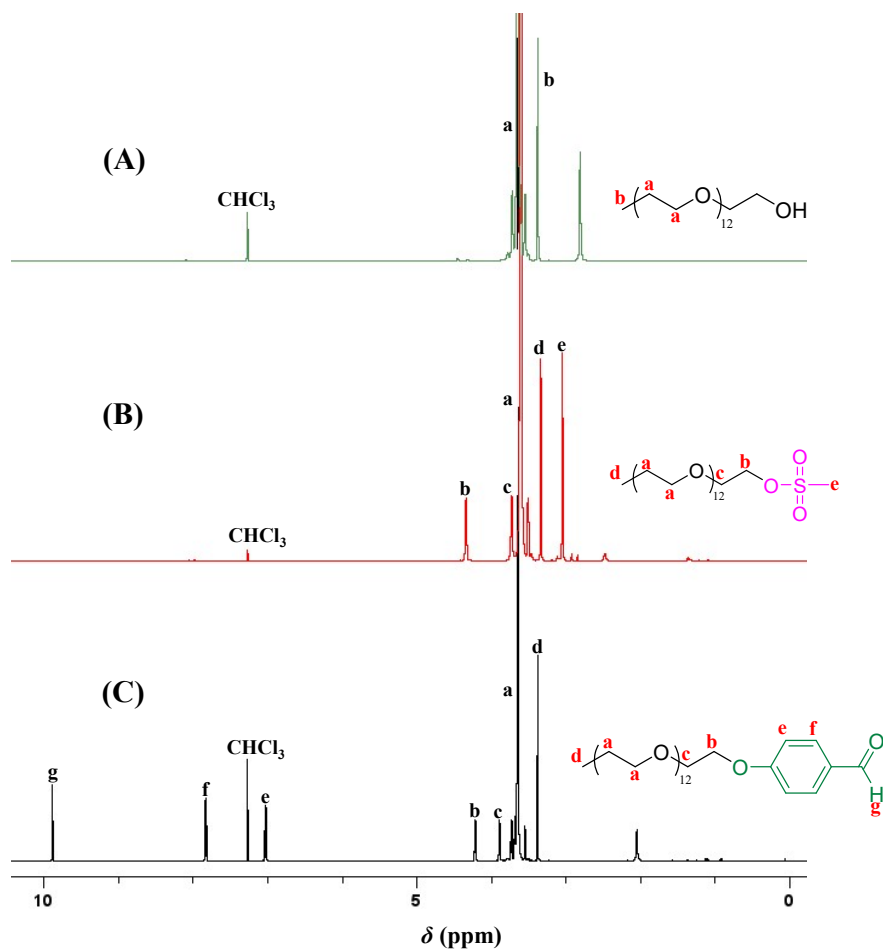


Figure S9. ^1H NMR spectra of (A) PEG-OH 550, (B) PEG-MS and (C) PEG-Bz linear monofunctionalized homopolymers in CDCl_3 .

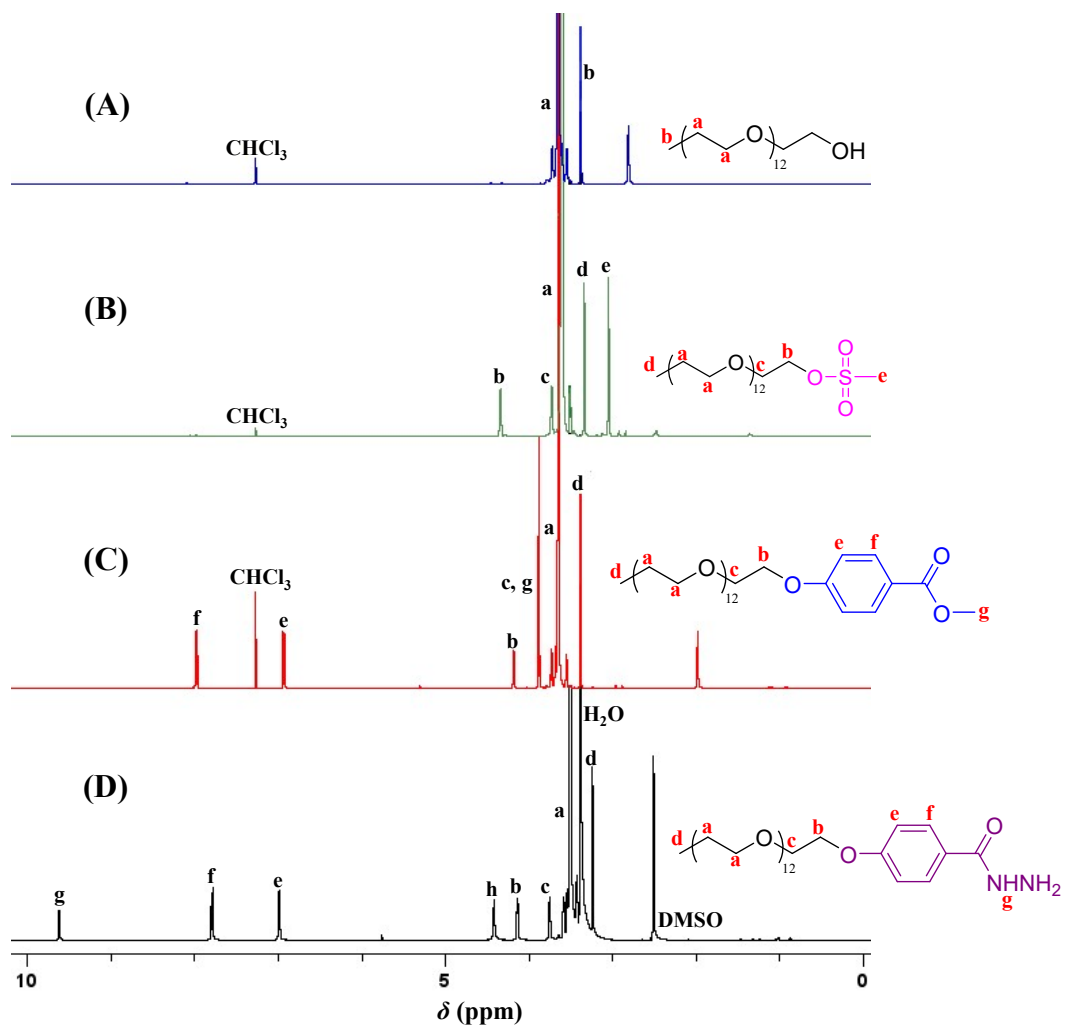


Figure S10. ^1H NMR spectra of (A) PEG-OH 550, (B) PEG-MS, and (C) PEG-PRHz linear monofunctionalized homopolymers in CDCl_3 , and (D) PEG-Hz linear monofunctionalized homopolymer in d_6 -DMSO.

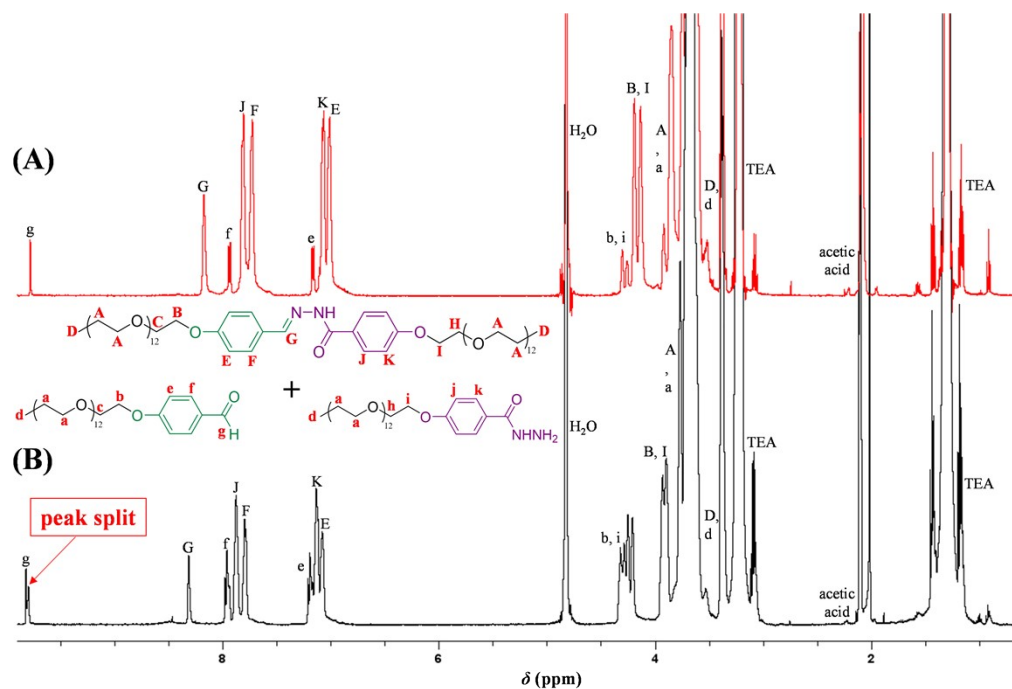


Figure S11. ^1H NMR spectra in D_2O of the linear PEG acylhydrazone adduct formed (A) after the first (one addition of DCI followed by one addition of triethylamine), and (B) after the seventh (seven alternating additions of DCI and triethylamine) reformation cycles.

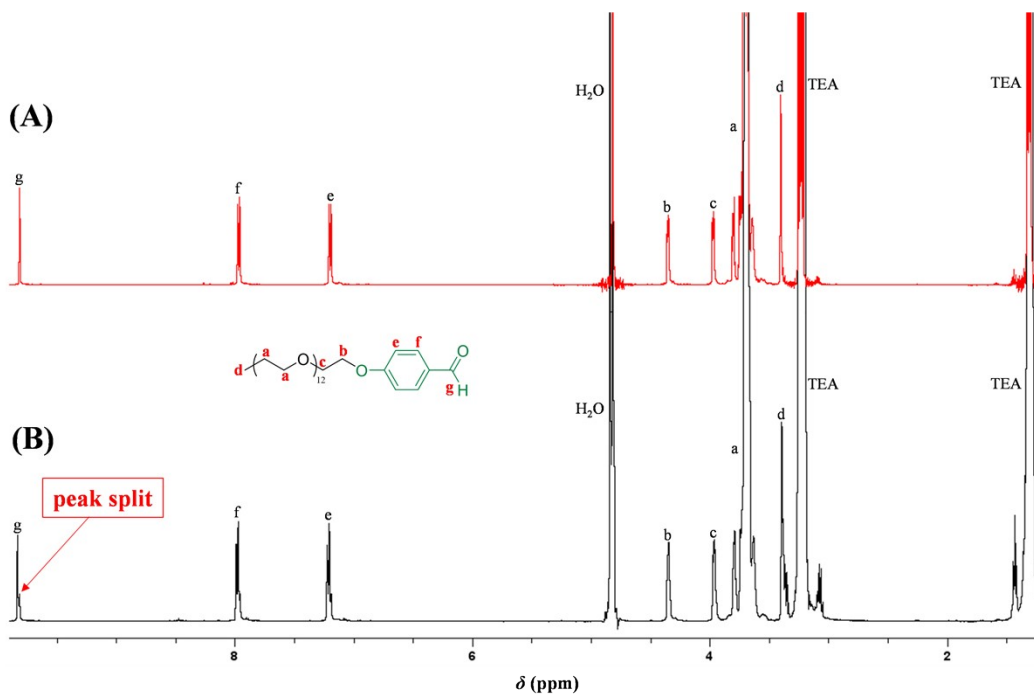


Figure S12. ^1H NMR spectra in D_2O of linear PEG-Bz (A) after one addition of DCI and one addition of triethylamine, and (B) after seven alternating additions of DCI and triethylamine.

SANS Analysis

Fits of the SANS data were performed in absolute units. The hydrophobic PPG parts of the block copolymer forming the small micelles concentrate in larger superstructures, composed of connecting PEG chains, remaining PPG, and water. Since the PPG and PEG parts of the block copolymer are all covalently bonded in a conetwork, complete phase separation is not possible. Thus, we assumed that only 55% of the total PPG is contained in the small micelles, while the rest is part of the matrix. In addition, both the PPG cores and the PEG/PPG matrix are swollen with water (ϕ_w) according to previous work on such copolymers [6,7].

To fit the peak at high q , we used a model of homogeneous spheres of radius R , described by a form factor $P(q,R)_{sph}$ (with a log-normal size distribution $L_N(R,R_m)$ to account for the polydispersity, described by the standard mean deviation σ , and centered around the mean radius R_m) that interact *via* a hard sphere potential, described by a structure factor $S(q)_{HS}$. The scattering intensity $I(q)$, the form and structure factors, as well as the other necessary quantities are defined as:

$$I(q) = {}^1NV^2\Delta SL D^2 \cdot P(q) \cdot S(q)_{HS} \quad (S1)$$

$$P(q,R)_{sph} = \left(3 \cdot \frac{\sin qR - qR \cdot \cos qR}{(qR)^3} \right)^2 \quad (S2)$$

$$\text{with: } L_N(R,R_m) = \frac{{}^1N}{R\sigma\sqrt{2\pi}} \cdot \exp\left(-\frac{(\ln(R,R_m))^2}{2\sigma^2}\right)$$

$$P(q) = \int_0^\infty L_N(R,R_m) \cdot P(q,R)_{sph} \cdot dR$$

$$S(q)_{HS} = \frac{1}{1 + 24\phi_{HS} \frac{G(\Phi_{HS},A)}{A}} \quad (S3)$$

$$G(\Phi_{HS},A) = \alpha \frac{\sin A - A \cos A}{A^2} + \beta \frac{2A \sin A - (2 - A^2) \cos A - 2}{A^3} + \gamma \frac{-A^4 \cos A + 4[(3A^2 - 6) \cos A + (A^3 - 6A) \sin A + 6]}{A^5}$$

$$A = 2R_{HS} \cdot q$$

$$\alpha = \frac{(1 + 2\Phi_{HS})^2}{(1 - \Phi_{HS})^4}; \quad \beta = -6\Phi_{HS} \frac{(1 + \Phi_{HS}/2)^2}{(1 - \Phi_{HS})^4}; \quad \gamma = \frac{\Phi_{HS} \cdot \alpha}{2}$$

where 1N is the number density of particles, V their volume, and ΔSLD is the contrast (difference in scattering length density between core and matrix). $P(q)_{sph}$ is the form factor of a homogeneous sphere, where the size is distributed with the log normal size distribution $L_N(R, R_m)$. $S(q)_{HS}$ is the hard sphere structure factor, with the hard sphere volume fraction Φ_{HS} and the hard sphere radius R_{HS} .

The aggregation number of polymer chains in the core N_{agg} was deduced from the molar mass, MM , obtained from the forward scattering intensity of the form factor:

$$MM = I(0)_{FF} \cdot \frac{\rho \cdot N_A}{\Phi \cdot \Delta SLD^2} \quad (S4)$$

The large aggregates at low q were described with the Guinier approximation:

$$I(q) = I(0) - \exp\left(-\frac{R_g^2}{3} \cdot q^2\right) \quad (S5)$$

with $I(0)$ being the forward scattering intensity, and R_g the Guinier radius. The number of micelles contained in one larger aggregate $N_{agg, mic}$ was obtained from the ratio of the two forward scattering intensities of the large aggregates and the form factor ($I(0)/I(0)_{FF}$).

Table S3. SANS analysis for the small spherical hydrophobic aggregates (micelles): percentage of water ϕ_w in the core (was kept fixed), mean radius R_m of the micelles, extrapolated intensity at $q = 0$, $I_{0,FF}$ (eliminating the structure factor $S(q)_{HS}$) aggregation number N_{agg} of T904 units, effective hard sphere radius R_{HS} , and the corresponding hard sphere volume fraction Φ_{HS} (the percentage of aggregated PPG ϕ_{PPG} was kept fixed at 55%) as obtained from modelling the SANS data of the 15% w/w sample. For the globular superstructure, radius of gyration, R_g , intensity at $q = 0$, I_0 , and aggregation number $N_{agg, mic}$ of micellar aggregates with this globular superstructure. The SLD values for the hydrated PPG micelles and PEG/PPG/D₂O matrix are also given.

T (°C)	25 (initial)	40	50
ϕ_w (fixed)	0.45	0.40	0.30
R_m (nm)	2.93	2.64	2.65
$I_{0,FF}$ (cm ⁻¹)	14.84	10.02	9.93
N_{agg}	8.6	5.8	5.7
R_{HS} (nm)	4.01	3.93	3.80
Φ_{HS}	0.217	0.316	0.310
R_g (nm)	60.0	50.0	45.7
I_0 (cm ⁻¹)	42171	26694	26364
$N_{agg, mic}$	2840	2670	2650
SLD_{mic} (nm ⁻²)	3.05×10^{-4}	2.75×10^{-4}	2.16×10^{-4}
SLD_{matrix} (nm ⁻²)	5.68×10^{-4}	5.69×10^{-4}	5.70×10^{-4}

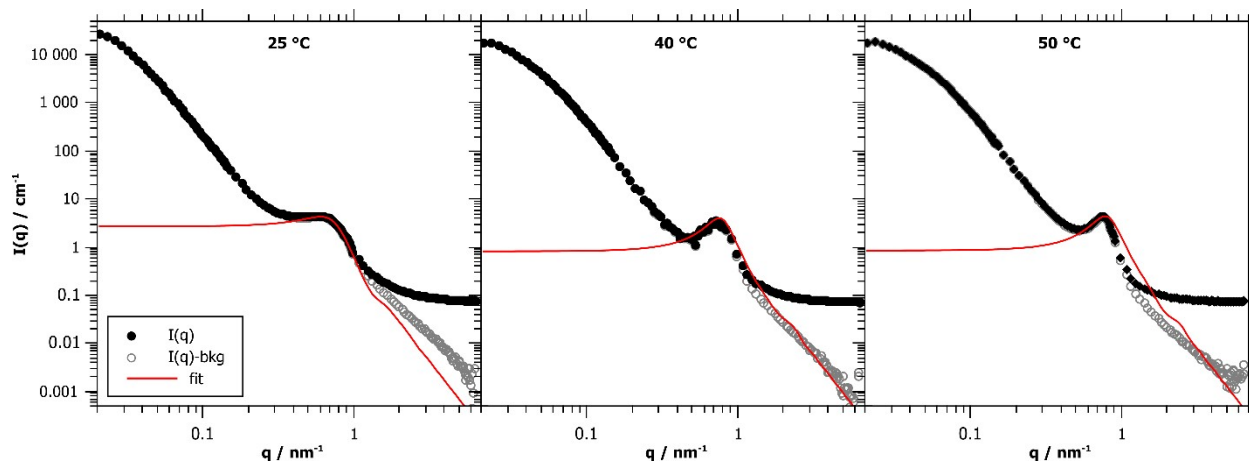


Figure S13. SANS profiles of the T904 APCNs at (from left to right) 25, 40, and 50 °C, without (closed symbols) and with subtracted background (open symbols) and the corresponding fits as solid lines (for parameters see Table S3).

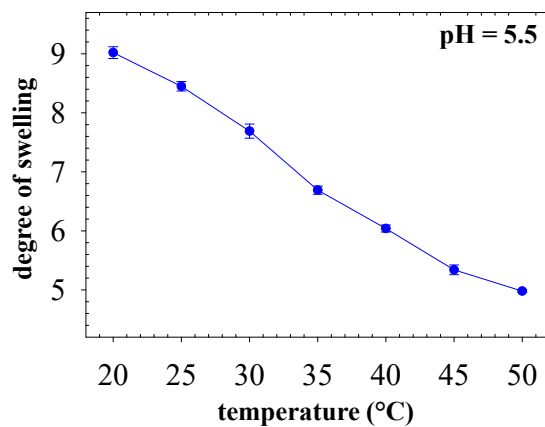


Figure S14. Temperature-dependence of the swelling degrees in a 200 mM acetate buffer of pH = 5.5 for an APCN prepared at a 15% w/v polymer concentration and also in a 200 mM acetate buffer of pH = 5.5.

References

- [1] D. E. Apostolides, T. Sakai and C. S. Patrickios, Dynamic covalent star poly(ethylene glycol) model hydrogels: A new platform for mechanically robust, multifunctional materials, *Macromolecules*, 2017, **50**, 2155–2164.
- [2] G. Deng, C. M. Tang, F. Y. Li, H. F. Jiang and Y. M. Chen, Covalent cross-linked polymer gels with reversible sol-gel transition and self-healing properties, *Macromolecules*, 2010, **43**, 1191–1194.
- [3] D. Suckau, A. Resema, M. Schuerenberg, P. Hufnagel, J. Franzen and A. A. Holle, Novel MALDI LIFT-TOF/TOF mass spectrometer for proteomics, *Anal. Bioanal. Chem.*, 2003, **376**, 952–965.
- [4] U. Keiderling and A. Wiedenmann, New SANS instrument at the BER II reactor in Berlin, Germany, *Physica B*, 1995, **213 & 214**, 895–897.
- [5] U. Keiderling, The new ‘BerSANS-PC’ software for reduction and treatment of small angle neutron scattering data, *Appl. Phys. A*, 2002, **74**, s1455–s1457.
- [6] M. Svensson, P. Alexandridis and P. Linse, Phase behavior and microstructure in binary block copolymer/selective solvent systems: Experiments and theory, *Macromolecules*, 1999, **32**, 637–645.
- [7] L. Yang, P. Alexandridis, D. C. Steytler, M. J. Kositza and J. F. Holzwarth, Small-angle neutron scattering investigation of the temperature-dependent aggregation behavior of the block copolymer Pluronic L64 in aqueous solution, *Langmuir*, 2000, **16**, 8555–8561.