Supplementary Information (SI) for Polymer Chemistry.
This journal is © The Royal Society of Chemistry 2026

Supporting Information for:

Highly swellable pH-responsive nanogels generated by polymerisation-induced self-assembly

Xueyuan Li,[† a,b] Xiaojing Lu, [† a,b] Jian Tang, [a,b] Francesca Patel-Burrows,[a,b] and Lee A. Fielding [* a,b]

a. Department of Materials, School of Natural Sciences, The University of Manchester, Oxford Road, Manchester, M13 9PL, U.K.

b. Henry Royce Institute, The University of Manchester, Oxford Road, Manchester, M13 9PL, U.K.

** Corresponding author: lee.fielding@manchester.ac.uk*

Materials and Methods

Materials

Potassium 3-sulfopropyl methacrylate (KSPMA, 98%), methacrylic acid (MAA, 99%), hydroxypropyl methacrylate (HPMA, 97%, a mixture of hydroxypropyl and hydroxyisopropyl methacrylates) and 4,4'-azobis(4-cyanovaleric acid) (ACVA, 98%) were purchased from Sigma-Aldrich (UK) and used as received. 2-hydroxyisopropyl methacrylate (isoHPMA, 98%) was obtained from Alfa Aesar. 1,4-dioxane (99%) was purchased from Honeywell (UK) and used as received. 4-((((2-carboxyethyl)thio)carbonothioyl)thio)-4-cyanopentanoic acid (CCCP, 95%) was supplied by Boron Molecular. Deuterium oxide (D_2O) for NMR characterisation was obtained from Cambridge Isotope Laboratories (UK). Dialysis tubing (regenerated cellulose, MWCO = 3.5 kDa, diameter = 29 mm) was received from Fisher Scientific (UK). Deionised (DI) water was obtained from a Fusion 320 purification system (Suez).

Synthesis of PKSPMA

The polymerisation of KSPMA was conducted using protocols related to those previously reported[1, 2] (**Figure 1a**). In a typical synthesis, KSPMA (5.37 g, 21.25 mmol), ACVA (24.6 mg, 0.09 mmol) and CCCP (135 mg, 0.46 mmol) were dissolved in a co-solvent comprised of water (16.47 g) and 1,4-dioxane (5.43 g). The resulting solution was degassed by purging with nitrogen for 20 minutes and subsequently immersed into a preheated oil bath at 70 ℃ for 100 minutes. During the polymerisation, aliquots were sampled at 10, 20, 30, 40, 60, 80 and 100 minutes for kinetic analysis. The reaction was then quenched in an ice bath. The final degree of polymerisation was determined by ^{1}H NMR as 44 ($PKSPMA_{44}$), using conversion analysis; and the molar mass distribution was characterised by gel permeation chromatography (GPC), M_n = 12,500 g mol^{-1} and M_w/M_n = 1.10.

Synthesis of $PKSPMA_{44}$-$P(HPMA_{1-x\%}$-$MAA_{x\%})_{300}$

The synthesis of $PKSPMA_{44}$-$P(HPMA_{1-x\%}$-$MAA_{x\%})_{300}$, where x represents a fraction between 0 and 1, was carried out in water (**Figure 1b**). A typical dispersion polymerisation of $PKSPMA_{44}$-$P(HPMA_{95\%}$-$MAA_{5\%})_{300}$ employing a (HPMA + MAA): $PKSPMA_{44}$: ACVA molar ratio of 300 : 1 : 0.2 at 10% w/w, was performed as follows. HPMA (754 mg, 5.23 mmol), MAA (27 mg, 0.31 mmol), $PKSPMA_{44}$ macro-CTA (225.9 mg, 18 µmol), ACVA (1.0 mg, 3.6 µmol) were weighted in a 14 mL vial. Deionised water (9 mL) was then added to dissolve the solids, and the resulting solution was purged with nitrogen for 15 minutes prior to being immersed in a preheated oil bath at 70 ℃. The polymerisation was allowed to proceed for 24 hours and was subsequently terminated by exposure to air.

Proton nuclear magnetic resonance (^{1}H NMR) spectroscopy. ^{1}H NMR spectra of PKSPMA samples were recorded on Bruker Advance III HD 500 MHz spectrometer with 128 scans averaged per spectrum at 25 ℃. Samples were dissolved in D_2O prior to ^{1}H NMR analysis.

Gel permeation chromatography (GPC). Molar mass distributions were determined using an Agilent Technologies 1260 Infinity II GPC system equipped with a refractive index detector and two PLAquagel OH Mixed M columns. Aqueous GPC measurements were conducted using phosphate buffer eluent (pH 9) containing 30% v/v methanol. The system was calibrated with polyethylene oxide standards. Samples were prepared as 5 mg/mL solutions in the phosphate buffer eluent at pH 9 prior to analysis.

Dynamic light scattering (DLS) and aqueous electrophoresis. Hydrodynamic diameters (D_h) and zeta potentials were determined using a Malvern Zetasiser Ultra instrument. The instrument was equipped with a 623.8 nm laser, detecting back-scattered light at a scattering angle of 173°. All dispersions were diluted to 0.1% w/w in deionised water prior to analysis. pH was adjusted between 4 and 10 using 0.025 M HCl and 0.025M KOH. Each measurement was performed in triplicate to minimise experimental error. Thermo-responsive behaviour was investigated by measuring the samples at pH 4 and 8 over a range of temperatures. The temperature was increased from 1 °C to 45 °C and subsequently decreased from 45 °C to 1 °C in 5 °C intervals. Measurements were repeated and averaged over three consecutive runs under identical conditions.

Transmission electron microscopy (TEM). TEM images were captured using a FEI Tecnai G2 20 instrument operating at 200 kV and equipped with a Gatan 1k CCD camera. Samples were diluted to 0.1% w/w, and 3 µL of the resulting dispersions were drop-cast onto 400-mesh plasma pre-treated carbon-coated grids (Agar scientific) and allowed to dry overnight at room temperature. The dried TEM grids were subsequently placed on 40 µL uranyl acetate (UA) solution droplets for 1 minute. Excess UA solution was subsequently carefully removed by blotting with clean filter paper.

Supporting data

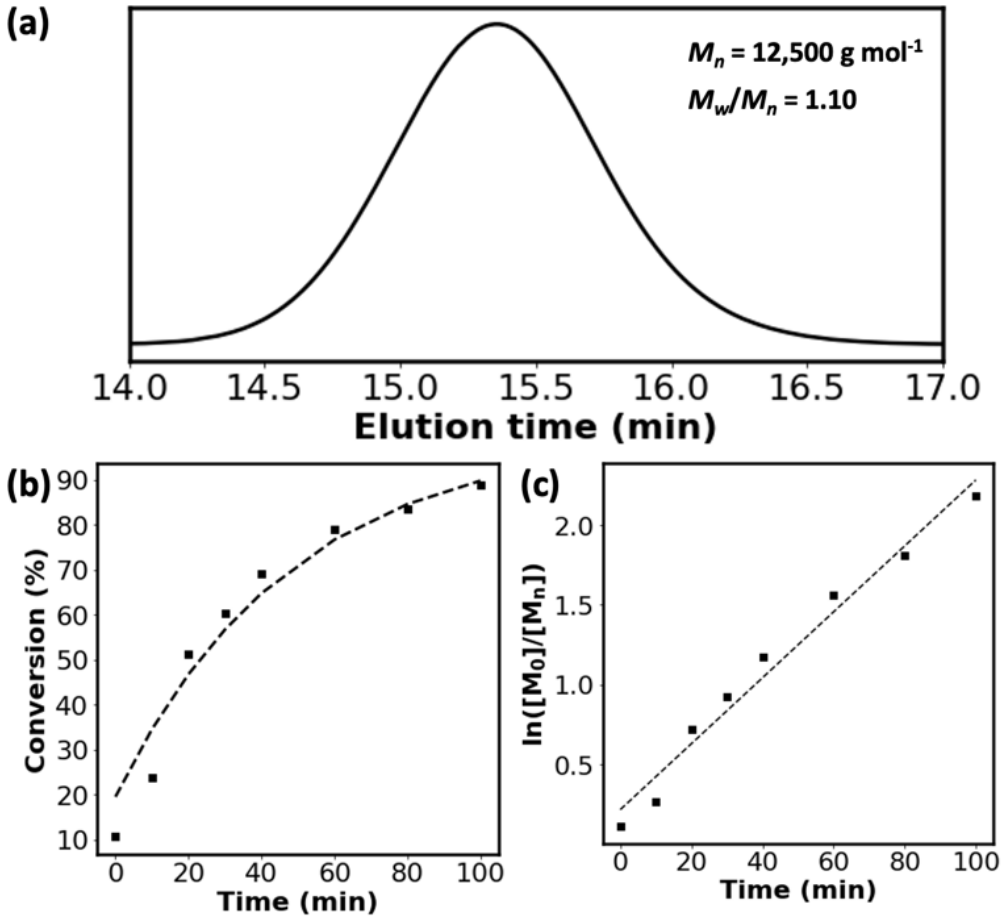

Figure S1. a) GPC trace of PKSPMA$_{44}$ macro-CTA. b) Monomer conversion and (c) ln([M_0]/[M_n]) as a function of time during the RAFT solution polymerisation of KSPMA.

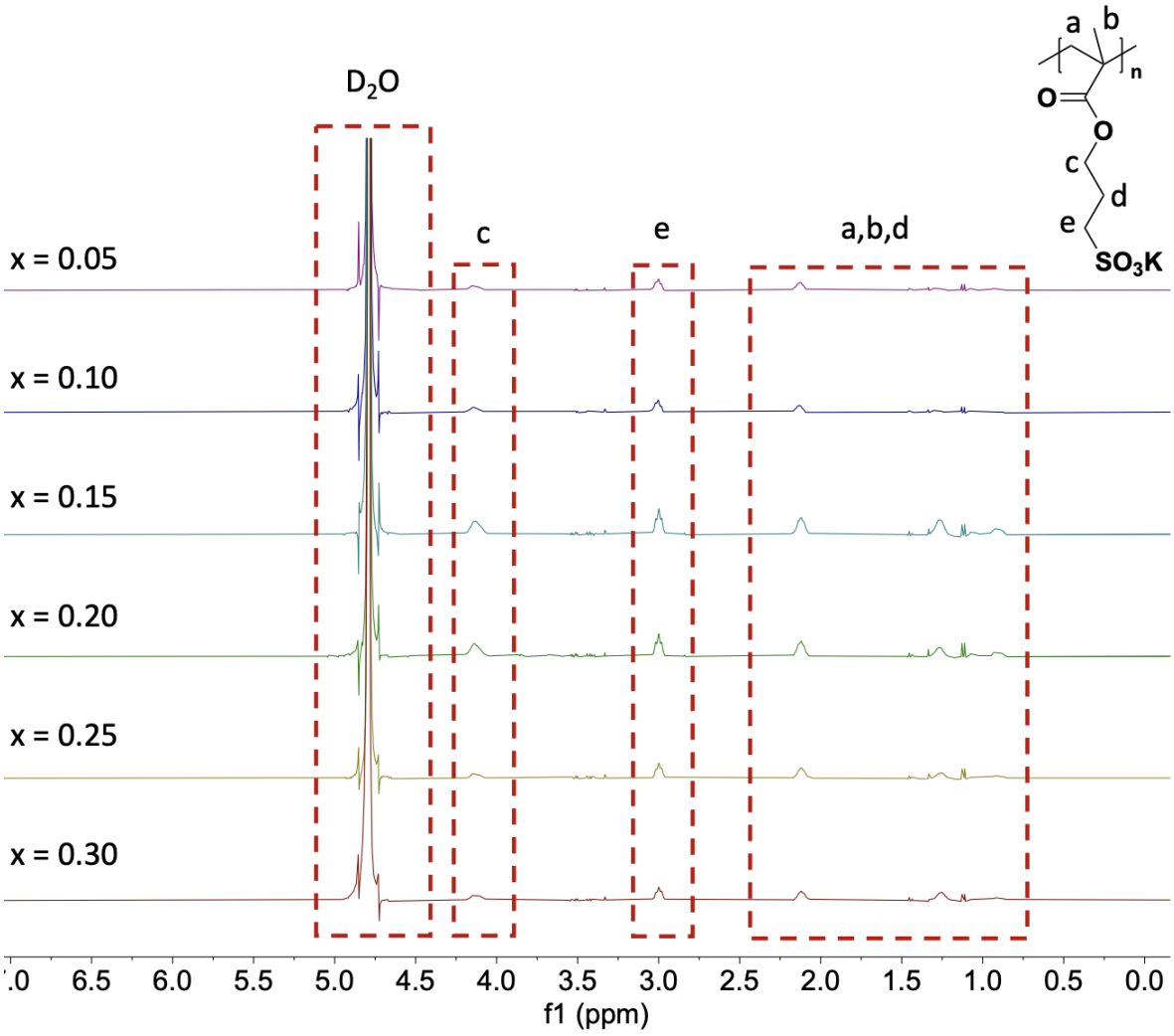

Figure S2. ^{1}H NMR spectra of PKSPMA$_{44}$-P(HPMA$_{1-x}$-MAA$_{x}$)$_{340}$ copolymers with varying MAA content (from x = 5% to 30%, top to bottom traces).

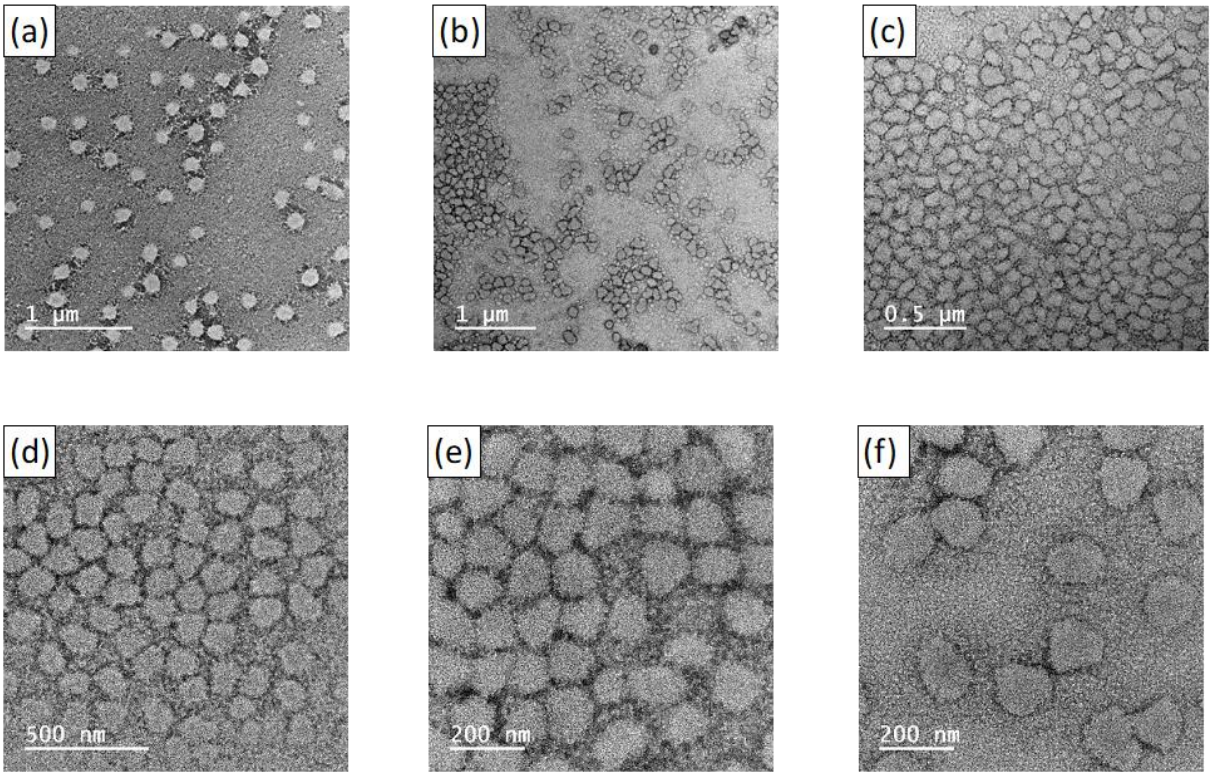

Figure S3. TEM images of PKSPMA$_{44}$-P(HPMA$_{75\%}$-MAA$_{25\%}$)$_{340}$, dried from dispersions at pH4.

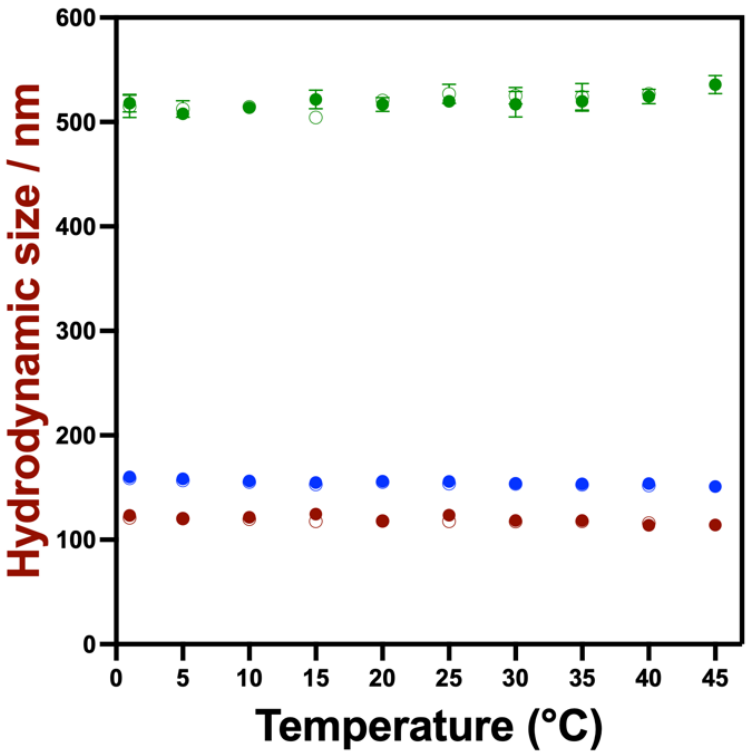

Figure S4. Particle size of S_{44}-(isoH$_{75\%}$-A$_{25\%}$)$_{300}$ at pH4 (blue) and pH8 (green), and S_{44}-(H$_{75\%}$-A$_{25\%}$)$_{300}$ at pH4 (red) as the temperature was increased from 1 °C to 45°C (solid circles), and then decreased to 1 °C (hollow circles), in 5 °C intervals.

Table S1. Hydrodynamic diameters (D_h) of PKSPMA$_{44}$-*b*-P(HPMA$_{1-x\%}$-*stat*-MAA$_{x\%}$)$_{300}$ nanogels at pH 4 and pH 8 with varying compositions, and their corresponding swelling ratios.

Sample	At pH4		At pH8		Swelling Ratio
	D_h (nm) *	PDI	D_h (nm) *	PDI	
S_{44}-H$_{300}$	205	0.006	224**	0.069**	1.1
S_{44}-(H$_{95\%}$-A$_{5\%}$)$_{300}$	204	0.013	424	0.098	2.1
S_{44}-(H$_{90\%}$-A$_{10\%}$)$_{300}$	147	0.136	374	0.166	2.6
S_{44}-(H$_{85\%}$-A$_{15\%}$)$_{300}$	185	0.022	540	0.030	2.9
S_{44}-(H$_{80\%}$-A$_{20\%}$)$_{300}$	168	0.088	530	0.123	3.2
S_{44}-(H$_{75\%}$-A$_{25\%}$)$_{300}$	152	0.019	653	0.178	4.3
S_{44}-(H$_{70\%}$-A$_{30\%}$)$_{300}$	123	0.051	447	0.151	3.6

*Obtained by DLS measurements at 25 °C.

**Measured at pH7

References

1. M. Semsarilar, V. Ladmiral, A. Blanazs and S. P. Armes, *Langmuir*, 2012, **28**, 914-922.
2. S.-P. Wen, J. G. Saunders and L. A. Fielding, *Polymer Chemistry*, 2020, **11**, 3416-3426.