

Supporting information

Polymerisation of 2-acrylamido-2-methylpropane sulfonic acid sodium salt (NaAMPS) and acryloyl phosphatidylcholine (APC) via aqueous Cu(0)-mediated radical polymerisation

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Materials

All chemicals were purchased from Sigma-Aldrich or Fischer Scientific unless otherwise stated. The water soluble initiator 2,3-dihydroxypropyl 2-bromo-2-methylpropanoate, and PEG-macroinitiator were prepared as reported in the literature.^{1, 2} Tris(2-(dimethylamino)ethyl)amine (Me₆TREN) was synthesized according to literature procedures and stored under nitrogen prior to use.³ Copper (I) bromide (CuBr), was sequentially washed with acetic acid and ethanol and dried under vacuum.

Instruments and analysis

¹H NMR spectra were recorded on Bruker DPX-300 and DPX-400 spectrometers using deuterated solvents (D₂O) obtained from Aldrich. Aqueous SEC traces were obtained on a PL-GPC50 system using a buffer (0.1M NaNO₃, pH 7.4) eluent at 30°C, equipped with a

refractive index detector, two PLaquagel-OH 30 (300×7.5 mm), PLaquagel guard (50×7.5 mm) and autosampler. Narrow linear poly(ethylene oxide) and poly(methacrylic acid) standards in range of 200 to 1.3×10^5 g.mol⁻¹ were used to calibrate the system. All samples were passed through 0.22µm PTFE filter before analysis.

General procedure for aqueous SET-LRP

To a Schlenk tube fitted with a magnetic stirring bar and a rubber septum, H₂O (2 mL) and Me₆-Tren (0.4 equiv.) were added and the mixture was bubbled with nitrogen for 15 min. CuBr (0.4 equiv.) was then carefully added under slight positive pressure of nitrogen. The mixture immediately became blue ([Cu(Me₆-Tren)]Br₂) and a precipitation (Cu(0)) was observed. A separate vial fitted with a rubber septum and magnetic stirring bar was charged with initiator (1 equiv.), monomer (*DP* equiv.) and H₂O (2 mL). The mixture was left to stir until complete dissolution of the monomer was obtained prior to deoxygenation by nitrogen sparging for 10 minutes. The solution was then cannulated into the Schlenk tube and the reaction was left to proceed at 0°C.

General procedure for chain extension/copolymerisation by aqueous SET-LRP

General procedure for homopolymerisation following using the appropriate [M] : [I] : [CuBr] : [Me₆-Tren] ratio. Homopolymerisations allowed to reach near quantitative conversion prior to addition of a degassed aliquot of the chosen monomer (*DP*, equiv.), in H₂O (50 wt%) *via* a nitrogen-purged syringe. The resulting solution was stirred at 0°C and progress was followed intermittent sampling with analysis by ¹H NMR and SEC .

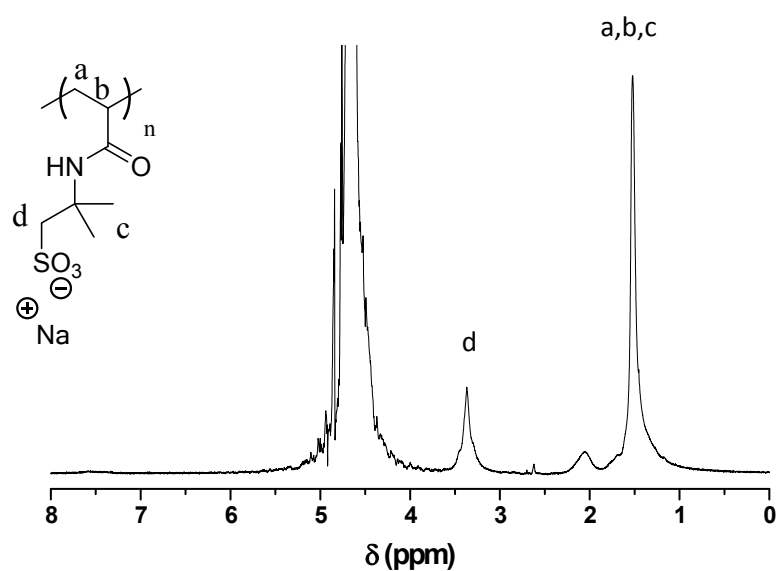


Figure S1: ^1H NMR (D_2O) spectrum of PNaAMPS_{20} utilising aqueous SET-LRP. Initial conditions: $[\text{NaAMPS}]:[\text{I}]:[\text{CuBr}]:[\text{Me}_6\text{-Tren}] = [20]:[1]:[0.4]:[0.4]$ in 4 mL H_2O at 0°C .

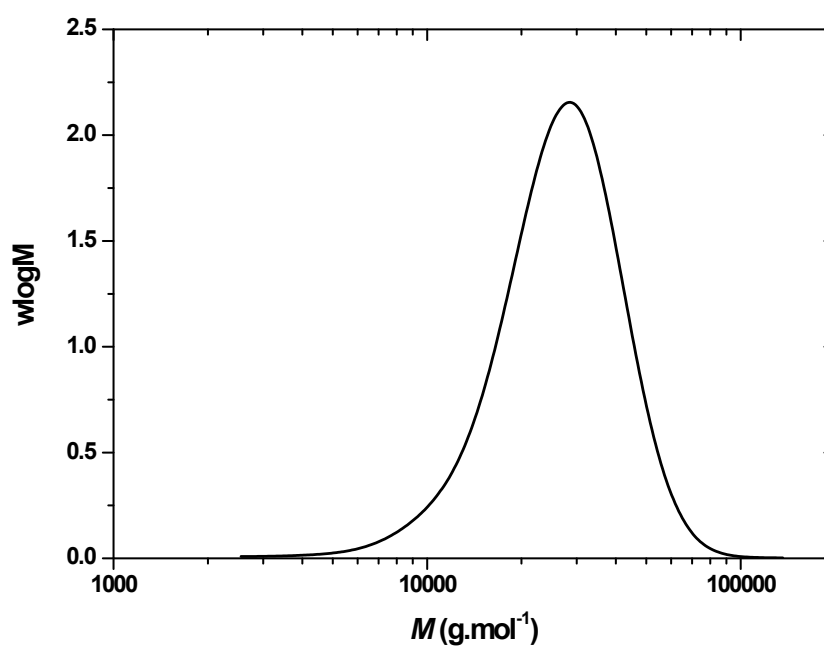


Figure S2: Aqueous SEC analysis for the synthesis of PNaAMPS_{40} utilising aqueous SET-LRP. Initial conditions: $[\text{NaAMPS}]:[\text{I}]:[\text{CuBr}]:[\text{Me}_6\text{-Tren}] = [40]:[1]:[0.4]:[0.4]$ in 4 mL H_2O at 0°C .

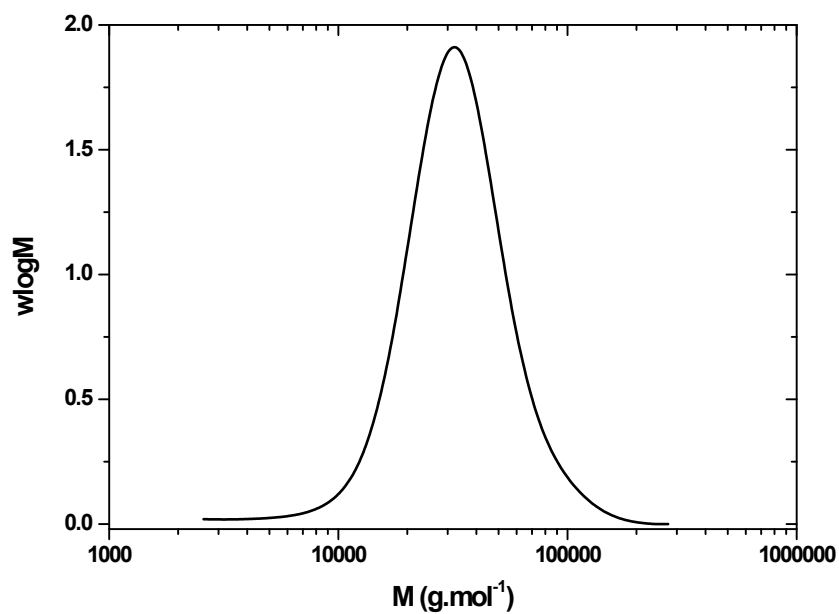


Figure S3: Aqueous SEC analysis for the synthesis of PNaAMPS₈₀ utilising aqueous SET-LRP. Initial conditions: [NaAMPS]:[I]:[CuBr]:[Me₆-Tren] = [80]:[1]:[0.8]:[0.4] in 4 mL H₂O at 0°C.

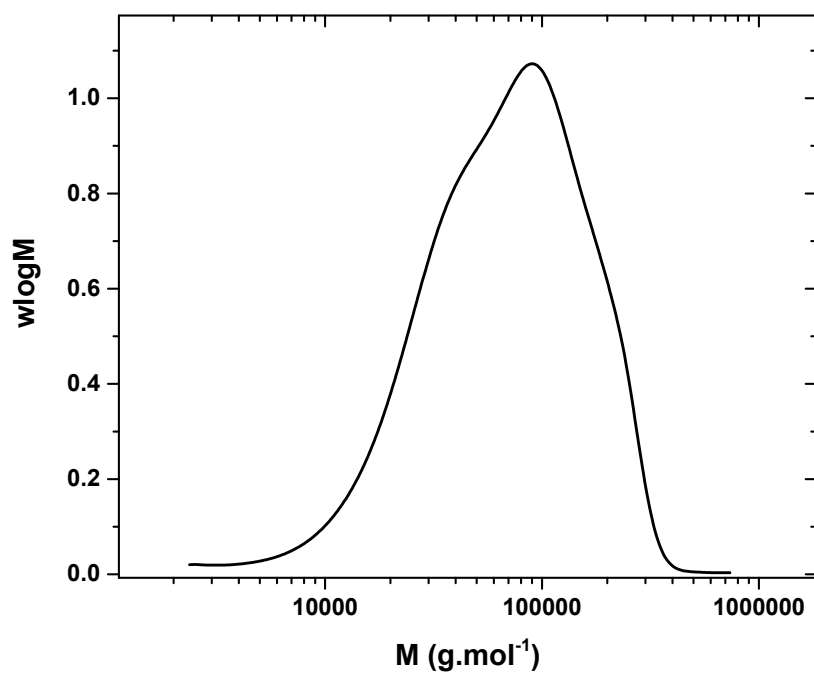


Figure S4: Aqueous SEC analysis for the synthesis of PNaAMPS₁₆₀ utilising aqueous SET-LRP. Initial conditions: [NaAMPS]:[I]:[CuBr]:[Me₆-Tren] = [160]:[1]:[0.8]:[0.4] in 4 mL H₂O at 0°C.

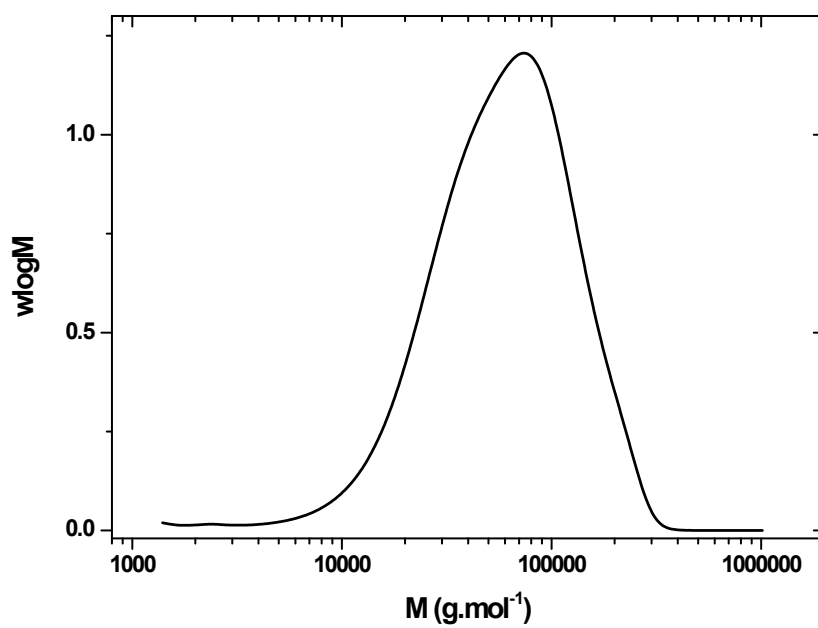
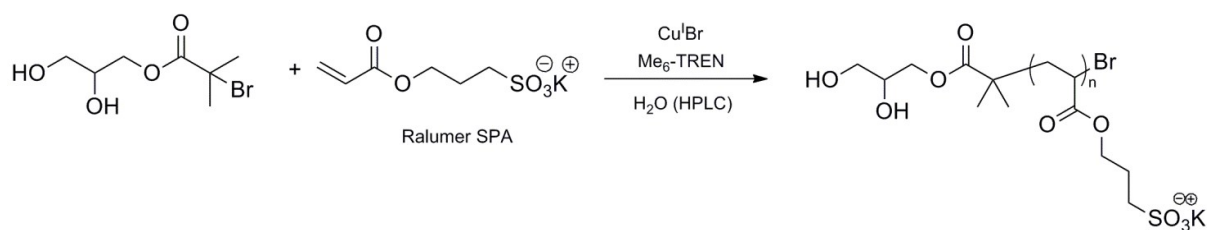


Figure S5: Aqueous SEC analysis for the synthesis of PNaAMPS₁₆₀ utilising aqueous SET-LRP. Initial conditions: [NaAMPS]:[I]:[CuBr]:[Me₆-Tren] = [160]:[1]:[1.6]:[1] in 4 mL H₂O at 0°C.

Table S1. Polymerisation of KSPA by aqueous SET-LRP



$\text{DP}_{n,\text{th}}$	T (°C)	Ratio (Cu-L)	Time	Conversion	$^*\text{D}$	$^*M_{n,\text{th}}$ (g.mol ⁻¹)	$^{**}M_{n,\text{NMR}}$ (g.mol ⁻¹)	$^*M_{n,\text{SEC}}$ (g.mol ⁻¹)
20	25	0.4-0.4	30min	Full	1.22	4900	5100	6600
40	25	0.4-0.4	30min	Full	1.18	9500	10500	9700
80	0	0.6-0.4	30min	Full	1.31	18800	16700	14700
160	0	0.6-0.4	1h	97%	1.47	37400	27900	22700
320	0	0.6-0.6	3h	97%	1.84	74600	75000	39700

* Determined by aqueous SEC

** Determined by ^1H NMR in D_2O

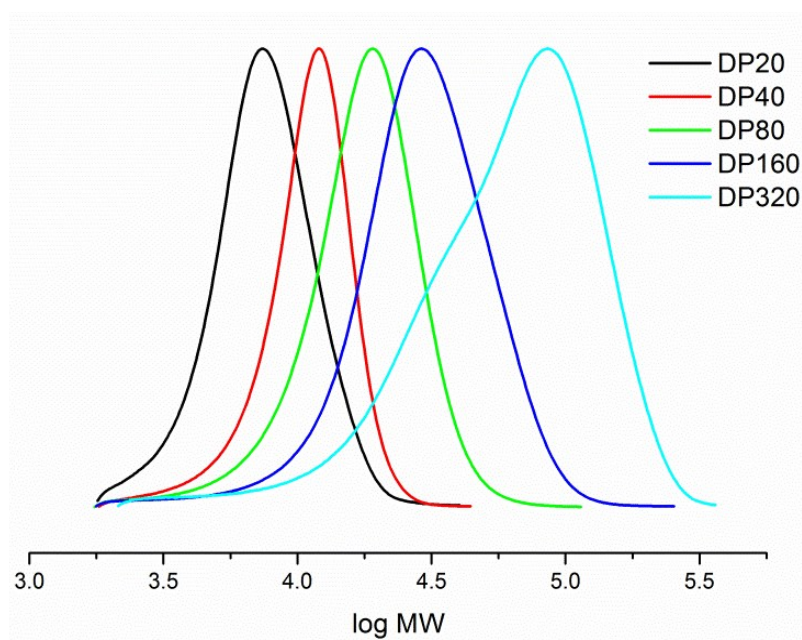


Figure S6: Aqueous SEC analysis for the synthesis of PKSPA utilising aqueous SET-LRP.

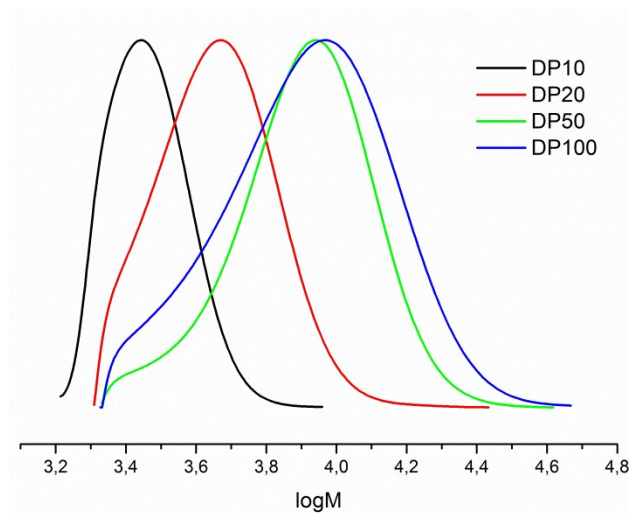
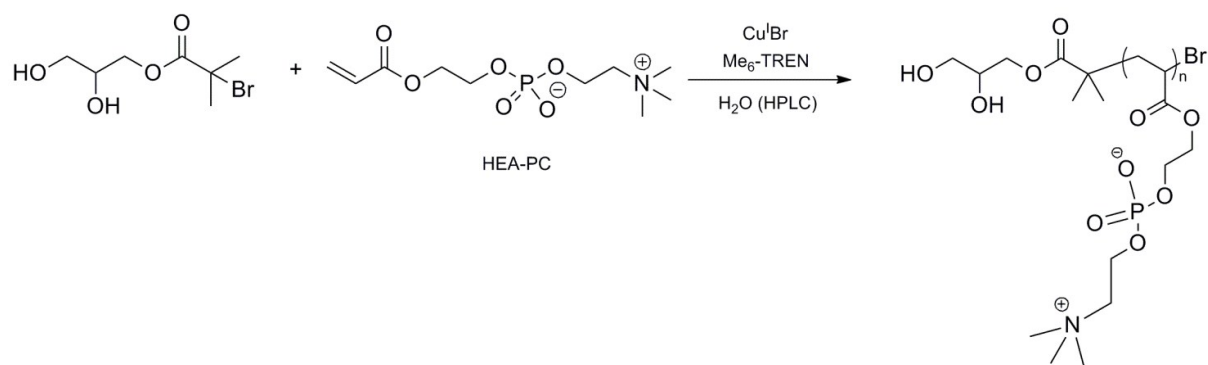


Figure S7: Aqueous SEC analysis for the synthesis of PAPC utilising aqueous SET-LRP.

Table S2. Synthesis of NaAMPS containing block copolymers by aqueous SET-LRP.

	Cycle	Time (min)	Conversion (%)	*M_n (g.mol ⁻¹)	*D
<i>In situ</i> Chain Extension	AMPS	30	> 99	11600	1.21
	AMPS	30	> 99	18000	1.21
Block (co)polymerisations	PEGA	30	100	5800	1.24
	AMPS	30	100	14100	1.30
	HEAm	30	100	2500	1.29
	AMPS	30	100	14000	1.15
	AMPS	30	100	11000	1.17
	NIPAm	30	100	-	-

* Determined by aqueous SEC

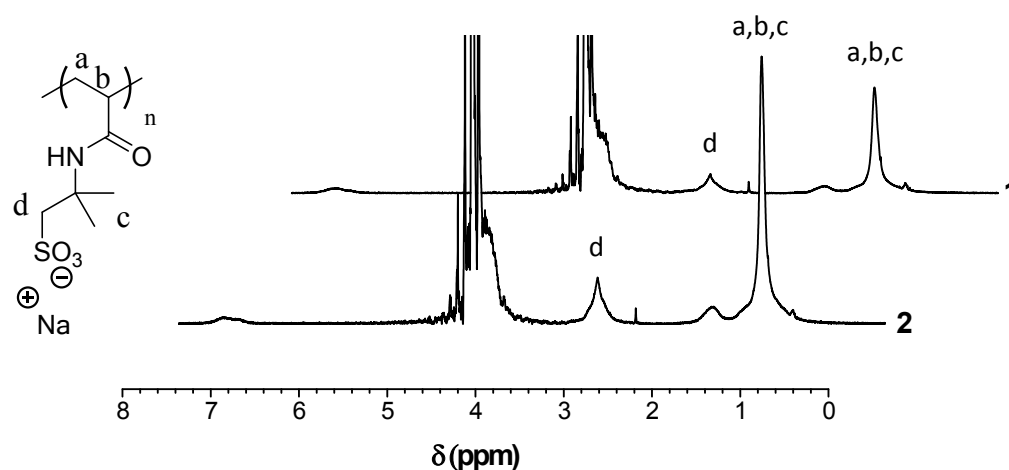


Figure S8: ¹H NMR analysis for the *in situ* chain extension from a PNaAMPS₂₀ macroinitiator utilising aqueous SET-LRP. Initial conditions: [NaAMPS]:[I]:[CuBr]:[Me₆-Tren] = [20]:[1]:[0.4]:[0.4]. Chain extension achieved upon addition of an aliquot of NaAMPS (20 equiv.) in H₂O (2 mL).

Table S3. Synthesis and chain extension of PAPC pseudo block copolymers by aqueous SET-LRP.

$DP_{n,th}$	T (°C)	Ratio (Cu-L)	Time	Conv.	*D	$M_{n,th}$ (g.mol ⁻¹)	$^{**}M_{n,NMR}$ (g.mol ⁻¹)	$^*M_{nSEC}$ (g.mol ⁻¹)
10	0	0.6-0.8	30min	92 %	1.16	3100	3100	2600
10+10	0	0.6-0.8	1h30	Full	1.14	5900	5900	4400
10+10+10	0	0.6-0.8	3h30	Full	1.23	8700	10400	5400
10+10+10+10	0	0.6-0.8	22h30	76 %	1.15	11500	14000	5800

* Determined by aqueous SEC

** Determined by ¹H NMR in D₂O

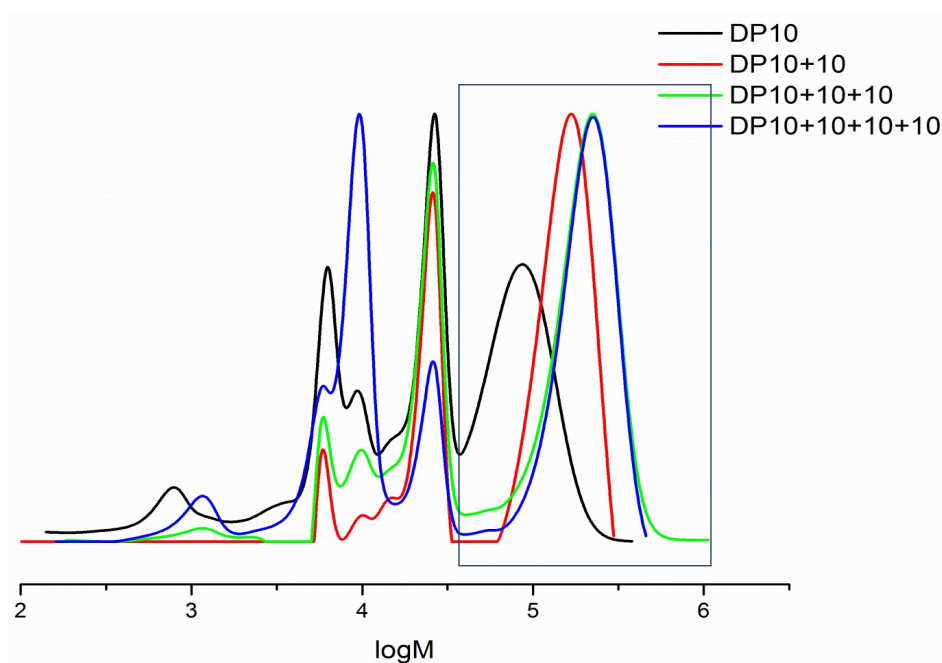


Figure S9: Aqueous SEC analysis for the synthesis and chain extension of PAPC pseudo block copolymer utilising aqueous SET-LRP. Numbers reported come from analysis of the peaks in the box. The low molecular weights peaks did not coincide with the monomer and have been assigned as unidentified impurities/system peaks.

Table S4. Synthesis PEG-*b*-NaAMPS copolymers by aqueous SET-LRP.

DP	Cu:L	* $M_{n,NMR}$ (g/mol)	** $M_{n,SEC}$ (g/mol)	$M_{n,th}$ (g/mol)	** \mathcal{D}	Conversion (%)
25	0.8:0.4	8000	8700	7800	1.21	>99
50	0.8:0.4	13500	17000	13600	1.34	>99
100	0.8:0.4	33000	23400	25000	1.88	>99

* Determined by ^1H NMR in D_2O

** Determined by aqueous SEC

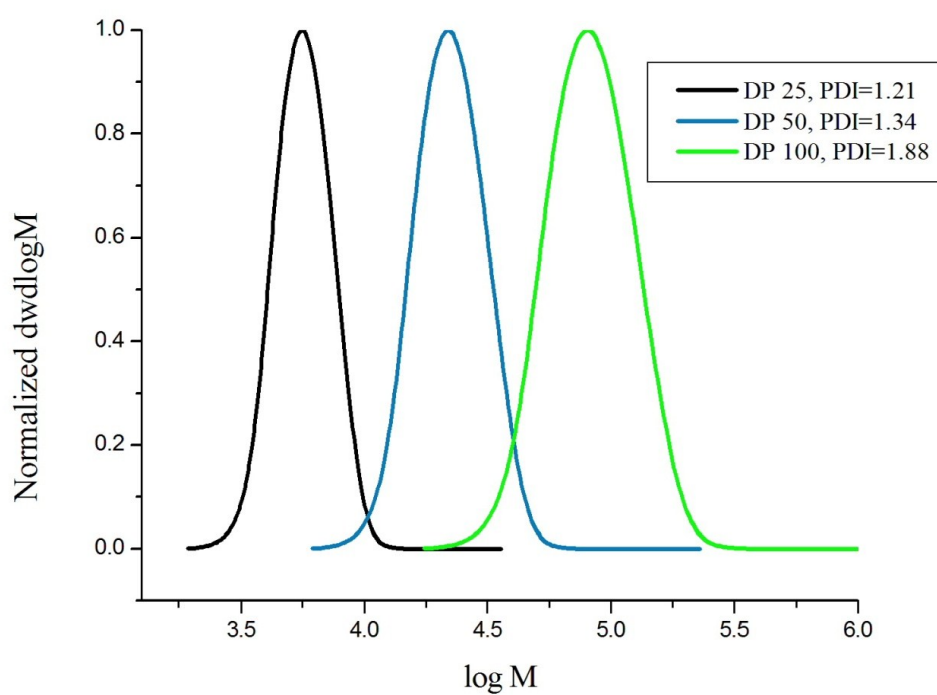


Figure S10: Aqueous SEC analysis for the synthesis of PEG-*b*-NaAMPS copolymer by aqueous SET-LRP.

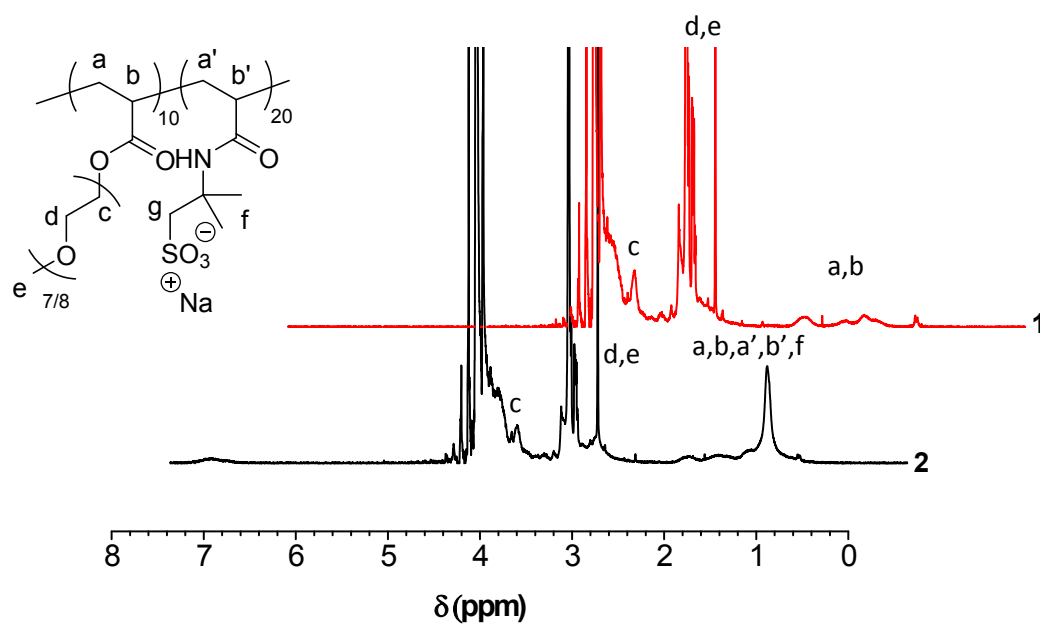


Figure S11: ^1H NMR analysis for the *in situ* chain extension from a PPEGA₁₀ macroinitiator utilising aqueous SET-LRP. Initial conditions: [PEGA]:[I]:[CuBr]:[Me₆-Tren] = [10]:[1]:[0.4]:[0.4]. Chain extension achieved upon addition of an aliquot of NaAMPS (20 equiv.) in H₂O (2 mL).

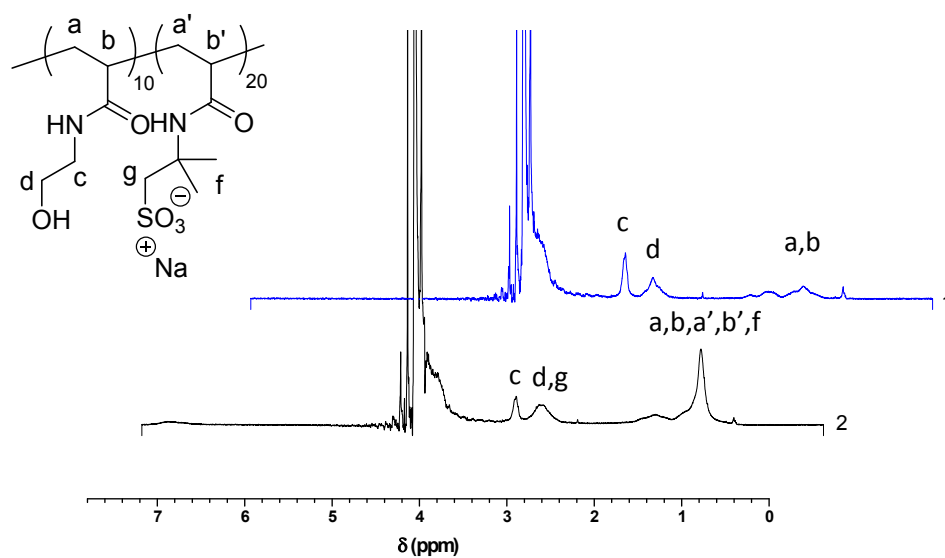


Figure S12: ^1H NMR analysis for the *in situ* chain extension from a PHEAm₂₀ macroinitiator utilising aqueous SET-LRP. Initial conditions: [HEAm]:[I]:[CuBr]:[Me₆-Tren] = [20]:[1]:[0.4]:[0.4]. Chain extension achieved upon addition of an aliquot of NaAMPS (20 equiv.) in H₂O (2 mL).

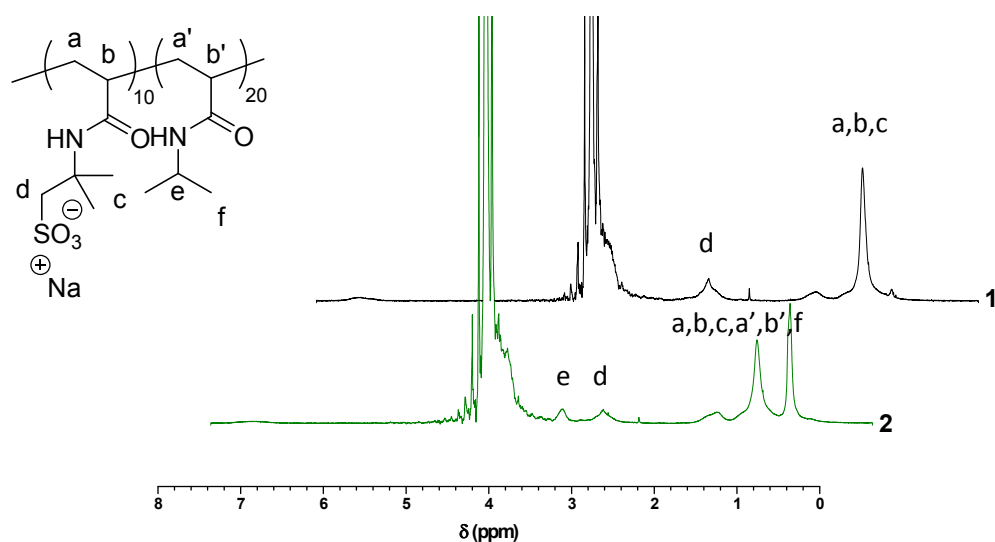


Figure S13: ^1H NMR analysis for the *in situ* block copolymerisation from a PNaAMPS_{20} macroinitiator utilising aqueous SET-LRP. Initial conditions: $[\text{NaAMPS}]:[\text{I}]:[\text{CuBr}]:[\text{Me}_6\text{-Tren}] = [20]:[1]:[0.4]:[0.4]$. Chain extension achieved upon addition of an aliquot of NIPAm (20 equiv.) in H_2O (2 mL).

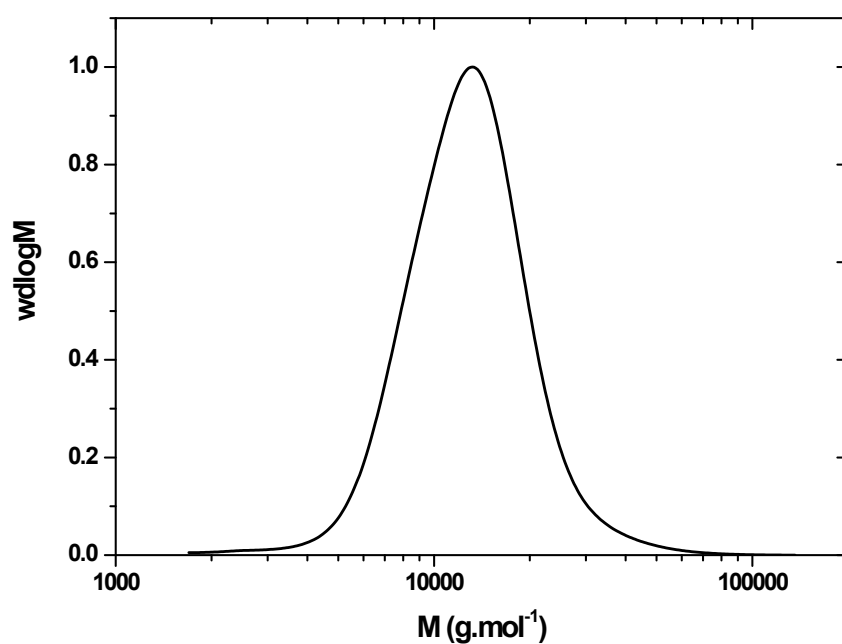


Figure S14: SEC analysis for the PNaAMPS_{20} macroinitiator utilising aqueous SET-LRP. Initial conditions: $[\text{NaAMPS}]:[\text{I}]:[\text{CuBr}]:[\text{Me}_6\text{-Tren}] = [20]:[1]:[0.4]:[0.4]$.

Table S5. Synthesis of P(APC)₁₀-*b*-(NIPAm)₈₀ by aqueous SET-LRP.

DP _{n,th}	T (°C)	Ratio (Cu-L)	Time	Conv.	*D	M _{n,th} (g.mol ⁻¹)	**M _{n,NMR} (g.mol ⁻¹)	*M _{nSEC} (g.mol ⁻¹)
10	0	0.8-0.6	1h	97 %	*	3100	3100(10)	*
10+80	0	0.8-0.6	5h	96 %	*	12100	-	*

* Determined by aqueous SEC

** Determined by ¹H NMR in D₂O

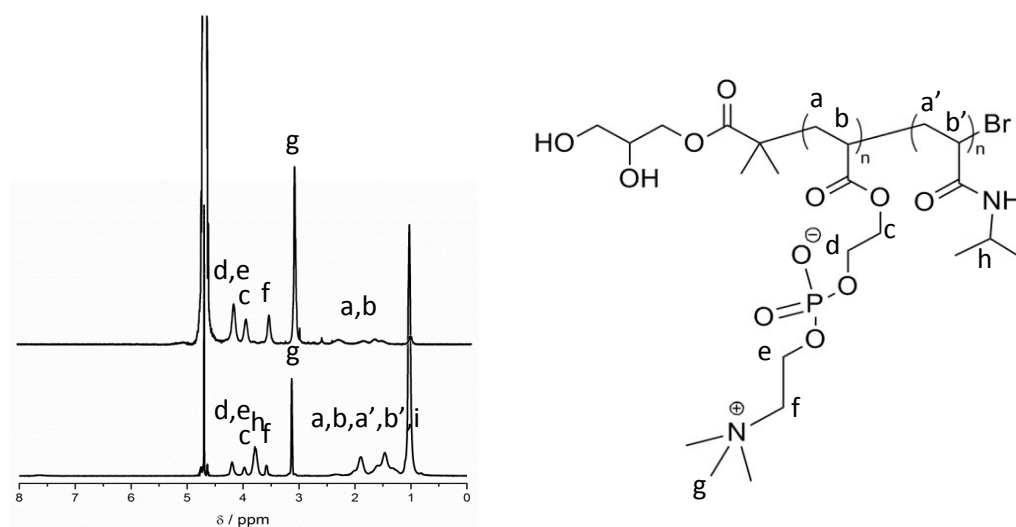


Figure S15: ¹H NMR analysis for the *in situ* block copolymerisation from a PAPC macroinitiator utilising aqueous SET-LRP. Initial conditions: [APC]:[I]:[CuBr]:[Me₆-Tren] = [10]:[1]:[0.4]:[0.4]. Copolymerisation achieved upon addition of an aliquot of NIPAm (80 equiv.) in H₂O (2 mL).

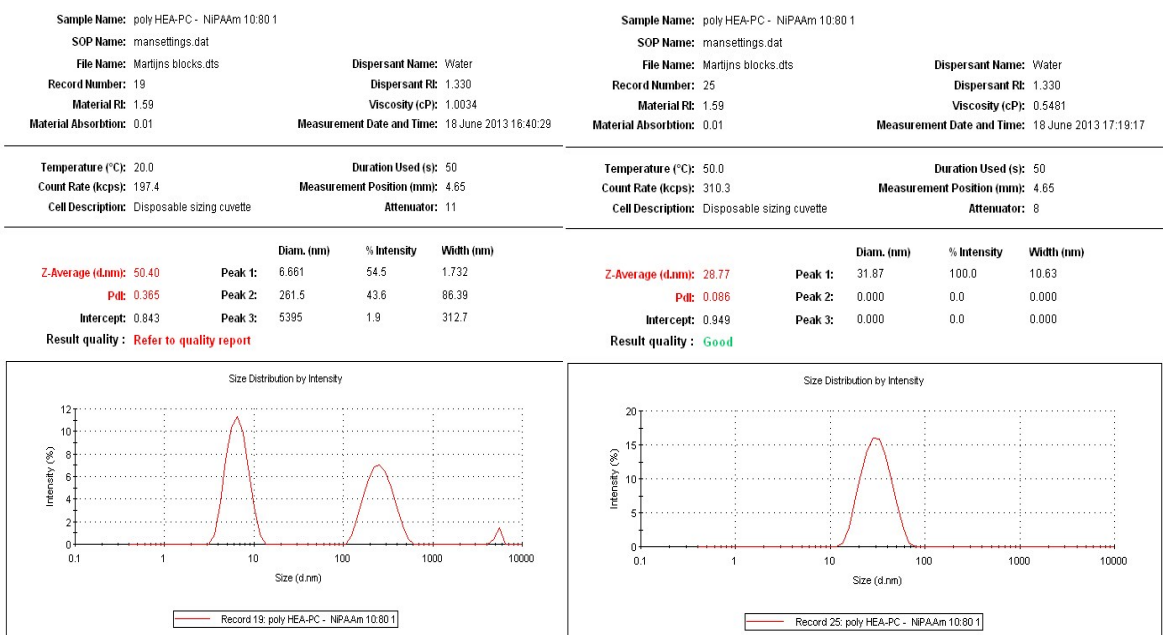


Figure S16: DLS data for P(APC)₁₀-*b*-(NIPAm)₈₀ in pure water at 20 °C (left) and above the LCST at 50 °C (right) showing temperature dependent transition to well defined nanoparticles.

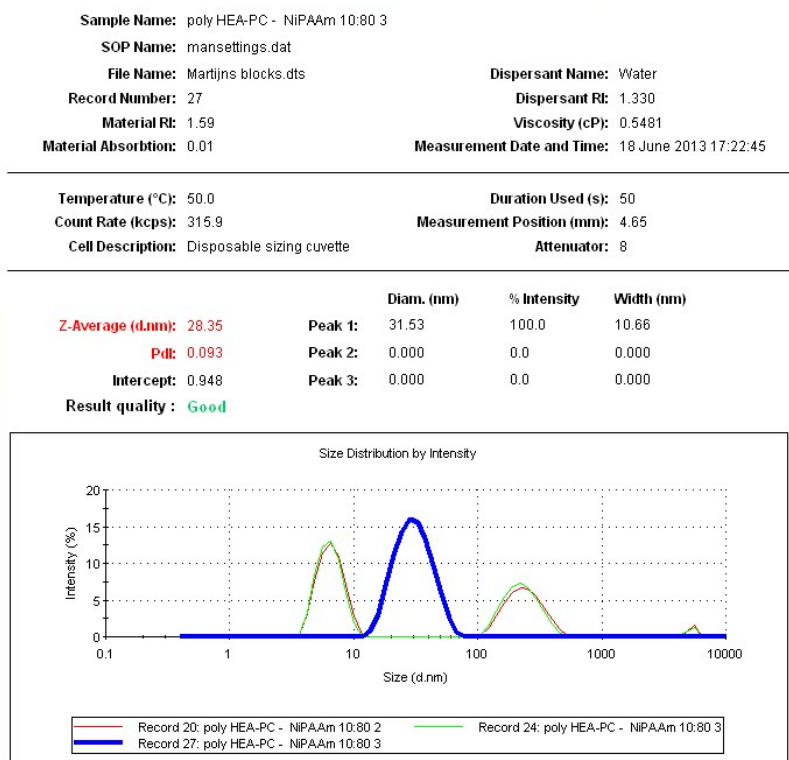


Figure S17: DLS data for heating-cooling cycles of the P(APC)₁₀-*b*-(NIPAm)₈₀ in pure water.

References

1. S. Perrier, S. P. Armes, X. S. Wang, F. Malet and D. M. Haddleton, *Journal of Polymer Science Part A: Polymer Chemistry*, 2001, **39**, 1696-1707.
2. S. Perrier and D. M. Haddleton, *European Polymer Journal*, 2004, **40**, 2277-2286.
3. M. Ciampolini and N. Nardi, *Inorganic Chemistry*, 1966, **5**, 41-44.