Supporting Information

Reversible Morphological Switching of Nanostructures in Solution

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Materials

AIBN (2,2'-Azo*bis*(2-methylpropionitrile)) was recrystallized from a 9:1 mixture of hexanes/acetone and stored in the dark at 4 °C. Methyl acrylate (MA) was purified *via* vacuum distillation over CaH_2 and then stored at 4 °C. *N-iso*-propyl acrylamide (NIPAM) was recrystallized from a 9:1 mixture of hexanes/acetone and stored at 4 °C. RAFT CTA, **1** was prepared as reported by the authors previously.[1] All other materials were used as received from Sigma-Aldrich Co. Tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF), dichloromethane (DCM), ethyl acetate and hexanes were used as received from Fisher Scientific unless otherwise stated. When used, dry solvents were collected and used directly from an in house drying and degassing solvent tower delivery system.

Instrumentation

^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker DPX-400 spectrometer respectively in $CDCl_3$ unless otherwise stated. Chemical shifts are reported in ppm (δ) relative to $CHCl_3$ (7.26 ppm for ^{1}H and 77.2 ppm for ^{13}C) using TMS as an internal reference. The number average molecular weight of each polymer block was determined by ^{1}H NMR spectroscopy (128 scans) to give M_n(NMR). This was calculated by comparing the integration of the signals corresponding to the RAFT CTA, **1** end groups (*e.g.* the phenyl ring protons at 7.20 ppm) to the NCO-C*H* peaks of the acryl amide at 4.02 ppm in the PNIPAM block and the methyl protons of the

PMA side chain at 3.60 ppm. All infrared spectra were collected on a Perkin Elmer Spectrum 100 FTIR ATR unit. Molecular weights M_n(GPC) and molecular weight distributions for all polymers were estimated by size exclusion chromatography (SEC) with HPLC grade DMF (Fisher) containing 1 wt % LiBr as eluent at 40 °C at a flow rate of 1.0 mL/min with two PLgel 5 μm mixed C columns and a PLgel 5 μm guard column. Data was analyzed with Cirrus GPC software (Polymer Laboratories) using polymethyl methacrylate standards (EasiCal PMMA, Polymer Laboratories).

Dynamic Light Scattering (DLS) Measurements

Apparent hydrodynamic diameters ($D_{h,app}$) and size distributions of the nanostructures in aqueous solutions were determined by dynamic light scattering (DLS). The DLS instrumentation consisted of a Malvern Zetasizer NanoS instrument operating at 25 °C or 65 °C with a 4 mW He-Ne 633-nm laser module. Measurements were made at a detection angle of 173° (back scattering), and Malvern DTS 5.02 software was used to analyze the data. DLS measurements during the transition were taken by transferring the cuvette to the DLS instrument (ensuring no heat loss occurred) and recording measurements in triplicate (with 15 runs recorded per measurement) at 65 °C, after equilibrating for 5 min. All size distributions and polydispersity data shown for micelles, **4, 5** and **6** and vesicles, **7**, **8** and **9** and cross-linked vesicles, **10** are averages of at least three DLS measurements.

Static Light Scattering (SLS) Measurements

SLS measurements were performed on a Malvern Instruments Autosizer 4800, equipped with an APD detector and a Malvern 7132 50 ns 16-bit digital auto-correlator, using a 50mW green laser beam. SLS measurements were carried out over

an angle range of 30-170° in 7° stepwise increments. Toluene was used as a calibration standard. SLS data was collected for 3 or more different concentrations of the vesicles, **7** at 20 different angles for each concentration and was analyzed using the Zimm plot method on Malvern PSW0078 – Advanced software to determine z-average radius of gyration (R_g).

Atomic Force Microscopy (AFM) Measurements

A Veeco MultiMode AFM was used with a Nanoscope IIIa controller and Quadrex module (Digital Instruments, Veeco Metrology Group; Santa Barbara, CA), the tips were silicon with nominal force constant and resonant frequency of 3.5 N/m and 75 kHz (NSC18/no Al from MikroMasch). The samples were prepared for AFM analysis by drop deposition of approximately 0.1 mL of sample at a concentration of 0.71 mg/mL onto freshly cleaved mica and dried ontop of an oven for *ca.* 2 hours. The number average-particle diameters (D_{av}) and standard deviations were generated using imageJ software and analysis of at least 50 particles.

Transmission Electron Microscopy (TEM) Measurements

To prepare samples for TEM analysis at room temperature, an argon plasma treated, carbon coated, copper grid was placed onto a droplet of the sample solution for 2 min (film side down) and excess liquid was removed by blotting onto filter paper and the sample was allowed to air dry. The sample was then stained using a 1% solution of uranyl acetate for 1.5 min, blotted with filter paper to remove any excess liquid and allowed to air dry. To prepare samples for TEM analysis at 65 °C, an argon plasma treated, carbon coated, copper grid was placed into the solution to be analyzed at 65 °C for 2 min and excess liquid was removed rapidly *via* placing under vacuum (to

prevent cooling of the sample upon drying). The samples were then stained using a 1% solution of uranyl acetate (unless otherwise stated) for 1.5 min, blotted onto filter paper to remove any excess liquid and allowed to air dry. All samples were then examined with a transmission electron microscope (JEOL TEM-1200), operating at 80 kV. Average sizes of micelles, **4, 5** and **6** and vesicles, **7**, **8** and **9** cross-linked vesicles, **10** were determined from counting the sizes of at least 50 particles.

VT-NMR Experiments

5 mg of the diblock copolymer, **3** was dissolved in D_2O (after stirring at 25 °C overnight) and 0.5 mg of 3-(trimethylsilane)-1-propane-sulfonic acid was added as a reference/ internal standard. The ^1H NMR spectrum of the diblock was then run at 10 different temperatures ranging from 25-65 °C at 5 °C intervals. The sample was equilibrated at each temperature for 10 min prior to the spectrum being run.

Synthetic Procedures

Chain-end Functionalized PNIPAM$_{47}$, 2.

N-iso-propyl-acrylamide (0.5 g, 4.42 mmol), RAFT CTA, **1** (0.051 g, 0.088 mmol mmol) and AIBN (0.0044 g, 0.027 mmol) were dissolved in dry DMF (1.0 mL) and placed in an oven-dried ampoule with a stirrer bar, under the flow of nitrogen. The ampoule was degassed at least three times *via* freeze/ pump/ thawing cycles and released to and sealed under nitrogen. The polymerization mixture was then heated and stirred at 65 ºC for 5 h. Upon completion, the polymerization mixture was cooled to stop the polymerization. The polymer was isolated *via* precipitation into di-ethylether (*ca.* 200 mL), affording chain end functionalized homopolymer, PNIPAM$_{47}$, **2** (0.486 g, 93 %). M_n^{NMR} = 5.9 kDa, M_n^{GPC} = 6.1 kDa (vs. PMMA

standards), M_w/M_n = 1.09. IR (ν_{max}/cm^{-1}): 1131, 1171, 1366, 1386, 1458, 1538, 1640, 2927, 2970, 3282. ^{1}H NMR ($CDCl_3$, 400 MHz 128 scans): δ 0.85 (t, 3H, C*H*$_3$(CH$_2$)$_{17}$) in CTA end group), 1.05-1.20 (br, 6H, (C*H*$_3$)$_2$CH in polymer side chain), 1.29-2.38 (br, 3H, C*H*$_2$ and C*H* in polymer backbone), 3.10 (br s, 6H, (C*H*$_3$)$_3$C in CTA end group), 3.19 (t, 2H, SC=SSC*H*$_2$ in CTA end group), 3.29 (q, 2H, NC*H*$_2$CH$_3$ in charged end group), 3.95 (br s, 1H, (CH$_3$)$_2$C*H* in PNIPAM side chain), 4.75 (s, 4H, C*H*$_2$PhC*H*$_2$ in CTA end group), 6.20-7.10 (br s, 1H, N*H*CO in PNIPAM side chain), 7.11 (d, 2H, Ar*H* in end group), 7.19 (d, 2H, Ar*H* in end group).

Chain-end Functionalized PMA$_{27}$-*b*-PNIPAM$_{47}$, 3.

MA (0.0865 g, 1.01 mmol), **2** (0.2 g, 0.0335 mmol) and AIBN (0.00165 g, 0.01005 mmol) were dissolved in dry DMF (0.6 mL) and placed in an oven-dried ampoule with a stirrer bar, under the flow of nitrogen. The ampoule was degassed at least three times *via* freeze/ pump/ thawing cycles and released to and sealed under nitrogen. The polymerization mixture was then heated and stirred at 65 ºC for 24 h. Upon completion, the polymerization mixture was cooled and precipitated into hexanes (*ca.* 200 mL). The resulting polymer was collected *via* decanting off the solution and dissolving the remaining polymer in THF and then removing the THF under reduced pressure to afford chain end functionalized diblock copolymer, PMA$_{27}$-*b*-PNIPAM$_{47}$, **3** (0.281 g, 98%) M_n^{NMR} = 8.2 kDa, M_n^{GPC} = 9.3 kDa, M_w/M_n = 1.25 (using PMMA standards). IR (ν_{max}/cm^{-1}): 822, 852, 1131, 1163, 1367, 1386, 1446, 1545, 1642, 1734, 2876, 2970, 3286. ^{1}H NMR ($CDCl_3$, 400 MHz, 128 scans): δ 0.83 (t, 3H, C*H*$_3$(CH$_2$)$_{17}$) in CTA end group), 1.05-1.20 (br, 6H, (C*H*$_3$)$_2$CH in PNIPAM side chain), 1.29-2.38 (br, 6H, C*H*$_2$ and C*H* in polymer backbone), 3.10 (br s, 6H, (C*H*$_3$)$_3$C in CTA end

group), 3.60 (br s, 3H, C*H*$_3$OCO in PMA side chain), 3.95 (br s, 1H, (CH$_3$)$_2$C*H* in PNIPAM side chain), 6.20-7.10 (br s, 1H, N*H*CO in PNIPAM side chain), 7.11 (d, 2H, Ar*H* in end group), 7.19 (d, 2H, Ar*H* in end group).

PMA$_{27}$-*b*-PNIPAM$_{47}$ Micelles in 1:9 THF/H$_2$O, 4

The diblock copolymer PMA$_{27}$-*b*-PNIPAM$_{47}$, **3** was dissolved in 1:9 THF/water at a concentration of 1 mg/mL, affording a clear solution of PMA$_{27}$-*b*-PNIPAM$_{47}$ micelles, **4** at a concentration of 1 mg/mL. The micelles were then filtered through a 0.45 μm Teflon syringe filter prior to analysis by DLS and heating to give vesicles. $D_{h.app}$ (DLS by number) = 30.5 nm (100%), $D_{h.app}$ (DLS by volume) = 32.1 nm (78%), 208 nm (22%), $D_{h,app}$ (DLS by intensity) = 208 nm (92%), 33.6 nm (8%), PDI (DLS) = 0.34; D_{avg} (TEM) = 20 ± 5 nm. D_{avg} (AFM) = 88 ± 9 nm.

PMA$_{27}$-*b*-PNIPAM$_{47}$ Micelles in 100% H$_2$O by Dialysis, 5

The diblock copolymer PMA$_{27}$-*b*-PNIPAM$_{47}$, **3** was dissolved in 1:9 THF/water at a concentration of 1 mg/mL. The opaque micelle solution was transferred to dialysis tubing (MWCO = 3.5 kDa) and dialyzed against deionized nanopure water exhaustively (incorporating 6 changes) to remove all of the THF, affording a clear solution of PMA$_{27}$-*b*-PNIPAM$_{47}$ micelles, **5** at a concentration of 0.71 mg/mL. The micelles were then filtered through a 0.45 μm Nylon syringe filter prior to analysis by DLS and heating to give vesicles. $D_{h,app}$ (DLS by number) = 16.9 nm (100%), $D_{h.app}$ (DLS by volume) = 18.2 nm (98%), 85.7 nm (2%), $D_{h,app}$ (DLS by intensity) = 104 nm (62%), 19.9 nm (38%), PDI (DLS) = 0.47; D_{avg} (TEM) = 17 ± 2 nm. Zeta potential +25 ± 8 mV.

PMA_{27}-*b*-$PNIPAM_{47}$ Micelles in 100% H_2O by Direct Dissolution, 6

The diblock copolymer PMA_{27}-*b*-$PNIPAM_{47}$, **3** was dissolved in water at a concentration of 1 mg/mL *via* stirring overnight at 25 °C, affording a clear solution of PMA_{27}-*b*-$PNIPAM_{47}$ micelles, **6** at a concentration of 1 mg/mL. The micelles were then filtered through a 0.45 μm Nylon syringe filter prior to analysis by DLS and heating to give vesicles. $D_{h.app}$ (DLS by number) = 17.4 nm (100%), $D_{h.app}$ (DLS by volume) = 20.2 nm (96%), 75.2 nm (4%), $D_{h.app}$ (DLS by intensity) = 89.3 nm (64%), 23.6 nm (36%), PDI (DLS) = 0.36.

PMA_{27}-*b*-$PNIPAM_{47}$Vesicles in 1:9 THF/H_2O, 7

A 2 mL solution of micelles, **4** was placed in a sealed glass cuvette equipped with a small stirrer bar and placed in an oil bath at 65 °C. The sample was then heated with stirring at 500 rpm for the desired time, to achieve the micelle to vesicle transition. $D_{h.app}$ (DLS by number) = 155 nm (100%), $D_{h,app}$ (DLS by volume) = 186 nm (100%), $D_{h,app}$ (DLS by intensity) = 188 nm (100%), PDI (DLS) = 0.27; D_{avg} (TEM) = 85 ± 16 nm. D_{avg} (AFM) = 178 ± 13 nm.

PMA_{27}-*b*-$PNIPAM_{47}$ Vesicles in 100% H_2O, 8

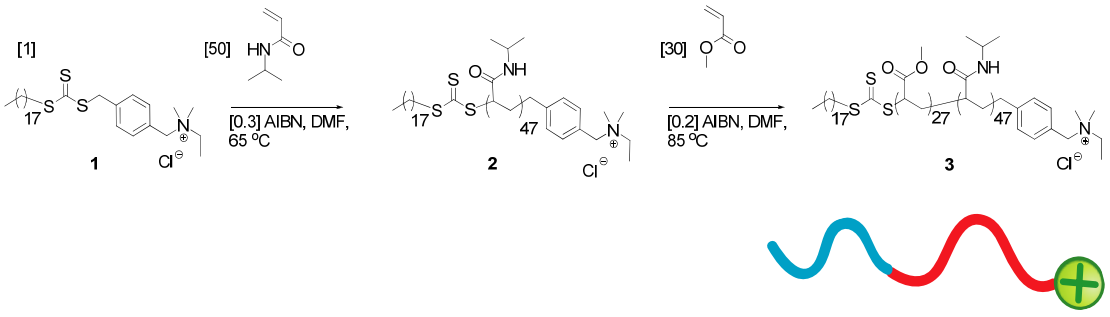
A 2 mL solution of micelles, **5** was placed in a sealed glass cuvette equipped with a small stirrer bar and placed in an oil bath at 65 °C. The sample was then heated with stirring at 500 rpm for the desired time, to achieve the micelle to vesicle transition. $D_{h.app}$ (DLS by number) = 140 nm (100%), $D_{h,app}$ (DLS by volume) = 143 nm (100%), $D_{h,app}$ (DLS by intensity) = 146 nm (100%), PDI (DLS) = 0.03.

PMA_{27}-*b*-$PNIPAM_{47}$ Vesicles in 100% H_2O, 9

A 2 mL solution of micelles, **5** was placed in a sealed glass cuvette equipped with a small stirrer bar and placed in an oil bath at 40 °C. The sample was then heated with stirring at 500 rpm for the desired time, to achieve the micelle to vesicle transition. $D_{h,app}$ (DLS by number) = 218 nm (100%), $D_{h,app}$ (DLS by volume) = 253 nm (100%), $D_{h,app}$ (DLS by intensity) = 249 nm (100%), PDI (DLS) = 0.41.

L-ascorbic acid "cross-linked" PMA_{27}-*b*-$PNIPAM_{47}$ Vesicles, 10

A 2 mL solution of micelles, **5** was placed in a sealed glass cuvette equipped with a small stirrer bar and placed in an oil bath at 65 °C. The sample was then heated with stirring at 500 rpm for 28 h, to achieve the micelle to vesicle transition. The vesicles were then cooled to 40 °C in the DLS instrument and 5 mg of *L*-ascorbic acid was added to the heated solution. The solution was then allowed to cool to 25 °C. $D_{h,app}$ (DLS by number) = 158 nm (100%), $D_{h,app}$ (DLS by volume) = 163 nm (100%), $D_{h,app}$ (DLS by intensity) = 166 nm (100%), PDI (DLS) = 0.30; D_{avg} (TEM) = 175 ± 12 nm.



Scheme S1. Synthesis of the 'head-group' chain end-functionalized diblock copolymer, **3**.

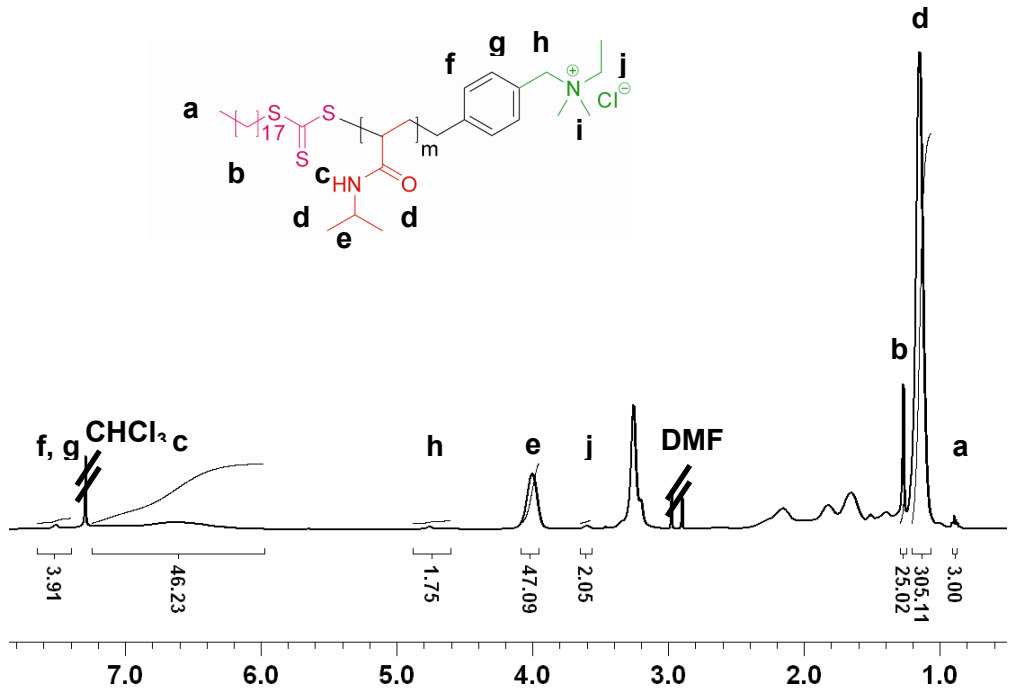


Figure S1. Assigned ^{1}H NMR spectrum of chain end functionalized homo-PNIPAM, **2** in $CDCl_3$.

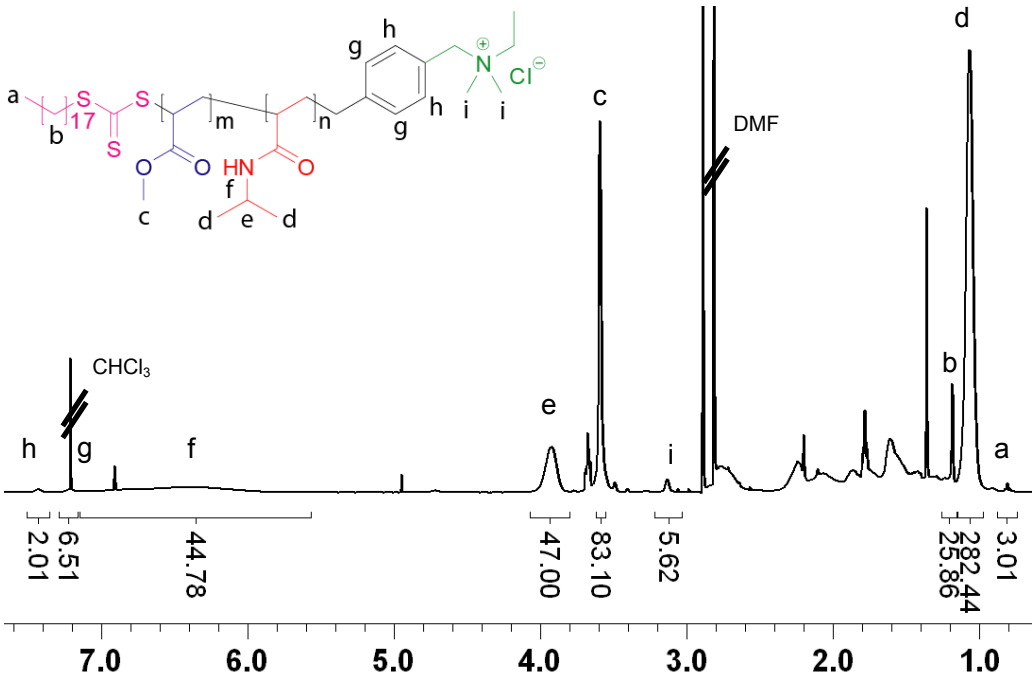


Figure S2. Assigned ^{1}H NMR spectrum of end functionalized diblock copolymer, PMA_{27}-*b*-$PNIPAM_{47}$, **3**, run in $CDCl_3$.

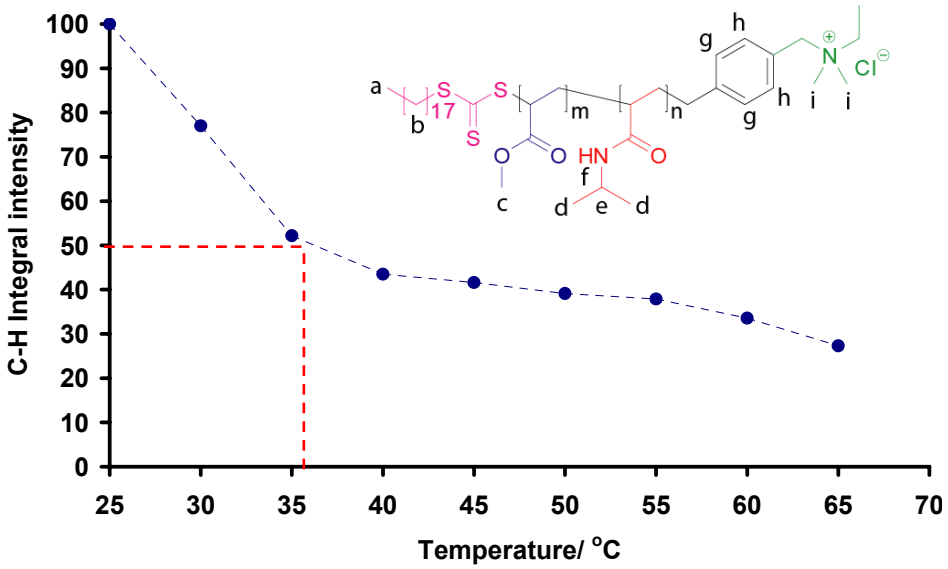


Figure S3. A graph to show the ratio of ^{1}H NMR signal intensities for PNIPAM C-H next to methyl groups (assigned as *e* in inset, at 3.8 ppm) as a function of temperature in D_2O solution (6 mg/mL) for the PMA_{27}-*b*-$PNIPAM_{47}$ diblock copolymer, **3.** The LCST was the temperature at which the PNIPAM signal intensity was reduced by 50% *versus* an internal standard**.**

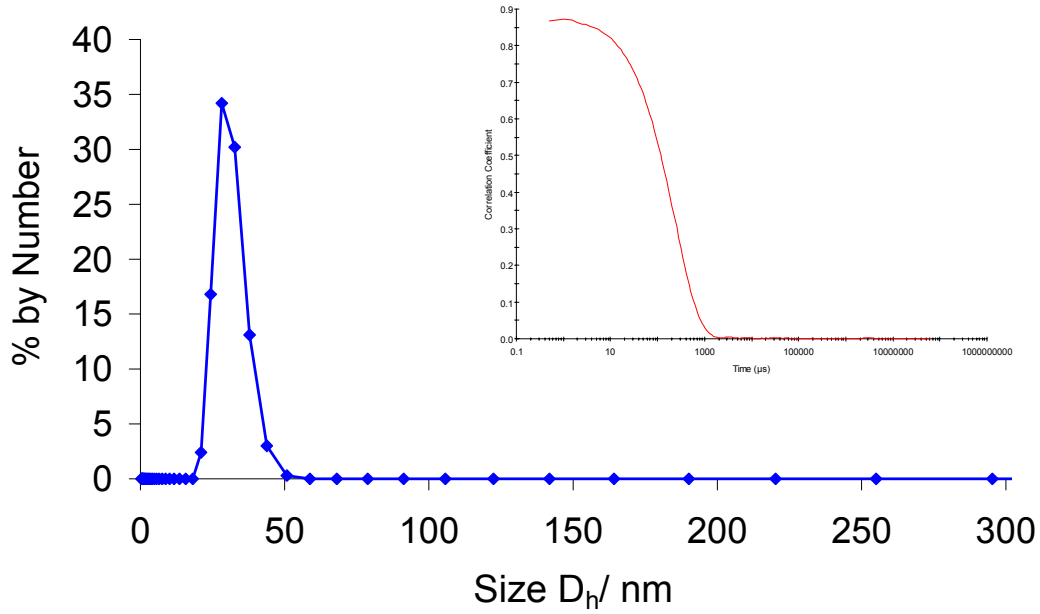


Figure S4. DLS data for the micelles, **4** at 25 °C, with inset showing the correlation function.

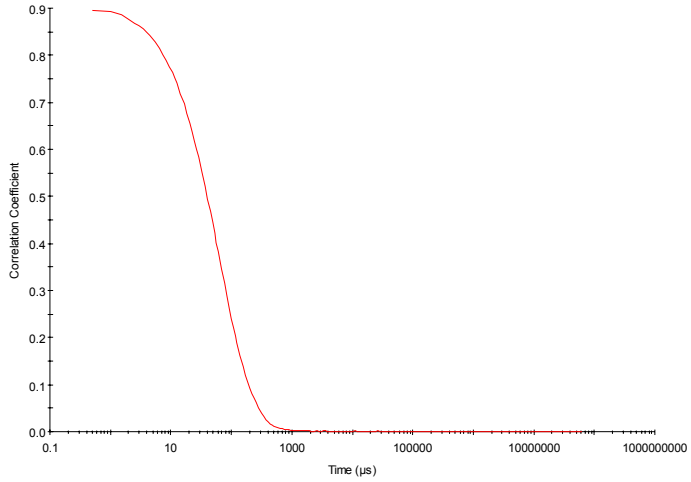


Figure S5. Correlation function from the DLS data for the micelles, **5** at 25 °C.

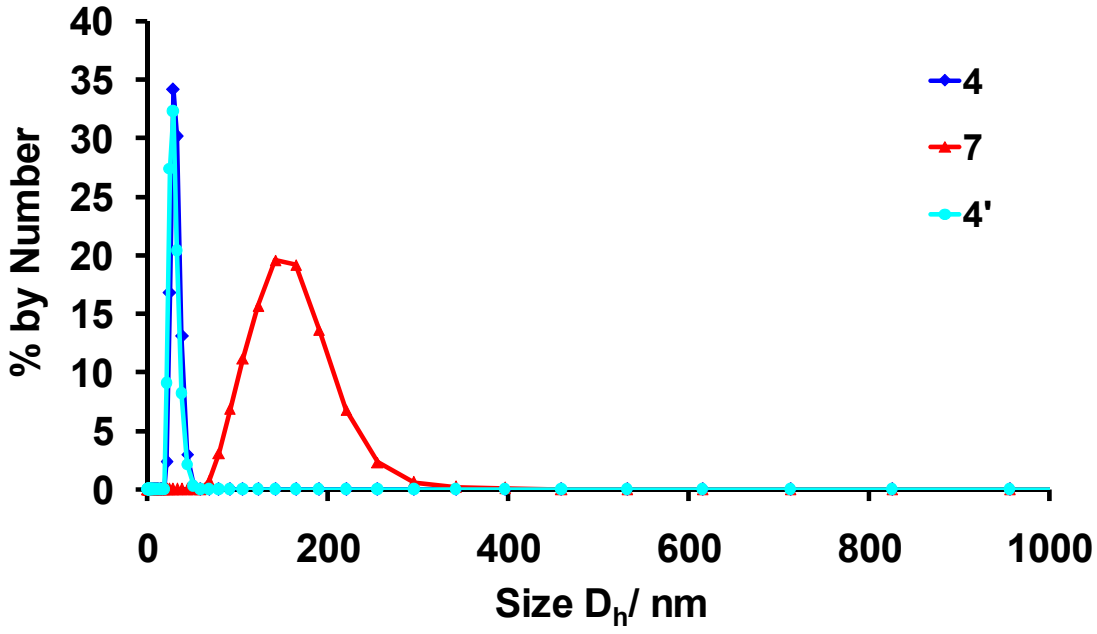


Figure S6. Apparent hydrodynamic diameters, $D_{h,app}$ (by number) of the PMA_{27}-*b*-$PNIPAM_{47}$ copolymer aggregates **4** upon heating and stirring a solution at 65 °C to form **7** followed by cooling to room temperature to afford **4'**.

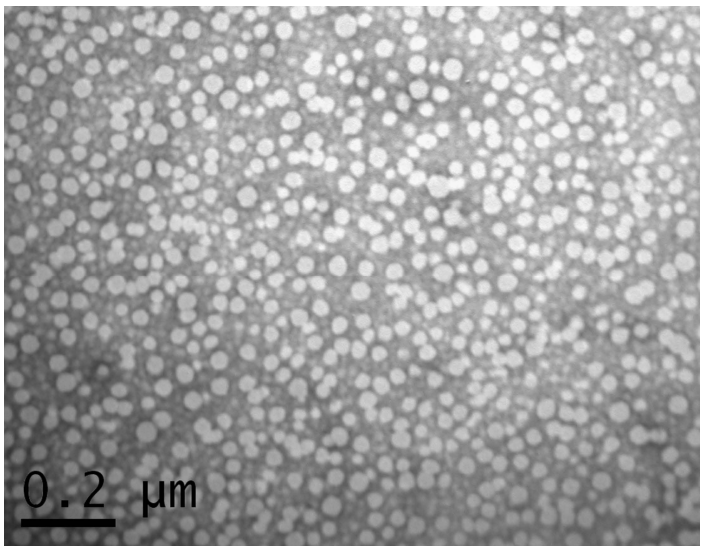


Figure S7. A representative TEM micrograph of aggregates, **7** upon cooling back to micelles **4'**, after 30 min cooling to 25 °C and stained with uranyl acetate. Samples were drop cast from a cooling solution at 25 °C.

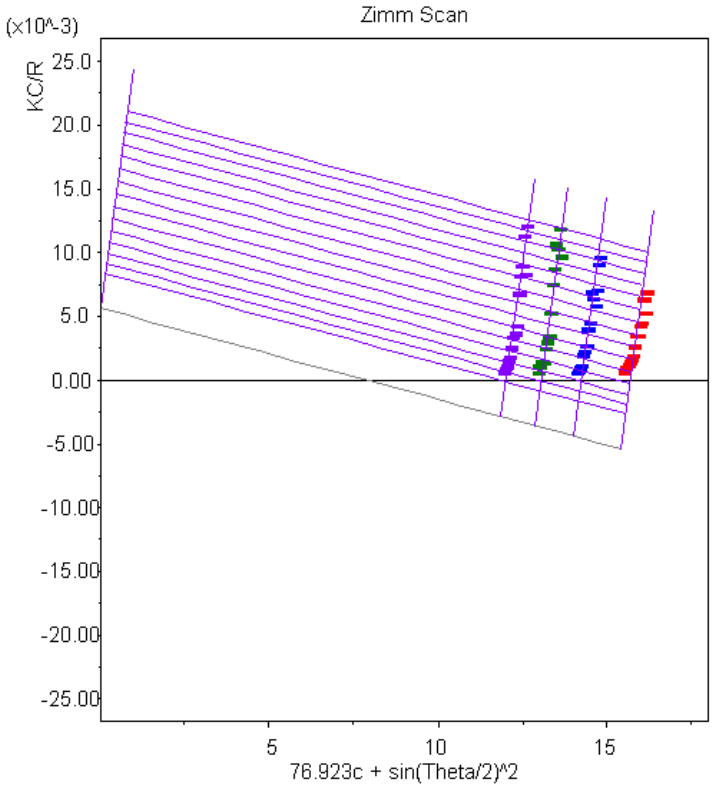


Figure S8. Zimm plot of the PMA_{27}-*b*-$PNIPAM_{47}$ vesicles, **7** performed at 65 °C.

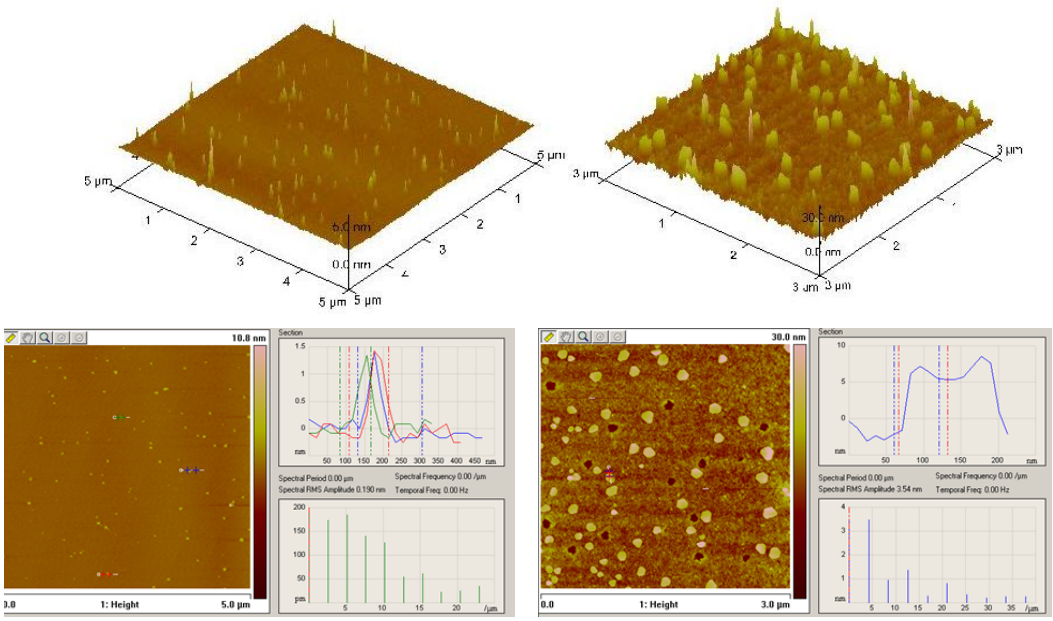


Figure S9. Representative AFM data for micelles **4** (LHS) and vesicles **7** (RHS). Note that the diameters measured by AFM are not reliable due to tip effects, however the cross-section view which is showed below each image highlights the solid and hollow nature of the micelles and vesicles respectively.

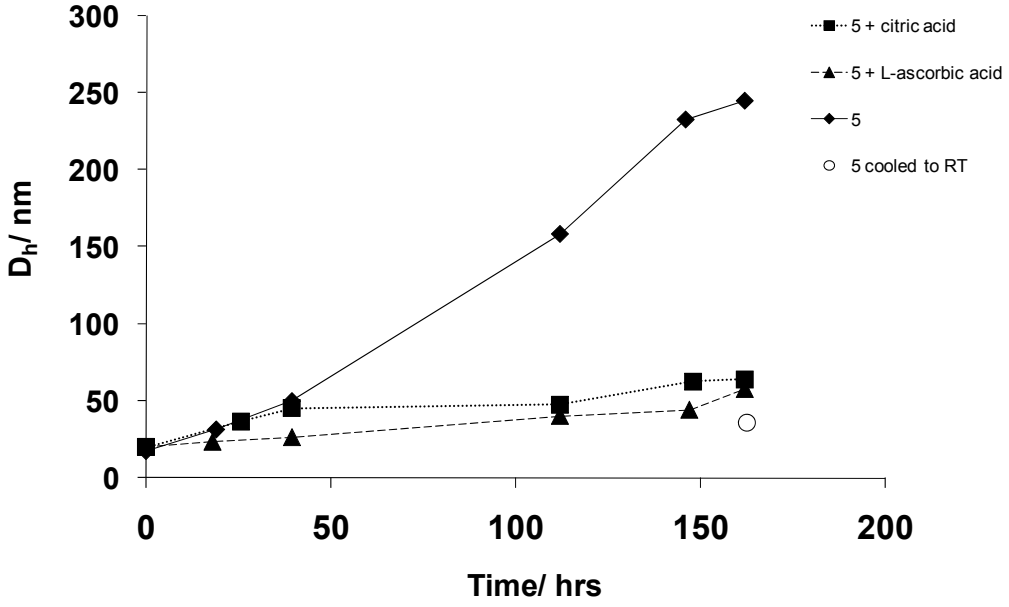


Figure S10. Apparrent hydrodynamic diameter, $D_{h,app}$ of **5** upon heating a 0.71 mg/mL solution at 40 °C, with no additive to form vesicles **9** and with 5 mg L-ascorbic acid or 5 mg citric acid additive. Lines are a guide for the eye only.

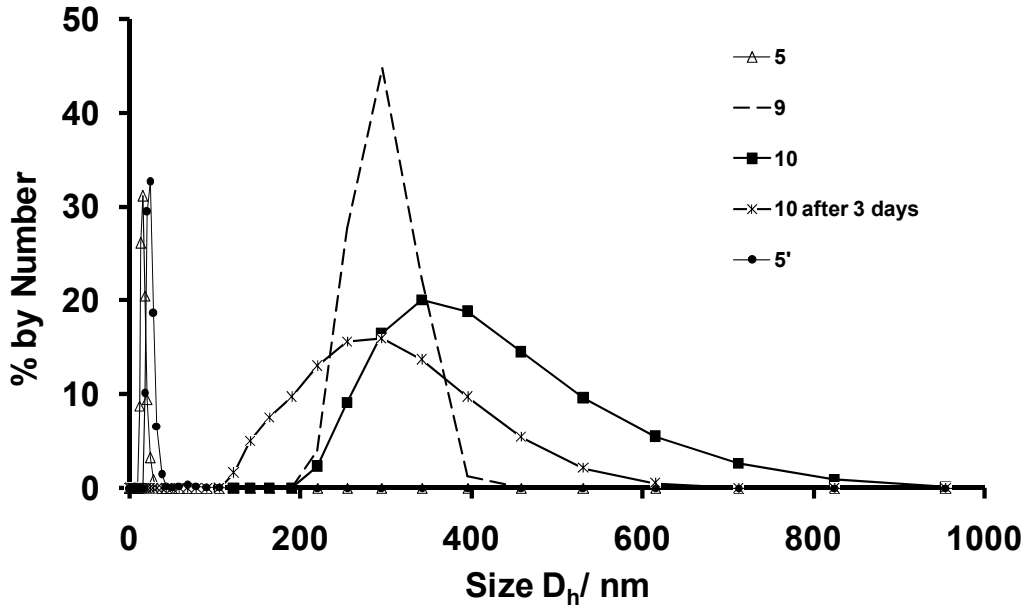


Figure S11. Apparent hydrodynamic diameter, $D_{h,app}$ (by number) of the PMA_{27}-*b*-$PNIPAM_{47}$ vesicles, **9** upon heating and stirring then 5 mg of *L*-ascorbic acid was added and the solution was cooled to 25 °C to give 'cross-linked' aggregates, **10**.

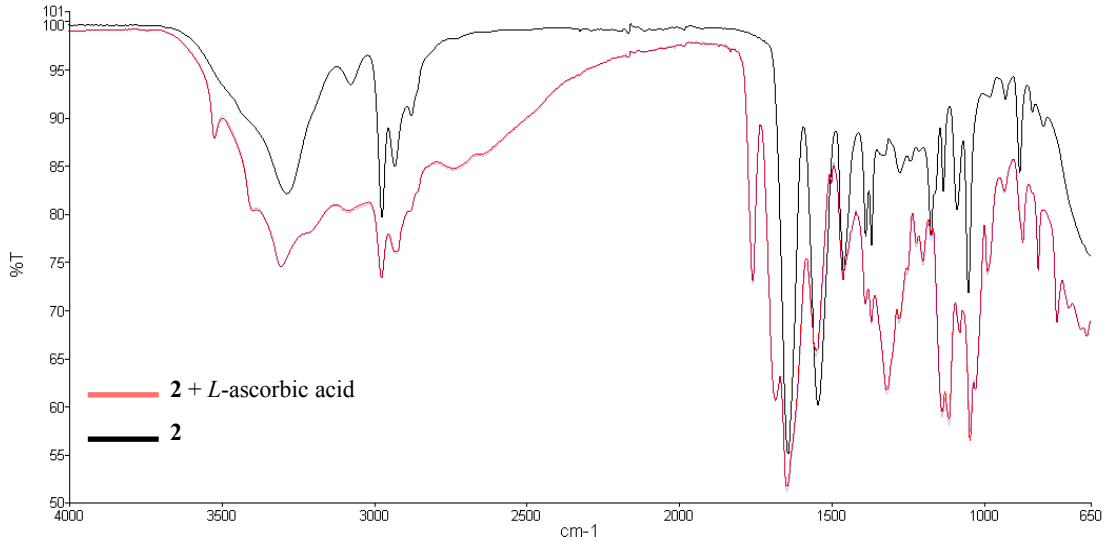


Figure S12. IR spectrum overlay showing possible interaction between $PNIPAM_{47}$, **2** and *L*-ascorbic acid.

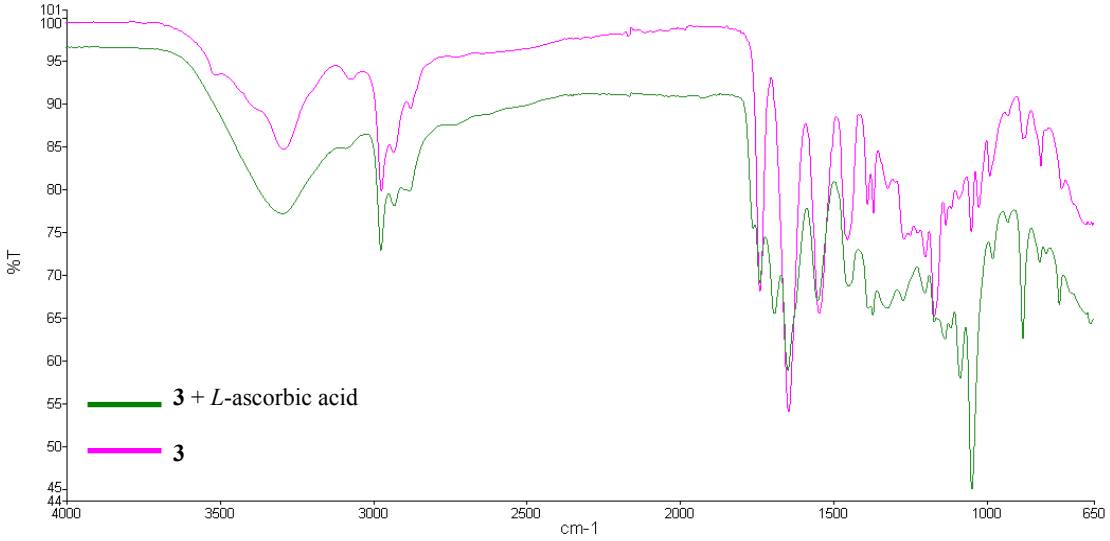


Figure S13. IR spectrum overlay showing possible interaction between PMA_{27}-*b*-$PNIPAM_{47}$, **3** and *L*-ascorbic acid.

The IR spectrum of **2** and **3** in the presence of *L*-ascorbic acid showed shifts in the N-H and C=O stretching frequencies. Furthermore, the OH region of the spectrum was significantly broadened, indicating possible H-bonding interactions.

Reference

1. A. O. Moughton, R. K. O'Reilly, *Chem. Commun.* **2010**, *46*, 1091.