Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information for:

Synthesis of well-defined diblock copolymer nano-objects by RAFT non-aqueous emulsion polymerization of *N*-(2-acryloyloxy)ethyl pyrrolidone in non-polar media

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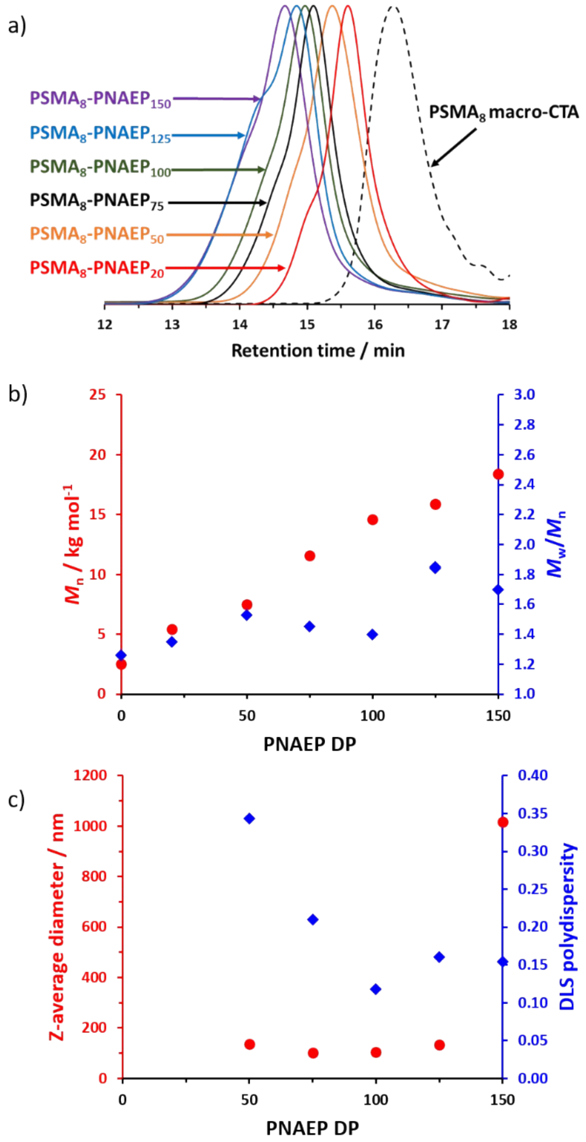

Figure S1. (a) Chloroform GPC curves recorded for a $PSMA_8$ precursor and a series of $PSMA_8$-$PNAEP_x$ diblock copolymers synthesized by the RAFT non-aqueous emulsion polymerization of NAEP at 90 °C in *n*-dodecane using a $PSMA_8$/T21s molar ratio of 4.0. (b) Evolution in M_n and M_w/M_n with target PNAEP DP for a series of $PSMA_8$-$PNAEP_x$ diblock copolymers as judged by GPC analysis (refractive index detector with calibration using a series of near-monodisperse PMMA standards). The GPC data for the corresponding $PSMA_8$ precursor is also shown as a reference. (c) Evolution in z-average diameter (and the corresponding DLS polydispersity) with increasing target PNAEP DP for a series of $PSMA_8$-$PNAEP_x$ diblock copolymers as judged by DLS after dilution from 20 to 0.1% w/w solids using *n*-dodecane.

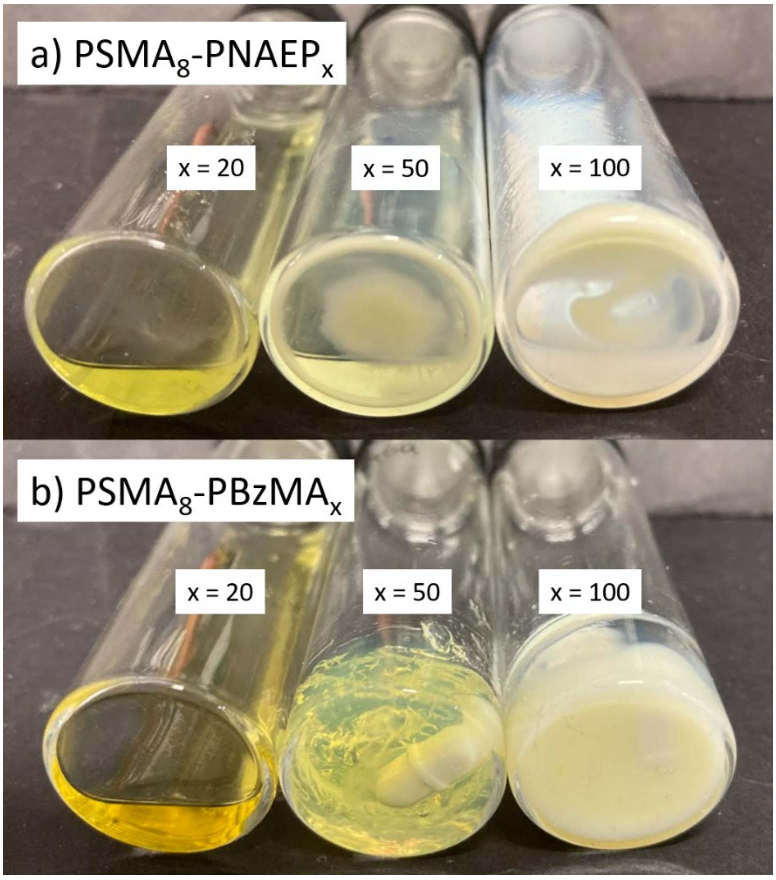

Figure S2. Digital images recorded for (a) $PSMA_8$-$PNAEP_x$ nano-objects prepared by RAFT non-aqueous emulsion polymerization of NAEP at 90 °C in *n*-dodecane indicating incipient flocculation (from left to right x= 20, 50 and 100) and (b) $PSMA_8$-$PBzMA_x$ nano-objects prepared by RAFT dispersion polymerization of NAEP at 90 °C in *n*-dodecane indicating colloidally stable dispersions (from left to right x= 20, 50 and 100).

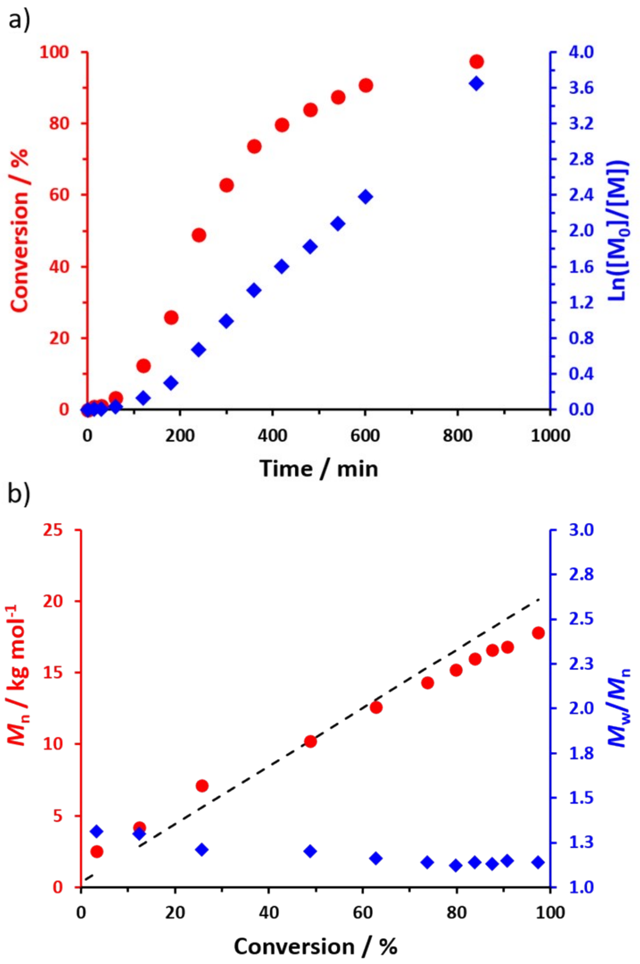

Figure S3. (a) Conversion *vs.* time curves obtained for the RAFT solution polymerization of SMA at 70 °C in toluene targeting a PSMA DP of 60 at 50% w/w solids using a PETTC RAFT agent and AIBN initiator (PETTC/AIBN molar ratio = 5.0). (b) Corresponding evolution in M_n and M_w/M_n with conversion observed for the same SMA homopolymerization. The dashed line indicates the theoretical M_n data. The experimental M_n data set differs from this theoretical line owing to a systematic GPC calibration error that is incurred by using PMMA standards.

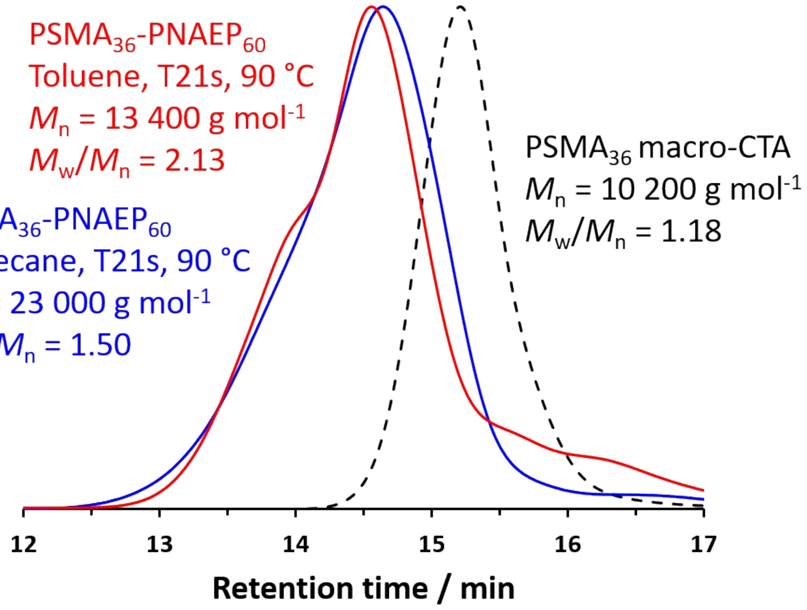

Figure S4. Chloroform GPC curves recorded for a $PSMA_{36}$ precursor and two corresponding chain-extended $PSMA_{36}$-$PNAEP_{60}$ diblock copolymers prepared by RAFT *solution* polymerization of NAEP in toluene at 90 °C (red trace) or by RAFT *non-aqueous* emulsion polymerization of NAEP in *n*-dodecane at 90 °C (blue trace). In each case, the $PSMA_{36}$/T21s molar ratio was 4.0. These GPC traces indicate relatively high blocking efficiencies (particularly for the synthesis conducted in *n*-dodecane) but the presence of a high molecular weight shoulder suggests that some chain transfer to polymer occurs in this case.

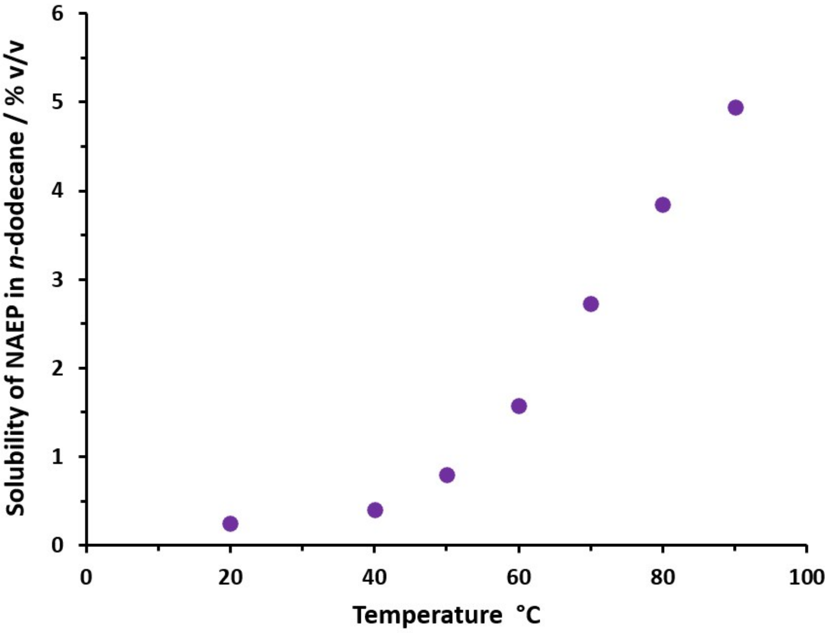

Figure S5. Solubility (v/v%) of NAEP monomer in *n*-dodecane between 20 and 90 °C as determined by visual inspection.

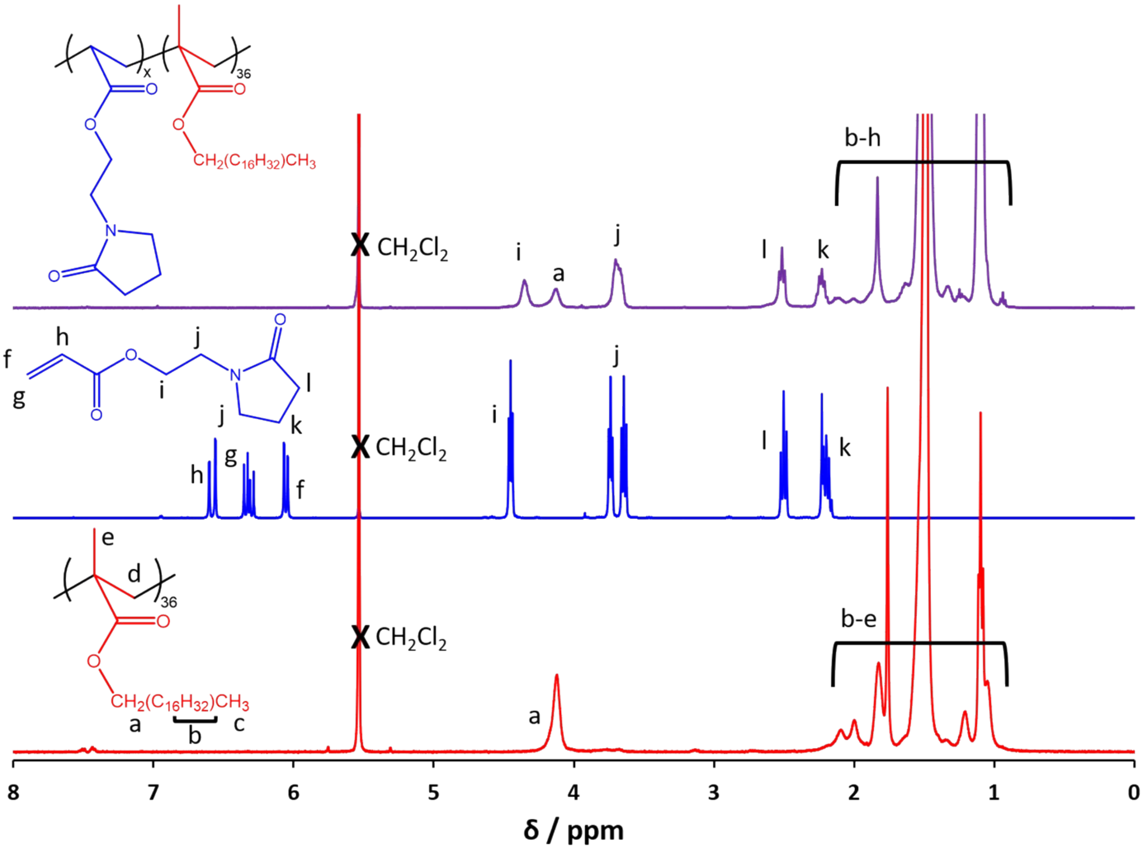

Figure S6. ^{1}H NMR spectra recorded in CD_2Cl_2 for the PSMA$_{36}$ precursor (red spectrum), NAEP monomer (blue spectrum) and a PSMA$_{36}$-PNAEP$_{60}$ diblock copolymer (purple spectrum) prepared at 20% w/w solids by RAFT non-aqueous emulsion polymerization in *n*-dodecane at 90 °C. Comparison of the integrated monomer vinyl signals with appropriate polymer signals in the latter spectrum indicate more than 99% conversion in this case.

Table S1. Summary of NAEP monomer conversion, diblock copolymer M_n and M_w/M_n data as determined by chloroform GPC and the z-average diameters and polydispersities (PDI) determined by DLS studies for linear $PSMA_{36}$-$PNAEP_x$ diblock copolymer nanoparticles prepared *via* RAFT dispersion polymerization prepared in various *n*-dodecane at 90 °C.

Target diblock copolymer composition	NAEP conversion^a / %	GPC^b			DLS^c	
		M_p / g mol^{-1}	M_n / g mol^{-1}	M_w/M_n	Z-average diameter / nm	DLS polydispersity
$PSMA_{36}$-$PNAEP_{10}$	98	14 400	13 700	1.26	$	$
$PSMA_{36}$-$PNAEP_{20}$	98	16 200	16 400	1.31	$	$
$PSMA_{36}$-$PNAEP_{30}$	98	17 800	18 300	1.31	$	$
$PSMA_{36}$-$PNAEP_{40}$	98	20 100	21 400	1.45	40	0.19
$PSMA_{36}$-$PNAEP_{50}$	98	21 900	22 600	1.50	45	0.17
$PSMA_{36}$-$PNAEP_{60}$	98	22 900	23 000	1.50	52	0.10
$PSMA_{36}$-$PNAEP_{60}$†	99	19 500	20 300	1.36	35	0.11
$PSMA_{36}$-$PNAEP_{70}$	99	25 700	25 800	1.76	60	0.12
$PSMA_{36}$-$PNAEP_{80}$	99	33 600	23 300	2.40	69	0.09
$PSMA_{36}$-$PNAEP_{90}$	99	39 700	23 200	3.00	76	0.08
$PSMA_{36}$-$PNAEP_{100}$	99	43 700	31 000	3.33	77	0.05
$PSMA_{36}$-$PNAEP_{110}$	99	48 900	26 500	3.87	86	0.05
$PSMA_{36}$-$PNAEP_{150}$	99	*	*	*	100	0.05
$PSMA_{36}$-$PNAEP_{200}$	99	*	*	*	128	0.03
$PSMA_{36}$-$PNAEP_{300}$	>99	*	*	*	164	0.10
$PSMA_{36}$-$PNAEP_{400}$	>99	*	*	*	202	0.02
$PSMA_{36}$-$PNAEP_{500}$	>99	*	*	*	261	0.10

a. NAEP conversion determined by ^1H NMR spectroscopy.

b. Molecular weight data determined by chloroform GPC against a series of PMMA calibrants.

c. DLS studies measured at 0.1% w/w dispersions by dilution with *n*-dodecane.

$ DLS analysis only indicated very low scattered light intensities, suggesting that micellar nucleation had not occurred in these syntheses.

* GPC analysis was not possible for these nanoparticles because molecular dissolution could not be achieved owing to core-crosslinking. Presumably, this is the result of extensive chain transfer to the acrylic polymer backbone.

† Diblock copolymer nanoparticles synthesized using AIBN initiator at a $PSMA_{36}$:AIBN molar ratio of 4.0.

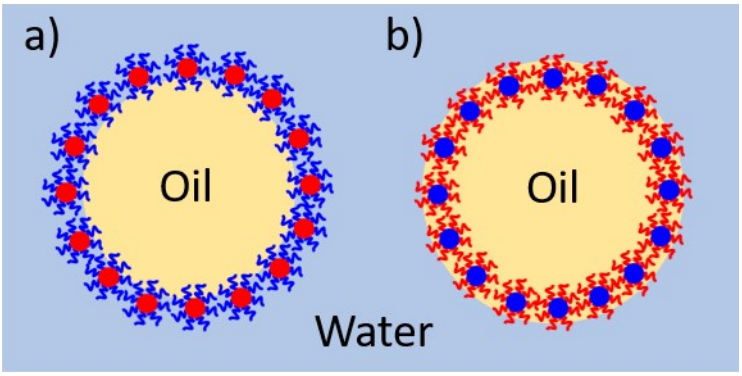

Figure S7. Schematic representation of the two possible explanations for the o/w Pickering emulsions that are formed after high-shear homogenization of an equal volume of deionized water and a 1.0% w/w dispersion of *hydrophobic* $PSMA_{36}$-$PNAEP_{70}$ nanoparticles in *n*-dodecane. (a) *In situ* nanoparticle inversion during homogenization produces *hydrophilic* $PNAEP_{70}$-$PSMA_{36}$ nanoparticles that then adsorb at the outer surface of the oil droplets. (b) The original *hydrophobic* $PSMA_{36}$-$PNAEP_{70}$ nanoparticles adsorb at the *inner surface* of the oil droplets. DLS studies of the aqueous continuous phase suggest that the second explanation is most likely to be correct. [N.B. Both schematic cartoons have been simplified for clarity. In scenario A, the excess (non-adsorbed) hydrophilic nanoparticles in the aqueous continuous phase have been omitted. Similarly, the excess (non-adsorbed) hydrophobic particles present within the oil droplet are not shown in scenario B].

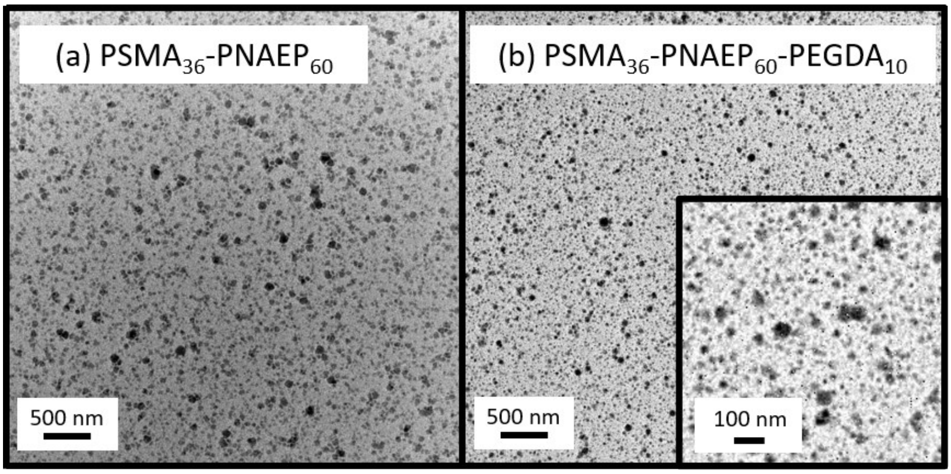

Figure S8. Representative TEM images recorded for linear $PSMA_{36}$-$PNAEP_{60}$ and cross-linked $PSMA_{36}$-$PNAEP_{60}$-$PEGDA_{10}$ nano-objects. The latter nanoparticles exhibit a more well-defined spherical morphology, whereas the former tend to undergo (partial) deformation during TEM grid preparation. Inset image shows the core-crosslinked nano-objects at a higher magnification.

Table S2. Summary of z-average diameters and DLS polydispersities (PDI) determined for linear $PSMA_{36}$-$PNAEP_{60}$ diblock copolymer nanoparticles and the corresponding core-crosslinked $PSMA_{36}$-$PNAEP_{60}$-$PEGDA_{10}$ triblock copolymer nanoparticles in *n*-dodecane (a poor solvent for PNAEP) and chloroform (a good solvent for PNAEP).

Target diblock copolymer composition	**DLS diameter / nm (PDI)**	
	n-Dodecane	Chloroform
$PSMA_{36}$-$PNAEP_{60}$	52 (0.10)	/
$PSMA_{36}$-$PNAEP_{60}$-$PEGDA_{10}$	57 (0.09)	84 (0.06)

SAXS model

In general, the intensity of X-rays scattered by a dispersion of nano-objects [usually represented by the scattering cross section per unit sample volume, $\frac{d\Sigma}{d\Omega}(q)$] can be expressed as:

$$\frac{d\Sigma}{d\Omega}(q) = NS(q)\int_0^\infty \ldots \int_0^\infty F(q,r_1,\ldots,r_k)^2 \Psi(r_1,\ldots,r_k)dr_1 \ldots dr_k \qquad \text{S1}$$

where $F(q, r_1, \ldots, r_k)$ is the form factor, $r_1, \ldots, r_k$ is a set of k parameters describing the structural morphology, $\Psi(r_1, \ldots, r_k)$ is the distribution function, S(q) is the structure factor and N is the nano-object number density per unit volume, which can be expressed as:

$$N = \frac{\varphi}{\int_0^\infty \ldots \int_0^\infty V(r_1,\ldots,r_k)\Psi(r_1,\ldots,r_k)dr_1 \ldots dr_k} \qquad \text{S2}$$

where $V(r_1, \ldots, r_k)$ is volume of the nano-object and φ is their volume fraction in the dispersion. For all SAXS experiments conducted herein, a dilute copolymer concentration of 1.0 % w/w was utilized. Thus it can be assumed that s(q) = 1 for all analysis and modeling.

Spherical model

The spherical micelle form factor equation for Equation S1 is given by[1]:

$$F_{sph}(q) = N_s^2\beta_s^2A_s^2(q,R_s) + N_s\beta_c^2F_c(q,R_g) + (q) \qquad \text{S3}$$

Where R_s is the core radius of the spherical micelle and R_g is the radius of gyration of the PSMA corona block. The core block and the corona block X-ray scattering length contrast is given by $\beta_s = V_s(\xi_s - \xi_{sol})$ and $\beta_s = V_c(\xi_c - \xi_{sol})$, respectively. Here ξ_s, ξ_c and ξ_{sol} are the X-ray scattering length densities of the core-forming block (ξ_{PNAEP} = 11.46 × 10^{10} cm^{-2}), the coronal stabilizer block (ξ_{PSMA} = 9.237 × 10^{10} cm^{-2}) and *n*-dodecane (ξ_{sol} = 7.322 × 10^{10} cm^{-2}). V_s and V_c are the volumes of the core-forming block and the coronal stabilizer block, respectively. Using the molecular weights of the PNAEP and PSMA blocks and their respective mass densities (ρ_{PNAEP} = 1.26 g cm^{-3} and ρ_{PSMA} = 0.97 g cm^{-3}), the individual block volumes can be calculated from $V = \frac{M_{n,pol}}{N_A\rho}$, where $M_{n,pol}$ corresponds to the number-average molecular weight of the block determined by ^{1}H NMR spectroscopy.

The sphere form factor amplitude is used for the amplitude of the core self-term:

$$A_c(q,R_s) = \Phi(qR_s)exp\left(-\frac{q^2\sigma^2}{2}\right) \qquad \text{S4}$$

Where $\Phi(qR_s) = \frac{3[sin(qR_s) - qR_s cos(qR_s)]}{(qR_s)^3}$. A sigmoidal interface between the two blocks was assumed for the spherical micelle form factor (equation S4). This is described by the exponent term with a width σ accounting for a decaying scattering length density at the micellar interface. This σ value was fixed at 2.2 during fitting.

The form factor amplitude of the spherical micelle corona is:

$$A_c(q) = \frac{\int_{R_s}^{R_s+2s} \mu_c(r)\frac{\sin(qr)}{qr} r^2 dr}{\int_{R_s}^{R_s+2s} \mu_c(r) r^2 dr} exp\left(-\frac{q^2\sigma^2}{2}\right) \qquad \text{S5}$$

The radial profile, $\mu_c(r)$, can be expressed by a linear combination of two cubic b splines, with two fitting parameters *s* and *a* corresponding to the width of the profile and the weight coefficient, respectively. This information can be found elsewhere,[2,3] as can the approximate integrated form of Equation S5. The self-correlation term for the corona block is given by the Debye function:

$$F_c(q,R_g) = \frac{2\left[\exp\left(-q^2R_g^2\right) - 1 + q^2R_g^2\right]}{q^4R_g^2} \qquad \text{S6}$$

Where R_g is the radius of gyration of the PSMA coronal block. The aggregation number of the spherical micelle, N_s, is given by:

$$N_s = (1 - x_{sol})\frac{\frac{4}{3}\pi R_s^3}{V_s} \qquad \text{S7}$$

Where x_{sol} is the volume fraction of solvent (in this case, *n*-dodecane) in the PNAEP micelle core. An effective structure factor expression proposed for interacting spherical micelles[4] is used in equation S1:

$$S_s(q) = 1 + \frac{A_{s\_mic}^{av}(q)^2\left[S_{PY}(q,R_{PY},f_{PY}) - 1\right]}{F_{s\_mic}(q)} \qquad \text{S8}$$

Herein the form factor of the average radial scattering length density distribution of the micelles is given by $A_{s\_mic}^{av}(q) = N_s\left[\beta_sA_s(q,R_s) + \beta_cA_c(q)\right]$ and $S_{PY}(q,R_{PY},f_{PY})$ is a hard-sphere interaction structure factor based on the Percus-Yevick approximation,[5] where R_{PY} is the interaction radius and f_{PY} is the hard-sphere volume fraction. A polydispersity for one parameter (R_s) is assumed for the micelle model, which is described by a Gaussian distribution. Thus, the polydispersity function in Equation S1 can be replaced with:

$$\Psi(r_1) = \frac{1}{\sqrt{2\pi\sigma_{R_s}^2}} exp\left(-\frac{(r_1 - R_s)^2}{2\sigma_{R_s}^2}\right) \qquad \text{S9}$$

Where σ_{R_s} is the standard deviation for R_s. In accordance with equation S2, the number density per unit volume for the micelle model is expressed as:

$$N = \frac{\varphi}{\int_0^\infty V(r_1)\Psi(r_1)dr_1} \qquad \text{S10}$$

Where φ is the total *volume fraction* of copolymer in the spherical micelles and $V(r_1)$ is the total *volume* of copolymer within a spherical micelle $[V(r_1) = (V_s + V_c)N_s(r_1)]$.

1 J. S. Pedersen, *J. Appl. Crystallogr.*, 2000, **33**, 637–640.

2 J. S. Pedersen and M. C. Gerstenberg, *Colloids Surfaces A Physicochem. Eng. Asp.*, 2003, **213**, 175–187.

3 J. S. Pedersen, C. Svaneborg, K. Almdal, I. W. Hamley and R. N. Young, *Macromolecules*, 2003, **36**, 416–433.

4 J. S. Pedersen, *J. Chem. Phys.*, 2001, **114**, 2839–2846.

5 D. J. Kinning and E. L. Thomas, *Macromolecules*, 1984, **17**, 1712–1718.