Supporting Information for:

Rational Synthesis of Novel Biocompatible Thermoresponsive Block Copolymer Worm Gels

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Supporting Figures and Tables



Fig. S1 Assigned ¹H NMR spectra (CD₃OD) for (A) the PMPC₁₅ precursor, (B) the PMPC₂₆ precursor, (C) the PMPC₁₅-PHPMA₁₅₀ diblock copolymer and (D) the PMPC₂₆-PHPMA₂₈₀ diblock copolymer.



Fig. S2 GPC curves (3:1 chloroform/methanol eluent, refractive index detector) recorded for the two $PMPC_x$ precursors and the corresponding $PMPC_x$ -PHPMA_y diblock copolymers. M_n and M_w/M_n data are expressed relative to a series of near-monodisperse poly(methyl methacrylate) (PMMA) standards.



Fig. S3 Representative TEM images recorded for (A) PMPC₁₅-PHPMA₁₅₀ diblock copolymer worms at 25 °C (B) PMPC₁₅-PHPMA₁₅₀ diblock copolymer spheres at 6 °C and (C) the reconstituted PMPC₁₅-PHPMA₁₅₀ diblock copolymer worms formed on returning to 25 °C. The corresponding inset digital photographs show the original 18 % w/w transparent free-standing worm gel at 25 °C, the free-flowing fluid obtained at 6 °C and the reconstituted free-standing worm gel at 25 °C. TEM images were recorded after dilution of an 18 % w/w aqueous dispersion to 0.1% w/w copolymer concentration at 25 and 6 °C followed by drying at ambient temperature.



Fig. S4 Reduction in the mean cross-sectional core radius associated with a sphere-to-worm (or cylinder) transition while maintaining a constant core volume.



Fig. S5 SAXS pattern recorded at 25 °C for a 1.0% w/w aqueous dispersion of $PMPC_{26}$ -PHPMA₂₈₀ worms. The white line indicates the data fit obtained using a worm-like micelle model.

Table S1 TEM assignment and various SAXS parameters determined from modeling SAXS data recorded for a 1.0% w/w aqueous dispersion of PMPC₂₆-PHPMA₂₈₀ nano-objects diluted from the as synthesized 25% w/w aqueous dispersion at 25 °C (Fig. S5) [N.B. R_w is the worm core radius and σ_{R_w} is its standard deviation, L_w is the worm contour length and b_w is the worm Kuhn length].

TEM	SAXS			
Morphology assignment	$R_{\rm w}$ / nm	$\sigma_{\!R_{ m w}}$ / nm	$L_{ m w}$ / nm	$b_{ m w}$ ª / nm
Worms	12.9	1.0	342	342

^a To achieve a satisfactory data fit, it was necessary to assume that b_w was equal to L_w , i.e. that the worms are relatively inflexible.



Fig. S6 Gel modulus vs. strain amplitude sweeps determined by oscillatory rheology indicating the linear viscoelastic region for aqueous dispersions of (A) 18% w/w PMPC₁₅-PHPMA₁₅₀ and (B) 10% w/w PMPC₂₆-PHPMA₂₈₀ diblock copolymer worms. These measurements were conducted at 25 °C and an angular frequency of 1.0 rad s⁻¹. The solid red and open blue symbols correspond to G' and G'', respectively.



Fig. S7 Gel moduli vs. angular frequency sweeps determined by oscillatory rheology for aqueous dispersions of (A) 18% w/w PMPC₁₅-PHPMA₁₅₀ and (B) 10% w/w PMPC₂₆-PHPMA₂₈₀ diblock copolymer worms recorded at 25 °C and an applied strain amplitude of 1.0 %. The solid red and open blue symbols correspond to G' and G'', respectively.



Fig. S8 SIPLI images recorded at 6, 25 and 37 °C for a 10% w/w aqueous dispersion of $PMPC_{15}$ -PHPMA₁₅₀ worms using a constant shear rate of 1.0 s⁻¹ at the sample edge. A thermal equilibration time of 10 min was allowed at each temperature prior to data acquisition. The white arrows indicate the orientation of the polarizer (P) and analyzer (A).



Fig. S9 Variation in gel moduli (G' and G'') over time as determined by oscillatory rheology for a series of aqueous dispersions of (A) PMPC₁₅-PHPMA₁₅₀ and (B) PMPC₂₆-PHPMA₂₈₀ diblock copolymer worms diluted from 25% w/w by serial dilution to varying copolymer concentrations in order to determine the critical gelation concentration (CGC) of the respective gels at 25 °C. An applied strain amplitude of 1.0% and an angular frequency of 1.0 rad s⁻¹ were used in these measurements. Digital photographs indicate the physical appearance (i.e. whether a free-standing gel or a free-flowing fluid) of these two worm dispersions at each copolymer concentration. These rheological time sweeps suggest critical gelation concentrations of approximately 15% w/w and 2.5 – 4.0% w/w for the PMPC₁₅-PHPMA₁₅₀ and PMPC₂₆-PHPMA₂₈₀ diblock copolymer worms, respectively. However, the CGC does not correspond to the formation of a free-standing gel for the PMPC₂₆-PHPMA₂₈₀ worms because only rather low gel moduli are observed at low copolymer concentrations for this system.

Small Angle X-ray Scattering (SAXS) Models

A general expression for the X-ray scattering intensity, I(q), resulting from a dispersion of uniform nano-objects can be expressed as:

$$I(q) = NS(q) \int_{0}^{\infty} \dots \int_{0}^{\infty} F(q, r_1, \dots r_k)^2 \Psi(r_1, \dots r_k) dr_1 \dots dr_k$$
(S1)

Here N is the number density of nano-objects per unit volume which is given by:

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

S(q) is the structure factor, $F(q, r_1, ..., r_k)$ is the form factor, $r_1, ..., r_k$ is a set of k parameters which describe the structural morphology, $\Psi(r_1, ..., r_k)$ is the polydispersity (distribution) function, $V(r_1, ..., r_k)$ is the volume of the nano-objects and φ is their volume fraction within the dispersion.

Spherical Micelle Model

The spherical micelle form factor to be used in equation S1 is expressed as:¹

$$F_{s}(q, r_{1}) = N_{s}^{2} \beta_{s}^{2} A_{s}^{2}(q, r_{1}) + N_{s} \beta_{c}^{2} F_{c}(q, R_{g}) + N_{s}(N_{s} - 1) \beta_{c}^{2} A_{c}^{2}(q) + 2N_{s}^{2} \beta_{s} \beta_{c} A_{s}(q, r_{1}) A_{c}(q)$$
(53)

where r_1 is the core radius of the spherical micelle and R_g is the radius of gyration of the corona block. The core and corona block X-ray scattering contrast is given by $\beta_s = V_s(\xi_s - \xi_{sol})$ and $\beta_c = V_c(\xi_c - \xi_{sol})$, respectively. ξ_s , ξ_c , and ξ_{sol} are the scattering length densities (SLDs) of the core block $(\xi_{HPMA} = 11.11 \times 10^{10} cm^{-2})$, the corona block $(\xi_{PMPC} = 11.6 \times 10^{10} cm^{-2})$ and the solvent $(\xi_{water} = 9.42 \times 10^{10} cm^{-2})$, respectively. V_s and V_c are the volumes of the core and corona block, respectively. Block copolymer volumes were obtained from the relation $V = \frac{M_{w,pol}}{\rho N_A}$ using $\rho_{PMPC} = 1.28 \text{ g cm}^{-3}$ and $\rho_{PHPMA} = 1.21 \text{ g cm}^{-3}$ as determined using a solution densitometer and helium pycnometry, respectively. Here $M_{w,pol}$ is the mean molecular weight of the PMPC₁₅ or PMPC₂₆ stabilizer block as determined by ¹H NMR spectroscopy and N_A is Avogadro's constant. The amplitude of the sphere form factor is used for that of the core self-term:

$$A_{\rm s}(q,r_1) = \Phi(qr_1) \exp\left(-\frac{q^2\sigma^2}{2}\right) \tag{S4}$$

where

$$\Phi(qr_1) = \frac{3[\sin(qr_1) - qr_1\cos(qr_1)]}{(qr_1)^3}$$
(55)

The spherical micelle form factor (equation S3) assumes a sigmoidal interface between the two blocks which is described by the exponent term in equation S4 with a width, σ , to account for the decaying SLD at the core-shell interface. During fitting the σ value was fixed at 2.5 Å. The self-correlation term for the corona block is expressed as the Debye function:

$$F_{\rm c}(q, R_{\rm g}) = \frac{2\left[\exp\left(-q^2 R_{\rm g}^2\right) - 1 + q^2 R_{\rm g}^2\right]}{q^4 R_{\rm g}^4}$$
(S6)

The form factor amplitude for the spherical micelle corona is given by:

$$A_{\rm c}(q) = \frac{\int_{r_1}^{r_1 + 2s} \mu_{\rm c}(r) \frac{\sin(qr)}{qr} r^2 dr}{\int_{r_1}^{r_1 + 2s} \mu_{\rm c}(r) r^2 dr} \exp\left(-\frac{q^2 \sigma^2}{2}\right)$$
(S7)

Here $\mu_c(r)$ denotes the radial profile, which can be expressed by the linear combination of two cubic splines using two fitting parameters *s* and *a* that correspond to the width of the profile and the weight coefficient, respectively. This information, along with the approximate integrated form of equation S7 can be found elsewhere.^{2,3}

The mean aggregation number for the spherical micelles is given by:

$$N_{\rm s} = (1 - x_{\rm sol}) \frac{\frac{4}{3} \pi r_1^3}{V_{\rm s}}$$
(S8)

where x_{sol} is the volume fraction of solvent (water) within the PHPMA micelle core. The micelle core radius, r_1 , is the only parameter that is assumed to be polydisperse and is described by a Gaussian distribution. Therefore, the polydispersity function in equation S1 can be written as:

$$\Psi(r_1) = \frac{1}{\sqrt{2\pi\sigma_{R_s}^2}} \exp\left(-\frac{(r_1 - R_s)^2}{2\sigma_{R_s}^2}\right)$$
(59)

Here R_s is the mean spherical micelle core radius and σ_{R_s} is the standard deviation of R_s . In accordance with equation S2, the number density per unit volume is expressed as:

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

Here φ represents the total volume fraction of copolymer forming the micelles and $V(r_1)$ is the total volume of copolymer in a micelle, which can be expressed as:

$$V(r_1) = (V_{\rm S} + V_{\rm C})N_{\rm S}(r_1)$$
(S11)

The structure factor, S(q), in equation S1 was assumed to be unity for this model as sufficiently low copolymer concentrations were used (1.0% w/w).

Worm-Like Micelle Model

For worm-like micelles, the form factor in equation S1 can be expressed as:⁴

$$F_{w}(q, r_{1}) = N_{w}^{2} \beta_{s}^{2} F_{sw}(q, r_{1}) + N_{w} \beta_{c}^{2} F_{c}(q, R_{g}) + N_{w} (N_{w} - 1) \beta_{c}^{2} S_{cc}(q) + 2N_{w}^{2} \beta_{s} \beta_{c} S_{sc}(q, r_{1})$$
(S12)

Where parameters previously defined in the spherical micelle model are the same unless otherwise stated. The worm-like micelle core (with radius, r_1) self-correlation term is given by:

$$F_{\rm sw}(q, r_1) = F_{\rm worm}(q, L_{\rm w}, b_{\rm w}) A_{\rm csw}^2(q, r_1)$$
(S13)

This is a product of a core cross-section term and a form factor for self-avoiding and semi-flexible chains which represents the worm-like micelle, $F_{worm}(q, L_w, b_w)$. Here L_w is the mean contour length of the worm-like micelle, and b_w is the Kuhn length of the worm-like micelle. A more complete expression for this chain form factor can be found in the original literature.² The core cross-section term is defined as:

$$F_{\rm csw}(q,r_1) = A_{\rm csw}^2(q,r_1) = \left[2\frac{J_1(qr_1)}{qr_1}\right]^2$$
(S14)

Here J_1 is the first-order Bessel function of the first kind. The corona blocks self-correlation term in equation S12 $[F_c(q, R_g)]$ is given by equation S6, while $S_{sc}(q, r_1)$, the interference cross-term between the corona chains and worm-like micelle core, is expressed as:

$$S_{\rm sc}(q, r_1) = \psi(qR_{\rm g})A_{\rm csw}(q, r_1)J_0[q(r_1 + R_{\rm g})]F_{\rm worm}(q, L_{\rm w}, b_{\rm w})$$
(S15)

where J_0 is the zero-order Bessel function of the first kind and $\psi(qR_g)$ is the corona chain form factor amplitude, which is expressed as:

$$\psi(qR_{\rm g}) = \frac{1 - \exp\left(-q^2 R_{\rm g}^2\right)}{\left(qR_{\rm g}\right)^2}$$
(S16)

 $S_{cc}(q)$ is the interference term between the worm corona chains, which is given by:

$$S_{\rm cc}(q) = \psi^2(qR_{\rm g}) J_0^2[q(r_1 + R_{\rm g})] F_{\rm worm}(q, L_{\rm w}, b_{\rm w})$$
(S17)

While the mean worm-like micelle aggregation number, $N_{\rm w}$, is expressed as:

$$N_{\rm w} = (1 - x_{\rm sol}) \frac{\pi r_1^2 L_{\rm w}}{V_{\rm s}}$$
(S18)

The worm-like micelle core radius, r_1 , is the only parameter that is assumed to be polydisperse and is described by a Gaussian distribution. Therefore, the polydispersity function in equation S1 can be written as:

$$\Psi(r_1) = \frac{1}{\sqrt{2\pi\sigma_{R_w}^2}} \exp\left(-\frac{(r_1 - R_w)^2}{2\sigma_{R_w}^2}\right)$$
(S19)

Here R_w is the *mean* worm-like micelle core radius and σ_{R_w} is its standard deviation. For this model the number density per unit volume is expressed similarly to equation S10. Again the structure factor, S(q), in equation S1 was assumed to be unity for this model as sufficiently low copolymer concentrations were used (1.0% w/w).

The programming tools available within Irena SAS macros for Igor Pro were used to implement the scattering models.⁵ Model fittings were performed using the least-squares method.

References

- 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.
- J. S. Pedersen and P. Schurtenberger, *Macromolecules*, 1996, **29**, 7602–7612.
- 5 J. Ilavsky and P. R. Jemian, J. Appl. Crystallogr., 2009, **42**, 347–353.