Electronic Supplementary Material (ESI) for Polymer Chemistry.

# Supporting Information

# Forced Gradient Copolymerisation: A Simplified Approach for Polymerisation-Induced Self-Assembly

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## EXPERIMENTAL SECTION

### Materials

Oligo(ethylene glycol) methyl ether methacrylate (OEGMA) ($M_n$ = 300 g mol$^{-1}$) (Sigma-Aldrich) and *N*,*N*-dimethyl acrylamide (DMA, Sigma-Aldrich) was deinhibited by passing through a column of basic alumina. Diacetone acrylamide (DAAm, Sigma-Aldrich) was purified by recrystallization from ethyl acetate. Zinc meso-tetra (*N*-methyl-4-pyridyl) porphine tetrachloride (ZnTMPyP, Frontier Scientific), 4-((((2-carboxyethyl)thio)carbonothioyl_thio)-4-cyanopentanoic acid (CTCPA, Boron Molecular), 2-hydroxypropyl methacrylate (HPMA, Sigma-Aldrich) and all other reagents were used as received unless otherwise specified.

### Instrumentation

All $^1$H-NMR spectra were recorded in d$_6$-DMSO using a Bruker 300 or 400 MHz spectrometer. All chemical shifts are reported in ppm (δ) relative to tetramethylsilane, referenced to the chemical shifts of residual solvent resonances.

The molecular weight and dispersity of the prepared polymers were measured by Gel Permeation Chromatography. The eluent was DMAc (containing 0.03% w/v LiBr and 0.05% w/v 2,6-dibutyl-4-methylphenol (BHT)) at 50 °C (flow rate of 1 mL/min) with a Shimadzu modular system comprising an SIL-20A auto-injector, a Polymer Laboratories 5.0 μm bead-size guard column (50 × 7.5 mm$^2$) followed by three linear PL (Styragel) columns (10$^5$, 10$^4$ and 10$^3$), an RID-10A differential refractive-index (RI) detector and a UV detector ($\lambda$ = 310 nm). The GPC was calibrated on commercial poly(methyl methacrylate) (PMMA) standards with molecular weights of 200 – 10$^6$ g mol$^{-1}$.

Dynamic Light Scattering (DLS) measurements were performed using a Malvern Zetasizer Nano Series running DTS software and using a 4 mW He−Ne laser operating at a wavelength of 633 nm and an avalanche photodiode (APD) detector. The scattered light was detected at an angle of 173°.

Transmission Electron Microscopy (TEM) studies of self-assembled copolymers were conducted at an accelerating voltage of 100 kV (JEOL-1400). The polymerization dispersions were diluted with water to give 0.2 - 0.5 wt% dispersions and deposited onto carbon-coated copper grids. Uranyl acetate stain was applied to all samples.

Photopolymerization reactions were performed using a Thorlabs M595L3 LED ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) equipped with a collimation adapter and powered by a DC4100 driver. The light intensity was measured using a Newport 843-R power meter.

A New Era NE-1000 multi-phaser syringe pump was used in conjunction with NormJect syringes to inject solutions into the reaction vial.

## Methods

### Kinetic studies of PET-RAFT dispersion polymerization of DMA and DAAm

Polymerization kinetics of the PET-RAFT dispersion copolymerization of DMA and DAAm ([DMA]:[DAAm]:[CTCPA]:[ZnTMPyP] = 30:270:1:0.02 and total solid content of 20 wt%) were conducted as follows: CTCPA (1.26 mg, $4.10\times10^{-6}$ mol), DMA (12.15 mg, 12.63 µL, $0.12 \times 10^{-3}$ mol), ZnTMPyP (72.21 µg, $8.17 \times 10^{-8}$ mol, 72.21 µL of a 1 mg/mL aqueous stock solution), DMF ( 7.31 mg, 10 µL, added as a $^1$H NMR internal standard), water (0.813 mL) and a 5mm magnetic stir bar were added to a 4 mL glass vial which was subsequently sealed with a rubber septum. The mixture was then purged with $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature with stirring at 200 rpm. Once the irradiation starts, deoxygenated DAAm (186.6 mg, $1.1 \times 10^{-3}$ mol, 186.6 µL in a 1 g/mL aqueous stock solution) was injected into the glass vial through a syringe pump in a gradient manner. In the first 20 minutes, DAAm was injected into the reaction at 0.58 µL/min. The injection rate was increased to 1.17 µL/min from 20-40 minutes, and 2.33 µL/min from 40-60 minutes. All DAAm was injected into the reaction from 60-80 minutes with 5.25 µL/min injection rate. At predetermined time points, aliquots were taken under $N_2$ for analysis by $^1$H NMR. Monomer conversions were calculated using $^1$H NMR ($d_6$-DMSO) relative to DMF as an internal standard. Unless otherwise stated, all monomer conversions were calculated using $^1$H NMR ($d_6$-DMSO) relative to DMF as an internal standard. DMA conversions were calculated using the following formula, $\alpha_{OEGMA} = 100 \times (1 - (DMA_t / DMF_t) / (DMA_0 / DMF_0))$, where $DMA_t = \int I^{5.8\text{-}5.6\text{ ppm}}$ at time, t; $DMA_0 = \int I^{5.8\text{-}5.6\text{ ppm}}$ of the initial polymerization mixture; $DMF_t = \int I^{7.9\text{-}8.1\text{ ppm}}$ at time, t and $DMF_0 = \int I^{7.9\text{-}8.1\text{ ppm}}$ of the initial polymerization mixture. DAAm conversion was calculated using the following equation $\alpha = 100 \times [p / (p+m)]$, where $m = \int I^{5.6\text{-}5.4}$ ppm and $p = [(\int I^{2.2\text{-}1.9}\text{ ppm} / 3) - (\int I^{5.6\text{-}5.4}\text{ ppm})]$.

## PET-RAFT dispersion polymerization of DMA and DAAm under orange light

A typical experiment ([DMA]:[DAAm]:[CTCPA]:[ZnTMPyP] = 30:270:1:0.02 and total solid content of 20 wt%) were conducted as follows: CTCPA (1.26 mg, $4.10\times10^{-6}$ mol), DMA (12.15 mg, 12.63 µL, $0.12 \times 10^{-3}$ mol), ZnTMPyP (72.21 µg, $8.17 \times 10^{-8}$ mol, 72.21 µL of a 1 mg/mL aqueous stock solution), DMF ( 7.31 mg, 10 µL, added as a $^1$H NMR internal standard), water (0.813 mL) and a 5mm magnetic stir bar were added to a 4 mL glass vial which was subsequently sealed with a rubber septum. The mixture was then purged with $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature with stirring at 200 rpm. Once the irradiation starts, deoxygenated DAAm (186.6 mg, $1.1 \times 10^{-3}$ mol, 186.6 µL in a 1 g/mL aqueous stock solution) was injected into the glass vial through a syringe pump in a gradient manner. In the first 20 minutes, DAAm was injected into the reaction at 0.58 µL/min. The injection rate was increased to 1.17 µL/min from 20-40 minutes, and 2.33 µL/min from 40-60 minutes. All DAAm was injected into the reaction from 60-80 minutes with 5.25 µL/min injection rate. The reaction was left at room temperature under irradiation for 24 hours before it was quenched by exposure to air (and storage in the dark). Monomer conversions were calculated using $^1$H NMR (d$_6$-DMSO) relative to DMF as an internal standard. GPC derived molecular weight values ($M_{n,GPC}$) and polymer dispersities ($Đ$) were determined against PMMA standards. Finally, TEM analysis was used to determine the size and the morphology of the self-assembled block copolymers.

## Kinetic studies of PET-RAFT dispersion polymerization of OEGMA$_{300}$ and HPMA

Polymerization kinetics of the PET-RAFT dispersion copolymerization of OEGMA$_{300}$ and HPMA ([OEGMA$_{300}$]:[HPMA]:[CTCPA]:[ZnTMPyP] = 80:320:1:0.02 and total solid content of 20 wt%) were conducted as follows: CTCPA (0.87 mg, $2.83\times10^{-6}$ mol), OEGMA$_{300}$ (68.14 mg, 64.90 µL, $2.16 \times 10^{-3}$ mol), ZnTMPyP (50.20 µg, $5.68 \times 10^{-8}$ mol, 50.20 µL of a 1 mg/mL aqueous stock solution), DMF (7.31 mg, 10 µL, added as a $^1$H NMR internal standard), water (1 mL) and a 5mm magnetic stir bar were added to a 4 mL glass vial which was subsequently sealed with a rubber septum. The mixture was then purged with dry $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature with stirring at 200 rpm. Once the irradiation started, deoxygenated HPMA (130.99 mg, 122.88 µL, $0.91 \times 10^{-3}$ mol) was injected into the glass vial through a syringe pump in a gradient manner. In the first 7 minutes, HPMA was injected into the reaction at 1.10 µL/min. The injection rate was increased to 2.19 µL/min from 7-14 minutes, and 4.39 µL/min from 14-21 minutes. All HPMA was injected into the reaction from 21-28 minutes with 9.87 µL/min injection rate with a total volume of 122.88 µL. At predetermined time points, aliquots were taken under $N_2$ for analysis by $^1$H NMR. Monomer conversions were calculated using $^1$H NMR (d$_6$-DMSO) relative to DMF as an internal standard. OEGMA$_{300}$ conversions were calculated using the following formula, $\alpha_{OEGMA} = 100 \times (1 - (OEGMA_t / DMF_t) / (OEGMA_0 / DMF_0))$, where $OEGMA_t = \int I^{\ 6.15\text{-}6.05\ ppm}$ at time, t; $OEGMA_0 = \int I^{\ 6.1\text{-}6.05\ ppm}$ of the initial polymerization mixture; $DMF_t = \int I^{\ 7.9\text{-}8.1\ ppm}$ at time, t and $DMF_0 = \int I^{7.9\text{-}8.1\ \mathrm{ppm}}$ of the initial polymerization mixture. HPMA conversion was calculated using the following equation $\alpha = 100 \times [p / (p+m)]$, where $m = \int I^{6.05\text{-}5.95}$ ppm and $p = [(\int I^{2.2\text{-}1.5}$ ppm / 3) - ($\int I^{6.05\text{-}5.95}$ ppm)].

### PET-RAFT dispersion polymerization of OEGMA$_{300}$ and HPMA under orange light

A typical experiment ([OEGMA$_{300}$]:[HPMA]:[CTCPA]:[ZnTMPyP] = 80:320:1:0.02 and total solid content of 20 wt%) were set up as follows: CTCPA (0.87 mg, $2.83 \times 10^{-6}$ mol), OEGMA$_{300}$ (68.14 mg, 64.90 µL, 2.16 $\times 10^{-3}$ mol), ZnTMPyP (50.20 µg, $5.68 \times 10^{-8}$ mol, 50.20 µL of a 1 mg/mL aqueous stock solution), DMF ( 7.31 mg, 10 µL, added as a $^1$H NMR internal standard), water (1 mL) and a 5mm magnetic stir bar were added to a 4 mL glass vial which was subsequently sealed with a rubber septum. The mixture was then purged with $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature with stirring at 200 rpm. Once the irradiation starts, deoxygenated HPMA (130.99 mg, 122.88 µL, $0.91 \times 10^{-3}$ mol) was injected into the glass vial through a syringe pump in a gradient manner. In the first 7 minutes, HPMA was injected into the reaction at 1.10 µL/min. The injection rate was increased to 2.19 µL/min from 7-14 minutes, and 4.39 µL/min from 14-21 minutes. All HPMA was injected into the reaction from 21-28 minutes with 9.87 µL/min injection rate. The reaction was left at room temperature under irradiation for 3 hours before it was quenched by exposure to air (and storage in the dark). Monomer conversions were calculated by $^1$H NMR (d$_6$-DMSO) using DMF as an internal standard. GPC derived molecular weight values ($M_{n,\ GPC}$) and polymer dispersities ($Đ$) were determined against PMMA standards. Finally, TEM analysis was used to determine the size and the morphology of the self-assembled block copolymers.

### Synthesis of POEGMA$_{300}$ macroRAFT agent by thermally initiated RAFT polymerization

OEGMA$_{300}$ (9.37 ml, 9.84 g, $3.28 \times 10^{-2}$ mol), CTCPA (0.05 g, $1.64 \times 10^{-4}$ mol), AIBN (1.64 mg, $1 \times 10^{-5}$ mol) and 20 mL toluene were added to a 100 mL round bottom flask which was sealed with a rubber septum and purged with $N_2$ for 30 min at 0 °C. The polymerization was carried out for 5 h at 70 °C before quenching in an ice bath and exposing to air. The resulting polymer was purified by repeated precipitation in a mixture (30:70, v/v) of petroleum spirits and diethyl ether.

### PET-RAFT dispersion polymerization of HPMA with POEGMA$_{300}$ macroRAFT agent

A typical experiment ([HPMA]:[MacroRAFT]:[ZnTMPyP] = 400:1:0.02 and a total solid content of 20 wt%) was set up as follows: MacroRAFT (68.44 mg, $2.28 \times 10^{-6}$ mol), HPMA (131.56 mg, 123.41 µL, $0.91 \times 10^{-3}$ mol), ZnTMPyP (40.34 µg, $4.56 \times 10^{-8}$ mol, 40.34 µL of a 1 mg/mL aqueous stock solution), DMF (7.31 mg, 10 µL added as a $^1$H NMR internal standard) and water (1 mL) were added to a 21 mL vial. The reaction mixture was transferred to a 4 mL glass vial equipped with a 5 mm magnetic stir bar and the vial subsequently sealed with a rubber septum. The mixture was then purged with $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature for 3 h with stirring at 200 rpm before it was quenched by exposure to air (and storage in the dark). Monomer conversions were calculated by $^1$H NMR (d$_6$-DMSO) using DMF as an internal standard. GPC derived molecular weight values ($M_{n,GPC}$) and polymer dispersities ($Đ$) were determined against PMMA standards. Finally, TEM analysis was used to determine the size and the morphology of the self-assembled block copolymers.

## Synthesis of PEG$_{113}$-CDTPA macroRAFT

The synthesis of PEG113-CDTPA was performed using a modified procedure from literature[1]: CDTPA (0.97 g, 2.4 mmol) in DCM (20 mL) was added to a flask containing PEG113 (6 g, 1.2 mmol) and a stirrer bar. Then a solution of DCC (0.5 g, 2.4 mmol) and DMAP (0.029 g, 0.24 mmol) in DCM (10 mL) was added dropwise to the reaction mixture at 0 °C. The flask was sealed with a rubber septum and purged with nitrogen for 30 min at 0 °C. The esterification reaction was stirred at room temperature for 48 h. The polymer was collected by repeated precipitation of the reaction mixture in cold diethyl ether.

## PET-RAFT dispersion polymerization of HPMA with PEG$_{113}$-CDTPA macroRAFT agent

A typical experiment ([HPMA]:[MacroRAFT]:[ZnTMPyP] = 400:1:0.02 and a total solid content of 20 wt%) was set up as follows: MacroRAFT (15.96 mg, 3.192 × 10$^{-6}$ mol), HPMA (184.04 mg, 172.65 µL, 1.27 × 10$^{-3}$ mol), ZnTMPyP (56.43 µg, 6.38 × 10$^{-8}$ mol, 56.43 µL of a 1 mg/mL aqueous stock solution), DMF (7.31 mg, 10 µL added as a $^1$H NMR internal standard) and water (1 mL) were added to a 21 mL vial. The reaction mixture was transferred to a 4 mL glass vial equipped with a 5 mm magnetic stir bar and the vial subsequently sealed with a rubber septum. The mixture was then purged with $N_2$ for 20 minutes followed by irradiation with orange LED light ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) at room temperature for 3 h with stirring at 200 rpm before it was quenched by exposure to air (and storage in the dark). Monomer conversions were calculated by $^1$H NMR (d$_6$-DMSO) using DMF as an internal standard. GPC derived molecular weight values ($M_{n,GPC}$) and polymer dispersities ($Đ$) were determined against PMMA standards. Finally, TEM analysis was used to determine the size and the morphology of the self-assembled block copolymers.

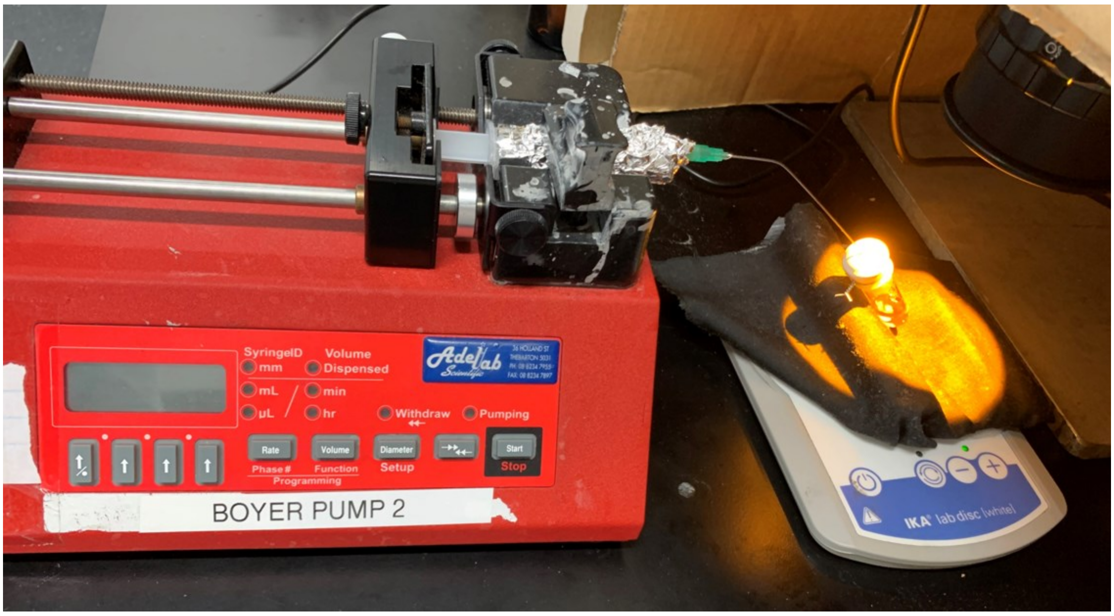


**Figure S1.** Digital photograph of a typical set-up for gradient PET-RAFT dispersion copolymerization.

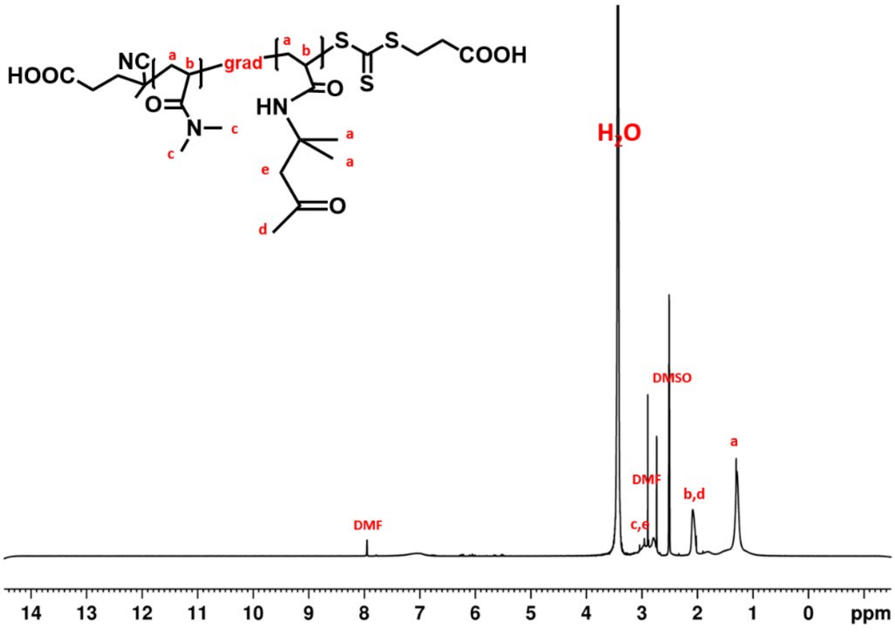


**Figure S2.** Typical $^1$H NMR spectrum (recorded in d$_6$-DMSO) of a poly(DMA-*gradient*-DAAm) copolymer synthesized via the dispersion PET-RAFT copolymerization of DMA and with injection of DAAm.

**Table S1.** Experimental and characterization data for the PET-RAFT dispersion copolymerization of DMA and DAAm with varying monomer ratios and target DPs at a total solids content of 15 wt%. Polymerizations were conducted under orange light irradiation (λmax = 595 nm, 10.2 mW/cm2) using [CTCPA]:[ZnTMPyP] = 1:0.02. S = Sphere, W = Worm, P = Precipitation. n/r = not run.

| Entry | [DAAm]:[DMA] | Overall DP | DMA Composition (mol%) | Overall Conversion (%) | $M_{n,\text{ Theo}}$ (g/mol) | $M_{n,\text{ GPC}}$ (g/mol) | Đ | Morphology (Major / Minor) |
|---|---|---|---|---|---|---|---|---|
| **PISA-19** | **210:90** | **300** | **30** | **93** | **41 600** | **39 100** | **1.26** | **S** |
| **PISA-20** | **225:75** | **300** | **25** | **85** | **38 900** | **27 500** | **1.12** | **S** |
| **PISA-21** | **240:60** | **300** | **20** | **83** | **38 900** | **20 900** | **1.11** | **S** |
| **PISA-22** | **255:45** | **300** | **15** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-23** | **270:30** | **300** | **10** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-24** | **285:15** | **300** | **5** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-25** | **280:120** | **400** | **30** | **82** | **48 800** | **34 800** | **1.10** | **S** |
| **PISA-26** | **300:100** | **400** | **25** | **90** | **54 800** | **43 800** | **1.14** | **S/W** |
| **PISA-27** | **320:80** | **400** | **20** | **87** | **54 200** | **44 900** | **1.14** | **W/S** |
| **PISA-28** | **340:60** | **400** | **15** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-29** | **360:40** | **400** | **10** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-30** | **380:20** | **400** | **5** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-31** | **350:150** | **500** | **30** | **80** | **59 500** | **31 600** | **1.1** | **W/S** |
| **PISA-32** | **375:125** | **500** | **25** | **85** | **64 700** | **30 200** | **1.09** | **W** |
| **PISA-33** | **400:100** | **500** | **20** | **80** | **62 300** | **30 700** | **1.11** | **W** |
| **PISA-34** | **425:75** | **500** | **15** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-35** | **450:50** | **500** | **10** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |
| **PISA-36** | **475:25** | **500** | **5** | **n/r** | **n/r** | **n/r** | **n/r** | **P** |

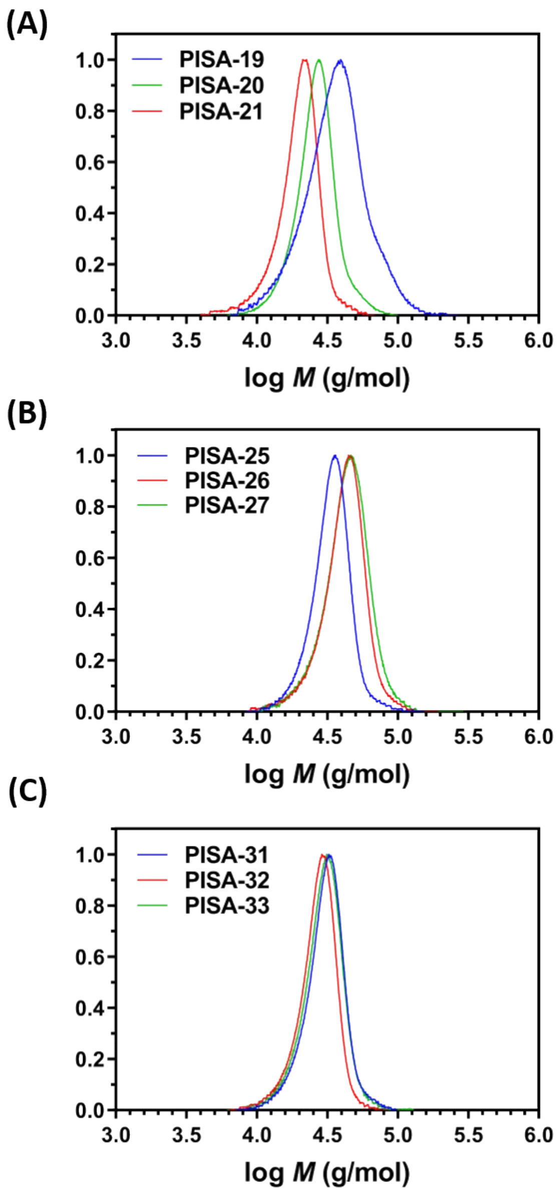


**Figure S3.** Molecular weight distributions from the PET-RAFT forced-gradient dispersion polymerization of DMA and DAAm with varying monomer ratios and target DPs at a total solids content of 15 wt%. Polymerizations were conducted under orange light irradiation (λmax = 595 nm, 10.2 mW/cm2) using [CTCPA]:[ZnTMPyP] = 1:0.02.

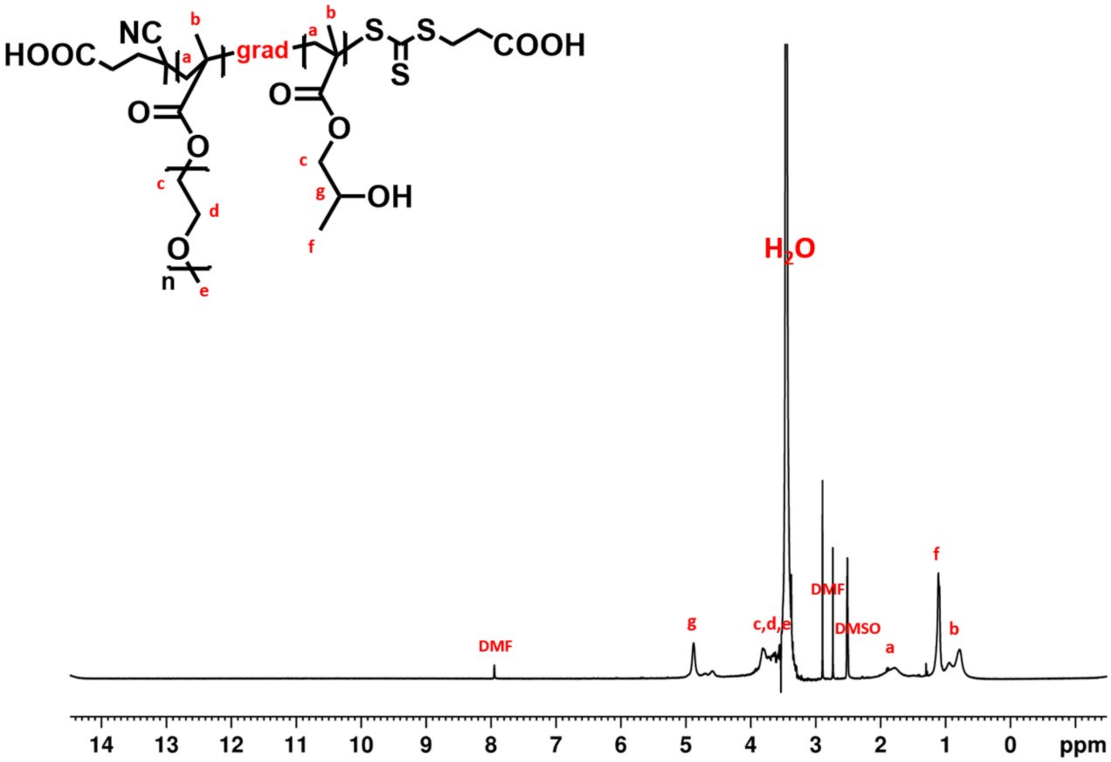


**Figure S4.** Typical $^1$H NMR spectrum (recorded in d$_6$-DMSO) of a purified poly(OEGMA$_{300}$-*grad*-HPMA) copolymer synthesized via the dispersion PET-RAFT copolymerization of OEGMA$_{300}$ and HPMA.

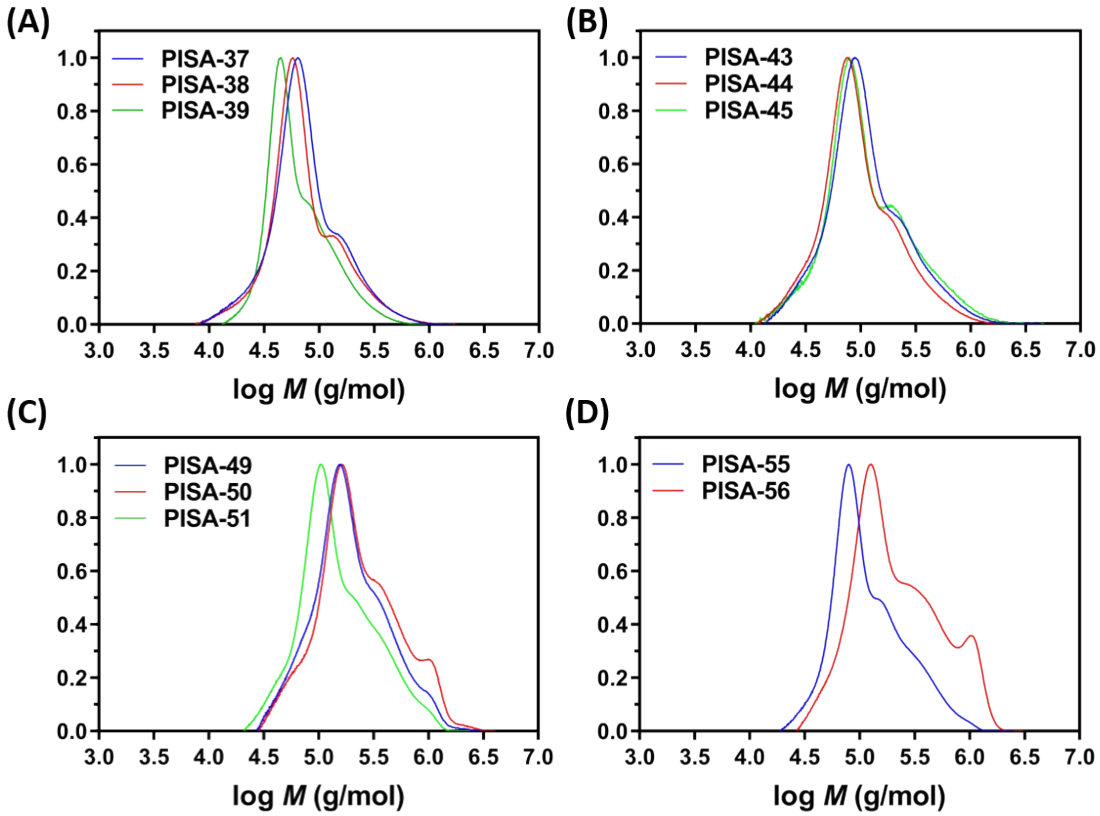


**Figure S5.** Molecular weight distributions from the PET-RAFT gradient dispersion polymerization of $OEGMA_{300}$ and HPMA with varying monomer ratios and target DPs at a total solids content of 20 wt%. Polymerizations were conducted under orange light irradiation ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) using [CTCPA]:[ZnTMPyP] = 1:0.02. (For detailed experimental and characterization data, please refer to **Table 2**)

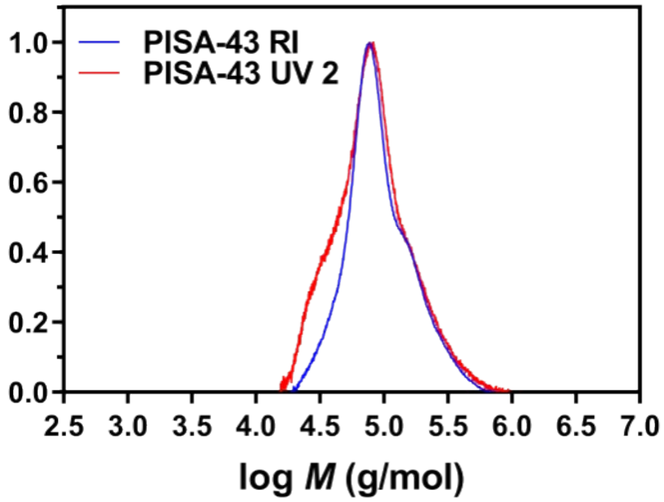
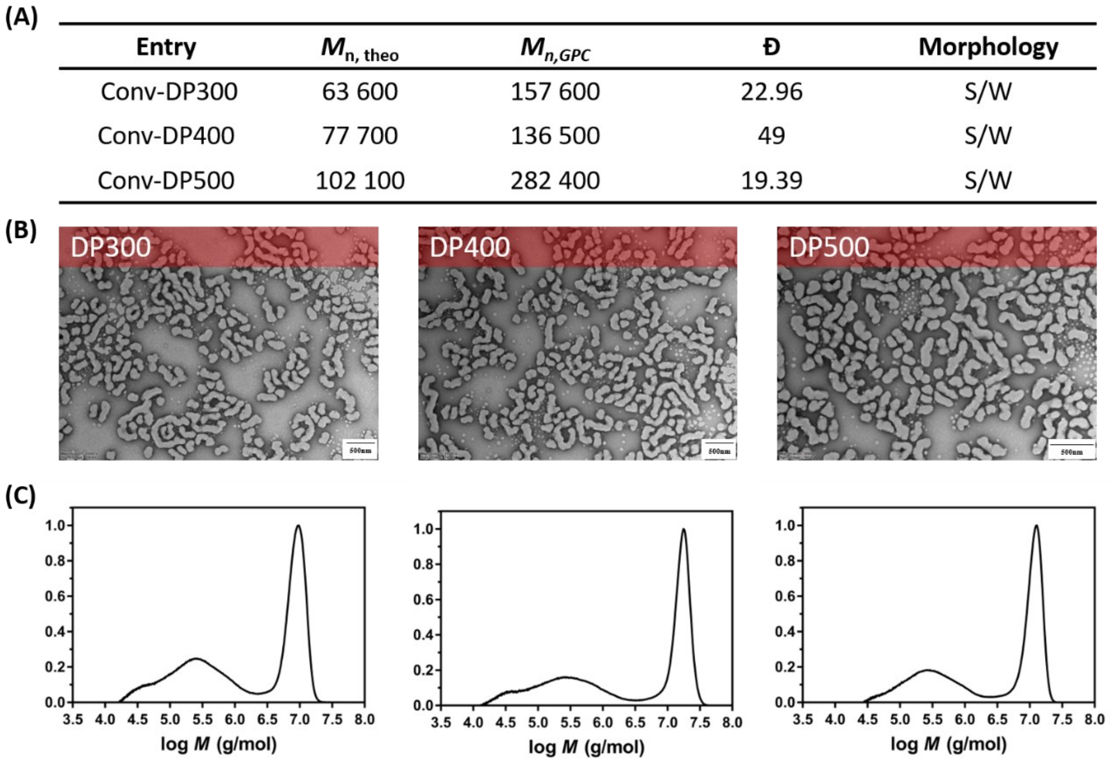


**Figure S6.** Overlay of molecular weight distributions of **PISA-43** obtained by RI and UV detector through GPC. Polymerization were performed by the PET-RAFT gradient dispersion polymerization of $OEGMA_{300}$ and HPMA at a total solids content of 20 wt%. Polymerizations were conducted under orange light irradiation ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) using [CTCPA]:[ZnTMPyP] = 1:0.02. (For detailed experimental and characterization data, please refer to **Table 2**)



(A)

| Entry | $M_{n,\,theo}$ | $M_{n,GPC}$ | Đ | Morphology |
|---|---|---|---|---|
| Conv-DP300 | 63 600 | 157 600 | 22.96 | S/W |
| Conv-DP400 | 77 700 | 136 500 | 49 | S/W |
| Conv-DP500 | 102 100 | 282 400 | 19.39 | S/W |

**Figure S7.** (**A**) Experimental and characterization data for the PET-RAFT dispersion polymerization of HPMA in the presence of $POEGMA_{300}$ as a macroRAFT agent. Polymerizations were conducted using a [CTCPA]:[ZnTMPyP] = 1:0.02 under orange light irradiation ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) for 3 h at a total solids content of 20 wt%. (**B**) representative TEM micrographs: S = Spheres, W = Worms, and (**C**) corresponding molecular weight distributions by GPC for nanoparticles shown in (B).

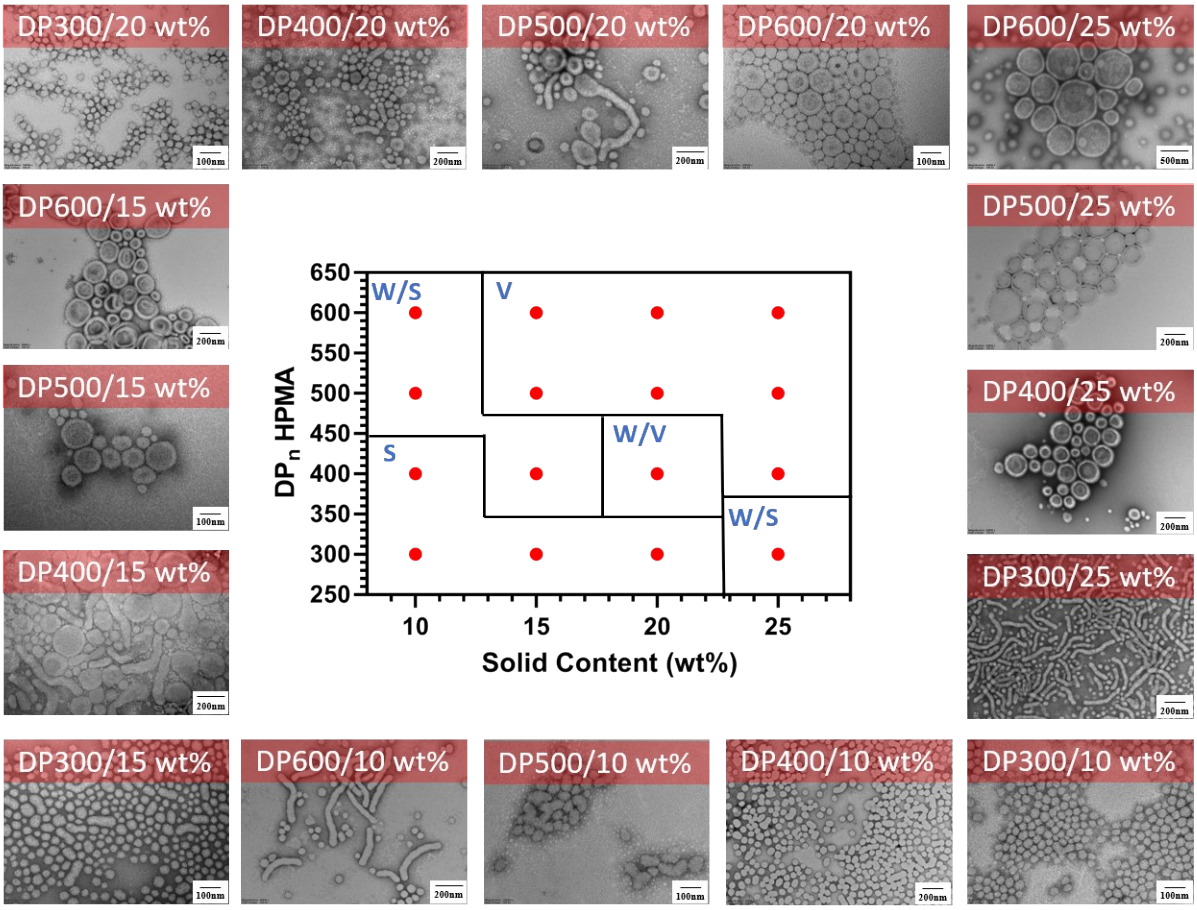


**Figure S8.** Representative TEM micrographs and corresponding phase diagram for a series of nanoparticles synthesized using PET-RAFT dispersion polymerization of HPMA in the presence of $PEG_{113}$-CDTPA macroRAFT with varying target DPs and total solids content. Polymerizations were conducted under orange light irradiation ($\lambda_{max}$ = 595 nm, 10.2 mW/cm$^2$) using [CTCPA]:[ZnTMPyP] = 1:0.02. S = Sphere, W = Worm, V = vesicles.

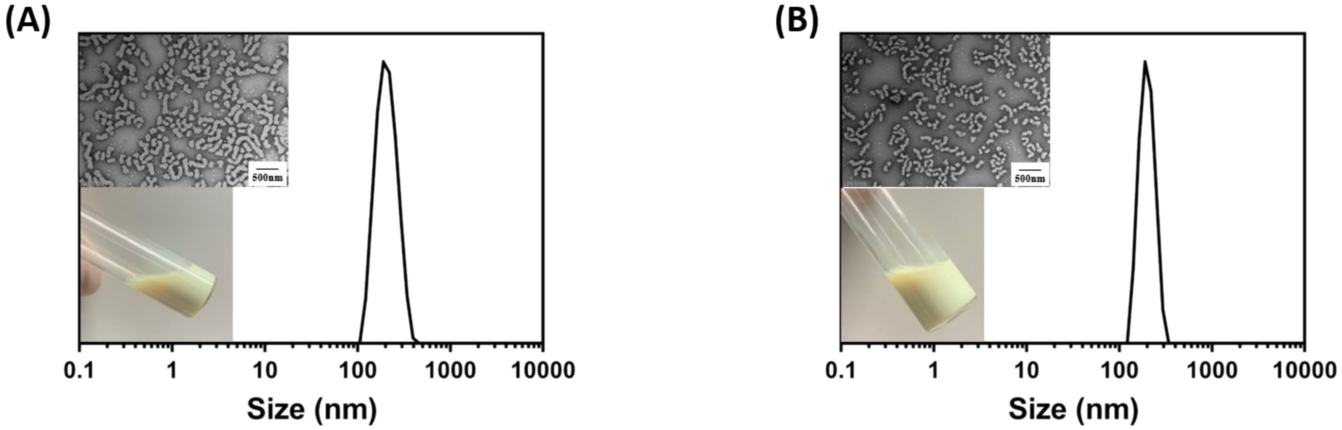


**Figure S9.** (**A**) DLS derived intensity-based size distributions, TEM micrographs and digital photograph of self-assembled POEGMA$_{300}$-*b*-PHPMA nanoparticles (**Conv-DP400**) at 25 ℃, and (**B**) POEGMA$_{300}$-b-HPMA nanoparticles (**Conv-DP400**) at 40 ℃.

## Additional References:

1. J. Tan, H. Sun, M. Yu, B. S. Sumerlin and L. Zhang, *ACS Macro Lett.*, 2015, **4**, 1249-1253.