Supporting Information for:

Optimization of the high-throughput synthesis of multiblock copolymer nanoparticles in aqueous media *via* polymerization-induced self-assembly

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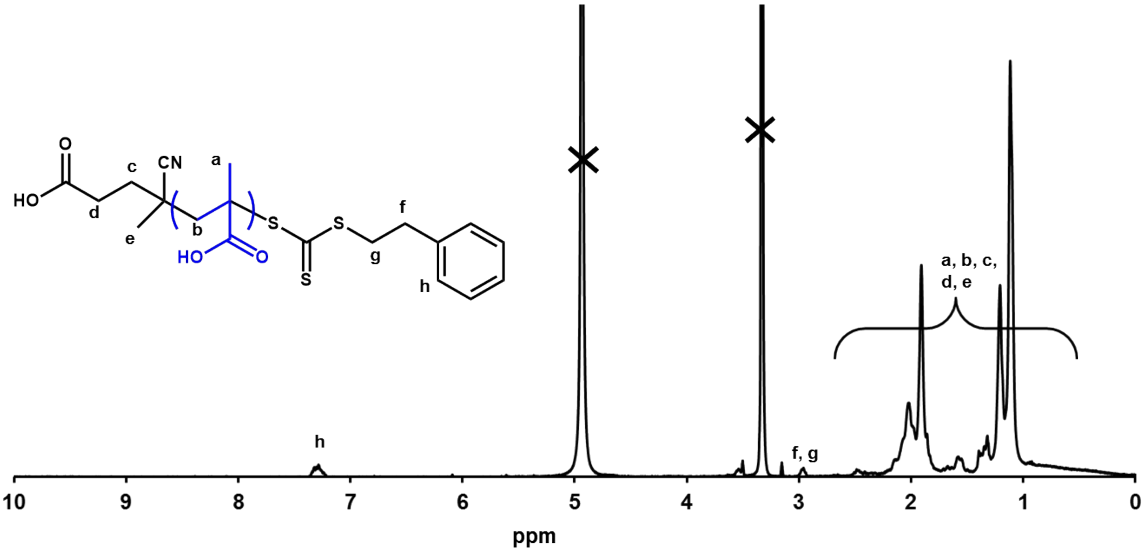
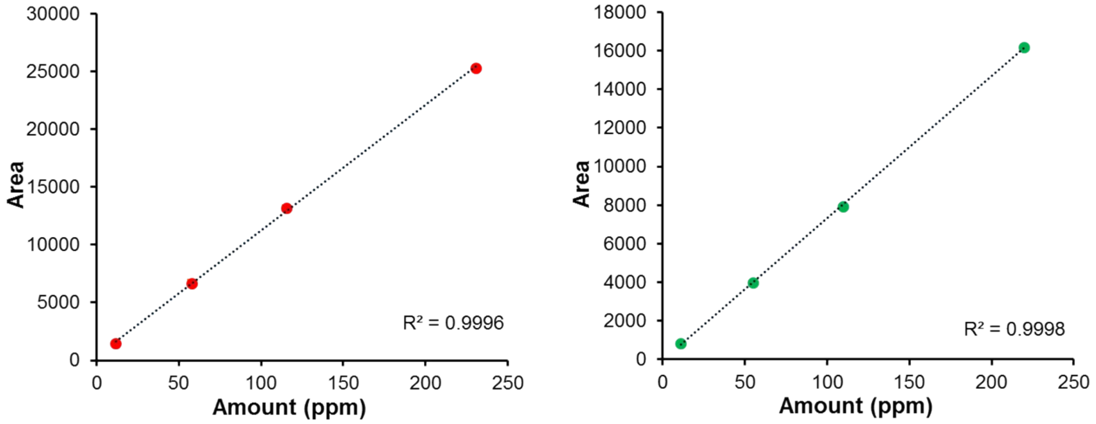
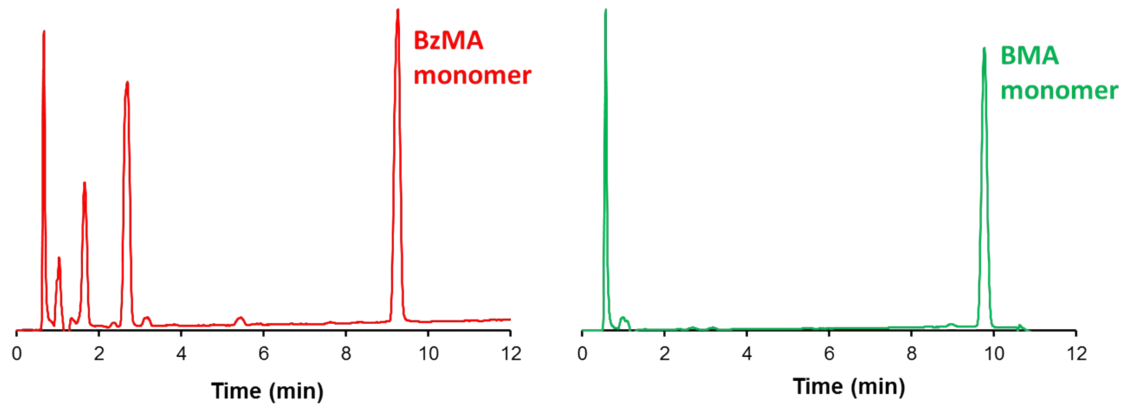


Figure S1. ^{1}H NMR spectra for purified PMAA$_{56}$ macro-CTA prepared *via* RAFT alcoholic solution polymerization. Integration of relevant peaks indicates a PMAA degree of polymerization (DP) of 56. The peaks marked with a cross are from the NMR solvent d_4-methanol (~3.3 ppm) and water (~3.5 ppm).



a) BzMA calibration plot

b) BMA calibration plot



c) $PMAA_{56}$-$PBzMA_{500}$

d) $PMAA_{56}$-$PBMA_{500}$

Figure S2. Monomer conversions for all high-throughput syntheses were determined by using HPLC to calculate the amount of residual monomer (ppm). Example calibration plots for (a) BzMA monomer and (b) BMA monomer and example chromatograms for (c) $PMAA_{56}$-$PBzMA_{500}$ and (d) $PMAA_{56}$-$PBMA_{500}$ are shown in this figure.

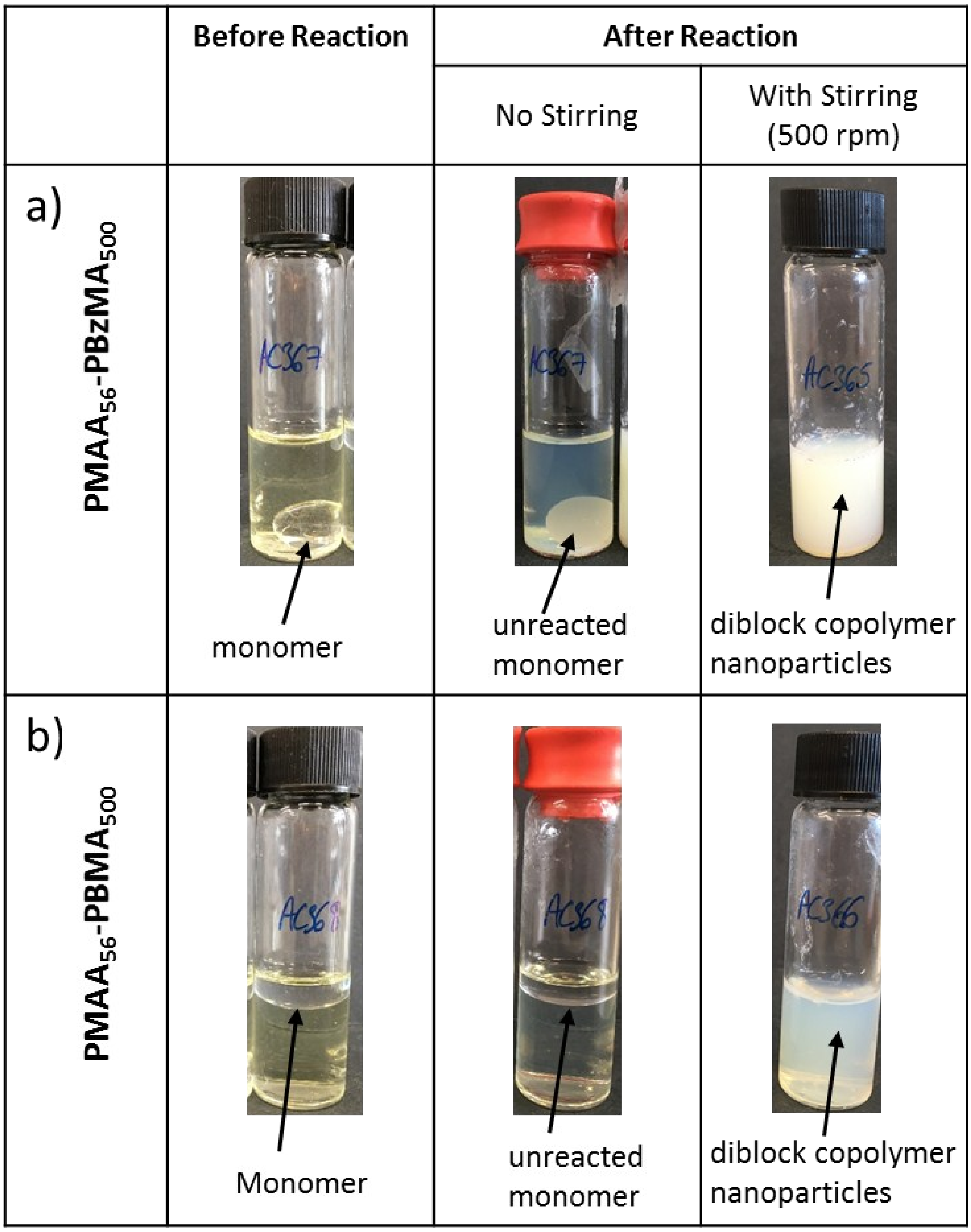


Figure S3. Digital photographs showing initial reaction mixtures and final diblock copolymer nanoparticle dispersions for the laboratory-scale synthesis of (a) $PMAA_{56}$-$PBzMA_{500}$ and (b) $PMAA_{56}$-$PBMA_{500}$. Reactions were either unstirred or stirred at 500 rpm with a magnetic flea. No significant polymerization was obtained for the *unstirred* reaction solution as judged by ^{1}H NMR spectroscopy.

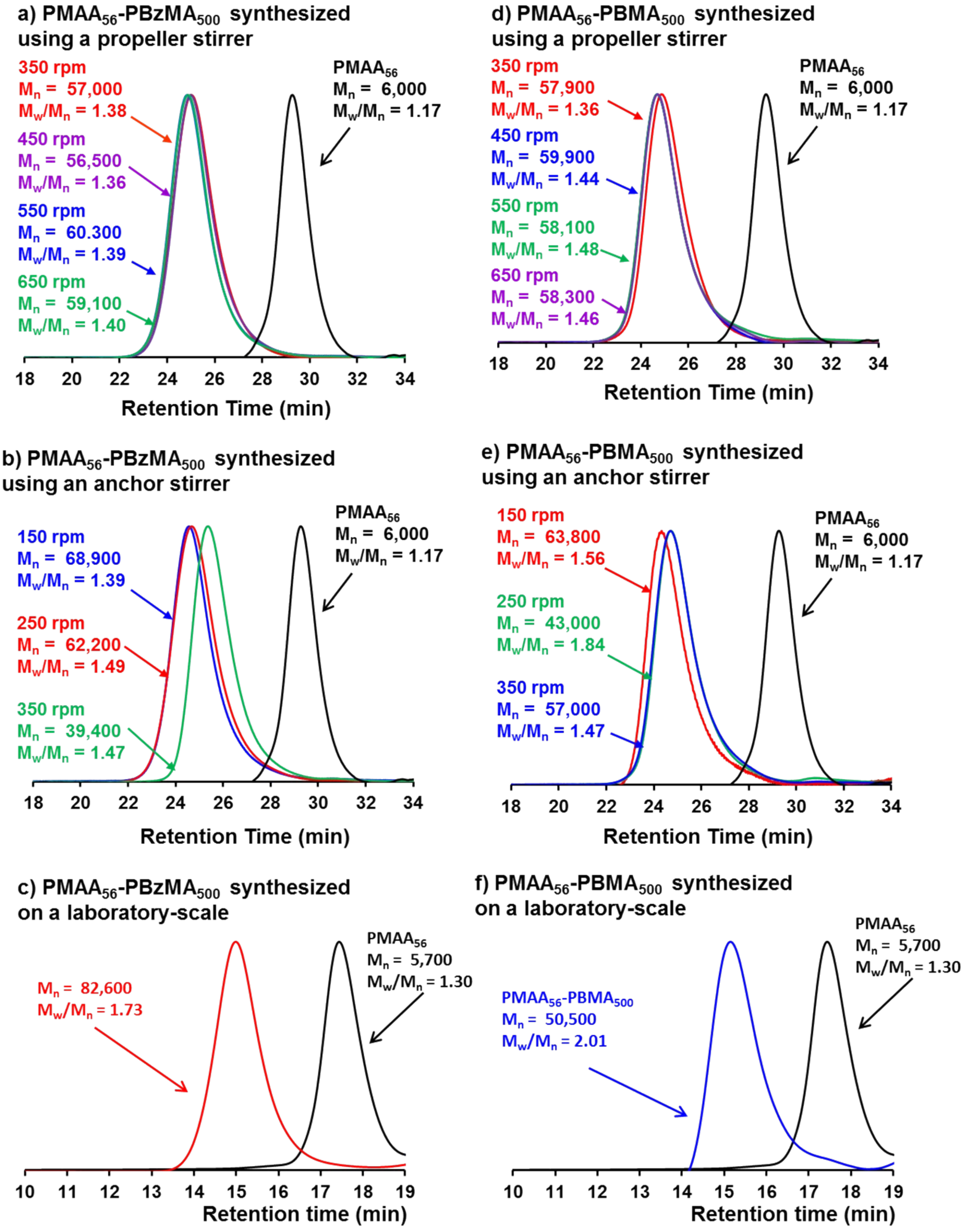
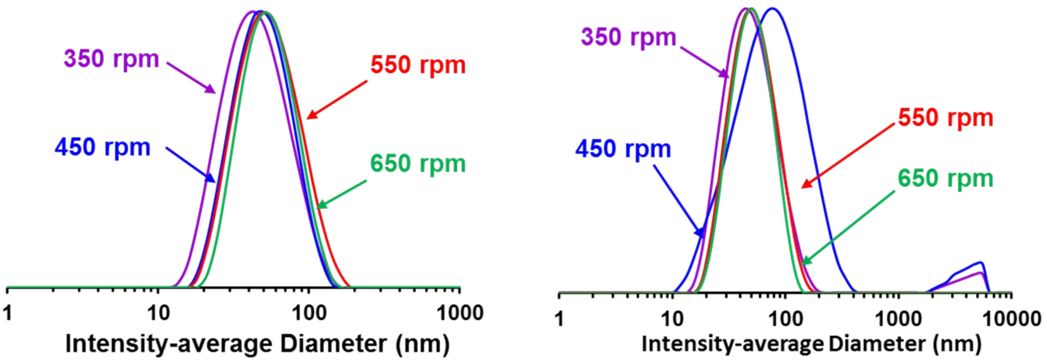
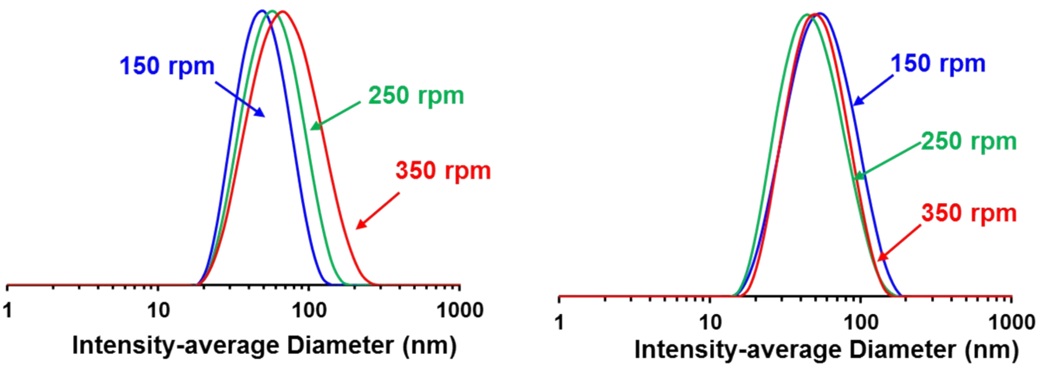


Figure S4. THF GPC chromatograms corresponding to the data reported in Table 2. This data demonstrates the effect of stirrer geometry and stirring rate (rpm) on the synthesis of PMAA$_{56}$-PBzMA$_{500}$ and PMAA$_{56}$-PBMA$_{500}$ diblock copolymer nanoparticles *via* high-throughput RAFT aqueous emulsion polymerization at 70 ^{o}C. Chromatograms for the corresponding laboratory-scale polymers are included for comparison. All reactions were performed at 20 % w/w solids using a macro-CTA/initiator molar ratio of 5.0.



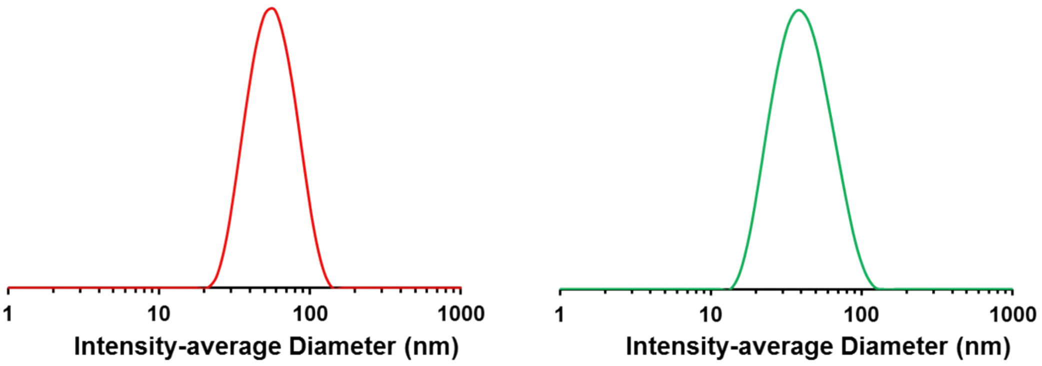
a) PMAA$_{56}$-PBzMA$_{500}$ synthesized using a *propeller* stirrer

d) PMAA$_{56}$-PBMA$_{500}$ synthesized using a *propeller* stirrer



b) PMAA$_{56}$-PBzMA$_{500}$ synthesized using an *anchor* stirrer

e) PMAA$_{56}$-PBMA$_{500}$ synthesized using an *anchor* stirrer



c) PMAA$_{56}$-PBzMA$_{500}$ synthesized on a laboratory scale

f) PMAA$_{56}$-PBzMA$_{500}$ synthesized on a laboratory scale

Figure S5. Intensity-average size distribution plots for dynamic light scattering data reported in Table 1 and Figure 2. This data demonstrates the effect of stirrer geometry and stirring rate (rpm) on the synthesis of PMAA$_{56}$-PBzMA$_{500}$ and PMAA$_{56}$-PBMA$_{500}$ diblock copolymer nanoparticles *via* high-throughput RAFT aqueous emulsion polymerization at 70 ^{o}C. All reactions were performed at 20 % w/w solids using a macro-CTA/initiator molar ratio of 5.0. Intensity-average size distribution plots for the equivalent laboratory-scale syntheses (c) and (f) are also included for comparison.

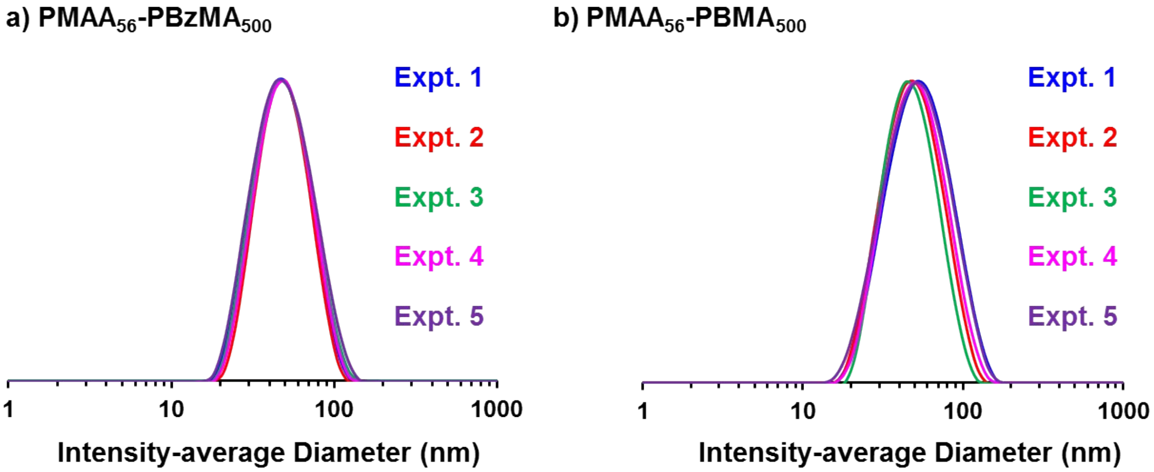
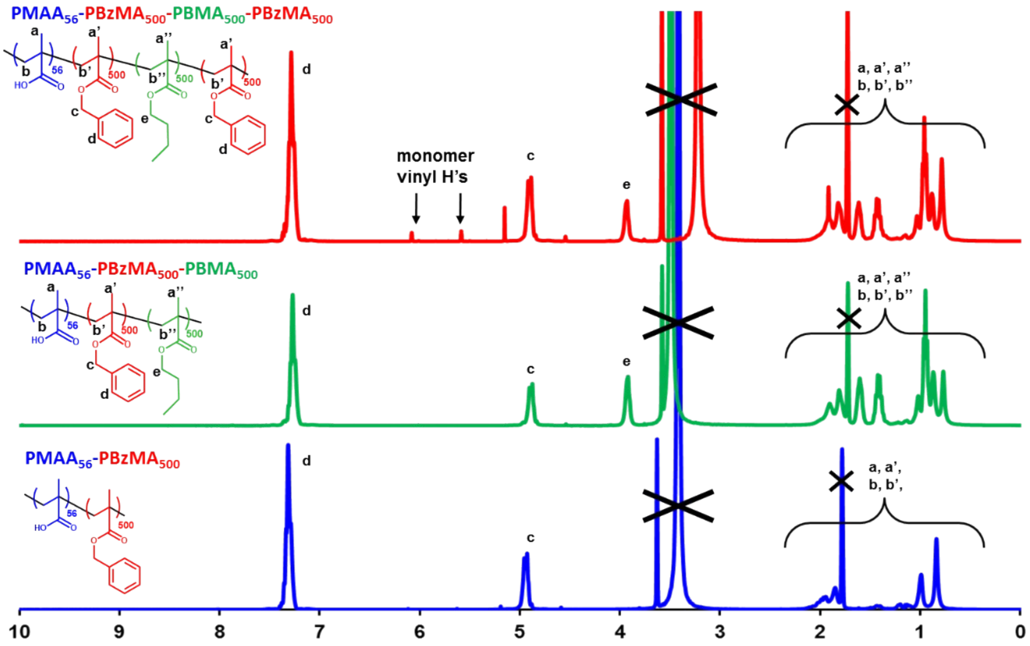


Figure S6. Intensity-average size distribution plots for dynamic light scattering data reported in Table 2. This data demonstrates the reproducibility of the PISA synthesis of diblock copolymer nanoparticles *via* high-throughput RAFT aqueous emulsion polymerization of either benzyl methacrylate (BzMA) or *n*-butyl methacrylate (BMA) at 70 °C using a $PMAA_{56}$ macro-CTA at pH 5.

a) Route A



b) Route B

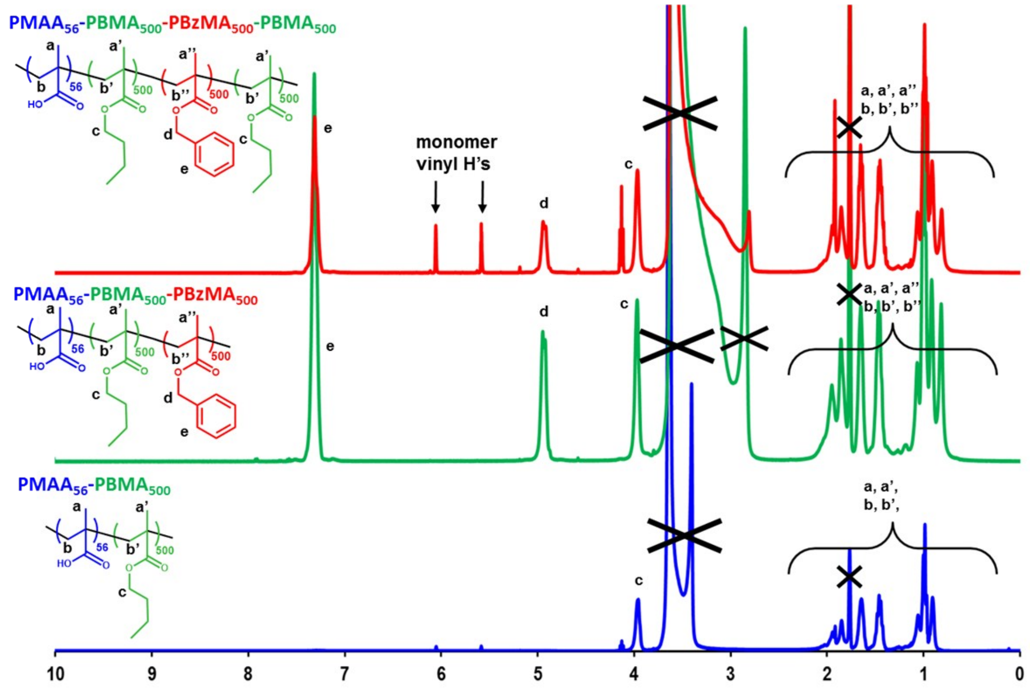


Figure S7. ^{1}H NMR spectra for diblock, triblock and tetrablock copolymers prepared *via* RAFT aqueous emulsion polymerization. These syntheses were performed on the high-throughput Chemspeed A100 robot synthesizer via either (a) Route A or (b) Route B as outlined in Scheme 2. The peaks labelled with a black cross correspond to solvent peaks from d_8-tetrahydrofuran (1.73 ppm and 3.58 ppm) and water (~3.5 ppm)

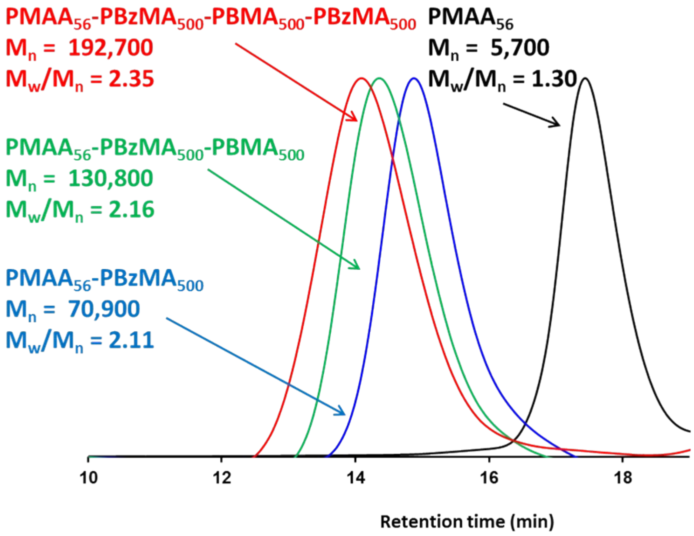
	Target Composition	Overall Monomer Conversion[a] (%)		Average Particle diameter (nm) by DLS	Average Particle PDI by DLS	Average Particle diameter (nm) by TEM	M_n[b]	M_w/M_n[b]
		BzMA	BMA					
High-Throughput Syntheses	$PMAA_{56}$-$PBzMA_{500}$	99	-	49	0.17	38	69,200	1.55
	$PMAA_{56}$-$PBzMA_{500}$-$PBMA_{500}$	> 99	> 99	86	0.09	60	95,500	1.59
	$PMAA_{56}$-$PBzMA_{500}$-$PBMA_{500}$-$PBzMA_{500}$	96	> 99	106	0.10	64	130,400	1.64
	$PMAA_{56}$-$PBMA_{500}$	-	94	47	0.21	40	69,000	1.62
	$PMAA_{56}$-$PBMA_{500}$-$PBzMA_{500}$	> 99	> 99	82	0.16	49	103,900	1.85
	$PMAA_{56}$-$PBMA_{500}$-$PBzMA_{500}$-$PBMA_{500}$	100	87	117	0.17	61	129,400	1.84
Laboratory-Scale Syntheses	$PMAA_{56}$-$PBzMA_{500}$	> 99	-	64	0.16	40	79,900	2.11
	$PMAA_{56}$-$PBzMA_{500}$-$PBMA_{500}$	> 99	> 99	80	0.13	57	130,800	2.16
	$PMAA_{56}$-$PBzMA_{500}$-$PBMA_{500}$-$PBzMA_{500}$	96	> 99	121	0.17	63	192,700	2.35
	$PMAA_{56}$-$PBMA_{500}$	-	> 99	62	0.15	48	87,800	2.00
	$PMAA_{56}$-$PBMA_{500}$-$PBzMA_{500}$	> 99	> 99	90	0.17	52	205,700	2.30
	$PMAA_{56}$-$PBMA_{500}$-$PBzMA_{500}$-$PBMA_{500}$	>99	> 99	109	0.16	67	280,200	2.25

Table S1. Summary of diblock, triblock and tetrablock copolymers prepared *via* RAFT aqueous emulsion polymerization. These syntheses were performed either on the high-throughput Chemspeed A100 robot synthesizer or on a laboratory-scale. These multiblock copolymer syntheses were performed at 70 °C using a $PMAA_{56}$ macro-CTA/initiator of 5.0, in aqueous solution at pH 5.

[a] Conversion determined by high-performance liquid chromatography (HPLC) for high-throughput syntheses and by ^1H NMR for laboratory-scale syntheses.

[b] Molecular weight data determined by GPC using THF eluent containing 4 % v/v glacial acetic acid (calibrated using a series of near-monodisperse poly(methyl methacrylate) standards). These two data sets were analyzed using separate GPC instruments with differing column sets. Moreover, the copolymers obtained from the laboratory-scale syntheses were methylated using excess trimethylsilyldiazomethane, whereas those prepared using the high-throughput protocol were not subjected to this chemical derivatization. See Experimental for more details.

a) Route A: THF GPC chromatograms



b) Route B: THF GPC chromatograms

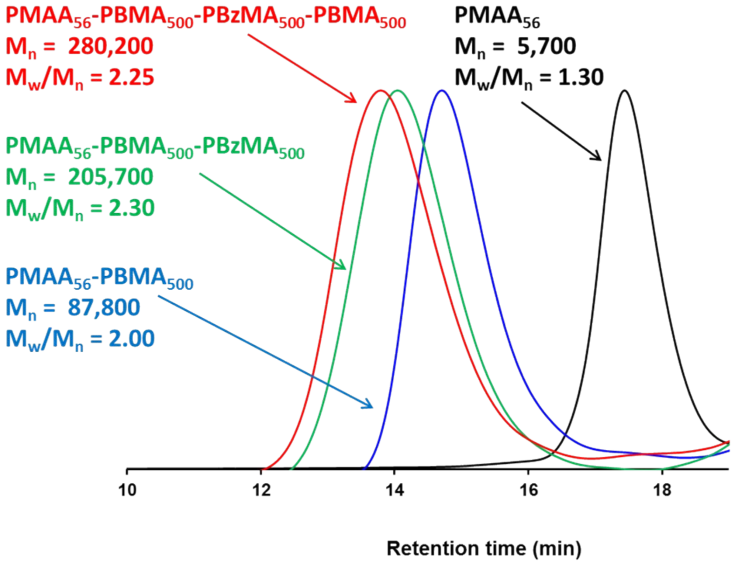


Figure S8. THF GPC chromatograms for diblock, triblock and tetrablock copolymers prepared *via* RAFT aqueous emulsion polymerization on a laboratory-scale. These block copolymers were prepared via either (a) Route A or (b) Route B as outlined in Scheme 2. The high-throughput and laboratory-scale polymers were analyzed using separate GPC instruments with differing column sets. Moreover, the copolymers obtained from the laboratory-scale syntheses were methylated using excess trimethylsilyldiazomethane, whereas those prepared using the high-throughput protocol were not subjected to this chemical derivatization. See Experimental for more details.

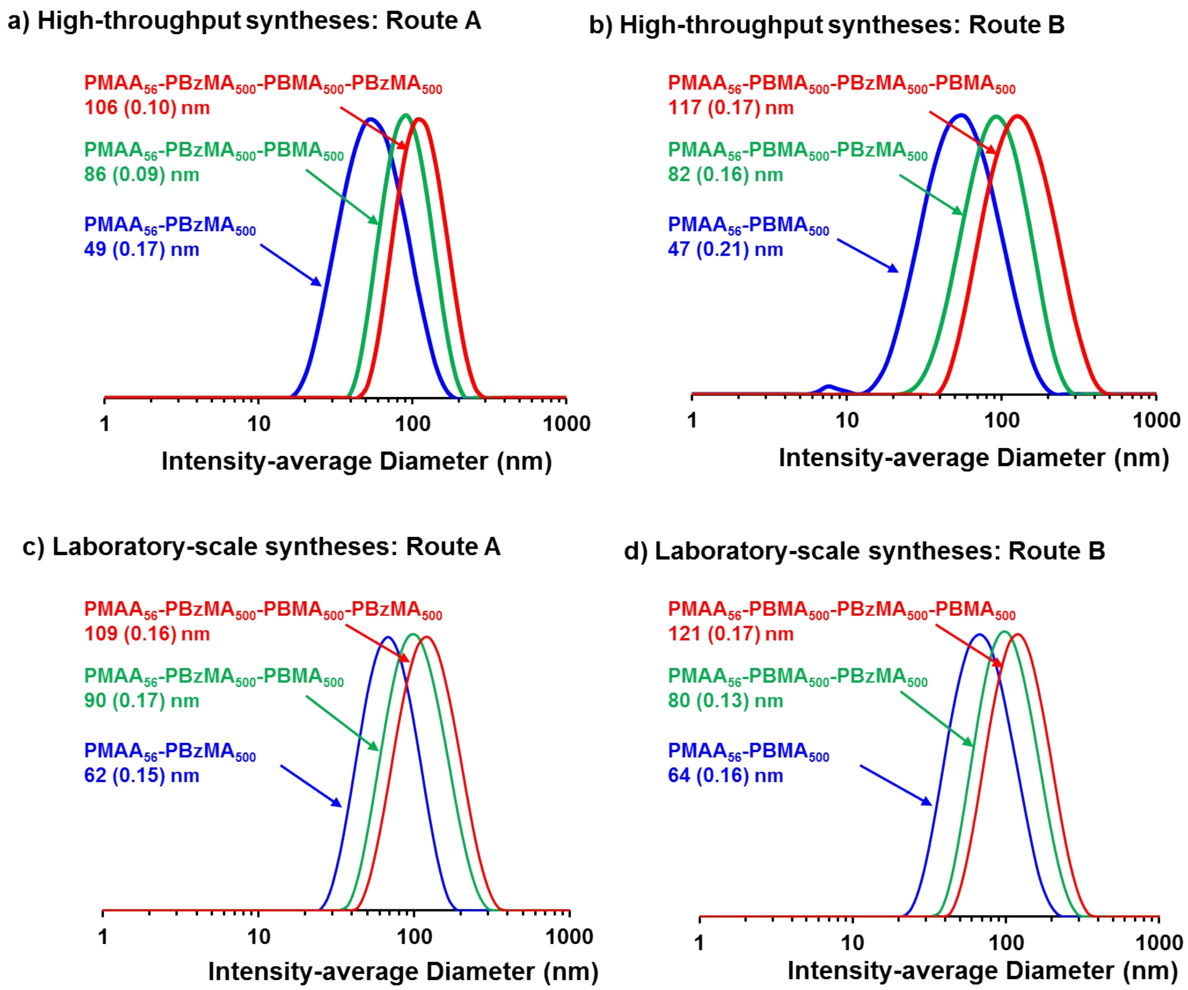


Figure S9. Intensity-average size distribution plots for dynamic light scattering data for diblock, triblock and tetrablock copolymers prepared *via* RAFT aqueous emulsion polymerization. These syntheses were performed either on the high-throughput Chemspeed A100 robot synthesizer or on a laboratory-scale. These block copolymers were prepared via either (a) Route A or (b) Route B as outlined in Scheme 2.

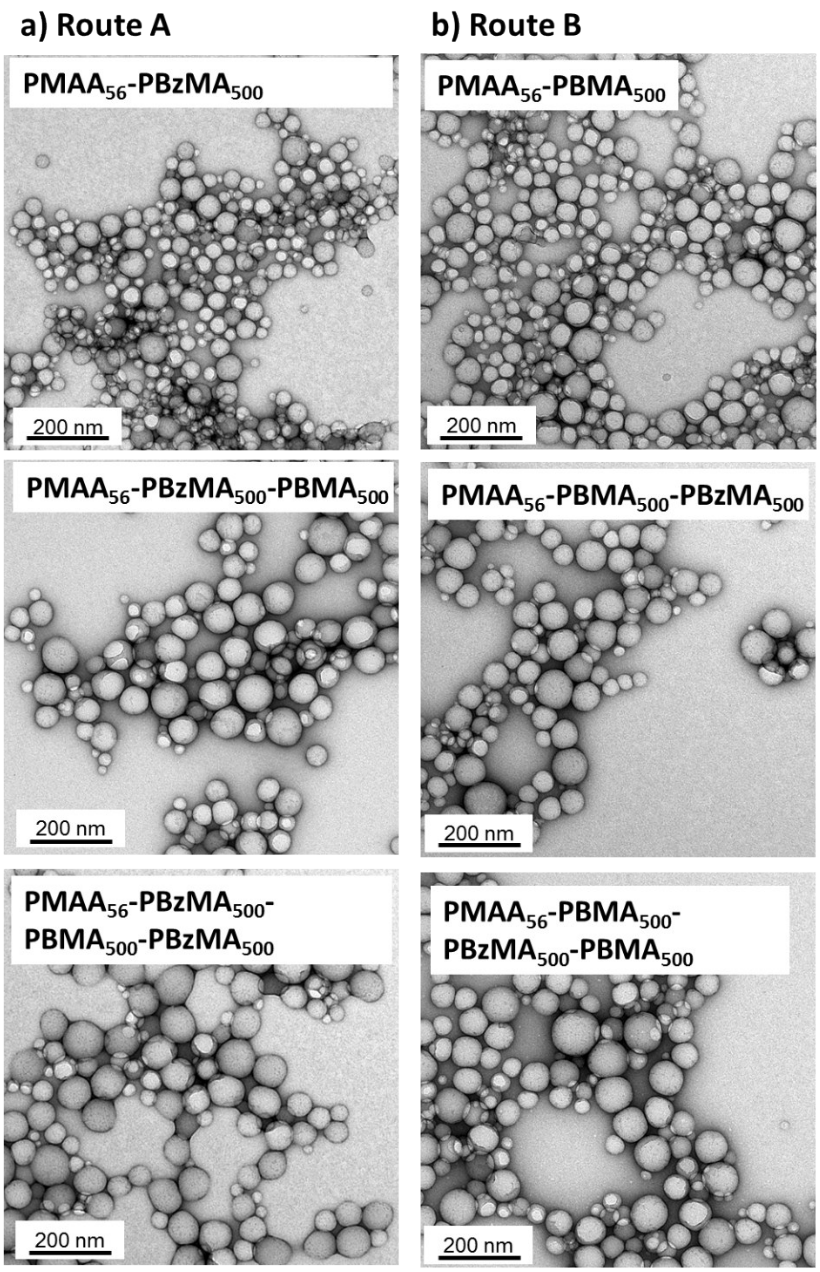


Figure S10. Representative TEM images obtained for the synthesis of diblock, triblock and tetrablock copolymers prepared on a laboratory-scale by RAFT aqueous emulsion polymerization. Spherical morphologies were obtained in all cases and an increase in mean nanoparticle diameter was observed by DLS and TEM with each subsequent block addition.