Supporting Information for:

PET-RAFT and SAXS: High Throughput Tools To Study Compactness and Flexibility of Single Chain Polymer Nanoparticles

Rahul Upadhya[1], N. Sanjeeva Murthy[2], Cody L. Hoop,[3] Shashank Kosuri[1], Vikas Nanda,[4] Joachim Kohn,[2] Jean Baum[3], Adam J. Gormley[*1]

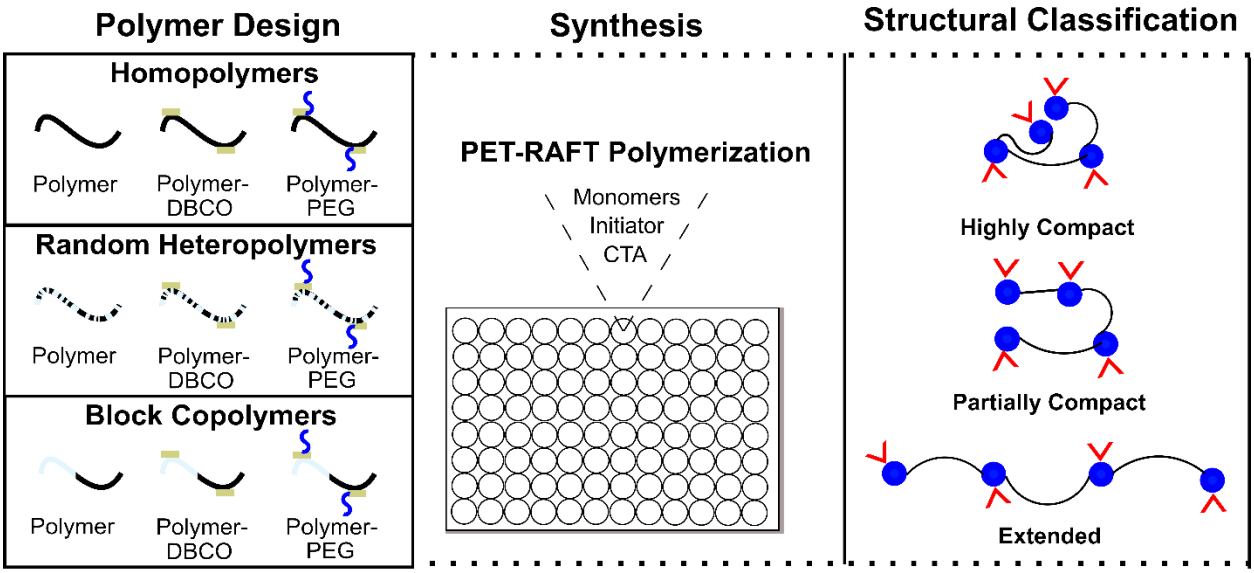
[1]Department of Biomedical Engineering, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

[2]New Jersey Center for Biomaterials, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

[3]Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

[4]Center for Advanced Biotechnology and Medicine and the Department of Biochemistry and Molecular Biology, Robert Wood Johnson Medical School, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

Corresponding Author E-mail: Adam.Gormley@rutgers.edu



S1. Supplemental Methods

S1.1: Definition of Homopolymers, Random Heteropolymers, and Block Copolymers

The general definition of homopolymers, random heteropolymers, and block copolymers is presented in **Table S1**. Each monomer column contains the number of units designed for the polymer chain (n) with the mol% (%). Included are definitions for all polymer backbones (labeled: homopolymer, RH/BC (1:1), RH/BC (1:1:1), and RH/BC (9:1), where RH = random heteropolymer, BC = block copolymer, and the included ratios are the feed ratios of monomer 1 : monomer 2).

Table S1. Summary of definitions for all polymer sub-types: homopolymers, random heteropolymers (RH), block copolymers (BC), and functionalized polymers.

Polymer Sub-Type	Monomer 1 n / %	Monomer 2 n / %	Monomer 3 n / %	NHS n / %	DBCO-NH_2 n / %	PEG-N_3 n / %	SI Table
Homopolymer	400 / 100%	--	--	--	--	--	Table S6
Homopolymer (PEG-Functionalized)	360 / 75%	--	--	40 / 8.33%	40 / 8.33%	40 / 8.33%	Table S6
RH/BC (1:1)	200 / 50%	200 / 50%	--	--	--	--	Table S7
RH/BC (1:1) (PEG-Functionalized)	180 / 37.5%	180 / 37.5%	--	40 / 8.33%	40 / 8.33%	40 / 8.33%	Table S7
RH/BC (1:1:1)	133 / 33.3%	133 / 33.3%	133 / 33.3%	--	--	--	Table S7
RH/BC (1:1:1) (PEG-Functionalized)	120 / 25%	120 / 25%	120 / 25%	40 / 8.33%	40 / 8.33%	40 / 8.33%	Table S7
RH/BC (9:1)	360 / 90%	40 / 10%	--	--	--	--	Tables S8-S11
RH/BC (9:1) (PEG-Functionalized)	324 / 67.5%	36 / 7.5%	--	40 / 8.33%	40 / 8.33%	40 / 8.33%	Tables S8-S11

S.1.2: logP Calculations

logP was calculated for each of the groups displayed in Table S1 by taking the weighted average of components as follows:

$$logP = (logP_{mon1} * x_{mon1}) + (logP_{mon2} * x_{mon2}) + (logP_{mon3} * x_{mon3}) + (logP_{NHS} * x_{NHS}) + (logP_{DBCO} * x_{DBCO}) + (logP_{PEG} * x_{PEG})$$

where x refers to the mol% of the individual monomers, NHS acrylic acid, DBCO-NH_2, or PEG-N_3.

This can also be re-expressed as:

$$logP = \sum_i (logP_i * x_i)$$

where i = 1, 2, 3, NHS, DBCO-NH_2, and PEG-N_3.

S2. Additional Information

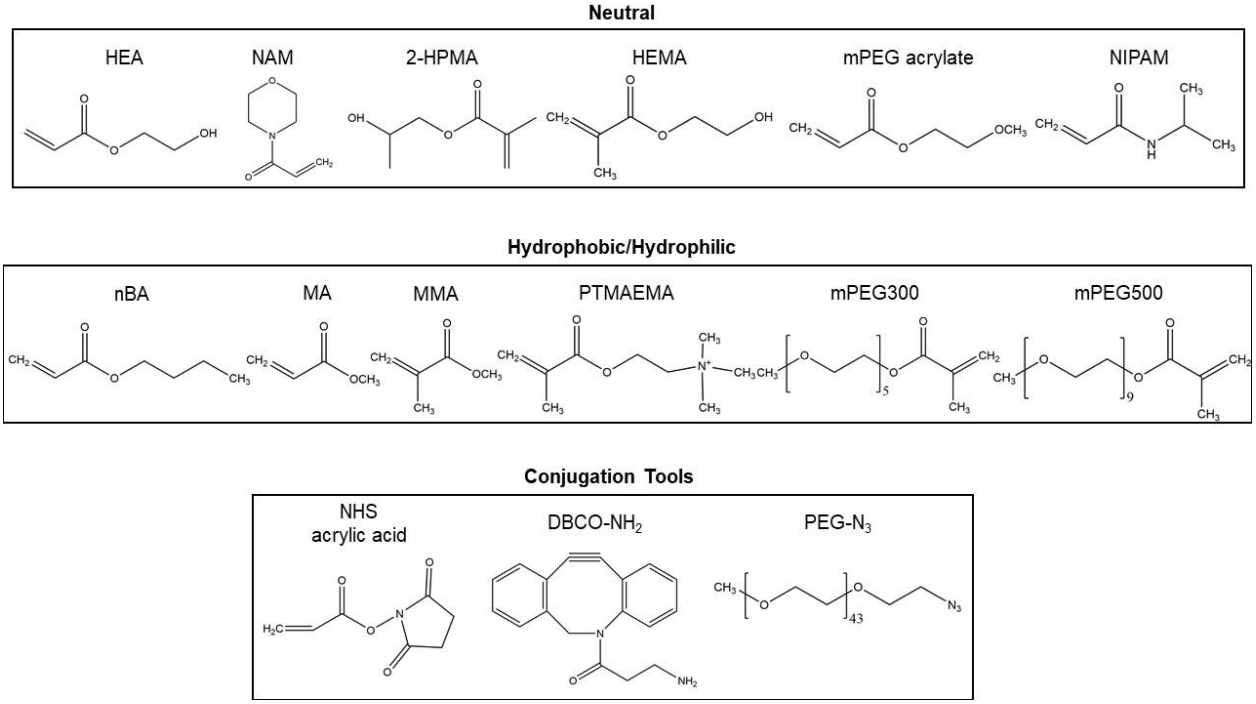


Figure S1. Chemical structures of neutral monomers (HEA, NAM, 2-HPMA, HEMA, mPEG acrylate, and NIPAM), hydrophobic monomers (nBA, MA, and MMA), hydrophilic monomers (PTMAEMA, mPEG300, and mPEG500), and conjugation tools (NHS acrylic acid, DBCO-NH_2, and PEG-N_3).

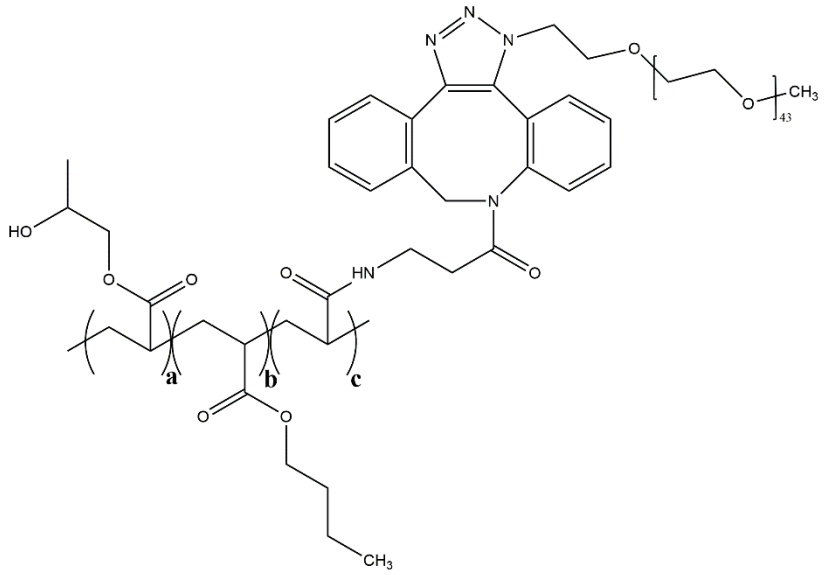


Figure S2. Illustrating the structure of a PEG-functionalized random heteropolymer (RH 2-HPMA-nBA 10% PEG). [a]Represents neutral 2-HPMA monomer (85% feed in the polymer backbone). [b]Represents hydrophobic nBA monomer (5% feed in the polymer backbone).[c]Represents the portion of the polymer chain at which NHS acrylic acid was originally polymerized (10% feed).

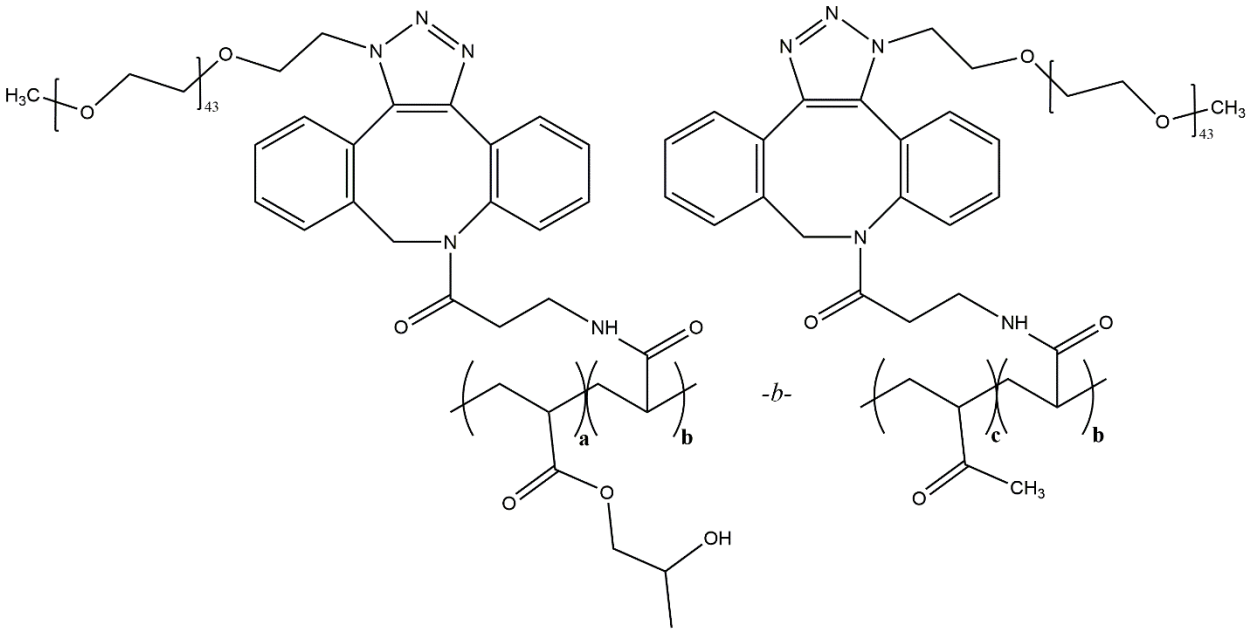


Figure S3. Illustrating the structure of a PEG-functionalized block copolymer (BC 2-HPMA-MA 10% PEG). [a]Represents neutral 2-HPMA monomer (85% feed in the polymer backbone). [b]Represents the portion of the polymer chain at which NHS acrylic acid was originally polymerized (10% feed in the polymer backbone). [c]Represents the hydrophobic nBA monomer (5% feed in the polymer backbone). Note that this design was selected in order for functionalization to be evenly dispersed.

Table S2. logP values determined for each compound.

Sample	logP
HEA	0.57
NAM	-0.13
DMA	0.21
NIPAM	0.72
2-HPMA	1.26
HEMA	0.85
mPEG acrylate	0.33
nBA	2.52
MA	0.49
MMA	1.59
mPEG300	0.77
mPEG500	0.11
PTMAEMA	-6.90
NHS acrylate	0.65
DBCO-NH_2	2.14
PEG-N_3	-7.09

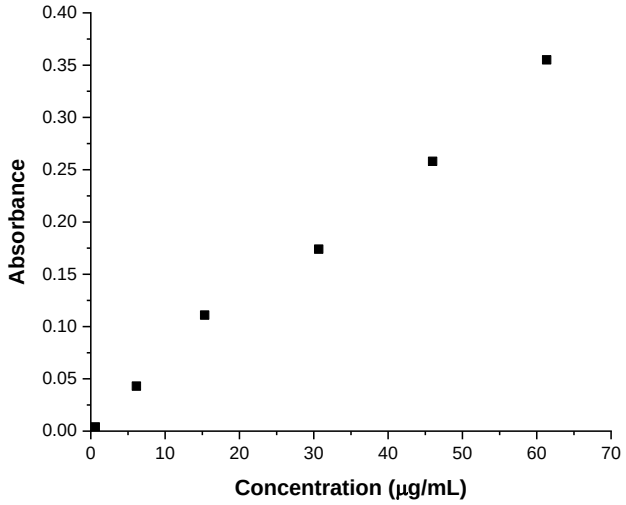


Figure S4. Standard curve for DBCO-NH_2 that was used to determine all concentrations post-purification for functionalization at a wavelength of 310 nm.

Table S3. DBCO incorporation percentages of all homopolymers. A background subtraction of polymer-NHS was done from the previous step to obtain only the concentration of DBCO present.

Polymer	DBCO Incorporation %
HEA	5.00
NAM	4.07
NIPAM	3.84
DMA	5.27
2-HPMA	1.28
HEMA	1.66
mPEG acrylate	2.59

Table S4. DBCO incorporation percentages of all random heteropolymers. A background subtraction of polymer-NHS was done from the previous step to obtain only the concentration of DBCO present.

Polymer	DBCO Incorporation %
RH HEA-NIPAM	12.1
RH HEA-2-HPMA	4.07
RH HEA-HEMA	4.60
RH HEA-NAM	13.4
RH HEA-NAM-HEA	13.8
RH HEA-mPEG300	10.5
RH HEA-mPEG500	11.2
RH HEA-PTMAEMA	4.71
RH HEA-nBA	10.8
RH HEA-MA	10.8
RH HEA-MMA	12.4
RH NIPAM-2-HPMA	5.50
RH NIPAM-PTMAEMA	5.47
RH NIPAM-nBA	8.58
RH NIPAM-MA	11.2
RH NIPAM-MMA	9.57
RH 2-HPMA-nBA	9.54
RH 2-HPMA-MA	3.04
RH HEA-MMA	12.4
RH 2-HPMA-MMA	10.4
RH HEMA-nBA	6.57
RH HEMA-MA	3.58
RH HEMA-MMA	9.31

Table S5. DBCO incorporation percentages of all block copolymers. A background subtraction of polymer-NHS was done from the previous step to obtain only the concentration of DBCO present.

Polymer	DBCO Incorporation %
BC HEA-NIPAM	11.1
BC HEA-2-HPMA	3.52
BC HEA-HEMA	2.97
BC HEA-NAM	8.55
BC HEA-NAM-HEA	13.5
BC HEA-mPEG300	10.5
BC HEA-mPEG500	8.73
BC HEA-PTMAEMA	8.78
BC HEA-nBA	8.93
BC HEA-MA	9.22
BC HEA-MMA	9.22
BC NIPAM-2-HPMA	3.99
BC NIPAM-PTMAEMA	7.27
BC NIPAM-nBA	7.51
BC NIPAM-MA	8.67
BC NIPAM-MMA	8.84
BC 2-HPMA-nBA	5.24
BC 2-HPMA-MA	6.69
BC HEA-MMA	9.22
BC 2-HPMA-MMA	6.69
BC HEMA-nBA	6.40
BC HEMA-MA	6.92
BC HEMA-MMA	6.20

Table S6. Characterization data for all homopolymers and homopolymers with PEG conjugated. M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to samples that precipitated.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
HEA	0.57	46,480	65,406	40,850	1.281	1.202	21.24	21.30	0.997	1.1	0.56
HEA 10% PEG	0.071	93,102	--	--	--	--	18.14	16.61	1.09	1.6	0.45
NAM	-0.13	56,468	25,882	30,580	1.118	1.058	13.04	9.65	1.35	1.5	0.47
NAM 10% PEG	-0.45	94,018	--	--	--	--	12.26	9.57	1.28	1.9	0.41
NIPAM	0.72	45,264	25,420	35,330	1.124	1.119	P	--	--	--	--
NIPAM 10% PEG	0.18	80,248	--	--	--	--	P	--	--	--	--
DMA	0.21	39,652	25,879	61,110	1.126	1.076	P	--	--	--	--
DMA 10% PEG	-0.20	94,242	--	--	--	--	10.53	9.06	1.16	1.5	0.47
2-HPMA	1.26	57,668	17,100	41,510	1.100	1.187	P	--	--	--	--
2-HPMA 10% PEG	0.59	69,469	--	--	--	--	17.14	14.64	1.17	1.1	0.56
HEMA	0.85	52,056	16,601	30,220	1.093	1.205	P	--	--	--	--
HEMA 10% PEG	0.28	67,430	--	--	--	--	20.57	20.76	0.991	1.5	0.47
mPEG acrylate	0.33	52,056	20,097	27,140	1.141	1.058	15.91	12.12	1.31	1.5	0.47
mPEG acrylate 10% PEG	-0.11	76,042	--	--	--	--	19.26	14.45	1.33	1.7	0.44

Table S7. Characterization data for all random heteropolymers (RH) and block copolymers (BC) only containing various neutral components. All polymerizations were done using a feed ratio of 1:1 for 2-component polymers and 1:1:1 for the 3-component polymer (HEA-NAM-HEA). M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to precipitated polymers.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
RH HEA-NIPAM	0.65	45,872	29,590	23,450	1.211	1.087	P	--	--	--	--
RH HEA-NIPAM 10% PEG	0.13	139,102	--	--	--	--	13.22	9.61	1.38	1.4	0.49
BC HEA-NIPAM	0.65	45,872	27,961	25,040	1.294	1.126	18.07	18.11	0.998	1.5	0.47
BC HEA-NIPAM 10% PEG	0.13	139,102	--	--	--	--	5.71	5.43	1.05	2.0	0.40
RH HEA-2-HPMA	0.92	52,074	70,165	66,960	1.479	1.454	20.23	14.85	1.36	1.9	0.41
RH HEA-2-HPMA 10% PEG	0.33	89,803	--	--	--	--	13.17	13.18	0.999	2.0	0.40
BC HEA-2-HPMA	0.92	52,074	86,765	52,830	1.539	1.135	14.57	11.91	1.22	1.6	0.45
BC HEA-2-HPMA 10% PEG	0.33	84,673	--	--	--	--	6.40	5.51	1.16	1.8	0.42
RH HEA-NAM	0.22	51,474	42,356	39,890	1.315	1.103	P	--	--	--	--
RH HEA-NAM 10% PEG	-0.20	144,144	--	--	--	--	8.75	6.11	1.43	1.5	0.47
BC HEA-NAM	0.22	51,474	28,355	38,890	1.317	1.159	8.04	5.59	1.44	1.5	0.47
BC HEA-NAM 10% PEG	-0.20	130,707	--	--	--	--	7.31	6.00	1.22	2.1	0.39
RH HEA-NAM-HEA	0.34	49,776	32,209	15,490	1.291	1.042	7.48	6.00	1.25	1.5	0.47
RH HEA-NAM-HEA 10% PEG	-0.10	142,616	--	--	--	--	7.47	5.66	1.32	1.5	0.47
BC HEA-NAM-HEA	0.34	49,776	20,814	69,620	1.225	1.100	8.41	6.55	1.28	1.8	0.42
BC HEA-NAM-HEA 10% PEG	-0.10	142,616	--	--	--	--	10.57	5.89	1.79	1.9	0.41
RH NIPAM-2-HPMA	0.99	51,466	47,979	38,150	1.437	1.349	P	--	--	--	--
RH NIPAM-2-HPMA 10% PEG	0.39	102,426	--	--	--	--	12.66	9.53	1.33	2.6	0.35
BC NIPAM-2-HPMA	0.99	51,466	37,019	40,900	1.256	1.075	P	--	--	--	--
BC NIPAM-2-HPMA 10% PEG	0.39	88,442	--	--	--	--	5.65	5.01	1.13	2.1	0.39

Table S8. Characterization data for all random heteropolymers (RH) and block copolymers (BC) only containing HEA along with a hydrophobic or hydrophilic monomer. All combinations were done using a feed ratio of HEA:hydrophobic/hydrophilic monomer of 9:1. M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to precipitated polymers.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
RH HEA-mPEG300	0.59	53,832	57,328	25,720	1.387	1.050	7.14	6.27	1.14	1.7	0.44
RH HEA-mPEG300 10% PEG	0.086	146,266	--	--	--	--	9.15	7.36	1.24	1.9	0.41
BC HEA-mPEG300	0.59	53,832	52,036	35,930	1.360	1.219	9.23	7.85	1.18	1.7	0.44
BC HEA-mPEG300 10% PEG	0.086	146,266	--	--	--	--	8.59	7.25	1.18	1.8	0.42
RH HEA-mPEG500	0.52	61,832	52,407	33,450	1.359	1.135	8.19	6.66	1.23	1.5	0.47
RH HEA-mPEG500 10% PEG	0.033	153,466	--	--	--	--	9.57	6.61	1.45	1.9	0.41
BC HEA-mPEG500	0.52	61,832	53,839	69,690	1.442	1.011	7.39	6.85	1.08	1.6	0.45
BC HEA-mPEG500 10% PEG	0.033	141,828	--	--	--	--	10.28	10.24	1.00	1.9	0.41
RH HEA-PTMAEMA	-0.18	50,140	36,566	42,020	1.279	1.099	15.03	12.36	1.22	1.5	0.47
RH HEA-PTMAEMA 10% PEG	-0.50	93,850	--	--	--	--	15.82	12.59	1.26	1.2	0.53
BC HEA-PTMAEMA	-0.18	50,140	35,137	30,770	1.367	1.159	8.97	5.92	1.52	1.7	0.44
BC HEA-PTMAEMA 10% PEG	-0.50	131,621	--	--	--	--	10.61	6.88	1.54	1.9	0.41
RH HEA-nBA	0.77	46,959	46,965	30,350	1.280	1.099	5.43	4.65	1.17	1.7	0.44
RH HEA-nBA 10% PEG	0.22	140,080	--	--	--	--	8.32	7.24	1.15	2.0	0.40
BC HEA-nBA	0.77	46,959	53,521	33,030	1.497	1.169	14.93	17.60	0.848	1.6	0.45
BC HEA-nBA 10% PEG	0.22	130,116	--	--	--	--	13.00	13.08	0.994	1.9	0.41
RH HEA-MA	0.56	45,276	41,882	20,770	1.206	1.110	7.70	6.57	1.17	1.7	0.44
RH HEA-MA 10% PEG	0.063	138,566	--	--	--	--	9.59	7.31	1.31	2.2	0.38
BC HEA-MA	0.56	45,276	47,715	38,550	1.388	1.149	12.34	8.82	1.40	1.6	0.45
BC HEA-MA 10% PEG	0.063	131,289	--	--	--	--	10.11	9.17	1.10	2.0	0.40
RH HEA-MMA	0.67	45,837	43,041	25,680	1.296	1.102	14.28	9.00	1.59	1.6	0.45
RH HEA-MMA 10% PEG	0.15	139,071	--	--	--	--	9.32	8.75	1.07	2.7	0.35
BC HEA-MMA	0.67	45,837	61,382	31,030	1.419	1.181	11.56	9.35	1.24	1.7	0.44
BC HEA-MMA 10% PEG	0.15	131,798	--	--	--	--	8.43	8.99	0.938	1.8	0.42

Table S9. Characterization data for all random heteropolymers (RH) and block copolymers (BC) only containing NIPAM along with a hydrophobic or hydrophilic monomer. All combinations were done using a feed ratio of NIPAM:hydrophobic/hydrophilic monomer of 9:1. M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to precipitated polymer.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
RH NIPAM-PTMAEMA	-0.042	49,046	41,395	36,480	1.403	1.043	23.47	25.40	0.92	1.5	0.47
RH NIPAM-PTMAEMA 10% PEG	-0.39	99,869	--	--	--	--	12.38	9.22	1.34	1.9	0.41
BC NIPAM-PTMAEMA	-0.042	49,046	36,449	35,850	1.355	1.073	14.99	12.56	1.19	2.9	0.34
BC NIPAM-PTMAEMA 10% PEG	-0.39	116,612	--	--	--	--	11.57	9.32	1.24	2.0	0.40
RH NIPAM-nBA	0.90	45,864	47,040	18,350	1.707	1.021	6.26	5.87	1.07	1.1	0.56
RH NIPAM-nBA 10% PEG	0.32	125,856	--	--	--	--	8.33	8.74	0.95	2.5	0.36
BC NIPAM-nBA	0.90	45,864	23,061	30,250	1.181	1.123	16.57	11.44	1.45	1.9	0.41
BC NIPAM-nBA 10% PEG	0.32	115,834	--	--	--	--	14.06	14.18	0.992	2.2	0.38
RH NIPAM-MA	0.70	44,181	35,710	37,550	1.339	1.085	P	--	--	--	--
RH NIPAM-MA 10% PEG	0.17	137,580	--	--	--	--	8.85	8.76	1.01	1.9	0.41
BC NIPAM-MA	0.70	44,181	23,481	23,730	1.237	1.061	P	--	--	--	--
BC NIPAM-MA 10% PEG	0.17	125,139	--	--	--	--	8.69	7.86	1.11	1.8	0.42
RH NIPAM-MMA	0.81	44,742	15,474	16,070	1.095	1.025	14.59	11.35	1.29	2.2	0.38
RH NIPAM-MMA 10% PEG	0.25	134,071	--	--	--	--	11.71	11.08	1.06	1.9	0.41
BC NIPAM-MMA	0.81	44,742	20,953	21,640	1.165	1.052	16.02	19.25	0.832	2.9	0.34
BC NIPAM-MMA 10% PEG	0.25	127,285		--	--	--	10.77	10.92	0.986	1.8	0.42

Table S10. Characterization data for all random heteropolymers (RH) and block copolymers (BC) only containing 2-HPMA along with a hydrophobic monomer. All combinations were done using a feed ratio of 2-HPMA:hydrophobic monomer of 9:1. M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to precipitated polymer.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
RH 2-HPMA-MMA	1.29	55,906	36,953	33,370	1.438	1.158	P	--	--	--	--
RH 2-HPMA-MMA 10% PEG	0.61	148,133	--	--	--	--	6.95	7.62	0.912	2.9	0.34
BC 2-HPMA-MMA	1.29	55,906	37,162	35,580	1.314	1.164	P	--	--	--	--
BC 2-HPMA-MMA 10% PEG	0.61	117,615	--	--	--	--	10.00	9.74	1.03	2.0	0.40
RH 2-HPMA-nBA	1.39	57,028	34,415	28,290	1.218	1.136	P	--	--	--	--
RH 2-HPMA-nBA 10% PEG	0.69	144,914	113,371	94,090	1.709	1.215	7.64	10.17	0.751	2.9	0.34
BC 2-HPMA-nBA	1.39	57,028	43,908	49,260	1.390	1.225	P	--	--	--	--
BC 2-HPMA-nBA 10% PEG	0.69	105,268	--	--	--	--	14.22	15.19	0.936	2.0	0.40
RH 2-HPMA-MA	1.18	55,345	75,562	44,250	1.366	1.083	12.13	10.93	1.11	1.2	0.53
RH 2-HPMA-MA 10% PEG	0.53	83,380	--	--	--	--	17.12	21.71	0.789	2.9	0.34
BC 2-HPMA-MA	1.18	55,345	47,352	44,250	1.279	1.103	P	--	--	--	--
BC 2-HPMA-MA 10% PEG	0.53	117,091	112,472	94,830	1.706	1.191	8.45	10.22	0.827	2.4	0.37

Table S11. Characterization data for all random heteropolymers (RH) and block copolymers (BC) only containing HEMA along with a hydrophobic or hydrophilic monomer. All combinations were done using a feed ratio of HEMA:hydrophobic/hydrophilic monomer of 9:1. M_w and $Đ$ was determined by SEC-MALS, R_g by SAXS, and R_h by DLS. P refers to precipitated polymer.

Polymer	logP	$MW_{Theoretical}$ (Da)	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$	R_g (nm)	R_h (nm)	R_g/R_h	Porod Exponent	v
RH HEMA-nBA	1.02	51,977	39,726	33,250	1.719	1.295	P	--	--	--	--
RH HEMA-nBA 10% PEG	0.41	112,828	--	--	--	--	7.00	8.52	0.822	2.6	0.35
BC HEMA-nBA	1.02	51,977	92,815	66,800	1.468	1.310	P	--	--	--	--
BC HEMA-nBA 10% PEG	0.41	111,253	--	--	--	--	9.49	8.32	1.14	2.5	0.36
RH HEMA-MA	0.81	50,294	70,662	33,630	1.381	1.121	P	--	--	--	--
RH HEMA-MA 10% PEG	0.25	83,512	--	--	--	--	5.34	5.76	0.927	1.8	0.42
BC HEMA-MA	0.81	50,294	85,878	69,320	1.619	1.308	P	--	--	--	--
BC HEMA-MA 10% PEG	0.25	114,531	--	--	--	--	8.60	8.41	1.02	2.0	0.40
RH HEMA-MMA	0.92	50,855	21,166	18,230	1.198	1.120	P	--	--	--	--
RH HEMA-MMA 10% PEG	0.33	137,188	--	--	--	--	8.21	7.71	1.06	1.9	0.41
BC HEMA-MMA	0.92	50,855	85,634	61,370	1.491	1.295	P	--	--	--	--
BC HEMA-MMA 10% PEG	0.33	108,312	--	--	--	--	8.69	10.58	0.821	2.6	0.35
RH HEMA-PTMAEMA	0.08	55,158	33,289	42,210	1.414	1.124	5.33	5.29	1.01	1.5	0.47
RH HEMA-PTMAEMA 10% PEG	-0.30	113,123	--	--	--	--	11.61	8.57	1.35	1.8	0.42
BC HEMA-PTMAEMA	0.08	55,158	95,176	76,850	1.637	1.265	24.05	20.29	1.19	1.0	0.60
BC HEMA-PTMAEMA 10% PEG	-0.30	146,167	--	--	--	--	23.89	22.23	1.07	1.4	0.49

Table S12. dn/dc values determined for each homopolymer (DP 400) using the Agilent 1200 Series differential RI detector. Weighted averages of dn/dc values were used to quantify MALS molar mass of random heteropolymers and block copolymers.

Polymer	dn/dc (mL/g)	R^2
HEA	0.152	0.9996
NAM	0.123	0.9913
DMA	0.081	0.9424
NIPAM	0.173	0.9981
2-HPMA	0.115	0.9992
HEMA	0.174	1.0000
mPEG acrylate	0.123	0.9984
nBA	0.117	0.9861
MA	0.081	0.9756
MMA	0.298	0.9961
mPEG300	0.132	0.9992
mPEG500	0.146	0.9950
PTMAEMA	0.078	0.9995

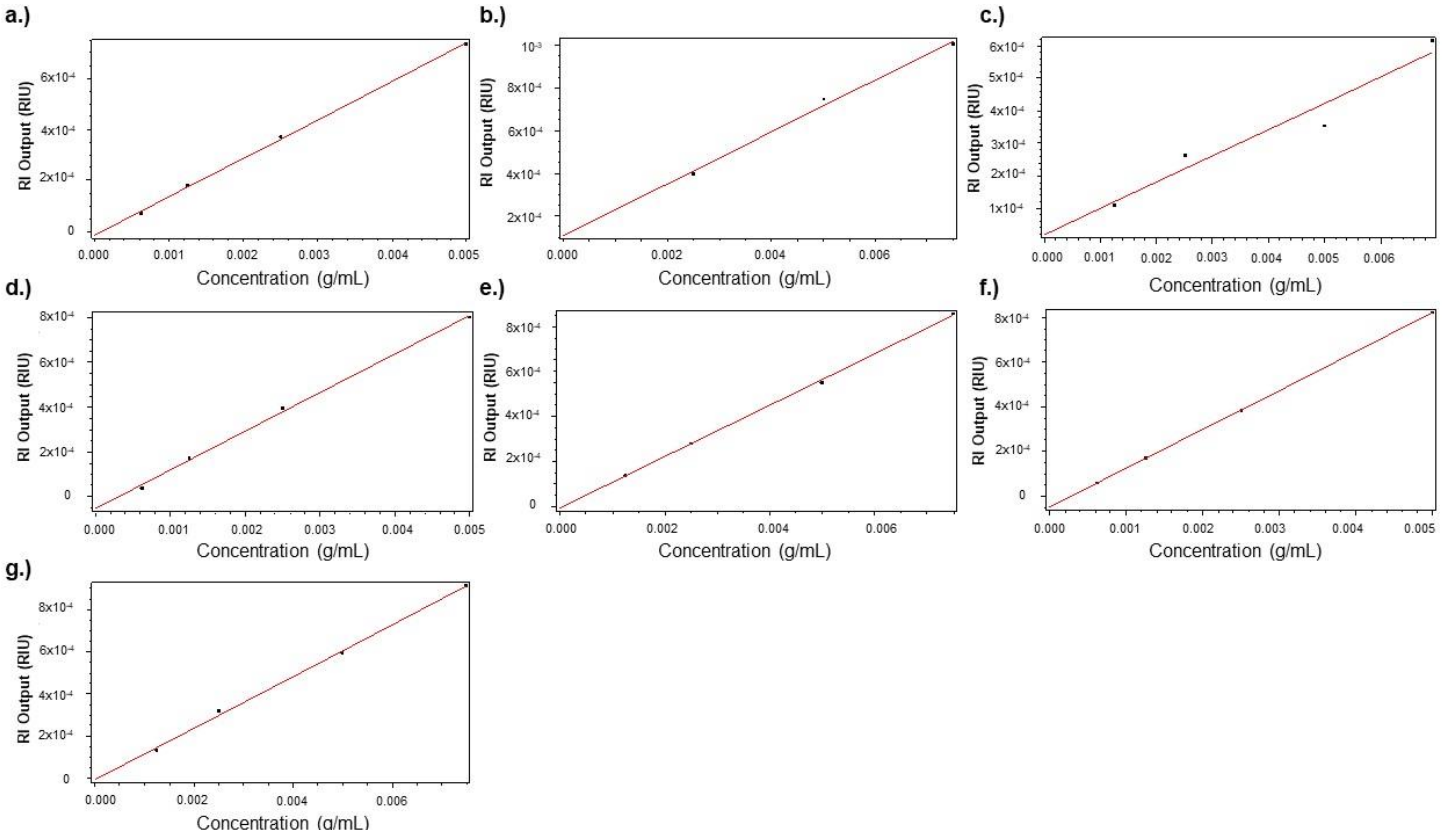


Figure S5. Plots of calibrated RI output (RIU) vs. concentration (g/mL) obtained from batch injections of the DP 400 neutral homopolymers using the Agilent 1200 Series differential RI detector (plots were processed in Astra chromatography software for light scattering (Wyatt Technology). Displayed are plots for the neutral monomers: (**a**) HEA; (**b**) NAM; (**c**) DMA; (**d**) NIPAM; (**e**) 2-HPMA; (**f**) HEMA; (**g**) mPEG acrylate.

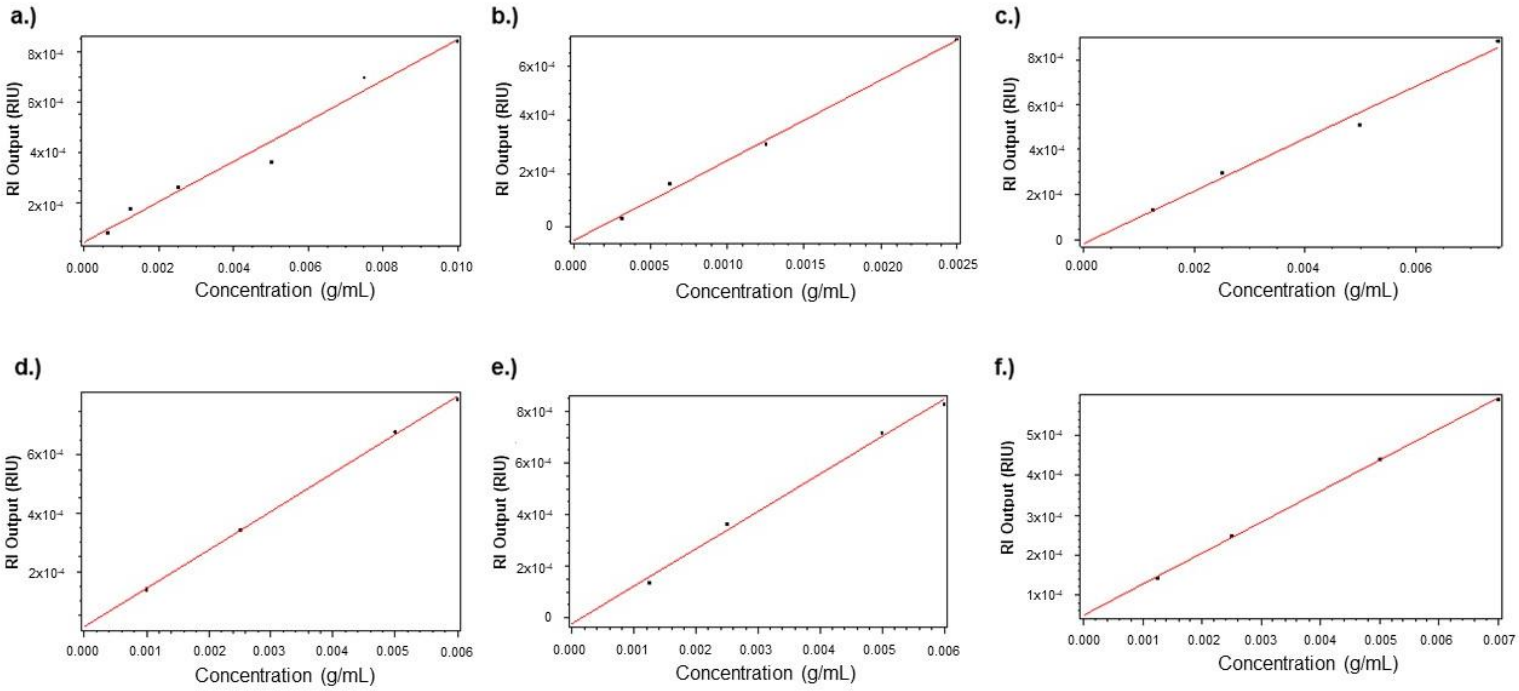


Figure S6. Plots of calibrated RI output (RIU) vs. concentration (g/mL) obtained from batch injections of the DP 400 hydrophobic and hydrophilic homopolymers using the Agilent 1200 Series differential RI detector (plots were processed in Astra chromatography software for light scattering (Wyatt Technology). Displayed are plots for the neutral monomers: (**a**) MA; (**b**) MMA; (**c**) nBA; (**d**) mPEG300; (**e**) mPEG500; (**f**) PTMAEMA.

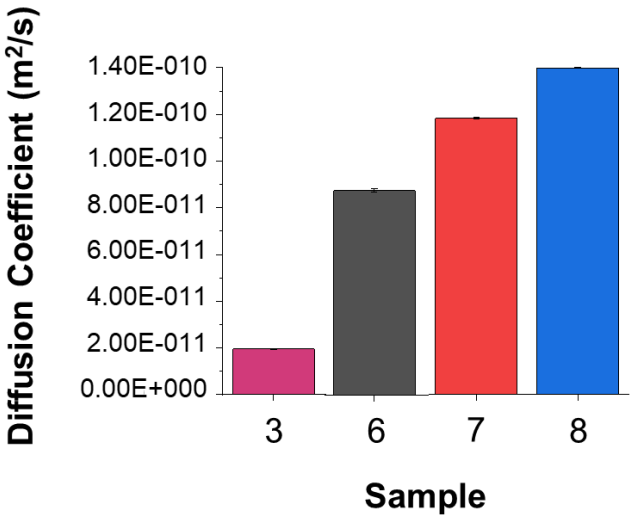


Figure S7. NMR diffusion coefficient summary. Column graph of diffusion coefficients quantified for mPEG acrylate (**3**), BSA (**6**), RH 2-HPMA-nBA 10% PEG (**7**), and BC 2-HPMA-MA 10% PEG (**8**).

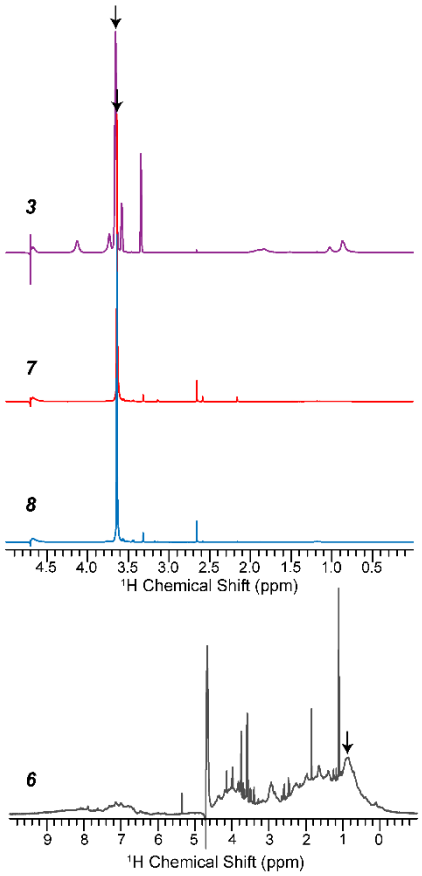


Figure S8. ^{1}H-NMR (in deuterated PBS) of mPEG acrylate 400 (3), BSA (6), RH 2-HPMA-nBA 10% PEG (7), BC 2-HPMA-MA 10% PEG (8). Arrows denote peaks considered for diffusion analysis.

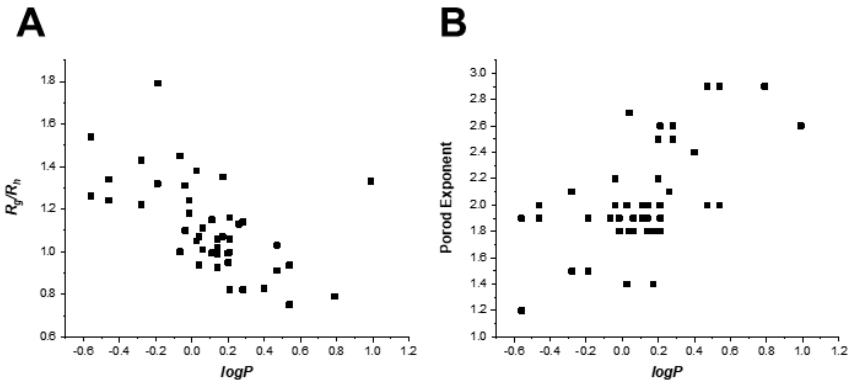


Figure S9. Association between logP and (A) R_g/R_h and (B) Porod exponent for all random heteropolymers and block copolymers functionalized with 10% PEG (combined). Note that in this case *logP* refers to *logP* of the entire polymer (accounting for the NHS acrylic acid, DBCO-NH_2, and PEG).

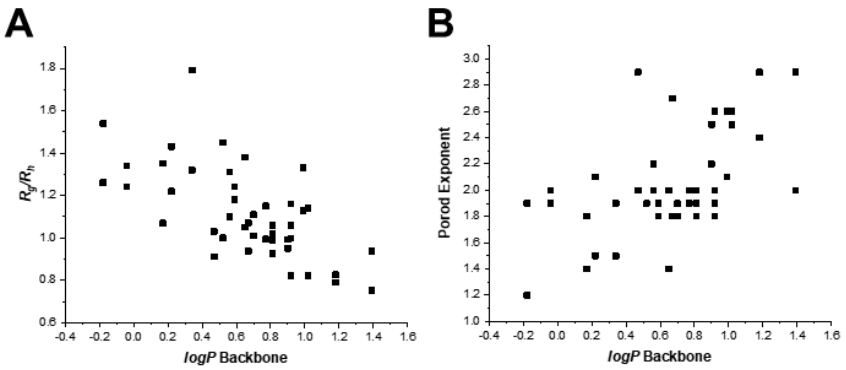


Figure S10. Association between backbone logP and (A) R_g/R_h and (B) Porod exponent for all random heteropolymers and block copolymers (pooled) functionalized with 10% PEG. Note that in this case *logP* refers to *logP* of the polymer backbone only.

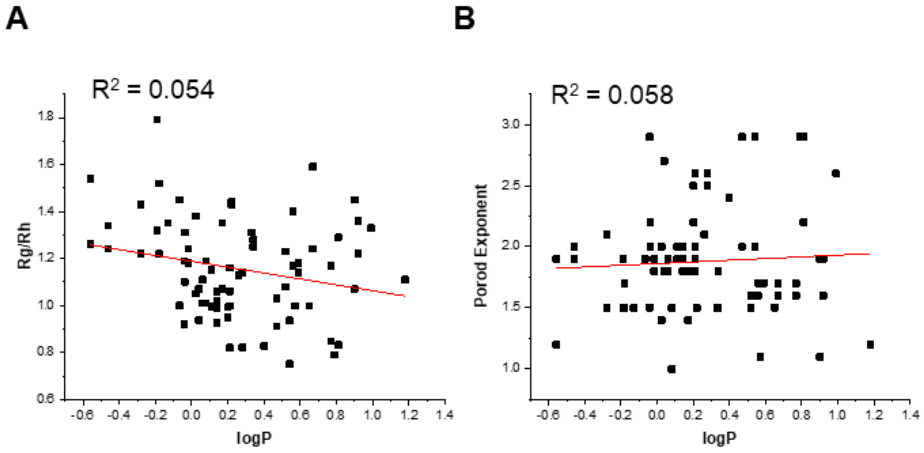


Figure S11. Association between *logP* and (A) R_g/R_h and (B) Porod exponent for all polymers characterized. Note that in this case *logP* refers to *logP* of the entire polymer (accounting for the NHS acrylic acid, DBCO-NH_2, and PEG). The R^2 displayed is for a linear fit.

Table S13. Molecular weight shift (weight-average MW) due to PEG incorporation of RH 2-HPMA-nBA 10% PEG (**7**) and BC 2-HPMA-MA 10% PEG (**8**).

Polymer	MW_{GPC} (Da)	MW_{MALS} (Da)	$Đ_{GPC}$	$Đ_{MALS}$
RH 2-HPMA-nBA 10% DBCO	54,827	53,430	1.466	1.068
RH 2-HPMA-nBA 10% PEG	113,371	94,090	1.709	1.215
BC 2-HPMA-MA 10% DBCO	50,978	55,440	1.419	1.130
BC 2-HPMA-MA 10% PEG	112,472	94,830	1.706	1.191

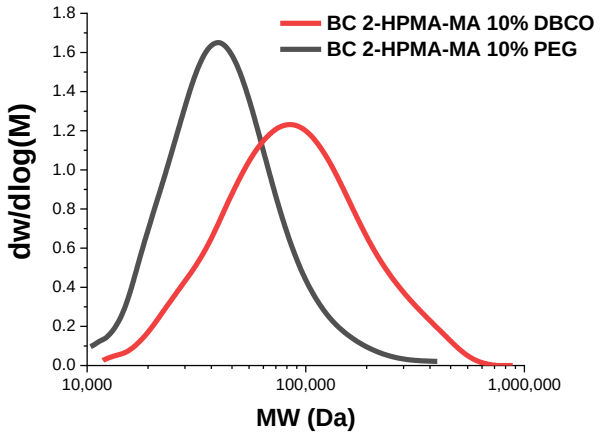


Figure S12. Molecular weight distribution for BC 2-HPMA-MA 10% DBCO and BC 2-HPMA-MA 10% PEG in which an increase in molecular weight is due to PEG incorporation. These molecular weight distributions are obtained by RI calibration.

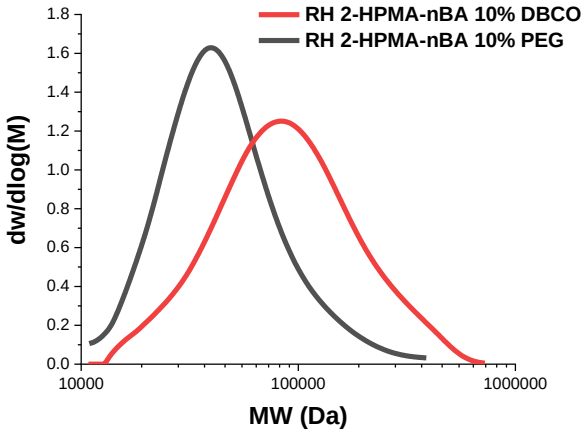


Figure S13. Molecular weight distribution for RH 2-HPMA-nBA 10% DBCO and RH 2-HPMA-nBA 10% PEG in which an increase in molecular weight is due to PEG incorporation. These molecular weight distributions are obtained by RI calibration.