Understanding the effect of monomer structure of oligoethylene glycol acrylate copolymers on their thermoresponsive behavior for the development of polymeric sensors.

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Synthesis of methoxy diethylene glycol acrylate (mDEGA) and methoxy triethylene glycol acrylate (mTEGA)

The synthesis of of methoxy diethylene glycol acrylate (mDEGA) and methoxy triethylene glycol acrylate (mTEGA) was adjusted from literature.[1] 50 mL of mDEG (0.43 mol, 1 eq.) was dissolved in 77 mL Et_3N (anhydrous, 0.55 mol, 1.29 eq.) and dry DCM (300 mL) and cooled to 0°C under argon atmosphere. Acryloyl chloride (42 mL, 0.52 mol, 1.22 eq) was added dropwise under vigorous stirring, after which the mixture was allowed to equilibrate to room temperature overnight. The yellowish mixture showed a precipitate, which was removed via column chromatography (Silica, EtOAc). The clear, slightly yellow liquid was further purified by double vacuum distillation (T_{vapour} = 50°C, P = 2.2 x 10^{-1} mbar). The resulting clear, colorless liquid product was stabilized by adding a small amount of hydroquinone. **Yield:** 55.81 g (75 %). **^{1}H NMR spectroscopy (300 MHz, DMSO-d_6):** δ(ppm) 6.34 (1H, dd, ^{3}J = 17.42 Hz, ^{2}J = 2.08 Hz, H_a); 6.19 (1H, dd, ^{3}J = 17.24 Hz, ^{3}J = 9.90 Hz, H_b); 5.95 (1H, dd, ^{3}J = 10.06 Hz, ^{2}J = 2.08 Hz, H_c); 4.22 (2H, multi, H_d); 3.64 (2H, multi, H_e); 3.54 (2H, multi, H_f); 3.44 (2H, multi, H_g); 3.24 (3H, s, H_h).

mTEGA was synthesized in a similar manner as mDEGA (T_{vapour} = 63°C, P = 2.2 x 10^{-1} mbar). **Yield:** 57.72 g (85 %). **^{1}H NMR spectroscopy (300 MHz, $CDCl_3$):** δ (ppm) 6.42 (1H, dd, ^{3}J = 17.50 Hz, ^{2}J = 1.54 Hz, H_a); 6.14 (1H, dd, ^{3}J = 17.27 Hz, ^{3}J = 10.18 Hz, H_b); 5.83 (1H, dd, ^{3}J = 10.18 Hz, ^{2}J = 1.85 Hz, H_c); 4.31 (2H, tr, ^{3}J = 4.85 Hz, H_d); 3.66 (10H, multi, H_e); 3.37 (3H, s, H_f).

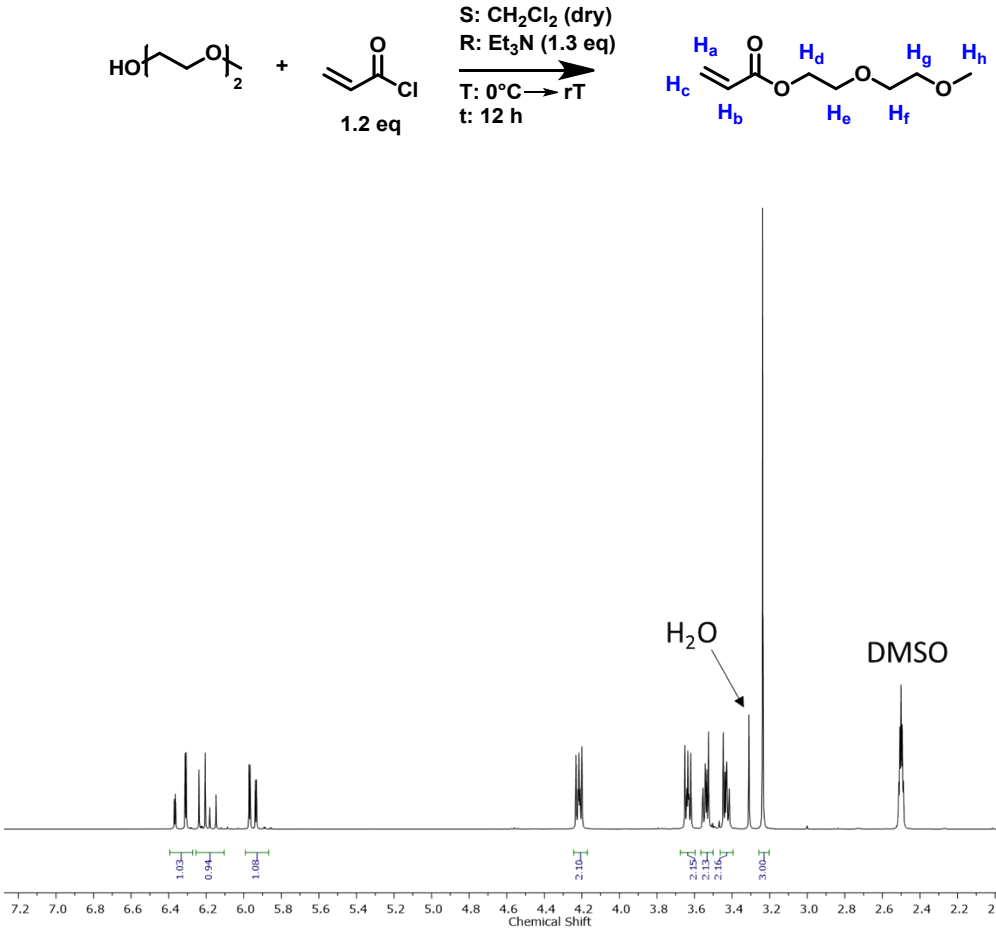

Figure S1. Synthetic conditions for the synthesis of mDEGA with respective ^{1}H NMR annotations and ^{1}H NMR spectrum.

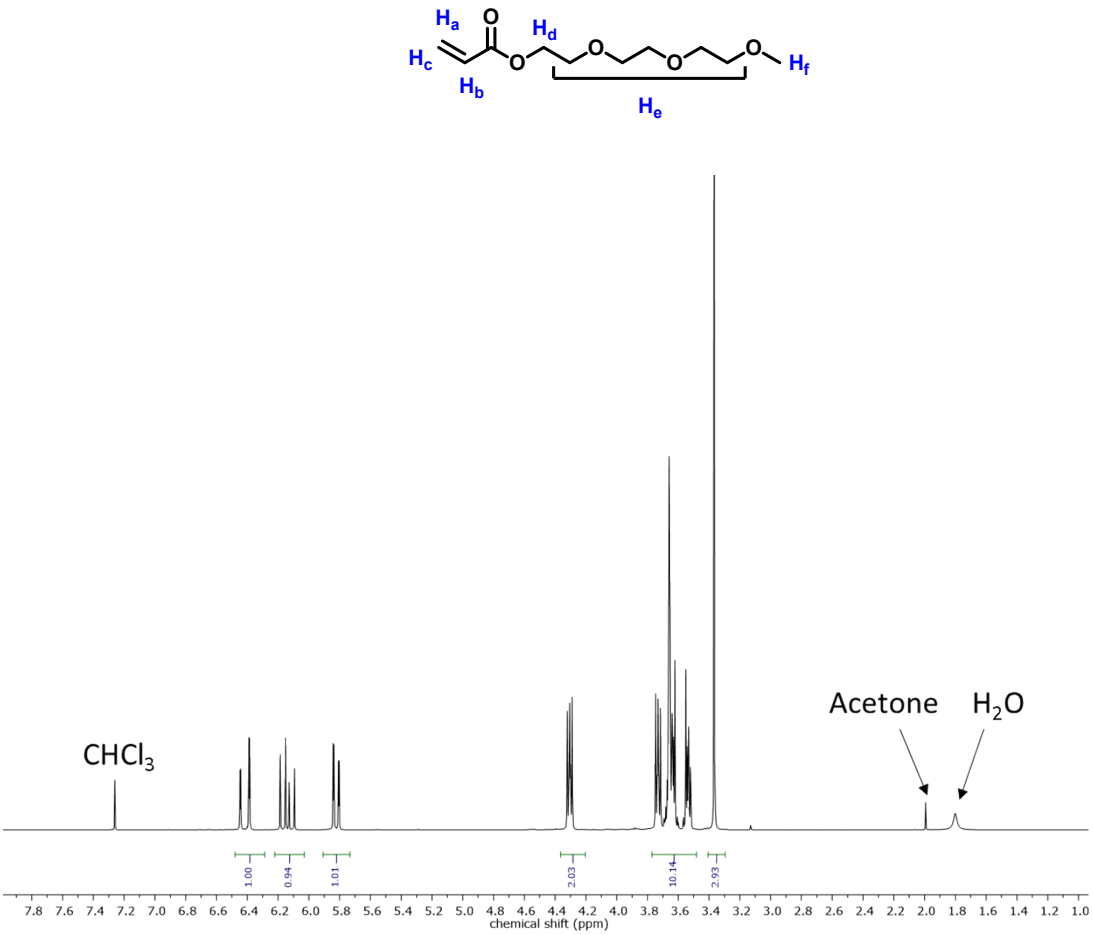

Figure S2. Structure of mTEGA with respective ^{1}H NMR annotations and ^{1}H NMR spectrum.

Synthesis of 2-(2-hydroxyethoxy)ethyl acrylate (hDEGA)

The synthesis of hDEGA was adapted from Shim *et al*.[2] Acryloyl chloride (12.9 g, 0.142 mol, 1 eq.) in 50 mL of 1,4-dioxane was slowly added to a mixture of DEG (30.1 g, 0.284 mol, 2 eq.) and 28.7 g of Et_3N (0.284 mol, 2 eq.) in 50 mL of 1,4 dioxane, with continuous stirring at 0°C. Next, the mixture was filtered and the solvent was evaporated under reduced pressure at room temperature. The compound was purified by silica gel chromatography using a gradient from *n*-hexane to 2:1 *n*-hexane:EtOAc and isolated as light yellow oil (11.8 g, 0.074 mol, 52% yield). **^{1}H NMR spectroscopy (300 MHz, $CDCl_3$):** δ(ppm) 6.43 (1H, dd, H_a); 6.15 (1H, dd, H_b); 5.87 (1H, dd, H_c); 4.34 (2H, t, H_d); 3.73-3.77 (4H, m, H_e); 3.62 (2, t, H_f); 2.85 (1H, s, H_g)

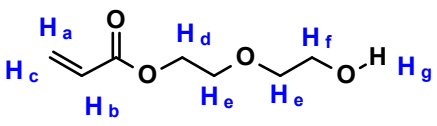

Figure S3. Structure of hDEGA with respective ^{1}H NMR annotations.

Polymer composition analysis via GC and characterization via SEC

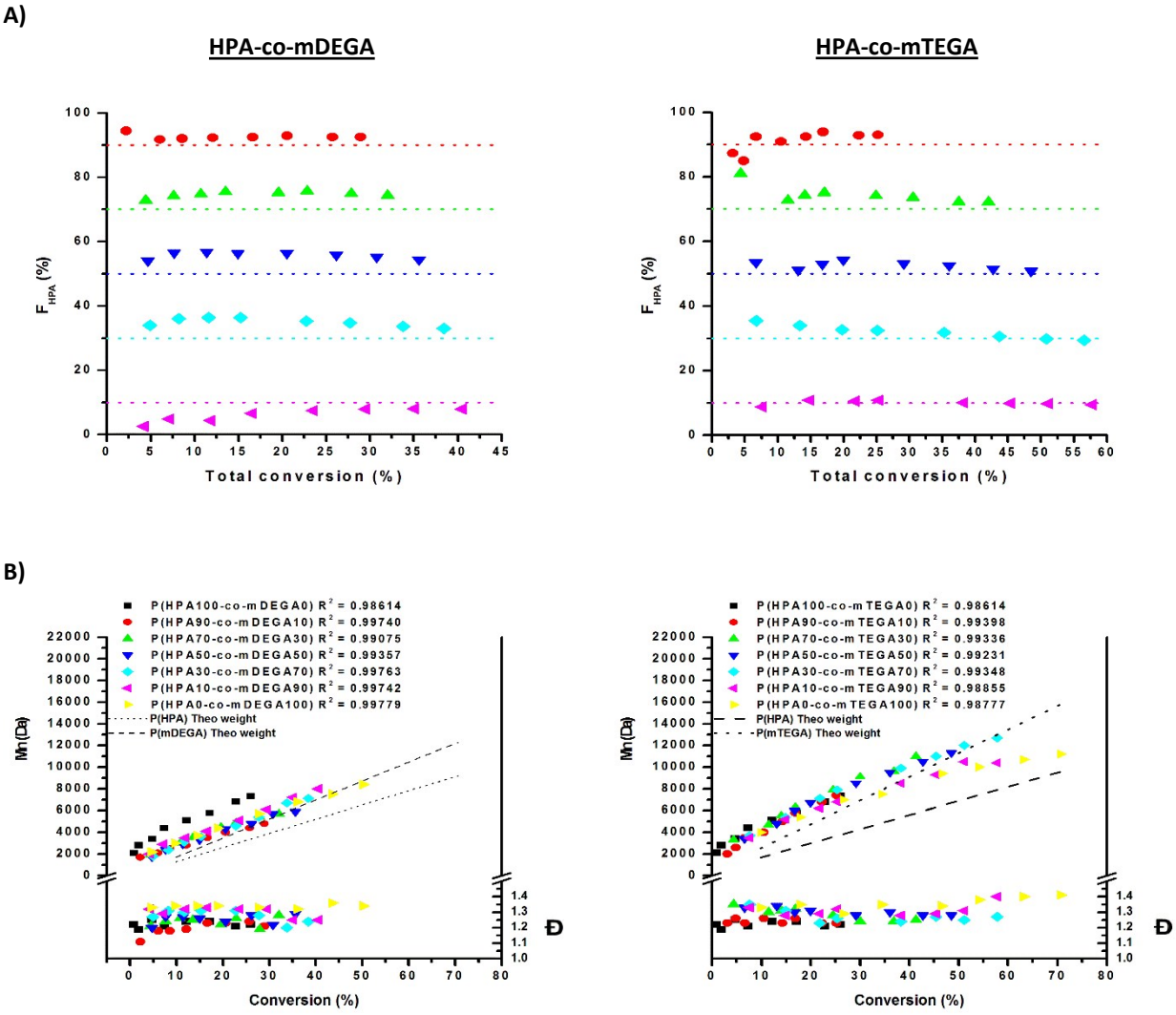

Figure S4: A) Fraction of incorporated HPA based on GC results for HPA-co-mDEGA (left) and HPA-co-mTEGA (right) and B) Molecular weight evolution measured using SEC for HPA-co-mDEGA (left) and HPA-co-mTEGA (right).

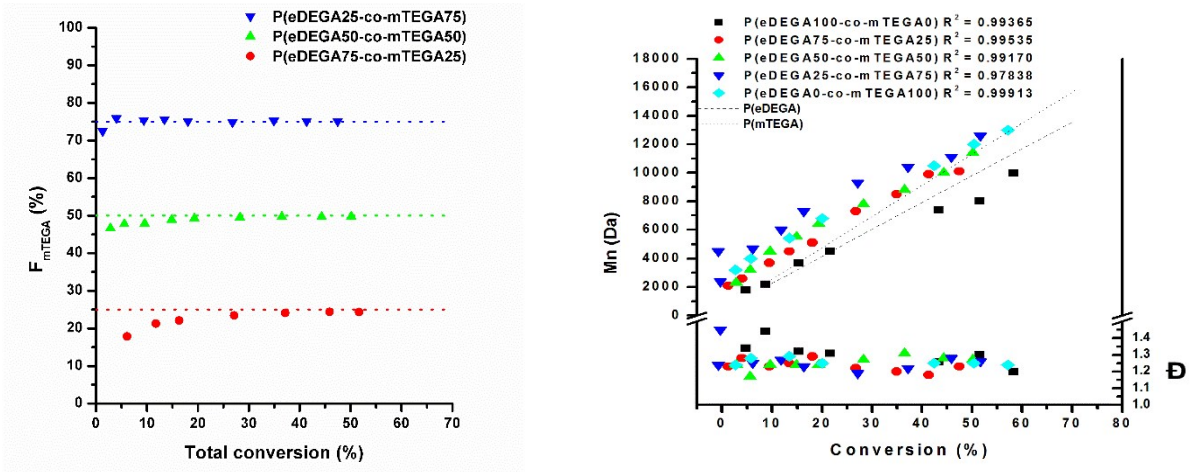

Figure S5: Fraction of incorporated mTEGA based on GC results for eDEGA-co-mTEGA (left) and molecular weight evolution measured using SEC for eDEGA-co-mTEGA (right).

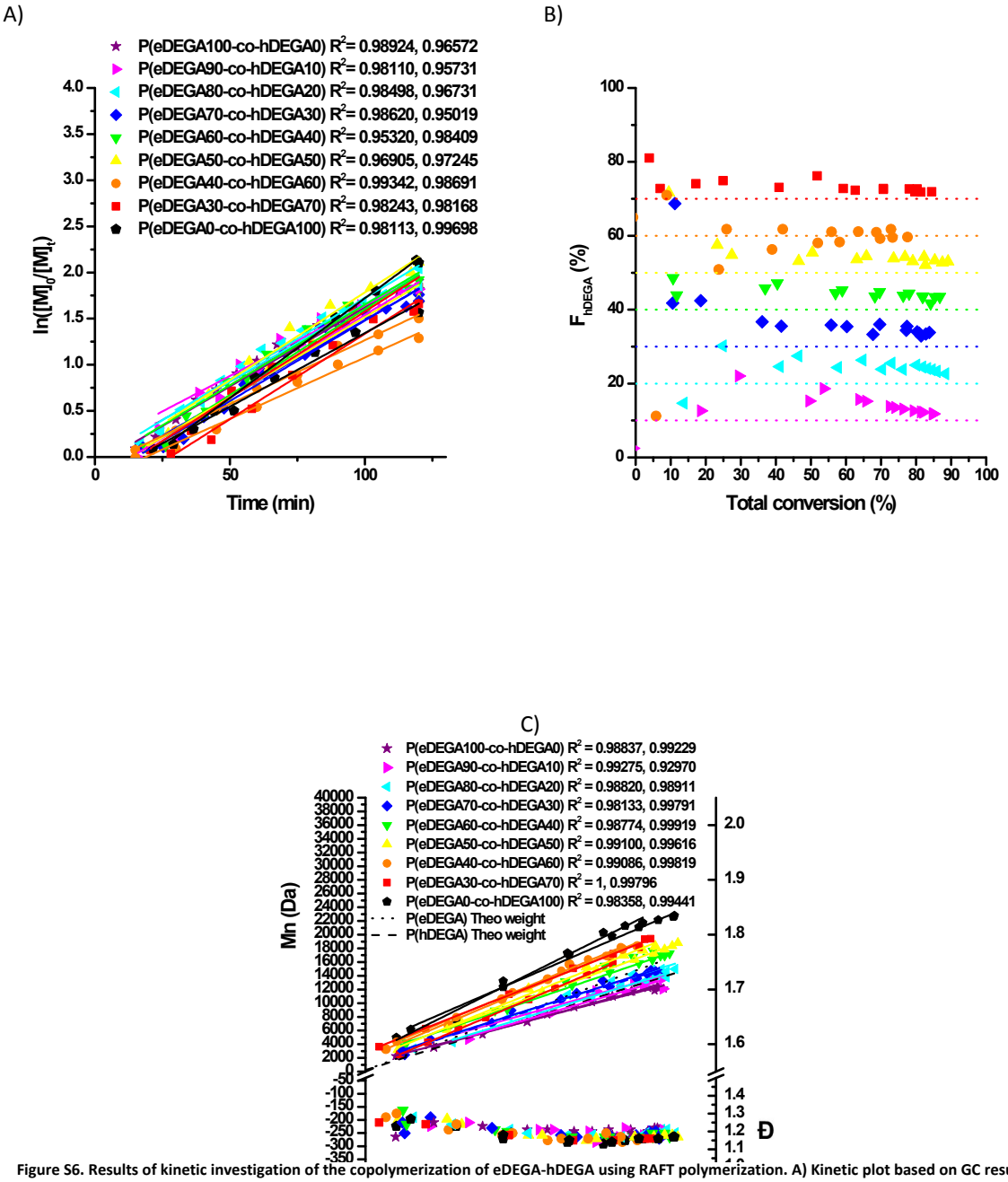

Figure S6. Results of kinetic investigation of the copolymerization of eDEGA-hDEGA using RAFT polymerization. A) Kinetic plot based on GC results B) Fraction of incorporated hDEGA based on GC results and C) Molecular weight evolution measured using SEC.

From the obtained kinetic data, the copolymerization parameters were calculated, utilizing the copolymerization mixtures with different ratios of monomer 1 and monomer 2. The polymer composition (F) was determined by the obtained conversion from GC data (Figure S4A, S5 and S6B). For comparison purposes the copolymerization parameters of the eDEGA-co-mTEGA via NMP were compared with the copolymerization parameters of the eDEGA-co-mTEGA via RAFT, which were calculated based on kinetic data from literature.[3] The copolymerization parameters r_{HPA}, r_{mTEGA}, r_{mDEGA}, r_{hDEGA} and r_{eDEGA} were calculated using equations S1 and S2 (for explanation of terms see footnote of Table S1-S5).

$$F_1 = \frac{r_1 f_1^2 + f_1 f_2}{r_1 f_1^2 + 2 f_1 f_2 + r_2 f_2^2} \quad \text{(S1)}$$

$$\eta = \left(r_1 + \left(\frac{r_2}{\alpha}\right)\right)\xi - \left(\frac{r_2}{\alpha}\right) \quad \text{(S2)}$$

The distribution of the repeating units along the copolymer chain were calculated using the Skeist model (equations S3 and S4)

$$X = 1 - \left(\frac{f_1}{f_1^0}\right)a\left(\frac{f_2}{f_2^0}\right)b\left(\frac{f_1^0 - d}{f_1 - d}\right)c \quad \text{(S3)}$$

$$\bar{F}_1 = \frac{f_1^0 - f_1(1 - X)}{X} \quad \text{(S4)}$$

where X is total monomer conversion, f_1^0 and f_2^0 are initial molar fractions of monomer 1 and 2, respectively; f_1 and f_2 are instant monomer fractions of monomer 1 respectively 2 and $\bar{F}_1$ is the cumulative molar fraction of repeating unit 1 in copolymer.

Table S1. Parameters used for calculation of monomer reactivity ratios in HPA/mDEGA copolymerization.

			Conversion						
Entry	F_{HPA}[a]	F_{HPA}[b]	ζ_{HPA}[c]	ζ_{mDEGA}[d]	Z[e]	G'[f]	H'[g]	η[h]	ξ[i]
1	0.9	0.93	0.297	0.215	1.459	7.852	5.850	1.153	0.859
2	0.7	0.74	0.340	0.274	1.299	1.461	1.717	0.546	0.641
3	0.5	0.54	0.387	0.325	1.244	0.152	0.769	0.088	0.444
4	0.3	0.34	0.379	0.320	1.235	-0.399	0.333	-0.308	0.257
5	0.1	0.08	0.281	0.359	0.742	-1.231	0.158	-1.099	0.141

[a] Molar fraction of HPA in monomer feed. [b]Molar fraction of HPA in polymer determined by GC. [c] HPA conversion determined by GC. [d]mDEGA conversion determined by GC [e]Z = log(1–ζ_{HPA})/log (1–ζ_{mDEGA}), [f]G' = (F-1)/Z where F = F_{HPA}/ $F_{mDEGA,}$ [g]H' = F/Z^2, [h]η = G'/(H'+α) where α = (H'$_{max}$ H'$_{min}$)$^{0.5}$, [i]ξ = H'/(H'+α).

Table S2. Parameters used for calculation of monomer reactivity ratios in HPA/mTEGA copolymerization.

			Conversion						
Entry	F_{HPA}[a]	F_{HPA}[b]	ζ_{HPA}[c]	ζ_{mTEGA}[d]	Z[e]	G'[f]	H'[g]	η[h]	ξ[i]
1	0.9	0.93	0.261	0.176	1.554	7.904	5.499	1.258	0.876
2	0.7	0.72	0.432	0.392	1.137	1.382	1.990	0.499	0.718
3	0.5	0.51	0.436	0.419	1.055	0.039	0.935	0.0225	0.545
4	0.3	0.31	0.452	0.431	1.066	-0.517	0.395	-0.439	0.336
5	0.1	0.1	0.454	0.454	1	-0.889	0.111	-0.996	0.124

[a] Molar fraction of HPA in monomer feed. [b]Molar fraction of HPA in polymer determined by GC. [c] HPA conversion determined by GC. [d]mTEGA conversion determined by GC [e]Z = log(1–ζ_{HPA})/log (1–ζ_{mTEGA}), [f]G' = (F-1)/Z where F = F_{HPA}/ $F_{mTEGA,}$ [g]H' = F/Z^2, [h]η = G'/(H'+α) where α = (H'$_{max}$ H'$_{min}$)$^{0.5}$, [i]ξ = H'/(H'+α).

Table S3. Parameters used for calculation of monomer reactivity ratios in hDEGA/eDEGA copolymerization.

			Conversion						
Entry	F_{hDEGA}[a]	F_{hDEGA}[b]	ζ_{hDEGA}[c]	ζ_{eDEGA}[d]	Z[e]	G'[f]	H'[g]	η[h]	ξ[i]
1	0.7	0.72	0.647	0.578	1.209	1.335	1.789	0.654	0.876
2	0.6	0.62	0.432	0.401	1.104	0.558	1.327	0.353	0.840
3	0.5	0.55	0.559	0.449	1.375	0.179	0.659	0.196	0.723
4	0.4	0.45	0.667	0.538	1.423	-0.122	0.408	-0.185	0.617
5	0.3	0.36	0.666	0.511	1.532	-0.288	0.238	-0.587	0.485
6	0.2	0.27	0.637	0.421	1.852	-0.336	0.110	-0.925	0.303
7	0.1	0.15	0.756	0.467	2.244	-0.365	0.036	-1.266	0.124

[a] Molar fraction of HPA in monomer feed. [b]Molar fraction of HPA in polymer determined by GC. [c] hDEGA conversion determined by GC. [d]eDEGA conversion determined by GC [e]$Z = \log(1-\zeta_{hDEGA})/\log(1-\zeta_{eDEGA})$, [f]$G' = (F-1)/Z$ where $F = F_{hDEGA}/F_{eDEGA}$, [g]$H' = F/Z^2$, [h]$\eta = G'/(H'+\alpha)$ where $\alpha = (H'_{max} H'_{min})^{0.5}$, [i]$\xi = H'/(H'+\alpha)$.

Table S4. Parameters used for calculation of monomer reactivity ratios in eDEGA/mTEGA copolymerization.

			Conversion						
Entry	F_{eDEGA}[a]	F_{eDEGA}[b]	Z_{eDEGA}[c]	Z_{mTEGA}[d]	Z[e]	G'[f]	H'[g]	η[h]	ξ[i]
1	0.25	0.25	0.414	0.414	1	-0.667	0.333	-0.518	0.259
2	0.5	0.5	0.443	0.443	1	0	1	0	0.512
3	0.75	0.76	0.465	0.441	1.077	2.012	2.730	0.546	0.741

[a] Molar fraction of HPA in monomer feed. [b]Molar fraction of HPA in polymer determined by GC. [c] hDEGA conversion determined by GC. [d]eDEGA conversion determined by GC [e]$Z = \log(1-\zeta_{eDEGA})/\log(1-\zeta_{mTEGA})$, [f]$G' = (F-1)/Z$ where $F = F_{eDEGA}/F_{mTEGA}$, [g]$H' = F/Z^2$, [h]$\eta = G'/(H'+\alpha)$ where $\alpha = (H'_{max} H'_{min})^{0.5}$, [i]$\xi = H'/(H'+\alpha)$.

Table S5. Parameters used for calculation of monomer reactivity ratios in eDEGA/mTEGA copolymerization via RAFT, generated with data from ref.[3]

			Conversion						
Entry	F_{hDEGA}[a]	F_{hDEGA}[b]	ζ_{hDEGA}[c]	ζ_{eDEGA}[d]	Z[e]	G'[f]	H'[g]	η[h]	ξ[i]
1	0.2	0.20	0.565	0.554	1.031	-0.723	0.240	-0.596	0.199
2	0.4	0.41	0.420	0.410	1.033	-0.307	0.641	-0.190	0.397
3	0.5	0.50	0.515	0.509	1.017	0.012	0.978	0.0060	0.501
4	0.6	0.60	0.513	0.507	1.018	0.509	1.464	0.209	0.601
5	0.8	0.80	0.497	0.493	1.012	2.998	3.941	0.610	0.802

[a] Molar fraction of HPA in monomer feed. [b]Molar fraction of HPA in polymer determined by GC. [c] hDEGA conversion determined by GC. [d]eDEGA conversion determined by GC [e]$Z = \log(1-\zeta_{eDEGA})/\log(1-\zeta_{mTEGA})$, [f]$G' = (F-1)/Z$ where $F = F_{eDEGA}/F_{mTEGA}$, [g]$H' = F/Z^2$, [h]$\eta = G'/(H'+\alpha)$ where $\alpha = (H'_{max} H'_{min})^{0.5}$, [i]$\xi = H'/(H'+\alpha)$.

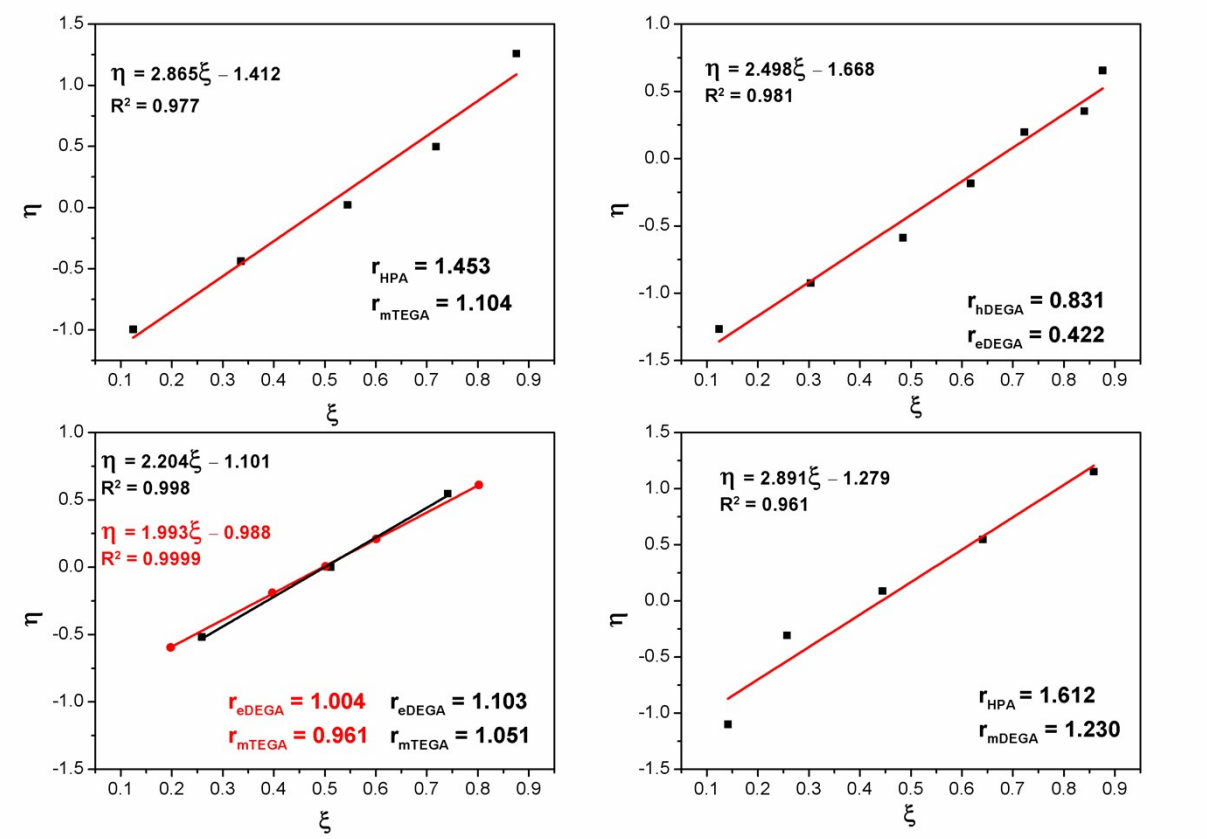

Figure S7. Extended Kelen-Tudos plots of the copolymerizations of HPA-mTEGA (top left), eDEGA-mTEGA via NMP (black) and via RAFT generated with data from ref [3] (red) (bottom left), hDEGA-eDEGA (top right) and HPA-mDEGA (bottom right).

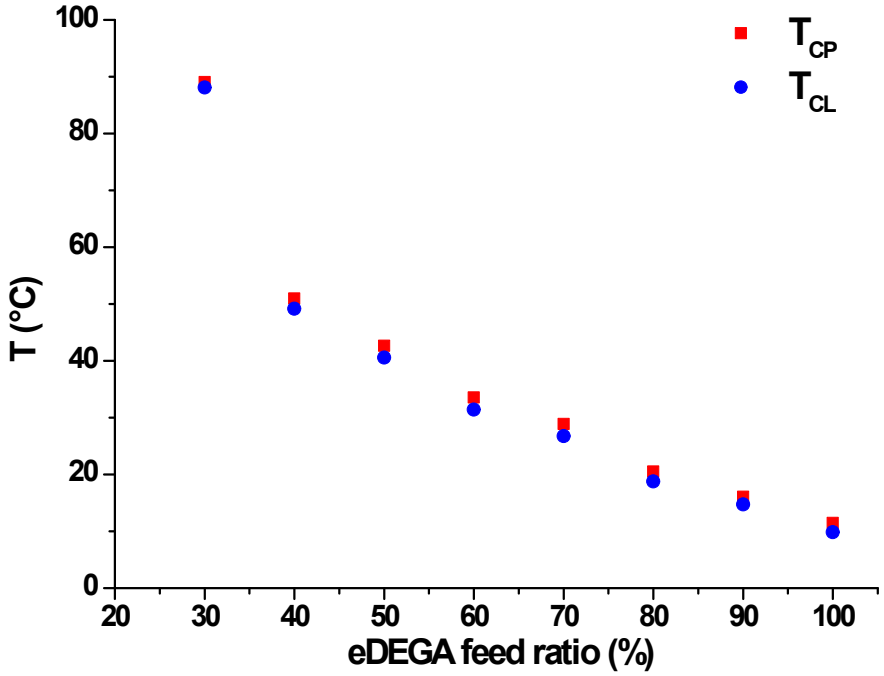

Figure S8. : Overview of Tcp and Tcl values and calculated trend in function fraction hydrophobic monomer for P(eDEGAx-co-hDEGA100-x) at a concentration of 20 mg/mL.

Table S6: Overview of the properties of the eDEGA-co-mTEGA combinations used for the T_{cp} measurements. Conversions and total DP were determined via GC, M_n and Đ were obtained via SEC.

Monomer feed ratio (eDEGA-mTEGA)	Conversion mTEGA (%)	Conversion eDEGA (%)	Total DP	M_n (kDa)	Đ	T_{cp}
0: 100	57	0	57	13.0	1.24	68
25:75	52	52	52	12.6	1.26	53
50:50	50	50	50	11.4	1.27	39
75:25	45	48	47	10.1	1.23	28
100:0	0	58	58	10.0	1.20	17

Table S7: Overview of the properties of the HPA-co-mTEGA combinations used for the T_{cp} measurements. Conversions and total DP were determined via GC, M_n and Đ were obtained via SEC.

Monomer feed ratio (HPA-mTEGA)	Conversion mTEGA (%)	Conversion HPA (%)	Total DP	M_n (kDa)	Đ	T_{cp}
0: 100	71	0	71	11.2	1.41	66
10:90	58	60	58	10.4	1.40	65
30:70	59	56	58	12.7	1.27	59
50:50	48	50	49	11.3	1.28	52
70:30	38	42	41	11.0	1.25	44
90:10	18	26	25	7.4	1.23	32
100:0	0	26	26	7.3	1.22	21

Table S8: Overview of the properties of the hDEGA-co-eDEGA combinations used for the T_{cp} measurements. Conversions and total DP were determined via GC, M_n and Đ were obtained via SEC.

Monomer feed ratio (hDEGA-eDEGA)	Conversion hDEGA (%)	Conversion eDEGA (%)	Total DP	M_n (kDa)	Đ	T_{cp} @ 5 mg/ (20 mg/mL)
100: 0	79	0	79	21.7	1.16	n.a. (n.a.)
70:30	83	76	81	19.4	1.16	n.a. (89)
60:40	77	78	78	18.3	1.15	62.4 (51)
50:50	88	78	83	18.3	1.18	50.0 (43)
40:60	91	79	84	16.9	1.21	38.3 (34)
30:70	95	79	84	14.5	1.16	33.3 (29)
20:80	99	85	88	15.0	1.19	25.4 (21)
10:90	100	83	85	13.8	1.17	18.5 (16)
0:100	0	85	85	12.1	1.2	14.4 (11)

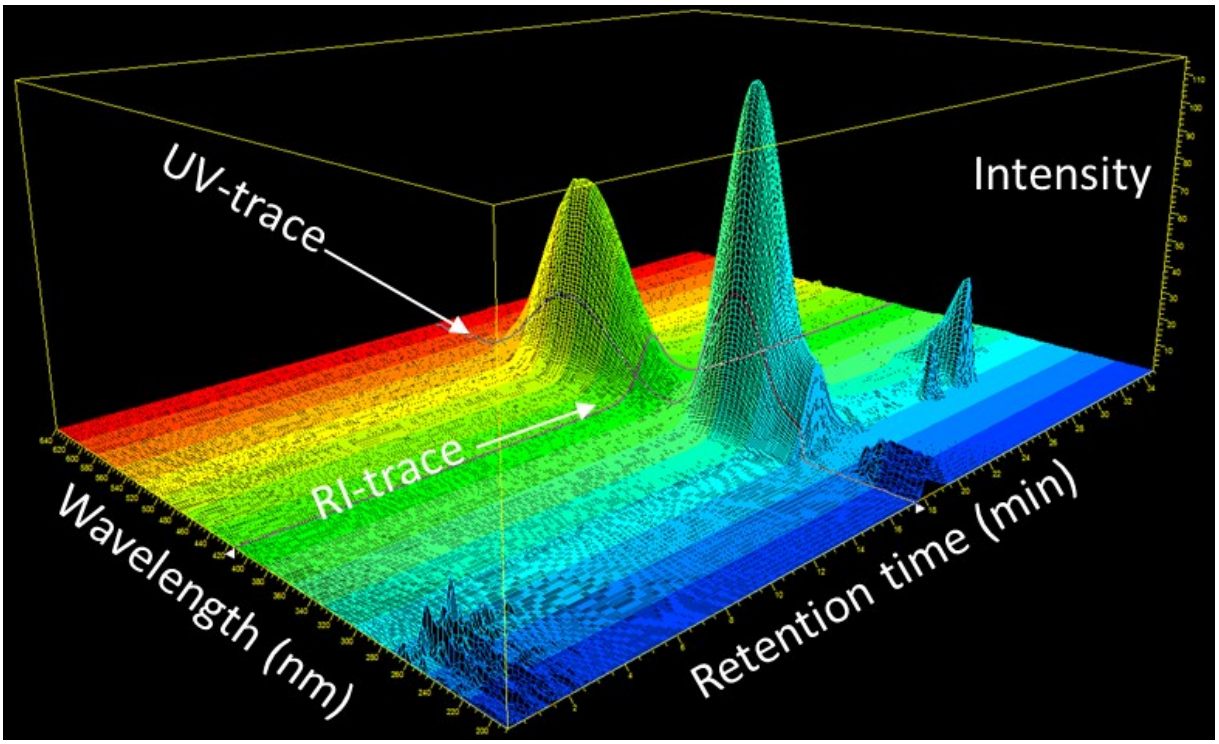

Figure S9. : 3D SEC-image, displaying the retention time of the polymer (x-axis), and the relative intensity (y-axis) as a function of wavelength (z-axis). Gray lines display the overall refractive index trace and UV-absorption spectrum of the polymer.

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(3) Voorhaar, L., Van Hecke, K., Vancoillie, G., Zhang, Q. & Hoogenboom, R. In Controlled Radical Polymerization: Materials. *High-Throughput Synthesis of Thermoresponsive Poly(oligoethylene glycol acrylate) Copolymers by RAFT Polymerization* **2015**) *1188,*