High throughput screening for the design of protein binding polymers

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SUPPLEMENTARY INFORMATION

Experimental methods

Materials

All solvents and chemicals were purchased from common commercial sources (Sigma Aldrich, Merck, etc.) unless otherwise stated. *Glucose oxidase* (GOx) from *Aspergillius niger, Bovine Serum Albumin* (BSA), *Trypsin*, *Uricase*, *Lysosyme (chicken egg white)*, *Casein*, *Manganese Peroxidase* (MnP) and *Carbonic Anhydrase* (CAn) were purchased from Sigma Aldrich, stored at -30 °C and used as received. Cy3-COOH and Cy5 acrylate were synthesized according to our previous report.[30] Monomers for the polymer synthesis have been purified over inhibitor remover columns (Sigma Aldrich) prior to synthesis. The recombinant human TRAIL protein was purchased from Abcam (ab256115) and represents a 19.5 kDa active fragment of the full-length protein (amino acids 115 to 281).

Instrumentation

Size Exclusion Chromatography (SEC) measurements were performed in a DMF eluent containing 0.1 % lithium chloride at 50 °C. Calibration was carried out using polyethylene glycol (PEG), on a Shimadzu system, equipped with an *RID-10A* detector and an Agilent *PolarGel M* column. ^{1}H NMR spectra were acquired with a Bruker 400 MHz spectrometer and processed using *MestreNova.* Conversion was estimated by addition of 1,3,5-triazole standard in the NMR samples. Quantification of the Cy3 to enzyme ratio and the FRET read-out and heat assays were performed on a *SpectraMax iD3* plate reader from Molecular Devices.

Small angle X-ray scattering

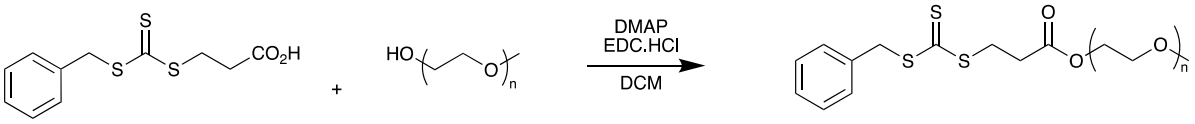
SAXS experiments were carried out at the Australian Synchrotron on the small-/wide-angle X-ray scattering beamline[36] using X-rays with a wavelength, λ, of 1.033 Å (12 keV). Isotropic scattering patterns were collected on a Pilatus 2 M detector with an active area of 981 × 1043 pixels of 170 m^2 each with a 2.3 m sample to detector distance. The magnitude of the scattering vector (q) is defined by $q = 4\pi/\lambda \sin(\theta/2)$, where θ is the scattering angle. The samples were placed in a 96-well plate solution autoloader from where samples were taken automatically, and the SAXS was measured in a consistent position in a quartz capillary. Scatterbrain (ANSTO) was used to radially average the raw pixels in the SAXS images and subtract the background patterns, which were collected for each solvent mixture. Data was fit to a core shell model, using the radius and SLD of the protein as the core, using SASview[37] and the NIST IgorPro macros.[38]

Protein labelling

Proteins were labelled with Cy3-COOH *via* amide coupling. The protein was dissolved in 50 mM carbonate buffer (pH 9.6). Stock solutions of the coupling reagents 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) hydrochloride (20 mg/mL) and *N*-hydroxy succinimide (NHS, 20 mg/mL) were prepared in 100 mM MES buffer (pH 5.5). Cy3-COOH (10 mg/mL) was

dissolved in a DMSO / water mixture. Cy3 CO_2H (18.8 µL, 40 eq.), EDC hydrochloride (26.4 µL, 300 eq.) and NHS (43.8 µL, 800 eq.) were mixed in MES buffer. After 15 mins the protein (e.g. GOx, 1.25 mg, 1 eq.) was added. The coupling reaction was left over night and purified the next day over a *Sephadex* G15 column in 50 mM phosphate buffer (pH 7.4). It was estimated that all enzyme was recovered from the column. The amount of Cy3 in each labelled protein batch was estimated with fluorescent reading (see table S2).

Synthesis of macro-RAFT agent



Poly(ethylene glycol) macro-RAFT agent was prepared by esterification of the carboxy functional in 3-benzylsulfanylthiocarbonylsulfanylpropionic acid (BSPA) RAFT agent, with the hydroxy functional in 1.9 kDa poly(ethylene glycol) methyl ether (mPEG) through EDC coupling approach. mPEG (2.00 g, 1.05 mmol) and DMAP (102.88 mg, 0.84 mmol) were dissolved in 5 mL cold anhydrous DCM. To the mixture was added a solution of BSPA (2.29 g, 8.42 mmol) and (EDC·HCl, 2.42 g, 12.63 mmol) in 5 mL of cold anhydrous DCM. The mixture was stirred in an ice bath for 10 minutes and the reaction was continued at room temperature for 18 hours. The solvent was condensed under reduced pressure. The product was precipitated from cold diethyl ether twice. The crude was purified by dialysis against water and freeze-dried to afford a pale-yellow powder. ^{1}H NMR (400 MHz, $CDCl_3$) confirmed the success of the EDC coupling of BSPA to PEG by showing peaks at 7.29-7.32 ppm (m, 5H, ArH), 4.59 ppm (s, 2H, $ArCH_2$), and 3.80−3.44 ppm (m, 168H, CH_2−O).

Polymer Synthesis on Automated Workstation

Polymer library synthesis was facilitated with a *Beckmann Coulter* Automated Workstation (Biomek NX^P MC). An oxygen insensitive *enz*-RAFT polymerisation technique was applied for the synthesis of the polymers. As a reaction solvent, 50 mM phosphate buffer (pH 7.4) with 10 % DMSO content was used. Additional to the monomer mixture (0.5 M), Cy 5 acrylate monomer (0.1 mM) was added to incorporate the relevant fluorescence dye in the polymers needed for the FRET transfer. The initiator VA-044 and RAFT agent 2-(butylthiocarbonothioylthio)propanoic acid (BTPA) were used in a ratio of 0.1 to achieve a degree of polymerisation (DP) of 100 units. In *enz*-RAFT, GOx was used to consume free oxygen in solution. For the activity of the enzyme relevant glucose (0.05 M) and pyruvate (0.05 M) were added. GOx was added last (0.002 mM). The enzyme was allowed to consume oxygen for 30 mins prior to putting the polymerisation batches into an oven overnight at 45 °C. The polymer libraries were used without further purification. Composition data, GPC characterisation and selected conversions for the full library can be found in tables S4-S5. Additionally, the logP of each monomer was estimated with **https://molinspiration.com/** (table S3a). With that, the hydrophobicity of the polymer was estimated by calculating the weighted average of all the monomer logP for each polymer. A table of the estimated log P is provided (Table S3b). The estimated logP for polymers ranges from –163.0 to +45.5 and –24.3 to +37.6 for library 1 and library 2, respectively.

FRET assays

FRET screening was performed with Cy3 labelled enzyme at different enzyme concentrations ranging from 0.1 to 1.00 µM in low volume 384 well plates with a total volume of 40 µL. The concentration of the polymer was based on molecular equivalents to the enzyme. Each FRET assay was duplicated. Fluorescence screens were performed at an excitation wavelength of 485 nm and the emission wavelength was measured at 570 nm (Ex 485 / Em 570), further at Ex 485 / Em 670 and Ex 610 / 670. Fluorescence screens at Ex 485 / Em 570 and Ex 610 / 670 are the corresponding signals related to Cy3 and

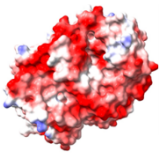
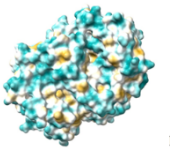
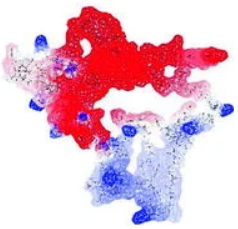
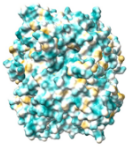
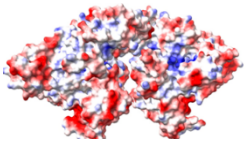
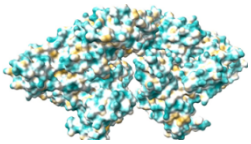
Cy5, respectively. The signal gained from Ex 485 / Em 670 can be interpreted as the FRET signal, where resonance transfer from one dye molecule (Cy3) to the other (Cy5) happens due the binding of polymer to enzyme and resulting low distance between dye molecules. FRET ratio results with an error of > 10 % were excluded from reporting.

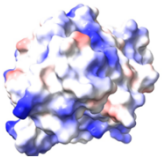
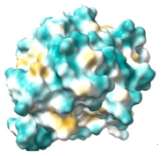
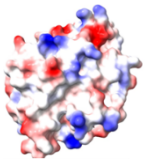
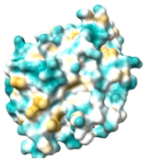
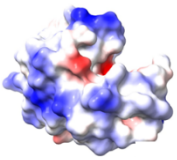
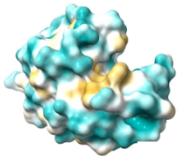
Stability assays

We screened the majority of the polymer libraries to investigate the influence of polymer binding on the stability of GOx towards heat stress. For this assay, 40 µg/mL GOx in 20 mM phosphate buffer (pH = 7.4) was incubated with 16 equivalents of polymer. Per plate, two controls of GOx without polymer were prepared accordingly. This was incubated in an oven at 60 °C for 20 mins. Activity of GOx in these conditions was screened before as to be seen in **Figure S4**.

After the incubation period, the GOx was diluted 100-fold to 400 ng/mL. The following heat assay was automated on the Biomek workstation. In 96 well plates, 50 µL of the dilution was incubated with 50 µL 0.1 M glucose (in 20 mM phosphate buffer). After 5 mins, 50 µL of 0.25 mM TMB with 2 ug/mL HRP (in 50 mM citrate buffer, pH = 5.5) were added and left to incubate for another minute. The reaction was quenched with 20 µL of 1 M H_2SO_4. Readout was performed on *SpectraMax iD3* plate reader at a wavelength of 450 nm.

Table S1. Characteristics of the proteins used in this study.

Protein	Molecular weight (kDa)	Isoelectric point (pI)	PDB ID codes	Coulombic electrostatic potential (ESP)	Molecular lipophilicity potential (MLP)
Manganese peroxidase	40	4.55	1MNP	-	-
Glucose oxidase	160	4.95	1CF3		
κ-casein	25	5.26	-		-
Uricase	34	5.54	4R8X		
Bovine serum albumin	69	5.82	4F5S		

Trypsin	27	6.08	1S81		
Carbonic anhydrase	35	6.36	1V9E		
Lysozyme	16	9.36	1DPX		

Protein crystal structures were retrieved from The Protein Data Bank.9 Electrostatic potential and hydrophobicity were calculated and visualised using UCSF ChimeraX program.10 (ESP) Ranging from **red** for negative potential through **white** to **blue** for positive potential. (MLP) maps ranging from **dark cyan** (most hydrophilic) to **white** to **dark goldenrod** (most lipophilic). No crystal structure is available for κ-casein, instead, sequence-obtained molecular modelling shows that it consists of two separate domains: a hydrophilic domain carrying a negative charge and a hydrophobic domain carrying a positive charge. Data obtained with permission from ref.14 Copyright 2013 Springer Science Business Media New York.

Table S2. Average Cy3 to enzyme ratio of labelled enzymes and standard deviation (SD) for all enzymes used as well as number of lysines per enzyme. N.D. = not determined.

Protein	MW [g/mol]	Average Cy3/enzyme ratio	SD	# lysines
MnP	39 557	0.22	± 0.00	9
GOx	160 000	1.41	± 0.35	15
Cas	25 000	N.D.	N.D.	12
Uri	34 000	N.D.	N.D.	29
BSA	66 463	1.39	± 0.16	60
Try	26 558	N.D.	N.D.	14
CAn	30 000	0.17	± 0.01	16
Lys	16 000	N.D.	N.D.	6

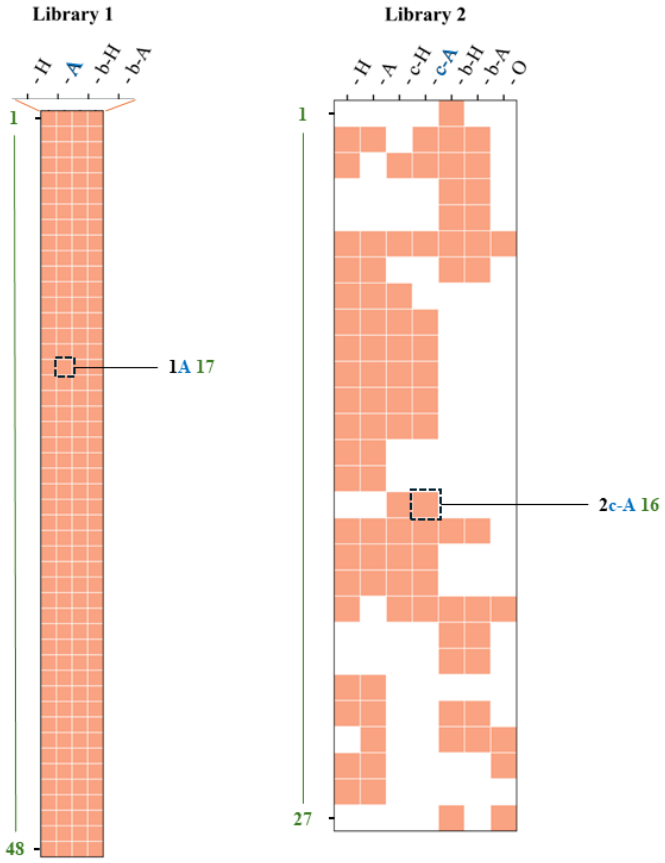


Figure S1. Overview over systematic index names of polymers of library 1 and 2.

Table S3a. LogP of each monomer used for the synthesis of library 1 and 2. LogP calculated with https://molinspiration.com/.

monomer	milogP
H	0.09
A	-0.31
N	0.74
S	-2.83
C	0.34
D	0.36
X	1.25
Q	-3.61
F	2.41
M	0.82
Y	2.26

Table S3b. Calculated logP of all polymers in library 1.

Index #	logP	Index #	logP	Index #	logP	Index #	logP
1H 1	-139.00	1A 1	-163.00	1b-H 1	-139.00	1b-A 1	-163.00
1H 2	-139.00	1A 2	-163.00	1b-H 2	-139.00	1b-A 2	-163.00
1H 3	-115.80	1A 3	-135.80	1b-H 3	-115.80	1b-A 3	-135.80
1H 4	19.80	1A 4	-4.20	1b-H 4	19.80	1b-A 4	-4.20
1H 5	43.00	1A 5	23.00	1b-H 5	43.00	1b-A 5	23.00
1H 6	-113.30	1A 6	-129.30	1b-H 6	-113.30	1b-A 6	-129.30
1H 7	45.50	1A 7	29.50	1b-H 7	45.50	1b-A 7	29.50
1H 8	-134.00	1A 8	-150.00	1b-H 8	-134.00	1b-A 8	-150.00
1H 9	-65.00	1A 9	-97.00	1b-H 9	-65.00	1b-A 9	-97.00
1H 10	-65.00	1A 10	-97.00	1b-H 10	-65.00	1b-A 10	-97.00
1H 11	24.80	1A 11	8.80	1b-H 11	24.80	1b-A 11	8.80
1H 12	14.40	1A 12	-17.60	1b-H 12	14.40	1b-A 12	-17.60
1H 13	-2.00	1A 13	-22.00	1b-H 13	-2.00	1b-A 13	-22.00
1H 14	7.00	1A 14	-29.00	1b-H 14	7.00	1b-A 14	-29.00
1H 15	5.00	1A 15	-27.00	1b-H 15	5.00	1b-A 15	-27.00
1H 16	1.00	1A 16	-23.00	1b-H 16	1.00	1b-A 16	-23.00
1H 17	-7.00	1A 17	-15.00	1b-H 17	-7.00	1b-A 17	-15.00

1H 18	12.65	1A 18	-25.35	1b-H 18	12.65	1b-A 18	-25.35
1H 19	20.60	1A 19	-17.40	1b-H 19	20.60	1b-A 19	-17.40
1H 20	14.80	1A 20	-23.20	1b-H 20	14.80	1b-A 20	-23.20
1H 21	16.30	1A 21	-19.70	1b-H 21	16.30	1b-A 21	-19.70
1H 22	32.20	1A 22	-3.80	1b-H 22	32.20	1b-A 22	-3.80
1H 23	20.60	1A 23	-15.40	1b-H 23	20.60	1b-A 23	-15.40
1H 24	-60.00	1A 24	-84.00	1b-H 24	-60.00	1b-A 24	-84.00
1H 25	19.40	1A 25	-4.60	1b-H 25	19.40	1b-A 25	-4.60
1H 26	0.50	1A 26	-15.50	1b-H 26	0.50	1b-A 26	-15.50
1H 27	35.00	1A 27	11.00	1b-H 27	35.00	1b-A 27	11.00
1H 28	22.00	1A 28	-10.00	1b-H 28	22.00	1b-A 28	-10.00
1H 29	-49.40	1A 29	-81.40	1b-H 29	-49.40	1b-A 29	-81.40
1H 30	-49.40	1A 30	-81.40	1b-H 30	-49.40	1b-A 30	-81.40
1H 31	14.00	1A 31	-18.00	1b-H 31	14.00	1b-A 31	-18.00
1H 32	12.00	1A 32	-16.00	1b-H 32	12.00	1b-A 32	-16.00
1H 33	17.65	1A 33	-12.35	1b-H 33	17.65	1b-A 33	-12.35
1H 34	25.60	1A 34	-4.40	1b-H 34	25.60	1b-A 34	-4.40
1H 35	19.80	1A 35	-10.20	1b-H 35	19.80	1b-A 35	-10.20
1H 36	10.00	1A 36	-14.00	1b-H 36	10.00	1b-A 36	-14.00
1H 37	21.30	1A 37	-6.70	1b-H 37	21.30	1b-A 37	-6.70
1H 38	37.20	1A 38	9.20	1b-H 38	37.20	1b-A 38	9.20
1H 39	25.60	1A 39	-2.40	1b-H 39	25.60	1b-A 39	-2.40
1H 40	27.00	1A 40	3.00	1b-H 40	27.00	1b-A 40	3.00
1H 41	40.00	1A 41	24.00	1b-H 41	40.00	1b-A 41	24.00
1H 42	19.00	1A 42	-5.00	1b-H 42	19.00	1b-A 42	-5.00
1H 43	-44.40	1A 43	-68.40	1b-H 43	-44.40	1b-A 43	-68.40
1H 44	-107.80	1A 44	-131.80	1b-H 44	-107.80	1b-A 44	-131.80
1H 45	-107.80	1A 45	-131.80	1b-H 45	-107.80	1b-A 45	-131.80
1H 46	-84.60	1A 46	-104.60	1b-H 46	-84.60	1b-A 46	-104.60
1H 47	-82.10	1A 47	-98.10	1b-H 47	-82.10	1b-A 47	-98.10
1H 48	-102.80	1A 48	-118.80	1b-H 48	-102.80	1b-A 48	-118.80

Table S3c. Calculated logP of all polymers in library 2.

Index #	logP	Index #	logP	Index #	logP	Index #	logP
2H 2	25.20	2A 2	9.20			2c-A 2	21.60
2H 3	22.50			2c-H 3	18.90	2c-A 3	14.90
2H 6	14.40	2A 6	-17.60	2c-H 6	10.80	2c-A 6	-5.20
2H 7	18.05	2A 7	-11.95				
2H 8	18.05	2A 8	-11.95	2c-H 8	14.45		
2H 9	25.25	2A 9	-4.75	2c-H 9	21.65	2c-A 9	7.65
2H 10	26.00	2A 10	-4.00	2c-H 10	22.40	2c-A 10	8.40
2H 11	21.70	2A 11	-6.30	2c-H 11	18.10	2c-A 11	6.10
2H 12	36.10	2A 12	8.10	2c-H 12	32.50	2c-A 12	20.50
2H 13	37.60	2A 13	9.60	2c-H 13	34.00	2c-A 13	22.00
2H 14	15.65	2A 14	-14.35				
2H 15	15.65	2A 15	-14.35				
				2c-H 16	8.10	2c-A 16	-11.90
2H 17	11.70	2A 17	-24.30	2c-H 17	13.30	2c-A 17	1.30
2H 18	16.90	2A 18	-11.10	2c-H 18	35.00	2c-A 18	27.00
2H 19	16.90	2A 19	-11.10	2c-H 19	35.00	2c-A 19	27.00
2H 20	9.00			2c-H 20	5.40	2c-A 20	-18.60
2H 23	19.00	2A 23	-5.00				
2H 24	21.50	2A 24	1.50				
		2A 25	8.00				
2H 26	29.00	2A 26	21.00				
2H 27	31.50	2A 27	27.50				
2b-H 1	36.00						
2b-H 2	25.20	2b-A 2	9.20				
2b-H 3	22.50	2b-A 3	2.50				
2b-H 4	25.00	2b-A 4	9.00				
2b-H 5	27.50	2b-A 5	15.50				
2b-H 6	30.00	2b-A 6	22.00	2O 6	35.20		
2b-H 7	14.40	2b-A 7	-17.60				
2b-H 17	11.70	2b-A 17	11.70				

2b-H 20	9.00	2b-A 20	9.00	2O 20	35.00	
2b-H 21	11.50	2b-A 21	11.50			
2b-H 22	14.00	2b-A 22	14.00			
2b-H 24	21.50	2b-A 24	21.50			
2b-H 25	24.00	2b-A 25	24.00	2O 25	34.40	
				2O 26	34.20	
2b-H 28	34.00			2O 28		

Table S4. Characterisation data (^{1}H NMR & GPC) of library 1. The polymerisations were conducted in 8-strip PCR tubes with 200 µL per vial for 16 hours at 45 °C in 10% DMSO. [M]/[RAFT] = 100, [RAFT]/[initiator] = 10, [GOx] = 2 µmol L^{-1}, and [M] = 0.5 mol L^{-1}.

Index #	polymer	RAFT agent	$M_{n,\,theo}$ [b] (g mol^{-1})	$M_{W,\,GPC}$ [c] (g mol^{-1})	$M_{n,\,GPC}$ [c] (g mol^{-1})	Đ [d]	conversion NMR[a] / %
1H 1	P(H_{60}-*co*-Q_{40})	BTPA	15500	5200	5100	1.04	N.D.
1H 2*	P(H_{60}-*co*-Q_{40})	BTPA	15500	10000	9400	1.06	N.D.
1H 3*	P(H_{50}-*co*-Q_{40}-*co*-F_{10})	BTPA	15900	44700	42100	1.06	N.D.
1H 4*	P(H_{60}-*co*-D_{40})	BTPA	13500	18600	14700	1.26	N.D.
1H 5*	P(H_{50}-*co*-D_{40}-*co*-F_{10})	BTPA	13900	16200	13300	1.22	N.D.
1H 6	P(H_{40}-*co*-Q_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	16200	48200	36900	1.31	N.D.
1H 7*	P(H_{40}-*co*-D_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	14200	18700	14800	1.27	N.D.
1H 8*	P(H_{40}-*co*-Q_{40}-*co*-C_{20})	BTPA	16000	44400	41200	1.08	N.D.
1H 9	P(H_{80}-*co*-Q_{20})	BTPA	13700	6800	4600	1.48	99
1H 10	P(H_{80}-*co*-Q_{20})	BTPA	13700	15000	9100	1.65	N.D.
1H 11*	P(H_{40}-*co*-D_{40}-*co*-C_{20})	BTPA	14000	28600	20100	1.42	100
1H 12*	P(H_{80}-*co*-D_{20})	BTPA	12700	31300	22800	1.38	N.D.
1H 13	P(H_{50}-*co*-N_{40}-*co*-Q_{10})	BTPA	12600	24800	16500	1.50	N.D.
1H 14	P(H_{95}-*co*-A_5)	BTPA	11600	24900	21100	1.18	N.D.
1H 15	P(H_{90}-*co*-A_{10})	BTPA	11400	24500	20700	1.18	N.D.
1H 16	P(H_{80}-*co*-A_{20})	BTPA	10900	21900	18500	1.18	N.D.
1H 17	P(H_{60}-*co*-A_{40})	BTPA	10000	16500	13800	1.19	N.D.
1H 18	P(H_{95}-*co*-M_5)	BTPA	11700	23000	17800	1.30	99
1H 19	P(H_{95}-*co*-F_5)	BTPA	12100	25300	21400	1.18	N.D.
1H 20	P(H_{95}-*co*-X_5)	BTPA	11900	24900	21100	1.18	N.D.
1H 21	P(H_{90}-*co*-M_{10})	BTPA	11500	23200	19600	1.18	N.D.

1H 22	P(H_{90}-*co*-F_{10})	BTPA	12300	24100	20200	1.19	N.D.
1H 23	P(H_{90}-*co*-X_{10})	BTPA	12000	24200	20400	1.18	N.D.
1H 24*	P(H_{60}-*co*-Q_{20}-*co*-C_{20})	BTPA	14200	29000	24700	1.18	N.D.
1H 25*	P(H_{60}-*co*-D_{20}-*co*-C_{20})	BTPA	13200	57400	41500	1.38	N.D.
1H 26*	P(H_{40}-*co*-N_{40}-*co*-Q_{10} -*co*-C_{10})	BTPA	12900	25300	20700	1.22	N.D.
1H 27	P(H_{60}-*co*-N_{40})	BTPA	11700	47500	32700	1.45	N.D.
1H 28	P(H_{80}-*co*-N_{20})	BTPA	11800	39000	28700	1.36	N.D.
1H 29*	P(H_{80}-*co*-S_{20})	BTPA	13700	15900	12600	1.26	N.D.
1H 30*	P(H_{80}-*co*-S_{20})	BTPA	13700	61500	60300	1.02	N.D.
1H 31	P(H_{80}-*co*-C_{20})	BTPA	12400	15400	11700	1.31	N.D.
1H 32	P(H_{75}-*co*-C_{20}-*co*-A_5)	BTPA	12200	14300	10800	1.33	N.D.
1H 33	P(H_{75}-*co*-C_{20}-*co*-M_5)	BTPA	12300	15900	11900	1.33	N.D.
1H 34	P(H_{75}-*co*-C_{20}-*co*-F_5)	BTPA	12600	19800	16700	1.19	N.D.
1H 35	P(H_{75}-*co*-C_{20}-*co*-X_5)	BTPA	12500	15100	11300	1.34	N.D.
1H 36	P(H_{70}-*co*-C_{20}-*co*-A_{10})	BTPA	12000	13800	10500	1.31	N.D.
1H 37	P(H_{70}-*co*-C_{20}-*co*-M_{10})	BTPA	12100	16700	14300	1.17	N.D.
1H 38	P(H_{70}-*co*-C_{20}-*co*-F_{10})	BTPA	12900	19300	16000	1.20	N.D.
1H 39	P(H_{70}-*co*-C_{20}-*co*-X_{10})	BTPA	12500	14600	11400	1.29	N.D.
1H 40	P(H_{60}-*co*-N_{20}-*co*-C_{20})	BTPA	12400	33000	25100	1.32	99
1H 41	P(H_{40}-*co*-N_{40}-*co*-C_{20})	BTPA	12300	36300	31800	1.14	N.D.
1H 42	P(H_{60}-*co*-C_{40})	BTPA	13000	36045	26978	1.34	N.D.
1H 43*	P(H_{60}-*co*-S_{20}-*co*-C_{20})	BTPA	14200	44800	41500	1.08	N.D.
1H 44	P(H_{60}-*co*-S_{40})	BTPA	15500	5772	5224	1.10	N.D.
1H 45*	P(H_{60}-*co*-S_{40})	BTPA	15500	44700	42400	1.05	N.D.
1H 46*	P(H_{50}-*co*-S_{40}-*co*-F_{10})	BTPA	16000	14900	12000	1.24	N.D.

1H 47	P(H_{40}-*co*-S_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	16200	36000	31500	1.14	73
1H 48*	P(H_{40}-*co*-S_{40}-*co*-C_{20})	BTPA	16100	46200	44400	1.04	N.D.
1A 1	P(A_{60}-*co*-Q_{40})	BTPA	12800	24400	13800	1.76	N.D.
1A 2*	P(A_{60}-*co*-Q_{40})	BTPA	12800	N.D.	N.D.	-	N.D.
1A 3*	P(A_{50}-*co*-Q_{40}-*co*-F_{10})	BTPA	13700	8800	8600	1.02	N.D.
1A 4*	P(A_{60}-*co*-D_{40})	BTPA	10800	62500	53500	1.17	N.D.
1A 5*	P(A_{50}-*co*-D_{40}-*co*-F_{10})	BTPA	11700	55100	50600	1.09	N.D.
1A 6*	P(A_{40}-*co*-Q_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	14400	8700	8500	1.02	N.D.
1A 7	P(A_{40}-*co*-D_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	12400	38800	34300	1.13	N.D.
1A 8*	P(A_{40}-*co*-Q_{40}-*co*-C_{20})	BTPA	14200	36400	33900	1.08	100
1A 9*	P(A_{80}-*co*-Q_{20})	BTPA	10100	N.D.	N.D.	-	N.D.
1A 10*	P(A_{80}-*co*-Q_{20})	BTPA	10100	16000	13600	1.17	N.D.
1A 11*	P(A_{40}-*co*-D_{40}-*co*-C_{20})	BTPA	12200	13800	11500	1.20	94
1A 12*	P(A_{80}-*co*-D_{20})	BTPA	9000	60400	52800	1.14	N.D.
1A 13	P(A_{50}-*co*-N_{40}-*co*-Q_{10})	BTPA	10400	27300	21500	1.27	N.D.
1A 14*	P(A_{95}-*co*-H_5)	BTPA	7600	13900	12300	1.13	N.D.
1A 15*	P(A_{90}-*co*-H_{10})	BTPA	7800	13700	12100	1.12	N.D.
1A 16	P(A_{80}-*co*-H_{20})	BTPA	8200	10200	7500	1.37	N.D.
1A 17	P(A_{60}-*co*-H_{40})	BTPA	9100	17400	12800	1.36	N.D.
1A 18*	P(A_{95}-*co*-M_5)	BTPA	7400	13500	11900	1.13	N.D.
1A 19*	P(A_{95}-*co*-F_5)	BTPA	7800	12700	11200	1.13	N.D.
1A 20*	P(A_{95}-*co*-X_5)	BTPA	7600	13400	11900	1.13	N.D.
1A 21*	P(A_{90}-*co*-M_{10})	BTPA	7500	13300	11800	1.13	N.D.
1A 22*	P(A_{90}-*co*-F_{10})	BTPA	8300	12500	11100	1.13	N.D.
1A 23*	P(A_{90}-*co*-X_{10})	BTPA	7900	13200	11600	1.14	N.D.

1A 24*	P(A_{60}-*co*-Q_{20}-*co*-C_{20})	BTPA	11500	22700	17200	1.32	N.D.
1A 25*	P(A_{60}-*co*-D_{20}-*co*-C_{20})	BTPA	10500	60900	58100	1.05	N.D.
1A 26	P(A_{40}-*co*-N_{40}-*co*-Q_{10} -*co*-C_{10})	BTPA	11100	41000	33200	1.23	N.D.
1A 27	P(A_{60}-*co*-N_{40})	BTPA	9000	25200	19400	1.30	99
1A 28	P(A_{80}-*co*-N_{20})	BTPA	8200	13100	10400	1.26	N.D.
1A 29*	P(A_{80}-*co*-S_{20})	BTPA	10100	11200	10200	1.10	N.D.
1A 30*	P(A_{80}-*co*-S_{20})	BTPA	10100	8500	7600	1.12	N.D.
1A 31*	P(A_{80}-*co*-C_{20})	BTPA	8800	34500	31000	1.11	N.D.
1A 32*	P(A_{75}-*co*-C_{20}-*co*-H_5)	BTPA	9000	36100	33100	1.09	N.D.
1A 33*	P(A_{75}-*co*-C_{20}-*co*-M_5)	BTPA	8900	35200	30200	1.16	95
1A 34	P(A_{75}-*co*-C_{20}-*co*-F_5)	BTPA	9300	280400	231900	1.21	N.D.
1A 35*	P(A_{75}-*co*-C_{20}-*co*-X_5)	BTPA	9100	35900	32300	1.11	N.D.
1A 36*	P(A_{70}-*co*-C_{20}-*co*-H_{10})	BTPA	9300	36700	33300	1.10	N.D.
1A 37*	P(A_{70}-*co*-C_{20}-*co*-M_{10})	BTPA	9000	34900	31200	1.12	N.D.
1A 38*	P(A_{70}-*co*-C_{20}-*co*-F_{10})	BTPA	9700	46800	41100	1.14	N.D.
1A 39*	P(A_{70}-*co*-C_{20}-*co*-X_{10})	BTPA	9400	34500	31200	1.10	N.D.
1A 40	P(A_{60}-*co*-N_{20}-*co*-C_{20})	BTPA	9600	64800	62000	1.05	N.D.
1A 41	P(A_{40}-*co*-N_{40}-*co*-C_{20})	BTPA	10500	13900	10600	1.30	N.D.
1A 42*	P(A_{60}-*co*-C_{40})	BTPA	10300	67700	55900	1.21	N.D.
1A 43	P(A_{60}-*co*-S_{20}-*co*-C_{20})	BTPA	11500	69500	66400	1.05	N.D.
1A 44*	P(A_{60}-*co*-S_{40})	BTPA	12800	9000	8400	1.07	83
1A 45	P(A_{60}-*co*-S_{40})	BTPA	12800	69100	65900	1.05	N.D.
1A 46	P(A_{50}-*co*-S_{40}-*co*-F_{10})	BTPA	13700	70200	67000	1.05	N.D.
1A 47	P(A_{40}-*co*-S_{40}-*co*-F_{10} -*co*-C_{10})	BTPA	14400	1100	1100	1.05	83
1A 48	P(A_{40}-*co*-S_{40}-*co*-C_{20})	BTPA	14300	70800	67700	1.05	N.D.

1b-H 1	PEG_{113}-*b*-P(H_{60}-*co*-Q_{40})	PEG 113 RAFT	20500	184200	157500	1.17	N.D.
1b-H 2	PEG_{113}-*b*-P(H_{60}-*co*-Q_{40})	PEG 113 RAFT	20500	6500	6300	1.03	N.D.
1b-H 3	PEG_{113}-*b*-P(H_{50}-*co*-Q_{40}-*co*-F_{10})	PEG 113 RAFT	21000	229000	158100	1.45	N.D.
1b-H 4*	PEG_{113}-*b*-P(H_{60}-*co*-D_{40})	PEG 113 RAFT	18500	14500	11600	1.24	N.D.
1b-H 5	PEG_{113}-*b*-P(H_{50}-*co*-D_{40}-*co*-F_{10})	PEG 113 RAFT	19000	5300	4100	1.27	91
1b-H 6	PEG_{113}-*b*-P(H_{40}-*co*-Q_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	21300	6000	5700	1.05	N.D.
1b-H 7	PEG_{113}-*b*-P(H_{40}-*co*-D_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	19200	71200	68700	1.04	N.D.
1b-H 8	PEG_{113}-*b*-P(H_{40}-*co*-Q_{40}-*co*-C_{20})	PEG 113 RAFT	21100	5900	5600	1.07	N.D.
1b-H 9	PEG_{113}-*b*-P(H_{80}-*co*-Q_{20})	PEG 113 RAFT	18700	14600	13100	1.12	85
1b-H 10	PEG_{113}-*b*-P(H_{80}-*co*-Q_{20})	PEG 113 RAFT	18700	6700	4600	1.45	99
1b-H 11	PEG_{113}-*b*-P(H_{40}-*co*-D_{40}-*co*-C_{20})	PEG 113 RAFT	19100	61700	50200	1.23	N.D.
1b-H 12	PEG_{113}-*b*-P(H_{80}-*co*-D_{20})	PEG 113 RAFT	17700	5200	4100	1.25	N.D.
1b-H 13*	PEG_{113}-*b*-P(H_{50}-*co*-N_{40}-*co*-Q_{10})	PEG 113 RAFT	17700	45100	42600	1.06	N.D.
1b-H 14	PEG_{113}-*b*-P(H_{95}-*co*-A_5)	PEG 113 RAFT	16700	19200	16300	1.17	N.D.
1b-H 15	PEG_{113}-*b*-P(H_{90}-*co*-A_{10})	PEG 113 RAFT	16400	21500	18200	1.18	N.D.
1b-H 16	PEG_{113}-*b*-P(H_{80}-*co*-A_{20})	PEG 113 RAFT	16000	26000	21400	1.22	N.D.
1b-H 17	PEG_{113}-*b*-P(H_{60}-*co*-A_{40})	PEG 113 RAFT	15100	21200	18400	1.16	N.D.
1b-H 18	PEG_{113}-*b*-P(H_{95}-*co*-M_5)	PEG 113 RAFT	16700	33300	26800	1.24	99
1b-H 19	PEG_{113}-*b*-P(H_{95}-*co*-F_5)	PEG 113 RAFT	17100	34700	27900	1.24	N.D.
1b-H 20	PEG_{113}-*b*-P(H_{95}-*co*-X_5)	PEG 113 RAFT	16900	34600	27900	1.24	N.D.
1b-H 21	PEG_{113}-*b*-P(H_{90}-*co*-M_{10})	PEG 113 RAFT	16600	35100	28200	1.24	N.D.
1b-H 22	PEG_{113}-*b*-P(H_{90}-*co*-F_{10})	PEG 113 RAFT	17300	35700	28800	1.24	95
1b-H 23	PEG_{113}-*b*-P(H_{90}-*co*-X_{10})	PEG 113 RAFT	17000	22900	19200	1.19	N.D.
1b-H 24	PEG_{113}-*b*-P(H_{60}-*co*-Q_{20}-*co*-C_{20})	PEG 113 RAFT	19300	184600	155700	1.19	N.D.
1b-H 25*	PEG_{113}-*b*-P(H_{60}-*co*-D_{20}-*co*-C_{20})	PEG 113 RAFT	18300	50800	35800	1.42	N.D.

1b-H 26*	PEG_{113}-*b*-P(H_{40}-*co*-N_{40}-*co*-Q_{10} -*co*-C_{10})	PEG 113 RAFT	18000	17000	13100	1.30	N.D.
1b-H 27	PEG_{113}-*b*-P(H_{60}-*co*-N_{40})	PEG 113 RAFT	16800	34600	28100	1.23	98
1b-H 28	PEG_{113}-*b*-P(H_{80}-*co*-N_{20})	PEG 113 RAFT	16800	32300	26100	1.24	N.D.
1b-H 29	PEG_{113}-*b*-P(H_{80}-*co*-S_{20})	PEG 113 RAFT	18700	6300	5700	1.10	N.D.
1b-H 30	PEG_{113}-*b*-P(H_{80}-*co*-S_{20})	PEG 113 RAFT	18700	5600	4900	1.15	N.D.
1b-H 31	PEG_{113}-*b*-P(H_{80}-*co*-C_{20})	PEG 113 RAFT	17400	34700	28200	1.23	N.D.
1b-H 32	PEG_{113}-*b*-P(H_{75}-*co*-C_{20}-*co*-A_5)	PEG 113 RAFT	17200	16400	14500	1.13	N.D.
1b-H 33	PEG_{113}-*b*-P(H_{75}-*co*-C_{20}-*co*-M_5)	PEG 113 RAFT	17300	34000	27800	1.22	N.D.
1b-H 34	PEG_{113}-*b*-P(H_{75}-*co*-C_{20}-*co*-F_5)	PEG 113 RAFT	17700	27400	22300	1.23	N.D.
1b-H 35	PEG_{113}-*b*-P(H_{75}-*co*-C_{20}-*co*-X_5)	PEG 113 RAFT	17500	23400	19500	1.20	87
1b-H 36	PEG_{113}-*b*-P(H_{70}-*co*-C_{20}-*co*-A_{10})	PEG 113 RAFT	17000	25300	22200	1.14	87
1b-H 37	PEG_{113}-*b*-P(H_{70}-*co*-C_{20}-*co*-M_{10})	PEG 113 RAFT	17100	33000	27200	1.21	N.D.
1b-H 38	PEG_{113}-*b*-P(H_{70}-*co*-C_{20}-*co*-F_{10})	PEG 113 RAFT	17900	24000	20000	1.21	N.D.
1b-H 39	PEG_{113}-*b*-P(H_{70}-*co*-C_{20}-*co*-X_{10})	PEG 113 RAFT	17600	22300	18600	1.19	89
1b-H 40*	PEG_{113}-*b*-P(H_{40}-*co*-N_{40}-*co*-C_{20})	PEG 113 RAFT	17300	66500	57400	1.16	N.D.
1b-H 41	PEG_{113}-*b*-P(H_{60}-*co*-N_{20}-*co*-C_{20})	PEG 113 RAFT	17400	32400	22900	1.42	N.D.
1b-H 42	PEG_{113}-*b*-P(H_{60}-*co*-C_{40})	PEG 113 RAFT	18000	28300	22800	1.24	N.D.
1b-H 43	PEG_{113}-*b*-P(H_{60}-*co*-S_{20}-*co*-C_{20})	PEG 113 RAFT	19300	6400	6200	1.03	N.D.
1b-H 44	PEG_{113}-*b*-P(H_{60}-*co*-S_{40})	PEG 113 RAFT	20500	5600	5400	1.04	N.D.
1b-H 45	PEG_{113}-*b*-P(H_{60}-*co*-S_{40})	PEG 113 RAFT	20500	5900	5300	1.11	N.D.
1b-H 46	PEG_{113}-*b*-P(H_{50}-*co*-S_{40}-*co*-F_{10})	PEG 113 RAFT	21000	5700	5100	1.13	N.D.
1b-H 47	PEG_{113}-*b*-P(H_{40}-*co*-S_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	21300	71000	68000	1.04	N.D.
1b-H 48*	PEG_{113}-*b*-P(H_{40}-*co*-S_{40}-*co*-C_{20})	PEG 113 RAFT	21100	8100	7600	1.07	N.D.
1b-A 1	PEG_{113}-*b*-P(A_{60}-*co*-Q_{40})	PEG 113 RAFT	17800	5000	4400	1.13	N.D.
1b-A 2*	PEG_{113}-*b*-P(A_{60}-*co*-Q_{40})	PEG 113 RAFT	17800	46000	42800	1.07	N.D.

1b-A 3*	PEG_{113}-*b*-P(A_{50}-*co*-Q_{40}-*co*-F_{10})	PEG 113 RAFT	18700	50000	45800	1.09	N.D.
1b-A 4	PEG_{113}-*b*-P(A_{60}-*co*-D_{40})	PEG 113 RAFT	15800	67300	60900	1.10	N.D.
1b-A 5	PEG_{113}-*b*-P(A_{50}-*co*-D_{40}-*co*-F_{10})	PEG 113 RAFT	16700	73800	70600	1.04	N.D.
1b-A 6	PEG_{113}-*b*-P(A_{40}-*co*-Q_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	19500	245800	151700	1.62	N.D.
1b-A 7	PEG_{113}-*b*-P(A_{40}-*co*-D_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	17400	73100	69800	1.05	N.D.
1b-A 8	PEG_{113}-*b*-P(A_{40}-*co*-Q_{40}-*co*-C_{20})	PEG 113 RAFT	19300	285400	179800	1.59	N.D.
1b-A 9	PEG_{113}-*b*-P(A_{80}-*co*-Q_{20})	PEG 113 RAFT	15100	6000	5300	1.12	N.D.
1b-A 10	PEG_{113}-*b*-P(A_{80}-*co*-Q_{20})	PEG 113 RAFT	15100	282200	184600	1.53	N.D.
1b-A 11	PEG_{113}-*b*-P(A_{40}-*co*-D_{40}-*co*-C_{20})	PEG 113 RAFT	17300	72700	69300	1.05	N.D.
1b-A 12	PEG_{113}-*b*-P(A_{80}-*co*-D_{20})	PEG 113 RAFT	14100	5900	5500	1.07	N.D.
1b-A 13	PEG_{113}-*b*-P(A_{50}-*co*-N_{40}-*co*-Q_{10})	PEG 113 RAFT	15400	242700	196900	1.23	N.D.
1b-A 14	PEG_{113}-*b*-P(A_{95}-*co*-H_5)	PEG 113 RAFT	12600	134500	115200	1.17	N.D.
1b-A 15	PEG_{113}-*b*-P(A_{90}-*co*-H_{10})	PEG 113 RAFT	12800	114800	100900	1.14	N.D.
1b-A 16	PEG_{113}-*b*-P(A_{80}-*co*-H_{20})	PEG 113 RAFT	13300	15000	13400	1.12	N.D.
1b-A 17	PEG_{113}-*b*-P(A_{60}-*co*-H_{40})	PEG 113 RAFT	14200	19600	17300	1.13	N.D.
1b-A 18	PEG_{113}-*b*-P(A_{95}-*co*-M_5)	PEG 113 RAFT	12500	7900	6500	1.22	N.D.
1b-A 19	PEG_{113}-*b*-P(A_{95}-*co*-F_5)	PEG 113 RAFT	12800	8000	6600	1.23	N.D.
1b-A 20	PEG_{113}-*b*-P(A_{95}-*co*-X_5)	PEG 113 RAFT	12700	8400	6800	1.24	N.D.
1b-A 21	PEG_{113}-*b*-P(A_{90}-*co*-M_{10})	PEG 113 RAFT	12500	8600	7100	1.22	N.D.
1b-A 22	PEG_{113}-*b*-P(A_{90}-*co*-F_{10})	PEG 113 RAFT	13300	7700	6400	1.21	N.D.
1b-A 23	PEG_{113}-*b*-P(A_{90}-*co*-X_{10})	PEG 113 RAFT	13000	7100	6000	1.19	N.D.
1b-A 24	PEG_{113}-*b*-P(A_{60}-*co*-Q_{20}-*co*-C_{20})	PEG 113 RAFT	16600	269000	207300	1.30	N.D.
1b-A 25*	PEG_{113}-*b*-P(A_{60}-*co*-D_{20}-*co*-C_{20})	PEG 113 RAFT	15500	12600	10600	1.19	N.D.
1b-A 26	PEG_{113}-*b*-P(A_{40}-*co*-N_{40}-*co*-Q_{10} -*co*-C_{10})	PEG 113 RAFT	16200	251500	212400	1.18	N.D.
1b-A 27*	PEG_{113}-*b*-P(A_{60}-*co*-N_{40})	PEG 113 RAFT	13200	22300	18600	1.20	N.D.

1b-A 28	PEG_{113}-*b*-P(A_{60}-*co*-N_{40})	PEG 113 RAFT	14100	29500	24500	1.21	N.D.
1b-A 29	PEG_{113}-*b*-P(A_{80}-*co*-S_{20})	PEG 113 RAFT	15100	6200	5600	1.10	N.D.
1b-A 30	PEG_{113}-*b*-P(A_{80}-*co*-S_{20})	PEG 113 RAFT	15100	6500	6400	1.02	N.D.
1b-A 31	PEG_{113}-*b*-P(A_{80}-*co*-C_{20})	PEG 113 RAFT	13800	6500	5600	1.15	N.D.
1b-A 32	PEG_{113}-*b*-P(A_{75}-*co*-C_{20}-*co*-A_5)	PEG 113 RAFT	13500	126300	108700	1.16	N.D.
1b-A 33	PEG_{113}-*b*-P(A_{75}-*co*-C_{20}-*co*-M_5)	PEG 113 RAFT	13900	6200	5200	1.18	N.D.
1b-A 34	PEG_{113}-*b*-P(A_{75}-*co*-C_{20}-*co*-F_5)	PEG 113 RAFT	14300	5900	4800	1.24	N.D.
1b-A 35	PEG_{113}-*b*-P(A_{75}-*co*-C_{20}-*co*-X_5)	PEG 113 RAFT	14100	6000	4900	1.23	N.D.
1b-A 36	PEG_{113}-*b*-P(A_{70}-*co*-C_{20}-*co*-A_{10})	PEG 113 RAFT	13100	152100	127900	1.19	N.D.
1b-A 37	PEG_{113}-*b*-P(A_{70}-*co*-C_{20}-*co*-M_{10})	PEG 113 RAFT	14000	6000	5100	1.17	N.D.
1b-A 38	PEG_{113}-*b*-P(A_{70}-*co*-C_{20}-*co*-F_{10})	PEG 113 RAFT	14800	6100	5100	1.21	N.D.
1b-A 39	PEG_{113}-*b*-P(A_{70}-*co*-C_{20}-*co*-X_{10})	PEG 113 RAFT	14400	6200	5200	1.19	N.D.
1b-A 40	PEG_{113}-*b*-P(A_{60}-*co*-N_{20}-*co*-C_{20})	PEG 113 RAFT	14700	16500	9100	1.81	N.D.
1b-A 41*	PEG_{113}-*b*-P(A_{40}-*co*-N_{40}-*co*-C_{20})	PEG 113 RAFT	15500	53700	44700	1.20	N.D.
1b-A 42	PEG_{113}-*b*-P(A_{60}-*co*-C_{40})	PEG 113 RAFT	15300	5600	5200	1.08	N.D.
1b-A 43	PEG_{113}-*b*-P(A_{60}-*co*-S_{20}-*co*-C_{20})	PEG 113 RAFT	16600	6300	5500	1.15	N.D.
1b-A 44*	PEG_{113}-*b*-P(A_{60}-*co*-S_{40})	PEG 113 RAFT	17800	8700	8000	1.09	N.D.
1b-A 45	PEG_{113}-*b*-P(A_{60}-*co*-S_{40})	PEG 113 RAFT	17800	238100	187800	1.27	N.D.
1b-A 46	PEG_{113}-*b*-P(A_{50}-*co*-S_{40}-*co*-F_{10})	PEG 113 RAFT	18700	215500	163800	1.32	N.D.
1b-A 47	PEG_{113}-*b*-P(A_{40}-*co*-S_{40}-*co*-F_{10} -*co*-C_{10})	PEG 113 RAFT	19500	73300	70000	1.05	N.D.
1b-A 48*	PEG_{113}-*b*-P(A_{40}-*co*-S_{40}-*co*-C_{20})	PEG 113 RAFT	19300	8300	7900	1.06	N.D.

[a] Monomers conversion of polymers calculated from ^{1}H NMR in DMSO, used standard 1,3,5-trioxane.

[b] Theoretical molecular weight calculated using the monomer conversion.

[c] Molecular weight obtained from GPC (DMF, 0.1% formic acid and calibrated to poly(ethylene glycol/oxide) standards).

[d] Dispersity (= *M*w/*M*n) calculated from GPC.

* GPC traces were collected on aqueous GPC with eluent of 40 % water and 60 % acetonitrile.

Note: BTPA = 2-(Butylthiocarbonothioylthio)propanoic acid, A = acrylamide, H = hydroxyethyl acrylate and D = *N*-[3-(Dimethylamino)propyl]acrylamide. PEGMEA = poly(ethylene glycol) methyl ether acrylate (*M*n = 480 g mol-1), M = methyl acrylate, Y = butyl acrylate, F = benzyl acrylate, C = carboxyethyl acrylate, and PEG = mPEG = poly(ethylene glycol) methyl ether (*M*n = 1900 g mol-1). N.D. (GPC) polymer not detectable in any GPC eluent. N.D. (NMR) not determined as all polymerisations are usually processed to a monomer conversion of >90.

Table S5. Characterisation data (^{1}H NMR & GPC) library 2. The polymerisations were conducted in 8-strip PCR tubes with 250 µL per vial for 8 hours at 44 °C in 14% DMSO. [M]/[RAFT] = 100, [RAFT]/[initiator] = 5, [GOx] = 2 µmol L^{-1}, and [M] = 1 mol L^{-1}.

Index #	polymer	RAFT agent	$M_{n,\,theo}$ [b] (g mol^{-1})	$M_{W,\,GPC}$ [c] (g mol^{-1})	$M_{n,\,GPC}$ [c] (g mol^{-1})	Đ [d]	conversion NMR[a] / %
2H 2	P(H_{40}-*co*-D_{60})	BSPA	14300	29600	25700	1.15	N.D.
2H 3	P(H_{50}-*co*-D_{50})	BSPA	13900	30600	25100	1.22	99
2H 6	P(H_{80}-*co*-D_{20})	BSPA	12700	26100	21200	1.23	N.D.
2H 7	P(H_{75}-*co*-D_{20}-*co*-M_5)	BSPA	12500	26900	19100	1.41	N.D.
2H 8	P(H_{75}-*co*-D_{20}-*co*-M_5)	BSPA	12500	26900	19100	1.41	N.D.
2H 9	P(H_{75}-*co*-D_{20}-*co*-Y_5)	BSPA	12700	22300	18100	1.23	N.D.
2H 10	P(H_{75}-*co*-D_{20}-*co*-F_5)	BSPA	12900	25300	20200	1.25	N.D.
2H 11	P(H_{70}-*co*-D_{20}-*co*-M_{10})	BSPA	12400	26000	18300	1.42	N.D.
2H 12	P(H_{70}-*co*-D_{20}-*co*-Y_{10})	BSPA	12800	21600	17300	1.25	100
2H 13	P(H_{70}-*co*-D_{20}-*co*-F_{10})	BSPA	13100	28500	20500	1.39	N.D.
2H 14*	P(H_{75}-*co*-D_{20}-*co*-C_5)	BSPA	12800	14900	12000	1.24	N.D.
2H 15*	P(H_{75}-*co*-D_{20}-*co*-C_5)	BSPA	12800	20500	19000	1.10	N.D.
2H 17	P(H_{90}-*co*-D_{10})	BSPA	12300	18700	15300	1.22	N.D.
2H 18*	P(H_{70}-*co*-D_{20}-*co*-C_{10})	BSPA	13000	30800	25000	1.23	N.D.
2H 19*	P(H_{70}-*co*-D_{20}-*co*-C_{10})	BSPA	13000	66100	62200	1.06	N.D.
2H 20	PH_{100}	BSPA	11900	8700	6500	1.34	98

2H 23*	P(C_{40}-*co*-H_{60})	BSPA	13000	66300	55300	1.20	N.D.
2H 24*	P(C_{50}-*co*-H_{50})	BSPA	13300	63800	53500	1.19	N.D.
2H 26*	P(C_{80}-*co*-H_{20})	BSPA	14100	41800	33100	1.26	N.D.
2H 27*	P(C_{90}-*co*-H_{10})	BSPA	14400	24000	15700	1.53	N.D.
2A 2	P(A_{40}-*co*-D_{60})	BSPA	12500	31600	28500	1.11	N.D.
2A 6	P(A_{80}-*co*-D_{20})	BSPA	9100	24100	20800	1.16	N.D.
2A 7	P(A_{75}-*co*-D_{20}-*co*-M_5)	BSPA	9200	24200	18300	1.32	99
2A 8	P(A_{75}-*co*-D_{20}-*co*-M_5)	BSPA	9200	24200	18300	1.32	99
2A 9	P(A_{75}-*co*-D_{20}-*co*-Y_5)	BSPA	9400	23800	20500	1.16	N.D.
2A 10	P(A_{75}-*co*-D_{20}-*co*-F_5)	BSPA	9500	26300	21900	1.20	N.D.
2A 11	P(A_{70}-*co*-D_{20}-*co*-M_{10})	BSPA	9200	22000	19000	1.16	N.D.
2A 12	P(A_{70}-*co*-D_{20}-*co*-Y_{10})	BSPA	9700	24600	21000	1.17	99
2A 13	P(A_{70}-*co*-D_{20}-*co*-F_{10})	BSPA	10000	27100	22000	1.23	N.D.
2A 14*	P(A_{75}-*co*-D_{20}-*co*-C_5)	BSPA	9500	26200	24300	1.07	N.D.
2A 15*	P(A_{75}-*co*-D_{20}-*co*-C_5)	BSPA	9500	22900	20800	1.10	N.D.
2A 17	P(A_{90}-*co*-D_{10})	BSPA	8200	18300	15800	1.16	N.D.
2A 18*	P(A_{70}-*co*-D_{20}-*co*-C_{10})	BSPA	9800	38300	29900	1.28	N.D.
2A 19*	P(A_{70}-*co*-D_{20}-*co*-C_{10})	BSPA	9800	24200	21100	1.15	N.D.
2A 23*	P(A_{60}-*co*-C_{40})	BSPA	10300	68500	59700	1.15	N.D.
2A 24	P(A_{50}-*co*-C_{50})	BSPA	11000	8200	6800	1.21	100
2A 25	P(A_{40}-*co*-C_{60})	BSPA	11800	8200	6300	1.30	N.D.
2A 26*	P(C_{80}-*co*-A_{20})	BSPA	13200	57500	50700	1.13	N.D.

2A 27*	P(C_{90}-*co*-A_{10})	BSPA	14000	53300	45400	1.17	N.D.
2c-H 3	P(PEG_{40}-*co*-H_{10}-*co*-D_{50})	BSPA	28400	36000	28800	1.25	100
2c-H 6	P($PEGMEA_{40}$-*co*-H_{40}-*co*-D_{20})	BSPA	27200	45500	30300	1.50	N.D.
2c-H 8	P($PEGMEA_{40}$-*co*-H_{35}-*co*-D_{20}-*co*-M_5)	BSPA	27100	40600	29000	1.40	100
2c-H 9	P($PEGMEA_{40}$-*co*-H_{35}-*co*-D_{20}-*co*-Y_5)	BSPA	27300	38100	27400	1.39	N.D.
2c-H 10	P($PEGMEA_{40}$-*co*-H_{35}-*co*-D_{20}-*co*-F_5)	BSPA	27500	41900	29300	1.43	N.D.
2c-H 11	P($PEGMEA_{40}$-*co*-H_{30}-*co*-D_{20}-*co*-M_{10})	BSPA	26900	39800	28600	1.39	N.D.
2c-H 12	P($PEGMEA_{40}$-*co*-H_{30}-*co*-D_{20}-*co*-Y_{10})	BSPA	27400	37100	27100	1.37	N.D.
2c-H 13	P($PEGMEA_{40}$-*co*-H_{30}-*co*-D_{20}-*co*-F_{10})	BSPA	27700	38800	28300	1.37	100
2c-H 16	P($PEGMEA_{40}$-*co*-H_{50}-*co*-D_{10})	BSPA	26800	33300	23800	1.40	N.D.
2c-H 17	P($PEGMEA_{40}$-*co*-H_{30}-*co*-D_{20}-*co*-C_{10})	BSPA	27500	28600	17500	1.64	N.D.
2c-H 18	P($PEGMEA_{40}$-*co*-H_{20}-*co*-D_{20}-*co*-C_{10}-*co*-Y_{10})	BSPA	27600	29369	17540	1.67	N.D.
2c-H 19	P($PEGMEA_{40}$-*co*-H_{20}-*co*-D_{20}-*co*-C_{10}-*co*-Y_{10})	BSPA	27600	30238	17734	1.71	N.D.
2c-H 20	P($PEGMEA_{40}$-*co*-H_{60})	BSPA	26400	22600	18100	1.25	100
2c-A 2	P($PEGMEA_{40}$-*co*-D_{60})	BSPA	28800	36800	30400	1.21	99
2c-A 3	P($PEGMEA_{40}$-*co*-A_{10}-*co*-D_{50})	BSPA	28000	34300	29800	1.15	N.D.
2c-A 6	P($PEGMEA_{40}$-*co*-A_{40}-*co*-D_{20})	BSPA	25400	30100	25700	1.17	N.D.
2c-A 9	P($PEGMEA_{40}$-*co*-A_{35}-*co*-D_{20}-*co*-Y_5)	BSPA	25700	29700	25400	1.17	100
2c-A 10	P($PEGMEA_{40}$-*co*-A_{35}-*co*-D_{20}-*co*-F_5)	BSPA	25900	31400	26600	1.18	N.D.
2c-A 11	P($PEGMEA_{40}$-*co*-A_{30}-*co*-D_{20}-*co*-M_{10})	BSPA	25600	30900	26000	1.19	100
2c-A 12	P($PEGMEA_{40}$-*co*-A_{30}-*co*-D_{20}-*co*-Y_{10})	BSPA	26000	28500	24400	1.17	N.D.
2c-A 13	P($PEGMEA_{40}$-*co*-A_{30}-*co*-D_{20}-*co*-F_{10})	BSPA	26400	33500	27900	1.20	N.D.

2c-A 16	P(PEGMEA$_{40}$-*co*-A$_{50}$-*co*-D$_{10}$)	BSPA	24600	26000	22400	1.16	N.D.
2c-A 17*	P(PEGMEA$_{40}$-*co*-A$_{30}$-*co*-D$_{20}$-*co*-C$_{10}$)	BSPA	26200	27800	17200	1.61	N.D.
2c-A 18*	P(PEGMEA$_{40}$-*co*-A$_{20}$-*co*-D$_{20}$-*co*-C$_{10}$-*co*-Y$_{10}$)	BSPA	26800	28000	17000	1.65	N.D.
2c-A 19*	P(PEGMEA$_{40}$-*co*-A$_{20}$-*co*-D$_{20}$-*co*-C$_{10}$-*co*-F$_{10}$)	BSPA	27100	28800	17500	1.64	N.D.
2c-A 20	P(PEGMEA$_{40}$-*co*-A$_{60}$)	BSPA	23700	20000	16800	1.19	100
2b-H 1	PEG-*b*-PD$_{100}$	mPEG-BSPA	17800	46200	39500	1.17	82
2b-H 2	PEG-*b*-P(H$_{40}$-*co*-D$_{60}$)	mPEG-BSPA	16200	55100	44800	1.23	N.D.
2b-H 3	PEG-*b*-P(H$_{50}$-*co*-D$_{50}$)	mPEG-BSPA	15800	46100	37500	1.23	97
2b-H 4*	PEG-*b*-P(H$_{40}$-*co*-D$_{50}$-*co*-C$_{10}$)	mPEG-BSPA	16000	5722800	5697200	1.00	N.D.
2b-H 5*	PEG-*b*-P(H$_{30}$-*co*-D$_{50}$-*co*-C$_{20}$)	mPEG-BSPA	16400	N.D.	N.D.	-	N.D.
2b-H 6*	PEG-*b*-P(H$_{20}$-*co*-D$_{50}$-*co*-C$_{30}$)	mPEG-BSPA	16600	N.D.	N.D.	-	N.D.
2b-H 7	PEG-*b*-P(H$_{80}$-*co*-D$_{20}$)	mPEG-BSPA	14600	35400	28300	1.25	N.D.
2b-H 17	PEG-*b*-P(H$_{90}$-*co*-D$_{10}$)	mPEG-BSPA	14200	27500	22200	1.24	N.D.
2b-H 20	PEG-*b*-PH$_{100}$	mPEG-BSPA	13800	13700	10000	1.37	98
2b-H 21	PEG-*b*-P(H$_{90}$-*co*-C$_{10}$)	mPEG-BSPA	14100	14000	10800	1.30	N.D.
2b-H 22	PEG-*b*-P(H$_{80}$-*co*-C$_{20}$)	mPEG-BSPA	14300	12400	9300	1.33	N.D.
2b-H 24	PEG-*b*-P(H$_{50}$-*co*-C$_{50}$)	mPEG-BSPA	15200	10200	8000	1.27	96
2b-H 25	PEG-*b*-P(H$_{40}$-*co*-C$_{60}$)	mPEG-BSPA	15500	8700	6100	1.43	N.D.
2b-H 28	PEG-*b*-PC$_{100}$	mPEG-BSPA	16600	4900	3800	1.28	96
2b-A 2	PEG-*b*-P(A$_{40}$-*co*-D$_{60}$)	mPEG-BSPA	14400	49100	40600	1.21	N.D.
2b-A 3	PEG-*b*-P(A$_{50}$-*co*-D$_{50}$)	mPEG-BSPA	13500	46800	38700	1.21	92
2b-A 4*	PEG-*b*-P(A$_{40}$-*co*-D$_{50}$-*co*-C$_{10}$)	mPEG-BSPA	14200	N.D.	N.D.	-	N.D.

2b-A 5*	PEG-*b*-P(A_{30}-*co*-D_{50}-*co*-C_{20})	mPEG-BSPA	15000	N.D.	N.D.	-	N.D.
2b-A 6*	PEG-*b*-P(A_{20}-*co*-D_{50}-*co*-C_{30})	mPEG-BSPA	15700	N.D.	N.D.	-	N.D.
2b-A 7	PEG-*b*-P(A_{80}-*co*-D_{20})	mPEG-BSPA	11000	33600	28000	1.20	N.D.
2b-A 17	PEG-*b*-P(A_{90}-*co*-D_{10})	mPEG-BSPA	10100	23700	20100	1.18	N.D.
2b-A 20	PEG-*b*-PA_{100}	mPEG-BSPA	9300	11500	9700	1.19	94
2b-A 21	PEG-*b*-P(A_{90}-*co*-C_{10})	mPEG-BSPA	10000	9400	7800	1.20	N.D.
2b-A 22	PEG-*b*-P(A_{80}-*co*-C_{20})	mPEG-BSPA	10700	9400	7800	1.20	N.D.
2b-A 24	PEG-*b*-P(A_{50}-*co*-C_{50})	mPEG-BSPA	12900	8700	7200	1.21	N.D.
2b-A 25	PEG-*b*-P(A_{40}-*co*-C_{60})	mPEG-BSPA	13700	8400	7000	1.20	N.D.
2O 6*	P(C_{40}-*co*-D_{60})	BSPA	15400	27800	23800	1.17	N.D.
2O 20*	P(C_{50}-*co*-D_{50})	BSPA	15300	33100	22700	1.46	N.D.
2O 25*	P(C_{80}-*co*-D_{20})	BSPA	14900	34000	23900	1.42	N.D.
2O 26*	P(C_{90}-*co*-D_{10})	BSPA	14800	18700	13200	1.42	N.D.
2O 28	PC_{100}	BSPA	14700	5000	3900	1.28	97

[a] Monomers conversion of polymers calculated from ^{1}H NMR in DMSO, used standard 1,3,5-trioxane.

[b] Theoretical molecular weight calculated using the monomer conversion.

[c] Molecular weight obtained from GPC (DMF, 0.1% formic acid and calibrated to poly(ethylene glycol/oxide) standards).

[d] Dispersity (= *M*w/*M*n) calculated from GPC.

* GPC traces were collected on aqueous GPC with eluent of 40 % water and 60 % acetonitrile.

Note: BTPA = 2-(Butylthiocarbonothioylthio)propanoic acid, A = acrylamide, H = hydroxyethyl acrylate and D = *N*-[3-(Dimethylamino)propyl]acrylamide. PEGMEA = poly(ethylene glycol) methyl ether acrylate (*M*n = 480 g mol-1), M = methyl acrylate, Y = butyl acrylate, F = benzyl acrylate, C = carboxyethyl acrylate, and PEG = mPEG = poly(ethylene glycol) methyl ether (*M*n = 1900 g mol-1). N.D. (GPC) polymer not detectable in any GPC eluent. N.D. (NMR) not determined as all polymerisations are usually processed to a monomer conversion of >90.

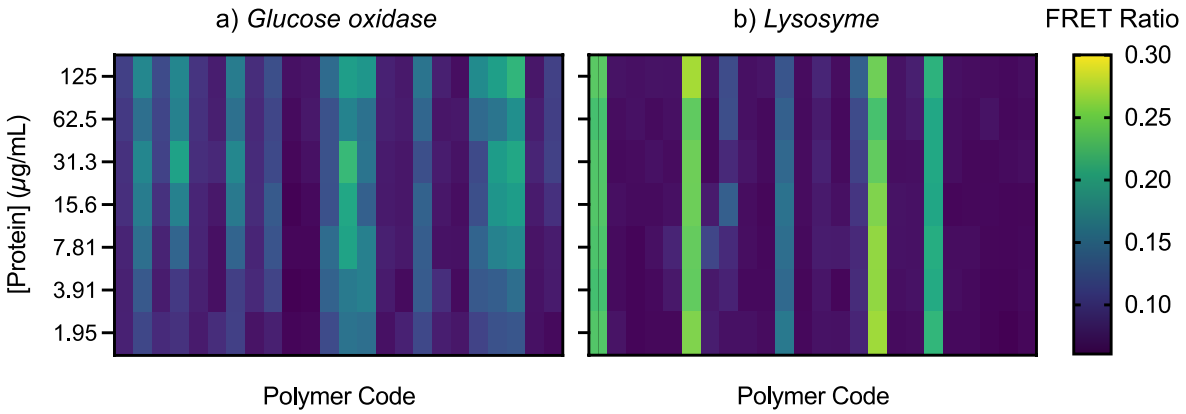


Figure S2. FRET results from dilution of a selection of polymers from library 2 against a) GOx and b) Lysosyme in 20 mM phosphate buffer (pH 7.4).

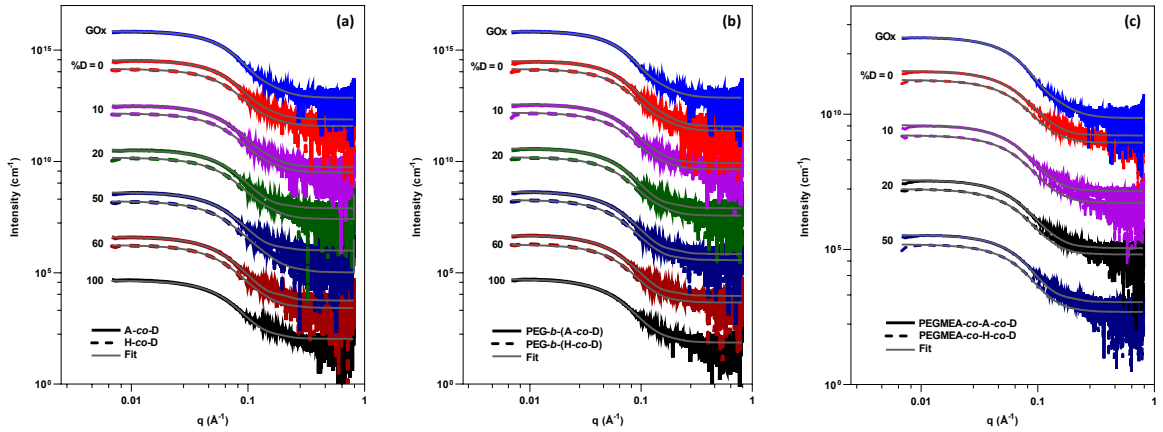


Figure S3. Small angle X-ray scattering (SAXS) data obtained upon mixing of polymers with GOx (1.0 mg.mL^{-1}) at poly/GOx = 8 with core-shell fits shown. Data is offset in the y-axis. Note: A = acrylamide, H = hydroxyethyl acrylate and D = N-[3-(Dimethylamino)propyl]acrylamide, PEG = polyethylene glycol methyl ether (M_n = 1900 g.mol^{-1}), PEGMEA = poly(ethylene glycol) methyl ether acrylate (M_n = 480 g.mol^{-1}).

Table S6. Core-shell model fitting parameters for small angle X-ray scattering (SAXS) fits shown in **Figure S3**a. Data was obtained upon assembly of the polymers with GOx (poly/GOx = 8) in PBS.

Polymer	Core radius (nm)	Core SLD ($Å^{-2}$)	Shell thickness (nm)	Shell SLD ($Å^{-2}$)	Overall size (nm)	solvent SLD ($Å^{-2}$)
GOx	3.0	1.0×10^{-5}	-	-	6.0	3.0×10^{-6}
PA_{100}	3.0	1.0×10^{-5}	2.2	2.9×10^{-6}	10.4	3.0×10^{-6}
$P(A_{90}$-*co*-$D_{10})$	3.0	1.0×10^{-5}	2.4	2.8×10^{-6}	10.8	3.0×10^{-6}
$P(A_{80}$-*co*-$D_{20})$	3.0	1.0×10^{-5}	3.6	2.7×10^{-6}	13.2	3.0×10^{-6}
$P(A_{50}$-*co*-$D_{50})$	3.0	1.0×10^{-5}	4.1	2.7×10^{-6}	14.2	3.0×10^{-6}
$P(A_{40}$-*co*-$D_{60})$	3.0	1.0×10^{-5}	4.3	2.7×10^{-6}	14.6	3.0×10^{-6}
PH_{100}	3.0	1.0×10^{-5}	1.2	2.5×10^{-6}	8.4	3.0×10^{-6}
$P(H_{90}$-*co*-$D_{10})$	3.0	1.0×10^{-5}	1.6	2.6×10^{-6}	9.2	3.0×10^{-6}
$P(H_{80}$-*co*-$D_{20})$	3.0	1.0×10^{-5}	2.0	2.7×10^{-6}	10.0	3.0×10^{-6}
$P(H_{50}$-*co*-$D_{50})$	3.0	1.0×10^{-5}	3.0	2.8×10^{-6}	12.0	3.0×10^{-6}
$P(H_{40}$-*co*-$D_{60})$	3.0	1.0×10^{-5}	3.2	2.8×10^{-6}	12.4	3.0×10^{-6}
PD_{100}	3.0	1.0×10^{-5}	4.6	2.9×10^{-6}	15.2	3.0×10^{-6}

Table S7. Core-shell model fitting parameters for small angle X-ray scattering (SAXS) fits shown in **Figure S3**b Data was obtained upon assembly of the polymers with GOx (poly/GOx = 8) in PBS.

Polymer	Core radius (nm)	Core SLD ($Å^{-2}$)	Shell thickness (nm)	Shell SLD ($Å^{-2}$)	Overall size (nm)	solvent SLD ($Å^{-2}$)
PEG-*b*-PA_{100}	3.0	1.0×10^{-5}	2.1	2.8×10^{-6}	10.2	3.0×10^{-6}
PEG-*b*-$P(A_{90}$-*co*-$D_{10})$	3.0	1.0×10^{-5}	2.8	2.8×10^{-6}	11.6	3.0×10^{-6}
PEG-*b*-$P(A_{80}$-*co*-$D_{20})$	3.0	1.0×10^{-5}	4.1	2.7×10^{-6}	14.2	3.0×10^{-6}
PEG-*b*-$P(A_{50}$-*co*-$D_{50})$	3.0	1.0×10^{-5}	4.1	2.7×10^{-6}	14.2	3.0×10^{-6}
PEG-*b*-$P(A_{40}$-*co*-$D_{60})$	3.0	1.0×10^{-5}	4.1	2.7×10^{-6}	14.2	3.0×10^{-6}
PEG-*b*-PH_{100}	3.0	1.0×10^{-5}	1.4	2.5×10^{-6}	10.4	3.0×10^{-6}
PEG-*b*-$P(H_{90}$-*co*-$D_{10})$	3.0	1.0×10^{-5}	1.9	2.6×10^{-6}	10.8	3.0×10^{-6}
PEG-*b*-$P(H_{80}$-*co*-$D_{20})$	3.0	1.0×10^{-5}	2.1	2.7×10^{-6}	13.2	3.0×10^{-6}
PEG-*b*-$P(H_{50}$-*co*-$D_{50})$	3.0	1.0×10^{-5}	3.6	2.8×10^{-6}	14.2	3.0×10^{-6}
PEG-*b*-$P(H_{40}$-*co*-$D_{60})$	3.0	1.0×10^{-5}	3.7	2.8×10^{-6}	14.6	3.0×10^{-6}
PEG-*b*-PD_{100}	3.0	1.0×10^{-5}	4.3	2.9×10^{-6}	14.6	3.0×10^{-6}

Table S8. Core-shell model fitting parameters for small angle X-ray scattering (SAXS) fits shown in **Figure S3**c. Data was obtained upon assembly of the polymers with GOx (poly/GOx = 8) in PBS.

Polymer	Core radius (nm)	Core SLD ($Å^{-2}$)	Shell thickness (nm)	Shell SLD ($Å^{-2}$)	Overall size (nm)	solvent SLD ($Å^{-2}$)
P(PEGMEA$_{40}$-*co*-A$_{60}$)	3.0	1.0 x 10^{-5}	2.8	2.6 x 10^{-6}	11.6	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-A$_{50}$-*co*-D$_{10}$)	3.0	1.0 x 10^{-5}	3.0	2.7 x 10^{-6}	12.0	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-A$_{40}$-*co*-D$_{20}$)	3.0	1.0 x 10^{-5}	3.0	2.7 x 10^{-6}	12.0	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-A$_{10}$-*co*-D$_{50}$)	3.0	1.0 x 10^{-5}	4.2	2.8 x 10^{-6}	14.4	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-H$_{60}$)	3.0	1.0 x 10^{-5}	2.3	2.6 x 10^{-6}	10.6	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-H$_{50}$-*co*-D$_{10}$)	3.0	1.0 x 10^{-5}	2.6	2.7 x 10^{-6}	11.2	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-H$_{40}$-*co*-D$_{20}$)	3.0	1.0 x 10^{-5}	2.9	2.8 x 10^{-6}	11.8	3.0 x 10^{-6}
P(PEGMEA$_{40}$-*co*-H$_{10}$-*co*-D$_{50}$)	3.0	1.0 x 10^{-5}	3.5	2.9 x 10^{-6}	13.0	3.0 x 10^{-6}

Table 3. GPC traces of chain length experiment.

Index #	**polymer**	$M_{n,\,theo}$ [b] (g mol^{-1})	$M_{W,\,GPC}$ [c] (g mol^{-1})	$M_{n,\,GPC}$ [c] (g mol^{-1})	$Đ$ [d]
1H 22 _ 25*	P(H$_{22.5}$-*co*-F$_{2.5}$)	3300	12200	10700	1.15
1H 22 _ 50*	P(H$_{45}$-*co*-F$_5$)	6300	16900	14600	1.16
1H 22 _ 100*	P(H$_{90}$-*co*-F$_{10}$)	12300	26800	21700	1.24
1H 22 _ 200*	P(H$_{180}$-*co*-F$_{20}$)	24400	43900	33100	1.33
1H 22 _ 400*	P(H$_{360}$-*co*-F$_{40}$)	48500	52300	40300	1.30
1H 13 _ 25	P(H$_{12.5}$-*co*-N$_{10}$-*co*-Q$_{2.5}$)	3300	6000	3700	1.62
1H 13 _ 50	P(H$_{25}$-*co*-N$_{20}$-*co*-Q$_5$)	6400	9200	5200	1.76
1H 13 _ 100	P(H$_{50}$-*co*-N$_{40}$-*co*-Q$_{10}$)	12600	14100	9000	1.57
1H 13 _ 200	P(H$_{100}$-*co*-N$_{80}$-*co*-Q$_{20}$)	25000	22300	15900	1.41
1H 13 _ 400	P(H$_{200}$-*co*-N$_{160}$-*co*-Q$_{40}$)	49600	25700	16600	1.55

[a] Monomers conversion of polymers calculated from ^{1}H NMR in DMSO, used standard 1,3,5-trioxane.

[b] Theoretical molecular weight calculated using the monomer conversion.

[c] Molecular weight obtained from GPC (DMF, 0.1% formic acid and calibrated to poly(ethylene glycol/oxide) standards).

[d] Dispersity (= *M*w/*M*n) calculated from GPC.

* GPC traces were collected on aqueous GPC with eluent of 40 % water and 60 % acetonitrile.

Note: BTPA = 2-(Butylthiocarbonothioylthio)propanoic acid, A = acrylamide, H = hydroxyethyl acrylate and D = *N*-[3-(Dimethylamino)propyl]acrylamide. PEGMEA = poly(ethylene glycol) methyl ether acrylate (*M*n = 480 g mol-1), M = methyl acrylate, Y = butyl acrylate, F = benzyl acrylate, C = carboxyethyl acrylate, and PEG = mPEG = poly(ethylene glycol) methyl ether (*M*n = 1900 g mol-1). N.D. (GPC) polymer not detectable in any GPC eluent. N.D. (NMR) not determined as all polymerisations are usually processed to a monomer conversion of >90.

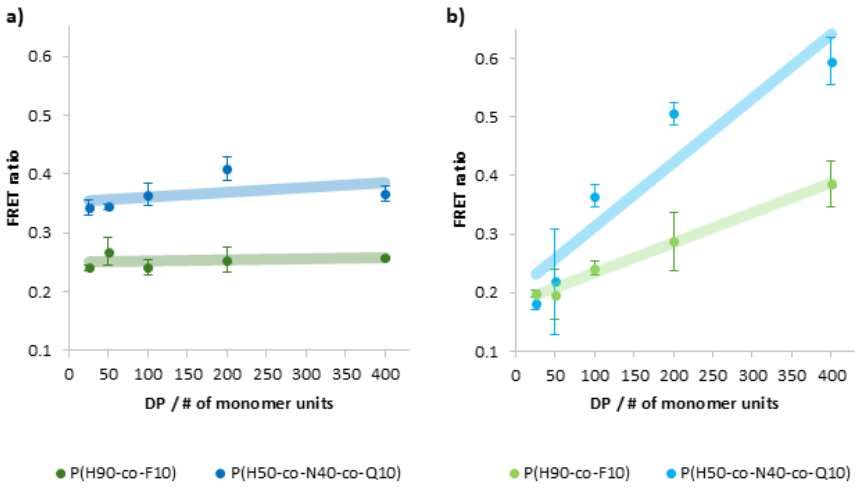


Figure S4. FRET ratio vs degree of polymerization of three different polymers. For **a)** different concentrations of polymer were used to hold concentration of Cy5 dye constant whereas for **b)** polymer concentration was constant at 16 eq. In comparison to GOx. All experiments were performed at 1 µM GOx in 20 mM phosphate buffer.

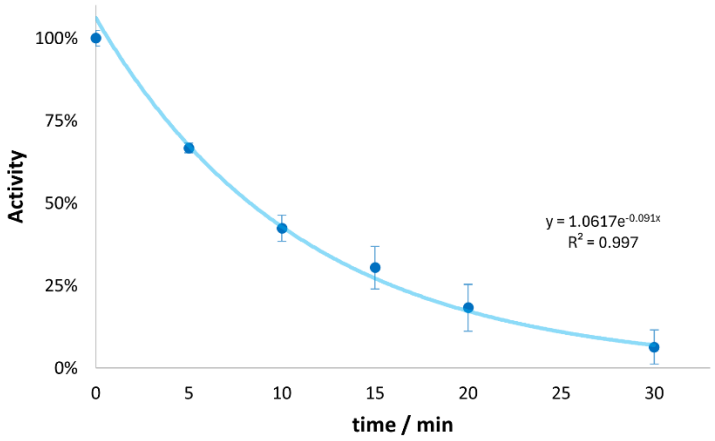


Figure S5. Stability in % of GOx over time in min, incubation in oven at 60C up until 30 mins.

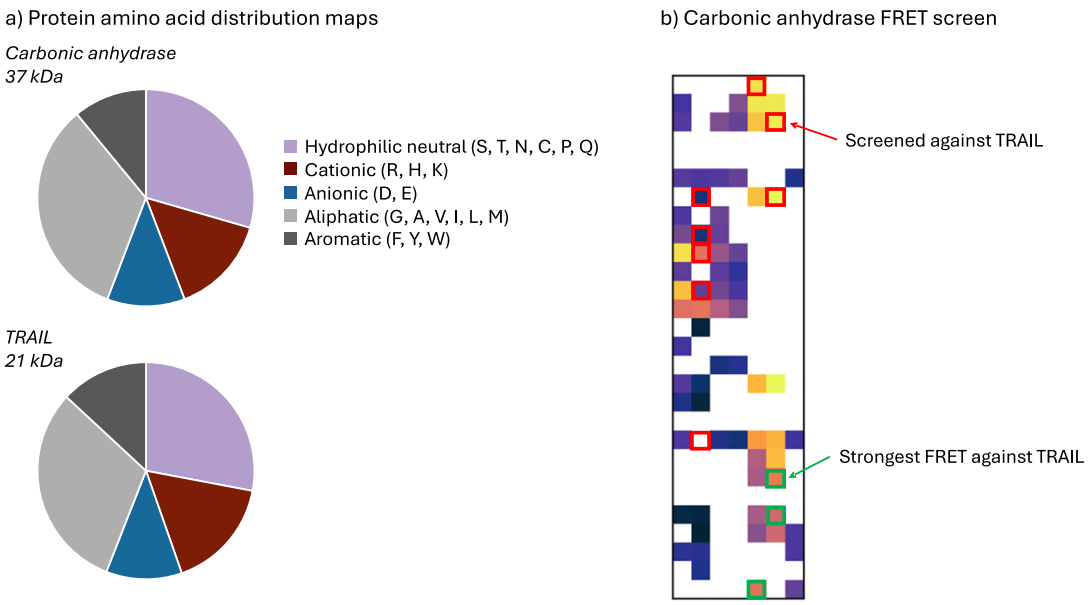


Figure S6. a) Percentage of each class of amino acid in the protein sequence for carbonic anhydrase and TRAIL, b) FRET map from the carbonic anhydrase screen with polymers selected for screening against TRAIL shown in the overlaid boxes. The best hits against TRAIL are highlighted in green.