Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting information

Synthesis of biscarboxylic acid functionalised EDTA mimicking polymers and their ability to form Zr(IV) chelation mediated nanostructures

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Figures

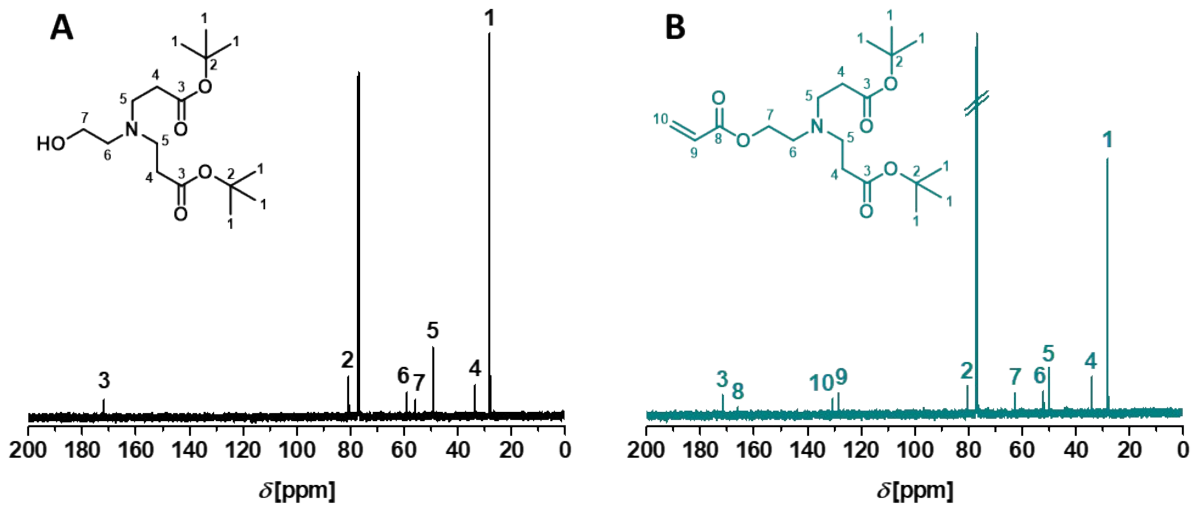

Figure S1. ^{13}C NMR (400 MHz, $CDCl_3$) of 1 (A) and tbAEAP (B).

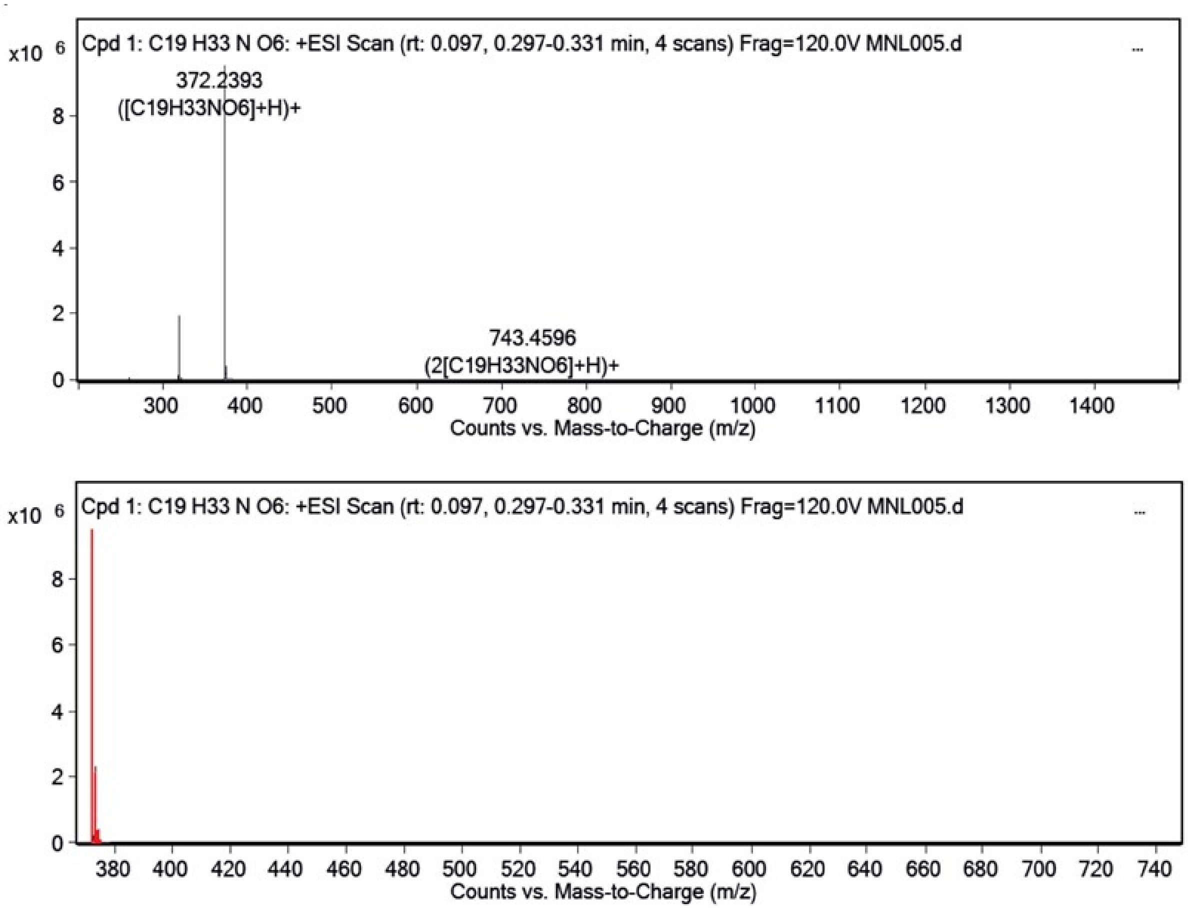

Figure S2. HR ESI-MS of *t*BuAEAP. Top: Full spectrum. Bottom: Magnification of the area of *m/z* 370 to 750. Black: Experimental data. Red: Calculated data.

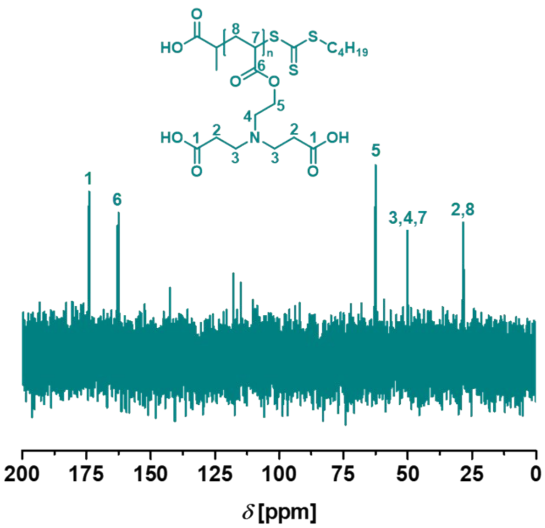

Figure S3. ^{13}C NMR (400 MHz, D_2O) of deprotected homopolymer PAEAP.

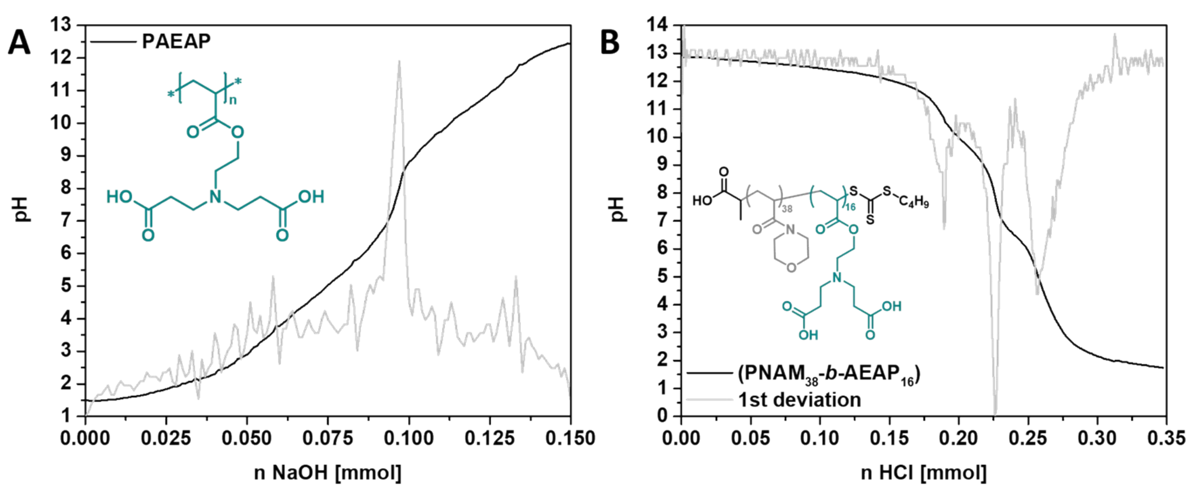

Figure S4. Titration of AEAP containing polymers (10 mg mL^{-1} in MQ). (A) Dependency of pH value on amount of NaOH (0.1 M) added to a solution of PAEAP. (B) Dependency of pH value on amount of HCl (0.1 M) added to a solution of $PNAM_{38}$-*b*-$PAEAP_{16}$.

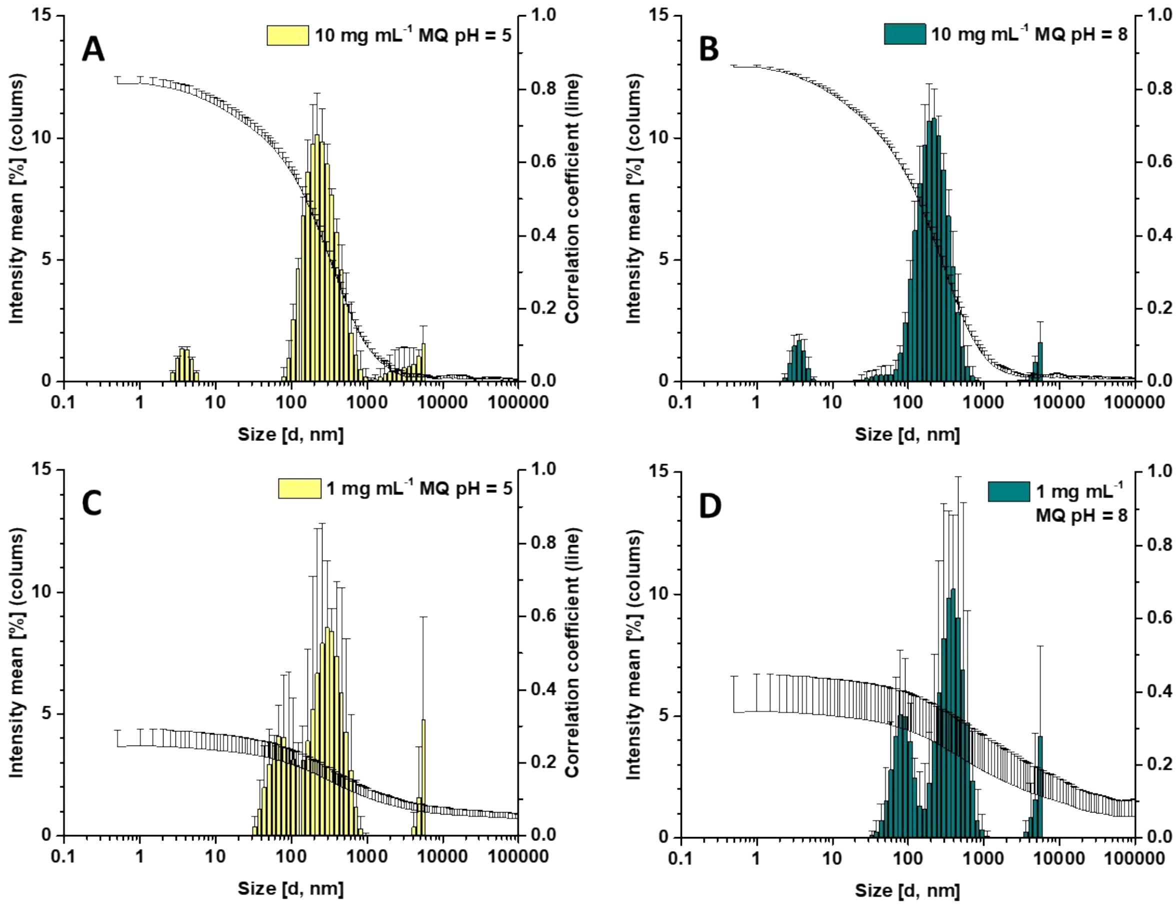

Figure S5. Mean intensity distribution and correlation coefficient of different complexes of PNAM$_{38}$-*b*-PAEAP$_{16}$ at different concentrations and pH values as determined by DLS measurements. Data represents the mean of three measurements with three runs each.

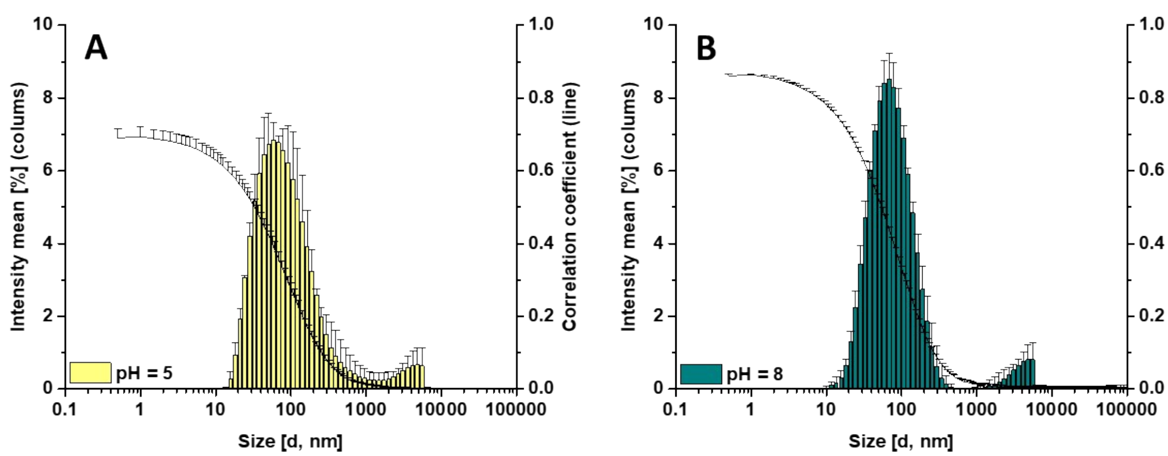

Figure S6. Mean intensity distribution and correlation coefficient of different complexes of PNAM$_{38}$-*b*-PAEAP$_{16}$ and Fe(III) as determined by DLS measurements. Polymer concentration: 1 mg mL^{-1} in MQ. 1.0 eq. Fe(III) per RU. Data represents the mean of three measurements with three runs each. A: pH = 5. B: pH = 8.

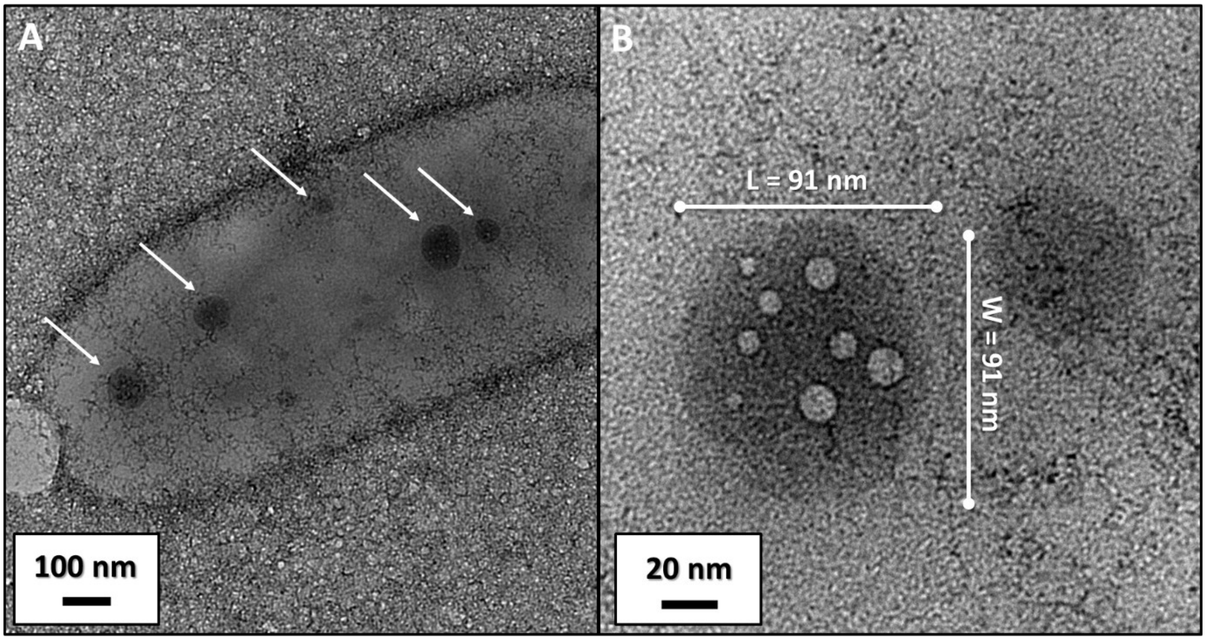

Figure S7. (A and B) TEM images of metal complexation mediated nano-assembly of $PNAM_{38}$-*b*-$PAEAP_{16}$ with 1 eq of Fe(III) at pH = 5 in MQ. (B) Magnification of A.

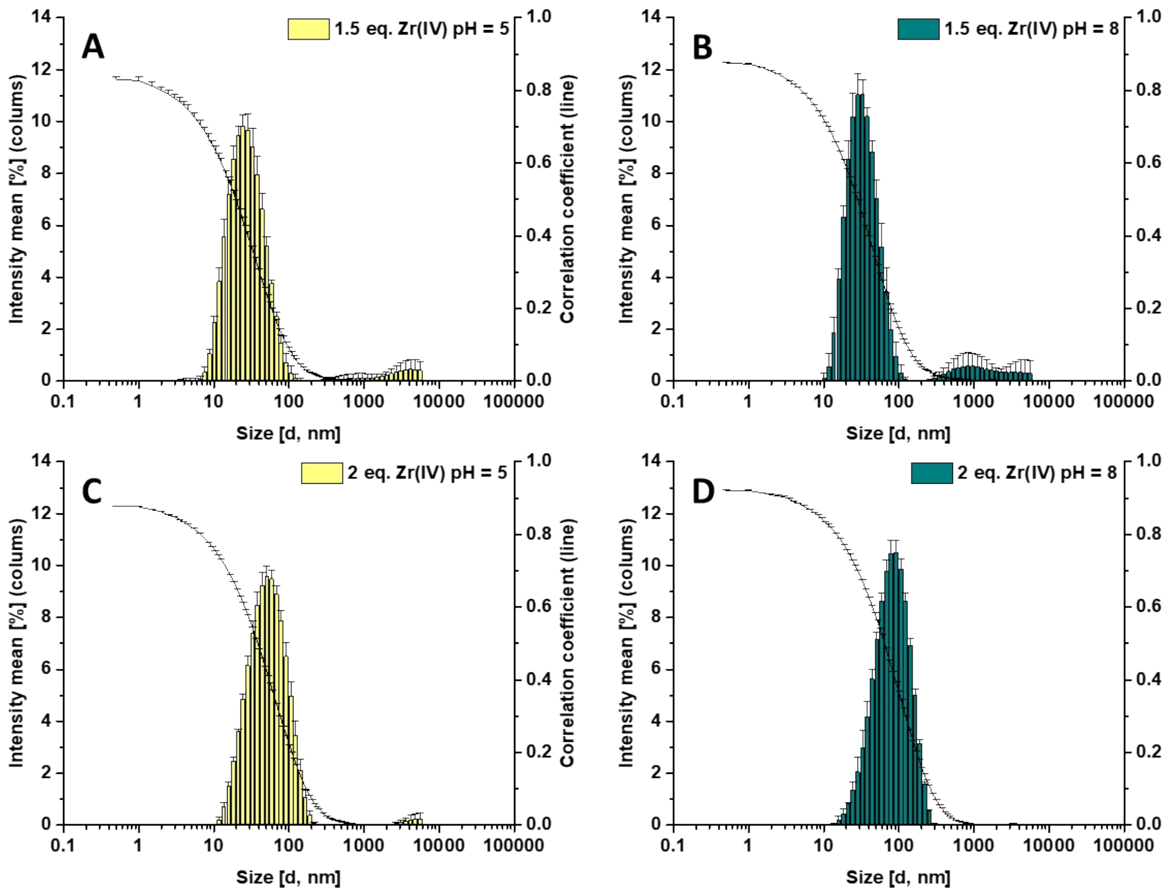

Figure S8. Mean intensity distribution and correlation coefficient of different complexes of $PNAM_{38}$-*b*-$AEAP_{16}$ and Zr(IV) as determined by DLS measurements. Data represents the mean of three measurements with three runs each. (A) 1.5 eq Zr(IV) per RU, pH = 5. (B) 1.5 eq Zr(IV) per RU, pH = 8. (C) 2 eq Zr(IV) per RU, pH = 5. (D) 2 eq Zr(IV) per RU, pH = 8.

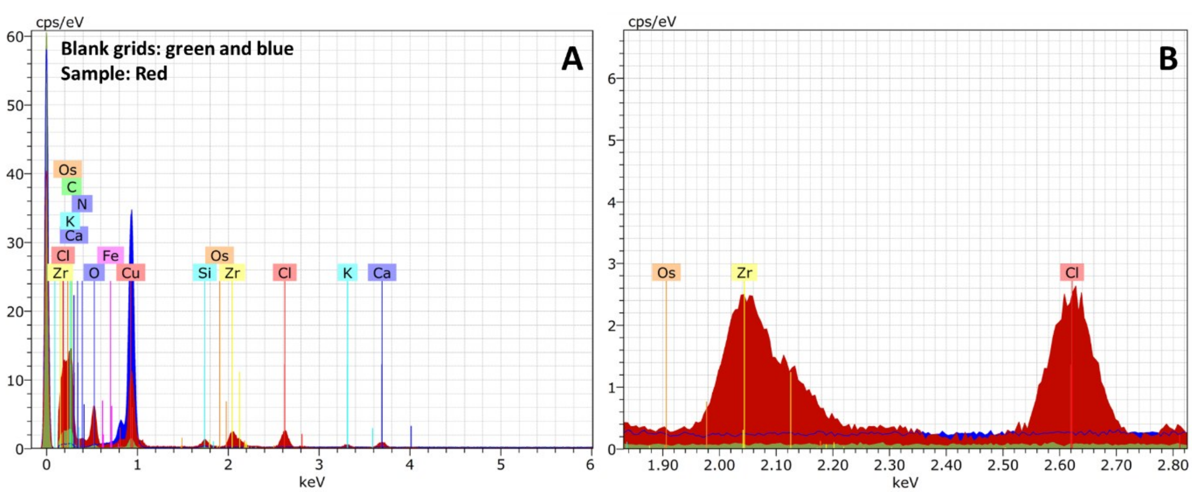

Figure S9. EDX of nanostructures of $PNAM_{38}$-*b*-$AEAP_{16}$ assembled using 2 eq of Zr(IV) in MQ at a pH value of 5.

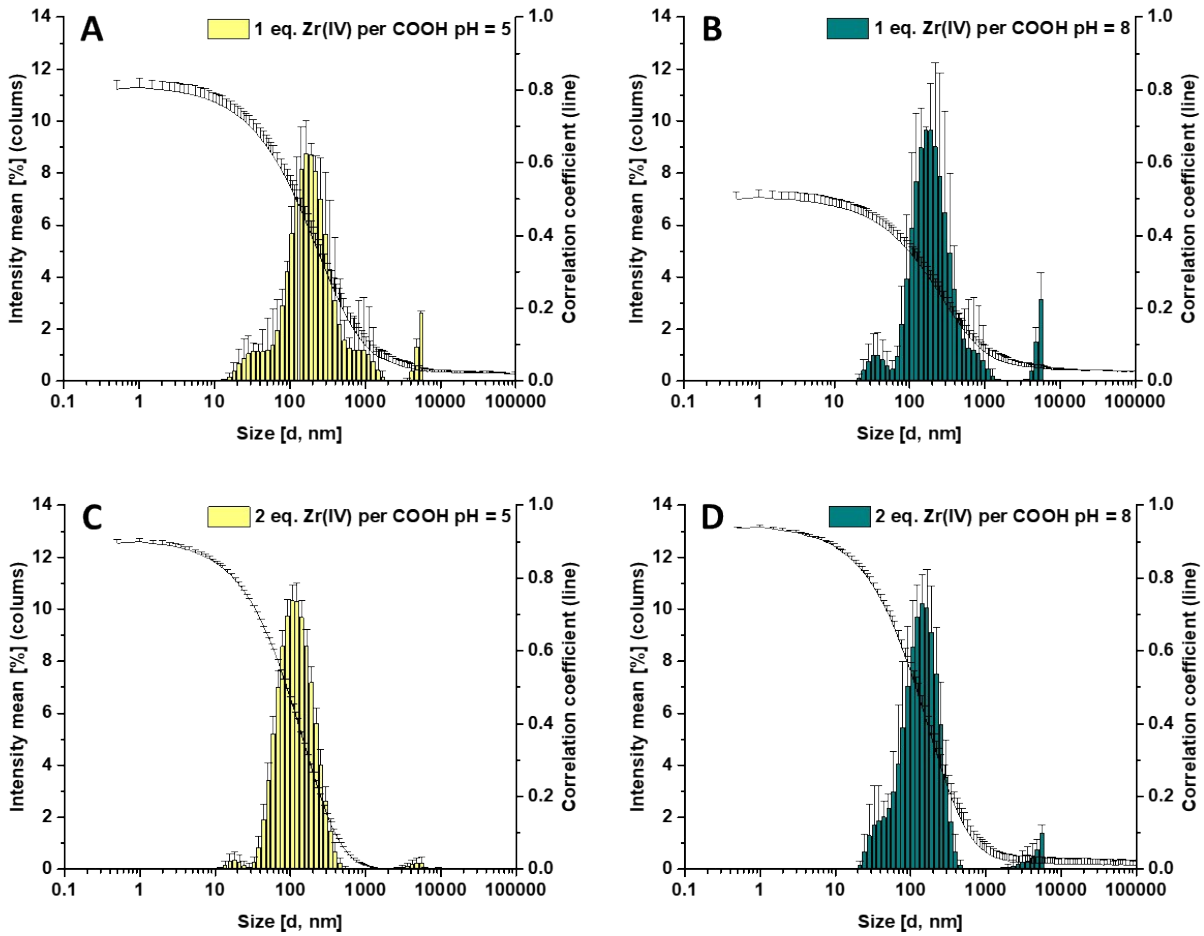

Figure S10. Mean intensity distribution and correlation coefficient of different complexes of PNAM$_{38}$-*b*-AA$_{16}$ and Zr(IV) as determined by DLS measurements. Polymer concentration: 1 mg mL^{-1} in MQ. Data represents the mean of three measurements with three runs each.

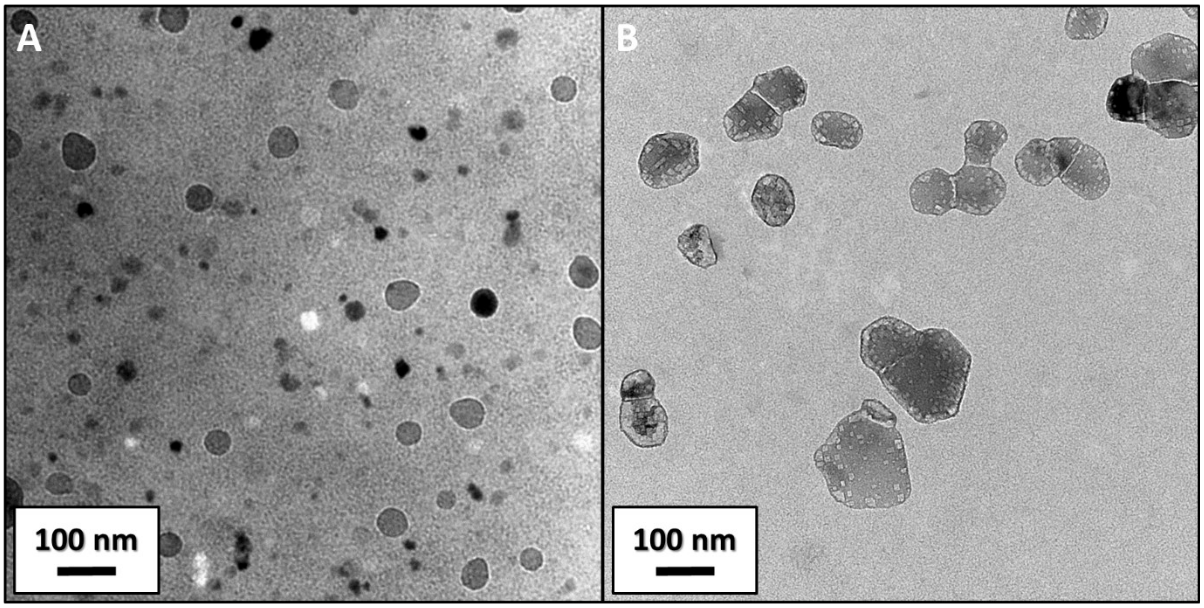

Figure S11. TEM images of metal complexation mediated nano-assembly of $PNAM_{38}$-*b*-PAA_{16} incubated with 2 eq Zr(IV) per COOH at (A) pH = 5, and (B) pH = 8.

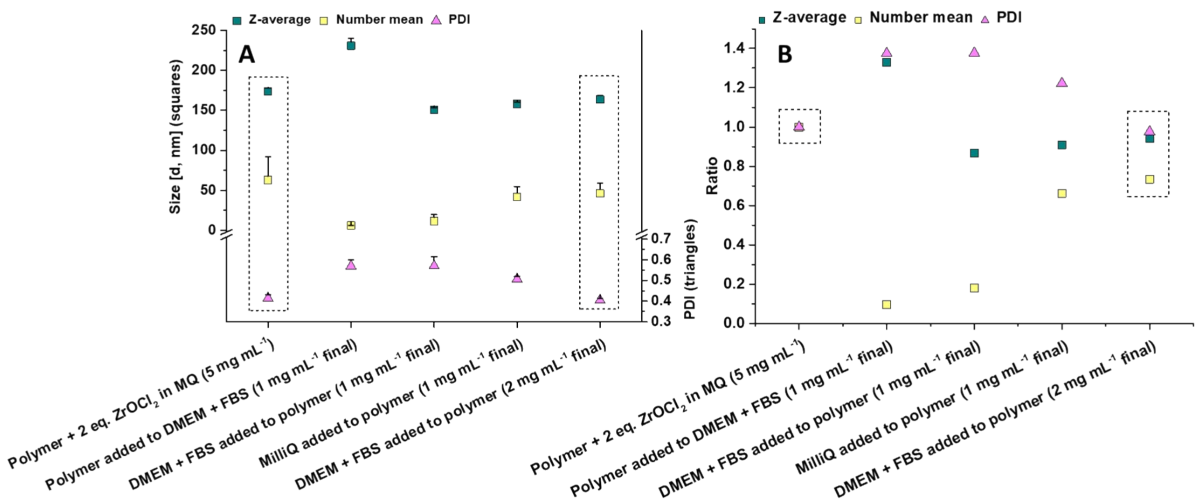

Figure S12. DLS results of Zr-polymer complexes in the presence of FBS containing cell culture media. $PNAM_{38}$-*b*-$AEAP_{16}$ was dissolved in 1 mL MQ (5 mg mL^{-1}) two equivalents per AEAP repeating unit of Zr(IV) have been added from an 0.1 M solution in MQ and 100 µL 0.1 M NaOH solution were added. Zr-polymer complex solutions have been diluted as indicated. Values represent the mean and SD of three measurements with three runs each. (A) Z-average, number mean and PDI obtained by DLS measurements. (B) Size and dispersity ratios obtained by division of each value by the value of the initial solution (5 mg mL^{-1} in MQ). Data represents the mean of three measurements with three runs each.

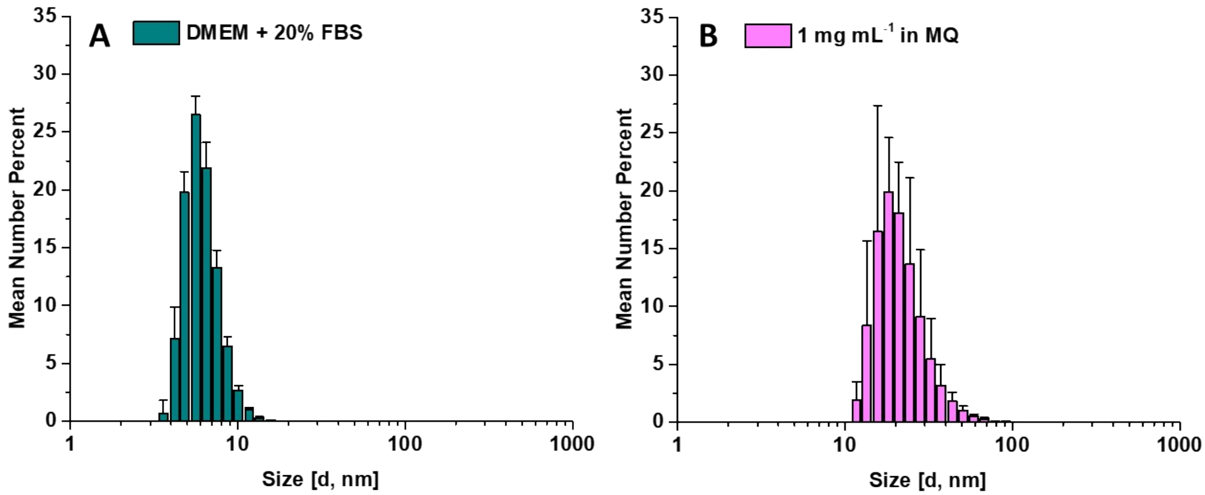

Figure S13. DLS (mean number percent) of (A) serum containing cell media, and (B) complexes of $PNAM_{38}$-*b*-$AEAP_{16}$ and Zr(IV) in MQ (2 eq Zr(IV) per RU, 1 mg mL^{-1}, pH = 8). Data represents the mean and SD of three measurements with three runs each.

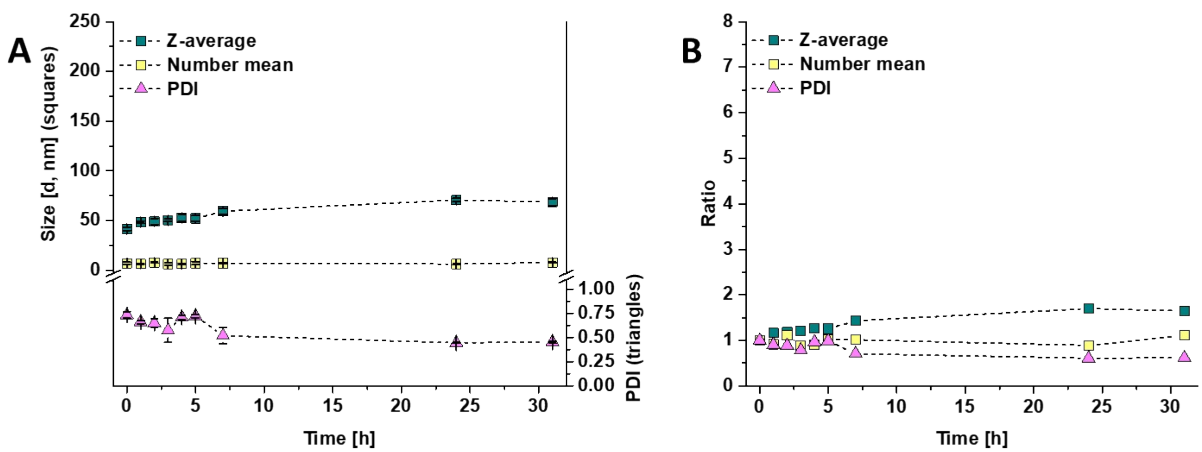

Figure S14. Time dependent stability of complexes of $PNAM_{38}$-*b*-$AEAP_{16}$ and Zr(IV) (2 eq. Zr(IV) per RU) in DMEM + 20% FBS determined by DLS measurements. Polymer concentration: 2 mg mL^{-1}. (A) Size and PDI. Values represent the mean and SD) of three measurements with three runs each. (B) Size and dispersity ratios obtained by division of each value by the value of the initial solution (t = 0 h).

Tables

Table S1. Evaluation of complexation experiments of PNAM$_{38}$-*b*-AEAP$_{16}$ and different amounts of Fe(III) by DLS measurements. Data represents the mean and SD of three measurements with three runs each.

	pH = 5				pH = 8			
Eq. of Fe(III) per RU	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept
0.0	446 ± 75	49 ± 11	0.49 ± 0.03	0.45 ± 0.04	677 ± 252	58 ± 17	0.72 ± 0.31	0.54 ± 0.08
0.7	127 ± 1	38 ± 5	0.43 ± 0.02	0.92 ± 0.01	109 ± 3	41 ± 15	0.31 ± 0.02	0.94 ± 0.00
1.0	66 ± 2	22 ± 2	0.38 ± 0.02	0.84 ± 0.02	65 ± 2	18 ± 5	0.30 ± 0.04	0.93 ± 0.00
1.3	85 ± 1	28 ± 8	0.31 ± 0.03	0.94 ± 0.00	90 ± 2	30 ± 4	0.33 ± 0.04	0.93 ± 0.01

Table S2. Evaluation of complexation experiments of PNAM$_{38}$-*b*-AEAP$_{16}$ and different amounts of Zr(IV) by DLS measurements. Data represents the mean and SD of three measurements with three runs each.

	pH = 5				pH = 8			
Eq. of Zr(IV) per RU	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept
0.0	446 ± 75	49 ± 11	0.49 ± 0.03	0.45 ± 0.04	677 ± 252	58 ± 17	0.72 ± 0.31	0.54 ± 0.08
0.5	80 ± 40	9 ± 1	0.64 ± 0.11	0.67 ± 0.03	53 ± 17	6 ± 3	0.72 ± 0.16	0.88 ± 0.02
1.0	25 ± 1	9 ± 1	0.54 ± 0.01	0.81 ± 0.02	30 ± 1	13 ± 0	0.44 ± 0.01	0.77 ± 0.03
1.5	25 ± 1	9 ± 3	0.26 ± 0.04	0.92 ± 0.01	32 ± 1	16 ± 2	0.26 ± 0.01	0.94 ± 0.00
2.0	45 ± 0	17 ± 1	0.24 ± 0.01	0.94 ± 0.00	69 ± 2	22 ± 3	0.21 ± 0.03	0.96 ± 0.00
2.5	60 ± 2	23 ± 4	0.31 ± 0.05	0.96 ± 0.00	77 ± 0	28 ± 4	0.25 ± 0.01	0.95 ± 0.00
3.0	102 ± 0	21 ± 1	0.28 ± 0.00	0.94 ± 0.00	819 ± 77	121 ± 56	1.00 ± 0.00	0.94 ± 0.01
0.006	194 ± 8	49 ± 20	0.46 ± 0.03	0.96 ± 0.01	Visible precipitate			

Table S3. Evaluation different amounts of Zr(IV) in aqueous solution by DLS measurements. Data represents the mean and SD of three measurements with three runs each. *Equal amounts as depicted in Table S1 have been used without polymer.

	pH = 5				pH = 8			
Eq. of Zr(IV) per RU*	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept	Z-average [d, nm]	Number mean [d, nm]	PDI	Intercept
0.5	1821 ± 929	138 ± 92	1.00 ± 0.00	0.85 ± 0.04	1315 ± 305	101 ± 36	0.86 ± 0.03	0.78 ± 0.04
1.0	217 ± 1	62 ± 23	0.49 ± 0.02	0.94 ± 0.00	Visible precipitate			
1.5	403 ± 71	69 ± 34	0.74 ± 0.12	0.95 ± 0.01	Visible precipitate			
2.0	1114 ± 153	90 ± 34	1.00 ± 0.00	0.94 ± 0.01	Visible precipitate			
2.5	360 ± 15	116 ± 63	0.89 ± 0.06	0.94 ± 0.00	Visible precipitate			
3.0	441 ± 16	126 ± 88	0.98 ± 0.02	0.94 ± 0.01	Visible precipitate			
4.0	419 ± 16	92 ± 41	0.87 ± 0.11	0.92 ± 0.01	Visible precipitate			

Equations

1. *Hydrolysis*

$$4\,ZrOCl_2 + 24H_2O \rightarrow [Zr_4(OH)_8(OH_2)_{16}]^{8+} + 8ClO_4^- \qquad (S1)$$

2. *Formation of anionic complexing agent*

$$R(COOH)_n + nOH^- \rightarrow R(COO^-)_n + nH_2O \qquad (S2)$$

3. *Complex formation*

$$[Zr_4(OH)_8(OH_2)_{16}]^{8+} + R(COO^-)_n \rightarrow \left[Zr_4(OH)_{8-n}(OH_2)_{16}\left(COO^-\right)_n R\right]^{8+} + nOH^- \qquad (S3)$$

Or

$$[Zr_4(OH)_8(OH_2)_{16}]^{8+} + R(COO^-)_n \rightarrow \left[Zr_4(OH)_8(OH_2)_{16-n}\left(COO^-\right)_n R\right]^{8-n+} + nH_2O \qquad (S4)$$

4. *Polymerisation*

$$2HOZrOCOR(COO^-)_{n-1} \rightarrow 2HOZrOCOR(COO^-)_{n-2}\,COOZrOCOR(COO^-)_{n-1} + OH^- \rightarrow Polymer \rightarrow Particle \rightarrow Sol-gel \qquad (S5)$$