Supplementary Information

Depolymerizable, Adaptive Supramolecular Polymer Nanoparticles and Networks

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I. General Experimental Details

Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without further purification. Anhydrous tetrahydrofuran, dichloromethane, and methanol were obtained from an Anhydrous Solvent Delivery System (SDS) equipped with activated alumina columns. *o*-Phthalaldehyde (98%, Alfa-Aesar) was purified according to a literature procedure.¹ 1,6-hexanediol (99% Aldrich) was dissolved in THF over CaH₂, filtered after stirring overnight, and collected by evaporation of the solvent.² 5-nitroisophthalaldehyde and 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydro-pyrimidin-2-yl)urea were prepared according to literature procedures.^{3,4} All reactions were performed in oven dried glassware under N₂ atmosphere unless otherwise indicated. Flash column chromatography was conducted with silica gel 60 (230-400 Mesh) from Silicycle.

¹H and ¹³C NMR spectra were obtained with a Varian 400 or Varian 500 MHz spectrometer in the School of Chemical Sciences NMR laboratory at the University of Illinois at Urbana-Champaign. Chemical shifts are reported in δ (ppm) relative to the residual solvent peak. Coupling constants (J) are expressed in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet), and b (broad).

Analytical gel permeation chromatography (GPC) analyses were performed on either of two systems. Most GPC analyses were performed on a system composed of a Waters 515 HPLC pump, a Thermoseparations Trace series AS100 autosampler, a series of three Waters HR Styragel columns (7.8' 300 mm, HR3, HR4, and HR5), and a Viscotek TDA Model 300 triple detector array, in HPLC grade THF (flow rate = 0.9 mL/min) at 25 °C. The GPC was calibrated using a series of monodisperse polystyrene standards. Triple detector analysis was carried out in Waters 1515 Isocratic HPLC pump, with a Waters (2707) 96-well autosampler, and a series of 4 Waters HR Styragel columns (7.8 X 300mm, HR1, HR3, HR4, and HR5) in THF at 30 °C, coupled to 4 detectors in sequence: Waters (2998) Photodiode Array Detector, a Waters (2414) Refractive Index Detector, Wyatt mini-DAWN TREOS multi-angle laser light-scattering, and a Wyatt Viscostar II viscometer. Analysis of the data was done using Wyatt's Astra 6 software. PPA dn/dc was calculated online to be 0.1515 as an average of three 100% mass-recovery experiments and was used for all samples.

Thermal gravimetric analysis (TGA) was done using a Mettler-Toledo TGA/DSC1 LF. Scans were collected in the range of 25 °C – 400 °C with a ramping rate of 10 °C/min under a dry nitrogen atmosphere. Hydrodynamic radii where determined by dynamic light scattering (DLS) on a Malvern Zetasizer Nano ZS. The laser power was 20mW at 633 nm. The polymer solutions were prepared by dissolving the polymer in THF at 1 mg/mL and filtering over a 0.45 μ m filter before being analyzed by DLS. Infrared spectra (percent transmittance) were acquired on a SmartITR ATR accessory for a Nicolet Nexus 670 FT-IR spectrometer.

Atomic force microscopy (AFM) was performed under ambient conditions on a Bruker Multimode NanoScope VIII. A silicon tip cantilever (SCANASYST-AIR, 50-90 kHz, 0.4 N/m from Bruker) was used in ScanAsyst mode with a scan size of 1-4 μ m, a 1 Hz scan rate and 512 scan lines. Atomic force microscopy samples were prepared by dropcasting 2 μ l of solution (0.1-10 μ g/mL in THF, filtered over a 0.45 μ m filter) on freshly cleaved mica in ambient conditions and allowing the sample to air dry.

II. Synthetic Procedures



In a glovebox, purified *o*-PA (2.62 g, 19.5 mmol) and 5-nitroisophthalaldehyde (1.01 g, 5.6 mmol) were weighed into a Schlenk flask and dissolved in THF (35 mL). The solution was removed from the glovebox and degassed by three freeze-pump-thaw cycles. Then, 1,6-hexanediol in THF (0.80 mL of a 0.03 M solution, 24 µmol) was added, and the solution stirred 2 minutes then cooled to -78 °C. Finally, P₂-t-Bu phosphazene base in THF (0.05 mL of a 2.0 M solution, 100 µmol) was added to initiate polymerization. The reaction was left stirring at -78 °C for 3 h, then the polymer end-capped by adding trichloroacetyl isocyanate (0.65 mL, 5.5 mmol) and allowing the mixture to stir an additional 2 h at -78 °C. The reaction mixture was then brought to room temperature and polymer precipitated by pouring into methanol (100 mL) and collected by filtration. Polymer **1** was further purified by dissolving in dichloromethane and reprecipitating from methanol and washed in diethyl ether (2.46 g, 68%). ¹H NMR (500 MHz, DMSO-d₆) δ 10.25-9.75 (b, 1H, aldehyde), 8.80-8.15 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal). GPC (RI): M_n = 13.5 kDa, PDI = 1.49.

Synthesis of PPA-HMNB (Polymer 2).



To a Schlenk flask were added 2.41 g PPA-NIPA (Polymer 1, 1.4 mmol –CHO) and sodium borohydride (0.10 g, 2.6 mmol). The solids were dissolved in dichloromethane (40 mL) and methanol (8 mL), and the reaction mixture left stirring 1 h at room temperature. Polymer **2** was then precipitated into excess methanol (200 mL) and washed in methanol and diethyl ether (1.74 g, 72%). ¹H NMR (500 MHz, DMSO-d₆) δ 8.45-7.75 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal), 5.70-5.40 (b, CH₂-OH), 4.75-4.25 (b, -CH₂-OH). GPC (RI): M_n = 15.7 kDa, PDI = 1.34.



In a glovebox, PPA-HMNB (Polymer 2, 0.20 g, 88 µmol –OH) and 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydro-pyrimidin-2-yl)urea (UPy-NCO, 28 mg, 95 µmol) were weighed into a Schlenk flask and dissolved in chloroform (60 mL, neutralized by stirring over K₂CO₃). To this solution was added 1,4-diazabicyclo[2.2.2]octane (DABCO, 0.65 mL of a 8.8 mM solution, 6 µmol) and the flask was closed and warmed to 60 °C overnight (18 hours). After overnight reaction, 1,6-hexanediamine (50 mg) was added to quench the PPA-UPy and the mixture filtered and concentrated in vacuo. The residue was dissolved in dichloromethane (20 mL) and filtered, then precipitated into methanol (150 mL) and washed in methanol and diethyl ether (0.17 g, 85%). ¹H NMR (500 MHz, CDCl₃) δ 13.3-12.9 (b, NH), 12.0-11.7 (b, NH), 10.3-9.9 (b, NH), 8.50-7.75 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal), 4.75-4.00 (b, -CH₂-O), 4.00-0.50 (b, aliphatic –CH₂-). GPC (RI): M_n = 15.3 kDa, PDI = 1.31.

Depolymerization of PPA-UPy.



In a Schlenk flask, PPA-UPy (Polymer 3, 40 mg) was dissolved in dichloromethane (0.4 mL). To the solution was added boron trifluoride etherate (1 drop, ~0.04 mmol) and the reaction stirred for 5 min at room temperature, turning deep yellow immediately. To the mixture was then added pyridine (0.10 mL, 1.2 mmol) and left stirring 2 h. The reaction mixture was concentrated in vacuo and collected as a yellow oil, identified as majority *o*-PA by ¹H NMR. ¹H NMR (500 MHz, CDCl₃) δ 10.54 (s, 2H, CHO), 7.98 (q, 2H, Ar-H), 7.78 (q, 2H, Ar-H). GPC (RI): No polymer.



In a Schlenk flask, PPA-UPy (Polymer 3, 40 mg) was dissolved in dichloromethane (0.4 mL). The solution was cooled to -78 °C, and boron trifluoride etherate (1 drop, ~0.04 mmol) was added. The reaction was stirred for 2 h at -78 °C, then quenched by adding pyridine (0.10 mL, 1.2 mmol) and left stirring 2 h. The solution was then warmed to room temperature and polymer collected by precipitation into methanol (50 mL) and washing in methanol and diethyl ether (30 mg, 75%). GPC (RI): $M_n = 2.5$ kDa, PDI = 2.00.

Formation of PPA-UPy Supramolecular Networks.



In a Schlenk flask, PPA-UPy (Polymer 3, 70 mg) was dissolved in dichloromethane (0.4 mL). The solution was cooled to -78 °C, and boron trifluoride etherate (0.01 mL, 0.08 mmol) was added. The reaction gels almost immediately, but was left for 2 h at -78 °C before quenching with pyridine (0.10 mL, 1.2 mmol) and left stirring another 2 h. The solution was brought to room temperature and the resulting solid polymer was washed in excess methanol and diethyl ether (71 mg, quantitative recovery). The white solid was insoluble in chloroform, dichloromethane, THF, and dimethyl sulfoxide (all good solvents for PPA-UPy).

As a control reaction, the above procedure was repeated with PPA-HMNB (Polymer 2, 70 mg in 0.4 mL dichloromethane). The reaction mixture remains soluble and colorless, and the polymer was collected as a white powder (34 mg, 49% yield). The polymer is soluble in all typical solvents for PPA. GPC (RI): $M_n = 2.0$ kDa, PDI = 1.80.

Depolymerization of PPA-UPy Supramolecular Networks (Figure 5).

Cross-linked PPA-UPy (10-20 mg) was suspended in CDCl₃ (~3 mL) in a small glass dish, turning to an opaque gel. To the suspension was added three drops trifluoroacetic acid. The solid sample shrank in size immediately and disappeared completely within 2 min. The solution was collected for analysis and identified as majority *o*-PA monomer by ¹H NMR. ¹H NMR (500 MHz, CDCl₃) δ 10.54 (s, 2H, CHO), 7.98 (q, 2H, Ar-H), 7.78 (q, 2H, Ar-H).

III. NMR Spectra



Figure S1 / ¹*H NMR spectra of PPA-NIPA*: *NMR spectra of* $M_n = 13.5$ *kDa PPA-NIPA (Polymer 1) in DMSO-d*₆. *Additional peak corresponds to water.*



Figure S2 $|^{1}H$ *NMR spectra of PPA-HMNB*: *NMR spectra of* $M_{n} = 15.7$ kDa PPA-HMNB (Polymer 2) in DMSO-d₆. Additional peaks correspond to monomer and solvent.



13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 *Figure S3* $|^{T}H$ *NMR spectra of PPA-HMNB*: *NMR spectra of* $M_{n} = 15.7$ *kDa PPA-HMNB (Polymer 2) in CDCl₃*. *Additional peaks correspond to monomer and solvent*.



13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 Figure S4 $/^{1}H$ NMR spectra of PPA-UPy: NMR spectra of $M_{n} = 15.3$ kDa PPA-UPy (Polymer 3) in CDCl₃. Additional peaks correspond to monomer and solvent.



Figure S5 / **Zoomed Region of** ¹**H** NMR spectra of PPA-UPy: NMR spectra of $M_n = 15.3$ kDa PPA-UPy (Polymer 3) in CDCl₃. Broad peaks correspond to hydrogen-bonded protons of UPy. Sharp peak is residual monomer.



Figure S6 / ¹*H NMR spectra of Depolymerized PPA-UPy*: NMR spectra of PPA-UPy (Polymer 3) in CDCl₃ after reaction with boron trifluoride etherate at room temperarature (blue trace, bottom) compared to purified o-PA monomer (red trace, top). Major peaks in depolymerization product correspond to o-PA.



Figure S7 / ¹*H NMR spectra of Reconstituted PPA-UPy*: *NMR spectra of* $M_n = 2.5$ *kDa PPA-UPy* (*Polymer 3*) *in CDCl*₃ *after reconstitution reaction with boron trifluoride etherate at -78* °*C*.



L1.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 *Figure S8* / ¹*H NMR spectra of Depolymerized PPA-UPy Supramolecular Network:* NMR spectra of product from reaction of cross-linked PPA-UPy (Polymer 3) with trifluoroacetic acid in CDCl₃. Major peaks in depolymerization product correspond to o-PA, and insets reveal the presence of benzaldehyde comonomer.



Figure S9 / ¹*H NMR spectra of Reconstituted PPA-HMNB*: NMR spectra of $M_n = 2.0$ kDa PPA-HMNB (Polymer 2) in CDCl₃ after reconstitution reaction with boron trifluoride etherate at -78 °C.



Figure S10 | Normalized GPC chromatograms of PPA-NIPA (1, green), PPA-HMNB (2, blue) and PPA-UPy (3, red) copolymers. Molecular weight and polydispersity data are summarized in Table S1.

Table S1 / GPC data for polymer samples.						
	Sample	Polymer	Yield	M_n $(kDa)^a$	M_p $(kDa)^a$	PDI^{a}
	PPA-NIPA	1	68%	13.5	20.0	1.49
	PPA-HMNB	2	72%	15.7	21.0	1.34
	PPA-UPy	3	85%	15.3	20.1	1.31

^aAverage molecular weights and polydispersity determined by gel permeation chromatography (GPC), calibrated with monodisperse polystyrene standards.



Figure S11 | Normalized GPC chromatograms of PPA-HMNB (2, blue), PPA-UPy (3, red), depolymerized PPA-UPy (yellow), and reconstituted PPA-UPy (green). Molecular weight of polydispersity data are summarized in Table S2.

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Sample	Polymer	Yield	M_n	M_p	PDI^{a}	
			$(kDa)^a$	$(kDa)^a$		
PPA-HMNB	2	72%	15.7	21.0	1.34	
PPA-UPy	3	85%	15.3	20.1	1.31	
Depolymerized PPA-UPy		100%	0.1	0.2	1.92	
Reconstituted PPA-UPy		75%	2.5	2.6	2.01	

Table S2 | GPC data for polymer samples

^aAverage molecular weights and polydispersity determined by gel permeation chromatography (GPC), calibrated with monodisperse polystyrene standards.



Figure S12 | Normalized GPC chromatograms of PPA-HMNB (2, blue), PPA-UPy (3, red), reconstituted PPA-HMNB (yellow), and reconstituted PPA-UPy (green). Molecular weight of polydispersity data are summarized in Table S3.

able 55 / GFC alla for polymer samples.						
Sample	Polymer	Yield	M_n	M_p	PDI^{a}	
			$(kDa)^a$	$(kDa)^a$		
PPA-HMNB	2	72%	15.7	21.0	1.34	
PPA-UPy	3	85%	15.3	20.1	1.31	
Reconstituted PPA-HMNB		49%	2.0	1.8	1.80	
Reconstituted PPA-UPy		75%	2.5	2.6	2.01	

Table S3 / GPC data for poly	ner samples
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^aAverage molecular weights and polydispersity determined by gel permeation chromatography (GPC), calibrated with monodisperse polystyrene standards.



Figure S13 | *Triple detector GPC data.* a) Normalized GPC chromatograms of PPA-HMNB (blue) and PPA-UPy (red); b) Plot of absolute molecular weight (logarithmic axis) versus retention time. Molecular weights are summarized in Table S4.

Table S4 / Comparison of PPA-HMNB and PPA-UPy absolute molecular weights.

Sample	M_n	M_p	PDI^{a}	R_h
×.	$(kDa)^a$	$(kDa)^{a}$		$(nm)^b$
PPA-HMNB	20.8	20.6	1.29	5.9
PPA-UPy	22.4	21.6	1.22	4.9

^aAverage molecular weights and polydispersity determined absolutely by triple detector GPC analysis. ^bHydrodynamic radius determined by light scattering.

V. AFM images



Figure S14 | AFM image of single-chain polymer nanoparticles. PPA-UPy (Polymer 3) nanoparticles on mica, casted from a 0.1 μ g/mL solution in THF. Nanoparticles are spherical and monodisperse, with heights of approximately 4 nm and average diameters of 46 nm.



Figure S15 | AFM images of single-chain polymer nanoparticles. Additional views of PPA-UPy (Polymer 3) nanoparticles on mica, cast from 0.1 μ g/mL solution. Nanoparticles are seen to be spherical and monodisperse.



Figure S16 | AFM images of PPA-HMNB (Polymer 2). Several views of PPA-HMNB (Polymer 2) aggregates on mica (cast from 10 μ g/mL solution) for comparison to PPA-UPy nanoparticles. The morphology of linear PPA-HMNB polymers differs significantly between regions and is observed as randomly associated aggregates.

<u>Author's note</u>: The following AFM images were collected on a second PPA-UPy sample with $M_w = 10.0$ kDa and PDI = 1.40, and a PPA/benzaldehyde ratio of 88/12. Polymers were cast from a 10 µg/mL solution in THF.



Figure S17 / *AFM images of single-chain polymer nanoparticles.* Additional views of PPA-UPy (Polymer 3) nanoparticles on mica, cast from 10 μ g/mL solution. Nanoparticles are seen to be spherical and fairly monodisperse. Dimensions of particles along cross-section: 19.7 nm diameter/2.5 nm height and 17.2 nm diameter/2.0 nm height.



Figure S18 / AFM images of single-chain polymer nanoparticles. Additional views of PPA-UPy (Polymer 3) nanoparticles on mica, cast from 10 μ g/mL solution. Nanoparticles are seen to be spherical and fairly monodisperse. Dimensions of particles along cross-section: 14.0 nm diameter/1.4 nm height, 14.0 nm diameter/1.8 nm height, and 14.0 nm diameter/1.6 nm height.



Figure S19 | Additional magnifications of single-chain polymer nanoparticles. PPA-UPy (Polymer 3) nanoparticles on mica, casted from a 10 μ g/mL solution in THF, at various magnification. Nanoparticles are spherical and monodisperse.





Figure S20 | TGA of PPA-HMNB and PPA-UPy: Normalized TGA curves of PPA-HMNB (2, blue) and PPA-UPy (3, red). Depolymerization temperatures are summarized in Table S5.

Polymer	Sample	Onset Temp	Endset Temp	Residue at
		$(^{\circ}C)$	$(^{\circ}C)$	300 °C
2	PPA-HMNB	211	240	6%
3	PPA-UPy	214	241	15%

Table S5 / TGA Samples. Depolymerization data for PPA-HMNB and PPA-UPy.



Figure S21 | ATR-IR spectra of PPA (green), PPA-UPy (red), and PPA-UPy network (blue).



Figure S22 | Expansion into ATR-IR spectra of PPA (green), PPA-UPy (red), and PPA-UPy network (blue).

VIII. References for Supporting Information

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