Multi-responsive copolymers: Using thermo-, light- and redox stimuli as three independent inputs towards polymeric information processing. †

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Electronic Supplementary Information (ESI) for Chemical Communications

Experimental Part

Materials. All chemicals and solvents were commercially available and used as received unless otherwise stated. Tetrahydrofuran (THF) was dried over sodium and freshly distilled before use. Triethylamine (Et_3N) was dried over calcium chloride and distilled previously. Membrane tube for dialysis was purchased from Roth (MWCO 3500) with an exclusion volume of 3500 Dalton. Poly(pentaflourphenylacrylate) (PPFPA) with a molecular weight of M_n = 14 000g mol^{-1} and a molecular weight distribution M_w/M_n = 1.3 was synthesized following a procedure described earlier[1]

Instrumentation. ^{1}H- NMR spectra were recorded on a Bruker 300 MHz FT-NMR spectrometer in deuterated solvents. ^{19}F-NMR spectra were recorded on a Bruker 400 MHz FT-NMR spectrometer. The chemical shifts (δ) were given in ppm relative to trimethylsilane (TMS). Gel permeation chromatography (GPC) was used to determine the molecular weight and the corresponding molecular weight distributions, (M_w/M_n), of the polymer samples with respect to polystyrene standards. GPC measurements were performed in THF. The flow rate was 1mL*min^{-1} at 25°C. IR spectra were recorded using a Bruker Vector 22 FT-IR spectrometer with an ATR unit. ESR spectra were recorded on a Miniscope MS300 in continuous wave mode. The samples were irradiated with a constant frequency of 9.5 GHz (X-band) which was generated by a Hewlett Packard frequency counter model 5340A. The internal standard was Mn^{2+} in zinc sulphide.

Synthesis of *N*-(2-Aminoethyl)-4-(2-phenyldiazenyl)benzamide (azobenzene) was synthesized according to a method published recently.[1] yield: 83% ^{1}H-NMR ($CDCl_3$): δ/ppm: 8.62 (s, 1H), 8.06 (d, 2H), 7.93 (m, 4H), 7.60 (m, 3H), 3.30 (q, 2H), 2.71 (t, 2H); FT-IR (ATR-mode): ν_{max}/ cm^{-1} 3296 (N-H), 1634 (C=O), 1539 (C=O)

Synthesis of 4-Oxy-2,2,6,6-tetramethyl-1-oxyl-piperidine (Oxy-TEMPO) was already published before.[2] yield: 57% FT-IR (ATR-mode): ν_{max}/ cm^{-1} 1726 (C=O), 1366 (C-N); ESR (continuous wave mode, in CH_2Cl_2): microwave: 9.42 GHz, g-value: 1.9897, A= 13.5 G; m/z 170 (92%), 171 (8%)

Synthesis of 4-Amino-2,2,6,6-tetramethyl-1-oxyl-piperidine (Amino-TEMPO) The procedure, which was published before, was slightly modified as follows.[2] 24.6 g (0.32 mol) of ammonium acetate was dissolved in 350 mL of dry methanol and molecular sieve were added. The pH value was adjusted to 7-8 using potassium carbonate. 5.4 g (0.032 mol) of Oxy-TEMPO were dissolved in 20 mL of dry methanol and were added dropwise into the ammonium acetate solution. After 30 min., 1.44 g (0.045 mol) of sodium cyanoborohydride were added at once. The reaction was kept at room temperature for 48 hours. The mixture was filtrated and the methanol was removed under low pressure. The red powder was dissolved in 50 mL of water. The pH value was adjusted to 5-6, using diluted hydrochloride acid and extracted with chloroform. Next, the pH

value of the aqueous phase was raised to 13, saturated with sodium chloride and extracted three times with chloroform. The organic layer was dried over $MgSO_4$, filtrated and evaporated completely. The product was further purified by column chromatography using neutral Al_2O_3 and ethanol as mobile phase. Pure red coloured amino-TEMPO was obtained. yield: 80% FT-IR (ATR-mode): ν_{max}/ cm^{-1} 3379 and 3297 (N-H), 1583 (N-H), 1363 (C-N valence); ESR (continuous wave mode, in CH_2Cl_2): microwave: 9.42 GHz, g-value: 1.9916, A= 14.2 G; m/z 171 (89%), 171 (11%)

General procedure for the synthesis of the triple responsive polymer (PI and PII) PPFPA and Et_3N were dissolved in 5 mL of freshly distilled THF. The solution was heated up to 45°C and azobenzene and amino-TEMPO (both dissolved in 0.5 mL of dry THF) were added. After 4 hours the solution was cooled down to room temperature. An excess amount of isopropylamine was added and the solution was allowed to stir for additional 18 hours at ambient temperature. Next, the solvent was evaporated and the residue was dissolved in 8 mL of Millipore water and dialyzed against Millipore water for 18 hours. The water was evaporated completely and the residue was dissolved in THF. After precipitation the polymer into dry diethylether, the polymer was centrifuged and dried for 5 hours in vacuum.

Synthesis of the triple responsive polymer PI 300 mg (1.3 mmol) of PPFPA, 0.25 mL (3.4 mmol) of Et_3N, 10 mg (0.037 mmol) of azobenzene (correspond to 3% in respective to the pentafluorophenyl moieties), 6 mg (0.037 mmol) of amino-TEMPO (correspond to 3% in respective to the pentafluorophenyl moieties) and 0.38 mL (9.3 mmol) of isopropylamine were used, following the general procedure for triple responsive polymers, to yield 146 mg of PI. FT-IR (ATR-mode): ν_{max}/ cm^{-1} 1641 (C=O), 1534 (C=O), 1364 (C-N valence); ESR (continuous wave mode, in CH_2Cl_2): microwave: 9.42 GHz, g-value: 1.9890

Synthesis of the triple responsive polymer P2 300 mg (1.3 mmol) PPFPA, 0.25 mL (3.4 mmol) Et_3N, 10 mg (0.037 mmol) azobenzene (correspond to 3% in respective to the pentafluorophenyl moieties), 11 mg (0.063 mmol) amino-TEMPO (correspond to 5% in respective to the pentafluorophenyl moieties) and 0.38 mL (9.3 mmol) isopropylamine were used, following the general procedure for triple responsive polymers, to yield 126 mg of PII. FT-IR (ATR-mode): ν_{max}/ cm^{-1} 1641 (C=O), 1534 (C=O), 1364 (C-N valence); ESR (continuous wave mode, in CH_2Cl_2): microwave: 9.42 GHz, g-value: 1.9890

Turbidity measurement Turbidity measurements were recorded on a JASCO V-630 photospectrometer with a JASCO ETC-717 peltier element. The optical transmittance of a light beam (λ = 632 nm) was plotted versus the temperature of the sample quartz cell. The heating rate was 1°C per minute and the sample was stirred during measurement. The sample was prepared by dissolving 5 mg of the polymeric material in 1 mL of a 0.1 molar sodium sulfate solution. The ascorbic acid and the red prussiate were directly added as a powder and the solution was stirred at 5°C. After 1 hour, the temperature was raised up to 45°C and the solution was separated with a syringe from the precipitated polymer. Next, the polymer was again dissolved in 1 mL of a 0.1 molar aqueous sodium sulfate solution per mg of polymer. In the case of the red prussiate this purification step was repeated twice.

Irradiation experiments of the polymer solution were performed in the 10 mm quartz cuvette placed in an ice bath and using an Oriel Instrument 500 W mercury lamp equipped with a 365 nm filter for 1.5 hours.

References

1 F. D. Jochum and P. Theato, *Polymer*, **2009**, *50*, 3079–3085
2 G. M. Rosen, *Journal of Medicinal Chemistry*, **1974**, *17*, 358–360
3 B. M. Weckhuysen, R. Heidler, R.A. Schoonheydt, *Mol. Sieves*, **2004**, *4*, 295-335

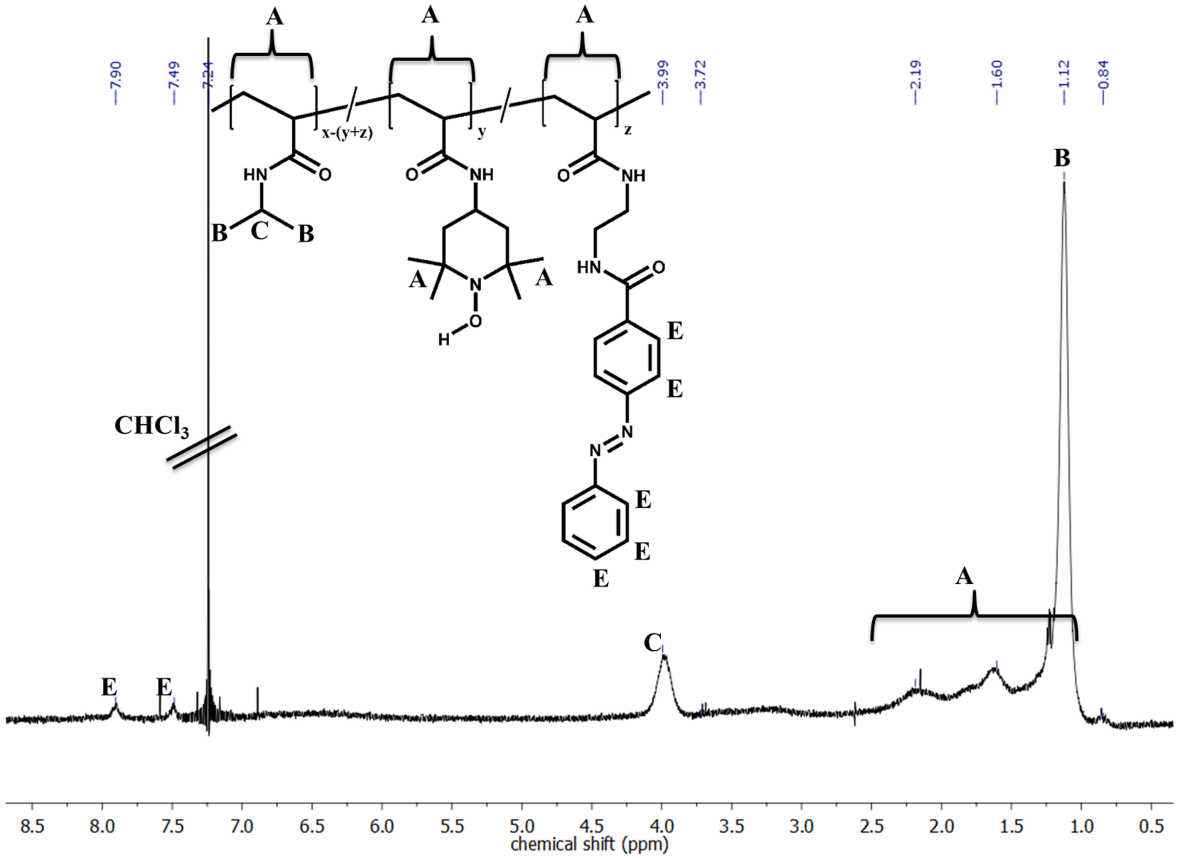

Figure S1. ^{1}H NMR spectra of PI in $CDCl_3$

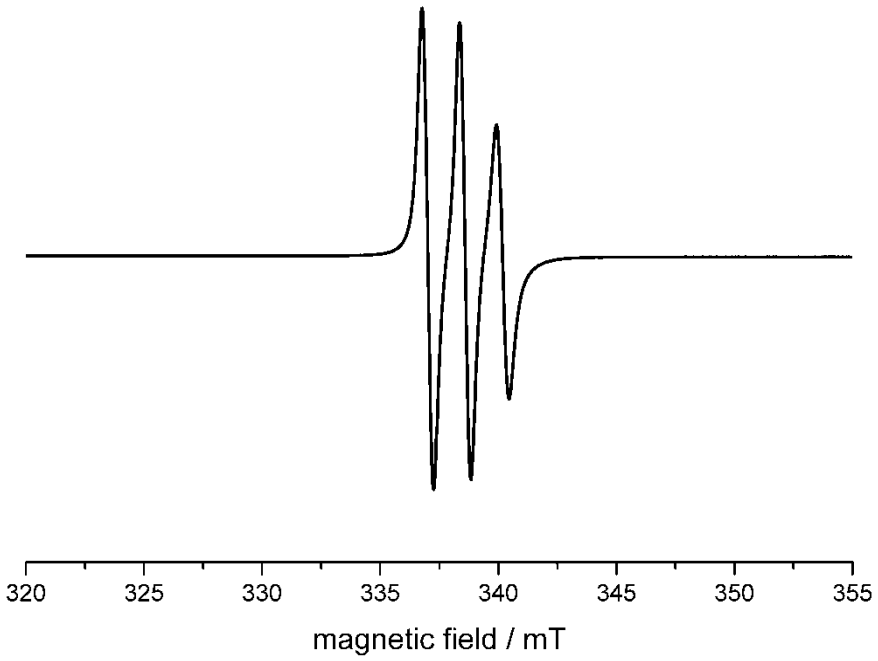

Figure S2. ESR spectra for PI in CH_2Cl_2. Continuous wave mode, microwave: 9.42 GHz

PNIPAM test model

In order to proof the influence of the added salts (ascorbic acid and red prussiate), a poly(*N*-isopropylamine) (PNIPAM) model system was prepared and treated with the corresponding salts. The addition of ascorbic acid yielded in a slight decrease of the LCST (figure S3). While 2.5 mg of ascorbic acid showed no difference, the addition of 29 mg lowered the LCST of PNIPAM of about 0.3°C. The effect of red prussiate was even more pronounced (figure S4). The addition of 128 mg red prussiate led to a decrease of the LCST of about 5°C. Removal of the red prussiate by precipitation of the polymer and followed by two washing steps could reverse the shift.

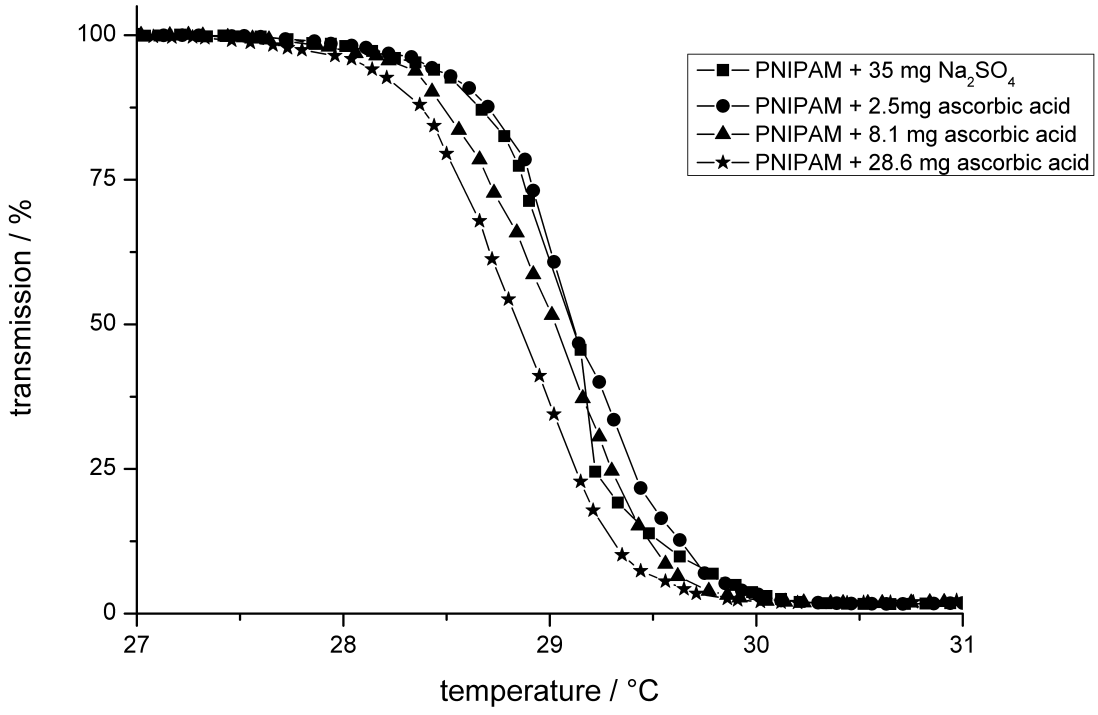

Figure S3. Turbidity measurements of a PNIPAM test model to proof the influence of ascorbic acid upon the clouding point. (a) pure PNIPAM (black squares), clouding point: 29.1°C, (b)addition of 2.5 mg ascorbic acid (black circles), clouding point: 29.1°C, (c) addition of 8.1 mg ascorbic acid (black triangles), clouding point: 29.0°C (d) addition of 28.6 mg ascorbic acid (black stars), clouding points: 28.8°C

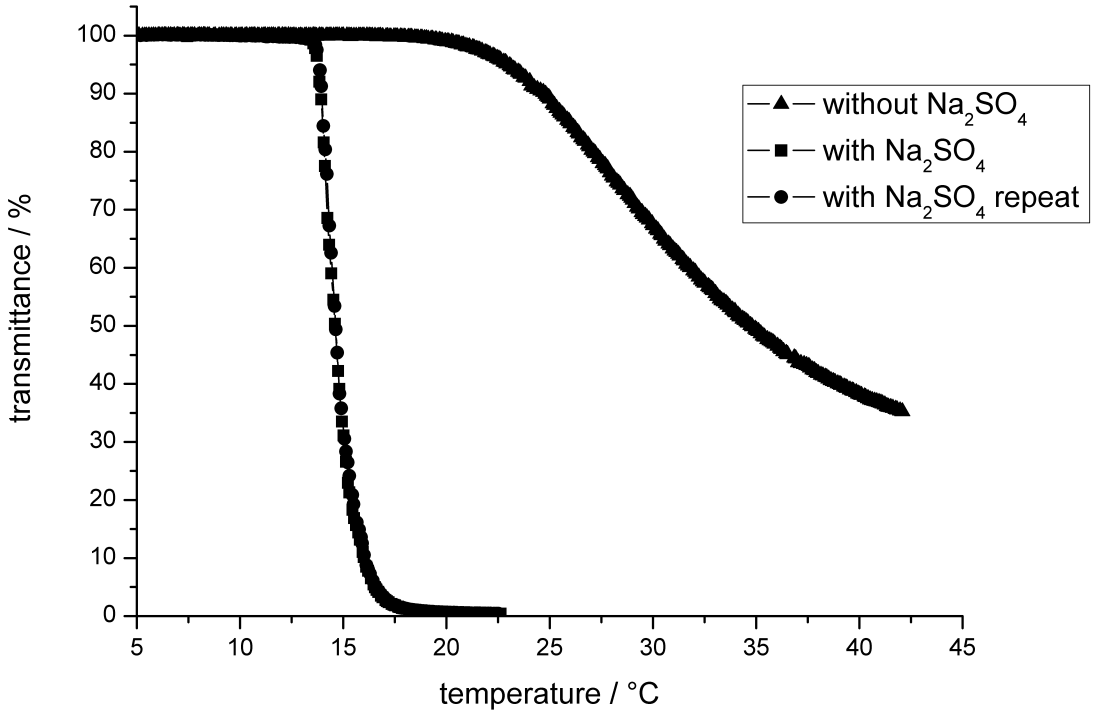

Figure S4: turbidity measurements of PI to proof the influence of the cosmotropic salt sodium sulfate. (a) pure PI (black triangles), broad clouding point estimated at 30.2°C, (b) addition of 38 mg of sodium sulfate (black squares), clouding point at 14.6°C, (c) repeat of the same measurement in order to proof the accuracy of the measurement technique (black circles), clouding point at 14.6°C

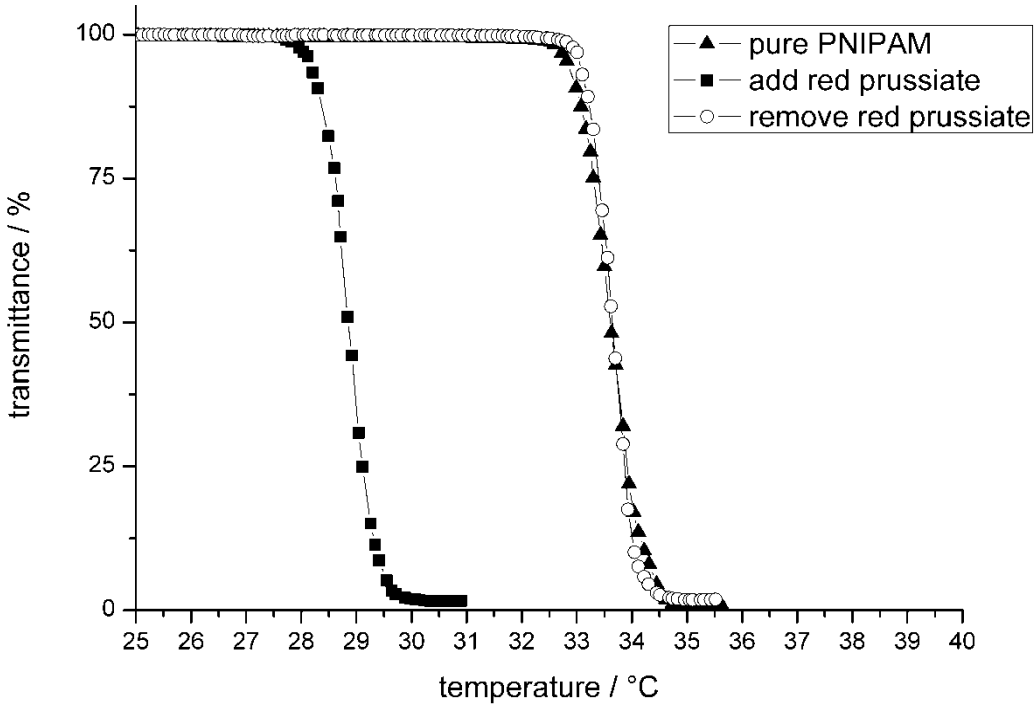

Figure S5. Turbidity measurements of a PNIPAM test model to proof the influence of red prussiate upon the clouding point. (a) pure PNIPAM (black triangles), clouding point: 33.6°C, (b) addition of 128 mg red prussiate (black squares), clouding point: 28.8°C, (c) two subsequent purification steps in order to remove the red prussiate (white circles), clouding point: 33.6°C

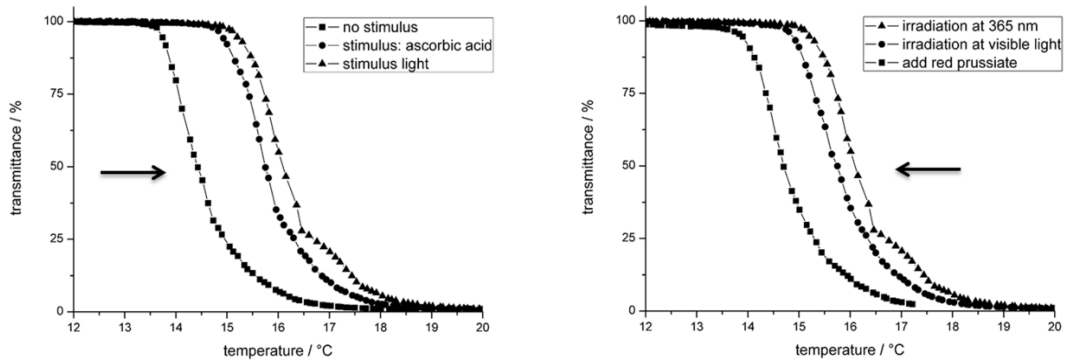

Figure S6. Turbidity measurements of the triple responsive polymer PI (first cycle). Left: (a) PI without any stimulus (black squares), (b) addition of 80 mg ascorbic acid (black circles), reduction of TEMPO, (c) irradiation with UV-light 365 nm for 2 hours (black triangles), cis-isomerization; right: (a) irradiated sample (black triangles), cis-conformation, (b) irradiation with visible light for 2 hours (black circles), trans-isomerization, (c) addition of 120 mg red prussiate (black triangles), oxidation of TEMPO

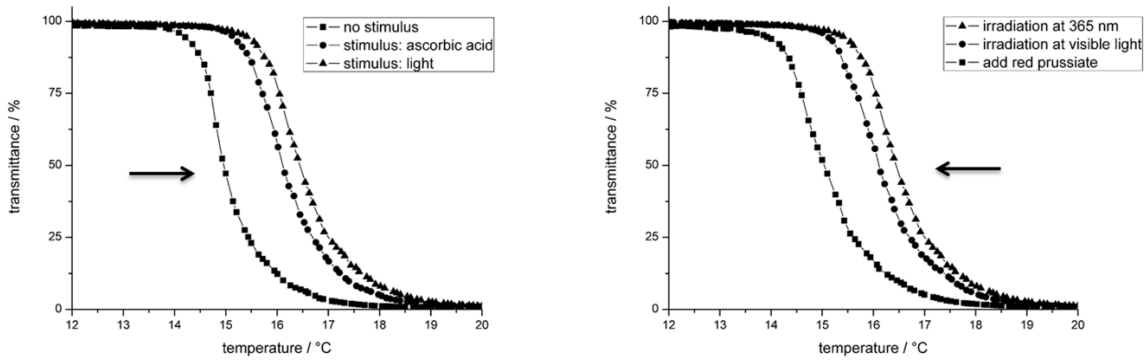

Figure S7. Second cycle:Turbidity measurements of the triple responsive polymer PI. Left: (a) PI without any stimulus (black squares), (b) addition of 80 mg ascorbic acid (black circles), reduction of TEMPO, (c) irradiation with UV-light 365 nm for 2 hours (black triangles), cis-isomerization; right: (a) irradiated sample (black triangles), cis-conformation, (b) irradiation with visible light for 2 hours (black circles), trans-isomerization, (c) addition of 132 mg red prussiate (black triangles), oxidation of TEMPO

	clouding point$_{first}$ / °C	clouding point$_{second}$ / °C
start	14.4	14.9
ascorbic acid	15.7	16.1
irradiation at 365 nm	16.0	16.4
irradiation sunlight	15.6	16.1
red prussiate	14.6	15.0

Table S1. Clouding points of the triple responsive polymer PI in dependence of the stimuli. Left the first cycle (fig. S6) and right the second cycle (fig. S7)

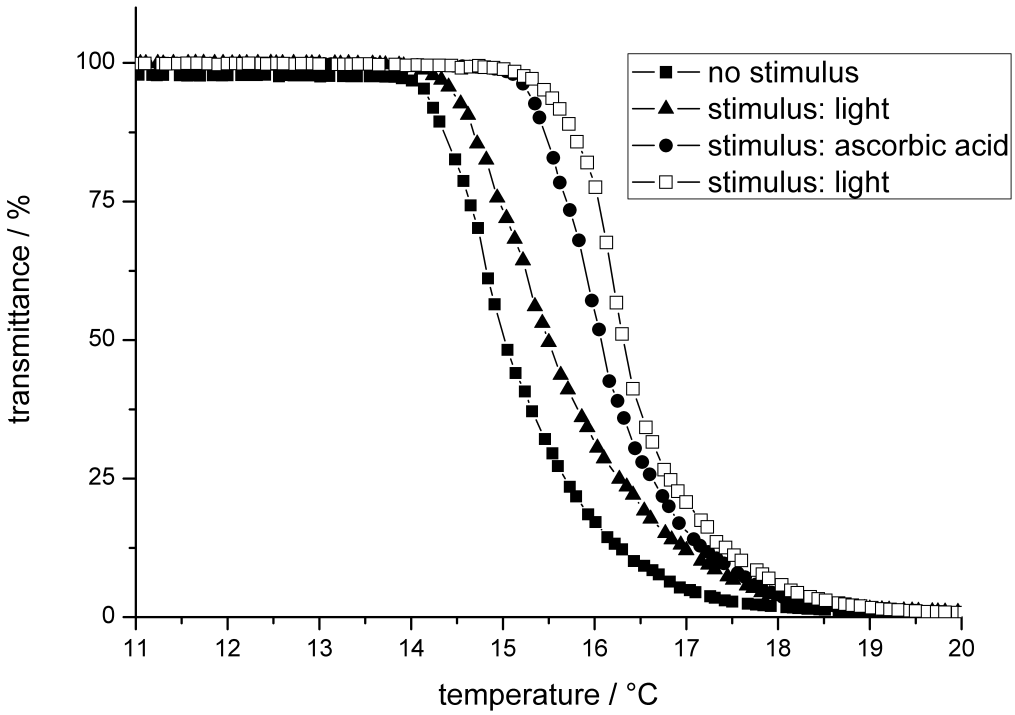

Figure S8. Turbidity measurements of the triple responsive polymer PI. (a) PI without any stimulus (black squares), (b) irradiation with UV-light 365 nm for 1.5 hours (black triangles), cis-isomerization (c) addition of 40 mg ascorbic acid (black circles), reduction of TEMPO, (d) irradiation with UV-light 365 nm for 1.5 h (white squares)

	clouding point$_{first}$ / °C
start	15.0
irradiation at 365 nm	15.5
ascorbic acid	16.0
irradiation at 365 nm	16.3

Table S2. Clouding points of the triple responsive polymer PI in dependence of the stimuli, when the polymer is irradiated with UV light first

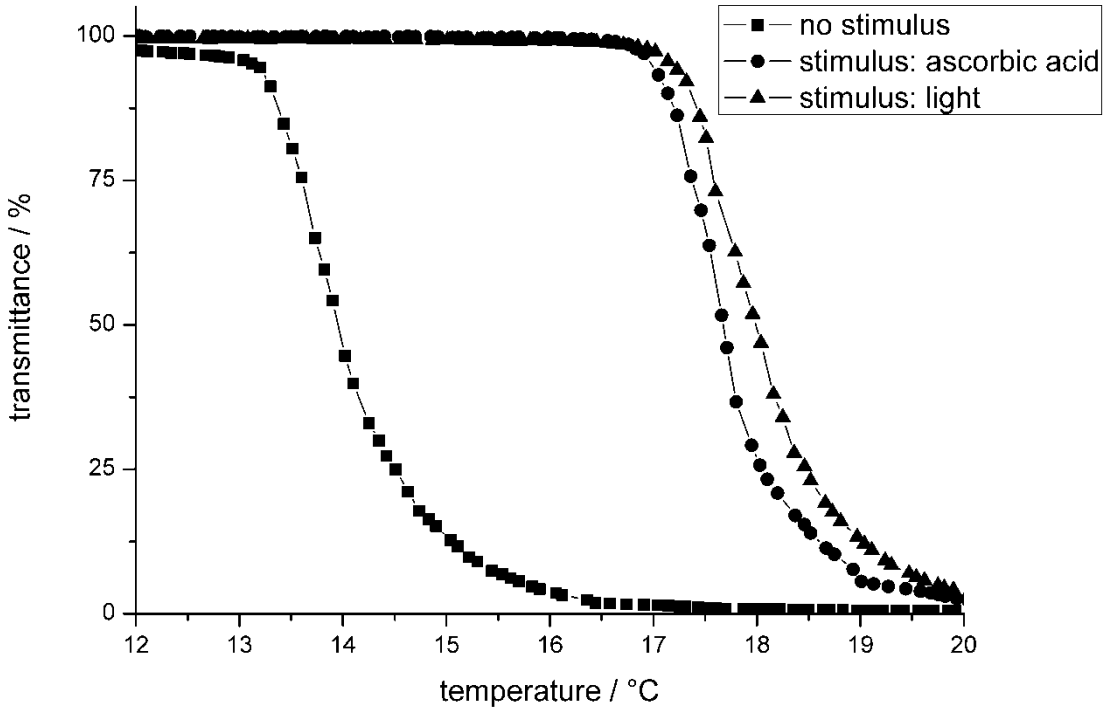

Figure S9. Turbidity measurements of the triple responsive polymer PII. (a) PII without any stimulus (black squares), (b) addition of 91.5 mg ascorbic acid (black circles), reduction of TEMPO, (c) irradiation with UV-light 365 nm for 2 hours (black triangles), cis-isomerization

	clouding point$_{first}$ / °C
start	13.9
ascorbic acid	17.7
irradiation at 365 nm	18.0
irradiation sunlight	17.7
red prussiate	14.0

Table S3. Clouding points of the triple responsive polymer PII in dependence of the stimuli.

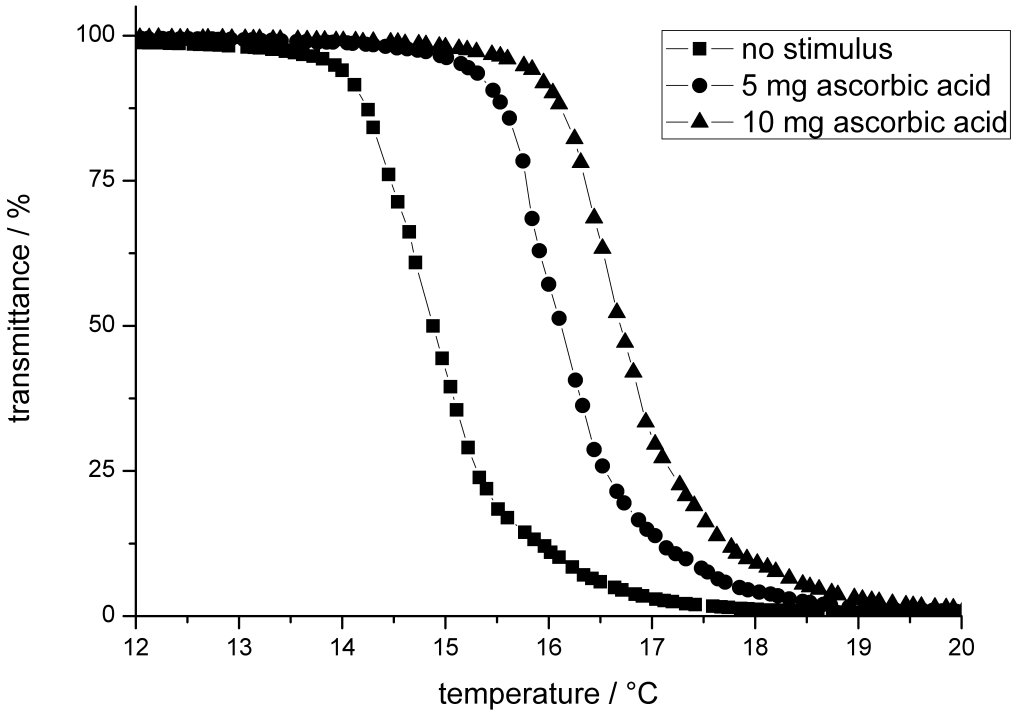

Figure S10. Successive reduction of the triple responsive polymer PII determined by turbidity measurement. (a) without any stimulus (black squares), clouding point: 14.8°C, (b) first addition of 5 mg ascorbic acid (black circles), clouding point: 16.1°C (c) second addition of 5 mg ascorbic acid (black triangles), clouding point: 16.7. Please note, that the determination of the conversion rate is rather difficult due to the paramagnetic character of the TEMPO moieties. A quantitative analyses cannot be achieved by NMR spectroscopy and even an internal calibration with TEMPO using ESR spectroscopy contains errors roughly about 20%.[3]

	S_1	R_1	Q_1	$_1$
A	**0**	**0**	**previous state**	
	1	**0**	**1**	**0**
	0	**1**	**0**	**1**

	S_2	R_2	Q_2	$_2$
B	**0**	**0**	**previous state**	
	1	**0**	**1**	**0**
	0	**1**	**0**	**1**

Table S4 Characteristics table A) TEMPO based flip-flop. Inputs are S_1 ascorbic acid (set) and R_1 red prussiate (reset). B) azobenzene based flip-flop. Inputs are S_2 UV light with 365 nm (set) and R_2 light > 400 nm (reset). Please note that only one input can be active at a time