SUPPORTING INFORMATION

Temperature driven self-assembly of a zwitterionic block copolymer that exhibits triple thermo-responsivity and pH sensitivity

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Figure S1. $^1$H NMR spectrum for the block copolymer poly(NIPAAm$_{114}$-$b$-MPDSAH$_{228}$) at 25 °C in D$_2$O with the addition of NaCl to increase solubility and homogeneity.

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Figure S2. GPC$_{\text{aq}}$ chromatograms for poly(NIPAAm$_{114}$-$b$-MAPSP$_{228}$) at 25 °C in Na$_2$PO$_4$ 10 mM and NaBr 25 mM eluent solution at a flow rate of 0.5 ml/min (thin black curve) or 0.75 ml/min (thick black curve); in Na$_2$PO$_4$ 10 mM and NaBr 100 mM eluent solution at a flow rate of 0.5 ml/min (red curve); and NaOH and NaBr 25 mM eluent solution (pH≈11) at a flow rate of 0.5 ml/min (blue curve).

Synthesis of poly(NIPAAm)-BBDT
In a Schlenk flask 0.162 moles of N-isopropylacrylamide monomer (NIPAAm) were mixed with 200 mL of 1,4-dioxane, 2.8x10$^{-6}$ moles of benzyl benzodithioate (BBDT) CTA (purchased from Sigma-Aldrich and used as received) and 1.4x10$^{-6}$ moles of AIBN using magnetic stirring. The flask was sealed and five cycles of freeze-pump-thaw were carried out to remove oxygen from the reaction solution. Then, Argon gas was bubbled in the solution for 30 minutes to remove the remaining oxygen. After that the flask was immersed in an oil bath at 65 °C for 9 hours (the reaction time is longer because the kinetics of the BBDT-CTA is slower compared with DDMAT-CTA). The reaction was stopped by cooling down the solution; the flask was first opened and then immersed in an ice-water bath followed by immersion in a liquid nitrogen bath.

Synthesis of poly(MPDSAH)-S1
In a Schlenk flask 0.12 moles of monomer [3-(methacryloylamino)propyl] dimethyl(3-sulfopropyl)ammonium hydroxide inner salt (MPDSAH) were mixed with 60 mL of water and HCl 0.5 M was added to reach pH 6. This solution was mixed with 60 ml of 1,4-dioxane, 2.0x10$^{-4}$ moles of AIBN and 5.0x10$^{-4}$ moles of DDMAT-CTA. However the solution was not homogeneous, so 80 ml of DMSO were added to have a homogeneous solution. The flask was sealed and five cycles of freeze-pump-thaw were carried out to remove oxygen from the reaction solution. Then, Argon gas was bubbled in the solution for 30 minutes to remove the remaining oxygen. Then the flask was immersed in an oil bath at 65 °C and after 3.5 hours the reaction was stopped because of precipitation of the polymer. The reaction was stop by cooling down the
solution; the flask was first opened and then immersed in an ice-water bath followed by immersion in a liquid nitrogen bath.

**Synthesis of poly(MPDSAH)-S2**

In a Schlenk flask 0.06 moles of MPDSAH were mixed with 60 mL of water and HCl 0.5 M was added to reach pH 6. This solution was mixed with 60 ml of 1,4-dioxane, 80 mL of DMSO, 1.0x10^{-4} moles of AIBN and 2.5x10^{-4} moles of DDMAT-CTA. The flask was sealed and five cycles of freeze-pump-thaw were carried out to remove oxygen from the reaction solution. Then, Argon gas was bubbled in the solution for 30 minutes to remove the remaining oxygen. Then the flask was immersed in an oil bath at 65 °C and after 24 hours the reaction was stopped because of precipitation of the polymer. The reaction was stop by cooling down the solution; the flask was first opened and then immersed in an ice-water bath followed by immersion in a liquid nitrogen bath. The RAFT agent was used here to obtained low polydispersity. The long reaction time was set with the goal of obtaining a high molecular weight poly(MAPDSP).

**Synthesis of poly(MPDSAH)-S3**

In a Schlenk flask 0.06 moles of MPDSAH were mixed with 60 mL of water and HCl 0.5 M was added to reach pH 6. This solution was mixed with 60 ml of 1,4-dioxane, 80 mL of DMSO and 1.0x10^{-4} moles of AIBN. The flask was sealed and five cycles of freeze-pump-thaw were carried out to remove oxygen from the reaction solution. Then, Argon gas was bubbled in the solution for 30 minutes to remove the remaining oxygen. Then the flask was immersed in an oil bath at 65 °C and after 24 hours the reaction was stopped because of precipitation of the polymer. The reaction was stop by cooling down the solution; the flask was first opened and then immersed in an ice-water bath followed by immersion in a liquid nitrogen bath. The long reaction time was set with the goal of obtaining a high molecular weight poly(MPDSAH).

**Separation of poly(MPDSAH)-S4**

From the purification of the block copolymer poly(NIPAAm_{114-b-MPDSAH_{228}}) using the chromatographic column packed with Sepharose 6B, we separated poly(MPDSAH) homopolymer. According to the retention time in GPC_{aq}, the polymer should have a M_n between 80-100 KDa; however, the M_n was not possible to calculate with more precision because the calibration curve using PEG standards was not appropriate.

**Purification of poly(MPDSAH)-S1, S2 and S3**

After the reaction flask was cooled down, the formed precipitate was separated by filtration in vacuum. The polymer was dried under vacuum and re-dissolved in water to carry out dialysis for one week in a 3500 MWCO membrane (Spectra/Por Biotech) to remove unreacted MPDSAH monomer. The polymer solution was freeze-dried and then GPC_{aq} in aqueous phase was carried out (see Fig. S4). The chromatograms showed high polydispersity. The fact that poly(MPDSAH) precipitates during the reaction makes it difficult to obtain a polymer with low polydispersity. The addition of the RAFT agent and working a low monomer concentration did not help to improve the polydispersity.

**Synthesis of Poly(NIPAAm-b-MPDSAH)-BBDT**

In the case of the synthesis using Poly(NIPAAm)-CTA-2, 0.125 mmol of polymer was mixed with 14.2 mmol of MPDSAH (dissolved in 10 mL of water, pH adjusted to 6) and 0.06 mmol of
AIBN in 60 mL of methanol. The temperature was set at 60 °C. The flask was sealed, five cycles of freeze-pump-thaw were carried out and Argon gas was bubble. The flask was immersed in an oil bath at 65 °C for 20 hours. The reaction was cooled down by using an ice-water bath followed by a liquid nitrogen bath. The same purification method described for Poly(NIPAAm-b-MPDSAH)-DDMAT was followed for Poly(NIPAAm-b-MPDSAH)-BBDT; however, the latter polymer GPC\textsubscript{aq} chromatogram showed impurities of homopolymers.

![Figure S3](image)

**Figure S3.** Effect of temperature on the UV-Vis transmittance when heating a 0.1% w/w polymer solution. A) poly(NIPAAm)-DDMAT (black curve, pH=7.5) and poly(NIPAAm)-BBDT (red curve, pH=6.8) in pure water. B) poly(MPDSAH)-S1 (black curve, pH=6.8), poly(MPDSAH)-S2 (red curve, pH=7.5), poly(MPDSAH)-S3 (blue curve, pH=7.3), poly(MPDSAH)-S4 (magenta curve, pH=7.8).

**Table S1.** Experimental characteristic data for the homopolymers, macro-CTAs and the block copolymer.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Method</th>
<th>M\textsubscript{n} (g/mol)</th>
<th>PD</th>
<th>Elution Time (min)</th>
<th>Monomer Units</th>
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<td>114</td>
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<td>---</td>
<td>23.83</td>
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<tr>
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<td>81</td>
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<tr>
<td></td>
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<td>28,100</td>
<td>---</td>
<td>28.63</td>
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<td>20.97</td>
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<tr>
<td>Poly(MPDSAH)-S2</td>
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<td>&gt;3</td>
<td>16.90 &amp; 18.65</td>
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</tr>
<tr>
<td>Poly(MPDSAH)-S3</td>
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Figure S4. GPC\textsubscript{aq} chromatograms for poly(MPDSAH)-S1 (black thick curve), poly(MPDSAH)-S2 (red curve), poly(MPDSAH)-S3 (blue curve) and poly(MPDSAH)-S4 (black thin curve) with 10 mM Na\textsubscript{2}HPO\textsubscript{4} and 25 mM NaBr solution as eluent and at a rate of 0.5 mL/min.

Figure S5. Effect of temperature on the UV-Vis transmittance of a polymer mixture solution with 0.05% of each. A) poly(NIPAAm)-DDMAT and poly(MPDSAH)-S1 (black curve), poly(NIPAAm)-DDMAT and poly(MPDSAH)-S2 (red curve), poly(NIPAAm)-DDMAT and poly(MPDSAH)-S3 (blue curve). B) poly(NIPAAm)-BBDT and poly(MPDSAH)-S1 (black curve), poly(NIPAAm)-BBDT and poly(MPDSAH)-S2 (red curve), poly(NIPAAm)-BBDT and poly(MPDSAH)-S3 (blue curve).
**Figure S6.** Effect of temperature on the UV-Vis transmittance of a polymer mixture solution of poly(NIPAAm)-DDMAT and poly(MPDSAH)-S4 at different ratios (black curve 3:1, red curve 1:1, blue curve 1:3 respectively) but a total of 0.1% w/w and pH=6.8.

**Figure S7.** Effect of temperature on the UV-Vis transmittance of a polymer mixture solution with poly(NIPAAm)-BBDT and poly(MPDSAH)-S4 at different ratios (black curve 3:1, red curve 1:1, blue curve 1:3 respectively) but a total of 0.1% w/w and pH=6.8.
Figure S8. Effect of temperature on the UV-Vis transmittance of polymer solution. A) a 0.1% solution of poly(NIPAAm)-DDMAT in a 0.025 M solution of NaOH (black curve, pH=11.2) and HCl (red curve, pH=1.8). B) a solution of poly(NIPAAm)-DDMAT and poly(MPDSAH)-S4 0.05%w/w each in a 0.025 M solution of NaOH (black curve, pH=11.7) and HCl (red curve, pH=1.9).
**Figure S9.** Effect of temperature on the UV-Vis transmittance (solid red, heating curve) and the hydrodynamic radius (blue solid circles) of a solution 0.1% w/w in ultra-pure water of the synthesized poly(NIPAAm-b-MPDSAH), using poly(NIPAAm)-BBDT as initial macro-CTA. This block copolymer used is impure and may contain residues of the homopolymers.