Supplementary Material for "Programming Nanoparticle Aggregation Kinetics with Poly(MeO₂MA-co-OEGMA) CoPolymers"

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Section S.1 Synthesis and structural characterization of DS-Poly(MeO₂MA_x-co-OEGMA_y)

Disulfide-functionalized random copolymers of oligo(ethylene glycol) methyl methacrylate (OEGMA) and 2-(2-methoxy-ethoxy) methyl methacrylate (MeO₂MA), named DS-Poly(MEO₂MA_x-*co*-OEGMA_y), were grown from a previously synthesized disulfide functionalized ATRP initiator, 2,2'-dithiobis[1-(2-bromo-2-methylpropionyloxy)ethane] (DTBE) where *x* and *y* represented the molar fractions of MEO₂MA and OEGMA, respectively.^[S1] A description of the synthesis of DS-Poly(MEO₂MA₈₀-*co*-OEGMA₂₀) follows. A 50 ml round-bottomed flask was filled with 156.2 mg (1 mmol) of 2,2'-dipyridyl, 226 mg (0.5 mmol) of DTBE, 9.51 g (20 mmol) of OEGMA, 15.01 g (80 mmol) of MEO₂MA, and 20 ml of ethanol. The mixture was degassed with argon for 30 min and then 72 mg (0.5 mmol) of Cu(I)bromide was added to the flask. The solution was bubbled with Argon for further 10 minutes, carefully sealed with a septum and stirred at 60 °C for 6-8 hours. The reaction was stopped by removing the septum and adding 5 mL of ethanol. The final mixture was dialyzed two times overnight against water and one time against absolute ethanol using Type T2 Dialysis Tube 6000 to 8000 Da MCWO (Fisher Scientific). Ethanol was removed by rotary evaporation, and residual solvent was removed under vacuum.

A schematic of the synthesis together with the structural information of the three copolymers is reported in **Figure S1**.



Figure S1. (A) Synthesis of DS-Poly(MEO₂MA_x-*co*-OEGMA_y) from a disulfide functionalized ATRP initiator; **(B)** Zimm plot obtained using static light scattering meausurements for aqueous dispersion of DS-Poly(MeO₂MA₈₀-co-OEGMA₂₀).

Structural information of the synthesized copolymers was obtained by the combination of static and dynamic light scattering in water dispersion. Relevant parameters obtained from the experiments are reported in **Table S1**.

Table S1. Structural parameters for the three copolymers in water obtained form the combination of static and dynamic light scattering: hydrodynamic radius, R_H , molecular weight, M_W , and degree of polymerization, r.

(x:y)	R_{H} , nm (PDI)	M_W , g mol ⁻¹	r
95:5	3.9 (0.22)	20000	98
90:10	3.3 (0.22)	22800	104
80:20	4.1 (0.12)	28100	112

From dynamic light scattering we analyzed the field correlation functions by using the methods of cumulants and an expansion up to the second order; we found a hydrodynamic radius of 3-4 nm with a polydispersity index of 0.1-0.2. From static measurements, the molecular weight of the polymer was found to be in the range 20kDa $< M_W < 30$ kDa, in agreement to the mass balance dictated by the reaction.

Section S.2 Synthesis and structural characterization of $Au(a)(MeO_2MA_x-co-OEGMA_y)$ NPs

Au@(MEO₂MA-*co*-OEGMA) NPs were synthesized from Au@citrate-stabilized NPs in a ligand exchange process according to the recipe reported by Edwards et al. ^[S2]. A 5mg/mL solution of the disulfide functionalized poly(MEO₂MA_x-*co*-OEGMA_y) in water was prepared. A 50 mL portion of Au@citrate-stabilized NPs previously prepared were placed in a 125 mL Erlenmeyer flask and stirred vigorously. A 1ml portion of DS-Poly(MEO₂MA_x-*co*-OEGMA_y) was added dropwise to the Au@citrate solution, and the mixture was gently stirred overnight at ambient temperature. Free polymer was removed from the Au@(MEO₂MA_x-*co*-OEGMA_y) solution by centrifugation multiple times at high speed [typically $3 \times (60 \text{ min } @ 10000 \text{ RCF})$ with redispersion after each centrifugation in water] until the aqueous solutions removed after centrifugation did not exhibit any thermoresponsive behavior. UV-VIS absorption measurements of the grafted nanoparticles confirm the removal of all the unreacted copolymers after purification (**Figure S2**).



Figure S2. UV-VIS absorption of Au@(MeO₂MA_x-co-OEGMA_y) in water before (dashed line) and after (solid line) centrifugation @10000 RCF; the absorption spectrum of the supernatant is also reported (dash-dotted line).

The dimensions of the gold nanoparticles before and after the grafting with the thermoresponsive copolymers are reported in **Table S1** together with the estimated grafting density. Polymer surface coverage was calculated from the increment (dn/dc) of refractive index *n* with concentration *C*:

$$\sigma_p = \frac{n_p - n_w}{\left(\frac{dn}{dC}\right)} \cdot \frac{N_A \delta}{M_W}$$
(eq. S1)

where δ is the copolymer shell thickness and M_W the molecular weight of the polymer estimated by static light scattering. The refractive index of the polymer was assumed to be $n_p=1.5$ and the refractive index of the medium was $n_w=1.3325$.

Table S2. Average hydrodynamic radius, R_H , at ambient temperature of the gold nanoparticles before and after coupling with the thermoresponsive copolymers, and estimated copolymer grafting density.

(x:y)	R_H , nm	δ, nm	σ_p , nm ⁻²
95:5	23.4	15.8	0.61
90:10	19.8	12.2	0.42
80:20	20.0	12.4	0.34

As a result of the presence of the oligo(ethylene glycol) side groups on the surfaces, Au@(MEO₂MA-*co*-OEGMA) NPs can be dispersed in water and their phase behavior can be tuned by temperature similarly as the free copolymers in solution.

Section S.3 Theoretical description for the aggregation kinetics of thermoresponsive nanoparticles

The rate of aggregation of monomeric nanoparticles into larger agglomerates can be represented as a kinetic process as shown in equation S2: ^[S3]

$$\frac{\partial C_z}{\partial t} = \frac{1}{2} k_{ij} C_i C_j - C_z \sum_{i=1}^{\infty} k_{iz} C_i$$
(eq. S2)

where C_z is the concentration of aggregates containing z-monomers, k_{ij} is the second order aggregation rate constant associated with aggregate formation, C_i , C_j are the concentration of aggregate or monomer where $z > i_i j$, and k_{iz} is the dissociation rate constant of aggregates of size z. For very small times, the aggregation kinetics can be approximated by the reversible association/disagglomeration of doublets, which dominated over other higher order aggregate formation:

$$\frac{dC_2}{dt} = \frac{1}{2}k_{11}C_1^2 - k_{21}C_1C_2$$
(eq. S3)

In case of an irreversible process or negligible dissociation, the increase in concentration of dimers, (C_2) is proportional to the product of the initial rate constant of aggregation k_{11} and the square of the initial concentration of nanoparticle monomer (C_1) , simplifying equation (S3) into:

$$\frac{dC_2}{dt} = \frac{1}{2}k_{11}C_1^2$$
 (eq. S4)

The experimental values of the aggregation rate, k_{11} , for Au@(MEO₂MA_x-*co*-OEGMA_y) NPs are reported in table S3-S7 against salt concentration and temperature.

Table S3: Aggregation rate values, k_{11} (m³ s⁻¹), for Au@(MeO₂MA₉₅-co-OEGMA₅) NPs in suspension.

	T=22.5 °C	T=25.2 °C	T=28.4 °C	T=31.0 °C
C _{NaCl} =40 mM				3.6 x 10 ⁻²⁰
C _{NaCl} =50 mM				4.8 x 10 ⁻²⁰
C _{NaCl} =100 mM				1.9 x 10 ⁻¹⁹
C _{NaCl} =120 mM				6.7 x 10 ⁻¹⁹
C _{NaCl} =140 mM			1.6 x 10 ⁻²⁰	1.1 x 10 ⁻¹⁸
C _{NaCl} =170 mM				1.7 x 10 ⁻¹⁸
C _{NaCl} =190 mM			2.2 x 10 ⁻²⁰	2.1 x 10 ⁻¹⁸
C _{NaCl} =240 mM			5.4 x 10 ⁻²⁰	2.5 x 10 ⁻¹⁸
C _{NaCl} =280 mM			1.0 x 10 ⁻¹⁹	1.8 x 10 ⁻¹⁸
C _{NaCl} =300 mM			3.7 x 10 ⁻¹⁹	
C _{NaCl} =320 mM			2.8 x 10 ⁻¹⁹	
C _{NaCl} =360 mM			7.2 x 10 ⁻¹⁹	
C _{NaCl} =400 mM		2.1 x 10 ⁻²⁰	1.6 x 10 ⁻¹⁸	
C _{NaCl} =440 mM		8.9 x 10 ⁻²⁰	1.3 x 10 ⁻¹⁸	
C _{NaCl} =480 mM			1.6 x 10 ⁻¹⁸	
C _{NaCl} =520 mM		1.5 x 10 ⁻¹⁹	1.8 x 10 ⁻¹⁸	
C _{NaCl} =550 mM		2.6 x 10 ⁻¹⁹		
C _{NaCl} =590 mM	2.9 x 10 ⁻²⁰	4.9 x 10 ⁻¹⁹		
C _{NaCl} =630 mM		8.7 x 10 ⁻¹⁹		
C _{NaCl} =650 mM	6.2 x 10 ⁻²⁰	1.3 x 10 ⁻¹⁸		
C _{NaCl} =700 mM	1.5 x 10 ⁻¹⁹	1.4 x 10 ⁻¹⁸		
C _{NaCl} =750 mM	2.5 x 10 ⁻¹⁹	1.9 x 10 ⁻¹⁸		

C _{NaCl} =800 mM	8.1 x 10 ⁻¹⁹	2.0 x 10 ⁻¹⁸	
C _{NaCl} =830 mM	1.1 x 10 ⁻¹⁸		
C _{NaCl} =840 mM	1.6 x 10 ⁻¹⁸		
C _{NaCl} =1000 mM	1.7 x 10 ⁻¹⁸		
C _{NaCl} =1210 mM	1.9 x 10 ⁻¹⁸		
C _{NaCl} =1390 mM	2.0 x 10 ⁻¹⁸		

Table S4: Aggregation rate values, k_{11} (m³ s⁻¹), for Au@(MeO₂MA₉₀-co-OEGMA₁₀) NPs in suspension.

	T=34.0 °C	T=36.0 °C	T=38.4 °C	T=40.0 °C
C _{NaCl} =230 mM				9.3 x 10 ⁻²¹
C _{NaCl} =280 mM				3.3 x 10 ⁻²⁰
C _{NaCl} =300 mM		2.1 x 10 ⁻²⁰	3.5 x 10 ⁻²⁰	
C _{NaCl} =320 mM				7.4 x 10 ⁻²⁰
C _{NaCl} =360 mM			1.7 x 10 ⁻¹⁹	2.2 x 10 ⁻¹⁹
C _{NaCl} =400 mM		2.9 x 10 ⁻²⁰	3.6 x 10 ⁻¹⁹	3.6 x 10 ⁻¹⁹
C _{NaCl} =420 mM				
C _{NaCl} =440 mM		1.4 x 10 ⁻¹⁹	6.4 x 10 ⁻¹⁹	6.5 x 10 ⁻¹⁹
C _{NaCl} =480 mM			1.1 x 10 ⁻¹⁸	8.4 x 10 ⁻¹⁹
C _{NaCl} =500 mM				9.7 x 10 ⁻¹⁹
C _{NaCl} =520 mM	4.5 x 10 ⁻²⁰	2.2 x 10 ⁻¹⁹	1.4 x 10 ⁻¹⁸	9.7 x 10 ⁻¹⁹
C _{NaCl} =540 mM				1.2 x 10 ⁻¹⁸
C _{NaCl} =560 mM		5.6 x 10 ⁻¹⁹		1.6 x 10 ⁻¹⁸
C _{NaCl} =600 mM	3.5 x 10 ⁻¹⁹	6.8 x 10 ⁻¹⁹	1.6 x 10 ⁻¹⁸	1.6 x 10 ⁻¹⁸
C _{NaCl} =630 mM		1.1 x 10 ⁻¹⁸	1.8 x 10 ⁻¹⁸	1.6 x 10 ⁻¹⁸
C _{NaCl} =650 mM				
C _{NaCl} =670 mM		1.3 x 10 ⁻¹⁸		
C _{NaCl} =700 mM	3.6 x 10 ⁻¹⁹	1.7 x 10 ⁻¹⁸		
C _{NaCl} =730 mM	7.7 x 10 ⁻¹⁹			
C _{NaCl} =800 mM	8.6 x 10 ⁻¹⁹	1.8 x 10 ⁻¹⁸		
C _{NaCl} =870 mM				
C _{NaCl} =890 mM	9.2 x 10 ⁻¹⁹	2.0 x 10 ⁻¹⁸		
C _{NaCl} =950 mM	1.3 x 10 ⁻¹⁸			

C _{NaCl} =1010 mM	1.7 x 10 ⁻¹⁸	2.0 x 10 ⁻¹⁸	
C _{NaCl} =1090 mM	1.3 x 10 ⁻¹⁸		
C _{NaCl} =1190 mM	2.2 x 10 ⁻¹⁸		

Table S5: Aggregation rate values, k_{11} (m³ s⁻¹), for Au@(MeO₂MA₉₀-co-OEGMA₁₀) NPs in suspension.

	T=22.5 °C	T=25.2 °C	T=28.0 °C	T=31.0 °C
C _{NaCl} =600 mM				3.2 x 10 ⁻²⁰
C _{NaCl} =700 mM				3.6 x 10 ⁻²⁰
C _{NaCl} =730 mM				1.1 x 10 ⁻¹⁹
C _{NaCl} =800 mM			2.5 x 10 ⁻²⁰	1.5 x 10 ⁻¹⁹
C _{NaCl} =860 mM				2.1 x 10 ⁻¹⁹
C _{NaCl} =890 mM			2.3 x 10 ⁻²⁰	5.0 x 10 ⁻¹⁹
C _{NaCl} =1010 mM		6.2 x 10 ⁻²¹	1.4 x 10 ⁻¹⁹	7.2 x 10 ⁻¹⁹
C _{NaCl} =1090 mM		6.2 x 10 ⁻²⁰	2.0 x 10 ⁻¹⁹	1.2 x 10 ⁻¹⁸
C _{NaCl} =1190 mM		2.6 x 10 ⁻¹⁹	7.6 x 10 ⁻¹⁹	1.4 x 10 ⁻¹⁸
C _{NaCl} =1290 mM	3.7 x 10 ⁻²⁰	4.3 x 10 ⁻¹⁹	9.7 x 10 ⁻¹⁹	1.8 x 10 ⁻¹⁸
C _{NaCl} =1400 mM	8.6 x 10 ⁻²⁰	4.9 x 10 ⁻¹⁹	1.3 x 10 ⁻¹⁸	1.9 x 10 ⁻¹⁸
C _{NaCl} =1500 mM	2.1 x 10 ⁻¹⁹	8.1 x 10 ⁻¹⁹	1.5 x 10 ⁻¹⁸	
C _{NaCl} =1590 mM	3.3 x 10 ⁻¹⁹	9.5 x 10 ⁻¹⁹	1.4 x 10 ⁻¹⁸	
C _{NaCl} =1650 mM		1.1 x 10 ⁻¹⁸		
C _{NaCl} =1700 mM	9.2 x 10 ⁻¹⁹	1.2 x 10 ⁻¹⁸	1.8 x 10 ⁻¹⁸	
C _{NaCl} =1800 mM		1.4 x 10 ⁻¹⁸		
C _{NaCl} =1850 mM	1.8 x 10 ⁻¹⁸			
C _{NaCl} =1900 mM	$1.7 \ge 10^{-18}$	1.8×10^{-18}		
C _{NaCl} =1950 mM	1.8 x 10 ⁻¹⁸			
C _{NaCl} =2000 mM	1.5 x 10 ⁻¹⁸			

	T=40.2 °C	T=43.1 °C	T=46.0 °C	T=49.0 °C
C _{NaCl} =140 mM				4.6 x 10 ⁻²¹
C _{NaCl} =190 mM			2.6 x 10 ⁻²⁰	2.7 x 10 ⁻²⁰
C _{NaCl} =230 mM			1.8 x 10 ⁻¹⁹	9.2 x 10 ⁻²⁰
C _{NaCl} =280 mM			7.5 x 10 ⁻¹⁹	6.1 x 10 ⁻¹⁹
C _{NaCl} =300 mM			9.4 x 10 ⁻¹⁹	8.8 x 10 ⁻¹⁹
C _{NaCl} =320 mM			1.1 x 10 ⁻¹⁸	9.7 x 10 ⁻¹⁹
C _{NaCl} =340 mM			2.1 x 10 ⁻¹⁸	1.5 x 10 ⁻¹⁸
C _{NaCl} =360 mM			1.7 x 10 ⁻¹⁸	1.7 x 10 ⁻¹⁸
C _{NaCl} =400 mM		2.8 x 10 ⁻²⁰	1.6 x 10 ⁻¹⁸	1.8 x 10 ⁻¹⁸
C _{NaCl} =440 mM		2.8 x 10 ⁻²⁰	1.9 x 10 ⁻¹⁸	2.2 x 10 ⁻¹⁸
C _{NaCl} =480 mM		3.5 x 10 ⁻²⁰		
C _{NaCl} =500 mM	4.6 x 10 ⁻²¹			
C _{NaCl} =520 mM		4.3 x 10 ⁻¹⁹		
C _{NaCl} =540 mM				
C _{NaCl} =560 mM	2.1 x 10 ⁻²⁰	7.0 x 10 ⁻¹⁹		
C _{NaCl} =590 mM	1.2 x 10 ⁻¹⁹	1.2 x 10 ⁻¹⁸	1.6 x 10 ⁻¹⁸	
C _{NaCl} =630 mM		1.4 x 10 ⁻¹⁸	1.8 x 10 ⁻¹⁸	
C _{NaCl} =650 mM	2.9 x 10 ⁻¹⁹	1.7 x 10 ⁻¹⁸		
C _{NaCl} =670 mM	9.1 x 10 ⁻¹⁹	1.5 x 10 ⁻¹⁸		
C _{NaCl} =690 mM	1.1 x 10 ⁻¹⁸	1.7 x 10 ⁻¹⁸		
C _{NaCl} =750 mM	1.7 x 10 ⁻¹⁸	2.0×10^{-18}		
C _{NaCl} =800 mM	2.1 x 10 ⁻¹⁸			
C _{NaCl} =840 mM	2.3×10^{-18}			

Table S6: Aggregation rate values, k_{11} (m³ s⁻¹), for Au@(MeO₂MA₈₀-co-OEGMA₂₀) NPs in suspension.

	T=22.5 °C	T=27.0 °C	T=31.2 °C	T=36.2 °C
C _{NaCl} =800 mM				1.8 x 10 ⁻²⁰
C _{NaCl} =860 mM				5.8 x 10 ⁻²⁰
C _{NaCl} =900 mM				1.7 x 10 ⁻¹⁹
C _{NaCl} =950 mM				4.2 x 10 ⁻¹⁹
C _{NaCl} =1000 mM				9.6 x 10 ⁻¹⁹
C _{NaCl} =1060 mM				1.7 x 10 ⁻¹⁸
C _{NaCl} =1110 mM				2.1 x 10 ⁻¹⁸
C _{NaCl} =1150 mM				1.9 x 10 ⁻¹⁸
C _{NaCl} =1200 mM			6.8 x 10 ⁻²¹	2.5 x 10 ⁻¹⁸
C _{NaCl} =1300 mM			1.1 x 10 ⁻¹⁹	
C _{NaCl} =1350 mM			3.4 x 10 ⁻¹⁹	
C _{NaCl} =1400 mM			6.8 x 10 ⁻¹⁹	
C _{NaCl} =1450 mM			1.4 x 10 ⁻¹⁸	
C _{NaCl} =1500 mM			1.5 x 10 ⁻¹⁸	
C _{NaCl} =1550 mM			2.0×10^{-18}	
C _{NaCl} =1570 mM			1.9 x 10 ⁻¹⁸	
C _{NaCl} =1650 mM		2.3 x 10 ⁻²⁰		
C _{NaCl} =1710 mM		1.2 x 10 ⁻¹⁹		
C _{NaCl} =1750 mM		3.7 x 10 ⁻¹⁹		
C _{NaCl} =1800 mM		4.6 x 10 ⁻¹⁹		
C _{NaCl} =1860 mM		$1.0 \ge 10^{-18}$		
C _{NaCl} =1900 mM		1.1 x 10 ⁻¹⁸		
C _{NaCl} =1950 mM		1.4 x 10 ⁻¹⁸		
C _{NaCl} =1990 mM	5.9 x 10 ⁻²⁰	2.5 x 10 ⁻¹⁸		
C _{NaCl} =2050 mM		2.9 x 10 ⁻¹⁸		
C _{NaCl} =2110 mM	1.5 x 10 ⁻²⁰	2.5 x 10 ⁻¹⁸		
C _{NaCl} =2200 mM	1.3 x 10 ⁻¹⁹			
C _{NaCl} =2300 mM	4.2 x 10 ⁻¹⁹			
C _{NaCl} =2320 mM	1.7 x 10 ⁻¹⁸			
C _{NaCl} =2350 mM	1.6 x 10 ⁻¹⁸			

Table S7: Aggregation rate values, k_{11} (m³ s⁻¹), for Au@(MeO₂MA₈₀-co-OEGMA₂₀) NPs in suspension.

C _{NaCl} =2390 mM	2.1 x 10 ⁻¹⁸		
C _{NaCl} =2430 mM	1.7 x 10 ⁻¹⁸		

Section S.4 Reversible association of thermoresponsive nanoparticles

The stability of Au@(MeO₂MA_x-co-OEGMA_y) NPs was studied by time resolved dynamic light scattering (tr-DLS) over a broad range of temperatures. As well as ionic strength, solution temperature is responsible for a change of the physical chemistry of the copolymer layer. Independent of the composition, a continuous decrease in the hydrodynamic radius, R_H , was observed upon heating or adding salt in the suspension. (see Figure S3).



Figure S3. Hydrodynamic radius of Au@(MeO₂MA_x-co-OEGMA_y) in pure water as a function of **(A)** salt and **(B)** temperature: (\bigcirc) Au@(MEO₂MA₉₅-*co*-OEGMA₅); (\square) Au@(MEO₂MA₉₀-*co*-OEGMA₁₀); (\triangle) Au@(MEO₂MA₈₀-*co*-OEGMA₂₀).

This behavior is ascribed to the shrinkage of the thermosensitive shell induced by dehydration of the swollen copolymer layer. As reported by other authors^[S4-S8] such a dehydration process leads to a coil-to-globule transition where the formation of hydrogen bonds between the ether oxygen of the ethylene glycol and water hydrogens is counterbalanced by the hydrophobicity of the apolar backbone. If T is increased over a critical solution temperature, T_C , the NPs become even more attractive; this is due to the hydrophobic effect between the copolymer layers for which water has become a poor solvent under these conditions. As a consequence of this effect aggregation occurs which is completely reversible upon cooling.

To quantify the T-dependent interaction energy between our thermosensitive nanoparticles we follow the treatment of Zaccone et al.^[S9], which consider the kinetics of reversible association between two particles to form a dimer. **Figure S4** shows a picture of the mechanism of

interaction between two Au@(MeO₂MA_x-co-OEGMA_y) NPs. In this scheme k_{11} and k_{21} denotes the association and dissociation rate constants, respectively.



Figure S4. Schematic of the reversible association of thermoresponsive NPs and the effective square well interaction, as a function of the surface separation, h.

To assess information on the reversible aggregation kinetics we monitored the evolution of the hydrodynamic radius as a function of time. Representative profiles for $Au@(MeO_2MA_{90}-co-OEGMA_{10})$ NPs at $C_{NaCl} = 0.45$ M are reported in **Figure S5a** in response to different temperatures.



Figure S5. **(A)** Hydrodynamic radius of Au@(MeO₂MA₉₀-co-OEGMA₁₀) NPs as a function of time: T = 34 °C (\bigcirc); T = 36 °C (\square); T = 38 °C (\triangle); T = 40 °C (\bigtriangledown). **(B)** Dissociation rate, k_{21} , as a function of temperature for Au@(MeO₂MA₉₅-co-OEGMA₅) NPs at different ionic strengths: C_{NaCl} = 0.45 M (\bigcirc); C_{NaCl} = 0.60 M (\square); C_{NaCl} = 0.80 M (\triangle); C_{NaCl} = 1.00 M (\bigtriangledown); C_{NaCl} = 1.20 M (\diamondsuit).

The time evolution of the R_H is linear in the early stage of association and, as expected, the growth rate, dR_H/dt , of the nanoparticle aggregates increases with increasing temperature. The data of figure S5a can be regressed to determine the effective association constant, K_{eff} , using the following equation:

$$\frac{1}{R_{H,1}}\frac{dR_{H}}{dt} = OC_{NPs}K_{eff} \approx OC_{NPs}k_{11}\left(\frac{4k_{11}C_{NPs}}{k_{21} + 4k_{11}C_{NPs}}\right)^{2}$$
(eq.S5)

where $R_{H,I}$ is the initial particle radius, and O is the optical factor depending on the scattering vector and on the ratio between the hydrodynamic radius of the doublet and the monomer, which is approximately 1.4.^[S3] In case of no dissociation, k_{2I} =0, equation S5 correctly recovers the well-known result for the irreversible aggregation kinetics.^[S3] Considering that for attractive colloids the association constant is given by the Smoluchowski diffusion limited rate, $k_{11} = (4/3)k_bT/\eta$, this equation allows us to extract the microscopic dissociation rate, k_{2I} from K_{eff} . Representative T-dependent profiles of the k_{2I} values are shown in **Figure S5b** for Au@(MEO₂MA_x-co-OEGMA)_y NPs at different NaCl concentrations. In all cases we found that k_{2I} decreases with increasing temperature (stability decreases), while increasing the ionic strength of the solution results in a shift of the dissociation curves to lower temperatures.

The knowledge of k_{21} also allows us to estimate the energy scales for the attraction between the nanoparticles. Considering the dissociation constant as the rate at which one particle escapes from the attractive potential well that binds it to the second particle, the depth of the square well potential, V_{min} , can be obtained:^[S10]

$$k_{21} = \frac{D}{\delta^2} e^{-V_{min}/k_b T}$$
 (eq. S6)

Here $D = k_b T / 6\pi \eta R_{H,1}$ is the diffusion constant and $\delta = 10 \text{ nm}^{[S11]}$ is the width of the square-well potential. A picture of the binding energy for both swollen and collapsed nanoparticles is reported in Figure S3.

Figure S6a shows the T-dependent binding energy normalized by the saturation value, V_{min}^{∞} , for Au@(MEO₂MA₉₀-co-OEGMA)₁₀ NPs for a family of NaCl concentrations.



Figure S6. **(A)** Experimental T dependence of the binding energy for Au@(MeO₂MA₉₀-co-OEGMA₁₀) NPs at different ionic strength: $C_{NaCl} = 0.45$ M (\bigcirc); $C_{NaCl} = 0.60$ M (\square); $C_{NaCl} = 0.80$ M (\triangle); $C_{NaCl} = 1.00$ M (\bigtriangledown); $C_{NaCl} = 1.20$ M (\diamondsuit). The dash-dotted lines are the fitting to the data by using equation S6. **(B)** Critical aggregation temperature T_C , and entropy ΔS , of transition for Au@(MeO₂MA₉₀-co-OEGMA₁₀) NPs as a function of salt.

In all cases V_{min}/V_{min}^{∞} increases sharply from zero to unity in a narrow T interval.

The observed sharp behavior of the thermoresponsive nanoparticles is associated to the transition from the hydrophilic to the hydrophobic state with increasing T.

Combining the statistical mechanics of this first order transition with the reversible kinetic model, the energetics of the transition between swollen and collapsed nanoparticles can be assessed:

$$\frac{V_{min}}{V_{min}^{\infty}} = \left(\frac{1}{1+e^{-\frac{(T_c-T)\Delta S}{k_b T}}}\right)^2; \quad \Delta H = -T_c \Delta S$$
(eq. S7)

In this equation T_C is the critical aggregation temperature (or LCST) and ΔS is the entropy of the hydrophilic to hydrophobic transition. Details on the derivation of equation S7 are reported in the work of Zaccone et al.^[S9]. Results of the fitting to the data of Figure S6a are reported in **Figure S6b**.

While the entropy of the transition is nearly independent from salt, ΔS =-400 k_b, the critical temperature linearly decreases with increasing C_{NaCl} , i.e. the stability of the nanoparticles decreases with increasing the ionic strength.

REFERENCES

- S1. E.W. Edwards, M. Chanana, D. Wang, H. Moehwald, Angewandte Chemie-International Edition, 2008, 47, 320.
- S2. E.W. Edwards, M. Chanana, D. Wang, *Journal of Physical Chemistry C*, 2008, 112, 15207.
- S3. H. Holthoff, S.U. Egelhaaf, M. Borkovec, P. Schurtenberger, H. Sticher, *Langmuir*, 1996, 12, 5541.
- **S4.** J.-H Lutz, *Advanced Materials*, 2011, **23**, 2237.
- S5. M.I. Gibson, D. Paripovic, H.-A. Klok, Advanced Materials, 2010, 22, 4721.
- S6. J. Israelachvili, *Proceedings of the National Academy of Sciences*, 1997, 94, 8378.
- 87. R. Begum, H. Matsuura, *Journal of the Chemical Society, Faraday Transactions*, 1997, 93, 3839.
- **S8.** K. Tasaki, *Journal of the American Chemical Society*, 1996, **118**, 8459.
- **S9.** A. Zaccone, J.J. Crassous, B. Béri, M. Ballauff, *Physical Review Letters*, 2011, **107**, 168303.
- **S10.** P.A. Smith, G. Petekidis, S.U. Egelhaaf, W.C.K. Poon, *Physical Review E*, 2007, **76**, 041402.
- **S11.** J. Israelachvili, *Nature*, 1982, **300**, 341.