Supporting Information for

Multicompartment Core/Shell Microgels

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Experimental Section

Materials. All chemicals were purchased from Aldrich unless otherwise noted. *N*-isopropylacrylamide (NIPAm, TCI) and *N*-isopropylmethacrylamide (NIPMAm) were recrystallized from hexane (J.T. Baker) before use. *N,N*'-methylenebis(acrylamide) (BIS), *N,N*'-(1,2-dihydroxyethylene)bisacrylamide (DHEA), acrylic acid (AAc), ammonium persulfate (APS), and sodium periodate ($NaIO_4$) were used as received. The 4-acrylamidofluorescein (AFA) was synthesized previously in our group via the reaction of 4-aminofluorescein with acryloyl chloride, as described in previous work.[1] The water used in all experiments was distilled and then purified using a Barnstead E-Pure system operating at a resistance of 18 MΩ. A 0.2 μm filter was incorporated into this system to remove particulate matter.

Aqueous buffer preparation

Aqueous buffers were prepared using recipes from buffer calculator developed by R. Beynon at the university of Livepool. The pH values were measured by a pH meter (pH 430, Corning Corp.) with an Accumet probe (Cole-Palmer). The ionic strength was controlled by adding the appropriate amount of NaCl based on the buffer calculation. Here, all the buffers had an ionic strength of 10 mM. The pH 3 buffer is formate buffer, while the pH 6.5 buffer is 2-(*N*-morpholino)ethanesulfonic acid (MES) buffer.

Microgel synthesis.

PNIPMAm core synthesis. pNIPMAm microgels were prepared by free-radical precipitation polymerization, using 140 mM total monomer concentration and a molar composition of 98% NIPMAm and 2% BIS. Polymerization was carried out in a three-neck, 250 mL round-bottom flask to which 100 mL of a filtered, aqueous solution of all monomers and 2 mM SDS was added. This solution was heated to ~ 65 ºC while being purged with N_2 gas and stirred vigorously for ~ 1 h. Then the reaction was immediately initiated by injection of an APS aqueous solution (to make a final APS concentration of 4 mM). The solution immediately turned turbid, indicating successful initiation. This solution was allowed to heat and stir for an additional 7 h while being purged with N_2 gas. The microgels were purified several times by centrifugation and resuspension in deionized water to remove unreacted monomer, oligomers and surfactant. The purified microgel solution was lyophilized prior to storage.

DHEA cross-linked pNIPMAm shell synthesis (CS microgel). The lyophilized pNIPMAm microgel powder was resuspended in deionized water to a concentration of 10 mg/mL. Here, the pNIPMAm microgels were used as seed particles, upon which a DHEA cross-linked shell was added. A solution of pNIPMAm core microgels (4 mL) and SDS (2 mg) in deionized water (10 mL) was heated to 65 ºC under a gentle stream of N_2. Separately, NIPMAm (192 mg), DHEA (33.6 mg) and AFA (1 mg) were dissolved in water (10 mL). This solution was purged with N_2 at room temperature and was then slowly added to the heated core solution. After the temperature remained stable at 65 ºC, an aqueous solution of APS (6 mg in 2 mL water) was added to initiate the polymerization. The reaction was allowed to proceed for 6 h. The microgels were purified several times by centrifugation and resuspension in deionized water.

BIS cross-linked pNIPAm-co-AAc shell synthesis (CDS microgel). This procedure is similar to that of CS microgel synthesis. A solution of CS microgels (7 mL) and SDS (2 mg) in deionized water (9 mL) was heated to 65 ºC, followed by the slow addition of 8 mL of aqueous monomer solution containing NIPAm (190 mg), AAc (14 mg) and BIS (6 mg). After the temperature remained stable at 65 ºC, APS aqueous solution (6 mg in 2 mL water) was added to initiate the polymerization. The reaction was allowed to proceed for 6 h. The microgels were then purified several times by centrifugation and resuspension in deionized water.

Microgel shell degradation. For both CS and CDS microgels, degradation was carried out by addition of excess $NaIO_4$, resulting in CS-D and CDS-D microgels, respectively. The reactions were carried out at room temperature overnight. Shell-degraded microgels were purified by repeated centrifugation and resuspension.

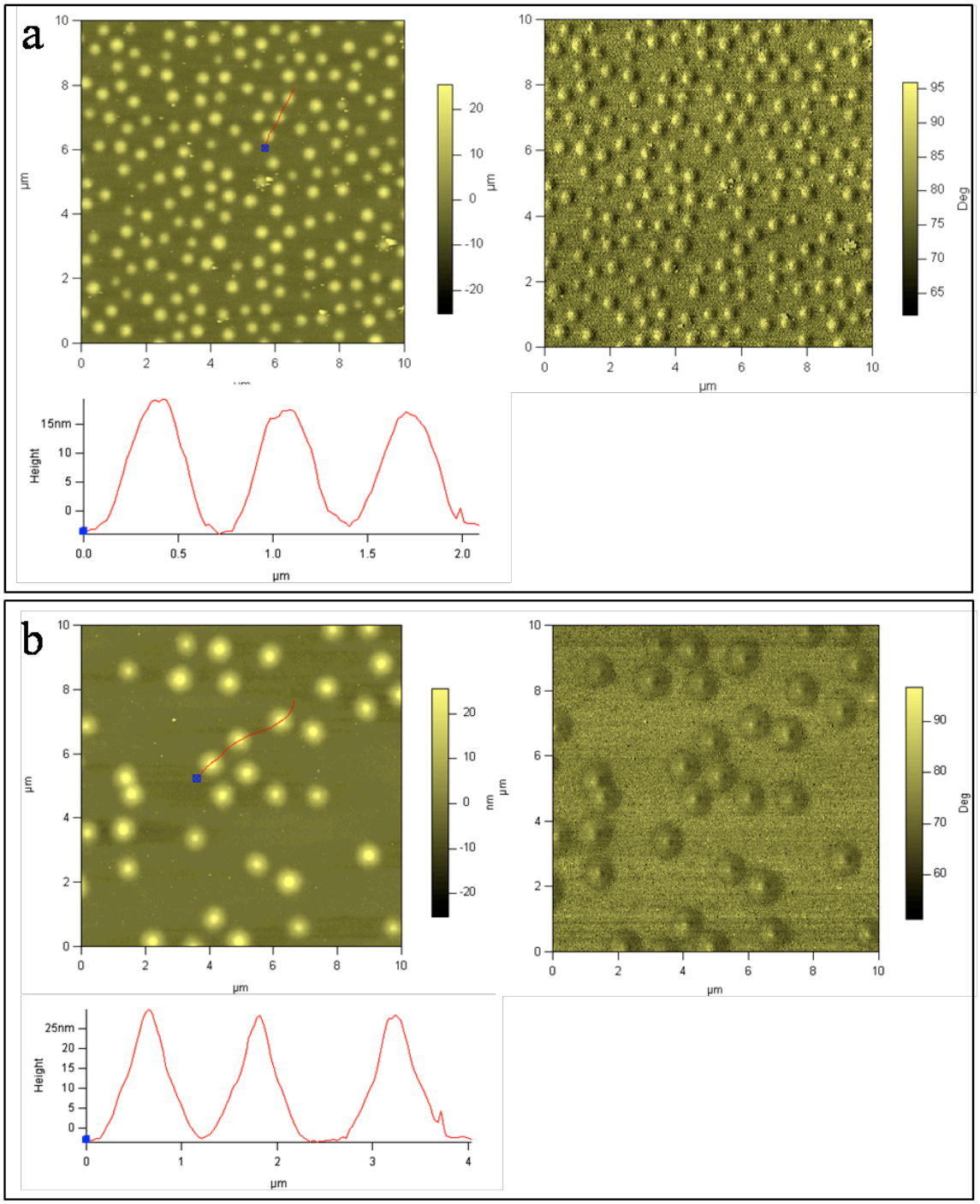
Characterization.

Atomic Force Microscopy (AFM). Glass coverslips (22 mm × 22 mm) were placed in a ceramic holder and cleaned using a sequential solvent sonication method. The following solvent sequence was employed using a Bransonic 2510 Ultrasonicator: 30 min in dilute soapy (Alconox) water, 15 min in deionized water, 15 min in acetone, 15 min in isopropyl alcohol, and 15 min in absolute ethanol. Afterward, the glass was incubated in a 1 v/v% solution of 3-aminopropyltrimethoxysilane (APTMS) in absolute ethanol (200 proof) for 2 h under gentle agitation. The functionalized glass was then rinsed with a 70% aqueous ethanol solution and deionized water, and then dried under a gentle stream of N_2.

The amine-functionalized glass was then dipped into a dilute microgel aqueous solution for ~2 h. The glass was gently rinsed with deionized water and dried under a gentle stream of N_2. Microgels were imaged using an Asylum Research MFP-3D AFM Instrument (Santa Barbara, CA). Imaging was performed and processed using the MFP-3D software under the IgorPro (WaveMetrics Inc., Lake Oswego, OR) environment. Non-contact mode, aluminum-coated silicon nitride cantilevers were purchased from NanoWorld (force constant = 42 N/m, resonance frequency = 320 kHz). All images were taken in air under ambient conditions.

Photon correlation spectroscopy (PCS). Microgel sizes were measured by PCS (Protein Solutions, Inc.) with a programmable temperature controller. Prior to taking measurements, the microgel solutions were allowed to thermally equilibrate at each temperature for 25 min. All correlogram analyses were performed with software supplied by the manufacturer (Dynamic v.5.25.44, Protein Solutions, Inc.). The data presented are the averaged values of 30 measurements, with a 10 s integration time for each measurement.

Steady-state fluorescence. Fluorescence spectra were recorded with a steady-state fluorescence spectrophotometer (Photon Technology International), equipped with a Model 814 PMT photon-counting detector. Fluorescein spectra were measured for the purified microgels at ambient temperature, with an excitation wavelength of 493 nm.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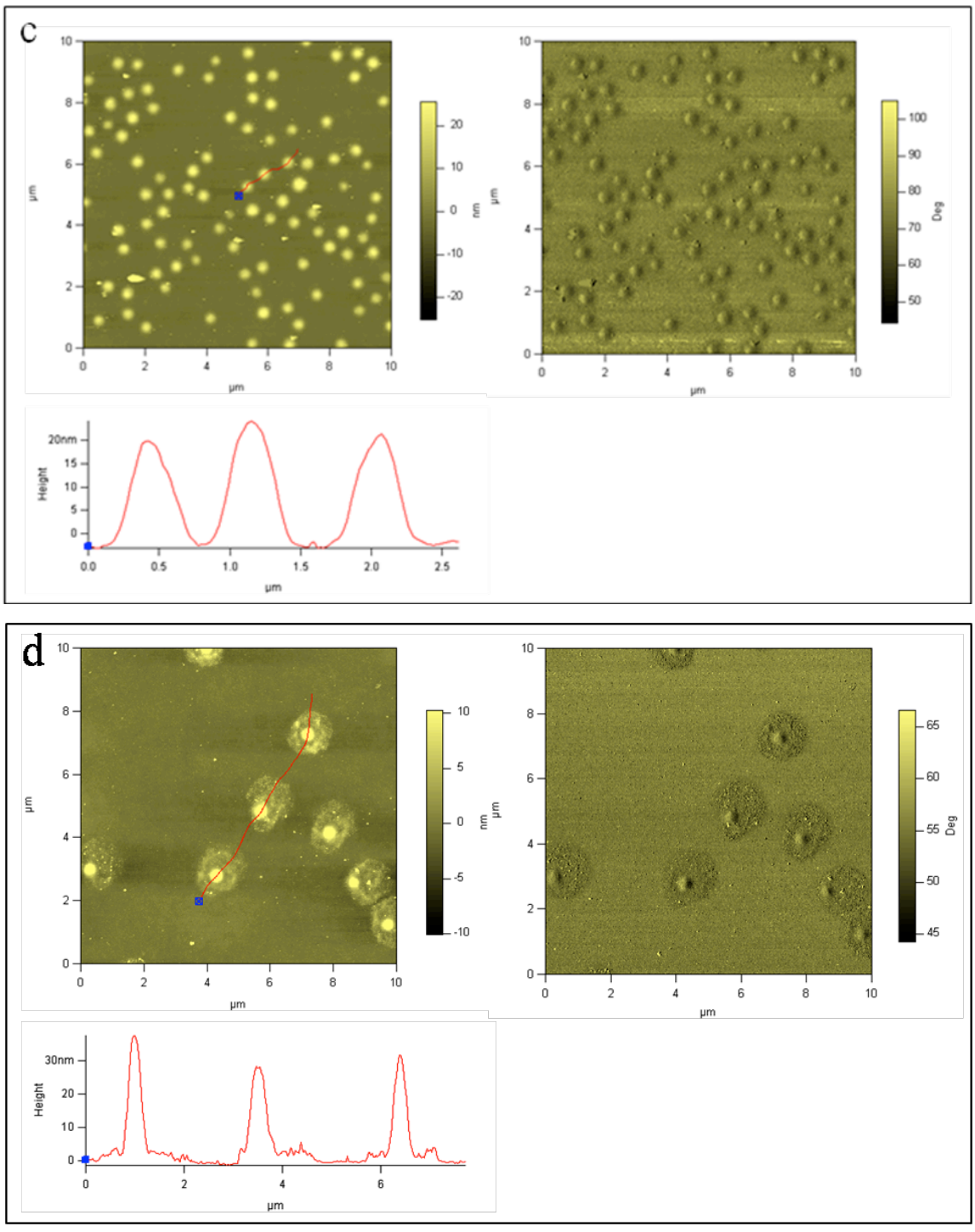

Figure S1. AFM height images (left), phase images (right), and line profiles of (a) Core, (b) CS, (c) CS-D, and (d) CDS-D microgels adsorbed and dried on amine-functionalized glass slides. For (a-c) the microgels were absorbed from deionized water, whereas (d) was absorbed from a pH 6.5 MES buffer. The images in panel (c) illustrate the complete removal of the DHEA-cross-linked shell. Panel (d) illustrates the effect of charge shielding on the mobility of the core within the shell component.

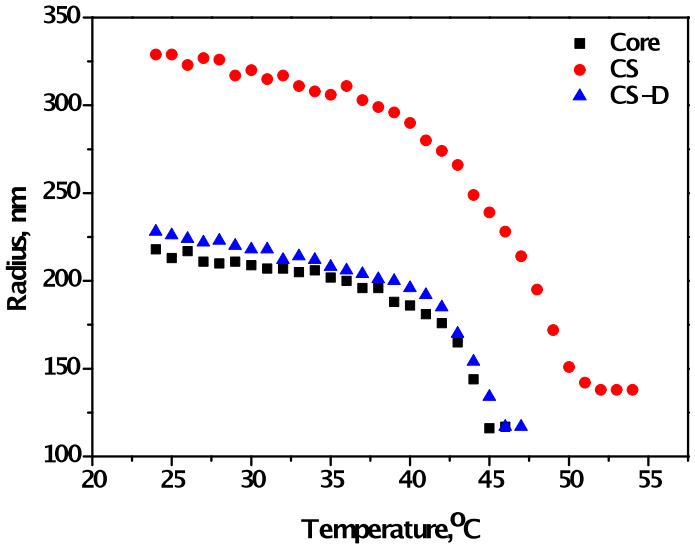

Figure S2. The variation in hydrodynamic radius of Core, CS and CS-D microgels as a function of temperature in pH 3 formate buffer (I = 10 mM).

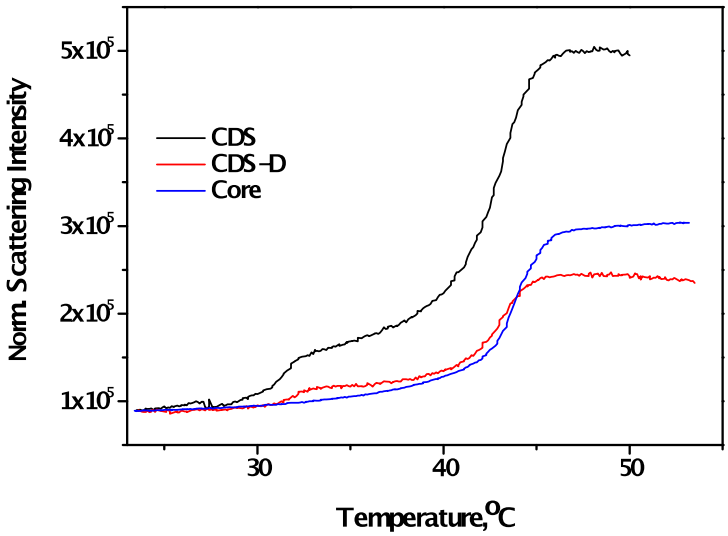

Figure S3. Light scattering intensity as a function of temperature in pH 3 media (ionic strength 10 mM).

(1) Serpe, M. J.; Jones, C. D.; Lyon, L. A. *Langmuir* **2003**, 19,8759-8764.