Microgels

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Interplay between Hydrogen Bonding and Macromolecular Architecture Leading to Unusual Phase Behavior in Thermosensitive Microgels**

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Generally, folding processes of proteins are caused by intra- and interchain hydrogen bonding, as well as hydrophobic and electrostatic interactions, and lead to rather complex bioactive structures. Some synthetic polymers can display macromolecular structures similar to proteins and thus may serve as simpler, though appropriate, model systems to study particular features of folding processes.[1]

Poly-*N*-isopropylacrylamide (PNIPAM) undergoes a reversible transition at 32 °C attributed to the formation of intra- and intermolecular hydrogen bonds. The coil-to-globule transition of linear PNIPAM has been investigated by calorimetry,[2] fluorescence spectroscopy,[3] light scattering,[4] and infrared spectroscopy.[5] Computer simulations show that the folding process is strongly influenced by the polymer structure.[6] The architecture of a synthetic polymer system can be modified by chemical cross-linking, copolymerization, or the formation of core–shell architectures. The latter leads to tunable phase transition temperatures and to variable inter- and intramolecular interactions between the different compartments.

Different core–shell microgel systems were reported recently by separate research groups. In particular, core–shell systems with a thermosensitive core and a stimuli-responsive shell show unique properties.[7] The coil-to-globule phase transition of thermosensitive polymers is attributed to a delicate balance between hydrophobic interaction and hydrogen bonding. A core–shell system is composed of different regions with specific interactions; on the one hand, the core and shell with their individual thermoresponsive hydrophobic interactions and on the other hand, the core/shell interface where the core and shell materials are directly connected, which leads to a mutual influence of core and shell swelling.[8]

Recently, we reported thermosensitive cross-linked copolymer microgels consisting of *N*-isopropylacrylamide (NIPAM) and *N*,*N*-diethylacrylamide (DEAAM) that reveal an unusual depression of the phase transition temperature depending on the composition.[9] The volume phase transition temperature (VPTT) has a minimum for the 1:1 copolymer, that is, the transition temperature is lower than that of the corresponding homopolymer particles. This unusual, synergistic behavior could be caused by strong hydrogen bonding between the mono- and disubstituted acrylamide repeating units in the copolymer microgel.

In this work we endeavored to investigate the hydrogen-bonding pattern of microgels consisting of NIPAM and DEAAM by Fourier-transform infrared (FTIR) spectroscopy, which has proved to be a useful tool to probe intra- and intermolecular hydrogen bonding.[10] The copolymer and core–shell microgels depicted in Figure 1 were investigated. We will show that different hydrogen bonds are formed in microgels containing mono- and disubstituted acrylamides and that the hydrogen-bonding pattern depends on the microgel morphology. As a consequence, copolymers, in contrast to core–shell systems, display synergistic effects leading to a distinct VPTT depression. To the best of our knowledge, the influence of the microgel architecture on its hydrogen-bonding pattern has not been reported before.

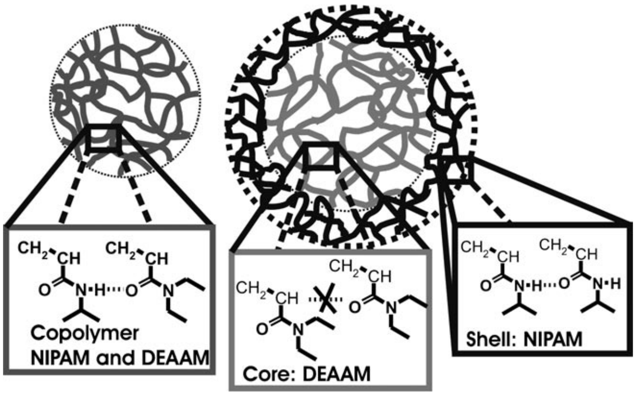

Figure 1. The different microgel types, copolymer (left) versus core–shell (right), and the intramolecular hydrogen bonds. The third system (PNIPAM core and poly(*N*,*N*-diethylacrylamide) (PDEAAM) shell) is not shown.

FTIR spectroscopic results on the interplay between the microgel morphology and intra- and intermolecular hydrogen-bonding pattern are presented for 1) the copolymer

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system PD(55/45) (the first number denotes the mol percent of DEAAM and the second of NIPAM in the microgel, as determined by NMR spectroscopy; PD = PDEAAM) and two core–shell systems, 2) PD/PN-CS(80/20) (the first number denotes the mol percent of the core and the second of the shell; PN = PNIPAM, CS = core–shell) with a PDEAAM core and a PNIPAM shell, and 3) the inverse core–shell microgel PN/PD-CS(25/75), with a PNIPAM core and a PDEAAM shell. Systems 1 and 2 are depicted schematically in Figure 1.

The transition temperatures and compositions of the microgel systems studied are summarized in Table 1. The synthesis of the copolymer and core–shell microgel systems was carried out by known procedures.[7b,9] The VPTT of the microgels was determined by light scattering. The core–shell microgels do not show a depression of the VPTT, in contrast to the copolymer microgel.

Table 1: Composition and volume phase transition temperature (VPTT) of the different microgels.

Sample	Monomer composition DEAAM/NIPAM [mol%]	VPTT [°C]
PNIPAM	0/100	32
PD(55/45)	55/45	20
PN/PD-CS(25/75)	75/25	26
PD/PN-CS(80/20)	80/20	27
PDEAAM	100/0	26

FTIR measurements were carried out over a temperature range of 10 to 50 °C with a temperature increment of 2 K and D_2O as solvent. The major advantage of using D_2O is a shift in the deformation band of water, which prevents the band from overlapping with the amide I′ band and facilitates the analysis of the hydration state of the amide C=O groups.[10] The amide I′ region consists mainly of the C=O stretching vibration with a minor contribution of N–H stretching. As the amide I′ region is very sensitive to hydrogen bonding, we focus on this band.[10,11]

The copolymer microgel PD(55/45) consists of DEAAM and NIPAM in a monomer ratio of nearly 1:1. PNIPAM consists of hydrogen-donor (–NH) and hydrogen-acceptor (C=O) functionalities, contrary to PDEAAM which provides only hydrogen-acceptor functionalities. The peak at 1597 cm^{-1} in Figure 2 is related to intermolecular hydrogen bonds (C=O···D-O-D) with the solvent D_2O and decreases with increasing temperature. This peak is mainly caused by strongly hydrated PNIPAM monomers (for the FTIR spectra of PDEAAM and PNIPAM, see the Supporting Information).[4,12] Intramolecular hydrogen bonds (C=O···D-N-) within the polymer can be assigned to the peak at about 1643 cm^{-1}, which increases at higher temperatures. The middle peak at 1625 cm^{-1}, which can be ascribed to C=O groups in a more hydrophobic (less hydrated) environment, shows a slight decrease at the phase transition only.[11,13] With increasing temperature, the intensity of the first peak (at 1597 cm^{-1}) decreases strongly and the second peak (at 1625 cm^{-1}) slightly, which indicates dehydration; that is, the local environment of the C=O groups becomes more hydrophobic in the collapsed state. In addition, the number and strength of intramolecular hydrogen bonds increase at the expense of intermolecular hydrogen bonds. This behavior is consistent with a rearrangement of the chains in the cross-linked microgel during the phase transition.

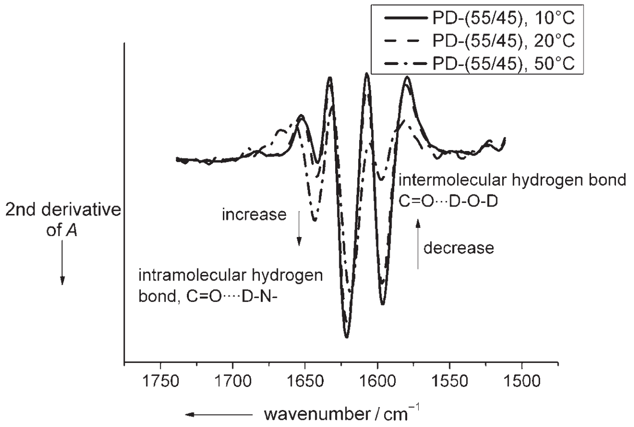

Figure 2. Second derivative of the amide I′ band of copolymer PD(55/45) in D_2O in the swollen state (10 °C), in the phase-transition region (20 °C), and in the collapsed state (50 °C).

Figure 3 exhibits the amide I′ region of the core–shell system PD/PN-CS(80/20). Two main peaks can be determined at 1597 and 1625 cm^{-1}. The first peak, which is related to intermolecular hydrogen bonds to D_2O, decreases at higher temperatures. A further small peak is visible at 1643 cm^{-1}, which increases slightly at higher temperatures and may be ascribed to vibrational modes of molecules at the interface between the core and the shell. This peak is related to the formation of an intramolecular C=O hydrogen bond and is, as expected, more pronounced in the collapsed high-temperature state. On comparing the core–shell (PD/PN-CS(80/20)) and the inverse core–shell (PN/PD-CS(25/75)) systems, no significant differences are found in the FTIR spectra.

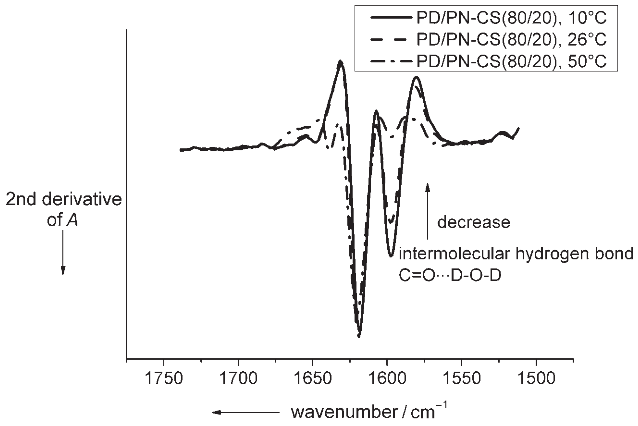

Figure 3. Second derivative of the amide I′ band of core–shell PD/PN-CS(80/20) in D_2O in the swollen state (10 °C), in the phase-transition region (26 °C), and in the collapsed state (50 °C).

For comparison, a further FTIR spectroscopic measurement was carried out on a mixture of the two homopolymer microgels in the ratio of 57 mol% PDEAAM and 43 mol% PNIPAM. The FTIR spectrum looks very similar to that of the core–shell system (all spectra are shown in the Supporting Information), which indicates the absence of marked hydrogen-bond interactions between different microgel particles.

Figure 4 shows the temperature-dependent intensity of the intramolecular hydrogen bonds of pure PNIPAM, the copolymer PD(55/45), the two core–shell systems, and the mixture of the two homopolymers. (The PDEAAM homopolymer cannot form intramolecular bonds.) The shape of all curves looks similar; however, a strong shift to lower temperatures is observed for the copolymer, thus indicating a significant strengthening of intramolecular bonds in agreement with the concomitant strong decrease of intermolecular bonds to water. Clearly, the microgel architecture governs the type and extent of hydrogen bond formation.

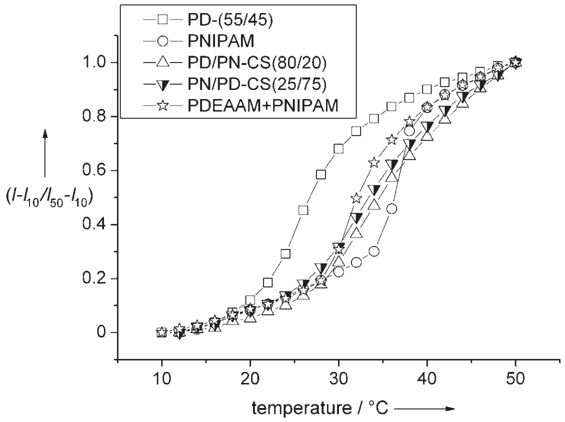

Figure 4. Temperature dependence of intramolecular hydrogen bonds (peaks normalized to the intensity of the wavenumber at 1643 cm^{-1} at 50°C) for PNIPAM, PD(55/45), the core–shell systems, and the mixture of PDEAAM and PNIPAM microgels.

The strong increase of the intramolecular hydrogen bonds in the copolymer PD(55/45) is caused by the direct neighborhood of the NIPAM and DEAAM units, thus favoring polymer–polymer interactions in the copolymer microgel which lead to the unusual depression of the phase transition temperature observed. In the core–shell systems, however, the different monomers are locally separated in core and shell, and intramolecular hydrogen bonding between mono- and disubstituted amide groups is hardly possible (Figure 1). Consequently, the core–shell systems do not display a reduction in VPTT.

Intramolecular hydrogen bonds can be formed between nearest neighbors and between units more widely spaced along the polymer network. The former will mainly influence solvation, whereas the latter can—depending on the degree of swelling—lead to the formation of additional physical cross-links and loops.[4] A temperature-dependent formation of loops and cross-links could lead to hysteresis in particle size between heating and cooling which, however, has not been observed with our systems.

More detailed information on the extent of formation of loops and physical cross-links could be obtained from computer simulations and by studying microgels with different densities of chemical cross-links.[14] Our small-angle neutron scattering and NMR data suggest that the two repeating units are in fact incorporated statistically in the microgel, which was also reported for other systems.[15] Therefore, we may speculate that hydrogen bonds are formed preferentially between neighboring units, as supported by the strong, cooperative increase of intramolecular bonds at the transition.

Finally, we discuss the temperature dependence of the intermolecular hydrogen bond (peak at 1597 cm^{-1}) for the different samples. As already mentioned, this peak probes the solvation of the amide group with D_2O and thus is also observable for the pure PDEAAM, in contrast to the peak correlated with intramolecular bonds. The observation that the copolymer reveals dehydration at temperatures lower than that for the pure PDEAAM indicates that the formation of intramolecular hydrogen bonds induces the release of water molecules and the collapse of the microgel.

In summary, by using temperature-dependent FTIR spectroscopy we were able to distinguish between intra- and intermolecular hydrogen bonds and to correlate the intra- and intermolecular hydrogen-bonding pattern with the microgel architecture. Homopolymers, copolymers, and core–shell systems form different amounts of intra- and intermolecular hydrogen bonds, and the unusual synergistic depression of the phase transition temperature of the copolymer microgel PD(55/45) is caused by strong hydrogen bonding between neighboring DEAAM and NIPAM groups.

The data clearly demonstrate the influence of the local environment of the mono- and disubstituted acrylamide repeating units on the phase transition temperature. The strong increase of the intramolecular hydrogen bonds in the copolymer PD(55/45) is caused by the direct neighborhood of the NIPAM and DEAAM units, thus fostering direct polymer–polymer interactions in the copolymer microgel, which lead to a marked depression of the phase transition temperature. Conversely, in core–shell systems the monomers are locally separated in the core and shell, and consequently no depression of the phase transition temperature is observed. These data clearly demonstrate the strong interplay of the microgel architecture and the hydrogen-bonding pattern that determines the temperature sensitivity of these materials. Thermosensitive microgels are used for different applications, such as in sensors and as carriers for biomolecules. As the copolymers allow tuning of the local molecular-interaction pattern, these materials offer additional features as compared to core–shell systems.

Experimental Section

NIPAM (Acros Organic), DEAAM (Polyscience), sodium dodecyl sulfate (Fluka), potassium peroxodisulfate (Merck), and cross-linker *N*,*N*′-methylenebisacrylamide (Merck) were used as received. The cross-linked copolymer microgels were synthesized by dispersion polymerization as described previously.[9] The dispersion was purified three times by repeated ultracentrifugation (30 min at 50000 rpm), decantation of the supernatant, and redispersion in bidistilled water.

For the FTIR measurements, CaF_2 transmission windows and 0.05-mm Mylar spacers were used. The temperature in the cell was controlled through an external water circuit. All the FTIR spectra were collected on a Nicolet 5700 FTIR spectrometer equipped with a liquid-nitrogen-cooled mercury cadmium telluride detector. For each spectrum, 256 interferograms of $2\,cm^{-1}$ resolution were co-added. The sample chamber was continuously purged with dry air. A corresponding solvent spectrum was subtracted from the spectrum of each sample, and all the spectra were baseline-corrected and normalized. All data processing was performed with GRAMS software.

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[1] H. Chens, G. Liu, C. Wang, G. Zhang, C. Wu, *J. Polym. Sci. Part B* **2006**, *44*, 770 – 778.
[2] V. Y. Grinsberg, A. S. Dubovik, D. V. Kuznetsov, N. V. Grinberg, A. Y. Grosberg, T. Tanaka, *Macromolecules* **2000**, *33*, 8685 – 8692.
[3] Y. Mylonas, G. Staikos, P. Lianos, *Langmuir* **1999**, *15*, 7172 – 7175.
[4] H. Cheng, L. Shen, C. Wu, *Macromolecules* **2006**, *39*, 2325 – 2329.
[5] a) S. Y. Lin, K. S. Chen, L. Run-Chu, *Polymer* **1999**, *40*, 2619 – 2624; b) O. Ramon, E. Kesselman, R. Berkovici, Y. Cohen, Y. Paz, *J. Polym. Sci. Part B* **2001**, *39*, 1665 – 1677; c) Y. Katsumoto, T. Tanaka, H. Sato, Y. Ozaki, *J. Phys. Chem. A* **2002**, *106*, 3429 – 3435; d) Y. Maeda, H. Yamamoto, I. Ikeda, *Colloid Polym. Sci.* **2004**, *282*, 1268 – 1273.
[6] A. R. Khokhlov, P. G. Khalatur, *Phys. Rev. Lett.* **1999**, *82*, 3456 – 3459.
[7] a) D. Gan, L. A. Lyon, *J. Am. Chem. Soc.* **2001**, *123*, 7511 – 7517; b) I. Berndt, W. Richtering, *Macromolecules* **2003**, *36*, 8780 – 8785; c) S. Nayak, L. A. Lyon, *Angew. Chem.* **2005**, *117*, 7862 – 7886; *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 7686 – 7708.
[8] a) C. D. Jones, L. A. Lyon, *Macromolecules* **2000**, *33*, 8301 – 8306; b) I. Berndt, J. S. Pedersen, W. Richtering, *J. Am. Chem. Soc.* **2005**, *127*, 9372 – 9373; c) I. Berndt, C. Popescu, F.-J. Wortmann, W. Richtering, *Angew. Chem.* **2006**, *118*, 1099 – 1102; *Angew. Chem. Int. Ed.* **2006**, *45*, 1081 – 1085; d) I. Berndt, J. S. Pedersen, W. Richtering, *Angew. Chem.* **2006**, *118*, 1769 – 1773; *Angew. Chem. Int. Ed.* **2006**, *45*, 1737 – 1741.
[9] M. Keerl, W. Richtering, *Colloid Polym. Sci.* **2006**, *285*, 471 – 474.
[10] a) H. Herberhold, S. Marchal, R. Lange, C. H. Scheyhing, R. F. Vogel, R. Winter, *J. Mol. Biol.* **2003**, *330*, 1153 – 1164; b) H. Zein, R. Winter, *Phys. Chem. Chem. Phys.* **2000**, *2*, 4545 – 4551; c) G. Panick, R. Malessa, R. Winter, G. Rapp, K. J. Frye, C. Royer, *J. Mol. Biol.* **1998**, *275*, 389 – 402.
[11] Y. Katsumoto, T. Tanaka, Y. Ozaki, *J. Phys. Chem. B* **2005**, *109*, 20690 – 20696.
[12] Y. Maeda, T. Higuchi, I. Ikeda, *Langmuir* **2000**, *16*, 7503 – 7509.
[13] Y. Maeda, T. Nakamura, I. Ikeda, *Macromolecules* **2002**, *35*, 10172 – 10177.
[14] T. Hoare, D. McLean, *J. Phys. Chem. B* **2006**, *110*, 20327 – 20336.
[15] E. Djopke, W. Vogt, *Macromol. Chem. Phys.* **2001**, *202*, 750 – 757.