Studies of the Thermal Volume Transition of Poly(*N*-isopropylacrylamide) Hydrogels by High-Sensitivity Differential Scanning Microcalorimetry. 2. Thermodynamic Functions

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Received March 24, 2000; Revised Manuscript Received September 7, 2000

ABSTRACT: We report the first accurate measurements of the partial heat capacity of poly(*N*-isopropylacrylamide) hydrogels with varying cross-link density. When the cross-link density is increased, the transition broadens and the transition temperature decreases, while the enthalpy, entropy, and heat capacity increment of the transition do not practically change. The transition heat capacity increment is negative, $\Delta_t c_p = -0.63 \pm 0.04$ J/g/K. This indicates the formation of a hydrophobic core of the gel upon the transition. The partial heat capacity of polymer network in the gel approaches the partial heat capacity of the unfolded linear poly(*N*-isopropylacrylamide) at low temperatures, indicating a complete disordering of the gel under these conditions. On the basis of the calorimetric data, thermodynamic functions of the transition were calculated from 0 to 150 °C. They allow one to compare enthalpic and entropic contributions to the stabilization of the collapsed gel. This state is found to be most stable at about 100 °C, and a reswelling transition could be expected only above 150 °C. Contributions of the dehydration of apolar and polar groups as well as residual factors to the transition enthalpy, entropy, and free energy were calculated. The role of apolar dehydration, i.e., of the hydrophobic effect, was not found to be predominant. Apparently, interactions of residues (van der Waals interactions and/or hydrogen bonding) contribute mainly to the stabilization of the collapsed state.

1. Introduction

In a previous communication,[1] the first results of studies of the volume phase transition in poly(*N*-isopropylacrylamide) (PNIPA) hydrogels by high-sensitivity differential scanning calorimetry (HS-DSC) were presented. The behavior of the low-concentration gels at different scanning rates was considered, and the dependences of the transition parameters on the heating rate were discussed. It was shown that HS-DSC measurements at the heating rate of 0.125 K/min seem to provide results closely approximating equilibrium.

In this paper results of the study of the volume phase transition in PNIPA hydrogels with varied cross-link density by the HS-DSC method are presented. The measurements were performed at a heating rate of 0.125 K/min. The transition temperature, enthalpy, and entropy as well as the transition width vs the cross-linking density are determined. They are compared with the theory of the polymer gel collapse. The calorimetric data are used to calculate the transition enthalpy, entropy, and free energy as a function of temperature over the range of 0−150 °C. Temperature dependences of the partial heat capacity of polymer network in the gels are obtained. They are compared with the partial heat capacity of linear PNIPA completely unfolded. This approach made it possible to estimate a change in the water accessible surface area of the polymer network. Contributions of apolar and polar dehydration as well as other residual factors into the thermodynamic functions of the gel collapse are discussed.

2. Experimental Section

PNIPA gels were prepared following the standard free-radical polymerization of *N*-isopropylacrylamide (NIPA) with the cross-linker, *N*,*N*′-methylenebis(acrylamide) (BIS).[2] The gelation was initiated by ammonium persulfate and accelerated by tetramethylenediamine. The NIPA concentration of 6 M was fixed, and the BIS concentration was varied (5, 20, and 40 mM) to prepare gel samples of different cross-link densities denoted by G-05, G-20, and G-40. The equilibrium polymer concentration in such gels at 20 °C was 4.2, 6.8, and 10.8%, respectively.

Aqueous suspensions of the gels with polymer concentration of about 2.5 or 4−7 mg/mL depending on the aim of the experiment were directly used in calorimetric measurements. An average size of gel particles in the suspensions was of about 10 μm. The procedure of preparation of gel suspensions was described in detail elsewhere.[3] The calorimetric measurements were carried out with the adiabatic differential scanning microcalorimeter DASM-4 (NPO BIOFIZPRIBOR, Pushchino, Russia). Measurements were performed under an excess pressure of 2 atm over the temperature range from 2 to 60 °C. As a rule, the heating rate of 0.125 K/min was used. However, experiments aimed at precise measurements of the partial heat capacity of polymer network in the gels were done at the heating rate of 1.00 K/min because the maximal baseline stability of the instrument was achieved at this rate. The time constant of the instrument determined in each experiment was of about 20 s. The dynamic deconvolution of calorimetric curves removing their instrumental broadening was carried out as described previously.[1] The corrected difference in apparent heat capacities of the gel suspension in the sample measuring cell and water in the reference measuring cell, $\Delta C_p(T)$, was transformed into the partial specific heat capacity of polymer network:[4]

$$c_p(T) = \frac{\Delta C_p(T)}{m} + \frac{\bar{v}(T)}{\bar{v}_0(T)} c_{p,0}(T) \qquad (1)$$

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10.1021/ma000527w CCC: $19.00
Published on Web 10/25/2000

where m is the mass of the polymer in the suspension, $\bar{v}(T)$ is the partial specific volume of the polymer, and $\bar{v}_0(T)$ and $c_{p,0}(T)$ are the specific volume and heat capacity of water.[5] The partial specific volume of linear PNIPA (PolyScience, lot. 470793) as a function of temperature was used in the calculations. It was determined by densimetric measurements.

In calculations of the excess heat capacity functions of the volume phase transition, its baseline was approximated by the progress line.[6] The transition temperature, T_t, and the transition enthalpy, $\Delta_t h(T_t)$, were determined as the first moment of the excess heat capacity function and as an area under this curve, respectively. In most cases T_t was very close to the peak temperature.

Measurements of the density of aqueous solutions of the linear PNIPA were carried out with the automatic vibration densimeter AD-1 (NPO BIOFIZPRIBOR, Pushchino, Russia). Polymer concentration in the solutions was varied over the range 1−10 mg/mL. The solutions were kept in the instrument at the given temperature for 2 h prior the measurements. Measurements were performed from 20 to 45 °C. The instrument was calibrated by densities of air and water at each temperature. Errors in the density determination did not exceed $\pm 8 \times 10^{-6}$ g/cm^3. The partial specific volume of the polymer was determined as a sum of the intercept and the slope of a straight line approximating the plot of the inverse density of solution vs polymer concentration. The average error in the determination of the partial volume was of ± 0.004 cm^3/g. It was found that the experimental temperature dependence of the partial specific volume of PNIPA is monotonic and does not display any singular point in the vicinity of the transition temperature of PNIPA (about 33 °C). It is well approximated by the linear function

$$\bar{v}(t) = 0.842 + 0.0014t \qquad (2)$$

where the partial volume is expressed in cm^3/g and temperature is given in °C. This function was used in calculations of the partial heat capacity of polymer network in the gel.

The Origin 4.0 software was mainly used for the calculations related to the data processing.

3. Results

The typical thermogram of the collapse of a PNIPA hydrogel is given in Figure 1. Such tracings allow one to determine main thermodynamic parameters of the phase transition: the transition temperature, T_t, and enthalpy, $\Delta_t h(T_t)$, as well as the transition heat capacity increment, $\Delta_t c_p$, in the course of a single experiment. However, more detailed considerations showed that such a procedure gives correctly only an order of magnitude of the heat capacity increment and a qualitative tendency of its changes among the gels studied. It probably overestimated slightly the $\Delta_t c_p$ because the transition baseline was fixed by a linear part of the calorimetric curve to left of the peak (beginning from 20 °C) not too distant from the transition temperature. Considering a broader range of temperatures, it was found that the transition already starts at about 20 °C, as a slight linear increase in the heat capacity. Actually, the baseline should be defined at lower temperatures where the heat capacity is practically independent of temperature. This condition introduced a negligible error in the determination of the transition enthalpy but affects probably the results of determination of the transition heat capacity increment more seriously. As an alternative estimate of the heat capacity increment $\Delta_t c_p$, the difference in the partial heat capacities of polymer network before and after the transition was used (see below).

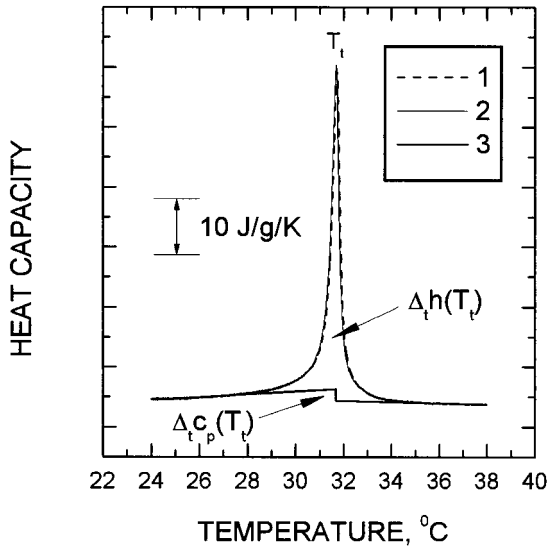

Figure 1. Typical calorimetric tracing for a PNIPA hydrogel: 1, experimental curve; 2, curve corrected for the limited time response of the instrument; 3, approximation of the transition baseline used to estimate the heat capacity increment of the transition, $\Delta_t c_p$. T_t is the transition midpoint temperature coincided practically with the peak temperature. $\Delta_t h(T_t)$ is the transition enthalpy at T_t. The polymer concentration in the calorimetric sample is of 2.5 mg/mL. Heating rate is of 0.125 K/min.

After subtraction of the transition baseline taking into account changes in the partial heat capacity due to the transition, the experimental thermograms were converted into excess heat capacity functions of the transition (Figure 2). These functions are asymmetric. As a rule, a slope of the ascending branch is significantly lower than that of the descending one. The asymmetry becomes more pronounced when the cross-linking density increases. It is also seen that with the increased cross-link density the heat capacity peak broadens out and decreases in the height. In other words, the transition becomes less cooperative. Figure 3 illustrates the main tendencies of changes in the thermodynamic parameters of the collapse with the change in the cross-link density. Clearly, the cross-link density affects only the transition temperature and width. The remaining parameters do not undergo significant changes. The transition heat capacity increment is negative, indicating a decrease in the water accessibility of hydrophobic groups of chains of the gel network as a result of the transition. To confirm this conclusion, careful measurements of the partial heat capacity of polymer network in the PNIPA gels were carried out. These measurements were done under the heating rate of 1 K/min and at a higher polymer concentration in calorimetric samples (Figure 4). The maximal stability of the instrument baseline is provided under this heating rate. This is of primary importance for precise measurements of the partial heat capacity. The baseline drifts under lower heating rates (however, this does not affect the transition parameters). A higher polymer concentration in the calorimetric sample was needed to make a measurable difference in the heat capacities before and after the transition more significant.

The partial heat capacity of a polymer is known to be a function of its chemical composition and the water accessibility of its residues.[7] According to the current methodology, structural interpretation of data on the partial heat capacity of polymer in PNIPA hydrogels

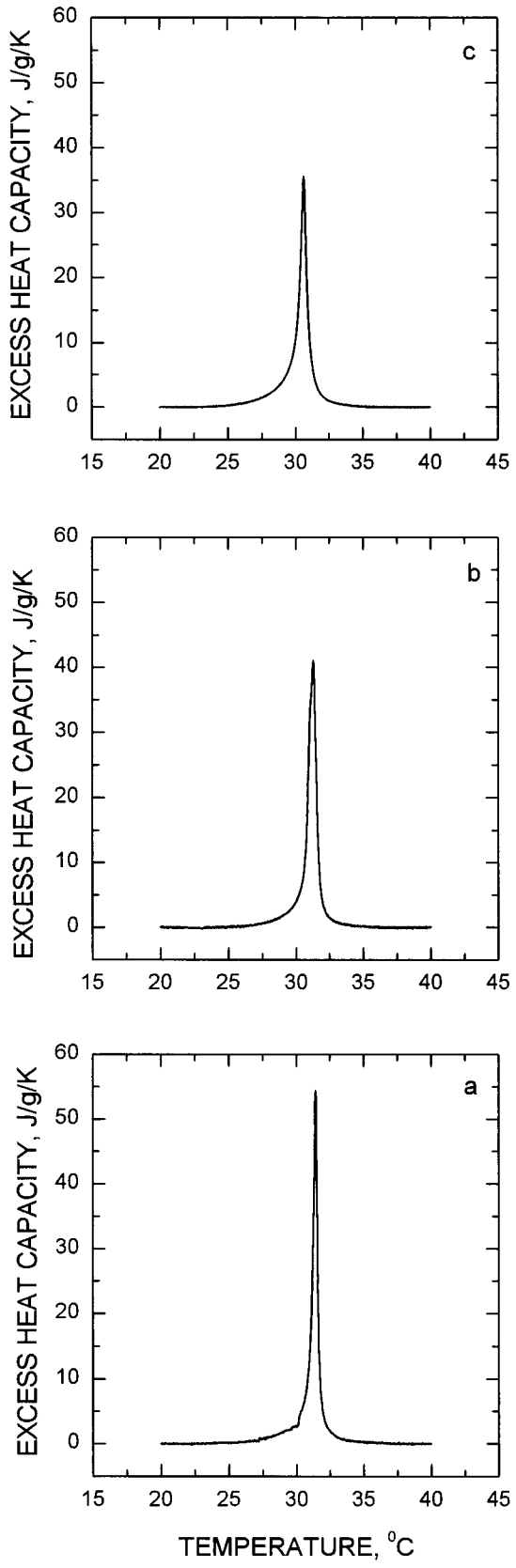

Figure 2. Excess heat capacity functions related to the volume phase transition for PNIPA hydrogels with different cross-link densities: (a) sample G-05 (6 M NIPA, 5 mM BIS); (b) sample G-20 (6 M NIPA, 20 mM BIS); (c) sample G-40 (6 M NIPA, 40 mM BIS). Heating rate is of 0.125 K/min.

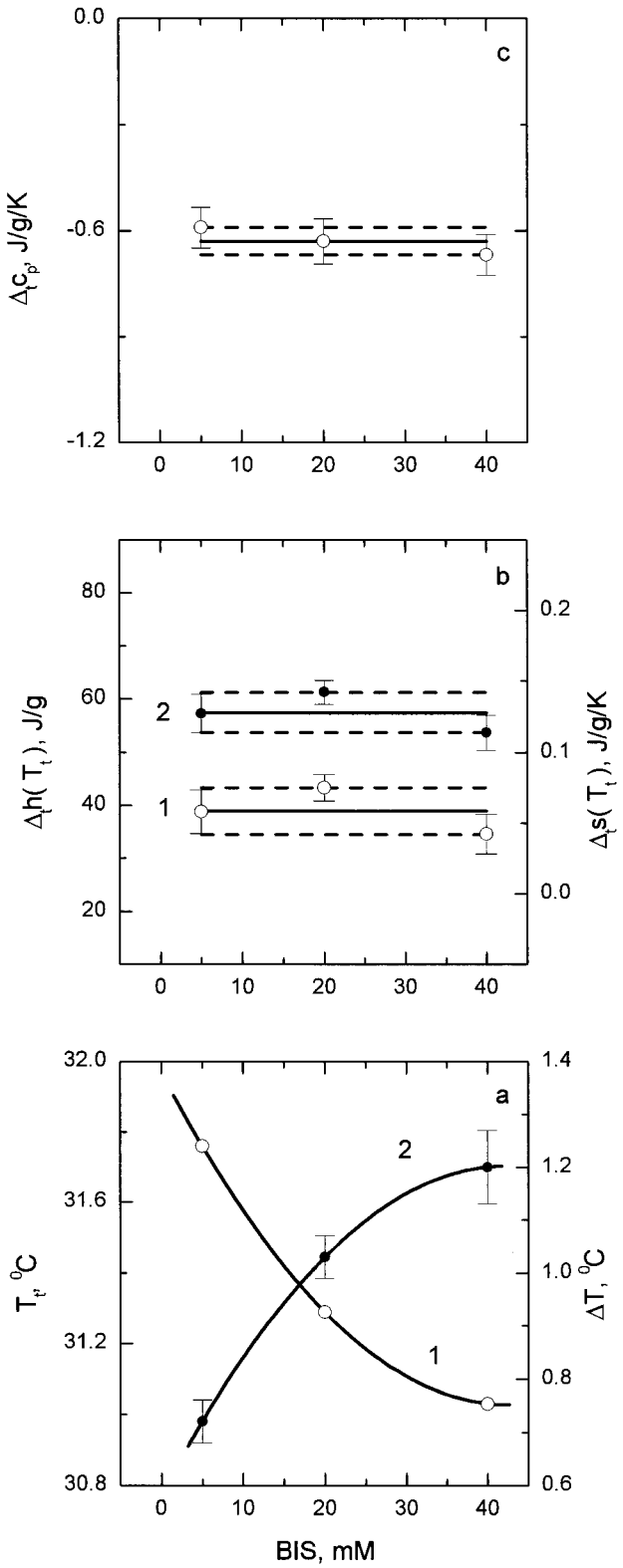

Figure 3. Parameters of the volume phase transition for PNIPA hydrogels against concentration of the cross-linking agent used for gel preparation at the constant NIPA concentration (6 M): (a) T_t is the transition temperature (curve 1, left ordinate axis); ΔT is the transition width (curve 2, right ordinate axis); (b) $\Delta_t h(T_t)$ is the transition enthalpy at T_t (curve 1, left ordinate axis), $\Delta_t s(T_t) = \Delta_t h(T_t)/T_t$ is the transition entropy at T_t (curve 2, right ordinate axis); (c) $\Delta_t c_p$ is the transition heat capacity increment determined as a difference in the partial heat capacities of polymer network after and before the transition (see Figure 4). $\Delta T = \Delta_t h(T_t)/c_p(T_t)$, where $c_p(T_t)$ is the excess heat capacity at T_t. Dashed lines represent confidence limits of the average values of the parameters.

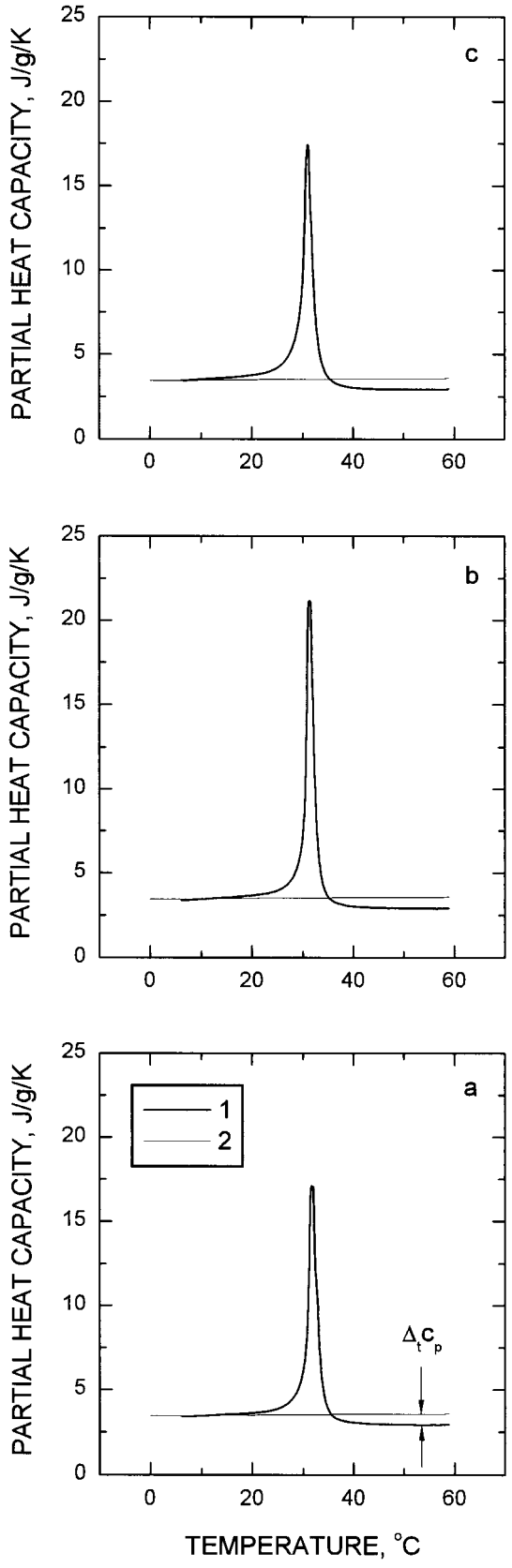

Figure 4. Partial heat capacity functions of polymer network in the PNIPA hydrogels with different cross-link densities (1) and calculated partial heat capacity of completely unfolded PNIPA chains (2): (a) sample G-05 (6 M NIPA, 5 mM BIS); (b) sample G-20 (6 M NIPA, 20 mM BIS); (c) sample G-40 (6 M NIPA, 40 mM BIS). $\Delta_t c_p$ is the heat capacity increment of the phase transition. Polymer concentration in the calorimetric samples is of 4−7 mg/mL. Heating rate is of 1.00 K/min.

should be based on the calorimetric data for oligomers of *N*-isopropylacrylamide of different chain lengths. Unfortunately, such data are not still accessible. Because of lack of better models, we chosen poly(leucine) as a model for our analysis. It consists of the same atoms as PNIPA,[8] and its partial heat capacity in the unfolded state, i.e., in the state with the complete water accessibility of residues, has been precisely measured over a wide temperature range and analyzed in detail from the structural point of view.[9,10] We believe that such an approach could be considered as a first approximation that would be specified when new thermodynamic information on more appropriate model compounds will become available.

In Figure 4 the data for poly(leucine) are given by curve 2. It seems reasonable to assume that this curve well approximates the partial heat capacity of unfolded PNIPA chains. It is seen that the partial heat capacity of the polymer network in the PNIPA gels approaches the heat capacity of unfolded PNIPA chains at low temperatures. This tendency is easy to understand. Indeed, in the swollen state of the gel, the network chains adopt coil conformations with a complete solvent accessibility of residues. The gel collapse results in the heat capacity decrease since a part of hydrophobic residues loses their contacts with water molecules. It is evident that the difference in the partial heat capacities of polymer network before and after the transition may be considered as its heat capacity increment $\Delta_t c_p$. In this case $\Delta_t c_p = -0.63 \pm 0.04$ J/g/K at 50 °C independent of degree of cross-linking of the gel.

4. Discussion

As starting point to discuss our observations, we use a mean-field theory of gel collapse. While there are a variety of versions of such a theory (see refs 11 and 21 and references therein), they all predict a sharpening of the transition with increasing chain length between cross-links or decreasing cross-link density. This agrees well with our data. We believe that the speed of swelling and shrinking and that of equilibration of microphase separation in a gel, under the conditions of slow quasi-equilibrium process examined in this work, is controlled by the collective diffusion of subchains. If that is indeed the case, then this speed increases with cross-link density. Therefore, we expect that the sharpening of the transition observed in our experiments is not related to these kinetic processes. Another theoretical prediction is that decreasing chain lengths should shift the transition to lower values of the Flory interaction parameter χ. The PNIPA−water system has LCST;[12] therefore, the χ value will decrease with lower temperature. Hence, one can expect that the transition temperature of PNIPA gels should decrease with increased cross-link density. Yet another theoretical prediction is that swelling curves (density or diameter of gel vs T) are practically independent of cross-link density except in the narrow vicinity of the transition point. They coincide practically at temperatures lower and higher than the transition temperature. This seems to explain why the enthalpy of the collapse of PNIPA gels does not depend on the cross-link density.

Let us assume that the partial enthalpy of polymer in the gel is

$$h(T,\phi) = h^0(T) + h^M(\phi) \qquad (3)$$

where $h^0(T)$ is the partial standard enthalpy of polymer, ϕ is the volume fraction of polymer in the gel, and $h^M(\phi)$ is the partial mixing enthalpy of polymer that is an increasing function of ϕ. In the course of a calorimetric experiment, a difference in the partial enthalpies of polymer at temperatures of the scan start and finish, T_1 and T_2, respectively, is measured:

$$\Delta_t h = h(T_2) - h(T_1) \cong h^M(\phi(T_2)) - h^M(\phi(T_1)) > 0 \quad (4)$$

where $\phi(T_2)$ and $\phi(T_1)$ are the volume fractions of polymer in the collapsed and swollen gel at the temperatures T_2 and T_1. Sufficiently far from the transition temperature, a change in the cross-link density in the range corresponding to the experimental conditions affects the function $\phi(T)$ only slightly. It follows that the calorimetric transition enthalpy $\Delta_t h$ must depend only slightly on the cross-link density. Since a change in the cross-link density is equivalent to a change in the polymerization degree of network subchains of the gel, this relationship agrees with data of Tiktopulo et al.,[13] who measured the enthalpy of the collapse of linear chains of PNIPA and poly(*N*-isopropylmethacrylamide) with the polymerization degree from about 100 to 3000. According to these data, the specific enthalpy of the collapse is of 34.4 ± 5.9 J/g, independent of the polymerization degree. It is of interest that this value coincides practically with our estimation of the specific enthalpy of the collapse of the PNIPA gels, $\Delta_t h(T_t) =$ 38.9 ± 4.4 J/g.

As indicated above, the excess heat capacity functions of the collapse of the PNIPA gels display the specific asymmetry, i.e., at points equidistant from the T_t its ascending slope is lower than the descending one. This feature should be reflected in the shape of the integral transition curve. It was of interest to compare transition curves of the collapse of PNIPA gels according to the volumetric[11] and HS-DSC data. To do this we compared the quantities

$$\alpha_V(T) = \frac{\phi(T) - \phi(T_1)}{\phi(T_2) - \phi(T_1)} \quad (5)$$

and

$$\alpha_H(T) = \frac{h(T) - h(T_1)}{h(T_2) - h(T_1)} \quad (6)$$

The transition curves are presented in Figure 5 relative to the transition temperature T_t. The curve $\alpha_V(T)$ resembles formally a curve of the second-order phase transition.[14] The conversion degree gradually increases with increasing temperature in the pretransitional range and then abruptly becomes unity at the transition point $T = T_t$. As a whole, the transition curve $\alpha_H(T)$ has the same form. However, it does not display the singularity at $T = T_t$ that may be caused by the dynamic mode of calorimetric measurements and the effect of the instrumental time response.

Let us consider the change in the partial heat capacity of polymer network upon the gel collapse in more detail. According to the definition,[10] the partial heat capacity of a polymer in aqueous solution can be written in the form

$$c_p(T) = c_p^g(T) + \Delta_g^w c_p(T) \quad (7)$$

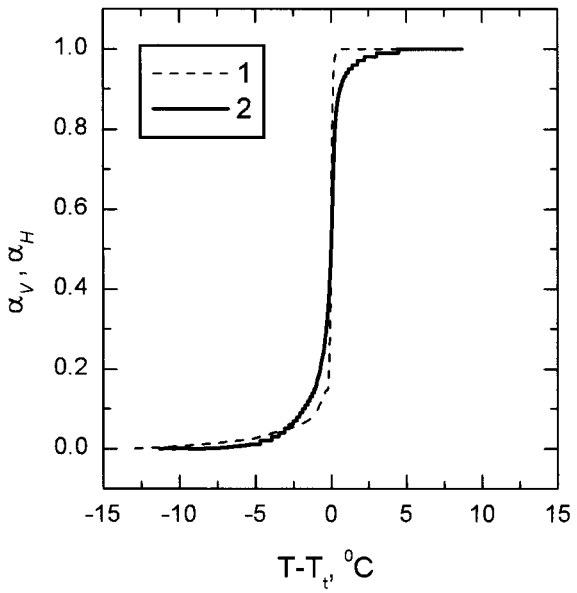

Figure 5. Reduced integral curves of the volume phase transition for PNIPA hydrogels according to volumetric[11] (1) and HS-DSC (2) data.

where $c_p^g(T)$ is the apparent heat capacity of the polymer in the gas phase which is determined by all freedom degrees of an isolated macromolecule and $\Delta_g^w c_p(T)$ is the change in the heat capacity upon a transfer of the macromolecule from the gas phase to water, i.e., the hydration heat capacity increment. The applicability of eq 7 to a swollen gel seems to be beyond doubt. On the other hand, in the case of the collapsed state this equation should involve an additional term related to noncovalent interactions[7,11] resulting from the condensed nature of this state. However, this contribution is hard to estimate with a reasonable precision even for proteins having a well-defined structure. Nonetheless, it can be assumed to vanish over the temperature range (0−50 °C)[7] of interest for this study. Therefore, it is reasonable to assume that eq 7 could be also applied to description of the collapsed gel state.

It was found out with a good precision that the hydration increment is proportional to the water accessible surface area of a macromolecule (ASA):[9,10]

$$\Delta_g^w c_p(T) = k(T)\mathrm{ASA} \quad (8)$$

where $k(T)$ is a constant depending on temperature. Hence, the heat capacity increment of the gel collapse can be defined in the form

$$\Delta_t c_p(T) = k(T)\Delta_t\mathrm{ASA} \quad (9)$$

where Δ_tASA is the change in the accessible surface area resulting from the collapse. This relation could be used to specify changes in the gel structure associated with the collapse from the transition heat capacity increment. This value comprised $\Delta_t c_p(50\ °C) = -0.63 \pm$ 0.04 J/g/K independent of the gel cross-link density. The value $k(50\ °C) = 1.34$ J/mol/K/Å^2 was calculated from the data for poly(leucine).[10]

Calculations showed that the change in the accessible surface area of the network chains resulting from the collapse represents about −53 Å^2/residue, while the ASA change upon folding a PNIPA chain to a dense globule should be over −170 Å^2/residue. Thus, our data do not

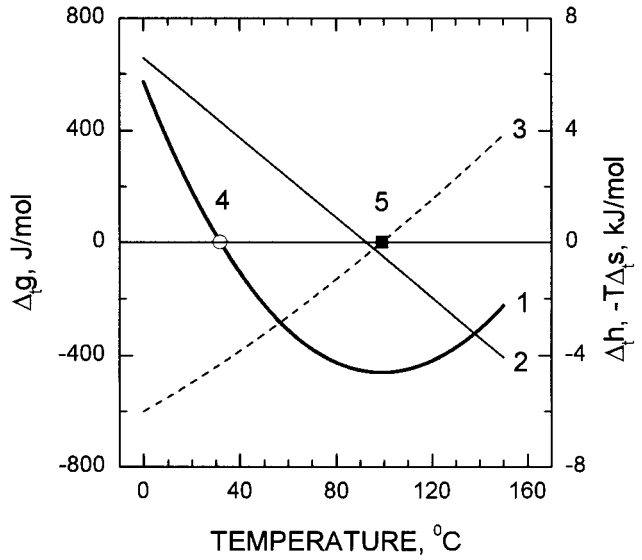

Figure 6. Free energy (1, left ordinate axis) of the volume phase transition and its enthalpy (2) and entropy (3) components (right ordinate axis) vs temperature for the gel G-05 (6 M NIPA, 5 mM BIS) calculated per mole of residues. Points 4 and 5 correspond to temperatures T_t and T_s where the functions 1 and 3 vanish.

support the simple image of the collapsed gel as a dense body similar to the interior of a dense globule. Instead, it seems reasonable to assume a microstructure with some more dense domains whose interior is not accessible to water, but whose surface remains in contact with water such as microphase-separated states. It would be premature to speculate on the possible shapes of such domains and their relations to the subchains.

From the calorimetric data obtained, temperature dependences of the enthalpy, entropy, and free energy of the collapse of the PNIPA hydrogels were calculated assuming that the heat capacity increment of the transition does not depend on temperature:[15]

$$\Delta_t h(T) = \Delta_t h(T_t) + \Delta_t c_p (T - T_t) \quad (10)$$

$$\Delta_t s(T) = \frac{\Delta_t h(T_t)}{T_t} + \Delta_t c_p \ln(T/T_t) \quad (11)$$

$$\Delta_t g(T) = \Delta_t h(T) - T\Delta_t s(T) \quad (12)$$

Results of the calculations for the gel sample G-05 (6 M NIPA, 5 mM BIS) are given in Figure 6. These are the free energy of the transition (1) and its enthalpic (2) and entropic (3) components. From a formal point of view, these functions are typical of processes driven by hydrophobic interactions.[16] When temperature increases, the free energy first changes from positive to negative, vanishes at the transition temperature T_t = 31.8 °C, passes through a minimum at temperature of about 100 °C, and begins to increase again remaining, however, negative. At low temperatures the enthalpic contribution is positive, but the entropic one is negative. With increasing temperature both contributions pass through zero and then change sign. The transition enthalpy and entropy vanish at temperatures T_h = 92.6 °C and T_s = 99.1 °C, respectively. These data show that the collapse is entropy-driven at low temperatures and enthalpy-driven at high temperatures. The low-temperature increase in the entropy of the system can be related to the dehydration of PNIPA residues, thanks to a large number of water molecules gaining additional degrees of freedom as well as to the elastic relaxation of network subchains. Note that the maximal stability of the collapsed state of the gel relative to the swollen one is expected at temperature of about 100 °C, corresponding to the minimal transition free energy. An increase in the free energy at higher temperatures allows one to suggest that the free energy would again vanish at some higher temperature (about 170 °C). A reentrant phase transition to the collapse will correspond to this temperature. We could not locate this transition because the working range of our instrument is confined to below 150 °C. Therewith, the reality of the reentrant transition is supported by the data on behavior of PNIPA gels in alcohol−water mixed solvent.[17] In this system, the reentrant transition was found at a rather lower temperature. A decrease in the temperature of the reverse transition in the presence of an alcohol is evident from general properties of the free energy function.

The free energy of the swollen state of the gel decreases more than that of the collapsed one upon addition of the alcohol which is a good solvent for PNIPA.[18] Thus, the transition free energy curve should shift upward and could cross the abscissa axis once more at a lower temperature in comparison with the expected temperature of the reverse transition in water.

Using the estimated change in the water accessible surface area of network chains of the PNIPA gel due to the collapse, $\Delta_t ASA = -53$ Å^2, it is possible to calculate dehydration contributions for apolar *(*apol*)* and polar *(*pol*)* groups of these chains into the thermodynamic functions of the transition.[19]

On the basis of thermodynamic data on solubility of a large set of model compounds in water and the principle of independent group contributions, it was shown that thermodynamic functions of hydration, reduced to ASA, are universal and specific for apolar and polar groups:[19]

$$\Delta_g^w h_{apol}^R(t) = -177.2 + 2.260t - 2.318t^2 \quad (13)$$

$$\Delta_g^w s_{apol}^R(t) = -0.7680 + 7.940 \times 10^{-3}t - 1.585 \times 10^{-5}t^2 \quad (14)$$

$$\Delta_g^w g_{apol}^R(t) = 33.27 + 0.7615t - 3.863 \times 10^{-3}t^2 + 4.514 \times 10^{-6}t^3 \quad (15)$$

$$\Delta_g^w h_{pol}^R(t) = -1654 - 1.891t + 1.884t^2 \quad (16)$$

$$\Delta_g^w s_{pol}^R(t) = -0.8533 - 7.622 \times 10^{-3}t + 3.381 \times 10^{-5}t^2 - 1.042 \times 10^{-7}t^3 \quad (17)$$

$$\Delta_g^w g_{pol}^R(t) = -1420 + 0.8759t + 2.448 \times 10^{-3}t^2 \quad (18)$$

where t is temperature in °C, reduced hydration enthalpies and free energies are expressed in J/mol/Å^2, and reduced hydration entropies are given in J/mol/K/Å^2. Contributions of dehydration of apolar and polar groups of PNIPA into specific thermodynamic functions of the collapse of the PNIPA gel were calculated as follows:

$$h^*_{apol}(T) = \Delta^w_g\, h^R_{apol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{apol}}{ASA^0}\right)\frac{1}{M^0_{apol}} \quad (19)$$

$$s^*_{apol}(T) = \Delta^w_g\, s^R_{apol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{apol}}{ASA^0}\right)\frac{1}{M^0_{apol}} \quad (20)$$

$$g^*_{apol}(T) = \Delta^w_g\, g^R_{apol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{apol}}{ASA^0}\right)\frac{1}{M^0_{apol}} \quad (21)$$

$$h^*_{pol}(T) = \Delta^w_g\, h^R_{pol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{pol}}{ASA^0}\right)\frac{1}{M^0_{pol}} \quad (22)$$

$$s^*_{pol}(T) = \Delta^w_g\, s^R_{pol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{pol}}{ASA^0}\right)\frac{1}{M^0_{pol}} \quad (23)$$

$$g^*_{pol}(T) = \Delta^w_g\, g^R_{pol}(T)\left(\Delta_t ASA\,\frac{ASA^0_{pol}}{ASA^0}\right)\frac{1}{M^0_{pol}} \quad (24)$$

where ASA^0_{apol} = 137 Å^2, ASA^0_{pol} = 45 Å^2, M^0_{apol} = 55 g/mol, and M^0_{pol} = 56 g/mol are accessible surface areas and molecular weights of the apolar and polar parts of a leucine residue and ASA^0 = 182 Å^2 is its total accessible surface area.[10] We remind the reader that the atomic composition of the leucine residue is identical with that of a PNIPA residue.

The differences between the experimental transition functions and the dehydration contributions, i.e., so-called residual functions, are very important for understanding. They are determined by nonhydration factors:[19]

$$\Delta_t h_{res} = \Delta_t h - (h^*_{apol} + h^*_{pol}) \quad (25)$$

$$\Delta_t s_{res} = \Delta_t s - (s^*_{apol} + s^*_{pol}) \quad (26)$$

$$\Delta_t g_{res} = \Delta_t g - (g^*_{apol} + g^*_{pol}) \quad (27)$$

It may be suggested[19,20] that the residual transition enthalpy is mainly determined by van der Waals interactions or hydrogen bonding of the residues in the collapsed state. The residual transition entropy may be considered as a sum of changes in the combinatorial entropy, connected with the change in gel composition, and in the conformational entropy of subchains caused by their elastic deformation.

Results of deconvolution of the thermodynamic functions of the collapse of the gel G-05 (6 M NIPA, 5 mM BIS) are shown in Figure 7 and partly in Table 1.

It is obvious that the dehydration contributions to the enthalpy hinder the transition (Figure 7a). Then it is of interest that the contribution of the polar dehydration far exceeds that of the apolar dehydration. Alternatively, the residual enthalpy is negative and rather large over the entire temperature range, superior to any of the dehydration contributions. Therefore, it can be concluded that one of most important driving forces of the collapse are cooperative interactions of the residues in the collapsed state. These interactions are most likely of van der Waals type although those due to hydrogen bonding cannot be excluded.[20] Note that in our case the residual enthalpy is about −40 kJ/residue. It falls within

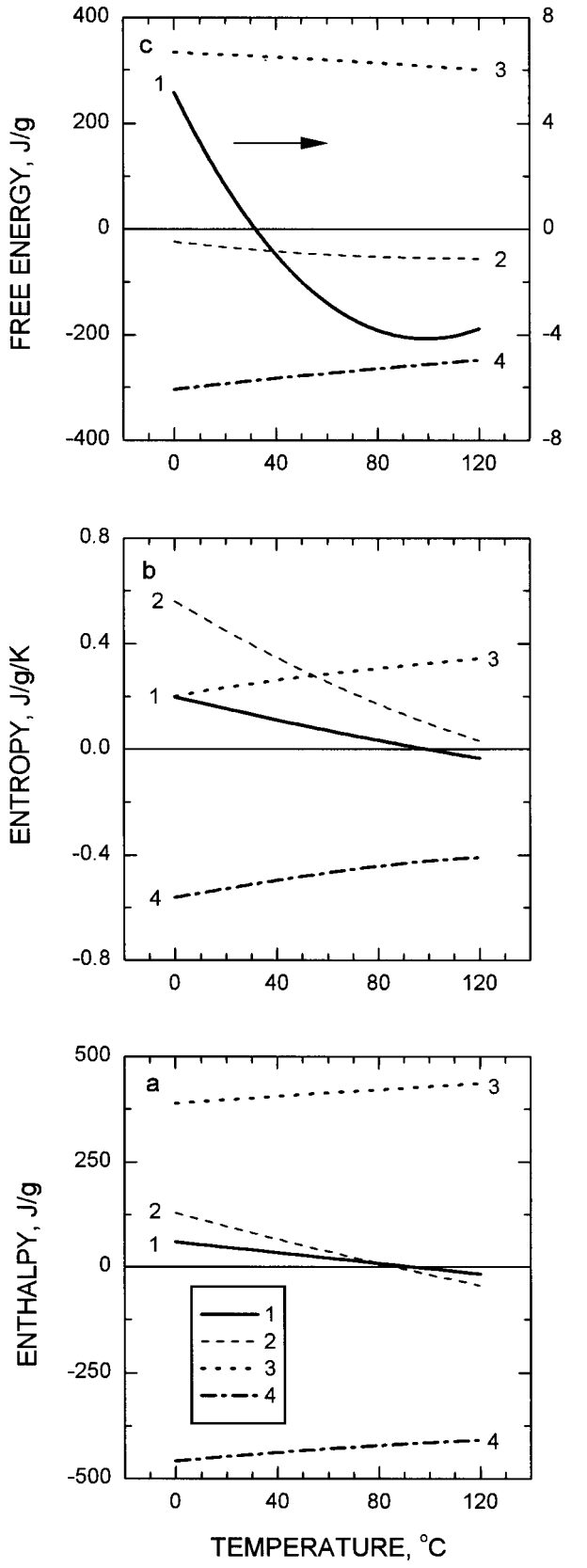

Figure 7. Results of deconvolution of the specific thermodynamic functions of the volume phase transition for the gel G-05 (6 M NIPA, 5 mM BIS): 1, experimental data; 2, contribution of apolar dehydration; 3, contribution of polar dehydration; 4, residual contributions connected with van der Waals interactions and/or hydrogen bonding (a) and combinatorial and chain conformation factors (b). The experimental free energy (c, 1) is plotted on the right ordinate axis.

Table 1. Contributions into Thermodynamic Functions of the Volume Phase Transition for the Gel G-05 (6 M NIPA, 5 mM BIS) at the Transition Temperature, T_t = 31.8 °C

function	enthalpy, J/g	entropy, J/g/K	free energy, J/g
experimental	39	0.13	0.0
apolar dehydration	78	0.39	−39
polar dehydration	402	0.25	326
total dehydration	480	0.64	287
residual	−441	−0.51	−287

the range of residual enthalpies for protein folding (from −30 to −50 kJ/residue).[19]

The dehydration contributions to the entropy favor the collapse transition (Figure 7b). The contribution of the apolar dehydration dominates over that of the polar dehydration at relatively low temperatures (up to 40−50 °C). The situation changes at higher temperatures. There the contribution of the apolar dehydration diminishes, and that of the polar dehydration increases somewhat. The residual entropy is negative at all temperatures. It overrides any of the dehydration contributions in absolute value. Its average value is of about −50 J/residue/K. This is also close to the residual entropy of protein folding.[19] Figure 7c sums up the balance of the considered factors. It becomes evident that the transition is mainly driven by the gain in the van der Waals or H-bonding interaction terms at the cost of strong interactions of residues of the polymer in the collapsed state and the effect of the dehydration of apolar groups. The former factor is dominant. By contrast, the effect of the dehydration of the polar group of the polymer counteracts the transition.

5. Conclusion

1. The mean field theory of polymer gels collapse specifies en bloc correctly main tendencies of changes in the transition parameters (its temperature, enthalpy, and width) with increased gel cross-linking density.

2. The featured asymmetry of the excess heat capacity function of the collapse of the PINPA gel arises from the form of the $V-T$ transition curve.

3. Polymer chains in the PNIPA hydrogel are completely unfolded at low temperatures so that each residue of the chain is accessible to water molecules.

4. The collapse of the PINPA gel is accompanied by a decrease in the accessible surface area of polymer chains resulting from the formation of a hydrophobic interior of the gel. Only a small part of the residues takes part in this process. The main part of the residues remains in the state accessible to the solvent. The interior structure of the collapsed gel does not seem to be highly affected by the gel cross-linking density.

5. The maximum stability of the collapsed state of the PNIPA gel is expected at the temperature of about 100 °C. The transition is entropy-driven up to this temperature and becomes enthalpy-driven at higher temperatures. The collapsed gel is suggested to undergo a reverse phase transition into the swollen state at temperatures of about 160−170 °C.

6. The main factor resulting in the collapse of the PNIPA gel is cooperative interaction of polymer units in the collapsed state. However, its contribution is inadequate to overcome the contribution of dehydration of polar groups of the polymer unfavorable for the transition. The balance needed for the transition is achieved at the cost of a small but crucial contribution of the dehydration of apolar groups of the polymer.

Acknowledgment. The research described in this publication was made possible in part due to the Award RC1-233 of the US Civilian Research & Development Foundation for the Independent States of the Former Soviet Union (CRDF). V.Y.G., N.V.G., A.S.D. and D.V.K. thank the Russian Foundation for Basic Researches for partial financial support (Grants 98-03-33370a and 98-03-33350a). Authors are grateful to Dr. T. V. Burova for useful discussions.

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MA000527W