*Macromolecules* **1999,** *32,* 1471−1475

# Studies of the Thermal Volume Transition of Poly(*N*-isopropylacrylamide) Hydrogels by High-Sensitivity Differential Scanning Microcalorimetry. 1. Dynamic Effects

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*Received July 15, 1998; Revised Manuscript Received December 11, 1998*

ABSTRACT: We present first results of studies of the volume phase transition in poly(*N*-isopropylacrylamide) (NIPA) hydrogels by high-sensitive differential scanning calorimetry (HS−DSC). We examine the behavior of the low-concentrated gels at different scanning rates and discuss the dependencies of the transition parameters upon heating rate. It is shown that HS−DSC measurements at heating rate of 0.125 K/min provide results closely approximating the equilibrium ones in every respect except for the value of transition temperature. At higher heating rates, the transition temperature appears to be practically rate-independent, and network exhibits signs of spatially nonuniform structures developing in the course of collapse, with some parts of the system collapsing under the restrictions of others being almost unperturbed. The apparent enthalpy of this constrained transition is higher than that observed at equilibrium. We discuss the hypothesis that the transition occurs through the spinodal decomposition.

## 1. Introduction

Poly(*N*-isopropylacrylamide) (NIPA) hydrogel is one of the most widely studied examples of gel systems undergoing a temperature-controlled volume phase transition.[1−8] This transition is governed mainly by the hydrophobic interactions between the monomers of the gel subchains, and thus collapse occurs upon heating. In many cases (depending on the amount of cross-linkers), NIPA gel collapse/swelling appears discontinuous and thus is interpreted as a true first-order phase transition. This transition can be also pretty well understood theoretically in terms of the models that essentially go back to classical Flory theory.[9] In this theory, phase transition is said to be governed by the competition between conformational entropy of polymers and volume interactions between monomers; in the specific case of the NIPA gel, the volume interactions at high temperatures are dominated by hydrophobic attraction. In this sense, it is sometimes said that gel collapse represents a macroscopic manifestation of coil−globule transition for the gel subchains. However illuminative is this Flory theory picture, it does not answer a number of questions, the first and foremost of which is about what happens to individual chains when gel macroscopically collapses? The two possible extreme answers to this question would be either (i) each subchain collapses by the same ratio as the gel as a whole, such that the degree of interpretation of neighboring subchains remains essentially unchanged, or (ii) each subchain only moderately changes its gyration radius (*exclusively* because subchain ends come closer to each other), but the overlap between subchains increases dramatically. Another related question is how uniform or nonuniform is the internal structure and/or density distribution inside the collapsed gel. Although these and similar questions are somewhat similar to the widely debated problem of affine or nonaffine deformation of elastomeric polymer network and to the problem of butterfly pattern (see ref 10 and the references therein), the issue for the collapsed gel remains rarely addressed experimentally and poorly understood theoretically. In this work, we plan to make a modest first step in this direction.

Experimentally, the easiest way to observe the polymer gel phase transition is by measuring gel volume, or the diameter of a cylindric gel sample. So far only relatively few works have been published in which gel phase transition has been examined thermodynamically, using conventional differential scanning calorimetry (DSC) technique.[11−15] Apart from measuring the transition temperatures, most of the above cited works dealt with enthalpy measurements for rather concentrated gels, while heat capacity remains hardly touched in the literature. Meanwhile, because of the role of hydrophobic interactions in the NIPA gel behavior, the transition heat capacity increment and the partial heat capacity of polymer in the gel give unique information on water accessibility of functional groups of the network, which is precisely the kind of information one would like to know in order to gain an insight into how subchains are locally organizing themselves within the collapsed gel.

Another problem with calorimetry data obtained for polymer gels is that calorimetric peaks were always pretty wide. This of course sharply contradicts what one would expect for the first-order phase transition. The width of the observed peaks suggests that the data were distorted during the measurements due to a low time response of the instrument. Clearly, one has to try to deconvolute the observed distorted calorimetric data in

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10.1021/ma9810924 CCC: $18.00

order to analyze the real peak shape quantitatively in terms of microscopic thermodynamic models of the transition.

It was shown in a recent paper[16] that one can successfully overcome a number of limitations of conventional DSC technique using its high-sensitivity version (HS−DSC). In this communication we present the first HS−DSC results on the volume phase transition of NIPA hydrogels. We will consider behavior of the low-concentrated gels at different scanning rates, discuss the dependencies of observed parameters of the transition upon heating rate and compare them with the equilibrium data. Specifically, we will show that under the conditions of our experiments the HS−DSC measurements at heating rate of 0.125 K/min yield results reasonably close to the equilibrium data.

## 2. Experimental Section

NIPA gels were prepared following the standard free-radical polymerization of *N*-isopropylacrylamide with cross-linker, *N*,*N*′-methylenebis(acrylamide) (BIS).[17] The gelation was initiated by ammonium persulfate and accelerated by tetramethylenediamine. To prepare gel samples of different cross-linking densities, we varied both monomer and crosslinker concentrations. Indeed, according to the work,[18] at higher monomer concentration the cross-linking is more effective, and thus both monomer and cross-linker concentrations, and not only their ratio, determine the gel structure. The majority of measurements were carried out for the gel with monomer concentration 800 mM and BIS concentration 9.7 mM, which corresponds to equilibrium mass concentration of the gel at 20 °C about $w$(20 °C) = 4.6%. We paid special attention to check that all major dynamic features found for this sample are typical for other gel samples undergoing discontinuous (first order) collapse transition. The later condition is important, because we know from other work[19] that gel phase transition may be continuous (second order) or discontinuous (first order) depending on the amount of cross-links. The gel we chose belongs to the later type. The motivation for this choice is due to the fact that our approach, based on calorimetry measurements, is particularly informative for the first-order phase transitions.

We perform our calorimetry experiments using gel in the form of aqueous suspension with average gel particle size of about $10^{-4}$ cm (10 $\mu$m), polymer concentration in the suspension was about 1 mg/mL. The procedure for preparation of gel suspensions was described elsewhere.[16] An adiabatic differential scanning microcalorimeter DASM-4 (NPO BIOFIZPRIBOR, Puschino, Russia) was used for calorimetric measurements. This calorimeter with capillary measuring cells seems to fit in the best possible way for the studies of heterogeneous systems by HS-DSC. Measurements were performed under heating rates 0.125, 0.250, and 0.500 K/min, and excess pressure of 2 atm over the temperature range from 2 to 80 °C. The time constant of the instrument, $\tau$, was determined by the single exponential fit of the rising and decaying parts of the calibration heating pulse for each experiment. The obtained values of $\tau$ fall in the range 23−28 s, with standard error ±0.5 s independently of heating rate. The dynamic deconvolution of calorimetric curves removing their instrumental broadening was carried out according to the formula (see refs 20 and 21):

$$C_p^{\mathrm{tru}}(T) = C_p^{\mathrm{obs}}(T) + \tau\beta\frac{\mathrm{d}C_p^{\mathrm{obs}}(T)}{\mathrm{d}T} \qquad (1)$$

Here $C_p^{\mathrm{tru}}(T)$ and $C_p^{\mathrm{obs}}(T)$ are the true and observed heat capacities, respectively; $\beta$ is the heating rate, and $T$ is the temperature. The meaning of that formula is simple indeed: with heating rate $\beta$, temperature changes by $\Delta T = \beta\tau$ during the time interval $\tau$; accordingly, the measured heat capacity at a current time moment relates to the time about $\tau$ *earlier*, or to the temperature $T - \Delta T$: $C_p^{\mathrm{obs}}(T) = C_p^{\mathrm{tru}}(T - \Delta T) \simeq C_p^{\mathrm{tru}}(T) - \Delta T(\mathrm{d}C_p^{\mathrm{tru}}/\mathrm{d}T)$. Assuming heat rate is slow, to the linear approximation in heat rate, we can replace $C^{\mathrm{tru}}$ by $C^{\mathrm{obs}}$ *in the correction term*, thus arriving at eq 1.

The specific partial heat capacity of polymer in the gel was calculated in accordance with ref 22

$$c_p(T) = \Delta C_p(T)/m + c_{p,\mathrm{o}}(T)\rho_{\mathrm{o}}(T)v \qquad (2)$$

where $\Delta C_p(T)$ is a difference of apparent heat capacities of the sample and the reference solvent (water), J/K; $m$ is weight of the polymer in the sample, $g$; $\rho_{\mathrm{o}}(T)$ and $c_{p,\mathrm{o}}(T)$ are density and specific heat capacity of water,[23] g/cm$^3$ and J/(g/K), respectively; $v$ is the specific partial volume of the polymer, cm$^3$/g. The specific partial volume of linear PNIPA at 33 °C, $v$(33 °C) = 0.902 cm$^3$/g, obtained by interpolation of data of Heskins and Guillet[24] was used in the calculations.

To calculate excess heat capacity functions of the volume phase transition, we approximated its base line by the so-called progress line.[25] This procedure allows one to eliminate contributions of temperature changes in heat capacity of the system before and after transition, i.e. in the swollen and collapsed states.

The majority of calculations were performed using Origin 2.9 software.

## 3. Results

Figure 1 presents the measurements data of the polymer partial heat capacity in the NIPA hydrogel as a function of temperature. The data shown are obtained at different heating rates ranging from 0.125 to 0.500 K/min. Experimental data were corrected according to eq 1 to take account of the instrumental retardation time. Therefore, artificial broadening of heat capacity peaks resulting from the finite instrument time response was removed. This was necessary because peaks are extremely narrow.

The experimental data shown in Figure 1 indicate that at the lowest heating rate a very narrow, sharp, and rather symmetric peak due to heat capacity is observed. This suggests a possibility of a true singularity in the heat capacity which could not be detected completely because of the finite instrument time response. Then, with an increase in heating rate the peak spreads to higher temperatures and decreases in the height. Hence, the transition appears less cooperative.

In Figure 2 excess heat capacity functions of the volume phase transition at different heating rates are compared with the data of Li and Tanaka[19] obtained by the equilibrium method.[28] From this figure one notices that the excess heat capacity functions determined at different dynamic regimes practically coincide to the left of the transition temperature and become widely separated to the right of it. Then, the higher the heating rate, the greater is a discrepancy between the dynamic curves. The dynamic curves are located markedly to the right of the equilibrium curve and differ strongly from it in shape. The equilibrium curve is well approximated by the function:[19]

$$c_p = A|t|^{\alpha}\,(1 + D|t|^{0.5}) \qquad (3)$$

where $A$, $D$ and $\alpha < 0$ are constants, $t = (T - T_t)/T_t$ is the reduced temperature, and $T_t$ is the transition temperature. In contrast, the dynamic curves are not compatible with this function. Even at the lowest heating rate fitting of the dynamic curve to the function in eq 3 was unsuccessful.

Dependencies of the transition temperature, enthalpy, and the transition half-width on heating rate are shown

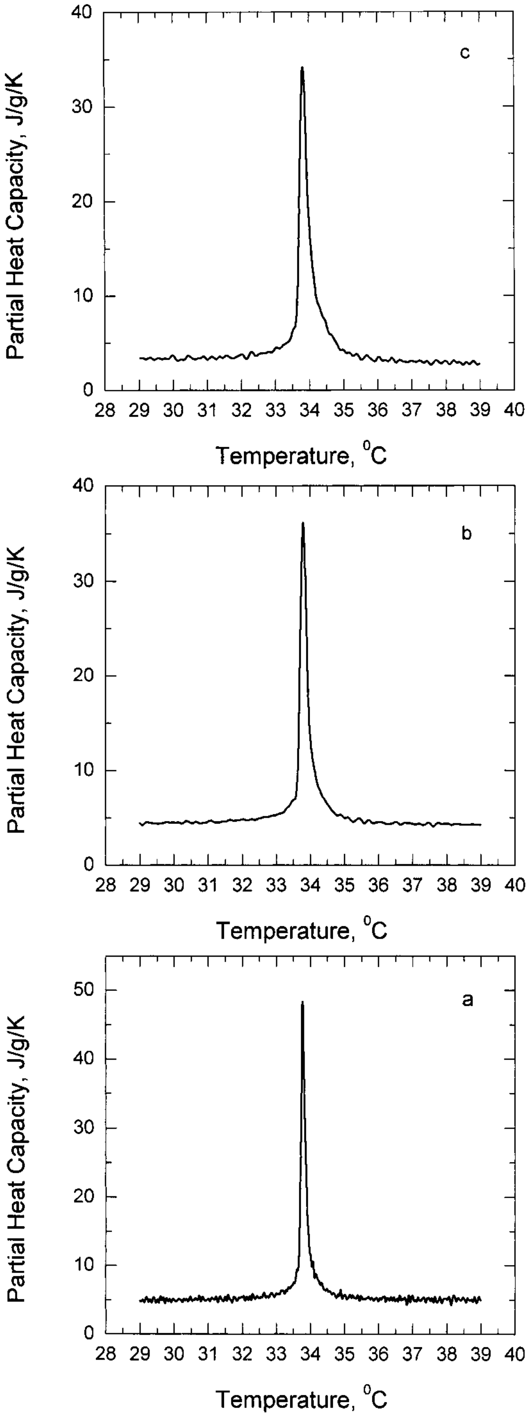

**Figure 1.** Partial heat capacities of polymer in the NIPA hydrogel against temperature at different heating rates: 0.125 (a), 0.250 (b), and 0.500 (c) K/min. The equilibrium gel concentration at 20 °C is 4.6%. The polymer concentration in the calorimetric sample is 1 mg/mL. Curves are dynamically deconvoluted to remove their artificial shape distortions due to the finite instrument response.

in Figure 3. Note that all these transition parameters increase linearly with heating rate. It is of importance here that extrapolation of the transition half-width and enthalpy to the zero heating rate yields values which are very close or practically coincide with equilibrium data. No such agreement is observed for the transition temperature.

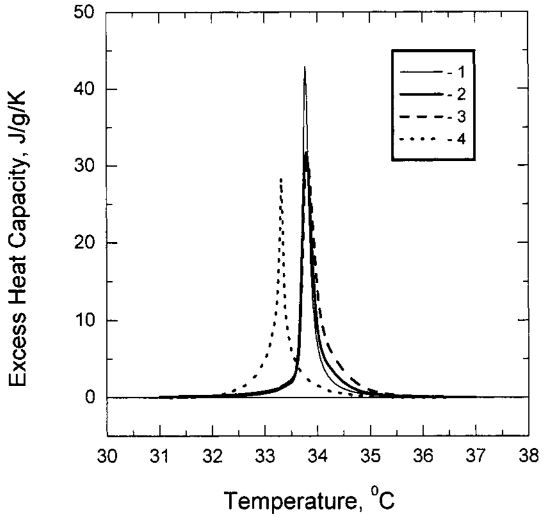

**Figure 2.** Excess heat capacities functions of the NIPA hydrogel coupled with the volume phase transition at different heating rates: 0.125 (1), 0.250 (2), and 0.500 (3) K/min. The equilibrium gel concentration at 20 °C is 4.6%. Curve 4 represents equilibrium data by Li and Tanaka.[19]

It is interesting to compare the dynamic effects and the dependence of phase transition characteristics on heating rate for the NIPA gels with similar characteristics for some biopolymer systems, as described in refs 26 and 27. On the one hand, the phase transition in NIPA gel exhibits certain similarity to kinetically controlled conformational transitions[26,27] in that the transition temperature dependence on heating rate is nonlinear. The fact is not only that changes in temperature are ahead of a response by the system but also that an increase in the heating rate affects the transition temperature differently, depending on the rate itself: the effect is strong at low rates and weak at high ones. On the other hand, there are also noticeable differences between NIPA gel phase transition and kinetically controlled transitions in biopolymers: while the transition enthalpy changes linearly with heating rate in the former, it is practically independent of the heating rate in the later.

## 4. Discussion

The NIPA gels with proper amount of cross-links undergo strong first-order-type collapse phase transition in response to the temperature increase.[19,29] As with other first-order phase transitions, kinetics of the gel collapse should be expected to proceed very differently depending on how fast the transition is triggered. The two extremes are to change the environment very slowly, adiabatically, or to use an instantaneous temperature quench. The former regime has been realized in the "equilibrium" experiments,[19] where temperature was changing gradually over a period of several days. There is every ground to believe that gels in that experiment were indeed equilibrated at each temperature. Not surprisingly, the calorimetric data for this regime agree well with predictions of the equilibrium theory. Indeed, the data presented in ref 19 support the expectation that gel collapse transition belongs to the 3*D* Ising universality class (see also eq 3). The later regime of the temperature quench is much less understood in general. Clearly, dynamics of the process is dramatically different depending on how far we quench the temperature behind the transition point. At moderate quenches, dynamics occurs via nucleation and growth mechanism; at stronger quenches, the so-called spinodal decomposition should be observed.

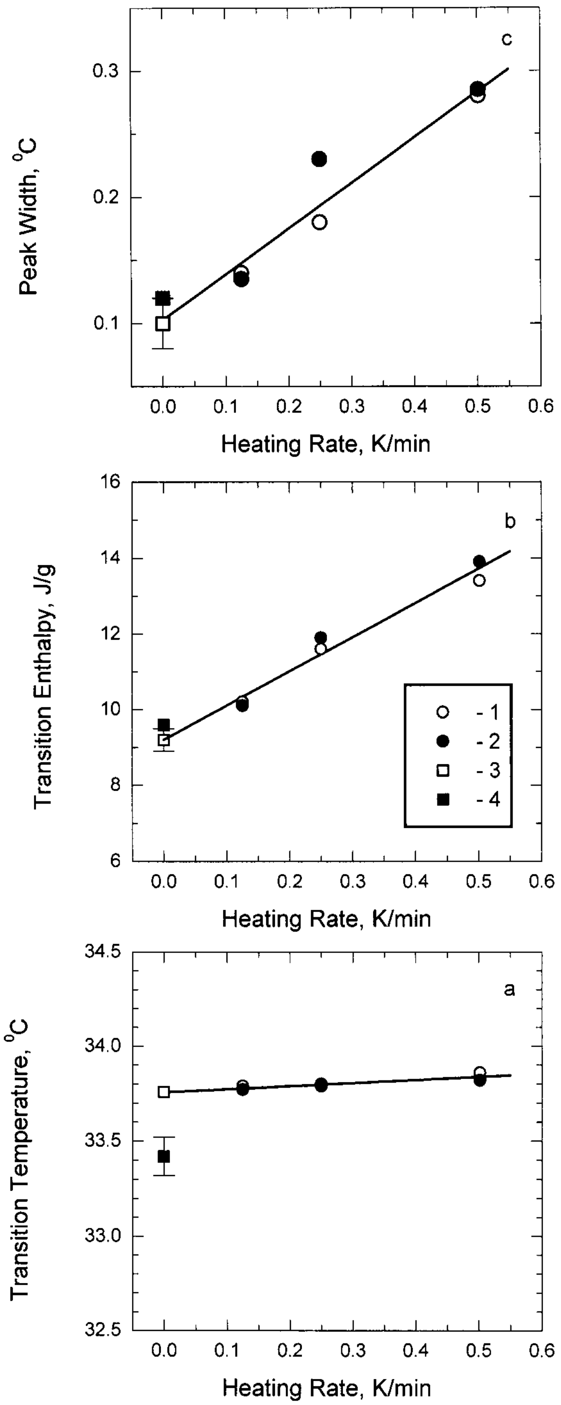

**Figure 3.** Parameters of the volume phase transition of the NIPA hydrogel against heating rate: 1, first scan; 2, second scan; 3, data from extrapolation to zero heating rate; 4, equilibrium data by Li and Tanaka.[19]

Speaking about gels, one has to keep in mind several serious complications which might affect dramatically the observed behavior. One aspect is that conformational transitions in the network subchains may occur faster than cooperative diffusion of the gel is able to establish the uniform density distribution. Another aspect has to do with the fact that gel network is always nonuniform, with the regions of higher and lower degrees of entanglements etc.

Considering our experimental data, one is tempted to speculate about the fact that the observed transition point becomes rate-independent when rate is fast enough—specifically, when it is faster than 0.125 K/min. One of the possibilities to explain this fact is to assume that the seemingly rate-independent observed transition temperature corresponds to the spinodal condition, where expanded state of the gel becomes locally unstable. Our understanding of spinodal decomposition in the gel, with an account made of the gel imperfections, inhomogeneities, and other poorly controlled structural features, are by far insufficient to make an quantitative theoretical statement and to explain further details of the observed calorimetric data. We are indebted to a reviewer for pointing out for another possible explanation, which is a possible calibration error of either the instrument used in this work or the one used in ref 19. Although this explanation seems unlikely because the results of both works are consistent in all other respects, we cannot rule it out completely.

Concerning the effect of heating rate on the calorimetric transition enthalpy, we can make the following argument. At low heating rate the gel has enough time to realize the necessary volume change by means of cooperative diffusion. Accordingly, what is measured by our calorimeter in this case is an isobaric heat effect of the volume phase transition, i.e., its true enthalpy. In contrast, at a high heating rate, phase separation of the gel progresses ahead of any significant volume change. Hence, what is measured under this condition is in effect a change in the internal energy rater than enthalpy. Since the transition is accompanied with the decrease of volume, it is not surprising that the heat effect measured at isobaric conditions appears less than that measured at isochoric conditions.

## 5. Conclusion

Studying the discontinuous volume phase transition of poly(*N*-isopropylacrylamide) hydrogels by high-sensitivity differential scanning microcalorimetry, measurements should be performed at heating rate not higher than 0.125 K/min to minimize perturbations related to the finite instrument response time and kinetics of the transition. The apparent transition enthalpy of the volume phase transition is an interesting function of heating rate.

**Acknowledgment.** The research described in this publication was made possible in part due to Award No. RC1-233 of the U.S. Civilian Research & Development Foundation for the Independent States of the Former Soviet Union (CRDF). N.V.G., V.Y.G., and E.E.M. also thank the RBRF Foundation (Grant No. 95-03-9474) for partial financial support.

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