Real-Time Temperature and Photon Transmission Measurements for Monitoring Phase Separation during the Formation of Poly(*N*-isopropylacrylamide) Gels

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ABSTRACT: Phase separation during the formation of poly(*N*-isopropylacrylamide) (PNIPA) hydrogels was investigated using real-time photon transmission and temperature measurements. The hydrogels were prepared by free-radical crosslinking polymerization of *N*-isopropylacrylamide (NIPA) in the presence of *N,N'*-methylenebisacrylamide (BAAm) as a crosslinker in an aqueous solution. The onset reaction temperature T_0 was varied between 20 and 28℃. Following an induction period, all the gelation experiments resulted in exothermic reaction profiles. A temperature increase of 6.5 ± 0.6℃ was observed in the experiments. It was shown that the temperature increase during the formation and growth process of PNIPA gels is accompanied by a simultaneous decrease in the transmitted light intensities I_{tr}. The decrease in I_{tr} at temperatures below the lower critical solution temperature of PNIPA was explained by the concentration fluctuations due to the inhomogeneity in the gel network. At higher temperatures, it was shown that the gel system undergoes a phase transition via a spinodal decomposition process. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 86: 3589–3595, 2002

Key words: hydrogels, phase separation; crosslinking; light scattering

INTRODUCTION

Hydrophilic gels, called hydrogels, are important materials of both fundamental and technological interest. The swelling behavior of hydrogels has been investigated repeatedly in the last four decades. In recent years, attention has turned to the swelling and collapse phenomena that are observed when a hydrogel network is brought into contact with a solvent. Poly(*N*-isopropylacrylamide) (PNIPA) gel is a typical temperature-sensitive gel exhibiting volume-phase transition at its lower critical solution temperature (LCST), which is approximately 34℃.[1,2] Below this temperature, the gel is swollen and it shrinks as the temperature is increased. The temperature sensitivity of PNIPA gels has attracted great attention in the last years due both to fundamental and technological interests.[3–6] These materials are useful for drug-delivery systems, separation operations in biotechnology, processing of agricultural products, sensors, and actuators.

PNIPA hydrogels have been prepared by free-radical crosslinking copolymerization of the *N*-isopropylacrylamide (NIPA) monomer with *N,N'*-methylenebisacrylamide (BAAm) as a crosslinker in aqueous solutions. It is worth noting, however, that a reproducible synthesis of PNIPA gels is difficult to achieve.[7–11] This is probably due to the LCST of the PNIPA chains, which is close to the usual polymerization temperatures. One may expect that the kinetic events of free-radical crosslinking copolymerization may cause a local or overall temperature increase in the reaction system above the LCST, resulting in a phase separation and formation of heterogeneous structures.[12] Indeed, depending on the heat-transfer characteristics of the synthesis molds, PNIPA gels prepared from the same monomer solution exhibit conflicting physical properties.[8,10] For example, the nature of the temperature-induced volume-phase transition in PNIPA gels has been reported as both continuous[8,13,14] and discontinuous.[1,6]

An *in situ* photon transmission study for aging in polyacrylamide (PAAm) gels due to multiple swelling was recently reported by our laboratory,[15] where it was observed that the transmitted light intensity I_{tr} decreases continuously as the PAAm gel swells. The decrease in I_{tr} was attributed to an increase in the scattered light intensity, which originated from the concentration fluctuations in the swollen gel.

In this work, *in situ* real-time photon transmission and temperature measurements are reported for the free-radical crosslinking copolymerization of NIPA
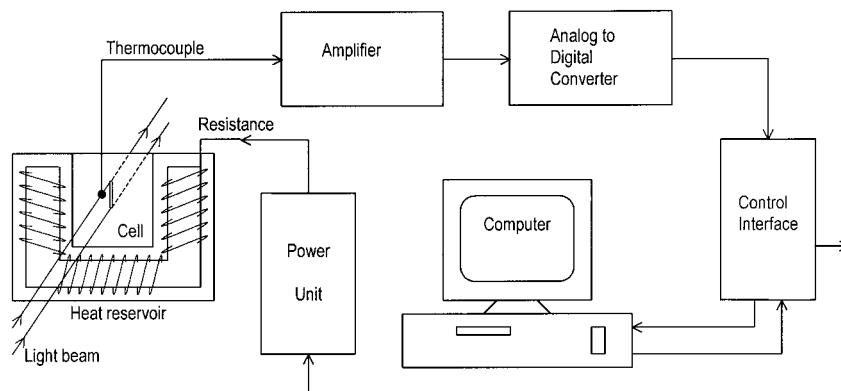

Figure 1 Experimental apparatus for real-time temperature and photon transmission measurements during the formation of PNIPA gels.

with BAAm as a crosslinker at various onset reaction temperatures and crosslinker contents. For this purpose, a special experimental setup was designed, which allowed us to monitor both the I_{tr} and temper-

ature from a small-volume element of the reaction system as a function of time. As will be shown below, the exothermicity of crosslinking NIPA polymerization and the resulting phase separation were verified
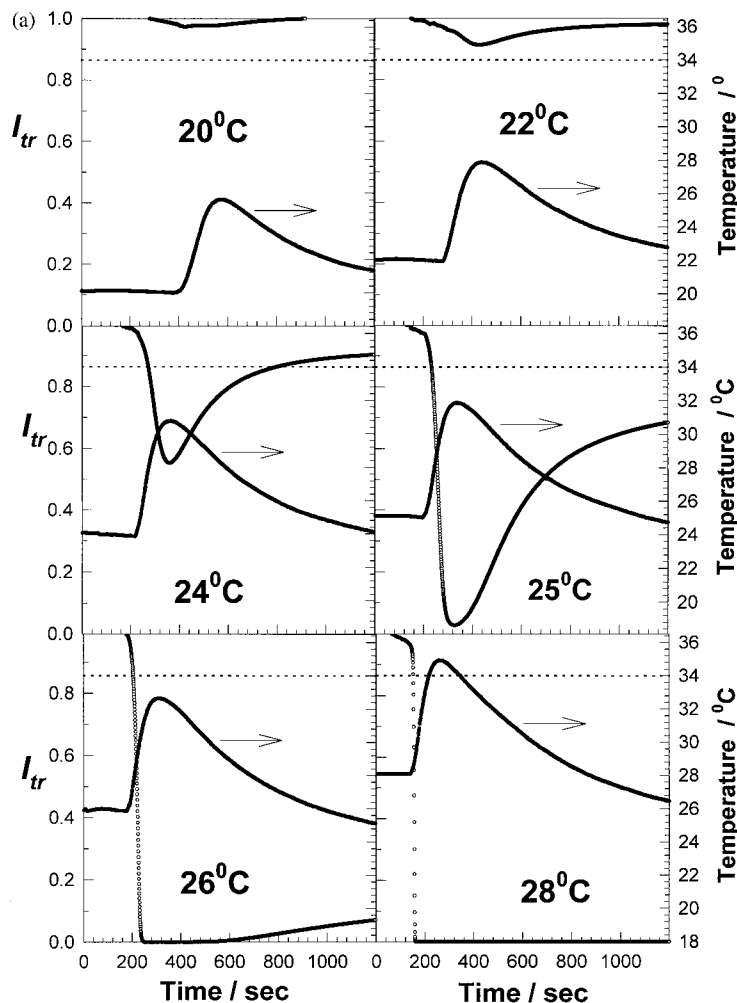

Figure 2A Variations of the transmitted light intensity I_{tr} and the temperature versus reaction time during the crosslinking copolymerization of NIPA and BAAm. The onset reaction temperatures T_0 are indicated in the figure. The dotted horizontal lines show the LCST of PNIPA. BAAm mol % = 2.

by the experiments. It was observed that I_{tr} decreases drastically even at temperatures below the LCST of PNIPA chains. A decrease in I_{tr} due to an increase in the scattered light intensity indicates spatial-phase separation, which appears during the formation of PNIPA gels due to the gel inhomogeneities.

EXPERIMENTAL

The free-radical crosslinking copolymerization of NIPA (Merck, Germany) was carried out using BAAm (Merck) as a crosslinker in aqueous solution. The initial monomer concentration was kept constant at 6.9 w/v %, while the onset reaction temperature T_0 and the crosslinker (BAAm) content were varied separately. Ammonium persulfate (APS; Merck) and N,N,N',N'-tetramethylethylenediamine (TEMED; Merck) were, respectively, the initiator and the accelerator.

The polymerization reactions were performed in glass cells, which were placed in a Perkin–Elmer UVV spectrometer. During the course of the reactions, the transmitted light intensity at 450 nm and the temper-

ature were recorded simultaneously from a reaction volume of less than 0.1 mL. For this purpose, a special setup was designed, as schematically shown in Figure 1. A mixture of 3 g of NIPA, 75 mg of APS, and various amounts of BAAm (75, 90, and 110 mg) was first dissolved in 45 mL of deionized and distilled water. After bubbling nitrogen through the solution, 6 mL of this solution was poured into a 30×22-mm glass cell of 13-mm path length. Thereafter, the glass cell containing the reaction components except the accelerator TEMED was placed into the water bath of the spectrometer.

The temperature of the water bath was computer-controlled with an accuracy of $\pm 0.1^0$C. The temperature of the reaction solution was measured at a single point near the center of the cell with a thermocouple. The distance between the location of the thermocouple in the solution and the path of the incident light was less than 3 mm. This provided the measurements of both the light intensity and the temperature in a small-volume element of the reaction system (less than 0.1 mL). Moreover, stirring of the reaction solution during the heating process provided temperature homogene-
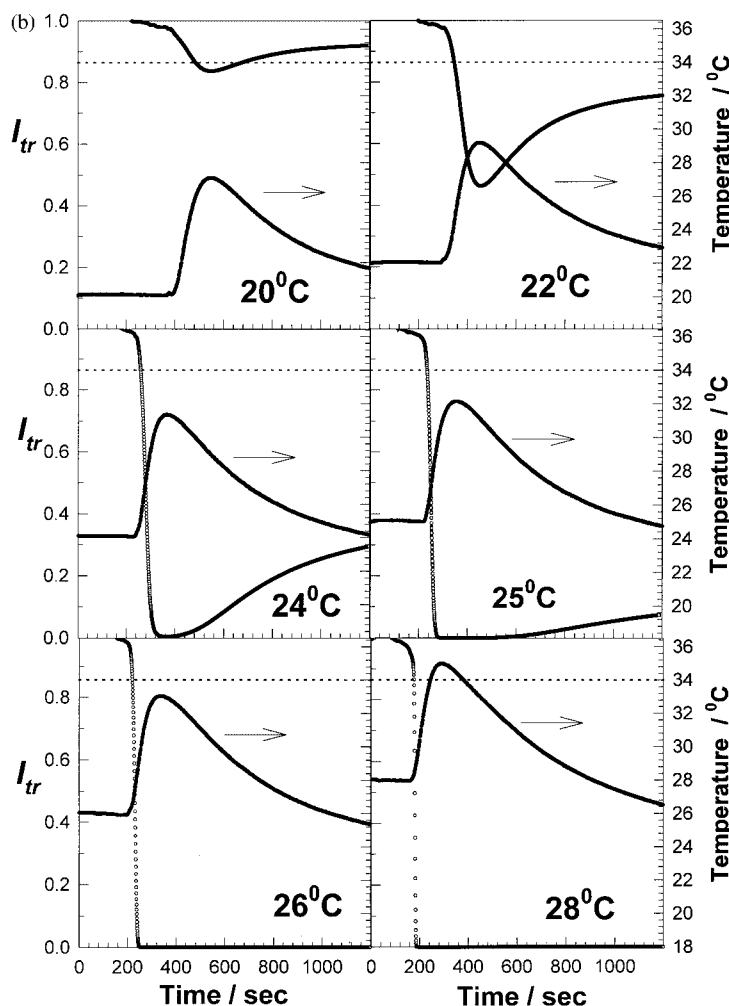

Figure 2B BAAm mol % = 3. (*Continued from the previous page*)

ity in the cell volume. After the cell content attained thermal equilibrium with the surrounding heat reservoir, 20 μL of TEMED was added into the reaction solution and the solution was stirred further for a few seconds. In our experiments, we always observed an induction period ranging from 2 to 7 min prior to the polymerization. During this period, the temperature of the reaction system was kept constant at $T_0 \pm 0.1$ by the heating of the reaction system. As long as the temperature starts to increase, the heating was switched off.

During the crosslinking copolymerization of NIPA, the transmitted light intensities were measured in real time using the time-drive mode of the spectrometer at a 450-nm wavelength. Simultaneously, the temperature of the system could be recorded every second. The timing of both the light intensity and temperature measurements was computer-controlled. In the following, the transmitted light intensities are given in terms of the normalized intensities I_{tr} with respect to the intensity at zero polymerization time.

RESULTS AND DISCUSSION

In Figure 2(A,B), the normalized transmitted light intensity I_{tr} and the temperature T are plotted as a function of the reaction time t for the reaction solutions containing 2 and 3 mol % of the crosslinker, respectively. The onset reaction temperatures T_0 were varied between 20 and 28^{0}C, as indicated in the figures. The LCST of PNIPA (34^{0}C) is also shown in the figures by the horizontal dotted lines. By all the gelation experiments, the temperature of the solution remained initially constant. This initial constant temperature period is the induction period of the polymerization. The induction time was calculated as the time period from the addition of TEMED into the solution until the start of the temperature increase. The induction times recorded for three different crosslinker contents are shown in Figure 3, plotted as a function of the onset temperature T_0. The induction time decreases almost linearly from 7 to 2 min as T_0 increases from 20 to 28^{0}C. Figure 3 also indicates that the induction time is almost independent of the crosslinker concentration of the feed.

Following the induction period, all the gelation experiments resulted in exothermic reaction profiles (Fig. 2). The temperature of the reaction system increases sharply with time, attains a maximum value, and then decreases continuously at longer reaction times, due to dissipation of the reaction heat to the surroundings. By separate experiments, we measured the reaction times for the onset of gelation in the reaction systems, as described previously.[16] We observed that the macrogelation in these gelling systems occurs at reaction times corresponding to the lower-left shoulder of the temperature peaks shown in Fig-

ure 2. This reveals that the temperature increase in NIPA polymerization is caused by the exothermic polymerization reactions as well as by the reduction of the termination rate constants due to the gel effect.

The maximum temperatures attained during the polymerization (T_{max}) corresponding to the peaks of the temperature versus time plots in Figure 2 are collected in Figure 4 as a function of the onset temperature T_0 for various crosslinker contents. The dotted line in Figure 4 represents the relation $T_{max} = T_0$, which would result in the case of athermal reactions. It is seen that T_{max} increases almost linearly with the onset temperature T_0. For onset temperatures $T_0 < 25^0$C, T_{max} is a slightly increasing function of the crosslinker content, whereas at higher T_0 values, T_{max} is independent of the crosslinker content. The increase of T_{max} with increasing crosslinker content at low onset temperatures is probably due to the simultaneous increase of the reaction rates,[16,17] which reduces the amount of heat dissipating from the cell to the surroundings. Moreover, the distance between the data points and the dotted line in Figure 4 corresponds to the largest temperature difference ΔT_{max} attained during the reaction. An average value of $\Delta T_{max} = 6.5 \pm 0.6^0$C was found by all the gelation experiments. Huglin and coworkers recorded similar ΔT_{max} values for the homopolymerization of NIPA, when carried out in vials of 25-mm diameter.[10] However, when the reactions were carried out in molds of 3-mm thickness, no temperature increase was observed by the same authors.[10] This means that the extent of the temperature increase strongly depends on the heat-transfer characteristics of the reaction vessel. Reaction heat generated in the glass cells of 13-mm thickness seems to be sufficient to increase the temperature of the reaction solution up to the LCST of PNIPA. Compared to the NIPA polymerization, acrylamide (AAm) polymerization leads to a temperature increase of only 1^{0}C, indicating that the NIPA polymerization is much more exothermic than is the AAm polymerization.[10] Indeed, the reaction enthalpies were reported to be 100 and 77.5 kJ/mol for NIPA and AAm polymerizations, respectively.[10] It must be noted that, in our gelation experiments, the distance between the location of the thermocouple in the reaction solution and the path of the incident light was less than 3 mm. Considering that the thermal conductivity of gels is very small, the temperatures reported in this work may be slightly lower than the actual temperature on the light path.

Figure 2 also shows that the temperature increase during the gel formation and growth process is accompanied by a simultaneous decrease in the transmitted light intensities I_{tr}. The time at which the temperature reaches a maximum value corresponds to the time at which I_{tr} becomes a minimum. This is a direct evidence that the appearance of turbidity in PNIPA gels is due to the exothermic nature of their formation
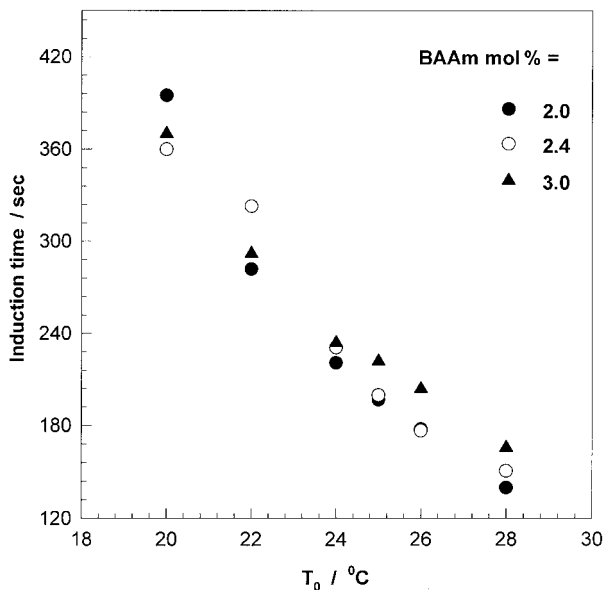
Figure 3 Induction time shown as a function of the onset reaction temperature T_0. The crosslinker contents are indicated in the figure.

process as well as due to the poor heat-transfer characteristics of the reaction vessels. The higher the temperature of the reaction system, the lower the I_{tr} intensities. Interestingly, even at temperatures below the LCST, I_{tr} decreases rapidly during the reactions. This is clearly seen in Figure 2 for onset temperatures below 25^0C, for which the maximum temperature remains below 31^0C. Another interesting point shown in
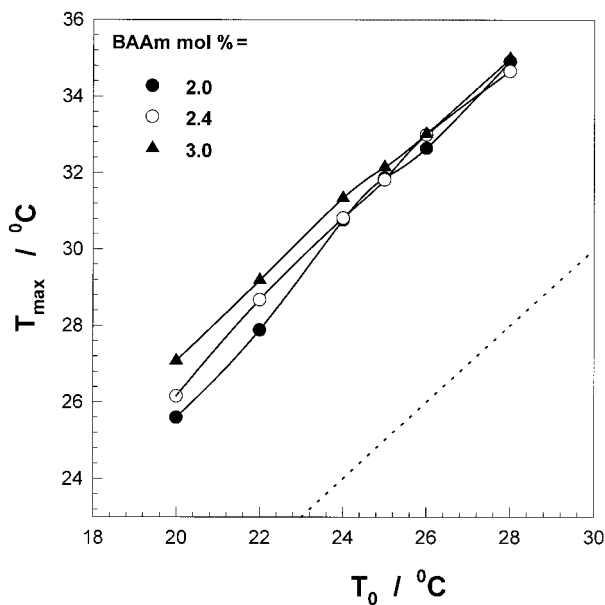

Figure 4 Maximum temperatures attained during the polymerization T_{max} is shown as a function of the onset temperature T_0 for various crosslinker contents. The solid curves only show the trend of the data. The dotted line represents the relation $T_{max} = T_0$.
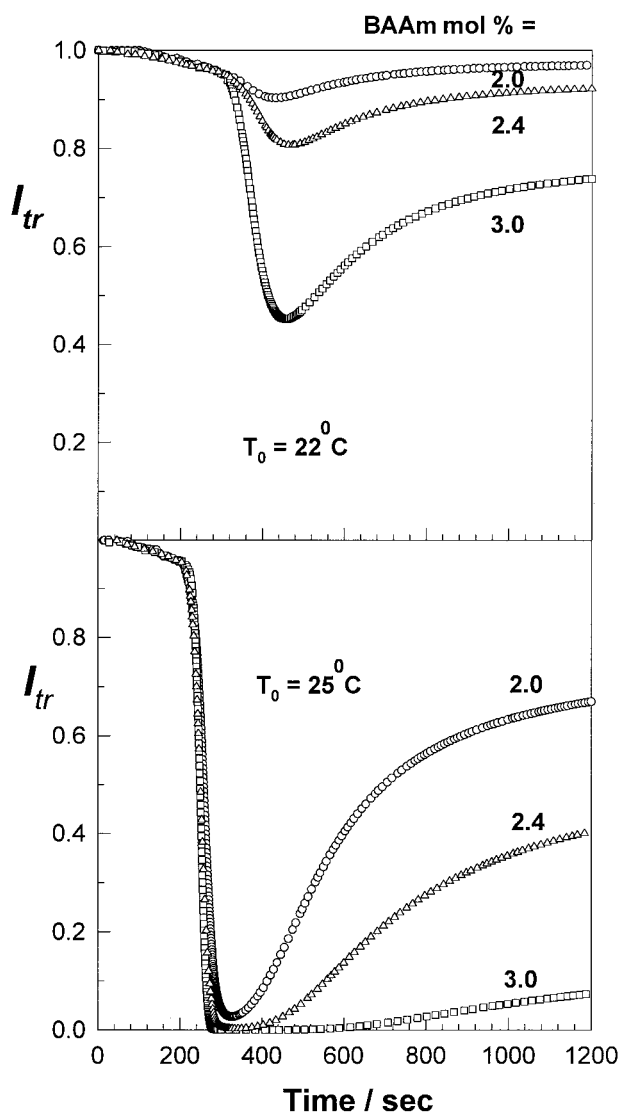

Figure 5 Transmitted light intensities I_{tr} shown as a function of the reaction time of crosslinking copolymerization of NIPA and BAAm. The onset reaction temperatures T_0 and the crosslinker contents are indicated in the figures.

Figure 2 is that, at onset reaction temperatures T_0 above 25^0C, I_{tr} attains a limiting value after a given reaction time, indicating formation of permanent turbidity in the final PNIPA gels. However, if the onset temperature is below 25^0C, I_{tr} starts to increase again at longer times, indicating that the turbidity that appeared due to the temperature increase disappears again as the system cools down later. Comparison of Figure 2(A,B) also shows that the amount of the crosslinker present during the gel-formation process influences drastically the I_{tr} intensities. Figure 5, showing the reaction time dependence of the I_{tr} intensities for three different crosslinker contents, indicates that the decrease in I_{tr} with time becomes more abrupt as the crosslinker concentration increases.

In Figure 6, the rates of change in I_{tr} with time $(-dI_{tr}/dt)$ for 2 and 3 mol % crosslinker samples are
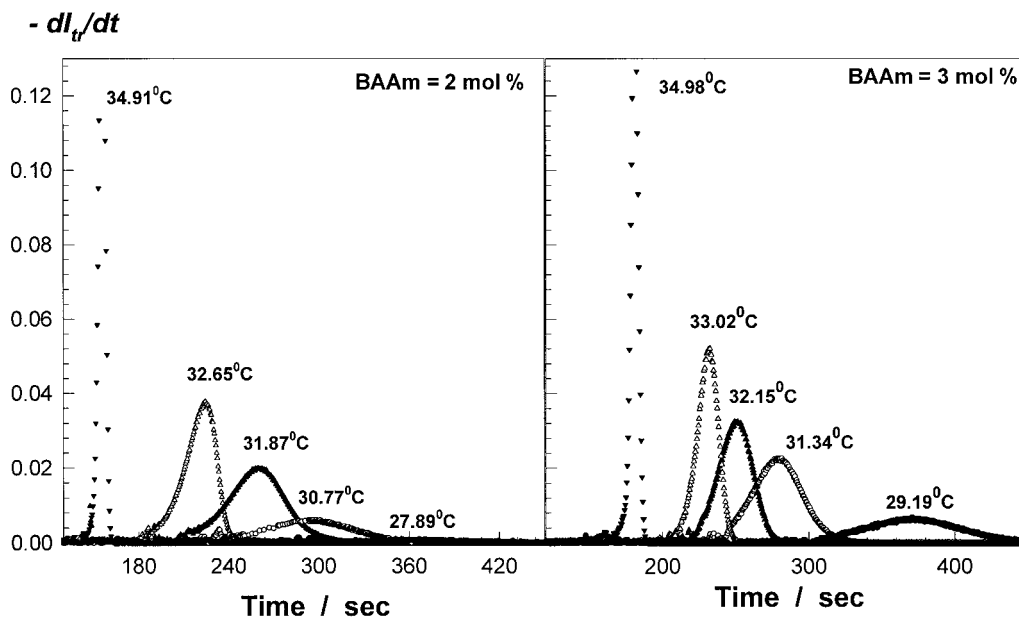
Figure 6 Rate of change in I_{tr} with time ($-dI_{tr}/dt$) for 2 and 3 mol % crosslinker samples shown as a function of the reaction time of crosslinking copolymerization of NIPA and BAAm for various onset temperatures. The onset reaction temperature = ($\bullet$) 22, ($\bigcirc$) 24, ($\blacktriangle$) 25, ($\triangle$) 26, and ($\blacktriangledown$) 28^{0}C. The maximum temperatures attained during the reactions are indicated in the figures.

plotted against the reaction time t for various onset temperatures. The maximum temperatures attained during the reactions are indicated in the figures. The peaks of these dependencies correspond to the inflection points in the I_{tr} versus time data of Figure 2 and give maximum rates $(-dI_{tr}/dt)_{max}$ on the y-axes. $-(dI_{tr}/dt)_{max}$ values calculated for three crosslinker samples are collected in Figure 7 as a function of the maximum temperature T_{max}. $-(dI_{tr}/dt)_{max}$ increases first slightly, then rapidly around the LCST of PNIPA. The dependence represents a power-law behavior, which typically gives evidence for critical phenomena. These observations are in accord with the light-scattering measurements of Matsuo et al. on PNIPA gels.[18] They also reported that the spatial fluctuations of scattered light intensity drastically increase around T_0 = 28^{0}C. According to Figure 4, this onset temperature corresponds to a maximum temperature slightly above the LCST of PNIPA.

Our experimental data consisted of the following scenario: When the polymerization is initiated by the decomposition of APS and TEMED molecules, the primary radicals formed start to grow by adding the monomer NIPA and the crosslinker BAAm. In comparing the reactivities of the monomers NIPA and BAAm in free-radical copolymerization, BAAm reactivity is at least twice the NIPA reactivity due to the existence of two vinyl groups on each BAAm molecule. Therefore, the molecules formed earlier should contain more BAAm units and, therefore, should be more highly crosslinked than those formed later.[19,20] PNIPA gels can thus be assumed to consist of lightly

crosslinked and highly crosslinked regions. The existence of these kinds of regions is known as inhomogeneities.

If the temperature of such a partially formed, inhomogeneous PNIPA gel is increased rapidly from T_0 to various T_{max} below the LCST, the loosely crosslinked regions can adjust their orientation to fit a new equilibrium. However, the highly crosslinked regions require much more time to reorganize. The difference in the relaxation time of various gel regions results in the density fluctuations along the gelling system, which scatter light and decrease the I_{tr} intensities. Further polymerization and crosslinking reactions fix these fluctuations in the final hydrogel. The observed decrease in I_{tr} at temperatures below the LCST can thus be explained with the concentration fluctuations due to the inhomogeneity within the gel network. Moreover, an increasing crosslinker content is known to increase the degree of inhomogeneity in PNIPA gels.[21] As a consequence, the I_{tr} intensities decrease further with an increasing crosslinker content of the feed (Fig. 5).

The rate of change in I_{tr} with time corresponds to the growth rate of phase-separated domains in the reaction system. As seen in Figures 6 and 7, the growth rate of domains is slow if T_{max} is less than the LCST, whereas it becomes rapid if T_{max} exceeds the LCST. This indicates that, if the temperature of the gel-forming system exceeds the LCST, as in the case of the experiments carried out at T_0 = 28^{0}C, a different mechanism of phase separation is operative in the PNIPA gels. In these experiments, the sample temper-
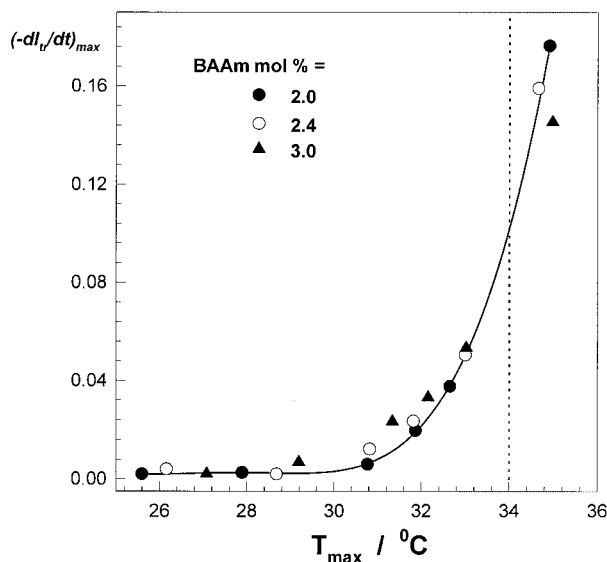
Figure 7 Maximum rates $(-dI_{tr}/dt)_{max}$ calculated for three crosslinker samples shown as a function of the maximum temperature T_{max}. The vertical dotted line represents the LCST of PNIPA

ature increases from T_0 to various temperatures above the LCST within 1 min, due to the exothermicity of the polymerization reactions (Fig. 2). During this heating process, the interior of the gel system remains under a constant volume condition due to the slowness of the volume change of the macroscopic gel samples near the critical point.[22] As a result, the gel system undergoes a transition from the one-phase to the two-phase coexistence state along the critical isochore path via a spinodal decomposition process.[23,24] The changes in I_{tr} and the corresponding derivative $-dI_{tr}/dt$ with time for samples with $T_0 = 28^0C$ give an indication of the different stages of the spinodal decomposition process (Figs. 2 and 6). During the early stage, I_{tr} decreases very slowly. In the intermediate stage, I_{tr} decreases rapidly due to the formation and growth of domains, which gives an increase to the peak in the derivative plot (Fig. 6). After the transition stage, I_{tr} becomes saturated, which implies that the domains have reached equilibrium concentration.

CONCLUSIONS

Phase separation during the formation of PNIPA hydrogels was investigated using real-time photon trans-

mission and temperature measurements. The hydrogels were prepared by the free-radical crosslinking polymerization of NIPA in the presence of BAAm as a crosslinker in an aqueous solution. The onset reaction temperature T_0 was varied between 20 and 28^0C. Following an induction period ranging from 2 to 7 min, all the gelation experiments resulted in exothermic reaction profiles. A temperature increase of 6.5 ± 0.6^0C was observed in the experiments. It was shown that the temperature increase during the formation and growth process of PNIPA gels is accompanied by a simultaneous decrease in the transmitted light intensities I_{tr}. Even at temperatures below the LCST, I_{tr} decreased rapidly during the reactions. The decrease in I_{tr} below the LCST was explained by the concentration fluctuations due to the inhomogeneity in the gel network. At higher temperatures, it was shown that the gel system undergoes a phase transition via a spinodal decomposition process.

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