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Swelling and deswelling pathways in non-ionic poly(*N*-isopropylacrylamide) hydrogels in presence of additives ☆

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Abstract

The behaviour of deswollen (D) and equilibrium swollen (S) non-ionic poly(*N*-isopropylacrylamide) (PNIPA) hydrogel samples in aqueous hydroxides and chlorides of Na and K are investigated. The samples respond in dramatically different styles to increasing concentrations of the additive in the external aqueous medium. Both samples exhibit volume phase transition at additive concentrations characteristic of the anion. Thereafter, if left undisturbed in the same medium, the D samples shrink with increasing concentrations of the additive, while the S samples in a critical concentration range initially shrink to an opaque mass, then develop a lump on the surface which eventually turns into a clear transparent bubble. The bubble wall is permeable and the size and shape stable for months implying the contents within are in osmotic equilibrium with the external fluid. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Poly(*N*-isopropylacrylamide); Hydrogels; Swelling and deswelling pathways

1. Introduction

Sharp volume phase transitions in certain polymeric hydrogels brought about by small changes in solvent composition [1–6], temperature [1,6–9], pH [10], ionic composition [10], or by application of electric field across the gel [11] have been extensively investigated in recent years. Most of these hydrogels are derivatives or copolymers of acrylamide. Each hydrogel system has its own unique chemistry, which in a large measure decides its swelling and deswelling characteristics. For instance, there is a general consensus that the volume phase transition observed in poly(*N*-isopropylacrylamide) (PNIPA) hydrogels, is due to the amphiphilic nature of the monomer unit itself. On one hand the hydrophilic nature of the –C=O and –N–H groups are well documented, while the hydrocarbon backbone and the pendent isopropyl groups are hydrophobic. Just as the delicate balance of hydrophilic and hydrophobic interactions leads to a stable tertiary structure for the proteins, such forces may be operative in PNIPA polymers. The H-bonding ability of –C=O and –N–H groups could be instrumental in stabilising a chain conformation in PNIPA below LCST in which polymer–water interactions predominate over polymer–polymer interactions. This has been indicated by a variety of studies of widely different experimental approaches such as influence of additives [12–15], influence of comonomer [16,17], effect of mixed solvent systems [18–20], determination of solvent chemical potential [21], Differential scanning calorimetry [22], fluorescence spectroscopy [23–25], dynamic light scattering [26], EPR [27]. The results are in conformity with the general hypothesis that a decrease in the solvent quality of water (caused by an increase in the ambient temperature or the presence of additives), could deplete the number of solvating water molecules around the polymer chain. The hydrophobic groups thus exposed would tend to aggregate forcing the polymer chain into a new conformation in which polymer–polymer interactions are dominant. The abruptness of the transition is indicative of a co-operative mechanism.

While investigating swelling and deswelling of PNIPA hydrogels in aqueous alkali, we recorded several dissimilarities between the two pathways. Significant among these is the unusual yet perfectly reversible pattern formation along the deswelling pathway, right after the volume phase transition. Such phenomena have so far been observed mostly in ionic hydrogels brought about by variations in the ambient temperature or solvent composition [8,28–30]. Matsuo and Tanaka [28] have reported that variation in acetone–water composition during shrinking can induce pattern formation in cylindrical acrylamide–sodium acrylate copolymer gels. Earlier they observed pattern

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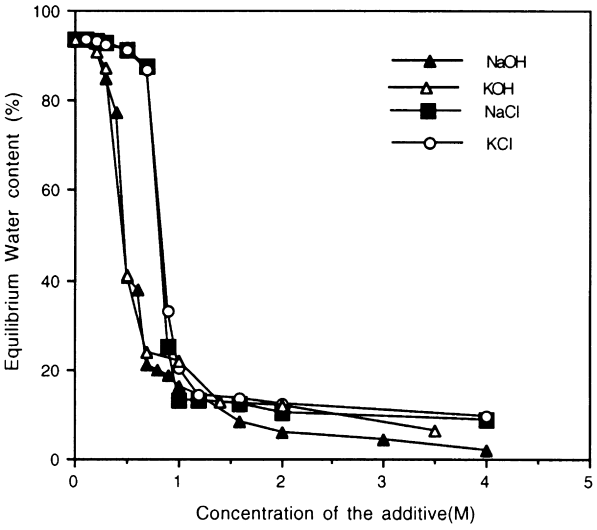

Fig. 1. Additive induced volume phase transition in D samples.

formation in spherical beads of NIPA–sodium acrylate copolymer gels [8].

Here we compare the behaviour of deswollen and swollen non-ionic PNIPA gels in aqueous solutions of the hydroxides and chlorides of sodium and potassium and for the first time report the occurrence of anion induced pattern formation in pure non-ionic PNIPA hydrogels.

2. Experimental

2.1. Materials

N-isopropyl acrylamide (NIPA) from Eastman Kodak was recrystallised from hexane, *N*,*N*′-methylenebisacrylamide (BIS), ammonium persulphate (APS) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) special

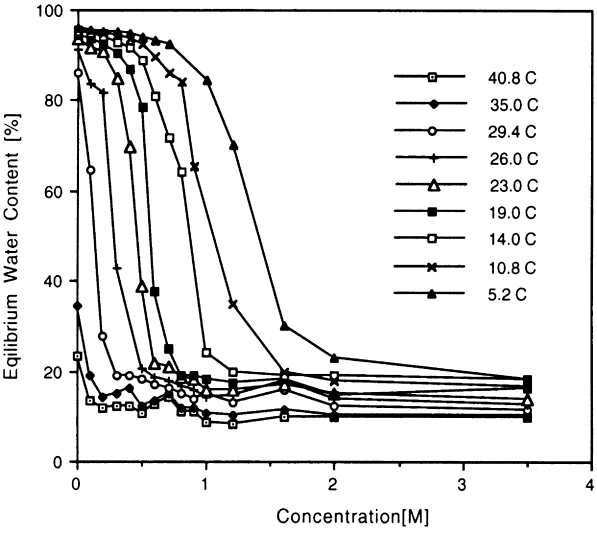

Fig. 2. Swelling of D samples in NaOH at different temperatures.

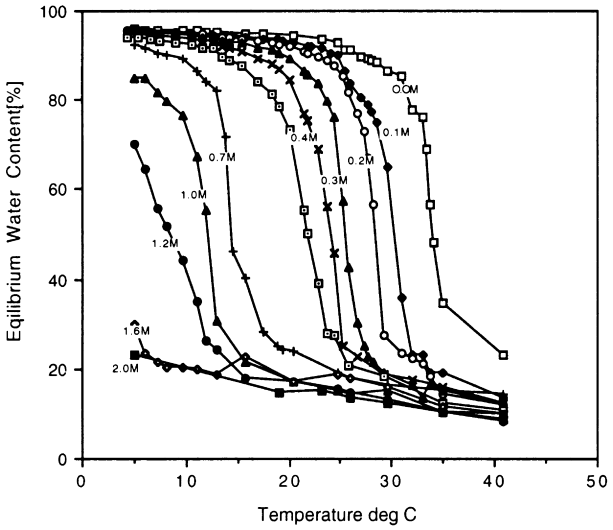

Fig. 3. Swelling of D samples as a function of temperature at different NaOH concentrations.

grade from SRL and Loba, Bombay, were used without further purification. All other chemicals and solvents were of analytical grade. Double distilled water was used for all the experiments.

2.2. Preparation of hydrogel discs

PNIPA gels were prepared by free radical polymerisation in water by following the usual procedure [14] at an ambient temperature of 24–25°C. A total of 7.786 g NIPA and 0.214 g BIS were dissolved in 100 ml double distilled water. As redox indicator 50 mg APS and 50 μl TEMED were added, the well-stirred mixture was poured between two siliconised glass plates separated by Teflon gasket (0.6 cm thickness). The gelled slab was dislodged carefully and punched into circular discs with a cork borer. Some of

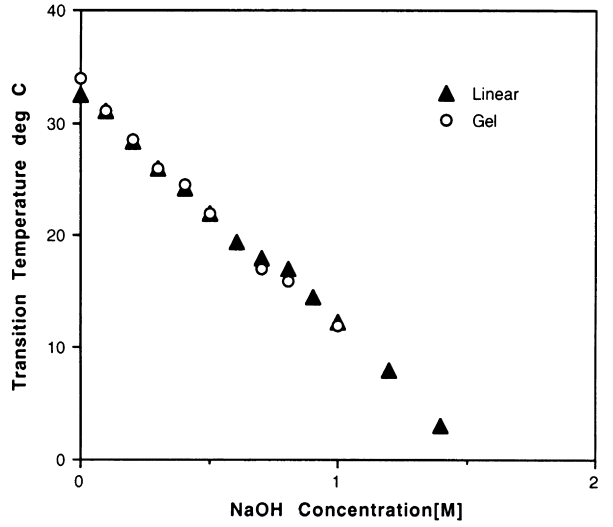

Fig. 4. Dependence of transition temperature on NaOH concentration for crosslinked and uncrosslinked PNIPA.

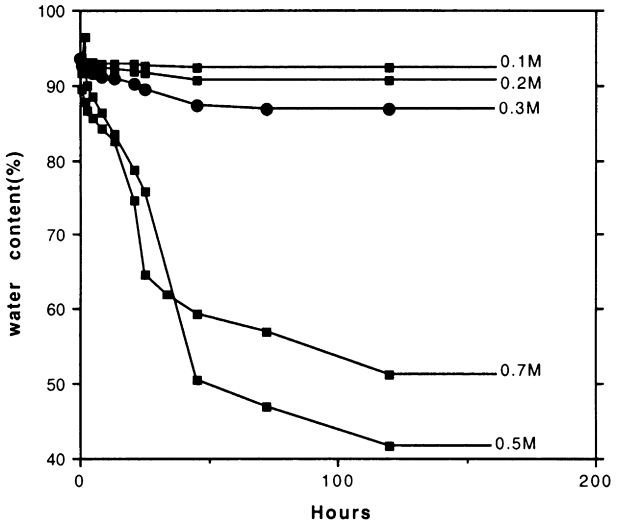

Fig. 5. Deswelling of S samples in dilute aqueous NaOH.

the discs were washed extensively with distilled water and dried at room temperature to constant weight (D samples). The rest of the samples were allowed to swell to equilibrium in water (S samples). Cylindrical and spherical gels were prepared by polymerising the pregel solution (as mentioned above) in respective glass moulds.

2.3. Swelling and deswelling studies

Temperature dependent studies, were carried out in a thermostatted water bath and all other studies were carried out at an ambient temperature of 24–25°C. In a typical experiment weighed samples were introduced into the required medium. At regular intervals the discs were removed from the solvent, the excess surface solvent blotted with a tissue paper, weighed and returned to the medium. This process of swelling and weighing was continued until the discs attained constant weight.

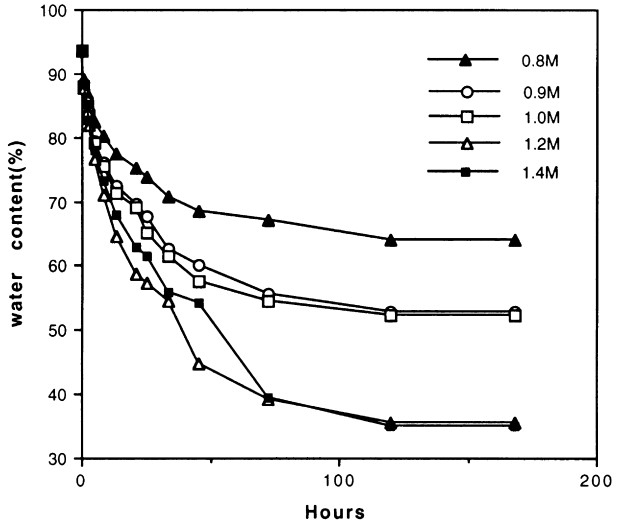

Fig. 6. Deswelling of S samples in 0.8–1.4 M aqueous NaOH.

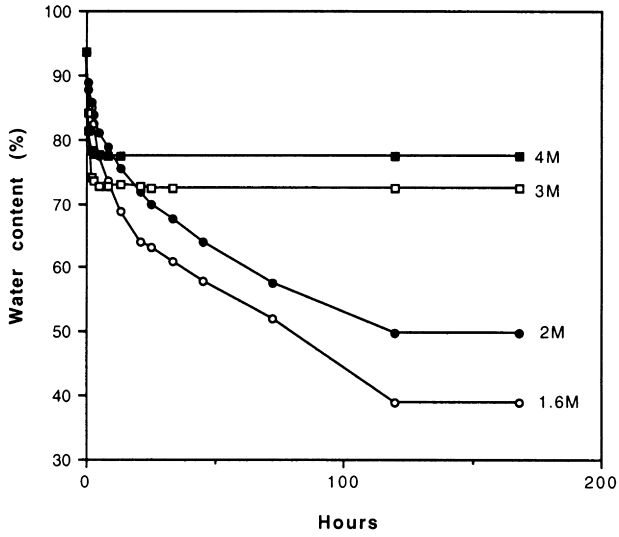

Fig. 7. Deswelling of S samples in concentrated aqueous NaOH.

For deswelling experiments the above process was reversed i.e. from swollen state to constant final weight. For the lower concentration of additive solutions the discs were immersing, but in an intermediate concentration range the discs were floating and they were allowed to float sidewise so that negligible portion of the discs is in contact with air. For further higher additive concentration the floating discs were constantly turned around. The water content of the gels was calculated on the basis of the dry and the equilibrium swollen weight [31,32]:

$$\text{Water content}(\%) = \frac{w_s - w_d}{w_s} \times 100$$

where w_s is the equilibrium swollen weight, and w_d the dry weight of the sample. The measurements were done in duplicate, since variations were negligible average values were taken.

2.4. Synthesis of linear PNIPA

NIPA was polymerised according to the method of Park and Hoffman [14] in toluene/terahydrofuran mixture (75/25, v/v) with azobis(isobutyronitrile) (AIBN) as an initiator at 60°C for 24 h. (mol. wt $\sim 10^4$).

2.5. Methods

The cloud point of linear PNIPA in NaOH solutions was determined by reading transmittance at 550 nm using a UV–Vis spectrophotometer (Perkin–Elmer UV–Vis spectrophotometer model Lambda 2]. For this PNIPA (1% w/v) was dissolved in a given NaOH solution at 4°C. The cell holder in the spectrophotometer was maintained at the required temperature by circulating water from a thermostat. The temperature was gradually raised from 4.0 to 40.0°C and the transmittance was recorded. The cloud point is taken as the temperature which registered 50%

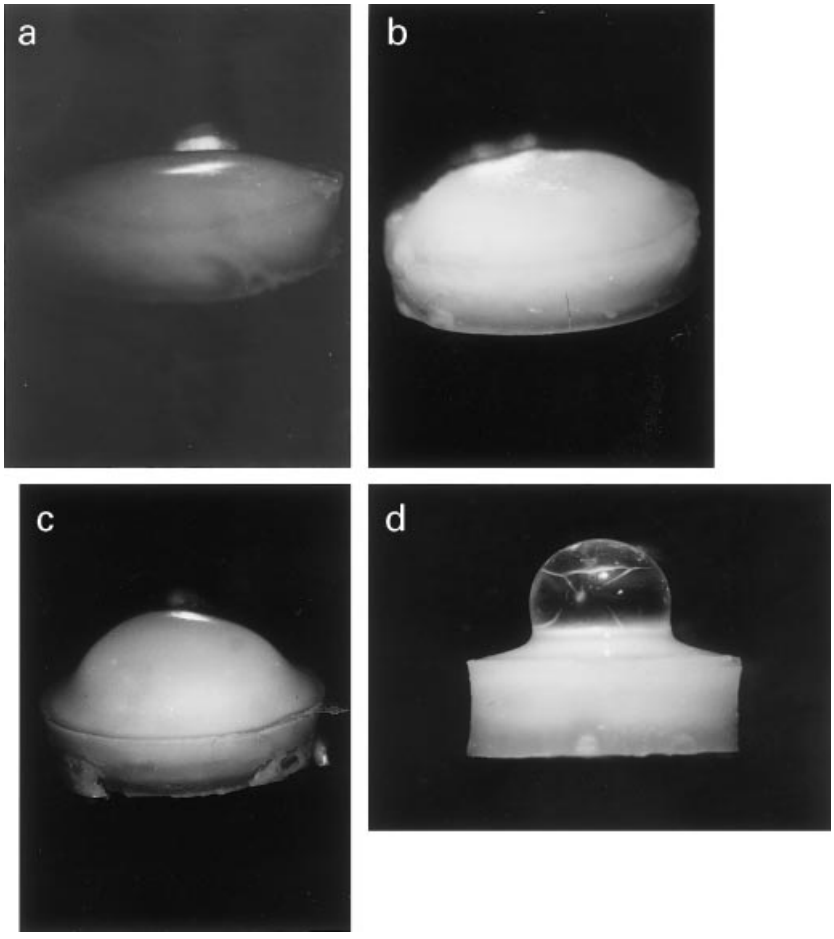

Fig. 8. Development of bubble when S sample is placed in aqueous 1 M NaOH at room temperature. (a) 13 h—the swollen sample becomes an opaque disc. (b) 21 h—a small lump appears on top. (c) 25 h—lump grows in size. (d) 34 h—the fully formed bubble.

decrease in transmittance. ^{1}H NMR spectra were produced on a Gemini 200 MHz spectrometer in D_2O. IR spectra were run on a Perkin–Elmer model 12C FTIR instrument. GPC was run on a Shimadzu unit, fitted with an RI detector using a Waters 100, 500 and 10^3 Å styragel columns connected in series, at a flow rate of 1.0 ml/min and THF was used as eluent.

3. Results and discussion

3.1. Volume phase transitions in D and S samples in aqueous solutions of NaOH, KOH, NaCl and KCl

Park and Hoffman [14] were the first to demonstrate that aqueous NaCl can induce volume phase transition in non-ionic PNIPA hydrogels. They monitored the effect of a series of sodium salts and concluded that the Cl^- ion is responsible for bringing about this transition. Several reports [12–15] have appeared on the effect of additives on the volume phase transition in pure non-ionic PNIPA hydrogels. Saito et al. [33] tried to extend the theory further by alluding to the primary and secondary water clusters. It is suggested that hydrophobic interactions outweigh the hydrophobic hydration as the salt concentration in the aqueous medium increases.

For the first time we report similar phenomenon in PNIPA hydrogel samples exposed to increasing concentrations of NaOH, KOH and KCl solutions at room temperature (Fig. 1). In hydroxides the samples register volume phase transition around 0.5 M whereas in chlorides, this transition occurs around 0.8 M. This reconfirms the observation of Park and Hoffman [14] that the transition is dependent not on the cation but on the anion and roughly on its position in the Hofmeister series. For instance in the series of alkali halides, the efficiency of lowering T_t follows the ranking $I < Br < Cl < F$ while remaining independent of the cation. The essential difference between an anion and a cation could be in the manner in which they interact with water. Although there are some qualitative disagreements, most experimental techniques which do not depend on specific ion(s) induced effects, show that water structure should be dependent on both the anion and the cation. However if we consider that central to water structure formation is the interaction of the amide group of the polymer with the anion then the issue is settled. Because anions have more

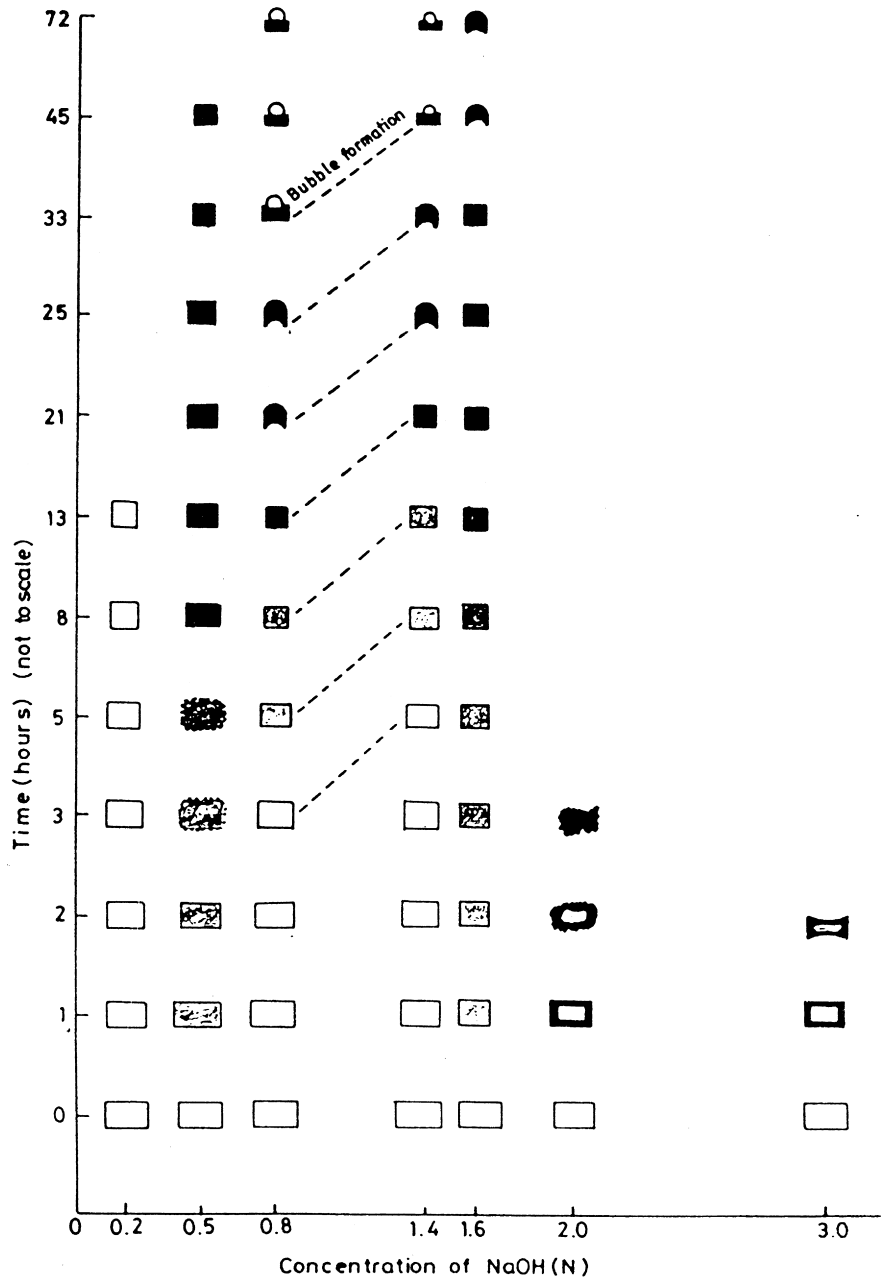

Fig. 9. Schematic diagram of the process of deswelling of S samples at different additive concentrations.

chemically inclined to interact with the amide group than the cations. The effect of OH^- ion appears stronger than that of Cl^-. That is the transition is sharper and occurs at a much lower concentration. This is understandable since given the unique chemistry of the OH group it is capable of hydrogen bonding in a multiplicity of ways.

The transition exhibits the usual dependence on temperature. The water content of the PNIPA gel plotted against the NaOH concentration for seven different temperatures (Fig. 2). Results are qualitatively the same for KOH and KCl and hence not shown. At each temperature the water content decreases sharply for a slight change in the NaOH concentration. The sharpness of the transition decreases as we reduce the temperature. For convenience we re-plot Fig. 2 as a function of temperature (Fig. 3). We observe that with increase in the NaOH concentration the transition shifted towards lower temperature and become more continuous. In Fig. 4 the transition temperatures for both linear and crosslinked PNIPA are plotted against the NaOH concentration. It is interesting to note that the LCST is same regardless of the molecular state of PNIPA.

3.2. Deswelling of equilibrium swollen (S) samples

All these experiments were carried out on initially dry samples; i.e. we were essentially monitoring the swelling

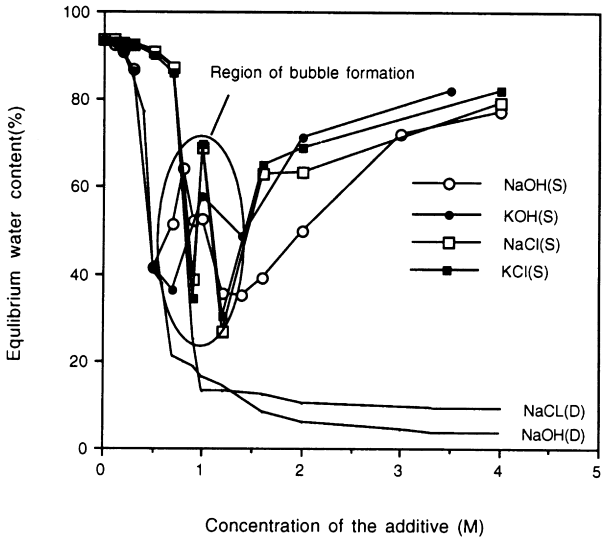

Fig. 10. Equilibrium water content of S samples in aqueous NaOH, KOH, NaCl and KCl.

pathways. What happens along the deswelling pathway? To monitor this, we first equilibrated the D samples in distilled water. The equilibrium swollen samples, designated as S samples, were then allowed equilibrate in aqueous solution of the desired additive. We scanned the whole range from 0.1 to 2.0 M of aqueous additive solution at intervals of 0.1 M. Our observations in aqueous solutions of the hydroxides and chlorides of Na^+ and K^+ are identical except that in chloride solutions the events occurred at slightly higher concentrations. Hence for clarity and convenience we confine our discussions to the events in sodium hydroxide solutions.

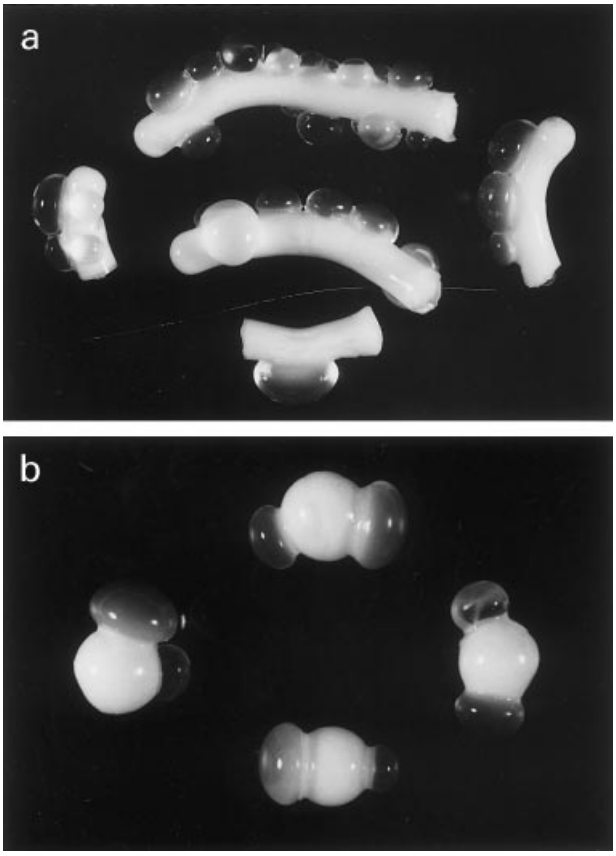

Fig. 11. Bubble formed in the equilibrium swollen cylindrical and spherical PNIPA gel on deswelling in 1 M aqueous NaOH. (a) Cylindrical gel; (b) spherical gel.

In dilute aqueous NaOH (0.1–0.30 M), the deswelling is marginal, but increases thereafter as shown in Fig. 5. At intermediate concentrations of 0.8–1.4 M the samples deswell extensively (Fig. 6). But with still higher NaOH concentrations, the deswelling decreases (Fig. 7). The samples undergo visible physical changes too. In 0.2 M NaOH, the sample retains its nature but turns cloudy and opaque when NaOH > 0.5 M. In the brief concentration range of $0.8 \leq C \leq 1.4$ M for NaOH the S samples first shrink homogeneously maintaining a clear appearance, then turn opaque. Gradually a lump appears on the surface which eventually develops into a clear bubble (Fig. 8). The bubble is stable for months if left undisturbed. In the concentration range of 1.4–1.8 M the discs develop a surface lump, but it does not turn to a transparent bubble; instead remains opaque throughout. With still higher concentrations of NaOH, (>2 M) the gel turns instantly into a hard white wrinkled mass with a thin hazy central zone.

The series of events is schematically illustrated in Fig. 9 as a function of NaOH concentration. The water content of the samples at equilibrium in each case is shown in Fig. 10 and the region of bubble formation is identified. For better visual comparison we have included the behaviour of D samples here. As is evident the VPT per se is not affected; but S samples have more water content than D samples at the transition point and thereafter.

Park and Hoffman [34] observed that the water content of PNIPA hydrogels above LCST is dictated by its initial state. Okano and his coworkers [35–40] have reported the formation of a collapsed skin layer on the hydrogel surface of PNIPA above the critical temperature. They observed that this skin thickens with time and virtually controls the rate of water permeation in either direction. If the surface collapse is rapid, then a pool of hydration water associated with collapsing polymer chain gets trapped in the gel interior, because the surface collapsed layer effectively prevents diffusion and transport in either direction.

3.3. Characteristics of the bubble

Bubble formation can be observed in gels of other geometry such as cylinder and sphere as well (Fig. 11), however the size and number of bubbles are very sensitive to ambient conditions, especially temperature. Usually the size of the bubble decreases with the concentration of the additive in the external medium. Also bubbles appear preferentially only on one surface of the opaque base. We have carried

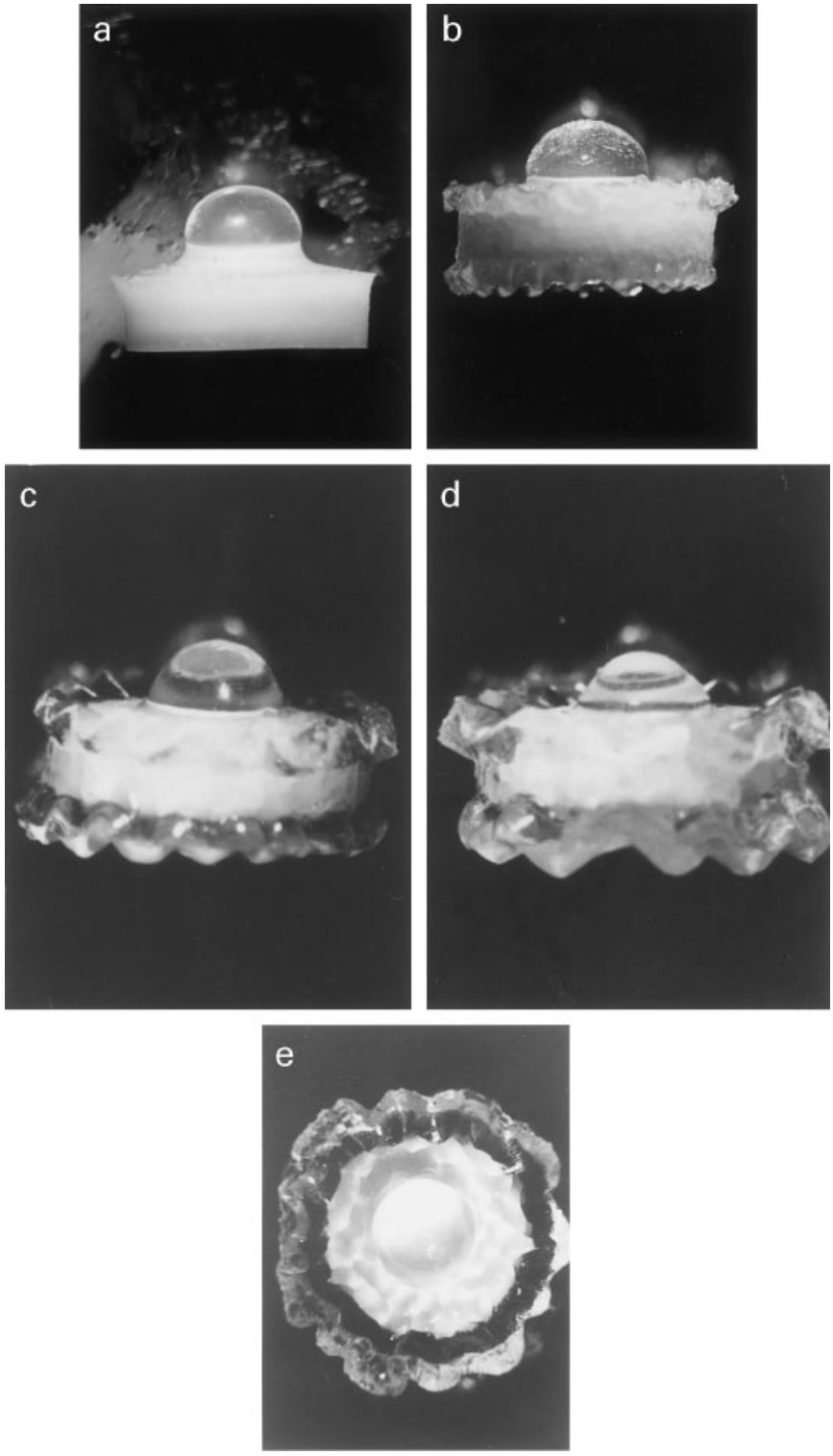

Fig. 12. Submersion of the bubble as the sample is re-swollen in distilled water. (a) 0 min; (b) 15 min; (c) 40 min; (d) 80 min; (e) 80 min (top view).

out experiments with varying percentages of crosslinking agent. We have studied with 0.014, 0.021, 0.028, 0.035% of crosslinker with respect to monomer. In these set of experiments also bubble formation was observed as shown in Fig. 11.

The most striking feature about the bubble is the permeability of its transparent wall. This can be demonstrated in several ways. A bubble formed in 1 M solution, when transferred to 4 M solution collapses; but reforms when returned to 1 M solution. An air-dried sample reforms the bubble when returned to the original solution. The series of happenings when the bubbled sample is placed in

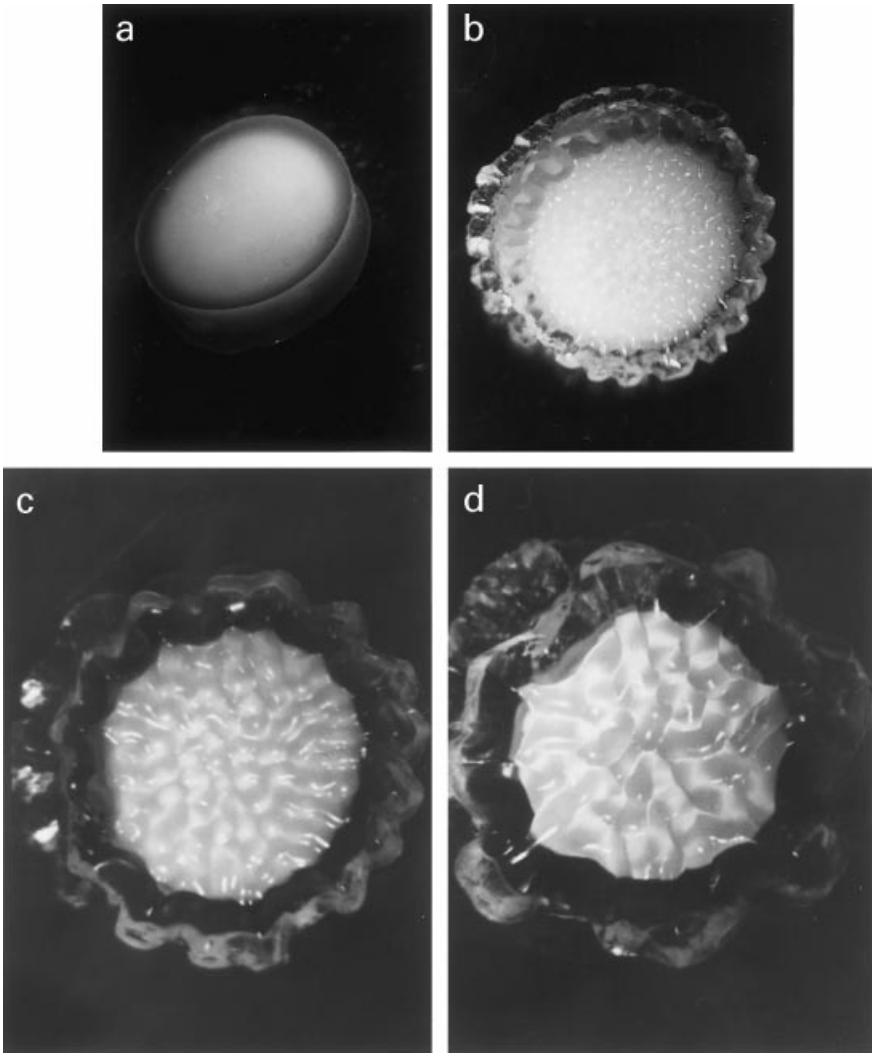

Fig. 13. Evolution of surface patterns on the flat bottom surface of the bubble when the sample is allowed to swell in water. (a) 0 min; (b) 40 min; (c) 80 min; (d) 150 min.

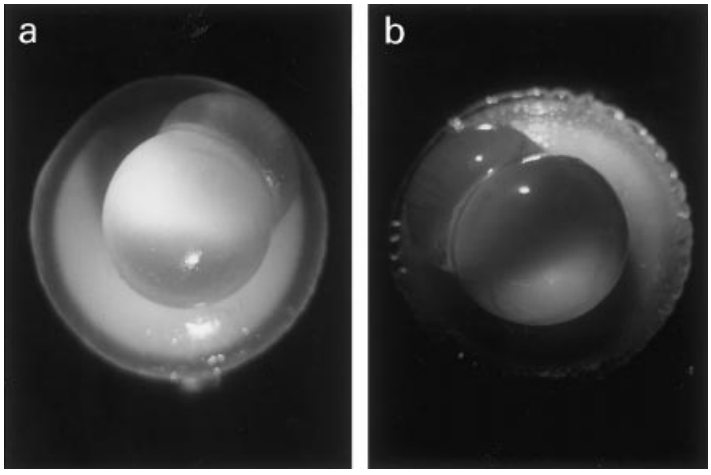

Fig. 14. Selective staining of the bubble with phenolphthalein: (a) initial; (b) after keeping the sample for 2 min in phenolphthalein solution.

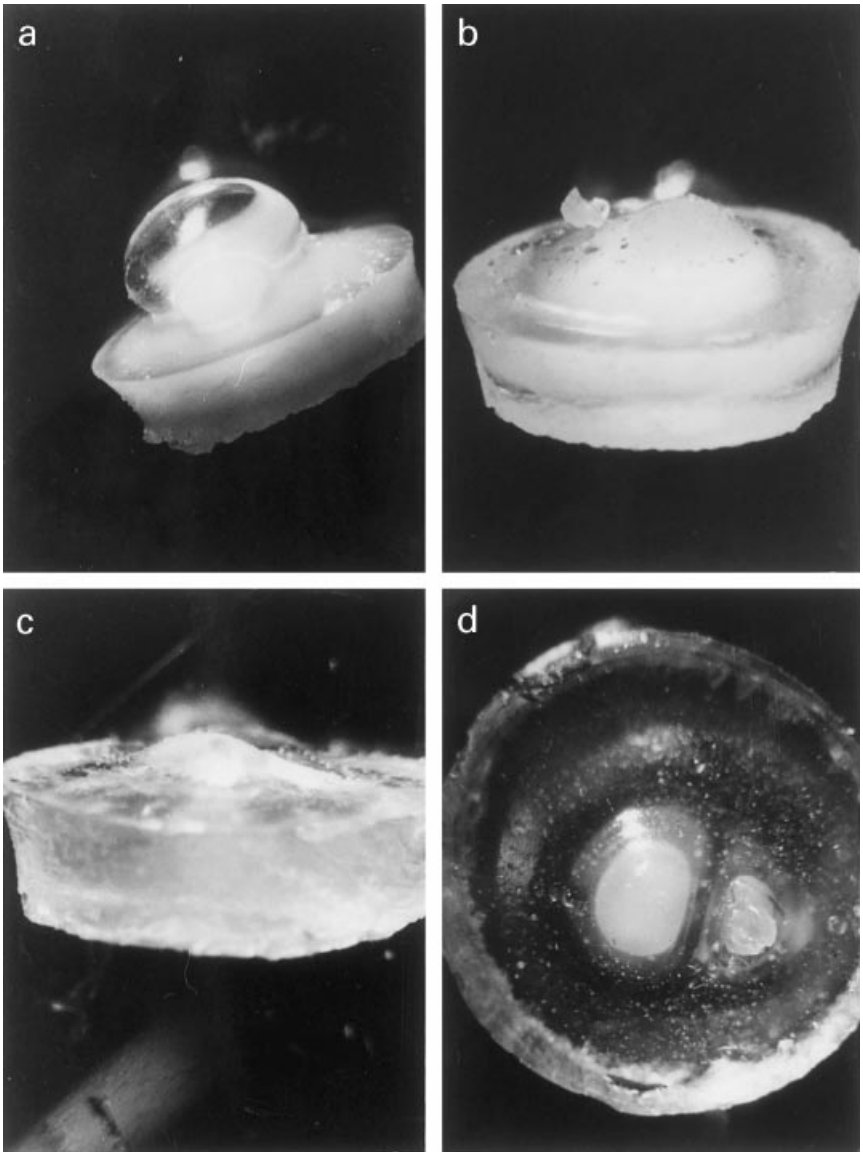

Fig. 15. Contraction of the bubble and swelling of the opaque base in acetone. (a) 0 min; (b) 30 min; (c) 60 min; (d) 120 min.

distilled water is shown in Fig. 12. The opaque base imbibes water, and swells to a transparent disc submerging the bubble. The bubble however leaves a crimp on the gel surface. When returned to alkali the bubble re-emerges. It is also interesting to note that the polymer density just below the bubble is less compared to the other portion of the opaque gel. When allowed to re-swell the portion just below the bubble gets transparent faster than the rest of the sample. During this re-swelling process the bubble does not changes its size. This could be because the polymer chains in the bubble wall are already stretched to their limit that they cannot be stretched any more. In fact we suspect this to be the reason for the surface crimp in the deswollen and reswollen samples. A similar explanation has been provided by Matsuo and Tanaka discussing pattern formation in ionic acrylamide gels [28]. Fig. 13 shows the simultaneous development of patterns on the flat bottom surface with time [41].

The permeability of the bubble wall can be demonstrated by a simple yet striking experiment. When a bubbled sample, extensively washed with distilled water is placed in a phenolphthalein solution, the bubble develops a pink colour due to the diffusion of phenolphthalein solution into the bubble (Fig. 14). Likewise when a thoroughly washed bubbled sample is placed in acetone, the opaque base gradually swells to transparency while the bubble turns turbid (Fig. 15). The explanation seems to be simple: acetone is a good solvent for PNIPA hence the collapsed base begins swelling; however as acetone from the exterior diffuses into the bubble, NaOH precipitates.

3.4. Discussion

A critical analysis of the data suggest that the bubble formation could be an osmotically driven process by the

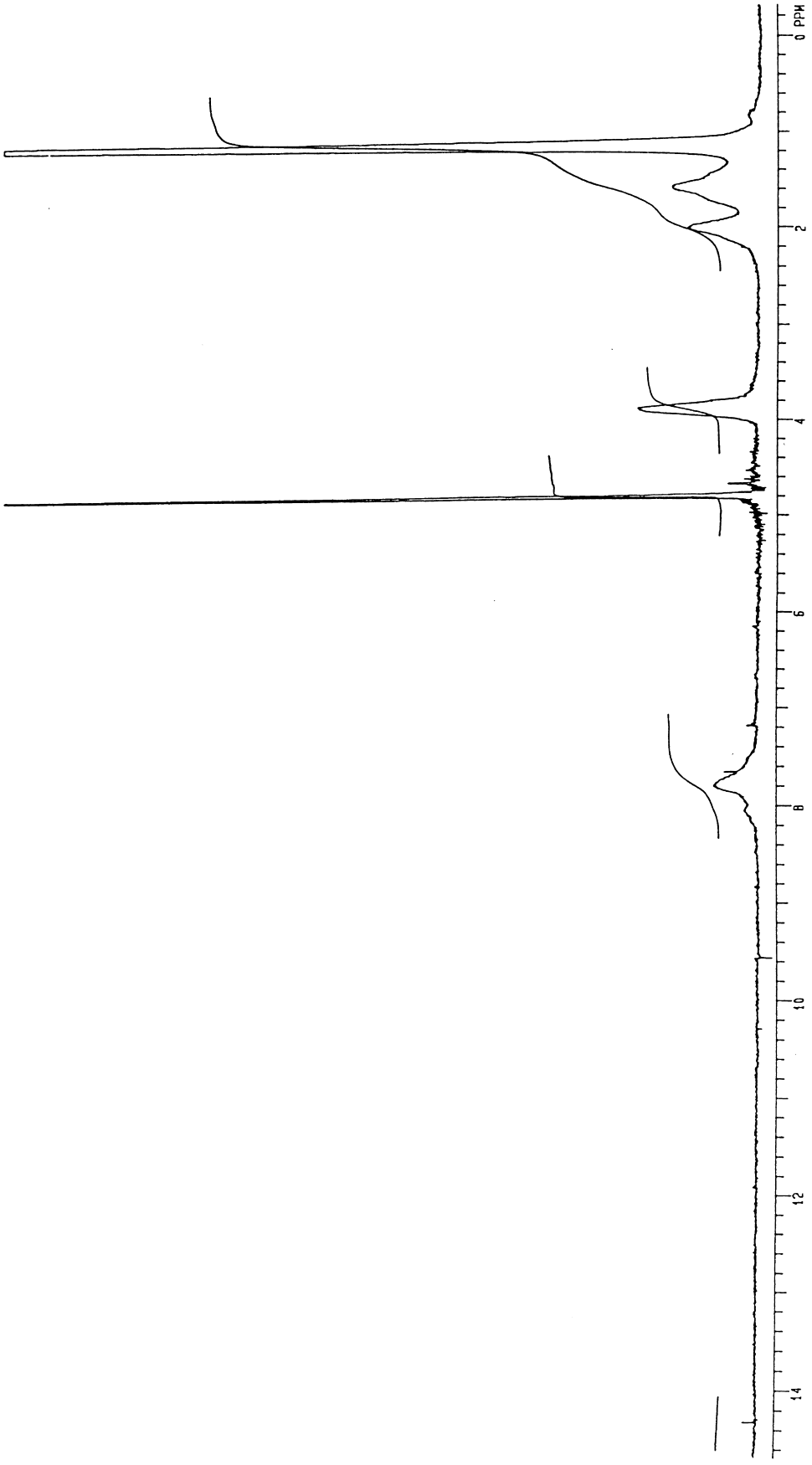

Fig. 16. ^{1}H NMR spectra of NaOH treated linear PNIPA (200 MHz, D_2O).

excess water trapped in the S samples. In presence of an additive, the D samples imbibe less amount of water, while equilibrium swollen S samples expel lesser quantities of water and this divergence amplifies as the additive concentration in the external solution increases. At present we have no accurate method to separately quantify the water associated with the bubble as well as with the polymer base and this prevents us from carrying out a detailed kinetic analysis of the whole process.

NaOH of low normality (<0.5 M) is a poor solvent for PNIPA gels, but not poor enough to collapse the polymer chains completely; the gel still has about 80% water content. Concentrated NaOH (>2 N) is an extremely poor solvent and the polymer chains collapse to a white tangled mass leaving a hazy central zone of trapped water pool. This can be construed as an osmotic shock that causes an abrupt collapse of the chains with consequent entrapment of water. The surface collapses at a fast rate forming a hard impermeable layer which prevents mass transfer or diffusion in either direction. This could be reason for the much higher values of the water content.

In the intermediate concentration range of $0.8 \leq C \leq 1.4$ M, the polymer chains with associated water collapse but not too densely so that permeation and diffusion are still possible. This results in the osmotically driven inward flux of alkali into the entrapped water pool. When the osmotic pressure of the internal water pool exactly matches that of the external fluid, the system spontaneously separates into two phases; polymer rich opaque base and solvent rich transparent bubble. The bubble is stable because the solution inside is in osmotic equilibrium with external medium.

It has been reported that substituted amides are not hydrolysed in alkali solution at room temperature [42]. Yet, to dispel the possibility that hydrolysed amide group could have somehow contributed to the observations presented here, we carried out a control experiment. Emulating the stringent experimental conditions, linear PNIPA samples (MW $\sim 10^4$) were treated with 4 M NaOH for 7 days under stirring at room temperature. The IR and NMR spectra (shown in Fig. 16) of this sample did not show the presence of carboxylic acid and were in fact identical with the original PNIPA. Molecular weight determination by GPC established no chain fragmentation has taken place. Above all LCST of the NaOH treated sample was identical with that of the original PNIPA.

4. Conclusions

There are quantitative differences in the water content of hydrogels along the swelling and deswelling pathways. It is presumed that the bubble formation observed during the anion induced deswelling of initially equilibrium swollen gels is the spontaneous separation of the partially collapsed gel into polymer-rich and solvent-rich domains. The permeability of the bubble wall and its stability imply that the phenomenon is osmotically driven.

Acknowledgements

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