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Rapid swelling and deswelling of thermoreversible hydrophobically modified poly(*N*-isopropylacrylamide) hydrogels prepared by freezing polymerisation

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Abstract

Rapid response thermally sensitive hydrophobically modified poly(*N*-isopropylacrylamide) hydrogels have been synthesised successfully using a two-step polymerisation method, the initial polymerisation being carried out at 20 °C, followed by polymerisation at − 28 °C for 24 h. The results show that the swelling/deswelling rates of poly[*N*-isopropylacrylamide-*co*-(di-*n*-propylacrylamide)] P(NIPA-*co*-DPAM) hydrogels prepared by two-step polymerisation are much faster than for the same type of hydrogels prepared via conventional methods (30 °C for 24 h), i.e. the time for the former xerogel to absorb 70 and 90 wt% is just 30 and 240 min, respectively, compared to the latter xerogel which takes 1600 and 2500 min to absorb the same amounts of water. During deswelling (shrinking), the hydrogel loses 95 wt% water in 1 min, compared to a timescale for the corresponding cross-linked copolymers prepared by conventional methods of about 5 h for 50 wt% water loss. Scanning electron microscopy, and flotation experiments together with swelling ratio studies reveal that the polymeric network of the former hydrogel is characterised by an open structure with more pores and higher swelling ratio but lower mechanical strength compared to the latter hydrogels. Such rapid response hydrogels have potential applications in separation and drug release technologies for example.

Keywords: *N*-isopropylacrylamide; Di-*n*-propylacrylamide; Hydrophobically modified polymers

1. Introduction

Poly(*N*-isopropylacrylamide) (PNIPA) hydrogel is a typical thermally sensitive gel due to the presence of both hydrophilic amide groups and hydrophobic isopropyl groups in its side-chains. These hydrogels exhibit a volume phase transition at a lower critical solution temperature (LCST) of approximately 33 °C [1–3]. When the swelling temperature is below the LCST, the gel is swollen, hydrated and hydrophilic. However, above the LCST, the gel shrinks and forms a collapsed, dehydrated and hydrophobic state due to disruption of the delicate hydrophilic/hydrophobic balance in the network structure.

This kind of hydrogel is of interest not only for industrial applications such as immunoassays [4], drug delivery systems [5,6], separation processes [7,8], and immobilisation of enzymes [9], but also in fundamental research [7,10–12]. Therefore these materials have attracted considerable attention from both fundamental and technological standpoints over the last two decades.

In a previous report [13], the synthesis and characterisation of a series of novel copolymeric thermosensitive hydrogels of NIPA with the double alkyl chain acrylamide monomers di-*n*-propylacrylamide (DPAM), di-*n*-octylacrylamide and didodecylacrylamide has been described, and their swelling behaviour in water and aqueous sodium dodecyl sulfate (SDS) solutions has been studied. The results indicated firstly that these gels exhibited a lower LCST (30 °C) in water and a higher LCST in aqueous SDS solutions in comparison to PNIPA. In particular, there were two discontinuous volume transitions at 36–40 and 70 °C, when the SDS concentration was above 0.5 wt%. Secondly, the swelling ratio changed according to either the hydrophobic content of the PNIPA gels or the nature of the swelling medium.

In the present paper, we report on work undertaken to

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improve the swelling/deswelling rate for these hydrophobically modified PNIPA hydrogels, motivated by the need for fast response systems for a number of applications such as separation processes [7,8] and drug delivery systems [5,6], where the use of conventional PNIPA hydrogels is restricted due to very slow swelling/deswelling, ranging from hours to days. In this regard, several strategies have been proposed in order to increase the response kinetics for PNIPA [14], which include (i) forming a heterogeneous network structure of the hydrogel through a phase separation method [15,16]; (ii) graft-copolymerisation, where the free ends of the grafts act to accelerate the dehydration rate [17–19]; (iii) use of silane cross-linking agents [20,21]; (iv) cold polymerisation methods [22] and (v) use of polyethylene glycol (PEG) as a pore-forming agent during the polymerisation reaction [14]. Here we report a new method to prepare rapid response hydrophobically modified PNIPA hydrogels via a two-step polymerisation method, and compare the swelling behaviour to that for conventional hydrogels. In addition, the morphology of hydrogels is characterised by scanning electron microscopy (SEM).

2. Experimental

2.1. Materials

NIPA, the cross-linker *N*,*N*-methylene bisacrylamide (BIS), the initiator ammonium persulphate (APS), and the activator *N*,*N*,*N*′*N*′-tetramethyl ethylene diamine (TEMED), were all purchased from Aldrich Chemical Co. DPAM was prepared according to the method described elsewhere [13]. NIPA was recrystallised from toluene/*n*-hexane (27/73 v/v) prior to use, other chemicals being used without further purification. For the preparation of hydrogels, deionised water was heated and cooled under bubbling nitrogen prior to use.

2.2. Synthesis of hydrogels

The hydrogels were prepared by free radical cross-linking copolymerisation in a water–dioxane (4:1 (w/w)) mixture. After preliminary experiments it was found that this composition of the solvent used for the monomer feed was critical for obtaining both a homogeneous feed and fast response. Water alone could not be used as solvent due to the sparing solubility of the hydrophobic monomers.

As in our previous studies on hydrophilically modified hydrogels based on NIPA [23], a ratio of 15/85 (w/w) for NIPA/solvent was adopted in all syntheses. However, here the solvent was not pure water but, as indicated above, a dioxan/water mixture. The content of hydrophobic comonomer DPAM was 5 mol% relative to NIPA. As before [23], the concentrations of APS, TEMED and BIS were each fixed at 1 mol% with respect to total monomers. The feed mixture of initiator, monomers and solvents was stirred well and degassed with oxygen-free nitrogen for 15 min in an ice/water bath. Then TEMED was added and the mixture was degassed for a short time. Following this, the reaction glass vials (20 mm in diameter and 58 mm in length) were sealed tightly, and the vials were placed in a constant temperature (20 °C) water bath. The polymerisation was carried out at 20 °C for 0, 15, 30, 45 and 60 min, respectively. After the first step of polymerisation was finished, the second polymerisation step was performed at −28 °C for 24 h. We call this step 'freezing polymerisation'. After the freezing polymerisation, the glass vials were broken and the frozen gels were cut into discs or disc-like pieces approximately 20 mm in diameter and ~3–4 mm in thickness. Finally the discs were washed with not only deionised water, but also using acetone to remove any possible unreacted monomers and/or linear homopolymers.

2.3. Nomenclature

The sample notation indicates the time (in minutes) for the first step of polymerisation at 20 °C (all samples having the same monomer content and the same initiator and activator concentrations). For example, S-15 is the sample for which the polymerisation at 20 °C was conducted for 15 min. A conventional sample was produced solely by polymerisation for 24 h at 30 °C without any subsequent low temperature step and is denoted S-C.

2.4. Conversion

The weight of xerogel, m_x, was obtained after removal of unreacted monomers and linear polymers by alternately swelling the hydrogels in deionised water/acetone for 1 week (the swelling medium being changed daily) in a refrigerator with temperature ~8 °C, drying the hydrogels in an oven at 47 °C for 48 h and then to constant weight, m_x, in a vacuum oven at 45 °C for ~24 h. The percentage conversion to cross-linked polymer is given by $100(m_x/m_m)$, where m_m is the total mass of monomers in the feed mixture.

2.5. Swelling and deswelling measurements

Temperature dependent measurements were carried out using samples in deionised water, either in a thermostated water bath or a constant temperature refrigerator. The xerogel disc was swollen to equilibrium in deionised water for a minimum of 48 h at various temperatures in the range 8–70 °C on both heating and cooling. After swelling equilibrium was reached (~48 h) at a particular temperature, the hydrogels were removed from the swelling medium, the excess surface water was lightly surface dried with filter paper, and the sample was weighed, the corresponding weight being m_h. The swelling ratio r was obtained as $r = m_h/m_x$ where m_h and m_x are the weights of hydrogel and xerogel, respectively. At least three samples of

each hydrogel were used to yield three values of m_h, the average of which was used to calculate r. The results indicate that the gel is stable and the response is reproducible.

2.6. Microscopic observation

The morphologies of the xerogels were observed using SEM. For this purpose, the water in the hydrogels was gradually exchanged by an ethanol/methanol mixture and finally acetone, then dried in a vacuum oven at 45 °C for 24 h [12]. In order to keep the pores of the xerogels intact for imaging, the xerogels were left in liquid nitrogen and then broken. The inner surfaces of xerogels were sputter-coated with gold for 3 min using an Emscope SC-500 instrument prior to the SEM examination. The electron microscope used was a CamScan series 4 with a magnification of 500 ×.

2.7. Kinetics of swelling/deswelling

To measure the swelling/deswelling response rate, disc or disc-like xerogel samples were used, their diameter being approximately 11–12 mm, and the thickness approximately 2–3 mm.

The kinetics of swelling of the xerogels were followed gravimetrically. Each xerogel of weight m_x was immersed in deionised water at 25 °C, and after a certain time, the hydrogel was lightly surface dried and weighed at regular time intervals (m_t), water uptake capacity (w_u) (%) being defined as follows:

$$w_u = 100 \times (m_t - m_x)/m_e, \quad (1)$$

where m_e is the weight of the hydrogel at swelling equilibrium at a particular temperature.

The kinetics of deswelling of hydrogels was also followed gravimetrically, in a constant temperature water bath (50 °C). Swollen hydrogels equilibrated first at 25 °C were transferred into a constant temperature (50 °C) water atmosphere, then after a certain time, hydrogels were surface dried with filter paper. The weight changes of the hydrogels were recorded during the course of deswelling at these time intervals. The percentage water retention (w_r) is calculated as follows:

$$w_r = 100 \times (m_t - m_x)/m_e, \quad (2)$$

where m_t is the weight of hydrogel at a given time.

3. Results and discussion

3.1. Observation of swelling

All xerogels discs were swollen in water at room temperature to become hydrogels and all gels swelled uniformly, and had smooth edges and compact shape except S-15. The gels sank in water and were white and opaque. The opacity of the samples can be attributed to the thickness of the sample and the fact that the polymerisation temperature was 30 °C, which is the same as the LCST in water [13]. As shown elsewhere [24], the polymerisation of NIPA is an exothermic reaction and an increase in temperature of 3–5 °C can be observed. This is sufficient to exceed the LCST of the copolymers, and thus lead to a phase separated (and hence opaque) structure. Hydrogel S-15 samples had ragged edges and a loose structure, floated in water and were translucent. This is a consequence of the polymerisation temperature of S-15 (20 °C) which is far below the LCST of P(NIPA-*co*-DPAM) in water.

Fig. 1 is a comparison of the structure of S-C and S-15 hydrogels in water at room temperature, after the hydrogels had reached equilibrium, at which point they had both expanded but to a different degree. It is clear that the S-15 hydrogel floats in water, whereas the conventional hydrogel sinks. Although the actual density of these xerogels can be measured according to literature methods [25], the flotation experiment gives a more direct comparative assessment, i.e. the density of xerogel S-15 is lower than that of conventional xerogel S-C. As the hydrogels had reached equilibrium, the density is related to the porosity of hydrogels; the higher the porosity the lower the density. Both hydrogels swelled in water indicating that the gels were permeable to water and that trapped air was unlikely to contribute significantly to the density of the gels. At the same time, the mechanical strength of the xerogel S-C is better than that of S-15 as assessed by manual manipulation. Although the S-C xerogel is fragile, it is harder to break and retains a smooth breaking surface/shape after breaking. In contrast, the S-15 xerogel resembles dried plastic foam, is very brittle and easily broken into a powder by hand.

The conversion of the hydrogels in terms of weight percentage is summarised in Table 1. For example, the final conversion of the conventional hydrogel S-C is 98.7 wt%, whereas it drops to approximately 36 wt% for S-0 when polymerisation at 20 °C was not carried out. However, when polymerisation is performed at this temperature for just 15 min, the conversion is 68 wt%, and the final conversion

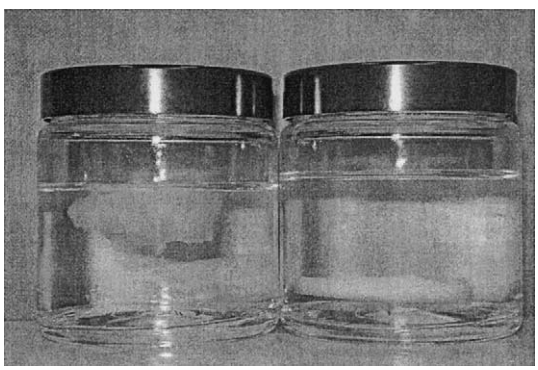

Fig. 1. Photographs taken under conditions of swelling equilibrium for hydrogels of S-15 (left) and S-C (right) in water at room temperature.

Table 1
The conversion of P(NIPA-*co*-DPAM) hydrogels after polymerisation at the temperatures indicated

Sample code	Conversion (20 °C) wt%	Conversion (−28 °C) wt%
S-C	–	98.7
S-0	–	36.4
S-15	67.7	83.3
S-30	91.3	98.2
S-45	95.2	98
S-60	96.8	100

increases to 83 wt%. For all samples except S-0 the conversion is high enough for the copolymer compositions to be the same, i.e. similar in magnitude to the feed composition. This may not be true for S-0, but monomer reactivity ratios, whereby compositional drift could be calculated, are not available for this system. In a sense, it seems rather surprising that the conversion for S-0 is as high as 36 wt% in view of the fact that polymerisation was only carried out at −28 °C. However, it should be remembered that polymerisation could proceed in the finite time taken for the temperature of the sample to attain −28 °C from the starting temperature of 20 °C.

3.2. Swelling ratios

Fig. 2 shows the temperature dependence of the swelling ratio obtained on heating for conventional hydrogels and hydrogels prepared via the two-step synthesis method. All curves display the same tendency with increasing temperature, viz. a fall in swelling ratio with temperature, which becomes sharper in the vicinity of the critical temperature. Finally, in the high temperature regime there is almost complete deswelling for all systems, and r attains a value close to unity. It should be noted that the value of r at low temperature increases slightly with decreasing reaction time at 20 °C, i.e. the value of r slightly increases with decreasing polymerisation conversion (see Table 1). However, the swelling ratio is not improved dramatically by performing a two-step polymerisation. Although the value of r for hydrogel S-0 is higher than for the other hydrogels, due to the lower conversion it was not possible to cut the sample into discs. Therefore this polymer was not suitable for swelling/deswelling kinetic studies.

For all the hydrogels, the cooling process was also carried out, and almost all the swelling ratios are the same as those obtained on heating (data not distinguished in the plots presented here). Thus the reversible nature of swelling and deswelling was confirmed.

3.3. Swelling and deswelling kinetics

The swelling and deswelling kinetics of the conventional and two-step polymerisation hydrogels were studied by gravimetry at defined time intervals. Fig. 3 shows a comparison of swelling kinetics for five xerogels. Except for xerogel S-60, the absorption of water is faster than for the conventional xerogel S-C. This can possibly be attributed to the formation of porous structures inside these gels, which enable water molecules to diffuse into the polymer network more easily. We suggest that the faster swelling observed for the two-stage polymerised samples was due to incomplete conversion of comonomers into a cross-linked polymeric network during the polymerisation at 20 °C for 15–45 min (see Table 1). After this first stage of polymerisation, mobile water molecules are able to diffuse into the porous gel, leading to an expansion of the network prior to freezing at −28 °C. During the freezing

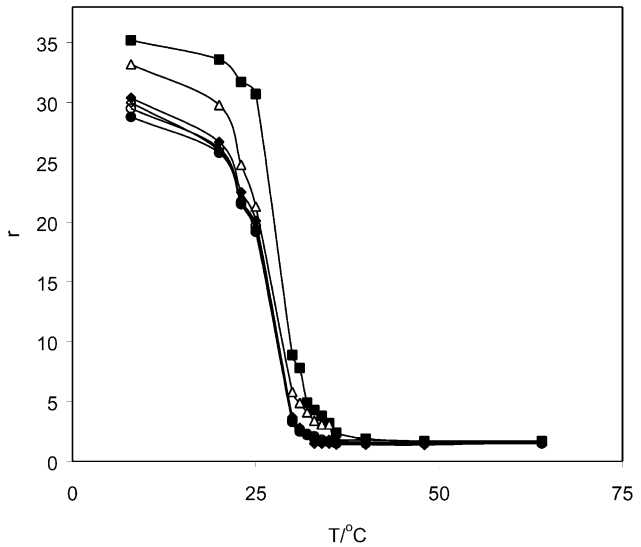

Fig. 2. Swelling ratios of the conventional and two-step polymerisation P(NIPA-*co*-DPAM) hydrogels as a function of temperature. (◆) S-C; (■) S-0; (△) S-15; (○) S-30; (◇) S-45; (•) S-60.

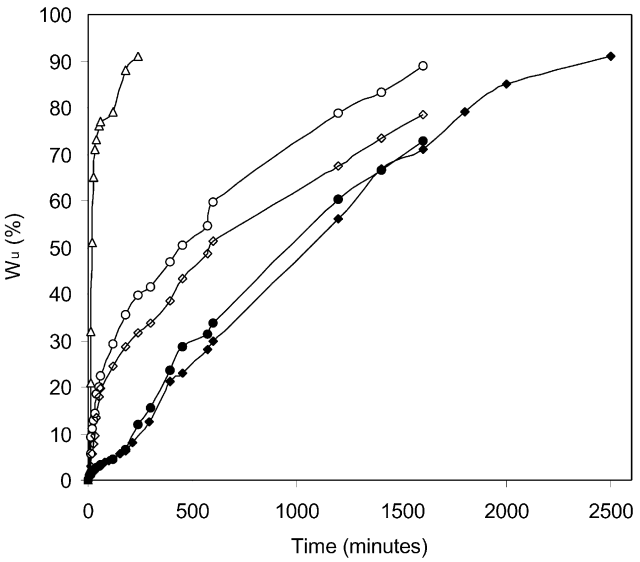

Fig. 3. Swelling kinetics of the conventional and two-step polymerisation P(NIPA-*co*-DPAM) hydrogels at 25 °C. (◆) S-C; (△) S-15; (○) S-30; (◇) S-45; (•) S-60.

polymerisation, the water itself seems to act as a porosigen [26,27] possibly due to ice crystal formation creating a network with a more open channel structure. After completion of the polymerisation reactions, the frozen hydrogel melts when the gel is returned to ambient conditions, and the ice crystals leave a highly porous structure, able to take up water more quickly. These conjectures are supported by SEM investigations of the gel structure (vide infra). As we have pointed out already in Section 2, the hydrogels were prepared in a water–dioxane (4:1 (w/w)) mixture. If the ratio of water–dioxane was changed to 1:1 (w/w), we could still obtain a homogeneous feed, but the gel did not display a fast response, this providing an additional indication of the key role of ice in forming pores in the polymer network.

Zhang and Zhou [22], who prepared a fast response PNIPA hydrogel via one-step cold polymerisation at −18 °C, attributed the fast response to a macroporous network formed when the polymerisation was conducted below the freezing point of water. They also suggested that the increase in molar volume of ice compared to water leads to an increase in pore size during low temperature polymerisation, although this seems hardly enough to lead to a significant change, which we believe is primarily related to ice crystal formation.

It also should be noted when increasing reaction time up to 30 min at 20 °C (i.e. S-30), the conversion increases dramatically compared with polymerisation for 15 min at this temperature. Fig. 3 also shows that the absorption of water by xerogel S-30 was much slower than for S-15. We ascribe this to the increased conversion after the first step of polymerisation, which hinders the diffusion of water into the S-30 network prior to the freezing polymerisation step. Hydrogel S-15 exhibits the fastest swelling response rate, the xerogel absorbing 70% water in 30 min. Why this gel displays the fastest swelling is still unclear at present. It appears that the polymerisation time at 20 °C must be controlled so that the network formed is sufficiently porous to accommodate free water before the freezing polymerisation step.

The xerogels of S-15, S-60 and S-C had distinct surface skins. The first was rough and loose without any surface layer. In contrast, the latter two xerogels were smooth, tight and formed a dense layer at the xerogel surface. The former observation is consistent with a more open and porous structure, as indicated by flotation experiments.

The deswelling kinetics of hydrogels S-C and of S-15, S-30, S-45, S-60 are shown in Figs. 4 and 5, respectively. Comparison of these figures shows that the deswelling of S-15, S-30, S-45 and S-60 hydrogels is much faster than that of the conventional hydrogel S-C (not the difference in time axes). The hydrogel S-15 loses 95 wt% water in 1 min, compared to loss of 50% water in 300 min for the conventional hydrogel. The results can be attributed to the more porous structure of hydrogel S-15 that allows faster shrinking upon water desorption. A similar observation of a faster deswelling rate of PNIPA hydrogel obtained via freezing polymerisation when compared to conventional PNIPA hydrogel was made by Zhang and Zhou [22].

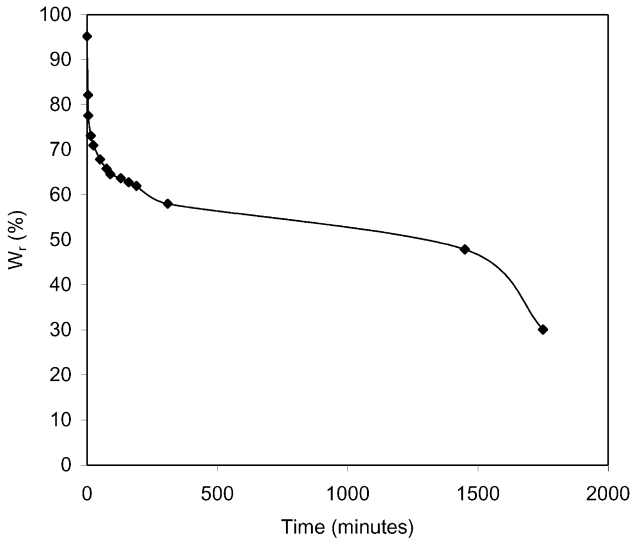

Fig. 4. Deswelling kinetics of the conventional P(NIPA-*co*-DPAM) hydrogel (S-C) at 50 °C.

3.4. SEM studies

The SEM images of xerogels prepared via two-step (S-15) and conventional polymerisation (S-C) methods are shown in Figs. 6 and 7, respectively. The S-15 xerogel displays a more open structure, which is in good agreement with the flotation experiments (see Fig. 1). These results suggest that xerogel S-15 is more porous and, thus displays faster swelling/deswelling response rate. The structure of S-C (Fig. 7) is less open, consistent with the higher observed density and explaining the slower response rate.

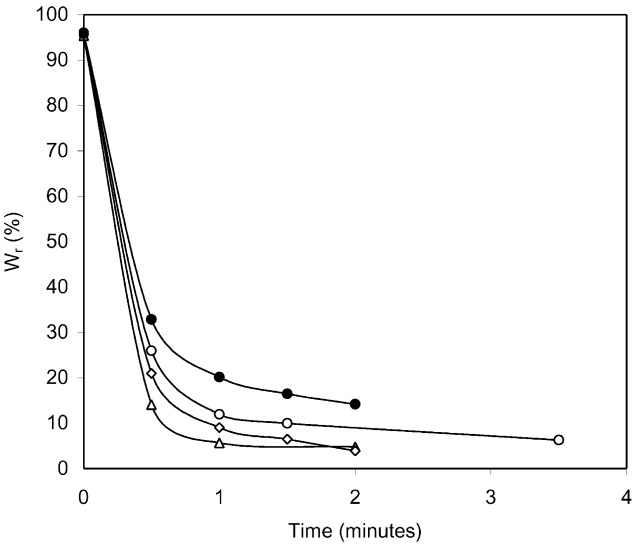

Fig. 5. Deswelling kinetics of two-step polymerisation P(NIPA-*co*-DPAM) hydrogels at 50 °C. (△) S-15; (○) S-30; (◇) S-45; (•) S-60.

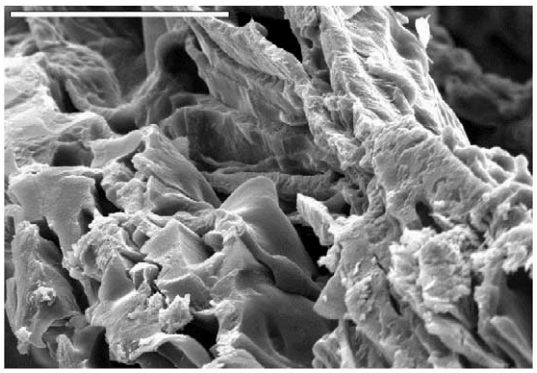

Fig. 6. Cross-sectional scanning electron microscopy image of S-15. The scale bar equals 100 μm.

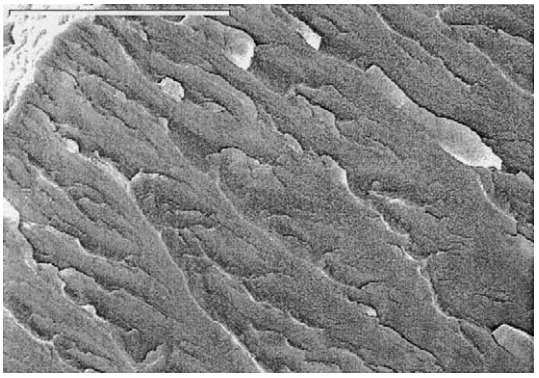

Fig. 7. Cross-sectional SEM image of S-C. The scale bar equals 100 μm.

4. Conclusions

Rapid response thermally sensitive P(NIPA-*co*-DPAM) hydrogels were successfully prepared via a two-step polymerisation method, in which the polymerisation is conducted at 20 °C for a short time and polymerisation is completed at − 28 °C. The results indicate that the response kinetics of these hydrogels can be adjusted according to the polymerisation time at 20 °C, which seems to influence the porosity of the network structure of xerogels. This two-step polymerisation technique could be useful in potential applications in controlled drug delivery, etc.

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