

Microporous, Responsive Hydroxypropyl Cellulose Gels. 1. Synthesis and Microstructure

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ABSTRACT: An effective technique for the synthesis of microporous gels is developed along with correlations between synthesis conditions and microstructure. Such gels have substantially different properties than their nonporous analogues. Microporous hydroxypropyl cellulose (HPC) gels were prepared by heating aqueous HPC solutions above their lower critical solution temperatures (LCST's) while cross-linking the polymer with divinyl sulfone. The effective porosity of the gel increased from 23 to 76% by decreasing HPC concentration from 22.6 to 9 wt %, as anticipated from the system phase diagram. The pore size range decreased from 0.5–9.0 to 0.05–0.2 μm by increasing reaction time before phase separation from 1.5 to 25 min, demonstrating that cross-linking in the homogeneous state limits the extent of phase separation possible. Gel morphology changed from open-celled to closed-celled by decreasing reaction time in the phase-separated state, which limits cross-linking in the polymer-rich phase.

Introduction

Some cross-linked, solvent-swollen gels exhibit large, reversible changes in their swollen volumes upon changes in external conditions. The most intensively studied volume changes are those of hydrogels in response to small changes in the temperature, solvent composition, pH, or ionic composition of the solution surrounding the gel.^{1–5} Volume changes can also be induced by pressure, external electric fields, irradiation by visible light, or specific chemical stimuli, such as glucose concentration.^{1,6,7} The volume change may occur gradually over a range of stimulus values or it may occur abruptly at a specific value of the stimulus. Thermodynamically, the latter case has been shown to be a phase transition.^{1–7} These gels are commonly referred to as “responsive gels,” “stimulus-sensitive gels,” or “environmentally sensitive gels.”

Since the solvent sorption capacity is one of the most important properties of a gel, the ability to actively control gel solvent content through the application of an external stimulus has led to many ideas for technological innovations based on these materials. Uses of these gels as recyclable absorbents, sensors, switches, artificial muscles, responsive drug delivery systems, and other concepts have all been examined in detail.^{1–10} For most of these applications, response rate is a critical factor for either technical success (as for sensors) or economic viability (as for recyclable absorbents). However, it has been shown that, in general, the kinetic behavior of these gels is determined by the cooperative diffusion coefficient of the polymer chains in the solvent.¹ Since this diffusion coefficient is on the order of 10^{-7} cm^2/s , the rate of swelling or shrinking of a macroscopic gel sample is generally quite slow: e.g., a 1 mm thick gel sample typically takes hours to reach a

new equilibrium water content in response to a stimulus.

Previous Work on Fast-Response Gels. The response time of environmentally sensitive gels can be dramatically reduced by decreasing the characteristic diffusion path length, since time scales with the square of the dimension for a diffusion-limited process. Unfortunately, reducing the dimensions of the gel may not be desirable or feasible for many potential applications of responsive gels. However, it has been previously shown that the response rate can be substantially faster for microporous responsive gels, i.e., gels possessing pores in the size range 0.01–100 μm . Hirasa and co-workers have prepared microporous responsive poly(vinyl methyl ether) (PVME) gels that respond quickly to temperature by γ -irradiation of PVME solutions under conditions which induce microscopic phase separation.^{11,12} We employed a similar process to prepare microporous PVME gels and found that the response rates of these gels were strongly influenced by the rate and dose of γ -irradiation.¹³ We have also produced microporous thermally sensitive poly(*N*-isopropylacrylamide) (PNIPA) gels that swell and shrink up to 3000 \times faster than the analogous nonporous PNIPA gels. In this case, a copolymerization/cross-linking reaction was initiated in a single-phase solution but completed in a phase-separated state by heating the solution above its lower critical solution temperature (LCST).¹⁴ Microporous, responsive poly(vinyl alcohol) gels also have been prepared by subjecting aqueous polymer solutions to repeated freeze and thaw cycles.¹² Wu et al. have generated microporous PNIPA gels by carrying out the copolymerization/cross-linking reaction entirely above the LCST in the presence of another LCST polymer, hydroxypropyl cellulose (HPC).¹⁵ Yoshida et al. have prepared combtype PNIPA grafted gels capable of shrinking rapidly but swelling slowly (similar to conventional nonporous gels).¹⁶ Such asymmetry in swelling and shrinking rates is common in many of the studies cited above but has not been fully examined.

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Thus a variety of protocols have been developed for creating microporous gels, but correlation of the synthesis conditions and resulting microstructure is clearly required. Furthermore, the relationship between microstructure and kinetics is similarly in need of examination. The transport mechanisms involved in the fast response kinetics must also be elucidated.

Research Hypothesis and Objectives. On a fundamental level, this project determines factors required for fast response of gels and identifies the steps which limit the volume change kinetics. It also develops an understanding of how chemical cross-linking influences polymer phase separation. On an applied level, the process described herein constitutes an effective route to the production of fast-response gels for use in a variety of technological applications.

The principal hypothesis employed here is that swelling and shrinking in a microporous gel with interconnected pores involves two distinct mass transfer steps: (1) diffusion in the polymer struts and (2) convection through the pores. Thus, the characteristic diffusional path length is half the thickness of the strut or pore wall, not the sample thickness, since solvent can be transported into or out of the gel through interconnected pores of sufficient size by convection. Since the rate of convection is generally much faster than the rate of diffusion, microporous gels with interconnected pores should respond much faster than nonporous gels. However, to allow convective transport through the pores, the pores must be interconnected, providing continuous channels for solvent transport through the gel. If the pores are unconnected, the kinetics of volume change in microporous gels will remain relatively slow.

Examination of mass transfer processes in microporous gels requires a method that can be (1) adapted to the synthesis requirements of responsive gels, (2) controlled to yield reproducible microstructures, and (3) varied to produce differing microstructures. The purpose of this work is to present the development of such a synthesis technique and to correlate synthesis conditions and the resulting microporosity. Subsequent work examines the connection between gel microstructure and equilibrium swelling and kinetics.

Microporous polymeric materials can be prepared by a variety of methods. They can be made by generating gas bubbles within the material during synthesis, leaching of soluble particles from within a polymer (leaving behind voids), copolymerization of a bicontinuous emulsion, inducing phase separation of a polymer solution followed by solidification of the polymeric microstructure, or copolymerization/cross-linking of monomers in a poor solvent for the polymer.^{1,14,17-31} On the basis of preliminary work with several of these methods, the technique found to be most readily suited to the production of microporous responsive gels with desired morphologies and pore size ranges was the temperature-induced phase separation (TIPS) process.^{1,20,21}

The TIPS process has been used to fabricate microporous foams and membranes from polymer solutions which phase-separate upon cooling. In such cases, the microstructure is locked-in upon vitrification of the polymer/solvent system, followed by solvent removal (typically by lyophilization).¹⁷⁻¹⁹ However, the standard approach to TIPS is not directly applicable to the water-soluble polymers used to prepare responsive hydrogels. These polymers generally exhibit lower critical solution temperature (LCST) behavior and thus must be heated,

not cooled, to induce phase separation, thereby precluding use of vitrification as a means of fixing the microstructure. Also, any such dried microporous materials could not be subsequently contacted with water without redissolution of the polymer (due to the absence of cross-links). By including a chemical cross-linking step concurrent with the phase separation step, we have successfully developed a method for producing fast-response microporous gels with considerable microstructural control. While there have been a number of studies on the copolymerization/cross-linking of monomer solutions undergoing simultaneous phase separation (especially for producing macroporous chromatographic media), cross-linking preformed polymers as in this work constitutes a different problem.^{14,25-31}

Since the rate of heat transfer is about 2 orders of magnitude faster than the rate of diffusion of ions or solvent in the gel, we have demonstrated greater enhancement in the volume change kinetics for thermally sensitive gels in comparison to pH-, ion-, or solvent-sensitive gels.²¹ Hence, the focus here was on thermally sensitive gels. The modified TIPS process described above has been used to make thermally sensitive microporous hydroxypropyl cellulose (HPC) gels. HPC is ideally suited to test the concepts described above for several reasons. First, it is thermally responsive; i.e., gels prepared from HPC display a reversible volume change with temperature.³² Also, aqueous solutions of HPC show LCST behavior in a convenient range; the transition temperature is $44 \pm 2^\circ\text{C}$.³³ Furthermore, the phase separation of HPC and water occurs by spinodal decomposition, yielding the bicontinuous phases we hypothesized would lead to the formation of open-celled rather than closed-cell materials.³⁴⁻³⁶ Finally, the rate of cross-linking HPC with divinyl sulfone can be controlled through the catalyst concentration and could occur fast enough to preserve the phase-separated state.³⁷

Experimental Procedure

Synthesis of Microporous HPC Gels. The following procedure was developed to produce microporous HPC gels.²⁰ Dry HPC powder (Aldrich Chemical, Milwaukee, WI; average molecular weight of 370 000) was dissolved in an aqueous pH 12.2 NaOH solution. The solution was kept at room temperature for at least 24 h to ensure complete mixing. Divinyl sulfone (DVS) (Aldrich Chemical, Milwaukee, WI; 97% purity) was added to the solution by a micropipet at ambient temperature (23°C), and the reaction was mixed thoroughly for 30 s. The solution was then sandwiched between glass plates separated by a silicon rubber gasket 1.6 mm thick; the mold was held together by spring clamps.

The cross-linking reaction proceeded over three different time/temperature intervals, or periods, as illustrated in Figure 1. Each temperature change was induced by immersing the reaction mold into a water bath at the designated temperature. In the first period, cross-linking was conducted in a homogeneous state at room temperature to initiate formation of an embryonic network. The temperature was then increased above the LCST of the polymer solution, to 47°C , into the unstable region of the phase diagram, thereby inducing phase separation of the solution. Cross-linking can continue during this second period but is anticipated to occur primarily in the polymer-rich phase. In the final period, the temperature is decreased back below the LCST of the solution, where some remixing of phases and further cross-linking could then occur before the reaction is quenched. The reaction times corresponding to these three steps are denoted t_{BP} , t_{DP} and t_{AP} , where the subscripts BP, DP and AP denote the reaction times before, during and after phase separation, respectively.

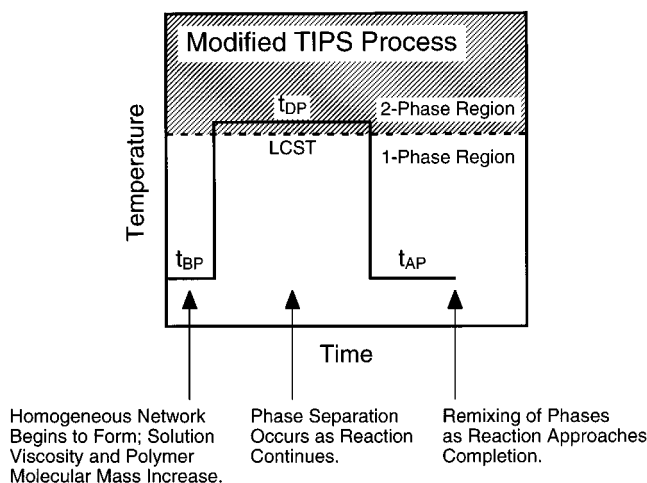


Figure 1. Schematic representation of the synthesis of microporous gels by the modified temperature-induced phase separation (TIPS) method.

The total cross-linking reaction time was held constant at 24 h since this time is adequate to carry out the cross-linked reaction to completion (subsequent work with this system has revealed that 12 h or less is sufficient).³⁷ The gel sheet produced was cut into square pieces measuring about 25 mm \times 25 mm. The NaOH catalyst was neutralized by soaking the gels in dilute HCl; the sol fraction remaining in the gel was leached away by repeatedly swelling and shrinking the gel in water between 23 and 60 $^{\circ}$ C.

Microstructural Characterization. Scanning electron microscopy (SEM) of freeze-dried gels was performed to obtain the gel pore and strut sizes, as well as to provide information regarding pore interconnectivity. The following procedure, also successfully utilized to examine the morphologies of cellulose gels in $\text{NH}_3/\text{NH}_4\text{SCN}$ as well as various other gels was followed to freeze-dry water-swollen gels while preserving their microstructures intact for imaging.^{38,39}

Small chunks (approximately 2 mm \times 2 mm) of gel were cut from a swollen gel sheet using a fresh razor blade. They were blotted on a filter paper to remove excess surface water and then quickly plunged into liquid ethane cooled by liquid nitrogen. These vitrified specimens were transferred in liquid nitrogen to a solid brass specimen stage, in which were drilled nine 3-mm (diameter) \times 3-mm (depth) holes. The stage was held in constant contact with liquid nitrogen. Once samples were placed in the holes, the stage was quickly transferred to a JEOL JFD-9000 C freeze fracture/etching unit to minimize frost buildup on the gel surfaces. Once inside the unit, the stage was held at -100 $^{\circ}$ C. A knife block located above the specimen stage was maintained at -164 $^{\circ}$ C to act as a coldfinger and collect contaminants during freeze-drying, which was conducted for 10 h at 3.2×10^{-7} Torr. After freeze-drying, samples were mounted on SEM stubs using carbon-impregnated (conductive) double-sided tape and sputter-coated with 25 nm of Au-Pd (2.5 nm/min in pulse mode to avoid sample heating). The microstructure of the freeze-dried gels was imaged using an ISI-SX-30 scanning electron microscope operated at 15 kV. Pore and strut size ranges were measured directly from the resultant electron micrographs.

Measurement of Effective Porosity. Voids generated in responsive gels will not enable the desired fast response unless the pores are open and of sufficient dimension to allow convective flow of solvent through them. Thus rather than attempting to determine absolute porosity (total void volume per sample volume) by conventional methods,²⁶ for these microporous gels, an "effective porosity" ϵ was defined as the fraction of total gel volume occupied by interconnected pores (void spaces) through which water can flow. From the mass lost by the sample under a known applied mechanical pressure, the effective porosity of the gel was calculated. To determine effective porosity, a gel sample swollen in water at

25 $^{\circ}$ C was weighed and placed between 24 layers of lint-free tissue paper (Kimwipes, Kimberly-Clark, Neenah, WI). This assembly was placed between glass plates; upon brief application of a mechanical pressure of 8–15 psi to the sample, expelled water was absorbed by the tissue paper. This procedure was repeated three more times using fresh Kimwipes until the gel stopped expelling water. The effective porosity results obtained from the final mass of the gels were reproducible to within $\pm 3\%$.

Results and Discussion

The modified TIPS process provides a great degree of control over the gel microstructure. Microporous HPC gels with different morphologies, effective porosities, pore sizes and strut thicknesses have been successfully prepared by altering synthesis conditions such as the initial polymer concentration (C_p) and the time allowed for each of the three cross-linking periods: time before phase separation (t_{BP}), during phase separation (t_{DP}), and after phase separation (t_{AP}). In the first period, an embryonic network is formed which will affect the degree and rate of phase separation and ultimately the gel morphology. If the first period is too long, a complete network may form, and the thermodynamic effect of the heating stage (t_{DP}) may be macroscopic phase separation (macrosyneresis) rather than the desired microscopic phase separation (microsyneresis). Also insufficient reagent may remain to cross-link the concentrated polymer regions and a microporous gel will not be produced. In contrast, if the first period is too brief, a latex of microgels rather than a macroscopic gel may form, especially if $t_{DP} \gg t_{AP}$. In the second period, sufficient time must be allowed to cross-link the polymer-rich regions into a permanent structure. In the final period, some remixing of the polymer-rich and polymer-dilute phases may occur to further alter the ultimate gel properties. To test these ideas, C_p , t_{BP} , t_{DP} , and t_{AP} were varied in combinations expected to critically test these hypotheses. From the results of these experiments, the likely effects of other variables which were not tested, such as the temperature of the phase separation or the relative rates of cross-linking (which can be controlled by catalyst concentration) and phase separation, can be predicted.

The focus of this effort is to study the effect of synthesis conditions on gel morphology. In subsequent work, the effect of microstructural parameters such as effective porosity, pore size, and pore connectivity on the temperature dependence of the swelling behavior and volume change kinetics of thermally sensitive hydrogels will be presented. Effective porosity and pore connectivity determine the amount of solvent that can be rapidly absorbed or expelled in response to the stimulus, and pore size affects the rate and mechanism by which the solvent can move through the gel. The rate-governing step of the volume change kinetics of microporous gels sensitive to other stimuli, such as solution ionic strength and solvent quality, has been previously established.²¹

Proof of Concept. The first synthesis experiment was designed to prove that a cross-linked microporous gel with interconnected pores can be prepared using the modified TIPS process. The synthesis procedure described in the experimental section was employed to prepare an HPC gel with an initial polymer concentration (C_p) of 9 wt %, and a cross-linker concentration (C_x) of 1.4 wt % (these values are in the range used in previous work to make homogeneous temperature-

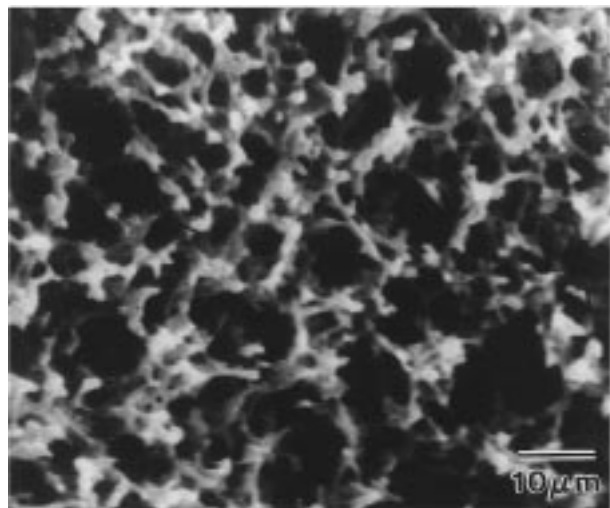


Figure 2. Representative cross-sectional SEM micrograph of the freeze-dried P24 gel, demonstrating that the gel is composed of a network of interconnected pores.

responsive gels).³² The reaction time before phase separation (t_{BP}) was minimal (equal to the time required to mix the polymer solution with the cross-linker, pour the solution in the mold, and heat it above the LCST), while the reaction time during phase separation (t_{DP}) was held at 24 h and the reaction time after phase separation (t_{AP}) was negligible.

The resulting microporous gel, designated P24, was freeze-dried and the gel microstructure was characterized by SEM using the procedure described in the previous section. From the SEM micrograph of P24, displayed in Figure 2, it is evident that this gel is microporous with pores measuring 0.5–9 μm in diameter. Note that the pores in this gel appear interconnected, as expected and desired. Also, the microstructure is quite reminiscent of those that develop during spinodal decomposition in conventional TIPS processes and distinctly different from the sorts of microstructures that develop during nucleation and growth.²⁷ Thus, the modified TIPS process was successful in producing microporous gels with interconnected pores, as hypothesized. The remainder of the paper tests this hypothesis more rigorously by examining whether key variables affect microstructural characteristics in manners consistent with this hypothesis.

Effect of Initial Polymer Concentration (C_p).

The initial polymer concentration plays a crucial role in the development of gel microstructure, since it governs the relative amounts of polymer-dilute and polymer-rich phases produced upon phase separation. This distribution should correlate with the relative amounts of polymer struts and pores (i.e., effective porosity), as well as pore size and strut thickness. The initial polymer concentration also affects whether a designated temperature change keeps the solution in the single-phase region of the phase diagram or moves the system into a metastable or unstable region. Since spinodal decomposition of an initially homogeneous polymer solution occurs by moving into the unstable phase region and leads to bicontinuous phase formation (which should yield the open-celled microstructures desired), all initial polymer concentrations have been chosen so that the solutions could be moved from below the LCST into the unstable region upon heating.^{33,40,41}

The synthesis parameters examined in this study and the microstructural characteristics of the gels obtained

Table 1. Effect of Initial Polymer Concentration (C_p) on Gel Morphology

Synthesis Parameters						
initial polymer concentration, C_p = 9–22.6 wt %						
initial cross-linker concentration, C_x = 1.3–2.2 wt %						
reaction time before phase separation, t_{BP} = 1.5–2.2 min						
reaction time during phase separation, t_{DP} = 23–24 h						
reaction time after phase separation, t_{AP} = 0 min						
overall reaction time \approx 24 h						
sample designation	C_p , wt %	cross-linker: polymer ratio, g/g	effective porosity, g/g	pore size cross section, μm	strut thickness, μm	pore morphology
P24	9.0	0.141	0.76	0.5–9.0	1.0–2.0	interconnected
P16S1	12.8	0.118	0.69	0.5–8.0	0.5–2.0	interconnected
P20	16.4	0.094	0.54	0.2–2.5	0.25–1.0	interconnected
P38	22.6	0.094	0.23	0.2–2.0	0.2–2.0	interconnected

are summarized in Table 1. Representative micrographs of these gels are provided in Figures 2 and 3. An important correlation identified here is that an increase in the initial polymer concentration induces a significant decrease in the effective porosity of these microporous gels. Effective porosity in these water-swollen gels at 23 $^{\circ}\text{C}$ represents the fraction of the microporous gel volume occupied with interconnected water-filled pores. The remaining volume is therefore occupied by water-swollen struts.

The reduction in microporous gel effective porosity from 0.76 to 0.23 accompanying an increase in the initial polymer concentration from 9.0 to 22.6 wt % can be readily explained using the lever rule for phase ratios. According to this rule, the ratio of the amount of the polymer-dilute phase to the polymer-rich phase at the phase separation temperature is equal to the ratio of the difference of the polymer-rich concentration and the system's average concentration to the difference of the system's average concentration and the polymer-dilute concentration. Reducing the initial polymer concentration consequently leads to a greater percentage of the dilute phase (but not necessarily different concentrations in the polymer-rich and polymer-dilute phases as this will depend on the phase boundaries of the two-phase system). Moreover, the depth of movement into the two-phase region may also alter the relative amounts of the polymer-rich and -dilute phases. This variable was not, however studied in this work since the phase boundaries of the HPC–water system rise steeply above the LCST (and therefore the changes in phase compositions with temperature are small), in which case the phase-separation temperature is not expected to have as significant an effect on gel microstructure as the variables investigated here.³³ Since the polymer-dilute phase leads to pores and the concentrated phase forms water-swollen struts in a water-swollen microporous gel, the effective porosity of microporous gels prepared by the phase inversion technique is expected a priori to decrease with an increase in the initial polymer concentration. Thus, the experimentally observed trend in effective porosity with increasing initial polymer concentration is in agreement with that dictated by the phase lever rule.

Additional important characteristics of gel morphology are pore and strut sizes, which are obtained from micrographs such as those shown in Figures 2 and 3 and tabulated in Table 1. As the initial polymer concentration increases, these characteristics are found to decline modestly, with the most marked change occurring between C_p values of 12.8% and 16.4% (the

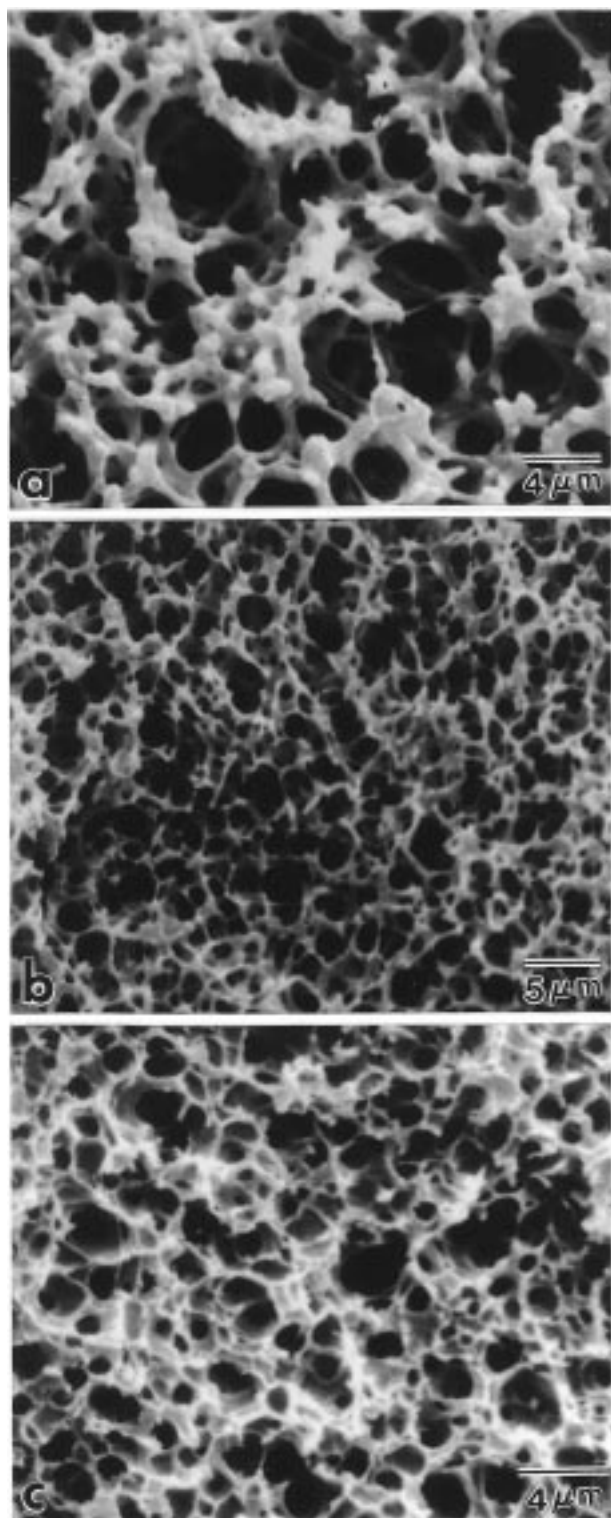


Figure 3. Series of cross-sectional SEM micrographs of the freeze-dried (a) P16S1, (b) P20, and (c) P38 gels, illustrating the effect of initial polymer concentration (C_p) on gel morphology. See Table 1 for synthesis conditions and microstructural characteristics.

modest reduction in cross-linker by 20% would have acted primarily to increase the time prior to gelation slightly; this would have tended to increase the pore and strut size, as discussed in detail in the next section). In all cases, however, the pores remain interconnected as expected if phase separation occurs via spinodal decomposition. Thus, by altering the initial polymer concentration, the effective porosity of microporous gels can

Table 2. Effect of Reaction Time before Phase Separation (t_{BP}) on Gel Morphology

Synthesis Parameters					
initial polymer concentration, $C_p = 9.0$ wt %					
initial cross-linker concentration, $C_x = 1.4$ – 1.6 wt %					
reaction time before phase separation, $t_{BP} = 1.5$ – 480 min					
reaction time during phase separation, $t_{DP} = 19$ – 24 h					
reaction time after phase separation, $t_{AP} = 0$ min					
overall reaction time ≈ 24 h					
sample designation	t_{BP} , min	effective porosity, g/g	pore size cross-section, μm	strut thickness, μm	pore morphology
P24	1.5	0.76	0.5–9.0	1.0–2.0	interconnected
P53B	2.9	0.77	0.5–8.0	0.5–2.0	interconnected
P35	8.4	0.73	0.5–8.0	0.5–1.0	interconnected
P34	15	0.72	0.25–3.0	0.25–1.0	interconnected
P70	20	0.69	0.075–0.5	0.1–0.2	interconnected
P41	25	0.47	0.05–0.2	0.1–0.2	interconnected
P69	60	0.08	0.03–0.15		partially interconnected
P73	177		no pores		nonporous
P74	480		no pores		nonporous

be controlled while maintaining pore interconnectivity, without substantially altering pore and strut dimensions.

Effect of Reaction Time before Phase Separation (t_{BP}). Only a modest change in the pore size (of about a factor of 3) was observed in these microporous HPC gels upon changing the initial polymer concentration. But as hypothesized earlier, pore size should be most strongly affected by t_{BP} since the degree of cross-linking prior to induction of phase separation will fix the average distance that polymer chains can move from one another. Thus, in this section, cross-linking reaction time before phase separation (t_{BP}) is varied from 1.5 to 480 min while keeping all other synthesis variables constant ($C_p = 9$ wt %, $C_x = 1.4$ – 1.6 wt %, $t_{DP} \approx 24$ h, and $t_{AP} = 0$ h).

As seen in Table 2, the pore size and strut thickness ranges decrease steadily (by about an order of magnitude overall) as t_{BP} is increased from 1.5 to 20 min. Note, however, that the effective porosity of the gels examined here remains nearly constant, supporting the phase considerations presented in the previous section. A similar reduction in domain size with increasing cross-linking reaction before phase separation has been reported by Hsich et al. upon the phase separation of an epoxy/carboxyl-terminated butadiene acrylonitrile (CTBN) copolymer blend.⁴² Furthermore, from the representative micrographs displayed in Figures 2 and 4, it is apparent that the gel morphology remains comparable; that is, the pores appear interconnected in all cases. However, at $t_{BP} = 25$ min, pore connectivity and microstructure begin to change. For $t_{BP} > 177$ min, the gels are clearly nonporous at the length scales that could be visualized with the SEM microscope employed here.

This observed decrease in the gel pore and strut (domain) sizes can be explained as follows: As the cross-linking reaction time before phase separation is increased, the polymer chains become increasingly more cross-linked in the homogeneous state, resulting in an increase in the solution viscosity and a decrease in polymer chain mobility (which, in turn, reduces the phase separation rate at the onset of phase separation). The rate of phase separation continues to decrease as the cross-linking reaction proceeds simultaneously with the phase separation process. Concurrently, the cross-linking of linear polymer chains locks them into a three-

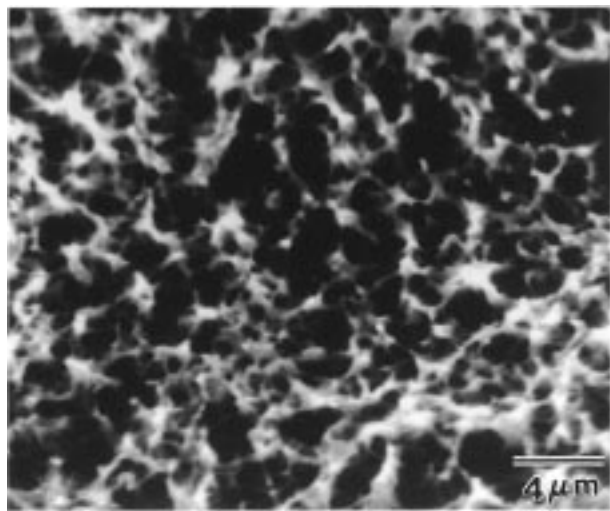


Figure 4. Cross-sectional SEM micrograph of the freeze-dried P34 gel, illustrating the effect of short reaction time before phase separation (t_{BP}) on gel morphology. See Table 2 for synthesis conditions and microstructural characteristics.

dimensional network, which may restrict the distance a polymer chain can move away from other neighboring polymer chains during phase separation. As a result, polymer chains may not be able to move very far from each other, resulting in smaller domain sizes of the concentrated and dilute phases. The smaller pore and strut sizes observed are therefore consistent with the increase in reaction time before phase separation. Thus, the synthesis variable t_{BP} provides a means by which to control the pore and strut sizes while maintaining pore interconnectivity.

As t_{BP} is increased to 60 min, the polymer solution undergoes gelation *before* the onset of phase separation. When the temperature is increased above the phase separation temperature for $t_{BP} > 60$ min, the gelled polymer solution begins to shrink (macrosyneresis) as the cross-linking reaction continues. Due to the continuing cross-linking, however, the gelled solution does not shrink completely; that is, it does not shrink to the same extent as a homogeneous gel of identical composition at the same temperature. This gel (designated P69) possesses pores in the size range 0.03–0.15 μm , indicating that an increase in temperature causes this gel to undergo internal phase separation (microsyneresis) simultaneously with shrinking as solvent is exuded (macrosyneresis). In the micrograph of this gel, the pores do not appear to be completely interconnected, which is consistent with effective porosity measurements (only 8% of the water present in the pores could be removed under mechanical pressure). Upon further increasing t_{BP} to 177 min (sample P73), the resulting gel is found to shrink substantially more relative to gel P69 as the temperature is increased. No pores are visible in the micrograph of the freeze-dried gel P73, although there appears to be two distinct phases comprising the gel.²⁰ Comparable shrinking of a gelled polymer solution with $t_{BP} = 480$ min is likewise observed.

Effective porosity of the gels does not change appreciably with an increase in t_{BP} up to 20 min, but under these conditions the pore and strut sizes decrease significantly. However, for $t_{BP} > 20$ min, the effective porosity decreases, reaching zero at 60 min. Thus the pore and strut sizes of microporous HPC gels can be effectively controlled by varying t_{BP} until gelation occurs,

while maintaining pore interconnectivity. If t_{BP} is increased beyond the gelation time, microporous gels with unconnected pores are produced, in which case t_{BP} should correlate strongly with the sorption/desorption kinetics of such gels (i.e., flow should be fastest in large interconnected pores, decline as the pore density decreases, and slow dramatically if pore interconnectivity is lost altogether). This issue is addressed further in the next section.

Effect of Reaction Time during Phase Separation (t_{DP}). By varying the initial polymer concentration and reaction time before phase separation, we have demonstrated that the pore size, strut thickness, and effective porosity of microporous gels can be varied in a controlled fashion. In most of these cases, the gel morphology is relatively invariant, consisting of interconnected pores, although some variation in the degree of pore interconnectivity has been achieved by increasing the reaction time before induction of phase-separation (t_{BP}).

In all of the gels discussed thus far, the reaction in the phase-separated state has been allowed to proceed for nearly 24 h, resulting in preservation of the phase-separated, interconnected domains comprising the gel network. Furthermore, the reaction time *after* phase separation (t_{AP}), has been maintained at zero. To explore the effect of t_{DP} on gel morphology, the cross-linking reaction in the phase-separated state has been conducted for shorter periods than in the previous section and thus may not be sufficiently long to promote either substantial phase separation or preservation of the interconnected phase domains obtained upon phase separation. After the cross-linking reaction is allowed to occur for a time t_{DP} , the temperature is returned to ambient temperature, which is well within the homogeneous region of the phase diagram. This change in temperature can lead to remixing of the phase-separated domains in both the concentrated and dilute phases. The degree of phase remixing should be inversely related to the extent of polymer cross-linking in the concentrated phase, from which the permanent microstructure develops.

In this section, the reaction time before phase separation (t_{BP}) is held constant at about 2 min, while the reaction time during phase separation (t_{DP}) has been varied from 1.5 to 5.1 min (the initial polymer and cross-linker concentrations held constant). After t_{DP} , the cross-linking reaction continues at ambient temperature in a single-phase region of the phase diagram.

A micrograph of gel P45 with a t_{DP} of 1.5 min is shown in Figure 5a (micrographs of gels P75 and P76 appear qualitatively similar and thus are not included here). The morphological characteristics of these gels are substantially different from those of the gels discussed in the previous sections. Micrographs of these gels reveal significantly fewer pores, most of which seem to be dispersed in a continuous solid phase, indicating incomplete pore interconnectivity. These results are further confirmed by effective porosity measurements. Upon application of pressure, these gels can expel only about 11% of their total water content. Thus keeping t_{DP} relatively low produces gels that lack complete pore interconnectivity. If t_{DP} is increased to 5.1 min, a completely interconnected porous structure results, as shown in the micrograph of gel P44, Figure 5b. The morphology of P44 appears similar to that of P24 (Figure 2) with $t_{DP} = 1380$ min. Pore sizes and porosi-

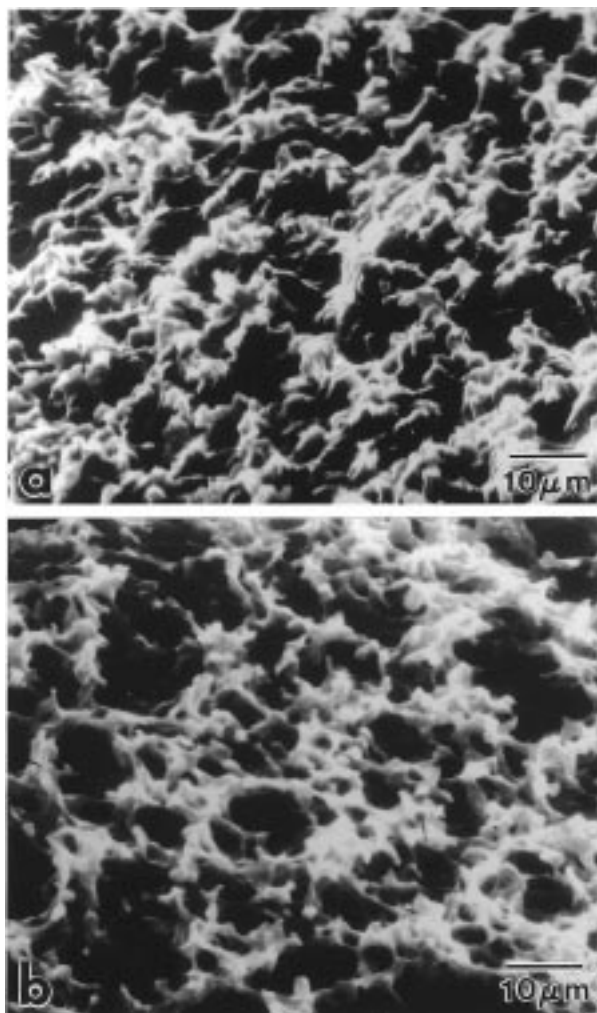


Figure 5. Pair of cross-sectional SEM micrographs of the freeze-dried (a) P45 and (b) P44 gels, illustrating the effect of reaction time during phase separation (t_{DP}) on gel morphology. See Table 3 for synthesis conditions and microstructural characteristics.

Table 3. Effect of Reaction Time during Phase Separation (t_{DP}) on Gel Morphology at Short Reaction Time before Phase Separation ($t_{BP} \approx 2$ min)

Synthesis Parameters						
initial polymer concentration, $C_p = 9.0$ wt %						
initial cross-linker concentration, $C_x = 1.4$ – 1.6 wt %						
reaction time before phase separation, $t_{BP} = 1.5$ – 2.2 min						
reaction time during phase separation, $t_{DP} = 1.5$ – 1380 min						
reaction time after phase separation, $t_{AP} = 0$ – 24 h						
overall reaction time ≈ 24 h						
sample designation	t_{DP} , min	t_{AP} , min	effective porosity, g/g	pore size cross section, μm	strut thickness, μm	pore morphology
P45	1.5	1620	0.12	3.0–8.0	2.0–6.0	partially interconnected
P75	3.7	1620	0.11	0.5–10.0	0.5–18.0	partially interconnected
P76	3.8	1600	0.11	0.5–8.0	0.5–20.0	partially interconnected
P44	5.1	1460	0.77	1.0–16.0	1.0–2.0	interconnected
P24	1380	0	0.71	0.5–9.0	1.0–2.0	interconnected

ties of gels with different t_{DP} are listed in Table 3. The dramatic differences in gel morphology and effective porosity between $t_{DP} = 3.8$ and 5.1 min and the minor corresponding changes for $t_{DP} > 5.1$ min suggest that the formation of a permanent, interconnected microstructure may be a critical phenomenon, perhaps related

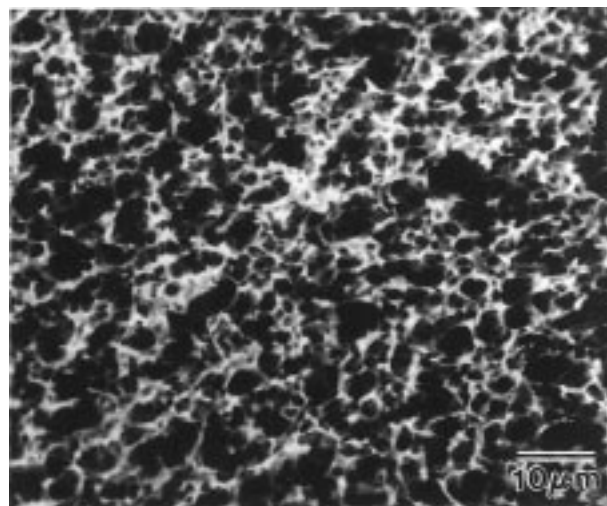


Figure 6. Cross-sectional SEM micrograph of the freeze-dried P46 gel, illustrating the effect of reaction time after phase separation (t_{AP}) on gel morphology. See Table 4 for synthesis conditions and microstructural characteristics.

Table 4. Effect of Reaction Time during Phase Separation (t_{DP}) on Gel Morphology at Long Reaction Time before Phase Separation ($t_{BP} = 8.9$ min)

Synthesis Parameters						
initial polymer concentration, $C_p = 9.0$ wt %						
initial cross-linker concentration, $C_x = 1.6$ wt %						
reaction time before phase separation, $t_{BP} = 8.9$ min						
reaction time during phase separation, $t_{DP} = 1.7$ – 1405 min						
reaction time after phase separation, $t_{AP} = 0$ – 40 h						
overall reaction time = 24 – 40 h						
sample designation	t_{DP} , min	t_{AP} , min	effective porosity, g/g	pore size cross section, μm	strut thickness, μm	pore morphology
P46	1.7	2390	0.64	0.5–8.0	0.5–1.0	interconnected
P35	1405	0	0.73	0.5–8.0	0.5–1.0	interconnected

to a percolation or gel point.

The value of t_{DP} at which the transition occurs from unconnected or partially connected pores to interconnected pores depends largely on the value of t_{BP} . This has been verified by conducting the reaction for longer periods in the homogeneous state (before phase separation). In the case of gel P46, t_{BP} and t_{DP} are fixed at 8.9 and 1.7 min, respectively. As seen in Figure 6, gel P46 exhibits an interconnected, porous microstructure even though t_{DP} is very short (see Table 4). The higher value of t_{BP} (8.9 min compared to 2.0 min in samples P45, P75, and P76) apparently allows sufficient cross-linking to occur prior to phase separation to create an incipient network just short of the gel point. Thus only a relatively short time in the phase-separated state is capable of locking-in a permanent, interconnected gel microstructure. It is possible, therefore, to vary in a systematic fashion the gel morphology from completely interconnected to partially connected or completely unconnected by varying the reaction time during phase separation (t_{DP}) in concert with the reaction time before phase separation (t_{BP}).

Conclusions

A modified version of the TIPS process has been successfully developed to prepare cross-linked, microporous gels with interconnected pores. The modification presented here requires cross-linking of the polymer chains during temperature-induced phase separation of

aqueous polymer solutions. This process facilitates tremendous control over microstructural parameters such as effective porosity, pore size, strut thickness, and pore interconnectivity. Resultant gels consequently exhibit a wide variety of swelling, permeability, and kinetic properties, which will be presented in subsequent work. Since this process is shown to be consistent with principles well-established in the scientific literature, the general conclusions presented here ought to apply to any polymer which can be chemically cross-linked while undergoing thermally induced phase separation.

Gel effective porosity can be tailored through the initial polymer concentration and can be manipulated in controlled fashion while maintaining pore interconnectivity as long as the reaction time during phase separation is sufficiently long to lock-in a phase-separated structure (while keeping the reaction time before phase separation t_{BP} as low as possible). Under these conditions, an increase in the initial polymer concentration results in a reduction in the effective porosity of the gel, in accord with the relative amounts of the polymer-rich and polymer-dilute phases found by applying the lever rule to the phase diagram of the system. The pore and strut sizes likewise can be controlled through the reaction time before phase separation. Pore and strut sizes decrease with increasing reaction time before phase separation, whereas pore interconnectivity is retained only at low t_{BP} . Long cross-linking reaction times before phase separation (nearly or greater than the gelation time) results in nonporous gels.

Moreover, the gel morphology, whether closed-cell or open-cell (i.e., extent of pore interconnectivity) can be readily altered by varying the reaction time either before phase separation or during phase separation. If the reaction time before phase separation is slightly longer than the gelation time, a gel with pores dispersed in a continuous polymer-rich phase is produced. In this case, the pore size is quite small (0.03–0.15 μm across). On the other hand, if both the reaction times before and during phase separation are kept short, a gel with partially connected pores is obtained. In this case, the pore sizes are considerably larger (0.5–10.0 μm).

The effect of reaction time during phase separation has been studied here at only one value of initial polymer concentration (9 wt %). However, it may be possible to prepare gels with partially connected or unconnected pores at different initial polymer concentrations if the reaction time in the phase-separated state is not long enough to completely lock-in an interconnected microstructure. The reaction time during phase separation required to fix an interconnected gel microstructure also depends on the extent of cross-linking prior to phase separation. For example, if a fraction of the gel network already exists prior to phase separation, the extent of cross-linking required in the phase-separated state to complete the network will be far less than that in the case where the entire network must form in the phase-separated state. Furthermore, the extent of cross-linking at the time of phase separation or phase dissolution also affects the respective rates of these phase transformations.

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References and Notes

- (1) Gehrke, S. H. *Adv. Polym. Sci.* **1993**, *110*, 81.
- (2) Beltran, S.; Hooper, H. H.; Blanch, H. W.; Prausnitz, J. M. *J. Chem. Phys.* **1990**, *92*, 2061.
- (3) Bae, Y. H.; Okano, T.; Kim, S. W. *J. Polym. Sci., Polym. Phys. Ed.* **1990**, *28*, 923.
- (4) Ilavsky, M. *Polymer* **1981**, *22*, 1687.
- (5) Tanaka, T.; Nishio, I.; Sun, S.-T.; Ueno-nishio, S. *Science* **1982**, *218*, 467.
- (6) Osada, Y.; Umezawa, K. *Biomedica* **1987**, *2*, 927.
- (7) Mamada, A.; Tanaka, T.; Kungwachakun, D.; Irie, M. *Macromolecules* **1990**, *23*, 1517.
- (8) Gehrke, S. H.; Andrews, G. P.; Cussler, E. L. *Chem. Eng. Sci.* **1986**, *41*, 2153.
- (9) Hoffman, A. S.; Affrassibi, A.; Dong, L. C. *J. Controlled Release* **1986**, *4*, 213.
- (10) Gehrke, S. H.; Lyu, L. H.; Barnhouse, K. *Sep. Sci. Technol.* in press.
- (11) Huang, X.; Unno, H.; Akehata, T.; Hirasa, O. *J. Chem. Eng. Japan* **1987**, *20*, 123.
- (12) Suzuki, M.; Hirasa, O. *Adv. Polym. Sci.* **1993**, *100*, 241.
- (13) Kabra, B. G.; Akhtar, M. K.; Gehrke, S. H. *Polymer* **1992**, *33*, 990.
- (14) Kabra, B. G.; Gehrke, S. H. *Polym. Commun.* **1991**, *32*, 322.
- (15) Wu, X. S.; Hoffman, A. S.; Yager, P. *J. Polym. Sci., Polym. Chem. Ed.* **1992**, *30*, 2121.
- (16) Yoshida, R.; Katsumi, U.; Kaneko, Y.; Sakai, K.; Kikuchi, A.; Sakurai, Y.; Okano, T. *Nature* **1995**, *374*, 240.
- (17) Kesting, R. E. *Synthetic Polymeric Membranes: A Structural Perspective*; John Wiley & Sons: New York, 1985.
- (18) Young, A. T.; Moreno, D. K.; Marsters, R. G. *J. Vac. Sci. Technol.* **1982**, *20*, 1094.
- (19) Aubert, J. H.; Clough, R. L. *Polymer* **1985**, *26*, 2047.
- (20) Kabra, B. G. Ph.D. Thesis, University of Cincinnati, 1993.
- (21) Kabra, B. G.; Gehrke, S. H. *ACS Symp. Ser.* **1994**, *573*, 76.
- (22) Cameron, N. R.; Sherrington, D. C. *Adv. Polym. Sci.* **1996**, *126*, 163.
- (23) Allan, D. S. In *Modern Superabsorbent Polymer Technology*; Buchholz, F. R.; Graham, A. T., Eds.; Wiley-VCH: New York, 1998; Chapter 6, p 223.
- (24) Kabra, B. G.; Gehrke, S. H., U.S. Patent No. 5,573,994, 1996.
- (25) Seidl, J.; Malinsky, J.; Dusek, K.; Heitz, W. *Adv. Polym. Sci.* **1967**, *5*, 113.
- (26) Wojaczynska, M.; Kolarz, B. N. *J. Appl. Polym. Sci.* **1995**, *56*, 433.
- (27) Bansil, R.; Liao, G. *Trends Polym. Sci.* **1997**, *5*, 146.
- (28) Kolarz, B. N.; Wojaczynska, M.; Trochimczuk, A. W. *Makromol. Chem.* **1993**, *194*, 1299.
- (29) Okay, O.; Balkas, T. I. *J. Appl. Polym. Sci.* **1986**, *31*, 1785.
- (30) Okay, O.; Gürün, C. *J. Appl. Polym. Sci.* **1992**, *46*, 421.
- (31) Küçük, I.; Kuyulu, A.; Okay, O. *Polym. Bull.* **1995**, *32*, 511.
- (32) Harsh, D. C.; Gehrke, S. H. *J. Controlled Release* **1991**, *17*, 175.
- (33) Fortin, S.; Charlet, G. *Macromolecules* **1989**, *22*, 2286.
- (34) Kyu, T.; Mukherjee, P. *Liq. Cryst.* **1988**, *3*, 631.
- (35) Kyu, T.; Zhuang, P.; Mukherjee, P. *ACS Symp. Ser.* **1989**, *384*, 266.
- (36) Chowdhury, A. H.; Russo, P. S. *J. Chem. Phys.* **1990**, *92*, 5744.
- (37) O'Connor, S. M.; Gehrke, S. H. *J. Appl. Polym. Sci.* **1997**, *66*, 1279.
- (38) Frey, M. W.; Cuculo, J. A.; Spontak, R. J. *J. Polym. Sci., Polym. Phys. Ed.* **1996**, *34*, 2049.
- (39) Dauben, M.; Platkowski, K.; Reichert, K. H. *Angew. Makromol. Chem.* **1997**, *250*, 67.
- (40) Tsai, F.-J.; Torkelson, J. M. *Macromolecules* **1990**, *23*, 775.
- (41) Cahn, J. W. *J. Chem. Phys.* **1965**, *42*, 93.
- (42) Hsieh, H. S.-Y. *J. Mater. Sci.* **1991**, *26*, 3209.

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