

Frontal Polymerization Synthesis of Temperature-Sensitive Hydrogels

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The study of hydrogels and their response to external environment is of special interest because of their potential as drug delivery systems,^{1,2} actuators,³ and separation devices.^{4,5} Temperature-sensitive hydrogels undergo a reversible swelling–deswelling transition with a small change of temperature near the phase transition point.⁶ A frequently studied thermosensitive hydrogel is based on solution free-radical cross-linking copolymerization of the monomer *N*-isopropylacrylamide and the cross-linker *N*-*N*-methylenebisacrylamide. The availability of preparation techniques allowing the synthesis of hydrogels with structural uniformity is limited by the exothermicity of the polymerization reaction which induces phase separation of linear poly(*N*-isopropylacrylamide) chains, PNIPAM, at 32 °C.⁷ Therefore, to generate uniform hydrogels, small-sized samples are usually produced at low monomer and initiator concentration and at low synthesis temperature that circumvent spatial inhomogeneities and microaggregation. Under these reaction conditions, the rates of polymerization and gelation are low, requiring longer time to synthesize hydrogels. We present here the first frontal polymerization synthesis of isopropylacrylamide (NIPAM) hydrogels at high monomer and initiator concentration. It has been found that, in addition to a more rapid synthesis of hydrogels, a substantial increase in the homogeneity of the microstructure of the hydrogel with respect to the solution polymerization is obtained. Moreover, large hydrogel samples with similar equilibrium swelling ratio can be readily produced without the effect of microaggregation and phase separation.

Frontal polymerization involves the conversion of monomer to polymer in a localized reaction zone which propagates due to the interplay of thermal conduction and temperature-dependent reaction rates.^{8,9} First introduced as a way to synthesize poly(methyl methacrylate) at high pressure,¹⁰ the method was later extended by Pojman and co-workers to include numerous polymers^{11,12} and cross-linked networks¹³ produced at ambient pressure. Thermochromic composite materials, polymer blends, and simultaneous interpenetrating polymer networks have been synthesized by frontal polymerization.^{14–16} In these examples, the

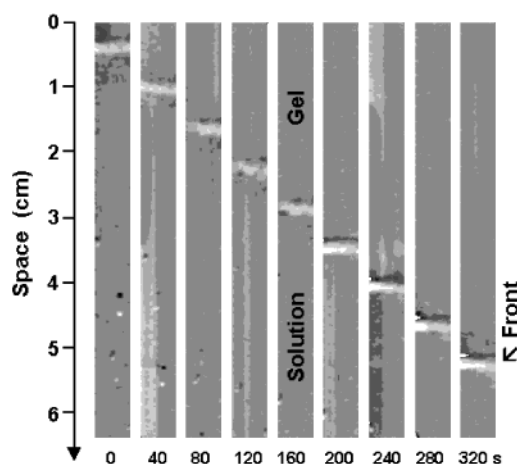


Figure 1. Sequence of image-processed video-frames illustrating the constant-speed propagation of the polymerization front. Initial conditions: 5 g of isopropylacrylamide, 0.02 g of ammonium persulfate, and 0.05 g of bisacrylamide in 2.5 mL of DMSO.

rapid reaction rate, observed in propagating fronts, circumvents phase separation that is common in batch studies. Consequently, the resulting materials are more uniform than ones synthesized in a batch reactor. At times, frontal polymerization may not be sufficient to arrest phase separation because the synthesis of polyacrylamide cross-linked with bisacrylamide leads to opaque gels, suggesting that phase separation does occur.¹³

Because the temperature of traveling fronts reaches close to the boiling point of water, DMSO was used as the solvent for producing isopropylacrylamide hydrogels. The gel system was typically studied for solutions containing NIPAM (2 g/mL), persulfate (0.008 g/mL), and bisacrylamide (0.02 g/mL). The monomer, NIPAM, the cross-linking agent, and the initiator were dissolved in a known amount of degassed DMSO. The homogeneous solution was purged with nitrogen for 10 minutes and transferred to a 10 cm long test tube (ID 13 mm). Initiation of the front was achieved by using a soldering iron as the heat source.

Figure 1 shows a representative time series of frontal polymerization of NIPAM hydrogel. The initial temperature perturbation dissociates the initiator, persulfate, into radicals that combine with monomer units resulting in a polymer network after subsequent cross-linking. The heat of the polymerization reaction disperses into the unreacted region by thermal conduction, and a propagation front ensues. A slight difference in refractive index between the synthesized hydrogel and the gelling solution allows us to optically monitor the progression of the front and to determine its velocity from distance versus time plots. Under the conditions specified in Figure 1, the propagating front traveled through the system at a constant velocity of 8.3 mm/min. For the given dimensions, the entire hydrogel sample was synthesized within 10 min. Furthermore, we found that the speed of the front depends strongly on the initial concentration of persulfate, which can be used to further shorten the synthesis time. For example, a 2-fold increase in persulfate (0.032 to 0.064 *m*) corresponds to an increase in propagation velocity from 8.3 to 12.6 mm/min. The concentration of bisacrylamide, however, has little effect on the front velocity.

To compare the macroscopic as well as microscopic properties of hydrogels obtained from frontal and conventional synthesis, reference gels with the same nominal composition were synthesized in a batch reactor at 60 °C. Both preparation schemes

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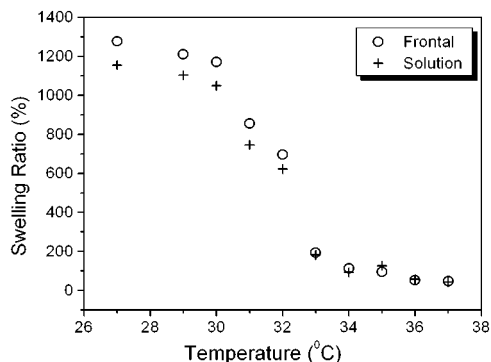


Figure 2. Temperature dependence of the equilibrium swelling ratio of hydrogels produced by frontal and solution polymerization. The swelling ratio, SR, was obtained by weighing the hydrogel at different temperatures and is calculated as: $SR = 100\% \times (\text{swollen mass} - \text{dry mass})/\text{dry mass}$.

produced transparent gels, suggesting that no macroscopic phase separation occurred during the gel formation. Two important features of the hydrogels are their temperature-dependent volume and their microscopic morphology, which will be discussed in the following. We investigated the water-uptake of dried hydrogel samples in aqueous solutions. The curves in Figure 2 show a sigmoidal dependence between the sample mass and the system temperature. These data reveal that the high-temperature synthesis of frontal polymerization does affect neither the equilibrium swelling ratios in the collapsed region nor the phase transition temperature of the obtained samples. Note that at low temperatures a slight increase in the swelling ratio is observed, which could be attributed to structural defects in the conventionally produced hydrogel. This presumption is confirmed by scanning electron microscopy (SEM) data which revealed a striking difference in the microscopic morphology of the two hydrogels. The samples used for SEM measurements were quickly frozen in liquid nitrogen and freeze-dried for 1 day. Two representative micrographs are shown in Figure 3. The hydrogel synthesized by frontal polymerization has a spongelike microporous structure with a relatively uniform pore size distribution. The solution-produced hydrogel, however, displays a morphology in which the microporous structure involves a dispersed microaggregated phase.

The well-defined pores obtained in the frontal synthesis of hydrogels can be attributed to the rapid increase in synthesis temperature at the polymerization front, which suppresses macroscopic phase separation and microaggregation, as well as sedimentation of domains of different density. To characterize the temperature profile along the reaction front, a thermocouple was inserted into the pregel solution, which recorded the temperature evolution at a particular point of the reaction system. These measurements showed that the temperature increases locally from 26 to 98 °C in less than one minute. According to the constant velocity, c , of the front, the temporal data, $T(t)$, were converted to spatial temperature profiles (i.e., $T(x) = T(c \cdot t)$). Figure 4 indicates that the temperature increase from 26 to 98 °C is localized to a (traveling) 20 mm interval. This localization and the related fast increase in temperature are the key features that allow for the rapid synthesis of hydrogels with a spatially uniform microstructure.

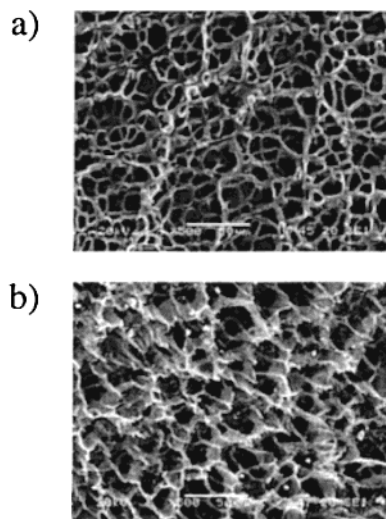


Figure 3. Scanning electron micrographs of hydrogels produced by frontal polymerization (a) and conventional batch polymerization at 60 °C (b). Field of view = $(220 \times 280) \mu\text{m}^2$.

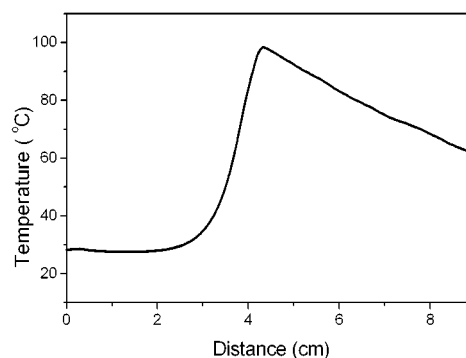


Figure 4. Temperature profile obtained during the frontal polymerization of the hydrogel. See Figure 1 for initial conditions.

In conclusion, we have demonstrated that the rapid polymerization in a localized reaction zone allows for controlled in situ frontal polymerization of isopropylacrylamide with no spatial inhomogeneities. This fast and efficient way of synthesizing hydrogels does not compromise their temperature-dependent properties, which make these systems promising candidates for various applications that call for environment-controlled volume changes. We have also been able to produce other hydrogels (e.g., the pH-sensitive acrylamide–dimethylaminoethyl methacrylate hydrogel) using frontal polymerization, indicating the versatility of the technique. Nevertheless, more studies are needed to explore the applicability of this approach to a wider class of hydrogels and to quantify the effect of the synthesis method on dynamic properties.

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