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Facile Glycerol-Assisted Synthesis of *N*-Vinyl Pyrrolidinone-Based Thermosensitive Hydrogels via Frontal Polymerization

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We report a facile strategy for quickly fabricating thermosensitive poly(HPMA-*co*-NVP) hydrogels in the presence of glycerol by using frontal polymerization (FP). The appropriate amounts of hydroxypropyl methacrylate (HPMA) and 1-vinyl-2-pyrrolinone (NVP), *N*,*N*′-methylenebisacrylamide (MBAA), and ammonium persulfate (APS)/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) couple redox initiator were mixed together at ambient temperature in the presence of glycerol as the medium. A variety of features for preparing hydrogel samples, such as ratios of NVP/HPMA, the presence of the glycerol and its concentration, and MBAA cross-linker concentration, were thoroughly investigated. We have found that the presence of glycerol can suppress the "fingering" of FP and overcome the formation of bubbles. Also, the ratio of NVP/HPMA for synthesis of hydrogels by FP plays an important role in its microstructure and swelling property. The morphology, thermosensitive behavior, and swelling studies of polymer hydrogels prepared via FP are comparatively investigated on the basis of environmental scanning electron microscopy (ESEM) and swelling measurement. Results show that the swelling capacity of the hydrogel prepared via FP is superior to that obtained by the traditional batch polymerization (BP) method. The glycerol-assisted FP can be exploited as an alternative means for synthesis of NVP-based copolymer hydrogels with additional advantages of fast and efficient way.

Introduction

Hydrogel, a kind of three-dimensional cross-linked polymer network imbibing large quantities of water while maintaining its integrity, has attracted academic and industrial interests.[1−4] Several hydrogels exhibit dramatic and reversible volume changes, in response to a variety of environment stimuli, such as temperature, pH, ionic strength, stress, magnetic, electrical, and ultrasound irradiation.[5−8] Numerous applications of hydrogels have been widely applied in soft contact lenses,[9] chemical sensors,[10] controlled drug delivery materials,[11] tissue engineering,[12] wound dressing,[13] and diagnostics[14] due to their excellent swelling−deswelling properties and stimuli-responsive behaviors. Up to now, many approaches for preparing versatile hydrogels have been rapidly achieved by using a variety of monomers via free-radical polymerization, such as 1-vinyl-2-pyrrolinone (NVP),[15] 2-hydroxyethyl methacrylate (HEMA),[16] *N*-isopropylacrylamide (NIPAM),[17] acrylamide (AAm),[18] and acrylic acid (AAc),[19] along with some chemical cross-linkers, such as *N*,*N*′-methylenebisacrylamide (MBAA). Among the hydrogel family, the poly(*N*-vinyl pyrrolidinone) (PVP) hydrogel, which is nontoxic and thermosensitive, has attracted great investigation efforts owing to its high biocompatibility and good affinity to water.[20] However, as a practical point of view, PVP has a poor mechanical strength, thus limiting its potential application. To obtain desirable mechanical properties of hydrogels, a great deal of research has been concentrated on reinforcing their

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(1) Osada, Y.; Gong, J. P. *Adv. Mater.* **1998**, *10*, 827.
(2) Nguyen, K. T.; West, J. L. *Biomaterials* **2002**, *23*, 4307.
(3) He, B.; Wan, E.; Chan-Park, M. B. *Chem. Mater.* **2006**, *18*, 3946.
(4) Ladet, S.; David, L.; Domard, A. *Nature* **2008**, *452*, 76.
(5) Sershen, S.; West, J. *Adv. Drug Delivery Rev.* **2002**, *54*, 1225.
(6) Matsukuma, D.; Yamamoto, K.; Aoyagi, T. *Langmuir* **2006**, *22*, 5911.
(7) Ehrick, J. D.; Stokes, S.; Bachas-Daunert, S.; Moschou, E. A.; Deo, S. K.; Bachas, L. G.; Daunert, S. *Adv. Mater.* **2007**, *19*, 4024.
(8) Kozlovskaya, V.; Kharlampieva, E.; Khanal, B. P.; Manna, P.; Zubarev, E. R.; Tsukruk, V. V. *Chem. Mater.* **2008**, *20*, 7474.
(9) Kim, S. H.; Opdahl, A.; Marmo, C.; Somorjai, G. A. *Biomaterials* **2002**, *23*, 1657.
(10) Lee, Y. J.; Braun, P. V. *Adv. Mater.* **2003**, *15*, 562.
(11) Dai, H. J.; Chen, Q.; Qin, H. L.; Guan, Y.; Shen, D. Y.; Hua, Y. Q.; Tang, Y. L.; Xu, J. *Macromolecules* **2006**, *39*, 6584.
(12) Luo, Y.; Shoichet, M. S. *Nat. Mater.* **2004**, *3*, 249.
(13) Balakrishnan, B.; Mohanty, M.; Umashankar, P. R.; Jayakrishnan, A. *Biomaterials* **2005**, *26*, 6335.
(14) van der Linden, H. J.; Herber, S.; Olthuis, W.; Bergveld, P. *Analyst* **2003**, *128*, 325.
(15) Fechine, G. J. M.; Barros, J. A.G.; Alcantara, M. R.; Catalani, L. H. *Polymer* **2006**, *47*, 2629.
(16) Stachowiak, A. N.; Bershteyn, A.; Tzatzalos, E.; Irvine, D. *J. Adv. Mater.* **2005**, *17*, 399.
(17) Jones, C. D.; Lyon, L. A. *Macromolecules* **2003**, *36*, 1988.
(18) Grassmann, O.; Muller, G.; Lobmann, P. *Chem. Mater.* **2002**, *14*, 4530.
(19) Moschou, E. A.; Peteu, S. F.; Bachas, L. G.; Madou, M. J.; Daunert, S. *Chem. Mater.* **2004**, *16*, 2499.
(20) Devine, D. M.; Higginbotham, C. L. *Eur. Polym. J.* **2005**, *41*, 1272.

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degree of cross-linking or using the copolymerization method.[21] For instance, poly(acrylic acid-*co*-*N*-vinyl pyrrolidinone) hydrogels,[22] poly(*N*-isopropylacrylamide-*co*-*N*-vinyl pyrrolidinone) hydrogels,[23] and poly(hydroxyethyl methacrylate-*co*-*N*-vinyl pyrrolidinone) hydrogels[24] were prepared for this purpose. It is considered that these copolymer hydrogels containing hydrogen bond interactions may enhance the mechanical properties of hydrogels.[25] Although much literature has been reported on PVP-based hydrogels, unfortunately, there is little information on the effect of altering monomer compositions and polymerization variables on the network structure of the resulting hydrogels.

In 2001, Washington and Steinbock first reported the synthesis of temperature-sensitive poly(*N*-isopropylacrylamide) hydrogels using frontal polymerization (FP) in the presence of dimethyl sulfoxide (DMSO) as the solvent.[26] Typically, FP is a mode of converting a monomer into a polymer via a localized reaction zone that propagates through the coupling of thermal diffusion and temperature-dependent reaction rate. Since the first pioneering work discovered by Chechilo and Enikolopyan in 1972 who studied methyl methacrylate polymerization under adiabatic conditions at high pressure,[27] a great deal of work on this versatile and facile methodology for synthesizing a wealth of uniform polymers and polymeric networks with spatially controlled microstructures and morphologies has been performed in a rapid fashion.[28−31] Pojman and co-workers demonstrated FP with thiol−ene systems,[32] ionic liquid,[33] and a microencapsulated initiator.[34] Mariani et al. obtained poly(dicyclopentadiene),[35] polyurethane,[36] epoxy resin−montmorillonite;[37] moreover, they developed an FP method for the consolidation of stone[38] and applied phosphonium-based ionic liquids as radical initiators in FP.[39] Chen et al. reported that segmented PU, poly urethane−nanosilica hybrids, epoxy resin−polyurethane hybrid networks, urethane−acrylate copolymers, poly(*N*-methylolacrylamide), poly(hydroxyethyl acrylate), and poly(*N*-methylolacrylamide)/poly(methyl acrylamide) hybrids were synthesized by FP.[40−47] Recently, some works in the literature reported synthesis of other hydrogels via FP. Ge et al. reported the FP synthesis of a graft copolymer superabsorbent hydrogel of acrylic acid onto starch in aqueous solution.[48] Mariani and co-workers prepared poly(*N,N*-dimethylacrylamide) hydrogels using different solvents via FP.[49] They found that the swelling ratio was influenced by the presence and type of solvents, with values ranging from 850 to 3500% for some samples prepared in water and DMSO. Very recently, in our previous work, we successfully prepared poly(*N*-vinyl pyrrolidinone) and poly(*N*-methylolacrylamide)/polyhededral oligomeric silsesquioxane graft copolymer hybrids via FP.[50,51]

In this work, we report on glycerol assisted synthesis of thermosensitive poly(HPMA-*co*-NVP) hydrogels via FP. To the best of our knowledge, there has been no precedent report on glycerol as the medium to fabricate hydrogels. The presence of glycerol not only suppresses the "fingering" of FP but also does not alter the three-dimensional network structure of hydrogels. The aim of this research is to evaluate the impact of varying the monomer compositions of the hydrogel on morphologies and swelling properties. The results will provide insights into the structure−property relationship for this range of hydrogels and the use of glycerol assisted synthesis in the preparation of other kinds of hydrogels.

Experimental Section

Materials. Hydroxypropyl methacrylate (HPMA), 1-vinyl-2-pyrrolidinone (NVP), glycerol, *N*-methyl-2-pyrrolidone (NMP), and *N*,*N*′-methylenebisacrylamide (MBAA) were purchased from Aldrich. The redox couple, ammonium persulfate (APS)/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as the redox initiator was also obtained from Aldrich. All chemicals were used as received, without further purification.

(21) Anseth, K. S.; Bowman, C. N.; Brannon-Peppas, L. *Biomaterials* **1996**, *17*, 1647.
(22) Devine, D. M.; Higginbotham, C. L. *Polymer* **2003**, *44*, 7851.
(23) Geever, L. M.; Minguez, C. M.; Devine, D. M.; Nugent, M. J. D.; Kennedy, J. E.; Lyons, J. G.; Hanley, A.; Devery, S.; Tomkins, P. T.; Higginbotham, C. L. *J. Mater. Sci.* **2007**, *42*, 4136.
(24) Mcbrierty, V. J.; Quinn, F. X.; Keely, C.; Wilson, A. C.; Friends, G. D. *Macromolecules* **1992**, *25*, 4281.
(25) Peppas, N. A.; Bures, P.; Leobandung, W.; Ichikawa, H. *Eur. J. Pharm. Biopharm.* **2000**, *50*, 27.
(26) Washington, R. P.; Steinbock, O. *J. Am. Chem. Soc.* **2001**, *123*, 7933.
(27) Chechilo, N. M.; Khvilivitskii, R. J.; Enikolopyan, N. S. *Dokl. Akad. Nauk SSSR* **1972**, *204*, 1180.
(28) Chechilo, N. M.; Enikolopyan, N. S. *Dokl. Phys. Chem.* **1974**, *214*, 174.
(29) Chechilo, N. M.; Enikolopyan, N. S. *Dokl. Phys. Chem.* **1975**, *221*, 392.
(30) Chechilo, N. M.; Enikolopyan, N. S. *Dokl. Phys. Chem.* **1976**, *230*, 840.
(31) Pojman, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 6284.
(32) Pojman, J. A.; Varisli, B.; Perryman, A.; Edwards, C.; Hoyle, C. *Macromolecules* **2004**, *37*, 691.
(33) Jiménez, Z.; Pojman, J. A. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2745.
(34) McFarland, B.; Popwell, S.; Pojman, J. A. *Macromolecules* **2004**, *37*, 6670.
(35) Mariani, A.; Fiori, S.; Chekanov, Y.; Pojman, J. A. *Macromolecules* **2001**, *34*, 6539.
(36) Fiori, S.; Mariani, A.; Ricco, L.; Russo, S. *Macromolecules* **2003**, *36*, 2674.
(37) Mariani, A.; Bidali, S.; Caria, G.; Monticelli, O.; Russo, S.; Kenny, J. M. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2204.
(38) Vicini, S.; Mariani, A.; Princi, E.; Bidali, S.; Pincin, S.; Fiori, S.; Pedemonte, E.; Brunetti, A. *Polym. Adv. Technol.* **2005**, *16*, 293.
(39) Mariani, A.; Nuvoli, D.; Alzari, V.; Pini, M. *Macromolecules* **2008**, *41*, 5191.
(40) Chen, S.; Sui, J. J.; Chen, L. *Colloid Polym. Sci.* **2005**, *283*, 932.
(41) Chen, S.; Sui, J. J.; Chen, L.; Pojman, J. A. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 1670.
(42) Chen, S.; Feng, C.; Sui, J. J. *Acta Polym. Sin.* **2005**, *1*, 1.
(43) Chen, S.; Tian, Y.; Chen, L.; Hu, T. *Chem. Mater.* **2006**, *18*, 2159.
(44) Hu, T.; Chen, S.; Tian, Y.; Pojman, J. A.; Chen, L. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 3018.
(45) Chen, S.; Hu, T.; Tian, Y.; Chen, L.; Pojman, J. A. *J. Polym. Sci., Part A: Polym. Chem* **2007**, *45*, 873.
(46) Chen, L.; Hu, T.; Yu, H.; Chen, S.; Pojman, J. A. *J. Polym. Sci., Part A: Polym. Chem* **2007**, *45*, 4322.
(47) Hu, T.; Fang, Y.; Yu, H.; Chen, L.; Chen, S. *Colloid Polym. Sci.* **2007**, *285*, 891.
(48) Yan, Q. Z.; Zhang, W. F.; Lu, G. D.; Su, X. T.; Ge, C. C. *Chem.—Eur. J.* **2005**, *11*, 6609.
(49) Caria, G.; Alzari, V.; Monticelli, O.; Nuvoli, D.; Kenny, J. M.; Mariani, A. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 1422.
(50) Cai, X. J.; Chen, S; Chen, L. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2177.
(51) Fang, Y.; Chen, L.; Chen, S. *J. Polym. Sci., Part A: Polym. Chem* **2009**, *47*, 1136.

FP. We chose the APS/TMEDA couple as the redox initiator to decrease the triggering temperature and front temperature, allowing monomers with lower boiling point to polymerize without bubbles. The appropriate amounts of HPMA, NVP, MBAA, and APS were mixed with glycerol at ambient temperature in a flask. A typical composition was NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, and APS = 0.1 wt %. The flask was shaken vigorously to obtain a homogeneous solution. Then, the mixture was added by the reductant TMEDA ([APS]/[TMEDA] = 1:4 mol/mol) and poured into a 10 mL (15 mm diameter) glass test tube. The reaction mixture was kept at about 18−25 °C to slow bulk polymerization. The upper side of the mixture was then heated by a soldering iron until the hot propagating front commenced.

The front position was recorded as a function of time. A plot of the front position versus time produced a straight line whose slope was the front velocity. Temperature profiles were measured using a K-type thermocouple connected to a digital thermometer, one end of which was immersed into the mixture at a certain distance from the free surface. Subsequently, temperature as a function of time was converted to a spatial profile using the front velocity.[32] After the completion of reaction, the samples were removed from the tube and cut into small pieces (2−5 mm) which were purified by immersion in deionized water for 7 days to remove all water-soluble materials. Then the pieces were dried in a vacuum oven at 60 °C until the weight of the specimen was constant.

Batch Polymerization (BP). Several batch runs were performed to compare the resultant samples with the corresponding ones obtained by FP. In a typical run, the same amounts of each component as quoted above were mixed with vigorous stirring in a reaction vessel and immersed in a thermostatted oil bath set at 60 °C for 2 h.

FT-Raman Spectroscopy. To identify the chemical structures of the products, FT-Raman spectra were obtained by Nicolet-6700 FT-IR spectrometer equipped with a NXR FT-Raman module and the research-grade 2.0 w nd:yvo$_4$ laser with wavelength of 1064 nm. The spectra were collected at a resolution of 4 cm^{-1}.

Environmental Scanning Electron Microscopy (ESEM) Measurements. The structures of hydrogels obtained were investigated by ESEM with a QUANTA 200 (Philips-FEI, Holland). The samples were immersed in deionized water at room temperature for 7 days. During this time, the water was changed daily to allow for the removal of water-soluble materials, and then the samples were dried in a vacuum oven at 60 °C. Dried samples were immersed again in deionized water to swell at room temperature. Hydrous samples used for ESEM measurement were cut to expose their inner structure.

Swelling Measurements. Water absorption measurements were performed by gravimetric analysis. Dried samples were weighed and then immersed in excessive amount deionized water at room temperature. At regular time intervals, the samples were taken out, wiped of excessive water with filter paper, weighed, and returned to the swelling medium. The experiment was continued until a constant weight of samples was achieved. The equilibrium swelling ratio (SR) in water was determined gravimetrically by the following equation:[26]

$$\text{Swelling Ratio (SR, \%)} = (W_s - W_{dry})/W_{dry} \times 100\%$$

where W_s is the weight of swollen samples after the certain time and W_{dry} is the weight of dried samples.

Results and Discussion

FP. For frontal polymerization, a stable front is essential to perform the FP process. If there is no stable flat front, such as the phenomenon of "fingering" observed under the descending front due to the interference of double-diffusive convection, the "fingering" effect associated with the formation of bubbles will affect the front velocity and even leave a hole in the polymer product. Thus, we cannot get the V_{front} data of FP at all. Up to now, a great deal of research has been concentrated on suppressing these phenomena: changing the initiator concentration or increasing the viscosity of the liquid phase by adding some kinds of fillers, such as silica and bis(acrylamide).[52,53] Moreover, since the temperature of traveling fronts usually reaches close to the boiling point of some common solvents, high boiling point solvents (e.g., DMSO and NMP) are employed for producing samples in FP avoiding the formation of bubbles.[53,54] Initially, we prepared poly(HPMA-*co*-NVP) hydrogel using NMP as the solvent. There exists obvious "fingering" during the FP in this system (see Supporting Information, Figure S1a). The formation of "fingering" in the tube may be due to the occurrence of Rayleigh-Taylor instabilities, which manifests itself as "fingering" of polymerizing solution that descends from the front.[55] In this case, no stable flat front exists, making it impossible to get the V_{front} data of FP. To address this problem, we chose glycerol as the medium to carry out the FP. We assessed the pot life by preparing tubes with the reactants, leaving them at ambient temperature and visually determining at what time they spontaneously polymerized. We found that the mixture of HPMA, NVP (NVP/HPMA = 3:7 (w/w)), glycerol (40 wt %), MBAA (0.3 wt %), APS (0.1 wt %), and TMEDA ([APS]/[TMEDA] = 1:4 mol/mol) is inert at the ambient temperature (18−25 °C) for more than 2 h but very reactive after being heated for several seconds with a soldering iron. Perhaps more interestingly, in the case of glycerol-assisted synthesis of poly(HPMA-*co*-NVP) hydrogel, the glycerol cannot only suppress the "fingering" of FP but also overcome the formation of bubbles during the FP process (see Supporting Information, Figure S1b). It can be explained by the fact that glycerol can effectively increase the viscosity of this system and exhibit good compatibility with NVP monomer. This finding allows us to perform pure FP runs without simultaneous occurrence of "fingering". Up to now, the utilization of glycerol as the medium to assist carrying out FP and to fabricate polymer hydrogel has not been previously described.

Figure 1a shows a representative time series of visual images illustrating the constant-speed propagation of the polymerization front of the poly(HPMA-*co*-NVP) hydrogel. The interface between the polymer and unreacted

(52) Pojman, J. A.; Craven, R.; Khan, A.; West, W. *J. Phys. Chem.* **1992**, *96*, 7466.
(53) Pojman, J. A.; Curtis, G.; Ilyashenko, V. M. *J. Am. Chem. Soc.* **1996**, *118*, 3783.
(54) Yu, H.; Fang, Y.; Chen, L.; Chen, S. *Polym. Int.* **2009**, *58*, 851.
(55) Pojman, J. A.; Ilyashenko, V. M.; Khan, A. M. *J. Chem. Soc. Faraday Trans.* **1996**, *92*, 2825.

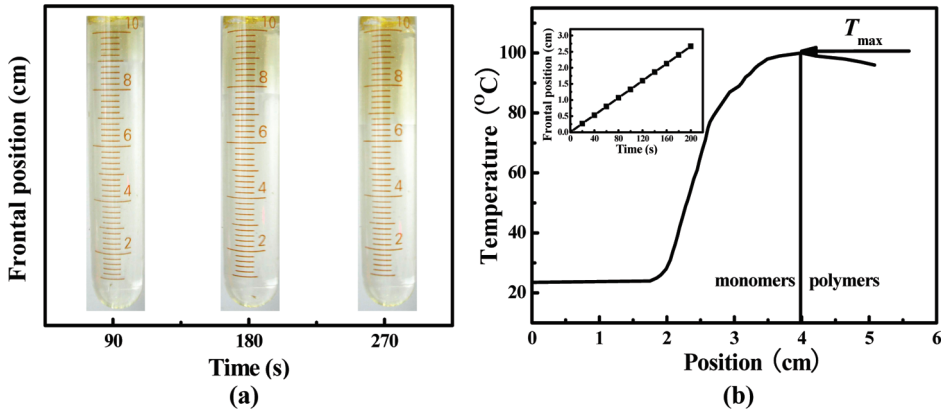

Figure 1. (a) Sequence of images illustrating the constant-speed propagation of the polymerization front of poly(HPMA-*co*-NVP) hydrogel. (b) Typical temperature profile of poly(HPMA-*co*-NVP) hydrogel prepared by FP. Inset: front position vs time for poly(HPMA-*co*-NVP) hydrogel prepared by FP. Initial conditions: NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol.

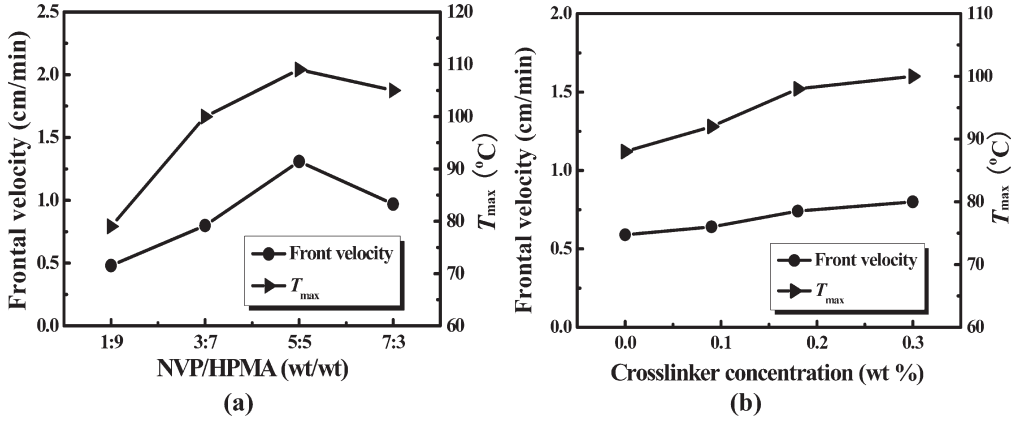

Figure 2. (a) Frontal velocity and T_{max} of poly(HPMA-*co*-NVP) hydrogels prepared by FP vs the NVP/HPMA weight ratios at glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol. (b) Frontal velocity and T_{max} of poly(HPMA-*co*-NVP) hydrogels by FP vs the concentration of cross-linker at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol.

monomer can be clearly seen. The upper layer of mixture is poly(HPMA-*co*-NVP), and the lower layer is unreacted monomer. Front propagation occurs at a constant velocity with almost no formation of bubbles. A fresh sample is transparent, while a cooled one becomes ivory-white. The opacity of the NVP-based hydrogels at NVP/HPMA = 3:7 (w/w) results from the incompatibility between glycerol and hydrophobic comonomer HPMA, causing phase separation.[56] The position of the front as a function of time at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol is given in Figure 1b (inset). As can be seen in Figure 1b (inset), the experimental data are well fitted by a straight line, thus indicating that a constant-velocity, self-sustaining front is obtained. This result represents the evidence that pure FP is occurring. Fronts are always performed in the descending mode to avoid buoyancy-driven convection. The typical temperature profile obtained is also given in Figure 1b. As shown in Figure 1b, in less than 2.2 cm, the temperature increases more than 77 °C, and the T_{max} (the highest temperature that the K-type thermocouple detected at a fixed point of 4 cm from the free surface) is 100 °C. It can be seen that no temperature increase has been observed before the front approached the fixed point, thus indicating that simultaneous polymerization is not occurring to a significant degree during front propagation. The position of the front for different NVP/HPMA weight ratios as a function of time is given in Figure S2 (see Supporting Information Figure S2). The experimental data for all sets of experiments are well fit by straight lines, meaning that the fronts propagate with constant velocities. In Figure 2a, T_{max} and front velocity, as function of the NVP concentration, are reported. When using NVP or HPMA alone, the "fingering" phenomenon occurs, meaning that only one monomer of HPMA or NVP in this case could not obtain a stable front because of occurrence of buoyancy-driven convection. The front velocities at NVP/HPMA = 1:9, 3:7, 5:5, and 7:3 (w/w) are 0.48, 0.80, 1.31, and 0.97 cm/min, respectively. The results show that there exists a maximum front velocity at NVP/HPMA = 5:5 (w/w), while its corresponding T_{max} (109 °C) reaches a maximum value. We emphasize that our experiments were performed under nonadiabatic conditions. For this reason, the increased velocity reduces the time for heat loss.

We investigated the effect of the cross-linker MBAA concentration on both T_{max} and front velocity. Figure 2b

(56) Kiritoshi, Y.; Ishihara, K. *Polymer* **2004**, *45*, 7499.

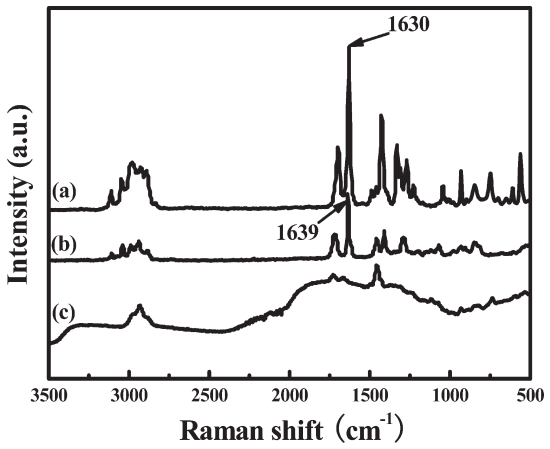

Figure 3. FT-Raman spectra (3500−500 cm^{-1}) of (a) HPMA, (b) NVP, and (c) poly(HPMA-*co*-NVP) hydrogel at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol prepared by FP.

shows the behaviors of these parameters as a function of MBAA concentration. As expected, increasing the MBAA concentrations from 0 to 30 wt % results in the increase in front velocity from 0.59 to 0.80 cm/min and in T_{max} from 88 to 100 °C. The increase of T_{max} is mainly attributed to the increased cross-linker concentration and the increased velocity, allowing heat loss decrease under nonadiabatic conditions. Also, we explored the effect of the glycerol concentration on both T_{max} and front velocity (see Supporting Information Table S1). To find the optimal glycerol concentration for obtaining poly(HPMA-*co*-NVP) hydrogels by FP, several runs were performed with no addition of cross-linker at different glycerol concentrations, varying from 0 to 80 wt %, while APS concentration was maintained at 0.1 wt %, [APS]/[TEMED] = 1:4 mol/mol and NVP/HPMA at a specific ratio of 3:7 (w/w). For glycerol concentration less than 20 wt %, no front propagated. Conversely, for glycerol concentration > 60 wt %, the "fingering" phenomenon occurred. Therefore, the data were obtained for glycerol concentrations between 20 and 60 wt %. As the glycerol concentration increases from 20 to 60 wt %, the front velocity decreases from 1.19 to 0.48 cm/min. An analogous decrease in T_{max} with increasing glycerol concentration is also observed.

FT-Raman Spectrometry Characterization. The structure of the poly(HPMA-*co*-NVP) hydrogel was determined from FT-Raman spectra. Figure 3 shows FT-Raman spectra in the range of 3500−500 cm^{-1} of (a) HPMA, (b) NVP, and (c) poly(HPMA-*co*-NVP) hydrogel at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol prepared by FP. It can be seen that a sharp peak at 1630 cm^{-1} of C═C group appears for pure HPMA sample, while a similar sharp peak at 1639 cm^{-1} is also observable for the pure NVP sample due to the C═C group.[57] However, the peak at around 1630 cm^{-1} nearly disappears in the poly(HPMA-*co*-NVP) sample. The disappearance in Raman peaks associated with the C═C double bond may be attributed to the copolymerization reaction between NVP and HPMA monomer.

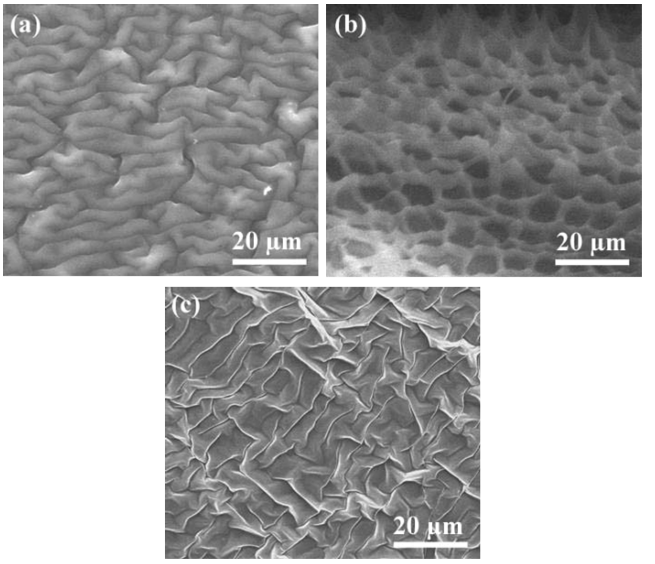

Figure 4. ESEM micrographs of poly(HPMA-*co*-NVP) hydrogels prepared by FP with glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt % and [APS]/[TMEDA] = 1:4 mol/mol at different NVP/HPMA weight ratios: (a) NVP/HPMA = 1:9 (w/w), (b) NVP/HPMA = 3:7 (w/w) and (c) NVP/HPMA = 5:5 (w/w).

Morphology of Hydrogels. The morphology of the hydrogels was investigated by ESEM measurement. Figure 4 is the ESEM micrographs of poly(HPMA-*co*-NVP) hydrogels with different NVP/HPMA weight ratios. On the microscale, the morphological structure of poly(HPMA-*co*-NVP) hydrogels with different NVP/HPMA weight ratios is distinctly diverse. As seen in Figure 4a, with NVP/HPMA = 1:9 (w/w), the hydrogel sample exhibits a regular surface arrangement and compact microstructure. The characteristic structural texture of the hydrogel is around 4 μm wide and 25 μm long. Perhaps more interestingly, with NVP/HPMA = 3:7 (w/w), the hydrogel sample has a spongelike microporous structure with a relatively uniform porous size distribution, along with the porous diameter of about 8 μm. As we expect, the hydrogel with microporous structure can retain a desirable swelling property, which is extremely important for the application of the hydrogels (seen in Figure 4b). The following swelling capacity measurement also confirms that this hydrogel prepared with NVP/HPMA = 3:7 (w/w) behaves with an excellent swelling capacity comparing with those at other NVP/HPMA weight ratios. Furthermore, for the weight ratio of NVP/HPMA = 5:5 (w/w), the hydrogel sample also illustrates a compact microstructure, along with the structural texture of 6 μm wide and 40 μm long (seen in Figure 4c).

Swelling Studies. The typical swelling behavior of the hydrogel at room temperature can be clearly seen in Figure 5. As seen in Figure 5a, the hydrogel sample at NVP/HPMA = 3:7 (w/w) presents ivory-white and opaque before swelling in deionized water. Interestingly, when it is fully swollen after 7 days, the hydrogel sample becomes transparent and long in macroscopic size, meaning the

(57) Silverstein, R. M.; Webster, F. X.; Kiemle, D. J. *Spectrometric Identification of Organic Compounds*, 7th ed.; John Wiley & Sons: Hoboken, NJ, 2005.

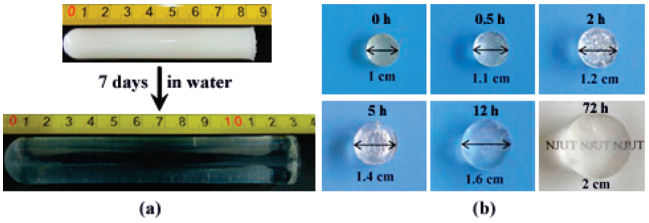

Figure 5. Typical swelling of hydrogel prepared by FP at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol. (a) The digital photos of the sample before swelling and after swelling in deionized water for 7 days. (b) Variation of swelling behavior of the treated sample as a function of swelling time.

glycerol has been completely removed from the hydrogel during the process of swelling. To obtain pure hydrogels, all the hydrogel samples should remove all glycerol and dry in a vacuum oven at 60 °C for overnight before the swelling measurement, guaranteeing all of them to be transparent. Figure 5b illustrates the macroscopic swelling variation of the hydrogel as a function of swelling time. Initially, the diameter of the dried sample is 1 cm. When immersed in deionized water after 0.5 h, the surface of the sample presents regular macroscopic surface texture and the diameter of the sample becomes 1.1 cm. With increasing swelling time, the diameter of the sample becomes larger and larger. After 5 h of swelling time, the texture on the surface of the sample partially disappears and the diameter of the sample becomes 1.4 cm. More interestingly, when the swelling time is more than 12 h, the texture on the surface of the sample completely disappears. The diameter of the transparent sample becomes 2 cm after 72 h of swelling in water, noticing that there is a 1-fold increase in the diameter of the sample after 72 h of swelling time.

The swelling kinetics behavior of hydrogels synthesized at different NVP/HPMA weight ratios was investigated using gravimetric analysis and is depicted in Figure 6. As seen in Figure 6, the equilibrium time (Q) of the hydrogels is a function of NVP/HPMA weight ratio. At 11 h of swelling time, the SRs of hydrogels at NVP/HPMA = 1:9, 2:8, 3:7, and 7:3 (w/w) are 121%, 241%, 789%, and 457%, respectively. The results indicate that the swelling rate for the sample at NVP/HPMA = 3:7 (w/w) is the fastest one. Furthermore, the equilibrium SRs at NVP/HPMA = 1:9, 2:8, 3:7, and 7:3 (w/w) are about 180% (Q = 50 h), 400% (Q = 60 h), 930% (Q = 80 h), and 810% (Q = 80 h), correspondingly. We believe the maximum SR is from a typical desirable porous structure of the as-prepared hydrogel at NVP/HPMA = 3:7 (w/w), which is consistent with the ESEM results (seen in Figure 4). Also, we investigated the effect of the cross-linker MBAA concentration on the SR value (see Supporting Information Table S2). As expected, increasing the MBAA concentration from 0 to 0.3 wt % causes an obvious decrease in SR from 3792 to 1059%. The results exhibit that the swelling capacity of hydrogels decreases with the increase of cross-linker concentration, which is in good agreement with the reported literature.[58]

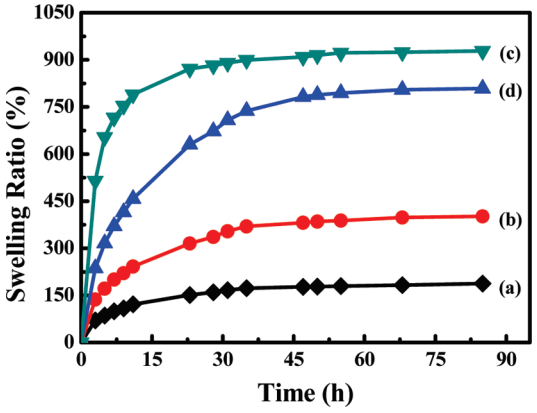

Figure 6. Swelling kinetics of poly(HPMA-*co*-NVP) hydrogels produced by FP with glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol at different NVP/HPMA weight ratios: (a) 1:9, (b) 2:8, (c) 3:7, and (d) 7:3 (w/w).

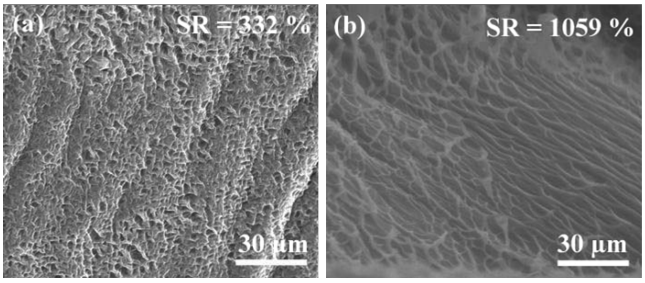

Figure 7. ESEM micrographs of poly(HPMA-*co*-NVP) hydrogels at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol synthesized by (a) BP (SR = 332%) and (b) FP (SR = 1059%).

Figure 7 presents ESEM micrographs of poly(HPMA-*co*-NVP) hydrogel prepared by FP at NVP/HPMA = 3:7 (w/w), glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol and the control sample with the same composition prepared by BP in a batch reactor at 60 °C for 2 h. As indicated in Figure 7, the hydrogel synthesized by FP displays a spongelike porous structure, and most of the pores are connected to each other to form capillary channels. For comparison, the control sample prepared by BP presents a thick and compact porous structure, and its pore size is much smaller than that prepared by FP. Another indication for comparing the swelling behavior of the hydrogel prepared by FP with that by BP comes from the SR value of hydrogels. The SR of the hydrogel synthesized by BP is 332%, whereas the SR of the one prepared by FP is 1059%, noticing that there is a 3-fold increase in SR by using the FP polymerization technique. Similar results have been reported.[26,48] This finding suggests that the swelling capacity of the hydrogel prepared using the FP method is superior to that obtained using traditional BP methods.

Thermosensitive Behavior of Hydrogels. To study the thermosensitive properties of hydrogels, the dried

(58) Hennink, W. E.; van Nostrum, C. F. *Adv. Drug Delivery Rev.* **2002**, *54*, 13.

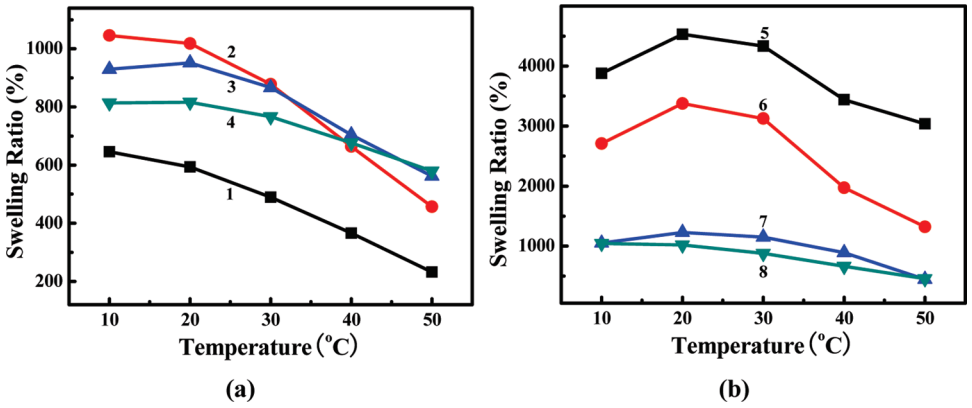

Figure 8. (a) Swelling ratio as a function of temperature of poly(HPMA-*co*-NVP) hydrogels produced by FP with glycerol = 40 wt %, MBAA = 0.3 wt %, APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol at different NVP/HPMA weight ratios: (1) 2:8, (2) 3:7, (3) 5:5, and (4) 7:3 (w/w). (b) Swelling ratio as a function of temperature of poly(HPMA-*co*-NVP) hydrogels produced by FP with glycerol = 40 wt %, NVP/HPMA = 3:7 (w/w), APS = 0.1 wt %, and [APS]/[TMEDA] = 1:4 mol/mol at different concentrations of cross-linker MBAA: (5) 0, (6) 0.06, (7) 0.18, and (8) 0.3 wt %.

hydrogel samples were completely swollen and equilibrated in deionized water at temperatures raging from 10 to 50 °C. The SRs of hydrogels as a function of temperature with different NVP/HPMA weight ratios are given in Figure 8a. As seen in Figure 8a, at NVP/HPMA = 2:8 (w/w), SR of the sample varies from SR = 645% at 10 °C down to 232% at 50 °C; at NVP/HPMA = 5:5 (w/w), SR of the sample varies from SR = 929% at 10 °C down to 561% at 50 °C, along with a slight increase in the SR of the sample at 20 °C; at NVP/HPMA = 7:3 (w/w), SR of the sample varies from SR = 813% at 10 °C down to 579 at 50 °C. However, at NVP/HPMA = 3:7 (w/w), the SR of the sample exhibits an SR as high as 1046% at 10 °C, the largest of all samples, and dramatically down to 457% at 50 °C. In this case, the poly(HPMA-*co*-NVP) hydrogel at NVP/HPMA = 3:7 (w/w) presents the optimal thermosentitive property due to its dramatic swelling capacity changes in response to temperature. Figure 8b displays the SRs of hydrogels as a function of temperature with different cross-linker MBAA concentrations while the weight ratio of NVP/HPMA is maintained at 3:7 (w/w). It can be seen that, with an increase MBAA from 0 to 0.3 wt %, the SR of the sample decreases under the same temperature. Meanwhile, with increasing temperature, the SR of the sample at MBAA concentrations ranged from 0 to 0.18 wt % exists in a slight increase in the SR at 20 °C. It could be attributed to structural defects in the low concentration of cross-linker hydrogels.[26] With $T > 20$ °C, the SR of the sample with all different MBAA concentrations decreases with the elevated temperature. These results suggest that there exists a definite relationship of the thermosensitive property and swelling capacity of these hydrogels with MBAA concentration and their NVP/HPMA composite.

Conclusion

We have demonstrated a new strategy for rapidly fabricating thermosensitive poly(HPMA-*co*-NVP) hydrogels in the presence of glycerol by using frontal polymerization. We have found that a variety of features of as-prepared hydrogel samples can be tuned by varying FP conditions, namely, ratios of NVP/HPMA, the presence of the glycerol and its concentration, and MBAA cross-linker concentration. Particularly, we first employ glycerol to assist carrying out FP and to synthesize polymer hydrogels. In this case, the presence of glycerol can suppress the "fingering" of FP and overcome the formation of bubbles. Another advantage is that the glycerol in the hydrogels can be easily removed during the process of swelling, profiting to enhance the swelling capacity of the hydrogels. For synthesis of poly(HPMA-*co*-NVP) hydrogels by FP, the ratio of NVP/HPMA in the hydrogel plays an important role in its microstructure and swelling property. The poly(HPMA-*co*-NVP) hydrogels both with NVP/HPMA = 1:9 and 5:5 (w/w) do not exhibit porous morphology, while the hydrogel with NVP/HPMA = 3:7 (w/w) has a spongelike microporous structure with a relatively uniform porous size distribution. An optimal NVP/HPMA weight ratio at NVP/HPMA = 3:7 (w/w) is determined in this case, which is a reference point to produce a porous hydrogel with better swelling capacity.

On the other hand, by comparing the SR value of the hydrogel prepared by FP with that by BP, the SR of the hydrogel using BP is 332%, whereas the SR of the one using FP is 1059%, noticing that there is a 3-fold increase in SR by using FP polymerization technique. This finding suggests that the swelling capacity of the hydrogel prepared by using the FP method is superior to that obtained by traditional BP methods. The results of thermosensitive behavior and swelling studies indicate that the poly(HPMA-*co*-NVP) hydrogels prepared by glycerol-assisted FP have both good swelling capacity and thermosensitive property. The above results allow us to conclude that glycerol-assisted FP can be exploited as an alternative means of NVP-based copolymer hydrogel synthesis with additional advantages of fast and efficient methods and better properties.

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Supporting Information Available: Tables S1 and S2 and Figures S1 and S2 present the dependences of the front velocity and front temperature on the NVP/HPMA ratios, the presence of the glycerol and its concentration, and MBAA cross-linker concentration (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.