Preparation of thermosensitive PNIPAAm hydrogels with superfast response

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A simple, effective strategy was developed and demonstrated to prepare thermosensitive poly(*N*-isopropylacrylamide) (PNIPAAm) hydrogel with a superfast response by using an organic solvent, tetrahydrofuran (THF), as a foaming agent as well as a precipitation agent during the polymerization/crosslinking in water at room temperature. The superfast response PNIPAAm hydrogel was attributed to the macroporous network and heterogeneous matrix, and it may contribute significantly to the construction of novel intelligent devices in the future.

Stimulated from natural feedback systems, synthetic intelligence or responsive systems have attracted great interest from researchers aiming to develop materials that mimic the natural feedback or response, and may contribute significantly to the construction of novel biomaterials. One particular feedback system is intelligent hydrogels,[1] which can change their shapes and volumes with a slight variation of external stimuli, such as temperature and/or pH.

Poly(*N*-isopropylacrylamide) (PNIPAAm) is a thermosensitive polymer, which phase separates from water at a lower critical solution temperature (LCST) of approximately 32 °C.[2] As the temperature rises above LCST, the hydrophobic groups in PNIPAAm polymer chains undergo a coil–globule transition and suddenly aggregate.[3] Accordingly, PNIPAAm hydrogels exhibit thermoreversible phase separations and collapse abruptly in volume at temperatures above the LCST.[4] Due to this unique intelligence, PNIPAAm hydrogel has been widely used in biomedical fields as a matrix for protein–ligand recognition, drug controlled release and artificial organs.[5]

A drawback of a normal PNIPAAm hydrogel is the slow response behavior to an applied signal, which greatly limits its potential applications especially in some cases,[6] such as artificial organs, actuators and on–off switches. As a result, improving the response rate has attracted a lot of research interest recently, and several approaches have been reported.[7] A successful approach was proposed to improve the shrinking rate of PNIPAAm hydrogel by grafting freely mobile PNIPAAm chains to the hydrogel network.[8] Here, we demonstrate a simpler, yet effective strategy to achieve a superfast response PNIPAAm hydrogel by using tetrahydrofuran (THF) as a foaming agent as well as a precipitation agent during the polymerization/crosslinking process.

In order to prepare modified PNIPAAm hydrogel, monomer NIPAAm (0.2 g) and crosslinker *N*,*N*′-methylenebisacrylamide (4.0 mg) were dissolved in distilled water to form a monomer solution (10.0 wt.%) and the free radical polymerization was carried out in a glass bottle of 25 mm in internal diameter at room temperature (22 °C). After mild shaking for a few minutes, ammonium persulfate solution (20 μl, 10 wt.% aqueous solution) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (20 μl) were added into the monomer solution to initiate the radical polymerization. 60 seconds later, 0.15 ml THF was added dropwise and the reacting medium became translucent and foamy in about 100 seconds. Then the polymerization was continued for another 30 minutes. After the polymerization, the prepared hydrogel was immersed in distilled water at room temperature for at least 48 h and the water was refreshed every several hours in order to allow the residue to leach out. The PNIPAAm hydrogel thus obtained was designated as the modified PNIPAAm hydrogel or MGel. The normal PNIPAAm

hydrogel control (NGel) was prepared without the adding of THF and other preparation conditions were the same as for MGel.

Morphology is a critical factor that determines response behaviors of PNIPAAm hydrogel; the interior morphology of the hydrogel was investigated using a scanning electron microscope (SEM, Hitachi S4500 SEM, Mountain View, CA). As illustrated in Fig. 1, the interior morphology of normal PNIPAAm hydrogel (NGel) is rather compact with small pores. In contrast, MGel presents a macroporous network structure with a heterogeneously distributed matrix. The macroporous network structure of MGel was attributed to the adding of organic solvent, THF during the gelation process. It was reported that organic solvents such as dichloromethane, acetone and methanol might act as foaming agents during the polymerization to generate a superporous hydrogel.[9] The macroporous network was generated from the blowing of THF and simultaneous evaporation of water at an increased reaction temperature due to the highly exothermic gelation process.

Besides the macroporous network, the heterogeneous matrix of MGel was supposed to be a result of the cononsolvency phenomenon of PNIPAAm chains. As we know, whether in water or in THF, PNIPAAm chains dissolve well and the hydrogel exhibits a swollen state at room temperature. However, PNIPAAm chains will collapse and precipitate when THF is added into the aqueous reaction system, and the solubility of the PNIPAAm chains is dramatically reduced in the mixture of water and THF.[10] With the introduction of THF during the polymerization, the propagating PNIPAAm chains precipitated from the monomer solution. From this viewpoint, THF acts as the precipitation agent during the polymerization. Finally, the resulting PNIPAAm hydrogel has obtained a heterogeneously distributed matrix from its conventional homogeneous one. Namely, THF acted as a chain precipitation agent as well as the foaming agent during the polymerization/crosslinking process.

The classical temperature dependent swelling ratios of hydrogels were investigated through a gravimetric method. Hydrogel samples were immersed in water at each testing temperature for at least 48 h and the average value of three measurements was taken for each sample. The equilibrium swelling ratio was calculated as W_s/W_d, where W_s is the weight of water in the swollen hydrogel and W_d is the dry weight of hydrogel. As presented in Fig. 2, at room temperature, the swelling ratio of MGel was higher than that of NGel. The swelling ratio (around 51) of MGel is around 2 times that of NGel (around 26) at room temperature. This may be explained
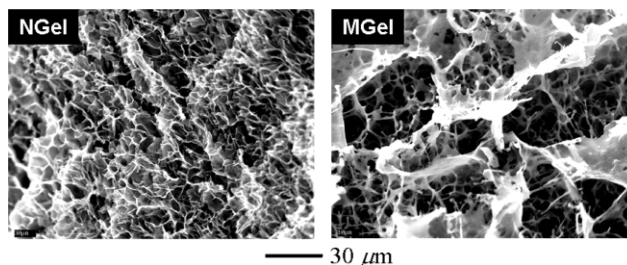

Fig. 1 SEM micrographs of normal (NGel) and modified (MGel) PNIPAAm hydrogels.

by the macroporous network of MGel and the increased free volume within the hydrogel network, thus, more water would reside. Data also show that both PNIPAAm hydrogels exhibited a similar temperature-dependence, but the magnitude of the thermo-induced swelling ratio variation of MGel was larger than that of NGel. Generally, the phase transition temperature or LCST of a PNIPAAm based network is regarded as the temperature at which the phase-separation degree (change of swelling ratio (ΔV) vs. temperature change (ΔT) around the transition temperature ($\Delta V/\Delta T$)) is the greatest. From Fig. 2, it is clear that LCSTs of both hydrogels lie in the vicinity of 33 °C, which is in agreement with findings of others.[4,7]

As mentioned above, the purpose of this research is finding a simple, but effective strategy to prepare PNIPAAm hydrogel with a fast response. Here, the response kinetics of hydrogels were examined gravimetrically at 48 °C (shrinking) and 22 °C (swelling) respectively as shown in Fig. 3. The water content of wet hydrogel was calculated to measure the response rate with the definition: [($W_t - W_d)/W_s$] × 100, where W_t is the weight of the wet hydrogel at a testing temperature and other terms are the same as defined above in the swelling ratio. In comparison to the slow response rate of NGel, MGel exhibits a superfast response rate when undergoing shrinking upon a temperature jump from 22 °C (below LCST) to 48 °C (above LCST). About 90% of the water was evacuated from MGel within 90 seconds and the gel reached a stable shrunk state in about 10 minutes, whereas NGel needed a week, even a month, to do it. This dramatically improved shrinking rate of MGel was attributed to its special microstructure because either the macro-porous network or heterogeneous matrix is favorable to accelerate the shrinking rate upon heating. The fact that a macroporous

network may increase the shrinking rate is easily understood because the freed water can diffuse out quickly and smoothly.[7a] It was also accepted that a heterogeneous matrix may lead to a fast response rate due to the existence of non-equilibrated shrinking force at different collapsed regions.[11] Because of the heterogeneous microstructure, many shrunk regions appeared but with a different collapsed phase during the shrinking process. Gradually, freed water in the water-rich regions may diffuse into the surrounding dilute regions, and this diffusion leads to the formation of an inter-connected water release channel among water-rich regions throughout the hydrogel. As a result, the freed water is evacuated quickly from the collapsing network, which contributed to the fast response rate of the heterogeneous hydrogel.

Figure 3 also demonstrates the swelling behavior of freeze dried hydrogels in water at room temperature, and MGel exhibits a much faster swelling rate compared with NGel. During the hydration process, water penetration is a crucial step in determining the swelling kinetics of hydrogels. In the case of NGel, its hydration was much slower from the beginning of the swelling process. NGel absorbed about 8% water within 5 minutes, and about 21% within 30 minutes. However, MGel absorbed about 43% and about 65% water within 5 minutes and 30 minutes respectively. The fast hydrating/swelling rate of MGel was also attributed to its macroporous network and heterogeneous matrix with similar reasons for its fast shrinking.

It is known that a hydrogel is able to keep a memory of its formation history, including molecular conformation as well as microstructure.[12] All the characteristics of a modified hydrogel are kept subsequent to its generation. Thus, the superfast response of the modified PNIPAAm hydrogel is supposed to be inherent and stable. In reality, based on our experimental observations, the fast shrinking and swelling processes of the modified hydrogel are reversible and recyclable, while the whole hydrogel remains intact.

Fig. 2 Equilibrium swelling ratios of normal (NGel) and modified (MGel) PNIPAAm hydrogels at different temperatures.

Fig. 3 Shrinking and swelling kinetics of normal (NGel) and modified (MGel) PNIPAAm hydrogels in water at 48 °C (shrinking) and 22 °C (swelling).

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12 (a) C. Alvarez-Lorenzo, O. Guney, T. Oya, Y. Sakai, M. Kobayashi, T. Enoki, Y. Takeoka, T. Ishibashi, K. Kuroda, K. Tanaka, G. Wang, A. Yu, G. S. Masamune and T. Tanaka, *Macromolecules*, 2000, **33**, 8693; (b) X. Z. Zhang, Y. Y. Yang, 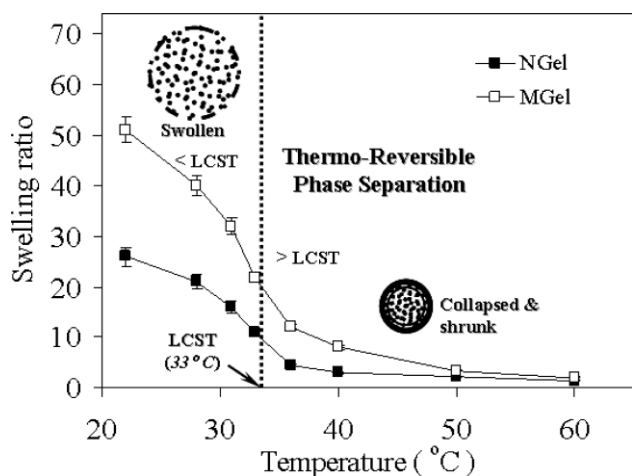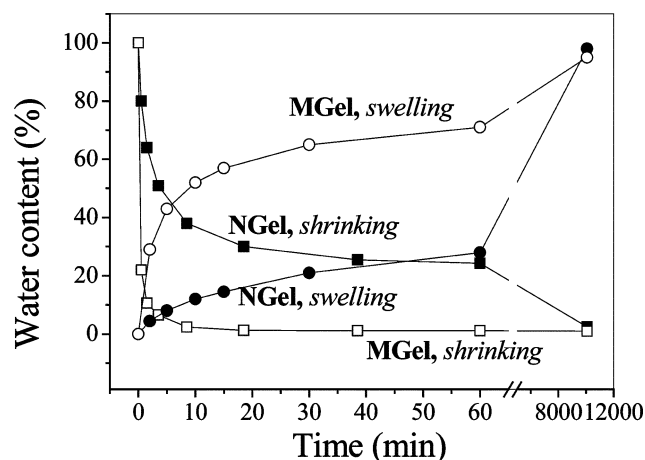F. J. Wang and T. S. Chung, *Langmuir*, 2002, **18**, 2013.