

Thermo- and pH-sensitive behavior of hydrogels based on oligo (ethylene glycol) methacrylates and acrylic acid

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Abstract Novel dual stimuli-responsive hydrogels were prepared by free-radical polymerization of 2-(2-methoxyethoxy) ethyl methacrylate (MEO₂MA) and oligo (ethylene glycol) methacrylate (OEGMA), as thermosensitive monomers, and acrylic acid (AAc), as a pH-sensitive monomer. Due to the thermosensitive monomers introduced in the macromolecular network, the synthesized materials possessed tunable thermal behavior. In addition, as well as by introducing in the polymerization feed pH-sensitive monomer AAc, the equilibrium swelling properties of the hydrogels can be tuned by three comonomers. Moreover, the de-swelling kinetics was studied by changing temperature and/or pH, and they could be well described with a first-order kinetics equation. Especially, the faster shrinking rates of hydrogels were observed when the simultaneous temperature and pH stimuli changed from pH 8/18 to pH 2/55 °C because of the cooperative thermo-/pH responses. The prepared dual temperature-/pH-sensitive P(MEO₂MA-co-OEGMA) hydrogels as a new material candidate may provide significant valuable information for various potential applications.

Introduction

In recent years, intelligent hydrogels have attracted much more attention due to their potential applications in many high-tech fields, such as biosensor, drug delivery devices, artificial muscles, and actuators [1–5]. They show variations

in their volume or phase transition in response to environmental stimuli such as temperature, pH, light, electric, and magnetic field and so on [6–16]. Among all of the above-mentioned stimuli, temperature and pH are the most popular investigated aspects [4, 8, 17–19], because both stimuli are important environmental parameters in biomedical and other systems. It is well known that poly (*N*-isopropylacrylamide) (PNIPAM) and their copolymers that undergo a sharp volume-phase transition at their lower critical solution temperature (LCST) are the most common thermosensitive hydrogels [20–24]. However, the excellent property of thermal response of PNIPAM and their copolymers hydrogels has not been widely used in biomedical field since the NIPAM monomer is carcinogenic or teratogenic. Until 2006, Lutz et al., who used two kinds of PEG derivatives of 2-(2-methoxyethoxy)ethyl methacrylate and oligo(ethylene glycol) methacrylate, have synthesized adjustable temperature-sensitive copolymer (P(MEO₂MA-co-OEGMA)) by atom transfer radical polymerization(ATRP), ending that only the amide-type polymer has a temperature sensitive behavior of the times [25–30]. Therefore, PNIPAM as an example of a thermosensitive polymer was challenged by the discovery that the random copolymer of P(MEO₂MA-co-OEGMA) exhibits a LCST in water, which can be tuned between 26 and 90 °C depending on the OEGMA content. Moreover, in contrast to PNIPAM, P(MEO₂MA-co-OEGMA) hydrogels are expected to be non-toxic and non-immunogenic. Thus, in recent years, this new type of thermosensitive hydrogel system was intensely investigated by researchers. On the one hand, microgels and nanogels based on the P(MEO₂MA-co-OEGMA) copolymers have been reported [31–33]. Cai et al. [31] synthesized monodisperse microgels of P(MEO₂MA-co-OEGMA) by traditional free-radical polymerization (FRP), with tunable LCST by changing the composition of monomers. In another work,

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Dong et al. [32, 33] reported thermoresponsive microgels of P(MEO₂MA-*co*-OEGMA) via activators generated by electron transfer for ATRP (AGET ATRP) in miniemulsion using anisole as oil phase and ethylene glycol dimethacrylate (EGDMA) as a crosslinker. Apart from microgels, a novel type of core-shell nanogel of P(MEO₂MA-*co*-OEGMA) with tunable sizes and thermosensitivities was synthesized by Shen and its coworkers [34], using reversible addition-fragmentation chain transfer (RAFT). On the other hand, Lutz et al. [35] further synthesized the blocks of the controllable sol-gel transitions networks by ATRP of MEO₂MA and OEGMA₄₇₅ in the presence of 4-arm star-shaped PEG macroinitiators, with a double hydrophilic character below the LCST due to the permanently hydrophilic PEG inner blocks and thermoresponsive P(MEO₂MA-*co*-OEGMA) outer blocks. Moreover, the swelling and de-swelling kinetics of this system of hydrogels has also been investigated [36–38], recently.

However, from the application point of view, hydrogels would be much more attractive if they could respond to at least double stimulation such as possessing temperature- and pH-sensitive behaviors simultaneously. Over the past few decades, the dual thermo- and pH-sensitive hydrogels have been prepared mainly by combining PNIPAM with a pH-sensitive polymer unit, such as acrylic acid (AAc) [39], methacrylate (MAA) [40], and 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS) [41]. In addition, there have been a few reports on incorporating the pH-sensitive units to the thermosensitive polymer of PMEO₂MA to form double-responsive copolymers [42, 43]. For example, Matyjaszewski et al. synthesized thermo- and pH-responsive brush copolymers of MEO₂MA with MAA and/or *N,N*-dimethylaminoethyl methacrylate (DMAEMA) by ATRP. The thermal properties of the copolymers and terpolymers depended on the composition of the copolymer side chains and pH [42]. Zhao et al. reported a thermo- and

pH-sensitive ABA triblock copolymer, poly (methoxydi(ethylene glycol)-*co*-methacrylic acid)-*b*-poly (ethylene oxide)-*b*-poly (methoxydi(ethylene glycol)-*co*-methacrylic acid) (P(DEGMMA-*co*-MAA)-*b*-PEO-*b*-P(DEGMMA-*co*-MAA)). They showed that the sol-gel transition temperature ($T_{\text{sol-gel}}$) of aqueous solutions of this ABA triblock copolymer can be controlled by pH, and multiple sol-gel-sol transitions can be realized via the combination of temperature and pH triggers [43].

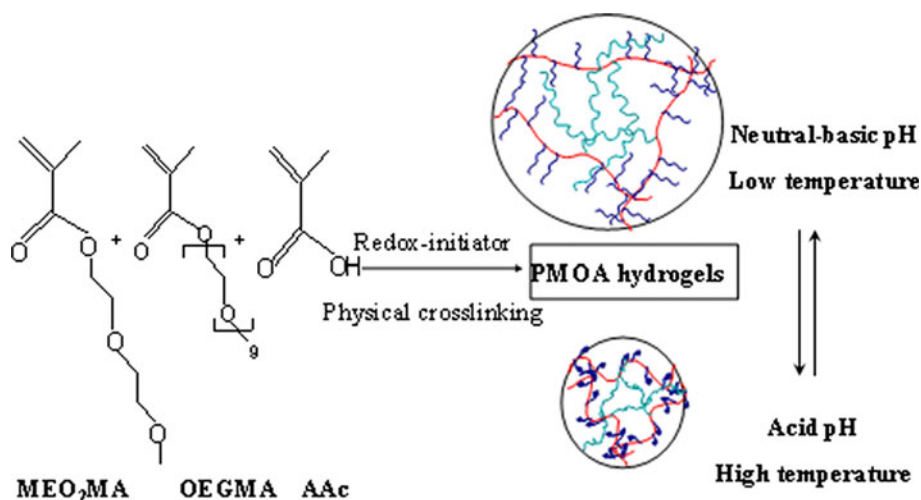
Herein, our interest is focused on double-responsive hydrogels that are switchable by both temperature and pH, which can be achieved by the incorporation of AAc monomer to the system of P(MEO₂MA-*co*-OEGMA) hydrogels. The chemical structures of the monomers employed for the preparation of the corresponding comb-type copolymeric hydrogels of MEO₂MA, OEGMA and AAc (P(MEO₂MA-*co*-OEGMA-*co*-AAc), PMOA) are represented in Scheme 1. In order to confirm the dual response of PMOA hydrogels, the swelling properties of hydrogels at different temperatures and buffer solutions were measured by gravimetric methods. In addition, the de-swelling behaviors of hydrogels were studied by changing temperature and/or pH.

Experiment

Materials

2-(2-Methoxyethoxy) ethyl methacrylate (MEO₂MA, 97%) was purchased from TCI Chemical Co. Tokyo, Japan. Oligo(ethylene glycol) methyl ether methacrylate (OEGMA, average $M_n = 475$, the number of EO units 8–9) was purchased from Sigma-Aldrich Co. AAc, potassium persulfate (K₂S₂O₈) and sodium hydrogen sulfite (NaHSO₃) were purchased from Sinopharm Chemical Reagent Co. Ltd. All these reagents were used as received.

Scheme 1 Molecular structures and synthesis of PMOA hydrogels



Synthesis of PMOA hydrogels

PMOA hydrogels were synthesized by free-radical polymerization without using chemical crosslinkers. First, MEO₂MA, OEGMA and AAc monomers were mixed in the three-necked flask with stirring and accessing nitrogen gas for 30 min. Then, a certain amount of redox initiators that were composed of potassium persulfate (K₂S₂O₈) and sodium hydrogen sulfite (NaHSO₃) were added to the flask with stirring for another 30 min. Second, the mixed solution was injected into small glass tubes (diameter = 5 mm, length = 120 mm), and then, the glass tubes were sealed by preservative film and kept inside the water bath at 55 °C for 5 h. Finally, the glass tubes filled with gels were carefully broken, and the gel columns were immersed in deionized water for at least 3 days to remove the unreacted chemicals. During this time, the water was replaced several times. After that, the hydrogels were dried at room temperature until constant weight. Different compositions of PMOA hydrogels were obtained employing the monomers described in Table 1. Hydrogels are expressed as PM_xO_yA-1 or PM_xO_yA-2, where *x* and *y* stand for 10 × MEO₂MA/(MEO₂MA + OEGMA) (mol/mol) and 10 × OEGMA/(MEO₂MA + OEGMA) (mol/mol), respectively, and 1 and 2 stand for 70 and 40 mmol AAc, respectively.

Characterizations of PMOA hydrogels

The swelling ratios of the PMOA hydrogels with varied compositions in the deionized water and Britton–Robinson buffer solutions were measured with a gravimetric method. After regular time intervals, the samples were taken out to measure gravimetrically after removing the excess water from the gel samples surface with filter paper and weighed, and the weight data presented are an average of three samples, as reported in the literature [17]. The effect of temperature on the equilibrium swelling ratio was measured in the temperature range from 18 to 55 °C.

The de-swelling kinetics of the PMOA hydrogels was measured in different conditions designed for the measurements. The temperature was maintained at 18 and 55 °C, respectively. Britton–Robinson buffer solutions

Table 1 Compositions for PMOA hydrogels

Sample	Feed composition	MEO ₂ MA (mmol)	OEGMA (mmol)	AAc (mmol)
PMOA-1	PM ₉ O ₁ A-1	45	5	70
	PM ₈ O ₂ A-1	40	10	70
PMOA-2	PM ₉ O ₁ A-2	45	5	40
	PM ₈ O ₂ A-2	40	10	40

Note: 1 wt% K₂S₂O₈ and NaHSO₃ as initiators = 2 mL

with the same ionic strength and pH values (pH = 8, 2) were used to measure the de-swelling process. The gel samples were left to fully swell in the deionized water or buffer solution of pH = 8 at 18 °C and then transferred to a given condition. At regular time intervals, the samples were weighed using the same method of swelling ratio as mentioned previously.

The equilibrium swelling ratio and water retention were defined using the following Eqs. 1 and 2, respectively.

$$\text{Equilibrium swelling ratio} = \frac{W_s - W_d}{W_d} \quad (1)$$

$$\text{Water retention } (t) = \frac{W_t - W_d}{W_s - W_d} \times 100 \quad (2)$$

where *W_s* is the weight of the swollen equilibrium hydrogel at below the LCST, *W_d* is the dry weight of the hydrogel, and *W_t* is the weights of de-swelling hydrogel at a given time, respectively.

Phase transition temperature of hydrogel was measured by dynamic mechanical thermal analysis Q800 (DMA). A fully swollen piece of hydrogel with a certain length, width and thickness (12 mm × 6 mm × 1.5 mm) was taken out from the deionized water for DMA testing. The frequency and amplitude of testing were maintained at 1 Hz and 10 μm, respectively. The temperature increased from 20 to 50 °C at a heating rate of 1 °C/min to ensure the accuracy of the observed phase transition temperature.

Results and discussion

Preparation of PMOA hydrogels

In this study, PMOA hydrogels with various monomeric contents based on two kinds of non-linear PEG derivatives of MEO₂MA with the number of EO units 2 (short side chain), OEGMA with the number of EO units 8–9 (long side chain) and AAc monomers were synthesized in the absence of chemical crosslinkers. Physical crosslink may be occurred in the hydrogels due to mutual entanglement of molecular chains between OEGMA long graft chains, MEO₂MA short chains and PAA backbone or the hydrogen-bonding interaction between the carboxyl groups of AAc and the ether oxygen of OEG side chain, as shown in Scheme 1. The properties of the hydrogels were stable, and the appearances of them were transparent.

Swelling behavior of PMOA hydrogels in different aqueous solutions

Figure 1 shows the equilibrium swelling ratios of the PMOA samples in the deionized water at room temperature (18 °C). It can be clearly seen from this figure that the

swelling ratio is directly related to the amount of OEGMA. Compared with the PM_9O_1A and PM_8O_2A hydrogels containing the same content of AAc, the PM_8O_2A hydrogels have higher equilibrium swelling ratios than the PM_9O_1A hydrogels. The differences could be due to the higher hydrophilic character of the longer PEG side chains of OEGMA. It has been shown that the hydrogel with long hydrophilic side chains forms a more open structure and locks more moisture [44]. Therefore, the equilibrium swelling ratios of the hydrogels can be tuned by varying the molar ratio of MEO_2MA and OEGMA.

From the above analysis, the swelling behavior in neutral environment was mainly related to the content of OEGMA. However, the AAc content also has an impact on the equilibrium swelling ratio, as obviously shown in Fig. 1. In general, the water uptake of the hydrogels should be increased with increasing hydrophilic monomer AAc introduced into the backbone of the gel. Oppositely, the equilibrium swelling ratio in this system decreased with the increasing AAc content. One possible reason is that the carboxyl groups of AAc interact with the ether oxygen of OEG side chains through hydrogen bonding, and such complexation results in shrinkage of the hydrogels (1). The water uptake capacity of the hydrogels' structure suffered limitation to some degree. Therefore, an increased content of AAc was related to a lower equilibrium ratio in water, and the hydrophilicity of the hydrogels decreased overall.

Figure 2 shows the further dynamic gravimetric swelling curves of PMOA hydrogels in pH 8 solution after equilibrium swelling in the deionized water. It is well known from the literature that the $P(MEO_2MA-co-OEGMA)$ hydrogel only respond to changes in temperature and does not respond to changes in pH [27, 38]. However, AAc as a typical pH-sensitive unit was successfully incorporated into the system of $P(MEO_2MA-co-OEGMA)$ hydrogels. As the

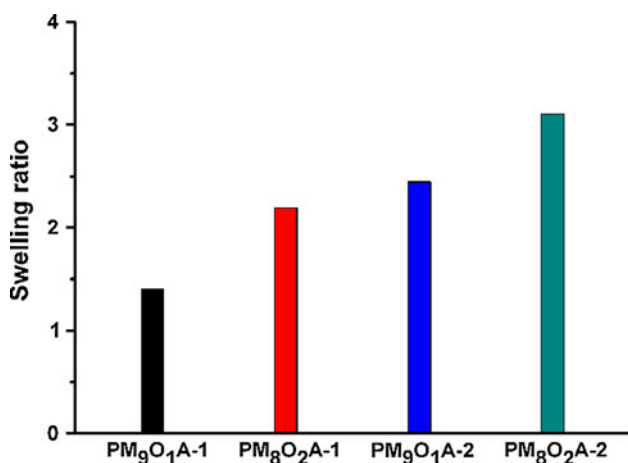


Fig. 1 Effect of the copolymer composition on the swelling at equilibrium of PMOA hydrogels in the deionized water at 18 °C

pH became more basic, ionization of the carboxylic groups in the gel structure increased, resulting in an electrostatic repulsive interaction between the OEG side chains and the PAAc backbone, and subsequent rupture of the hydrogen bonds. This phenomenon led to hydrogels decomplexation, and consequently, hydrogels can further swell. Because of the higher density of AAc in the backbone than that of the PMOA-2 hydrogels, the PMOA-1 hydrogels had a significantly higher sensitivity to pH in the same buffer solution. In addition, as can be found from the PM_9O_1A and PM_8O_2A hydrogels with the same content of AAc, the swelling rate of PM_9O_1A hydrogels was obviously faster than that of PM_8O_2A hydrogels. This may be attributed to the decomplexation between ethenoxy groups of OEG side chains and carboxyl groups of AAc at higher pH. The number of carboxyl groups of AAc which unreacted with the ether oxygen of OEG side chain in PM_9O_1A was more than in PM_8O_2A . PM_9O_1A with more remained carboxyl groups can deprotonate quickly in basic solution, resulting in faster further swelling.

The dependence of the swelling capacity on the temperature

It is a well-known fact that $P(MEO_2MA-co-OEGMA)$ hydrogels have tunable LCST behaviors between 26 and 90 °C with different composition of MEO_2MA and OEGMA [25, 28]. Thermoresponsive hydrogels of this system were attributed to changing in the hydrophilic and hydrophobic balance with respect to the H-bonding interactions between ethenoxy polar groups and water. At temperature below the LCST, strong H-bonding interactions lead to good solubility, resulting in higher swelling ratios. When the temperature is

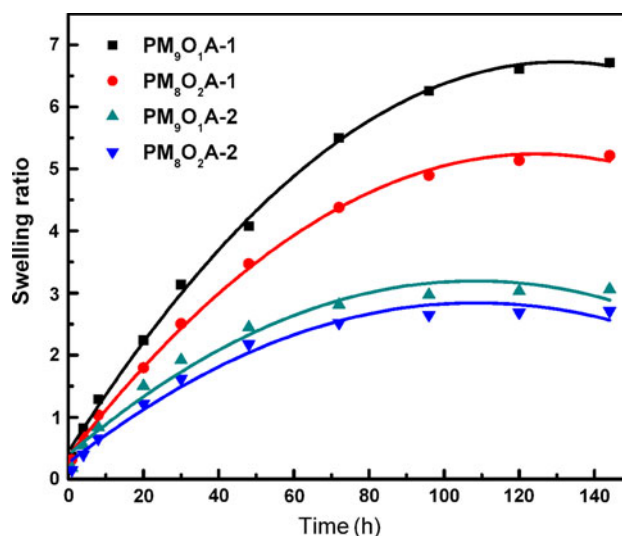


Fig. 2 Swelling kinetics of PMOA hydrogels in pH = 8 at 18 °C after equilibrium swelling in the deionized water

beyond the LCST, conformational transition of OEG side chains decreased the polarity of ethenoxy groups and hydration is weakened. Therefore, the macroscopic appearances of the hydrogels transferred from transparent to opaque, resulting in a phase separation [38]. Similar to P(MEO₂MA-co-OEGMA) hydrogels, PMOA hydrogels as expected still have thermoresponsive behavior, and their swelling ratios decreased with increasing temperature, although AAc was introduced into the system. They became swollen at temperature below the LCST, but shrunken at temperature above the LCST. The experimental results of changes of swelling ratios of PMOA hydrogels with the temperature in the deionized water are plotted in Fig. 3. However, the changes of the swelling at equilibrium with the temperature are not instantaneous; hydrogels required at least 12 h to swell water and to achieve the new equilibrium. In addition, it should be pointed out that the phase transition point of hydrogels using this method is not obvious as a result of the swelling curves that did not have distinct inflection points.

On the other hand, as mentioned earlier, conformational transition of OEG side chains in PMOA hydrogels sharply decreased the polarity of ethenoxy groups at the phase transition temperature, the H-bonding between ethenoxy groups and water was broken suddenly, as well as the intermolecular associations between OEG side chains and the PAAc backbone were enhanced, and thus, the modulus of the hydrogels may have an abrupt transition. Therefore, based on the changes of modulus, we preliminary designed the faster and more straightforward method and compared its results with those of the conventional method. Dynamic mechanical thermal analysis (DMA) was used to investigate the changes of modulus of the hydrogels with the temperature range of 20 to 50 °C and at a heating rate of

1 °C/min. The length, width and thickness of hydrogel pieces were around 12, 6 and 1.5 mm, respectively. The hydrogel piece with less thickness (1.5 mm) was selected to allow a fast heat transfer into them.

It should be pointed out that the samples for DMA testing require a range of stiffness (100–10⁷ N/m). The strength of hydrogels was correlated with the conventional swelling ratio; the stronger gels had the lower swelling ratio. However, the series of PMOA-2 hydrogels' stiffness were less than 100 N/m, which was out of the range of DMA testing. Therefore, only the system of PMOA-1 hydrogels was tested to study the changes of phase transition temperature. The results of storage modulus change for PMOA-1 hydrogels were presented in Fig. 4. As expected, PM₉O₁A-1 and PM₈O₂A-1 hydrogels have an abrupt transition corresponding to the modulus with temperature at around 31 and 37 °C, respectively. The results of the transition temperature are almost consistent with the phase transition temperature of PMOA-1, that corresponding to the visible pictures of two samples from transparent to opaque, and were also shown in Fig. 4. The values of phase transition temperature increase with the molar fraction of OEGMA in the hydrogels. Moreover, compared with the curves of PM₉O₁A-1 and PM₈O₂A-1, PM₉O₁A-1 has a relatively sharper jump than PM₈O₂A-1 and that may be depended on the whole movement rate of OEG side chains to backbone in hydrogel at the phase transition temperature. Such behaviors could be a consequence of the ratio of the long side chains, which moved to the backbone chains slower than the short side chains. Therefore, the range of phase transition of PM₈O₂A-1 was much wider than that of PM₉O₁A-1. The modulus of PM₈O₂A-1 changed upon heating with hysteresis.

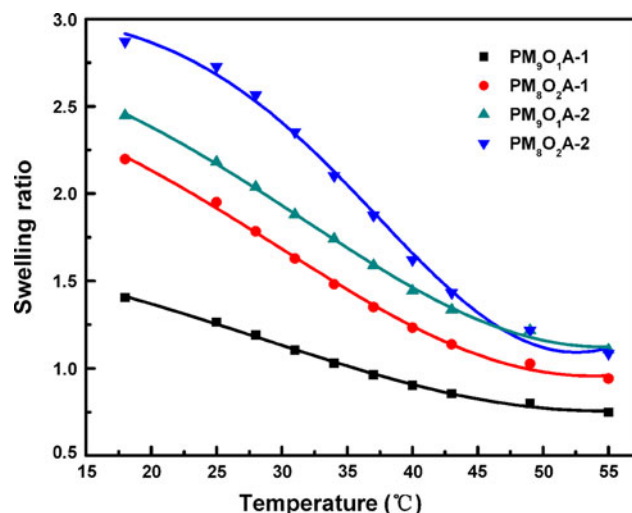


Fig. 3 Changes of swelling ratios of PMOA hydrogels with the temperature in the deionized water range from 18 to 55 °C

De-swelling kinetics of hydrogels under various conditions

De-swelling kinetics of PMOA hydrogels in response to temperature change

Considering the possible application of PMOA hydrogels, such as matrices in drug delivery systems, it is necessary to determine their de-swelling kinetics. Figure 5 shows the de-swelling ratios of hydrogels with time from the equilibrium swelling state in the deionized water at 18 °C to above the LCST at 55 °C. As expected, the higher content of OEGMA hydrogels (PM₈O₂A-1 and PM₈O₂A-2) showed accelerated de-swelling. The PM₈O₂A hydrogels shrank rapidly on the time scale, and entrapped water was quickly squeezed out from the hydrogels' interior. Such improvement of de-swelling kinetics can be attributed to the presence of the more longer OEGMA side chains in the PM₈O₂A hydrogels, which can potentially act as

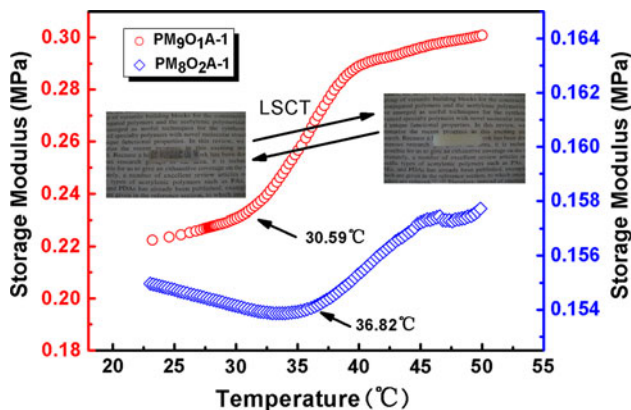


Fig. 4 Changes of modulus of PM₉O₁A-1 (red line) and PM₈O₂A-1 (blue line) hydrogels with the increase in temperature from 20 to 50 °C

water-release channels within the network and therefore boost the de-swelling kinetics [27]. In addition, when the temperature is above the LCST of hydrogels, incorporated AAc segments which maintained hydration also restricted the shrinkage of hydrogels synchronously. The PMOA-2 hydrogels with less AAc exhibited a faster rate of de-swelling than PMOA-1 hydrogels with more AAc.

De-swelling kinetics of PMOA hydrogels in response to pH change

Before the test, the hydrogels had been immersed in buffer solution of pH 8 at 18 °C to the equilibrium state. Then, significant de-swelling behaviors were observed in the de-swelling process of all hydrogels that were suddenly transferred to a buffer solution of pH 2. In this process, just a change in pH was measured, without changing the temperature. The de-swelling kinetics results are obviously shown in Fig. 6. As expected, the de-swelling rates of all hydrogels were relatively accelerated corresponding to pH change from alkaline to acidic, because of the introduction of the AAc into the temperature-sensitive hydrogel system. Each hydrogel can protonate their carboxyl moieties from alkaline to acidic solution quickly under the changeable environment, and the carboxyl moieties form a lot of hydrogen bonds, which pull back the whole network chain segments and squeeze more solution out of the hydrogels, resulting in de-swelling rapidly. In addition, with the same AAc content, the de-swelling rate increased with an increasing number of OEGMA side chains. Moreover, compared with the de-swelling kinetics of PMOA-1 hydrogels, PMOA-2 hydrogels with less AAc possessed much faster de-swelling behaviors. The ability of this system that responds to the changes of pH was quite different from the system of P(NIPAM-co-AAc) hydrogels that the de-swelling rate increased with increasing amount

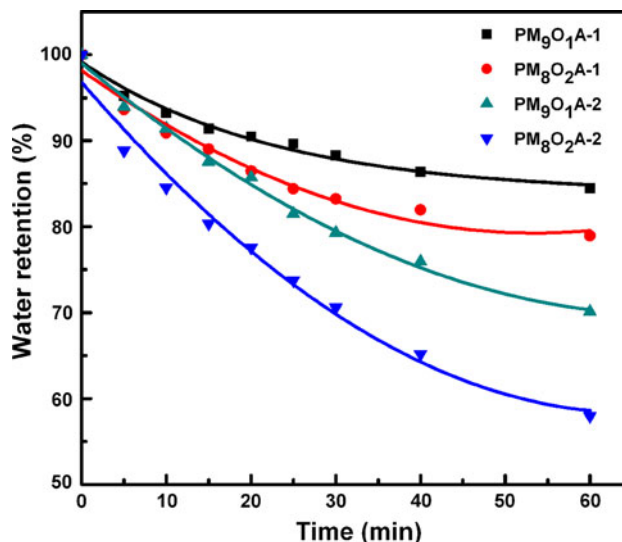


Fig. 5 De-swelling kinetics of hydrogels at 55 °C in water

of AAc units [17]. This phenomenon can be interpreted that the relatively weakened interaction force among molecular chains in PMOA-2 system was formed due to the interactions between the ethenoxy groups of the side chains and the carboxylic acid groups of AAc, just as mentioned earlier. When the environment is mutated, PMOA-2 with more free carboxylic acid groups would be deionized, which would reform hydrogen bonds and increase hydrophobic interaction compared to the electrostatic interaction; thus, the moisture was squeezed out quickly from the network and reduce the response time, resulting in faster de-swelling.

De-swelling kinetics of PMOA hydrogels in response to both temperature and pH changes

It is not difficult to see that the above-discussed experimental conditions and results only responding to one of the stimulus factors (temperature or pH) were changed, and the other was fixed to study the de-swelling behaviors of all hydrogels. However, as far as we know, the temperature and pH as two important physiological parameters were often changed synchronously in practical applications. Figure 7 shows the de-swelling kinetics of hydrogels in a buffer solution of pH 2 at 55 °C after an abrupt change from pH 8 and 18 °C. It was found that the shrinking trends from the curves of hydrogels are similar to those in Fig. 6. The only difference is that all the hydrogels shrunk more rapidly, exceeding the de-swelling rates of them in response to either temperature or pH alone. Especially, in PM₈O₂A-1 and PM₈O₂A-2 hydrogels, the amounts of release of water almost reach 90 and 100% at 80 min, respectively, proving that the elevated temperature is more suitable for accelerating the response. One possible

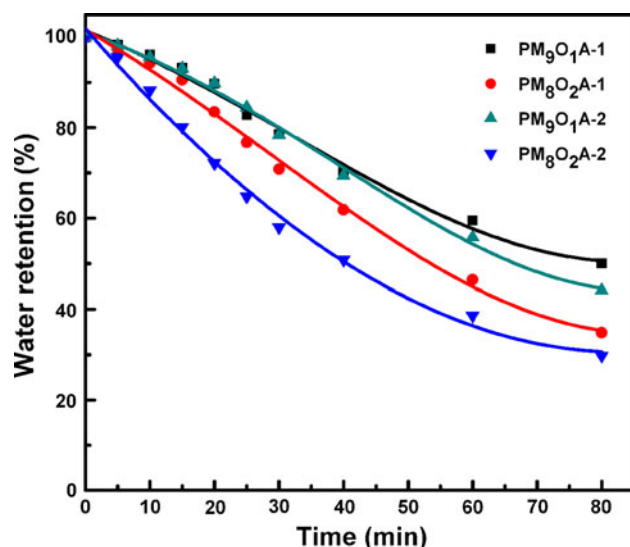


Fig. 6 De-swelling kinetics of hydrogels in buffer at pH 2 as measured from an equilibrium swelling condition in buffer at pH 8 at 18 °C

explanation for this phenomenon would be that the smooth surface skins of all hydrogels in the testing process began to crack and even peel within several minutes (about 10 min) after an abrupt environmental change. The actual shrinking force of internal hydrogels brought about by the low pH surrounding and high temperature further enhanced dramatically due to the increasing hydrophobic interaction of the pH-sensitive AAc groups and the temperature-sensitive ethenoxy groups side chains simultaneously. Therefore, faster releasing rate of the entrapped water from the hydrogels was observed.

In order to compare the de-swelling processes under different conditions more quantitatively, a semilogarithmic plot as first-order rate analysis was applied to the time dependence of de-swelling rate as follows: [23, 45, 46]

$$\ln \frac{W_t - W_e}{W_0 - W_e} = -kt \quad (3)$$

where W_e and W_0 are the weights of hydrogel in the de-swelling equilibrium state under certain conditions and the initial weight of the hydrogel at 18 °C and/or pH 8, respectively, k is the rate constant and t is the de-swelling time. According to de-swelling kinetic curves of the PMOA hydrogels, their de-swelling rate constants can be found out according to Eq. 3.

Corresponding to Figs. 5, 6 and 7, Figs. 8, 9 and 10 show that the plots of $\ln [(W_t - W_e)/(W_0 - W_e)]$ versus time for de-swelling of the hydrogels approached linear relation. From the slopes of these lines, the de-swelling rate constants of the gels were obtained. Table 2 lists the de-swelling kinetic parameters of the hydrogels as well as the correlation coefficients (R^2) for the linear regression of the data presented in Figs. 8, 9 and 10, respectively. The

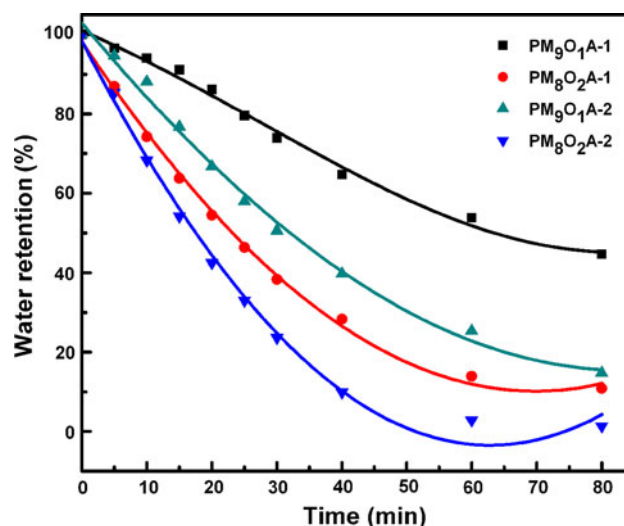


Fig. 7 De-swelling kinetics of hydrogels in buffer at pH 2 and 55 °C as measured from an equilibrium swelling condition in buffer at pH 8 and room temperature (18 °C)

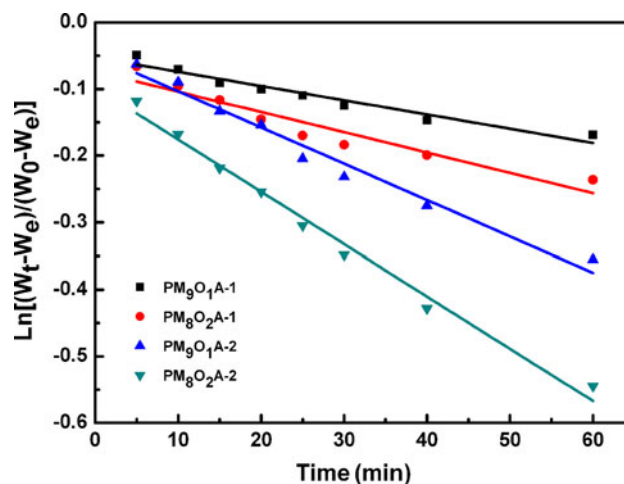


Fig. 8 Dependence of the $\ln [(W_t - W_e)/(W_0 - W_e)]$ of de-swelling PMOA hydrogels on time at 55 °C in water

plots are linearly fitted with the correlation coefficients of more than 0.90, which indicates that the de-swelling processes can be apparently governed by the first-order kinetics equation. It was observed from the Table 2 that with the same AAc content, the de-swelling rate constants of the PM_8O_2A hydrogels are greater than those of the PM_9O_1A hydrogel. It suggests that the growing content of OEGMA long side chains, act as water-release channels in PMOA hydrogels when collapse occurs, is beneficial for improving the responsive kinetics. Also, the de-swelling rate constants of the PMOA-2 hydrogels were more than those of PMOA-1 hydrogels in the same condition. It was mainly ascribable to the relatively weakened inter-macromolecular interaction between OEG side chains and the PAAc backbone, as mentioned earlier. In addition, the data

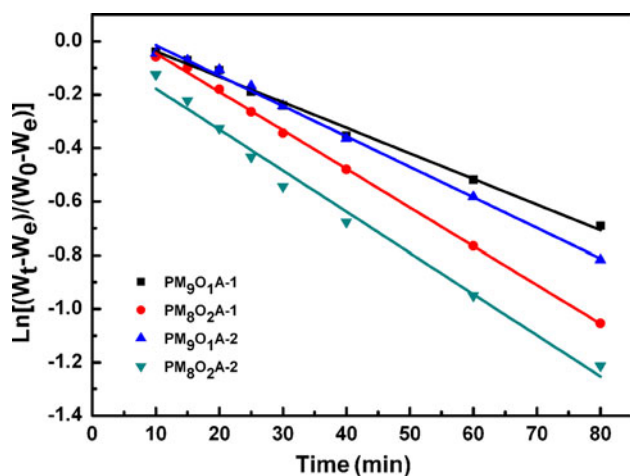


Fig. 9 Dependence of the $\text{Ln} [(W_t - W_e)/(W_0 - W_e)]$ of de-swelling PMOA hydrogels on time at 18 °C (pH = 2)

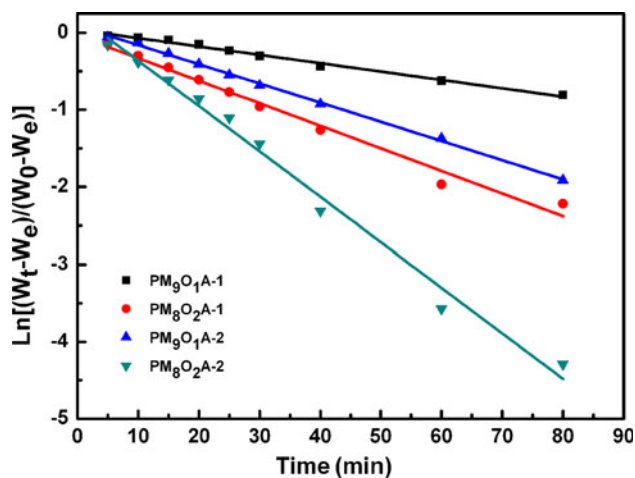


Fig. 10 Dependence of the $\text{Ln} [(W_t - W_e)/(W_0 - W_e)]$ of de-swelling PMOA hydrogels on time at 55 °C (pH = 2)

in Table 2 indicated that the de-swelling rate constants of the PMOA hydrogels undergoing two stimulus (T and pH) variations were much larger than those only changing one stimulus. The kinetic experiments showed that the PMOA hydrogel had a good sensitivity to temperature and pH. Accordingly, it is possible to design a hydrogel with the desired de-swelling rate by controlling the OEGMA and AAc contents or controlling the de-swelling conditions.

Conclusions

Novel dual temperature- and pH-sensitive PMOA hydrogels have been successfully prepared by the free-radical polymerization. The hydrogels exhibit reversible LCST behaviors in the deionized water with changing temperatures. In addition, the phase transition temperature

Table 2 De-swelling kinetic parameters of PMOA hydrogels

Sample code	$k \times 10^3$	R^2
From $T = 18^\circ$ to 55°		
PM ₉ O ₁ A-1	2.14	0.9304
PM ₉ O ₁ A-2	5.44	0.9028
PM ₈ O ₂ A-1	3.05	0.9712
PM ₈ O ₂ A-2	7.83	0.9864
From pH = 8 to 2		
PM ₉ O ₁ A-1	9.57	0.9930
PM ₉ O ₁ A-2	11.39	0.9990
PM ₈ O ₂ A-1	14.44	0.9960
PM ₈ O ₂ A-2	15.36	0.9864
From pH 8/18 to pH 2/55 °C		
PM ₉ O ₁ A-1	10.84	0.9908
PM ₉ O ₁ A-2	24.94	0.9984
PM ₈ O ₂ A-1	29.28	0.9824
PM ₈ O ₂ A-2	58.83	0.9872

determination by tracking the change of equilibrium swelling ratios with temperature was consistent with the DMA testing results. The LCST values corresponding to PM₉O₁A-1 and PM₈O₂A-1 are around 31 and 37 °C, respectively. Apart from the investigation of temperature sensitivity, the equilibrium swelling and de-swelling behaviors of all hydrogels have also been studied in detail under various environmental stimuli. The equilibrium swelling ratio of hydrogels increased with increase in the content of OEGMA and decrease in the content of AAc. In addition, the de-swelling behaviors of hydrogels were observed in given conditions and they could be well described with a first-order kinetics equation. In comparison with the three given conditions, the PMOA hydrogels exhibited faster de-swelling rates by changing the temperature and pH values simultaneously from pH 8/18 to pH 2/55 °C. The proposed hydrogels in response to dual temperature and pH stimuli suggest that they are promising new material candidates for various applications, such as for drug delivery, novel biosensors, biotechnology, actuators and so on.

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