

## pH 진동계 안에서 pH 감응성 자기진동 IPN 하이드로젤의 합성과 분석

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(2014년 3월 14일 접수, 2014년 11월 18일 수정, 2014년 12월 6일 채택)

### Synthesis and Characterization of pH-sensitive and Self-oscillating IPN Hydrogel in a pH Oscillator

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(Received March 14, 2014; Revised November 18, 2014; Accepted December 6, 2014)

**Abstract:** A self-oscillating interpenetrating polymer network (IPN) poly(acrylic acid)/poly(ethylene glycol) (PAA/PEG) hydrogel was prepared by using radical polymerization with a two-step method. The IPN hydrogel was characterized by FTIR spectroscopy and morphological analysis. The results indicated that the chains of PEG and PAA twined to form porous structure which is beneficial to water molecules entering inside of the hydrogel. In addition, the pH-responsive behavior, salt sensitivity, swelling/de-swelling oscillatory behaviors and self-oscillation in a closed pH oscillator were also studied. The results showed that the prepared hydrogel exhibited pH-sensitivity, good swelling/de-swelling reversibility and excellent salt sensitivity. The self-oscillating behavior of swelling/de-swelling for the prepared hydrogel was caused by pH alteration coupled with the external media. This study may create a new possibility as biomaterial including new self-walking actuators and other related devices.

**Keywords:** PAA/PEG IPN hydrogel, reversibility, self-oscillation, pH-responsiveness.

## Introduction

Hydrogels are a kind of new materials with three-dimensional networks, which swell but do not dissolve in water or aqueous solution. In the past decades, hydrogels, especially stimuli-responsive hydrogels have attracted considerable attentions.<sup>1-6</sup> However, the conventional stimuli-responsive hydrogels exhibit only one behavior: either swelling or de-swelling in response to environment stimulus such as temperature,<sup>7</sup> pH,<sup>8,9</sup> electricity.<sup>10</sup> Such materials have been applied to design intelligent materials and imitate stimuli-responsive functions in living system due to their abrupt changes in response to external stimuli. However, in order to stimulate the material, an external device is necessary. Recently, Yoshida and his co-workers<sup>11,12</sup> reported a novel kind of intelligent hydrogels which autonomously swelled and de-swelled periodically in a

closed homogenous solution without any external stimuli. The BZ oscillating reaction<sup>13,14</sup> was used to develop the driving force of materials producing swelling/de-swelling self-oscillating behavior. The main idea for self-oscillating polymers or gels is based on that the catalyst of the BZ reaction ruthenium tris-(2,2'-bipyridine)(Ru(bpy)<sub>3</sub>) periodically changes in the oxidized state and the reduced state. The Ru(bpy)<sub>3</sub> is covalently bonded on the polymer main chains, the periodic solubility change of the Ru(bpy)<sub>3</sub> in the polymer system caused swelling/de-swelling self-oscillating for the polymers and aggregation/disaggregation self-oscillating for the polymer chains. Bilici *et al.*<sup>15</sup> investigated the behavior of poly(acrylic acid) (PAA) cryogels in bromate-sulfite-ferrocyanide pH oscillating reaction and the results indicated that the cryogels oscillated between swelling and de-swelling states periodically. Due to the special dynamic rhythms, the self-oscillating hydrogels are expected to be used in self-walking actuators, novel biomimetic walking-gel actuator, microdevices, pacemakers, mass transport surface, drug delivery systems *etc.*<sup>16-19</sup>

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Some works have been done to combine two or three monomers forming interpenetrating polymer networks (IPNs). Because there is no chemical bond existing among the component networks, each network may keep its own property independently, and interpenetration of two networks may lead to much better mechanical strength and flexibility.<sup>20</sup> Because of its excellent advantages, IPN hydrogels can be chosen to form self-oscillating materials which generate autonomic swelling/de-swelling oscillation under non-oscillatory outer conditions.

In this study, we attempted to synthesize a novel hydrogel which possessed both the characteristics of self-oscillating without external stimulating device and IPN with excellent mechanical strength and flexibility. So PAA/PEG IPN hydrogel was synthesized successfully and the results indicated that the prepared material had excellent swelling/de-swelling behavior, salt sensitivity and good pH reversibility. The  $\text{BrO}_3^-$ - $\text{SO}_3^{2-}$ - $\text{Fe}(\text{CN})_6^{4-}$ - $\text{H}_2\text{SO}_4$  pH oscillator<sup>21,22</sup> in closed system was chosen to investigate the self-oscillating behavior and the results indicated it appeared obviously oscillating in volume. The excellent properties of PAA/PEG hydrogel and the biocompatibility of PAA and PEG would lead to a more applications in biomaterial fields such as oral drug delivery media, self-walking actuators and other devices.

## Experimental

**Materials.** Acrylic acid (AA,  $\text{C}_3\text{H}_4\text{O}_2$ ) and potassium ferrocyanide ( $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$ ) were purchased from Tianjin Kaixin chemical industry Co., Ltd. Polyethylene glycol (PEG2000) and *N,N'*-methylene bisacrylamide (MBA) were obtained from Shanghai Zhongqin chemical reagent Co., Ltd. Potassium bromate was obtained from Tianjin Guangfu chemical reagent Co., Ltd. Citric acid monohydrate (CA,  $\text{C}_6\text{O}_7\text{H}_8 \cdot \text{H}_2\text{O}$ ), sodium sulfite ( $\text{Na}_2\text{SO}_3$ ) and ammonium persulfate (APS) were obtained from Yantai Shuangshuang chemical Co., Ltd. NaOH,  $\text{Na}_3\text{PO}_4$ , and other reagents were purchased from Tianjin Kaitong chemical reagent Co., Ltd. All reagents were analytical grade and were used without further purification.

**Preparation of the PEG/PAA IPN Gel.** The IPN hydrogels of PEG/PAA were prepared by radical cross-linking copolymerization. The synthesis process of PEG/PAA hydrogels as following: Typically, AA (15.00 g) monomer was introduced into 10 mL distilled water and then neutralized with sodium hydroxide solution which obtained by adding sodium hydroxide (6.6 g) into distilled water (10 mL). The mixture was added

**Table 1. Composition and Designation of PEG/PAA IPNs**

Sample	Mass of AA (g)	Mass of PEG (g)	Mass of MBA (g)	Mass of APS (g)
IPN 1	15.00	1.5	0.01	0.09
IPN 2	15.00	2.5	0.01	0.09
IPN 3	15.00	3.5	0.01	0.09

into a 250 mL three-neck flask equipped with a stirring bar and a nitrogen line, and cooled to room temperature. Then MBA (0.005 g) was added to the above monomer solution. After being purged with nitrogen for 30 min to remove the oxygen dissolved in the solution, the mixed solution was heated at 75 °C for 5 min, and then the radical initiator, APS (0.045 g) was added. When the solution began to polymerize, different concentrations of PEG (10 mL), MBA (0.005 g) and APS (0.045 g) were added into the mixture quickly and it was removed from oil bath after it became epinephelos. Then the solution was stirred at 65 °C for 4 h and the hydrogel was obtained. The feed compositions of the hydrogels in this study are listed in Table 1.

**Structural and Morphological Characterizations.** Fourier Transform Infrared (FTIR) Spectroscopy: The hydrogels were cut into disks and immersed into distilled water for a month, and the water refreshed several times in order to remove un-reacted monomers and cross-linking agents. Then the hydrogels were dried at 60 °C under vacuum for FTIR measurement. The FTIR spectra were obtained on the FTS3000 spectrometer (DIGILABGON, USA).

**Scanning Electron Microscopy (SEM):** To identify the morphological differences in the IPN hydrogel, the swollen hydrogels at room temperature were cut into pieces and were frozen-dried for three days to remove water completely. The samples were sputter-coated and utilized for imaging their microstructure using the JSM-5600LV scanning electron microscope (JSM-5600LV, Japan).

**Swelling Ratio Measurements of the Hydrogels.** pH Sensitivity of the Hydrogels: The hydrogels which reached swelling equilibrium in distilled water were cut into cylinder with 10 mm in diameter and 10 mm in highness. Then the particles were immersed into absolute ethyl alcohol to obtain networks followed by drying at 40 °C under vacuum condition. Finally, uniform dimensional particles with diameters and highness about 0.8 mm were received.

The obtained hydrogels were immersed in various different pH solutions with ionic strength kept at 0.1 mol/L. The swell-

ing equilibrium was tested by measuring the diameters of the samples using a digital vernier caliper. The swelling measurement in different pH solution was made on the basis of the relative volume swelling ratio  $Q$ , which was determined according to the following equation:

$$Q = (D/D_0)^3 \quad (1)$$

where  $D$  is the diameter of the equilibrium swollen hydrogel sample in solution and  $D_0$  is the diameter after dried, respectively.

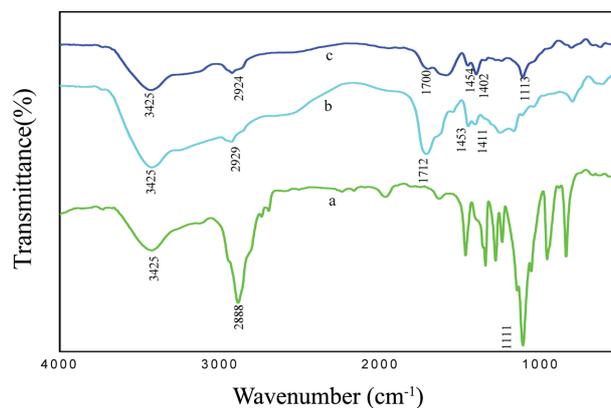
**Salt Sensitivity of the Hydrogels:** To measure equilibrium lost water content (LWC) of the hydrogels, the swollen samples in distilled water were immersed in various concentration of NaCl aqueous solutions. The weights of de-swelling samples were measured at different intervals until the weight did not change. The LWC was calculated as following expression:

$$\text{LWC (\%)} = [(W_s - W_d)/W_s] \times 100 \quad (2)$$

where  $W_s$  is the weight of the equilibrium swollen sample in water and  $W_d$  is weight of the equilibrium de-swelling sample in NaCl aqueous solution.

**Oscillatory Swelling/De-swelling Behavior of the Hydrogels:** The swollen hydrogel samples in distilled water were firstly soaked in the solution with pH=3 to equilibrium, and then transferred into the solution with pH=7 for 2 h. This cycle was repeated continuously. The diameters of hydrogels were recorded before each immersion. The relative volume swelling ratio  $Q$  of cycle-swollen samples were obtained through the eq. (1).

**Self-oscillatory Behavior of the Hydrogels in Batch pH Oscillator:** The swollen hydrogel samples fixed by one end was suspended in the mixed solution of  $\text{H}_2\text{SO}_4$  (0.03 mol/L),  $\text{KBrO}_3$

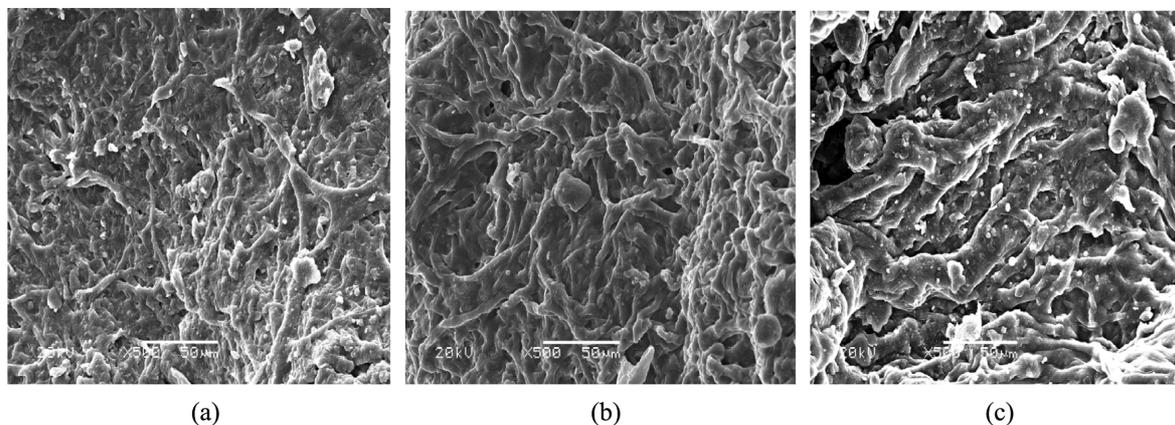


**Figure 1.** FTIR spectra of (a) PEG; (b) PAA; (c) PEG/PAA IPN hydrogel.

(0.195 mol/L),  $\text{Na}_2\text{SO}_3$  (0.225 mol/L) and  $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$  (0.06 mol/L) in batch reactor (volume=50 mL). At the same time, the pH of the system were monitored continuously with a pH meter (PHSJ-4F) connected with computer and the dimensional changes of the hydrogel were measured with a digital vernier caliper at various intervals.

## Results and Discussion

**FTIR Spectra of Hydrogel.** The FTIR spectra of PEG, PAA and PEG/PAA hydrogel were shown in Figure 1. In Figure 1(a), the peak at  $3425 \text{ cm}^{-1}$  is the O-H stretching vibration absorption peak and the band is wide because of the formation of associated hydrogen bond in PEG. The bending vibration absorption peak of C-H appears at  $2888 \text{ cm}^{-1}$  and the C-O-C stretching vibration absorption peak at  $1111 \text{ cm}^{-1}$ . The spectrum of PAA (Figure 1(b)) is similar to Figure 1(a) partly whereas a new C=O stretching vibration appears at  $1712 \text{ cm}^{-1}$ .

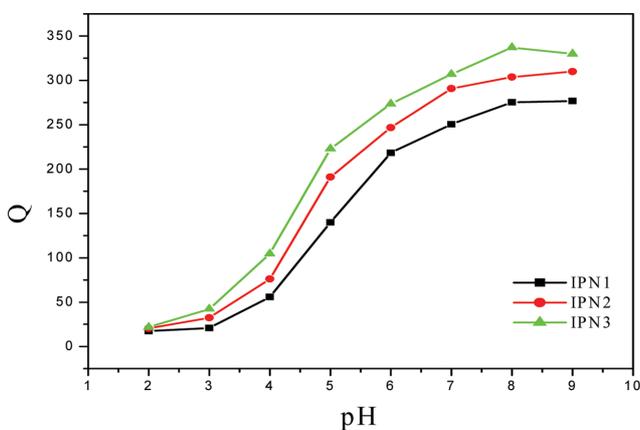


**Figure 2.** SEM images of PEG/PAA hydrogels: (a) IPN1; (b) IPN2; (c) IPN3.

The C-O-C stretching vibration absorption peak of PEG appears around  $1113\text{ cm}^{-1}$  in Figure 1(c). The results indicated that we synthesized PEG/PAA IPN hydrogel successfully.

**Morphological Analysis of Hydrogel.** Surface morphologies of the PEG/PAA IPN hydrogels were shown in Figure 2. From Figure 2, it is found that the surface of PEG/PAA hydrogel is homogeneous and rough which reveals agglomeration phenomena do not happen in synthetic process. In addition, the numerous uniform pores enlarge the contract area of the hydrogel with water molecules and it is beneficial to water molecules diffusion into the hydrogel. It is obvious that the chains of PAA and PEG twine mutually and form interpenetrating polymer network. The incorporating of PEG chain into the PAA network strengthens the PAA gel's tenacity and intensity obviously and also enhances the rate of the swelling and deswelling processes.

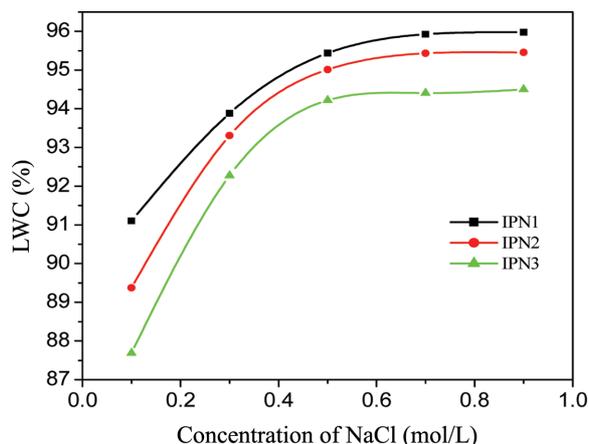
**pH Sensitivity of the Hydrogel.** To investigate the effect of pH value on the swelling ratios, three hydrogels with different contents of PEG were prepared and immersed into buffer solutions with pH range from 2 to 9. As shown in Figure 3, the relative swelling ratio of the hydrogel increases quickly with the increasing of pH value in the range of 2-9 at room temperature. However, the increasing rate of the relative swelling ratio changes with pH value. When pH is lower than 4, AA in the hydrogel exists as  $-\text{COOH}$  groups. That is to say, the ionization degree of AA is low and the charge repulsion between negatively charged groups is so weak that the pores inside the hydrogel are not open thoroughly and plenty water molecules can't spread into the hydrogel. With the pH increasing in the range of 4 to 6, the  $-\text{COOH}$  groups on polymer chain are ionized into  $-\text{COO}^-$  because of the  $\text{pK}_a$  of AA being about 4.25.<sup>15</sup>



**Figure 3.** Volumetric changes of PEG/PAA IPN hydrogel as a function of pH at room temperature.

The charge repulsion between negatively charged groups increases distinctly and the surface of hydrogel begins to swell, which makes water enter inside of hydrogel easily and the relative volume swelling ratio increases abruptly. Due to the increasing of ionization rate of AA in the polymer chain becomes slower and slower from pH 7 to 9, the relative swelling ratio also becomes slower and slower even roughly maintains a flat. In addition, it can be seen from Figure 3 that with the increasing of the feed amount of PEG, the relative swelling ratio of the hydrogel also increases gradually. It is may be account to two reasons. The one is PEG used as a pore-forming agent during the gelation process usually.<sup>23</sup> More PEG could form porous structure in hydrogel which makes water molecules outside easily diffuse into the inside of the hydrogel. The other may be due to the hydrophilic group of  $-\text{OH}$  of PEG chain. And in the experiments, we found that PEG influenced the hardness and suppleness of the hydrogel. Less of PEG in the hydrogel leads the hydrogel too hard to cut into the desired shapes, but excessive of PEG in it causes the water absorbent ability of the hydrogel decreasing. The main reason may be large amount of PEG making the hydrogel more intensive which prevents water molecules to enter inside of hydrogel. In addition, excessive PEG chain decreases the hydrophilicity of hydrogel for the backbone of PEG is a hydrophobic group.

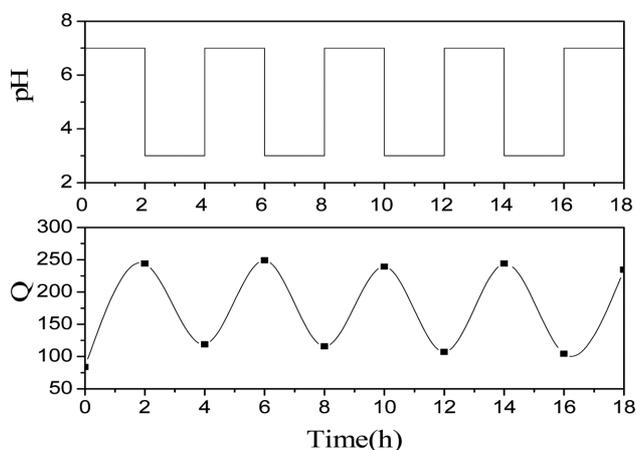
**Salt Sensitivity of the IPN Hydrogels.** Considering the important effect of salts on water absorbency capacity and the application in animals and plants of the hydrogels, the equilibrium dehydration behaviors of the prepared hydrogel in NaCl solution were investigated. Figure 4 shows the lose water content (LWC) of the IPN hydrogel in NaCl aqueous solution. It indicates that the dehydration rate of the IPN hydrogel increases with increasing of the NaCl concentrations. According to the Donnan osmotic pressure equilibrium,<sup>24</sup> with increasing of moveable counter ions in external environment, the osmotic pressure within the hydrogel decreases and the network structure of it shrinks. It also can be seen from Figure 4 that the LWC increases with the decreasing of PEG in the hydrogel in the same NaCl solution. The main reason maybe lie in that PEG plays the role of supporting the hydrogel's interpenetrating polymer network structure and is beneficial to water absorbing and losing and moderate PEG makes the network of the hydrogel more perfect. If no enough pores inside of the hydrogel, water molecules cannot be squeezed easily. But if more PEG in the hydrogel, the chains of PEG and PAA crosslink closely, the strong interaction forces among them make the hydrogel keep its original structure and water mol-



**Figure 4.** Equilibrium lost water content of the IPN hydrogels in NaCl solution.

ecules are blocked in the pores. So, the IPN3 contains more water retention space and relative lower lose of water property, and IPN1 hydrogel has higher salt sensitivity.

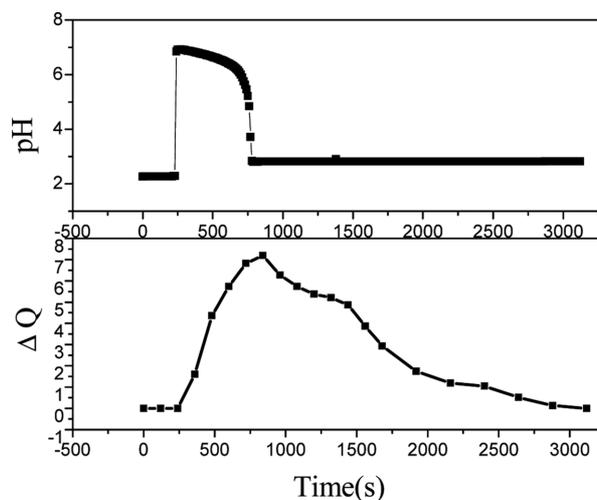
**Oscillatory Swelling/De-swelling Behavior of the Hydrogels.** To investigate the reversible swelling behavior of the prepared hydrogels with the pH of the external environment, the swelling/de-swelling oscillatory experiments were carried out and the results were shown in Figure 5. When the equilibrium swollen hydrogel in the solution of pH=3 immersed into the solution of pH=7, it began to swell quickly, and shrink when it returned back to the solution of pH=3. Then the sample was transferred into the solution of pH=7 again, it swelled fast. It can be seen from Figure 5 obviously that with the increasing number of cycles, the  $Q$  of the prepared hydrogel remained constantly. It is obvious that the pH-dependent swelling/de-swelling is reversible. We also found in the pro-



**Figure 5.** Oscillatory swelling/de-swelling behavior of the IPN2 hydrogel between pH 3.0 and 7.0. ( $I=0.1$  mol/L).

cess of experiments that the hydrogel were not broken and the shape kept very well after several cycles, which indicated the hydrogel has a good reversibility and flexible. This may be attributed to the incorporating of PEG in the IPN hydrogels. The excellent reversibility and flexible demonstrated that the hydrogel could be expected to use as pH-responsive materials in many fields of biological.

**Self-oscillatory Behavior of the Hydrogels in Closed pH Oscillator.** The  $\text{BrO}_3^-$ - $\text{SO}_3^{2-}$ - $\text{Fe}(\text{CN})_6^{4-}$  system in acidic media is known to exhibit oscillating behavior in which the concentration of  $\text{H}^+$  changes periodically as shown in Figure 6. When the swollen hydrogel was immersed in the pH oscillator, it began to swell with the increasing of pH by adding  $\text{SO}_3^{2-}$  into the system. The hydrogel continued to swell and its volume increased about 7 times to the original size when the pH began to decrease. With the decreasing in pH of the oscillator, the hydrogel started to shrink. The de-swelling rate was slower than that of swelling one, and it took about 30 min for its restoration to its original size. This slower reversible phenomenon may be attributed to the strong hydrogen bonding interaction among the carboxylic groups of hydrogel network and the slowing down diffusion rate of water outside the hydrogel. Just as we know, oral route is the most important and convenient path of administering drugs. Useful oral drug delivery demands the drug carrier is resistant to the impact of enzymes and pH change that is changing from pH 1-3 in the stomach to pH 6-7 in the intestine.<sup>25</sup> The synthesized hydrogel swells significantly in pH 6-7 and shrinks dramatically in solution of lower pH. In addition, PAA and PEG are biocompatibility,



**Figure 6.** Self-oscillatory behavior of the IPN2 hydrogel in a closed pH oscillator.

which could be degraded in biology environment. So it is also suitable to use as an efficient oral drug delivery media.

## Conclusions

In this work, IPN hydrogel were prepared via in radical polymerization of AA and PEG monomers in the presence of *N,N'*-methylene bisacrylamide as a cross-linker. The results showed that the hydrogel exhibited good pH and salt sensitivity and excellent reversibility of pH-responsive. The sensitive characteristics of the hydrogel increased with the increasing PEG content at the same conditions. Also the response of the present hydrogel in the  $\text{BrO}_3^-$ - $\text{SO}_3^{2-}$ - $\text{Fe}(\text{CN})_6^{4-}$  oscillating system indicates that it exhibits good swelling/deswelling self-oscillating behavior coupled with pH oscillator. Therefore, the prepared PEG/PAA IPN hydrogel can be useful for the various future applications in bioengineering and biotechnology.

**Acknowledgments.** This work was supported in part by the Basic Project of Science and Research of Colleges and Universities of Gansu Province (5001-109), the Natural Science Foundation of Gansu Province (1010 RJZA015; 096RJZA120).

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