

Preparation of Hydrogels Composed of Poly(vinyl alcohol) and Polyethyleneimine and Their Electrical Response

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ABSTRACT: Semi- and full-interpenetrating polymer network (IPN) hydrogels composed of poly(vinyl alcohol) and polyethyleneimine (PEI) were prepared to investigate the bending behavior under the electric response. To find out the characteristics of the hydrogel in the medium, swelling ratio, and rate and water state of the hydrogels were measured. The swelling ratio of the semi-IPN hydrogels increased with PEI content in the matrix, whereas that of full-IPN hydrogels dramatically decrease with increase of PEI contents in the hydrogels. In the water state of hydrogel, the bound water and free water of semi-IPN hydrogels increased with PEI weight ratio. The full-IPN hydrogels show the lower free water content in comparison with the

semi-IPN hydrogel. The IPN hydrogels exhibited bending angle change in response to external stimulus such as voltage, the bending angle increased with PEI concentration. In addition, the repeated bending behaviors according to the magnitude of the applied electric field revealed that the bending angle is reversible without collapse of formation of hydrogel in all samples. Thus, the hydrogels will be useful as novel modulation systems in the field of artificial organ and matrix for drug delivery. © 2007 Wiley Periodicals, Inc. *J Appl Polym Sci* 107: 2136–2141, 2008

Key words: hydrogels; interpenetrating networks (IPN); biopolymers

INTRODUCTION

Smart materials can reversibly change their volume and shape in response to external stimuli such as pH, temperature and electric field.^{1–4} In particular, the electrically responsive hydrogels are recently focused on their potential scientific importance in the actuator, artificial muscle, and sensor.⁵

The electro-active polymer (EAP) system can also widen the applications to biomedical applications such as tissue engineering and gene/drug delivery system because the electrical stimulus has influenced on the proliferation of cell and tissue regeneration. Note that the change in volume and shape caused by electrical stimulus can be acted as a stimulus in the tissue or cells. The stimulus can play an important role in altering the characterization of extracellular matrix.⁶ In particular, the pulsatile mechanical stimulus improved the mechanical strength and collagen production in the tissue-engineered artificial organ.^{7–11} Furthermore, the mechanical stimulus can be controlled by EAP system.

For the introducing the EAP system into biomedical applications, the polyethyleneimine (PEI), and

poly(vinyl alcohol) (PVA) were used to prepare the electro responsive matrix because these polymers has been often used in the drug/gene delivery system and tissue engineering.^{12–20} In particular, PEI has been extensively used to deliver plasmid DNA into mammalian cells,^{12–15} because not only cationic groups of PEI main chain could be conjugated with phosphate groups of DNA but also the ion group of PEI can activate the movement under electrical current. As the other component, PVA has been known as excellent mechanical strength, good film forming, and long-term temperature.^{19,20} In addition, PVA is bio-compatible and nontoxic, and exhibits minimal cell adhesion and protein absorption, as desired in biomedical applications requiring contact with bodily fluid.^{19,20}

Several research groups have focused on the electro-responsive behavior of PVA-based hydrogels under the influence of applied electric field. Kim et al. reported that the interpenetrating polymer network (IPN) hydrogels composed of PVA and poly(*N*-isopropylacrylamide), chitosan, polymethacrylic acid, hyaluronic acid, and poly(diallyldimethylammonium chloride) have electrical sensitivity behavior at various pHs and salt concentrations in the medium.^{21–25} Kim et al. reported that the PVA/poly(acrylic acid) IPN hydrogels exhibited the electrically sensitive behaviors on the equilibrium bending angle and swelling–deswelling ratios.²⁶

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In this study, the hydrogel was prepared using the IPN which is an assembly of interpenetrating networks of two crosslinked polymers. Semi-IPN means that one component of the assembly is crosslinked leaving the other in linear form, whereas full-IPN shows all polymer chains are crosslinked. The PEI was chemically crosslinked with adipic acid and the PVA chains were alternatively physically crosslinked using the freeze-thawing.

The goals of the present study are to prepare the electro-sensitive hydrogel composed of PEI and PVA and to investigate the swelling and bending angle behaviors. Furthermore, the difference of IPN-types is discussed by comparing semi-IPN hydrogels with full-IPN hydrogels.

EXPERIMENTAL

Materials

PVA, 99% hydrolyzed, with average molecular weight from 8.50×10^4 to 1.46×10^5 g/mol and PEI (50 wt % solution in water) were purchased from Aldrich Chemicals (Milwaukee, WI). Adipic acid, N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride (EDC) and N-hydroxysuccinimide (NHS) were purchased from Sigma Chemicals (St. Louis, MO). Water was first treated with a reverse osmosis system and further purified with a Milli-Q Plus system (Waters, Millipore, Billerica, MA). Other chemicals were reagent grade and used without any further purification.

Preparation of semi-IPN hydrogels

PVA was dissolved in deionized water at 70°C for 3 h to prepare 5 wt % aqueous solutions. The PVA and PEI solutions were mixed with various weight ratios, as shown in Table I. To crosslink the PEI, adipic acid was used as a crosslinking agent. The equivalence molar ratio between PEI and adipic acid was confirmed with the titration method using a conductivity

meter. Molar ratio of PEI/Adipic acid/NHS was 1 : 1 : 2 with reference to the PEI amino group. This solution was poured into a petri dish, and dried at room temperature for one day. The dried film was immersed in deionized water containing EDC (1 : 2, by molar ratio of adipic acid) to activate forming amide bondages between amino groups of PEI and carboxylic groups of adipic acid, and slowly shaken overnight at room temperature. After crosslinking, any unreacted residues were washed with deionized water and dried in a 30°C vacuum oven.

Preparation of full-IPN hydrogels

The PVA/PEI solution poured into a petri dish was frozen at -50°C for 6 h and thawed at room temperature for 6 h. These freezing-thawing cycles were repeated four times. After finishing the freezing-thawing cycles, the samples were dried in vacuum oven at 30°C. The crosslinking method using the EDC was same as semi-IPN hydrogels.

Measurement of swelling behaviors

A swelling study was conducted on the hydrogels to observe the kinetic behavior and swelling ratio in the swelling medium. To measure the swelling ratio, preweighed dry samples were immersed in deionized water solutions. After the excessive surface solution was removed with filter paper, the swollen samples were weighed at various time intervals. The swelling ratio and equilibrium water content (EWC) were calculated using the following formula:

$$\text{Swelling ratio} = (W_s - W_d)/W_d$$

$$\text{EWC}(\%) = (W_s - W_d)/W_s \times 100$$

where W_s is the weight of hydrogel in the swollen state, and W_d is the dry weight of the hydrogel after drying the gels in a dry oven for 2 days.

TABLE I
Composition and Water States of Hydrogels

Hydrogel types	Sample codes	Weight ratio (wt%)		Water state ^a		
		PVA	PEI	EWC (%)	Free water (%)	Bound water (%)
Semi-IPN hydrogel	sAI91	90	10	62.66	7.24	55.42
	sAI82	80	20	69.96	13.66	56.30
	sAI73	70	30	71.34	13.91	57.43
	sAI64	60	40	74.54	14.55	59.99
Full-IPN hydrogel	fPVA	100	0	73.36	8.52	64.83
	fAI91	90	10	71.11	7.42	63.69
	fAI82	80	20	70.69	6.99	64.70
	fAI73	70	30	69.87	6.15	63.72
	fAI64	60	40	65.96	5.57	60.39

^a Samples were fully swollen in distilled water (pH = 5.4) at 25°C for 2 h.

Measurement of bending angle under electric stimulus

The bending angle measurement was investigated in the noncontact direct current (DC) electric field.²⁷ The hydrogels were fully swollen in 0.01N NaCl aqueous solution at room temperature and cut into a $50 \times 2 \times 2 \text{ mm}^3$ rectangular column. After the one end of the sample column was fixed and placed vertically between two carbon electrodes in NaCl aqueous solution, its bending behavior was investigated under DC electric field. The bending degree of hydrogels was measured by varying the applied electric potential.

Characterizations

Fourier transform infrared (FTIR, Nicolet model Magna IR 550, Madison, WI) spectroscopy was used to confirm the crosslinking between PEI and adipic acid. The state of water in the hydrogels was investigated by differential scanning calorimetry (DSC, TA Instruments, DSC910, New Castle, DE) in the temperature range of -20 to 30°C with a heating rate of $5^\circ\text{C}/\text{min}$ under N_2 flow. The amount of free water and bound water were calculated from the respective melting enthalpies. The following equation assumes that the heat of fusion of free water in the hydrogel (Q_{endo}) is the same as that in ice (Q_f , 79.7 cal/g):

$$W_b(\%) = W_t - (W_f + W_{fb}) = W_t - (Q_{\text{endo}}/Q_f) \times 100$$

where, W_b is the amount of bound water (%); W_f and W_{fb} are the amounts of free water and freezing bound water, respectively; and W_t is the EWC [EWC (%)].

RESULTS AND DISCUSSION

Preparation of IPN hydrogels

FTIR spectroscopic measurement was carried out to confirm the formation of amide bonds, based on the changes in chemical structure of the hydrogel. Figure 1 shows the FTIR spectra for PVA (a), PEI (b), the semi-IPN hydrogels (c–f) and adipic acid (g). The FTIR spectrum of PEI indicated that a peak appeared at 1588 cm^{-1} could be assigned to $N-H$ bending vibration of a primary amino group. In addition, Figure 1(g), adipic acid shows a characteristic peak at 1746 cm^{-1} , which can be attributed to the characteristic peaks of a carbonyl stretching vibration. In the case of the IPN hydrogel [Fig. 1(c–f)], the formation of amide groups were confirmed by appearance of amide I at 1655 cm^{-1} and amide II at 1559 cm^{-1} and the disappearances of free amino group of PEI at 1588 cm^{-1} and carboxyl group in adipic acid at 1746

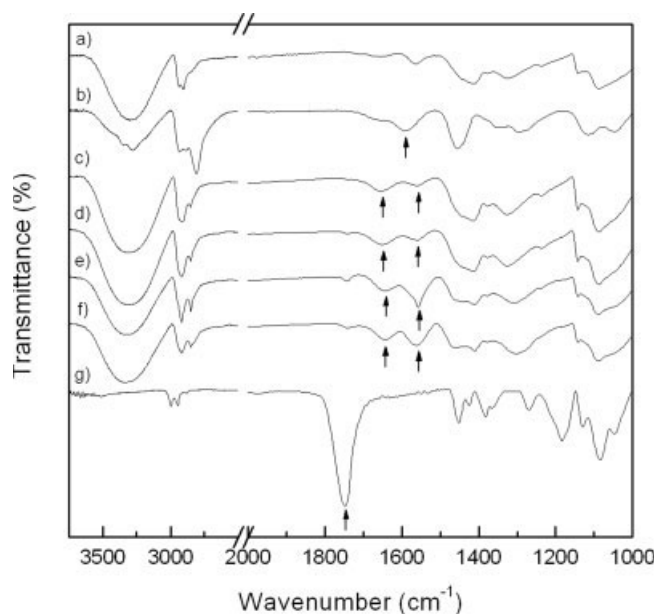


Figure 1 Fourier transform infrared spectra for (a) PVA, (b) PEI, (c) sAI91, (d) sAI82, (e) sAI73, (f) sAI64, and (g) adipic acid.

cm^{-1} because of the formation of amide bondages, compared with PEI and adipic acid.

Swelling kinetics of the IPN hydrogel

Figure 2 shows swelling kinetics behaviors of IPN hydrogels in deionized water at 25°C . As shown in Figure 2(a), the swelling ratio of sAI82, sAI73, and sAI64 hydrogels reached an equilibrium swelling state within about 20 min and that of sAI91 hydrogel did 40 min. The relatively slow swelling kinetics of sAI91 may be due to the higher content of PVA. In addition, the swelling ratio of the sAI hydrogels increased with PEI content in the matrix. Rapid swelling kinetics and high swelling ratio of sAI hydrogels arose from the fast and strong hydration of PEI chains which maintain high mobility and ionic charge. In the previous studies, hyaluronic acid and chitosan which have ionic groups such as carboxyl and amino groups, respectively, in the semi-IPN PVA hydrogels also showed the rapid swelling kinetics.^{22,24}

Figure 2(b) shows the swelling kinetics of the fAI hydrogels which reached an equilibrium swelling state within about 60 min, because the fAI has a more compact complex structure in comparison with sAI. Note that sAI hydrogels have only PEI crosslinking molecular structure, whereas the fAI hydrogels additionally have physically crosslinked PVA after freeze-thawing procedure. The decrease of swelling ratio was more dramatic in the higher PEI containing hydrogels. As a similar result, Rao et al. reported that the crosslinked PVA/PEI membrane

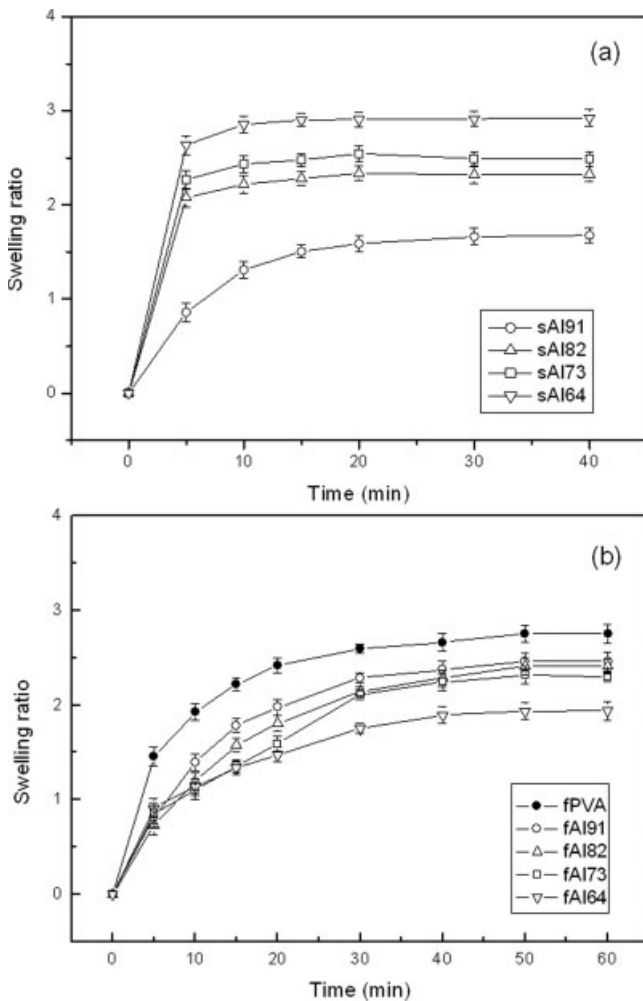


Figure 2 Swelling kinetics of (a) semi-IPN hydrogels and (b) full-IPN hydrogels in 0.01N NaCl aqueous solution (pH = 5.4) at 25°C.

using glutaraldehyde also showed the lower sorption in comparison with the non-cross-linked PVA/PEI membrane because of forming the compact structure after crosslinking.²⁸

Water states of semi-IPN and full-IPN hydrogels

To further elucidate the swelling behavior of hydrogel, the water state of the hydrogels was investigated by DSC which is used for the quantitative determination of the amounts of freezing and nonfreezing water. Generally, the state of water in the polymer hydrogel can be divided into free water, freezing bound water, and nonfreezing bound water. The free water had no interaction with polymer chains, whereas the bound water was involved in the hydrogen bonding with polymer. The endothermic peak appeared at around 0–10°C and was attributed to the presence of free water in the hydrogels. The fraction of free water in total water was approximately calcu-

lated as the ratio of the endothermic peak area for the water-swollen hydrogel to the melting endothermic heat of fusion (79.9 cal/g) for pure water.

Table I displays the water states of the hydrogels. The water states were affected on the weight ratio and the type of IPN. In semi-IPN hydrogels, the bound water and free water increased with PEI weight ratio because the PEI has the ionic groups which can bind the water, in the result of increasing the EWC in the hydrogel. The full-IPN hydrogels show the lower free water content in comparison with the semi-IPN hydrogel. The physically cross-linked PVA chains can not have more free volumes to be able to contain the free water than semi-IPN hydrogels due to compact structure.

Bending behavior of the IPN hydrogels under electric fields

When an electric field was applied to the hydrogel strip in aqueous NaCl solutions, the hydrogel

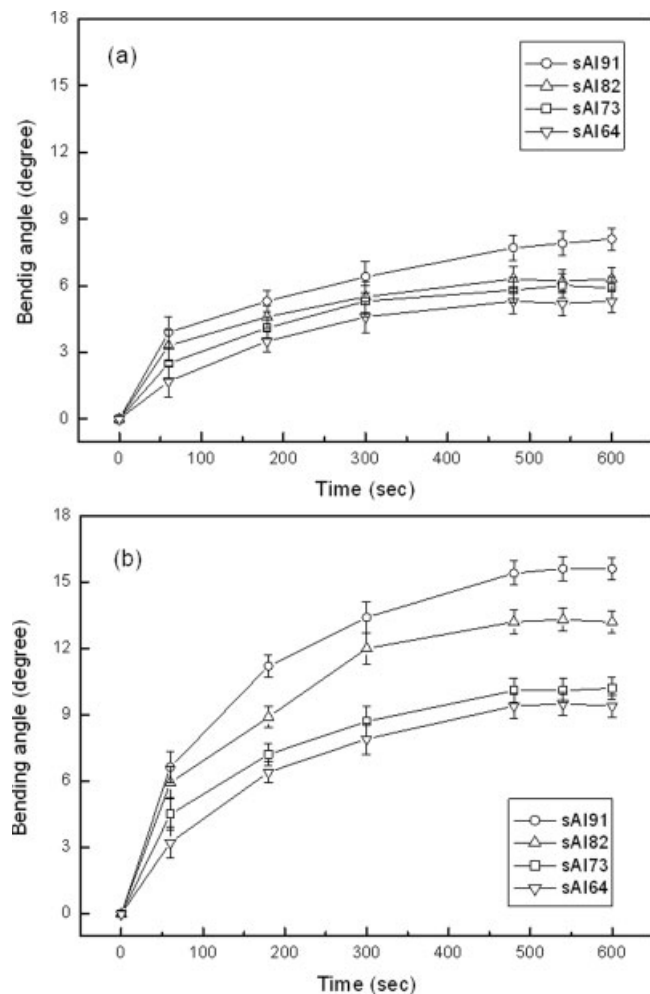


Figure 3 Bending angle of semi-IPN hydrogels at (a) 5 V and (b) 10 V in 0.01N NaCl aqueous solution (pH = 5.4) at 25°C.

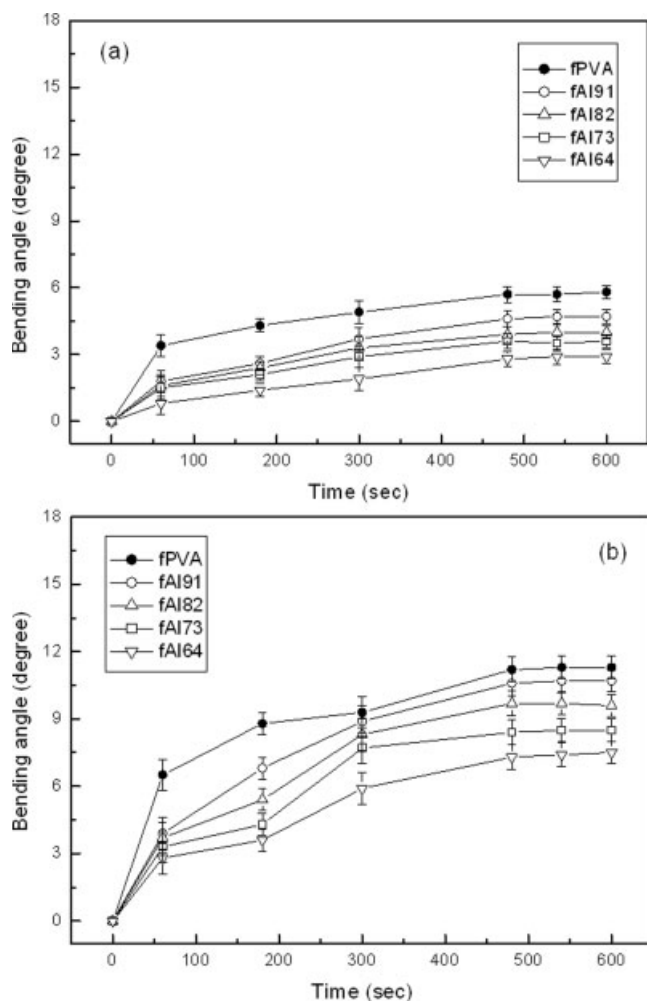


Figure 4 Bending angle of full-IPN hydrogels at (a) 5 V and (b) 10 V in 0.01N NaCl aqueous solution (pH = 5.4) at 25°C.

showed significant bending. The hydrogel returned to its original position after the electric stimulus was removed. The altering the polarity of the electric field induces the hydrogel movement toward the opposite direction. The mechanism of bending behavior is caused by the deformation of a hydrogel under an electric field. The voltage-induced motion of ions has influence on the deformation, indicating the concomitant expansion of one side of the other. Unfortunately, it is not clear completely to explain the chemo-mechanical kinetics due to the lack of well-developed theories.

Figures 3 and 4 show the variation of the bending angle of the sAI and fAI hydrogels, as a function of the applied voltage, in 0.01N NaCl solution at room temperature. The bending angle increased with the voltage applied across the hydrogel, indicating that the bending was induced by the electric current.

The bending angle of IPN hydrogel increased with PVA content in the hydrogel regardless of IPN-

types. It seems that the crosslinked PEI chains restrict the mobility of the hydrogel toward the electrode. The bending angle depended on the restriction caused by PVA crosslinking in comparison with the driving force based on ionic charges of non-cross-linked amino groups. In addition, the bending angle of full-IPN hydrogels is low in comparison with that of semi-IPN hydrogels because of physically cross-linking of PVA.

Previously reported IPN hydrogels composed of PVA and poly(acrylic acid)(PAA) showed the similar results with bending kinetics and bending angles of the PEI/PVA IPN hydrogel at the 5 V, whereas the bending angle of PVA/PAA IPN above 10 V was higher than the PVA/PEI hydrogels.²⁶ In addition, the PVA/poly(methacrylic acid), PVA/chitosan and PVA/hyaluronic acid IPN hydrogels have the higher bending angle in comparison with the PVA/PEI hydrogel.^{22–24} It may be due to the more compact structure of the PVA/PEI hydrogel and the various bending tested conditions of the medium under the applied voltages. Note that not only polymer structure and thickness of the tested hydrogel but also the medium conditions such as added salts concentrations and temperature affect on the bending angle of the hydrogels.

Figure 5 shows the reversible bending behaviors according to the magnitude of the applied electric field. The bending angle is reversible without collapse of formation of hydrogel in all samples. The rate of bending behavior was so late as for the hydrogel to be incompatible in the application to the rapid motion system. However, the biomedical system for gene release or artificial organic matrix requires not the rapid motion but the sustained motion.

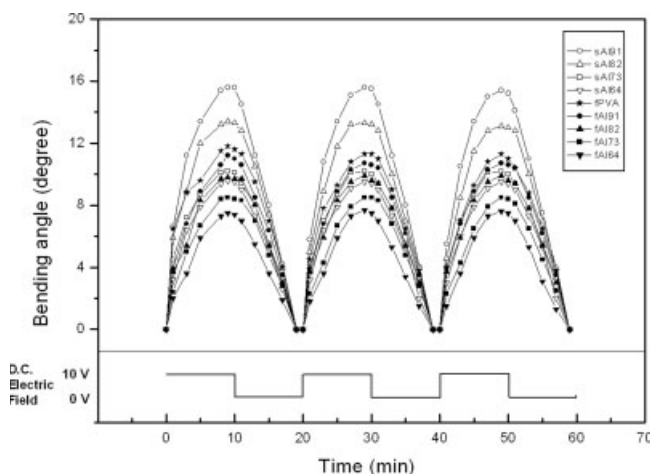


Figure 5 Pulsatile bending behaviors of IPN-hydrogels with changes in the applied voltage of 10 V in 0.01N NaCl aqueous solution (pH = 5.4) at 25°C.

CONCLUSIONS

FTIR spectroscopic measurement confirmed the formation of amide bonds between amino groups of PEI and carboxylic groups of adipic acid. The swelling behaviors revealed that the swelling ratio of the semi-IPN hydrogels increased with PEI content in the matrix, whereas that of full-IPN hydrogels dramatically decrease with increase of PEI contents in the hydrogels. In the water state of hydrogel, the bound water and free water of semi-IPN hydrogels increased with PEI weight ratio because the PEI has the ionic groups which can bind the water, in the result of increasing the EWC in the hydrogel. The full-IPN hydrogels show the lower free water content in comparison with the semi-IPN hydrogel. The bending angle increased with the voltage applied across the hydrogel and with PVA content in the hydrogel regardless of IPN-types. In addition, the bending angle of full-IPN hydrogels is low in comparison with that of semi-IPN hydrogels because of physically cross-linking of PVA. The IPN-hydrogels showed the reversible bending behavior.

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