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Novel polyion complex with interpenetrating polymer network of poly(acrylic acid) and partially protected poly(vinylamine) using *N*-vinylacetamide and *N*-vinylformamide

Hiroharu Ajiro [a,b], Yukie Takemoto [b], Taka-aki Asoh [b], Mitsuru Akashi [a,b,*]

[a] The Center for Advanced Medical Engineering and Informatics, Osaka University, 2-2 Yamada-oka, Suita, Osaka 565-0871, Japan
[b] Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamada-oka, Suita, Osaka 565-0871, Japan

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ABSTRACT

Poly(vinylamine), the simplest polycation with primary amines, was applied to interpenetrating polymer networks (IPN) with poly(acrylic acid). *N*-Vinylformamide (NVF) was employed for amino-protected monomers to control electrostatic balance. pH-responsivities of IPNs varied, depending on the hydrolysis conditions and acrylic acid (AAc) concentration of the second network. Poly(*N*-vinylacetamide)-*co*-poly(*N*-vinylformamide) (4/6, mol/mol) was employed for the first network, subsequently hydrolyzed with 50% amide groups, and the second network was polymerized with 0.25 mol L^{-1} AAc, extremely shrunken hydrogels with polyion complex were formed at pH 7, showing that the controlled amount of highly active primary amines are available in IPN.

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1. Introduction

Poly(vinylamine) (PVAm) is an attractive polycation, because it contains the highest nitrogen content among polycations, possessing high reactivity of primary amines. From this point of view, PVAm is distinguished from conventional polycations, such as poly(ethylenimine) and poly(allylamine), however, only a few dozen examples of PVAm gels exist in the literature at present [1,2]. The limited number of examples is attributed to the fact that vinylamine monomers are unstable and easily convert to acetaldehyde imines. Therefore, PVAm is usually transformed from precursor polymers, such as poly(*N*-vinylformamide) (PNVF), poly(*N*-vinylacetamide) (PNVA), and other poly(*N*-vinylalkylamides).

Since a convenient synthesis method for *N*-vinylalkylamides was developed within our group [3], many poly(*N*-vinylalkylamide)s have since been synthesized. Copolymerization is one of approaches to produce functional materials. For example, thermosensitive copolymers are produced when *N*-vinylformamide (NVF) is polymerized with *N*-vinylalkylamides [4,5]. *N*-Vinylacetamide (NVA) also produces thermosensitive and pH-responsive polymers by copolymerization with vinylacetate [6]. Hydrophilic PVAm plays an important role in expressing stimuli sensitivity, but the considerably different radical polymerizability between non-conjugated *N*-vinylalkylamide monomers and common vinyl monomers limit the variety of copolymerization. On the other hand, layer-by-layer (LbL) assembly produces functional materials using electrostatic interactions with polyanions such as PAAc [7–9] and poly(sodium styrenesulfonate) [10]. Strong PVAm cationic features are effectively utilized in the LbL technique, however, the obtained functionality is only limited only to substrate surfaces.

We recently applied interpenetrating polymer network (IPN) [11,12] to poly(*N*-vinylalkylamide) gels [13–15]. IPN enables poly(*N*-vinylalkylamide)s to combine with polyanions at all ratios, because there is no need for radical polymerization between *N*-vinylalkylamides and other vinyl monomers. Furthermore, considering that amide groups properly convert to cationic PVAm inside IPN, it is therefore possible to produce electrostatically controllable polyelectrolytes and polyion complexes (PICs).

PIC gels are widely applicable to functional materials, including biomedical applications [16–18], drug delivery systems [19–22], damping materials [23], and film improvements [24]. Basic PICs with PAAc bearing IPN have been synthesized with combinations of modified poly(aspartic acid)/PAAc [25], chitosan/PAAc [26], and alginate/amine-terminated poly(*N*-isopropylacrylamide) [27]. These PIC gels show pH-, temperature-, and

* Corresponding author. Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamada-oka, Suita, Osaka 565-0871, Japan. Tel.: +81 6 6879 7356; fax: +81 6 6879 7359.
E-mail address: akashi@chem.eng.osaka-u.ac.jp (M. Akashi).

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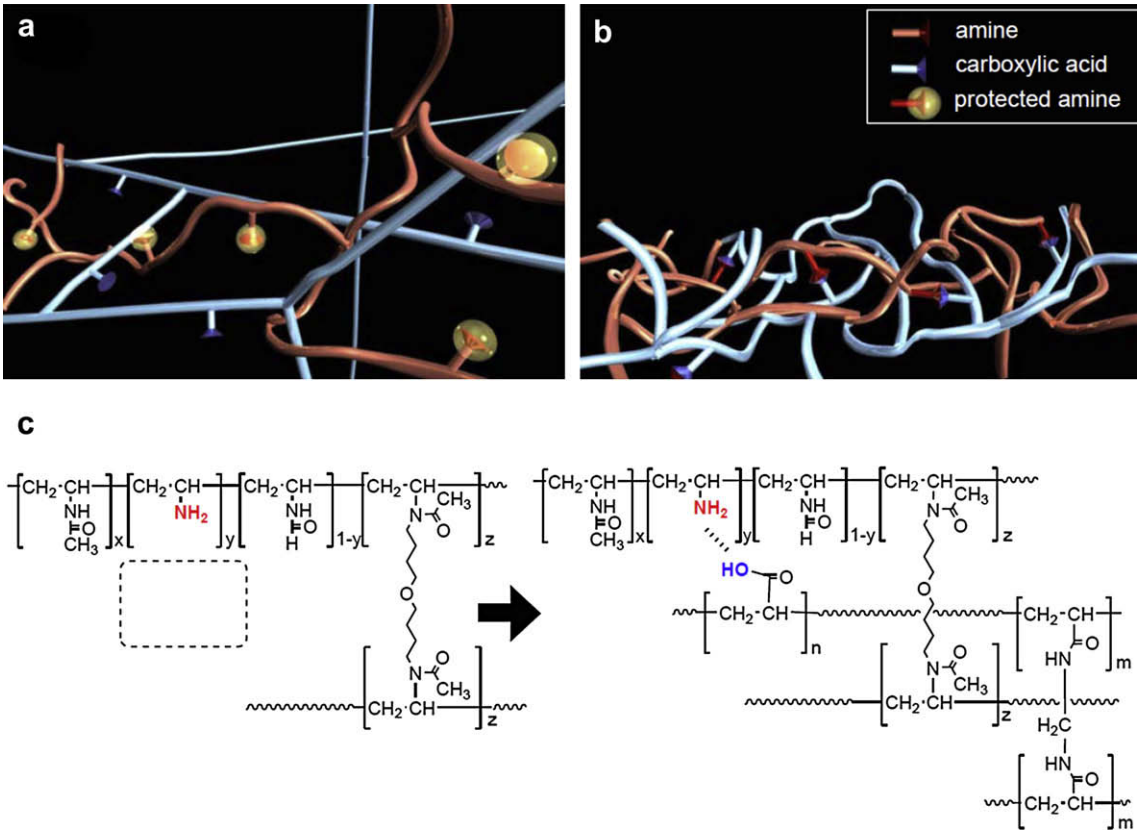

Scheme 1. An illustration of PNVA-*co*-PNVF/PAAc IPNs, whose amino groups are protected with amide groups (a) and shrunken PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN at pH 7 (b). The reaction scheme of PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN from PNVA-*co*-PNVF-*co*-PVAm gels, bearing an AAc associating place at the second polymerization stage (c).

salt-responsive characteristics, when the balance of anions and cations is properly controlled by the initial monomer load. However, it is somewhat difficult to precisely control amounts of cations and anions under circumstances that include dilute hydrogels, without adroit handling conditions [28] and strict molecular design [29].

In this study, we focused on NVF as a precursor of cationic PVAm in IPN preparations. Differing from conventional PICs, the amount of introducing cations could be well controlled by PNVF hydrolysis conditions [5,30], with constant polymer densities and neutral PNVF. Herein we report novel pH-responsive IPNs by an approach with protected PVAm, using PNVF and PNVA (Scheme

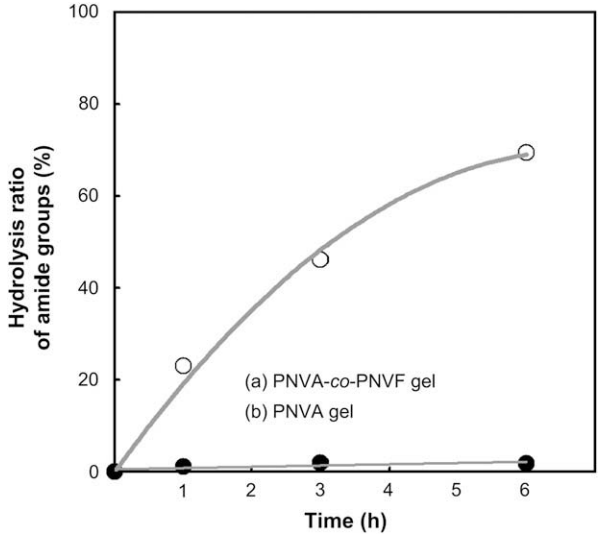

Fig. 1. Hydrolysis behaviors of PNVA-*co*-PNVF (4/6, mol/mol) gels (a) and PNVA gels (b).

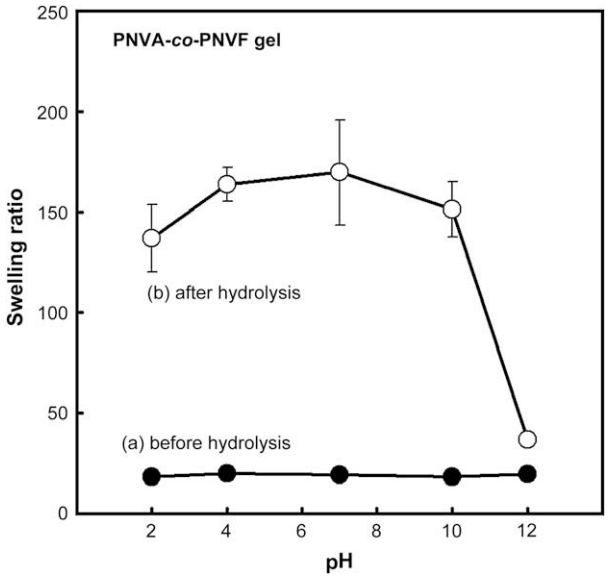

Fig. 2. Swelling ratios of PNVA-*co*-PNVF gels (a) and 50% hydrolyzed PNVA-*co*-PNVF gels (b) ($n = 3$).

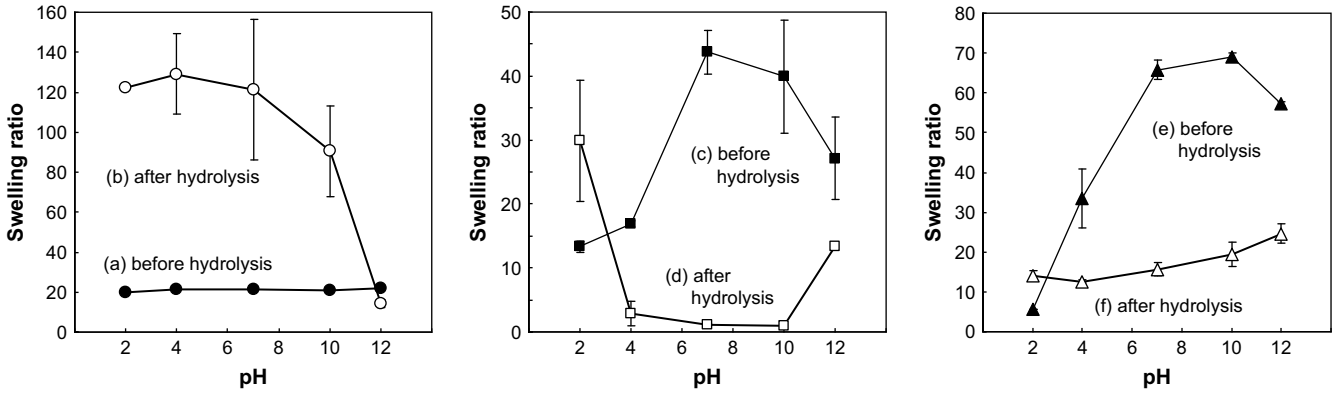

Fig. 3. Swelling ratio *versus* pH of PNVA-*co*-PNVF/PAAc IPN with an AAc concentration of 0.1 mol L^{-1} (a) the hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN with an AAc concentration of 0.1 mol L^{-1} (b) PNVA-*co*-PNVF/PAAc IPN with an AAc concentration of 0.25 mol L^{-1} (c) the hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN with an AAc concentration of 0.25 mol L^{-1} (d) PNVA-*co*-PNVF/PAAc IPN with an AAc concentration of 0.5 mol L^{-1} (e) the hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN with an AAc concentration of 0.5 mol L^{-1} (f) ($n = 3$).

1a), and we prepared PIC gels by hydrolysis (deprotection) (Scheme 1b).

2. Experimental section

2.1. Materials

NVA (Showa Denko K.K., Japan) was recrystallized from toluene/cyclohexane (1/3) and dried under vacuum at room temperature. NVF (Mitsubishi Chemical Co., Ltd., Japan) and AAc were purified by distillation. *N*,*N*-methylenebisacrylamide (MBAAm) (Wako, Ltd., Japan), 2,2′-azobis(2-methylpropionamidine)dihydrochloride (V-50) (Wako, Japan), ammonium peroxodisulfate (APS) (Nakarai Tasque, Japan), and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) (Nakarai Tasque, Japan) were used without further purification. *N*,*N*-5-Oxanonamethyene-bis-*N*-vinylacetamide (5ON-bis-NVA) was used as an NVA crosslinker, and was prepared according to a previously reported method [13].

2.2. Preparation of PNVA-co-PNVF-co-PVAm gel

NVA (136 mg, 1.6 mmol), NVF (448 μL, 6.4 mmol), V-50 (22 mg, 0.08 mmol) as a radical initiator, and 5ON-bis-NVA (71 mg, 0.24 mmol) as a crosslinker were combined in degassed water (8 mL, 0.2 mol L^{-1} for NVA, 0.8 mol L^{-1} for NVF). Solutions were injected between double glass plates that were separated by a silicon gasket (1.0 mm thickness) under a nitrogen atmosphere. The mixture was then almost quantitatively polymerized at 37 °C for 8 h. After repeatedly washed by water, elemental analysis of the freeze-dried gel showed the ratio of PNVA/PNVF was 4/6. Obtained PNVA-*co*-PNVF gels were treated with 2 M aqueous NaOH at 60 °C to hydrolyze amide groups on PNVF parts, and adequately rinsed with 0.01 M aqueous HCl.

2.3. Preparation of PNVA-co-PNVF-co-PVAm/PAAc IPNs

A typical experimental procedure is described for IPN with an AAc concentration of 0.25 mol L^{-1}. AAc was neutralized by aqueous NaOH for use in polymerizations. An AAc solution (26%, 2 mL, 8 mmol), MBAAm (62 mg, 0.40 mmol), and APS in water (10%, 91 μL, 0.04 mmol) were combined with 0.01 M aqueous HCl (32 mL total) and degassed by N_2 purges. Gel membranes were cut into disks (8 mm diameters) in advance. PNVA-*co*-PNVF-*co*-PVAm gels, which were hydrolyzed for 3 h, were introduced to solutions, the mixture was left untouched for AAc monomer diffusion into gels over 12 h. TEMED (14 μL, 0.09 mmol) was introduced to mixtures an hour before heating up to 37 °C for 8 h to prepare IPNs. Each gel was immersed into a large amount of ultrapure water for 1 week to remove reaction residues. The swelling ratio of the hydrogel was calculated by the following equation: $(W_s - W_d)/W_d$, where W_s is the weight of swollen hydrogels at room temperature and W_d is that of dried gels.

2.4. Swelling experiments

To study hydrogel swelling at different pH-values, hydrogel samples were put into aqueous solutions of 0.01 M HCl or 0.01 M NaOH at a desired pH (30 mL of solution per each hydrogel). Swelling experiments were performed in capped vials in order to avoid CO_2 uptake. Hydrogel samples remained in solution at 25 °C

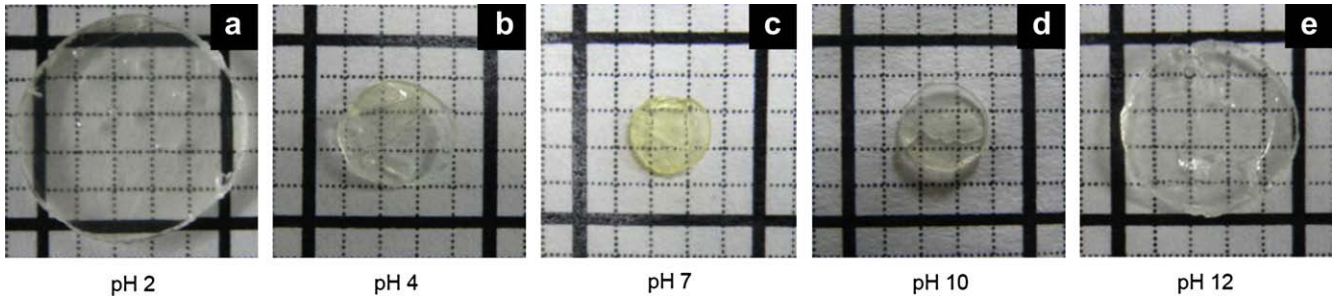

Fig. 4. Photos of 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc IPNs, prepared with a 0.25 mol L^{-1} AAc concentration under various pH conditions. (a) pH 2, (b) pH 4, (c) pH 7, (d) pH 10, and (e) pH 12.

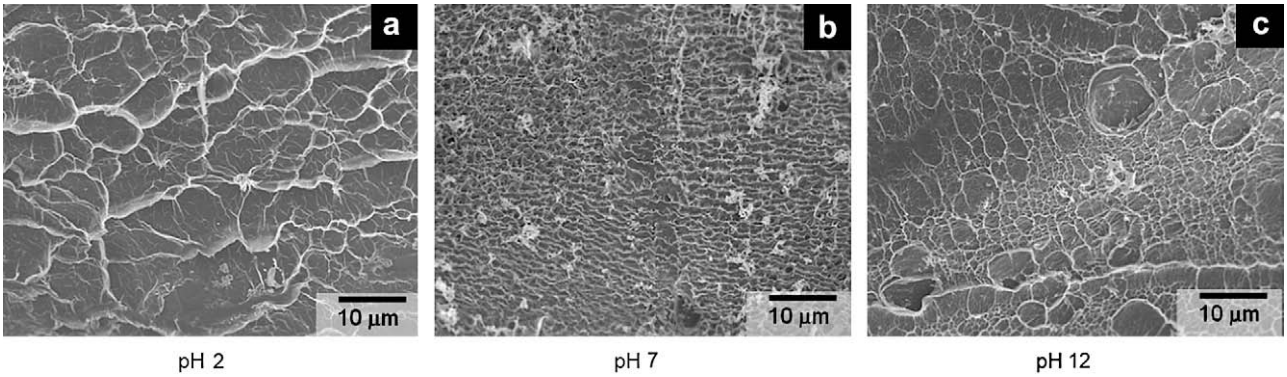

Fig. 5. SEM image of a freeze dried gel of 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc IPNs at pH 2 (a), pH 7 (b), and pH 12 (c).

for the time required to attain equilibrium. After equilibrium was attained (from 12 to 24 h), hydrogel samples were weighed and the pH of the exterior solution was measured.

3. Results and discussion

In this study, we selected PNVA-*co*-PNVF (4/6, mol/mol) for the first network in IPN, because additional PNVA improves the mechanical strength of PNVF gels. Hydrolysis of PNVA-*co*-PNVF was achieved by 2 M aqueous NaOH, under which only PNVF changed to PVAm [4,31]. Firstly, the hydrolysis behavior of PNVA-*co*-PNVF (4/6, mol/mol) was investigated in order to estimate the emerging amount of polycation (PVAm) in the absence of PAAc.

Fig. 1 shows the hydrolysis behavior of PNVA-*co*-PNVF gels (open circles) and PNVA gels (closed circles), determined by elemental analyses. Whereas PNVA gels were stable even after 6 h in alkali conditions, PNVA-*co*-PNVF gels gradually hydrolyzed over 6 h. In short, around 50% of amide groups in PNVA-*co*-PNVF were converted to PVAm after 3 h. The aforementioned hydrolysis ratios were in good agreement with those determined by ^{1}H NMR analyses using linear PNVA-*co*-PNVF copolymers (Supporting Information, Fig. S1) [30]. Therefore, we estimated that 50% amide groups (83% PNVF and ~0% PNVA) were converted to PVAm after 3 h, and we checked the swelling ratios of 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm gels at various pH conditions. In this study, we assumed there was no ionic strength effect toward the swelling ratio due to very dilute salt concentrations (0.01 mol L^{-1} HCl and NaOH).

Compared with PNVA-*co*-PNVF before hydrolysis (Fig. 2a), larger swelling ratios were observed between pH 2 and pH 10, suggesting the deprotection of amino groups and the existence of polycations (Fig. 2b), which is in good agreement with the ammonium proton's dissociation constant ($pK_b \sim 10$). Then, 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm gels were employed to the IPN preparation with PAAc.

Prior to the IPN preparation with polycations and polyanions, we examined proper AAc concentrations to observe anionic repulsion in PNVA-*co*-PNVF gels without hydrolysis. When 0.25 mol L^{-1} AAc and 0.5 mol L^{-1} AAc were chosen in PNVA-*co*-PNVF/PAAc IPN preparations, swelling curves resembled those of PAAc (Fig. 3c and e), while there was no pattern change with 0.1 mol L^{-1} AAc (Fig. 3a). So, using 50% hydrolyzed PNVA-*co*-PNVF gels (PNVA-*co*-PNVF-*co*-PVAm gels) in Fig. 1, pH responsivities of IPNs were investigated by preparations with different concentrations of AAc; 0.1 mol L^{-1}, 0.25 mol L^{-1}, and 0.5 mol L^{-1}. Under these conditions, bare amino groups in PNVA-*co*-PVAm polymer chains can associate with the second monomer AAc before polymerization, which may result in effective polycation–polyanion interactions (Scheme 1c).

Compared with PNVA-*co*-PNVF/PAAc IPNs (Fig. 3a, c, and e), which were not hydrolyzed as controls, swelling ratios *versus* pH plots for each PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN (Fig. 3b, d, and f) were investigated. When 0.1 mol L^{-1} AAc was employed at the second gelation, non-hydrolyzed PNVA-*co*-PNVF/PAAc IPNs showed similar patterns with PNVA gels (Fig. 3a). After hydrolysis, IPNs possessed typical swelling ratio dependences to the pH of PVAm ($pK_b \sim 10$), implying that the amount of polyanion (PAAc) was deficient (Fig. 3b). Interestingly, a largely shrunken gel (swelling ratio = 1.1) was obtained at pH 7, when 0.25 mol L^{-1} AAc was employed for PNVA-*co*-PNVF-*co*-PVAm/PAAc IPN preparations (Fig. 3d), showing polyion complex formations. The aforementioned was also supported by swelling ratios at pH 2 (swelling ratio = 30) and at pH 12 (swelling ratio = 13), which were 27 times and 12 times as large as those at pH 7, respectively. The estimated amount of PVAm in IPN was equivalent to PAAc, determined by the increased weight on IPN preparation (Supporting Information, Table S1). However, when 0.5 mol L^{-1} AAc was used, the relationship between swelling ratio and pH resembled that of PAAc ($pK_a \sim 4$) (Fig. 3e). Even after the hydrolysis, due to excess polyanions (PAAc) relative to generated polycations (PVAm), electrostatic interactions were not strong enough to shrink neutralized gels at pH 7 (swelling ratio = 16), although cationic repulsive interactions existed at pH 2 (Fig. 3f).

Additionally, largely shrunken gels were also observed at pH 7, when more than 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc was employed, controlling AAc concentration in IPN preparations. Therefore, the ionic balance could be the central parameter governing the swelling behavior.

Photos of each gel under various pH conditions are depicted in Fig. 4. It is notable that the swelling ratio decreased to around 1 at pH 7, almost all the water inside was expelled (Fig. 4c). Thus, PIC formation was achieved, possessing an equivalent cationic and anionic balance. By controlling PNVA/PNVF initial ratios, hydrolysis times, and AAc amounts with dexterity, various pH-responsive IPNs were prepared.

SEM images of the freeze-dried gels in Fig. 4 are shown in Fig. 5. Despite the fact that the same hydrogel was used, pore sizes at pH 2 (Fig. 5a) and pH 12 (Fig. 5c) were enlarged compared to those at pH 7 (Fig. 5b), suggesting higher density polymers at pH 7 than at other pH values because of the polyion complex formation. The previous observation is in good agreement with pH-responsive hydrogel characteristics.

4. Conclusions

By taking advantage of NVF structural features as amino-protected monomers, polycations were introduced into IPNs with PAAc gels. The resulting 50% hydrolyzed PNVA-*co*-PNVF-*co*-PVAm/PAAc

IPNs showed various pH-responsivities, dependant on molar ratios of anions and cations inside of hydrogels. Shrunken PICs were formed by selecting proper NVA/NVF ratios (4/6) of the first network, hydrolysis conditions (3 h), and AAc concentration (0.25 mol L^{-1}) of the second network. The pH-responsivity was controlled by hydrolysis times of PNVA-*co*-PNVF gels. In conclusion, by using NVF and NVA we showed that highly reactive primary amines were available in IPNs as polyion complexes, and were able to control the polymer density and the amount of polycations.

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Appendix. Supporting information

The supplementary material associated with this article can be found in the on-line version at doi:10.1016/j.polymer.2009.06.016.

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