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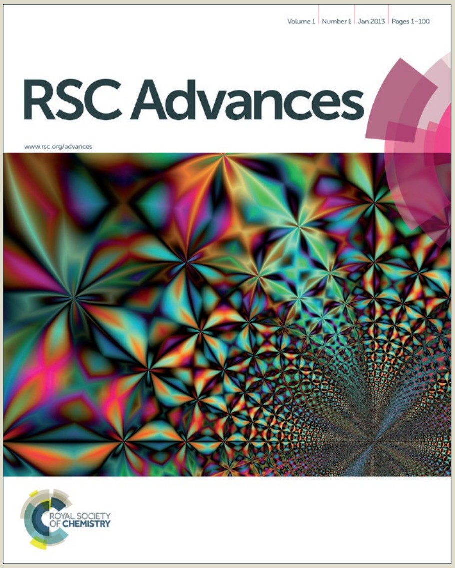

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Paper

Fabrication of rapidly-responsive switches based on coupling effect of polyacrylamide and poly(acrylic acid) without IPN structure

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Huan-Huan Du and Xin-Cai Xiao*

Interpenetrating polymer networks (IPN) structure have been applied to stimuli-responsive drug delivery systems. However this structure may restrict stimuli-responsive speed. In this paper, this traditional IPN structure was not applied and a novel coupling system comprising of two different membranes immobilizing different polymers such as polyacrylamide (PAAM) and poly(acrylic acid) (PAAC) was studied for the first. The formation and microstructures of the immobilizing membranes were investigated systematically by XPS and SEM. The thermoresponsive characteristics of the coupling membranes system were investigated by tracking the diffusional permeability of NaCl at temperatures from below the upper critical solution temperature (UCST) to above the UCST. The results show that PAAM and PAAC were successfully immobilized onto the porous N6 membrane substrates, respectively. And the proposed system had a positive switch effect with higher responsive speed under the same condition. The dates provide valuable guidance for increasing thermoresponsive speed, the design and preparation of new thermoresponsive switch membranes system for different applications.

Introduction

Environmental stimuli-sensitive polymeric systems exhibit volume or phase transitions in response to slight environmental changes such as temperature [1-10], pH [2, 9, 11-14], glucose concentration [15-17], ethanol concentration [18], different ions and molecules [9, 19-25]. They have attracted a widespread interest in the last two decades due to their potential applications in numerous fields, including drug delivery, chemical separations, sensors, and catalysis. As there are many cases in which environmental temperature fluctuations occur naturally, and in which the environmental temperature stimuli can be easily designed and artificially controlled, thermosensitive hydrogels or microgels have been focused much attention.

An important aim is to improve thermoresponsive speed for thermosensitive system [26]. Because a slowly-responsive speed to temperature limits its applications in many fields such as "smart" actuators and on-off switches. Several strategies [27-31] to increase responsive dynamics have been explored.

It is well known that polyacrylamide (PAAM) and poly(acrylic acid) (PAAC) with interpenetrating polymer networks (IPN) structure can form polycomplexes in solution through hydrogen bonding [10, 26]. When the environmental temperature is lower than upper critical solution temperature (UCST) of PAAM/PAAC, the two polymer chains form so-called chain-chain zipper effect or intermolecular hydrogen bonds, which results to the IPN structure keeping shrinking state. On the other hand, when the environmental temperature is higher than the UCST, PAAC dissociates intermolecular hydrogen bonds with PAAM, and the IPN structure keeps swelling state for the relaxation of the two polymer chains. Consequently, when the temperature increases from below the UCST to above the UCST, the membrane pores change from "open" to "close" [10] while the state of the microspheres is from shrinking to swelling [26].

From shown as Reference 10 and 26, the responsive range to temperature based on the PAAM/PAAC with IPN structure is about 10 °C. However, this range displays that the thermoresponsive speed is relatively slow compared with the responsive range of poly(*N*-isopropylacrylamide), another thermoresponsive polymeric material, (about 4 °C) [27].

Our groups thought that this IPN structure might restrict the thermoresponsive speed while can increase mechanical strength. In this project, the traditional IPN structure was broken and the zipper effect of PAAC and PAAM was utilized. Firstly, the polymers PAAC and PAAM were immobilized on the surfaces of porous nylon 6 (N6) membranes, respectively. Then the two immobilizing membranes

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School of Pharmacy, South-Central University for Nationalities,Wuhan 430074, China. E-mail: xcxiao@mail.scuec.edu.cn. Fax: +86-27-6784-1196; Tel: +86-27-6784-1196.

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were closely contacted. We hoped that when the environmental temperature was lower than the UCST, PAAC chains formed intermolecular hydrogen bonds with PAAM chains. The entanglement between the two polymers made the coupling membranes system in a closed state. However, when the environmental temperature was higher than the UCST, the intermolecular hydrogen bonds between PAAM chains and PAAC chains were disrupted and the coupling effect between two polymers no longer existed, which made the proposed system in an opened state. A schematic illustration of the proposed positively thermoresponsive switch membranes is shown as Figure 1. The object of this project was to obtain some guidance for higher thermoresponsive speed and to design and prepare thermoresponsive delivery system with desired response temperatures for different applications. To our knowledge, this is the first report to break the traditional IPN structure and study their coupling effect.

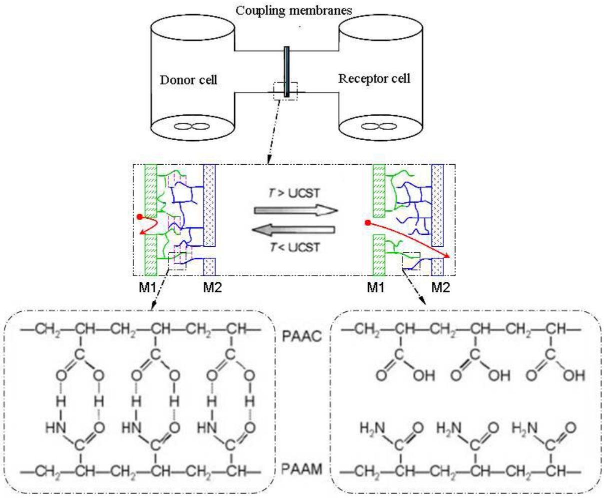

Fig.1 Schematic illustration of the concept of the proposed positively thermoresponsive switch membranes.

Experimental

Materials

Porous N6 membranes were used as the flat membranes substrates. The N6 substrates, with pore size of 0.22*μm*, were supplied by Xidoumen Membrane Co. Ltd., China. The acrylamide (AAM), acrylic acid (AAC), sodium hydroxide (NaOH), formic acid and ammonium cerium (Ⅳ) nitrate ($(NH_4)_2Ce(NO_3)_6$), as a initiator, were provided by Sinopharm Chemical Reagent Co., Ltd., China. The AAM was used after purification by recrystallization in hexane and acetone and then dried in vacuo at room temperature. The AAC was used after vacuum distillation. The *N,N'*-methylene bisacrylamide (BIS), as a cross-linker, was supplied by Changsha Oumay Biotech Co., Ltd., China. The sulfuric acid (H_2SO_4) was supplied by Kaifeng Dongda Chemical Co., Ltd., China. Other reagents were all analytical grade and used without further purification. The water used in the experiment was ultrapure water, and its resistance was 18MΩ.

Preparation of polyacrylamide (PAAM) solution or poly(acrylic acid) (PAAC) solution

To testify the relation of mixing PAAM solution and PAAC solution, PAAM solution and PAAC solution were obtained respectively. The PAAM solution was synthesized as follows: 1 g of AAM was dissolved in 20 mL of ultrapure water. And 100 mg of APS was dissolved in 5 mL of water. Nitrogen was bubbled into the two solutions to remove oxygen for 30 min. The AAM and APS solutions were then mixed. The mixture was poured immediately into 190 mL of water at 70 °C under stirred at a rate of 1000 rpm. The polymerization was carried out at 70°C for 24 h.

Preparation of the PAAC solution was the same procure of PAAM solution except only changing from 1 g of AAm to 1 mL of AAC.

The optical relation between PAAM solution and PAAC solution

A series of mixing samples including different volume ratio of PAAM solution and PAAC solution were obtained. All samples were put in constant-temperature baths kept from 15 to 40 °C and stored at pointed temperature for 8h, then were taken photographs. Finally all photographs about one sample were put together with increasing temperature.

Preparation of immobilizing PAAM or PAAC membranes

In the present project, the immobilizing PAAM or PAAC membranes (N6-*i*-PAAM or PAAC) were prepared by applying the chemical copolymerization method. Firstly the N6 membranes were washed with 4% (*W/V*) of NaOH and dried to constant weight, and then the membranes were placed in 20% (*W/V*) of the formic acid solution for 2h, then they were placed in the mixed solution including AAM or AAC monomer, $(NH_4)_2Ce(NO_3)_6/H_2SO_4$ and BIS. The AAM and AAC monomer concentrations in solution were 1 and 0.2 *wt.*-%, respectively. The weight percentage ratio of BIS to the monomer was 5:100. The solution was stirred and the polymerization was carried out in a constant-temperature bath at 60 °C for 4h to obtain a immobilizing membrane. All sample membranes were immersed in ultrapure water at the room temperature for 24 h to remove any unreacted monomer and homopolymer, and then were dried in oven at 40 °C overnight. The immobilizing yield of the membrane was defined as the weight increase of the membrane after the immobilizing process and could be calculated according to the equation:

$$Y = (m_g - m_0) / m_0 \times 100\% \qquad (1)$$

where Y stands for the immobilizing yield [%] of PAAM/PAAC on the membrane substrate, and m_g and m_0 stand for the mass [g] of the membrane after and before immobilizing, respectively [32].

Characterization of membranes

X-ray photoelectron spectroscopy (XPS, XSAM800, Kratos, U.K.) was employed to study the composition of the membrane surface before and after immobilizing PAAM or PAAC. It was using a monochromatic Al Kα X-ray source (1486.6 eV photons). The core-level signals were obtained at the photoelectron take-off angle (α, with respect to the sample surface) of 90°.

Scanning electron microscopy (SEM, Hitachi S-450, Japan) was employed to study the microscopic configuration of the N6-*i*-PAAM or PAAC membranes. To observe the cross-sections, the sample membranes were put into liquid nitrogen for enough time, then cut with a slice, finally gilded.

Thermoresponsive diffusion experiments

The main aim of this project was to check the thermoresponsive speed different from that with the IPN structure and the switch effect of the coupling system. The NaCl was used as a model drug and the release experiments were carried out according to previously published method [32]. To measure the permeability through the flat membrane, all membranes were dialyzed against aqueous NaCl with a known concentration for more than 3 days. and all dialysises were carried out in constant-temperature bath kept from 15 to 40 °C. The permeability of the solute across the membrane(s) was measured by determining the increase in the solute concentration of the surrounding medium with time. During the measurements, the liquid's temperature was kept constant using a thermostatic unit. The concentration of NaCl was determined by measuring the electrical conductance with an electrical conductivity meter.

The diffusion coefficient of the solute across the flat membrane, D, could be calculated using the following equation, derived from Fick's first law of diffusion [32]:

$$D = - V\, L\, \ln[1-2(C_2)t / (C_1)0] / (2\, A\, t) \qquad (2)$$

where D is the diffusional coefficient [cm^2/s], $(C_1)_0$ and $(C_2)_t$ are the initial and intermediary concentrations (at time t) of the solute in the donor and receptor compartments, respectively [mol/L], V is the volume of the liquid in the donor compartment and that in the receptor compartment [cm^3], L is the thickness of the dry membrane [cm], and A is the effective diffusion area of the membrane [cm^2].

Results and discussion

Thermoresponse of the mixture including PAAM solution and PAAC solution

Figure 2 displays optical photographs of the mixture including different volume ratio of PAAM solution and PAAC solution at different temperature. From these photoes, the transmittance of all mixtures changed from turbid to clear with increasing temperature. Because when the environmental temperature was lower than UCST of PAAM/PAAC, the two polymer chains linked together by intermolecular hydrogen bonds, which resulted to scatter dramatically to light and the mixtures displayed turbid. On the other hand, when the environmental temperature was higher than the UCST, PAAC dissociates intermolecular hydrogen bonds with PAAM, and the two polymer chains relax, which made scatter weakly to light and the mixtures displayed clear. The results verified the mixtures solution including the two polymers chains had thermoresponse and two polymer chains formed intermolecular hydrogen bonds like that of IPN structure.

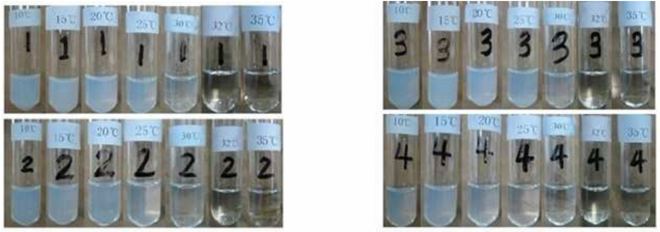

Fig.2 The optical photographs of the mixture including PAAM solution and PAAC solution at different temperature.

Immobilizing yields of the sample membranes

A series of the immobilizing PAAM or PAAC membranes were prepared by controlling the monomer concentration and the reaction time. To study effects of the immobilizing yield and the ratio of the immobilizing yield (R= Y_{PAAC}/Y_{PAAM}) of the coupling membranes on the thermoresponsive switch characteristics, two types of the coupling membranes with the same R were chosen and listed in Table1.

Table 1 The immobilizing yields and the ratio of the immobilizing yields (R) of the different type of the coupling membranes

Number of the coupling membranes	Y_{PAAC} [%]	Y_{PAAM} [%]	R [-]	The type of coupling membranes
a	-	-	-	Single virgin membrane
b	5.47		-	Single membrane
c		6.43	-	Single membrane
d	-	-	-	Double virgin membranes
e	5.47	6.43	0.85	*C-M*※
f	5.47	6.43	0.85	*M-C*※

※When the diffusional solute went across the immobilizing-PAAC membrane and then the immobilizing-PAAM membrane, this type of the coupling membranes was assigned as *C-M*, otherwise assigned as *M-C*.

The chemical characterization and morphological analysis of the N6-*i*-PAAM or PAAC membrane

Figure 3 shows the XPS O1s core-level spectra of the virgin N6 membrane, the immobilizing-PAAM membrane, and the immobilizing-PAAC membrane. For binding energy of the C=O species (531.2 eV), compared with the peak area between the virgin N6 membrane and the immobilizing-PAAM membrane (52844.6 and 57152.9, respectively), the differences of the peak area confirmed that the PAAM were successfully immobilized on the porous N6 membrane substrates. Compared with the binding energy for the C=O species and for the O-H species between the virgin N6 membrane and the immobilizing-PAAC membrane (531.0 eV and 532.2 eV, respectively), the results proved that the PAAC were successfully immobilized on the porous N6 membrane substrates.

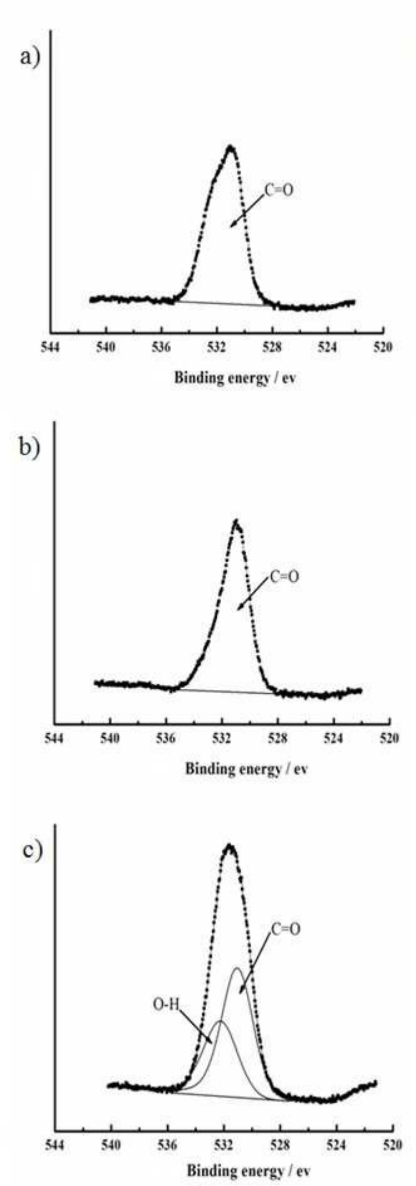

Fig.3 XPS O1s core-level spectra of a) the virgin N6 membrane, b) the immobilizing-PAAM membrane, and c) the immobilizing-PAAC membrane.

The SEM images of the cross section of the virgin porous N6 substrate, the immobilizing PAAM membrane and the immobilizing PAAC membrane are shown as Figure 4. Compared with the inner pore surfaces and thickness near the membranes surface of the virgin (Figure 4a), the immobilizing-PAAM membrane (Figure 4b), and the immobilizing-PAAC membrane (Figure 4c), the change of the microstructures indicated that PAAM and PAAC were successfully immobilized onto the porous N6 membrane substrates, respectively.

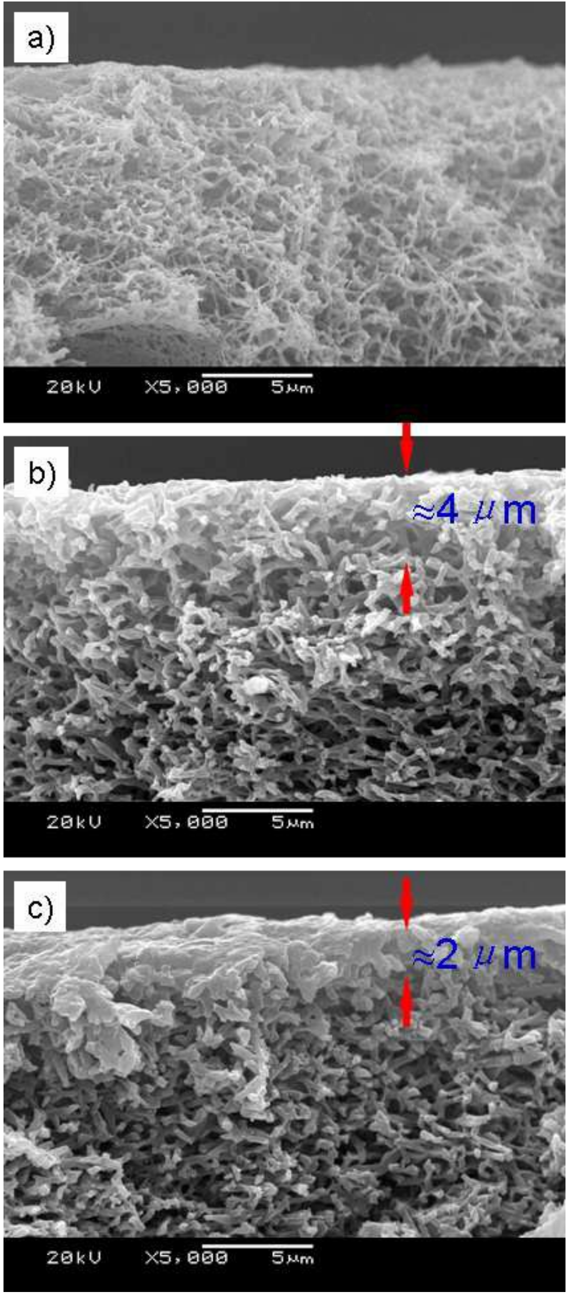

Fig.4 SEM micrographs of the cross sections of a) the virgin N6 membrane, b) the N6-*i*-PAAM membrane (Y_{PAAM}=6.43%), c) the N6-*i*-PAAC membrane (Y_{PAAC}=5.47%). Scale bar 5µm.

Thermoresponsive diffusional permeability of the coupling system

Figure 5a–f shows the diffusional dynamics of the modle drug permeating throngh the virgin N6 substrate membrane, the immobilizing-PAAM membrane, the immobilizing-PAAC membrane, two virgin N6 substrate membranes and the coupling membranes at different temperature. The diffusional coefficient of the drug permeating throngh the single substrate membrane (as shown in Figure 5a) increases simply with increasing the environmental temperature in the range of 15-40 °C. And the diffusional coefficient of the drug permeating throngh the immobilizing PAAM or PAAC membrane (as shown in Figure 5b, c) was also simple, which means that the singly-immobilizing membranes had no thermoresponsive characters. Because single PAAM or PAAC had no sensitivity to the temperature. The reason of the diffusional coefficient increasing was only because of thermal motion resulting from increasing temperature.

As shown in Figure 5d, the diffusional coefficient of the drug running across the two virgin membranes kept unchanged when the temperature increased from 15 to 40 °C, which displays that this system had no thermoresponsive characters. However, under the same experimental conditions, the diffusional coefficient of the drug running across the coupling membranes comprising of the immobilizing-PAAM membrane and the immobilizing-PAAC membrane appeared an interesting phenomenon. The diffusional coefficient changed dramatically at temperatures around the UCST (as shown in Figure 5e and f). These systems exhibited positively thermoresponsive characteristics, which meaned that the permeability of the coupling membranes increased with increasing the environmental temperature and was different from that the membrane system with IPN structure [10]. This phenomenon demonstrated that the switch effect existed. The effect made the membranes system in a closed state when the environmental temperature was lower than the UCST because PAAC chains formed intermolecular hydrogen bonds with PAAM chains. However the system displayed an opened state when the environmental temperature was higher than the UCST for intermolecular PAAM chains-PAAC chains hydrogen bonds being disrupted. The results testified again the two polymer existed coupling relation when the temperature was lower than the UCST.

It is also interesting that the thermoresponsive trend was obvious when the order of the immobilizing-PAAM membrane and the immobilizing-PAAC membrane was exchanged (as seen in Figure 5e and f). A sharp transition of the permeability occurred when the temperature increased from 25 to 30 °C under the drugs running across firstly the immobilizing-PAAC membrane and then the immobilizing-PAAM membrane (as seen in Figure 5e). While the transition range was from 20 to 35 °C under the drugs running across firstly immobilizing-PAAM membrane and then the immobilizing-PAAC membrane (as seen in Figure 5f). The reason may be that immobilizing PAAC and PAAM were all bulgy gels, and the dilatability of PAAC was larger than that of PAAM. The relative reason are still continuing. However this transition temperature range (5 °C) tested the responsive speed to temperature was higher than that system with the IPN structure under the same condition [10, 26], which means that our previous speculation was reasonable.

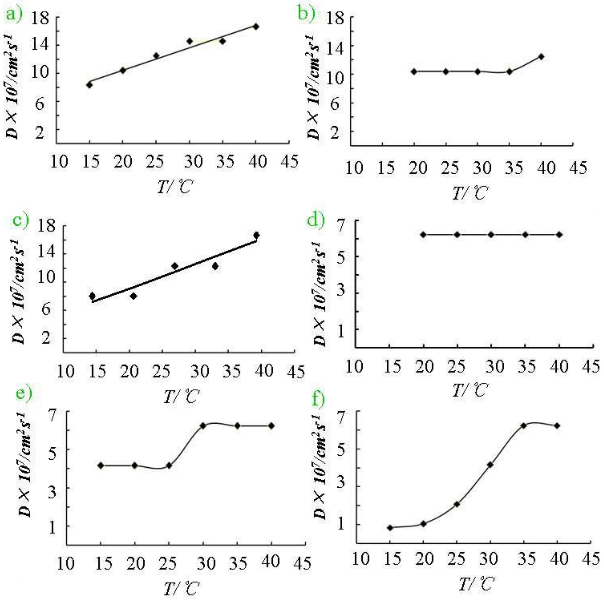

Fig.5 Effect of temperature on the permeation of NaCl through different membrane(s) with PAAC or PAAM switches. a) the Virgin N6 membrane. b) the N6-*i*-PAAC membrane (Y_{PAAC}=5.47%). c) the N6-*i*-PAAM membrane (Y_{PAAM}=6.43%). d) Two virgin N6 membranes. e) the *C-M* coupling membranes. f) the *M-C* coupling membranes (Y_{PAAC}=5.47% and Y_{PAAM}=6.43%).

Conclusions

In summary, a novel family of thermoresponsive switch membranes composing of a immobilizing-PAAM membrane and a immobilizing-PAAC membrane has been successfully developed. This system did not adopt the traditional IPN structure of PAAM and PAAC and applied their coupling effect resulting from intermolecular hydrogen bonds. The results show that PAAM and PAAC were successfully immobilized onto the porous membrane substrates, respectively, by XPS and SEM technology. The diffusional permeability of the coupling system exhibits significantly positive switch characteristics and higher thermoresponsive speed than that with IPN structure under the same condition. The coupling membranes provides a new mode of behavior for thermoresponsive “smart” or “intelligent” membrane actuators, which is highly attractive for targeting delivery systems, chemical separations, and sensors.

Acknowledgements

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