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Positively K^+-Responsive Membranes with Functional Gates Driven by Host–Guest Molecular Recognition

Zhuang Liu, Feng Luo, Xiao-Jie Ju, Rui Xie, Tao Luo, Yi-Meng Sun, and Liang-Yin Chu**

A novel positively K^+-responsive membrane with functional gates driven by host-guest molecular recognition is prepared by grafting poly(*N*-isopropylacrylamide-*co*-acryloylamidobenzo-15-crown-5) (poly(NIPAM-*co*-$AAB_{15}C_5$)) copolymer chains in the pores of porous nylon-6 membranes with a two-step method combining plasma-induced pore-filling grafting polymerization and chemical modification. Due to the cooperative interaction of host-guest complexation and phase transition of the poly(NIPAM-*co*-$AAB_{15}C_5$), the grafted gates in the membrane pores could spontaneously switch from "closed" state to "open" state by recognizing K^+ ions in the environment and vice versa; while other ions (e.g., Na^+, Ca^{2+} or Mg^{2+}) can not trigger such an ion-responsive switching function. The positively K^+-responsive gating action of the membrane is rapid, reversible, and reproducible. The proposed K^+-responsive gating membrane provide a new mode of behavior for ion-recognizable "smart" or "intelligent" membrane actuators, which is highly attractive for controlled release, chemical/biomedical separations, tissue engineering, sensors, etc.

1. Introduction

Smart membranes with porous substrates and stimuli-responsive gates, which could control or adjust their permeation properties by functional gates in response to external chemical and/or physical stimuli, are attracting increasing interest due to their potential applications in many fields, such as controlled release of substances, chemical separations, water treatment, tissue engineering, chemical sensing, and so on.[1–5] Ion-responsive membranes which can selectively respond to specific metal ions are of unique interests and importance among smart membranes,[6–18] because some metal ions such as potassium and sodium ions are very important for chemical signal transduction in biological systems whereas heavy metal ions show serious toxicity to human beings and other living organisms. Among physiologically important metal ions, potassium ions (K^+) is the most abundant intracellular metal ion and plays an important role in biological systems, which not only involves in the maintenance of extracellular osmolarity with sodium ion (Na^+) but also regulates the concentration of other ions such as calcium ion (Ca^{2+}) and chloride ion (Cl^-) in the living cell.[19] The intracellular K^+ concentration is about 30 times as high as that outside of the cell due to the active function of ion channels across the cell membrane.[20] A disorder of K^+ concentrations between intracellular and extracellular fluids is always associated with certain diseases, for example, serious cytoclasis or disabled K^+-Na^+ pump in the cell membrane would result in abnormal increase of extracellular K^+ concentration at some pathological sites in the body.[21] Therefore, strategies for specific recognition of potassium ion (K^+) attract particular attention, because such systems are highly attractive for various applications such as tissue engineering,[12,13] targeted drug delivery systems,[18,22] sensors and/or actuators,[23–27] and so on. The fabrication of K^+-responsive membranes is of both scientific and technological interest.

Up to now, almost all of the K^+-responsive gating membranes have featured negatively K^+-responsive characteristics, that is, the trans-membrane permeability decreases suddenly responding to the presence of K^+ ions in the environment, because all of the K^+-responsive functional gates in the gating membranes were constructed from poly(*N*-isopropylacrylamide-*co*-benzo-18-crown-6-acrylamide) (poly(NIPAM-*co*-$B_{18}C_6$Am)).[7–11,14,15,17] In these cases, the membrane pores change from an "open" to a "closed" state when K^+ ions appear in the environment, as a result of the K^+-responsive isothermal swelling conformational change of the poly(NIPAM-*co*-$B_{18}C_6$Am). In certain applications such as K^+-triggered controlled release, however, an inverse mode of the K^+-responsive gating behavior of the membranes is preferred. Unfortunately, positively K^+-responsive membranes with functional gates driven by host-guest molecular recognition have not been reported yet.

In this study, we report on a novel family of K^+-responsive gating membranes with positively K^+-responsive gating characteristics, that is, the "opening" of membrane pores is induced by the presence rather than the absence of K^+ ions in the environment. The proposed membrane is designed with functional gates composed of PNIPAM chains and 15-crown-5 units. Due to the cooperative interaction of host-guest complexation and phase transition of the grafted poly(*N*-isopropylacrylamide-*co*-acryloylamidobenzo-15-crown-5) (poly(NIPAM-*co*-$AAB_{15}C_5$)),

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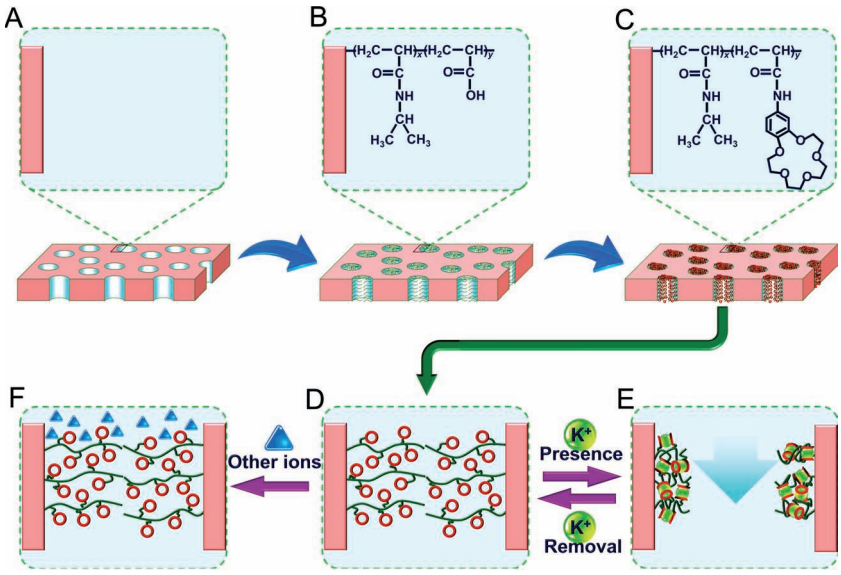

Figure 1. Schematic illustration of the preparation process (A–C) and the positively K^+-responsive property (D–F) of the proposed smart membrane with functional gates. The functional gates of the membrane are composed of grafted thermo-responsive PNIPAM chains acting as the actuators and pendent 15-crown-5 moieties acting as the sensors to recognize K^+. A) Porous nylon-6 membrane substrate. B) Poly(NIPAM-*co*-AA) copolymers are grafted into the membrane pores as gates by a plasma-graft pore-filling polymerization method. C,D) Poly(NIPAM-*co*-$AAB_{15}C_5$) copolymeric gates are prepared by modifying the grafted poly(NIPAM-*co*-AA) copolymers with $AB_{15}C_5$. When K^+ ions appear in the environment, they can be recognized and captured by the 15-crown-5 receptors to form 2:1 "sandwich" complexes, as a result the grafted copolymer chains shrink and the membrane pores "open" (E). On the contrary, when the K^+ ions are removed from the crown ether receptors, the grafted polymer chains swell and "close" the membrane pores (D). However, other ions (e.g. Na^+, Ca^{2+} or Mg^{2+}) can not trigger such responsive switching function of the membrane pores (F).

the synthetic gates in the membrane pores spontaneously switch from a "closed" to an "open" state by recognizing K^+ ions in the environment, and the positively K^+-responsive gating action of the membrane is rapid, reversible and reproducible.

2. Results and Discussion

2.1. Fabrication Strategy

The concept of the proposed positively K^+-responsive gating membrane with functional gates and the fabrication procedure are schematically illustrated in **Figure 1**. The functional gates of the membrane are constructed from poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers, in which the pendent 15-crown-5 units act as host receptors for sensing K^+ ions and the PNIPAM units act as actuators. PNIPAM is an excellent thermo-responsive polymer, which exhibits a dramatic swelling/shrinking conformational change when environmental temperature is changed across its lower critical solution temperature (LCST) around 32 °C. The crown ether 15-crown-5, a well-known host molecule, could selectively recognize K^+ to form stable 2:1 (ligand:ion) "sandwich" host-guest complexes.[28,29] It has been discovered recently that the LCST of the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer shifts to a lower value when the 15-crown-5 units selectively capture K^+.[18,22,30] When the operation temperature is selected between the two LCST values before and after the crown ether receptors capture K^+ ions, the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers have a K^+-responsive volume phase transition characteristic that is on the reverse of that of poly(NIPAM-*co*-$B_{18}C_6Am$), that is, the copolymer shrinking is induced by the presence of K^+ rather than the absence of K^+ in the environment.[18,22,30] Once K^+ ions are added to the environmental solution, the 15-crown-5 receptors from adjacent poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer chains capture the K^+ ions and form stable 2:1 "sandwich" complexes, which disrupt the hydrogen bonding between the oxygen atoms in the crown ether and the hydrogen atoms of water and cause the copolymer chains to contract. As a result, the hydrophobicity of the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer is enhanced at the operation temperature, and thus the LCST for phase transition shifts negatively to a lower value. Consequently, the copolymer changes its physical state abruptly and reversibly from swollen state to shrunken state responding to the presence of K^+ when the environmental temperature is maintained between above-mentioned two LCST values.[18,22,30] Therefore, the proposed membrane gates shrink in response to K^+-recognition as a result of the host-guest complex formation. As a result, the membrane pores change from "closed" gates to "open" gates when the K^+ ions present in the environment. The "closed/open" switching function of the membrane gates is reversible and selectively responsive to K^+ ions, that is, the grafted copolymers swell again and the membrane pores turn back to a "closed" state after removal of K^+, while other ions can not trigger the pores "opening" action.

In this study, the proposed positively K^+-responsive membranes are fabricated in a two-step process, in which the linear poly(*N*-isopropylacrylamide-*co*-acrylic acid) (poly(NIPAM-*co*-AA)) copolymers are grafted in the membrane pores and then the 15-crown-5 units are synthesized onto the grafted copolymers subsequently. In the first step, linear poly(NIPAM-*co*-AA) copolymers are grafted into the membrane pores as gates by a plasma-graft pore-filling polymerization method[7–15,17,31–37] with porous nylon-6 membranes as substrates and both *N*-isopropylacrylamide (NIPAM) and acrylic acid (AA) as co-monomers. In the second step, the grafted poly(NIPAM-*co*-AA) copolymers are modified with 4′-aminobenzo-15-crown-5 ($AB_{15}C_5$) by using 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (EDC) as a dehydration catalyst, and finally poly(*N*-isopropylacrylamide-*co*-acryloylamidobenzo-15-crown-5) (poly(NIPAM-*co*-$AAB_{15}C_5$)) copolymer gates with both PNIPAM and 15-crown-5 units are formed in the membrane pores (see the Experimental Section for experimental details). Scanning electron microscopy (SEM) is used to ascertain the microstructures of membranes and Fourier transform infrared spectrometry (FT-IR) is

employed to chemically confirm the fabrication of the functional gates. K^+, Na^+, Ca^{2+} and Mg^{2+} ions, which are very important for chemical signal transduction in biological systems, are chosen as the test environmental metal ions. K^+-responsive characteristics of both linear poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers and the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) gates in the membrane pores are experimentally studied systematically. Pressure-driven filtration experiments are carried out to determine the "closed/open" switching performance of membranes with poly(NIPAM-*co*-$AAB_{15}C_5$) gates.

2.2. Ion-Responsive Characteristics of the Linear Poly(NIPAM-*co*-$AAB_{15}C_5$) Copolymer

In order to confirm the ion-recognizable characteristics of the linear poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers fabricated by the above-mentioned two-step method and the optimum operation conditions for the proposed gating membrane, a series of linear poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers with different contents of crown ether units are prepared and tested. The conversion of poly(NIPAM-*co*-AA) copolymers to poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers is confirmed using ^{1}H nuclear magnetic resonance spectrometry (^{1}H-NMR) via comparing the molar ratio of AA to NIPAM with that of $AAB_{15}C_5$ to NIPAM. The conversion rate could almost achieve 100% according to the results of ^{1}H-NMR spectra. For example, the molar ratio of AA to NIPAM in the poly(NIPAM-*co*-AA) copolymers is 15.92% (Figure S1, see Supporting Information), and the followed molar ratio of $AAB_{15}C_5$ to NIPAM is 15.84% (Figure S2, see Supporting Information). The temperature-dependent transmittance changes of poly(NIPAM-*co*-AA15.92%) and poly(NIPAM-*co*-$AAB_{15}C_5$15.84%) linear copolymer solutions containing different metal ions are shown in **Figure 2**A,B respectively. For poly(NIPAM-*co*-AA15.92%) copolymers without ion-recognizable units, the phase transition behaviors of the copolymers in various metal ion solutions are almost the same as that in pure water (Figure 2A). However, with introducing crown ether 15-crown-5 units in the copolymers, the LCST of poly(NIPAM-*co*-$AAB_{15}C_5$15.84%) copolymers exhibits obvious negative shift in 0.1 M K^+ solution compared with that in other solutions (Figure 2B). Such distinct change of the phase transition temperature is resulted from the formation of stable 2:1 "sandwich" host-guest complexes of 15-crown-5 with K^+. With increasing K^+ concentration from 0.005 M to 0.2 M, the negative shift degree of LCST is increased (Figure 2C,D).

The K^+-triggered phase transition behaviors of prepared poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers with different contents of crown ether units are studied systematically (**Figure 3**). The

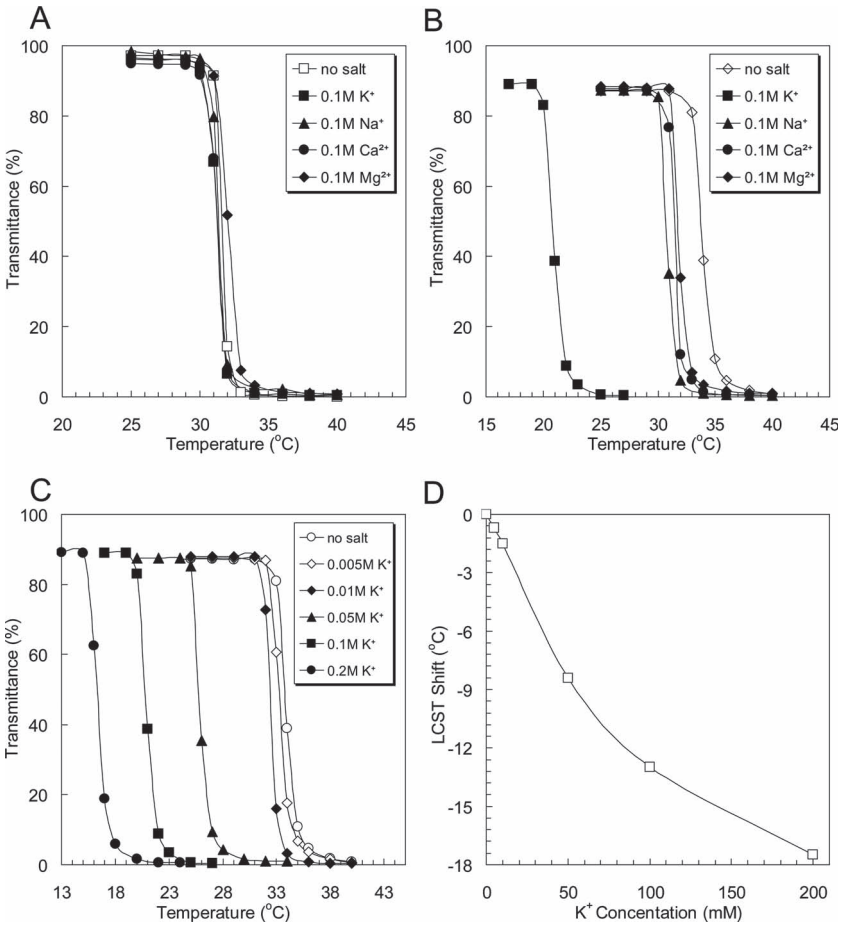

Figure 2. The LCST shift for phase transition of poly(NIPAM-*co*-AA15.92%) and poly(NIPAM-*co*-$AAB_{15}C_5$15.84%) linear copolymers solutions containing different metal ions. A) Phase transition behaviors of poly(NIPAM-*co*-AA15.92%) copolymer. B) Phase transition behaviors of poly(NIPAM-*co*-$AAB_{15}C_5$15.84%) copolymer. Phase transition behaviors (C) and LCST shift (D) of poly(NIPAM-*co*-$AAB_{15}C_5$15.84%) copolymer in response to K^+ with different concentrations.

molar ratios of $AAB_{15}C_5$ to NIPAM in the copolymers are confirmed by ^{1}H-NMR analyses (Figure S2–S4, see Supporting Information). The LCST shift in response to K^+ is remarkably enhanced with increasing the content of crown ether units in poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers while setting the K^+ concentration at 0.1 M, which is closed to the intracellular K^+ concentration.[19,20] The LCST values of the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers with different contents of 15-crown-5 units in pure water are about 34 °C; however, when the surrounding pure water is replaced by 0.1 M K^+ solution, the LCST values of the poly(NIPAM-*co*-$AAB_{15}C_5$15.84%), poly(NIPAM-*co*-$AAB_{15}C_5$13.26%) and poly(NIPAM-*co*-$AAB_{15}C_5$6.66%) copolymers negatively shifts to about 21 °C, 25 °C and 28 °C, respectively (Figure 3A). The more the amount of crown ether units in poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers, the more the K^+ ions could be captured to form more complexes; as a result the more the LCST shift of the copolymers (Figure 3B). The above results suggest that when the environmental solution is changed from pure water to 0.1 M K^+ solution, the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers with the content of 15-crown-5 units about 15.84%

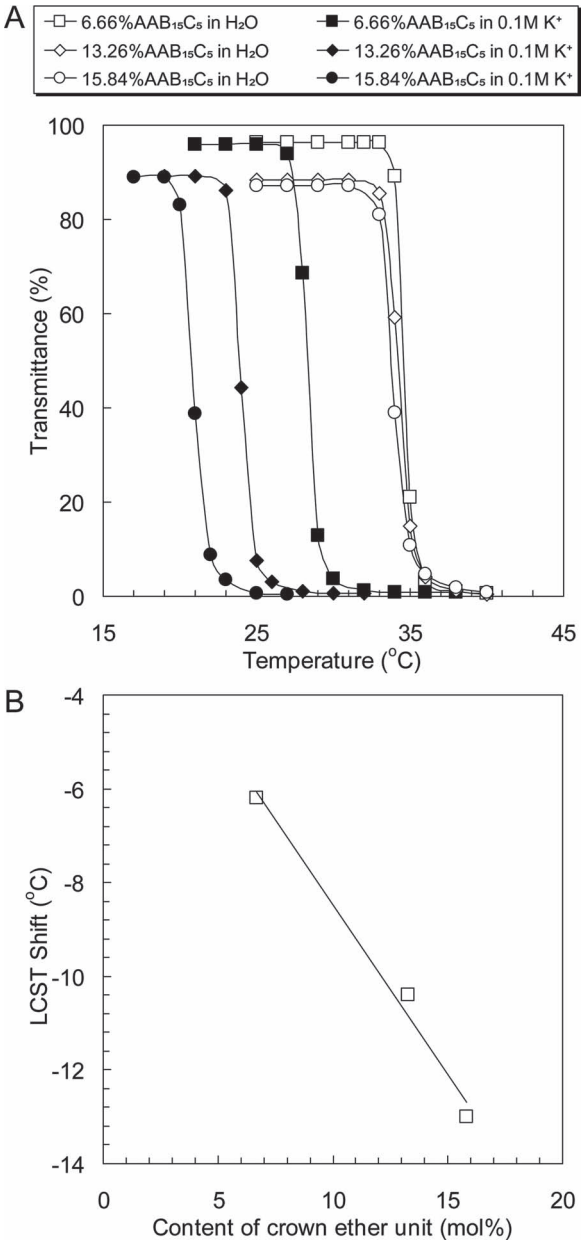

Figure 3. Phase transition behaviors of the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers with different contents of crown ether units in pure water and 0.1 M K^+ solution (A) and effect of the content of crown ether units on the LCST shift of the poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers in 0.1 M K^+ solution (B).

could exhibit a satisfactory isothermal swelling/shrinking conformational change at room temperature (about 25 °C).

2.3. Morphological and Compositional Analyses of the Grafted Membranes

In the first step of fabrication of the proposed gating membrane, the grafting yield Y_{PNAA} (wt%) of the poly(NIPAM-*co*-AA) copolymers on the membrane is estimated as the mass

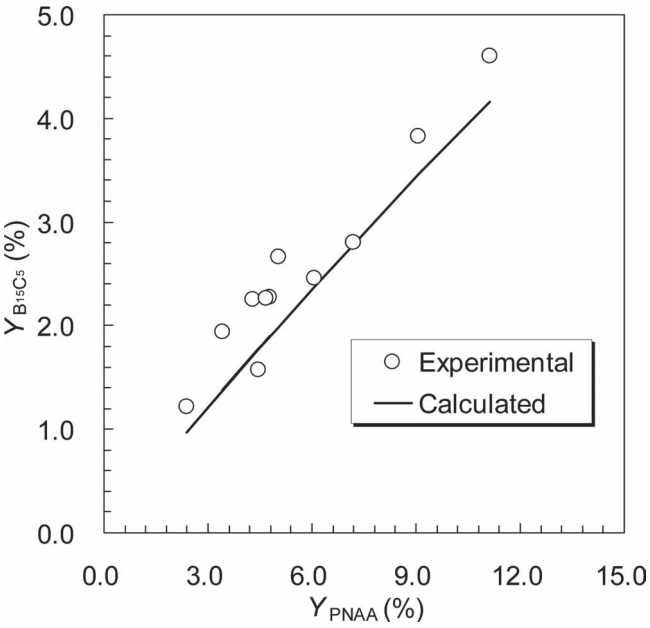

Figure 4. The relationship between the grafting yields Y_{PNAA} and Y_{B15C5} in the preparation of poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane, in which the solid line is calculated from Equation (3) and the circle dots are experimental data.

increase ratio of the membrane after grafting poly(NIPAM-*co*-AA) according to the following equation:

$$Y_{PNAA} = \frac{M_{mem(PNAA)} - M_{sub}}{M_{sub}} \times 100\% \quad (1)$$

where, M_{sub} and $M_{mem(PNAA)}$ are the masses of the membrane substrate and the poly(NIPAM-*co*-AA)-grafted membrane, respectively.

In the second step of chemical modification, the poly(NIPAM-*co*-AA) copolymers are converted to poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers. The grafting yield Y_{B15C5} (wt%) of crown ether units is estimated as the mass increase ratio of the membranes after introducing $AB_{15}C_5$:

$$Y_{B_{15}C_5} = \frac{M_{mem(PNB_{15}C_5)} - M_{mem(PNAA)}}{M_{mem(PNAA)}} \times 100\% \quad (2)$$

where, $M_{mem(PNAA)}$ and $M_{mem(PNB15C5)}$ are the masses of the poly(NIPAM-*co*-AA)-grafted membrane and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane, respectively.

There exists a relationship between Y_{PNAA} and Y_{B15C5}, which can be expressed by the following equation:

$$Y_{B_{15}C_5} = \frac{M_{AB_{15}C_5} - M_{H_2O} \times N_{(AA/NIPAM)} \times C_R}{M_{AA} \times N_{(AA/NIPAM)} + M_{NIPAM}} \times \frac{Y_{PNAA}}{1 + Y_{PNAA}} \quad (3)$$

where, M_{AB15C5}, M_{H2O}, M_{AA} and M_{NIPAM} stand for the molecular weight (g mol^{-1}) of $AB_{15}C_5$, H_2O, AA and NIPAM, respectively; $N_{(AA/NIPAM)}$ is the molar ratio of AA to NIPAM, which is supposed the same as the feed ratio of 20%; and C_R is the conversion ratio of AA units to crown ether units, which is supposed as 100%. **Figure 4** illustrates the relationship between grafting

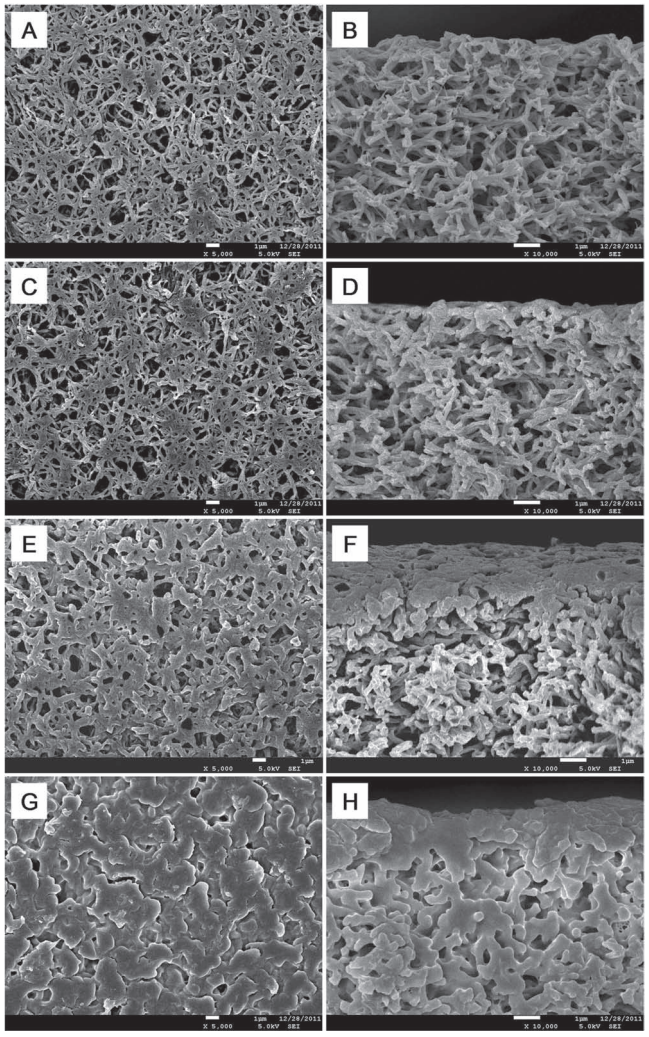

Figure 5. SEM images of surfaces (A,C,E,G) and cross sections (B,D,F,H) of ungrafted nylon-6 membrane substrate (A,B) and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted nylon-6 membranes with grafting yields of Y_{PNAA} = 2.39%/Y_{B15C5} = 1.22% (C, D), Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% (E, F) and Y_{PNAA} = 7.18%/Y_{B15C5} = 2.80% (G, H). Scale bars are 1 μm.

yields Y_{PNAA} and Y_{B15C5} in the preparation of poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane, in which the solid line is calculated from Equation (3). Obviously, the experimental data fit in well with the calculated data, which indicates that the result of grafted copolymers is close to our design.

Figure 5 shows SEM images of the surfaces and cross sections of the ungrafted nylon-6 membrane substrate and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes with different grafting yields. The ungrafted nylon-6 membrane substrate is constructed with a thin functional porous top layer (Figure 5A), and honeycombed pores can be clearly seen in the membrane (Figure 5B). After grafting, it can be seen that the surface pores of the grafted membrane are smaller compared with those of the ungrafted membrane. And, the more the copolymers are grafted, the smaller the pores size (Figure 5A,C,E,F). From the cross-sectional SEM images (Figure 5B,D,F,H), it can be clearly seen that the grafted copolymers are formed inside the pores throughout the entire membrane thickness. The above results confirm that, the functional copolymers can be grafted onto both the outer surfaces of the membrane and the inner surfaces of the membrane pores by using the two-step fabrication method in this study.

Figure 6 shows FT-IR spectra of the ungrafted nylon-6 membrane substrate, poly(NIPAM-*co*-AA)-grafted membrane with Y_{PNAA} of 7.18%, and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes with different grafting yields. From comparative analyses of the FT-IR spectra, the successful fabrications of poly(NIPAM-*co*-AA)-grafted membrane and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes are confirmed. Specifically, the characteristic double peaks at 1388 and 1366 cm^{-1} for isopropyl group of NIPAM and a band at 1713 cm^{-1} for carboxylic group of AA all appear in the FT-IR spectrum of poly(NIPAM-*co*-AA) grafted membrane (Curve B). For poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes, the characteristic band of carboxylic group at 1713 cm^{-1} disappears after the EDC modification, which indicates that almost all AA units are converted to $AAB_{15}C_5$ units (Curve C–E). In addition, the characteristic bands of benzo-15-crown-5

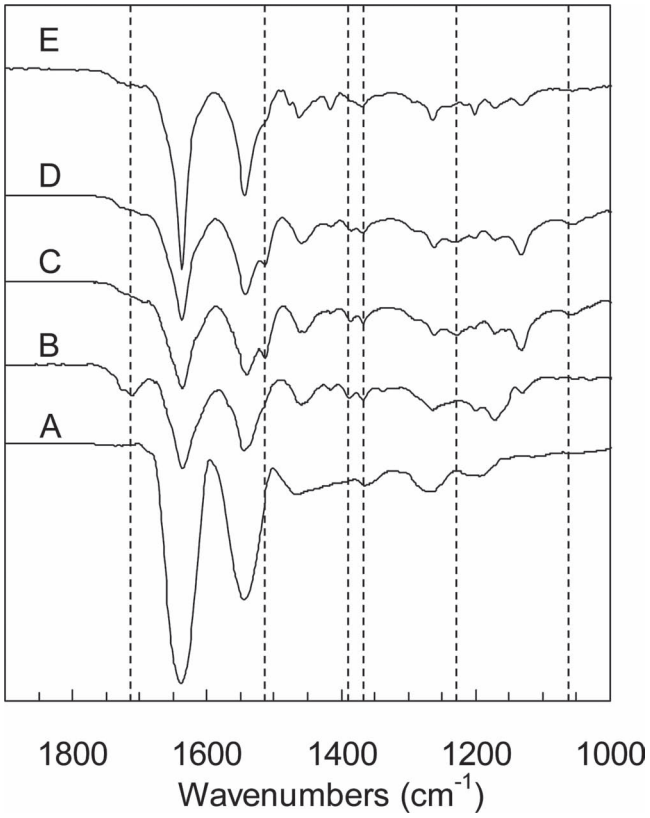

Figure 6. FT-IR spectra of ungrafted nylon-6 substrate membrane (Curve A), poly(NIPAM-*co*-AA)-grafted nylon-6 membrane with grafting yield of Y_{PNAA} = 7.18% (Curve B), and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted nylon-6 membranes with grafting yields of Y_{PNAA} = 7.18%/Y_{B15C5} = 2.80% (Curve C), Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% (Curve D) and Y_{PNAA} = 2.39%/Y_{B15C5} = 1.22% (Curve E).

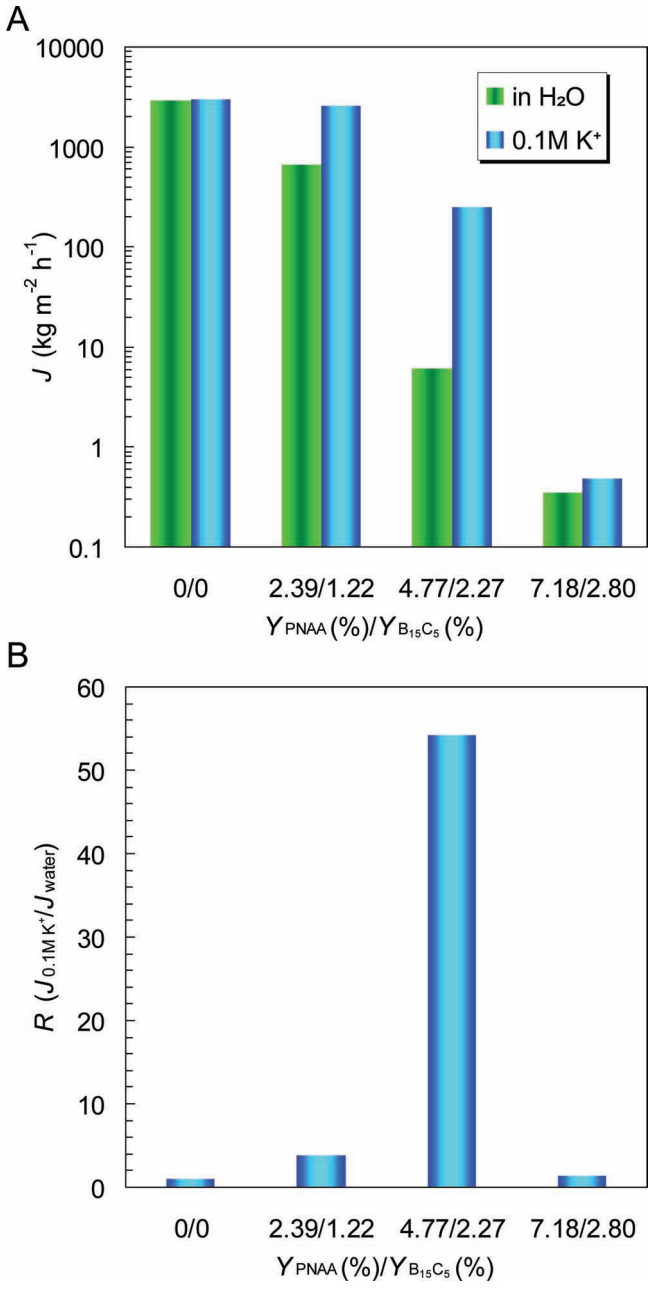

Figure 7. Effect of grafting yield on the solution flux through poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes in pure water and 0.1 M K^+ solution (A) and the K^+-triggered gating coefficient (R) of the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes (B).

group, including a strong peak at 1516 cm^{-1} (shoulder peak) for C=C skeletal stretching vibration in the phenyl ring, a peak at 1228 cm^{-1} for C–O asymmetric stretching vibration in Ar–O–R, and a peak at 1055 cm^{-1} for C–O symmetric stretching vibration in Ar–O–R, are all found in the FT-IR spectra of poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes. Furthermore, the peak intensity of the crown ether groups at 1516 cm^{-1} (shoulder peak) is increased with increasing the grafting yield of crown ether units.

2.4. Positively K^+-Responsive Gating Characteristics of Membranes with Grafted Poly(NIPAM-*co*-$AAB_{15}C_5$) Gates

Figure 7 shows the K^+-responsive switching effect of poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes with different grafting yields, in which the K^+-triggered gating coefficient (R) is defined as follows:

$$R = \frac{J_{0.1\text{M K}^+}}{J_{\text{water}}} \tag{4}$$

where, $J_{0.1\text{M K}^+}$ and J_{water} are the measured solution fluxes at 25 °C in 0.1 M K^+ solution and in pure water, respectively. With increasing the grafting yield, the solution fluxes reduce in both 0.1 M K^+ solution and pure water at 25 °C (Figure 7A). The larger the grafting yield is, the larger the density and length of the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer chains. As a result, the solution flux across the grafted membrane decreases with increasing the grafting yield. When the grafting yields are Y_{PNAA} = 7.18%/Y_{B15C5} = 2.80%, the solution fluxes across the grafted membranes become very small in both 0.1 M K^+ solution and pure water. As expected, the solution flux of the gating membrane in 0.1 M K^+ solution is obviously larger than that in pure water due to the K^+-triggered "opening" of the membrane pores. When the grafting yields are Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27%, the K^+-triggered gating coefficient (R) is the largest in this study (as large as 54.2), which indicates that the grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% provide the optimal density and length of the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer chains for the gating effect (Figure 7B). So, this gating membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% is selected for subsequent investigations of K^+-responsive characteristics.

The dynamic changes in solution fluxes across the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% in pure water and aqueous solutions containing different metal ions at 25 °C are shown in **Figure 8**A. When pure water is used, the grafted copolymer chains swell and the membrane pores are "closed" at 25 °C, as a result that water flux is as low as 4.5 kg m^{-2} h^{-1}. In contrast, the presence of K^+ in the environment at 25 °C induces an isothermal shrinkage of the copolymer chains that causes the "opening" of membrane pores, and thus the flux suddenly increases to as large as 245.4 kg m^{-2} h^{-1}. As expected, Na^+, Ca^{2+} and Mg^{2+} ions nearly do not cause any obvious change of the solution flux across the membrane. The very slight differences between the flux in pure water and those in Na^+, Ca^{2+} and Mg^{2+} solutions are the results of the salting-out effects on the grafted copolymers.[38,39] Repeatability of K^+-responsive switching function is also investigated by repeatedly changing the environmental solution between pure water and 0.1 M K^+ solution. Once the environmental solution is changed from 0.1 M K^+ solution into pure water at 25 °C, the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers exhibit a rapid shrinking response behavior to "close" the pores; as the result, the flux decreases suddenly. The results show that, the fabricated membrane with grafted poly(NIPAM-*co*-$AAB_{15}C_5$) gates satisfactorily exhibits positively K^+-responsive characteristics. The response behavior, which is driven by host-guest molecular recognition, is reversible and reproducible.

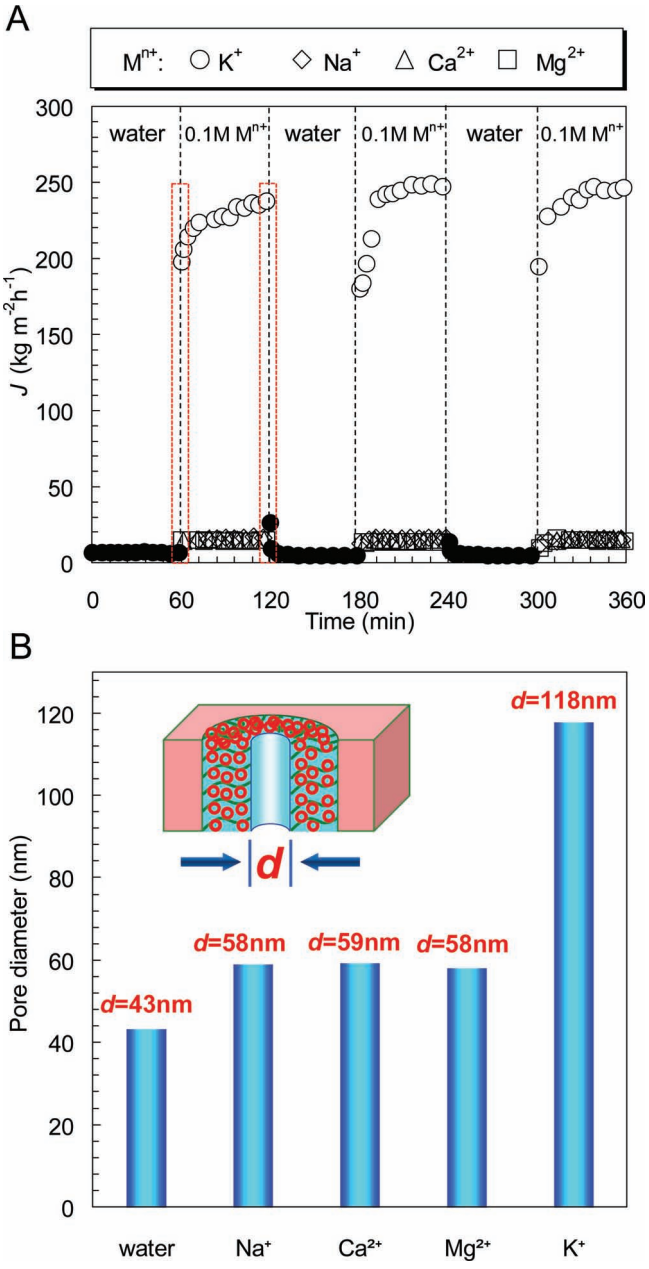

Figure 8. Isothermally dynamic change in solution flux though the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% in pure water and aqueous solutions containing different metal ions (A) and the change of estimated pore size of the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% in pure water and aqueous solutions containing different metal ions (B). The concentration of metal ion is 0.1 M. The details of the K^+-responsive flux changes in the dotted frames in Figure 8A nearby t = 60 min and t = 120 min are displayed in Figure 9.

The effective pore size of the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane can be estimated using the Hagen-Poiseuille's equation.[40] According to the Hagen-Poiseuille's equation, the water flux of a porous membrane can be expressed as:

$$J = \frac{n\pi d^4 P\rho}{128nl} \quad (5)$$

where, J stands for the water flux (kg m^{-2} s^{-1}); n for the number of pores per unit area (m^{-2}); d for the effective pore diameter (m); P for the trans-membrane pressure (Pa); ρ for the density of the solution (kg m^{-3}); η for the viscosity of flowing liquid (Pa s); and l for the membrane thickness (m). From Equation (5), the effective mean pore diameter of porous membrane can be expressed as:

$$d = \sqrt[4]{\frac{128nlJ}{n\pi P\rho}} \quad (6)$$

Figure 8B shows the change of estimated pore size of the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yield of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% in pure water and aqueous solutions containing different metal ions. The pore size of the membrane substrate is *ca.* 220 nm. After grafted with the copolymers, the pore size of the membrane reduces to 43 nm in pure water at 25 °C as a result of the blocking effect of the swollen copolymer chains. Just as expected, the effective pore size of the membrane in 0.1 M K^+ solution increases to 118 nm due to the shrinkage of the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers. The pore sizes of the membrane in 0.1 M Na^+, Ca^{2+} or Mg^{2+} solutions increase slightly to about 58 nm, because the above-mentioned salting-out effects[38,39] cause very slight shrinkage of the grafted copolymers. The results show that the fabricated membrane gates have reversible and specifically K^+-responsive "open/closed" switching function.

Figure 9 shows the rapid change of solution flux across the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with the grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% when the environmental solution is changed from pure water to 0.1 M K^+ solution (nearby t = 60 min in Figure 8A) and reversely changed from 0.1 M K^+ solution to pure water (nearby t = 120 min in Figure 8A). The solution flux increases immediately within 60 s when the pure water is replaced with 0.1 M K^+ solution at 25 °C (Figure 9A). That is to say, the response time is very short because the grafted poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers are linear chains with fast responsiveness. When the membrane is washed with pure water at 25 °C, the water flux decreases significantly and rapidly within 50 s (Figure 9B). This is attributed to the quick removal of the K^+ from crown ether units in the copolymer chains by washing the membrane with pure water under pressure of 0.06 MPa. The grafted poly(NIPAM-*co*-$AAB_{15}C_5$) linear chains swell rapidly in the membrane pores. The results show that the rapid and reversible K^+-responsive switching functions of the membrane gates are effectively achieved.

The fast and positively K^+-responsive function to control the flux across the membrane would bring a new mode for smart controlled release systems, which could self-regulatively release drugs in response to the presence of K^+ or abnormal increase of K^+ concentration. And, the function of membrane pore size change governed by the presence/absence of K^+ ions would bring novel materials for chemical/biomedical separations, tissue engineering and sensors that could respond to K^+ ion signals.

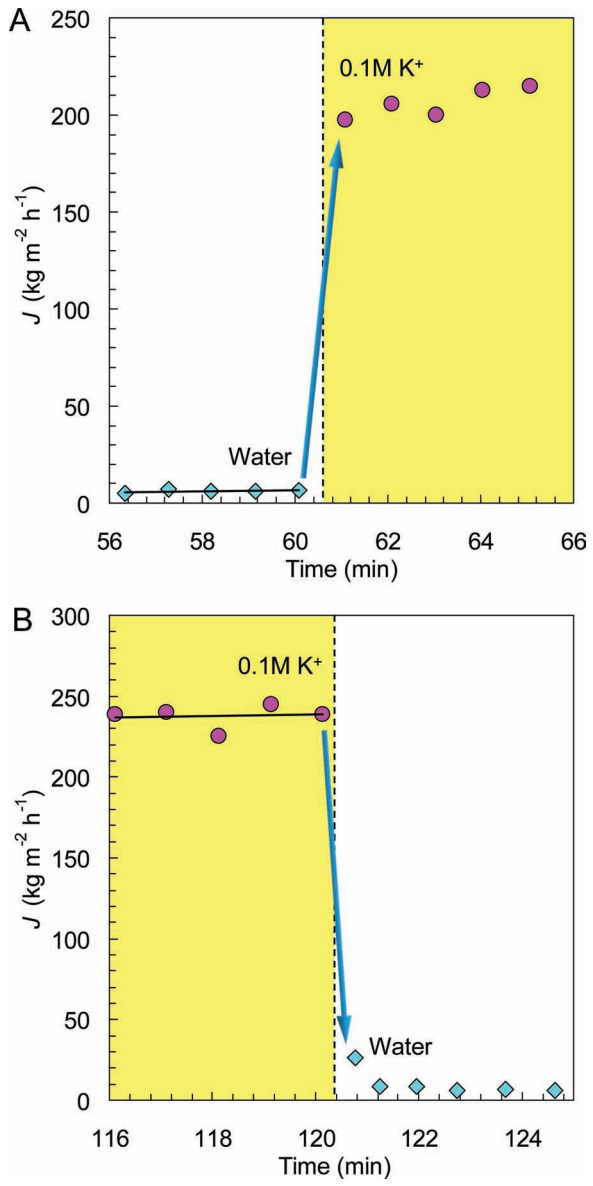

Figure 9. The rapid change of solution flux across the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% when the environmental solution is changed from pure water to 0.1 M K^+ solution (A) and reversely changed from 0.1 M K^+ solution to pure water (B).

3. Conclusions

In summary, a novel positively K^+-responsive membrane, which is composed of a porous membrane with linear grafted poly(NIPAM-*co*-$AAB_{15}C_5$) chains acting as ion-recognition functional gates, has been successfully developed. The prepared poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane could spontaneously control the solution flux across the membrane in response to the presence of K^+ as a result of the isothermal K^+-responsive shrinking transformation of the grafted copolymer chains occurred in the membrane pores, and the K^+-responsive characteristics are satisfactorily reproducible and rapid. The gating membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% exhibits the largest K^+-triggered switching effect in this study. This kind of smart membranes would be promising to serve as material candidates for drug delivery systems which could control the release of drugs in response to the presence of K^+ or abnormal increase of K^+ concentration, as well as material candidates for novel chemical/biomedical separation systems in response to K^+ ion signals. Furthermore, such smart gating membranes are also potential for artificial internal organs, sensors, early indicators of diseases related with abnormal K^+ concentration in vitro and/or in vivo.

4. Experimental Section

Materials: Porous nylon-6 membranes with an average pore size of 0.22 μm (supplied by Xidoumen Membrane Co. Ltd, China) were used as porous membrane substrates. *N*-isopropylacrylamide (NIPAM, purchased from Sigma-Aldrich) was purified by recrystallization with a hexane/acetone mixture. Acrylic acid (AA) was purchased from Chengdu Kelong Chemical Engineering Co., Ltd. 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride (EDC) was purchased from Sigma-Aldrich. 4′-aminobenzo-15-crown-5 ($AB_{15}C_5$) was synthesized from benzo-15-crown-5 ($B_{15}C_5$, purchased from Sigma-Aldrich) according to previously reported procedures.[30,41] 2,2′-Azobisisobutyronitrile (AIBN, purchased from Shanghai Reagent Fourth Factory) was recrystallized with ethanol and used as initiator. All other chemicals were of analytical grade and used as received. Pure water (18.2 MΩ at 25 °C) from a Milli-Q Plus water purification system (Millipore) was used throughout the experiments.

Synthesis of Linear Poly(NIPAM-co-AA) and Poly(NIPAM-co-$AAB_{15}C_5$) Copolymers: The linear poly(NIPAM-*co*-AA) copolymers with different AA contents were synthesized by free-radical copolymerization of NIPAM and AA monomers in tetrahydrofuran (THF) under N_2 atmosphere at 60 °C for 12 h. The concentration of total monomers (NIPAM and AA) was 0.1 mol L^{-1}. The feed molar ratios of AA to NIPAM were 10, 15 and 20%, and that of AIBN to total monomers (NIPAM and AA) was 1%. The poly(NIPAM-*co*-AA) copolymers were obtained and purified by precipitation with ethyl ether from THF for several times and then dried under vacuum at 40 °C for 12 h.

The linear poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers were synthesized by modifying poly(NIPAM-*co*-AA) copolymers with $AB_{15}C_5$ as follows: a mixture solution of poly(NIPAM-*co*-AA) copolymer (0.5 g) dispersion in anhydrous ethanol (20 mL) mixed with $AB_{15}C_5$ (0.2 g) and EDC (0.25 g) was stirred below 4 °C for 24 h under N_2 atmosphere. Then, the ethanol was removed by vacuum distillation, and then the residue was dispersed in THF again. The poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers were obtained by precipitation with ethyl ether from THF for several times and then dried under vacuum at 40 °C for 48 h..

The poly(NIPAM-*co*-AA) and poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers were characterized by ^{1}H-NMR (Bruker-400, Bruker Co., Germany) (Figures S1 to S6, see Supporting Information). The average molecular weights (M_w) of the poly(NIPAM-*co*-AA) copolymers were *ca.* 9000 ~ 9700 after methanol esterifiable treatment with methanol determined by Gel Permeation Chromatography (GPC, Waters 2410 refractive index detector) using THF as the mobile phase and polystyrene as the standard (Figures S7 to S9, see Supporting Information).

Characterization of Ion-Responsive Properties of Linear Poly(NIPAM-co-AA) and Poly(NIPAM-co-$AAB_{15}C_5$) Copolymers: The ion-responsive properties of linear poly(NIPAM-*co*-AA) and poly(NIPAM-*co*-$AAB_{15}C_5$) copolymers were evaluated by measuring their corresponding LCST values in aqueous solutions containing various metal ions with different concentrations. The LCST values of the copolymers were determined by measuring the transmittance of the aqueous polymer solutions at 500 nm as a function of temperature using a UV-visible spectrophotometer (Shimadzu, UV-1700, Japan) equipped with a temperature-controlled cell (Shimadzu, TCC-240A, Japan). The polymer concentration in the aqueous solutions was fixed at 0.5 wt%.

Preparation of Poly(NIPAM-co-$AAB_{15}C_5$)-Grafted Membranes: Preparation of poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes included two steps as shown in Figures 1A–C. In the first step, plasma-graft pore-filling

polymerization was employed to graft linear poly(NIPAM-*co*-AA) copolymer chains onto nylon-6 membrane substrates according to the method described previously.[7–15,17,31–37] Briefly, the membrane substrate was placed in a transparent glass tube, which was filled with argon gas and evacuated to a pressure of 10 Pa beforehand, and then was treated by plasma at 30 W for 60 s. After that, the membrane was dunked into the monomer solution of NIPAM and AA, and the grafting polymerization took place in a shaking constant-temperature bath at 30 °C for a predetermined time. The feed molar ratio of AA to NIPAM in the monomer solution was 20%, and the polymerization time varied from 4 to 24 h to get membranes with different grafting yields. The grafted membrane was rinsed in pure water under vibration in a constant-temperature bath (30 °C) for 24 h to remove any unreacted monomers and ungrafted polymers, and then was dried in an oven at 50 °C overnight.

In the second step, the grafted poly(NIPAM-*co*-AA) copolymers on the membranes were modified with $AB_{15}C_5$ by using EDC as a dehydration catalyst. Poly(NIPAM-*co*-$AAB_{15}C_5$) copolymer gates were then formed in the membrane pores. Briefly, the poly(NIPAM-*co*-AA)-grafted membrane was dipped in anhydrous ethanol (80 mL) overnight, and then $AB_{15}C_5$ (0.2 g) was added in below 4 °C under N_2 atmosphere. An anhydrous ethanol (20 mL) containing EDC (0.25 g) was dropwise added to the above-mentioned anhydrous ethanol solution containing membrane and $AB_{15}C_5$ within 30 min. Then, the reaction was occurred in a hermetical glass tube below 4 °C for 24 h. The modified membrane was rinsed in ethanol under vibration in a constant-temperature bath (30 °C) for 24 h to remove any unreacted reagents, and then was dried in an oven at 50 °C overnight.

Morphological and Compositional Analyses of Membranes: SEM (JSM-5900LV, JEOL, Japan) was employed to study the microscopic configuration of ungrafted and grafted membranes. Before observation, the membranes were put into liquid nitrogen for enough time and fractured mechanically. Surface and cross sectional structures of membranes were observed at an accelerating voltage of 5.0 kV. FT-IR spectra of the ungrafted and grafted membranes were measured on a spectrophotometer (IR Prestige-21, Shimadzu) to make sure that the crown groups were successfully introduced into the copolymer chains of the membranes.

Characterization of Ion-Responsive Permeation Across Membranes: The ion-responsive properties of the prepared poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes were estimated by hydraulic permeability of aqueous solutions containing various metal ions across the membranes. The hydraulic permeability coefficients of ungrafted and poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membranes with different grafting yields were determined by measuring the solution fluxes using a filtration apparatus under a constant trans-membrane pressure of 0.06 MPa. In the experiments, the operation temperature was controlled at 25 °C by a thermostatic unit, and the diameter of the effective membrane area for filtration was 40 mm. The solution fluxes across the poly(NIPAM-*co*-$AAB_{15}C_5$)-grafted membrane with grafting yields of Y_{PNAA} = 4.77%/Y_{B15C5} = 2.27% were measured by alternately changing the solutions from pure water to aqueous solutions with addition of 0.1 M KNO_3, 0.1 M $NaNO_3$, 0.1 M $Ca(NO_3)_2$, or 0.1 M $Mg(NO_3)_2$, respectively.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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