Stimuli-Responsive Membranes through Sustainable Aqueous Phase Separation

Joshua D. Willott, Wouter M. Nielen, and Wiebe M. de Vos

Membrane Surface Science (MSuS), Membrane Science and Technology cluster, Mesa+ Institute for Nanotechnology, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands

ABSTRACT: Polymeric membranes are used on huge scales for kidney dialysis, wastewater treatment, and drinking water production. However, almost all polymeric membranes are fabricated by a process reliant on the use of unsustainable, expensive, and reprotoxic dipolar aprotic solvents. In this work, we propose an aqueous phase separation approach for preparing porous membranes. Poly(4-vinylpyridine) (P4VP), a pH-responsive polymer, is first dissolved at low pH where the polymer is charged and subsequently cast as a thin film. Switching to a high pH where the polymer is uncharged and insoluble results in controlled phase separation and solidification of the polymer into porous membrane structures. This approach gives a large degree of control over membrane structure, leading to symmetric porous microfiltration membranes and asymmetric dense nanofiltration membranes. Moreover, the use of a pH-responsive polymer leads directly to a pH-responsive membrane, where the degree of responsive behavior can be tuned by the degree of cross-linking. Such responsive behavior allows effective cleaning of the membrane, without the use of harsh chemicals. This work outlines an approach toward preparing membranes in a more sustainable fashion—an approach that allows control over the membrane structure and one that naturally leads to advanced membranes with responsive properties.

KEYWORDS: aqueous phase separation, polyelectrolytes, membranes, stimuli-responsive, nanofiltration, non-solvent-induced phase separation

INTRODUCTION

Membrane technology received its great breakthrough in the early 1960s with the invention of non-solvent-induced phase separation (NIPS). NIPS made it possible to fabricate, in a continuous process, defect-free polymeric membranes with symmetric and asymmetric structures. Because of this breakthrough, membranes are now used on massive scales for the production of drinking water, in kidney dialysis, for the separation of chemicals for biomedical applications, for the separation of gases, and for the treatment of wastewater. Each year this amounts to tens of millions of square meters of membrane material and tens of billions of US dollars. But all this comes at a price. The NIPS process is heavily reliant on the use of dipolar aprotic organic solvents like N-methylpyrrolidone (NMP), N,N-dimethylacetamide (DMAC), and N,N-dimethylformamide (DMF). These solvents are expensive, flammable, and most significantly harmful to humans (reprotoxic) and the environment. Therefore, residual solvent must be removed from the membranes by post-treatment, and because of high costs and environmental legislation, the solvents must be recycled. REACH legislation first implemented by the European Union in 2008 imposes strict time and concentration (in air) limits for NMP, DMAC, and DMF. As of October 2017, the REACH committee agreed to further restrict the exposure limit for NMP with legislation coming into effect in 2020. It is highly likely that similar restrictions will be extended to include other aprotic solvents like DMAC and DMF. Finding alternatives to avoid the use of these solvents is key to the future development and success of the synthetic membrane industry.

In the traditional NIPS process, the aprotic solvent has two important properties: it acts as a good solvent for the chosen polymer(s), and it is strongly miscible with water (the typical
nonsolvent). When a thin film of the polymer casting solution is immersed in the nonsolvent water, solvent diffuses out of the film and mixes with the water, while the water diffuses into the film. The gradual change in solvent quality leads to a controlled precipitation of the polymer into a porous film. A major advantage of this approach is the control it gives over membrane structure, as the speed of the precipitation process and the rates of solvent and nonsolvent movement (kinetics) together with the type of demixing event (thermodynamics) that occur during phase separation govern the final membrane porosity and structure.\(^\text{3}\) In more recent years, some attention has been focused on the preparation of membranes without the use of dipolar aprotic solvents.\(^\text{10–11}\) Unfortunately, this has simply not led to a real alternative to NIPS—one that gives the same control over the membrane structure without requiring toxic solvents.

For certain responsive polymers, a transition from soluble to insoluble is possible in a completely aqueous environment, for example, by changes in pH or ionic strength for polyelectrolytes.\(^\text{12,13}\) Poly(4-vinylpyridine) (P4VP) is one such polymer. P4VP is a weak polyelectrolyte that consists of monomers with basic pyridine groups that have an effective p\(_K_a\) value of 4.5–5.0 when free in solution.\(^\text{14,15}\) Because of the basicity of the pyridine groups, the hydrophilicity of P4VP increases significantly upon lowering pH, which makes P4VP water-soluble under acidic conditions.\(^\text{16}\) For higher pH values, the polymer charge is neutralized and P4VP is insoluble in water. Salt concentration also affects the fraction of charged monomer residues and hence the aqueous solubility of the polymer. In this work we propose that the use of pH-responsive polymers such as P4VP could lead directly to an alternative to NIPS, where water is employed as both the solvent and nonsolvent for the polymer. We term this pH-induced phase separation process aqueous phase separation (APS) and will demonstrate that APS provides a clear route to produce membranes with a variety of structures without harmful aprotic organic solvents.

P4VP is already an often-studied polymer for membrane modification due to its desired responsive properties, typically by one of two approaches.\(^\text{17,18}\) In the first method, porous support membranes (prepared by NIPS) are coated with P4VP,\(^\text{19,20}\) while in the second approach, asymmetric isoporous membranes are fabricated via a NIPS-based process utilizing the self-organizing properties of P4VP-containing diblock copolymers, where P4VP forms the walls of the pores.\(^\text{21–23}\) Pore-filled P4VP membranes exhibit pH-responsive filtration properties, where the water flux decreases drastically below approximately pH 4, slightly lower than the effective p\(_K_a\) of P4VP in free solution. Here, at low pH, the pyridine groups are protonated, and the P4VP phase swells to fill the pore volume, thus reducing the effective pore volume of the membrane. Because of the pH-tunable charge density of the P4VP-coated membranes, charge-selective separation has also been reported for diblock copolymer membranes.\(^\text{21}\) Similarly, this responsive behavior can be used as an effective cleaning step, where a change in membrane surface properties allows easy detachment of fouling agents. This means that membrane cleaning can be achieved using much lower quantities of chemical cleaning agents.

In this work, the soluble-to-insoluble transition for P4VP that is present with varying pH (that also exists for many other weak polyelectrolytes) is exploited to prepare porous membranes in a water-based approach. The membranes consist entirely of P4VP and are made by using the aqueous phase separation (APS) approach in which water acts as both the solvent and the nonsolvent for the polymer. Membranes can be prepared with great control over their properties, and we study in detail the membrane properties of a microfiltration and a nanofiltration type membrane prepared in this way. The P4VP, which makes up the membranes, retains its pH- and salt-responsive properties, and variations in cross-link density can be used to control the extent of the responsive behavior. This work thus provides a clear approach for the preparation of membranes with advanced properties without the need for toxic solvents.

### RESULTS AND DISCUSSION

This section is divided into three main parts. First, the aqueous phase separation (APS) process used to prepare the P4VP membranes is presented and discussed together with covalent cross-linking steps used to improve the chemical and mechanical properties of the membranes. Second, the preparation, morphology, and performance of symmetric porous membranes are discussed. Third, the preparation of asymmetric membranes with dense top layers supported by porous support substrates is discussed along with some performance characteristics. We will show that the water-based APS process is well-suited to preparing membranes with a variety of structures and that it can offer a sustainable alternative to the solvent-based NIPS process.

**Membrane Fabrication by Aqueous Phase Separation.** Flat sheet P4VP membranes were prepared by the novel
aqueous phase separation process, in which a thin film of polymer solution at low pH is immersed in an alkaline coagulation bath. The APS process is shown schematically in Figure 1. P4VP is a weakly basic polyelectrolyte with an effective pK_a of 4.5−5.0,\textsuperscript{14,15} that dissolves in aqueous solutions at low pH due to protonation of the of the pyridinyl nitrogens within the repeating units. At high pH, the charge of P4VP is neutralized and the polyelectrolyte precipitates. This switch in polymer solubility as a function of pH can be exploited to prepare membranes. For the specific APS approach used in this work, a thin film of acidic P4VP solution is cast onto a nonwoven mesh supported by a glass plate and then immersed in an alkaline coagulation bath. After immersion, an immediate exchange takes place where the alkaline bath neutralizes the acidic casting solution and thus the charge of the polyelectrolyte. In the bath, the polyelectrolyte begins to precipitate, and at a given point the polyelectrolyte solidifies, forming the membrane matrix. The compositions of both the polymer casting solution and coagulation bath were fine-tuned to achieve the optimal membrane cross-section structures and homogeneity (uniformity across the membrane surface area). The polymer concentration, acid type, and amount as well as the pH of the coagulation bath were all varied systematically. The importance of these factors will be discussed in the following sections, and akin to the traditional NIPS process, the polymer concentration and phase separation time are important in governing the final structure of the P4VP membranes.

**Symmetric Membrane Preparation, Morphology, and Performance.** Before the most successful membranes were obtained (Figure 2), many parameters were explored. Polymer concentration was one factor studied in the preparation of the symmetric membranes. Polymer concentrations in the casting solution less than 17 wt % resulted in membranes that were inhomogeneous or patchy. Here the solution viscosity is too low, and the cast film breaks apart in the coagulation bath during precipitation. Polymer concentrations of 20, 22, and 25 wt % produced much more homogeneous membranes, and 20 wt % was found to produce the most consistent and reproducible membranes. Above 25 wt % of polymer, the casting step became difficult due to the high viscosities of the casting solutions.

Another factor investigated was the difference in pH between the casting solution and the coagulation bath. In principle, this pH difference drives the exchange of H^+/OH\textsuperscript{-} occurring within the cast polyelectrolyte film, which in turn leads to the precipitation of the polyelectrolyte. Therefore, this factor will determine the precipitation speed of the polymer and thus the structure of the resultant membrane. Varying the acidity of the casting solution by changing the amount of hydrochloric acid had little effect on overall membrane structure and homogeneity (for a given bath condition). However, the addition of acetic acid (a weak acid) to the casting solution, in combination with hydrochloric acid, substantially improved the cross-section structure and reproducibility of the membranes. It is believed that the buffering capacity of acetic acid assists in controlling the phase separation process. Acetic acid is a green solvent\textsuperscript{24} that can be produced in a sustainable fashion in biorefineries and that can be easily recovered from water streams.\textsuperscript{25} The final casting solution composition used to prepare the symmetric membranes is presented in the Experimental Methods section.

Varying the alkalinity of the coagulation bath had a much more noticeable impact on overall membrane cross-section structure and homogeneity. At bath pH values of 12.5 and 12.7 (NaOH concentrations of 0.032 and 0.05 M), the precipitation was slow (>15 min) and the membrane surface was inhomogeneous. The precipitation was faster (~3 min) at higher bath pH values—as expected, since the driving force for precipitation is greater at higher bath pH (for a given casting solution composition). However, at bath pH values of 13.3 and 13.5 (NaOH concentration of 0.2 and 0.316), the faster

---

**Figure 2.** Top panel: scanning electron microscopy images of the non-cross-linked P4VP symmetric membrane: (a, b) cross-section view at magnification of ×1000 and ×3000, respectively, and (c) top view at magnification of ×10000. Bottom panel on left: (d) zeta-potential measurements as a function of pH (5 mM KCl) for the non-cross-linked membrane (yellow ○) and the “low” (blue △) and “high” (red ◇) cross-link extent membranes. Symbols are the average and error bars the standard deviation of two distinct measurements. Bottom panel on right: pure water flux of (e) the non-cross-linked (yellow ○) membrane and (f) membranes cross-linked to varying extents: “low” (blue △), “medium” (green □), and “high” (red ◇) as a function of transmembrane pressure (TMP). All water flux measurements were performed from 0.5 bar of TMP progressively up to 4 bar of TMP. The dashed arrow in (e) and the solid symbols in (e, f) represent the pure water flux measured at 1 bar of TMP after 4 bar of TMP was reached. For all water flux data, the symbols are the average of three distinct measurements on separate membrane samples, and the error bars are the standard deviation of those measurements.
The non-cross-linked P4VP membrane has a pH-dependent linking, but the membrane charge would still increase as one linker molecule. This scenario would not result in cross-molecule reacted, which would result in grafting of the cross-linked P4VP membrane. For both the cross-link extent membrane, the surface charge is more positively charged quaternary pyridine groups are formed, leading to smaller pore sizes. The cross-linking reaction occurred between two pyridine groups in the P4VP membrane and is thus a quaternization reaction. Therefore, with every successful cross-link, two positively charged quaternary pyridine groups are formed, which is seen in Figure 2d through zeta-potential measurements performed on the membranes. Quaternary amines are known for their high chemical stability and are stable against oxidative cleaning agents such as hypochlorite. It is also possible that in some cases only one end of the cross-linking molecule reacted, which would result in grafting of the cross-linker molecules. This scenario would not result in cross-linking, but the membrane charge would still increase as one pyridine group would become quaternized. From Figure 2d, the non-cross-linked P4VP membrane has a pH-dependent zeta-potential—negative at high pH and increasingly more positive with decreasing pH. The non-cross-linked membrane dissolves at pH values <4.0 (below the effective pKₐ of P4VP) and is also solubilized by alcohols (ethanol and isopropanol) due to favorable hydrogen-bonding interactions. For the “low” cross-link extent membrane, the surface charge is more positive at higher pH values compared to the non-cross-linked membrane, suggesting quaternization of the pyridine groups. The “high” cross-link extent membrane has a positive zeta-potential (on average +50 mV) from pH 10 to pH 4, suggesting substantial quaternization and therefore significant cross-linking. For both the “low” and “high” cross-link extent membranes, at pH values <4.0, the pyridine residues that have not undergone cross-linking become charged (below the effective pKₐ of P4VP), and consequently the measured zeta-potential increases substantially (pH-responsive surface charge). Significantly, all of the cross-linked membranes no longer dissolve in acidic water and alcohols because the covalent cross-linking maintains the structural integrity of the membrane. Across the pH range studied, no visible swelling of any cross-linked membranes was observed. As will be shown in the next section, varying the degree of cross-linking is an important control parameter to tune the water permeance and magnitude of the responsive properties of the P4VP membranes.

Figures 2e and 2f present the pure water flux as a function of transmembrane pressure (TMP) for the non-cross-linked and cross-linked P4VP membranes, respectively. The non-cross-linked membrane experienced irreversible structural (pore) compaction as shown by the drastic decrease in flux with increasing applied pressure beyond 0.5 bar. Importantly, for all the chemically cross-linked membranes, pure water flux increases as a function of pressure. The flux increase is linear as a function of applied pressure for the “low”, “medium”, and “high” cross-link extent membranes, and thus no structural compaction was observed over this pressure range (up to 4 bar, which is beyond the standard operating pressure for these class of membranes). The pure water permeance of the cross-linked membranes is 930 ± 510, 580 ± 50, and 250 ± 80 L m⁻² h⁻¹ bar⁻¹ for the “low”, “medium”, and “high” cross-link extents, respectively. These values are expected for membranes in the ultra- to microfiltration range. Increasing the extent of cross-linking results in a progressive decrease in the pure water permeance, which is not surprising as the swelling of the polyelectrolyte matrix is reduced at higher cross-link extents, leading to smaller pore sizes.

An important application for microfiltration and ultrafiltration membranes is the removal of suspended oil from industrial wastewater. In addition to the pure water permeance measurements, the separation of oil droplets from water was investigated for the “high” cross-link extent membrane by using a SDS-stabilized hexadecane-in-water emulsion. The mean oil droplet size was 3–4 μm. The retention of hexadecane droplets was high at 96.6 ± 1.2% (data from three distinct measurements). Fouling experiments using the same oil-in-water emulsion revealed the self-cleaning capability of the P4VP membrane in response to a simple pH switch; the data are presented in Table 1. Fouling resulted in a drastic decrease in water flux with a water permeance recovery of only ~20%. Cleaning of the membrane by soaking in a pH 7 solution of 5 mM NaCl was largely ineffective with the water permeance recovery only slightly improving to be ~40%. After cleaning in an acidic solution of pH 3 (5 mM NaCl), the water permeance recovery substantially increased to be ~90%. Switching to pH 3 results in an increase in the surface charge (see zeta-potential measurements in Figure 2d) of the cross-linked P4VP membrane and therefore its hydrophobicity; this combination of effects is most likely responsible for the desorption of the hydrophobic oil droplets (i.e., self-cleaning response). These data (Table 1) nicely

Table 1. Self-Cleaning Response to pH of the “High” Cross-Link Extent P4VP Membrane

| membrane condition | water permeance (L m⁻² h⁻¹ bar⁻¹) | water permeance recovery (%) |
|--------------------|-----------------------------------|-----------------------------|
| fresh              | 210 ± 20                          |                            |
| fouled             | 40 ± 10                           | ~20                         |
| post pH 7 clean    | 85 ± 10                           | ~40                         |
| post pH 3 clean    | 190 ± 25                          | ~90                         |

DOI: 10.1021/acsapm.9b01006
ACS Appl. Polym. Mater. 2020, 2, 659–667
demonstrate the pH-responsive self-cleaning ability of the P4VP membrane prepared by APS and are in line with the cleaning behavior of P4VP pore-filled membranes.29

The pH- and salt-responsive water permeance was studied for the “low” cross-link extent membrane. Figure 3a presents the pH-responsive water permeance measured for 0.005 mM NaCl solutions (water flux was measured at a TMP of 1 bar, and before these measurements pure water filtrations were performed at 4 bar for 30 min). At pH 9.0 and pH 5.5 (pH > effective pKₐ of P4VP) the permeance is the same as in pure water (within error), as expected for the weakly basic P4VP since the polymer and hence overall membrane charge from P4VP protonation is low. At pH 4.25 the permeance increases slightly (from ∼900 to ∼1000 L m⁻² h⁻¹ bar⁻¹), while at pH 3.0 (pH ≪ effective pKₐ of P4VP) the permeance increases substantially compared to that measured at pH 5.5 (from ∼1000 to ∼1600 L m⁻² h⁻¹ bar⁻¹, an increase of ∼85%). At low pH, the weakly basic pyridine groups are protonated, and the increased electrostatic repulsion between the charges together with swelling due to counterion and solvent absorption results in an increase in the effective pore size of the membrane and thus the higher permeance values. Importantly, cross-linking restricts the amount of swelling, and the membrane and water permeance is stable. This pH-induced swelling of the membrane is similar to the swelling response of cross-linked spin-coated P4VP thin films reported by Harnish and co-workers.30 Figure 3b shows the influence of ionic strength on the permeance at a fixed pH of 3.0 (measured at TMP of 1 bar). With increase in ionic strength from 0.005 to 0.05 M, the permeance does not change. However, at 0.5 M, the permeance drops, which can be attributed to greater charge screening at higher ionic strengths that results in a reduction in the swelling and hence a decrease in the effective pore size of the membrane.

The influence of cross-linking extent on the magnitude of the pH response of the membrane upon switching to pH 3 was also investigated. Figure 3c shows the percentage increase in water permeance observed at pH 3.0 (in 0.005 M NaCl) compared to the permeance measured in pure water for the three different cross-linking extents. At “low” cross-link extent, the permeance increases by ∼85% at pH 3. The magnitude of the pH-triggered increase in permeance is much less for higher cross-linking extents: ∼28% and ∼7% increase in permeance for the “medium” and “high” cross-link extent membranes, respectively. The degree of cross-linking can thus be used to tune the responsive properties of the membrane. This provides a useful additional tuning parameter to optimize membranes produced by APS toward a specific application.

Clearly with the APS approach used here we can prepare porous membranes that show good separation properties. Moreover, the chemical and mechanical stability can be guaranteed by cross-linking, which even allows additional control over membranes properties including the responsiveness of the membrane. Still, an important feature of the traditional NIPS process is its excellent control over membrane structure, allowing a variety of membranes to be produced with a single approach. It becomes important to show that also APS allows this control over membrane structure by preparing asymmetric and much denser membranes.

Asymmetric Membrane Preparation, Morphology, and Performance. For the preparation of asymmetric membranes, the polymer concentration in the casting solution was 20 wt %—the same amount used for preparing the symmetric membranes. The major differences between the preparation of the symmetric and the asymmetric membranes is that for the latter the pH of the coagulation bath was higher and the amount of acetic acid in the casting solution was greater.

As discussed earlier, increasing the pH difference between the casting solution and the coagulation bath increases the driving force for precipitation, and therefore shorter precipitation times should be expected. This is indeed the case for when the pH of the coagulation bath is increased progressively from pH 13 up to pH 14 (0.1 M up to 1 M NaOH). However, when the same casting solution is used to prepare the symmetric membranes, increasing the bath pH results in inhomogeneous films in which more than half of the cross-section structure is completely dense. These films were unsuitable to be used as membranes. To overcome this issue, changes in the composition of the casting solution were made. The first result to note is that varying the concentration of hydrochloric acid in the casting solution did not improve the structure of the resultant films. Next, it is important to recall from the preparation of symmetric membranes, that the addition of acetic acid to the casting solution significantly improved the structure and homogeneity of the films. Therefore, casting solutions with no hydrochloric acid and only acetic acid were prepared and studied. The lowest acetic acid concentration that resulted in a homogeneous (single fluid phase) casting solution was 8 wt %. However, the resultant

Figure 3. Water permeance of the “low” cross-link extent P4VP membrane to (a) changes in pH at fixed NaCl concentration of 0.005 M and (b) changes in ionic strength at fixed pH of 3.0. All measurements were performed at 1 bar of TMP from high to low pH and from low to high NaCl concentration. (c) pH-triggered permeance increase (%) observed for pH 3.0 (in 0.005 M NaCl background electrolyte) compared to pure water as a function of cross-linking extent. All data are the average of three distinct measurements on separate membrane samples, and the error bars are the standard deviation of those measurements.
films had very thick (>20 μm) dense top layers. Increasing the concentration of acetic acid in the casting solution results in films with progressively thinner dense top layers, and indeed this trend can be observed by following the SEM images in Figure 4. For 20 wt % acetic acid (Figure 4a,b) the thickness of the top layer is ~15 μm. For 30 wt % acetic acid (Figure 4c,d) the thickness of the top layer decreases to ~10 μm. At 40 wt % acetic acid (Figure 4e,f) the thickness of the dense top layer decreases further to ~2 μm, which importantly is within the thickness range seen for the separation layers of typical nanofiltration membranes. It is postulated that the buffering capacity of acetic acid acts to control the phase separation process. Consequently, at higher acetic acid concentrations, increasingly more porous films are formed.

The asymmetric membrane prepared by using 40 wt % acetic acid in the casting solution was selected for further studies since the thickness of the dense top layer was low (~2 μm by Figure 4f), and SEM images (Figure 4g) show that the top of the film was defect-free (within the resolution of the SEM). The pure water flux of the non-cross-linked and cross-linked 40 wt % acetic acid membranes were measured as a function of transmembrane pressure, and the results are presented in Figure 4h. Starting with the non-cross-linked membrane, the water flux increases with higher pressures, and this behavior is linear up to 2 bar of applied pressure. Beyond 2 bar of pressure, the increase in water flux is no longer linear and the size of the error bars increases substantially. This reveals again that the non-crosslinked membrane suffers from structural instabilities, and most likely defects form in the top layer, at increased pressures. To address this problem, the asymmetric films were also subjected to chemical cross-linking. After cross-linking, the flux increases linearly with pressure (see Figure 4b). The pure water permeance of the cross-linked membrane is 2.2 ± 0.2 L m⁻² h⁻¹ bar⁻¹ (average for three distinct measurements on separate membrane samples). The combination of the SEM images (Figure 4e−g) and water permeance value for the 40 wt % acetic acid membrane suggests that it resides in the nanofiltration category, albeit the water permeance is lower than many commercially available nanofiltration membranes.

To further study the performance of this membrane, the retention of the small organic molecule calcein (M₇ of 623 Da) was studied (see Figure 4i). The average retention of calcein for the non-cross-linked and cross-linked membranes was 68 ± 9% and 94 ± 2%, respectively supporting the claim that these membranes have the qualities of nanofiltration membranes. The results in this section nicely show the adaptability of the APS approach. With APS it is possible to prepare not only symmetric porous membranes but also asymmetric membranes with dense separation layers—all from a single polymer and significantly without the need for aprotic organic solvents.

### CONCLUSIONS

The production of polymeric membranes is currently dominated by NIPS—a simple and powerful approach to prepare membranes with great control over membrane structure. However, NIPS is heavily reliant on unsustainable, expensive, and toxic aprotic solvents such as NMP. We propose, as an alternative, a novel water-based phase inversion approach (termed APS) that provides similar control over membrane structure. Moreover, the very nature of this approach produces membranes with responsive properties that allow for easy membrane cleaning.

The APS approach was used to prepare P4VP membranes with a porous symmetric structure exhibiting pure water permeance (250−900 L m⁻² h⁻¹ bar⁻¹) and retention characteristics for the ultra- to microfiltration ranges. Covalent cross-linking was used to improve chemical and mechanical stability. Irreversible structural compaction was observed for the non-cross-linked symmetric membranes under applied water pressure, but importantly this problem was eliminated through covalent cross-linking that furnished membranes with stable pure water permeance up to 4 bar of transmembrane pressure. With higher cross-link extents, the measured pore size and pure water permeance progressively decreased showing that cross-linking degree can be used to tune membrane performance. An excellent retention of n-
hexadecane droplets (~97%) from a hexadecane-in-water emulsion was found. Moreover, the membranes were found to be self-cleaning in response to pH, due to the responsive properties of P4VP, with a water permeance recovery of >90% after immersion in a pH 3 solution. Indeed, pH- and salt-responsive permeance behavior of the cross-linked symmetric membranes was found with higher permeant fluxes observed below pH 4 where P4VP becomes charged. The magnitude of the permeance increase triggered at low pH decreased with higher cross-linking extents, showing again that the cross-linking is an adjustable parameter to tune membrane properties; in this case its degree of responsiveness. It was also demonstrated that APS provides substantial control over membrane structure. By tuning the acetic acid content in the casting solution, we could also prepare stable asymmetric membranes with water permeance $(2.2 \pm 0.2 \text{ L m}^{-2} \text{ h}^{-1} \text{ bar}^{-1})$ and retention (94% Calcein) values characteristic for nanofiltration membranes.

The APS approach presented here is a simple and scalable approach that gives a large degree of control over membrane structure. It thus demonstrates all the advantages of traditional NIPS, but in a much more sustainable fashion without requiring toxic aprotic solvents. Moreover, the APS approach naturally results in responsive membranes, with the degree of cross-linking determining the extent of the responsive behavior. We thus see the APS approach as an important tool toward more sustainable membrane preparation. While we have shown that APS works for P4VP we expect that this approach can be extrapolated to many other responsive polymers, allowing for many novel and sustainable membranes to be prepared in the near future. Performing APS with, for example, polycarboxylic acids will allow water-based chemical cross-linking methods to be used—a step toward making APS a completely aqueous approach.

### EXPERIMENTAL METHODS

**Materials.** Poly(4-vinylpyridine) (P4VP, $M_w = 200 \text{ kDa}$) was purchased from Scientific Polymer Products Inc. (Ontario, Canada) and used without further purification. Hydrochloric acid (fuming, 37%, ACROS Organics), acetic acid (glacial, >99.9%, Merck Millipore), sodium hydroxide (>97%, Merck Millipore), potassium chloride (>99%, VWR International), sodium chloride (>99%, Akzo Nobel), n-hexane (>96%, Merck Millipore), 1,4-dibromobutane (99%, Merck), sodium dodecyl sulfate (SDS, ≥99%, Merck), n-hexadecane (≥99%, Merck Millipore), and the fluorescent molecule Calcein (Sigma-Aldrich/Merck) were used as received.

**Membrane Preparation and Cross-Linking.** P4VP was added to a solution of water and acid (hydrochloric acid and/or acetic acid) and stirred for several hours (using a magnetic stirrer bar) until fully dissolved, making the homogeneous membrane casting solutions. Final compositions used herein are given in Table 2.

**Table 2. Composition of the Final Membrane Casting Solutions**

| component     | concentration (wt %) for symmetric membranes | for asymmetric membranes |
|---------------|---------------------------------------------|--------------------------|
| P4VP          | 20                                          | 20                       |
| water         | 67                                          | 50                       |
| hydrochloric acid$^a$ | 6.5                                          | 30                       |
| acetic acid   | 6.5                                          | 40                       |

$^a$In terms of 100% HCl.

To prepare all the membranes, the given polymer casting solution was poured onto a nonwoven fabric (poly(phenylene sulfide)) supported by a glass substrate, and a thin film of polymer was formed by using a manual film applicator with a gate height of 300 μm. Immediately afterward, the cast polymer film was carefully transferred, through gentle submersion by hand, to the bottom of an alkaline coagulation bath (pH 12.5–14.0, 0.032–1 M NaOH) where the phase inversion process took place forming the symmetric or asymmetric membranes. The membranes were left in the coagulation bath for 30 min. The precipitated and solidified polymer film was transferred to a deionized water bath (pH 5.5) for rinsing and storage.

A selection of the membranes were subjected to a chemically cross-linking process. To achieve this, the membranes were first dried overnight in air, then transferred to a sealed glass vessel, and last immersed in a solution of hexane containing the cross-linking agent 1,4-dibromobutane: at concentrations of either 0.5, 2.0, or 4.0% v/v to achieve the “low”, “medium”, or “high” cross-link extent symmetric membranes, respectively. The asymmetric membranes were cross-linked with 4.0% v/v of the cross-linking reagent. The solution was heated to 50 °C with slow stirring by using a magnetic stirrer bar; a temperature sensor was immersed in the solution to control the heating. The cross-linking reaction was allowed to proceed for 1 h. Afterward, the cross-linked membranes were rinsed with hexane, followed by ethanol, and last deionized water before being placed in a deionized water bath (pH 5.5) for storage. While the cross-linking approach used is simple and successful, we do acknowledge that the cross-linking agent and solvent used are toxic. However, importantly, the quantity of solvent and cross-linker used is very small, and its usage does not lead to a polluted wastewater stream, which is the case for the solvents used in the traditional NIPS process. In a continuation of this work, alternative cross-linking strategies using greener molecules and solvents are being explored.

**Morphology Characterization.** Scanning electron microscopy (SEM, JEOL JSM-6010LA and JEOL JSM-7610F, operated at an acceleration voltages of 5 and 2 kV, respectively) was used to study the morphology of the polymeric membranes. For cross-section analysis, the samples were fractured in liquid nitrogen, mounted in cross-section holders with adhesive carbon tape, and dried overnight in a vacuum oven at 30 °C. Before SEM analysis, the samples were coated with a 10 nm conducting layer of chromium using a Quorum Technologies Q150T sputter coater.

**Water Permeance.** The flux (L m$^{-2}$ h$^{-1}$) of pure water and various pH-controlled salt solutions through the P4VP membranes (ϕ 25 mm) were measured at different transmembrane pressures, ranging from 0.5 to 4 bar, at 20 °C, using a dead-end filtration setup. Transmembrane pressure (TMP) is defined as the difference in pressure between the feed and permeate side of the membrane. At each pressure, data were collected for at least 15 min after a steady-state flux was achieved. Water permeance (L m$^{-2}$ h$^{-1}$ bar$^{-1}$), defined as the flux divided by the TMP, was calculated for each measurement. The reported flux and permeance values are the average of at least two measurements, and the standard deviation of the repeats gives the error bars. For each measurement, the membrane was on top of a nonwoven fabric to provide additional mechanical support. The nonwoven fabric had a mesh size of >100 μm and therefore a significantly higher permeance (≈7.5 × 10$^6$ L m$^{-2}$ h$^{-1}$ bar$^{-1}$) than the P4VP membranes. Consequently, it was assumed that the nonwoven support had no influence on the obtained permeance results. To investigate the pH and salt response of the P4VP membranes, dead-end filtration measurements were performed with 0.005 M (pH 3.0, 4.25, 5.5, and 9.0), 0.05 M (pH 5.5), and 0.5 M (pH 5.5) sodium chloride solutions in addition to the pure water (pH 5.5). Here, pH adjustments were made using a minimal volume of 1 M HCl or 1 M NaOH solutions.

**Oil Retention, Membrane Self-Cleaning, and Calcein Retention.** To study retention for the symmetric porous membranes, an oil-in-water emulsion of hexadecane-in-water stabilized by sodium dodecyl sulfate (SDS) was used. A stock emulsion was prepared and then diluted immediately before the filtration measurements. The stock emulsion was prepared by mixing 2 g of hexadecane and 0.02 g...
Before each measurement, the membranes (GmbH, Berlin, Germany) for the symmetric porous membranes were immersed for 15 min in perfluorotributylamine (Fluorinert FC-43, 3M Belgium). Measurements were performed from 0.1 to 6.0 bar of nitrogen pressure. Reported values for mean pore size are the concentration range (0–2000 mg/L), the Beer–Lambert law applied. Here the relationship between the absorbance of the solutions and concentrations of the absorbing species was linear. The reported retention value is the average of four measurements (two measurements on two different membrane), and the error bar is the standard deviation of the four measurements.

To investigate membrane self-cleaning performance, fouling experiments were performed by using the same oil-in-water emulsion. First, the pure water flux was measured for 30 min. Next, the fouling experimentation was performed using 100 mg/L of the emulsion for 30 min. The fouled membrane was removed and placed in the cleaning solution, either pH 7 or pH 3 5 mM NaCl, for 15 min with slow stirring. Afterward, the pure water flux was measured again. The self-cleaning capacity is expressed as water permeance recovery, which is calculated from the pure water permeability before and after the fouling experiments. Water permeance recovery (%) = \((P_{\text{initial}}/P_{\text{fouled}})\times 100\), where \(P_{\text{initial}}\) is the water permeance of the fresh membrane and \(P_{\text{fouled}}\) is the water permeance of the fouled membrane.

Calcine (also named Fluorexon, \(M_c = 623\) Da) retention was measured for a selection of the asymmetric P4VP membranes. A feed concentration of 10 mg/L was used. Filtrations were performed for 2 h, and then the permeate was collected and analyzed. The initial 2 h of filtration before collection of the permeate was performed to help eliminate the effect of calcine adsorption to the membrane on the reported retention values. The feed, retentate, and permeate were measured with a fluorometer (Qubit 4 fluorometer, Invitrogen). For the concentration range studied, the fluorescence intensity was directly proportional to the concentration of calcine, and therefore the retention was calculated by using eq 1.

Porometry. The membrane pore size distribution was characterized by using a Porolux 500 capillary flow porometer (IB-FT GmbH, Berlin, Germany) for the symmetric porous membranes. Before each measurement, the membranes (\(\phi = 25\) mm) were immersed for 15 min in perfluorotributylamine (Fluorinert FC-43, 3M Belgium). Measurements were performed from 0.1 to 6.0 bar of applied nitrogen pressure. Reported values for mean pore size are the average of at least two measurements with the standard deviation of the repeats used for the error bars.

Zeta-Potential. The membrane zeta-potential was studied by using a SurPASS electrokinetic analyzer (Anton Paar, Graz, Austria). The zeta-potential was calculated by measuring the streaming current as a function of pressure, in 5 mM potassium chloride solution, via the expression

\[
\zeta = \frac{dI_l}{dP_{\text{Pref}}} \tag{2}
\]

where \(\zeta\) is the zeta potential (V), \(I_l\) is the streaming current (A), \(P\) is the pressure (Pa), \(\eta\) is the dynamic viscosity of the electrolyte solution (Pa-s), \(\epsilon\) is the dielectric constant of the electrolyte, \(\varepsilon_0\) is the vacuum permittivity (F m\(^{-1}\)), and \(L\) (m) and \(A\) (m\(^2\)) are the length and cross section, respectively, of the streaming channel.

AUTHOR INFORMATION

Corresponding Author *(W.M.d.V.) E-mail w.m.devos@utwente.nl, phone +31 53 4894495.

ORCID®

Joshua D. Willott: 0000-0003-1870-755X
Wouter M. Nielen: 0000-0001-9590-4894
Wiebe M. de Vos: 0000-0002-0133-1931

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Lieke van Ginkel is thanked for some performance tests on the asymmetric membranes. The authors acknowledge funding support from the “Vernieuwingsimpuls” programme through project VIDI 723.015.003 (financed by The Netherlands Organisation for Scientific Research, NWO) and from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (ERC StG 714744 SAMBA).

REFERENCES

(1) Loeb, S.; Sourirajan, S. Seawater demineralization by means of an osmotic membrane. *Adv. Chem. Ser.* 1965, 36, 117–132.
(2) Strathmann, H.; Kock, K.; Amar, P.; Baker, R. W. The formation mechanism of asymmetric membranes. *Desalination* 1975, 16, 179–203.
(3) Guillon, G. R.; Pan, Y.; Li, M.; Hoek, E. M. V. Preparation and characterization of membranes formed by nonsolvent induced phase separation: a review. *Ind. Eng. Chem. Res.* 2011, 50, 3798–3817.
(4) Strathmann, H. *Introduction to Membrane Science and Technology*; Wiley-VCH: 2011.
(5) Prat, D.; Hayler, J.; Wells, A. A survey of solvent selection guides. *Green Chem.* 2014, 16, 4546–4551.
(6) Bergkamp, L.; Herbstscheck, N. Regulating chemical substances under REACH: the choice between authorization and restriction and the case of dipolar aprotic solvents. *Rev. Eur. Community Int. Environ. Law* 2014, 23, 221–245.
(7) Commission Regulation (EU) 2018/588 of 18 April 2018 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards 1-methyl-2-pyrrolidone (accessed October 2019); http://data.europa.eu/eli/reg/2018/588/oj.
(8) Xing, D. Y.; Peng, N.; Chung, T.-S. Formation of cellulose acetate membranes via phase inversion using ionic liquid, [BMIM]-SCN, as the solvent. *Ind. Eng. Chem. Res.* 2010, 49, 8761–8769.
(9) M’barki, O.; Hanaia, A.; Bouyer, D.; Faur, C.; Sescousse, R.; Delabre, U.; Blot, C.; Guenoun, P.; Deratani, A.; Quekener, D.; Pochat-Bohatier, C. Greener method to prepare porous polymer membranes by combining thermally induced phase separation and crosslinking of poly(vinyl alcohol) (accessed October 2019); http://data.europa.eu/eli/reg/2018/588/oj.
(10) Diggi, A.; Marino, T.; Simone, S.; Di Nicola, E.; Li, X. M.; He, T.; Tornaghi, S.; Drioli, E. Towards non-toxic solvents for membrane preparation: a review. *Green Chem.* 2014, 16, 4034–4059.
(11) Hanaia, A.; Faur, C.; Deratani, A.; Guenoun, P.; Garate, H.; Quekener, D.; Pochat-Bohatier, C.; Bouyer, D. Fabrication of novel porous membrane from biobased water-soluble polymer (hydroxypropylcellulose). *J. Membr. Sci.* 2017, 526, 212–220.
(12) Cohen Stuart, M. A.; Huck, W. T. S.; Genzer, J.; Muller, M.; Ober, C.; Stamm, M.; Sukhorukov, G. B.; Szleifer, I.; Tsukruk, V. V.;
Urban, M.; Winnik, F.; Zauscher, S.; Luzinov, I.; Minko, S. Emerging applications of stimuli-responsive polymer materials. Nat. Mater. 2010, 9, 101–113.

(13) Willott, J. D.; Murdoch, T. J.; Webber, G. B.; Wanless, E. J. Physicochemical Behaviour of Cationic Polyelectrolyte Brushes. Prog. Polym. Sci. 2017, 64, 52–75.

(14) Satoh, M.; Yoda, E.; Hayashi, T.; Komiyama, J. Potentiometric titration of poly (vinylpyridines) and hydrophobic interaction in the counterion binding. Macromolecules 1989, 22, 1808–1812.

(15) Tantavichet, N.; Pritzker, M. D.; Burns, C. M. Proton uptake by poly(2-vinylpyridine) coatings. J. Appl. Polym. Sci. 2001, 81, 1493–1497.

(16) Kennemur, J. G. Poly(vinylpyridine) segments in block copolymers: synthesis, self-assembly, and versatility. Macromolecules 2019, 52, 1354–1370.

(17) Zhao, C.; Nie, S.; Tang, M.; Sun, S. Polymeric pH-sensitive membranes – a review. Prog. Polym. Sci. 2011, 36, 1499–1520.

(18) Wandera, D.; Wickramasinghe, S. R.; Husson, S. M. Stimuli-responsive membranes. J. Membr. Sci. 2010, 357, 6–35.

(19) Mika, A. M.; Childs, R. F.; Dickson, J. M.; McCarrvy, B. E.; Gagnon, D. R. A new class of polyelectrolyte-filled microfiltration membranes with environmentally controlled porosity. J. Membr. Sci. 1995, 108, 37–56.

(20) Wandera, D.; Wickramasinghe, S. R.; Husson, S. M. Stimuli-responsive membranes. J. Membr. Sci. 2010, 357, 6–35.

(21) Prat, D.; Hayler, J.; Wells, A. A survey of solvent selection guides. Green Chem. 2014, 16, 4546–4551.

(22) Closs, J. I.; Filiz, V.; Rangou, S.; Buhr, K.; Abetz, C.; Höche, D.; Hahn, J.; Jung, A.; Abetz, V. Double stimuli-responsive isoporourous membranes via post-modification of pH-sensitive self-assembled diblock copolymer membranes. Adv. Funct. Mater. 2013, 23, 731–738.

(23) Vriezekolk, E. J.; Nijmeijer, K.; de Vos, W. M. Dry–wet phase inversion block copolymer membranes with a minimum evaporation step from NMP/THF mixtures. J. Membr. Sci. 2016, 504, 230–239.

(24) Prat, D.; Hayler, J.; Wells, A. A survey of solvent selection guides. Green Chem. 2014, 16, 4546–4551.

(25) Pal, P.; Nayak, J. Acetic acid production and purification: critical review towards process intensification. Sep. Purif. Rev. 2017, 46, 44–61.

(26) de Grooth, J.; Haakmeester, B.; Wever, C.; Potreck, J.; de Vos, W. M.; Nijmeijer, K. Long term physical and chemical stability of polyelectrolyte multilayer membranes. J. Membr. Sci. 2015, 489, 153–159.

(27) Dickhout, J. M.; Moreno, J.; Biesheuvel, P. M.; Boels, L.; Lammertink, R. G. H.; de Vos, W. M. Produced water treatment by membranes: a review from a colloidal perspective. J. Colloid Interface Sci. 2017, 487, 523–534.

(28) Dickhout, J. M.; Kleijn, J. M.; Lammertink, R. G. H.; de Vos, W. M. Adhesion of emulsified oil droplets to hydrophilic and hydrophobic surfaces – effect of surfactant charge, surfactant concentration and ionic strength. Soft Matter 2018, 14, 5452–5460.

(29) Liu, H.; Yang, S.; Liu, Y.; Miao, M.; Zhao, Y.; Sotto, A.; Gao, C.; Shen, J. Fabricating a pH-responsive membrane through interfacial in-situ assembly of microgels for water gating and self-cleaning. J. Membr. Sci. 2019, 579, 230–239.

(30) Harnish, B.; Robinson, J. T.; Pei, Z.; Ramström, O.; Yan, M. UV-cross-linked poly(vinylpyridine) thin films as reversibly responsive surfaces. Chem. Mater. 2005, 17, 4092–4096.