

Membrane formation via non-solvent induced phase separation using sustainable solvents: A comparative study

Catharina Kahrs^{a,b,*}, Jan Schwellenbach^a

^a Sartorius Stedim Biotech GmbH, 37079, Goettingen, Germany

^b Leibniz University Hannover, Institute for Technical Chemistry, 30167, Hannover, Germany

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ABSTRACT

Non-solvent induced phase separation (NIPS) is a frequently used technique for the production of polymeric membranes. It enables the production of membranes with a broad range of different characteristics. Current solvents used in membrane preparation are often toxic, environmentally unfriendly and prepared from non-sustainable resources. This is why a replacement of solvents like *N*-methyl-2-pyrrolidone (NMP) and dimethylacetamide (DMAc) is highly desirable. In order to substitute a solvent whilst achieving the same desired membrane properties, it is necessary to understand the formation mechanisms and its influencing factors. One important set of parameters for controlling the membrane features is the polymer solution composition. This is why the aim of this study was to improve the understanding of membrane formation by gaining a holistic picture of the influences of systematic additive variations, focusing on the comparison between conventional and alternative sustainable solvent systems. Thus, 72 different polyethersulfone (PES) membrane prototypes were produced by immersion precipitation from polymer solutions prepared in NMP and DMAc, as well as in the sustainable alternatives 2-pyrrolidone (2P) and dimethylacetamide (DML). In all four solvent systems varying concentrations and molecular weights of the polymeric additives polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) were applied. The viscosity of the polymer solutions was determined, and thereof formed membranes were analyzed in terms of permeability, protein retention, surface properties, mechanical stability and morphology. The results indicate that both, solvents and additives, significantly impact the membrane properties. It was shown that the influences of the additives on all investigated membrane features were strongly dependent on the applied solvent. The observed effects were similar for the conventional solvents NMP and DMAc, but differed from those found for the alternative solvents 2P and DML, which among themselves also showed comparable outcomes. In conclusion, this study proves that it is possible to obtain desired membrane properties with 2P or DML as long as the solution composition is chosen appropriately.

1. Introduction

Filtration describes a mechanical separation process which is used to remove small particles or molecules from an aerosol or a fluid stream [1–4]. Typical areas of application are the purification of products in the food industry, the treatment of waste water, drinking water purification, the use for medical purposes such as dialysis, and the purification of pharmaceutical products [4–7]. In order to fulfill the requirements for different applications, filtration membranes have to meet certain criteria in terms of structure and performance [1]. Apart from determining these criteria through adjusted process parameters, the desired membrane characteristics such as pore size distribution, permeability, rejection

capability and surface properties can be controlled during the production process [8–10]. Due to their good capability of forming membranes with different morphologies and different performances, polymeric membranes are frequently chosen for filtration purposes [6,11–13].

A commonly applied manufacturing method for producing polymeric membranes is the phase separation of polymer solutions with a defined composition [14,15]. In this context one of the most applied approaches is the non-solvent induced phase separation (NIPS) [16–18]. It involves the formation of two phases through an exchange of the solvent from the polymer solution through a non-solvent from a precipitation bath. One of the phases contains a high polymer solution and is responsible for the formation of the membrane matrix, whereas the

* Corresponding author. August-Spindler-Straße 11, 37079, Goettingen, Germany.

E-mail address: catharina.kahrs@sartorius.com (C. Kahrs).

second phase contains only a very small proportion of the polymer and is washed out during the membrane formation process. This causes the development of the pore network within the matrix of the membrane until structure solidification sets in Refs. [19–21].

For controlling the membrane morphology, many factors have to be considered. Apart from the process conditions the composition of the initial polymer solution has a major impact on the thermodynamics and kinetics of the membrane formation process [19,22–24]. In this context, different membrane-forming polymers, different solvents and various non-solvent or polymeric additives can be used to alter the fundamental progress of phase inversion [8,25,26].

Among different membrane-forming polymers such as polysulfone (PSf), polyvinylidene fluoride (PVDF), polyamide (PA), or cellulose acetate (CA), polyethersulfone (PES) is one of the most commonly applied polymers for membrane preparation [8,27–29]. PES features favorable characteristics, which include a high thermal, chemical, and mechanical stability, as well as a high glass transition temperature and a good processability [30–32].

In order to prepare a membrane casting solution, the polymer and potential non-solvent or polymeric additives have to be dissolved in an appropriate solvent. Currently, common solvents which are used for preparing membrane casting solutions include *N*-methyl-2-pyrrolidone (NMP), dimethylacetamide (DMAc), dimethylformamide (DMF) and dioxane [8,19,33]. However, all these solvents have in common that they bring up several issues regarding safety, health and environmental sustainability during transport, storage and handling [33–35]. Another concern with these solvents is their disposal. They often cannot be reused due to certain quality requirements and regulatory demands [36, 37]. Therefore, the listed solvents implicate environmental issues and are further regarded as dangerous for human health [38–40].

In case of PES the most frequently used solvents are NMP and DMAc, which both belong to the list of the hazardous solvents. Consequently, there is a high interest in replacing these harmful solvents through sustainable alternatives, which at best meet the criteria of green chemistry [41–43]. A fundamental principle of green chemistry is the promotion of applying non-toxic and eco-friendly solvents in order to replace the conventionally used ones [19]. Furthermore, it requires the development of sustainable processes and products in order to minimize the risk factors, which emanate from the applied materials and in particular from chemicals such as solvents [37]. Finally, the replacement of conventional solvents through more sustainable ones shall reduce the environmental impact and simultaneously increase the sustainability of membrane fabrication [34,37,44–48].

As a result of the raising interest to improve the sustainability of membrane production, several different solvents have been investigated in the recent past with respect to their suitability for replacing harmful solvents. The non-toxic and biodegradable solvents which have been tested so far for their ability to form PES ultrafiltration membranes include dimethyl sulfoxide (DMSO), as well as the bio-derived solvents Rhodiasolv®Polarclean, γ -Valerolactone (GVL) and Cyrene™ [21,33, 35,41,42,48–51]. Furthermore, it has been reported that several other bio-based solvents, which are basically different derivatives of glycerol, can be used to prepare membranes with different polymers [35].

Apart from dissolving the selected polymer, the membrane which is formed from the prepared polymer solution has to be adjustable with regard to structure and performance. For polymeric systems with NMP and DMAc the control parameters have been frequently studied [8,20, 32,52–64]. The main parameters which have been found to influence the resulting membrane features include the casting solution composition and the precipitation conditions, since both affect the kinetics and thermodynamics of the formation process [8,19,22,60,65–70]. In addition to polymer, solvent and non-solvent, polymeric or non-solvent additives can be used to alter the thermodynamic and kinetic properties of polymer solution and membrane formation process [8,32,70,71]. Two of the most commonly used polymeric additives are polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) [20]. Apart from creating a more

hydrophilic membrane surface when the membrane-forming polymer has a quite hydrophobic character, PVP and PEG can impact the viscosity of the casting solution and therefore the diffusive exchange rate during NIPS. As a consequence it affects the resulting pore sizes as well as the formation of macrovoids in the sub-structure of the membrane. This is based on the change in coalescence of the polymer-poor phase and therefore on the alteration of the sizes of the remaining holes within the membrane matrix when the viscosity is altered [14,20,22,72]. Furthermore, PVP and PEG are designated as pore-forming agents because both additives have been shown to influence the permeability, the rejection properties, the stability and the structure of the resulting membranes [53,56,58,60,61,73,74].

In the past various studies were conducted which investigate the influence of varying concentrations and molecular weights of PVP and PEG on membrane structure and performance to understand their impact on the membrane formation process. However, as this process is very complex and strongly depends on the combination of several different variables, there is still a huge interest to further enhance the knowledge of the fundamentals of the formation mechanisms [8,20,25, 26]. On top of that, the studies on polymeric additives are limited to polymer solutions prepared with hazardous solvents. If the existing studies are compared among each other, the results are somewhat contradictory as well [20].

This is why in this work a comparative study is presented, which on one hand investigates the effects of polymeric additive variations in the conventional solvents NMP and DMAc, and on the other hand compares the outcomes of the conventionally used systems to those of the alternative solvents 2-pyrrolidone (2P) and dimethylacetamide (DML). These two alternative solvents exhibit similar characteristics to the conventional ones with regard to their physicochemical properties, which are summarized for all four solvents in Table 1.

In contrast to NMP and DMAc, 2P and DML are not classified as substances of very high concern. Instead, they are both regarded as non-toxic solvents and are readily biodegradable, which is why they have been categorized into the lowest water pollution class. Therefore, 2P and DML can be considered as sustainable solvents, which are safe for human health [75,76]. In contrast to 2P, which is mainly produced from γ -butyrolactone [77], DML can even be regarded as a bio-derived substance. It is the dimethylamide of natural lactic acid and therefore meets the principles of green chemistry, since it is produced from renewable sources [76].

2P was chosen as it has previously been shown that it is a suitable sustainable alternative for PSf membrane preparation [59,78]. However, until now no studies have been conducted which address the production of PES membranes with 2P as solvent. Furthermore, the effects caused by addition of additives have also not been studied so far for a 2P-based system. In contrast, DML was chosen as alternative solvent because to date it has not been presented as solvent in the context of membrane fabrication at all. However, DML has been reported to be a suitable non-toxic alternative for hazardous solvents in other application areas [79]. This is why a first trial was conducted to use DML for the production of PES membranes.

Table 1
Physicochemical properties of the applied solvents.

Characteristics	NMP	DMAc	2P	DML
Molar mass	99.13 g/mol	87.12 g/mol	85.11 g/mol	117.2 g/mol
Density (at 20 °C)	1.03 g/mol	0.94 g/cm ³	1.11 g/cm ³	1.05 g/cm ³
Melting point	- 24 °C	- 20 °C	25 °C	- 2 °C
Boiling point	204 °C	166 °C	250 °C	223 °C
Miscibility with water	completely miscible	completely miscible	completely miscible	completely miscible
Substance of very high concern	yes	yes	no	no

Consequently, the aim of this comparable study was to prove that 2P and DML are suitable for substituting NMP and DMAc in PES membrane production via NIPS. This shall contribute to the reduction of the environmental impact of the production process and therefore to the increase of the membrane process sustainability. Furthermore, a holistic picture of the influences on membrane formation during immersion precipitation should be gained by comparing additive influences among all four solvent systems. Therefore, concentration variations as well as the influences of different molecular weights of both additives, PVP and PVP, were studied in the four different solvent systems which have different affinities for dissolving the solution components as well as varying physical and chemical properties. A row of different casting solutions was prepared and used to produce PES membrane prototypes. Finally, the effects of the variables on the membrane properties were studied by determining the polymer solution viscosity, by evaluating the membrane structure and by determining the membrane performance in terms of permeability, retention capacity, mechanical stability and surface characteristics.

2. Experimental

2.1. Materials

Commercial PES Ultrason® E6020 with a molecular weight of 75,000 g/mol was purchased from BASF (Ludwigshafen, Germany) and applied as the membrane-forming polymer. The different solvents which were applied included the two conventional solvents NMP and DMAc (Carl Roth, Karlsruhe, Germany), as well as the two alternative solvents 2P (Carl Roth, Karlsruhe, Germany) and DML (BASF, Ludwigshafen, Germany). Different types of PVP Luvitec® powder with molecular weights of 9 kDa (Luvitec® K17), 50 kDa (Luvitec® K30) and 1400 kDa (Luvitec® K90) were acquired from BASF (Ludwigshafen, Germany), while PEG with molecular weights of 400 Da, 1500 Da, and 6000 Da were supplied by Sigma-Aldrich (St. Louis, MO, USA). Reverse-osmose (RO) water (Sartorius Stedim Biotech GmbH, Goettingen, Germany) was used as non-solvent. For measurements of the membrane permeability 0.9 wt% sodium chloride (Merck, Darmstadt, Germany) in RO-water was used. In case of the protein retention measurements lysozyme (Carl Roth, Karlsruhe, Germany) was applied as model molecule, whereas the used diluent potassium phosphate buffer with a pH of 7.0 (Carl Roth, Karlsruhe, Germany).

2.2. Polymer solution preparation

In order to study the influence of the polymeric additives in different solvent systems, membranes with varying concentrations and molecular weights of PVP and PEG were prepared, while the PES concentration was constantly held at 15 wt%. Since the water content can influence the final membrane characteristics, it was also held at a constant level. Therefore, the water proportion in all raw materials and their contribution to the final water amount in the polymer solution was determined using a moisture analyzer (Sartorius Lab Instruments GmbH & Co. KG, Goettingen, Germany) for solids, and a Karl Fischer Titrando (Metrohm, Herisau, Switzerland) for liquids. The necessary amount of RO-water was calculated to reach a final concentration of 0.5 wt% water in each casting solution. The compositions of the polymer solutions for preparing different membrane prototypes are listed in Table 2. All specified solution compositions were applied with each of the four chosen solvents so that in total 72 different membrane prototypes were produced. Each prototype was assigned with a code consisting of a letter and a number. The letter refers to the respectively applied solvent, where A stands for DMAc, N for NMP, M for DML and P for 2P. The number refers to the casting solution composition as it is listed in Table 2.

In order to prepare the polymer solutions, the defined amounts of RO-water and the respective solvent were filled into a 500 mL twin-neck flask (Carl Roth, Karlsruhe, Germany). The flask was placed into a

Table 2

Casting solution compositions for the preparation of PES membrane prototypes with variations in additive concentrations and molecular weights.

Composition	Components [wt.%]				
	PES	PVP 50 kDa	PEG 400 Da	Water	Solvent
1	15	0	0.0	0.5	84.5
2	15	1	0.0	0.5	83.5
3	15	2	0.0	0.5	82.5
4	15	3	0.0	0.5	81.5
5	15	4	0.0	0.5	80.5
6	15	5	0.0	0.5	79.5
7	15	1	0.0	0.5	83.5
8	15	1	2.5	0.5	81.0
9	15	1	5.0	0.5	78.5
10	15	1	7.5	0.5	76.0
11	15	1	10.0	0.5	73.5
12	15	1	12.5	0.5	71.0
13	15	1	15.0	0.5	68.5

Composition	Components				
	15 wt %	2.5 wt%	7.5 wt%	0.5 wt %	74.5 wt %
14	PES	PVP 9 kDa	PEG 400 Da	Water	Solvent
15	PES	PVP 50 kDa	PEG 400 Da	Water	Solvent
16	PES	PVP 1400 kDa	PEG 400 Da	Water	Solvent

Composition	Components				
	15 wt %	1.0 wt%	7.5 wt%	0.5 wt %	76.0 wt %
17	PES	PVP 50 kDa	PEG 1500 Da	Water	Solvent
18	PES	PVP 50 kDa	PEG 6000 Da	Water	Solvent

heated oil bath and tempered to 60 °C. Under constant stirring at 250 rpm (IKA overhead stirrer RW20, IKA, Staufen, Germany), the respective additives and finally the membrane-forming polymer were added to the flask. In case of all four solvents the mixture was then stirred overnight at 60 °C to dissolve the PES in the respective solvent, so that finally a homogenous casting solution was obtained. In a last step each solution was degassed in an oven at 50 °C for at least 2 h.

2.3. Preparation of membrane prototypes

In order to produce membrane prototypes, the previously prepared polymer solutions were cooled to 25 °C, poured onto a glass plate and evenly spread with a casting rake (AWU Precision Slovakia k.s., Prešov, Slovakia). The casting rake was made of stainless steel and had a defined casting thickness of 250 µm. Subsequently, the glass plate with the casting film was immediately immersed into a precipitation bath, which consisted of the non-solvent (RO-water) tempered to 25 °C. In order to allow the complete exchange of solvent and non-solvent, which resulted in a self-initiated detaching of the membrane from the glass support and the formation of the final membrane structure, the samples were left in the precipitation bath for 5 min. Subsequently, the membrane sheets were impregnated with 40 wt% glycerol in RO-water to prevent the collapse of the pore structure during storage of the samples. Finally, the samples were dried in an oven at 50 °C for 10 min and stored in airtight sealed bags until used for further investigation.

2.4. Characterization

2.4.1. Dynamic solution viscosity

The dynamic viscosity of each casting solution was determined using a HAAKE™ falling ball viscometer (ThermoFisher Scientific, Waltham, MA, USA). Therefore, the casting solution and an appropriate nickel-steel ball were filled into the viscometer tube and then tempered to 25 °C for at least 15 min using a thermostat (Lauda, Lauda-

Koenigshofen, Germany) connected to the viscometer. Finally, the falling time of the ball was measured in a fivefold determination and the dynamic viscosity was calculated as follows:

$$\eta = \frac{t_m \cdot (\phi_B - \phi_S) \cdot K}{1000} \quad (1)$$

where η is the dynamic viscosity (Pa·s), t_m is the mean falling time of the ball (sec), ϕ_B is the density of the ball (g/cm³), ϕ_S is the density of the solution (g/cm³), and K the constant of the ball (mPa·cm³·g⁻¹), which is determined through the calibration of the ball.

2.4.2. Cloud point titration

Cloud point measurements were conducted to compare the amount of water which can be added to the four different solvent systems until demixing is induced. For each solvent a 5 wt% PES solution was prepared and filled into a reactor (HWS, Mainz, Germany) tempered to 25 °C. Under constant stirring at 300 rpm (IKA overhead stirrer RW20, IKA, Staufen, Germany), 0.03 g/min of water were added to the polymer solution using an automatic titration unit (Metrohm900 Touch Control, Metrohm846 Dosing Interface, Metrohm 807 Dosing Unit and Metrohm800 Dosino, Metrohm GmbH and Co. KG, Filderstadt, Germany). During the titration experiment, the light transmittance was recorded as a function of time, until the transmittance dropped below a value of 5%. Finally, the inflection point of the function, which represents the cloud point of the solution, was determined with Origin 2018b (Northampton, MA, USA).

2.4.3. Scanning electron microscopy

In order to wash out the glycerol from the membrane structure, a small piece of each membrane sample was cut and flushed with RO-water for at least 15 min. Subsequently, the wet membranes were immersed into liquid nitrogen and cross-section samples were prepared by creating smooth breaks of the frozen membranes using a razor blade. The samples were placed into specimen stubs, marginal coated with conductive silver and sputter coated with a thin film of argon. Finally, the images were recorded using a FEI Quanta 200 ESEM (ThermoFisher Scientific, Waltham, MA, USA) under high vacuum and at a potential of 12.5 kV.

2.4.4. Sponge layer thickness

The recorded cross-section images were used to determine the thickness of the sponge-like layer on the skin-side of each membrane. The sponge layer was defined as the layer from the surface of the membrane to the first appearance of finger-like voids [80]. The software Image J (National Institutes of Health, Bethesda, MD, USA) was used as an image analysis tool.

2.4.5. Membrane permeability

The permeability of the manufactured membrane prototypes was determined with a solution of 0.9 wt% sodium chloride diluted in RO-water. Together with a fibrous support, a round membrane sample with a diameter of 26 mm was integrated into a 10 mL stirred cell (Sartorius Stedim Biotech GmbH, Goettingen, Germany), which was then filled with the previously prepared salt solution. The lid of the stirred cell was connected to a pressure supply and the measurement module was exposed to a pressure of 1 bar. By doing so, the salt solution was filtrated over the membrane sample with an effective filtration area of 3.8 cm², and the time which was needed to collect 10 mL of the filtrate was stopped. During the filtration run the solution was stirred on a magnetic stirrer at 1100 rpm (IKA color squid, IKA, Staufen, Germany). Finally, the membrane permeability was calculated as follows:

$$J = \frac{V_F}{A_M \cdot t \cdot p} \quad (2)$$

where J is the membrane permeability (L·m⁻²·h⁻¹·bar⁻¹), V_F is the

filtration volume (L), A_M is the effective filtration area of the membrane (m²), t is the filtration time (h) and p is the applied pressure (bar).

2.4.6. Protein retention

The protein retention of the membrane prototypes was determined by applying lysozyme (Lot. 235225855, Carl Roth, Karlsruhe, Germany) as model protein. Using a 20 mM potassium phosphate buffer (pH 7.0) as diluent, a lysozyme solution with a concentration of 0.2 g/L was prepared and mixed at 250 rpm on a magnetic stirrer (IKA color squid, IKA, Staufen, Germany), until the protein was completely dissolved. The prepared modules from the permeability measurements were emptied and filled with 10 mL of the lysozyme solution. Then the filtration was started by applying a pressure of 1 bar to the stirring cell. During the filtration the solution within the cell was constantly stirred at 1100 rpm on a magnetic stirrer (IKA color squid, IKA, Germany) to simulate cross-flow filtration, and the filtrate was collected in a test tube. After collecting 9.5 mL of the filtrate, the filtration was stopped and the cell was flushed twice with the pure salt solution. Subsequently, the cell was filled with the salt solution and the filtration at 1 bar and 1100 rpm was continued to a final filtrate volume of 12 mL in order to collect the remaining protein filtrate from the dead volume of the module. Finally, the lysozyme concentrations in the feed solution and the filtrates were measured by a UV-Vis spectrophotometer (Infinite® 200 PRO, Tecan, Maennedorf, Switzerland) at a wavelength of 280 nm. As the protein concentration is proportional to the extinction of the protein solution, the lysozyme rejection was calculated as follows:

$$R = 1 - \frac{c_p}{c_f} \cdot 100 \quad (3)$$

where R is the protein rejection (%), c_p is the protein concentration in the filtrate (g/L) and c_f is the protein concentration in the feed solution (g/L).

2.4.7. Bursting pressure

In order to evaluate the mechanical stability of the membrane prototypes, the bursting pressure was determined. The bursting pressure is defined as the pressure which is needed to rupture the membrane. First the membrane samples were wetted with water and then placed with the skin-side facing down into the bursting pressure device. The actual measurement was started by moving the plunger of the device directly onto the membrane sample. A continuously raising pressure was applied to the membrane sample until the bursting pressure was reached, which was indicated through an audible rupture of the membrane. Finally, the reached pressure was read from the meter of the device.

2.4.8. Water contact angle

The hydrophilicity of the membrane surface was evaluated by measurements of the contact angle, which was determined by application of the sessile drop method using an OCA 15 EC contact angle system (DataPhysics Instruments GmbH, Filderstadt, Germany). For the measurement a drop of 10 µL RO-water was injected onto the surface of a dry membrane sample with a micro-syringe. The drop was visualized with the integrated camera of the measurement system and the contact angle was determined at room temperature 10 s after placing the water drop onto the membrane surface. Three measurements of different locations on the membrane sample were recorded and averaged.

2.4.9. Unspecific protein binding

An indirect method to analyze the surface hydrophilicity is the measurement of the unspecific protein binding to the membrane surface. Therefore, 10 mm membrane blanks were placed into a 48-well plate. A protein solution of 3 g/L lysozyme (Lot. 235225855, Carl Roth, Karlsruhe, Germany) was prepared with 20 mM potassium phosphate buffer (pH 7.0) as diluent. Each well containing a membrane sample was supplied with 200 µL of the protein solution and the plate was incubated

for 16 h at room temperature on a Heidolph Titramax 100 plate shaker (Heidolph Instruments, Schwabach, Germany) at 300 rpm. After 16 h the protein solution was removed and the samples were washed twice for 20 min and once for 3 h with the phosphate buffer. In the meantime, a calibration standard row was prepared by serial dilution of the protein stock solution and 30 μL of each standard was added in duplicates to empty wells of the plate. 300 μL of the BCA reagent (ThermoFisher, Waltham, MA, USA) were added to each well and the plate was incubated at 300 rpm on the plate shaker for 1 h. Afterwards, 200 μL of each well were transferred into a new well plate and finally the absorbance was measured at 562 nm using a Infinite M2000 well-plate reader (Tecan, Männedorf, Switzerland). A calibration curve was created from the absorbance data and used to calculate the concentration of the protein concentration bound to the membrane samples.

2.4.10. Specific surface area

The specific surface area was determined by application of a normal BET procedure with a Gemini V device (Micromeritics, Norcross, GA, USA). In preparation for the measurement the samples were heated at 120 $^{\circ}\text{C}$ and under vacuum for at least 3 h. The weight of the dry samples was determined and finally the specific surface area was determined using the 11 point method of the Gemini device. The BET method detects the specific surface area on the basis of nitrogen gas adsorption to the membrane sample [81]. It can be described as follows:

$$S_{\text{BET}} = \frac{N_A \cdot A_M \cdot V_{\text{Mono}}}{m_{\text{ges}} \cdot V_M} \quad (4)$$

where N_A is the Avogadro constant, A_M is the area of the adsorbed nitrogen molecules, V_{Mono} is the volume of the adsorbed monolayer, m_{ges} is the mass of the sample and V_M is the molar volume of adsorbed nitrogen

molecules.

3. Results and discussion

3.1. Dynamic solution viscosity

The viscosity is an important variable with regard to the processability of the casting solution. In all cases, the viscosities of the polymer solutions was dependent on the additive type which was added to the solution (Fig. 1).

Furthermore, the viscosity showed a dependence on the respective additive concentration and molecular weight (Fig. 1). Although the magnitude of the viscosities differed between the four solvent systems, the main trends which were found for the tested variables were the same, independently of the solvent which was used. Therefore, the results show that the solvent which is applied for dissolving polymer and additives has an important impact on the final casting solution viscosity. Regardless of the type of additive and its respective concentration or molecular weight, the use of DMAc always resulted in the lowest solution viscosity when it is compared to one of those having the same composition, but were prepared in one of the other three solvents. In case of DMAc the viscosities ranged from 0.2 Pa·s to around 2 Pa·s. In comparison to casting solutions prepared with DMAc, polymer solutions which were prepared with NMP exhibited viscosities which were only slightly higher, as they ranged from 0.4 Pa·s to approximately 4 Pa·s. In contrast to these two commonly used solvents, polymer solutions which were prepared with 2P or DML showed significantly higher viscosities. In general, the use of 2P resulted in the highest viscosity values. While the viscosities of polymer solutions with DML ranged from around 3 Pa·s up to 28 Pa·s, the solutions prepared with 2P exhibited viscosities

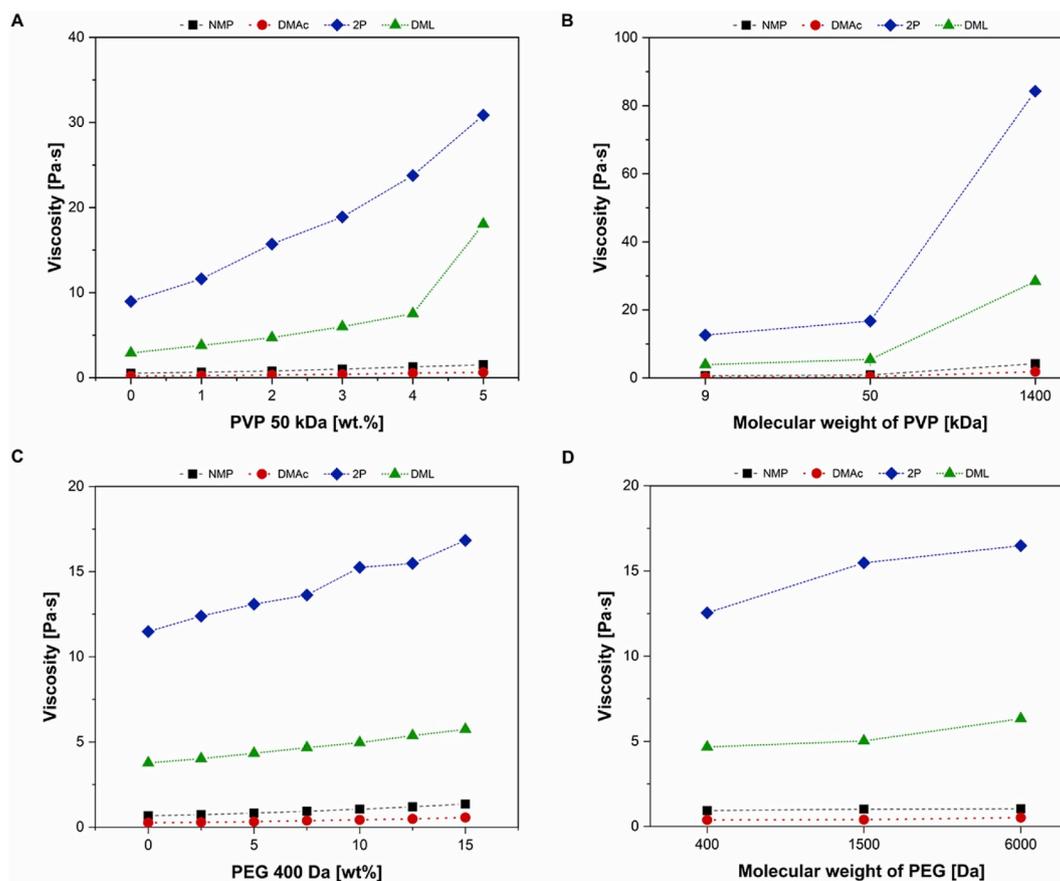


Fig. 1. Dynamic viscosity of polyethersulfone casting solutions at 25 $^{\circ}\text{C}$ in dependence of the PVP 50 kDa concentration (A), the PVP molecular weight (B), the concentration of PEG 400 Da (C), and the PEG molecular weight (D), determined with a falling ball viscometer.

ranging from 9 Pa·s up to 84 Pa·s. Comparing the viscosity ranges of the four systems among each other it becomes evident that the upper value in all cases is approximately ten times higher than the lower value. This implies that the increase of the viscosity caused by the additive variations lies in the same order of magnitude for all solvents.

Similarly to the results found after the polymers have been dissolved, sole DMAc exhibits the lowest viscosity, followed by NMP, which has almost twice the viscosity of DMAc. The viscosity of pure DML is about five times higher in comparison to DMAc, while 2P is even above 1.3 times higher (Table 3).

If the relation of the values for the pure solvents are compared to the relations of the complete viscosity range for each solvent after polymer and additives have been dissolved in it, it becomes apparent that the viscosities of the pure solvents NMP and DMAc differ by a factor of two. The range for NMP is also twice as high as the one of DMAc. This correlation between the pure solvent viscosity and the viscosity of the final casting solution could not be found for the other two solvents. While the viscosity of pure DML is only about five times higher than the one of DMAc, the range which was found for the whole set of casting solutions prepared in DML was approximately 15 times higher than the range determined for solutions in DMAc. In case of 2P this range was roughly 45 times higher in comparison to the one found for DMAc. An explanation for this could be that the viscosity is influenced by the interaction between solvent and polymer. The interaction of each solvent to another solvent or to a certain polymer can be characterized by their Hansen solubility parameters (HSP). The HSP data can be used to predict the affinity between two solvents, as well as the affinity between a polymer and a solvent. These affinities can be expressed by a so called distance value, which indicates how likely a polymer will dissolve in a certain solvent as the rule applies that like dissolves like. Hereby a low distance value indicates a good solubility of the polymer within the solvent, while a high distance value indicates that the solubility is rather poor [84]. The HSP for the four chosen solvents and their distance values to PES can be taken from Table 4.

The affinity between solvent and polymer affects the viscosity because the shape of the dissolved polymer chains has an influence on the resulting solution viscosity. Therefore both, the shape of the polymer molecules, as well as their arrangement and their behavior within the solvent play an important role. Depending on the interaction between polymer and solvent, the conformation of the polymer can change and the solvent can either be immobilized due to high interaction, or move about freely due to low interaction, which in turn changes the solution viscosity [85].

For both examined additives a rising concentration or the use of higher molecular weight additives resulted in an increase of the polymer solution viscosity. This trend could be observed for all four solvents, however, the magnitude of the final viscosity was solvent-dependent. Nonetheless, the proportions of the effects were similar in all four solvents, as the multiplication factor between the lowest and the highest viscosities, which yields the total viscosity interval, was the same for all tested systems.

The viscosity enlargement which was seen for an increase in PVP or PEG molecular weight is based on the general fundamentals of polymer physics. The viscosity increases when the polymer chains of the additives become longer because the internal friction between the coiled and swollen macromolecules becomes stronger, so that the chains interact with each other and cause polymer entanglement [86–88].

Table 3

Dynamic viscosities of the pure applied solvents at 25 °C.

Solvent	Dynamic viscosity at 25 °C [mPa·s]	Reference
N-methyl-2-pyrrolidone	1.7	[82]
N,N-dimethylacetamide	0.9	[83]
2-pyrrolidone	13.3	[82]
N,N-dimethylacetamide	5.1	[76]

Table 4

Hansen solubility parameters of polymer and solvents which were applied for membrane preparation, including the calculated distance values between the polymer and each solvent.

Solvent/Polymer	δ_d [MPa ^{0.5}]	δ_p [MPa ^{0.5}]	δ_h [MPa ^{0.5}]	Distance value to PES
Polyethersulfone	19.6	10.8	9.2	–
N-methyl-2-pyrrolidone	18.0	12.3	7.2	2.97
N,N-dimethylacetamide	16.8	11.5	10.2	3.05
2-pyrrolidone	18.0	16.6	7.4	6.28
N,N-dimethylacetamide	18.4	12.9	15.9	7.12

Furthermore, the larger the hydrodynamic size of the molecules, the more they slow down their movement. In turn, these circumstances result in a more confined position of the polymers and therefore in a more viscous solution. This also explains why the results for solutions with variations of PVP molecular weights showed a more pronounced effect in comparison to the variations with PEG because the molecular weight range which was tested in case of PVP was much higher than in case of PEG. An elevation of the viscosity could also be observed when the concentration of PVP or PEG was increased. Again this can be explained by the movement of the molecules within the solution as well as by the interactions between the polymer molecules. When the amount of polymeric additives in the solution rises, the polymer molecules more likely tend to interact with each other, which consequently favors the entanglement of the polymer chains. As a result, the position of the polymer molecules becomes more inflexible and in turn the viscosity of the solution increases [87,88]. This is also the reason why the viscosity raised at higher concentrations of polymeric additives, since the movement of the molecules becomes more restricted when their quantity increases. Again, the observed effect on the viscosity with increasing PVP concentration was more pronounced in comparison to the effect seen in case of PEG. Again, the chain length of the used PVP was higher than the one of PEG, which as discussed before influences the solution viscosity.

The trends which were observed in this study agree to the findings other groups made with similar systems or systems containing other solvents or polymers, as well as a different combination of both [14,62,64,71,72,89].

3.2. Cloud point titration

The cloud points of 5 wt% PES solutions prepared in the four different solvents NMP, DMAc, 2P and DML were determined and compared to each other. The compositions at the determined cloud points of each solution are shown in Table 5.

It was found that the ternary system with NMP has the highest water tolerance, so that in comparison to the other three solvents the most water is needed to induce precipitation. In contrast, a solution containing the same starting concentration of PES but DMAc as solvent tolerates around 2.5 wt% less water than the NMP solution. The reason for this could be the better solubility of PES in NMP, which in turn results in a larger miscibility gap. Similar observations for PES in NMP and DMAc were previously reported in literature [90,91].

Table 5

Cloud points of 5 wt% PES solutions prepared with NMP, DMAc, 2P and DML as solvents.

Solvent system	Water [wt.%]	Polymer [wt.%]	Solvent [wt.%]
NMP	12.01	3.86	83.43
DMAc	9.54	4.19	86.27
2P	5.91	4.47	89.62
DML	3.81	4.71	91.48

However, no phase diagrams have been reported for PES-2P or PES-DML so far. Therefore, a first trial was made in this study to compare the water tolerance of the alternative solvents to the conventional ones. It was found that both alternative solvent systems tolerate less water than the conventional ones, so that less water is needed to induce membrane formation. This can be explained by a lower solvent power of 2P and DML for PES [90].

From these results can be concluded that in case of the same PES concentration different membrane characteristics will be obtained when changing the solvents. The higher the water tolerance, the lower the polymer concentration in the solution when demixing sets in. As a consequence the proportion of solvent in the matrix-forming phase is reduced after onset of phase separation. This is why the nascent pore size after demixing is strongly influenced because higher polymer concentrations lead to tighter pore structures. It has been previously shown that higher polymer concentrations in the dope solution, which also cause an entry into the miscibility gap at higher polymer concentrations, result in tighter membranes [55]. Consequently membranes prepared with the same polymer concentration but with different solvents should exhibit different performances with respect to permeability and retention capability.

3.3. Membrane structure

In order to evaluate the influence of the additive and solvent variations on the membrane structure, cross-sections of each membrane prototype were recorded. It was found that all membranes had an asymmetric structure with a dense retentive layer on the top-side, which is commonly known as skin, and a porous sublayer below the skin. This sublayer can either contain macrovoids, finger-like cavities, or a sponge-

like morphology. These typical structural characteristics have been frequently published in literature [23,61,92–96].

Although the membranes had the asymmetric structure in common, the thickness of the dense top layer and the morphology of the sublayer differed in dependence of the type, concentration and molecular weight of the additive which was used. Furthermore, the resulting structure was strongly dependent on the applied solvent. The structures of the membranes prepared with the low viscosity solvents NMP and DMAc were similar, and differed to those of the membranes prepared with the high viscosity solvents 2P and DML, which on the other hand also exhibited similar morphological properties among each other.

If the structures of these two groups are compared to each other, it is striking that the sponge-like layer on the skin side of the membranes become thicker when a more viscous solvent is used. While the thickness of the sponge-like layer of the NMP and DMAc membranes is in the nanometer range (Fig. 2), its thickness is rather in the micrometer range for 2P and DML membranes (Fig. 3).

Apart from the sponge layer thickness, the substructures of the resulting membranes from both solvent groups differed as well. The morphology which was observed directly below the thin sponge-like layer can be distinguished between the different systems, as the cavities in the porous sublayer differ in size and shape in dependence of the applied solvent.

The influences of solvents and additives variations on the membrane morphology are in the following discussed based on selected representative membrane samples. For the whole set of cross-section images refer to Figs. S1–S4 in the supplementary material.

The left half of Fig. 4 depicts the sole influences of the respective solvent on the membrane morphology. The figure shows membrane cross-sections which were prepared without any additives. It was found

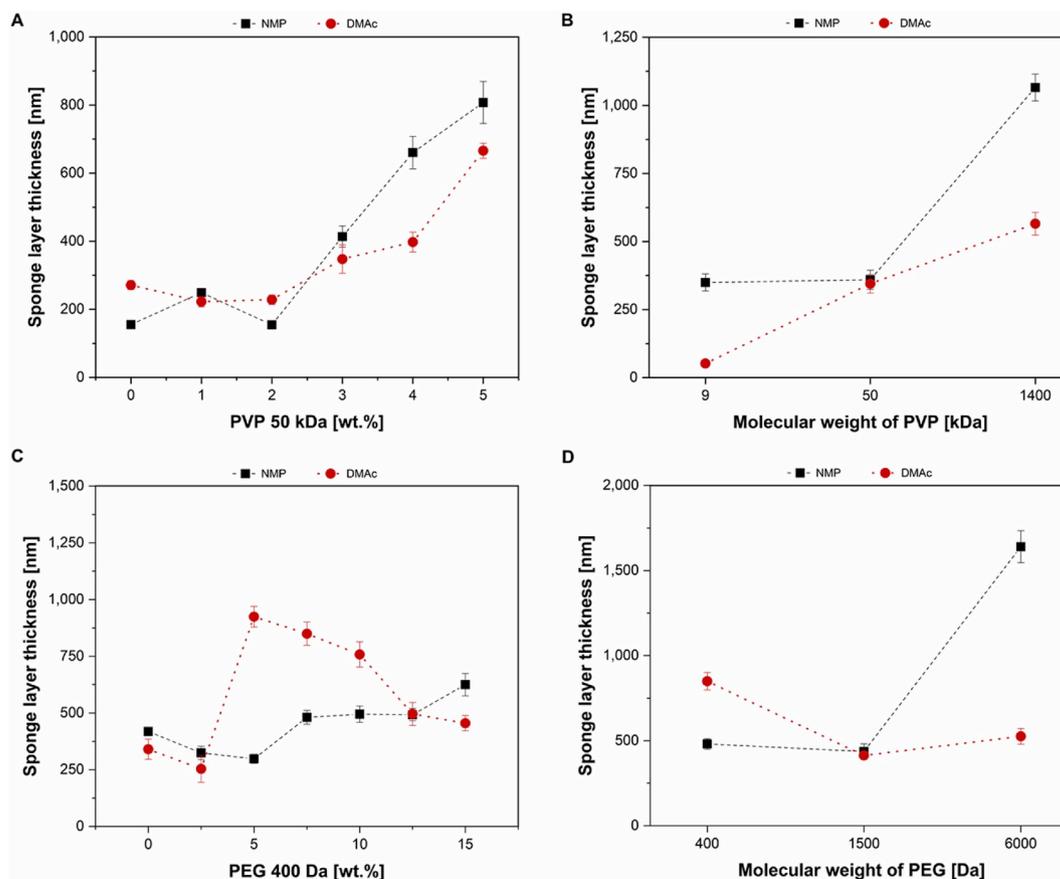


Fig. 2. Average sponge layer thickness \pm standard deviation ($n = 5$) in dependence of the PVP 50 kDa concentration (A), the PVP molecular weight (B), the concentration of PEG 400 Da (C), and the PEG molecular weight (D) of membrane prototypes prepared by immersion precipitation using NMP and DMAc as solvents.

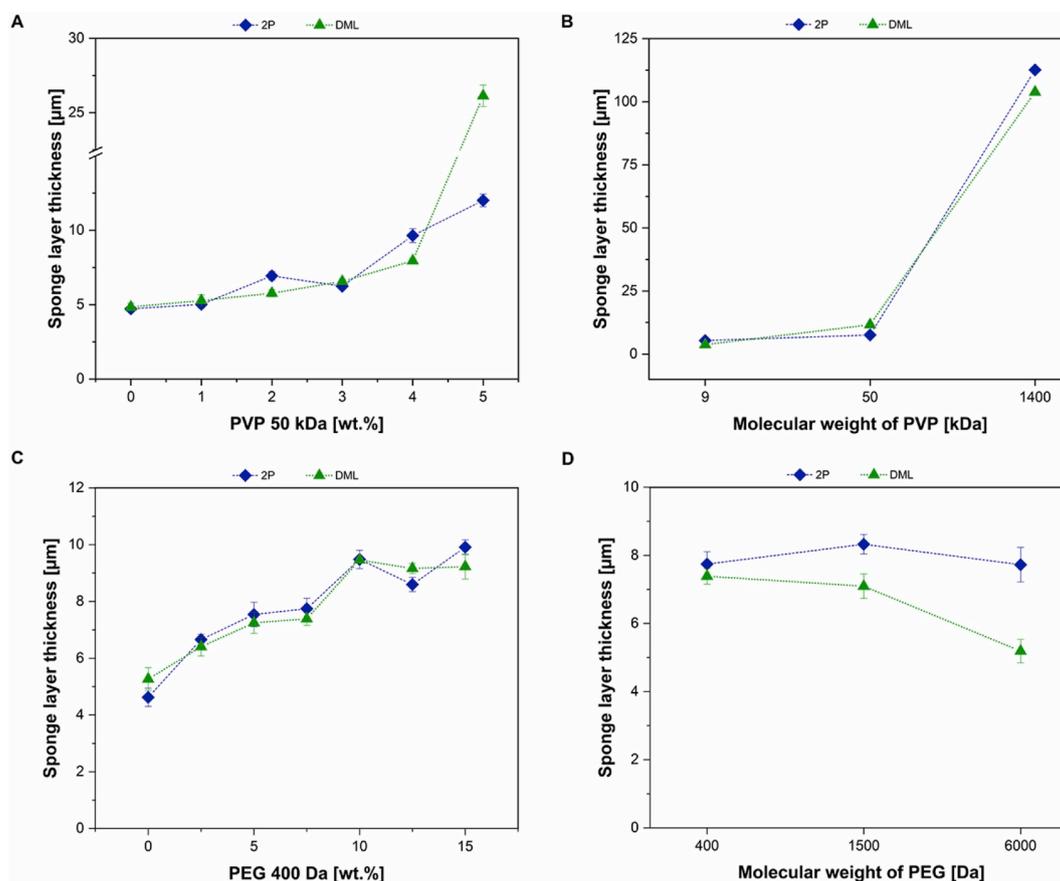


Fig. 3. Average sponge layer thickness \pm standard deviation ($n = 5$) in dependence of the PVP 50 kDa concentration (A), the PVP molecular weight (B), the concentration of PEG 400 Da (C), and the PEG molecular weight (D) of membrane prototypes prepared by immersion precipitation using 2P and DML as solvents.

that if low-viscosity solvents were used for the membrane production, the comparatively thin retentive skin layer is directly followed by a porous sublayer. This sublayer is dominated by a finger-like morphology, which is characterized by narrow, but vertically elongated cavities. Below this layer so-called macrovoids are predominant, which in this case are large and oval-shaped cavities surrounded by sponge-like areas. In contrast to the upper sponge-like layer, this sponge-like morphology can be distinguished by a rather cellular and closed pore structure. In contrast, membranes prepared with solvents having a higher viscosity exhibited a significantly thicker sponge structure on the skin side. In turn, the finger-like structure begins deeper within the membrane cross-section. In addition, contrarily to the case of NMP and DMAc, the voids are smaller in size than the ones which can be found in membranes prepared with conventional solvents. Merely the lower third of the DML cross-section is crossed by a horizontally extended, large cavity. Below this cavity and below the macrovoids in the 2P membrane a sponge-like structure follows, which in comparison to the NMP and DMAc structure is relatively narrow. A reason for this could be that the coalescence of the pore-forming nuclei and the diffusive exchange of solvent and non-solvent are suppressed by the higher dope solution viscosity in case of 2P and DML. As a consequence the growth of the pore-forming domains is slowed down, which consequently results in smaller pore sizes [97]. The results fit those of the performance experiments which are addressed later. It confirms the assumed mechanisms and points out that structure and performance of the membrane are closely related to each other.

As indicated, nucleation and growth is also influenced by the viscosity. The growth of the developing nuclei is dependent on the diffusion rate of the solvent into the nucleus, where higher diffusion allows the formation of larger macrovoids [92,94]. In turn, this causes that the

macrovoids remain smaller at higher viscosities. On top of that, the choice of the solvent is crucial for the demixing speed of the solution, which is known to be a critical influencing factor for the nucleation and growth mechanism. The demixing speed is not only dependent on the diffusion rate but also on the location of the miscibility gap in relation to the location of the solution composition within the phase diagram. In this case it is similar for NMP and DMAc, as well as for 2P and DML, however, both solvent groups differ from each other.

The right part of Fig. 4 representatively expresses the effect of PVP 50 kDa on the morphology when it is added to the casting solution using the highest PVP concentration as example. It was found that the structure in all four solvent systems changed in the presence of PVP, although the behavior again differed between membranes prepared from conventional and alternative solvents. The PVP content in the casting solution strongly affects the thickness of the sponge-like layer. Figs. 2 and 3 show that the layer thickness increased from twofold up to fivefold, depending on the solvent which was used. On one hand this can be attributed to changes in the solution viscosity, which in turn slow down the diffusive processes. On the other hand it can also be attributed to the altered thermodynamics of the system caused by the addition of PVP. The change of the skin thickness can be one reason for a decreasing permeability, which is addressed later. The sponge-like layer significantly contributes to the flow resistance. If the thickness of this layer is considerably increased, it effects the permeability as a consequence of the raise in flux resistance.

In the substructure an increase of the PVP concentration caused an enlargement of the voids, however, at the same time the number of the voids in the substructure decreased. A possible reason for this could be that PVP has a dual effect on the membrane morphology [60]. On one hand it affects the thermodynamic stability of the casting solution,

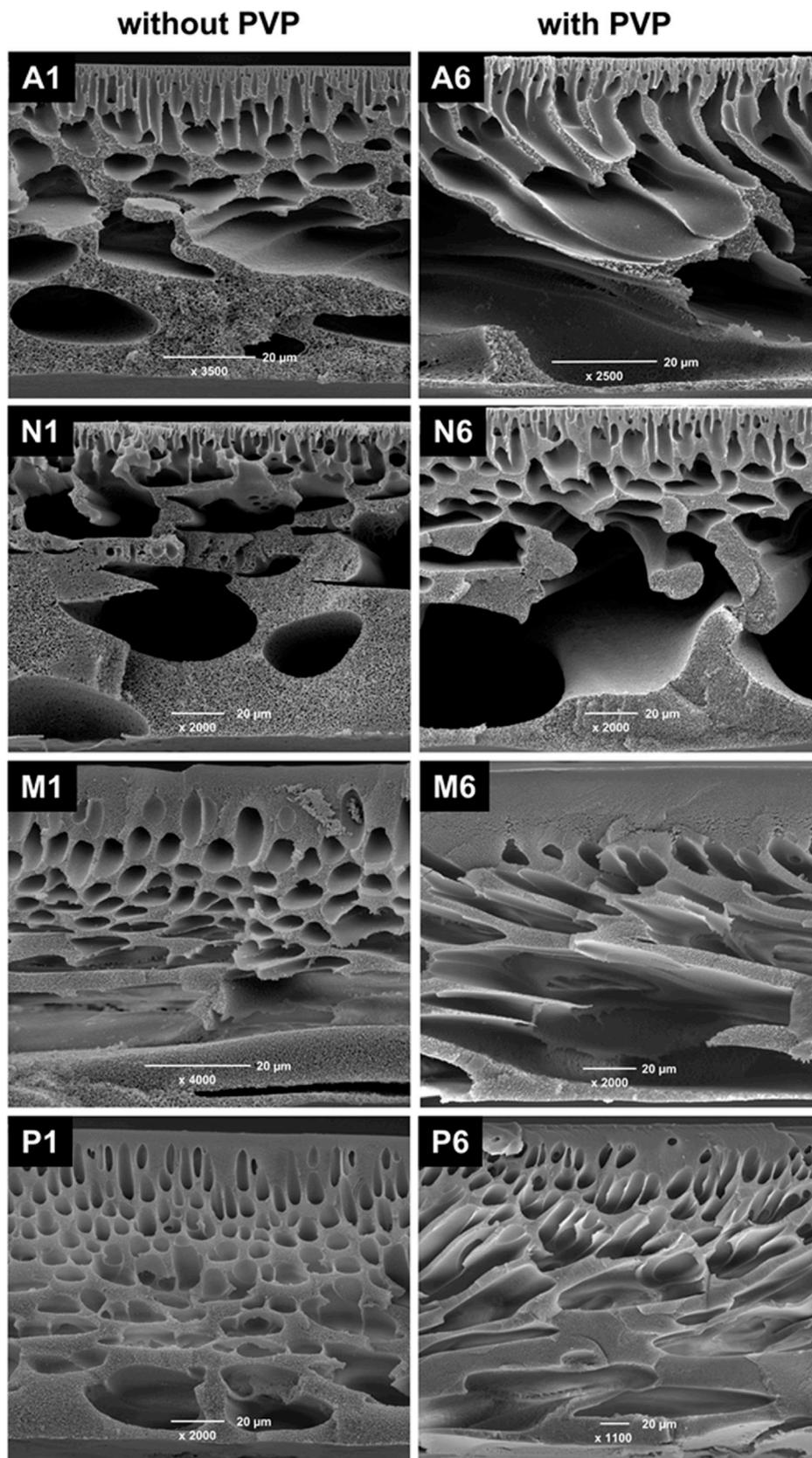


Fig. 4. Scanning electron microscopy cross-section images of membrane prototypes prepared by immersion precipitation with different solvents and without any PVP or with PVP 50 kDa added to the casting solution (image recording potential of 12.5 kV).

which leads to a change in demixing time. On top of that it affects the affinity between the solvent and the forming nuclei, which is responsible for the formation of macrovoids. Therefore, the uptake rate of the solvent by the nuclei is changed. As a consequence the size of the developing macrovoid is altered, since the size of the macrovoid is dependent on the ability of the nuclei to take up the solvent from its surroundings [60,96]. On the other hand the addition of PVP hinders the diffusion speed of the solvent and the non-solvent so that the uptake into the forming nuclei is slowed down. Hence, the resulting macrovoids should be smaller. However, in this case the first effect seems to superimpose so that larger macrovoids were able to form. Yet another reason for the larger sizes of the macrovoids could be that the sponge-like layer acts as a diffusion barrier for the non-solvent to diffuse into the casting film. Therefore, the time which the demixing solution needs to reach the solidification of the structure is prolonged. It has been previously reported that the size of the macrovoids is dependent on vitrification [98]. Therefore, the growth of the nuclei and their coalescence can proceed longer, which finally would lead to larger voids in the membrane substructure.

The membrane morphology is not only influenced by the presence of PVP, but also by the molecular weight of the added PVP. Both, the sponge-layer thickness and the morphology of the substructure are strongly influenced by the PVP molecular weight (Fig. 5).

If the added PVP has a low molecular weight, the sponge-like layer is rather thin. However, the thickness again differed in dependence on the viscosity of the used solvent. With an increase in the PVP molecular weight, the sponge-layer thickness visibly increased. Especially in case of the high viscous solvent systems the sponge-like morphologies occupies almost the complete cross-section of the membrane. This can be explained by the large effect of the PVP molecular weight on the viscosity as shown in Fig. 1. The viscosity raises above a point where the viscosity effect, which hinders the diffusion of solvent into the polymerlean phase, overcomes the effect of PVP on the thermodynamics of the casting solution. Therefore, the growth of the nuclei is prevented and a sponge-like morphology is formed. In contrast, with respect to the proportions of sponge-like and finger-like morphology across the complete cross-section for DMAc and NMP membranes with PVP of 1400 kDa (Fig. 5), a similar structure was observed as for the membranes with PVP of 50 kDa (Fig. 4). The reason for the morphology in the substructure of the membrane with high molecular weight PVP, which is dominated by vertically elongated macrovoids, could be that the point at which the viscosity effect overcomes the effect on the thermodynamic stability of the casting solution has not been reached. Consequently, the difference between conventional and alternative solvent membranes when using high molecular weight PVP is likely due to the different viscosities in dependence of the solvent, which determine the effect that superimposes.

In contrast to the apparent effect of PVP on the membrane morphology, PEG 400 Da has a lower influence on the membrane structure. However, similar to the results found for PVP, the increase of the PEG concentration in the casting solution increased the thickness of the sponge-layer in membranes prepared with NMP, 2P and DML (Figs. 2 and 3). Comparable to the PVP results, the addition of PEG has an effect on the viscosity, however, it is less pronounced than in case of PVP. As the viscosity influences the formation of a sponge-like morphology [98], an increase in the sponge-layer thickness is caused. However, this effect is less obvious than in case of PVP, which can be explained by the comparatively lower increase of the viscosity. Furthermore, PEG slightly influences the thermodynamic stability of the system, which also contributes to the formation of a sponge-like morphology [99,100]. In contrast to the other three solvents, the trend for the concentration row in DMAc was found to be different. Although the skin thickness increased up to a concentration of 5 wt% PEG, with a further elevation of the PEG concentration the sponge layer thickness started to decrease again (Fig. 2). This observation might have several reasons. One explanation could be that the influence of the viscosity in DMAc is

relatively low, especially in contrast to 2P and DML, so that other effects are dominating. Another reason could be that the change in the thermodynamic stability of the solution is different than in the other solution systems. Yet another possible reason for the divergent trend might be the difference in the affinity of the various solvents to PEG. Regarding to the HSP values DMAc has the lowest affinity to PEG, which could be the reason for causing the different behavior in contrast to the other solvents.

Although it has been reported in literature that an increase of the PEG concentration can suppress the formation of macrovoids [100], this could not be confirmed in this study. If comparing the SEM images of membranes without PEG to those made with PEG, no obvious differences in the substructure can be observed (Fig. 6). A reason could be that the influence of the PEG content on the casting solution viscosity is rather low, so that the viscosity effect is not large enough to cause structural changes in the sublayer. Furthermore, the influence of PEG on the thermodynamic stability is in comparison lower than the influence of PVP on the solution thermodynamics, so that the increase of PEG is not sufficient to visibly affect the morphology of the substructure. However, there might be a PEG concentration above the tested 15 wt% at which the effects of the viscosity and the influence on the thermodynamics are high enough to cause any structural changes in the membrane substructure.

Although an increase of the PEG molecular weight affected the thickness of the sponge-layer, no significant changes could be observed in the substructure of the membrane (Fig. 7).

In case of DMAc, 2P and DML membranes the thickness of the sponge-like layer was found to decrease with an increase in the molecular weight of PEG. In contrast, the sponge layer thickness of NMP membranes remained constant when the PEG molecular weight was raised from 400 Da to 1500 Da. However, a further increase of the molecular weight to 6000 Da resulted in an increase of the sponge layer thickness by a factor of about three. The same trend has been previously reported for a system of PSf, PEG and NMP and was explained by the change in the thermodynamic stability of the solution [64]. Furthermore, the use of high molecular weight additives induces an increase in the solution viscosity. This in turn can promote the formation of a sponge-like morphology.

In contrast to the trend observed for NMP membranes, it has been previously reported that the dissolving of PES in DMF or DMAc results in membranes which exhibit an opposite behavior. It has been shown previously that the thickness of the sponge-like structure decreases with a rising PEG molecular weight [14,57], which is similar to the results found in this study for DMAc, 2P and DML membranes. Therefore, the opposing trends seem to be solvent-dependent. One explanation could be that the solvents have different affinities for both, the additives and the non-solvent. Since the affinity between the components contributes to the rate of phase separation, because they influence the thermodynamic stability as well as the exchange rate of solvent and non-solvent, this may be the reason for the observed differences. If the distance values of the HSPs of PEG and the different solvents are compared to each other, the distance value of NMP and PEG is lower in comparison to the distance between PEG and the other three solvents. Furthermore, it has been previously shown that the use of higher molecular weight PEG can shift the phase boundary, which in turn influences the resulting membrane morphology and in particular the formation of a sponge-like morphology [20,99]. Although the PEG molecular weight affected the structure on the skin-side of the membrane, no obvious differences could be observed for the morphology of the substructure. A reason could be that the parameters which influence the sponge layer thickness were not large enough to cause structural changes in the sublayer. Again, the influence of PEG on the thermodynamic stability is rather low in comparison to PVP so that higher molecular weights of PEG might not cause a visible change in the morphology of the substructure.

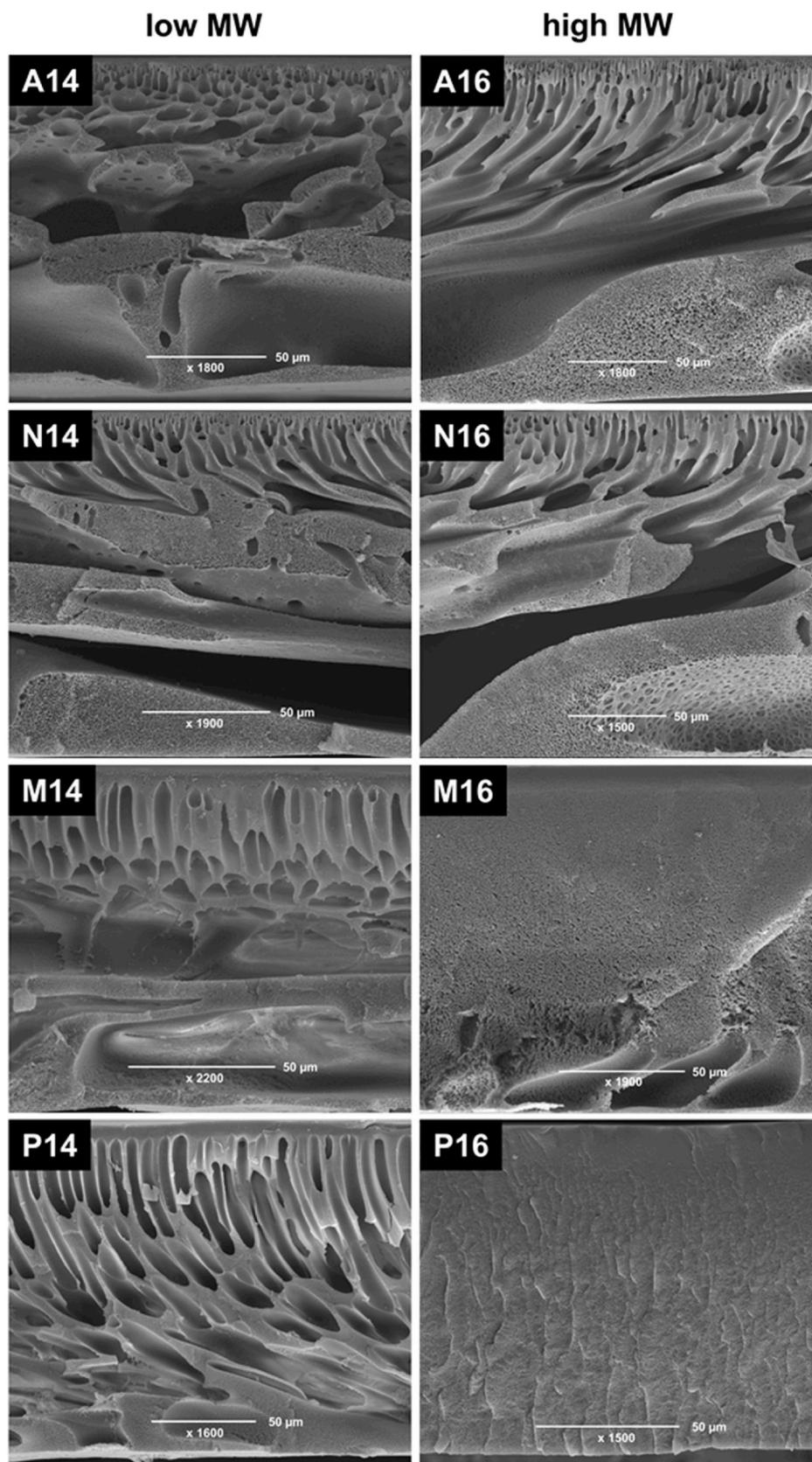


Fig. 5. Scanning electron microscopy cross-section images of membrane prototypes prepared by immersion precipitation with different solvents and PVP of different molecular weights (9 kDa or 1400 kDa) as additives (image recording potential of 12.5 kV).

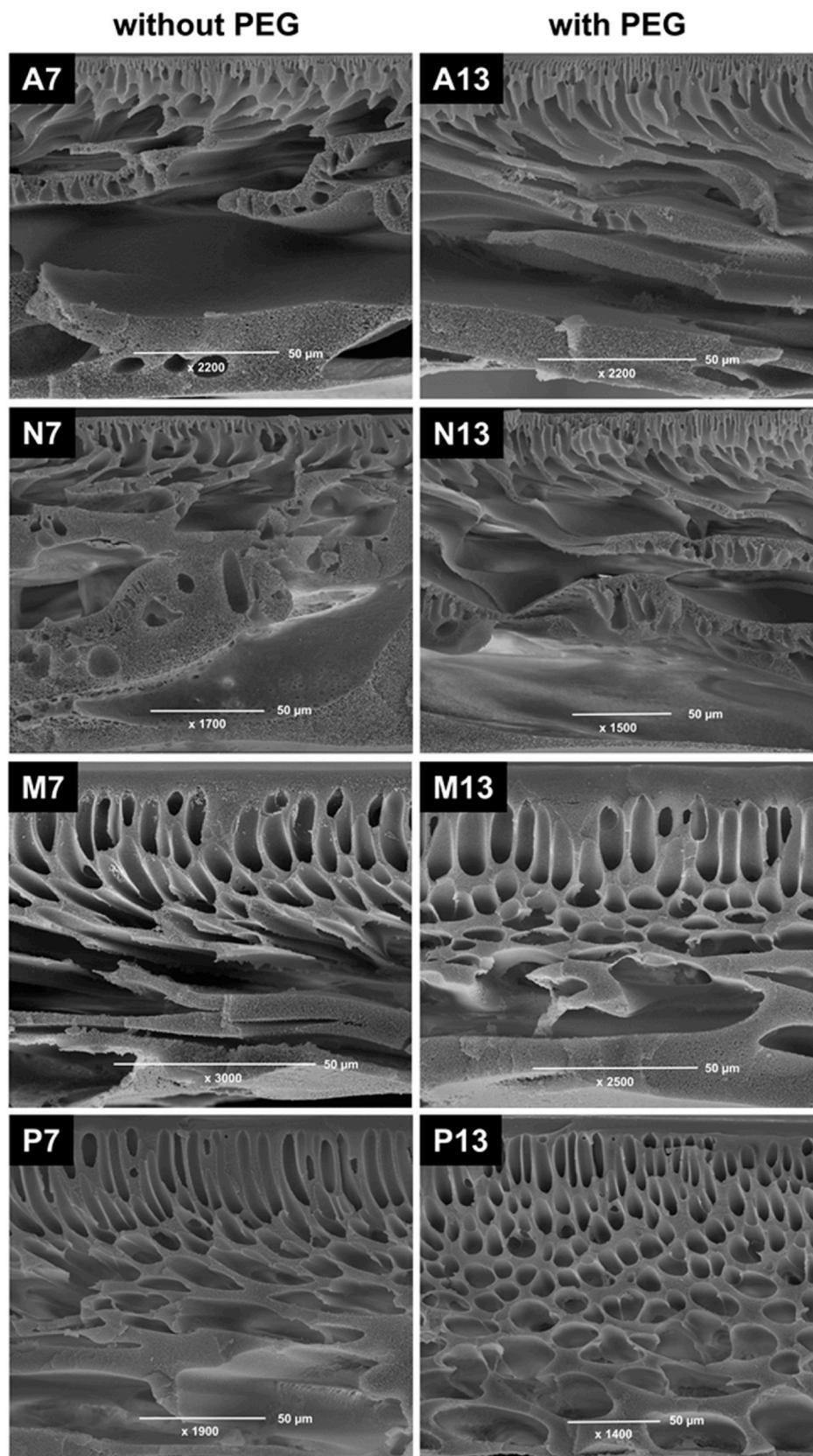


Fig. 6. Scanning electron microscopy cross-section images of membrane prototypes prepared by immersion precipitation with different solvents and without any PEG or with PEG 400 Da added to the casting solution (image recording potential of 12.5 kV).

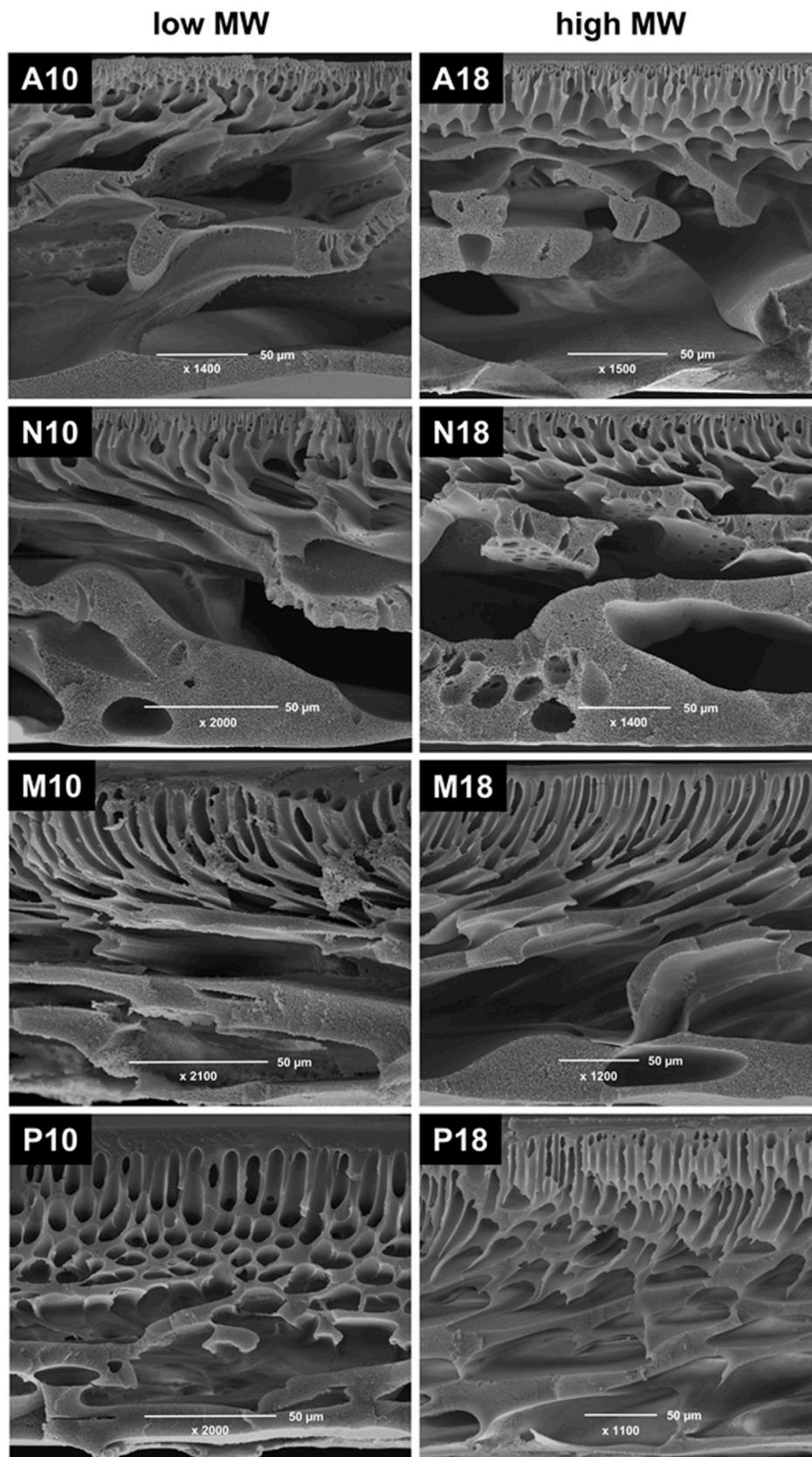


Fig. 7. Scanning electron microscopy cross-section images of membrane prototypes prepared by immersion precipitation with DMA or DML as solvent and PEG of different molecular weights (400 Da or 6000 Da) as additives (image recording potential of 12.5 kV).

3.4. Membrane permeability

It was found that the addition of PVP or PEG to the casting solution had an influence on the membrane permeability and that the observed effect is dependent on the concentration and molecular weight of the additive (Fig. 8).

For varying PVP 50 kDa concentrations in the casting solution the permeability of the manufactured membrane prototypes exhibited two different behaviors in dependence of the applied solvent. If the solvents 2P or DML were used for the preparation of the membrane samples, an increase of the PVP concentration lead to a decrease of the membrane permeability. In contrast, for DMAc and NMP membranes an increase of the PVP content in the casting solution resulted in an increase in the membrane permeability, until a certain concentration was reached. However, as it was also the case for 2P and DML membranes, a further addition of PVP to the solution lead to a reduction of the permeability. This behavior has already been reported in literature [55,60,62]. Anyhow it has been shown that the observed turning point can vary in dependence of the type and the concentration of the membrane-forming polymer which is applied. This is why the reported PVP concentration considerably varies, at which the permeability has its maximum in systems with NMP or DMAc.

The observation of a permeability maximum can be explained by two contrary effects. On one hand PVP acts as a pore-forming agent and can thus lead to an increase in permeability if its concentration is raised. On the other hand the addition of PVP to the solution results in a significant enlargement of the solution viscosity, which has an influence on the formation of the pore structure. During phase separation the pore network develops from the polymer-poor phase. When the solution composition during the NIPS process reaches a composition within the

miscibility gap, the solution separates into areas of polymer-rich phase and droplets of polymer-poor phase. Until the solidification sets in, the liquid polymer-poor phase is able to coalesce so that smaller droplets of this phase converge to larger droplets [101,102]. As a consequence the pores which are formed through these droplets increase in size. Therefore, the faster and the longer the coalescence can take place, the larger the pores will get during the phase separation process. Due to an increasing viscosity e.g. caused by the addition of higher PVP amounts, the coalescence is hindered and the developing pores remain smaller compared to solutions which exhibit a lower viscosity. As the pore size correlates with the membrane permeability, this is also the reason why the viscosity of the casting solution can impact the permeability. If this would be the reason why the permeability decreases, the protein retention should in turn increase due to the smaller pores. However, as this effect could not be observed, it is more likely that the flux decline can be attributed to the formation of a thicker sponge-like layer, which is also promoted by a higher viscosity. As the sponge-like structure contributes more to the flow resistance than a finger-like structure, this would explain why the previously discussed increase in the sponge layer thickness causes a decrease in permeability.

As mentioned, the two described effects of PVP act against each other. At low viscosities, the pore-forming properties of PVP dominate, which is why membranes prepared with DMAc or NMP show an increase in permeability when the concentration of PVP in the casting solution is raised. However, when a critical viscosity range is reached, the effect of PVP on the viscosity and thus on the coalescence overcomes the pore-forming effect. This is why the permeability reaches a maximum before it starts decreasing again. When 2P or DML are used as solvents, the viscosities of the casting solution are above the described critical viscosity, even without additional PVP in the polymer solution. In turn,

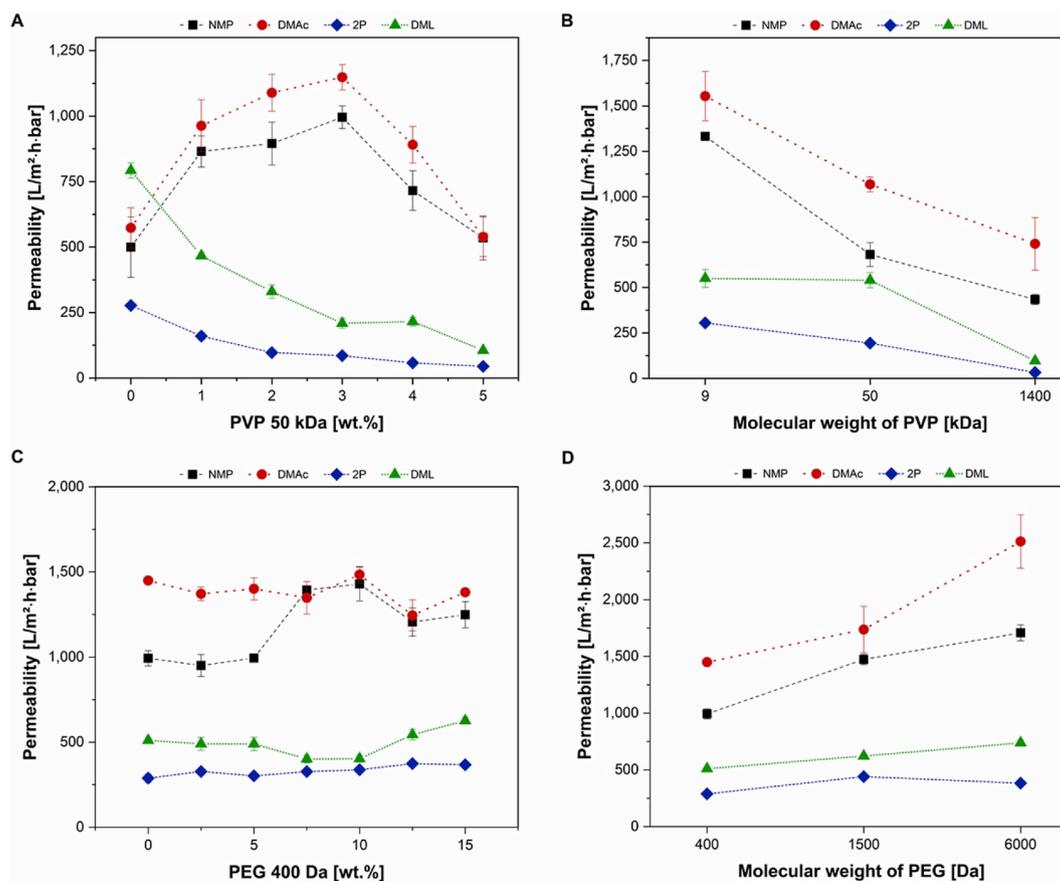


Fig. 8. Average permeability \pm standard deviation ($n = 3$) of a 0.9 wt% sodium chloride solution in dependence of the PVP 50 kDa concentration (A), the PVP molecular weight (B), the concentration of PEG 400 Da (C), and the PEG molecular weight (D) of membrane prototypes prepared in four different solvent systems.

an addition of PVP immediately reduces the permeability of the membrane, since the effect on the coalescence is outweighing the pore-forming impact of PVP immediately.

Apart from the viscosity effects, other influences such as the distribution of the PVP molecules within the polymer-poor and the polymer-rich phase can impact the pore development during phase inversion. It can influence the nucleation and growth mechanism, which has been described as one of the key mechanisms for the formation of polymeric membranes [23,103]. As the distribution is dependent on the location of the miscibility gap, which in turn is strongly influenced by the applied solvent, this could also be a reason for the contrasting behaviors observed for the different solution systems. According to the HSP distance values, which are quite similar for DMAc and NMP, these two substances are better solvents for PES than 2P and DML, which are with respect to the HSPs likewise similar (Table 4). As a consequence, the miscibility gaps of NMP and DMAc are smaller than the ones of 2P and DML [59,90]. This could be confirmed by the cloud point experiments in this study (Table 5). In turn, together with the influence of the differences in viscosity between the two solvents groups, these properties influence the composition of the two phases and therefore the PVP concentration within them.

In contrast to the different trends found in case of varying PVP concentrations, the observed behavior for variations in the PVP molecular weight was the same for all four solvent systems. It was found that the higher the molecular weight of PVP which is added to the casting solution, the lower is the permeability. This can be explained by the impact of the chain length on the viscosity, which strongly affects the formation of macrovoids and the development of a sponge layer, respectively [89,98]. An increase of the chain length of PVP results in an increase of the casting solution viscosity. As a result, the coalescence of the polymer-lean droplets during the membrane formation process is suppressed due to the higher flow resistance in the polymer solution, and the nucleation and growth mechanism is influenced. Consequently the formation of macrovoids is hindered, and in comparison to solutions containing PVP of lower molecular weight thicker sponge-like areas are formed by adding PVP with higher molecular weight, which strongly contribute to the membrane's flow resistance.

In addition to the effects on the solution viscosity, the type of PVP also influences the thermodynamics of the polymeric system. It has previously been shown that the phase diagram and therefore the demixing time can be altered by changing the molecular weight of PVP [89,104]. Furthermore, the composition of the developing phases can be influenced by the PVP molecular weight. For the membrane-forming polymer the low molecular weight polymeric contents primarily tend to remain in the polymer-poor phase, while the higher molecular weight contents primarily stay in the polymer-rich phase and therefore form the matrix of the membrane [105]. Likely, PVP will behave similarly, so that PVP with a higher molecular weight will increase the polymer content in the membrane matrix. This will in turn result in a tighter membrane structure. In contrast, PVP with lower molecular weight is predominantly accumulated in the polymer-poor phase and therefore washed out, so that the membrane matrix in comparison has a lower polymer content. This hypothesis could be confirmed by Matsuyama et al. who showed that the PVP retention factor increases with higher molecular weight [89]. Furthermore, the leaching of short-chained PVP from the membrane matrix is generally higher than the leaching of long-chained PVP [20].

For effects caused by variations of the PEG concentration, a dependence on the applied solvent could be observed. Similarly to the results of the PVP concentration row two different behaviors were found. In case of the low viscosity solvents DMAc and NMP, at low concentrations of PEG within the casting solution the permeability was not significantly influenced compared to membranes prepared without any PEG. However, a maximum for both systems was found in the middle concentration range, after which the permeability started to decrease again when even higher PEG concentrations were applied. A possible explanation for

the observed trend could be an interference of two opposite effects. In the literature, PEG 400 Da is described as a pore-forming agent [106]. The incorporation of PEG into the membrane matrix can lead to higher porosities and larger pores when it subsequently leaches out of the forming structure during the course of the immersion precipitation. This effect will account for the rising permeability at higher PEG concentrations, however a critical concentration is needed to create a visible effect. On the other hand, the addition of PEG increases the casting solution viscosity. Since a higher viscosity leads to a reduction in coalescence of the polymer-poor phase, it ultimately favors the formation of thicker sponge-like layer. Therefore, this effect will account for the decrease in permeability when a certain viscosity is reached, so that the pore-forming characteristics of PEG are compensated. The experimental results indicate that this critical viscosity lies at a value of around 1 Pa·s. For the solvents 2P and DML no visible effect on the permeability could be observed. This can be explained by the higher viscosities of the resulting casting solutions. As described before, the pore-forming characteristics of PEG might be compensated or superimposed by the hindrance of the coalescence at a viscosity of 1 Pa·s or above. When the pore-forming properties that lead to an increase of the permeability are compensated, the rise in flux is missing and the permeability stays at the same level or even decreases. As the use of 2P and DML results in casting solutions exhibiting viscosities already higher than 1 Pa·s, no flux increase could be achieved through a rising PEG concentration.

In contrast to the concentration variations of PEG, changes of the PEG molecular weight caused similar effects in all four solvent systems. It was observed that an increase in the PEG molecular weight induced a raise in permeability. This can be explained by the pore-forming properties of PEG. The concentration for the experiments with different molecular weights was set to 7.5 wt% PEG. Referring to the results of the concentration row, at this concentration the permeability results indicate a pore-forming effect of PEG in NMP and DMAc systems. The higher the molecular weight of the PEG molecule which is applied, the larger is its hydrodynamic diameter. During membrane formation the PEG molecules initially are embedded into the membrane matrix. However, in the course of the process PEG is washed out into the precipitation bath so that pores form at the positions where the PEG molecules were located [20]. Therefore, the larger the molecules are, the bigger will be the pores which result from their leaching.

While the effect for membranes prepared with NMP and DMAc is clearly visible, the effect for membranes prepared with 2P or DML is much less pronounced. As indicated before, a reason for this could be the influence of the viscosity, since it counteracts the pore-forming effect of PEG. As the viscosity of casting solutions prepared with 2P or DML is much higher than the ones prepared with DMAc or NMP, the contrary effect of the viscosity is compensating the pore forming impact of PEG and the permeability is only slightly influenced.

Another reason for the observed trend could be that the use of larger polymeric molecules shifts the position of the casting solution within the phase diagram towards the miscibility gap, as well as the location of the miscibility gap itself [20]. As a result, the path the solution composition follows to reach the heterogeneous two phase region is modified, and consequently the compositions of the developing phases are altered. Since the path into the miscibility gap and the thereof resulting compositions of the two developing phases are crucial for the resulting membrane structure, this in turn can influence the permeability of the resulting membrane.

3.5. Protein retention

The effect of the applied additive variations on the retention of the model protein lysozyme is shown in Fig. 9.

In case of size exclusion based filtration, usually a correlation between the membrane permeability and its retention capacity of the target molecule can be observed. This is based on the dependence of both membrane properties on the pore size distribution of the

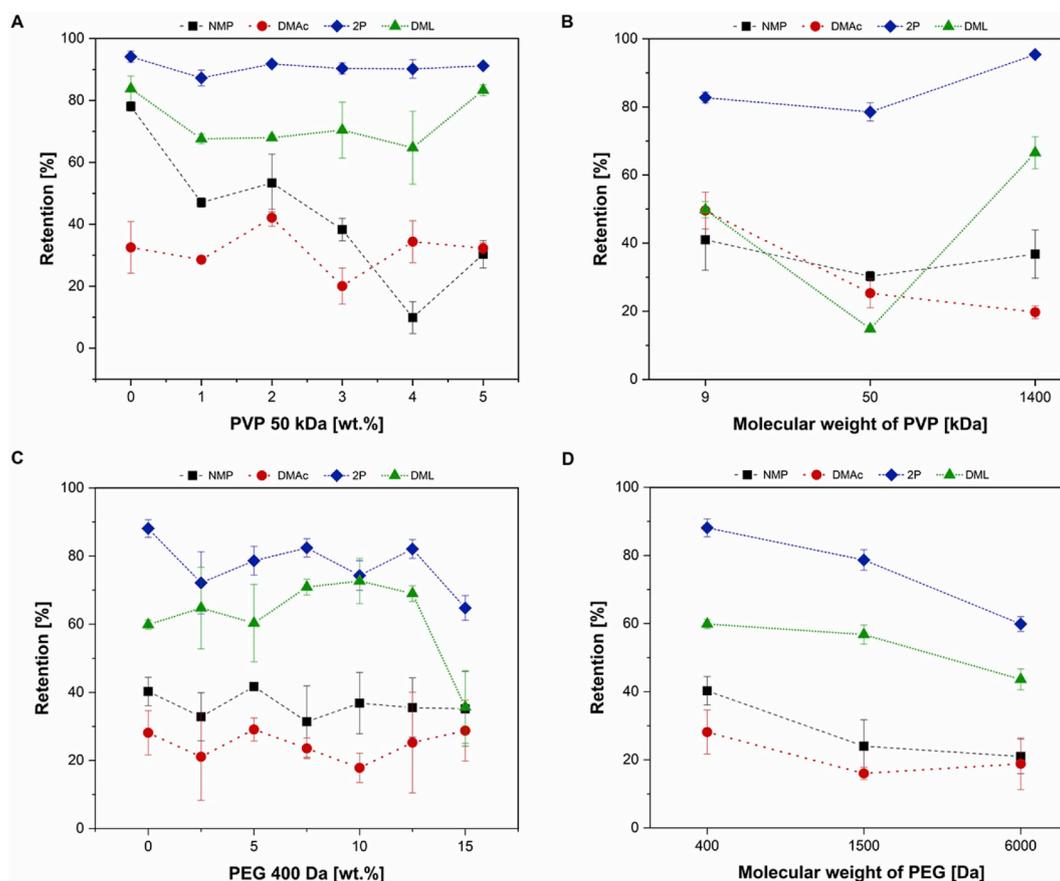


Fig. 9. Average lysozyme retention \pm standard deviation ($n = 3$) in dependence of the PVP 50 kDa concentration (A), the PVP molecular weight (B), the concentration of PEG 400 Da (C), and the PEG molecular weight (D) of membrane prototypes prepared in four different solvent systems, measured with a filtration medium consisting of 1 g/L protein in 20 mM phosphate buffer (pH 7.0).

membrane, its porosity and especially of the pore sizes within the retentive layer [25]. Nevertheless, this correlation can be superimposed by absorptive effects during filtration as well as by influences of the membrane substructure. In case of NMP membranes the correlation between permeability and retention of lysozyme could be observed to some extent. A rising PVP 50 kDa content in the casting solution decreased the retention, while a simultaneous increase in the permeability could be observed. However, at higher PVP concentrations the results deviate from the expected correlation. A reason for this could be that the increase of the hydrophilic PVP molecules in the casting solution, and therefore in the membrane matrix, can reduce the adsorption of lysozyme to the membrane surface. Although the main retention mechanism is size exclusion, the absorption of molecules can significantly contribute to the protein rejection of the filter as the adsorption to the pore walls leads to a net decrease in size of the pore. For DMAc membranes no correlation between permeability and retention could be observed. The lysozyme rejection fluctuated between 20% and 40% with no visible trends in dependence of changes in the PVP concentration. The same could be observed for 2P and DML. Although the permeability decreased with increasing PVP concentration in both cases, the retention was barely influenced. This indicates that the flow resistance of the membrane changes due to structural modifications, whereas the retention is not affected. However, it sticks out that the retention for both used solvent systems, and additionally also in the case of NMP, the retention is slightly higher in the absence of PVP than in its presence. This can be attributed to adsorptive effects. Since PVP should hydrophilize the membrane surface, fewer protein molecules can adhere to the surface through hydrophobic or unspecific interactions. As a result of this the retention tends to decrease. An explanation for the absence of

this influence in the DMAc system could be that the added PVP hardly remains in the membrane structure, but instead is washed out during the precipitation process.

Another sample which stands out is the DML membrane with the highest PVP concentration. At a concentration of 5 wt% PVP 50 kDa the retention increased, which correlates to the decrease in permeability. In this case, the cause could be a saturation of the membrane surface with PVP. As a consequence of this saturation, the retention does not decrease further due to a reduction of the protein absorption to the membrane. In this case size exclusion is almost solely responsible for the particle retention. Since the flux is decreasing as well, this observation is in agreement with the assumption that flux and retention are correlating.

A slight decrease of the lysozyme retention was observed for NMP and DMAc membranes when the molecular weight of PVP was increased. The longer the chains of the PVP molecule, the lower is the leaching of the molecules from the membrane structure during the formation process. If more PVP remains in the membrane structure, and in particular on the surface, the membrane hydrophilicity increases. This results in a decrease of the protein adsorption and since adsorption contributes to the retention, the lysozyme rejection thus decreases.

The effect should also be visible for membranes prepared with more viscous solvents. As expected, initially an increase in the molecular weight from 9 kDa to 50 kDa resulted in a decreased retention. However, when the molecular weight was further raised, the retention significantly increased, which can be attributed to a viscosity effect. If longer PVP chains are applied, the casting solution becomes more viscous. In particular, the addition of PVP 1400 kDa to casting solutions with 2P or DML resulted in a significant increase in viscosity (Fig. 1). As a result of the coalescence of the polymer-poor phase is hindered, the pore sizes in the

retentive layer remain smaller and thus the retention is increasing. In comparison, even in the presence of PVP 1400 kDa the viscosity of NMP and DMAc solutions is significantly lower than the one of 2P and DML so that the coalescence is not considerably effected. In turn, the effect of reduced adsorption superimposes the viscosity effect and the retention does not raise.

For the influence of PEG 400 Da concentration variations on the protein retention no obvious trends could be observed for all four solvent systems. These results agree with the outcomes of the permeability measurements. Although PEG in the literature is described as a hydrophilizing agent [14], no significant effect on the surface hydrophilicity could be observed. If the membrane surface gets more hydrophilic, it is expected that the retention decreases due to reduced adsorption, which in turn contributes to the protein rejection. A reason for the lack of this effect could be that most of the PEG is washed out during the formation process so that the membrane surface is not significantly hydrophilized. Yet, one conspicuous result was found for the highest PEG concentration in 2P and DML. In both cases the retention visibly decreased in comparison to the other applied PEG concentrations. A reason for this could be the reaching of a critical PEG concentration which is necessary to achieve that enough PEG will remain within the membrane matrix to hydrophilize the membrane surface. This could be caused by the increase of the viscosity. If a viscosity is reached that significantly prevents the leaching of PEG from the forming structure, the enrichment of the hydrophilic molecules on the membrane surface could reduce the adsorption of lysozyme molecules to the membrane surface during filtration and thus result in a decreased retention of these molecules.

In contrast, the molecular weight variations showed, that regardless of the solvent system which was applied, an increase of the PEG molecular weight causes a decrease in the retention of lysozyme. These results correlate to the permeability measurements, which showed a permeability increase when the added PEG molecules had higher molecular weights. As described before, the effect on the permeability and thus on the retention capacity can be explained by the removal of the PEG molecules from the membrane matrix during immersion precipitation. This leaching of larger PEG molecules results in the formation of larger pores in comparison to the leaching of smaller PEG chains. On the other hand the effect can result from a shift of the casting solution composition within the phase diagram [20].

3.6. Mechanical stability

In order to gain information about the mechanical stability of the membrane prototypes the bursting pressure was determined. The results of selected membrane samples are summarized in Table 6.

It was found that the PVP 50 kDa concentration has an effect on the mechanical stability. A decrease was observed for the conventional solvents, while membranes prepared with the alternative solvents exhibited higher bursting pressures when the PVP concentration was raised. The different behaviors can be explained by two opposing effects. On one hand the increase of the PVP concentration leads to a higher porosity, which in turn leads to a decrease of the mechanical stability [15]. On the other hand it was found that a higher PVP concentration leads to a thicker sponge-layer, which exhibits a higher mechanical stability than structures containing macrovoids [55]. While the effect on the porosity seems to be superimpose in case of NMP and DMAc membranes, the effect on the sponge-layer thickness seems to dominate in case of 2P and DML membranes. This is why different solvent-dependent trends were found.

In contrast, variations in PVP molecular weight, PEG 400 Da concentration and PEG molecular weight did not cause any significant changes in the mechanical strength. The slight differences can rather be attributed to the experimental error than to an actual effect of the variations.

Table 6

Bursting pressure, water contact angle, unspecific protein binding determined with lysozyme and specific surface area of selected membrane prototypes prepared in DMAc, NMP, DML or 2P and with variations in additive concentrations and molecular weights.

Sample	Bursting pressure [bar]		Water contact angle [°]		Unspecific protein binding [$\mu\text{g}/\text{cm}^2$]		Surface area [m^2/g]
	Average (n = 3)	\pm	Average (n = 3)	\pm	Average (n = 4)	\pm	
A1	0.32	0.005	67.5	2.9	14.2	0.8	19.6
A6	0.18	0.008	60	1.0	16.2	1.1	20.8
N1	0.32	0.050	76.2	1.8	76.2	1.8	19.5
N6	0.18	0.005	63	1.9	63.0	1.9	21.0
M1	0.22	0.031	74.5	0.7	54.3	2.8	39.5
M6	0.39	0.017	63.6	1.2	29.5	2.1	33.0
P1	0.37	0.031	66.8	1.7	53.6	3.6	50.6
P6	0.44	0.024	54.9	6.0	29.2	1.3	44.8
A14	0.28	0.042	62.1	2.3	24.1	1.6	19.4
A16	0.25	0.012	56.2	3.7	21.7	0.8	25.3
N14	0.38	0.033	67	3.4	20.2	1.7	24.4
N16	0.39	0.021	56	1.4	23.2	1.6	21.1
M14	0.26	0.045	54.7	1.7	35.0	2.0	39.5
M16	0.27	0.026	45.4	1.4	30.5	1.6	42.0
P14	0.28	0.009	68.6	1.9	43.9	1.5	49.4
P16	0.37	0.004	47.5	4.8	29.9	2.5	45.2
A7	0.17	0.029	64.6	2.9	19.5	1.2	20.8
A13	0.15	0.033	62.8	3.6	20.0	1.3	28.0
N7	0.20	0.012	57.9	3.5	22.8	1.5	22.2
N13	0.22	0.005	56.3	3.2	28.2	4.6	24.5
M7	0.22	0.012	65.5	4.2	31.5	2.0	58.5
M13	0.22	0.028	66.7	2.3	34.3	0.7	44.1
P7	0.29	0.012	60.9	1.5	43.8	3.5	41.6
P13	0.29	0.017	50	2.9	53.3	1.6	47.8
A10	0.25	0.039	57.2	4.1	22.4	2.1	24.5
A18	0.19	0.034	59.3	1.5	32.9	1.2	15.8
N10	0.25	0.045	60.3	2.5	27.3	4.4	24.7
N18	0.21	0.052	68	1.8	30.9	5.1	22.6
M10	0.25	0.031	61.2	4.5	32.6	2.6	42.1
M18	0.23	0.017	64.8	1.2	47.5	2.0	22.8
P10	0.24	0.012	66.2	2.3	45.5	2.5	52.2
P18	0.29	0.012	63.9	2.1	58.7	0.5	29.9

3.7. Surface characteristics

The surface characteristics were evaluated by measurements of the contact angle, the unspecific protein binding capacity using lysozyme as model protein, and the specific surface area. The results for selected membrane samples are summarized in Table 6.

The higher the hydrophilicity, the lower should be the protein binding to the membrane surface. However, the protein binding is not only influenced by the surface hydrophilicity but also by the surface area of the membrane [107]. This is why both properties were determined, so that all three surface characteristics can be interpreted in dependence of each other.

In general, if comparing the membranes prepared from the different solvents among each other without considering the additive effects, it can be seen that the contact angles lie in the same order of magnitude. However, a difference can be observed in case of protein binding and specific surface area, which correlate with each other, however. In most cases the surface area and therefore the protein binding is lower for membranes prepared with conventional solvents than for those prepared with the alternative ones. The reason for this could be that different structure-forming mechanisms take place in dependence of the applied solvent [5]. The different mechanisms can either result in a closed pore structure with a lower surface area, as observed for NMP and DMAc membranes, or a bicontinuous structure with a higher surface area, as observed for 2P and DML membranes [102].

However, not only the solvent has an impact on the surface characteristics, but also the applied additives. It was found that both, an increase of the PVP 50 kDa concentration and the use of PVP with a higher

molecular weight, lead to a slight decrease of the water contact angle. This increase of the surface hydrophilicity can be explained by the hydrophilic nature of PVP [55]. The more of the hydrophilic additive is used, the more hydrophilic will be the originally hydrophobic surface caused by the hydrophobic nature of PES. The increase of the surface hydrophilicity could not only be confirmed through the water contact angle, but also through the determination of the unspecific protein binding. It was found that an increase of the PVP concentration decreased the lysozyme binding to NMP, DML and 2P membranes. In case of NMP this can mainly be attributed to the hydrophilicity, since the protein binding decreased although the surface area slightly increased. In case of 2P and DML the decreased protein binding is not solely caused by the surface hydrophilicity, but also by the decrease of the surface area. In case of DMAc neither the surface area nor the protein binding was found to change.

When the PVP molecular weight was increased the specific surface was found to increase as well. In turn, more surface is available to which protein molecules can bind. However, the protein binding was found to remain constant when the PVP molecular weight was changed, or it even decreased when PVP 1400 kDa was used. Therefore, these results confirm that a higher molecular weight of PVP results in an increased surface hydrophilicity.

For changes in the PEG 400 Da concentration the effects on the surface characteristics are not straightforward. For membranes prepared with the conventional solvents the surface area slightly increased with raised PEG concentration. A similar effect was observed for 2P membranes. However, in case of DML membranes an opposite behavior was seen. Although PEG is frequently used to increase the membrane surface hydrophilicity [108], it was found that both, the water contact angle and the protein binding, are not significantly affected by a raise in the PEG concentration. The only exception was observed for 2P membranes, where a decrease of the contact angle and a simultaneous increase of the protein binding was observed.

In contrast, an increase of the PEG molecular weight resulted in more definable effects. It was found that the surface area in case of DMAc, DML and 2P membranes is decreasing with increasing PEG molecular weight, whereas the unspecific protein binding was increasing at the same time. This indicates that the surface hydrophobicity is raising when using high molecular weight PEG. A reason for this could be that the share of the hydrophilic part of the PEG molecule in relation to the hydrophobic part of the PEG molecule is changed when the chain length increases.

4. Conclusion

A comparative study was conducted to prove that it is possible to substitute the hazardous solvents NMP and DMAc through the sustainable alternatives 2P and DML. Furthermore this study improves the understanding of polymeric membrane formation by creating a holistic picture of different influencing variables. The impact of the two commonly applied additives PVP and PEG was studied in dependence of the solvent used for the preparation of different PES membranes. In this context, concentrations and molecular weights of the two chosen additives in each of the investigated solvents was varied systematically.

It was found that the viscosity is strongly dependent on the choice of the additive conditions and on the applied solvent. Since the viscosity strongly impacts the demixing process, it determines the properties of the forming membrane. This is why concentration and molecular weight variations of PVP and variations of the PEG molecular weight considerably influenced the water permeability. In contrast, changes in PEG concentration did not exhibit clear effects on the permeability, since the influence of the PEG concentration on the viscosity was found to be smaller. The effects of the variations on the lysozyme retention largely correlated with the influences they had on the permeability. These correlations can be attributed to structural changes. The determination of the sponge layer thickness on the skin-side confirmed this assumption,

as it was influenced by all varied parameters. Since the results regarding the morphology particularly showed correlations to the trends found for the permeabilities, the observed effects on the membrane permeability can be attributed to structural changes of the membrane, which are caused by additives and solvent choice. However, not only membrane morphology and performance are influenced by variations in additives and solvents, but also the mechanical stability as well as the surface characteristics.

The results show that the influences of the additives strongly depend on the applied solvent. The effects of additive variations on polymer solution and membrane characteristics were found for all four solvents systems, however, in general they were more pronounced for 2P and DML membranes. The observed differences can be explained by the respective solvent properties, since mainly the solubility criteria of the solvent and the solution viscosity play an important role.

Thus, 2P and DML are suitable sustainable alternatives for replacing hazardous solvent for PES membrane production. However, the influencing parameters have to be well-controlled to obtain membranes with similar characteristics. This study proved that the use of the appropriate solvent in combination with a suitable choice of the additives enables the production of membranes with desired properties. All in all, this study creates a holistic picture on the membrane formation process which can be applied to create new membrane casting solutions with new sustainable solvents.

Credit author statement

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Declaration of competing interest

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Appendix A. Supplementary data

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