Charged Polyethersulfone Ultrafiltration Membranes

By

Na Li

A dissertation submitted in partial fulfillment of the

requirements for the degree of

Doctor of Philosophy

(Food Science)

at the

UNIVERSITY OF WISCONSIN-MADISON
2021

Date of final oral examination: 12/12/2019

The dissertation is approved by the following members of the Final Oral Committee:

Mark R. Etzel, Professor, Food Science

John A. Lucey, Professor, Food Science

Regina M. Murphy, Professor, Chemical and Biological Engineering

Arnoldo Lopez-Hernandez, Instructor, Food Science

ACKNOWLEDGMENT

First, I would like to express my sincere gratitude to my advisor, Professor Mark Etzel, for his continuous support for my Ph.D study, for his encouragement, his kindness, and his guidance. Professor Etzel cared for me and nurtured the potential he saw me. Because of his wise guidance, I had the direction and support necessary to become an independent researcher and make great progress in my PhD project. I am very grateful for the many hours and efforts he devoted on my research project and my personal development. At the beginning of the PhD program, I was mildly clueless and did not know how to overcome research challenges. I was unsure to create a recipe to make polyethersulfone membranes charged in the lab after many unsuccessful experiments. However, because Professor Etzel reached out to me and built an effective communication bridge between us, I was able to make significant progress. Thanks to his tactful guidance and enormous patience, as a team we created a novel modification method to make PES membranes charged. Professor Etzel also taught me project management skills, such as literature research, design of experiments, experimental data analysis, critical thinking, problem solving and effective communication. My working experience with Professor Etzel was precious and inspiring, and he has given me the confidence to be confident in my skills and ability as an independent scientist. Professor Etzel's positive impact on me is long-lasting, and I cannot repay him for all he had done.

I would also like to thank the rest of my thesis committee: Professor John Lucey, Professor Regina Murphy, and Dr. Lopez-Hernandez for their insightful comments and encouragement. Professor Lucey provided open-ended questions and thoughtful feedback, from an industrial perspective, in an industrial aspect for potential applications of charged PES membranes. Professor Murphy gave input on the modification method mechanism used to make charged PES membrane and the related experimental designs. Dr. Lopez-Hernandez emphasized the assumptions I made in experimental design and gave me a lot of emotional supports.

The discovery of the modification method was possible because I stood on the shoulder of giants. I would like to thank Professor Mark R Etzel at UW-Madison and Professor Andrew Zydney at Pennsylvania State University for their excellent work in membrane science and Professor Charles Hansen for his creation of Hansen solubility parameters. My special thanks goes to Dr. Abhiram Arunkumar, a former labmate, for his excellent work in the development of a mass model of a one-stage ultrafiltration membrane system and for his encouragement through text messages and phone calls.

I would like to acknowledge Mike Molitor and Mellisa Houfe of the Center for Dairy Research for their collaboration on pilot plant scale-up experiments. Mike enthusiastically introduced to me the WPC manufacturing process and ultrafiltration applications in the dairy industry and he helped me with materials and system set up. Mellisa Houfe assisted in the 3.8-inch scale-up experiment. I also thank the biochemistry department for the unconditional access to the TYPHOON scanner and Wisconsin Centers for Nanoscale Technology for the access to FTIR spectroscopy and SEM Zeiss. My sincere thanks also goes

to my peers and the staff in Babcock hall: including but not limited to Tamala Noll, Marcia Verhage, Kathy Pool, Theresa Pillar, Dr. Daiki Murayama, Marielle Kouassi, Dr. Ruisong Pei, Dr. Nilushni Sivapragasm Sivaparan, Byran Lee, Dr. Jiayang Jin, Dr. Katherine Payne, Erin Aversa, Claire Collins and Cameron Wicks.

During my stay in Madison, I met a lot of good-hearted people all around the world: from Japan, France, India, Sri Lanka, Korea, Philippines, Malaysia, Singapore and Mexico and many other countries. I appreciated the multicultural environment and the diversity embraced by UW-Madison. I also enjoyed all the small and big conversations with people coming from different cultural backgrounds and all the kindness they had offered. I had an amazing experience learning English thanks to International Friendship Center of Madison.

Last but not the least, I would like to thank my parents and my husband for supporting me spiritually throughout my Ph.D. program and my life in general. I appreciate the encouragement and freedom given by my parents. My husband, Ze, has been a perfect companion to me during this long and arduous Ph.D. Journey. Having him in my life completes and fulfills every part of me.

ABSTRACT

Polyethersulfone (PES) ultrafiltration membranes of 5-10 kDa molecular weight cut off (MWCO) are widely used for cheese whey concentration, but these tight membranes are slow to filter whey through the membrane. Although membranes having a larger MWCO speed filtration, more proteins leak through the wider pore of the membrane. By placing an ionic charge on the surface of the wide pore membrane, proteins of like charge are rejected by electrostatic repulsion rather than size-based filtration and prevent protein leakage. In the present work, a new method is described that places charges on the surface of a finished PES ultrafiltration membrane by passing an incubation solution through the membrane. The incubation solution contains an organic solvent, water, and a charged polymer. The proposed mechanism is that the organic solvent swells the membrane allowing diffusion of the charged polymer into the membrane and removal of the organic solvent un-swells the membrane trapping the charged polymer in the membrane. The Hansen solubility parameter distance (Ra) predicts swelling of a polymer in a solvent. It was found that solvent-water blends having Ra values of 19.9 to 23.9 $MPa^{1/2}$ work best to swell the membrane and facilitate the diffusion transfer of the charged polymer. It was also found that a charged polymer having a phenyl ring had a greater thermodynamic affinity for the PES membrane polymer than for the solvent blend. This affinity provided a thermodynamic driving force for diffusion transfer of the charged polymer. Negatively charged polymers, such as polystyrenesulfonate and hydrolyzed styrene-maleic anhydride,

and positively charged polymers, such as styrene-maleic anhydride imide and poly(diallyldimethylammonium chloride), were used to make charged membranes successfully. Scale-up experiments from disc membranes to spiral-wound membranes were successful, resulting in a 1,500x increase in membrane area, and a transition from a dead-end to a crossflow mode of operation. A 200 kDa MWCO negatively charged spiral-wound membrane increased protein retention by 34% compared to a 10 kDa uncharged spiral-wound membrane, and at twice the whey filtration flux. This work benefits the dairy industry because high speed charged membranes use less energy, reduce protein losses, and lower the cost of manufacture of dairy protein ingredients.

TABLE OF CONTENTS

ABBREVIATIONS

ALA	Alpha-lactalbumin
BLG	Beta-lactoglobulin
DMF	Dimethylformamide
HSP	Hansen solubility parameter
L_p	Hydraulic permeability
MSP	Milk serum permeate
MWCO	Molecular weight cut off
NPN	Non-protein nitrogen
PDADMAC	Poly(diallyldimethylammonium chloride)
PES	Polyethersulfone
PSS	Poly(4-styrenesulfonic acid)
PVP	Polyvinyl pyrrolidone
PVSA	Poly(vinylsulfonic acid, sodium salt)
Ra	Hansen solubility parameter distance
SMA	Styrene-maleic anhydride
SMAH	Hydrolyzed styrene-maleic anhydride
SMAI	Styrene-maleic anhydride imide
S_o	Sieving coefficient
TS	Total solids
WPI	Whey protein isolate

Chapter 1 Literature review

1.1 Background and motivation

The whey is a by-product of making cheese. About 9 pounds of whey is generated for every pound of cheese manufactured, and a large cheesemaking plant can produce over 1 million liters of whey daily (Smith, 2008). As whey is generated, about 50% of milk solids appear in the whey, together with 20% of the milk protein and 90-100% of the lactose (Smithers, 2008). Before the late of 20th century, whey was not valued. Whey was returned to farms as pig feed or spread on farm fields. In the 1970s, concentration of whey protein from whey using ultrafiltration membranes transformed this waste by-product into a valuable product. In the manufacturing process of whey protein concentration, whey obtained from cheese makers was first centrifuged to remove whey cream (lipids) and cheese fines, pasteurized to kill bacteria, ultrafiltered or diafiltered to remove water and other small molecules, and then spray dried to produce whey protein concentrate (WPC) powder.

Ultrafiltration is an essential step in WPC manufacture. Sweet whey contains: water (93.5%), lactose (4.5 -5.0%) and protein (0.6%) after lipid removal (Zydney, 1998). The purpose of ultrafiltration and diafiltration is to increase the protein-to-dry-solids content from about 12 % to 34 % (WPC 34) and 80 % (WPC 80) by removing lactose and other small molecules while retaining proteins. Polyethersulfone (PES) membranes of molecular

weight cut off (MWCO) 5-10 kDa are widely used for ultrafiltration of whey (Ganju & Gogate, 2017; Rabiller-Baudry, Bégoin, Delaunay, Paugam, & Chaufer, 2008; Tang, Flint, Bennett, & Brooks, 2010). The problem with these membranes is the long processing time to pass the whey through the membrane at a low permeate flux of about 12 $L/m^2/h$ (LMH). Although a membrane with a larger MWCO would speed the filtration process, it would not beneficial to use it to replace the 5-10 kDa PES membrane because more protein would leak through the membrane. However, placing an ionic charge on the surface of a membrane having a larger MWCO solves this problem (Arunkumar & Etzel, 2015). The membrane having a larger MWCO allows whey to pass through faster. The membrane having charged groups on the surface that are alike to the protein might reject proteins by electrostatic repulsion. Thus, wide pore ionically charged membranes achieve both high filtration speed and high protein retention.

For example, the predominant whey proteins are alpha-lactalbumin (ALA) and beta-lactoglobulin (BLG). The molecular masses and isoelectric points (pI) are 14.4 kDa and pI 4.4 for ALA, 18.4 kDa and pI 5.2 for BLG. Based on size alone, these proteins would pass through an uncharged 300 kDa membrane. However, proteins carry a net negative charge when the pH is more than the pI. By adjusting the pH of whey to 6.8, the whey proteins carry a net negative charge and might be rejected by a negatively charged 300 kDa membrane. As a result, a wide pore ionically charged membranes might replace the tight 10 kDa PES membrane and achieve the same protein retention but at a greater filtration speed.

PES membranes are widely used in the dairy industry to concentrate proteins in milk and whey. PES consists of repeating phenyl groups connected to alternating sulfone groups by ether linkages (Figure 1.1). Due to its chemical structure, PES membranes have the unique properties of outstanding resistance to oxidative, thermal, mechanical, and hydrolytic attack (Zhao, Xue, Ran, & Sun, 2013). Resistance to chemical attack is important because hot caustic and acid solutions that contain the strong oxidizer chlorine are commonly used as daily cleaners and sanitizers of the membrane after use. However, the chemical resistance of PES also makes it difficult to chemically modify to contain an ionic charge. The goal of the present study was to modify wide-pore, high MWCO PES membranes to create ionically charged PES membranes that simultaneously provide a high permeate flux and a high protein recovery.

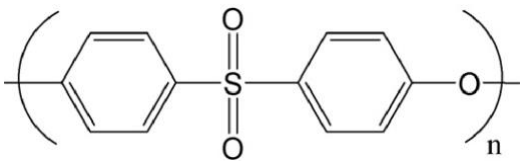

Figure 1.1 Chemical structure of polyethersulfone (PES).

1.2 Short history of membrane processes

There are a number of thorough reviews of the history of membrane science (Lonsdale, 1982; Strathmann, Giorno, & Drioli, 2011; Tamime, 2012). The following is a selection of some important events related to modern membrane technology and serves as a mini review of the history of membrane processes. The membrane process of separating

water from solutes has been known since 1748, when the French Catholic priest and physicist, Jean Antoine Nollet, discovered that a pig's bladder passes preferentially alcohol into water (Nollet, 1752). Nollet was the first to describe this phenomenon as osmosis. During the following century, membranes of animal (bladder) and plant (onion) origin were used primarily for laboratory applications. In 1855, Fick produced the first synthetic membranes formed from collodion and used these membranes to formulate his law of diffusion (Fick, 1855). Bechhold further developed methods for controlling pore size and measuring pore diameters in 1907, which allowed manufacturing of collodion membranes (Bechhold, 1908). He is generally credited for the first use of the term ultrafiltration (UF). In 1922, Zsigmondy patented a membrane filter as an ultrafilter to separate fine particles from an aqueous solution. Based on this patent, Sartorius GmbH commercially produced collodion membranes with various pore sizes in 1927. The primary use of these membranes was in research until the 1950, when the practical use of membranes became a focus of interest. A breakthrough in membrane science was the development of reverse osmosis membranes made of cellulose acetate by Sidney and Srinivasa in the early 1960s (Sidney & Srinivasa, 1964). The membrane developed by Sidney and Srinivasa provided enough salt rejection, water flux, and defect free area to desalinate seawater. The preparation of asymmetric cellulose acetate membranes by Sidney and Srinivasa was by a phase inversion process in which a polymer was precipitated in a controlled way from a liquid phase to solid phase by addition of an anti-solvent. Advances in polymer chemistry also led to the use of other polymers for the preparation of new membranes with improved mechanical strength and chemical and thermal stability, such as polyamides, polysulfone,

polyethylene, polyethersulfone. Membranes made from inorganic materials, known as ceramic membranes, became commercially available in the mid-1980s and offered further improved chemical and thermal stability. Membrane modules also expanded from plate-and-frame and shell-and-tube geometries to spiral-wound and hollow-fiber and stacked-sheet geometries. A wide variety of membrane materials and geometric configurations and membrane operating systems were generated for different commercial applications in this time period.

Most of the industrial developments of membrane technology in the food industry originated in the dairy industry (Bhattacharya, 2014). The pioneering use of membrane technology in the dairy industry was the concentration of whey proteins from cheese whey in the 1970s (Short, 1995; Zeman & Zydney, 1996) . The use of ultrafiltration for the production of whey protein concentrates grew rapidly, followed by applications of membrane technology in milk processing and cheese manufacturing. Nowadays, applications in the food industry account for 20% to 30% of the total production of membranes worldwide (Kotsanopoulos & Arvanitoyannis, 2015). The food industry is now the second biggest industrial market for membrane technology, and the major applications in the food industry are in the dairy industry (Kumar et al., 2013; Lipnizki, 2010).

1.3 Types of membrane separations

A membrane can be considered as a thin selective barrier between two phases (Howell, Sanchez, & Field, 2012). Certain components pass through the membrane under a driving force such as an applied pressure or an osmotic pressure. The majority of

commercial membranes are made from polymers, and polyethersulfone is one of the most common polymers used for production of commercial ultrafiltration and microfiltration membranes (Pinnau & Freeman, 2000). In a membrane filtration process, certain components in a feed stream are passed through the membrane into a permeate stream, while others are retained by the membrane forming a retentate stream (Zeman & Zydney, 1996). In common practice, a membrane is typically described by its pore size or nominal molecular weight cut-off (MWCO). MWCO of a membrane is defined as the molecular weight in Daltons of a solute that is 90% retained by the membrane (van Reis & Zydney, 2007).

Based on the membrane MWCO, pressure driven membrane filtration processes are classified into four main categories: reverse osmosis (RO), nanofiltration (NF), ultrafiltration (UF), and microfiltration (MF). The four membrane processes differ in their pore size and components that they retain. RO is a pressure-driven membrane filtration process that allows passage of water molecules but not the majority of dissolved solutes. RO membranes retain solutes having a molecular mass below 1 kDa. NF membranes have a slightly more open structure allowing water and monovalent ions to pass through the membrane while rejecting divalent ions and other larger solutes. NF membranes retain solutes having a molecular mass of 1 to 3 kDa. UF membrane pore sizes range from 1 nm to 100 nm and retain solutes having a molecular mass of 3 to 500 kDa. UF membranes were designed to retain proteins, colloids, viruses and other macromolecules. MF membranes retain particles in the range of 0.1 μm to 10 μm such as bacteria or fat droplets. The pore size ratings of MF membranes have been developed historically based on performance in

sterile filtration (Zeman & Zydney, 1996). The length of the rejected particles is often used for the pore size rating of a MF membrane, while MWCO is used to rate UF membranes.

1.4 Membrane structure and membrane fabrication

A membrane is a thin barrier that selectively permeates different solutes at different rates. Membranes either have a symmetric or an asymmetric structure (Pinnau & Freeman, 2000). Symmetric membranes have a uniform structure at all depths within the barrier layer, while asymmetric membranes consist of two or more structural layers of non-identical morphologies (Koros, Ma, & Shimidzu, 1996). The separation properties of symmetric membranes are determined by the entire barrier structure, but for asymmetric membranes the densest portion of the barrier layer, often the top layer, determines the separation properties.

Many asymmetric membranes are made of at least three layers (Rabiller-Baudry, Gouttefangeas, Le Lannic, & Rabiller, 2012). First, a top layer directly in contact with the feed liquid is commonly called the active or selective layer. The active layer determines the selectivity of the membrane. The material used for the active layer is either hydrophilic (polyvinyl alcohol, polyvinyl pyrrolidone, polyacrylamide, regenerated cellulose) or hydrophobic (polyethersulfone, polysulfone, polyvinylidene fluoride). Second, an intermediate layer often made of polysulfone or sometimes polyethersulfone. Third, a bottom layer, a macro-porous support material often made of nonwoven polyester. The support layer gives mechanical strength to the multilayer membrane structure. For PES

membranes, the active and intermediate layers are made using the phase inversion process.

Phase inversion via immersion precipitation is the most widespread technology for manufacturing polymeric membranes (Zeman & Zydney, 1996). A thin layer of the membrane polymer dissolved in an appropriate organic solvent is cast onto a suitable support and then submerged in a coagulation bath of non-solvent. Due to an exchange of solvent and non-solvent, the membrane is formed on the support. Figure 1.2 shows the possible pathways of membrane formation during the phase inversion process in a schematic ternary phase triangle. There are two immiscibility processes happening during the phase separation: liquid-liquid phase separation and gelation. In liquid-liquid phase separation, the solution separates into two liquid equilibrium phases by nucleation and growth of droplets of the second phase (Wijmans, Baaij, & Smolders, 1983). The porous sub-layer is the result of this phase separation. The active layer at the top is formed by gelation.

According to Wijmans and Smolders (1983), immediately after immersion in a bath containing a non-solvent, there is a rapid extraction of the organic solvent from the polymeric film and relatively small penetration of non-solvent into the polymeric film. The polymer concentration at the film-bath interface increases and the gel boundary is crossed (path “a” in Figure 1.2). This forms a thin and dense gel layer called the active layer. Beneath the active layer, the polymer concentration is lower, and the non-solvent concentration is higher, and liquid-liquid phase separation occurs (path “b” in Figure 1.2). This forms the porous sub-layer. The final membrane structure and its properties are

influenced by the composition of the polymer solution (polymer concentration, solvent, additive), the thickness of the cast polymer film, the non-solvent in the coagulation bath, the processing temperature and air moisture content, and the support material (Barth, Goncalves, Pires, Roeder, & Wolf, 2000; Pinnau & Freeman, 2000).

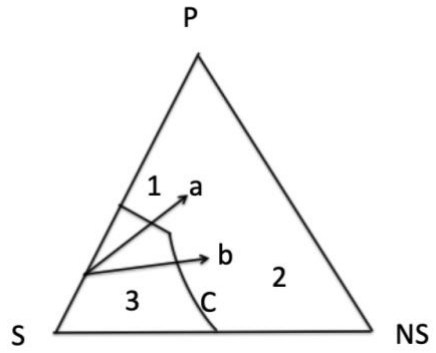

Figure 1.2 Schematic ternary phase triangle; P: polymer; S solvent; NS: non-solvent; C: critical phase separation boundary; 1: gelation region; 2: liquid-liquid phase separation region; 3: homogeneous solution region (adapted from Wijmans, Baaij, & Smolders, 1983).

A PES membrane made by the phase inversion process typically uses one of the following organic solvents: dimethylformamide (DMF), N-methyl-2-pyrrolidone (NMP), or dimethylacetamide (DMAc), and water as the non-solvent (Barth et al., 2000; Madaeni & Rahimpour, 2005; Pinnau & Freeman, 2000; Xu & Qusay, 2004; L. Zeman & Tkacik, 1988). DMF is one of the solvents widely used in the preparation of phase inversion PES membrane (Arthanareeswaran & Starov, 2011). Water is the most preferred non-solvent

for preparation of phase inversion membrane because it is nontoxic and nonflammable (Koros & Pinnau, 1994). To make a PES membrane, a homogenous solution of the PES polymer dissolved in an organic solvent, such as DMF, is prepared and coated onto the support layer. The coated web is then immersed in the coagulation bath of pure water to form the active layer and the porous sub-layer. Madaeni and Rahimpour (2005) investigated the effect of type of solvent and non-solvent on the morphology and performance of PES ultrafiltration membranes. The casting solution comprised of the PES polymer (58 kDa) and polyvinylpyrrolidone (PVP), as a pore forming additive, were dissolved in one of the commonly used solvents, including DMF, DMAc, and NMP. The non-solvents were water, 2-butanol, a mixture of water and 2-butanol, a mixture of water and 2-propanol, and a mixture of water and 1-butanol. They found that the main factor affecting the membrane structure was the solubility parameter difference between solvents and non-solvents. When DMAc was used as solvent in the polymer solution, the porosity of the membrane (pore area percentage on a cross-sectional micrograph of the membrane, including both upper dense layer and lower finger-like porous layer), was 88% for PES. The porosity was 84% using NMP and 80% using DMF. The solubility parameter difference was highest between DMF and the non-solvents tested, which means there was a lower miscibility between DMF and the non-solvent than for the other organic solvents. When the solvent and non-solvent were less miscible, the non-solvent diffused into the polymer film more slowly resulting in a delay in the phase separation of PES from the casting solution. This delay in phase separation is often associated with the formation of a denser top layer and lower porosity of the membrane. Changing the non-solvent lead to a change in the

solubility parameter difference between the solvent and the non-solvent causing a change in the porosity of PES membrane. For example, pure water had a larger solubility parameter difference for DMAc than the mixture of 50% 2-butanol in water. When the mixture of 50% 2-butanol in water was replaced with pure water as a non-solvent, the porosity of PES membrane decreased 4%.

To enhance the phase inversion method, an pore forming additive, such as PVP or polyethyleneglycol (PEG), has been used frequently in membrane fabrication for improved membrane pore structure (Amirilargani, Saljoughi, Mohammadi, & Moghbeli, 2010; Lafreniere, Talbot, Matsuura, & Sourirajan, 1987; Torres, Soriano, De Abajo, & dela Campa, 1993; Xu & Qusay, 2004). Amirilargani et al. (2010) studied the effect of PVP concentration as the pore former on the morphology and performance of PES membranes. It was found that increasing the PVP concentration from 1 wt.% to 9 wt. % in the PES/ethanol/NMP casting solution caused the fingerlike sub-layer of the membranes to have more large macro-voids. PVP is a hydrophilic additive that has a low affinity for NMP and PES in the casting solution, so it facilitated de-mixing in the coagulation bath, forming macro-voids in the membrane structure. Water flux of the modified PES membrane was increased significantly by increasing the PVP concentration from 0 to 1%, 3% or 6%. Malek, Seman Johnson and Hilal (2012) investigated the effect of PVP concentration on the performance of PES membranes. A PVP concentration from 5 wt.% to 25wt.% was added to the PES/NMP casting solution at a PES concentration of 15 wt.% or 20 wt.%. The permeability of pure water for the membranes was found to increase by 0% to 15% with increasing PVP concentration. When the PVP concentration was further increased by 15% to 20%, the

permeability of pure water decreased. Further addition of PVP above 15% led to an increase in viscosity of the casting solution actually slowing down the exchange rate of the solvent and the non-solvent during phase separation process in a water coagulation bath. This delay in de-mixing led to formation of a denser structure decreasing the water permeability.

1.5 Water and protein permeation through the membrane

1.5.1 Water permeation

The transport of water through membrane is a well-studied problem. The membrane is assumed to be a parallel array of uniform cylindrical pores. The filtration velocity, V, through a cylindrical pore is equal to:

$$V = \frac{r^2 \Delta P_{TM}}{8\mu\delta_m} \tag{1.1}$$

where ΔP_{TM} is trans-membrane pressure difference, r is pore radius, μ is solvent viscosity and δ_m is the thickness of the active layer (Zeman & Zydney, 1996). The filtration velocity (V) has units of m/s. The flux of clean water through an ultrafiltration membrane is given by hydraulic permeability, L_p:

$$L_p = \frac{J_v}{\Delta P_{TM}} = \frac{\varepsilon r^2}{8\mu\delta_m} \tag{1.2}$$

where J_v is the volumetric filtrate flux (volumetric flow rate per unit area of membrane), which is equal to εV where ε is the membrane porosity or pore area per unit membrane

area. L_p has units of LMH/bar. The membrane porosity (ε) is the fractional area occupied by the cylindrical pores given by:

$$\varepsilon = \frac{n\pi r^2}{A} \tag{1.3}$$

where n is the number of pores and A is the membrane area. Substituting Equation 1.3 to equation 1.2, the hydraulic permeability is given by:

$$L_p = \frac{n\pi r^4}{8A\mu\delta_m} \tag{1.4}$$

According to Equation 1.4, L_p increases with increasing pore radius to the fourth power and decreases with increasing viscosity.

1.5.2 Bulk mass transport

Bulk mass transport of proteins through a membrane was explained by Etzel and Arunkumar (2017). As pressure drives flow of water through the membrane, convection transports protein to the upstream surface of the membrane. If the membrane is partially retentive to the protein, then protein will accumulate at the upstream surface of the membrane and form a polarized boundary layer (deposit layer) (Figure 1.3). This phenomenon is generally known as concentration polarization. The protein concentration in solution is highest at the wall of the membrane (C_w) and falls to the bulk solution value (C_b) over a distance equal to the thickness of the polarized boundary layer, δ.

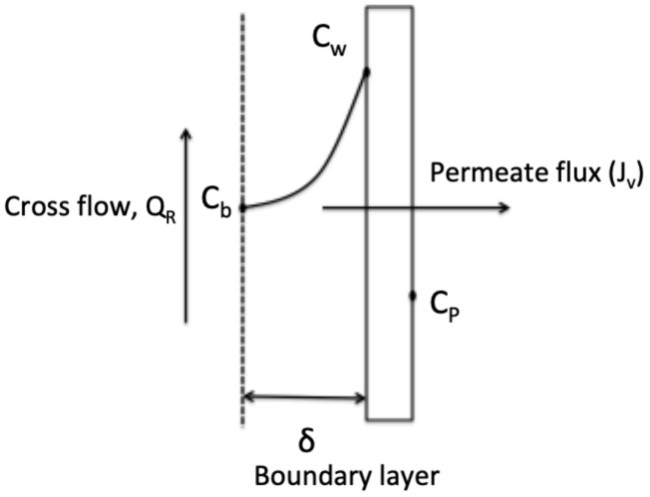

Figure 1.3. Schematic diagram of concentration polarization during membrane filtration.

The stagnant film model was proposed by Michaels (1968) to explain concentration polarization. The following mass balance was used:

$$J_v C - J_v C_P = -D\frac{dC}{dx} \tag{1.12}$$

where C is the protein concentration upstream at a distance x from the membrane surface, C_p is the protein concentration in the permeate stream, and D is the protein diffusion coefficient. The first term on the left hand side of equation accounts for protein moving toward the membrane by convection, and the second term on the left hand side accounts for protein leaking through the membrane. The term on the right hand side accounts for protein diffusion away from membrane. At steady state, the rate of protein transport by back diffusion is exactly balanced by the net rate of forward protein transport by

convection. Equation 1.12 can be integrated over the boundary layer thickness (i.e. from y = 0, C = C_w to y = δ, C = C_b) yielding:

$$J_v = k\ ln\frac{(C_w - C_P)}{(C_b - C_p)} \tag{1.13}$$

where the protein mass transfer coefficient (k) is equal to the ratio of the protein diffusion coefficient to the boundary layer thickness ($k = D/\delta$).

The observed sieving coefficient (S_o) is a fundamental measure of ultrafiltration membrane performance:

$$S_o = \frac{C_p}{C_b} = \left(\frac{C_w}{C_b}\right) S_a \tag{1.14}$$

where the ratio $C_p/C_w = S_a$, the actual sieving coefficient. C_w can be substituted by Equation 1.13 yielding:

$$S_o = \frac{S_a}{(1 - S_a)exp\left(-\frac{J_v}{k}\right) + S_a} \tag{1.15}$$

At low filtrate flux, the observed sieving coefficient (S_o) is equal to the actual sieving coefficient (S_a). Another useful form of Equation 1.13 is to solve for C_w in terms of S_o:

$$C_w = C_b\left[S_o + (1 - S_o)\exp\left(\frac{J_v}{k}\right)\right] \tag{1.16}$$

The solute concentration at the wall (C_w) increases with decreasing k and increasing C_b and J_v. For protein filtration, S_o decreases as the deposit layer thickness increases. The term in the exponent (J_v/k) is defined as the polarization index (β). Deposit layer thickness increases as β increases. For a spiral wound membrane in cross flow, β is given by:

$$\beta = J_v/k = 1.225J_v/\left(\frac{6Q_R}{hV_{HR}}D^2\right)^{1/3} \quad (1.17)$$

where h is the thickness of the feed-spacer mesh material, V_{HR} is the retentate hold up volume equal to hA_m where A_m is the membrane area and Q_R is the crossflow rate.

Keeping β constant during membrane filtration and scale-up is important. The polarization index (β) indicates the extent of deposit layer formation in spiral-wound membranes. In spiral wound membranes, the average transmembrane pressure (TMP) decreases linearly on the retentate side from membrane inlet to outlet (Piry et al., 2008). This decline in TMP leads to a decrease in the thickness of the deposit layer axially down the membrane. Scale-up based on constant wall concentration was proposed by van Reis et al. (1997). The constant wall concentration approach uses Equation 1.16 to control the flux. To maintain constant C_w, C_b and J_v must also remain constant. C_b is changing with the volume concentration factor (VCF), which is equal to the volume ratio of feed solution (V_F) over the retentate (V_R). When the large pore charged membranes are used, the permeate flux as well as β increase. This results in increasing in C_w and forms a protein deposit layer on the membrane surface that acts like a finer filter than the membrane itself. The protein deposit layer must be controlled for maintaining high filtration speed of the wide pore membrane. This means that permeate flux should be held constant during filtration. In the present work, when scaling-up, β was kept constant by controlling the permeate flux, J_v and the recirculation flow rate, Q_R. Flux control was implemented by placing a pump on the permeate stream.

1.5.3 Mass balance model for a batch operation

Mass balance models to predict the performance of ultrafiltration systems were developed to supersede time-consuming guess-and-check experimental methods of the past (Arunkumar & Etzel, 2013, 2015). A batch single-stage ultrafiltration/diafiltration system is shown in Figure 1.4. A feed solution of volume V_F and protein concentration C_F is placed into a feed tank at time zero. Let V_P be the permeate volume at time t. Permeate is drawn from the membrane at a constant flow rate Q_p and feed solution is applied to the membrane at a constant flow rate Q_F. The final mixing-cup retentate concentration $<C_R>$ is given by:

$$ln\frac{\langle C_R\rangle}{C_F} = \left(1-\widehat{S_o}\right)ln(V_F/V_R) \tag{1.17}$$

where $\widehat{S_o}$ is equal to:

$$\widehat{S_o} = \frac{S_o}{1-\hat{Q}(1-S_o)} = \frac{C_P}{\langle C_R\rangle} \tag{1.18}$$

The dimensionless flow rate $\hat{Q}$ is defined as:

$$\hat{Q} = \frac{Q_P}{Q_F} \tag{1.19}$$

When the flow rate of the permeate is much smaller than the flow rate of the feed solution, then $\widehat{S_o} \approx S_o$.

The overall mass balance in a batch operation is:

$$\langle C_R\rangle V_R = V_F C_F - V_P\langle C_P\rangle \tag{1.20}$$

Substituting Equation 1.20 to Equation 1.17, S_o is expressed as:

$$S_o = 1 - \frac{\ln[V_F/V_R - \langle C_P\rangle/\langle C_F\rangle\,(V_F/V_R - 1)]}{ln\,V_F/V_R} \qquad (1.21)$$

The observed sieving coefficient (S_o) is a dimensionless ratio comparing the concentration of protein that undesirably flows through a given membrane to the concentration of protein applied to the membrane. A smaller value of S_o means a more retentive filter.

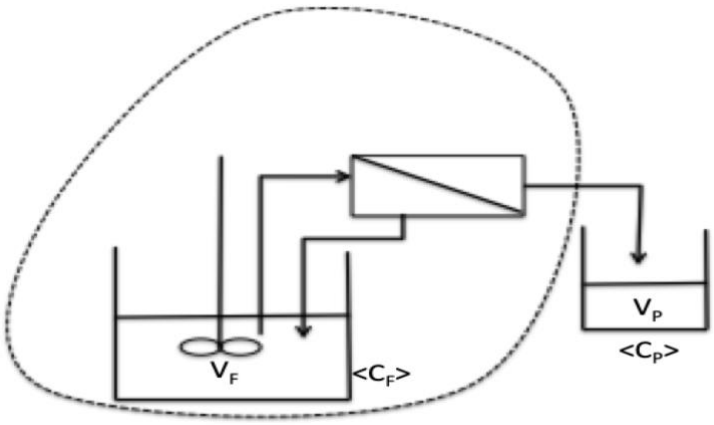

Figure 1.4. Stirred cell filtration system for sieving coefficient measurement based on the mass balance model of Arunkumar & Etzel (2013).

1.6 Membrane technology in whey processing

Whey is the yellowish liquid produced as a result of milk coagulation during cheese manufacture. There are two types of cheese whey: sweet whey and acid whey (Park, Haenlein, 2013). Sweet whey, with a pH no less than 5.6, is produced by rennet coagulation of milk, such as in Cheddar cheese manufacture. Acid whey, with pH not exceeding 5.1, is produced during the manufacturing of acid-coagulated cheeses, such as Cottage cheese.

Concentration of whey components varies slightly with the type of whey. Both types of whey are composed of water (93.5%), proteins (0.7-0.8%), lactose (4.4-4.8%), ash (0.5 - 0.6%), and fat (0.3%) (Smith, 2008). Whey contains about 50% of the milk solids, 20% of the proteins, and nearly 100% of the lactose from the original whole milk (Smithers, 2008).

About 9 pounds of whey are generated from every pound of cheese manufactured, and a large cheese plant can produce over 1 million liters of whey daily (Smith, 2008). Worldwide whey production is estimated at 180 to 190 x 10^6 ton/year (Mollea, Marmo, & Bosco, 2013). Whey was discarded as sewage or returned to dairy farms to be fed to pigs or spread on the farm fields in the past (Smithers, 2008). Concentration of whey protein from whey by ultrafiltration transformed this waste by-product into valuable products. There is a new expression in the dairy business: "cheese to break even, whey for profit."(Onwulata & Huth, 2009). Whey accounts for 11% of the revenue for a cheese manufacturer in the major cheese-producing regions (Balagtas, Hutchinson, Krochta, & Sumner, 2003). Balagtas et al. (2003) mentioned that the processing of whey into its components has been made profitable because of the demand for whey components, the development of whey processing techniques, and the cost of environmental regulations.

The dairy industry is one of the first large-scale commercial applications of membrane ultrafiltration (Rektor & Vatai, 2004). Since the early-1970s, the use of ultrafiltration for the production of whey protein concentrates has spread rapidly throughout the world (Zeman & Zydney, 1996). Nowadays the presence of membrane equipment in a dairy facility is common and it is used for a large variety of different processes, including whey protein concentration, standardization of cheese milk,

concentration of skim milk, and diafiltration of whey proteins. Ultrafiltration and diafiltration are an essential step in the manufacture of whey protein powders, whey protein concentrate (WPC) and whey protein isolates (WPI). The main purpose of ultrafiltration of whey is to concentrate the whey proteins on a dry solids basis for production of a whey protein powder having varied protein, lactose and ash contents (Atra, Vatai, Bekassy-Molnar, & Balint, 2005). WPC powder contains not less than 25% protein on a dry-solids basis. The main WPC products available as food ingredients are WPC34, which contains more than 34% whey protein on a dry solids basis, and WPC80, which contains more than 80% protein on a dry solids basis.

The processes to make WPC and WPI are described below following Smith (2008). Whey from the cheese maker is sent to a cream separator or centrifuge to remove cheese fines and whey cream. Regardless of whether the whey came from raw or pasteurized milk, all whey is then pasteurized. The pasteurized whey is fed to an ultrafiltration membrane to separate proteins from small molecules, such as water, lactose, and ash. In the production of WPC80, diafiltration is used after ultrafiltration to wash out lactose and ash from the final product. The last step is to spray dry the concentrated whey. Whey protein isolate (WPI) is whey protein having at least 90% protein on a dry-solids basis. WPI is produced by either microfiltration/ultrafiltration or ion exchange. The processes for the manufacture of WPC and WPI by membranes are similar. Pretreated whey is microfiltered to remove lipids and then subjected to ultrafiltration and diafiltration to concentrate the whey protein on a dry-solids basis. The protein concentrate is then spray dried. WPI contains 90-92% proteins, 0.5-1.0% lactose, 2.0-3.0% ash, 0.5-1.0% fat, and 4.0-5.0% moisture.

Membranes made of polyethersulfone (PES) of 5-10 kDa MWCO are widely used in the ultrafiltration and diafiltration steps (Ganju & Gogate, 2017; Rabiller-Baudry et al., 2008; Tang et al., 2010). The PES membrane has outstanding oxidative, thermal, mechanical and hydrolytic stability (Zhao et al., 2013). However, these tight membranes have a low permeate flux of about 12 $L/m^2/h$ (LMH) and require a significantly long time to pass the whey though the membrane. A membrane with a larger MWCO, for example, 300 kDa, speeds the filtration process, but also results in more proteins passing through the membrane.

Placing an ionic charge on the surface of the membrane having a larger MWCO than 10 kDa prevents proteins from passing through. The predominant whey proteins are alpha-lactalbumin (ALA) and beta-lactoglobulin (BLG). The molecular masses and isoelectric points (pI) of these proteins are 14.4 kDa and pI 4.4 for ALA, 18.4 kDa and pI 5.2 for BLG. By adjusting the pH of whey to 6.8, the whey proteins carry a net negative charge and are rejected by a negatively charged membrane having a larger MWCO than 10 kDa due to electrostatic repulsion. The advantage of a charged membrane having a large MWCO is to allow lactose to rapidly pass through the membrane while still rejecting whey proteins by electrostatic repulsion. Thus, wide pore ionically charged membranes achieve both high filtration speed and high protein retention. The goal of the present work was to modify wide pore, large MWCO PES membranes to create ionically charged PES membranes that simultaneously provide a high whey flux and a high protein recovery.

1.7 Modification method

PES is a one of the most widely used polymeric materials in membrane manufacture. PES polymer consists of alternating phenyl groups and sulfone groups connected by ether linkages. There are three approaches to modify the surface of PES membranes to contain charged groups: bulk chemical modification of the liquid PES material before fabrication into a membrane, a wet blending method, and modification of the solid PES surface.

1.7.1 Bulk modification of the PES polymer

Bulk chemical modification of the PES polymer to create charged groups mainly involves sulfonation and carboxylation. Sulfonation of PES is the addition of sulfonic acid groups to the aromatic backbone of PES. This is an electrophilic aromatic substitution reaction. It is notoriously difficult to sulfonate or carboxylate the PES matrix due to the electron withdrawing effect of the sulfone linkages (Lu, Zou, Guan, Dai, & Lu, 2005).

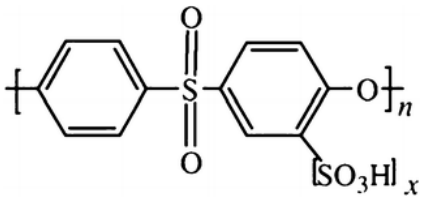

Figure 1.5. Chemical structure of sulfonated PES.

Sulfonation is carried out before membrane synthesis, using sulfonating agents such as sulfonic acid (H_2SO_4), sulfur trioxide (SO_3), oleum (SO_3 in H_2SO_4), sulfur trioxide-

triethylphosphate complex (SO_3-TEP), triethylphosphate, and trimethyl silylchlorosulfate ($(CH_3)_3SiSO_3Cl$) (Blanco, Nguyen, & Schaetzel, 2002; Blanco, Sublet, Nguyen, & Schaetzel, 2006; Dyck, Fritsch, & Nunes, 2002; I. Kim, Choi, & Tak, 1999; Lu et al., 2005). The sulfonic acid groups introduced in these methods are often located in the ortho position on the aromatic ring next to the ether group because of the electron donating ether oxygen at the para position (Figure 1.5) (J.-F. Blanco et al., 2006; Iojoiu, Maréchal, Chabert, & Sanchez, 2005). The sulfonation method for most reagents starts with adding the reagent to a PES polymer solution at constant temperature. The charged polymer is then precipitated in a cold liquid, separated by filtration, washed with deionized water and dried. The degree of sulfonation depends on several factors, including the strength of the sulfonating agent, the sulfonating solvent, reaction time, reaction temperature, and concentration of polymers. In general, the disadvantages of sulfonation are low reactivity, the heterogeneous reaction, chain cleavage, crosslinking side reactions and expense (Dyck et al., 2002). Chlorosulfonic acid is inexpensive sulfonation reagent, but chain degradation, branching, or crosslinking reactions may occur. However, if the reaction is carried out under controlled conditions, side reactions can be suppressed. PES polymer has been modified by sulfonation with chlorosulfonic acid as the sulfonating agent and concentrated sulfuric acid as the solvent (Lu et al., 2005). To prepare the sulfonated PES polymer, PES was dissolved in concentrated sulfuric acid. Chlorosulfonic acid was added to the PES solution drop by drop while stirring. After reaction, the mixture was gradually precipitated into ice-cold deionized water under agitation. The precipitate was recovered by filtration and washed with deionized water. Higher temperature (30 ˚C) led to a higher degree sulfonation but

also chain scission of the PES. At lower temperature (10 ˚C), the degree of sulfonation was controlled without chain scission of PES when varying reaction time and the quantity of chlorosulfonic acid. In addition, Blanco, Nguyen and Schaetzel (2002) used concentrated sulfuric acid and chlorosulfonic acid to sulfonate PES polymers before membrane fabrication. The PES polymer powder was dissolved in sulfuric acid. The resulted sulfonated polymers were then precipitated as the acid form in water. Recovery yield was calculated by comparing the weight of the polymer recovered by precipitation to the weight of the initial sample. The degree of sulfonation for 40 min at ambient temperature was 12.5% calculated from ion exchange capacity. The recovery yield at ambient temperature and 40 min of reaction time was 80% due to chain degradation during the reaction caused by the hydrolysis of the ether link in the main polymer chain. The recovery yield was increased slightly to 112% by cooling the reaction temperature to 4 ˚C and lengthening the reaction time to 3 h, but the degree of sulfonation was only slightly higher at 14%. To increase the degree of sulfonation, the polymer was dissolved in dichloromethane first before adding the sulfonation reactant. However, the recovery yield decreased drastically to 28.8% due to the dissolution of a fraction of the modified polymer in the precipitation medium. Blanco et al. (2006) used the same procedure to make the sulfonated PES polymer and fabricate PES membranes by the phase inversion method. The sulfonated polymer at a concentration of 25%-40% was dissolved in N-methyl-pyrrolidone (NMP) by heating the mixture at 70 ˚C for 1 d under mild stirring. The cooled solution was then cast onto a glass plate by immersing in a water bath. The membrane prepared with sulfonated PES polymers showed a macroscopically homogeneous and dense structure.

Blanco et al. (2006) mentioned that a membrane of such morphology is not suitable for application due to its low water permeability.

Similar to sulfonation, carboxylation of PES polymers before membrane fabrication can also create charges on the membrane surface. Deng et al. (2008) synthesized carboxylated PES polymer and made microfiltration membranes using the phase inversion method. To graft the carboxylic group onto the PES polymer, acrylic acid (AA) aqueous solution and PES powder were put into glass tubes, followed by gamma-ray irradiation. The powder was filtered, washed, and dried. The grafted PES powder and polyvinylpyrrolidone (PVP) as a pore forming agent were then dissolved in NMP and kept at 70 ˚C for 6 d. The membrane was cast onto a stainless-steel plate and immersed in a bath of deionized water at 20 ˚C. The degree of grafting increased with rising AA concentration below 30% but decreased with further increase in AA concentration above 30%. A high degree of grafting resulted in poor solubility of the AA grafted PES powder, which hindered membrane fabrication. With increased degree of grafting from 12.5 to 21%, the membrane made from carboxylated PES polymers showed increased pore dimension, higher water flux, and twisted fingerlike structure at the sub-layer of the membrane.

1.7.2 Blending method

In the blending method, polymers having hydrophilic functional groups are mixed with PES polymers before membrane fabrication. The limiting factor is the miscibility of the polymers in the organic casting solvent (J. Kim & Kim, 2005). Blending requires hydrophobic and hydrophilic polymers to be dissolved in the same organic solvents such as

Dimethylformamide (DMF) and N-Methylformamide (NMP), which are often used as coating solvents in membrane fabrication. Hydrophilic polymers, such as chitosan, cellulose acetate, phosphatidlcholine, poly(amide-imide), sulfonated poly(ether ketone), poly(ethylene glycol) and sulfobetaine, have been blended with PES (Ma, Su, Sun, Wang, & Jiang, 2007; Mahendran, Malaisamy, Arthanareeswaran, & Mohan, 2004; Manea & Mulder, 2002; Wang, Wang, Su, & Jiang, 2006; Y.-q. Wang et al., 2006; Wilhelm, Pünt, Van der Vegt, Strathmann, & Wessling, 2002). Rahimpour, Madaeni and Mehdipour-Ataei (2008) blended PES with a hydrophilic polymer to prepare ultrafiltration membrane using the phase inversion method. Poly(amide-imide) (PAI) and PES polymers were dissolved in dimethylacetamide (DMAC) with addition of PVP as the pore former. The solution was then cast onto a glass plate and moved to a non-solvent bath for immersion precipitation. The morphologies of blended PES/PAI membranes were different from the pure PES membrane. Higher PAI polymer concentration in the casting solution led to more porous membranes in the sub-layer with larger finger-like pores, but lower mean pore size of membrane. The pure water flux, and protein rejection were increased as PAI concentration increased in the casting solution. The thermal stability of the PES/PAI membrane was lower than the PES membrane based on thermo-gravimetric analysis. Because the glass transition temperature of PAI (157 ˚C) is lower than of PES (225 ˚C), the addition PAI in the PES membrane reduced the thermal stability. J. Kim and Kim (2005) made of blend of PES and hydrophilic poly(1-vinylpyrrolidone-co-styrene) (PVPS) copolymer to obtain a membrane with increased hydrophilicity. They observed that miscibility was limited to a narrow concentration range of vinyl pyrrolidone from 59% to 92%. Miscible PES blends with PVPS

polymers underwent phase separation on heating. Membranes were fabricated from the blend of PES and PVPS. The morphology of the membrane prepared from miscible blends of PES/PVPS was similar to that of a PES membrane, while the morphology of the membrane prepared from immiscible blends of PES/PVPS exhibited two phases: a PES-rich phase and a PVPS rich phase. Membranes prepared from the miscible blends of PES/PVPS showed increased solute rejection and water flux compared to the PES membrane alone.

1.7.3 Surface modification

Surface modification of the finished hydrophobic PES membranes post fabrication is an attractive approach to change the selectivity of the membrane while preserving its macroporous structure (Alenazi, Hussein, Alamry, & Asiri, 2017; Brink, Elbers, Robbertsen, & Both, 1993; Cheng et al., 2012; Jiang, Zhu, Li, Xu, & Zhu, 2010; K. Kim, Fane, & Fell, 1988; Van der Bruggen, 2009). Reddy (2003) reported that surface modification of a PES ultrafiltration membrane was achieved by physical adsorption of poly(4-styrenesulfonic acid) (PSS). The rejection of inorganic solutes such as NaCl and Na_2SO_4 was improved due to electrostatic repulsion without decreasing water flux. However, whether or not the PSS that adsorbed onto these membranes was washed off with use was not tested (Van der Bruggen, 2009). Cowan and Ritchie (2007) modified PES membranes by polymerization of styrene in a toluene solvent onto the surface of the membrane followed by sulfonation of the resulting polystyrene grafts using sulfuric acid in water. Permeation of ALA and BLG at pH 7.2 through the modified membrane decreased 5-fold compared to the raw membrane due to electrostatic repulsion. This method used three steps. First, the PES membrane was

treated with 0.5 N sulfuric acid in water to sulfonate the surface and serve as the initiator for cationic polymerization. Second, polystyrene chains were formed by polymerization of styrene dissolved in toluene onto the membrane surface. Third, the polystyrene chains were sulfonated using 0.5 N sulfuric acid in water. However, there are three challenges in this method. Sulfonation of PES membrane using diluted sulfuric acid in water is not easy if it occurs at all. The degree of polymerization of styrene in toluene onto the sulfonated membrane surface is difficult to control. In addition, toluene as an organic solvent can cause some damage to the PES membrane structure.

Other surface modification methods have also been investigated, including: plasma treatment, plasma-induced polymer grafting, UV-induced polymer grafting, gamma ray and electron beam-induced polymer grafting, and redox-grafting (Akbari, Desclaux, Rouch, Aptel, & Remigy, 2006; Iwa, Kumazawa, & Bae, 2004; N. Saxena, Prabhavathy, De, & DasGupta, 2009; Tyszler et al., 2006; Wavhal & Fisher, 2002a, 2002b, 2003; Yamagishi, Crivello, & Belfort, 1995a, 1995b). However, the equipment involved in plasma and radiation induced grafting is expensive. These methods also often lead to the degradation of the PES membrane by attacking the polymer backbone (Van der Bruggen, 2009; Zhao et al., 2013). A variety of plasma treatments have been employed to form a hydrophilic surface from a hydrophobic membrane. Ionization of a gas can occur by means of an electrical discharge at high frequencies. The creation of a plasma can be carried out in a microwave plasma generator or an induction coupled radiofrequency plasma generator (Kato, Uchida, Kang, Uyama, & Ikada, 2003) . Possible gases include Ar, CO_2, N_2, NH_3, O_2 and H_2O. The surface is bombarded with ionized plasma components to generate free radical

sites. Bonds that can be attacked by free radicals are C-C, C-H, and C-S bonds in the PES polymer. The generated free radicals can subsequently react with gas molecules. Remaining free radical sites bind with oxygen or nitrogen after contacting with air. For example, CO_2 plasmas were used to modify PES membranes (Wavhal & Fisher, 2002b). The CO_2 plasma treatment introduced several oxygen functional groups into the PES polymer, including carboxylic acid, ketone/aldehyde, and ester groups. The top surface of the treated membrane was adversely affected by the treatment, with fewer pores seen on the surface. Although CO_2 plasma treatment resulted in increased surface hydrophilicity, the mechanical and filtration properties of the membranes were significantly degraded. In addition, on most polymer surfaces, the hydrophilicity gained after plasma treatment was usually not permanent. A method that was used to avoid the loss of the desirable surface properties gained after plasma modification was the graft polymerization of hydrophilic monomers. Wavhal and Fisher (2002a) modified a PES membrane by argon plasma treatment followed by polyacrylic acid (PAA) grafting from the vapor phase. The pure water flux for the modified membranes increased. UV-induced grafting involves the chemical attachment of hydrophilic compounds to the membrane surface. PES membranes can be treated without photoinitiators, because PES materials are intrinsically photosensitive (Yamagishi et al., 1995a). Generally, with the radiation technique, absorption of energy by the polymer backbone initiates a free radical process (Akbari et al., 2006). The mechanism of UV-induced graft polymerization has two steps. In the first step, light absorption by the phenoxyphenyl sulfone chromophores in the polymer chain occurs. In the second step, photoexcitation results in a hemolytic cleavage of a C-S bond at the

sulfur bond at the sulfone linkage. This step yields two radical sites. Both radicals are reactive, and polymerization of monomer may occur at these sites. For example, Yamagishi et al. (Yamagishi et al., 1995a, 1995b) applied the UV-induced grafting method to modify PES membranes. UV radiation was carried out under a nitrogen atmosphere in a photochemical reactor equipped with sixteen low pressure mercury lamps. Examined were the effect of irradiation conditions and the monomer concentrations of three monomers: 1-hydroxyethylmethacrylate (HEMA), glycidylmethacrylate (GMA), and methacrylic acid (MAA). By choosing appropriate radiation and solution conditions, the modified membranes had increased flux and comparable protein retention to unmodified membranes. Gamma ray induced radiation grafting is seldom used for the modification of PES membranes because high-energy gamma rays induce breakage of the PES polymer backbone. Ion beam radiation is another alternative method to induce polymer grafting by creation of active sites on the membrane surface (Keszler, Kovacs, Tóth, Bertóti, & Hegyi, 1991; Schulze et al., 2010). Schulze et al. (2010) modified a PES membrane by electron beam radiation of membranes soaked with an aqueous solution of functional molecules. Irradiation was performed in an N_2 atmosphere using an electron beam accelerator. Some selected functional molecules had reduced protein adsorption to the modified membrane. Redox grafting is an effective method to generate free radicals under mild conditions with the use of redox initiators. The advantage of this method is that modification of a membrane can be carried out in aqueous solution at room temperature. The redox system $K_2S_2O_8/Na_2S_2O_5$ is often used, and it generates free radicals on the membrane surface for subsequent grafting. Belfer et al. (2000) modified PES membranes by redox grafting to

create functional groups on the membrane surface. The modified membrane surfaces were characterized by FTIR-ATR spectroscopy. The performance of the modified membranes was not tested.

1.8 Summary

Ultrafiltration is the most widely used membrane process in the dairy industry (Kumar et al., 2013). About 2/3 of the membrane area installed in the dairy industry is used for whey protein concentration (Saxena, Tripathi, Kumar, & Shahi, 2009). Whey was once considered a waste by-product by cheese makers. However, modern membrane technology, including ultrafiltration and diafiltration sparked a transformation that turned whey from a waste product to a valuable dairy ingredient (Smithers, 2008). Polyethersulfone (PES) ultrafiltration membranes of molecular weight cut off 5-10 kDa are widely used for ultrafiltration of whey (Ganju & Gogate, 2017). The problem with these membranes is the long processing time required to pass whey through a tight membrane at a low permeate flux of about 12 $L/m^2/h$ (LMH). A wide pore ionically charged PES membranes can replace the 10 kDa PES membranes and deliver equivalent protein retention at greater filtration speed.

The technology to place ionic charges on a PES membrane is the subject of the present work. Therefore, it is important to know how PES membranes are made and characterized. PES membranes are made by the phase inversion process using an organic solvent to dissolve the PES polymer and the non-solvent water to precipitate the polymer and form pores in the membrane. The observed sieving coefficient (S_o) is a fundamental

measure of ultrafiltration membrane permeability to proteins. The value of S_o of a membrane decreases after charges are placed on the membrane. The transport of clean water through membranes is also often used to evaluate membrane performance. The membrane hydraulic permeability (L_p) is the water flux per unit transmembrane pressure drop. L_p is a function of the membrane thickness, the pore radius, the solvent viscosity, and the membrane porosity. L_p is an important indicator of filtration speed.

The PES polymer consists of repeating phenyl groups connected to alternating sulfone groups by ether linkages. Due to its chemical structure, PES membranes are resistant to chemical attack. There are three approaches to modify the surface of PES membranes to contain charged groups: bulk chemical modification of the liquid PES material before fabrication into a membrane, liquid blending of charged polymers and PES, and surface modification of PES. The above methods for modification of PES membrane are commonly conducted on flat-sheet membranes. It is difficult to apply these methods to finished membrane end products, such spiral-wound membranes. Thus, there is a need to develop a modification method to convert finished PES membrane end products into charged PES membranes by simply pumping chemicals through membranes. In the modification method developed in this study, a mixture of organic solvent and water was used to swell PES membranes, but not dissolve the membrane polymer, to facilitate the diffusion transfer of a charged polymer into the PES membrane polymer. The development of this new method to make charged PES membranes will provide cheese whey manufacturers a cost-effective filtration process for the continued expansion of whey protein as a food ingredient.

1.9 Reference

Akbari, A., Desclaux, S., Rouch, J., Aptel, P., & Remigy, J. (2006). New UV-photografted nanofiltration membranes for the treatment of colored textile dye effluents. *Journal of membrane science, 286*(1-2), 342-350.

Al Malek, S., Seman, M. A., Johnson, D., & Hilal, N. (2012). Formation and characterization of polyethersulfone membranes using different concentrations of polyvinylpyrrolidone. *Desalination, 288*, 31-39.

Alenazi, N. A., Hussein, M. A., Alamry, K. A., & Asiri, A. M. (2017). Modified polyether-sulfone membrane: a mini review. *Designed monomers and polymers, 20*(1), 532-546.

Amirilargani, M., Saljoughi, E., Mohammadi, T., & Moghbeli, M. (2010). Effects of coagulation bath temperature and polyvinylpyrrolidone content on flat sheet asymmetric polyethersulfone membranes. *Polymer Engineering & Science, 50*(5), 885-893.

Arthanareeswaran, G., & Starov, V. M. (2011). Effect of solvents on performance of polyethersulfone ultrafiltration membranes: Investigation of metal ion separations. *Desalination, 267*(1), 57-63.

Arunkumar, A., & Etzel, M. R. (2013). Fractionation of α-lactalbumin from β-lactoglobulin using positively charged tangential flow ultrafiltration membranes. *Separation and Purification Technology, 105*, 121-128.

Arunkumar, A., & Etzel, M. R. (2015). Negatively charged tangential flow ultrafiltration membranes for whey protein concentration. *Journal of Membrane Science, 475*, 340-348.

Atra, R., Vatai, G., Bekassy-Molnar, E., & Balint, A. (2005). Investigation of ultra-and nanofiltration for utilization of whey protein and lactose. *Journal of food engineering, 67*(3), 325-332.

Balagtas, J., Hutchinson, F., Krochta, J., & Sumner, D. (2003). Anticipating market effects of new uses for whey and evaluating returns to research and development. *Journal of dairy science, 86*(5), 1662-1672.

Barth, C., Goncalves, M., Pires, A., Roeder, J., & Wolf, B. (2000). Asymmetric polysulfone and polyethersulfone membranes: effects of thermodynamic conditions during formation on their performance. *Journal of Membrane Science, 169*(2), 287-299.

Bechhold, H. (1908). Durchlässigkeit von Ultrafiltern. *Zeitschrift für Physikalische Chemie, 64*(1), 328-342.

Belfer, S., Fainchtain, R., Purinson, Y., & Kedem, O. (2000). Surface characterization by FTIR-ATR spectroscopy of polyethersulfone membranes-unmodified, modified and protein fouled. *Journal of Membrane Science, 172*(1-2), 113-124.

Bhattacharya, S. (2014). *Conventional and advanced food processing technologies*: John Wiley & Sons.

Blanco, J., Nguyen, Q., & Schaetzel, P. (2002). Sulfonation of polysulfones: Suitability of the sulfonated materials for asymmetric membrane preparation. *Journal of applied polymer science, 84*(13), 2461-2473.

Blanco. J, Sublet, J., Nguyen, Q. T., & Schaetzel, P. (2006). Formation and morphology studies of different polysulfones-based membranes made by wet phase inversion process. *Journal of membrane science, 283*(1-2), 27-37.

Brink, L., Elbers, S., Robbertsen, T., & Both, P. (1993). The anti-fouling action of polymers preadsorbed on ultrafiltration and microfiltration membranes. *Journal of membrane science, 76*(2-3), 281-291.

Cheng, C., Li, S., Zhao, W., Wei, Q., Nie, S., Sun, S., & Zhao, C. (2012). The hydrodynamic permeability and surface property of polyethersulfone ultrafiltration membranes with mussel-inspired polydopamine coatings. *Journal of membrane science, 417*, 228-236.

Deng, B., Li, J., Hou, Z., Yao, S., Shi, L., Liang, G., & Sheng, K. (2008). Microfiltration membranes prepared from polyethersulfone powder grafted with acrylic acid by simultaneous irradiation and their pH dependence. *Radiation Physics and Chemistry, 77*(7), 898-906.

Dyck, A., Fritsch, D., & Nunes, S. (2002). Proton‐conductive membranes of sulfonated polyphenylsulfone. *Journal of applied polymer science, 86*(11), 2820-2827.

Etzel, M. R., & Arunkumar, A. (2017). Charged ultrafiltration and microfiltration membranes for antibody purification. *Process Scale Purification of Antibodies, 43*, 246.

Fick, A. (1855). V. On liquid diffusion. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science, 10*(63), 30-39.

Ganju, S., & Gogate, P. R. (2017). A review on approaches for efficient recovery of whey proteins from dairy industry effluents. *Journal of Food Engineering, 215*, 84-96.

Howell, J. A., Sanchez, V., & Field, R. W. (2012). *Membranes in bioprocessing: theory and applications*: Springer Science & Business Media.

Iojoiu, C., Maréchal, M., Chabert, F., & Sanchez, J. Y. (2005). Mastering sulfonation of aromatic polysulfones: crucial for membranes for fuel cell application. *Fuel cells, 5*(3), 344-354.

Iwa, T., Kumazawa, H., & Bae, S. Y. (2004). Gas permeabilities of NH3‐plasma‐treated polyethersulfone membranes. *Journal of applied polymer science, 94*(2), 758-762.

Jiang, J.-H., Zhu, L.-P., Li, X.-L., Xu, Y.-Y., & Zhu, B.-K. (2010). Surface modification of PE porous membranes based on the strong adhesion of polydopamine and covalent immobilization of heparin. *Journal of Membrane Science, 364*(1-2), 194-202.

Kato, K., Uchida, E., Kang, E.-T., Uyama, Y., & Ikada, Y. (2003). Polymer surface with graft chains. *Progress in Polymer Science, 28*(2), 209-259.

Keszler, B., Kovacs, G., Tóth, A., Bertóti, I., & Hegyi, M. (1991). Modified polyethersulfone membranes. *Journal of membrane science, 62*(2), 201-210.

Kim, I., Choi, J., & Tak, T. (1999). Sulfonated polyethersulfone by heterogeneous method and its membrane performances. *Journal of Applied Polymer Science, 74*(8), 2046-2055.

Kim, J., & Kim, C. (2005). Ultrafiltration membranes prepared from blends of polyethersulfone and poly (1-vinylpyrrolidone-co-styrene) copolymers. *Journal of membrane science, 262*(1-2), 60-68.

Kim, K., Fane, A., & Fell, C. (1988). The performance of ultrafiltration membranes pretreated by polymers. *Desalination, 70*(1-3), 229-249.

Koros, W., Ma, Y., & Shimidzu, T. (1996). Terminology for membranes and membrane processes (IUPAC Recommendations 1996). *Pure and Applied Chemistry, 68*(7), 1479-1489.

Koros, W., & Pinnau, I. (1994). *Membrane formation for gas separation processes*: CRC Press: Boca Raton, FL.

Kotsanopoulos, K. V., & Arvanitoyannis, I. S. (2015). Membrane processing technology in the food industry: food processing, wastewater treatment, and effects on physical, microbiological, organoleptic, and nutritional properties of foods. *Critical reviews in food science and nutrition, 55*(9), 1147-1175.

Kumar, P., Sharma, N., Ranjan, R., Kumar, S., Bhat, Z., & Jeong, D. K. (2013). Perspective of membrane technology in dairy industry: A review. *Asian-Australasian journal of animal sciences, 26*(9), 1347.

Lafreniere, L. Y., Talbot, F. D., Matsuura, T., & Sourirajan, S. (1987). Effect of poly (vinylpyrrolidone) additive on the performance of poly (ether sulfone) ultrafiltration membranes. *Industrial & engineering chemistry research, 26*(11), 2385-2389.

Lipnizki, F. (2010). Cross-flow membrane applications in the food industry. *Membranes for food applications. Peinemann KV, Pereira S, Giorno L, Editores. Estados Unidos de América: Willey-VCH*, 1-23.

Lonsdale, H. (1982). The growth of membrane technology. *Journal of membrane science, 10*(2-3), 81-181.

Lu, D., Zou, H., Guan, R., Dai, H., & Lu, L. (2005). Sulfonation of polyethersulfone by chlorosulfonic acid. *Polymer Bulletin, 54*(1-2), 21-28.

Ma, X., Su, Y., Sun, Q., Wang, Y., & Jiang, Z. (2007). Preparation of protein-adsorption-resistant polyethersulfone ultrafiltration membranes through surface segregation of amphiphilic comb copolymer. *Journal of Membrane Science, 292*(1-2), 116-124.

Madaeni, S., & Rahimpour, A. (2005). Effect of type of solvent and non‐solvents on morphology and performance of polysulfone and polyethersulfone ultrafiltration membranes for milk concentration. *Polymers for advanced technologies, 16*(10), 717-724.

Mahendran, R., Malaisamy, R., Arthanareeswaran, G., & Mohan, D. (2004). Cellulose acetate–poly (ether sulfone) blend ultrafiltration membranes. II. Application studies. *Journal of applied polymer science, 92*(6), 3659-3665.

Manea, C., & Mulder, M. (2002). Characterization of polymer blends of polyethersulfone/sulfonated polysulfone and polyethersulfone/sulfonated polyetheretherketone for direct methanol fuel cell applications. *Journal of membrane Science, 206*(1-2), 443-453.

Michaels, A. S. (1968). New separation technique for CPI. *Chemical Engineering Progress, 64*(12), 31-&.

Mollea, C., Marmo, L., & Bosco, F. (2013). Valorisation of cheese whey, a by-product from the dairy industry. In *Food industry*: IntechOpen.

Nollet, J.-A. (1752). Recherches sur les causes du bouillonnement des liquides. *Hist Acad Roy Sci, 1*, 57-104.

Onwulata, C., & Huth, P. (2009). *Whey processing, functionality and health benefits* (Vol. 82): John Wiley & Sons.

Park, Y. W., Haenlein, G., & Ag, D. S. (2013). Milk and dairy products in human nutrition. *Production, Composition and Health. Ed. Wilet-Blackwell. A John Wiley&Sons, Ltd, Publication*, 700.

Pinnau, I., & Freeman, B. D. (2000). Formation and modification of polymeric membranes: overview. In: ACS Publications.

Piry, A., Kühnl, W., Grein, T., Tolkach, A., Ripperger, S., & Kulozik, U. (2008). Length dependency of flux and protein permeation in crossflow microfiltration of skimmed milk. *Journal of Membrane Science, 325*(2), 887-894.

Rabiller-Baudry, M., Bégoin, L., Delaunay, D., Paugam, L., & Chaufer, B. (2008). A dual approach of membrane cleaning based on physico-chemistry and hydrodynamics: application to PES membrane of dairy industry. *Chemical Engineering and Processing: Process Intensification, 47*(3), 267-275.

Rabiller-Baudry, M., Gouttefangeas, F., Le Lannic, J., & Rabiller, P. (2012). Coupling of SEM-EDX and FTIR-ATR to (quantitatively) investigate organic fouling on porous organic composite membranes. *Current microscopy contributions to advances in science and technology*, 1-11.

Rahimpour, A., Madaeni, S., & Mehdipour-Ataei, S. (2008). Synthesis of a novel poly (amide-imide)(PAI) and preparation and characterization of PAI blended polyethersulfone (PES) membranes. *Journal of membrane science, 311*(1-2), 349-359.

Rektor, A., & Vatai, G. (2004). Membrane filtration of Mozzarella whey. *Desalination, 162*, 279-286.

Saxena, A., Tripathi, B. P., Kumar, M., & Shahi, V. K. (2009). Membrane-based techniques for the separation and purification of proteins: An overview. *Advances in colloid and interface science, 145*(1-2), 1-22.

Saxena, N., Prabhavathy, C., De, S., & DasGupta, S. (2009). Flux enhancement by argon–oxygen plasma treatment of polyethersulfone membranes. *Separation and purification technology, 70*(2), 160-165.

Schulze, A., Marquardt, B., Kaczmarek, S., Schubert, R., Prager, A., & Buchmeiser, M. R. (2010). Electron Beam‐Based Functionalization of Poly (ethersulfone) Membranes. *Macromolecular rapid communications, 31*(5), 467-472.

Short, J. (1995). *Membrane separation in food processing*: Marcel Dekker, Inc. New York.

Sidney, L., & Srinivasa, S. (1964). High flow porous membranes for separating water from saline solutions. In: Google Patents.

Smith, K. (2008). *Dried Dairy Ingredients.* Wisconsin Center for Dairy Research.

Smithers, G. W. (2008). Whey and whey proteins—from 'gutter-to-gold'. *International Dairy Journal, 18*(7), 695-704.

Strathmann, H., Giorno, L., & Drioli, E. (2011). *Introduction to membrane science and technology* (Vol. 544): Wiley-VCH Weinheim.

Tamime, A. Y. (2012). *Membrane processing: dairy and beverage applications*: John Wiley & Sons.

Tang, X., Flint, S., Bennett, R., & Brooks, J. (2010). The efficacy of different cleaners and sanitisers in cleaning biofilms on UF membranes used in the dairy industry. *Journal of Membrane Science, 352*(1-2), 71-75.

Torres, M., Soriano, E., De Abajo, J., & dela Campa, J. (1993). Comparative study of the behaviour of experimental polyamide UF membranes. The effect of polyvinylpyrrolidone used as an additive. *Journal of membrane science, 81*(1-2), 31-42.

Tyszler, D., Zytner, R. G., Batsch, A., Brügger, A., Geissler, S., Zhou, H., . . . Melin, T. (2006). Reduced fouling tendencies of ultrafiltration membranes in wastewater treatment by plasma modification. *Desalination, 189*(1-3), 119-129.

Van der Bruggen, B. (2009). Chemical modification of polyethersulfone nanofiltration membranes: a review. *Journal of Applied Polymer Science, 114*(1), 630-642.

Van Reis, R., Goodrich, E., Yson, C., Frautschy, L., Whiteley, R., & Zydney, A. (1997). Constant Cwall ultrafiltration process control. *Journal of membrane science, 130*(1-2), 123-140.

van Reis, R., & Zydney, A. (2007). Bioprocess membrane technology. *Journal of Membrane Science, 297*(1-2), 16-50.

Wang, T., Wang, Y.-Q., Su, Y.-L., & Jiang, Z.-Y. (2006). Antifouling ultrafiltration membrane composed of polyethersulfone and sulfobetaine copolymer. *Journal of membrane science, 280*(1-2), 343-350.

Wang, Y.-q., Wang, T., Su, Y.-l., Peng, F.-b., Wu, H., & Jiang, Z.-y. (2006). Protein-adsorption-resistance and permeation property of polyethersulfone and soybean phosphatidylcholine blend ultrafiltration membranes. *Journal of membrane science, 270*(1-2), 108-114.

Wavhal, D. S., & Fisher, E. R. (2002a). Hydrophilic modification of polyethersulfone membranes by low temperature plasma-induced graft polymerization. *Journal of Membrane Science, 209*(1), 255-269.

Wavhal, D. S., & Fisher, E. R. (2002b). Modification of porous poly (ether sulfone) membranes by low‐temperature CO2‐plasma treatment. *Journal of Polymer Science Part B: Polymer Physics, 40*(21), 2473-2488.

Wavhal, D. S., & Fisher, E. R. (2003). Membrane surface modification by plasma-induced polymerization of acrylamide for improved surface properties and reduced protein fouling. *Langmuir, 19*(1), 79-85.

Wijmans, J., Baaij, J., & Smolders, C. (1983). The mechanism of formation of microporous or skinned membranes produced by immersion precipitation. *Journal of Membrane Science, 14*(3), 263-274.

Wilhelm, F., Pünt, I., Van der Vegt, N., Strathmann, H., & Wessling, M. (2002). Cation permeable membranes from blends of sulfonated poly (ether ether ketone) and poly (ether sulfone). *Journal of membrane science, 199*(1-2), 167-176.

Xu, Z.-L., & Qusay, F. A. (2004). Polyethersulfone (PES) hollow fiber ultrafiltration membranes prepared by PES/non-solvent/NMP solution. *Journal of Membrane Science, 233*(1-2), 101-111.

Yamagishi, H., Crivello, J. V., & Belfort, G. (1995a). Development of a novel photochemical technique for modifying poly (arylsulfone) ultrafiltration membranes. *Journal of Membrane Science, 105*(3), 237-247.

Yamagishi, H., Crivello, J. V., & Belfort, G. (1995b). Evaluation of photochemically modified poly (arylsulfone) ultrafiltration membranes. *Journal of Membrane Science, 105*(3), 249-259.

Zeman, & Zydney, A. L. (1996). *Microfiltration and ultrafiltration: principles and applications*: CRC Press.

Zeman, L., & Tkacik, G. (1988). Thermodynamic analysis of a membrane-forming system water/N-methyl-2-pyrrolidone/polyethersulfone. *Journal of Membrane Science, 36*, 119-140.

Zhao, C., Xue, J., Ran, F., & Sun, S. (2013). Modification of polyethersulfone membranes–a review of methods. *Progress in Materials Science, 58*(1), 76-150.

Zydney, A. L. (1998). Protein separations using membrane filtration: new opportunities for whey fractionation. *International Dairy Journal, 8*(3), 243-250.

Chapter 2 Development of charged polyethersulfone ultrafiltration membranes in a stirred cell

2.1 Introduction

Whey is a by-product of making cheese. The primary components of sweet whey are water (93.5%), lactose (4.5 -5.0%) and proteins (0.6%) (Zydney, 1998). The purpose of whey protein concentration is to increase the protein-to-dry-solids content from 12 % to 80 % by removing water and other small molecules while retaining proteins. A tight ultrafiltration membrane having a molecular weight cut-off (MWCO) of 10 kDa is typically used to achieve high protein retention (Ganju & Gogate, 2017). However, these membranes have a low permeate flux of about 12 $L/m^2/h$ (LMH) and require a long time for the whey to pass through the membrane. As the MWCO of the membrane increases, there is a trade-off between the shorter time needed to complete the filtration process and the higher amount of protein that leaks through the membrane (Mehta & Zydney, 2005). A membrane with a larger MWCO speeds the filtration process, but also results in more protein passing through the membrane. Wide pore charged membranes are used to overcome this trade-off. By placing an ionic charge on the surface of the membrane, proteins of like charge are rejected by electrostatic repulsion as well as size. This extra rejection mechanism allows the use of higher MWCO membranes without increasing protein leakage. For example, Arunkumar and Etzel (2015) found that a negatively charged 100 kDa ultrafiltration

membrane made of regenerated cellulose had the same protein leakage as a 10 kDa unmodified membrane but offered about a two-fold higher flux and increased passage of small molecules such as lactose.

The dairy industry, however, does not use regenerated cellulose ultrafiltration membranes. Membranes made of polyethersulfone (PES) of MWCO 5-10 kDa are most widely used in the dairy industry for the concentration of whey and milk (Rabiller-Baudry et al., 2008; Tang et al., 2010). The PES polymer is resistant to chemical attack, which is important because hot caustic and acid solutions that contain the strong oxidizer chlorine as a sanitizer are commonly used to the clean the membrane daily after use. The chemical resistance of PES also makes it difficult to chemically modify. The goal of the present study was to modify wide-pore, high MWCO PES membranes to create ionically charged PES membranes that simultaneously provide high permeate flux and high protein recovery.

PES is a high-performance polymer widely used in separation science. PES consists of repeating phenyl groups connected to alternating sulfone groups by ether linkages. Due to its chemical structure, PES membranes have unique properties such as outstanding oxidative, thermal, mechanical, and hydrolytic resistance (Van der Bruggen, 2009; Zhao et al., 2013). However, these unique properties also make PES membranes resistant to modification.

There are three approaches to modify PES membranes: bulk chemical modification of the liquid PES material before fabrication into a membrane, blending charged molecules into the PES liquid before membrane fabrication, and surface modification of the fabricated solid PES membrane. Bulk chemical modification of the PES polymer includes sulfonation

and carboxylation. It is notoriously difficult to sulfonate or carboxylate PES due to the electron withdrawing effect of the sulfone linkage (Lu et al., 2005). Harsh chemicals, such as concentrated sulfuric acid and acetyl chloride are often used to modify PES before membrane fabrication (Blanco et al., 2002, 2006). In the blending method, molecules having hydrophilic functional groups are mixed with the PES polymer in liquid form before membrane fabrication. The limiting factor is the miscibility of the charged molecules and the PES polymer in the organic casting solvent (J. Kim & Kim, 2005). Organic solvents such as dimethylacetamide (DMAc) and dimethylformamide (DMF) that dissolve PES, and that are used as casting solvents in PES membrane fabrication, do not dissolve hydrophilic molecules such as charged anions.

Surface modification of the finished hydrophobic PES membrane post-fabrication is an attractive approach to charge modification of the membrane while preserving its macroporous structure (Alenazi et al., 2017; Brink et al., 1993; Cheng et al., 2012; Jiang et al., 2010; K. Kim et al., 1988; Van der Bruggen, 2009). Reddy (2003) reported that surface modification of a PES ultrafiltration membrane was achieved by physical adsorption of poly(4-styrenesulfonic acid) (PSS). The rejection of inorganic solutes such as NaCl and Na_2SO_4 was improved due to electrostatic repulsion without decreasing the water flux. However, the long-term stability of the adsorbed PSS on the membranes was not measured (Van der Bruggen, 2009). Cowan and Ritchie (2007) modified PES membranes by polymerization of styrene in a toluene onto the surface of the membrane followed by sulfonation of the resulting polystyrene grafts. The permeation of both alpha-lactalbumin and beta-lactogloblin at pH 7.2 through the modified membrane decreased 5-fold

compared to the raw membrane due to electrostatic repulsion. This method used three steps. First, the PES membrane was treated with sulfuric acid in water to sulfonate the surface and serve as the initiator for cationic polymerization. Second, polystyrene chains were formed by polymerization of styrene dissolved in toluene onto the membrane surface. Third, the polystyrene chains were sulfonated using sulfuric acid in water. However, sulfonation of PES membrane with diluted sulfuric acid is problematic, and the chain polymerization process of styrene in toluene is difficult to control.

Other surface modification methods for PES have also been investigated, including radiation grafting: plasma radiation, UV-radiation, gamma ray radiation and electron beam radiation (Akbari et al., 2006; Iwa et al., 2004; Wavhal & Fisher, 2002a; Yamagishi et al., 1995a) . However, the equipment involved in these methods is expensive. These methods also often lead to the degradation of the PES membranes by attacking the polymer backbone (Van der Bruggen, 2009; Zhao et al., 2013).

Furthermore, the above methods for modification of PES membrane are commonly conducted on flat-sheet membranes. It is difficult to apply the above methods to finished membrane end products such as hollow fiber membranes and spiral wound membranes. Thus, there is a need to develop a method to modify PES membranes after the membranes are assembled into finished end products. In this way, new membrane products need not be made, and end users do not have to enter the membrane manufacturing business to modify PES membranes.

The present work sought to create a method that places charged functional groups on the surface of a finished PES membrane product without damaging the membrane. The

present work uses a new method for the surface modification of PES ultrafiltration membranes involving diffusion transfer of charged polymers into the PES membrane surface. A charged polymer is dissolved in a mixture of organic solvents in water and passed through membranes. The hypothesis is that the organic solvent blend swells the membrane polymer, without dissolving it, making it receptive to diffusion transfer of the charged polymer. A subsequent water wash removes the solvent blend and un-swells the membrane trapping the charged polymer onto the surface of the PES membrane. The extent of this modification depends on the solvent blend and the type of charged polymers. The solvent blend must dissolve the charged polymer and swell the PES without completely dissolving it. The charged polymer must have a greater thermodynamic affinity for the PES polymer than for the solvent blend so that it will not be back extracted into the solvent blend. The workable boundaries and possible mechanisms of action for this diffusion transfer method are the subject of the present work.

2.2 Materials and methods

PES flat sheet ultrafiltration membranes of 300 kDa MWCO were from Synder Filtration (Vacaville, CA, USA). Poly(4-styrenesulfonic acid)(PSS) (75 kDa, 200 kDa, and 1000 kDa) and poly(vinylsulfonic acid, sodium salt) (PVSA) were from Sigma-Aldrich (St. Louis, MO). Styrene-maleic anhydride (SMA) copolymer that had been hydrolyzed (SMAH) was from Polyscope Polymers B.V. (XIRAN® 1000HNa, 5 kDa, Geleen, The Netherlands). A tertiary amine derivative of SMA copolymer was from Cray Valley (SMA1000I, 5 kDa, Houston, Texas). Both the SMAH and SMAI copolymers were made from the same

unreacted SMA (SMA 1000, 5 kDa) that comprises styrene and maleic anhydride moieties in a 1: 1 molecular ratio. N,N-Dimethylformamide (DMF) and acetone were from Fisher Scientific (Pittsburgh, PA, USA). Ethanol was from Decon labs (200 proof, King of Prussia, PA, USA). Whey protein isolate (WPI) was from Davisco Foods International (Le Sueur, MN, USA) and contained 92.7% protein, 2.0% ash, 5.0% moisture, 0.0% lactose, and 0.3% lipids. Other chemicals were from Fisher Scientific (Pittsburgh, PA, USA).

2.2.1 Membrane modification method and characterization

Surface modification of PES membranes was carried out by permeating an incubation solution consisting of a charged polymer (PSS, PVSA, SMAH, SMAI) dissolved in a mixture of organic solvent (DMF, ethanol, tert-butyl alcohol or acetone) in water through the membrane using an 400 mL Stirred cell (Amicon® model UFSC40001, Burlington, MA, USA). A 76mm diameter disc was cut from the PES flat sheet membrane using a compass circle cutter. Each membrane was modified and characterized using the following protocol:

1. After fixing the disc in the stirred cell, each membrane was thoroughly washed with deionized (DI) water to remove preservatives. Hydraulic permeability (L_p) was measured by permeating DI water through the membrane at four different air pressures. The slope of the water flux ($L/m^2/h$, LMH) versus pressure drop (bar) was the hydraulic permeability of the membrane before use (L_{p0}).

2. Incubation solution was prepared by dissolving the charged polymer in the solvent blend. For example, 3.75% (w/v) PSS was dissolved in 250 mL of organic solvent (5%-50%) in water. For SMAH, the pH was adjusted to pH 4.3 or pH 7 using 1-4 M HCl to

dissolve SMAH in 50% DMF. For 3.75% SMAI, the incubation solution was pure ethanol. PVSA did not dissolve in 50% DMF at either 3.75% or 1.875% concentration. Therefore, the incubation solution was acidified to pH 0.8 by addition of 37.4 % (w/w) HCl to protonate the sulfonic acid moiety, making the PVSA soluble at a concentration of 1.875% (w/v).

3. The incubation solution was then pushed through the membrane by air pressure for 0.5 h to 16 h at 22 ˚C or in a refrigerator at 3 ˚C. A magnetic stir bar that was an integral part of the stirred cell created agitation during incubation. It was operated at 400 rpm using a Cimarec+ stirring hotplate from Thermo Fisher Scientific (Waltham, MA, USA).

4. The membrane was washed with DI water thoroughly in the stirred cell and the hydraulic permeability measured after modification (L_{p1}). When SMAH was used as polymer in the incubation solution in step 2, the membrane was rinsed with 0.1 M NaOH solution prior to DI water to deprotonate the carboxylic acids and remove excess SMAH that was not trapped in the membrane by making it water-soluble once more.

5. Protein passage was measured using 1 g/L WPI dissolved in 50 mM sodium phosphate, pH 6.8 (negatively charged membranes) or pH 3.5 (positively charged membranes). Whey proteins have a net negative charge at pH 6.8 and are repelled by membranes modified by negatively charged polymers. Whey proteins have a net positive charge at pH 3.5 and are repelled by membranes modified by positively charged polymers. Half the WPI solution (100 g of 200 g) was permeated through the membrane, and then the accumulated permeate and retentate samples analyzed for protein concentration. In order to calculate the observed sieving coefficient (S_o), a mass balance equation was used:

$$S_o = 1 - \frac{\ln[V_F/V_R - \langle C_P\rangle/\langle C_F\rangle\,(V_F/V_R - 1)]}{ln\,V_F/V_R} \quad (2.1)$$

where V_F/V_R = the volume ratio of feed solution to accumulated retentate solution, and C_P/C_F = the protein concentration ratio of accumulated permeate solution to the feed solution. This equation is necessary because the sieving coefficient is the instantaneous ratio of the protein concentration in the permeate to that in the retentate. For batch ultrafiltration these instantaneous protein concentrations are not constant and increase over time. Lower S_O means higher protein retention.

6. For cleaning, the membranes were placed into a beaker and soaked in 0.2% Alconox (Alconox Inc., NY, USA) solution for 1 h with agitation using an orbital table rotator (model 2314, Thermo Fisher Scientific, Waltham, MA, USA).

7. After steps 4 -6 described above were repeated using two other cut discs to obtain two more values of S_o and L_p. The end result was triplicate measurements of S_o (S_{o1}, S_{o2}, S_{o3}) and quadruplicate measurements of L_p (L_{p0}, L_{p1}, L_{p2}, L_{p3}) for each of three different discs.

2.2.2 Back extraction experiment

Back extraction of the charged polymer into the solvent blend was attempted to examine the mechanism of trapping. The membranes used for the back-extraction experiment were modified by 3.75 % SMAH in 50 % DMF at pH 7 and 22 ˚C for 16 h as described in Section 2.3. To back extract the SMAH polymer from the membrane, the incubation solution without any charged polymer was permeated through the membrane in the 400 mL stirred cell for 16 h by gravity. The membrane was then washed with water

thoroughly. For each membrane disc, the protein filtration experiment was repeated three times to measure S_o and L_p following steps 4-7.

2.2.3 Hansen solubility parameter distance

The Hansen solubility parameter (HSP) is widely used to predict solubility of polymers in solvent blends and the swelling of polymers (Hansen, 2007). The basis of the HSP is that the total cohesive energy of a liquid consists of three individual molecular contributions: dispersion, polarization, and hydrogen bonding forces. The solubility parameter is the square root of the ratio of the total cohesive energy divided by the molar volume of the liquid. The square of the total Hansen solubility parameter (δ_t) is the sum of the squares of each of the three individual Hansen solubility parameters due to: dispersion forces (δ_d), polarization forces (δ_p), and hydrogen bonding forces (δ_h) (Hansen, 2007). The HSP distance (Ra) is the difference between the HSP for a solvent (1) and polymer (2), and is calculated using the equation:

$$(Ra)^2 = 4(\delta_{d2} - \delta_{d1})^2 + (\delta_{p2} - \delta_{p1})^2 + (\delta_{h2} - \delta_{h1})^2 \quad (2.2)$$

Ra is a measure of molecular solvation. The smaller the HSP distance, the better the solvent is for the polymer. As the HSP distance decreases, the polymer is swollen more and more by the solvent and eventually dissolves in the solvent. Solvent blends are handled using the volume ratio of each of the solvents to calculate the three individual HSP values, which are then used to calculate Ra between the solvent blend and PES polymer. For example, PES has δ_d = 19 $MPa^{1/2}$, δ_p = 11 $MPa^{1/2}$, and δ_h = 8 $MPa^{1/2}$. Water has δ_d = 15.5 $MPa^{1/2}$, δ_p = 16 $MPa^{1/2}$, and δ_h = 42.3 $MPa^{1/2}$. DMF has δ_d = 17.4 $MPa^{1/2}$, δ_p = 13.7 $MPa^{1/2}$,

and δ_h = 11.3 $MPa^{1/2}$. A blend of 50 % DMF in water has δ_d = 16.5 $MPa^{1/2}$, δ_p = 14.9 $MPa^{1/2}$, and δ_h = 26.8 $MPa^{1/2}$. The HSP distance between PES and 50 % DMF is equal to 19.9, given by:

$$(Ra)^2 = 4(16.5 - 19)^2 + (14.9 - 11)^2 + (26.8 - 8)^2 = 394 \quad (2.3)$$

2.2.4 Hydraulic permeability

The flux of clean water through an ultrafiltration membrane is given by the hydraulic permeability (L_p) as follows (Reddy, Mohan, Bhattacharya, Shah, & Ghosh, 2003; Zeman & Zydney, 1996):

$$L_p = \frac{n\pi r^4}{8\mu\delta_m A} \quad (2.4)$$

where n is the number of pores of radius r per unit area A of the membrane, μ is solvent viscosity, and δ_m is thickness of the membrane. In the modification procedure, the number of pores, solvent viscosity, membrane thickness, and membrane area do not change. Only the pore radius might change due to dissolution of some of polymers in the membrane such as PES and the pore forming polymer polyvinylpyrrolidone (PVP) in the solvent blend or by the addition of the charged polymer to the pores. Because L_p varies to the fourth power of the pore radius, L_p is a sensitive measure of changes in the pore radius. For example, a 20% increase in pore radius results in a 107% increase in L_p.

2.2.5 SEM

The surface morphology of the dried membrane was measured using a scanning electron microscope (LEO Gemini 1530 SEM, Carl Zeiss AG, Oberkochen, Germany). The

dried membrane samples were cut into 9.5 mm diameter circles and attached to sample stubs using carbon tape. A conducting layer was deposited onto the membrane sample by using a sputter coater (Leica EM ACE600, Leica, Germany). Images were taken at the electron beam voltage of 3 kV.

2.2.6 FTIR Spectra

SMAI modified membranes were prepared following steps 1-4 in Section 2.2.1 and air-dried overnight at 22 °C in a fume hood. Membrane discs were mounted onto a Horizontal Attenuated Total Reflectance (HATR) accessory (Pike Technologies, Fitchburg, WI, USA). ATR-FTIR (Attenuated Total Reflection Fourier Transform Infra-Red) spectra were recorded on a Nicolet Magna 860 FTIR spectrometer (Thermo Fisher Scientific Inc., Waltham, MA, USA). The ATR accessory contained a ZnSe flat crystal (80 mm x 10 mm x 4 mm) at a nominal incident angle of 45 ˚ yielding about 10 internal reflections at the sample surface. All spectra (10 scans at 4 cm^{-1} resolution and ratio to the background spectra) were recorded at 22 ˚C. The instrument was purged with dry nitrogen to prevent interference of atmospheric moisture with the spectra.

2.3 Results

The following section contains the results of surface modification of PES ultrafiltration membranes by the diffusion transfer of charged polymers into the PES membrane surface. These results were used to examine the metes and bounds of the diffusion transfer technology and to make improvements in the charged membrane

technology. First, the negatively charged polymer polystyrene sulfonate (PSS) was dissolved in 50% DMF in water and contacted with the PES membrane. Next, other solvent blends were evaluated such as 20% DMF, 5% DMF, 50% ethanol, 10% ethanol, 50% tert-butyl alcohol, and 50% acetone. Then other charged polymers, such as PVSA, SMAH and SMAI were evaluated to examine the importance of the chemical structure of the charged polymer. Back extraction of the charged polymer from the modified PES membrane was attempted to examine the reversibility of the diffusion transfer method. Different combinations of incubation time, temperature, and pH were investigated to examine the effect on membrane performance. FTIR spectra of the modified membrane were used to confirm the presence of charged polymers on the surface of the modified membrane.

2.3.1 Modification of polyethersulfone membranes using a negatively charged polymer

Charged membranes were made from raw 300 kDa MWCO PES membranes using the negatively charged polymer polystyrene sulfonate (PSS). Values of S_o were measured for each membrane using 1 g/L WPI solution at pH 6.8 (Table 2.1). The raw membrane was not modified. The H_2O-PSS membrane was made by permeation of 3.75% of 75 kDa PSS in water through the membrane. The DMF membrane was made by permeation of a 50:50 mixture of DMF in water through the membrane without using PSS. The DMF-PSS membrane was made by permeation of 3.75% of PSS in 50% DMF through the membrane. Membrane discs were prepared in triplicate for measurement of L_p and S_o.

S_o of the H_2O-PSS membrane was not significantly different from S_o of the raw PES membrane ($p > 0.05$). In other words, there was no effect of PSS when water alone containing PSS was used as the incubation solution. The membrane made using 50% DMF in water with no PSS as the incubation solution had a higher value of S_o than the raw PES membrane ($p < 0.05$). Comparing the raw PES membrane to the DMF-PSS membrane S_o decreased dramatically by 14-fold. In other words, there was a strong decrease in the passage of protein through the membrane when 50% DMF in water was used as the incubation solution for the PSS.

The predominant proteins in cheese whey are alpha-lactalbumin (ALA) and beta-lactoglobulin (BLG). The isoelectric point (pI) of ALA (14.4 kDa) is pI = 4.4 and for BLG it is pI = 5.2 (18.4 kDa). These whey proteins are charged negative at pH 6.8. PSS has multiple sulfonic acid groups in the polymer backbone and is also strongly charged negative at pH 6.8. Given that these whey proteins are much smaller than the pores of the DMF-PSS membrane (MWCO = 300 kDa), the observed increase in protein rejection by the DMF-PSS membrane was attributed to electrostatic repulsion of the negatively charged proteins by the negatively charged membrane and not size-based filtration. In conclusion, the simultaneous presence of both PSS and 50% DMF in the incubation solution were essential for the successful modification of the PES membrane by PSS for the purpose of protein rejection.

Table 2.1. Sieving coefficients (S_o, n = 9) of a 300 kDa membrane using the charged polymer 75 kDa PSS for modification. Different letters in the same column of S_o indicate significant statistical differences ($p < 0.05$). Hydraulic permeability (L_p) was measured before (L_{p0}) and after (L_{p1}) modification. Different letters in the same row indicate significant statistical differences ($p < 0.05$)

Membranes	S_O	L_{p0}	L_{p1}
Raw membrane, no PSS (raw)	0.217 ± 0.022^{A}	333 ± 41	---
Water, 75kDa PSS alone, no DMF (H_2O-PSS)	0.196 ± 0.009^{A}	331 ± 18^{a}	181 ± 16^{b}
50% DMF alone, no PSS (DMF)	0.390 ± 0.034^{B}	338 ± 18^{a}	666 ± 110^{b}
50% DMF and PSS (DMF-PSS)	0.015 ± 0.003^{C}	309 ± 31^{a}	492 ± 31^{b}

Hydraulic permeability (L_p) before and after modification was compared for each membrane (Table 2.1). L_{p0} is the hydraulic permeability of the raw membrane before modification. L_{p1} is the hydraulic permeability of the membrane after modification, but before contact with the protein solution. L_{p0} of the H_2O-PSS membrane was larger than L_{p1} ($p < 0.05$). As shown in Equation (2.4), L_p is a function of pore size to the fourth power. PSS adsorption from water alone onto the membrane narrowed the membrane pores. Based on the values of L_{po} and L_{p1} the pore size decreased by 14%. However, this did not change the value of S_o.

An incubation solution consisting of 50% DMF alone (no PSS) made L_p increase by 97% and S_o increase by 80% compared to the raw membrane (Table 2.1). DMF is a good solvent for the membrane polymer. In fact, DMF is often used to completely dissolve PES polymer in preparation of the casting solution for membrane fabrication. The 50% DMF alone might have dissolved some membrane polymer, making the membrane pores somewhat (18%) larger and permitting more protein to pass through the membrane.

An incubation solution consisting of PSS in 50% DMF made L_p increase by 59% and S_o decrease by 14-fold compared to the raw membrane (Table 2.1). Opposing factors likely caused the increase in L_p for the DMF-PSS membrane: adsorption of PSS onto the membrane, narrowing the pores, and dissolution of the membrane polymer by 50% DMF, enlarging the pores. Although the DMF-PSS membrane had larger pores than the raw membrane (calculated to be 12%), protein passage decreased 14-fold likely due to electrostatic repulsion.

2.3.2 Effect of the type of organic solvent

The effect of the type of organic solvent used in the incubation solution on membrane performance (values of S_O and L_p) was measured in triplicate for each of three discs using 75 kDa PSS as the charged polymer (Table 2.2). The HSP distance (Ra) between the PES polymer and various solvent blends are also listed in Table 2.2. For example, 50% DMF in water has Ra = 19.9 $MPa^{1/2}$, whereas 20% DMF in water has Ra = 29.1 $MPa^{1/2}$.

Decreasing the DMF percentage in the solvent blend from 50% to 5% made S_o increase by 9-fold and L_p decrease by 2.8-fold. As the pore size decreased, protein

permeation increased. Decreased electrostatic repulsion between the protein and PSS was the likely cause of the decrease in S_o. The HSP distance increased from Ra = 19.9 $MPa^{1/2}$ to Ra = 33.8 $MPa^{1/2}$, which means that 5% DMF was a poorer solvent for the PES membrane than 50% DMF. These results were attributed to less diffusion transfer of PSS onto the membrane surface as the solvent blend lost its ability to swell the membrane. In other words, a value of Ra = 33.8 $MPa^{1/2}$ (5% DMF) was insufficiently small to trap as much PSS on the membrane surface as a value of Ra = 19.9 $MPa^{1/2}$ (50% DMF). Increasing the percentage DMF beyond 50% was not examined. The PES membrane completely dissolves in 100% DMF (Ra = 5.3 $MPa^{1/2}$), and 50% DMF alone made L_p increase by 97% compared to the raw PES membrane. Therefore, somewhere between 50% to 100% DMF, the membrane will dissolve, but it is possible that the value of S_o may continue to decrease before reaching that point.

Table 2.2. The effect of organic solvent type on the values of S_o and L_p measured before (L_{p0}) and after (L_{p1}) modification. Different letters in the same column (uppercase) or in the same row of L_p (lowercase) indicate significant differences ($p < 0.05$).

Solvents	S_0	L_{p0} (LMH/bar)	L_{p1} (LMH/bar)	Ra ($MPa^{1/2}$)
50% DMF and PSS	0.015 ± 0.003^{A}	309 ± 31^{a}	492 ± 31^{bA}	19.9
20%DMF and PSS	0.112 ± 0.015^{BC}	322 ± 17^{a}	284 ± 40^{aB}	29.1
5% DMF and PSS	0.136 ± 0.026^{BD}	334 ± 27^{a}	177 ± 16^{bC}	33.8
50% ethanol and PSS	0.031 ± 0.018^{AE}	270 ± 9^{a}	425 ± 62^{bAD}	23.9
10% ethanol and PSS	0.193 ± 0.026^{D}	293 ± 12^{a}	169 ± 19^{bC}	33.0
50% t-butyl alcohol and PSS	0.043 ± 0.017^{AEC}	380 ± 26^{a}	507 ± 56^{bA}	21.8
50% acetone and PSS	0.097 ± 0.039^{BCE}	312 ± 16^{a}	363 ± 49^{aBD}	18.2

Ethanol at 50% (S_o = 0.031) was not statistically different than 50% DMF (S_o = 0.015), whereas 10% ethanol (S_o = 0.193) was worse. The HSP distance is similar for 50% ethanol (Ra =23.9 $MPa^{1/2}$) and 50% DMF (Ra =19.9 $MPa^{1/2}$), whereas for 10% ethanol it is significantly higher (Ra =33.0 $MPa^{1/2}$). The value of L_{p1} was similar for 50% ethanol and 50% DMF, but significantly lower for 10% ethanol. These results were attributed to the values of the HSP distance and its relationship to swelling of the PES membrane polymer and the resulting diffusion transfer and trapping of PSS on the membrane surface.

Solvent blends of 50% tert-butyl alcohol (Ra = 21.8 $MPa^{1/2}$), and 50% acetone (Ra = 18.2 $MPa^{1/2}$) were also examined. The value of S_o was not different for 50% tert-butyl alcohol (S_o = 0.043) compared to 50% DMF (S_o = 0.015), whereas for 50% acetone (S_o = 0.095) S_o was higher. The value of L_{p1} was the same for 50% tert-butyl alcohol and 50% DMF, but significantly lower for 50% acetone. Disruption of the PES membrane surface was observed after using 50% acetone. It appeared that the applied air pressure deformed the membrane as witnessed by impressions of the rings of the stirred cell support plate embossed into the membrane. It is possible that 50% acetone at Ra = 18.2 $MPa^{1/2}$ may be close to a lower limit where the solvent blend becomes too good a solvent for the PES membrane.

2.3.3 Effect of PSS molecular mass

PSS of molecular mass 75kDa, 200kDa and 1000kDa in 50% DMF was examined (Table 2.3). Membranes modified by PSS had lower values of S_o than the raw membrane.

The PSS molecular mass had no effect on S_o. The membrane modified by 75 kDa PSS had a higher value of L_{p1} than the raw membrane, but not so for 200 and 1000 kDa PSS.

Table 2.3. Values of S_o and L_p for membranes modified by PSS of different molecular mass using 50% DMF. Different letters in the same column of S_o and L_{p1} (uppercase) or in the same row of L_p (lowercase) indicate significant differences ($p < 0.05$).

Membrane	S_o	L_{po} (LMH/bar)	L_{p1} (LMH/bar)
Water, raw membrane, no PSS	0.217 ± 0.022^{A}	333 ± 41^{a}	333 ± 41^{aA}
50% DMF and 75 kDa PSS	0.015 ± 0.003^{B}	309 ± 31^{a}	492 ± 31^{bB}
50% DMF and 200 kDa PSS	0.024 ± 0.004^{B}	294 ± 46^{a}	433 ± 56^{aAB}
50% DMF and 1000 kDa PSS	0.055 ± 0.008^{B}	330 ± 15^{a}	377 ± 8^{aAB}

2.3.4 Examination of charged polymer structure on performance

The effect of charged polymer structure was examined by comparing membranes modified by the charged polymers PVSA and 75 kDa PSS (Table 2.4). Both PVSA and PSS have similar chemical structures except PVSA does not contain a phenyl ring in the polymer backbone. The values of S_o for PVSA in 50% DMF were 25-fold higher than that for PSS in 50% DMF. PVSA did not work. This result was attributed to the lack of a phenyl ring in the PVSA. The phenyl moiety in PSS may create a thermodynamic affinity between PSS and the

phenyl ring of PES. This thermodynamic affinity is absent when using PVSA. This thermodynamic affinity might create a driving force for diffusion transfer of the PSS charged polymer into the PES membrane. Because PVSA did not contain a phenyl moiety, it did not diffuse into the PES membrane to make it negatively charged.

The importance of the phenyl moiety inspired a search for a charged polymer that could be used generically for either a positively or a negatively charged PES membrane. The co-polymer styrene maleic anhydride (SMA) is such a generic polymer. SMA has repeating styrene and maleic anhydride moieties in the polymer backbone. The styrene moiety provides the phenyl ring and thermodynamic affinity to the PES membrane, while the reactive maleic anhydride moiety can be made either charged positive or negative. Hydrolyzed styrene maleic anhydride copolymer (SMAH) contains negatively charged carboxylic acid groups and was used to make a negatively charged membrane (Table 2.4). Membrane modified using 3.75 % SMAH or 3.75 % 75 kDa PSS in 50% DMF had the same values of S_o and L_{p1} ($p > 0.05$).

In an attempt to back extract SMAH polymer from the PES membrane, 50% DMF without SMAH was permeated through the modified membrane overnight. S_o of the SMAH membrane after back extraction did not change ($p > 0.05$). In other words, the SMAH that had transferred into the membrane did not come out when washed using 50% DMF. This result was attributed to the SMAH having a higher thermodynamic affinity for the PES membrane than the 50% DMF incubation solution. At equilibrium, the SMAH partitioned into the PES polymer in preference to remaining in the 50% DMF incubation solution.

These results highlight importance of a hydrophobic character to the charged polymer in order to create a charged PES membrane by the diffusion transfer method.

Table 2.4. Values of S_o and L_p for membranes modified by PSS, PVSA or SMAH in 50% DMF. Different letters in the same column of S_o and L_{p1} (uppercase) or in the same row of L_p (lowercase) indicate significant differences ($p < 0.05$).

Membranes	S_o	L_{p0} (LMH/bar)	L_{p1} (LMH/bar)
50% DMF and 75 kDa PSS	0.015 ± 0.003^{A}	309 ± 31^{a}	492 ± 31^{bA}
50% DMF and PVSA*	0.377 ± 0.070^{B}	331 ± 21^{a}	701 ± 66^{bB}
50% DMF and SMAH	0.016 ± 0.003^{A}	251 ± 27^{a}	386 ± 11^{bAC}
Back extraction of 50% DMF and SMAH	0.010 ± 0.002^{A}	314 ± 37^{a}	334 ± 51^{aC}

*DMF at 1.875% PVSA

2.3.5 Effect of incubation time, temperature, and pH

Effects of incubation time, temperature, and pH on S_o using 3.75% SMAH in 50% DMF were investigated (Table 2.5). S_o did not change as incubation time increased from 0.5 h to 16 h, or as incubation temperature decreased from 22 to 3 °C. The diffusion transfer process was complete after the first half hour of contact with the incubation solution, and independent of the incubation temperature.

However, S_o decreased as pH increased from 4.3 to 7, and the incubation solution went from turbid to clear. SMAH has two pKa values (~4.4 and ~9.0) from the two carboxylic acid groups in the SMAH backbone (Scheidelaar et al., 2016). Increasing the pH of the incubation solution increased the negative charge on SMAH, increasing solubility. This likely increased diffusion transfer of the SMAH because only soluble SMAH can undergo the diffusion transfer process.

Table 2.5. Effect of time, temperature, and pH of the incubation solution on S_o using SMAH in 50% DMF. Different letters in the same column and row indicate significant differences ($p < 0.05$).

Time (h)	Incubation conditions		
	pH 4.3, 22 °C	pH 7.0, 22 °C	pH 7.0, 3 °C
0.5	0.058 ± 0.022[a]	0.037 ± 0.006[b]	0.028 ± 0.018[b]
1	0.048 ± 0.022[a]	0.046 ± 0.011[b]	0.020 ± 0.005[b]
4	0.040 ± 0.018[a]	0.023 ± 0.009[b]	0.015 ± 0.012[b]
16	0.040 ± 0.022[a]	0.016 ± 0.003[b]	0.013 ± 0.003[b]

2.3.6 SEM observations

Fig. 2.1 contains images of the top view of the raw membrane and the SMAH-PES membrane from the scanning electron microscope (SEM). The calibration bar length is 100 nm. A 300 kDa membrane has pore diameter of about 23 nm based on the diameter of the polymer (polyethylene glycol) used to measure the MWCO (Zhang et al., 2018). The modified membrane appeared to be no different in morphology or pore structure than the raw unmodified membrane. The conclusion from viewing the SEM images was that the active layer of the membrane was not changed by the modification procedure.

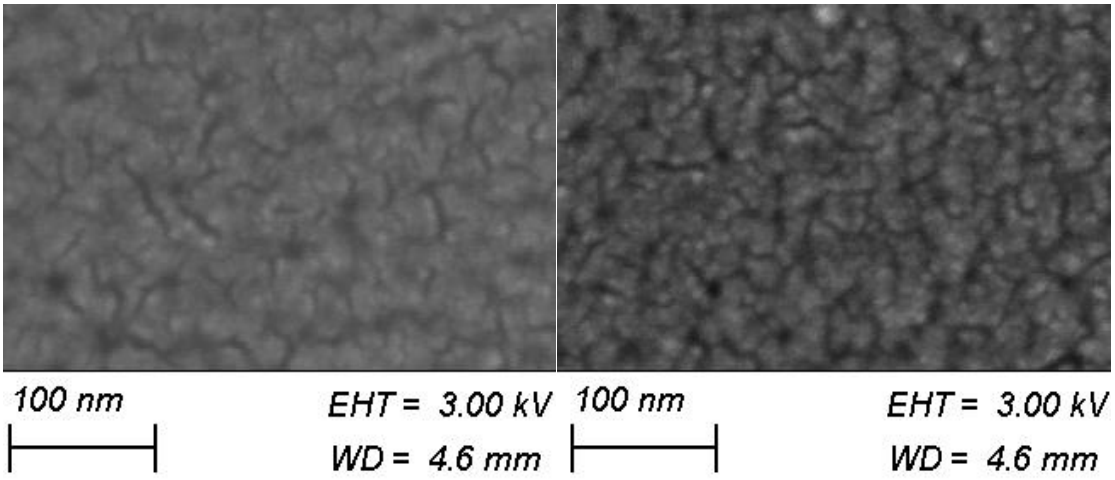

Figure 2.1. SEM photographs of the top views of (a) Raw PES and (b) SMAH-PES membranes

2.3.7 FTIR

FTIR spectroscopy was used to observe any changes in the chemistry of the membrane surface before and after modification using the positively charged polymer

SMAI. SMAI is a copolymer of styrene and dimethylaminopropylamine maleimide. Reacting the maleic anhydride moiety of SMA with dimethylaminopropylamine makes SMAI. Compared to 100% ethanol alone, the membrane modified by SMAI resulted in a 5.6-fold decrease in S_o, from 0.333 to 0.059 (Table 2.6). Thus, SMAI worked, as did SMAH. SMAI was not soluble in 50% DMF but was soluble in 100% ethanol. For 100% ethanol, Ra = 12.9, which is smaller than 50% DMF. Thus, it was not surprising that 100% ethanol alone dissolved some membrane material and resulted an increase in L_p of 79%. Adding SMAI to the 100% ethanol decreased L_{p1} by 78%, which corresponds to a calculated decrease in pore size of 32% compared to 100% ethanol alone. Thus, SMAI caused a strong decrease in S_o and in L_{p1}, both of these observations are evidence that a significant amount of SMAI was incorporated into the PES membrane by the diffusion transfer process.

Table 2.6. S_o and L_p of membranes modified by SMAI in 100% ethanol measured using 1 g/L WPI at pH 3.5. Different letters in the same column of S_o and L_{p1} (uppercase) or in the same row of L_p (lowercase) indicate significant differences ($p < 0.05$).

Membranes	S_o	L_{p0} (LMH/bar)	L_{p1} (LMH/bar)	Ra ($MPa^{1/2}$)
Raw membrane, no SMAI	0.321 ± 0.059^{A}	350 ± 32^{a}	---	35.4
100% ethanol alone, no SMAI	0.333 ± 0.025^{A}	353 ± 21^{a}	632 ± 26^{bA}	12.9
100% ethanol and SMAI	0.059 ± 0.010^{B}	314 ± 69^{a}	138 ± 62^{aB}	12.9

Figure 2.2 shows the FTIR spectra of the raw membrane and the SMAI modified membrane after modification for 0.5 h and 16 h. The SMAI modified membrane exhibited a new absorption peak at 1700 cm^{-1} which is the signature peak of the succinimide group in SMAI (Moghadam, Hasanzadeh, Fathi, & Nasr, 2013). Therefore, SMAI was detected on the surface of the PES membrane after modification. The penetration depth of the FTIR beam into PES polymers was calculated as 2.36 μm at 1700 cm^{-1} at a 45˚ angle of incidence using the ZnSe prism. The PES active layer is about 2 μm based on SEM images (data not shown). Therefore, the FTIR spectra provide evidence that the SMAI diffused into the active layer of the PES membrane.

The raw membrane had a peak at 1650 cm^{-1} that disappeared after membrane modification. An explanation for the disappearance of the peak at 1650 cm^{-1} is that the 100% ethanol swelled the PES membrane and released polyvinyl pyrrolidone (PVP). PVP is often used as a pore forming additive in PES membrane fabrication (Al Malek et al., 2012; Amirilargani et al., 2010). In confirmation, others have found using FTIR that PVP containing PES membranes show an absorption peak at 1677 cm^{-1} while PES membranes do not (Vatsha, Ngila, & Moutloali, 2014).

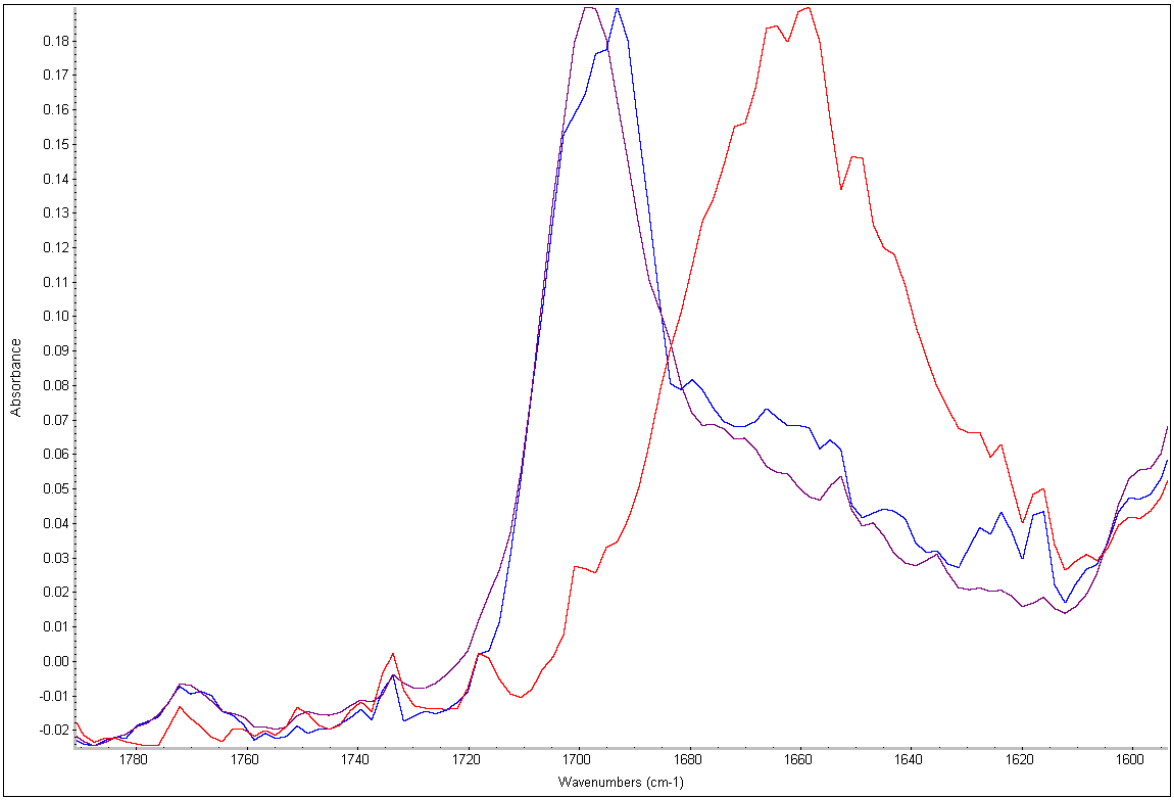

Figure 2.2. Infrared spectra of PES-SMAI at 0.5 h (blue), PES-SMAI at 16 h (purple) and PES (red).

2.3.8 Effect of solvent contact on Lp of the raw PES membrane

In order to test the hypothesis that the pore forming additive PVP was released from the membrane by 100% ethanol, a raw membrane disc was contacted with 100% ethanol four times in a row each time for 16 h, and L_p measured before and after. It was expected that L_p would decrease only once if 100% ethanol extracted PVP only, and each time if 100% ethanol dissolved the membrane polymer PES.

As shown in Table 2.7, L_p doubled after the first contact with 100% ethanol and did not change after the second and third contact. This result supports the hypothesis that

disappearance of the peak at 1650 cm^{-1} in the FTIR spectra of Figure 2.2 was from dissolution of PVP. Thus, 100% ethanol likely extracts PVP from the membrane but not PES, and the increase in L_p observed after contact of the membrane with the incubation solution was likely not from dissolution of PES.

After the fourth contact of the membrane with pure ethanol there was a small decrease in the L_p value compared to the first, second, third, and fourth contacts taken as a group. However, the pair-wise comparison of L_p for the third and fourth contacts alone was not statistically different ($p > 0.05$.).

Table 2.7. Hydraulic permeability (Lp) of raw PES membranes contacted with 100% ethanol several different time. Different letters in the same row indicate significant differences ($p < 0.05$).

Contact #	0	1	2	3	4
L_p (LMH/bar)	314 ± 14^a	687 ± 10^b	655 ± 0^b	612 ± 22^b	523 ± 11^c

2.4 Discussion

The aim of the present work was to convert an uncharged PES membrane to an ionically charged PES membrane simply by passing an incubation solution through a finished membrane product. The method developed in this work used an incubation solution composed of an organic solvent, water, and a charged polymer. The mechanism

proposed was that the charged polymer had an equilibrium affinity for the PES membrane polymer but could not diffuse into the membrane polymer without using an organic solvent in the incubation solution to swell the membrane polymer. Contact of the incubation solution with the membranes allowed the PES membrane to swell and the charged polymer to diffuse into the membrane. Removal of the incubation solution trapped the charged polymer on the surface of the PES membrane. Thus, to modify the membrane, the incubation solution should swell the membrane material; the charged polymer should have an equilibrium affinity for the membrane; and the charged polymer should dissolve in the incubation solution.

To facilitate diffusion of the charged polymer into the membrane substrate, the incubation solution should swell the membrane. The Hansen solubility parameter distance (Ra) predicts the swelling of a polymer in a solvent. If Ra is too small, then the solvent dissolves the membrane. If Ra is too large, then the solvent does not swell the membrane. For example, PES dissolves completely in 100% DMF where Ra = 5.3 $MPa^{1/2}$. On the other extreme, PES does not swell in water where Ra = 35.4 $MPa^{1/2}$. In the middle, PES swells in 50% DMF, but does not dissolve, where Ra = 19.9 $MPa^{1/2}$.

Workable values of Ra for the incubation solution were determined in the present work using the charged polymer PSS. Incubations solutions composed of, 50% ethanol (Ra = 23.9 $MPa^{1/2}$) and 50% tert-butyl alcohol (Ra = 21.8 $MPa^{1/2}$) had the same sieving coefficient as 50% DMF (Ra = 19.9 $MPa^{1/2}$) where S_o = 0.015. Incubations solutions composed of 5% DMF (Ra = 33.8 $MPa^{1/2}$) and 10% ethanol (Ra = 33.0 $MPa^{1/2}$) had a 9-fold greater sieving coefficient than 50% DMF (Ra = 19.9 $MPa^{1/2}$). Incubation solutions

composed of 50% acetone (Ra = 18.2 $MPa^{1/2}$) and 100% ethanol (Ra = 12.9 $MPa^{1/2}$) appeared to slightly damage the membrane. Lencki and Williams (1995) found that for polysulfone ultrafiltration membranes there was disruption to the membrane when Ra was small. Thus, based on the present work, values of Ra between 19.9 $MPa^{1/2}$ to 23.9 $MPa^{1/2}$ worked best for PES membranes made using the negatively charged polymer PSS. However, PES membrane using and positively charged SMAI in 100% ethanol (Ra = 12.9 $MPa^{1/2}$) also worked. Therefore, although the values of Ra may provide a useful guide to candidate compositions of the incubation solution, experimental verification remains the only sure way to measure success.

The molecular structure of the charged polymer was investigated in the present work. Because PES has two phenyl rings in each monomer of the repeating polymer structure, it is a hydrophobic polymer. The charged polymers PSS and PVSA both have a sulfonic acid moiety in the monomer structure, but PVSA does not have a phenyl ring. PSS worked and PVSA did not. Based on this result, a generic polymer SMA was examined that has a phenyl ring in the monomer structure and a reactive maleic anhydride moiety. The maleic anhydride was converted into a negatively charged moiety by hydrolysis to form two carboxylic acids (SMAH), and a positively charged moiety by reaction with dimethylaminopropylamine that contains one primary and one tertiary amine (SMAI). Both derivatives of SMA worked. Thus, the presence of a phenyl ring in the charged polymer was important, but other charged polymers having a hydrophobic moiety might also work.

Back extraction of the SMAH using the incubation solution did not work. The charged polymer preferred to stay in the PES membrane phase rather than diffuse back

into the incubation solution that contained 50% DMF. This is evidence of a thermodynamic affinity of the charged polymer for the PES polymer phase. This thermodynamic affinity would provide the driving force for diffusion transfer of the charged polymer from the incubation solution to the PES membrane phase. The inability to back extract the charged polymer in 50% DMF means that back extraction of the charged polymer into water is not likely.

The present work found that the charged polymer did not wash off the PES membrane using water or water containing detergent. The membrane could be used and cleaned several times without changes to the sieving coefficient or the hydraulic permeability. This is important for the dairy industry because the membranes are used and cleaned in entirely aqueous solutions. The observation that charged PES membranes can be made from raw PES membranes simply by pumping an incubation solution through the membranes is a major discovery of the present work. It allows end users of PES membranes to make a charged PES membrane without getting into the membrane manufacturing business. The charged PES membranes have a higher hydraulic permeability and lower protein leakage rate than existing 10 kDa uncharged PES membranes commonly used in the dairy industry. Thus, the charged membranes operate at higher speed and higher protein recovery than membranes in use in industry today. This is potentially an important economic benefit to the dairy industry.

2.5 Conclusions

A diffusion transfer method was developed to place a charge on polyethersulfone (PES) ultrafiltration membranes and the method can be used on assembled and finished membrane end products. The charge modification of PES membranes was accomplished by diffusion transfer of charged polymers into a swollen membrane. A charged polymer was dissolved in an organic solvent blend and passed through membranes. The organic solvent blend swelled the membrane allowing the diffusion of charged polymer into the membrane surface. The diffusion of charged polymers into the membrane created charged groups on the membranes and improved the rejection of proteins having like charges due to electrostatic repulsion. Protein rejection of the modified membrane was increased as much as high as 14-fold compared to the uncharged unmodified membrane.

The success of the membrane modification method depended on the type and amount of organic solvent in the solvent blend and the hydrophobic character of the charged polymer. The solvent blend and the membrane polymers were found to require a Hansen solubility parameter distance in the range of 12 to 33 $MPa^{1/2}$ so that the solvent blend swelled the membrane to facilitate the diffusion transfer of the charged polymer but without dissolving the membrane. It was also important that the charged polymer had a greater thermodynamic affinity for the membrane polymer than for the solvent blend in order to provide a driving force for diffusion transfer of the charged polymer from the solvent blend into the membrane. The diffusion of charged polymer occurred in a short of amount time, a half hour. This work is meaningful because it provides a new method to

convert a PES ultrafiltration membrane to an ionically charged PES membrane. This method can be applied to finished membrane end products without disrupting the membrane structure.

2.6 References

Akbari, A., Desclaux, S., Rouch, J., Aptel, P., & Remigy, J. (2006). New UV-photografted nanofiltration membranes for the treatment of colored textile dye effluents. *Journal of membrane science, 286*(1-2), 342-350.

Al Malek, S., Seman, M. A., Johnson, D., & Hilal, N. (2012). Formation and characterization of polyethersulfone membranes using different concentrations of polyvinylpyrrolidone. *Desalination, 288*, 31-39.

Alenazi, N. A., Hussein, M. A., Alamry, K. A., & Asiri, A. M. (2017). Modified polyether-sulfone membrane: a mini review. *Designed monomers and polymers, 20*(1), 532-546.

Amirilargani, M., Saljoughi, E., Mohammadi, T., & Moghbeli, M. (2010). Effects of coagulation bath temperature and polyvinylpyrrolidone content on flat sheet asymmetric polyethersulfone membranes. *Polymer Engineering & Science, 50*(5), 885-893.

Arunkumar, A., & Etzel, M. R. (2015). Negatively charged tangential flow ultrafiltration membranes for whey protein concentration. *Journal of Membrane Science, 475*, 340-348.

Blanco, J., Nguyen, Q., & Schaetzel, P. (2002). Sulfonation of polysulfones: Suitability of the sulfonated materials for asymmetric membrane preparation. *Journal of applied polymer science, 84*(13), 2461-2473.

Blanco, J., Sublet, J., Nguyen, Q. T., & Schaetzel, P. (2006). Formation and morphology studies of different polysulfones-based membranes made by wet phase inversion process. *Journal of membrane science, 283*(1-2), 27-37.

Brink, L., Elbers, S., Robbertsen, T., & Both, P. (1993). The anti-fouling action of polymers preadsorbed on ultrafiltration and microfiltration membranes. *Journal of membrane science, 76*(2-3), 281-291.

Cheng, C., Li, S., Zhao, W., Wei, Q., Nie, S., Sun, S., & Zhao, C. (2012). The hydrodynamic permeability and surface property of polyethersulfone ultrafiltration membranes with mussel-inspired polydopamine coatings. *Journal of membrane science, 417*, 228-236.

Ganju, S., & Gogate, P. R. (2017). A review on approaches for efficient recovery of whey proteins from dairy industry effluents. *Journal of Food Engineering, 215*, 84-96.

Hansen, C. (2007). *Hansen solubility parameters* (Hansen Ed. 2nd ed.). Boca Raton, FL: CRC Press.

Iwa, T., Kumazawa, H., & Bae, S. Y. (2004). Gas permeabilities of NH3‐plasma‐treated polyethersulfone membranes. *Journal of applied polymer science, 94*(2), 758-762.

Jiang, J.-H., Zhu, L.-P., Li, X.-L., Xu, Y.-Y., & Zhu, B.-K. (2010). Surface modification of PE porous membranes based on the strong adhesion of polydopamine and covalent immobilization of heparin. *Journal of Membrane Science, 364*(1-2), 194-202.

Kim, J., & Kim, C. (2005). Ultrafiltration membranes prepared from blends of polyethersulfone and poly (1-vinylpyrrolidone-co-styrene) copolymers. *Journal of membrane science, 262*(1-2), 60-68.

Kim, K., Fane, A., & Fell, C. (1988). The performance of ultrafiltration membranes pretreated by polymers. *Desalination, 70*(1-3), 229-249.

Lencki, R., & Williams, S. (1995). Effect of nonaqueous solvents on the flux behavior of ultrafiltration membranes. *Journal of Membrane Science, 101*(1-2), 43-51.

Lu, D., Zou, H., Guan, R., Dai, H., & Lu, L. (2005). Sulfonation of polyethersulfone by chlorosulfonic acid. *Polymer Bulletin, 54*(1-2), 21-28.

Mehta, A., & Zydney, A. L. (2005). Permeability and selectivity analysis for ultrafiltration membranes. *Journal of Membrane Science, 249*(1), 245-249.

Moghadam, P. N., Hasanzadeh, R., Fathi, F., & Nasr, N. (2013). Comparative study for adsorption of AL (III) ions from aqueous solutions with series of nano functional copolymers. *Journal of Macromolecular Science, Part A, 50*(12), 1167-1181.

Rabiller-Baudry, M., Bégoin, L., Delaunay, D., Paugam, L., & Chaufer, B. (2008). A dual approach of membrane cleaning based on physico-chemistry and hydrodynamics: application to PES membrane of dairy industry. *Chemical Engineering and Processing: Process Intensification, 47*(3), 267-275.

Reddy, A., Mohan, D. J., Bhattacharya, A., Shah, V., & Ghosh, P. (2003). Surface modification of ultrafiltration membranes by preadsorption of a negatively charged polymer: I. Permeation of water soluble polymers and inorganic salt solutions and fouling resistance properties. *Journal of Membrane Science, 214*(2), 211-221.

Scheidelaar, S., Koorengevel, M. C., van Walree, C. A., Dominguez, J. J., Dörr, J. M., & Killian, J. A. (2016). Effect of polymer composition and pH on membrane solubilization by styrene-maleic acid copolymers. *Biophysical journal, 111*(9), 1974-1986.

Tang, X., Flint, S., Bennett, R., & Brooks, J. (2010). The efficacy of different cleaners and sanitisers in cleaning biofilms on UF membranes used in the dairy industry. *Journal of Membrane Science, 352*(1-2), 71-75.

Van der Bruggen, B. (2009). Chemical modification of polyethersulfone nanofiltration membranes: a review. *Journal of Applied Polymer Science, 114*(1), 630-642.

Vatsha, B., Ngila, J. C., & Moutloali, R. M. (2014). Preparation of antifouling polyvinylpyrrolidone (PVP 40K) modified polyethersulfone (PES) ultrafiltration (UF) membrane for water purification. *Physics and Chemistry of the Earth, Parts A/B/C, 67*, 125-131.

Wavhal, D. S., & Fisher, E. R. (2002). Hydrophilic modification of polyethersulfone membranes by low temperature plasma-induced graft polymerization. *Journal of Membrane Science, 209*(1), 255-269.

Yamagishi, H., Crivello, J. V., & Belfort, G. (1995). Development of a novel photochemical technique for modifying poly (arylsulfone) ultrafiltration membranes. *Journal of Membrane Science, 105*(3), 237-247.

Zeman, L. J., & Zydney, A. L. (1996). *Microfiltration and ultrafiltration: principles and applications*: CRC Press.

Zhang, D., Karkooti, A., Liu, L., Sadrzadeh, M., Thundat, T., Liu, Y., & Narain, R. (2018). Fabrication of antifouling and antibacterial polyethersulfone (PES)/cellulose nanocrystals (CNC) nanocomposite membranes. *Journal of membrane science, 549*, 350-356.

Zhao, C., Xue, J., Ran, F., & Sun, S. (2013). Modification of polyethersulfone membranes–a review of methods. *Progress in Materials Science, 58*(1), 76-150.

Zydney, A. L. (1998). Protein separations using membrane filtration: new opportunities for whey fractionation. *International Dairy Journal, 8*(3), 243-250.

Chapter 3 Evaluation of charged spiral-wound ultrafiltration membranes

3.1 Introduction

Membrane filtration is an important unit operation for protein concentration and fractionation in the dairy industry. The presence of membrane equipment in a dairy processing facility is common and it is used for many different processes, such as standardization of cheese milk, concentration of skim milk, and whey protein concentration. The present work focused on the application of charged ultrafiltration membranes in whey protein concentration. Whey is a by-product of making cheese. About 9 pounds of whey is generated for every pound of cheese manufactured, and a large cheese making plant can produce over 1 million liters of whey daily. Whey contains about half of the dry solids of the original whole milk and 20% of the milk proteins (Smithers, 2008). Whey is essentially a dilute protein and lactose solution, consisting mainly of water (93.5%), lactose (4.5-5%) and protein (0.6%) (Zydney, 1998). The purpose of ultrafiltration is to concentrate proteins from the whey. A tight membrane made of polyethersulfone (PES) of molecular weight cut off (MWCO) 5-10 kDa is most widely used for ultrafiltration of whey (Ganju & Gogate, 2017; Rabiller-Baudry et al., 2008; Tang et al., 2010). Although a 10 kDa PES membrane offers high protein retention, the filtration speed is slow due to its small, tight pores. A membrane having a larger MWCO, although it

operates at higher filtration speed, it is not beneficial because more protein leaks through the membrane. There is trade-off between the hydraulic permeability (filtration speed) and protein retention of the membrane (Mehta & Zydney, 2005). Ionically charged ultrafiltration membranes can overcome this trade-off. Charged membranes made of regenerated cellulose have been proven to have same or increased hydraulic permeability and protein retention as a 10 kDa uncharged membranes (Arunkumar & Etzel, 2013, 2015; Arunkumar, Molitor, & Etzel, 2016).

In the last chapter, a diffusion transfer technology was developed to place a negative or positive charged into disc membranes using a stirred cell. A charged polymer was dissolved in a mixture of organic solvent in water to prepare an incubation solution. The incubation solution was passed through the disc membrane the stirred cell using applied air pressure. The membrane was then washed with water to remove the incubation solution. Whey protein in buffer was permeated through the membrane to evaluate the separation performance of the modified membrane. It was found that the 300 kDa charged disc membrane had 14-fold decrease in the value of the sieving coefficient (S_o) of the protein compared to the 300 kDa raw disc membrane. The objective of this chapter is to scale up the diffusion transfer technology 1500x from 76 mm diameter disc membranes to 1.8-inch and 3.8-inch spiral-wound membranes. Spiral-wound membranes consist of layered sheets of membrane and screen materials rolled around a central core tube. The dairy industry uses spiral-wound membranes instead of flat sheet membranes common in the biotechnology and biopharmaceutical industries. Flat sheet membrane discs were used in the previous chapter because the membrane material can be modified and tested in a

stirred cell quickly and at a low cost. Spiral-wound membranes are larger, more expensive, and consume more chemicals and time when performing experiments. Furthermore, because of the closed configuration of spiral-wound membranes, it is hard to observe any changes in the membrane surface resulting from the modification procedure. The diffusion transfer technology developed using disc membrane was applied to spiral-wound membranes. A total 1500x scale-up was successful: from a flat sheet disc membrane of 76 mm diameter to 1.8-inch and 3.8-inch spiral-wound membranes. In the scale-up, the type of the membrane material and the extent of concentration polarization were kept constant. It was found that a 200 kDa negatively charged spiral-wound membrane offered the same protein retention as an industry standard 10 kDa unmodified membrane but at higher flux.

3.2 Materials and methods

Polyethersulfone flat sheet and spiral wound ultrafiltration membranes (MWCO: 10 kDa, 100kDa, 200kDa, 300kDa) were obtained from Synder Filtration (Vacaville, CA, USA). Poly(4-styrenesulfonic acid)(PSS) (75 kDa, 200 kDa, and 1000 kDa) and poly(diallyldimethylammonium chloride) (PDADAMC) (100-200 kDa) were from Sigma-Aldrich (St. Louis, MO). Styrene-maleic anhydride (SMA) copolymer that was hydrolyzed (SMAH) was from Polyscope Polymers B.V. (XIRAN® 1000HNa, 5kDa, Geleen, The Netherlands). N,N-Dimethylformamide (DMF) was from Fisher Scientific (Pittsburgh, PA, USA). Ethanol was from Decon labs (200 proof, King of Prussia, PA, USA). Whey protein isolate (WPI) was from Davisco Foods International (Le Sueur, MN, USA). WPI contained

92.7% protein, 2.0% ash, 5.0% moisture, 0.0% lactose, and 0.3% lipids. Other chemicals were from Fisher Scientific (Pittsburgh, PA, USA).

3.2.1 Membrane modification method and characterization

Disc membranes were modified and characterized using the procedure described in Chapter 2. Modification of the spiral-wound ultrafiltration membrane elements was carried out by contacting the membrane with an incubation solution consisting of a charged polymer (PSS, SMAH, PDADMAC) dissolved in a mixture of organic solvent (DMF or ethanol) in water using the following flow system shown in Figure 3.1.

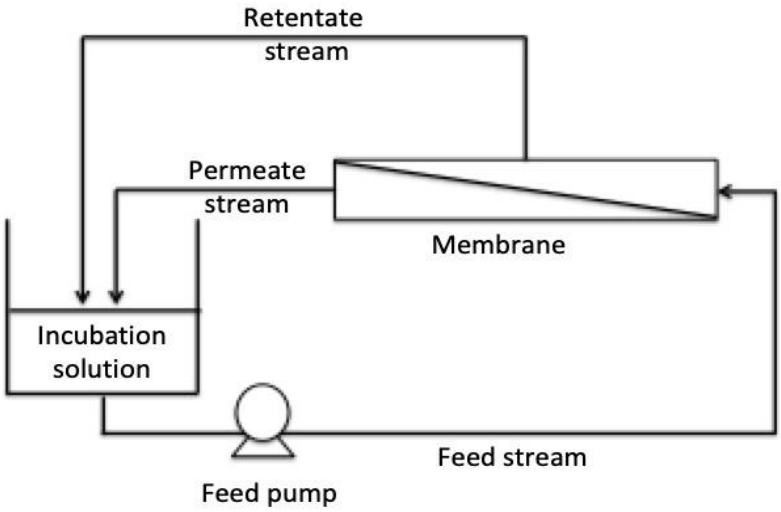

Figure 3.1. Set-up of the filtration system used for modification of spiral-wound membrane elements.

The following procedure was used for spiral-wound membrane elements:

1. After fixing a spiral-wound membrane in the filtration system, the membrane was thoroughly washed with deionized (DI) water at 22 °C to remove preservatives. Hydraulic permeability (L_p) was measured by passing deionized water through the membrane at four different retentate outlet pressures (5, 8, 10, and 15 psi) and 22 °C, which were set by restraining the retentate tubing using a pinch clamp. The slope of the pure water flux ($L/m^2/h$, LMH) versus pressure drop (bar) was the hydraulic permeability.

2. For the 1.8-inch diameter membrane, the incubation solution was prepared by dissolving 1.875% (w/v) SMAH, 3.75% PSS or 3.75% PDADMAC in 1 L of a mixture of 50% organic solvent (DMF or ethanol) in water. For the 3.8-inch diameter membrane, the incubation solution was prepared by dissolving 3.75% (w/v) SMAH in 10 L of a mixture of 50% DMF in water.

3. For the 1.8-inch diameter membrane, the incubation solution was then recirculated through the filtration system using a tubing pump (Masterflex peristaltic pump, model 7549-30; pump head, model 7019; Cole-Parmer, IL) for 16 h at 22 ˚C. For the 3.8-inch diameter membrane, the incubation solution was recirculated for 4 h at 22 ˚C using the same model of tubing pump.

4. The membrane was washed with DI water at 22 °C and the hydraulic permeability measured after modification. When SMAH was used as polymer in the incubation solution, the membrane was rinsed with 0.1 M NaOH solution prior to the DI water rinse in order to deprotonate the carboxylic acids and remove excess SMAH that was not trapped in the membrane by making it water-soluble once more.

5. Sieving coefficient (S_o) was measured using 1 g/L WPI solution dissolved in 50 mM sodium phosphate, pH 6.8 (negatively charged membrane) or pH 3.5 (positively charged membrane). S_o was measured under conditions of total recycle (Figure 3.2). This procedure was called "total recycle" because both permeate and retentate streams were recycled back to the feed solution container. For the 1.8-inch diameter membrane, in order to establish steady state prior to taking samples, 2 L of WPI solution was recirculated at 750 LMH (4 L/min) through the membrane for 6 h at 22 ˚C. For the 3.8-inch diameter membrane, 10 L of WPI solution was recirculated at 120 LMH (9 L/min) for 5 h at 22 ˚C. Permeate was recycled back to the feed solution container at 6-24 LMH. Samples of 5 mL were taken from permeate and retentate tubing at the end of total recycle. S_o was determined by the absorbance ratio of permeate to retentate at 280 nm using a UV spectrophotometer (Ultrospec 1000, Pharmacia Biotech, Uppsala, Sweden). When cheese whey or milk serum permeate was used as the feed solution, samples were sent to Eurofins DQCI (Minneapolis, MN) for measurement of non-protein-nitrogen (NPN) by the trichloroacetic acid (TCA) protein precipitation method, and Total Kjeldahl Nitrogen (TKN). True protein = 6.38*(TKN-NPN).

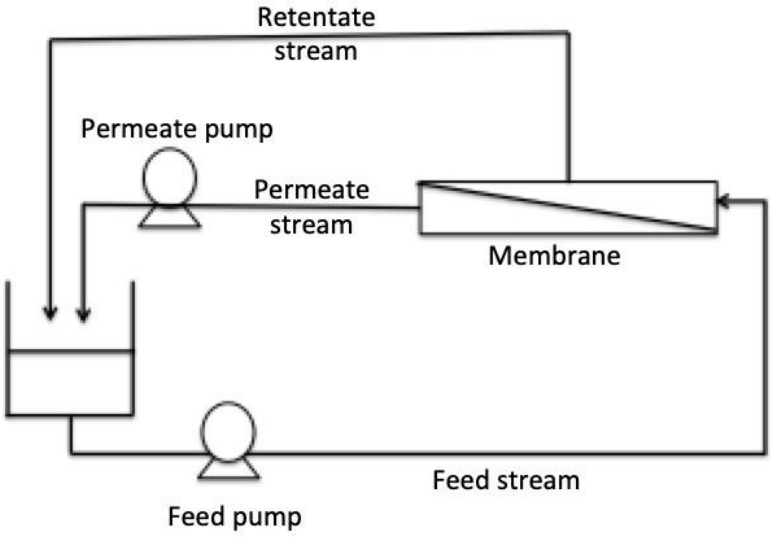

Figure 3.2. Flow system for spiral-wound membrane element.

6. The membrane element was washed using 2 L of 0.2% Alconox detergent (Alconox Inc., NY, USA) for the 1.8-inch diameter membrane and 10 L for the 3.8-inch diameter membrane under total recycle at 22 °C, rinsed thoroughly using DI water at 22 °C and stored in basic water (~ pH 9) at 3 ˚C. For membranes modified by PDADMAC, it was necessary to pump pure ethanol through the membranes under a total recycle at 22 ˚C following 0.2% Alconox detergent washing step in order to restore the hydraulic permeability. The purpose of pure ethanol washing step was to quench hydrophobic interactions that prevented release of the negatively charged hydrophobic surfactant (sodium linear alkylaryl sulfonate) in Alconox from the positively charged PDADMAC on the surface of the hydrophobic PES membrane surface. The PDADMAC membranes were

rinsed using DI water at 22 ˚C after the pure ethanol-washing step and stored in basic water (~pH 9) at 3 ˚C.

7. Steps 4-6 described above were repeated to obtain another value of S_o and L_p. The end results were duplicates measurements for each spiral-wound element.

3.2.2 Gel electrophoresis

For positively charged membranes made using PDADMAC, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed to measure the amount of alpha-lactalbumin and beta-lactoglobulin in the milk serum permeate feed stream and in the retentate and permeate after membrane filtration. Liquid samples without dilution were subjected to the SDS-PAGE sample preparation procedure, loaded into the gel, and visualized by Coomassie Blue staining following the protocol of Bund et al. (2012). Fluorescence laser densitometry after staining by SYPRO Red was used for protein quantification following the protocol of Arunkumar and Etzel (2013). Gels were scanned on a TYHOON FLA 9000 laser densitometer (GE Healthcare, Piscataway, NJ, USA) in fluorescence mode using excitation at 532 nm and emission at 610 nm. Bands were quantified using ImageQuantTL software (GE Healthcare).

3.3 Results

3.3.1 Scale-up to negatively charged 1.8-inch spiral-wound membranes

Table 3.1 contains the values of S_o and L_p for the raw and modified membranes for both 76 mm diameter discs and 1.8-inch diameter by 12-inch long spiral-wound elements (1812 elements). The feed stream was 1 g/L WPI in 50 mM sodium phosphate, pH 6.8. The values of S_o were similar for the 76 mm discs and the spiral-wound elements in each row for a given membrane MWCO and charge (Table 3.1). For example, S_o of the 10 kDa raw disc membrane was not different from the 10 kDa raw spiral-wound membrane. Values of L_p were greater for the 76 mm discs compared to the spiral-wound elements in each row. The lower values of L_p for the spiral-wound elements compared to the 76 mm discs was attributed to the permeate spacer screen in the spiral-wound elements. It was determined that the permeate spacer screen was a significant resistance to flow that was absent when using the 76 mm discs. Spiral-wound membrane elements consist of two layers: (1) a sandwich layer consisting of two sheets of membrane on either side of a permeate diamond-mesh spacer screen, and (2) and a diamond-mesh spacer retentate screen in between each membrane sandwich layer. These two layers are rolled into a cylinder to form the spiral-wound membrane element.

Because the 10 kDa spiral-wound membrane is widely used in the dairy industry for concentration of whey and milk, it was desired to have a charged membrane of similar protein sieving coefficient (S_o = 0.006), but a higher value of the hydraulic permeability

coefficient (L_p = 35 LMH/bar). The 100 kDa and 200 kDa SMAH membranes met this goal. Because the value of S_o was similar and the value of L_p was higher for the 200 kDa SMAH compared to the 100 kDa SMAH spiral-wound membrane, the 200 kDa SMAH spiral-wound membrane was chosen for further study. Thus, the 75x scale-up of the diffusion transfer technology was successful going from a 76 mm diameter disc membrane to an 1812 spiral-wound membrane.

Table 3.1. Values of S_o and L_p for PES discs and spiral-wound elements using 1 g/L WPI in buffer at pH 6.8. Error bars are ± standard deviation.

	76 mm disc		1812 spiral-wound element	
MWCO	S_o	L_p (LMH/bar)	S_o	L_p (LMH/bar)
10 raw	0.006 ± 0.001[a†]	61 ± 4[†]	0.006 ± 0.002[a*]	35 ± 1[*]
100 raw	0.010[a]	162	0.014 ± 0.001[a*]	35 ± 1[*]
100 SMAH	0.006[a]	183	0.003 ± 0.000[b*]	37 ± 1[*]
200 raw	0.023[a]	302	0.025 ± 0.001[a*]	53 ± 1[*]
200 SMAH	0.004[a]	367	0.005 ± 0.001[a*]	54 ± 5[*]
200 PSS	0.010[a]	525	0.012 ± 0.001[a*]	54 ± 5[*]
300 raw	0.217 ± 0.022[a†]	322 ± 23[†]	0.146 ± 0.032[a#]	58 ± 1[#]
300 PSS	0.031 ± 0.018[a†]	405 ± 40[†]	0.017 ± 0.006[a#]	46 ± 2[#]

*Replicates of S_o measured for one membrane.
[#]Triplicates of S_o measured for one membrane.
[†]Triplicates of S_o measured for three membranes.
[a-b]Different letters in the same row indicate significant differences ($p < 0.05$)

3.3.2 Cheese whey filtration experiments using an 1812 negatively charged spiral-wound membrane

The 200 kDa SMAH spiral-wound membrane was compared to the 10 kDa raw spiral-wound membrane using cheese whey as the feed stream. Sweet cheese whey that was cream separated by centrifugation and pasteurized was obtained from the Bioriginal Company (Reedsburg, WI). Whey was adjusted to pH 6.8 by addition of 2 M NaOH and vacuum filtered through a 0.7 μm glass fiber filter (GF/F, Whatman plc, UK). The filtered whey was fed to the spiral-wound membrane filtration system containing the 1812 element (Figure 3.2). Whey permeate flux was controlled to 12 LMH for the 10 kDa raw membrane, and 24 LMH for the 200 kDa charged PES. After whey was recycled for 6 h, 15 mL samples were taken from permeate and retentate tubing. Samples were sent to Eurofins DQCI (Minneapolis, MN) for estimation of NPN and true protein as discussed above.

The result is shown in Table 3.2. Compared to the 10 kDa raw membrane, the 200 kDa negatively charged SMAH membrane had the same value of S_o for true protein and for non-protein nitrogen (NPN). The 200 kDa SMAH membrane had twice the whey flux of the 10 kDa raw membrane. The value of L_p for the 200 kDa SMAH membrane was 36% higher than L_p for the 10 kDa raw membrane.

Table 3.2. Values of S_o and L_p for 1812 spiral-wound elements using cheese whey, pH 6.8. Error bars are ± standard deviation.

1812 Spiral-wound Element	S_o True Protein	S_o NPN	Whey Flux (LMH)	L_p (LMH/bar)
10 raw	0.052 ± 0.025[a*]	0.70 ± 0.009[b*]	12	33 ± 2*
200 SMAH	0.029 ± 0.000[a*]	0.74 ± 0.021[b*]	24	45 ± 6*

*Duplicate experiments for one membrane.
[a-b]Different letters in the same column indicate significant differences ($p < 0.05$)

3.3.3 Scale-up from 1812 to 3838 spiral-wound membranes using cheese whey

Table 3.3 contains the values of S_o and L_p for the 10 kDa raw, 200 kDa raw and 200 kDa charged membrane using sweet cheese whey at pH 6.8 as the feed stream. Sweet cheese whey that was cream separated by centrifugation and pasteurized was obtained from Klondike Cheese Co. (Monroe, WI). The natural pH of the whey was 6.6. It was adjusted to pH 6.8 by addition of 2 M NaOH prior to ultrafiltration. The whey was fed to a spiral-wound membrane filtration system where the 10 kDa raw, 200 kDa raw and 200 kDa charged membranes were mounted in parallel flow. Whey permeate flux was controlled to 12 LMH for the 10 kDa raw membrane, and 24 LMH for the 200 kDa charged and uncharged membranes. After the whey was recycled for 3 h, 50 mL samples of the permeate and retentate were taken from each of the three permeate streams coming from the three different membrane modules and from the common retentate and feed streams.

Samples were sent to Eurofins DQCI (Minneapolis, MN) for analysis as mentioned previously.

Compared to the 10 kDa raw membrane, the 200 kDa raw membrane had the same S_o for true protein while the 200 kDa negatively charged membrane had a 34% lower S_o for true protein (Table 3.3). S_o for non-protein nitrogen (NPN) was slightly higher for the 10 kDa charged membrane than either the 200 kDa raw membrane or the 200 kDa charged membrane. S_o for total solids (TS) was lower for the 200 kDa charged membrane than either the 10 kDa raw membrane or the 200 kDa charged membrane. The 200 kDa charged membrane had lower S_o for true protein, NPN and TS than the 10 kDa raw membrane.

Table 3.3. Values of S_o and L_p for 3838 spiral-wound spiral wound membranes.

MWCO	Whey Flux (LMH)	S_o True Protein	S_o NPN	S_o TS	L_p (LMH/bar)
10 raw	12	0.041	0.78	0.85	38
200 raw	24	0.041	0.70	0.86	55
200 SMAH	24	0.027	0.70	0.77	48

3.3.4 Scale-up from positively charged discs to 1812 spiral-wound membranes

Table 3.4 contains values of S_o and L_p for disc membranes and 1812 spiral wound elements with and without modification to impart a positive charge using PDADMAC. The

positively charged membranes showed more than 5-fold decrease in S_o compared to the raw membranes. For example, comparing the 300 kDa raw disc membrane to the 300 kDa PDADMAC disc membrane, S_o decreased by 7.5-fold while L_p remained unchanged. The decrease in S_o was attributed to rejection of the positively charged ALA and BLG at pH 3.5 by the positively charged quaternary amine groups of PDADAMC. Comparing the 300 kDa raw to the 300 kDa PDADMAC spiral-wound membranes, S_o decreased by 5-fold while L_p decreased by 38 % ($p < 0.05$). The 75x scale-up from positively charged disc membranes to spiral-wound membranes was successful.

Table 3.4. Performance of positively charged PES discs and 1812 spiral-wound membranes using 1 g/L WPI at pH 3.5.

	76 mm flat sheet disc		1812 spiral-wound element	
MWCO	S_o	L_p (LMH/bar)	S_o	L_p (LMH/bar)
300 raw	$0.369 \pm 0.041^{a\S}$	$315 \pm 21^{a\S}$	$0.258 \pm 0.001^{a*}$	$61 \pm 2^{a*}$
300 PDADMAC	$0.049 \pm 0.004^{b\S}$	$357 \pm 43^{a\S}$	$0.034 \pm 0.011^{b*}$	$37 \pm 5^{b*}$

$^{a-b}$Different letters in the same column indicate significant differences ($p < 0.05$)
*Replicates of S_o measurement for one membrane.
§Triplicates of S_o measurement for one membrane.

3.3.5 Fractionation of whey proteins in milk serum permeate using 1812 positively charged spiral-wound membranes

The 1.8-inch 300 kDa PDADMAC positively charged membrane was used to separate alpha-lactalbumin (ALA) from beta-lactoglobulin (BLG). Milk serum permeate (MSP) was obtained from the Babcock Hall Dairy Plant. MSP was adjusted to pH 4.3 by addition of 2 M HCl and vacuum filtered through a 0.7 μm glass fiber filter (GF/F, Whatman plc, UK). The filtered MSP solution was fed to the spiral-wound membrane filtration system containing the 1.8-inch diameter element (Figure 3.2). MSP permeate flux was controlled to 24 LHM or 6 LMH. After MSP was recycled for 6 h, 5 mL samples were taken from the permeate and retentate tubing. The amounts of ALA and BLG in the samples were determined by laser fluorescence densitometry of the SDS-PAGE gel stained by SYPRO Red (Figure 3.3). S_o was calculated from the band volume. The SD lane was a standard solution consisting of 0.3 g/L BLG (upper band) and 0.1 g/L ALA (lower band).

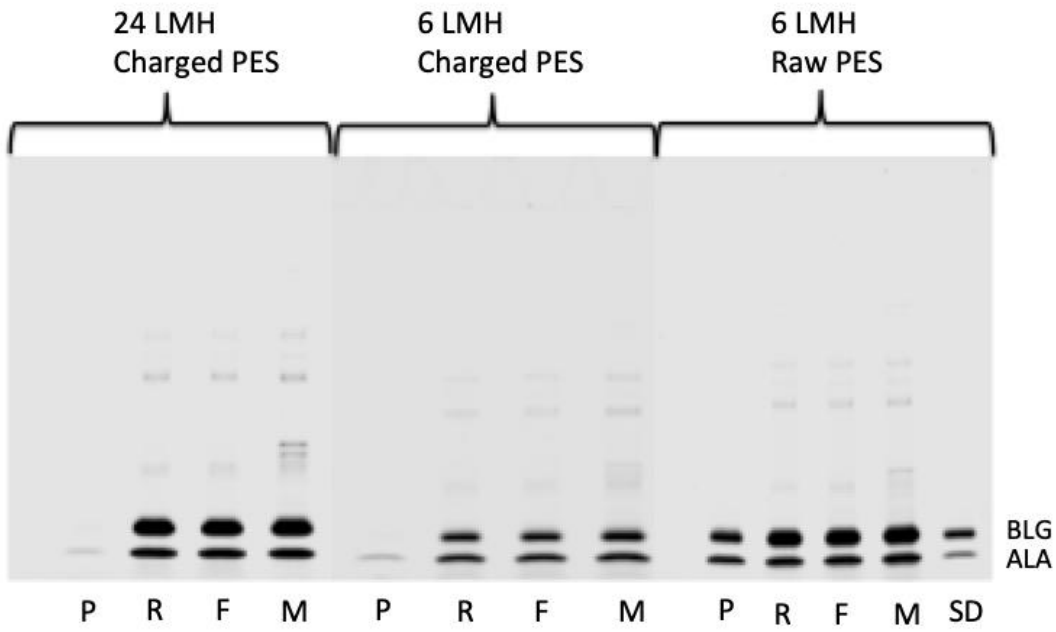

Figure 3.3 SDS-PAGE gels after SYPRO Red staining of the retentate (R), permeate (P), feed solution (F) and the original MSP (M) for the PDADMAC charged membrane and the raw membrane. SD = standard.

As shown in Table 3.5, the raw 300 kDa membrane had S_o = 0.75 for ALA and S_o = 0.45 for BLG. Both ALA and BLG were able to pass freely through the uncharged 300 kDa raw spiral-wound membrane. The goal was for BLG to be rejected by the PDADMAC membrane and for ALA to pass through into the permeate stream. This did not happen. For the 300 kDa positively charged PDADMAC membrane, S_o = 0.042 for ALA and S_o = 0.00 for BLG at a permeate flux of 6 LMH, and S_o = 0.025 for ALA and S_o = 0.00 for BLG at a permeate flux of 24 LMH. S_o for ALA for the positively charged PDADMAC membrane (S_o = 0.042) was

18-fold smaller than for the uncharged spiral-wound membrane at a permeate flux of 6 LMH, and 30-fold smaller at 24 LMH. Thus, although the PDADMAC membrane rejected BLG, the ALA did not pass freely through. This was attributed to excessive positive charge on the membrane resulting from too much PDADMAC. As seen in Table 3.4, this was likely not from pore restriction because values of L_p were not affected substantially by the PDADMAC. Future work should examine placing less PDADMAC on the membrane surface by using an incubation solution of 10-fold less PDADMAC dissolved in 10-50% ethanol.

Table 3.5. Values of S_o for ALA and BLG for a 300 kDa 1812 positively charged spiral-wound membrane determined by scanning SDS-PAGE gels of Figure 3.3.

Membrane	S_o ALA	S_o BLG	Permeate Flux (LMH)
Raw	0.75	0.45	6
3.75% PDADMAC	0.042	0.000	6
3.75% PDADMAC	0.025	0.000	24

3.3.6 Effect of PDADMAC concentration on S_o

In order to reduce the amount of positive charge on the PDADMAC membrane, disc membranes were modified using PDADMAC at successively lower PDADMAC concentrations in 50% ethanol (Table 3.6). The value of S_o for WPI in buffer at pH 3.5 increased 11-fold as the concentration of PDADMAC decreased from 3.75% to 0.38%. S_o increased linearly with decreasing PDADMAC concentration ($R^2 = 0.98$).

Table 3.6. Values of S_o, L_{p0} and mean L_p (L_{p1}, L_{p2}, L_{p3}) for a 300 kDa membrane discs modified using different concentrations of PDADMAC in 50% ethanol (S_o measured using WPI pH 3.5). Different letters in the same row of L_p indicate significant statistical differences ($p < 0.05$).

Concentration of PDADMAC	S_o	L_{p0} (LMH/bar)	L_p (LMH/bar)
3.75%	0.0487 ± 0.004[§]	332[a]	357 ± 43[§a]
3.50%	0.087	298	268
3.20%	0.148 ± 0.092[§]	373[a]	244 ± 46[§a]
3.00%	0.205 ± 0.086[§]	328[a]	262 ± 35[§a]
2.50%	0.277	312	328
1.875%	0.37	333	469
1.00%	0.449	318	473
0.375%	0.522	327	474

[§]Triplicate measurement of S_o and L_p for one membrane disc

In order to scale up, 1.8-inch 300 kDa PDADMAC membranes were made using 3.0% or 2.5% PDADMAC in 50% ethanol, and then tested to separate alpha-lactalbumin (ALA) from beta-lactoglobulin (BLG). Milk serum permeate (MSP) was filtered through the

modified membranes following the procedure in Section 3.3.5. MSP permeate flux was controlled to 6 LMH. The amounts of ALA and BLG in the samples are shown in Figure 3.4. Comparing Figures 3.3 and 3.4, more ALA permeated through the positively charged membranes when 3.0% or 2.5% PDADMAC was used versus 3.75% PDADMAC.

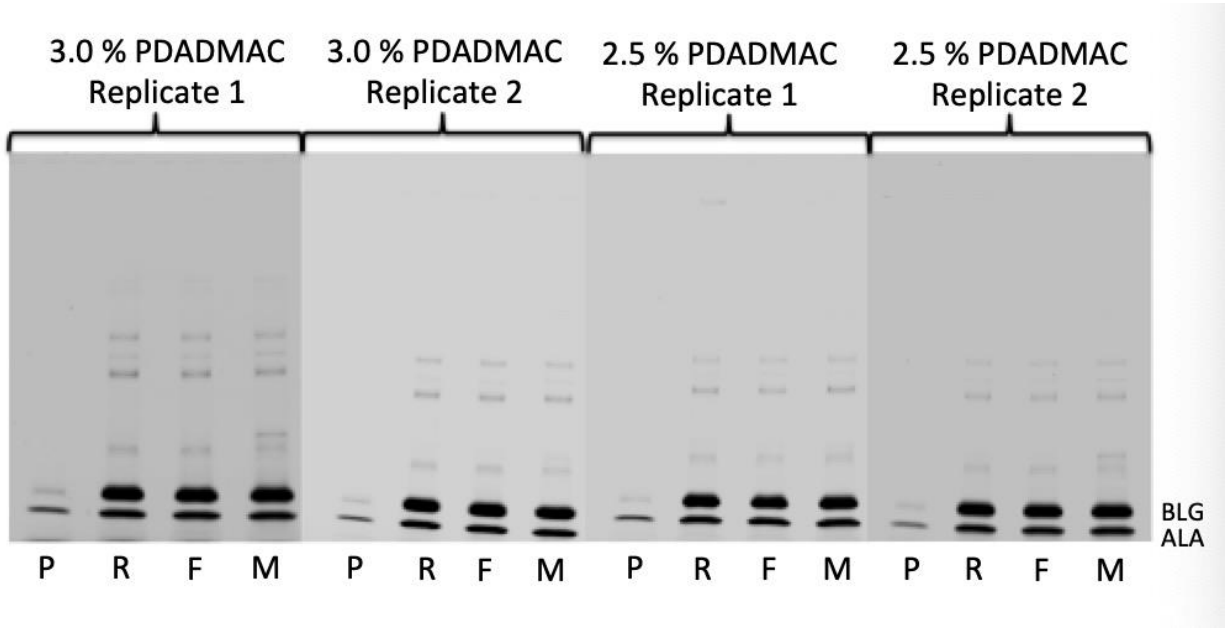

Figure 3.4 SDS-PAGE gels after SYPRO Red staining of the retentate (R), permeate (P), feed solution (F) and the original MSP (M) for the PDADMAC membranes.

Decreasing the PDADMAC concentration from 3.75% to 3.0% and 2.5% led to a 5-fold increase in permeation of ALA while only slight increase in permeation of BLG (Table 3.7). The 300 kDa positively charged membrane made using 3.0% PDADMAC had S_o = 0.218 for ALA and S_o = 0.027 for BLG. Decreasing the PDADMAC concentration from 3.0% to 2.5% did not change the sieving coefficients of ALA or BLG ($p > 0.05$). The increase in

permeation of ALA using lower concentration of PDADMAC was attributed to less positive charge on the membrane resulting from less PDADMAC in the incubation solution.

Table 3.7. Values of S_o for ALA and BLG for a 300 kDa 1812 positively charged spiral-wound membrane determined by scanning SDS-PAGE gels of Figure 3.4. Different letters in the same column of S_o indicate significant statistical differences ($p < 0.05$).

Concentration of PDADMAC	S_o ALA	S_o BLG	Permeate Flux (LMH)
3.75%	0.042	0.000	6
3.0%	$0.218 \pm 0.042^{a*}$	$0.027 \pm 0.010^{a*}$	6
2.5%	$0.207 \pm 0.040^{a*}$	$0.019 \pm 0.001^{a*}$	6

*Duplicate measurement of S_o for one membrane element.

3.3.7 Effect of cleaning solutions on charged membranes

In the dairy industry, membranes are subjected daily to a clean-in-place (CIP) procedure that uses strong acids, caustics, and chlorine sanitizer solutions. The 100 kDa and 200 kDa SMAH modified 1812 spiral-wound membranes were subjected to the CIP procedure recommended by Synder Filtration. This CIP procedure involves three steps: (1) circulating DI water through the membrane at 40 ˚C and then diluted NaOH solution at pH 10.5 for 30 min at 40 ˚C, and flushing the system using DI water at 40 ˚C, (2) circulating DI water at 40 ˚C through the membrane and then diluted phosphoric acid solution at pH 3,

and flushing with DI water at 40 ˚C, (3) circulating DI water at 40 ˚C and then 150 ppm chlorine solution for 20 min, and flushing with DI water at 40 ˚C.

Values of S_o for the 100 kDa SMAH modified membrane before and after each CIP step are shown in Table 3.8. Data were obtained by filtering 1 g/L WPI in buffer at pH 6.8 through the membrane after each cleaning step. The values of S_o were not changed by the CIP procedure. The SMAH modified membranes were resistant to the CIP treatment. Values of S_o for a 200 kDa SMAH modified membrane were also measured after the three CIP steps in Table 3.8. The value of S_o did not change after the CIP procedure.

Table 3.8. Negatively charged 1812 spiral-wound membrane before and after CIP.

CIP step	S_o of 100 kDa SMAH	S_o of 200 kDa SMAH
Before CIP	0.003	0.0053
After caustic wash	0.004	---
After acid wash	0.004	---
After chlorine sanitation	0.005	0.0059

3.4 Discussion

Going from a 76 mm diameter disc to a 3838 spiral-wound membrane is a 1,500x scale-up in membrane area. It is also a scale-up in flow geometry: going from dead-end flow using a single flat sheet membrane to tangential-flow using a multi-layer membrane sheet rolled into a spiral. The membranes were modified to carry a negative charge or a positive charge by permeation of a mixture of organic solvent in water that contained a charged polymer through the membranes. The scale-up experiments from disc to spiral-wound membrane were successful. The charge modified spiral-wound membranes had a lower value of S_o than the unmodified spiral-wound membranes of the same MWCO. The negatively charged 200 kDa spiral-wound membranes (1812 and 3838) had same or lower value of S_o when compared to the unmodified 10 kDa spiral-wound membranes used currently in the dairy industry.

Cheese whey contains primarily the proteins alpha-lactalbumin (ALA) and beta-lactoglobulin (BLG). The isoelectric point is pI = 4.4 for ALA and pI = 5.2 for BLG. The whey proteins are charged negative at pH 6.8. The negatively charged polymers tested in the present work impart a negative charge to the membrane: PSS polymer has sulfonic acid groups, while SMAH polymer has carboxylic acid groups. The negatively charged ALA and BLG proteins were repelled by negative charges on the modified membrane. Although ALA and BLG are smaller than the pores of the 200 kDa modified membranes, electrostatic repulsion dominated over size-based filtration to prevent the proteins from passing through the charged membrane.

In the present work, three 3838 spiral-wound membranes were tested: 10 kDa raw, 200 kDa raw, and the negatively charged 200 kDa SMAH membrane. Whey at pH 6.8 was the feed stream. The 200 kDa SMAH membrane permeated less protein (S_o = 0.027) than the 10 kDa raw membrane (S_o = 0.041). Permeation of NPN was also less for the 200 kDa SMAH membrane (S_o = 0.70) than the 10 kDa raw membrane (S_o = 0.78). Glycomacropeptide (GMP) is a small 8.6 kDa peptide in cheese whey that is charged negative at pH 6.8. The lower permeation of NPN using the negatively charged 200 kDa membrane was attributed to less permeation of GMP compared to the unmodified 10 kDa membrane.

3.5 Conclusions

A flow system was built to convert uncharged spiral-wound membranes to charged membranes (Figure 3.1). A charged polymer (PSS, SMAH, PDADMAC) dissolved in a mixture of 50% organic solvent (DMF, ethanol) in water was passed through the spiral-wound membrane to make it permanently charged negative or positive. Scale-up experiments from a 76 mm diameter disc membrane to a 3.8-inch spiral-wound membrane were successful. This represents a 1,500x scale up in membrane area, and a scale up from a dead-end flow to a cross flow mode of operation. The 1.8-inch diameter 200 kDa negatively charged spiral-wound membrane modified by SMAH offered equally high protein retention as the 10 kDa raw membrane but at a higher water flux. A 3.8-inch 200 kDa spiral-wound membrane modified to carry a negative charge by using SMAH was also successfully modified. Membranes are flushed daily in the dairy industry following a clean-in-plate

(CIP) procedure. Resistance to the cleaning solution is an important feature for charged membranes. It was found that the performance of the charged membranes did not change after the CIP procedure. Thus, the 200 kDa negatively charged spiral-wound membrane might potentially replace the 10 kDa raw spiral-wound membrane in industrial use.

Positively charged 300 kDa membranes modified by PDADMAC were also tested. The goal was for BLG to be rejected by the PDADMAC membrane and for ALA to pass through into the permeate stream. Both ALA and BLG were able to pass freely through the uncharged 300 kDa raw spiral-wound membrane. For the positively charged membrane modified using 3.0% or 2.5% PDADMAC in 50% ethanol, BLG was mostly rejected by the PDADMAC membrane, and ALA passed through the membrane ten-times more freely than BLG. Thus, fractionation of ALA from BLG was successful using the PDADMAC membrane.

3.6 References

Akbari, A., Desclaux, S., Rouch, J., Aptel, P., & Remigy, J. (2006). New UV-photografted nanofiltration membranes for the treatment of colored textile dye effluents. *Journal of membrane science, 286*(1-2), 342-350.

Al Malek, S., Seman, M. A., Johnson, D., & Hilal, N. (2012). Formation and characterization of polyethersulfone membranes using different concentrations of polyvinylpyrrolidone. *Desalination, 288*, 31-39.

Alenazi, N. A., Hussein, M. A., Alamry, K. A., & Asiri, A. M. (2017). Modified polyether-sulfone membrane: a mini review. *Designed monomers and polymers, 20*(1), 532-546.

Amirilargani, M., Saljoughi, E., Mohammadi, T., & Moghbeli, M. (2010). Effects of coagulation bath temperature and polyvinylpyrrolidone content on flat sheet asymmetric polyethersulfone membranes. *Polymer Engineering & Science, 50*(5), 885-893.

Arthanareeswaran, G., & Starov, V. M. (2011). Effect of solvents on performance of polyethersulfone ultrafiltration membranes: Investigation of metal ion separations. *Desalination, 267*(1), 57-63.

Arunkumar, A., & Etzel, M. R. (2013). Fractionation of α-lactalbumin from β-lactoglobulin using positively charged tangential flow ultrafiltration membranes. *Separation and Purification Technology, 105*, 121-128.

Arunkumar, A., & Etzel, M. R. (2015). Negatively charged tangential flow ultrafiltration membranes for whey protein concentration. *Journal of Membrane Science, 475*, 340-348.

Arunkumar, A., Molitor, M. S., & Etzel, M. R. (2016). Comparison of flat-sheet and spiral-wound negatively-charged wide-pore ultrafiltration membranes for whey protein concentration. *International dairy journal, 56*, 129-133.

Atra, R., Vatai, G., Bekassy-Molnar, E., & Balint, A. (2005). Investigation of ultra-and nanofiltration for utilization of whey protein and lactose. *Journal of food engineering, 67*(3), 325-332.

Balagtas, J., Hutchinson, F., Krochta, J., & Sumner, D. (2003). Anticipating market effects of new uses for whey and evaluating returns to research and development. *Journal of dairy science, 86*(5), 1662-1672.

Barth, C., Goncalves, M., Pires, A., Roeder, J., & Wolf, B. (2000). Asymmetric polysulfone and polyethersulfone membranes: effects of thermodynamic conditions during formation on their performance. *Journal of Membrane Science, 169*(2), 287-299.

Bechhold, H. (1908). Durchlässigkeit von Ultrafiltern. *Zeitschrift für Physikalische Chemie, 64*(1), 328-342.

Belfer, S., Fainchtain, R., Purinson, Y., & Kedem, O. (2000). Surface characterization by FTIR-ATR spectroscopy of polyethersulfone membranes-unmodified, modified and protein fouled. *Journal of Membrane Science, 172*(1-2), 113-124.

Bhattacharya, S. (2014). *Conventional and advanced food processing technologies*: John Wiley & Sons.

Blanco, J., Nguyen, Q., & Schaetzel, P. (2002). Sulfonation of polysulfones: Suitability of the sulfonated materials for asymmetric membrane preparation. *Journal of applied polymer science, 84*(13), 2461-2473.

Blanco, J.-F., Sublet, J., Nguyen, Q. T., & Schaetzel, P. (2006). Formation and morphology studies of different polysulfones-based membranes made by wet phase inversion process. *Journal of membrane science, 283*(1-2), 27-37.

Brink, L., Elbers, S., Robbertsen, T., & Both, P. (1993). The anti-fouling action of polymers preadsorbed on ultrafiltration and microfiltration membranes. *Journal of membrane science, 76*(2-3), 281-291.

Bund, T., Allelein, S., Arunkumar, A., Lucey, J. A., & Etzel, M. R. (2012). Chromatographic purification and characterization of whey protein–dextran glycation products. *Journal of Chromatography A, 1244*, 98-105.

Cheng, C., Li, S., Zhao, W., Wei, Q., Nie, S., Sun, S., & Zhao, C. (2012). The hydrodynamic permeability and surface property of polyethersulfone ultrafiltration membranes with mussel-inspired polydopamine coatings. *Journal of membrane science, 417*, 228-236.

Deng, B., Li, J., Hou, Z., Yao, S., Shi, L., Liang, G., & Sheng, K. (2008). Microfiltration membranes prepared from polyethersulfone powder grafted with acrylic acid by simultaneous irradiation and their pH dependence. *Radiation Physics and Chemistry, 77*(7), 898-906.

Dyck, A., Fritsch, D., & Nunes, S. (2002). Proton‐conductive membranes of sulfonated polyphenylsulfone. *Journal of applied polymer science, 86*(11), 2820-2827.

Etzel, M. R., & Arunkumar, A. (2017). Charged ultrafiltration and microfiltration membranes for antibody purification. *Process Scale Purification of Antibodies, 43*, 246.

Fick, A. (1855). V. On liquid diffusion. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science, 10*(63), 30-39.

Ganju, S., & Gogate, P. R. (2017). A review on approaches for efficient recovery of whey proteins from dairy industry effluents. *Journal of Food Engineering, 215*, 84-96.

Hansen, C. (2007). *Hansen solubility parameters* (Hansen Ed. 2nd ed.). Boca Raton, FL: CRC Press.

Howell, J. A., Sanchez, V., & Field, R. W. (2012). *Membranes in bioprocessing: theory and applications*: Springer Science & Business Media.

Iojoiu, C., Maréchal, M., Chabert, F., & Sanchez, J. Y. (2005). Mastering sulfonation of aromatic polysulfones: crucial for membranes for fuel cell application. *Fuel cells, 5*(3), 344-354.

Iwa, T., Kumazawa, H., & Bae, S. Y. (2004). Gas permeabilities of NH3‐plasma‐treated polyethersulfone membranes. *Journal of applied polymer science, 94*(2), 758-762.

Jiang, J., Zhu, L.-P., Li, X.-L., Xu, Y.-Y., & Zhu, B.-K. (2010). Surface modification of PE porous membranes based on the strong adhesion of polydopamine and covalent immobilization of heparin. *Journal of Membrane Science, 364*(1-2), 194-202.

Kato, K., Uchida, E., Kang, E.-T., Uyama, Y., & Ikada, Y. (2003). Polymer surface with graft chains. *Progress in Polymer Science, 28*(2), 209-259.

Keszler, B., Kovacs, G., Tóth, A., Bertóti, I., & Hegyi, M. (1991). Modified polyethersulfone membranes. *Journal of membrane science, 62*(2), 201-210.

Kim, I., Choi, J., & Tak, T. (1999). Sulfonated polyethersulfone by heterogeneous method and its membrane performances. *Journal of Applied Polymer Science, 74*(8), 2046-2055.

Kim, J., & Kim, C. (2005). Ultrafiltration membranes prepared from blends of polyethersulfone and poly (1-vinylpyrrolidone-co-styrene) copolymers. *Journal of membrane science, 262*(1-2), 60-68.

Kim, K., Fane, A., & Fell, C. (1988). The performance of ultrafiltration membranes pretreated by polymers. *Desalination, 70*(1-3), 229-249.

Koros, W., Ma, Y., & Shimidzu, T. (1996). Terminology for membranes and membrane processes (IUPAC Recommendations 1996). *Pure and Applied Chemistry, 68*(7), 1479-1489.

Koros, W., & Pinnau, I. (1994). *Membrane formation for gas separation processes*: CRC Press: Boca Raton, FL.

Kotsanopoulos, K. V., & Arvanitoyannis, I. S. (2015). Membrane processing technology in the food industry: food processing, wastewater treatment, and effects on physical, microbiological, organoleptic, and nutritional properties of foods. *Critical reviews in food science and nutrition, 55*(9), 1147-1175.

Kumar, P., Sharma, N., Ranjan, R., Kumar, S., Bhat, Z., & Jeong, D. K. (2013). Perspective of membrane technology in dairy industry: A review. *Asian-Australasian journal of animal sciences, 26*(9), 1347.

Lafreniere, L. Y., Talbot, F. D., Matsuura, T., & Sourirajan, S. (1987). Effect of poly (vinylpyrrolidone) additive on the performance of poly (ether sulfone) ultrafiltration membranes. *Industrial & engineering chemistry research, 26*(11), 2385-2389.

Lencki, R., & Williams, S. (1995). Effect of nonaqueous solvents on the flux behavior of ultrafiltration membranes. *Journal of Membrane Science, 101*(1-2), 43-51.

Lipnizki, F. (2010). Cross-flow membrane applications in the food industry. *Membranes for food applications. Peinemann KV, Pereira S, Giorno L, Editores. Estados Unidos de América: Willey-VCH*, 1-23.

Lonsdale, H. (1982). The growth of membrane technology. *Journal of membrane science, 10*(2-3), 81-181.

Lu, D., Zou, H., Guan, R., Dai, H., & Lu, L. (2005). Sulfonation of polyethersulfone by chlorosulfonic acid. *Polymer Bulletin, 54*(1-2), 21-28.

Ma, X., Su, Y., Sun, Q., Wang, Y., & Jiang, Z. (2007). Preparation of protein-adsorption-resistant polyethersulfone ultrafiltration membranes through surface segregation of amphiphilic comb copolymer. *Journal of Membrane Science, 292*(1-2), 116-124.

Madaeni, S., & Rahimpour, A. (2005). Effect of type of solvent and non‐solvents on morphology and performance of polysulfone and polyethersulfone ultrafiltration

membranes for milk concentration. *Polymers for advanced technologies, 16*(10), 717-724.

Mahendran, R., Malaisamy, R., Arthanareeswaran, G., & Mohan, D. (2004). Cellulose acetate–poly (ether sulfone) blend ultrafiltration membranes. II. Application studies. *Journal of applied polymer science, 92*(6), 3659-3665.

Manea, C., & Mulder, M. (2002). Characterization of polymer blends of polyethersulfone/sulfonated polysulfone and polyethersulfone/sulfonated polyetheretherketone for direct methanol fuel cell applications. *Journal of membrane Science, 206*(1-2), 443-453.

Mehta, A., & Zydney, A. L. (2005). Permeability and selectivity analysis for ultrafiltration membranes. *Journal of Membrane Science, 249*(1), 245-249.

Michaels, A. S. (1968). New separation technique for CPI. *Chemical Engineering Progress, 64*(12), 31-&.

Moghadam, P. N., Hasanzadeh, R., Fathi, F., & Nasr, N. (2013). Comparative study for adsorption of AL (III) ions from aqueous solutions with series of nano functional copolymers. *Journal of Macromolecular Science, Part A, 50*(12), 1167-1181.

Mollea, C., Marmo, L., & Bosco, F. (2013). Valorisation of cheese whey, a by-product from the dairy industry. In *Food industry*: IntechOpen.

Nollet, J.-A. (1752). Recherches sur les causes du bouillonnement des liquides. *Hist Acad Roy Sci, 1*, 57-104.

Onwulata, C., & Huth, P. (2009). *Whey processing, functionality and health benefits* (Vol. 82): John Wiley & Sons.

Park, Y. W., Haenlein, G., & Ag, D. S. (2013). Milk and dairy products in human nutrition. *Production, Composition and Health. Ed. Wilet-Blackwell. A John Wiley&Sons, Ltd, Publication*, 700.

Pinnau, I., & Freeman, B. D. (2000). Formation and modification of polymeric membranes: overview. In: ACS Publications.

Piry, A., Kühnl, W., Grein, T., Tolkach, A., Ripperger, S., & Kulozik, U. (2008). Length dependency of flux and protein permeation in crossflow microfiltration of skimmed milk. *Journal of Membrane Science, 325*(2), 887-894.

Rabiller-Baudry, M., Bégoin, L., Delaunay, D., Paugam, L., & Chaufer, B. (2008). A dual approach of membrane cleaning based on physico-chemistry and hydrodynamics: application to PES membrane of dairy industry. *Chemical Engineering and Processing: Process Intensification, 47*(3), 267-275.

Rabiller-Baudry, M., Gouttefangeas, F., Le Lannic, J., & Rabiller, P. (2012). Coupling of SEM-EDX and FTIR-ATR to (quantitatively) investigate organic fouling on porous organic composite membranes. *Current microscopy contributions to advances in science and technology*, 1-11.

Rahimpour, A., Madaeni, S., & Mehdipour-Ataei, S. (2008). Synthesis of a novel poly (amide-imide)(PAI) and preparation and characterization of PAI blended polyethersulfone (PES) membranes. *Journal of membrane science, 311*(1-2), 349-359.

Reddy, A., Mohan, D. J., Bhattacharya, A., Shah, V., & Ghosh, P. (2003). Surface modification of ultrafiltration membranes by preadsorption of a negatively charged polymer: I.

Permeation of water soluble polymers and inorganic salt solutions and fouling resistance properties. *Journal of Membrane Science, 214*(2), 211-221.
Rektor, A., & Vatai, G. (2004). Membrane filtration of Mozzarella whey. *Desalination, 162*, 279-286.
Saxena, A., Tripathi, B. P., Kumar, M., & Shahi, V. K. (2009). Membrane-based techniques for the separation and purification of proteins: An overview. *Advances in colloid and interface science, 145*(1-2), 1-22.
Saxena, N., Prabhavathy, C., De, S., & DasGupta, S. (2009). Flux enhancement by argon–oxygen plasma treatment of polyethersulfone membranes. *Separation and purification technology, 70*(2), 160-165.
Scheidelaar, S., Koorengevel, M. C., van Walree, C. A., Dominguez, J. J., Dörr, J. M., & Killian, J. A. (2016). Effect of polymer composition and pH on membrane solubilization by styrene-maleic acid copolymers. *Biophysical journal, 111*(9), 1974-1986.
Schulze, A., Marquardt, B., Kaczmarek, S., Schubert, R., Prager, A., & Buchmeiser, M. R. (2010). Electron Beam‐Based Functionalization of Poly (ethersulfone) Membranes. *Macromolecular rapid communications, 31*(5), 467-472.
Short, J. (1995). *Membrane separation in food processing*: Marcel Dekker, Inc. New York.
Sidney, L., & Srinivasa, S. (1964). High flow porous membranes for separating water from saline solutions. In: Google Patents.
Smith, K. (2008). *Dried Dairy Ingredients*. In K. Smith (Ed.).
Smithers, G. W. (2008). Whey and whey proteins—from 'gutter-to-gold'. *International Dairy Journal, 18*(7), 695-704.
Strathmann, H., Giorno, L., & Drioli, E. (2011). *Introduction to membrane science and technology* (Vol. 544): Wiley-VCH Weinheim.
Tamime, A. Y. (2012). *Membrane processing: dairy and beverage applications*: John Wiley & Sons.
Tang, X., Flint, S., Bennett, R., & Brooks, J. (2010). The efficacy of different cleaners and sanitisers in cleaning biofilms on UF membranes used in the dairy industry. *Journal of Membrane Science, 352*(1-2), 71-75.
Torres, M., Soriano, E., De Abajo, J., & dela Campa, J. (1993). Comparative study of the behaviour of experimental polyamide UF membranes. The effect of polyvinylpyrrolidone used as an additive. *Journal of membrane science, 81*(1-2), 31-42.
Tyszler, D., Zytner, R. G., Batsch, A., Brügger, A., Geissler, S., Zhou, H., . . . Melin, T. (2006). Reduced fouling tendencies of ultrafiltration membranes in wastewater treatment by plasma modification. *Desalination, 189*(1-3), 119-129.
Van der Bruggen, B. (2009). Chemical modification of polyethersulfone nanofiltration membranes: a review. *Journal of Applied Polymer Science, 114*(1), 630-642.
Van Reis, R., Goodrich, E., Yson, C., Frautschy, L., Whiteley, R., & Zydney, A. (1997). Constant Cwall ultrafiltration process control. *Journal of membrane science, 130*(1-2), 123-140.

van Reis, R., & Zydney, A. (2007). Bioprocess membrane technology. *Journal of Membrane Science, 297*(1-2), 16-50.

Vatsha, B., Ngila, J. C., & Moutloali, R. M. (2014). Preparation of antifouling polyvinylpyrrolidone (PVP 40K) modified polyethersulfone (PES) ultrafiltration (UF) membrane for water purification. *Physics and Chemistry of the Earth, Parts A/B/C, 67*, 125-131.

Wang, T., Wang, Y.-Q., Su, Y.-L., & Jiang, Z.-Y. (2006). Antifouling ultrafiltration membrane composed of polyethersulfone and sulfobetaine copolymer. *Journal of membrane science, 280*(1-2), 343-350.

Wang, Y.-q., Wang, T., Su, Y.-l., Peng, F.-b., Wu, H., & Jiang, Z.-y. (2006). Protein-adsorption-resistance and permeation property of polyethersulfone and soybean phosphatidylcholine blend ultrafiltration membranes. *Journal of membrane science, 270*(1-2), 108-114.

Wavhal, D. S., & Fisher, E. R. (2002a). Hydrophilic modification of polyethersulfone membranes by low temperature plasma-induced graft polymerization. *Journal of Membrane Science, 209*(1), 255-269.

Wavhal, D. S., & Fisher, E. R. (2002b). Modification of porous poly (ether sulfone) membranes by low‐temperature CO2‐plasma treatment. *Journal of Polymer Science Part B: Polymer Physics, 40*(21), 2473-2488.

Wavhal, D. S., & Fisher, E. R. (2003). Membrane surface modification by plasma-induced polymerization of acrylamide for improved surface properties and reduced protein fouling. *Langmuir, 19*(1), 79-85.

Wijmans, J., Baaij, J., & Smolders, C. (1983). The mechanism of formation of microporous or skinned membranes produced by immersion precipitation. *Journal of Membrane Science, 14*(3), 263-274.

Wilhelm, F., Pünt, I., Van der Vegt, N., Strathmann, H., & Wessling, M. (2002). Cation permeable membranes from blends of sulfonated poly (ether ether ketone) and poly (ether sulfone). *Journal of membrane science, 199*(1-2), 167-176.

Xu, Z.-L., & Qusay, F. A. (2004). Polyethersulfone (PES) hollow fiber ultrafiltration membranes prepared by PES/non-solvent/NMP solution. *Journal of Membrane Science, 233*(1-2), 101-111.

Yamagishi, H., Crivello, J. V., & Belfort, G. (1995a). Development of a novel photochemical technique for modifying poly (arylsulfone) ultrafiltration membranes. *Journal of Membrane Science, 105*(3), 237-247.

Yamagishi, H., Crivello, J. V., & Belfort, G. (1995b). Evaluation of photochemically modified poly (arylsulfone) ultrafiltration membranes. *Journal of Membrane Science, 105*(3), 249-259.

Zeman, & Zydney, A. L. (1996). *Microfiltration and ultrafiltration: principles and applications*: CRC Press.

Zeman, L., & Tkacik, G. (1988). Thermodynamic analysis of a membrane-forming system water/N-methyl-2-pyrrolidone/polyethersulfone. *Journal of Membrane Science, 36*, 119-140.

Zhang, D., Karkooti, A., Liu, L., Sadrzadeh, M., Thundat, T., Liu, Y., & Narain, R. (2018). Fabrication of antifouling and antibacterial polyethersulfone (PES)/cellulose nanocrystals (CNC) nanocomposite membranes. *Journal of membrane science, 549*, 350-356.

Zhao, C., Xue, J., Ran, F., & Sun, S. (2013). Modification of polyethersulfone membranes–a review of methods. *Progress in Materials Science, 58*(1), 76-150.

Zydney, A. L. (1998). Protein separations using membrane filtration: new opportunities for whey fractionation. *International Dairy Journal, 8*(3), 243-250.

Chapter 4 **FUTURE WORK**

New inventions such as the diffusion transfer technology developed in this work always raise as many unanswered questions as the work answered. In addition, new applications for the new technology might be explored beyond the initial work. Some unanswered questions that remain are:

1. Where does the charged polymer reside on the membrane surface after diffusion transfer?
2. Is the charged membrane stable to years of daily clean-in-place solutions that are strong oxidizers, and strong acids and bases, and hot?
3. What new challenges will be encountered to use the charged membranes for protein fractionation?
4. Can the diffusion transfer technology be used for nanofiltration membranes to increase flux while rejecting toxic heavy metal ions such as arsenic, lead, copper, cadmium, chromium, nickel, zinc, cobalt, and manganese?
5. What are the factors that we can use to manipulate the diffusion transfer of charged polymers into the membrane?

These five unanswered questions were selected for further discussion.

One

The proposed mechanism for the diffusion transfer process is that the organic solvent swells the membrane allowing diffusion of the charged polymer into the membrane and then removal of the organic solvent un-swells the membrane trapping the charged polymer in the membrane. It is thought that the charged polymer has an equilibrium affinity for the membrane polymer and that provides a thermodynamic driving force for the diffusion transfer process. But where does the charged polymer reside on the membrane surface after diffusion transfer? Is it on the surface of the membrane or distributed throughout the volume of the membrane polymer? The charged polymer might be analogous to a surfactant that has a hydrophilic head and a hydrophobic tail. In that case, the hydrophobic or lipophilic tail might bury itself into the hydrophobic membrane polymer and the polar hydrophilic charged head might reside at the surface protruding into the aqueous liquid phase. In this situation, the charged polymer would be found at the surface only of the membrane polymer and would not be distributed into the bulk volume of the membrane polymer. Alternatively, the charged polymer might diffuse throughout the membrane polymer, where only some of the charged polymer is presented at the membrane surface. Surface spectroscopy techniques might reveal the answer to this question. Why does it matter? By better understanding the mechanism of the diffusion transfer process we might better choose charged polymers and organic solvents, and we might better understand ways to improve the chemistry to make a more stable, reproducible, and widely useful product.

Two

In the dairy industry, ultrafiltration membranes are cleaned daily. Hot (50 °C) caustic solutions (sodium hydroxide, pH 11), acid solutions (nitric acid, pH 2.0), and caustic/chlorine (sodium hypochlorite, 150 ppm chlorine) solutions are used. Each solution is contacted with the membrane for 30 min (caustic or acid) or 20 min (chlorine). Membrane life in excess for 6 months is expected. This means that the membrane must withstand hundreds of cleaning cycles, and hundreds of hours of exposure to the hot cleaning solutions. Preliminary data from the present work shows that the charged membranes made using the diffusion transfer process are stable these cleaning solutions, but only one or two cycles performed at 40 °C were tested. Future work should examine more extensive testing of the stability to the cleaning solutions, and if one diffusion transfer chemistry versus another performs better.

Three

The process of protein concentration is distinctly different from the process of protein fractionation. Protein concentration does not change the ratio of one protein to another in the mixture while it elevates the concentration of all proteins. Protein fractionation does change the ratio of one protein to another in the mixture while it needn't elevate the concentration of all proteins. Protein concentration is generally easier than protein fractionation, because protein fractionation requires selective permeation of one protein through the membrane compared to the other protein. If the membrane is too permissive to protein permeation, then all proteins pass through the membrane and

fractionation does not occur. If the membrane is too tight, then no proteins pass through the membrane, and fractionation does not occur. Thus, protein fractionation requires a balancing act in selective permeation that protein concentration does not require. This means that for mixtures of protein, where only one protein is desired in the permeate, there must be a balancing act between the values of the sieving coefficients (S_o) where S_o for the permeating protein is much higher than for the retained protein. This means that if the amount of charged polymer on the membrane is too high, then both values of S_o may be too low, and vice versa.

In general, for charged ultrafiltration membranes, fractionation works best when the protein in the permeate is small and has an acidic isoelectric point (pI). In this way, the pH is adjusted such that the protein to be permeated has zero net charge (pH = pI). Because that protein is smaller than the other proteins and has no net charge, it passes through the membrane while the other proteins that are larger and charged are rejected by the membrane. The following proteins are examples of small acidic proteins that would work in this manner: human insulin (5.8 kDa, pI = 5.3), erythropoietin (30.4 kDa, pI = 4.5), soy hemoglobin (15.4 kDa, pI = 4.9), glycomacropeptide (9.0 kDa, pI = 3.8), alpha-lactalbumin (14.4 kDa, pI = 4.4), soy Bowman-Birk inhibitor (8.8 kDa, pI = 4.2). All these proteins are small and acidic and would permeate a charged membrane at pH = pI, while the other proteins that are larger and less acid would not. Future work to expand the application of charged ultrafiltration membranes to fractionation of food and pharmaceutical proteins might be a fruitful endeavor. Use of charged membranes for fractionation of these and other proteins would be advantageous because currently protein fractionation is not

feasible using uncharged ultrafiltration membranes, and chromatography is used. Chromatography is a slow and expensive cyclical batch process that uses a lot of water and generates a lot of wastewater. Replacing chromatography with charged ultrafiltration membranes would ameliorate these problems of chromatography and lower the cost of manufacture of fractionated proteins.

Fractionation of whey proteins in milk serum permeate using positively charged membranes was studied in this present work. It is found that although the membrane modified using an incubation solution containing 3.75% PDADMAC in 50% ethanol rejected BLG, the ALA did not pass freely through. However, reducing PADAMAC concentrations led to rejection of most BLG but permeation of more ALA. Thus, the amount of charges placed on the membrane surface is important to reject charged proteins and permeate uncharged proteins. Future work could focus on methods to control the amount of charge placed on the membrane surface by the diffusion transfer method: (1) decreasing the concentration of the charged polymer in the incubation solution to decrease the amount of charge applied to the membrane and (2) having two polymers in the incubation solution that compete for adsorption, one charged and the other not, for example polystyrene sulfonate and polyhydroxy styrene, such that alteration of the ratio of the two polymers alters the amount of charge on the membranes surface. Furthermore, a method to directly measure the charge on the surface of the membrane, rather than the indirect method of measurement of S_o, would provide useful information. For example, measurement of the zeta potential or the displacement of bound sodium or hydroxide ions would be a direct method of measuring the surface charge on the membrane.

Four

Toxic heavy metal ions such as lead, cadmium, and chromium occur in drinking water in some regions such a rural China and other rural areas where industrial pollution has contaminated the drinking water in rivers and ground aquifers. These are large positively charged cations that might be rejected more by charged nanofiltration membranes than uncharged nanofiltration membranes. The diffusion transfer method developed in the present work is not specific to ultrafiltration membranes. Any polymeric membrane might be suitable. If the diffusion transfer technology was used successfully on nanofiltration membranes, then one might obtain a higher water flux with the same rejection of heavy metal ions using a positively charged nanofiltration membrane than an uncharged nanofiltration membrane. This would increase the amount of safe drinking water available to poor people living in rural regions of the world that have been polluted by unchecked industrial activity.

Five

To manipulate the diffusion transfer of charged polymers into a polymeric membrane and control the amount of charges applied, we can vary factors, such as charged polymer size, charge density of charged polymer, charged polymer hydrophobicity and the organic solvent percentage in the solvent blend.

Firstly, the size of a charged polymer is likely to affect the diffusion transfer of the charged polymer into a polymeric membrane and the separation performance of the

resulted charged membrane. For example, 200 kDa disc membrane modified using SMAH (5 kDa) as the charged polymer in the incubation solution showed 2.5-fold a higher value of sieving coefficient than 200 kDa disc membrane modified using PSS (75 kDa). Smaller size charged polymers, and higher concentrations of charged polymers might increase diffusion transfer into the membrane. Future work can study how charged polymer size affects the kinetics and thermodynamic of the diffusion transfer of charged polymers into the membrane.

Secondly, hydrophobicity of a charged polymer determines both the solubility of the charged polymer in the organic solvent blend and the thermodynamic affinity between the charged polymer and the surface of the modified membranes. The present work used SMA with a ratio of styrene and maleic anhydride at 1:1 to place charges on membrane. In SMA copolymer, the ratio of styrene and maleic anhydride moieties can actually vary from 1:1 to 4:1. SMAH having a higher styrene content is more likely to dissolve in the organic solvent blend consisting of 50% DMF due to the increased hydrophobic character. For example, the SMAH 1:1 variant was only dissolved in 50% DMF by adding concentrated HCl at 15% (w/v) to protonate SMAH. The SMAH 4:1 variant may have a higher solubility in 50% DMF and need less HCl to protonate SMAH. SMAH having a higher styrene content also might create a greater thermodynamic affinity to the PES membrane material due to increased hydrophobicity. In addition, the solubility of SAMI polymer in a solvent blend might be changed by converting the tertiary amine functional group to quaternary amine. Quaternization of SMAI polymer using an alkyl halide (such as methyl or benzyl chloride) forms tetra-alkyl ammonium halide salt, and protonation of SMAI polymer with an acid

yields ammonium salts. The resulted SMAI salt product might be able to dissolve in a 50% ethanol, unlike SMAI polymer with tertiary amine groups.

Thirdly, the organic solvent blend can be further optimized. DMF from 5% to 50% and ethanol from 10% to 50% were already investigated. Higher percentage of organic solvent in water might also work or even work better to swell a polymeric membrane allowing charged polymers to diffuse into the membrane. Higher percentage of organic solvent will swell the membrane more and make the membrane more receptive to diffusion transfer of charged polymers but without dissolving the membrane. Since charged polymers have different thermodynamic affinity to a membrane, the amount of organic solvent needed to swell the membrane would depend on the charged polymers. For example, PDADMAC polymer has a great affinity to PES membrane. Without an organic solvent to swell the membrane, PDADMAC can still be adsorbed on the membrane surface. The value of S_o of the membrane modified using PDADMAC in water dropped 2.4-fold, compared to the raw membrane. Future work can optimize the organic solvent percentage depending on charged polymers in the diffusion method.

These five topics are examples of future work that might provide fruitful paths forward.

APPENDIX

A. Full data set for charged polyethersulfone ultrafiltration membranes in a stirred cell

A.1. Introduction

A method of making charged polyethersulfone (PES) ultrafiltration membranes was developed using a stirred cell to contact the uncharged raw PES membrane with an incubation solution consisting of a solvent and a charged polymeric solute. The performance of the charged membranes was evaluated by measuring sieving coefficient and hydraulic permeability. Section A contains the full experimental data set for sieving coefficient (S_o) and hydraulic permeability (L_p) measurements. It also contains the experiment result for modified polyvinylidene difluoride (PVDF) membranes using the diffusion transfer method.

A.2. Experiment

A.2.1 Modification of polyethersulfone membranes using a negatively charged polymer

The full data set for surface modification of PES ultrafiltration membranes by the diffusion transfer of negatively charged polymers into the PES membrane surface is listed in Table A.1. The surface modification method and characterization of the PES ultrafiltration membrane were introduced in Section 2.2.1 of Chapter 2. For each treatment,

experiments were conducted on three membrane discs. For each disc, the sieving coefficient was measured three times using 1 g/L WPI in buffer at pH 6.8. The mean of the three S_o values was calculated, and the mean values for each membrane disc were then averaged to obtain the mean S_o of the three membrane discs. The value of mean S_o using the H_2O-PSS incubation solution was not significantly different from mean S_o for the raw membrane ($p > 0.05$). The membrane made using 50% DMF in water with no PSS as the incubation solution had a higher value of mean S_o than the raw PES membrane ($p < 0.05$). Comparing the raw PES membrane to the DMF-PSS membrane, mean S_o decreased dramatically by 14-fold ($p < 0.05$).

Table A.1 Sieving coefficients of a 300 kDa membrane using the charged polymer 75 kDa PSS for modification. Different letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
Raw membrane, no PSS (raw)	1	0.196	0.261	0.285	0.217 ± 0.022^a
	2	0.191	0.167	0.226	
	3	0.196	0.198	0.232	
Water, 75kDa PSS alone, no DMF (H_2O-PSS)	1	0.19	0.221	0.216	0.196 ± 0.009^a
	2	0.138	0.196	0.23	
	3	0.152	0.228	0.194	
50% DMF alone, no PSS (DMF)	1	0.236	0.364	0.441	0.390 ± 0.034^b
	2	0.397	0.531	0.365	
	3	0.336	0.386	0.458	
50% DMF and PSS (DMF-PSS)	1	0.019	0.02	0.02	0.015 ± 0.003^c
	2	0.017	0.015	0.011	
	3	0.008	0.01	0.019	

As shown in Table A.2, L_p was measured once before modification (L_{p0}) and four times after modification (L_{p1}, L_{p2}, L_{p3}, L_{p4}) for each of the three discs. The mean L_p for each disc was calculated from the mean values of L_{p1}, L_{p2}, L_{p3}, and L_{p4}. The value of mean L_p for the DMF-PSS membranes was not significantly different from that of the raw membranes ($p > 0.05$). For the membranes modified by the incubation solution containing 50% DMF alone, mean L_p increased compared to the raw membranes and compared to the H_2O-PSS membranes ($p < 0.05$).

Table A.2 Hydraulic permeability (L_p, n=12) of cleaned 300 kDa membranes using the charged polymer 75 kDa PSS for modification, measured before protein filtration. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	L_{p1}	L_{p2}	L_{p3}	L_{p4}	Mean L_p
Raw membrane, no PSS (raw)	1	276.14	287.16	310.31	285.74	322 ± 23^{a}
	2	367.77	301.1	372.95	306.01	
	3	355.3	351.26	327.62	320.21	
Water, 75kDa PSS alone, no DMF (H_2O-PSS)	1	178.49	288.04	291.96	277.3	283 ± 23^{a}
	2	201.45	320.29	369.11	386.43	
	3	161.72	286.43	315.07	323.7	
50% DMF alone, no PSS (DMF)	1	514.63	435.75	400.86	411.68	529 ± 63^{b}
	2	708.48	530.76	552.37	477.32	
	3	773.97	528.68	520.08	494.29	
50% DMF and PSS (DMF-PSS)	1	474.71	433.52	385.77	327.77	405 ± 40^{ab}
	2	465.35	373.53	290.81	296.3	
	3	535.82	473.1	425.5	381.05	

In Table A.3, the values of L_p after the protein filtration experiment but before the cleaning step are listed for each disc. The mean of four L_p values for each disc was calculated and then averaged to obtain the mean L_p for the three discs. Comparing the DMF-PSS to the raw membrane, mean L_p after protein filtration remained same ($p > 0.05$). The membranes modified by the incubation containing 50% DMF alone showed a larger mean L_p value, compared to the DMF-PSS and the raw membranes ($p < 0.05$).

Table A.3 Hydraulic permeability (L_p, n=12) of fouled 300 kDa membranes using the charged polymer 75 kDa PSS for modification, measured after protein filtration. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	L_{pA}	L_{pB}	L_{pC}	L_{pD}	Mean L_p
Raw membrane, no PSS (raw)	1	142.56	184.06	157.5	143.52	158 ± 5[a]
	2	153.2	160.07	160.07	141.26	
	3	164.52	157.53	174.12	162.37	
Water, 75kDa PSS alone, no DMF (H_2O-PSS)	1	109.94	153.7	150.01	118.53	141 ± 12[a]
	2	126.63	172.73	170.89	164.6	
	3	96.23	151.85	144.41	135.46	
50% DMF alone, no PSS (DMF)	1	252.35	229.43	234.27	227.55	249 ± 9[b]
	2	275.3	249.39	251.23	239.83	
	3	267.2	242.17	256.76	260.14	
50% DMF and PSS (DMF-PSS)	1	165.13	124.02	128.78	154.96	150 ± 24[a]
	2	116.19	106.14	103.45	172.39	
	3	176.8	115.12	125.52	312.3	

A.2.2 Salt tolerance of the charged membranes made by diffusion transfer of charged polymers

Salt tolerance of the negatively charged membrane was evaluated. 1 M NaCl was added to the solution of 1 g/L WPI in 50 mM sodium phosphate, pH 6.8, and the solution pumped through a charged membrane disc to obtain the sieving coefficient. This experiment was conducted after the three sieving measurements in Table A1. In Table A.4, S_{o4} was from the fourth sieving coefficient measurement with 1 M NaCl added in the feed solution. S_{o5} was from the fifth sieving coefficient measurement without adding salt. The L_p value before and after the sieving measurement was also reported in Table A.4.

Comparing S_{o4} to S_{o5} for the DMF-PSS membrane, S_o increased ($S_{o4} > S_{o5}$) when 1 M NaCl was added to the protein solution ($p < 0.05$) whereas salt had no effect on S_o for the raw membrane ($p > 0.05$). This result was attributed to salt shielding the charges on the charged polymers that diffused into the membranes so that electrostatic repulsion between proteins and the charges on the membranes was reduced. Comparing S_{o4} to S_{o5} for the Alcohol-PSS membrane, S_o did not increase statistically when 1 M NaCl was added to the protein solution ($p = 0.06$).

Table A.4. Sieving coefficients of a 300 kDa membrane using the negatively charged polymer 75 kDa PSS for modification. L_{p5} and L_{pE} were the hydraulic permeability measured before and after the fifth sieving coefficient measurement. A paired t-test was conducted to compare S_{o4} and S_{o5} for each treatment, and different uppercase letters in the same row of mean S_o indicate significant statistical differences ($p < 0.05$). Different lowercase letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	S_{o4}	Mean S_{o4}	L_{p5}	S_{o5}	Mean S_{o5}	L_{pE}
Raw membrane, no PSS (raw)	1	0.400	0.299 ± 0.072^{Aab}	291.84	0.340	0.278 ± 0.049^{Aa}	161.56
	2	0.250		413.37	0.219		176.34
	3	0.246		391.72	0.275		178.38
Water, 75kDa PSS alone, no DMF (H_2O-PSS)	1	0.23	0.261 ± 0.071^{Aa}	322.05	0.228	0.266 ± 0.056^{Aa}	161.1
	2	0.359		417.29	0.346		194.73
	3	0.193		340.75	0.225		160.45
50% DMF alone, no PSS (DMF)	1	0.414	0.449 ± 0.026^{Ab}	433.18	0.355	0.385 ± 0.021^{Ba}	216.88
	2	0.476		428.15	0.397		226.05
	3	0.458		450.8	0.403		242.17
50% DMF and PSS (DMF-PSS)	1	0.072	0.091 ± 0.024^{Ac}	377.33	0.017	0.018 ± 0.003^{Bb}	121.72
	2	0.125		236.8	0.022		104.49
	3	0.077		337.18	0.016		118.11
50% t-butyl alcohol and PSS (Alcohol-PSS)	1	0.122	0.131 ± 0.030^{Aac}	423.35	0.030	0.043 ± 0.009^{Ab}	144.25
	2	0.172		432.41	0.046		148.21
	3	0.100		472.95	0.052		146.09

A.2.3. Effects of organic solvent type and percentage usage

Effects on membrane performance of the organic solvent type and percent solvent usage in the incubation solution were measured. DMF percentage usage ranging from 5%

to 50% was investigated. The values of S_o and L_p were measured in triplicate for each of three discs using 75 kDa PSS as the charged polymer (Table A.5 and A.6). As the percentage of DMF decreased from 50% to 5%, the value of mean S_o increased 9-fold (Table A.5) while the value of mean L_p remained unchanged (Table A.6). These results were attributed to the fact that 50% DMF is a better solvent than 5% DMF for the PES membrane, which led to less swelling of the PES membranes and less diffusion transfer of PSS onto the membrane surface for 5% DMF.

Table A.5. Effect of DMF percentage usage on S_o. Different letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Solvent Usage	Disc #	S_{01}	S_{02}	S_{03}	Mean S_o
50% DMF and PSS	1	0.019	0.02	0.02	0.015 ± 0.003^a
	2	0.017	0.015	0.011	
	3	0.008	0.01	0.019	
30% DMF and PSS	1	0.07	0.09	0.106	0.089
20% DMF and PSS	1	0.064	0.107	0.1	0.112 ± 0.015^b
	2	0.095	0.139	0.129	
	3	0.027	0.183	0.163	
10% DMF and PSS	1	0.04	0.108	0.124	0.091
5% DMF and PSS	1	0.013	0.145	0.152	0.136 ± 0.026^b
	2	0.098	0.213	0.184	
	3	0.046	0.114	0.144	

A.6. Effect of DMF percentage usage on L_p. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Solvent Usage	Disc #	L_{p1}	L_{p2}	L_{p3}	Mean L_p
50% DMF and PSS	1	474.71	433.52	385.77	405 ± 40[a]
	2	465.35	373.53	290.81	
	3	535.82	473.1	425.5	
30% DMF and PSS	1	236.45	287.31	259.98	261
20% DMF and PSS	1	228.82	286.47	220.26	332 ± 63[a]
	2	302.98	379.25	386.16	
	3	320.29	434.56	428.53	
10% DMF and PSS	1	247.74	300.98	308.7	286
5% DMF and PSS	1	190.58	297.99	329	327 ± 39[a]
	2	154.08	439.67	441.55	
	3	186.59	432.30	472.75	

Effects of other organic solvents besides DMF and percentage usage in the incubation solution on membrane performance were studied and values of S_o and L_p measured in triplicate for each of three discs using 75 kDa PSS as the charged polymer (Table A.7 & A.8). The values of mean S_o and mean L_p were not different among three solvent types at 50% usage: 50% ethanol, 50% tert-butyl alcohol and 50% acetone. These three solvents at 50% usage have very similar values of the HSP distance for PES. The HSP distance determines the extent of swelling of the PES membrane polymer and the resulting diffusion transfer and trapping of PSS on the membrane surface. When solvent usage decreased from 50% to 10% ethanol the HSP distance increased and the value of mean S_o increased ($p < 0.05$).

A.7. Effects of organic solvent type and percentage usage on mean S_o. Different letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Solvent	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
50% ethanol and PSS	1	0.019	0.02	0.02	0.015 ± 0.003^a
	2	0.017	0.015	0.011	
	3	0.008	0.01	0.019	
10% ethanol and PSS	1	0.123	0.264	0.313	0.193 ± 0.026^b
	2	0.033	0.14	0.37	
	3	0.049	0.234	0.218	
50% t-butyl alcohol and PSS	1	0.024	0.038	0.031	0.043 ± 0.017^a
	2	0.079	0.071	0.051	
	3	0.027	0.031	0.032	
50% acetone and PSS	1	0.069	0.099	0.061	0.097 ± 0.039^a
	2	0.055	0.06	0.068	
	3	0.04	0.108	0.124	

A.8. Effects of organic solvent type and percentage usage on the values of L_p. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Solvent	Disc #	L_{p1}	L_{p2}	L_{p3}	Mean L_p
50% ethanol and PSS	1	500.05	421.09	388.69	398 ± 32^{ab}
	2	428.96	420.13	347.04	
	3	347.43	371.03	355.22	
10% ethanol and PSS	1	191.04	282.9	259.98	306 ± 58^{a}
	2	172.93	450.64	526.88	
	3	144.14	385.35	336.49	
50% t-butyl alcohol and PSS	1	582.46	552.06	480.55	486 ± 37^{b}
	2	446.81	489.45	460.39	
	3	492.14	463.47	408.46	
50% acetone and PSS	1	432.3	471.6	445.77	384 ± 47^{ab}
	2	332.03	351.61	357.10	
	3	323.63	337.18	406.73	

A.4. Effect of PSS molecular mass

PSS of molecular mass 75 kDa, 200 kDa and 1000 kDa in 50% DMF was examined. Values of S_o are reported in Table A.9. Values of L_p are reported in Tables A.10 and A.11. Membranes modified by PSS had lower values of mean S_o compared to raw membrane ($p < 0.05$), but the values of mean S_o did not depend on PSS molecular mass ($p > 0.05$). The value of mean L_p was not statistically different for the raw membrane and membranes modified by PSS regardless of whether L_p was measured before or after protein filtration ($p > 0.05$). In conclusion, PSS molecular mass had no effect on S_o and L_p.

Table A.9. Sieving coefficients of 300 kDa membranes modified by PSS of different molecular mass using 50% DMF. Different letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
Raw membrane, no PSS (raw)	1	0.196	0.261	0.285	0.217 ± 0.022^a
	2	0.191	0.167	0.226	
	3	0.196	0.198	0.232	
50% DMF and 75 kDa PSS	1	0.019	0.02	0.02	0.015 ± 0.003^b
	2	0.017	0.015	0.011	
	3	0.008	0.01	0.019	
50% DMF and 200 kDa PSS	1	0.029	0.02	0.016	0.024 ± 0.004^b
	2	0.023	0.019	0.021	
	3	0.049	0.021	0.02	
50% DMF and 1000 kDa PSS	1	0.034	0.52	ND	0.055 ± 0.008^b
	2	0.031	0.056	0.054	
	3	0.054	0.066	0.066	

Table A.10. L_p measured before protein filtration for 300 kDa membranes modified by PSS of different molecular mass using 50% DMF. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	L_{p1}	L_{p2}	L_{p3}	L_{p4}	Mean L_p
Raw membrane, no PSS (raw)	1	276.14	287.16	310.31	285.74	322 ± 23[a]
	2	367.77	301.1	372.95	306.01	
	3	355.3	351.26	327.62	320.21	
50% DMF and 75 kDa PSS	1	474.71	433.52	385.77	327.77	405 ± 40[a]
	2	465.35	373.53	290.81	296.3	
	3	535.82	473.1	425.5	381.05	
50% DMF and 200 kDa PSS	1	355.64	314.26	ND	292.92	338 ± 59[a]
	2	486.65	399.32	401.01	380.67	
	3	456.75	349.65	27.16	269.43	
50% DMF and 1000 kDa PSS	1	525.38	659.69	384.74	ND	410 ± 16[a]
	2	315.68	368.77	445.39	445.65	
	3	384.74	502.54	446.19	373.11	

Table. A.11. L_p measured after protein filtration for membranes modified by PSS of different molecular mass using 50% DMF. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	L_{pA}	L_{pB}	L_{pC}	L_{pD}	Mean L_p
Raw membrane, no PSS (raw)	1	142.56	184.06	157.5	143.52	158 ± 5[a]
	2	153.2	160.07	160.07	141.26	
	3	164.52	157.53	174.12	162.37	
50% DMF and 75 kDa PSS	1	136.65	114.43	117.46	129.47	150 ± 24[a]
	2	137.61	145.29	120.18	126.56	
	3	146.02	137.92	133.62	152.39	
50% DMF and 200 kDa PSS	1	136.65	114.43	117.46	129.47	135 ± 8[a]
	2	137.61	136.42	119.15	161.3	
	3	146.02	137.92	133.62	152.39	
50% DMF and 1000 kDa PSS	1	165.13	124.02	128.78	154.96	144 ± 2[a]
	2	116.19	106.14	103.45	172.39	
	3	176.8	115.12	125.52	312.3	

The effect of PSS molecular mass on salt tolerance was also examined by addition of 1 M NaCl to the protein solution of 1 g/L WPI dissolved in 50 mM sodium phosphate, pH 6.8, used to measure S_o. In Table A.12, S_{o4} was from the fourth sieving coefficient measurement with salt added in the protein solution. S_{o5} was from the fifth sieving coefficient measurement without salt. L_p values before and after the measurement of S_o are also reported in Table A.12. The value of S_o increased ($S_{o4} > S_{o5}$) after addition of salt for the membranes modified using 75 kDa and 200 kD PSS, but not for the raw membrane ($p < 0.05$) or the 1000 kDa PSS ($p = 0.088$). In the presence of added salt (S_{o4}), the membranes modified using 75 kDa and 200 kDa PSS had lower values of S_o than the raw membrane ($p < 0.05$) but not lower than the 1000 kDa PSS membrane ($p > 0.05$). These results were attributed to salt shielding the negative charges on the charged polymers that diffused into the membranes so that electrostatic repulsion between the negatively charged proteins and the negatively charged polymer groups was reduced.

Table A.12. Effect of PSS molecular mass on S_o and L_p using a 300 kDa membrane. L_{p5} and L_{pE} are the hydraulic permeability measured before and after the fifth sieving coefficient measurement. Different letters (lower case) in the same column of mean S_o indicate significant statistical differences ($p < 0.05$). Different letters (upper case) in the same row of mean S_o indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	S_{o4}	Mean S_{o4}	L_{p5}	S_{o5}	Mean S_{o5}	L_{pE}
Raw membrane, no PSS (raw)	1	0.400	0.299 ± 0.072^{Aa}	291.84	0.340	0.278 ± 0.049^{Aa}	161.56
	2	0.250		413.37	0.219		176.34
	3	0.246		391.72	0.275		178.38
50% DMF and 75 kDa PSS	1	0.072	0.091 ± 0.024^{Ab}	377.33	0.017	0.018 ± 0.003^{Bb}	121.72
	2	0.125		236.8	0.022		104.49
	3	0.077		337.18	0.016		118.11
50% DMF and 200 kDa PSS	1	0.070	0.087 ± 0.013^{Ab}	303.44	0.017	0.021 ± 0.003^{Bb}	94.58
	2	0.103		303.44	0.021		94.58
	3	0.088		258.1	0.025		112.88
50% DMF and 1000 kDa PSS	1	ND	0.173 ± 0.023^{Aab}	ND	ND	0.069 ± 0.008^{Ab}	ND
	2	0.150		434.87	0.060		136.08
	3	0.196		357.79	0.077		192.58

A.5. Examination of charged polymer structure on performance

The effect of charged polymer structure on performance was examined by comparing membranes modified by the charged polymers: poly(vinylsulfonic acid, sodium salt) (PVSA) and 75 kD PSS (Table A.13 & A.14). Both PVSA and PSS have similar chemical structures except that PVSA does not contain a phenyl ring in the polymer backbone. The values of mean S_o for PVSA in 50% DMF were 25-fold higher than that for PSS in 50% DMF

($p < 0.05$). The phenyl ring in PSS is important because it may create a thermodynamic affinity between PSS and the phenyl ring of PES.

Hydrolyzed styrene maleic anhydride (SMAH) contains negatively charged carboxylic acid groups and a styrene group in the repeating unit. Compared to 75 kDa PSS, the membrane modified using 3.75% SMAH in 50% DMF had the same values of mean S_o and mean L_p ($p > 0.05$).

In an attempt to back extract SMAH polymer from the PES membrane, 50% DMF without SMAH was permeated through the modified membrane overnight. The values of mean S_o and mean L_p for the SMAH membrane after back extraction did not change ($p > 0.05$). These results highlight importance of a hydrophobic character to the charged polymer in order to create a thermodynamic affinity of the charged polymer for the PES membrane that is greater than for the 50% DMF incubation solution.

Table A.13. Sieving coefficients of a 300 kDa membrane using different charged polymers for modification. Different letters in the same column of mean S_o indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
50% DMF and 75 kDa PSS	1	0.019	0.02	0.02	0.015 ± 0.003^a
	2	0.017	0.015	0.011	
	3	0.008	0.01	0.019	
50% DMF and PVSA*	1	0.313	0.284	0.278	0.377 ± 0.070^b
	2	0.413	0.418	0.299	
	3	0.469	0.462	0.459	
50% DMF and SMAH	1	0.019	0.016	0.011	0.016 ± 0.003^a
	2	0.036	0.014	0.011	
	3	0.017	0.012	0.010	
Back extraction of 50% DMF and SMAH	1	0.01	0.008	0.008	0.010 ± 0.00^a
	2	0.014	0.014	0.012	
	3	0.01	0.01	0.009	

*DMF at 1.875% PVSA

Table A.14. L_p of a 300 kDa membrane using different charged polymers for modification. Different letters in the same column of mean L_p indicate significant statistical differences ($p < 0.05$).

Membrane	Disc #	L_{p1}	L_{p2}	L_{p3}	Mean L_p
50% DMF and 75 kDa PSS	1	474.71	433.52	385.77	429 ± 42[a]
	2	465.35	373.53	290.81	
	3	535.82	473.1	425.5	
50% DMF and PVSA*	1	680.30	654.20	587.53	665 ± 17[b]
	2	739.26	647.98	648.75	
	3	755.39	691.51	582.27	
50% DMF and SMAH	1	384.31	289.69	366.54	341 ± 8[ac]
	2	373.26	325.85	290.77	
	3	399.05	339.48	303.86	
Back extraction of 50% DMF and SMAH	1	304.97	284.44	269.62	306 ± 33[c]
	2	292.11	282.86	263.09	
	3	403.51	350.80	301.63	

*DMF at 1.875% PVSA

A.6. Effects of incubation time, temperature, and pH

Effects of incubation time, temperature and pH on S_o were investigated using 3.75% SMAH in 50% DMF (Table A.15). S_o did not change as incubation time increased from 0.5 h to 16 h, or as incubation temperature decreased from 22 to 3˚C ($p > 0.05$). However, S_o decreased as pH increased from 4.3 to 7 ($p < 0.05$).

Table A.15. S_o of a 300 kDa membrane using SMAH in 50% DMF. Different letters in the same column of mean S_o indicate significant differences ($p < 0.05$).

Temperature and pH	Time (h)	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
pH 4.3, 22˚C	0.5	1	0.086	0.104	0.065	0.058 ± 0.022[a]
		2	0.023	0.035	0.037	
		3	0.034	0.055	0.086	
pH 4.3, 22˚C	1	1	0.016	0.015	0.025	0.048 ± 0.022[a]
		2	0.021	0.097	0.046	
		3	0.029	0.081	0.102	
pH 4.3, 22˚C	4	1	0.007	0.040	0.031	0.040 ± 0.018[a]
		2	0.049	0.076	0.074	
		3	0.035	0.019	0.031	
pH 4.3, 22˚C	16	1	0.01	0.008	0.008	0.040 ± 0.022[a]
		2	0.048	0.086	0.071	
		3	0.012	0.018	0.014	
pH 7.0, 22˚C	0.5	1	0.043	0.043	0.027	0.037 ± 0.006[b]
		2	0.059	0.027	0.046	
		3	0.040	0.023	0.023	
pH 7.0, 22˚C	1	1	0.030	0.027	0.038	0.046 ± 0.011[b]
		2	0.037	0.076	0.060	
		3	0.034	0.063	0.049	
pH 7.0, 22˚C	4	1	0.019	0.023	0.018	0.023 ± 0.009[b]
		2	0.010	0.015	0.014	
		3	0.059	0.025	0.022	
pH 7.0, 22˚C	16	1	0.019	0.016	0.011	0.016 ± 0.003[b]
		2	0.036	0.014	0.011	
		3	0.017	0.012	0.010	
pH 7.0, 3˚C	0.5	1	0.006	0.013	0.012	0.028 ± 0.018[b]
		2	0.018	0.023	0.027	
		3	0.054	0.069	0.032	
pH 7.0, 3˚C	1	1	0.010	0.013	0.015	0.020 ± 0.005[b]
		2	0.029	0.028	0.022	
		3	0.027	0.020	0.019	
pH 7.0, 3˚C	4	1	0.011	0.009	0.005	0.015 ± 0.012[b]
		2	0.028	0.040	0.026	
		3	0.007	0.003	0.005	
pH 7.0, 3˚C	16	1	0.020	0.011	0.017	0.013 ± 0.003[b]
		2	0.015	0.014	0.013	
		3	0.006	0.009	0.008	

A.7 Effect of the positively charged polymer SMAI in 100% ethanol

SMAI is a copolymer of styrene and dimethylaminopropylamine maleimide. It was dissolved in 100% ethanol to make the incubation solution. As shown in Table A.16, compared to 100% ethanol alone, the membrane modified by SMAI had a 5.6-fold decrease in mean S_o. Adding SMAI to the 100% ethanol caused a strong decrease in mean S_o and in mean L_p because a significant amount of SMAI diffused into the PES membrane and made it positively charged.

Table A.16. S_o of membranes modified by SMAI in 100% ethanol measured using 1 g/L WPI at pH 3.5. Different letters in the same column of mean S_o indicate significant differences ($p < 0.05$).

Membrane	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
Raw membrane, no SMAI	1	0.327	0.425	0.356	0.321 ± 0.059^a
	2	0.198	0.256	0.261	
	3	0.48	0.272	0.317	
100% ethanol, no SMAI	1	0.197	0.39	0.355	0.333 ± 0.025^a
	2	0.363	0.300	0.291	
	3	0.410	0.371	0.324	
100% ethanol and SMAI	1	0.086	0.061	0.073	0.059 ± 0.010^b
	2	0.038	0.051	0.055	
	3	0.060	0.049	0.062	

Table A.17. L_p of membranes modified by SMAI in 100% ethanol measured using 1 g/L WPI at pH 3.5. Different letters in the same column of mean L_p indicate significant differences ($p < 0.05$).

Membrane	Disc #	L_{p1}	L_{p2}	L_{p3}	Mean L_p
Raw membrane, no SMAI	1	345.16	298.68	301.86	353 ± 27[a]
	2	375.72	358.56	384.66	
	3	391.15	316.03	410.11	
100% ethanol, no SMAI	1	605.53	505.15	525.23	569 ± 21[b]
	2	666.68	563.34	561.27	
	3	625.53	554.78	512.94	
100% ethanol and SMAI	1	224.59	351.53	304.09	226 ± 50[c]
	2	107.25	183.18	224.63	
	3	83.45	280.60	275.15	

A.8 Modification of a PVDF membrane

Polyvinylidene difluoride (PVDF) is another common polymer used to make ultrafiltration membranes, like PES. A 250 kDa PVDF membrane was made negatively charged using 75 kDa PSS or SMAH dissolved in 50% DMF. In Table A.18 and Table A.19, comparing to the raw membrane to the one where PSS was trapped on the surface of the membrane,mean S_o dropped about 3.6-fold while mean L_p dropped about 1.7-fold. For SMAH, mean S_o dropped about 3.2-fold while mean L_p dropped about 1.1-fold. PVDF has similar HSP distance values to PES in 50% DMF. Therefore, it was expected that 50% DMF would swell the PES and PVDF membranes similarly and allow diffusion transfer of charged polymers. In addition, although PVDF does not have the phenyl rings of PES, the difluoroethyl repeating moiety of PVDF is hydrophobic, which creates a thermodynamic

affinity between the phenyl ring of the charged polymers PSS and SMAH and the hydrophobic polymer PVDF.

Table A.18. S_o of PVDF membranes modified by PSS or SMAH in 50% DMF measured using 1 g/L WPI at pH 6.8.

Membrane	Disc #	S_{o1}	S_{o2}	S_{o3}	Mean S_o
Water, raw membrane	1	0.473	0.61	0.603	0.553 ± 0.009*
	2	0.398	0.615	0.618	
50% DMF alone	1	0.314	0.446	0.519	0.426
50% DMF and PSS	1	0.063	0.162	0.239	0.170
50% DMF and SMAH (1.875%)	1	0.034	0.18	0.232	0.155 ± 0.022*
	2	0.084	0.216	0.276	

*Triplicate measurements of S_o for each of two discs.

Table A.19. L_p of PVDF membranes modified by PSS or SMAH in 50% DMF measured using 1 g/L WPI at pH 6.8.

Membrane	Disc #	L_{p1}	L_{p2}	L_{p3}	Mean L_p	HSP
Water, raw membrane	1	334.15	345.2	327.12	270 ± 66*	32.5
	2	227.09	217.88	166.21		
50% DMF alone	1	115.62	154.46	175.84	149	16.9
50% DMF and PSS	1	134.66	148.82	90.55	156	16.9
50% DMF and SMAH (1.875%)	1	272.19	327.45	207.22	242 ± 42*	16.9
	2	257.11	168.55	172.06		

B. Development of a chemistry to place charges on polyethersulfone ultrafiltration membranes

B.1. Introduction

A charged ultrafiltration membrane has more flexibility compared to an uncharged membrane due to three variables: sign of the charge, density of the charge, and pore size of the membrane (Nakao, Osada, Kurata, Tsuru, & Kimura, 1988). Modification of existing uncharged PES membranes to impact the charge properties on membranes has been shown to improve membrane selectivity because the charged membrane repels charged solutes that bear charges of the same sign. For modification of polyethersulfone (PES) membranes, both chemical and physical reactions were attempted to make the membranes negatively charged, such as Blanc chloromethylation, and direct sulfonation, Friedel-Crafts reaction, radical grafting using a redox initiator, and physical adsorption on the membrane surface. However, when attempted in our laboratory, none of these methods were successful. None resulted in a modified PES membrane that permeated less protein than a raw membrane. The following is a recount of those attempts.

B.2. Experiment

B.2.1. Blanc reaction to chloromethylate PES and then sulfonate PES

The reaction solution for chloromethylation was prepared by mixing 30 mL 37% HCl aqueous solution with 20 mL formalin and 1.36 g $ZnCl_2$ in a flask (Yang & Lin, 2002). A PES disc with a diameter of 25 mm was cut from a flat sheet membrane (Millipore Biomax), and then placed into the reaction solution and heated at 50˚C for 24 h. The membrane was

then soaked in DI water for 24 h to remove chemical residues. To sulfonate the resulted membrane, the membrane was then soaked at 50 ˚C in a solution made by dissolving 6.3 g of Na_2SO_3 in 20 mL DI water and 0.1 mL ethanol. Values of S_o were measured in a stirred cell using a protein solution of 1 g/L whey protein isolate (WPI) dissolved in 50 mM sodium phosphate, pH 6.8. The value of S_o was calculated from the absorbance ratio at 280 nm of permeate to retentate solution. The hydraulic permeability was determined from the slope of water flux versus pressure drop.

Results and discussion

Comparing the raw membrane to the modified one, S_o and L_p essentially did not change (Table B.1). Yang and Ling (2002) sulfonated polysulfone hollow fiber membranes using the Blanc chloromethylation reaction. However, the method by Yang and Ling (2002) did not work for PES membranes. A methyl group is present exclusively in polysulfone rather than polyethersulfone (Belfer, Fainchtain, Purinson, & Kedem, 2000). The sulfonic group in polyethersulfone has an electron repulsing effect that deactivates the aromatic ring for substitution. Thus, poyethersulfone is less reactive than polysulfone.

Table B.1. Membrane modified by Blanc reaction

Membrane	S_o	L_p (LMH/bar)
Raw 100 kDa PES membrane	0.909 ± 0.106*	385 ± 45*
Modified 100 kDa PES membrane	0.857 ± 0.119*	371 ± 17*

*Single measurement of S_o and L_p for each of two discs.

B.2.2 Direct sulfonation of PES using diluted sulfuric acid

Flat sheet PES membrane discs having a pore size of 300 kDa and a diameter of 76 mm from both Millipore and Synder Filtration were used. Membrane discs were soaked in diluted H_2SO_4 solution at different temperature and incubation time combinations. Convective permeation of diluted H_2SO_4 solution instead of soaking was also conducted in a Mac Disc Holder (Amicon). The value of S_o was calculated using the mass balance model:

$$S_o = 1 - \frac{\ln[V_F/V_R - (C_P/C_F)(V_F/V_R - 1)]}{\ln(V_F/V_R)}$$

where V_F/V_R = the volume ratio of feed to retentate solution, and C_P/C_F = the protein concentration ratio of feed solution to permeate solution (Cowan & Ritchie, 2007). The absorbance ratio at 280 nm was used to determine C_P/C_F. The hydraulic permeability was determined from the slope of water flux versus pressure drop.

Results and Discussion:

Table B.2. Membranes modified by direct sulfonation

Membrane	Modificati-on method	Concentration	Time and temperature	L_{p0} (LMH /bar)	L_{p1} (LMH /bar)	S_o
100 kDa Biomax	raw	NA	NA	635	NA	0.208
100 kDa Biomax	soaking	0.5 N H_2SO_4	3 h at 22 ˚C	584	408	0.266
100 kDa Biomax	soaking	5 N H_2SO_4	3 h at 22 ˚C	498	416	0.245
100 kDa Biomax	convection	5 N H_2SO_4	17 h at 22 ˚C	506	386	0.189
100 kDa Synder	raw	NA	NA	126 ± 20*	NA	0.016 ± 0*
100 kDa Synder	convection	5 N H_2SO_4	3 h at 22 ˚C	127 ± 30*	79 ± 25	0.013 ± 0.002*

*Single measurement of S_o and L_p for each of two discs.

Comparing the raw 100 kDa Biomax to the modified 100 kDa Biomax by either soaking or convection in diluted sulfuric acid (Table B.2), S_o and L_p essentially remained unchanged. Longer soaking time, higher concentration of sulfuric acid, and increased flow by changing from soaking to convection did not result in a lower S_o. Comparing the raw Synder membranes and the modified Synder membranes, S_o and L_p were unchanged. Sulfonation of PES using diluted sulfuric acid is problematic because the electron repulsing effect of the sulfonic acid group deactivates the aromatic ring for substitution (Lu, Zou, Guan, Dai, & Lu, 2005). The raw 100 kDa Synder membrane has a small value of S_o, 20-fold smaller than the raw 100 kDa Biomax membrane. Biomax membranes are not conventional

PES membranes because the surface has been modified to reduce non-specific protein binding, based on the information provided by the manufacturer. Therefore, we focused on the modification of PES membranes made by Synder Filtration in the further investigations. Because the sieving coefficient of the 100 kDa Synder membrane was small, membranes having higher MWCO were modified using diluted sulfuric acid in hopes of better performance (Table B.3). Comparing the raw membrane and the membrane modified using 5 N sulfuric acid by convection, the values of S_o did not change for both the 200 kDa and 300 kDa Synder membranes. Increasing the concentration of sulfuric acid from 5 N to 50% (w/w) was not successful as the membrane was partially dissolved as seen by the increased L_p. The 300 kDa raw membranes showed 4-fold increase in S_o compared to the 200 kDa raw membrane. Therefore, it was decided to use 300 kDa membranes in future work in order to make changes in S_o more obvious.

Table B.3. Synder membranes modified by direct sulfonation

Membr-ane	Modification method	Concentr-ation	Time and temperature	Lp_0 (LMH/bar)	Lp_1 (LMH/bar)	S_o
200 kDa	raw	NA	NA	225 ± 58[#]	NA	0.024 ± 0.005[#]
200 kDa	convection	5 N H_2SO_4	3 h at 50 ˚C	219 ± 8[†]	84 ± 55[†]	0.021 ± 0.014[†]
300 kDa	raw	NA	NA	362 ± 6[#]	NA	0.103 ± 0.008[#]
300 kDa	convection	5 N H_2SO_4	3 h at 50 ˚C	353	404	0.110
300 kDa	convection	50 % (w/w) H_2SO_4	18 h at 90 ˚C	315	636	NA

[#] Single measurement of S_o and L_p for each of three discs.
[†] Single measurement of S_o and L_p for each of two discs.

B.2.3. Surface modification via cationic polymerization

Flat sheet PES membrane discs having a pore size of 300 kDa and a diameter of 76 mm from Synder Filtration were used. The functionalized membranes in this section were prepared by a three step procedure following the modification procedure by Cowan and Ritchie with some minor modifications (2007). Convective permeation of 22 % or 50 % H_2SO_4 (w/w) solution through the membrane disc was conducted in a Mac Disc Holder (Amicon) to sulfonate the raw membrane and provide sites for the second step of cationic polymerization of styrene monomer. The third step was sulfonation of the newly created styrene polymer using diluted sulfuric acid. Because 5 % styrene in toluene did not permeate through the pores of the PES membrane in a metal holder, because of capillarity, the membrane was soaked in 5 % styrene in toluene for 3 h instead of using convection. The values of S_o and L_p were determined following the method in section B.2.2.

Results and Discussion

Comparing L_p values of the membrane after the 1st sulfonation step to that after the styrene polymerization step, L_p decreased 5.8-fold for 50 % (w/w) sulfuric acid and 2.7-fold for 22 % (w/w) sulfuric acid. However, the sieving coefficient of the modified membrane was unexpectedly higher compared to the raw membrane (S_o = 0.103 ± 0.008 in Table B.3) after the polymerization step or the 2nd sulfonation step. This method failed to create charged membranes of lower S_o. In addition, both sulfonation of PES polymers and polymerization of styrene via cationic sulfonation were difficult to conduct.

Table B.4. Synder membranes modified via cationic polymerization

Membrane	1st sulfonation	L_p after the 1st sulfonation (LMH/bar)	L_p after the styrene polymerization (LMH/bar)	S_o	2nd sulfonation	S_o
300 kDa	50 % H_2SO_4 22 ˚C, 3 h	654	112	0.127	NA	NA
300 kDa	22 % H_2SO_4 50 ˚C, 3 h	404	148	0.149	5 N H_2SO_4 22 ˚C, 3 h	0.206

B.2.4. Surface modification via redox polymerization

Flat sheet PES membrane discs having a pore size of 300 kDa and a diameter of 76 mm from Synder Filtration were used. The flat sheet PES membrane discs were surface modified by grafting redox polymerization following the procedure by Belfer et al. (2000). Using 64 ml of water containing 15.8 g of sulfopropylmethacrylate (SPM), a mixture of 0.19 g $K_2S_2O_8$ and 0.15 g of $K_2S_2O_5$ was added and stirred until completely dissolved. The PES membrane was then soaked in the SPM solution overnight. The membrane was then taken out and washed thoroughly with water. The values of S_o and L_p were measured following the method in B.2.2.

Results and Discussion

Comparing to the raw 300 kDa PES membrane in Table B.3, the 300 kDa membrane modified via redox polymerization showed slightly lower S_o (Table B.5). Belfer et al. (2000) modified PES membranes by radical grafting with the aid of redox initiator to create new functional groups on the surface. The new functional groups on the modified membrane surfaces were characterized by FTIR-ATR spectroscopy. There were no performance tests

of the modified membranes in the literature. It is possible that the method did not result in the formation of a significant amount of charged polymers on the membrane surface, so the value of S_o would not change significantly after modification.

Table B.5. Synder membranes modified via redox polymerization

	L_{p0} (LMH/bar)	L_{p1} (LMH/bar)	S_o
300 kDa	367	278	0.093

B.2.5. Surface adsorption using negatively charged polymers

Flat sheet PES membrane discs having a pore size of 300 kDa and a diameter of 76 mm from Synder Filtration were used. The flat sheet PES membrane discs were surface modified via adsorption of 3.75% poly(sodium 4-styrenesulfonate) (PSS) (w/v) when PSS aqueous solution was permeated through membrane discs in a stirred cell (Reddy, Mohan, Bhattacharya, Shah, & Ghosh, 2003). Before and after passing the PSS solution through the membranes, the membranes were washed thoroughly with DI-water. After surface adsorption of the PSS from DI-water, the membranes were heated in an oven for about 40 min at 50 ˚C and 70 ˚C to create crosslinking between the sulfonate groups in PSS (Martins, Ruggeri, & De Paoli, 2003). The values of S_o and L_p were determined following the method in B.2.2.

Results and Discussion

Comparing the raw membrane to the modified membrane heated at 50 ˚C, S_o dropped about 2.7-fold and L_p decreased about 28 %. Heating at 70 ˚C instead of 50 ˚C did not change the value of S_o. Wash using an Alconox detergent solution at room temperature did not result in a significant increase in S_o. Permeation of 3.75% PSS twice did not change the value of S_o. The permeation of aqueous solution of PSS is thought to result in the physical adsorption of the negatively charged polymer onto the PES membrane surface and in the pore walls, which might arise from hydrophobic interaction, hydrogen bonding and Van Der Waals interaction (Reddy et al., 2003). Heating after permeation of PSS was conducted to fix PSS on the PES surface through proposed formation of crosslinking between the sulfonate groups in PSS (Martins et al., 2003).

To test if the physically adsorbed PSS polymer could be washed off the membrane at higher temperatures than ambient, 400 mL of 0.2% (w/w) Alconox at 50 ˚C was pumped through a modified membrane. S_o increased from 0.044 to 0.100 after the permeation of the Alconox detergent solution. Further investigation on how to prevent PSS from washing off the membrane was deemed necessary.

Table B.6. Synder membranes modified by surface adsorption of PSS

Membrane	Modification method	L_{p0}	L_{p1}	S_o
300 kDa	1. Permeate 0.47 % PSS and then 3.75% PSS, and water 2. Heat at 50 ˚C	390	282	0.038
300 kDa	1. Permeate 3.75 % PSS and water 2. Heat at 70 ˚C	ND	91	0.041
300 kDa	1. Permeate 3.75 % PSS, and water 2. Heat at 50 ˚C 3. Wash with Alconox	381	309	0.024
300 kDa	1. Permeate 3.75 % PSS and water 2. Heat at 50 ˚C; 3. Permeate 3.75 % PSS and water 4. Heat at 50 ˚C 5. Wash with Alconox	339	224	0.043
300 kDa	1. Permeate 3.75 % PSS (pH 1.7) and water 2. Heat at 50 ˚C 3. Permeate 3.75 % PSS (pH 1.7) and water 4. Heat at 50 ˚C 5. Wash with Alconox	307	298	0.083

B.2.6 Surface coating via deposition of chitosan/polystyrene sulfonate multilayers

Flat sheet PES membrane discs having a pore size of 300 kDa and a diameter of 76 mm from Synder Filtration were used. The membrane disc was dipped in chitosan (CHI) and polystyrene sulfonate (PSS) solutions following the deposition procedure by Aravind, Mathew, and Aravindakumar (2007). The membrane disc was first in a 0.01 M CHI in 1 M Nacl aqueous solution at pH 1.7 for 15 min. After dipping, the membrane was rinsed with 50 mL DI-water for 1 min. Then the membrane was dipped in 0.01 M PSS in 1 M Nacl aqueous solution at pH 1.7 for 15 min. The membrane was then rinsed with 50 mL DI-

water. The above dipping steps were repeated three times to build successive CHI/PSS layers. The values of S_o and L_p were determined following the method in B.2.2.

Results and Discussion

Compared to the raw 300 kDa PES membrane in Table B.3, the 300 kDa membrane modified by chitosan/polystyrene sulfonate multilayers showed 2.6-fold decrease in S_o (Table B.7). The value of L_p after modification dropped about 4.6-fold. However, it is unknown if the decrease in S_o was caused by the CHI/PSS multilayer coated on the surface of PES membranes or the CHI/PSS complex precipitated in the pores. This approach was abandoned because precipitation of CHI/PSS complex was observed on the surface of the membrane each time the membrane transferred from CHI to PSS solution. CHI/PSS complex might plug the membrane pores and cause a decrease in both S_o and L_p. Precipitation of CHI/PSS complex also made it impossible to modify finished membrane products, like spiral-wound membranes.

Table B.7. Synder Membranes Modified via deposition of CHI/PSS multilayers

	L_{p0} (LMH/bar)	L_{p1} (LMH/bar)	S_o
300 kDa	361	79	0.039

B.2.7. Surface coating using polystyrene

The intent of this work was to first coat the membrane with PS, and then sulfonate the PS using sulfuric acid to create a negatively charged PES membrane. The following experiments were important for the selection of a solvent blend for the diffusion transfer method in which PS dissolved in a solvent blend and diffused into the surface of the PES membrane without dissolving the PES membrane. A strip of 300 kDa PES membrane was cut and soaked in different solvent combinations for a short time and then taken out to assess surface changes by visual observation.

Results and Discussion

The dissolution of PES and PS in different organic solvents is shown in Table B.8. Pure DMF is a good solvent for both PES and PS, while pure ethanol is not a good solvent for either polymer. Pure toluene can dissolve PS but not PES. To coat PS onto PES, a solvent blend should consist of at least two types of solvents: one solvent swells PES to facilitate the diffusion transfer of PS into the membrane, and one solvent dissolves PS but not PES. Compatibility of different solvents and solvent blends for coating PS onto a PES surface are listed in Table B.8. Solvents that dissolves PS but not PES are considered to "work" to coat PS onto PES. For example, a solvent blend consisting of 1% DMF in toluene dissolves PS but not PES, so the solvent blend potentially works to coat PS onto PES. To test if the solvent blend consisting of 1% DMF in toluene could coat PS onto PES successfully, a membrane was soaked in a solvent blend consisting of 1% DMF in toluene at first. The resulted membrane was then soaked in a solvent blend containing 28% ethanol and 72% toluene

overnight to wash off unbound PS. The solvent blend consisting of 28% ethanol and 72% toluene was chosen to wash off unbound PS instead of 1% DMF in toluene because 28% ethanol and 72% toluene is a poorer solvent for PS and would not wash off the bound PS theoretically. The resulted membrane was soaked in pure ethanol to wash off toluene residues, followed by water to wash off ethanol residues. However, L_p increased dramatically after the above experiment. This indicates that the solvent mixtures dissolved the membrane during soaking, even though there was no obvious visual change on the membrane. In addition, D-limonene was used to coat PS onto PES. D-limonene is a nature flavor chemical in food manufacturing. D-limonene dissolves PS but not PES, so D-limonene potentially works to coat PS on PES. However, coating PS on the PES membrane using D-limonene was unsuccessful based on the observation on the dramatic increase in L_p after incubation in D-limonene.

Table B.8. Compatibility of PES and PS with different solvents

Solvent	Dissolves PES?	Dissolves PS?	Works?
100 % DMF	Yes	Yes	No
100 % ethanol	No	No	No
100 % toluene	No	Yes	Yes
1 % DMF in toluene	No	Yes	Yes
3 % DMF in toluene	Yes	Yes	No
20 % DMF in toluene	Yes	Yes	No
10 % DMF in ethanol	No	No	No
28 % ethanol & 72 % toluene	No	Yes	Yes
10 % DMF in water	No	No	No
47 % ethanol in DMF	Yes	Yes	No
47 % ethanol in THF	Yes	Yes	No
33 % ethanol in D-limonene	No	Yes	Yes

Because it was challenging to find an organic solvent blend to dissolve PS but not PES in the coating method, we shifted focus to hydrophilic charged polymers, including poly (sodium 4-styrenesulfoneate) (PSS) and sodium dodecyl sulfonate (SDS). Both PSS and SDS were dissolved completely in solvent blends consisting of 1-50% DMF in water. The hypothesis was that water can be used to dissolve PSS or SDS, while DMF works as a swelling agent to facilitate the diffusion transfer of PSS or SDS into PES membranes. To test the hypothesis, a solvent blend containing 1-50% DMF in water was permeated through a PES membrane in a stirred cell for 8~30 min, followed by a water rinse step. L_p of the

resulted PES membranes was measured before (L_{p0}) and after (L_{p1}) the permeation of 1-50% DMF in water, and the result was shown in Table B.9. L_p remained unchanged when DMF percentage in the solvent blend was below 15% but increased above 15 % DMF. DMF is a good solvent for PES. As DMF percentage in the solvent increased, the solvent blend became a better solvent for PES and resulted in a higher L_p. Since 50 % DMF in water did not cause significant change in L_p, 50% DMF was used for future modification experiments. Further experiments using PSS in 50% DMF were reported in chapter 2. Permeation of SDS in 50% DMF did not result in significant change in sieving coefficient of PES membrane. However, permeation of PSS in 50% DMF led to up to 14-fold decrease in sieving coefficient of PES membrane.

Table B.9 Values of L_p for PES discs after permeation of 1-50% DMF in water

Solvents	L_{p0}	L_{p1}
1% DMF	205	188
5% DMF	215	203
10% DMF	241	233
15% DMF	268	278
20% DMF	206	270
30% DMF	247	352
40% DMF	224	355
50% DMF	266	398

References

Aravind, U. K., Mathew, J., & Aravindakumar, C. (2007). Transport studies of BSA, lysozyme and ovalbumin through chitosan/polystyrene sulfonate multilayer membrane. *Journal of Membrane Science, 299*(1-2), 146-155.

Belfer, S., Fainchtain, R., Purinson, Y., & Kedem, O. (2000). Surface characterization by FTIR-ATR spectroscopy of polyethersulfone membranes-unmodified, modified and protein fouled. *Journal of Membrane Science, 172*(1-2), 113-124.

Cowan, S., & Ritchie, S. (2007). Modified polyethersulfone (PES) ultrafiltration membranes for enhanced filtration of whey proteins. *Separation Science and Technology, 42*(11), 2405-2418.

Lu, D., Zou, H., Guan, R., Dai, H., & Lu, L. (2005). Sulfonation of polyethersulfone by chlorosulfonic acid. *Polymer Bulletin, 54*(1-2), 21-28.

Martins, C. R., Ruggeri, G., & De Paoli, M.-A. (2003). Synthesis in pilot plant scale and physical properties of sulfonated polystyrene. *Journal of the Brazilian Chemical Society, 14*(5), 797-802.

Nakao, S., Osada, H., Kurata, H., Tsuru, T., & Kimura, S. (1988). Separation of proteins by charged ultrafiltration membranes. *Desalination, 70*(1), 191-205.

Reddy, A., Mohan, D. J., Bhattacharya, A., Shah, V., & Ghosh, P. (2003). Surface modification of ultrafiltration membranes by preadsorption of a negatively charged polymer: I. Permeation of water soluble polymers and inorganic salt solutions and fouling resistance properties. *Journal of Membrane Science, 214*(2), 211-221.

Yang, M.-C., & Lin, W.-C. (2002). Ultrafiltration of myoglobin using surface-sulfonated polysulfone hollow fiber. *Journal of Polymer Research, 9*(1), 61-67.