Doctoral Thesis

Porous polymer membranes: synthesis and applications

Author(s):
Kellenberger, Christoph Ruedi

Publication Date:
2014

Permanent Link:
https://doi.org/10.3929/ethz-a-010266408

Rights / License:
In Copyright - Non-Commercial Use Permitted
POROUS POLYMER MEMBRANES: SYNTHESIS AND APPLICATIONS

A thesis submitted to attain the degree of

DOCTOR OF SCIENCES

(Dr. sc. ETH Zurich)

presented by

CHRISTOPH RUEDI KELLENBERGER

MSc Micro- & Nanosystems, ETH Zurich

born on 21.07.1983
citizen of Zürich (ZH)
Switzerland

accepted on the recommendation of

Prof. Dr. Wendelin J. Stark, examiner
Prof. Dr. André R. Studart, co-examiner

2014
To my family
and all the people
who are always by my side.

Rien n'est plus fort qu'une idée dont l'heure est venue.

Victor Hugo
Acknowledgments

During the last three years I enjoyed the unique opportunity of doing a PhD at ETH Zurich. ETH offers an environment that not only fosters creativity and collaboration but also helps researchers to develop freely and to make an effective contribution to a better future. On my way to my PhD I always felt strongly encouraged and supported by all sides to realize new ideas with full commitment. Doing a PhD at ETH Zurich always felt like a great privilege to me. I am grateful to have had the chance to work with wonderful people and to have been surrounded by them during the past three years.

Sincere gratitude goes to my advisor, Prof. Dr. Wendelin J. Stark. Without you, I would have never even considered doing a PhD. I was overwhelmed when I first worked for you as a master student. Your way of thinking, your enthusiasm and motivational skills were a constant enrichment to my PhD time. The way you and your group work was an incentive to me, to always be better. You have built an exceptional group of scientists and students that for sure will keep up the extraordinary work. I will always be proud to be a part of this.

Prof. Dr. André R. Studart is kindly acknowledged for his interest in my work and spending his valuable time being my co-examiner. I would also like to thank Prof. Dr. Massimo Morbidelli for being the chairman of my examination.

At the same time, I want to thank Dr. Robert Grass. You were the first person I talked to when I first contacted the Functional Materials Laboratory. I will always remember how glad I was to have finally found a person to share my passion about realizing great ideas. I have always enjoyed our fruitful discussions and I am looking forward to ongoing collaborations with you. I wish you all the best.

Special thanks go to the workshop, especially Urs Krebs. As a trained mechanical engineer I have always enjoyed working with you on my projects and discussing your plans and prototypes. Your expertise, know-how and enthusiasm have made my life much easier.

A big thank you goes to all the former and actual members of the group. When I started my work in the Functional Materials Laboratory I have been welcomed with open arms and ever since felt comfortable and motivated around you. We shared a lot of laughs and I will always remember the time we spent together. Stephi, Luc, Norman, Sam, Nora, Aline, Dirk, Roli, Fabian, Michael, Schätz, Evagelos, Inge, Oli, Lüde, Tino, Alex, Daniela, Philipp, Jonas,
Schumi, Renzo, Carlos, Vladimir, Michela, Röbi, Corinne, Elia Madeleine; I have always felt surrounded by friends rather than just colleagues. Thank you!

I also want to highlight all the exceptional students and assistants that worked with me during my PhD: Julien, Florian, Marcel, Conny and Jeremy. Some are now PhD candidates in the group of Prof. Stark: Sam, Michi and Mario. I learned a lot from you.

Many thanks go to Bianca for proofreading this work. Being with you makes me happy.

Last but not least I want to thank all my family for their endless support and patience throughout the years of my studies. Feeling your support has always strengthened me to continue my way.
# Table of contents

Acknowledgments 3

Zusammenfassung 8

Summary 11

1. Synthesis and Applications of Polymeric Membranes 13
   1.1 Introduction and history 14
   1.2 Membrane terminology 17
   1.3 Preparation of polymeric membranes 19
      1.3.1 Phase inversion membranes 19
      1.3.2 Membranes from stretching 20
      1.3.3 Track etch membranes 20
      1.3.4 Block copolymer membranes 21
      1.3.5 Template removal membranes 22
   1.4 Areas of application 25
      1.4.1 Microfiltration 25
      1.4.2 Ultrafiltration 26
      1.4.3 Reverse osmosis and nanofiltration 28

2. Soluble Nanoparticles as Removable Pore Templates for the Preparation of Polymer Ultrafiltration Membranes 30
   2.1 Introduction 32
   2.2 Experimental
      2.2.1 Continuous preparation of CaCO₃ and SrCO₃ nanoparticles 33
      2.2.2 Nanoparticle dispersion in polymers 33
      2.2.3 Composite films, pore leaching and membrane preparation 34
      2.2.4 Dextran rejection profile test and flow rate 35
   2.3 Results and Discussion
      2.3.1 Characterization of pore templating nanoparticles 37
      2.3.2 Membrane morphology 38
2.3.3 Membrane performance 42
2.4 Conclusions 44

3. Nanoparticle Pore Template Manufactured Cellulose Acetate and Triethyl Citrate Modified PES Dialysis Membranes with Narrow Pore Size Distribution 45
3.1 Introduction 47
3.2 Experimental 49
   3.2.1 Nanoparticle-polymer dispersions 49
   3.2.2 Membrane preparation 49
   3.2.3 Membrane morphology and contact angle measurement 50
   3.2.4 Preparation of dialysis devices 50
   3.2.5 Buffer exchange 50
   3.2.6 Dextran recovery test for dialysis membranes 51
   3.2.7 Protein adsorption 51
3.3 Results and Discussion 52
   3.3.1 Membrane morphology and water contact angle 52
   3.3.2 Buffer exchange rate and wettability 54
   3.3.3 Membrane sample recovery and protein adsorption 56
3.4 Conclusions 57

4. Roll-to-Roll Preparation of Mesoporous Membranes by Nanoparticle Template Removal 58
4.1 Introduction 60
4.2 Experimental 61
   4.2.1 Nanoparticle – polymer dispersion 61
   4.2.2 Lab scale membrane samples 62
   4.2.3 pH effect and template removal mechanism 62
   4.2.4 Roll-to-roll coating 63
   4.2.5 Gravity driven filtration setup and 24 h operation 64
   4.2.6 Flow cytometric absolute cell counting 64
4.3 Results and Discussion 65
   4.3.1 pH effect and template removal mechanism 65
   4.3.2 Roll-to-roll coating 68
   4.3.3 Drinking water production 69
4.4 Conclusions 72
5. Conclusion and Outlook

5.1 Narrow pore size distribution

5.2 Functionalization and modification of membrane polymers

5.3 New membrane materials

Appendix: Supplementary Material

A.1 Supporting information to chapter 4

References

CURRICULUM VITAE
Zusammenfassung


Die vorliegende Arbeit befasst sich mit einer neuen Methode zur Herstellung poröser Polymermembranen. Dazu wird das sogenannte Partikeltemplat-Verfahren angewendet. Dieses neuartige Membranherstellungsverfahren ermöglicht eine im Vergleich zum Phasentrennverfahren einfache und direkte Steuerung der Porengröße. Zudem lassen sich damit grundsätzlich alle löslichen Polymere in nano- bis mikroporöse Strukturen überführen, was sich als weiterer entscheidender Vorteil herausstellen könnte. Im Gegensatz zu anderen neuartigen Membranverfahren, lassen sich die in dieser Arbeit beschriebenen Partikeltemplat-Membranen relativ einfach auf industriell bewährten Beschichtungsanlagen herstellen.

In Kapitel 1 wird nun also dieses Verfahren detailliert beschrieben. Genauer gesagt, werden säurelösliche Salzpartikel als Porentemplat verwendet. Die verwendeten Partikel wurden mittels der sogenannten Flammenspräsyanalyse hergestellt. Dabei wird ein mit Lösungsmittel verdünnter Salzprecursor unter kontrolliertem Sauerstoffzufuss in einer Sauerstoff-Methan


Das Partikeltemplat-Verfahren wird in diesem Kapitel zum ersten Mal auf einer industriellen Pilotanlage umgesetzt. Dazu werden über 700 mL der Partikel-Polymer Dispersion von einer kontinuierlichen Beschichtungsanlage auf einer Länge von 100 m aufgetragen. Die so erzeugte Membran (17 m²) wird zur Sterilfiltration von Teichwasser verwendet. Es zeigt sich,
dass die Membran über die gesamte Rollenlänge keine Fehlstellen aufweist und einen Bakterienrückhalt von über 99,99 % gewährleistet.

**Kapitel 4** schliesst die vorliegende Arbeit ab und gibt einen Ausblick über sinnvolle zukünftige Forschungsschwerpunkte des Partikeltemplat-Verfahrens. Ein Hauptaugenmerk sollte selbstverständlich darauf gelegt werden, die Vorzüge gegenüber dem heute am weitesten verbreiteten Membranverfahren, dem PhasentreNNverfahren, zu verstärken und weiterzuentwickeln.
Summary

Separation processes play a key role in the chemical industry due to their relatively low energy consumption. Polymer membranes for microfiltration and ultrafiltration are being used since their invention in the 1960s. Most common membrane separation processes are sterile filtration of drinking water, concentration and purification of proteins and antibodies as well as virus removal in the pharmaceutical industry. New fields for membrane applications have come up during the past two decades. Thin film composite membranes are applied as reverse osmosis membranes for the desalination of seawater, breathable membranes from fluoropolymers are an integral part of functional outdoor wear and temperature resistant and electrolyte stable high performance membranes separate the electrodes in lithium ion batteries as well as in fuel cells. The majority of these commercially available membranes are currently produced by the so called phase inversion process. Phase inversion stems from the 1920s and remained to date the most common industrial membrane manufacturing procedure. However, this technology has gradually reached its limits. The broad pore size distribution and the fact that only a limited number of polymers can be applied, has prompted research to develop novel membrane manufacturing techniques.

The present work describes a novel route towards the production of porous polymer membranes applying the particle template removal method. Compared to the phase inversion process, this novel membrane manufacturing technique allows for simple and straightforward pore size tuning. Besides, a main advantage of this process is its applicability on basically all kinds of soluble polymers. In contrast to other recently developed membrane manufacturing techniques, the herein presented process can be easily applied on industrially proven coating devices.

In chapter 1, the general concept of the process is described in detail. More precisely, acid soluble salt nanoparticles are applied as pore forming template. The particles were produced by the so called flame synthesis. Therefore, a salt precursor is diluted in an appropriate solvent, dispersed by a controlled flow of oxygen and ignited by a premixed methane–oxygen flame. The resulting nanoscale combustion product can then be collected on a glass fiber filter where it forms a filter cake. Subsequently, it can be removed by use of a spatula for further use. These particles are then embedded into a polymer matrix to form a polymer-particle composite. Later selective dissolution of the template reveals an interconnected porous
structure. Application of differently sized nanoparticles indeed leads to membranes with differently sized pores. The pore morphology was investigated using scanning electron microscopy and by applying the dextran rejection profile test.

**Chapter 2** deals with the application of hydrophilic membranes with narrow pore size distribution for use as biotechnological dialysis membranes. Two novel routes towards hydrophilic membranes are being presented as a result of the low flux rates reported in chapter 1. Membranes with inherent self-wetting properties are essential for dialysis applications. Pretreatment steps by soaking the membranes in ethanol or glycerol are undesired due to possible contamination of the dialysis solution. Hydrophilic and self-wetting membranes are being produced by the application of a naturally hydrophilic polymer and by the addition of a plasticizer to an originally hydrophobic membrane polymer. It can be shown that the addition of a plasticizer does not lead to a significant change in pore size distribution. This finding is of fundamental interest to the membrane community. With current membrane production processes, the addition of high amounts of additives has always led to undesired drastic changes to the original pore morphology.

**Chapter 3** focusses on the industrial implementation of the described membrane manufacturing process. In a first step, the pore formation process is investigated in detail. Therefore, the diffusion of the acid into the pore template is mathematically modeled and the rate of the template dissolution is illustrated by scanning electron microscopy. It is shown that low pH values between 0 and 1 are essential for a fast and complete dissolution of the pore forming template. Undesired contamination of the permeate by residual template particles is investigated as well.

The particle template removal method is for the first time applied on an industrial pilot scale. Thus, 700 ml of particle-polymer dispersion are continuously cast by a roll coating device over a length of 100 m. The as produced membrane (17 m²) is then applied to sterilize heavily contaminated pond water. It is demonstrated that the produced membrane roll is defect free. Furthermore, the rate of bacteria rejection proved to be higher than 99.99 %.

**Chapter 4** summarizes the present work. The chapter suggests future research activities for the particle template removal method. A main focus should clearly be laid on identifying the merits of this novel membrane manufacturing process over the currently applied phase inversion processes.
1. Synthesis and Applications of Polymeric Membranes
1.1 Introduction and history

A membrane can be described as a selective-permeable interface between two phases. The first commercially available polymer membranes were produced by Sartorius in 1920. These filter membranes were invented by the two Göttingen based chemists Wilhelm Bachmann and Richard Zsigmondy. Six years later Zsigmondy was awarded the Nobel Prize of Chemistry "for his demonstration of the heterogeneous nature of colloid solutions and for the methods he used, which have since become fundamental in modern colloid chemistry". However, these membranes suffered from low flux rates and were therefore only implemented in very few fields of application. The invention of the first asymmetric membrane in 1960 by Lob and Sourirajan then led to the first breakthrough in membrane separation processes [1]. This asymmetric membrane consisted of a very thin selective layer (skin) on top of a nonwoven support and thus yielded previously unattained high flow rates. Research in the field of polymeric membranes increased perpetually over the past 5 decades and has evolved into numerous applications until the present day. Membrane based separation processes have become indispensable in the production of drinking water, dialysis, desalination as well as pharmaceutical purification. As an energy efficient alternative to ordinary thermal separation, the membrane market is forecasted with continual growth due to constantly rising energy demands.

Selectivity of a membrane can be achieved through three methods which will be demonstrated in the following:

1.) Size exclusion is a procedure through which the selectivity of a membrane is predominately achieved. Polymeric membranes cover a pore size range of 0.001 to 10 μm. Items that are smaller than the pores can permeate through the membrane whereas larger items are rejected. Common size exclusion process steps performed by polymeric membranes involve protein purification [2-4], virus filtration [5-9], water sterilization and drinking water production [10-19] as well as particle filtration [11, 20].

2.) Another well-established method to create selectivity of a membrane is the introduction of charged species on the membrane’s surface. Selectivity can here be achieved in two opposite ways: electric repulsion or attraction. So called ion exchange membranes are capable of repelling ions of the same charge whereas oppositely charged ions can pass through unrestricted by following the applied electric field [21-23]. The charge of these membranes can be either positive or negative. A positively
charged membrane is termed “anion exchange membrane” and a negatively charged membrane is termed “cation exchange membrane”. Furthermore, electric attraction is also being used to selectively separate charged species. More precisely, polymer membranes with positively charged surface groups can adsorb viruses. The negatively charged protein shell of the virus (capsid) [24] is electrically attracted to the oppositely charged membrane surface whereas uncharged species can travel unhindered through the membrane by the applied pressure [25-30].

3.) Affinity membranes are an approach to achieve high specificity and selectivity. These kind of membranes were mainly developed to overcome the problems that arise from the use of membranes that operate purely on the size exclusion principle in which broad pore size distributions lead to a lack of selectivity. Chemical modification and radiation grafting are the methods of choice to bind ligands or functional groups to the membrane surface [31-34]. These functional groups can then bind specific molecules, thus creating selectivity of the membrane. However, despite promising research results, only very few affinity membranes made it to the market due to difficult up-scaling of these membrane modification techniques[31].

A combination of the above described methods is desirable to achieve highest possible selectivity. The 3M zeta plus™ filter, for example, uses a combination of size exclusion and electric attraction to achieve high values of virus retention [35].
**Figure 1.1:** (a) Size exclusion principle: physical rejection of particles or molecules by size is the most common method used in filtration. (b) Electric repulsion principle: a charged membrane can repel ions of the same charge whereas differently charged ions can pass through unrestricted. Ion exchange membranes generally work with this functional principle. (c) Electric attraction principle: polymer membranes with positively charged surface groups can adsorb viruses and other negatively charged molecules. (d) Affinity membranes: functional groups attached to the membrane surface can bind specific molecules while letting other molecules pass freely.

The driving component in most membrane separation applications is pressure. The volume flow through the membrane can be described by the Hagen Poiseuille’s relationship which assumes a certain number of equally sized cylindrical holes (simplified model assumption) as follows:

\[
V = \frac{A \phi d^2 \Delta p}{32 \eta t} \quad (1.1)
\]

with volume flow \( V \) (m\(^3\) s\(^{-1}\)), membrane area \( A \) (m\(^2\)), area porosity \( \phi \) (%), pore size \( d \) (m), differential pressure \( \Delta p \) (Pa), viscosity \( \eta \) (Pa s) and membrane thickness \( t \) (m).
Figure 1.1 b) illustrates the functional principle of an ion exchange membrane. The key part in this separation application is the implemented electric field. The electric force $F$ between two differently charged plates (electrodes) is described by the Coulomb force equation:

$$F = \frac{AE_0V^2}{2d^2} \quad (1.2)$$

with area $A$ ($m^2$), vacuum permittivity $\varepsilon_0$ ($\approx 8.85 \times 10^{-12} \, A^2 \, s^4 \, kg^{-1} \, m^{-3}$), voltage $V$ ($kg \, m^2 \, A^{-1} \, s^{-3}$) and distance between the two plates $d$ (m).

Another driving component in membrane separation processes is diffusion. The membrane acts as a separator between two phases with different molecular concentrations. Molecules will then travel from the side of large concentration to the side of low concentration. Diffusion through a membrane is described by Fick’s law:

$$J = -\frac{k_BT}{6\pi \eta r} \frac{d\phi}{dx} \quad (1.3)$$

with flux $J$ (mol m$^{-2}$ s$^{-1}$), Boltzmann constant $k_B$ ($1.38 \times 10^{-23} \, J \, K^{-1}$), Temperature $T$ (K), dynamic viscosity $\eta$ (kg m$^{-1}$ s$^{-1}$), hydrodynamic radius $r$ (m) and concentration gradient described by $\frac{d\phi}{dx}$ (mol m$^{-4}$).

### 1.2 Membrane terminology

A stringent terminology is essential for all contributions to the membrane science and industry. Therefore, in 1996, IUPAC has recommended a basic set of terms applicable to polymer membranes and processes [36]. The present work was written following these recommendations and the most frequently used terminologies are described below.

- **Membrane**: structure, having lateral dimensions much greater than its thickness, through which mass transfer may occur under a variety of driving forces
- **Homogeneous / symmetric membrane**: membrane with essentially the same structural and transport properties throughout its thickness
- **Asymmetric membrane**: membrane constituted of two or more structural planes of nonidentical morphologies
- **Selective membrane skin**: region, often located at the upstream face of an asymmetric membrane, that forms a thin, distinguishable layer primarily responsible for determining the permeability of the asymmetric membrane
- **Flux / flow rate**: number of moles, volume or mass of a specified component passing per unit time through a unit of membrane surface area normal to the thickness direction
- **Permeate**: stream containing penetrants that leaves a membrane module (Note: see Figure 1.2)
- **Retentate (raffinate)**: stream that has been depleted of penetrants which leaves the membrane modules without passing through the membrane to the downstream (Note: see Figure 1.2)
- **Dead-end flow**: flow through a membrane module in which the only outlet for upstream fluid is through the membrane (Note: see Figure 1.2)
- **Cross flow**: flow through a membrane module in which the fluid on the upstream side of the membrane moves parallel to the membrane surface and the fluid on the downstream side of the membrane moves away from the membrane in the direction normal to the membrane surface (Note: see Figure 1.2)
- **Fouling**: process resulting in loss of performance of a membrane due to the deposition of suspended or dissolved substances on its external surfaces, at its pore openings, or within its pores
- **Microfiltration**: pressure-driven membrane-based separation process in which particles and dissolved macromolecules larger than 0.1 μm are rejected
- **Ultrafiltration**: pressure-driven membrane-based separation process in which particles and dissolved macromolecules smaller than 0.1 μm and larger than about 2 nm are rejected
- **Nanofiltration**: pressure-driven membrane-based separation process in which particles and dissolved molecules smaller than about 2 nm are rejected
Figure 1.2: (a) Schematic of a dead-end flow: the feed (F) flows perpendicularly through the membrane (M). (b) Schematic of a cross flow: the feed flows horizontally over the membrane (M) and is divided into permeate (P) and retentate (R).

1.3 Preparation of polymeric membranes

1.3.1 Phase inversion membranes

Besides many emerging membrane processes, phase inversion is still the predominant membrane production process especially for commercial membranes [37-38]. Phase separation in a polymer matrix can be achieved through several methods [39-48], of which immersion precipitation [49-56] and thermally induced phase separation (TIPS) are the most widely applied [57-77]. Immersion precipitation is basically executed as a three step procedure. First, a polymer is dissolved in an adequate solvent. Then, the solution is cast on a support structure (typically polymer nonwoven) by doctor blade coating or continuous roll coating. In the industry, the coating speed is typically between 1 and 50 m min\(^{-1}\). The final step consists of immersing the casting solution into a coagulation bath to precipitate the polymer. The bath has to consist of a non-solvent that is miscible with the polymer solvent. Since the non-solvent is typically water, most immersion precipitation membrane polymers are restricted to water miscible solvents. Typical polymers and adequate solvents for immersion precipitation are presented in the following:

- Polyethersulfone (PES): dimethyl acetamide (DMAc), N-methylpyrrolidone (NMP)
- Cellulose and cellulose acetate (CA): dimethyl acetamide (DMAc), N-methylpyrrolidone (NMP), dimethyl sulfoxide (DMSO)
- Polyvinylidene fluoride (PVDF): dimethyl acetamide (DMAc), N-methylpyrrolidone (NMP), dimethyl sulfoxide (DMSO), dimethylformamide (DMF)
- Polyacrylonitrile (PAN): dimethyl acetamide (DMAc), N-methylpyrrolidone (NMP); dimethylformamide (DMF)

When the casting solution is immersed into the non-solvent, the solvent rapidly diffuses into the non-solvent while the non-solvent induces the precipitation of the polymer. The pores are thus created in polymer-poor phases whereas the polymer matrix is built in polymer-rich phases.

While immersion precipitation is particularly suitable for the manufacture of ultrafiltration membranes, microfiltration membranes are typically produced by TIPS. A polymer is dissolved in a low molecular weight compound that acts as solvent and non-solvent at high temperatures and at low temperatures, respectively. Once cooled down, the phases are separated by glass transition or crystallization and the low molecular weight compounds can be extracted. TIPS is especially suited for polymers which are difficult to dissolve, such as polypropylene.

1.3.2 Membranes from stretching

Phase inversion is the main process in the industrial production of ultrafiltration and microfiltration membranes. However, pore size and pore size distribution are difficult to control and the number of applicable polymers for ultrafiltration is restricted by the solvent – non-solvent miscibility. Therefore, different membrane manufacturing techniques have been developed with the aim to overcome the above described challenges related to the phase inversion process. Stretching is a method to create micro-pores in crystalline and semi-crystalline polymers that are not accessible by phase inversion. The well-known Gore-Tex® (polytetrafluoroethylene) and Celgard® (polypropylene) membranes are produced by this functional principle which was invented in the late 1960s and subsequently protected by several patents [78-81].

1.3.3 Track etch membranes

The track etch technology is another example of industrial microporous membrane fabrication [38]. Polymeric films (mostly polycarbonate and polypropylene) are irradiated by pulsing or continuous ion beams from accelerators [82]. As a consequence, free chemical bonds evolve which can be removed by subsequent etching. This results in almost perfectly straight capillaries through the polymer film [83]. These membranes stand out because of their highly uniform pore size distribution that to date remains unsurpassed. Unfortunately, poor reproducibility and high cost of the final product are the reasons why track etch
membranes remain a niche product for highly qualified analytical and scientific applications [84-87].

1.3.4 Block copolymer membranes

Selective removal of one component from self-assembled block copolymers displays a very remarkable and emerging technique to achieve polymeric porous membranes of high uniformity [88]. Two (diblock) or more (e.g. triblock) covalently bonded blocks of immiscible polymers (e.g. polystyrene and polyisoprene) form a block copolymer. This immiscibility favors the formation of structures that minimize the contact between the unlike polymers. Solutions of these block copolymers can be cast on substrates and further annealing leads to the formation of highly oriented structures. Depending on the volume fraction of the involved components and on the composition of the copolymers, the following structures can occur [89-92]:

- Lamellae (diblock copolymer)
- Cubic gyroid (diblock copolymer)
- Cylinders (diblock copolymer)
- Spheres (diblock copolymer)
- Cylinders between lamellae (triblock copolymer)
- Rings around cylinders (triblock copolymer)
- Tricontinuous diamond network (triblock copolymer)

The first serious results about mesoporous morphologies derived from self-assembled block copolymers were published by Lee et al. in 1989 [93]. In their study, a series of mesoporous membranes with pore sizes of 7 to 28 nm were produced by varying the block lengths. Thus, the block copolymer was prepared by the anionic living polymerization of (4-vinylphenyl) dimethyl-2-propoxysilane (PPS) and isoprene, by cross-linking the PPS domain and by subsequent ozonolysis of the polyisoprene (PI) block. This new method of creating porous polymers led to more fundamental research on the synthesis, morphology and control of pore structure in the following decade [94-99]. In 2001 it was found that the addition of a homopolymer to a diblock copolymer system generates cylindrical structures that are normal to the surface [100]. The generation of cylindrical pores normal to the coated surface are of substantial interest for the membrane community and has led to several publications demonstrating the use of block copolymer derived structures for filtration [6, 9, 101]. A
schematic of the fabrication of mesoporous polymer membranes manufactured by this process is given below.

Figure 1.3: Diblock copolymer filtration membrane produced by the method described by Yang et al. [9]. (a) Poly(methyl methacrylate) (PMMA) is added to polystyrene-block-poly(methyl methacrylate) (PS-b-PMMA) forming cylinders normal to the surface. (b) The PS block forms the polymer matrix and the PMMA homopolymer forms cylinders normal to the surface surrounded by the PMMA block. (c) The PMMA homopolymer can be selectively removed by acetic acid revealing a highly structured porous membrane.

So far, no commercial membrane products based on the self-assembly of block copolymers are available. On the one hand, this is due to the fact that this technology is fairly new and certain issues like pore size tuning, range of applicable polymers and mechanical stability remain to be investigated [9, 97]. On the other hand, no attempts towards industrial upscaling of this technique have been reported to date. This can partially be explained by the fact, that block copolymer structures have only recently been investigated for use as filtration membranes. More studies stem from micro-processing (mainly lithography) research where continuous production processes are generally less established [89, 97, 102].

1.3.5 Template removal membranes

Hard template removal from a polymer matrix is a similar approach towards the fabrication of highly structured porous membranes as in block copolymer membranes. Here, a (mostly) inorganic template is infiltrated by a monomer. Subsequent polymerization and template removal leads to an interconnected porous structure [103-107]. Because a highly precise templating will replicate one structure into another, the main focus lies on the application of ordered mesoporous silica nanoparticles or more generally colloidal crystals as templates [108-111]. Unfortunately, such highly ordered templates accompanied by large specific surface areas generate high interface energies when removed and therefore require stiff or highly cross-linked polymers [104, 112-113].
As described above, many promising new membrane production techniques have emerged during the past two decades. The main focus was laid on the tight control of pore size and pore size distribution as well as the accessibility of new polymers. This goal was clearly achieved by the above presented new methods. Nevertheless, due to a lack of large scale production, none of these new membranes can currently compete or even replace phase inversion membranes. This might be scientifically irrelevant and publications that demonstrate the upscale of lab processes to an industrial level generally receive scant attention from the research society. However, this growing divisiveness between research and industry hinders scientific breakthroughs from becoming available for a broad public. Recent publications questioning the reproducibility of scientific results confirm the need for more robust processes and will hopefully trigger a rethinking on the importance of upscaling, reproducibility and processability of scientific results that are substantially publicly funded [114-118].

In this work, a new route towards the fabrication of porous polymer membranes is presented. This new manufacturing process combines the straightforward physical pore size control as achieved through templating with the possibility of continuous production known from commercial phase inversion membranes. Therefore, the templating particles (nano- to microparticles) are directly mixed into a solution of dissolved polymer (dispersion). Once cast on a suitable substrate, the solvent can be evaporated to build a thin film polymer-particle composite. Subsequent immersion in a mild acid leads to removal of the template particles. A
high particle to polymer ratio guarantees an interconnected pore structure necessary for membrane applications.

Figure 1.5: Schematic of the particle template removal method. (a) Templating particles are directly mixed into a solution of dissolved polymer (dispersion). (b) Casting and subsequent solvent evaporation lead to a polymer-particle composite. The particles form an unordered array throughout the polymer matrix. (c) Dissolution of pore template reveals an open and interconnected porous structure.

The size and size distribution of the chosen templating particles determines the final morphology of the membrane. The template structure is formed on its own during the evaporation of the solvent. With this method, no template forming and monomer infiltration steps are necessary and the issue of high surface tensions related to previously formed ordered arrays of particles is eliminated [104, 112-113]. Thus, the membranes are significantly less brittle and more flexible. The starting dispersion can be applied using the doctor blade technique for small volume lab samples or by roll to roll coating for continuous large scale production [119-120]. The pore size distribution might not be as excellent as in track etch or block copolymer membranes. However, increasing quality of commercially available nano- and microparticles will continuously improve pore size distribution and enable pore size control over a wide range. Due to the mainly physical character of the pore formation, the choice of polymer is not restricted to solvent – non-solvent miscibility as in predominant phase inversion membranes. Thus, the template removal method may basically turn every polymer into a porous membrane as long as the polymer can be dissolved. So far, this new technology has turned out to be very versatile and has already been applied on different polymer-rs [20, 105]. Recently, incorporation of lanthanum nanoparticles into template removal membranes has led to phosphate removal during drinking water filtration [16].
Furthermore, membranes with high ionic conductivity for the utilization as battery separators have been attained as well [105].

1.4 Areas of application

The size of the pores determines the possible applications of a membrane. As described at the beginning of chapter 1, polymer membranes cover a pore size range of 0.001 to 10 μm. Choosing the right pore size is crucial for efficient and selective membrane processes. In filtration, a rejection of at least 90% of the contaminant is typically requested. Often, membrane providers recommend using a membrane with a molecular weight cut-off (MWCO) half the weight of the contaminant. This precautionary measure can be mainly attributed to the broad pore size distribution of the predominant phase inversion membranes. However, high rejection rates are therefore achieved at the expense of fast separation processes. In the following section, the three most common types of membrane processes and applications will be briefly described. The figure below gives an overview on membrane types and their applications.

![Figure 1.6: Overview on polymeric membrane types by pore size and applications.](image)

1.4.1 Microfiltration

Microfiltration covers the largest pore size range in polymeric membranes. The pore sizes range from 0.1 μm to approximately 5 μm. Mainly suspended solids, colloids and bacteria are rejected by a sieving (size exclusion) mechanism. These membranes typically offer high water flux rates at a low pressure. However, germs and viruses cannot be removed. Thus, microfiltration membranes are generally used for the disinfection steps of drinking water.
production and biotechnology [4, 19, 121]. Microfiltration membranes are primarily produced by TIPS [57, 62-64, 66-67, 70] or stretching of semi-crystalline polymer films [78-81]. Microfiltration membranes of highly uniform pore structure can be manufactured by the track etch method [84]. The most common polymers for microfiltration therefore are the hydrophobic polytetrafluoroethylene (PTFE), polypropylene (PP), PVDF and polyethylene (PE), whereas hydrophilic microfiltration membranes can be produced from CA, polycarbonate (PC), PES, polysulfone (PSU) and polyamide (PA) [18]. Hydrophobic membranes produced by the stretching method are very well known to a broad public under their registered brand names. Gore-Tex® is produced from the chemically highly stable PTFE. Due to its hydrophobic nature, this membrane has excellent properties as functional textile membrane. The membrane will not wet when in contact with water but the pores are large enough to let water vapor (perspiration) pass through easily. Another example for a well-established brand name is Celgard®. This stretched film from PP is a proven lithium ion battery separator with excellent resistance to acids, bases and oxidation. Battery membranes separate the electrodes to prevent a short circuit while ions can travel through unrestrictedly.

Hydrophilic microporous membranes produced by phase inversion (mainly TIPS) are essential components in the processing of water and beverages. Microorganisms such as bacteria, fungi, algae and protozoa as well as viruses pose a severe health risk and thus have to be removed during drinking water and beverage production. Due to the pore size difference that separates micro- from ultrafiltration, these two types are usually coupled to ensure full removal of biologically hazardous components [18, 122-123]. On the other hand, semiconductor and electronics industries as well as the pharmaceutical sector have a relatively constant demand for highly purified water. Here again, micro- and ultrafiltration are usually coupled to achieve the needed purity. Microfiltration commonly acts as prefiltter to remove bacterial contamination [19, 124]. ASTM F838 defines a microfiltration membrane as sterile filter when at least 99.99 % of *brevomundis diminuta* at a concentration of 10⁷ cells ml⁻¹ is removed after filtration [125-126].

1.4.2 Ultrafiltration

As described above, ultrafiltration experienced its breakthrough thanks to the invention of high flux asymmetric membranes at MIT in the 1960s [1]. Ultrafiltration membranes cover the pore size range of 0.002 μm to 0.1 μm. Therefore, this membrane type is ideally suited for purification and concentration of biomolecules, antibodies and proteins [2-3, 127]. Due to the small pore size of ultrafiltration membranes, even the smallest paroviruses (appr. 20 nm) can
be removed by ultrafiltration. This is of great significance for the pharmaceutical industry as well as for the treatment of drinking water [5-6, 8-9, 128-129]. The majority of the commercially available ultrafiltration membranes are produced by the phase inversion process, more precisely the immersion precipitation method. Common polymers are PSU and PES, PVDF and products from cellulose, such as cellulose nitrite and cellulose acetate. Immersion precipitation allows for the production of a wide range of pores in PSU and PES. Besides, these materials exhibit excellent pH and temperature stability. The glass transition temperature of PSU is 195 °C [38]. However, their hydrophobic properties put these membranes at a disadvantage when applied for the treatment of aqueous solutions. This leads to reduced water flux and increased binding of microorganisms due to hydrophobic interactions, an effect called fouling [130-134]. Polysulfone membranes are thus typically turned hydrophilic by the use of a wetting agent [135], blending with hydrophilic polymers [18, 136] or by surface modification [137]. Once rendered hydrophilic, these membranes are applied for general water treatment and clarification, sterile filtration, buffer filtration as well as tissue culture media filtration. The major providers are Merck Millipore and Pall Corporation, both located in the United States.

Compared to PSU and PES, PVDF has much better resistance to organic solvents and oxidizing agents. With a glass transition temperature of –40 °C, the semi-crystalline PVDF feels soft and offers a certain elasticity. Being soluble in DMAC and NMP it can still be processed by the immersion precipitation method. Naturally, PVDF is extremely hydrophobic and exhibits high protein and nucleic acid binding. Therefore, unmodified PVDF membranes with pore sizes of 0.2 µm and 0.45 µm are ideally suited for use as transfer membranes in blotting applications [138-140]. Similar techniques as with PES and PSU can be applied to render PVDF hydrophilic. Hydrophilized PVDF membranes represent a valid alternative to PES membranes for the treatment of aqueous solutions in applications like sterile filtration and protein purification [141-143].

Cellulose membranes are one of the few naturally hydrophilic membranes [38]. Most common products are membranes from cellulose nitrate, cellulose ester and cellulose acetate. Due to the self-wetting properties, these membranes are predestined for use in dialysis applications [3]. Tubes from cellulose ester or membrane cassettes are filled with solutions of biomolecules, antibodies or proteins. Immerses into deionized water, the molecules and contaminants will diffuse through the membrane following the concentration gradient. Small particles will diffuse faster than large particles. Additionally, the pore size of the membrane
acts as a size exclusion barrier. Thus, dialysis process steps efficiently remove residuals from biomolecule synthesis and can also be applied for buffer exchange. Unfortunately, these dialysis processes are generally slow. Dialysis can take days, and the dialysate has to be replaced at least once a day to maintain a high concentration gradient. Spectrum Labs, a California based dialysis membranes manufacturer, has therefore developed the so called dynamic dialysis. A constant counterflow of solution and dialysate guarantees a steady and highest possible concentration gradient thus increases diffusion rate and efficiency [144-146].

1.4.3 Reverse osmosis and nanofiltration

Nanofiltration membranes and membranes for reverse osmosis (RO) consist of a highly open porous support structure covered by a thin non-porous skin layer. In a strict sense, these membranes are not actual porous polymers. Nevertheless, their increasing importance in the fields of water desalination and the treatment of organic solvents, justify a short treatise within this chapter.

As the name suggests, RO means the inverse of an osmotic pressure driven membrane process. If the applied pressure is high enough (typically > 30 bar), the dissolved components will travel from the area of lower concentration to the area of higher concentration against the osmotic pressure [147]. Today, RO has its main application in the desalination of seawater as proposed by Reid and Breton in 1959 [148]. There are basically two types of commercial RO membrane materials: integral asymmetric cellulose acetate and polyamide thin film composites (TFCs). The asymmetric cellulose RO membranes are produced by ordinary phase inversion such that the thin skin layer (0.1 – 1 μm) remains non-porous. TFC RO membranes on the other hand consist of a porous polysulfone support covered by a thin polyamide skin layer (appr. 0.1 μm). This thin layer is prepared by in situ interfacial polymerization [38, 149]. The dense skin layers of these membranes, when in contact to water, will swell and thus tiny channels form that allow for water molecules to pass through, whereas monovalent ions are still rejected.

Nanofiltration is a relatively new terminology and definitions vary in literature [38, 149]. In this work, nanofiltration membranes are considered to consist of a dense, non-porous skin layer on top of a support structure that reject particles and multivalent ions smaller than 2 nm. While RO membranes focus on the treatment of aqueous solutions, new nanofiltration membranes have recently been developed for the treatment of organic solvents [150-152]. Emphasis is to be laid on the work of the group of Prof. Livingston from Imperial College, London. Their chemically cross-lined polyimide (PI) nanofiltration membranes were the first
to withstand aggressive solvents such as tetrahydrofuran (THF), DMF and NMP [153]. The process is based on the formation of integral asymmetric membranes rather than predominant TFC nanofiltration membranes. Therefore, a PI membrane prepared by the immersion precipitation method is immersed into a bath of methanol and crosslinker for 24 h. These nanofiltration membranes showed superior solvent stability compared to ordinary PI and MWCOs between 250 Da and 400 Da were reported. This innovation led to the foundation of Membrane Extraction Technology (MET) Ltd. which was acquired by Evonik Industries in 2010.
2. Soluble Nanoparticles as Removable Pore Templates for the Preparation of Polymer Ultrafiltration Membranes

Published in parts as:

Christoph R. Kellenberger, Norman A. Luechinger, Alexandros Lamrou, Michael Rossier, Robert N. Grass, Wendelin J. Stark

Abstract

A novel, nanoparticle-assisted process for the continuous fabrication of polymer (polyethersulfone) ultrafiltration membranes is reported. Incorporating acid-soluble carbonate nanoparticles into polymers and subsequent roll coating or solvent casting of these composites provides a low cost access to large area membrane preforms. Contacting these films with dilute acids removes the nanoparticle template and results in highly porous polymer films. The pore size of the membrane can be modified by the size and morphology of the nanoparticle templates, typically carbonates. The template forming nanoparticles and the morphology of the polymer ultrafiltration membranes were characterized by electron microscopy. The molecular weight cut off (MWCO) of the membranes was determined by a dextran rejection profile test and the amount of residue inorganic material was investigated by thermal gravimetric analysis (TGA) and inductively coupled plasma optical emission spectrometry (ICP-OES). The here outlined process may provide an alternative to the current phase inversion production processes particularly since pore templating by soluble nanoparticles is broadly applicable to technically attractive polymers.
2.1 Introduction

Filtration of particles in the sub-100 nm range such as viruses, nanoparticles or proteins is called ultrafiltration. Polymer ultrafiltration membranes are playing an important role in mass separation processes in the chemical and biopharmaceutical industry, food and beverage manufacturing and water treatment and recovery. Ultrafiltration membranes allow protein isolation, concentration and purification and virus clearance [6, 154-156]. Today, polymer ultrafiltration membranes are produced by the so called phase inversion process [40, 42-43, 45, 64, 157-158]: A phase separation is induced in a previously homogeneous polymer solution at a precise moment in processing, precise temperature and solvent to non-solvent ratio. As a result, the phase inversion process requires simultaneous and tight control on a broad range of parameters during production and its often broad pore size distribution decreases the selectivity of the resulting membrane [6, 155]. Such ultrafiltration membranes have therefore been considered unsuitable for demanding applications such as virus filtration [5-9, 159]. Recently, several novel approaches towards the fabrication of ultrafiltration membranes have been reported on the basis of micro fabrication [6, 9, 108]. Laser interference lithography and silicon micro machining technology have been used to fabricate membranes with 100 nm pore size [160]. Colloidal self-assembly of inverse opal materials has led to highly uniform pores in the sub-100 nm range [108, 161]. These approaches showed excellent characteristics concerning selectivity but cannot easily be applied on larger scales due to speed restrictions of micro processing and crack formation. Another approach towards the simple and rapid production of membranes is the formation of nanoporous films through block copolymer self-assembly [13]. Such membranes have been investigated for their use in ultrafiltration and showed promising characteristics concerning selectivity and porosity [162-164].

In this work, we report on a scalable approach towards large scale fabrication of ultrafiltration polymeric membranes based on a two-step procedure: First, a polymer sheet containing soluble (degradable) carbonate nanoparticles is prepared and optionally brought into a specific form. The nanoparticles act as pore templates (Scheme 1). In a second step the polymer film is turned porous by simple dissolution of the soluble nanoparticles upon contact to a mild acid. The pore formation of the resulting membrane is different than in conventional preparations: Here, the pore size and number of pores can be exactly defined by the size and number of nanoparticles, as they serve as a direct template of the finally obtained pores. Therefore, the pore size can be tuned through the particle properties. The pore formation
happens under well-defined conditions, separated from other processing variables. This may ultimately yield to narrow pore size distributions with associated improved selectivity.

![Diagram of membrane preparation]

**Figure 2.1:** Membrane preparation: A polymer/nanoparticle dispersion is cast onto a substrate and forms a composite film. The pore templates (carbonate nanoparticles) can be dissolved in diluted acid releasing the filtration membrane.

2.2 Experimental

2.2.1 Continuous preparation of CaCO₃ and SrCO₃ nanoparticles

The here applied nanoparticles were synthesized using a dry, continuous process adapted from the preparation of pigmented titania, tire soot and fumed silica, by so called flame spray synthesis [165-168].

Preparation of the CaCO₃ precursor: Ca-2-ethylhexanoate in 2-ethylhexanoic acid (Molekula) was diluted with tetrahydrofuran (THF) to a final Ca content of 3.9 wt% (weight-%; determined gravimetrically). SrCO₃ precursor: Strontium-2-ethylhexanoate in 2-ethylhexanoic acid (Strem Chemicals) was diluted with tetrahydrofuran (THF) to a final Sr content of 4.7 wt%. The precursor solutions were fed (9 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (9 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH₄, 1.2 l/min; O₂, 2.2 l/min). The nanoparticle-loaded aerosol off-gas was filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder was collected on glass fiber filters. The size distribution of the nanoparticles was analyzed optically using transmission electron microscopy (TEM). For the nanoparticle size distributions more than 400 single particles were measured.

2.2.2 Nanoparticle dispersion in polymers

The nanoparticles were dispersed in dissolved polyethersulfone (PES) at precise mass ratios (nanoparticle/polymer mass ratio) of 1.5. The related volume ratio (nanoparticle/polymer) was 0.7 for the lime stone (CaCO₃)-based membranes and 0.5 for the corresponding strontium carbonate based membranes. The PES (Veradel A-201, Dolder AG, Switzerland) was dissolved in dimethylacetamide (DMAC, puriss, Aldrich). The mass ratio of solids (CaCO₃
and PES) to solvent (DMAC) was 0.79 for lime stone (CaCO₃)-based membranes and 0.39 for the corresponding strontium carbonate based membranes. More specifically, the nanoparticle/PES dispersions were prepared from the following samples (all ratios and percentages given are referring to weight): A sample of 5.0 g of 15% PES solution in DMAC was mixed with 1.125 g of CaCO₃ or SrCO₃ nanoparticles in a small glass beaker and then vigorously shaken using a vortexer (Heidolph, Germany). An additional 0.57 g of DMAC was added to the SrCO₃-PES mixture to enhance its dispersibility. For a better dispersion of the nanoparticles in the solution, an ultrasonic finger has to be used (Hielscher UP400s, Germany) to sonicate the dispersions for 1 min at 400 W. The milky liquids were stable for several hours (Figure 2.2a) before the particles in the solution started to significantly agglomerate and subsequently sediment. This effect can be reversed by renewed sonication prior to film casting.

2.2.3 Composite films, pore leaching and membrane preparation

Suitable nanoparticle/polymer dispersions can be directly applied to produce ultrafiltration membranes. For laboratory scale samples, the dispersions were applied on 30 mm x 30 mm square glass substrates using spin-coating (Laurell Technologies Corp., WS-650SZ, USA). A drop of approximately 500 μl is pipetted onto the substrate and then spun for 10 seconds at 1000 rpm using an acceleration of 1000 rpm/s. Subsequent heating for 1 minute at 120 °C in an air circulation oven (Memmert GmbH, Germany) affords solvent evaporation and results in transparent composite films adhering to the glass substrate. The final membrane is obtained by dissolving the template nanoparticles through immersion into diluted hydrochloric acid (1 Molar; HCl) for 1 minute. The acid bath also detaches the polymer film from the glass substrate and results in free swimming membranes of sufficient mechanical stability for subsequent handling. The membranes were washed thoroughly in de-ionized water (Millipore, electrical resistivity > 18 MΩcm) and ethanol and dried in air for 2 hours. Scheme 1 shows a schematic of the production process and Figure 2.2b shows a picture of a transparent PES membrane above a Swiss franc coin.

The morphology and structure of the composite films (preforms) and final filtration membrane were analyzed using scanning electron microscopy to determine the pore size distribution. Cross section views were obtained from breaking membranes after immersion into liquid nitrogen. At least 200 pores per sample were optically measured in electron micrographs for each membrane type (CaCO₃ or SrCO₃ nanoparticles as pore template, subsequently denoted as CaCO₃-derived membrane or SrCO₃-derived membrane). Pore
density on the skin side of the membrane was optically measured in electron micrographs of 8.5 µm² area. The pore density was calculated as ratio between pore surface area to total surface area.

**Figure 2.2:** Polyethersulfon/nanoparticle dispersion (a) as starting material for film preparation and nanoporous PES membrane after removing the acid-soluble carbonate nanoparticle pore templates (b). A high degree of transparency confirms the absence of light-scattering impurities (right: Swiss coin).

Thermogravimetric analysis and inductively coupled plasma optical emission spectrometry was carried out by TGA (Linseis, STA PT 1600, Germany) and ICP-OES (Horiba Ultra 2) to investigate any residue inorganic content after acid leaching. For TGA the temperature range was set to 20 - 1200 °C under air atmosphere with a flow of 6 l/h, heating rate of 10 °C/min. The mass of the samples was about 20 mg. ICP-OES was conducted on membrane samples of 50 mg that were first incinerated at 600 °C in an ordinary sinter oven (Nabertherm, Germany) and then dissolved in 10 ml of 1M HCl.

### 2.2.4 Dextran rejection profile test and flow rate

The performance of ultrafiltration membranes is typically measured using a dextran rejection profile test. This testing procedure is widely accepted in industrial and academic research [154, 169-170]. Commercially available dextran standard molecules mixtures (Fluka Analytical, Switzerland) were used to measure the CaCO₃ – derived membrane using the following molecular weights: 1, 5, 25, 80, 150, 270, 410, 670, 1400 kDa. For the SrCO₃ –
derived membranes, a smaller set of molecular weight standards was used, i.e. 1, 5, 25, 80, 150 kDa. The dextran concentration was 0.5 g/l for all molecular weights. All samples were dissolved in 0.100 mol/l reagent grade sodium nitrate (NaNO₃) solution to keep the ion strength constant. The same NaNO₃ solution was also used as the mobile phase for gel permeation chromatography (GPC) analysis described in details below.

The setup for the filtration experiments is a crucial step in the determination of the filtration performance and the reproducibility of the results. It has been reported that different experimental setups (stirred cell, unstirred cell, dead-end operation, tangential flow) for ultrafiltration lead to different results and comparison of results from different setups can be deceptive [4, 170]. Besides, Wickramasinghe [8] had reported that the use of stirred cells for filtration experiments can cause leakage of the feed solution around the O ring seal between membrane and cell. Therefore a different experimental setup was chosen (Figure 2.3)[4]. The dextran solution was continuously pipetted onto the membrane that was flatly positioned on a suction strainer. A high-vacuum pump (Edwards, UK) was used to maintain a pressure difference of 1 bar. The membrane was wetted in ethanol prior to use and a support membrane (kindly sponsored by Freudenberg Filtration Technologies KG, Germany) was used to prevent damage to the membrane caused by the pressure difference. All experiments were carried out in duplicate and average values were given.

Figure 2.3: Experimental setup. Test membranes were positioned onto a mechanical support and various dextran solutions were fed through the filter.
Feed and filtrate samples (1 ml samples) were analyzed by Gel Permeation Chromatography (GPC) through two PSS Suprema 100 and Suprema 10000 (2x8x300 mm) GPC columns connected in series and calibrated against dextran standards of the following molecular weights: 1, 5, 25, 80, 150, 270, 410, 670 and 1400 kDa. For these analyses a Hitachi L-7000 HPLC system was used, equipped isocratic pump and RI detector, operated at 25 °C with 0.1M aqueous NaNO₃ as mobile phase at 1 ml/min. Dextran rejection profile curves were obtained from the GPC data following established procedures [154, 169-170]. The GPC curve of the filtrate was compared to the GPC curve of the mixed dextran molecules used to challenge the membranes. The characteristic rejection curve of the tested membranes was calculated as the ratio of dextran molecule concentration in the filtrate to dextran molecule concentration in the mixture as a function of molecular weight. The rejection profiles can be used to determine the molecular weight cut off (MWCO) of the specific membranes. The MWCO refers to the molecular weight of the molecule that is rejected by the membrane to at least 90 %. The flow rate of deionized water (Millipore, electrical resistivity > 18 MΩcm) through the membranes was measured for 30 minutes for each membrane at a pressure difference of 1 bar using the same experimental setup as in Fig 2. The results were normalized to ml / min / cm² at a pressure difference of 1 bar.

2.3 Results and Discussion

2.3.1 Characterization of pore templating nanoparticles

Soluble pore templates based on calcium and strontium carbonate nanoparticles were prepared by flame spray synthesis [165-168] and yielded particles of 51 and 42 nm average size for CaCO₃ and SrCO₃, respectively. This size range is in agreement with earlier reports on nano-limestone [166] or nano-glass particles [171]. Figure 2.4 shows transmission electron microscopy images of rather spherical CaCO₃ and SrCO₃ particles with their corresponding optically determined particle size distributions. The log-normal size distribution is in full agreement with theoretical predictions [172] and earlier reports [165-168]. The CaCO₃ particles were generally larger than the SrCO₃ nanoparticles, which stays in agreement with their difference in melting point and chemical stability. Similar trends have routinely been observed during flame synthesis of nanoparticles [173]. The particles consist mainly of individual primary particles and little sintering (formation of hard bonds between particles) is observable.
Figure 2.4: Transmission electron microscopy (TEM) images of CaCO$_3$ (a) and SrCO$_3$ nanoparticles (b) and their corresponding particle size distributions (c, d). The log-normal distribution stays in full agreement with theoretical predictions [172].

2.3.2 Membrane morphology

The preparation of polymer composite films with high (> 50 wt %) carbonate nanoparticle loadings stays in agreement with the above particle’s characteristics, namely the absence of significantly sintered large agglomerates. Embedding of high nanoparticle loadings in composites has been earlier observed to depend on the presence of predominantly individual nanoparticles in the case of calcium phosphates in biomaterials [174-175].

Removal of the pore template afforded porous polymer films as depicted in Figure 2.5. The substrate side of the membrane shows a very smooth surface with rather narrow pore size distribution and is therefore called the skin side. The skin side is one of the main factors determining the size of the rejected molecules. The reverse side of the membrane shows a higher porosity but also a larger distribution of pore sizes and a rough surface. The cross...
section micrographs reveal a highly porous structure with the capability for deep filtration. Due to the different viscosity during film casting, the SrCO$_3$-derived membranes are a little thinner than the CaCO$_3$-derived ones. The cross section further reveals large pores within the bulk of the material. It is expected that they resulted from fusion of pores (coalescence). Their formation may also have been facilitated by the presence of some agglomerates or air inclusions. Besides, agglomerates could have also been the result of a limited particle wetting by the polymer itself. Those large pores can have a positive effect (higher porosity) enabling higher filtrate flux as long as at least part of the membrane cross-section maintains its fine porosity.

![Micrographs of membranes](image)

**Figure 2.5**: Scanning electron microscopy images of membranes after template nanoparticle dissolution. Top view of CaCO$_3$- (a) and SrCO$_3$-derived membrane (b), skin (substrate side) of CaCO$_3$-membrane (c) and SrCO$_3$-membrane (d) and cross-sections of CaCO$_3$-membrane (e) and SrCO$_3$-membrane (f).

In order to provide a quantitative evaluation, the pore size distribution of the skin side of both membranes was determined by measuring at least 200 pores of both membranes in representative electron micrographs (Figure 2.6). The average pore diameter of the CaCO$_3$-derived membrane was 39 nm whereas the SrCO$_3$-derived membrane had an average pore diameter of 18 nm. The pore density of the skin side of the membranes was analyzed on 8.5
\( \mu m^2 \) area representative electron micrographs. The pore density of the CaCO\(_3\)-derived membrane was 2\% and 4.6\% for the SrCO\(_3\)-derived membrane, respectively.

**Figure 2.6:** Pore size distributions of the skin sides of polymer membranes derived from pore templation using acid soluble nanoparticles of nano-limestone, CaCO\(_3\) (a) and strontium carbonate, SrCO\(_3\) (b). The black curves indicate a log normal distribution.

Comparing the average particle size of the nanoparticles used for pore structure formation (template) revealed a possible correlation between pore size distribution and particle size distribution (Figure 2.7). But further, more detailed studies will be required to elucidate the details of this control parameter. It is expected that the mechanical properties of the polymer also influence the correlation of template size and resulting pore size as materials may anisotropically shrink after template removal.
Figure 2.7: Average template particle and resulting pore size of membranes derived from CaCO₃ (left) and SrCO₃-membrane (right). The columns show average values whereas the black error bars indicate standard deviations.

TG analysis (Figure 2.8) revealed low residue material from 3.3 wt % for the pure PES sample, 5.5 wt % for the CaCO₃ derived membrane and 4.0 wt % SrCO₃ derived membrane. Low residue content may be associated to resulting ashing. Therefore ICP-OES was used to ultimately determine the amount of residue calcium and strontium carbonate nanoparticles. The CaCO₃-derived membrane had 2.7 mg residual CaCO₃ per gram of membrane and the SrCO₃-derived membrane had 15.1 mg residual SrCO₃ per gram of membrane respectively. These results prove that there are few residue particles remaining after the leaching process. Nevertheless, the smaller SrCO₃ nanoparticles seem to be more prone to encapsulation by polymer. This shows that the SrCO₃ nanoparticle template is less interconnected than the CaCO₃ nanoparticle template.
Figure 2.8: TG analysis of pure PES and PES membranes after leaching of pore templating nanoparticles

2.3.3 Membrane performance

The ultrafiltration performance was tested using a number of dextran test molecules of various sizes. Figure 2.9 shows the dextran rejection profile of the CaCO$_3$-derived (a) and SrCO$_3$-derived membrane (b) with a cut-off at 1400 kDa or 70 kDa (rejection >95 %), respectively. The water permeability of the membranes was measured as 0.2 ml / min / cm$^2$ at 1 bar pressure difference for the CaCO$_3$-derived membrane and 0.05 ml / min / cm$^2$ for the SrCO$_3$-derived membrane. Figure 2.9a shows that the CaCO$_3$-derived membrane has a diffuse section (10 – 100 kDa) in its rejection profile. This plateau most likely refers to a broad pore size distribution in this specific area. Due to the narrower pore size distribution of the SrCO$_3$-derived membrane, no such diffuse areas can be found on the rejection profile shown in Figure 2.9b.
The size (diameter) of the molecule that corresponds to the molecular weight cut-off was calculated using the following formula \[ D = 0.053 \times MW^{0.5} \] (2.1)

with diameter D (nm) and weight of the dextran molecule MW (Da). Thus, the molecular weight of 1400 kDa refers to a size of 63 nm whereas 70 kDa refers to a size of 14 nm.

The present low flux of the here prepared membranes can be related to two reasons: First, if we consider the present porous membranes to have a certain number of equally sized cylindrical holes (simplified model assumption), the Hagen Poiseuille’s relationship can be written as

\[ V = \frac{A\varphi d^2 \Delta p}{32\eta t} \] (2.2)

with volume flow V (m³ s⁻¹), membrane area A (m²), area porosity φ (%), pore size d (m), differential pressure Δp (Pa), viscosity η (Pa s) and membrane thickness t (m). Equation (2.2) confirms that the flow rate decreases linearly with membrane thickness. The present membranes have a thickness of about 2 - 3 μm. A large thickness was chosen to facilitate the handling of the membranes during experimentation. For large scale applications, the membrane would obviously be cast directly onto a mechanical support substrate. This would allow the membrane to be produced much thinner, and hence allow for a larger flow. The
present demonstrative study has been using roll or spin coating which can form films as thin as 100 nm. For example, a membrane having a skin thickness of 400 nm instead of 2 µm would allow a five-time higher flow (2.2). Thus, the current spin-coating parameters and/or the viscosity of the dispersions will have to be adjusted. This step will of course require further investigations on the distribution of the nanoparticles in the polymer matrix when spin-coating or dispersion parameters are being changed from the current setup. Second, the porosity could be further enlarged by increasing the content of nanoparticles in the dispersion and therefore increasing the flow rate. The ability to embed higher amounts of nanoparticles in the PES solution and the creation and process ability of stable dispersions thereof should be investigated in a subsequent work.

2.4 Conclusions
The present work provides a simple and versatile alternative production process for the fabrication of polymeric ultrafiltration membranes. The use of soluble nanoparticles as pore templates allows broad process possibilities with the possibility to adapt pore size and, potentially, morphology. Separating the steps of polymer shaping (i.e. film preparation) and pore formation (leaching out of the nanoparticle pore template) may allow the design of more complex filter shapes, since the composite preform is amenable to conventional polymer processing. If roll coating is used to handle large area polymer films, the resulting beneficial cost structure of the resulting membranes may open these fascinating materials to new markets (off-site water purification) or enable low cost single-use operation in biotechnology and food manufacturing.
3. Nanoparticle Pore Template Manufactured Cellulose Acetate and Triethyl Citrate Modified PES Dialysis Membranes with Narrow Pore Size Distribution

Submitted for publication in parts as:

Christoph R. Kellenberger, Florian C. Pfleiderer, Renzo. A. Raso, Cornelia H. Burri, Christoph M. Schumacher, Robert N. Grass, Wendelin J. Stark
Abstract

In this study, unaltered and triethyl citrate (TEC) modified polyethersulfone (PES) membranes (30 wt % TEC) as well as membranes from cellulose acetate (CA) were produced using readily dissolvable nanoparticles as pore templates. These novel separators were implemented as dialysis membranes and characterized by means of buffer exchange rate, molecular weight cut-off (MWCO), protein adsorption, pore size distribution and water contact angle. The herein prepared membranes were further benchmarked against commercially available dialysis membranes with comparable average pore size. They showed narrow pore size distributions, fast dialysis rates at low protein adsorption and MWCOs of around 12 kDa. Interestingly, the PES TEC membranes displayed only moderate change in pore size distribution as a result of the plasticizer additive compared to pure PES membranes. This is a matter of substantial interest considering the fact that additive modifications of membranes produced by the predominant phase inversion process typically show alteration in morphology that lead to undesired changes in membrane performance. Furthermore, a dextran recovery test was introduced that meets the requirements for the specific dialysis membrane characterization and benchmarking.
3.1 Introduction

Porous polymeric membranes are of continuously growing importance in the field of filtration and dialysis. Ultrafiltration and microfiltration are commonly used for separation and purification of proteins and particles where the target is smaller than the contamination [2, 14, 156]. Dialysis on the other hand is applied, when the proteins and particles, that need to be purified, are larger than the contamination of the sample [127, 177-179]. Compared to filtration, dialysis is a pressureless, diffusion driven process. The membrane separates two liquid solutions with different protein or salt concentrations. The molecules then diffuse through the membrane following the concentration gradient as described by Fick’s law:

\[ J = -D \frac{d\varphi}{dx} \]  

(3.1)

with flux J, diffusion coefficient D and dimensional concentration gradient described by \( \frac{d\varphi}{dx} \). Diffusion coefficient D can be described by the following relation

\[ D = \frac{k_B T}{6\pi \eta R} \]  

(3.2)

with Boltzmann constant (\( k_B \)), Temperature (T), dynamic viscosity (\( \eta \)) and hydrodynamic radius (R). Thus, we get

\[ J = -\frac{k_B T}{6\pi \eta R} \frac{d\varphi}{dx} \]  

(3.3)

The difference in flux - as a result of the different hydrodynamic radius of the molecules - and the pore size of the membrane can therefore be used to separate larger from smaller molecules. Such membranes are currently being produced by the phase inversion process [40, 42, 45, 64, 157-158]. Low selectivity due to broad pore size distribution of these membranes has frequently been reported [6, 120, 155]. Research on this type of membrane has mainly focussed on chemical functionalization [131, 180-181] or addition of particles [132, 182-183] to increase hydrophilicity. However, phase inversion is complicated by the numerous parameters that have to be precisely controlled during production. Therefore, surface
modification and functionalization often leads to undesired structure changes and degradation in membrane performance [183-185].

Recently, we presented a novel type of polymeric membrane production based on the nanoparticle template removal method [104, 106, 120, 186]. This method uses a dense, interconnected nanoparticle structure as pore forming template in a polymer matrix. Later dissolution of the template leads to the formation of a nanoporous polymer. This process proved to be very versatile and was recently applied on different polymers [20, 105], showed to be functionalizable by addition of nanoparticles [16] and demonstrated the opportunity to obtain membranes with high ionic conductivity for use as battery separators [105]. Recently, we demonstrated the first large scale production of this new membrane type for use as water filters in the production of safe drinking water [119]. Unfortunately, water flux was rather low due to the bad wettability of the PES membrane surface.

In this work, we report on the modification of pure PES membranes by use of a plasticizer and on the application of CA as membrane polymer targeting the formation of hydrophilic, self-wetting dialysis membranes. Both, PES and CA are well known polymers for membrane production, especially for the phase inversion based processes [38, 187-188]. PES was altered by addition of 30 wt% of TEC. Environmentally friendly TEC [189] successfully decreased the water contact angle of PES by more than 3 ° and turned the PES more water-wettable without any drastic change in membrane morphology and performance. CA was for the first time used as membrane polymer using nanoparticles as pore templates and showed faster dialysis rates than comparable commercial membranes. All tested membranes were fully characterized regarding dialysis rate, protein adsorption properties, pore size distribution, water contact angle and MWCO. MWCO’s of ultrafiltration membranes are generally determined by the so-called dextran rejection profile test [169]. This membrane characterization method is widely accepted among membranologists [154, 170, 190]. However, even though ultrafiltration and dialysis membranes are basically the same from a morphological point of view, the separation processes of filtration and dialysis are completely different. Equation (3.3) describes the size dependance of the diffusion process. In a typical dialysis step, a biomolecule (10 nm-100 nm) is separated from a highly concentrated salt solution (monovalent cations, appr. 0.6 – 0.8 nm). This difference in size leads to a flux ratio of 10 to 150 in favor of the salt molecules. Therefore, pore size may be the determining factor in filtration. However, separation processes in dialysis are much more flux dependent than pore size dependent. Hence, dialysis membranes should not be characterized by a filtration test. This is why we
here propose a simple dextran recovery test. A dextran standard (12 kDa) was used to challenge the membranes as direct dialysis solution, instead as permeate in a filtration experiment. The solutions were then analyzed using gel permeation chromatography (GPC).

3.2 Experimental

3.2.1 Nanoparticle-polymer dispersions

The herein applied nanoparticle dispersions were prepared as described in detail earlier [119-120]. The PES (Veradel A-201, Dolder AG, Switzerland) and the CA (CA-398-6, Eastman, USA) dispersions were prepared as follows: 10 g of polymer were dissolved in 90 g of N,N-dimethylacetamide (DMAc, ABCR Chemicals, Germany) by stirring overnight. Then, 15 g of calcium carbonate nanoparticles were added (CaCO₃, American Elements, USA) and mixed to reach a particle-polymer ratio of 1.5. The average particle diameter and particle size distribution was determined by SEM. More than 400 particles were counted optically using scanning electron microscopy (SEM, FEI NovaNanoSEM450). This mixture was then shaken vigorously and sonicated for 1 minute at 400 W using an ultrasonic finger (Hielscher UP400s, Germany) to generate a stable dispersion. The PES TEC dispersion was prepared similarly, except that 3 g of TEC was added before the sonication step. Dispersions were applied to form membranes within 48 h after preparation to prevent the formation of particle agglomerates.

3.2.2 Membrane preparation

The membranes with approximate dimensions of 10 x 20 cm were produced using a doctor knife. Therefore, roughly 5 mL of the above described dispersion was cast onto a glass substrate. The solvent was subsequently evaporated in a circulating air oven at 80 °C for 10 minutes. Then the polymer-particle composite was given into a bath of 1 M HCl for 1 minute to remove the particle template. The membranes were then washed thoroughly under deionized water and dried on air. Commercial dialysis membranes with similar or slightly larger pore size for comparison were purchased from Millipore and Spectrum laboratories (Millipore V50 and Spectrum Spectra/Por 1000 kDa). These commercial membranes were chosen for comparison since they show the largest average pore size offered by these providers and therefore guarantee the fastest dialysis rate.
3.2.3 Membrane morphology and contact angle measurement

The morphology of the membranes was analyzed using SEM to determine the pore size distribution. At least 400 pores per membrane were optically evaluated (using commercially available imaging software). Hydrophilicity of the membranes was tested by determining the water contact angle of flat, non-porous polymer surfaces prepared from CA, PES and PES TEC. 150 μL of deionized water were carefully pipetted onto the polymer surfaces that were previously cast on glass slides. Photographs were taken and contact angle was measured optically. The average of 4 replicates (angles measured on both sides of the drop) and the corresponding standard error are displayed in Figure 3.2.

3.2.4 Preparation of dialysis devices

Membrane pieces of each membrane type were glued onto one side of an acrylonitrile butadiene styrene (ABS) ring produced by rapid prototyping (Stratasys UPrint SE Plus). The ring had an outer diameter of 30 mm, an inner diameter of 15 mm and a height of 9 mm giving a volume of 1.6 mL and a dialysis surface area of 1.76 cm². This device was capable of floating on the dialysate (e.g. deionized water) surface while the ring acted as a reservoir for the dialysis solution. The integrated membrane separated the solution from the dialysate.

3.2.5 Buffer exchange

The herein prepared membranes were tested in a buffer exchange experiment and benchmarked against the two commercially available dialysis membranes. The membranes were used dry, except the PES membrane in one experiment was wetted in ethanol prior to use to guarantee wetting (PES EtOH). The commercial membranes were pretreated according to the manufacturer’s requirements prior to use. The spectrum membrane was soaked in de-ionized water for 30 minutes to remove glycerol and then rinsed thoroughly in de-ionized water, the Millipore membrane was used as received. 1 mL of 1 M potassium permanganate (KMnO₄) was pipetted into the above described dialysis rings that were previously put onto the surface of 1 L of 1 M phosphate buffered saline (PBS). 50 μL of potassium permanganate solution were pipetted out of the dialysis ring every ten minutes over a period of 110 minutes. These samples were then diluted in 1 mL of deionized water and further analyzed spectroscopically (Tecan infinite F200, Switzerland) to determine the rate of buffer exchange for each membrane type. Furthermore, pictures of the dialysis progress were taken from every membrane after 10 s and 1 min of dialysis to optically determine wettability and rate of dialysis.
3.2.6 Dextran recovery test for dialysis membranes

The sample recovery of the membranes was investigated by applying a dextran test formerly known from the characterization of ultrafiltration membranes [154, 169-170]. Commercially available dextran standard molecules (Fluka Analytical, Switzerland) with a weight of 12 kDa were applied. The dextran concentration was 1.0 g L⁻¹ in 1M aqueous NaNO₃. 1 mL of dextran solution was pipetted onto the different types of membranes (dialysis rings) and dialyzed against 1 L of deionized water over a period of 110 minutes. After this period, the solution was pipetted out of the dialysis ring and compared to the original dextran standard using gel permeation chromatography (GPC). Two PSS (Suprema 100 and Suprema 10000, 2x8x300 mm) GPC columns were therefore connected in series and calibrated against the 12 kDa dextran standard. For analysis, a Hitachi L-7000 HPLC system was applied, equipped with an isocratic pump and RI detector, operated at 25 °C with 0.1 M aqueous NaNO₃ as mobile phase at 0.5 mL min⁻¹. Dextran recovery curves were obtained from the GPC data following well-known procedures [154, 169-170]. The GPC curve of the dialyzed solution was compared to the GPC curve of the starting dextran standard used to challenge the membranes. The characteristic rejection of the tested membranes was calculated as the ratio of dextran molecule concentration in the dialyzed solution to dextran molecule concentration in the starting solution.

3.2.7 Protein adsorption

Protein adsorption to the dialysis membrane surface possibly leads to unwanted loss of the purified target protein. Therefore, the amount of protein adsorption to the membrane during a typical dialysis period is a crucial element of the overall membrane performance. The herein applied membranes were tested for protein adsorption. A solution containing 1 g L⁻¹ bovine serum albumin (BSA, Sigma Aldrich, USA) was used as model protein. 1 mL of the BSA solution was pipetted onto the membrane surface of the above described dialysis ring. After a time period of 110 minutes the solution was pipetted out and compared to the original BSA solution. BSA concentration was determined using high performance liquid chromatography (HPLC, Agilent 1100 series). The applied column was a Zorbax Eclipse 4.6 x 150 mm run at 40 °C, with a flux of 0.75 mL / min and injection volume of 5 μL. All experiments were carried out in duplicate. Average values are given and normalized to μg of BSA cm⁻².
3.3 Results and Discussion

3.3.1 Membrane morphology and water contact angle

The size distribution of the applied CaCO$_3$ nanoparticles and the pore size distribution of the herein prepared and commercially available membranes were evaluated in Figure 3.1. The PES membrane shows the smallest average pore size (30 nm) and the most narrow pore size distribution of all tested membranes. The addition of TEC to the PES membrane resulted in a moderate increase of the average pore size (39 nm). However, the pore size distribution remained narrow. The CA membrane shows an average pore size of 48 nm, whereas the Millipore V50 membrane exhibits an average pore size of 73 nm and the Spectrum Labs membrane 57 nm, respectively. Figure 3.1 clearly depicts that the pore size distribution is generally narrower for membranes prepared by nanoparticle pore templating than for the commercial membranes produced by ordinary phase inversion. The correlation between pore templating particles and the resulting membrane morphology has been discussed earlier [120]. Narrow pore size distribution of the herein prepared membranes can be explained by a lack of agglomerates in the applied dispersion. The size distribution of the pores was only slightly larger than the size distribution of the templating nanoparticles. This underlines the significance of the availability of templating particles that combine exceptional dispersability with narrow size distribution. As can be seen from Figure 3.1a, b, c and d, the pore morphology seems to be depending on the affinity of the polymer to the template as well. CA tends to form more spherically shaped pores, whereas the PES derived membrane pores seem more angular similar to the shape of the templating particles. Good templating properties of the CaCO$_3$ – PES system has also been reported earlier [120]. Addition of the TEC plasticizer to the PES membrane resulted in a slight shift of the pore size distribution towards larger pores. However, the overall pore size distribution did not seem to broaden significantly and the angular character of the pores remained.
Figure 3.1: Particle size distribution a) and membrane morphology for b) PES membrane, c) PES TEC membrane, d) CA membrane, e) Millipore V50 and f) Spectrum Labs 1000 kDa membrane. The black curve indicates a log normal distribution.
Figure 3.2 displays the water contact angles of the non-porous CA, PES and PES TEC flat polymer surfaces. The addition of TEC to the PES membrane led to a decrease of the contact angle by 3 ° compared to untreated PES (six times larger than standard error). CA polymer surface showed the lowest water contact angle of all three surfaces.

![Figure 3.2](image)

**Figure 3.2:** Membrane contact angle measurements for a) PES surface, b) PES TEC surface, c) CA surface. Standard error is given for each measurement.

### 3.3.2 Buffer exchange rate and wettability

The buffer exchange rates were analyzed over a time period of 110 min. As becomes apparent in Figure 3.3, the untreated PES membrane shows a very slow dialysis rate. After 110 min., only 50% buffer exchange was achieved. This can be directly ascribed to the low wettability of PES. If pretreated in ethanol (PES EtOH) or modified by TEC (PES TEC), the rate of buffer exchange increased drastically.

![Figure 3.3](image)

**Figure 3.3:** Buffer exchange rate (1 M KMnO₄ vs. 1 M PBS) for different types of membranes. The grey line depicts 90% of buffer exchanged.
Only the CA, PES TEC and Millipore V50 membrane achieve over 90% buffer exchange within the given time period. This proves that TEC modified PES and CA are well suited membrane materials. However, the ethanol wetted PES membrane and the Spectrum membrane achieved only slightly lower dialysis rates. Figure 3.4 a, b, c display the generally weak wettability of modified and unmodified PES membranes whereas CA, Millipore V50 and Spectrum membranes were readily wetted and buffer exchange started within only 10 s (see Figure 3.4 d, e, f).

**Figure 3.4:** Buffer exchange rate (1 M KMnO$_4$ vs. 1 M PBS) for different types of membranes after ten seconds (left) and 60 seconds (right). (a) PES, (b) ethanol pretreated PES and (c) TEC modified PES membranes show slow wettability, whereas (d) CA, (e) Millipore V50 and (f) Spectrum membranes are readily wettable.
3.3.3 Membrane sample recovery and protein adsorption

Besides a fast dialysis rate, sample recovery and protein adsorption are key factors concerning the performance of dialysis membranes. Protein or antibody sample recovery should be as high as possible to prevent loss of precious target molecules. Hence, undesired protein adsorption to the membrane surface due to affinity or hydrophobic interactions should be as low as possible. Evaluation of sample recovery of the applied membranes was performed by implementing a variation of the well-known dextran rejection profile test [169]. Here, the dextran standard molecule was not filtered through the membranes but used as model compound in the dialysis solution. Since dialysis is basically a pressureless process, this variation simulates membrane sample recovery more accurately. The results of the sample recovery for each of the tested membranes are summarized in Table 3.1.

The sample recovery of the 12 kDa dextran standard molecule was about 90 % for all the tested membranes. This is in good agreement with the generally similar average pore sizes and diffusion rates through these membranes. CA (88 %), PES (89 %) and PES TEC (91 %) were very close to one another. The Spectrum membrane showed the highest sample recovery of 98 %. This might be attributed to its slightly slower dialysis rate (Figure 3.3) and generally low protein adsorption properties as is presented later. The V50 membrane from Millipore seemed to show opposite effects. The low sample recovery of 85 % may have been caused by the interaction of a fast dialysis rate (Figure 3.3) with adsorptive properties of the nitrocellulose membrane material. The ethanol pretreated PES membrane had a lower dextran recovery than the PES TEC membrane. This may be ascribed to hydrophobic interactions that may have arisen after the wetting effect of ethanol. A model protein adsorption (by BSA) showed little to no protein adsorption (within error range) for all of the tested membranes. Only the Millipore V50 showed a low protein adsorption value of 80 μg cm⁻². A summary of the overall performance of the herein tested membranes is given in Table 3.1.
Table 3.1

Detailed parameters of each membrane.

<table>
<thead>
<tr>
<th>membrane</th>
<th>buffer exchange after 110 min</th>
<th>12 kDA dextran recovery</th>
<th>BSA adsorption [μg cm⁻²]</th>
<th>average pore diameter</th>
<th>water contact angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>PES</td>
<td>51%</td>
<td>n.a.</td>
<td>0</td>
<td>30 nm</td>
<td>74 °</td>
</tr>
<tr>
<td>PES EtOH</td>
<td>86%</td>
<td>89 %</td>
<td>n.a.</td>
<td>30 nm</td>
<td>n.a.</td>
</tr>
<tr>
<td>PES TEC</td>
<td>92%</td>
<td>91 %</td>
<td>0</td>
<td>39 nm</td>
<td>71 °</td>
</tr>
<tr>
<td>CA</td>
<td>99%</td>
<td>88 %</td>
<td>0</td>
<td>48 nm</td>
<td>59 °</td>
</tr>
<tr>
<td>Millipore V50</td>
<td>97%</td>
<td>85 %</td>
<td>85</td>
<td>73 nm</td>
<td>n.a.</td>
</tr>
<tr>
<td>Spectrum 1000</td>
<td>88%</td>
<td>98 %</td>
<td>0</td>
<td>57 nm</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

3.4 Conclusions

Following the nanoparticle template removal method, CA was implemented as a membrane polymer and showed superior buffer exchange rates. For comparison a PES membrane was altered by the addition of a citrate plasticizer. The addition of 30 wt % of TEC reduced the water contact angle by more than 3 °. This improved wettability and turned the PES TEC membrane into a readily self-wetting dialysis membrane. Besides, this chemical modification only led to slight changes in the membrane morphology. Therefore, formerly reported undesired structure changes by additive modifications of membranes produced by the phase inversion process could be overcome by nanoparticle pore templating. This might be of fundamental interest for the filtration community. Rendering filtration membranes hydrophilic at unchanged performance by the addition of environmentally friendly TEC could be used to address membrane fouling issues more efficiently in the future. To our knowledge, the self-wetting and hydrophilizing effect of TEC is presented here for the first time. Additionally, the here presented membranes show narrower pore size distributions than commercial membranes produced by phase inversion. In principle, the uniformity of the pores is mostly dependent on the particle size distribution and could be significantly increased if appropriate particles would be used as templates. Furthermore, a variation of the generally accepted dextran rejection test was applied on the herein prepared membranes and on two commercially available membranes. This dextran recovery test proofed to meet the circumstances of the specific dialysis separation process and might therefore become a valid future tool for dialysis membrane characterization.
4. Roll-to-Roll Preparation of Mesoporous Membranes by Nanoparticle Template Removal

Published in parts as:

Christoph R. Kellenberger, Samuel C. Hess, Christoph M. Schumacher, Michael Loepfe, Jeremy E. Nussbaumer, Robert N. Grass, and Wendelin J. Stark

**Abstract**

Mechanistic and kinetic insights into the removal of soluble nanoparticles as templates for meso-pores now permit scale-up of mesoporous polymer membranes. Investigations on the effect of pH and nanoparticle dissolution time showed that pH levels of 0 or 1 are necessary to enable fast pore template dissolution. Approximately 5 % wt of the originally applied nanoparticles remained in the membrane due to complete encapsulation by the polymer matrix but did not contaminate the permeate during prolonged use. We demonstrated continuous production of 17 m² (100 m length) of membrane using a commercial roll-to-roll coating unit. These membranes were successfully applied in gravitation driven water filtration. The rates of rejection of bacteria from heavily contaminated natural pond water were higher than 99.99 %.
4.1 Introduction

Mesoporous membranes are widely used in biotechnology, the pharmaceutical sector and in the production of safe drinking water [11, 14, 155-156]. The market for such membranes is constantly growing and worth billions of dollars per year [191]. However, their high manufacturing costs currently prohibit broad use in developing countries [192]. Current commercial nanofilters are not produced by actual nanotechnology, but by a process called phase inversion that was developed in the 1970’s [40, 158, 193]. This technology has meanwhile reached its limits and presents weaknesses, such as difficult pore size tuning and low selectivity [6, 8, 42, 44]. Recently, new approaches based on the self-assembly of block copolymers [99, 130, 194] or on the basis of microfabrication [9, 108, 195] were suggested. These methods result in membranes with promising properties. But, so far these techniques lack an up-scale to required sizes [89, 196-197]. The use of inorganic hard templates or molecular imprinting and further polymerization around the template led to the formation of true meso- and microporous structures [104, 106, 186]. In this work, we report on the continuous production of mesoporous membranes using the nanoparticle template removal (nanoPTR) method [20, 120, 198]. This procedure is similar to the hard templating method but uses commodity scale inorganic nanoparticles as template in a dissolved polymer without polymerization step. A systematic investigation of the particle template removal mechanism provides fundamental insights into this novel and promising membrane production process. Industrial processing of these membranes was for the first time achieved by using low cost roll-to-roll coating equipment. A total of 17 m² of membrane area with a thickness of 2.5 μm was produced within 2 hours of production. The membrane with an average pore size of 39 nm [120] was able to remove more than 99.99 % of bacteria and has shown to enable preparation of safe and sterile drinking water.

We previously used nanoparticles as pore templates to synthesize polymeric ultrafiltration membranes with tunable pore sizes [120]. The fabrication process is shown schematically in Figure 4.1. This technique offers potential to be up-scaled to an industrial level. Thus, their application as low cost filters for the production of safe and sterile drinking water will become possible.
**Figure 4.1.** Use of soluble nanoparticles as templates for meso-pores. A limestone (CaCO₃) nanoparticle-polymer dispersion is first roll coated and then heated to evaporate the solvent providing a composite film. An acid treatment allows dissolution of the limestone particles and generates an interconnected and freestanding mesoporous structure.

With regard to manufacturing speed and safety the crucial step towards mastering large area membrane fabrication is the removal of the particle template from the polymer matrix and the evaluation of a suitable continuous processing unit. So far, no investigations on the influence of time and pH on the removal of the particle template are available. Besides, the need of strong acids to remove the template has recently risen questions in terms of polymer stability [199]. The scope of this work was to gain a more fundamental understanding of this removal process. In a second step, these findings were directly adopted in the large scale production of mesoporous membranes. The membrane was then tested as sterile filter in the production of drinking water.

### 4.2 Experimental

#### 4.2.1 Nanoparticle – polymer dispersion

A mixture of 15 % wt of polyethersulfone (PES, Veradel A 201, Dolder AG, Switzerland) in dimethylacetamide (DMAC, Puriss, Aldrich) was prepared by stirring overnight. In a second step, the CaCO₃ nanoparticles (American Elements, 97.5 %, USA) were added using a weight ratio of (nanoparticle/polymer mass ratio) of 1.5. We therefore added 135 g of CaCO₃ nanoparticles to 600 g of 15 % wt of PES solution. The mixture was then shaken vigorously. We further used an ultrasonic finger (Hielscher UP400s, Germany) for dispersing the nanoparticles. The mixture was sonicated 10 times at 400 W for 10 minutes. The sonication steps were alternated by shaking.
4.2.2 Lab scale membrane samples

The membranes used for investigating the pH effect and template removal mechanism were produced on the lab scale using a doctor knife. Therefore, approximately 10 ml of the above described dispersion was cast onto a glass substrate and subsequently given into a circulating air oven at 100 °C to let the solvent evaporate. Then the polymer-particle composite was put into a bath of deionized water to remove the film from the substrate and finally dried on air.

4.2.3 pH effect and template removal mechanism

The CaCO₃ template is dissolved by hydrochloric acid in the following reaction:

\[
\text{CaCO}_3(s) + 2H^+(aq) + 2Cl^-(aq) \rightarrow \text{Ca}^{2+}(aq) + 2Cl^-(aq) + \text{H}_2\text{O}(aq) + \text{CO}_2(g) \quad (4.1)
\]

First, we analyzed the dissolution behavior of the CaCO₃ template at different pH levels whereas time was held constant. 0.1 M buffered acid solutions were prepared for pH levels of pH 1 to 6. Compositions of these buffered acid solutions can be found in the Supporting Information. Membrane pieces with undissolved template were weighed (sample size around 10 mg) and immersed in the different pH solutions (10 ml) for 1 minute. The membranes were then taken out of the acid solution and immediately rinsed with deionized water. Subsequently, the membranes were put into separate containers with 10 ml of 1 M HCl for 12 hours to dissolve residual particles. These solutions were then analyzed for Ca content using inductively coupled plasma optical emission spectroscopy (ICP OES, Horiba Ultra 2). In a second experiment, the time dependence of the template dissolution at a constant pH 0 was tested. In order to distinguish whether the dissolution of the template at different pH levels is diffusion driven or mainly limited by the surface dissolution reaction rate, more investigations were carried out. Pills (radius 6 mm, height 1.63 mm) pressed from CaCO₃ nanopowder (approx. 0.25 g, American Elements, 97.5 %, USA) were immersed into 150 ml of buffered pH 1 and pH 3 solution (described in Supporting Information). The dissolution of the compressed nanopowder pills was then analyzed gravimetrically up to 12 h.

The diffusion coefficient for the 1-1 electrolyte HCl in water can be calculated as follows [200]:

\[
D_{\text{HCl}} = \frac{2}{\frac{1}{D_{\text{H}^+}} + \frac{1}{D_{\text{Cl}^-}}} = 3.3 \times 10^{-9} \text{ m}^2 \text{ s}^{-1} \quad (4.2)
\]
with a diffusion coefficient of $\text{H}^+$ ($9.31 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) and $\text{Cl}^-$ ($2.03 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) in water at 25 °C [200]. The mathematical model for the diffusion of HCl into the membrane was applied on analogous principles to heat transfer constrained by Dirichlet boundaries [201-202].

$$\frac{c - c_d}{c_o - c_d} = 4 \sum_{n=0}^{\infty} \frac{(-1)^n}{(2n+1)} \exp\left(-\left(\frac{\pi}{2}\right)^2 \left(2n + 1\right)^2 \frac{D_{\text{HCl}} t}{d^2}\right) \cos\left(\frac{\pi}{2} \left(2n + 1\right) \frac{x}{d}\right)$$  \hspace{1cm} (4.3)

With $c$ molar concentration as a function of time $t$ and location $x$, $c_o$ concentration at the membrane HCl solution boundary, $c_d$ molar concentration in the membrane at the beginning and membrane half-thickness $d$. This mathematical model was implemented using MATLAB (Mathworks Inc., software). Additionally, membranes obtained from the dissolution of the template in a 1 M HCl solution (pH 0) for 1 minute were used to filter 10 ml of deionized water at a pressure of 1 bar and analyzed for traces of CaCO₃ in the permeate using ICP OES. All experiments were carried out in triplicate. The intermediate stages during pure templating particle dissolution were analyzed by recording scanning electron microscopy (SEM, FEI NovaNanoSEM450) cross sections images of membranes treated at pH 0, pH 3 and pH 7 for 1 minute.

4.2.4 Roll-to-roll coating

The previously described nanoparticle-polymer dispersion was applied on a pilot scale foil processor. As support material for roll coating, a roll of high density polyethylene (HDPE) foil with a width of 0.17 m and a length of 100 m was chosen. The pilot-scale foil processor was kindly provided by Perlen Converting AG (Switzerland). The dispersion was continuously coated onto the HDPE foil at a line speed of 3 m / min and the solvent was subsequently evaporated in a hot air stream at 140°C. The thickness of the coating was adjusted to achieve a final thickness of the dry membrane of 2.5 µm. This final thickness can be varied by adjusting the gap between the rubber rolls of the coating unit. After drying the coated HDPE foil was rolled up again at the end of the line. The foil was then further processed in our laboratories. The roll was first cut into six pieces of equal length for storing. Then, the particles were etched in 1 M HCl for 1 minute and the membranes were lifted off from the HDPE support foil, washed in deionized water and dried on air. To prove the integrity of the production process, membrane pieces used in experiments were taken from all six rolls over their whole length. The emission of DMAC into the environment due to evaporation was calculated assuming complete evaporation of the solvent during production (details are presented in the Supporting Information). DMAC vapor stream was removed in an
air stream at a rate of 400 m$^3$ h$^{-1}$. Commercial membranes for comparison were purchased from Macherey-Nagel GmbH & Co. KG, Germany (Chromafil Xtra PES-20/25 0.2 µm).

4.2.5 Gravity driven filtration setup and 24 h operation

A square sheet of membrane with approximately 40 mm side length was first glued to the thread end of a plastic centrifuge tube with a diameter of 28 mm which accords to a filtration area of 6.16 cm$^2$ (Techno Plastic Products AG, Switzerland). The closed end of the tube was previously cut away. In order to mechanically support the membrane, a nonwoven (pore size 4 µm, kindly sponsored by Freudenberg Filtration Technologies KG, Germany) and a metallic grid were placed between our membrane and the perforated cap that was screwed back on the tube. Supporting Figure S1 shows a detailed picture of this filtration setup. In order to prove the functional efficiency of our membrane to work in a gravitation driven filtration device (no pump needed), the free end of the tube was glued into one end of a polyvinylchloride (PVC) hose. We used a 3.2 m long plastic hose with a diameter of 35 mm to establish a gravitational pressure of 0.3 bar. The hose was vertically installed and slowly filled with approximately 2 l of pond water. This pond water was taken from a pond located at the ETH Science City campus (ETH Zurich, 8093 Zurich, Switzerland, GPS: 47.409429,8.507696). The permeate was then collected in a glass beaker to analyze the flow rate gravimetrically. More detailed measurements on the long term application of the herein applied filter were also carried out. A 50 cm$^2$ filter was applied in a stainless steel filter housing and connected to a 5 l vessel filled with the described pond water. A pressure of 0.3 bar was established to simulate the pressure of the gravity driven filtration setup and the flow was measured over a period of 24 h by means of a flow meter (Sensirion SLQ-QT 500, CH).

4.2.6 Flow cytometric absolute cell counting

To characterize the membrane’s grade of bacteria impermeability, the filtration experiment was additionally performed under sterile conditions. Therefore, the membrane was again installed in the filter-tube described above. Instead of connecting it to a water hose, the filter setup was connected with a tube to N$_2$ pressure. Approximately 10 ml of pond water was pipetted into the filter tube. The filter tube was then connected to N$_2$ pressure of 1 bar equivalent to a 10 m water column. 1 ml of permeate was then collected in a sterile plastic tube for later analysis. All experiments were carried out in a flow hood. The effectiveness of bacteria removal was analyzed using flow cytometry (FCM). Staining for intact cell counts and FCM were carried out as follows. For a working solution, SYBR Green I (SG)
(Invitrogen AG, Basel, Switzerland) was diluted in anhydrous dimethyl sulfoxide (DMSO) at a ratio of 1:1000. This stock solution was stored at 20°C until use. 1 ml of filtered water was stained with 10 μl of SG and incubated in the dark for at least 15 min at 37 °C before measurement. FCM was performed using a BD Accuri C6 flow cytometer (BD Biosciences, San Jose, California, USA).

4.3 Results and Discussion

4.3.1 pH effect and template removal mechanism

As can be seen in Figure 4.2a, only the use of low pH levels allowed a satisfying removal of the inorganic pore template within a short time period of 1 minute. pH values of 3 and higher led to a delayed dissolution. In a separate experiment, the pH was held constant at 0 during 1 minute and for up to 12 hours. Figure 4.2b shows low differences in template dissolution during the first 60 minutes. However, embedding the polymer-particle composite sheets overnight (12 hours) even dissolved otherwise well protected CaCO₃ particles. Supporting Figure S2 shows the modeled HCl concentration in a membrane as a function of time (t) and place (x) neglecting the role of porosity and tortuosity and assuming an effective diffusion coefficient as in water. Diffusion into the membrane is very fast (within microseconds), confirming that the acid transport is not diffusion limited. Figure 4.2c on the other hand clearly shows that the dissolution rate of the CaCO₃ is strongly dependent on acidity. The pressed CaCO₃ pills were dissolved faster at pH 1 than at pH 3.
**Figure 4.2.** Effect of pH on CaCO₃ nanoparticle removal (1 minute, a). (b) shows the CaCO₃ content in the membrane at a constant pH 0 at different times. Different dissolution rates measured using a pill of compressed CaCO₃ nanoparticles at pH 1 and pH 3 in (c) demonstrate that the reaction rate depends on acidity.

The intermediate stages during particle template removal were also followed by SEM. Figure 4.3 shows different states of dissolution of the template. At pH 7, the membrane remains with most nanoparticle template after 1 minute of exposure. The membranes typically form smaller pores on the substrate side due to a reduced contact area of the template during film preparation. The air side (top side during film preparation) on the other hand forms larger pores. Supporting Figure S3 shows SEM pictures of air and substrate side illustrating this difference in pore size. At pH 3, the template particles are partially dissolved after 1 minute (41 % remaining). The particles closer to the original substrate side have dissolved slower than on the air side. This is in line with a reduced HCl mass flow through the smaller pores at the substrate side of the membrane. Therefore, the dissolution of the particle template is asymmetrical. Membrane samples treated at pH 0 for 1 minute showed almost full removal of the template particles (approx. 95 %). However, as illustrated schematically in Figure 4.3,
some isolated particles remain in the membrane if completely encapsulated and therefore without contact to the acid.

**Figure 4.3.** The mechanism of particle template removal is shown schematically (left) for different pH levels and experimentally (right). Scanning electron images of cross-sections of membranes show subsequent formation of pores and loss of the limestone (CaCO$_3$) nanoparticles.

Approximately 5% of the template particles are partially or even completely encapsulated by the polymer matrix and usually remained in the membranes. This encapsulation leads to a delayed dissolution and negatively affects fast and economic membrane production. A prolonged acid treatment is undesirable as it may affects the membrane morphology [199]. Obviously, short time acid treatments would be preferred. We thus investigated whether the encapsulated part of the template that results from short dissolution times may lead to contamination of the permeate during later use of the membrane. Supporting Figure S4 demonstrates that the purity of the permeate was not negatively affected by these residual
particles. The obtained permeate did not contain detectable quantities of \( \text{Ca}^{2+} \) which proved that the remaining undissolved part of the \( \text{CaCO}_3 \) template is rather inert and not released during use. Thus, prolonged acid treatments are not necessary.

### 4.3.2 Roll-to-roll coating

Seeking a simple and industrially established production process, we developed a method to fabricate the membranes on ordinary roll-to-roll foil processors. Foil processors are routinely used in industry to coat polymer foils with a functional surface or a different kind of polymer. Within two hours of production we fabricated 100 m of membrane foil with a width of 0.17 m yielding 17 m\(^2\) area. The amount of DMAC in the air stream used to carry away the solvent vapor was calculated to be 65 ppm (Supporting Table 2). The pore forming \( \text{CaCO}_3 \) templates were later dissolved in 1 M HCl solution for 1 minute according to the above described findings. Figure 3a shows a photography of the foil and in Figure 3b a SEM image of the mesoporous membrane is given.

![Figure 3a](image)

![Figure 3b](image)

**Figure 4.4.** Membrane roll produced by roll-to-roll coating (a) and SEM image the membrane surface morphology (b).
4.3.3 Drinking water production

The removal of bacteria is essential for the production of safe drinking water and for the sterilization of fluids for research and medical purposes. In recent years doubt emerged concerning the established grading system for sterile filters. This system is currently based on the filtration of *Brevundimonas diminuta* [19]. Several studies have shown that bacteria from marine water, sewage water, fresh water and even drinking water can still pass through sterile filters due to their shape and flexibility [12, 19]. A different test species (*Hylemonella*) was even suggested as alternative sterile filter testing organism [121]. We thus decided to use heavily contaminated water from a pond situated at the ETH campus (ETH, Science City, Switzerland) to test our membranes’ capability to remove bacteria and act as a sterile filter. This water had a bacterial contamination of over $5 \times 10^6$ cells per ml as measured by flow cytometry (Figure 4.5b). We implemented our membrane into a simple and inexpensive filtration setup without need for external energy supply. The same setup could be used in places that lack safe drinking water. The as prepared water hose was vertically fixed to the limb of a tree and filled with the previously described pond water to a height of 3.0 m thus creating a pressure of 0.3 bar. The experimental setup can be seen in Figure 4.5a and in Supporting Figure S1.
Figure 4.5. As a model for gravitational filtration a waterhose-filter setup was used at a hydrostatic pressure of 0.3 bar (a). The filtered pond water was collected and analyzed. Flow cytometry analysis of the untreated pond water is displayed in (b). Pure drinking water as a result of the filtration is displayed in (c). The framed area presents the demarcation from the background signal. Each point represents one bacteria.

As a result of the rather hydrophobic surface of the PES membrane, it took 15 minutes until the membrane was wetted and the first drop appeared. The permeate was then collected in a glass beaker to analyze the flow rate. After 10 hours, the permeate flux reached a rate of 0.037 ml / min which corresponds to a normalized flow of 120 l h⁻¹ m⁻² MPa⁻¹ (0.02 ml min⁻¹ cm⁻² bar⁻¹). Long term filtration over a period of 24 h using a filter area of 50 cm² showed a clear decrease in flow due to formation of a fouling layer (Figure 4.6, detailed statistics see Supporting Figure S5). However, the membrane remained operational and was capable of producing 0.445 l of drinking water. Such long term flux stabilization due to the formation of
a bio-fouling layer has been reported earlier [133, 203]. Hence, 225 cm$^2$ of membrane (approx. 15 x 15 cm$^2$) can generate about 2 l of safe drinking water per day.

![Image](image.png)

**Figure 4.6.** Flow rate analysis over a period of 24 h. Embedded SEM pictures show a highly porous membrane surface at the beginning of the filtration experiment. After 2.5 h a fouling layer formation can be seen and a dense fouling layer has formed after 24 h of filtration. The scale bar corresponds to 500 nm.

The here observed significant reduction in membrane thickness (for current phase inversion membranes about 100 μm; nanoPTR: 2.5 μm) is particularly relevant with regards to flow if considering the Hagen Poiseuille equation

$$V = \frac{\Delta \rho \phi^2 \Delta \rho}{32 \eta d}$$

(4.4)

with volume flow (V), membrane area (A), area porosity ($\phi$), pore size (s), differential pressure ($\Delta \rho$), viscosity ($\eta$) and membrane thickness (d). Experiments concerning the determination of the bacterial cell concentration in the pond water and the permeate were carried out in a laminar flow bench. Sterile conditions are essential to reliably determine the
bacterial retention of a filter. The permeate was compared to the original pond water using flow cytometry and showed 100 cells / ml whereas the original pond water contained $5 \times 10^6$ cells / ml corresponding to a reduction of the bacteria count $> 99.99 \%$ as depicted in Figure 4.5b and 4.5c. Regrowth of potentially harmful bacteria has recently been successfully suppressed by a lanthanum oxide functionalized membrane that has been produced by the template removal method [16]. Sterile filtration of liquids is most often performed using filters with pore sizes of 0.2 μm. Such sterile filtration is common practice and proposed by several microbiological textbooks [204-205]. However, recent publications have shown, that certain bacteria can still pass through these filters as described previously [12, 19, 121]. In order to compare our measurements to a typical 0.2 μm pore size filter, we additionally performed filtration of pond water with Chromafil Xtra PES-20/25 filter (pore size 0.2 μm, Macherey-Nagel GmbH & Co. KG, Germany). 98.77 % of bacteria were filtered out which is in accordance with previous reports by Wang et al 2007 [19]. The flux of deionized (DI) water through the Chromafil filter was 147’960 l h$^{-1}$ m$^{-2}$ MPa$^{-1}$ (24.66 ml min$^{-1}$ cm$^{-2}$ bar$^{-1}$) which is significantly higher to the measured DI water flux of 162 l h$^{-1}$ m$^{-2}$ MPa$^{-1}$ (0.027 ml min$^{-1}$ cm$^{-2}$ bar$^{-1}$) for the herein presented PES membrane. These drastic differences in bacteria rejection and water flux between these filters stand as a good example for given physical limits of filtration (4.4).

4.4 Conclusions

The herein presented findings lead to a more fundamental understanding of the particle template removal characteristics and enabled the production of large-scale mesoporous structures at low material cost (0.21 USD / m$^2$, see Supporting Table 1). This allows access to 2 l of safe drinking water at 0.48 US cents material cost per day if the filter is changed daily (labor not included). Formerly reported [89, 196-197] reproducibility and upscaling issues associated to other manufacturing techniques were overcome by nanoparticle template removal based production. Compared to phase inversion technique, which is the current industrial membrane manufacturing standard, here, the applied solvent is evaporated during production. This eliminates the need for a subsequent disposal of the precipitation bath. The solvent vapor that is carried away by the applied air flow can basically be incinerated or filtered to reduce release into the environment. However, DMAC is neither considered to be mutagenic nor carcinogenic and is even exempted from VOC (volatile organic compounds) taxes in Switzerland [206-207]. Therefore, this method provides a solid platform not only for
the production of safe drinking water in developing countries, but also shows great potential to generally advance membrane driven technologies such as gas and liquid filtration, protein purification and battery separators.
5. Conclusion and Outlook
In this work, a novel manufacturing process for porous polymeric membranes is presented as well as an overview on current membrane formation processes and applications. The membranes were produced by the particle template removal method. In a first step, detailed descriptions of the membrane formation process are given. This method appears to be very versatile. Not only can the pore size be easily and directly controlled by the size of the applied template particles. The membranes can also be modified by the addition of a plasticizer and the manufacturing process has been successfully upscaled to an industrial pilot scale. Continuous roll-to-roll coating allowed for the production of 17 m² of membrane. In a second step, the presented work also puts emphasis on membrane applications. The herein produced ultrafiltration membranes were characterized by dextran rejection profile tests and used as sterile filters according to the corresponding ASTM standard. Furthermore, comprehensive investigations on the use of self-wetting membranes for dialysis were conducted. The membranes produced by the particle template removal method performed well and have no reason to shun comparison with commercially established dialysis membranes.

The particle template removal has proven itself to be a flexible membrane manufacturing method. It can even be industrially produced and the cost structure basically resembles the predominant phase inversion process. However, a new technology can only replace an existing technology if it offers tremendous advantages. Otherwise, the technology will gradually disappear or merely remain as a niche technology. In the following section, an outlook for future research and investigation is given which aims to reach this new technology’s full potential.

5.1 Narrow pore size distribution

Ultrafiltration membranes produced by the template removal method display narrower pore size distribution than membranes fabricated by the immersion precipitation method. Even narrower pore size distributions can be expected in the future from commercially available particles of constantly increasing quality. Currently, membrane providers suggest using membranes with a MWCO half the size of the contaminant. This precautionary measure is at the cost of a fast and efficient separation. Membranes with better and more reliable selectivity will speed up biotechnological separation processes such as protein purification and concentration as well as virus filtration.
5.2 Functionalization and modification of membrane polymers

Phase inversion depends on numerous parameters which are difficult to control. The addition of additives, blending and chemical modifications of the existing membrane polymers thus remain limited. Therefore, the performance of current polymer membranes rest restricted to the performance of the applied polymer itself. However, increasing the wettability of filtration membranes could result in membranes with highly improved flux rates and better fouling properties. To date, most commercial ultrafiltration membranes are infiltrated with glycerol for better wetting, an additive that is quickly washed away. In the present study, we described a method to render PES membranes hydrophilic by the simple addition of a plasticizer. Although the added amount (30 % wt) was rather high, the change in pore size remained moderate and the overall pore size distribution was still very narrow. This can be attributed to the mainly physical pore size formation of the particle template removal process. This method therefore promises a multitude of options towards the modification and functionalization of membrane polymers. It will be essential to drive research in this area in order to create membranes with unparalleled flux and fouling properties or with enhanced mechanical strength. Functionalization or chemical modification could also lead to membranes with highly specific binding properties which are predestined for use in the demanding biotechnological separation processes.

5.3 New membrane materials

The herein presented work deals with common membrane polymers, such as PES and CA. The use of these polymers is ideal for implementation by phase inversion since the involved solvents allow good miscibility with water, which is the most common non-solvent for the necessary precipitation step. However, the particle template removal method is not constrained by any solvent – non-solvent miscibility. The process can essentially be applied on every kind of soluble polymer. Future investigations should therefore focus on the implementation of high performance polymers which, so far, could not be applied by current commercial membrane manufacturing techniques. Two types of requirements for future membrane materials clearly stand out: solvent resistance and temperature stability. To date, especially ultrafiltration membranes can only deal with aqueous solutions. Solvent stable membranes from high performance polymers such as polyether ether ketone (PEEK) or PVDF would open up a completely new field of ultrafiltration, such as solvent clarification or protein removal from antibiotics. On the other hand, completely stable organic solvent nanofiltration
membranes from PEEK could someday replace energy intensive distillation in the production of high purity solvents.

The energy storage sector urgently needs battery separators that can withstand high temperatures. The recent Boeing 787 grounding and reports about battery fires have harmed the reputation of Li-ion batteries. Therefore, battery separators from polyimide (PI), which are able to run at temperatures above 180 °C, could present a valid alternative to current separators made from PE, that shut down at a temperature of approximately 135 °C. All of the mentioned high performance polymers; PEEK, PVDF and PI, can be dissolved in the appropriate solvent or mix of solvents and are therefore basically applicable by the particle template removal method.

The field of porous polymeric membranes has been intensely researched and, in consequence, it has not only left its mark on a multitude of industries but is also of great importance to them. Nevertheless, as the outlook has shown, the potential of this field has not been completely reached which is why more research is needed in this area to grasp the full potential that it can provide.
Appendix: Supplementary Material
A.1 Supporting information to chapter 4

Buffered acid solutions

For the pH 1 solution 50 ml KCl was added to 134 ml HCl, for the pH 2 solution 100 ml KCl was added to 26 ml HCl, for the pH 3 solution 100 ml C₈H₅KO₄ was added to 44.6 ml HCl, for the pH 4 solution 200 ml C₈H₅KO₄ was added to 0.4 ml HCl, for the pH 5 solution 100 ml C₈H₅KO₄ was added to 45.2 ml NaOH and for the pH 6 solution 100 ml C₈H₅KO₄ was added to 90 ml NaOH. 1 M HCl was used as pH 0 solution.

Filtration setup

![Image of filtration setup]

**Figure S1.** Picture of the filtration setup. A flat piece of membrane is first glued to a plastic tube. A nonwoven and a metal grid form a mechanical support-intermediate before the sandwich structure is closed with a perforated screw cap.
Diffusion model

Figure S2. Modeled HCl concentrations in the membrane (a) as a function of place at different time intervals, (b) as a function of the time in the membrane center and (c) as a function of time and place.
NanoPTR membranes by roll-to-toll coating

Figure S3. Picture of membrane roll produced by roll-to-roll coating. The SEM pictures on the right show the bottom side of the membrane that faced the substrate during coating and evaporation (top right) and the other side of the membrane that has larger pores and higher surface roughness (bottom right).

NanoPTR membranes were applied using ordinary pilot scale roll-to-roll coating. The resulting membrane roll and the characteristic membrane pore morphology can be seen on supplementary Figure S3.
Residual CaCO$_3$ in permeate

**Figure S4.** ICP OES signal from permeate and background (1M HCl). The permeate signal is slightly below the background signal but lies within the error range.
24 hour flow rate analysis

Figure S5 depicts all the data collected during 24 h of filtration of pond water. The blue line depicts the original data measured every 5 s averaged over 10 minutes. The green line gives a Savitzky-Golay smoothening of these data points and the red line depicts a polynomial trendline to the original data.

![Graph depicting flow rate analysis](image)

**Figure S5.** original flow rate data (blue), smoothed data (green) and polynomial trend line (red).
Material Cost

The cost of 1 m² (thickness 4 µm) of membrane was calculated based on the prices we paid to the mentioned providers. A separate price was also calculated based on commodity scale prices that can be found online (e.g. www.alibaba.com). Energy cost was calculated on the basis of the evaporation enthalpy of DMAC and compared to current power costs in Switzerland (worst case 0.45 USD / kWh).

<table>
<thead>
<tr>
<th>material &amp; energy</th>
<th>amount needed</th>
<th>provider</th>
<th>cost [USD]</th>
<th>commodity scale cost [USD]</th>
</tr>
</thead>
<tbody>
<tr>
<td>membrane polymer (PES)</td>
<td>1.6 g</td>
<td>Dolder AG (Switzerland)</td>
<td>0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>CaCO₃ nanoparticles</td>
<td>2.4 g</td>
<td>American Elements (USA)</td>
<td>1.17</td>
<td>0.02</td>
</tr>
<tr>
<td>solvent (DMAC)</td>
<td>10.7 g</td>
<td>ABCR Chemicals (Germany)</td>
<td>0.31</td>
<td>0.02</td>
</tr>
<tr>
<td>support foil (HDPE)</td>
<td>50.0 g</td>
<td>Folietec AG (Germany)</td>
<td>0.14</td>
<td>0.14</td>
</tr>
<tr>
<td>energy</td>
<td>0.0015 kWh</td>
<td>Swiss power supply</td>
<td>0.0007</td>
<td>0.0007</td>
</tr>
<tr>
<td><strong>total cost per m²</strong></td>
<td></td>
<td></td>
<td><strong>1.74</strong></td>
<td><strong>0.21</strong></td>
</tr>
</tbody>
</table>

**Supporting Table 1:** material costs for lab and commodity scale.
VOC emission rate

Rates of DMAC as volatile organic compounds (VOC) emission were calculated using the data given in the table below.

<table>
<thead>
<tr>
<th>data</th>
<th>production rate</th>
<th>3</th>
<th>[m/min]</th>
</tr>
</thead>
<tbody>
<tr>
<td>foil width</td>
<td>0,17</td>
<td>[m]</td>
<td></td>
</tr>
<tr>
<td>area density foil</td>
<td>2,5</td>
<td>[g/m²]</td>
<td></td>
</tr>
<tr>
<td>annual production time</td>
<td>8000</td>
<td>[hr/yr]</td>
<td></td>
</tr>
<tr>
<td>mass rate</td>
<td>produced foil area</td>
<td>0,51</td>
<td>[m²/min]</td>
</tr>
<tr>
<td>mass rate</td>
<td>1,28</td>
<td>[g/min]</td>
<td></td>
</tr>
<tr>
<td>DMAC content</td>
<td>mass fraction polymer</td>
<td>40</td>
<td>[wt%]</td>
</tr>
<tr>
<td>polymer mass rate</td>
<td>0,51</td>
<td>[g/min]</td>
<td></td>
</tr>
<tr>
<td>whereas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mass fraction DMAC</td>
<td>85</td>
<td>[wt%]</td>
<td></td>
</tr>
<tr>
<td>DMAC mass rate</td>
<td>0,43</td>
<td>[g/min]</td>
<td></td>
</tr>
<tr>
<td>emission</td>
<td>exhauste mass rate</td>
<td>400</td>
<td>[kg/hr]</td>
</tr>
<tr>
<td>concentration DMAC</td>
<td>65,03</td>
<td>[ppm]</td>
<td></td>
</tr>
<tr>
<td>annual emsission</td>
<td>208</td>
<td>[kg/yr]</td>
<td></td>
</tr>
</tbody>
</table>

**Supporting Table 2:** calculated DMAC emission rates during membrane production.
References


12. Hahn, M. W. Broad diversity of viable bacteria in ‘sterile’ (0.2 μm) filtered water. Research in Microbiology 2004, 155 (8), 688-691.


116. Mobley, A.; Linder, S. K.; Braeuer, R.; Ellis, L. M.; Zwelling, L. A survey on data reproducibility in cancer research provides insights into our limited ability to translate findings from the laboratory to the clinic. *PloS one* **2013, 8** (5), e63221.


149. Ramakrishna, S.; Ma, Z.; Matsuura, T. *Polymer membranes in biotechnology: Preparation, functionalization and application*; World Scientific2011.


CURRICULUM VITAE

Christoph Ruedi Kellenberger

Functional Materials Laboratory
Institute for Chemical and Bioengineering
Department of Chemistry and Applied Biosciences
ETH Zurich, Vladimir-Prelog-Weg 1, HCI E113
8093 Zurich
Switzerland

Private Address:
Christoph Kellenberger
Geissbergweg 27
8006 Zurich
Switzerland

Phone: +41 44 633 27 40
Fax: +41 44 633 15 71
Email: christoph.kellenberger@chem.ethz.ch
Homepage: www.fml.ethz.ch

Born July 21th, 1983 in Zurich (ZH)
Citizen of Switzerland
Personal details
Date of birth  21.07.1983
Marital status  unmarried

Work experience
February 2013 - now  Co-Founder & CEO Novamem LLC
September 2010 - now  ETH Zurich, PhD student
November 2006 – March 2007  Phonak Hearing Systems Stäfa, internship
September 2004 – October 2004  ABB Turbosystems Baden, internship
October 2002 – January 2003  BBVA Privanza Bank SA Zürich, back office

Education
October 2003 – June 2010  Mechanical Engineering, ETH Zürich (Master of Science in Micro- and Nanosystems)

Awards
Alan Cussens Memorial Award 2011, European Aerosol Conference 2011, Manchester UK

Languages
German  • Native speaker
English  • Fluent
  • Five months language stay in Vancouver, BC, CAN
  • First Certificate in English (FCE)
French  • Business fluent

Hobbies
• Tournament director and vice president of a tennis club
• Golf, tennis, soccer
• Cooking
Refereed journal articles


Patents


Conference presentations and proceedings


Ch. R. Kellenberger, N. A. Luechinger, W. J. Stark, Fast and reproducible fabrication of polymer ultrafiltration membranes using nanoparticles as pore-forming template, 6th MRC Graduate Symposium, ETH Zurich, June 8, 2011.
**Student and assistant supervision**

Mario Stucki (master thesis 2013) - Nanoporous membranes for sustainable breathable fabrics  
- Now PhD student at FML / ETHZ

Samuel Hess (civilian services 2013) - PES membranes for virus filtration  
- Now PhD student at FML / ETHZ

Michael Loepfe (research project 2012) - Efficient filtration membrane integrity test protocol using size specific fluorescent nanoparticles  
- Now PhD student at FML / ETHZ

Jeremy Nussbaumer (civilian services 2013-now) - Hydrophilic PES membrane for drinking water production

Florian Pfleiderer (research assistant 2012-now) - Microporous membranes

Julien Kohler (research assistant 2012) - Cross-flow dialysis devices

**Courses and Laboratories**

Chemistry, ETHZ 529-0010-00L, administrative deputy of Prof. Stark, 2012-2013

Chemical Engineering Laboratory I, ETHZ 529-0639-01L, Teaching Assistant, 2012.

Laboratory Course: Elementary Chemical Techniques, ETHZ 529-0030-00L, Assistant 2011