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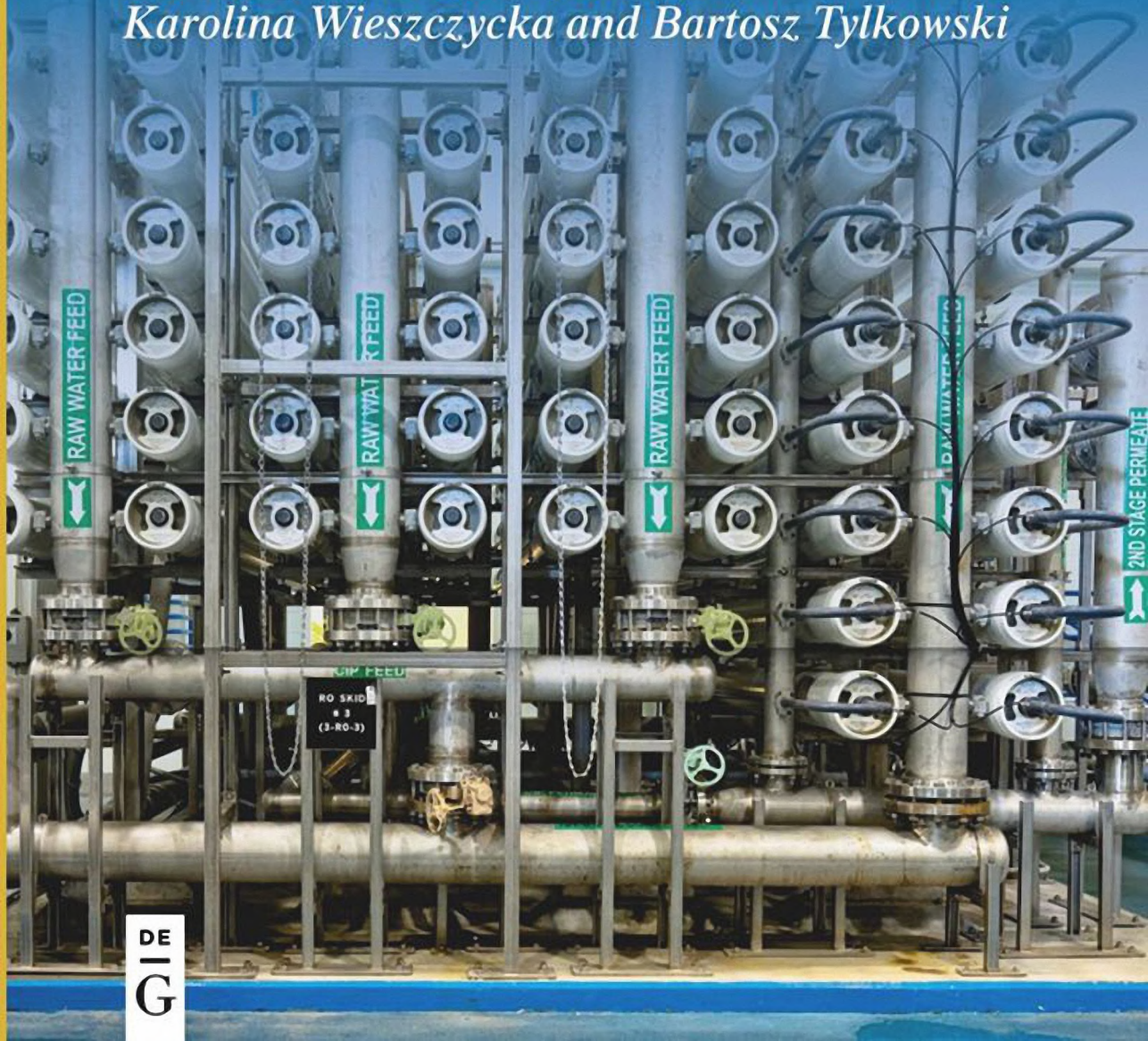
FROM ACADEMIA TO INDUSTRY

Edited by Katarzyna Staszak, Karolina Wieszczycka and Bartosz Tylkowski



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Membrane Technologies

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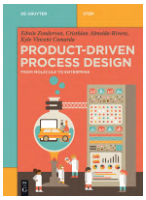

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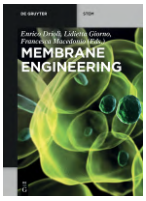

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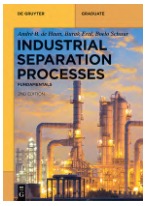

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Preface

The groundbreaking discovery that transformed membrane technology from a laboratory to an industrial process was the development of defect-free, high-flux, anisotropic membranes invented by Sidney Loeb and Srinivasa Sourirajan and disclosed in the United Stat Patent 3133132A filled by the University of California on November 29th 1960 and granted on May 12th 1964. With 60 years of fast advancement, today, membrane-based technologies are essential parts of numerous industrial processes which have brought significant benefits to improve human life.

This book aims to review the state of the art and to provide the readers with a comprehensive and in-depth understanding of recent developments and innovation analysis of the selected membrane applications. Chapter 1 emphasizes recent advancements in the design of membrane systems used either for separation or creation of mixtures from the perspective of industry 4.0 and data management. Chapter 2 focuses on the description of membrane processes, characterization of protein products, biological issues related to bacteriophages contamination, and modeling of the processes. Membrane applications in the food industry and in the production of beverages are detailed in Chapter 3 and Chapter 4, respectively. Chapter 5 discusses various applications of polymeric membranes in three significant areas of biomedicine, including tissue engineering, drug delivery systems, and diagnostics. Liquid membranes for separation of metal ions from wastewaters are the subject of Chapter 6. Essential oils are compounds extracted from plants which are usually utilized to produce perfumes, soaps, lotions, and flavorings as well as other well-being or aromatherapy products with antioxidant and antimicrobial properties. Membrane processes which have been proposed as a method for purification of essential oils extract is discussed in Chapter 7. We believe that the large number of references, to all significant topics mentioned, should make this book useful not only to undergraduates but also to graduate students and academic and industrial researchers.

Having an idea is one thing, turning it into a book is tough, however much satisfying!

We wish to acknowledge all contributing authors for making this book project a success.

Katarzyna Staszak
Karolina Wieszczycka
and
Bartosz Tylkowski

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1 Design of membrane systems

Abstract: Membrane separation systems have been used in process industry since decades; however, their designs are based mainly on experienced-based and use of trial-and-error approach, especially in case of membrane selection. This chapter reviews recent advancements in the design of membrane systems used either for separation or creation of mixtures from the perspective of industry 4.0 and data management. Additionally, computer-aided design tools have been reviewed with aim of possible use in the design of membrane separation systems.

Keywords: digital twins; membrane database; membrane selection; process design; process modelling; process simulation.

1.1 Introduction and definitions

The design of any matter, whether it is a table, pen, computer or chemical plant, is an art. Design of membrane systems is similar to the design of any other process unit and it involves the use of membrane science along with mathematics, engineering methods and tools such as models, simulations, drawings and spreadsheets [1]. These data and tools can only support the professional judgement and will never eliminate the professionals, since people are probably smarter than computers (and hopefully always will be). Professionals use imagination, analogies, knowledge of practise and knowledge of past disasters and experience which in some circumstances is like the hand of God while sometimes is like the sword of Damocles for ground-breaking endeavours.

In general, the goal of process design can be defined as the selection of the best opportunities among seemingly countless options to achieve the production goal within the foreseen operational and economical window with fulfilment of legal issues. Such definitions highlight the multi-objective nature of process design which in practise leads

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to various designs of the same design problem delivered by different professionals. Moran [2] noticed that the aim of process design is normally focused on determination of certain key dimensions, areas and volumes based on a number of parameters. Therefore, for non-novel processes, there may be set of rough rules of thumb, design guides, standards or codes of practise. Nevertheless, the process design has to include considerations and calculations (if possible) related to material selection (i.e. construction materials, active materials such as catalysts, solvents, membranes, etc.), operating conditions (i.e. normal operating conditions, start-up, shutdown, emergency situations, etc.), energy carriers and usage, environmental considerations, plausible disasters, investment and operational costs, variations in feed stock characteristics and influence on normal operations (more extreme conditions must be also carefully considered). The above range is not limited and can be expanded by professionals, but provides the range of typical considerations in process design practise.

In research and educational university practise, the process design of separation technologies is mainly related either to the experimental confirmation of separation concept in the laboratory scale, calculations of mass and energy balance or to fluid dynamics. Typical engineering considerations of process design pointed above are mainly outside the mainstream. In this chapter, the authors focus on the review of aspects which can be supportive for process design professionals while designing the membrane systems. Although at some points the Readers might have a feeling that the process design calculations require proficiency in mathematics, chemistry or IT skills, we keep in mind that the results should provide a minimum specification for an item, so that the purchase of commercially available unit with a reasonable confidence of its robustness would be possible [2]. Opaque outputs from modelling and simulation programs are not a substitute for transparent process design calculations, therefore in cases when it is possible, the short-cut methods would be also presented.

Regardless of which field would be considered, a membrane will be defined as the object which allows some components to pass while others will not. Membrane, as an object, can be solid or liquid in nature. Membranes can be biological, organic, inorganic or hybrid in nature. Aside from which definition would be considered, the utilisation of a membrane by humans requires the understanding of their nature, which is reflected in the ability to design its usage.

For the purpose of this chapter, a membrane is defined as the semi-permeable barrier for components, either chemical substances or biological compounds, synthesised or made by humans for separation purposes. The separation goal is usually achieved with only physical-based interactions (sorption, dissolution, solution, diffusion, desorption, sieving, electrochemical rejection etc.). However, it has to be kept in mind that when chemical substances are meeting and the membrane is one of them, reactions between the chemicals and biochemicals can occur. Therefore, the separation goal can be also achieved with accompanying chemical reactions, which is not the scope for this chapter.

It is important to point out that membranes are also used to create mixtures with tailored properties. The inorganic and even metallic membranes with narrow pore-size distribution are effectively used for preparation of monodisperse emulsions.

Additionally, membranes with precisely created holes are used as gas dispersers in wastewater treatment plants.

The membrane system is defined here as the closed process equipment with a membrane which actively separates two process streams (liquid, vapour, gas, suspension or any of their mixtures). Such systems can be operated in batch, semi-batch, semi-continuous or continuous mode. If continuous mode is considered, there will be at least one inlet (feed) and two outlet streams (permeate and retentate). However, in most of continuous processes, especially with no phase change, there will be one addition inlet stream for permeate side which is called the carrier or sweep.

Despite the fact that the design of a process is made either as a wild guess (i.e. *ad-hoc* solution) or experience-based, there is a need for a mathematical base. It is especially needed in the contemporary engineering world, because only that which can be measured can be used and reused. Designing is about reusing knowledge with the aim to achieve the defined goal. Moreover, designing with sufficient mathematical understanding is a key point in building the digital twins, which are essential for the on-going revolution of Industry 4.0. With this broadly drawn introduction, the following chapters are constructed as follows: (1) need for digital twins and modelling, (2) membrane-based separation systems, (3) mixture creation with membrane-based systems and (4) process modelling and simulation tools.

1.2 Requirements for digital twins and modelling

To facilitate the management, either from operational, economic or safety point of view, it is beneficial to measure, validate and store data which can be used to control and operate the plant in the best possible way. All that implies a need for virtual and digital twins. The virtual twin reflects the object with use of idealised models [3] which are based on well-defined physical and chemical relations. On other hand, the digital twins are data-based [3] and can be used to generate surrogate models describing the dependence of a quality metric on process parameters and other measurements [3]. The digital twins force the so-called Industry 4.0 revolution [4] which involves the use of different digital technologies to collect data from various internal (e.g. various equipment and departments within the same process facility) and/or external sources (e.g. consumers, producers, manufacturers, security services or other tiers using the product) consisting of the Internet of Things (IoT), centralisation, unification and harmonisation of various data in digital form (i.e. process and assets data). Both concepts of virtual and digital twins are merged in a concept of hybrid twins [3] to provide the holistic data and model environment of the whole plant. The trend of building the digital and virtual twins is undoubtedly a part of the building information modelling (BIM) methodology, which allows unification design documentation as well as managing and sharing information [4].

Life cycle of process plants by various authors and institutions is split in different stages but nevertheless, the baseline is that the life cycle of the plant starts with research and design, proceeds with construction and operation, and is finished with its decommissioning [5]. Here, for purpose of defining the life cycle of any process-oriented plant, the division based on [6] has been adopted, consisting of seven steps: (1) research and development, (2) process plant design (consisting of process design and plant design as distinguished sub-steps), (3) procurement, commissioning and construction, (4) start-up, (5) operation, maintenance and down-times, (6) modifications and updates and (7) decommissioning. All the steps of process-plant life cycle are presented graphically in Figure 1.1, in which the list of generated documentation and types of various computer-aided tools is also presented.

Main stages of the life cycle of a process plant require and generate various sets of data, which are bases for making decisions shortly or in an extended time. In general, two sets of data can be defined. The first are these which define principal knowledge generated through experiments, experience and already gathered data (e.g. literature, standards, codes of practise, etc.) which are used for process modelling, simulation and design. The second set of data takes its origin form process operations and in the framework of this chapter is called operational data. The growth of these sets of data changes over the life cycle with extreme growth of data for principal knowledge at the beginning which decreases substantially over the life cycle, while operational data

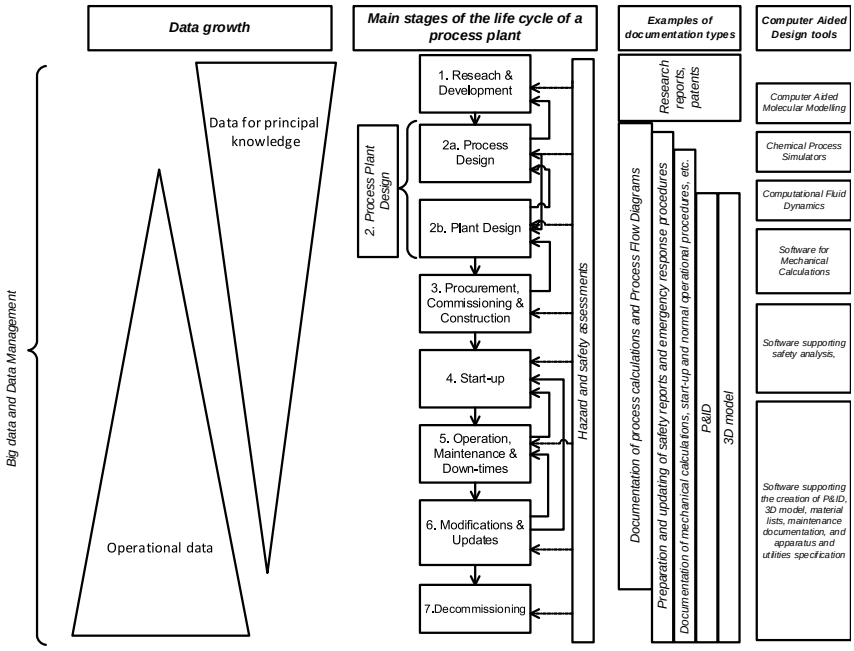

Figure 1.1: Process-plant life cycle (based on ref. [6]).

substantially grows since the start-up up to the decommissioning (see Figure 1.1). Both sets of data create the big data issue and a substantial need of data management. Research and development build-up enormous amounts of experimental data usually gathered in various reports and patents. These data are utilised in the following step of process design which is accomplished along with approved economic analysis and feasibility study. The process plant design is about transforming the selected process flow sheet into hardware by means of detailed engineering of equipment, piping, utilities, constructions, locations, etc. with the use of specification sets based on specific industrial standards or codes. After the process plant design is completed, the procurement, construction and commissioning (stage 3) of the facility can progress which is concluded with start-up (stage 4). The life cycle of a plant usually consists of long-term operation stages interrupted by maintenance and related planned down-times (stage 5) which can be related to modification and updates (stage 6). The cycle is finished with decommissioning and final close-off of the plant (stage 7). Additionally, it is important to highlight that each of the stages generates various sets of data and documentation, require adequate hazard and risk assessment, and the use of appropriate computer-aided tools and methods.

Plant design requires the cooperation of many groups of designers which may range from chemists and physics, biochemical, chemical, safety, mechanical, electrical and automation engineers up to civil engineers and architects. Therefore, it is necessary to ensure an adequate exchange of data between them in a multi-discipline environment, in order to organise the data generated by all disciplines and allow synthesis of knowledge and distribution of information required by certain disciplines at certain time. In that area, a plant design software (PDS) is a necessity and a tool which provides an environment for multi-disciplinary and multi-user collaboration within one computer-aided system with utilisation of material and equipment specifications. The short review of PDS delivered, for example, by AVEVA, Bentley, CADSchrorer, Haxagon, Autodesk, Alignex, Cadmatic IT and Factory is given in [4]. It is important to notice that PDS gives the possibility to build the digital twin which might involve data used in whole process design but also provides the possibility to collect process and use data for the asset management during the operational period of a process plant.

Adequate data management is needed at any step of the process-plant life cycle which consists of collection of data from various origins (e.g. literature, experiments, operational process, etc.) and first principles or grey-box models (i.e. models which have physical meaning or insides). Use of data and models creates a cycle of deductive and inductive processes around the collected data, as is presented in Figure 1.2. Usually, the design of any process requires the use of a first principles model or at least a grey-box model which provide the essential physical relations between incoming and outgoing streams. On this basis, the design can be deducted, leading to either an experimental or fully operational process. Operating the process will deliver measurements which can be analysed and provides a possibility for performance

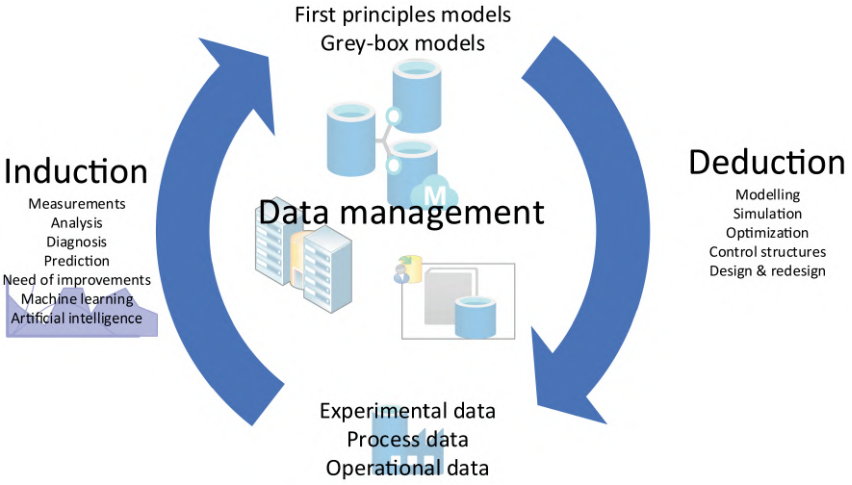

Figure 1.2: Inductive and deductive perspective on data management in process-plant design.

prediction and improvements. Inductive approaches through monitoring and diagnosis of processes can lead to their better understanding, ultimately improving the grey-box models. Actually, the cycle can be carried on infinitely. The presented deductive-inductive cycle can be considered at any single stage of the process-plant lifecycle or as on the whole.

1.3 Membrane-based separation systems

In membrane-based separation systems the membrane is an active barrier that separates the molecules based on either the sieving, diffusion, solution-diffusion mechanism or their combination. Principles of modelling of membrane-based separation systems have been widely discussed in the literature [7–15]. The driving force which describes any membrane separation between feed and retentate (see Figure 1.3) can be expressed as the difference of component chemical potential $\Delta\mu_i$ between the feed and permeate. Although it should be noted that from a physicochemical point of view the difference in chemical potentials between feed and permeate, and membrane surfaces can play significant role in establishing the actual driving force.

The membrane-based separation is characterised by component flux J_i and membrane area A. In the view of Figure 1.3, the component flux J_i depends on component concentration c_i and the coefficient of proportionality P_i, which is not necessarily constant, however it is linking the difference of chemical potential μ_i over the membrane thickness x (Eq. (1.1)).

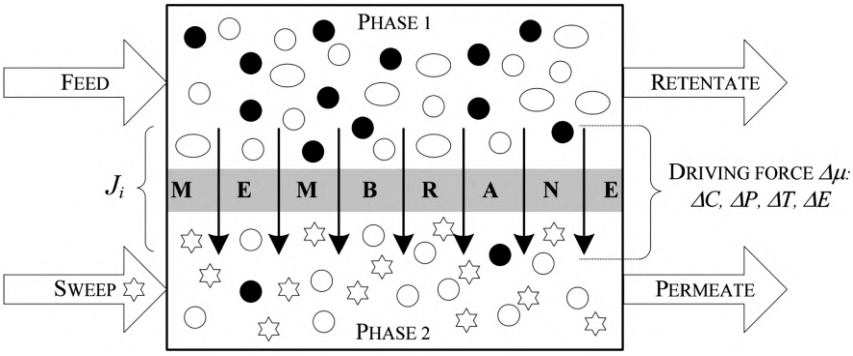

Figure 1.3: Concept of membrane-based separation (based on ref. [15]).

$$J_i = P_i \frac{d\mu_i}{dx} \tag{1.1}$$

From an experimental and operational point of view, three parameters namely selectivity ($\alpha_{i,j}$), rejection (R_i) and fraction of permeated (θ) feed need to be defined. The selectivity of membrane process $\alpha_{i,j}$ towards component i is defined by Eq. (1.2). Component rejection defines the ratio of difference in component concentration on the feed side $c_{i,F}$ and the permeate side $c_{i,P}$ (Eq. (1.3)). Fraction of permeated feed θ is defined as the ratio between the product of membrane area and sum of permeate component fluxes, and inlet flowrate as it is expressed by Eq. (1.4).

$$\alpha_{i,j} = \frac{J_i}{J_j} \cong \frac{P_i}{P_j} \tag{1.2}$$

$$R_i = \frac{c_{i,F} - c_{i,P}}{c_{i,F}} \tag{1.3}$$

$$\theta = \frac{A \sum_{i=1}^{NC} J_i}{F_F} = \frac{F_P}{F_F} \tag{1.4}$$

The most challenging part of modelling membrane-based separation is the mathematical description of physical interactions between separated component(s) and membrane material, and definition of driving forces from a practical point of view. Since there is a substantial amount of literature dealing with modelling of membrane-based separations, the authors decided to list the recommended literature in that matter.

The comprehensive review of nanofiltration and solvent resistant nanofiltration is available in [16, 17]. Influence of all components present in the feed, even those originating from solutions used to adjust the pH, on the separation in nanofiltration process have been recently discussed through the Donnan–Steric partitioning model

[18, 19]. Recently Ravichand and co-authors [14] reviewed works dealing with modelling of pressure-driven membrane-based liquid separations, membrane-based gas separations and membrane distillation. Van der Bruggen and Luis [20] discussed modelling strategies of mass transfer in pervaporation with use of solution-diffusion, sorption, diffusion models as well as with pore-flow model for binary, ternary and multicomponent mixtures.

The literature examples shortly presented above deal with modelling of membrane-based separation with models which are deeply linked to physical bases of the processes. Nevertheless, when facing a challenging problem with significant amount of experimental data but with limited physical inside which makes it impossible to use the first principal or grey-box models, the artificial intelligence (AI) is coming to the scene and plays the main role. The AI based on artificial neural networks (ANN) is an approach in which a system mimics how the human mind processes information and makes decisions [21]. ANNs have been applied to various membrane-based separations [22], for example to model microfiltration [23], ultrafiltration [23–26], nanofiltration [27], reverse osmosis [28–30], membrane distillation [30], pervaporation [31] and even membrane-based reactors [30].

All models for membrane-based separations are carried out under idealised flow patterns. In general, there can be differentiated six flow patterns in a membrane unit which differ due to inlet and outlet flow configurations, and flow conditions in the feed's and permeate's chambers (see Figure 1.4). The idealised membrane unit with well-mixed chambers on both sides of a membrane is presented in Figure 1.4a. That configuration will justify the assumption of constant flux and constant concentrations along the length of the membrane, which is schematically presented on the right in Figure 1.4a. More realistic patterns are shown in Figure 1.4b and c. Actually, countercurrent is more frequently found than cocurrent since it offers better usage of driving force and yields better separation at the lowest membrane area for the same operating conditions as in the cocurrent configuration. The majority of laboratory tests of membranes are conducted in configuration presented in Figure 1.4d, in case of which typical cross flow is assumed. From a practical point of view, in most laboratory tests it is assumed that fluid in the feed chamber is well-mixed. In some industrial processes, especially in membrane distillation, the sweeping agent (also called carrier) is used in order to ensure sufficient removal of permeating component(s). The carrier is usually inert and does not permeate through the membrane to the feed side. The use of a sweeping agent is usually performed in two configurations, i.e. cocurrent (Figure 1.4e) and countercurrent (Figure 1.4f). It has to be remembered that all of the idealised flow patterns in membrane separations presented in Figure 1.4 are rather more unique than frequently found in industrial cases. But they are useful for modelling purposes. In industrial units, it is possible to find a mixture of the configurations presented above. The two most common arrangements are spiral wound and hollow fibber modules. In the spiral wound, a flat membrane sheet is separated by spacers and inserted in a pressure vessel. Spacers play a significant role not only for giving the space between membrane but also influence

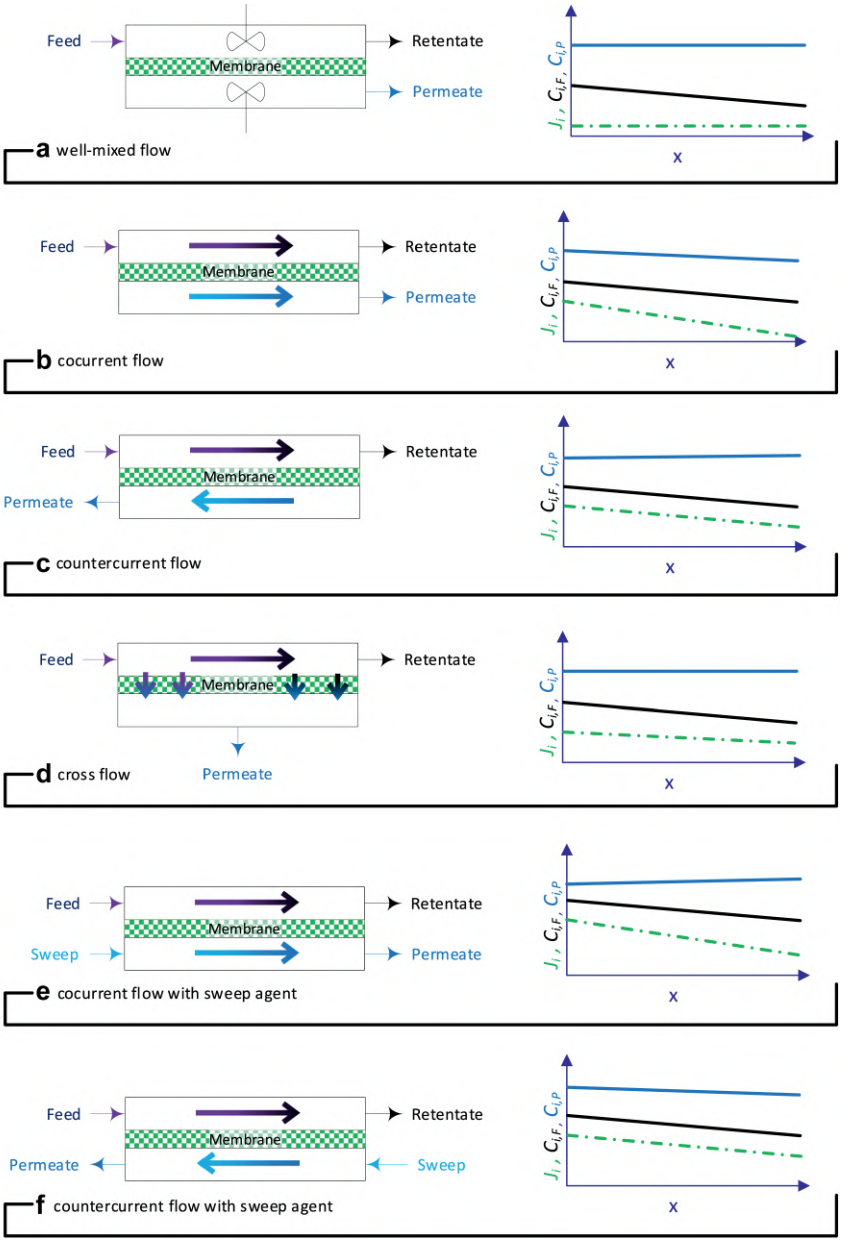

Figure 1.4: Idealised flow patterns and concentration profiles in modules in membrane-based separations (J_i – flux of component i, $c_{i,F}$ – component i concentration on the feed side, $c_{i,F}$ – component i concentration on the permeate side). a) well-mixed flow in feed and permeate sides; b) cocurrent flow pattern; c) countercurrent flow pattern; d) cross flow pattern; e) cocurrent flow pattern with sweep agent; f) countercurrent flow pattern with sweep agent.

the polarisation and fouling phenomena [32]. Hollow fibre arrangement consists of cylindrical membranes arranged in series in a pressure vessel. The selective layer is on the outside of the fibres. Usually, the feed enters the shell-side and the permeate passes through the membrane to the centre of the hollow fibres [33, 34].

When membrane-based separation is modelled, even with short-cut models, the question which might arise will be related to the increase of overall process efficiency and how to build the process based on available sizes of membrane units. If the designer is interested in the scale-up of the membrane process, the simplest option to consider is the sequential cascade as it is presented in Figure 1.5a. When not only scale-up is of interest, but also separation efficiency and purity, the sequential counter current cascade (Figure 1.5b) should be considered. If a single module ensures a high enough concentration of the compound in need but scale-up is required, then the designer should consider a parallel cascade configuration (Figure 1.5c). The following stripping and enrichment cascades networks (Figure 1.5d–F) present configurations focused on obtaining high purity with a relatively high efficiency.

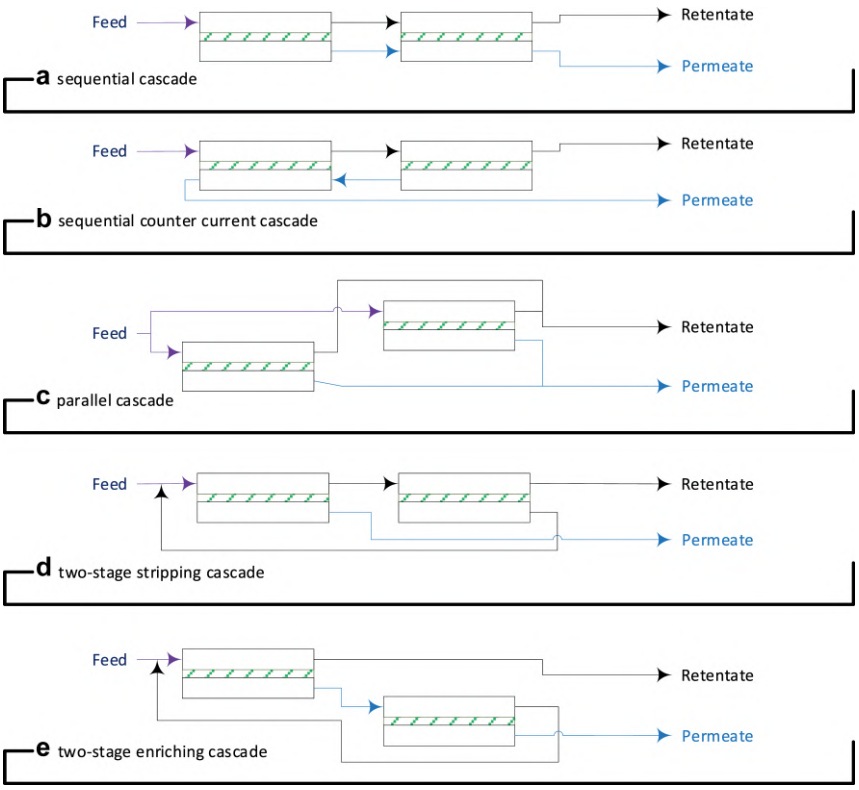

Figure 1.5: Examples of membrane networks. a) sequential cascade; b) sequential counter current cascade; c) parallel cascade; d) two-stage stripping cascade; e) two-stage enriching cascade.

Integration of membrane-based separation with and within other unit operations was applied since the first membrane processes were proposed. However, Lipnizki et al. [35] presented a feasible configuration and interrelations between membrane separations and other process units. Since then, hybrid process got significant attention in research [12, 36–41] but there is little information about their application industry except integration in dehydration of alcohols [42]. Figure 1.6 illustrates some common integration of membrane-based separation with reactor (Figure 1.6a and b) and

Figure 1.6: Configuration examples of membrane unit enhancing reaction and distillation processes. a) membrane unit enhancing reactor; b) hybrid process: membrane integrated with reactor; c) hybrid process: membrane unit enhancing distillate with permeate recycled; d) hybrid process: membrane unit enhancing distillate with retentate recycled; e) hybrid process: membrane unit fully integrated with distillation column; f) hybrid process: membrane unit enhancing side stream and retentate recycled; g) membrane unit enhancing bottom product with permeate recycled; h) membrane unit enhancing bottom product with retentate recycled.

with other separation technique (i.e. distillation, Figure 1.6c–h). Not all here presented configuration can be called as hybrid processes but nevertheless they show possible configuration of membrane-based separation with other separation and reaction processes. Integration of membrane with other unit operations is looked for when removal of single component, rather than set of components, which differ in size or permeability through membrane is enhancing the overall processes efficiency. This is especially looked for in distillation of azeotropic mixture [43] or dehydration of reactive mixture in order to move the reaction equilibrium towards required product [40].

1.4 Mixture creation with membrane-based systems

Unique application of membrane-based systems is related to the creation of multiphase mixtures of either immiscible liquids leading to emulsions, or dispersion of gas in liquids. Illustrative examples of the membrane emulsification process configurations are presented in Figure 1.7.

Porous membranes have found application in emulsification processes, especially in the pharmaceutical sector [44] and drug delivery [45]. The dispersed phase is pressed through the pores of a microporous membrane while the continuous phase flows along the membrane surface. Droplets grow at pore outlet until they reach a certain size or they are cut-off the membrane surface by the flowing liquid of the continuous phase. The detachment of a droplet is determined by the balance between the drag force on the droplet from the continuous phase flowing through the porous medium, the buoyancy of the droplet, the interfacial tension forces and the driving pressure [45, 46].

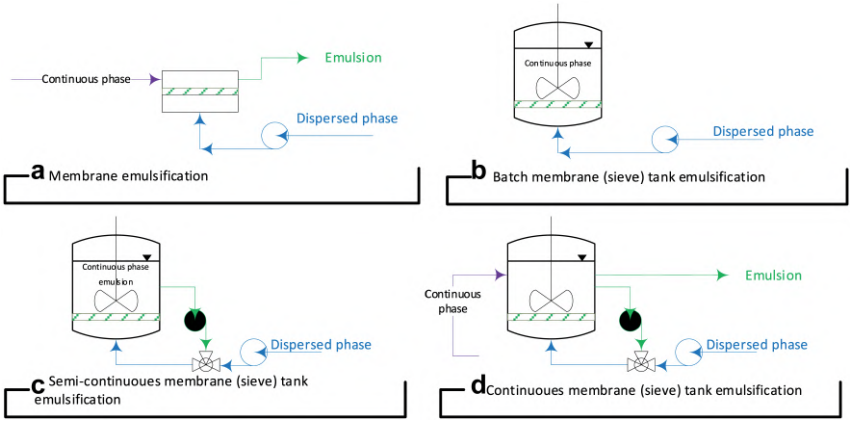

Figure 1.7: Illustrative configuration for membrane emulsification. a) membrane emulsification; b) sieve emulsification tank in batch mode; c) sieve emulsification tank in semi-continuoues mode; d) sieve emulsification tank in continuoues mode.

The stability and size of droplets are particularly important in terms of the applicability of emulsions. The stability of an emulsion is based on physical interactions between the components forming and acting on the interfacial surface [47]. Stability is also influenced by the droplet size distribution [48, 49], which is characterised by the span value $[(D_{90}–D_{10})/D_{50}]$. For example, narrow distribution of droplet sizes is characteristic for monodisperse emulsions which are more stable in comparison to multidisperse emulations [50]. From an operational point of view, it is possible to assess the droplet size based on empirical (i.e. grey-box) models.

Suárez et al. [44] reviewed and proposed a set of model expressions for estimation of the droplet size D_d in the stirred tank equipped with a flat membrane and for oil-in-water emulsions. The key parameter for droplet detachment is the shear stress τ on the membrane surface. When balance between drag force and interfacial tension force is considered, then droplet diameter $D_{[4,3]}$ (diameter of the sphere with volume equivalent to the droplet) can be estimated with Eqs. (1.5) or (1.6). Additionally, rough estimation of the minimum droplet size produced with use of membranes with round pores were proposed in the form of Eq. (1.7).

$$D_{[4,3]} = \left(\frac{4D_p\sigma}{6k_x\tau}\right)^{\frac{1}{2}} \tag{1.5}$$

$$D_{[4,3]} = \frac{1}{3\tau}\left(\frac{9}{2}\tau^2D_p^2 + 2\left(\frac{81}{16}\tau^4D_p^4 + \left(\sigma\tau D_p\right)^2\right)^{\frac{1}{2}}\right)^{\frac{1}{2}} \tag{1.6}$$

$$D^*_{dSDB} = \left(\frac{2\sigma}{3k_xD_p\tau}\right)^{\frac{1}{3}} \tag{1.7}$$

where D_p – pore diameter, σ – interfacial tension (N m^{-1}), k_x – wall correction factor for a simple sphere touching an impermeable wall and τ – shear stress (Pa).

In some cases, especially in wastewater treatment and aerobic fermentation, membrane diffusers are utilised in order to create gas-liquid(s) systems [51–53]. The membrane diffusers gained attention due to their large aeration area with evenly distributed gas bubbles, easy operation and maintenance. The use of membrane diffusers allows to deliver fine gas bubbles, therefore significantly increases the ratio of gas interfacial area to its volumetric flowrate. This leads to an improvement of mass transfer coefficient from gas phase into the liquid phase and has significant impact on decreasing the energy requirement [54]. Although there are reported studies regarding aeration or gas-delivering into the liquid phase with use of membrane diffusors, there is little information about the design equation for correlating the size of gas bubbles, liquid phase properties and volumetric gas flowrate, although there are some works which correlated the mass transfer and bubble size [51] as well as gas flowrate and hydrodynamics in a vessel with the gas hold-up [53].

1.5 Database for membrane selection

Specific membrane-based separation is selected by designers, engineers and/or researchers mainly based on their experience. The available information regarding prediction of component fluxes through membranes is rather limited, especially in multicomponent mixtures which are typical for industrial applications. Therefore, widespread literature surveys and queries to producers are required, causing difficulties in the identification of the promising membrane-based separation techniques along with appropriate membrane and process conditions for a given separation task. The need of extensive survey and lack of information result in challenges during the implementation of membrane-based separation techniques in the development of chemical and biochemical processes. Therefore, a need to search through some membrane-based separation processes databases seems to be a good choice and is looked for.

Authors have been monitoring the availability of the membrane and separation-oriented databases over the last decades. There were several attempts in the development of membrane databases such as the: database developed by Günther and Hapke [55], MBR database provided by MBR Network, Catalogue Membrane Technology provided by Dechema, and MemData [15, 56], which unfortunately were suspended and are no longer available.

The specialised membrane separation database was developed by Günther and Hapke [55]. That database aimed to assist the specialist, i.e. engineers and researchers, in selecting modules for the pilot scale and engineering analysis. The database contained two essential parts which presented the organised data with respect to: (1) basic information about the membrane module and the data delivered by the manufacturer and (2) extended data related to the application and separation performance of the membrane module (including experimental separation characteristic of the membrane). Within the database it was possible to carry on the separation efficiency calculation but only for the reverse osmosis modules. Nevertheless, the database collected information about four types of membrane-based separation processes: ultrafiltration, microfiltration, nanofiltration and reverse osmosis.

The MBR database was developed by the MBR Network and contained data related to the membrane bioreactors (MBRs) utilised only in the wastewater applications. The MBR database contained data about producers of MBR and possible application scale (e.g. household, municipal, etc.) but without membrane characteristic data. That online database was suspended a few years ago and appropriate reference is missing.

The Catalogue Membrane Technology aimed at providing a wide-ranging survey on the developers, manufacturers and suppliers of membranes and modules of any membrane-based separation process, which were in Germany, Austria and Switzerland. The collected data could have been searched with respect to separation technique and application field, institution and research topic, also with regard of

researcher. The catalogue did not make available information about the separation efficiency or process operation.

The data in the MemData was classified into different categories related to process module description, membrane information, experimental set-up, flux experimental data, modelling and permeability of pure compound. The structure of the database allowed gathering information about polymer-based membrane used in pervaporation, vapour permeation and gas separation. It was reported [56] that the MemData included information regarding 277 membranes, 112 experimental points of flux measurements of multicomponent mixtures and 1123 data points of pure component permeability through polymer membranes. Moreover, four models and correlations were also included. Further development of the MemData was suspended in 2016.

Recently, the open membrane database (OMD) which focuses on reverse osmosis membranes was reported [57]. That database is available online under the address www.openmembranedatabase.org and represents data of over 600 water purification and desalination membranes that have been gathered from peer-reviewed journals, reports and commercial product data. It is important that the authors provided clear information regarding the transport theory underlying the membrane performance calculations and best practises for membrane performance testing and reporting.

With respect to gas separation membrane systems, it is important to point out that the Polymer Handbook [58] also provides information about permeability, diffusivity and solubility of pure components (mainly gases) through polymeric membranes. These data are usually sufficient in order to find a promising membrane for gas separation applications.

A summary of all existing databases related to the membrane-based separation processes is given in Table 1.1. It is clear that the module database (Günther and Hapke [55]) would be most valuable from the point of view of the design engineer, as it could

Table 1.1: Summary of data reported in the reviewed membrane databases.

Database	Producers	Separation characteristic	Operational conditions	Information modules	Membrane processes
Catalogue Membrane Technology	Available	NA	NA	NA	[a]
MBR database	Available	NA	NA	NA	membrane bioreactors[b]
Module database of Günther and Hapke [55]	Available	Available	Available	Available	reverse osmosis nanofiltration ultrafiltration microfiltration
Open membrane database (OMD)	Available	Available	Available	Available	reverse osmosis[c]

[a]The database consists of the list of companies which are providing their service with respect to all kind of membrane-based separation. [b]Utilise microfiltration or ultrafiltration. [c]Authors of [57] claimed other application.

have provided extensive information about four types of membrane-based separation processes. The other two databases provide only a list of producers that design engineers can contact with respect to their specific applications. Currently, only the OMD is available for the design engineers for use at an early stage of membrane system design.

1.6 Process modelling and simulation tools – a brief review

Process simulation and modelling tools can be divided into three groups: (1) process simulation software (PSS), (2) modelling-simulation software (MSS) and (3) modelling and process simulation software (M&PSS) (M&PSS). PSS use predefined unit operations within the software but without the possibility to view the used equations. In contradiction to general process simulation tools, the modelling simulation software provides complete definition of modelling equations for which appropriate mathematical solvers are provided. The most modern and quite recently developed attempt involves software which is based on creating flowsheets that consist of predefined unit operations with the possibility of defining custom models. Within the last group, some of software incorporated the unique possibility to dig into the governing equations for all models, i.e. models of predefined unit operations and custom models.

To fulfil the requirement of a brief review and its general purpose in the volatile business environment, it should be remembered that software developers usually provide an environment which might include a set of various software and programs. Therefore, the authors of this chapter limited to name a set of environments rather than the specific software. The general overview of the reviewed software suits is presented in Table 1.2. One of the vast computer-aided modelling environments is delivered by Aspen® [59] which can be used for modelling, design, simulation and optimisation of batch and continuous processes, troubleshooting and monitoring the plant performance through online and real-time optimisation. Aspen offers interfaces for proprieties models and its parameter estimation. CHEMCAD® [60] software is an integrated suite of Chemstations, designed to improve the productivity and solve the process flowsheets with limited use of build-in custom models. Similarly, the CAD tool is a steady state and dynamic process simulator PRO/II [61] delivered by AVEVA, which has an in-built membrane unit with the permeate pressure, component permeability constants and membrane area as inputs. SuperPro Designer [62] is an interesting flowsheet simulator for batch or continuous processes as well as their combination with the possibility of process scheduling, equipment sizing and costing. Within SuperPro Designer there is a possibility to use microfiltration, ultrafiltration and reverse osmosis units. Another approach to simulation of membrane systems is presented in the WAVE [63] design software which focuses only on ultrafiltration, reverse osmosis and ion-exchange processes.

Table 1.2: Modelling and simulation tools.

Type	Name of software	Presence of membrane unit	2D model	3D model	Process simulation	Dynamic simulation	Batch simulation	Control structure	Build-in optimisation	Properties and thermodynamic databank	Model predictive control	Custom model	External connections	AI
PSS	ChemCad®	–	x	x[b]	x	x	x	x	x	x	x	With external tools	MS VBA, Excel, CAPE-OPEN, COM, DCOM, OPC, XML	NA
PSS	Pro/II®	x	x	x[b]	x	x	x	x	NA	x	NA	With external tools	MS VBA, Excel,	NA
M&PSS	AVEVA™ Process Simulation	–	x	x[c]	x	x	x	x	x	x	NA	Built-in and external with equation modification	MS VBA, Excel	NA
M&PSS	Aspen®	–	x	x[a]	x	x	x	x	x	x	x (adaptive process control)	Built-in and external	MS VBA, Excel	x
PSS	ProSim®	–	x	NA	x	x	x	x	NA	x	NA	External	MS VBA, C++, Visual Fortran, CAPE-Open	NA
PSS	SuperPro Designer®		x	x[b]	x	x	x	x	x	x	NA	Build-in and external	Excel, Matlab, C#, COM, MS Project	NA
M&PSS	gPROMS®	x	x	x[a]	x	x	x	x	x	x	x	Build-in	MS VBA, Excel, CAPE-OPEN, PRO/II,	NA

Table 1.2: (continued)

Type	Name of software	Presence of membrane unit	2D model	3D model	Process simulation	Dynamic simulation	Batch simulation	Control structure	Build-in optimisation	Properties and thermodynamic databank	Model predictive control	Custom model	External connections	AI
MSS	Matlab®	–	x	x[a]	x[d]	x[d]	x[d]	x[d]	x	NA	x	Built-in and external	ANSYS FLUENT, Matlab, Aspen Plus Excel, CAPE-Open, C++, etc.	x
MSS	MathCAD	–	x	x[a]	x[d]	x[d]	x[d]	x[d]	x	NA	NA	Built-in and external	Excel, C++, CAD, API	x
PSS	WAVE design software	x (UF, RO, IonEx)	x	NA	x	NA	NA	x[a] (limited to specific req.)	NA	x	NA	NA	NA	NA

x[a] – partial differential equations. x[b] – sizing and cost. x[c] – sizing, cost and transfer to plant design. x[d] – depending on model representation.

The group of MSS contains software which allows the user to define almost any mathematical model and solve it with possibility of selecting various and dedicated solvers. Matlab [64] and MatCAD [65] are the first choices for that group. Although MathCAD does not provide of any flow sheeting experience, its benefits include user-friendly symbolic-like input of model equations which can be easily organised with notes experience. In contradiction, Matlab offers more programmer-like experience with a combination of flowsheet-like experience with use of Simulink.

Here, the gPROMS [66] is opening the basket M&PSS software with an advanced equation-oriented process modelling environment, which can be used to model, analyse and optimise any equation-based model in a user-friendly flow sheeting environment. An interesting upcoming star of M&PSS is the AVEVA™ Process Simulation [67] software. Process Simulation offers novel approach to the equation-based environment for process simulation which includes possibility to track every equation used in the simulation and easy-to-use switching between process, fluid flow and dynamic modes. It is important to point out that the process simulator delivered by AVEVA allows the unique possibility to transfer the model and the data to the process plant design and operational environment developed and delivered by AVEVA for more than four decades. Even though gPROMS® and AVEVA™ Process Simulation include specific models of membrane units, it is recommended to adopt these models to the specific requirements of modeller.

From a practical point of view, the use of the included membrane models in any commercial software should be carried out carefully with outstanding verification of used parameters and included assumptions with the models. Therefore, many researchers and process designers develop their own models directly in the MSS or M&PSS software, or develop models in external environments (e.g. MS Excel, VBA, etc.) which can be used within simulators directly or with use of COM or CAPE-Open standards.

1.7 Summary

The main question in design of membrane systems is how to select the appropriate membrane process and membrane itself with respect to the separation efficiency and operational performance. Selection of a membrane process is a matter of defining the purpose i.e. separation or creation. The membrane-based separation processes are selected mainly due to the difference in size (sieve mechanisms) or in diffusivity (solution-diffusion mechanism) of separated components. Designers must make their choices based on their experience, literature review or external expertise's. In recent years, a significant increase in experimental research on membrane-base separations is observed while process modelling works are rather limited.

In this chapter, the design of membrane systems has been reviewed and placed within a wide perspective of challenges encountered within industry 4.0, big data

perspective and data management. The possible membrane configuration with other separation processes as well as with reactive processes has been presented.

For process designers, the important part of the work is related to process modelling and simulation tools. The available computer-aided tools have been divided into three groups and their main futures have been presented. It is important to note, that almost all software environments include the possibility to communicate with other CAD tools, allowing some model or process simulation capabilities along with other company-specific analysis. In this area, the usability of AI is observed, which is also reflected by the possibilities offered by three out of 10 modelling and simulation environments.

To summarise, the main drawbacks for designers of membrane systems are related to the lack or extremely limited predictive mathematical modelling, membrane physical properties and membrane process separation databases, making the design of the membrane separation system challenging and highly dependent on specific expert knowledge. These issues are even more noticable for membrane systems used for mixture creation.

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Maciej Staszak*

2 Membrane technologies for sports supplementation

Abstract: The important developments in membrane techniques used in the dairy industrial processes to whey manufacturing are discussed. Particular emphasis is placed on the description of membrane processes, characterization of protein products, biological issues related to bacteriophages contamination, and modeling of the processes. This choice was dictated by the observed research works and consumer trends, who increasingly appreciate healthy food and its taste qualities.

Keywords: bacteriophages; dairy; membrane process; ultrafiltration; whey.

2.1 Introduction

The human body has evolved on the basis of survival needs, developing features predestining it to lead a life requiring high motor activity with relatively low food supply. Over the last two hundred years, there has been a rapid civilizational change in the way of life, which has become much less demanding in terms of physical activity and mobility while increasing the availability of food. In addition, the industrialization of food production has resulted in a significant decrease in its nutritional quality while increasing its caloric content. This has led to consequences in the form of civilization diseases related to or caused by the growing problem of obesity. At the same time, it has been noted that one of the factors that have a positive impact on health is appropriately balanced physical activity. Human physical activity is therefore one of the key elements of a healthy society. Many sports disciplines use supplementation with the use of preparations with an increased concentration of protein, branched-chain essential amino acids such as BCAA, or minerals from the group of magnesium, zinc, or copper. The World Health Organization WHO has included relevant recommendations [1] concerning the necessary amount of exercise in the life of modern people, which is supposed to provide a possibly healthy lifestyle. It is considered that adults should undertake weekly 150–300 min of moderate-intensity physical activity or 75–150 min of high-intensity physical activity, or a corresponding combination of moderate-intensity and high-intensity aerobic activity. Recommendations for children and adolescents recommend an average of 60 min per day of moderate- to high-intensity aerobic physical activity throughout the week. The guidelines

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recommend regular muscle-strengthening activity in all age groups. In addition, a reduction in sedentary lifestyles is recommended in all age groups and ability types.

Popularization of the use of sports supplements is particularly widespread in bodybuilding, strength and, to a lesser extent, endurance sports. The T-Nation [2] website, which is run by experienced professionals in the field of sports and popular in the strength sports community, devotes a lot of attention to the issue of proper nutrition and supplementation, also raising difficult issues related to doping with anabolic substances, which are not approved for sports or recreational use in many countries. The articles appearing in the area of this website are in many cases formulated on the basis of reports from the scientific community and classic publications in professional journals. A number of other websites also contribute to the popularization of active lifestyles and devote much attention to the correct use of this type of supplementation.

In this work, the main focus is on problems that accompany the manufacturing processes for sports supplements using membrane techniques. Membrane techniques are a well-known and popular method of concentrating a variety of substances, from metal ions to large organic structures like proteins. Proteins are the main component in most nutritional supplements for athletes or people who are undergoing rehabilitation.

The worldwide nutritional supplements market volume was estimated to be $10.7 billion in 2020 and is projected to grow at a compound annual growth rate of 10.9% from 2021 to 2028. The number of consumers centered on personal wellness and fitness self-care and prevention is increasing. In addition, there is growing realization about the elevated threat of serious health conditions in COVID-19 patients affected by obesity, diabetes, and heart disease. Furthermore, the amount of consumptive consumers suffering from lifestyle-related diseases such as diabetes and obesity is quickly increasing. Based on the International Diabetes Federation, 463 million adults aged 20 to 79 had diabetes in 2019, and it is expected that this number will rise to 700 million by 2045. It is estimated that all these elements will boost fitness activities participation and drive usage of various supplements especially athletic nutrition supplements products over the predicted forecast period [3].

Increasing attention to the accessibility of athletic nutritional supplements is quickly increasing, therefore in turn propelling the market. In addition, health enthusiasts are increasingly learning about the advantages of various components and nutritional supplements from a variety of sources. Based on a survey released by Friesland Campina Ingredients [4], by 2020, in addition to healthcare professionals, 45% of adults look to fitness gyms and personal trainers for dietary guidance, and 53% look to friends and family for nutritional information. Furthermore, there is a surge in consumer need for plant-derived and immune-boosting nutritional foods. Major market leaders are releasing new products to cater to consumer demand. As an example, in May 2020, Orgain [5] launched several types of plant-based organic protein powders, including Organic Sport Protein Powder, Organic Sports Recovery Powder, and Organic Sport Energy Powder targeted at different customer groups, e.g. adults, children, or diabetics.

The increasing population of individuals with active lifestyles is pushing the sports supplements market. As reported by International Health, Racquet, and Sportsclub Association (IHRSA) [6], the amount of health club consumers in 2010 was 58 million, which has increased to 73.6 million in 2019. Furthermore, sportsmen are concentrating on satisfying nutritional demands together with athletic activities to improve their physical performance.

Many major and local market contributors are launching new tastes, compounds, and technologies. Ostrovit [7] introduced a number of new tastes of several whey and casein protein supplements, ranging from white chocolate, vanilla, strawberry, and cocoa to other coffee-based and inspired by desserts. Lonza [8] launched TWK10 [9, 10], a probiotic for use in athletic nutrition, in September 2020. TWK10 is an extract of *Lactobacillus plantarum*, derived from the Kimchi plant from Taiwan, that aids in improving athletic performance by increasing energy gathering and muscle endurance.

Therefore, the increase in demand for dietary supplements including protein nutrients in particular is expected to generate and will continue to drive strong growth in the dietary supplements market (Figure 2.1).

2.2 Types and classification of dietary supplements

A simple correlation between nutritional intake and physical performance does not exist, but there is a relationship between proper supplementation and physical performance [11–15]. Many researchers [16–18] point out that the physical performance of the individuals is a resultant of many factors, including aptitude, training and diet quality, and the mental predisposition of the person. They also emphasize that many supplements exhibit a "placebo effect" in sportspersons at best. The increased physical activity that accompanies sports results in an increased demand for energy and many nutrients. However, scientific studies show [19–22] that a properly composed diet,

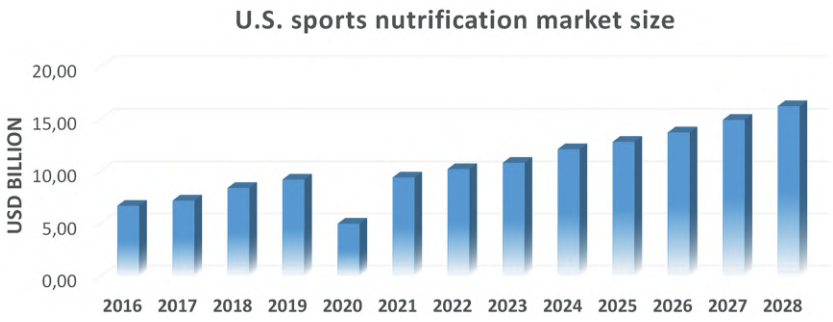

Figure 2.1: Expected market size for sports supplements [3].

based on natural products alone is able to provide increased amounts of energy and all necessary nutrients. Yet the supplementation for professional athletes is advisable, especially under high training loads. When using nutritional supplements, the primary goal is to take care of the health of the individuals, therefore the supplements used should be safe, effective, and allowed for use in sports. Nutritional supplements for the sporting population are a group of products with poorly researched side effects, which is why great care and moderation are required when using them. Currently, on the market, there are many products aimed at physically active people, whose effects have not been confirmed by reliable scientific studies. The effectiveness of many of them is therefore problematic. In addition, nutritional supplements may contain substances prohibited in sport and their use carries a risk of disqualification [23–25].

2.3 Proteins in the view of food functional classification

Functional properties of proteins are classified according to their respective physicochemical properties, the most important of which are hydrophilicity, phase boundary behavior, intermolecular interactions, and organoleptic properties that impart desirable characteristics to food products [26]. Therefore, the functional properties of proteins are defined as the properties that have the greatest influence on the texture, appearance, viscosity, mouthfeel, or taste of a product. In addition to their nutritional value, proteins should also have certain functional properties that enhance processing and provide the foundation for an efficient product. Dietary functional properties of proteins refer to the physicochemical properties that control the behavior of proteins in products [27]. To further understand these functional contexts, it is necessary to comprehend more than just the physicochemical properties of proteins, as well as their structural architecture (beginning with primary chains and ending with quaternary structures) and the diverse set of interactions that help stabilize higher-order protein structures [28].

Most of the major functional properties of proteins can be divided into two main groups: surface and hydration related. Functional properties that are associated with hydration involve dispersibility, solubility, swelling, viscosity, and gelation. The properties associated with surface activity include emulsification, foaming, and air–water and oil–water interface adsorption. Additional functional properties that do not fall into either of these two classes include diffusion and denaturation processes, and proteins intermolecular interactions that comprise protein–protein, protein–ion, and protein–ligand bonds forming.

Whey proteins are the proteins remaining in milk serum after the coagulation of caseins in an environment of pH 4.6 and a temperature of 20 °C. In industrial practice,

acid whey is a by-product of caseinate or cottage cheese production. It is made by adapting the pH of skim milk to a value of 4.6 by adding glucono delta lactone acid or a culture of lactic acid bacteria, then cutting and cooking the curds and draining the resulting whey. Sweet whey is produced by inoculating milk with lactic acid bacterial cultures to acidify it to a pH in the range of 6.2–6.4 and adding a coagulating enzyme, rennet for rennet cheese production.

Whey proteins are characterized by a compact globular structure, with a molecular weight in the range of 14–1000 kDa. One of the primary properties of whey proteins is their high content of sulfhydryl amino acid residues. During high-temperature processing of whey and whey protein concentrate (WPC) solutions, it is this property that allows whey proteins to form intermolecular covalent bonds. Disulfide intermolecular bonds play a key role during the heat-induced formation of whey protein gels and act to stabilize foam structures. However, the formation of these bonds during the manufacture and storage of WPC is highly undesirable as it leads to a product with low solubility and usability.

When planning and designing appropriate installations for the production of whey protein, there are two main issues to consider, namely the source of the protein [29] and the target form of the protein [30]. The primary sources are milk, eggs, beans, soy, rice, and in some rare cases beef. Figure 2.2 shows the typical protein forms which are ranked in the direction of increasing processing. The resultant protein concentrate can be regarded as the primary form of a protein supplement containing up to 80% protein. Isolate is the next step in increasing protein concentration and hydrolysate is the final form in which protein molecules are pre-hydrolyzed into shorter and more nutritionally absorbable chains.

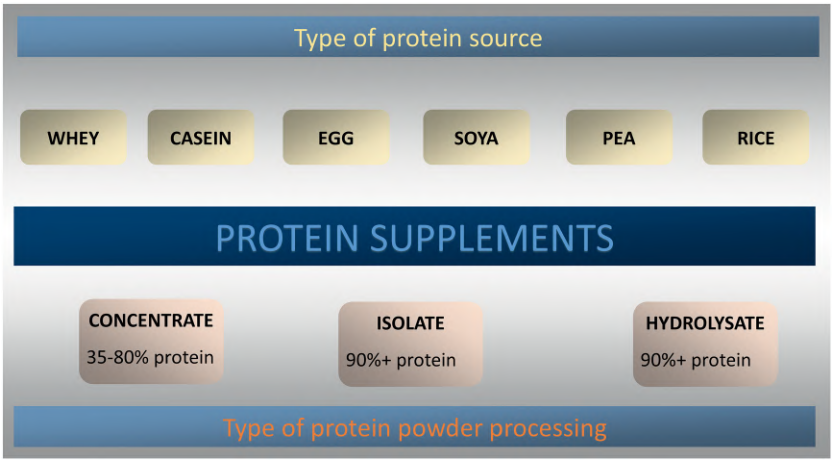

Figure 2.2: Source of proteins for typical supplements.

2.4 Membranes in food industry

A typical classification of membranes is ordered by average pore size. Membranes belong to the so-called dense membranes, when the transport of components has two steps: dissolution and diffusion through the membrane material. Membranes used in microfiltration usually have a pore size in the range of 0.1–10 μm. Membranes used in ultrafiltration have pore sizes in the range of 0.001–0.1 μm and are capable of retaining substances with molecular weights in the range of 300–10^6 Da. Membranes used in reverse osmosis are capable of retaining solvents with a molar mass below 1000 Da, while nanofiltration membranes are suitable for retaining solvents in the molar mass range between 1000 and 3000 Da.

Two typical membrane systems used are dead-end and cross-flow [31–35]. In the dead-end type of operation, the liquid to be filtered is forced through the pores of the membrane usually by exerting pressure on the feed side of the membrane. In the cross-flow type of operation, the feed fluid flows in a parallel direction to the surface of the membrane and penetrates the membrane by means of a pressure difference. Cross-flow minimizes the build-up of filter cake, thus keeping it at a low size. In cross-flow mode, the most widely utilized membrane units incorporate hollow fibers, tubular fibers, flat plates, and spiral wound devices. Hollow fiber and spiral wound types of modules offer the densest membrane packing because they have the channels of the smallest diameter. Though, this makes them more sensitive to fouling and may impede the cleanup process. Either of these cross-flow configurations of devices can also be used in dead-end operations. However, such setups are subject to high fouling rates.

At present, traditional chromatography is still considered as the most efficient way to separate and purify whey proteins on an industry scale [36]. Various chromatographic techniques such as affinity, ion exchange, and hydrophobic exchange have been used to perform protein separation, but they have drawbacks such as fouling, long cycle times, and complex control systems for the process [37, 38]. To address these shortcomings, macroporous membrane based monoliths have recently been used to improve the separation rate and decrease the backpressure, thus preventing nonspecific product binding and degradation. The benefits of using such monoliths are comparable to those of conventional chromatography [39]. The pressure processes using membrane technology are extremely important for the removal of mineral salts from whey. Whey is condensed by vaporization or reverse osmosis and subjected to demineralization by electrodialysis or using ion-exchange resins at present [40–42]. Nanofiltration membranes have the potential to be applied to perform demineralization due to their permeability to single-valent salts and organic species, enabling at the same time to reduce energy expense and wastewater output [43–46]; reverse osmosis ensures the retention of approximately 99.8% of lactose and its overall recovery of 74%, thus making water evaporation or crystallization easier [47]; microfiltration is most commonly used to eliminate microorganisms and remaining lipids, reducing to a

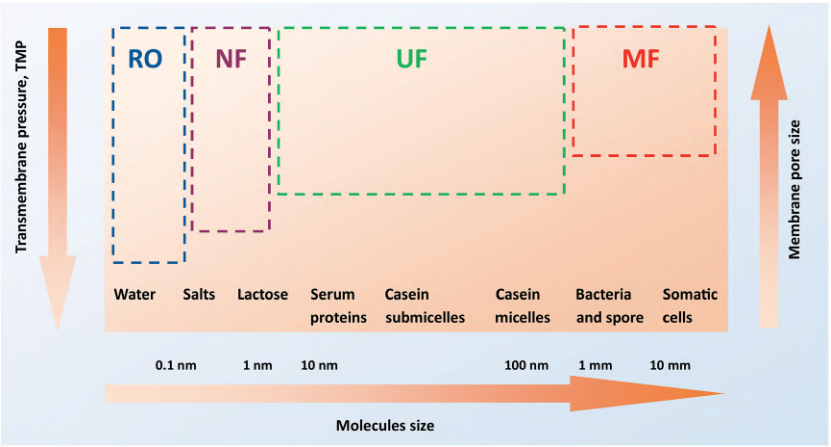

Figure 2.3: Application of each membrane technique to the separation of mixtures containing contaminants of different sizes.

minimum the fouling phenomenon and its impact on downstream processes [48, 49]. Figure 2.3 presents area of each usability of membrane techniques to the separation of mixtures that contain contaminants of various sizes.

Membrane processes that use the pressure difference between the feed and permeate sides to drive solvent transport across the membrane involve microfiltration, ultrafiltration, nanofiltration, and reverse osmosis [50]. Table 2.1 illustrates the categorization of membrane processes based on particle kind and size [51]. Membrane processes based on the pressure principle are the most essential membrane processes, which are typical unit operations in the field of dairy industry. Microfiltration is primarily used for clarification and skimming of cheese whey. Several studies [52–56] presented in detail the application of ceramic and polymeric membranes for microflushing of skimmed milk; reverse osmosis is used for partially demineralizing or preconcentrating whey, and nanofiltration is adequately capable of providing concurrent demineralization and concentration of whey [57].

Table 2.1: Classification of membrane techniques in the view of diary/whey separation.

Technique	Microfiltration	Ultrafiltration	Nanofiltration	Reverse osmosis
Structure/ mechanism	Largest pores/sieve mechanism	Medium pores/ sieve mechanism	Smallest pores/ sieve mechanism	App. no pores/solution-diffusion mechanism
Particle/solute size, nm	100–10,000	1–100	1–10	0.1–1
Class of separated species	Bacteria, cells emulsions, colloids, polymers	Sugars, viruses proteins, vitamins	Sugars, vitamins	Low molecular weight substances, salts.

The application of membrane filtration process technologies provides a broad spectrum of benefits to both the consumer and the producer. Membrane filtration technique is an innovative, nonthermal, environmentally safe, sustainable technology with many opportunities for the future that mitigates the negative effects of rising temperatures such as phase change, proteins denaturation and alteration of the sensory attributes of the resultant good. Membranes eliminate undesirable contaminants such as bacteria, medicines, or residues that adversely affect the quality of the product, resulting in a more attractive consistency and longer product lifespan. The membranes are highly selective because of their specific mechanisms of functioning such as ion exchange, diffusion of the solution, etc. The membranes are well suited for various kinds of installations and development because of their space-saving construction and require very little servicing. The functioning of membranes is quite straightforward, competitive, and does not need any specialist expertise to maintain or work with them. To achieve the expected results, it is occasionally required to employ a battery of membranes instead of an individual membrane [58–61] and to re-engineer the entire production of an industrial plant by incorporating different membrane operations already invented [62–64].

Several other membrane techniques are used to obtain whey in higher concentrations. Membrane chromatography is employed for the retrieval and purification of proteins. Nevertheless, membrane adsorption technology allows the recovery of high-value minority proteins from whey along with the optimization of process expenses. Consequently, membrane chromatography is a promising and innovative protein separation technique that combines filtration and liquid chromatography in a one-step approach [65].

Ion-exchange membrane chromatography is another technique that allows the concentration of proteins. Protein separation by ion exchange membranes is based on the electrostatic effect between charged proteins and the surface of adsorption. Ion exchange membranes find widespread use for the isolation of amino acids and proteins. The target molecule is found to repel the counter ion bound to the active surface region, and this counter ion is subsequently removed with a complimentary buffer salt. To achieve high separation efficiency, it is essential to select a suitable buffer to protect the target native protein [66]. The dynamic binding capacity of a given membrane system relies on both the size of the target protein molecule and the conditions such as protein concentration, pH, and ionic strength.

Membrane Affinity Chromatography is commonly used for protein recovery. This technology is based on the strong interactions occurring between ligands and target proteins due to their biological features. The entire process consists of three steps: loading, washing, and elution. The main assets of membrane based chromatography over conventional chromatography are short diffusion time (because of the intermolecular effects inside the pores), small pressure drop, high flux rate and high efficiency. This method is preferable for bigger proteins as they seldom penetrate inside the pore as they are blocked at the outer surface. Some researchers also indicate that membrane

chromatography is adequate for treating high volumes of liquids with low concentrations of the desired proteins [39].

2.5 Phages issues

Bacteriophages refer to viruses that affect microbial cultures and have a high reproduction rate. For this reason, they are commonly the cause of serious fermentation difficulties, particularly in the industrial dairy sector. The problem is well known for several years and the constant risk of serious bacteriophage infections in the dairy industry demands thorough phage detection as the primary means of bacteriophage control [67]. Temperature-induced phage inactivation is overall feasible, but the required temperatures impact the whey product functionality because of denaturation of whey proteins. It is proposed to introduce a "phage filtration" process stage before further processing of dairy whey into whey products to minimize the possibility of fermentation due to phage contamination [68]. Furthermore, the extremely high stability of phage in whey powder samples during long-term storage for four years has been documented [69]. Lactococcal phages remained detectable after pasteurization of milk followed by spray drying. There was no decrease in phage titer detected during the nine-month storage of milk powder [70], indicating that phage populations were highly stable in the dry powder matrix. A publication of Samtlebe et al. [71], showed the applicability of organic membranes with 100–500 kDa cutoff to isolate *Lactococcus lactis* phage from main whey proteins in native whey. This yielded a reduction of phage by 3.7 log units using a 300 kDa membrane. On the other hand, polymeric membranes exhibit a low protein permeability of 50% with a filtrate flux of 120 L/(h m^{-2}).

Figure 2.4 presents a simplified schematic of a process for dairy processing to produce whey powder. The indicated stage presents the phase when phages are processed to be removed.

The "phage-free" whey is an important issue during the manufacturing of several whey products. In Michel et al. work [72], this problem is addressed. Bacteriophages are typically present in raw milk in levels up to 10^4 plaque-forming units (pfu) mL^{-1}. To obtain better bacteriophage removal (≥9 log units), an orthogonal process approach that is a combined version of various techniques that support each other was used.

In recent years, there have been a number of different studies on combining separation and purification techniques for bacteriophages in whey. One approach is to merge them in an orthogonal way, well known as hurdle concept or hurdle technology [73, 74]. An orthogonal process is characterized by the use of at least two different, independent techniques in such a way as to make the best possible use of the synergistic phenomenon. For whey proteins, UV light is used in combination with membrane filtration. To obtain satisfactory bacteriophage removal and the mildest possible treatment of whey, a process is proposed [72] that integrates two techniques: cross-flow membrane filtration followed by UV-C treatment or heat treatment. Consequently,

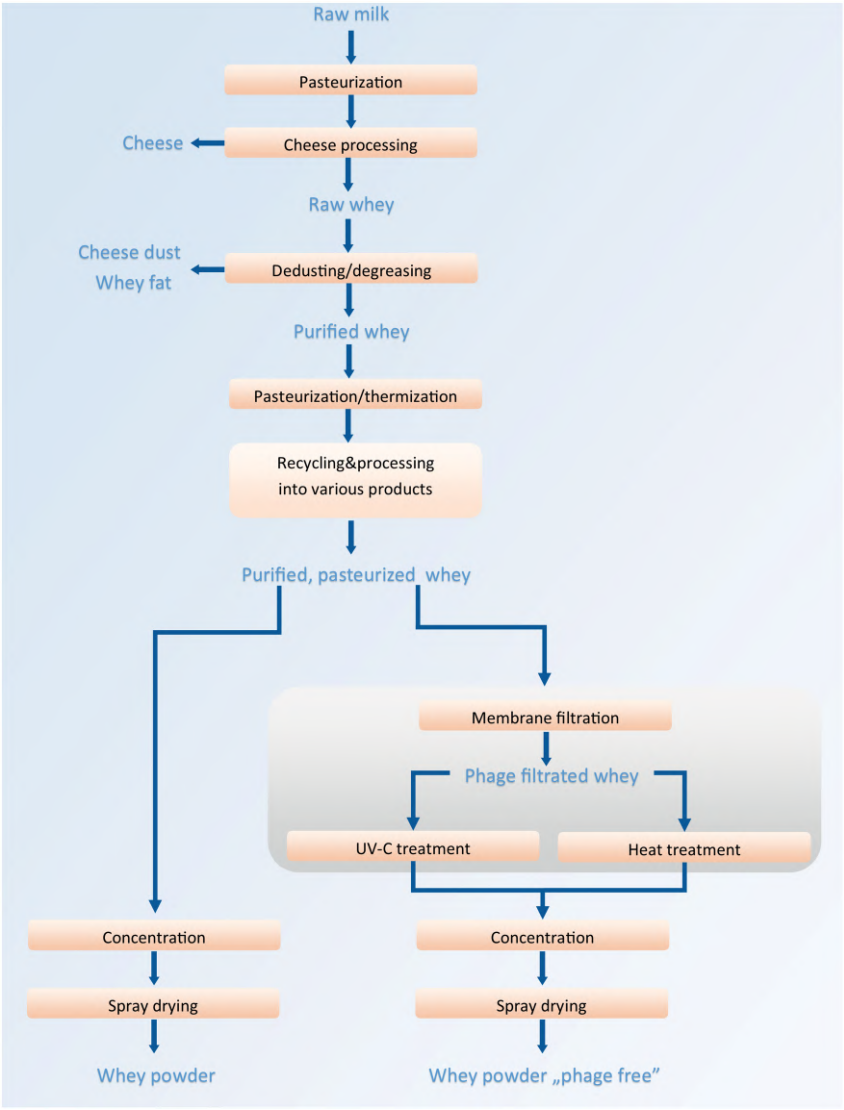

Figure 2.4: A simplified schematic of the cheese making process and the potential for further processing of dairy whey.

three common viral contaminants in dairy, i.e. *L. lactis* bacteriophages (P001, P008, and P680), which infect acidogenic starter bacterial cultures, were investigated in detail for their behavior during inactivation in filtered whey by UV-C treatment and heat treatment. Heat processing was found to be merely partially successful because the different degrees of heat resistance required, in the worst scenario, a temperature and time combination over pasteurization conditions. On contrary, UV-C processing

involved application rates of up to 2.25 J cm^{-2} for effective inactivation, thus providing a viable route to investigate the possibility of establishing a new "phage-free" whey production process.

Although there have been extensive research studies in the struggle to control phages over the years following their discovery, they remain a serious economic problem for dairy manufacturers. Effective approaches have been suggested e.g. phage-resistant strains, starter culture management, enhanced industrial design, and proper sanitizing measures, to maintain phages under general control. Yet, these remedies have not fully overcome the challenge, in part because of the continued evolution of phages and the conglomeration of the milk industry with growing dairy facilities operating huge amounts of milk each year [75].

2.6 Simulations and modeling concerned on membrane whey production

2.6.1 Fluid dynamics

One of the techniques that is used to perform an analysis based on calculations and simulations for the whey proteins ultrafiltration is computational fluid dynamics. CFD is a method applied to solve equations representing fluid flow through numerical methods. The use of this sort of approach gives the remarkable potential for studying flow phenomena, facilitates their better understanding, and at the same time provides an opportunity to optimize available solutions. For many years it has been implemented at the stage of developing new solutions as a tool reducing the development time of a product, enabling to outperform the competition not only in terms of time but at the same time on the degree of quality of the offered results. In most cases, sophisticated software is necessary to take benefit of the available potential. It enables to provide detailed results in a relatively short span of time even taking into account that quite high computational power is required.

$$\rho \frac{\mathrm{D}v}{\mathrm{D}t} = \rho g - \nabla p + \eta \cdot \left(\nabla^2 v + \frac{1}{3} \nabla \left(\nabla \cdot v \right) \right)$$

$$\frac{\mathrm{D}}{\mathrm{D}t} = \frac{\partial}{\partial t} + \left(v \cdot \nabla \right)$$

Although a number of components of membrane process are well-understood, the development of more productive membrane modules and the selection of optimal operational parameters is impeded by the absence of a well-validated and reliable model to depict this process: In other words, there is at present essentially no existing model that can forecast the whey sample filtration efficiency of a particular filtration

unit, based on quantifiable sample volumes and under different operating environments. Bottlenecks to address involve relying on single-dimensional or averaged models in forecasting a spatially inhomogeneous process, and the uncertainties concerning the nature and significance of filtration resistances, particularly mashing mechanisms. There are several reduced-dimensional (for example one dimension or surface-averaged) models that are widely used to characterize filtration processes. Among them are the film model, the gel polarization model, the shear-induced diffusion model, and the osmotic pressure model [76–78]. Although each is derived from a mechanistic process model, all of them depict process properties using space independent quantities (for example single whey concentration or surface area or amount of protein impurities). Two interpretations of this mathematical structure exist, the process is either one-dimensional (1D), implying that all characteristics in solution and on the membrane do not vary with the tangential position in the filtration channel or the values utilized in the study constitute variables averaged over the membrane region. For dead-end filtration, in which there is no tangential flow pattern over the length of the membrane, such reduced dimensionality models precisely reflect reality because there are no substantial mechanisms for the formation of uneven regions at the membrane area. In more industrially significant cross-flow filtration, however, the pressure drop over the length of the channel is driving the tangential flow to the membrane, resulting in changing conditions in the mixture and on the membrane surface at different locations. A previous study presented a comparison of permeate flux predicted using an area-averaged model for UF crossflow of bovine serum albumin with a comparative CFD calculation that accounted for spatial variations along the membrane interface [79]. Previous experiments and studies by Schausberger et al. [80, 81] showed that for all except the smallest transmembrane pressures, nonlinearities in the properties of the fluid suspension, such as osmotic pressure, viscosity, and diffusivity, resulted that area-averaged and 1D models considerably understated permeate flux relative to corresponding CFD calculations, and none of the mass transfer correlations needed by reduced-dimensional models seemed to be able to capture the resistance to filtration in the mixture (known as concentration polarization, or CP) computed by CFD models. Remarkably, all accessible mass transfer correlations ignore the effect of permeate flow into the membrane, rather they are strictly applied to the mass transfer of dissolved substances adjacent to the wall.

To study the UF process of whey proteins, mixture models are similarly used [82] to predict the concentration and velocity distribution of the solid in the vicinity of the membrane, in both dead-flow and cross-flow regimes. Because whey proteins have a reasonably dense globular structure, hard-sphere theory is employed to model solid suspension permeability and osmotic pressure: these features rely only on parameters that can be tested on an independent basis, like size and concentration of the protein. The model predictions appear to be in reasonable agreement with experimental results for both flow regimes, importantly in the lack of any complementary resistance models accounting for (for example) blockage of pores, superficial adsorption, or gel/cake

buildup. The authors concluded that when dead-end filtration is performed, the degree of flux drop is reasonably related to the thickness of the concentration layer and the peak concentration of solids reached the surface of the membrane. During cross-flow regime, advection of suspension from the bulk space in the direction of the membrane raises the flux of the permeate, especially along the membrane boundary. Modeling the system using simple two-dimensional geometry yields qualitative versus quantitative correspondence with the experiment, emphasizing the requirement to precisely grasp the system geometry to model concentration polarization (CP) phenomena effects. It is shown that filtration of whey proteins of industrial importance can be predicted and described by multiphase suspension modeling of a hard-sphere paradigm with the experimentally measured size of particles and provides the opportunity for improved optimization and UF system design for whey separation. Independent continuity and momentum balance equations for each component present (i.e., the fluid forming a continuous medium and the protein) are solved. Multifluid mixture models are the multiphase approach in the way that they incorporate explicitly the forces between and upon each of the components, i.e., for the case of ultrafiltration, the fluid-protein resistance and the osmotic pressure induced by the proteins. Authors summarize that the hard-sphere theory for the mixture model is shown to be predictive of experimentally measured permeate fluxes for whey ultrafiltration for either dead-end or cross-flow regimes, under conditions suitable for industrial applications. According to the authors applying the particle size measured in the modeling gives transient permeate fluxes that agree with the experimental data with an accuracy of 10% for dead-end filtration and agree with the reported published results for steady-state cross-flow filtration with an accuracy of 20%. These two discrepancies are close to the equivalent reproducibility of the experimental results. Importantly, the model accomplishes the aforementioned match with experimental results without considering any fouling-related resistances or using any variables that are not independently measured from the separation experiment.

2.6.2 Neural networks

The approach of assembling a model from two separate parts is presented in the work of Krippl et al. [79]. The authors present a model that uses a neural network in the first stage and a classical balance model in the second stage. The hybrid modeling was related to the classical mechanistic modeling method using stagnant film theory. The hybrid models were able to precisely predict flux and concentration within a broad range of both process parameters and product-purity relationships for a small number of training experiments. Considering these two elements in the approach to modeling was necessary to obtain accurate predictions. The stagnant film model was characterized by bigger errors and did not allow for the prediction of contaminant content because the basis of its calculations was only the main product. In addition, the hybrid

models created have very good interpolation capabilities and can be used for both prediction of multi-stage ahead flux and prediction of pollutants over time, which is seen as an important quality factor in many bioprocesses.

The submerged membrane bioreactor (SMBR) neural network model was presented by Yusof et al. [83] and modeled for cheese whey wastewater treatment by Çinar et al. [84]. The authors state that a typical neural network model cannot successfully be used to perform control actions predictions and control strategies creation. Accordingly, this work concentrates on formulating the SMBR filtration system process using the ANN-ARX (nonlinear autoregressive with exogenous input) time series simulation modeling technics, generally referred to as the nonlinear NARX model [85]. Such models are subsequently contrasted with linear ARX filtration modeling [86], an approach that is then used in the development of a control strategy for the membrane filtration process system. A proportional-integral-derivative (PID) controller was tuned for flux control to provide that process operating is as straightforward as possible for an industrial membrane bioreactor. There are two single-input single-output PID controllers designed for addressing two different strategies of control. The primary strategy is to control the permeate stream at the same time observing the behavior of the transmembrane pressure (TMP). The latter strategy is to control the TMP and observe the permeate flux. Finally, the simulation as well as actual experimental runs have been carried out for both these control strategies.

The potential use of artificial neural networks for whey desalination is presented in Kovács et al. work [87]. A neural network is considered to be part of mathematical modeling for whey filtration and is referred to as data-driven model. A numerical workflow for the simulation of whey diafiltration processes is presented. Both transport models and actual experimental datasets can be used without modifying the governing equations. The suggested routine can be used for various batch diafiltration approaches and for multicomponent solute systems. The authors recommended an empirical design that reduces the possibility of prior experiments to a minimum and allows us to obtain high-value information from the observed experimental data. Authors applied statistical models, such as response surface methodology, partial least-squares regression, and artificial neural networks tools to transform the raw data into information that is exploitable. The simulation strategy was verified on a series of experimental runs of the process under different diluent usage scenarios. It was found that there was quite good correspondence among the simulated and measured filtration datasets.

The newer researches [88] aim to develop a new LSTM-based fouling model to evaluate filtration efficiency and fouling growth. Experiments of filtration were performed to acquire training data of the model under variable water feed and working conditions. At the same time, the parameters and variables to quantify water quality variables and real-time optical coherence tomography images need to be prepared as input data to the LSTM model. While the suggested LSTM model demonstrated reasonable results under a variety of experimental settings, the proposed model

continued to exhibit small problems that still remain to be resolved. However, in order to be used as a general model for realistic real-world scenarios, the deep learning modeling technique for pollution prediction still needs considerable effort and continued development. Hence, it is proposed to consider additional operational scenarios and case studies to construct a more workable model in further research.

2.6.3 Balance approach

A balance approach refers to the mathematical description based on the equations formulated based on the mass and/or energy balances. Such a typical approach is used mainly to calculate fluxes and pressure drops and allows estimations of efficiency of membrane processes.

An equation oriented balance membrane ultrafiltration mathematical model for the whey filtration process was formulated in [89], and its associated parameters were quantified, and the model was statistically verified. The membrane blocking effect is included in the model as an auxiliary term, the phenomenon called membrane resistance, in addition to the mass balance equations. Finally, the impact of experimental conditions is represented by the variables of membrane flux and retention factor. A parameter fitting estimation task is addressed for the designed model by regressing the collected experimental results to the equations of the mathematical model. The statistical properties demonstrate that the proposed model has the potential to be applied for both control and estimation objectives. A comparison across three separate functions of static membrane resistance reveals that either the simple (polynomial) approach or the complex (logarithmic-exponential) approach do not achieve statistical trustworthiness when matched against the exponential static membrane resistance. Using the model built, a number of simulation tests were conducted to examine the model under stressed conditions. The initial simulation investigation checks the predictive performance of the developed model for rapid variations in feedstream concentration, whereas the latter shows that the timing approach strategy needs to be determined based on the operating profile of the pressure. The third simulation run indicates that given a sequential schedule strategy, the membrane (model) in question is able to be controlled with high performance, even for varying characteristics. While the fourth and fifth tests illustrate steady feed and pressure actions, the last test demonstrates that the model has the ability to be easily applied with varying performance characteristics. The simulation research demonstrates the prospective application of the membrane model to both optimum performance and scheduling scenarios.

A standardized model is presented [90] to characterize the time-dependent flux reduction during extended duration operation of whey UF processes. The model suggested is composed of three exponential decay patterns that account for the three phases of fouling: concentration polarization, protein deposition, and sediment

consolidation. Pilot-scale experiments have provided evidence to confirm the occurrence of these three phases. The empirical constant model values were estimated from the experimental data achieved in the whey ultrafiltration process on the pilot-scale system. The comparison of the values of the constants in the models evaluated for different process operating parameters, for example, TMP and feed concentration, can be used to identify their influence on the rate of permeate flux decline. Pilot-scale test setup based experimental data indicate that when proteinaceous sediment aggregation is prevalent, i.e., after several hours, the impact of TMP and feed concentration on the permeate flux decline rate is statistically negligible.

The authors conclude that a subsequent advantage of the designed unified model is the analogous character of the equation representing the fouling dynamics within the three phases. Besides the permeate flux absolute magnitude, the fouling dynamics are also able to influence the dynamic response behavior of the whey UF process. Because the unified model constants are essential functions of process operating parameters for example TMP, the unified model has the potential to be applied to identify the attainable efficiency of a regulator's automatic controls before designing the regulator. The impact of a long time fouling dynamics upon the attainable efficiency of automatic regulators is important, considering the operating duration of commercial membrane processes.

In view of the fact that TMPs and feed concentrations are independent of long-term fouling dynamics, to express the process dynamics by a time-varying model approach the convenient approach is to represent model coefficients as time-varying functions of time. In such a way the transient process model is represented as a transfer function, for example, the polynomial coefficients in both the numerator and denominator are defined as time-varying variables. According to and based on this time-dependent model of process dynamics, variations in attainable controller parameters at different fouling phases of the process can be examined. The model evaluated could be used to analyze the effectiveness of automatic regulators when developing and designing the control systems for the optimized whey ultrafiltration scenario.

2.7 Conclusions

The above examples demonstrate the widespread use of membrane techniques in the production of sports supplements. Both research work and the already applied technologies in the industry show that nowadays these processes are mature but there is still research to be done to improve the efficiency of these processes, mainly by eliminating the problem of membrane fouling and the need to remove bacteriophages. Hence the importance of research and development to improve the filtration performance of the membranes, to continuously improve the product quality and the environmental sustainability of the processes.

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3 Membrane applications in the food industry

Abstract: Current trends in the food industry for the application of membrane techniques are presented. Industrial solutions as well as laboratory research, which can contribute to the improvement of membrane efficiency and performance in this field, are widely discussed. Special attention is given to the main food industries related to dairy, sugar and biotechnology. In addition, the potential of membrane techniques to assist in the treatment of waste sources arising from food production is highlighted.

Keywords: dairy; fermentation broths; membranes; sugar.

3.1 Introduction

Membrane technology is well established in many areas of industry and everyday life. The materials presented here as well as numerous reports in the literature, including those from professional specialist journals, confirm the still dynamic development of membranes in many areas of industry, also in the food processing. It is assumed that about 30% of the membranes produced are used in the food industry [1]. As shown in Figure 3.1, both the purpose of membrane techniques and their application to specific food industries are very diverse. It should be noted that the examples given are not exhaustive of all membrane applications in this area.

It should be noted here that the food industry is a brunch of business with a high financial turnover which is extremely resistant to both economic and, for example, pandemic turbulence [2, 3]. Whatever the situation, to provide food is to provide for people's basic needs. Hence, food production and processing is a branch of the economy with high growth potential. On the other hand, more and more attention is being paid to the quality of food products produced. The society with a growing awareness of leading a healthy lifestyle expects from food producers products with preserved taste and nutritional values. It should be emphasized that this trend related to the rational use of food and its consumption is reflected, among others, in the 17 UN Sustainable Development Goals (SDGs) [4]. In this plan, which aims at sustainable global development for present and future generations, point 2 (SDG-2) focuses on food

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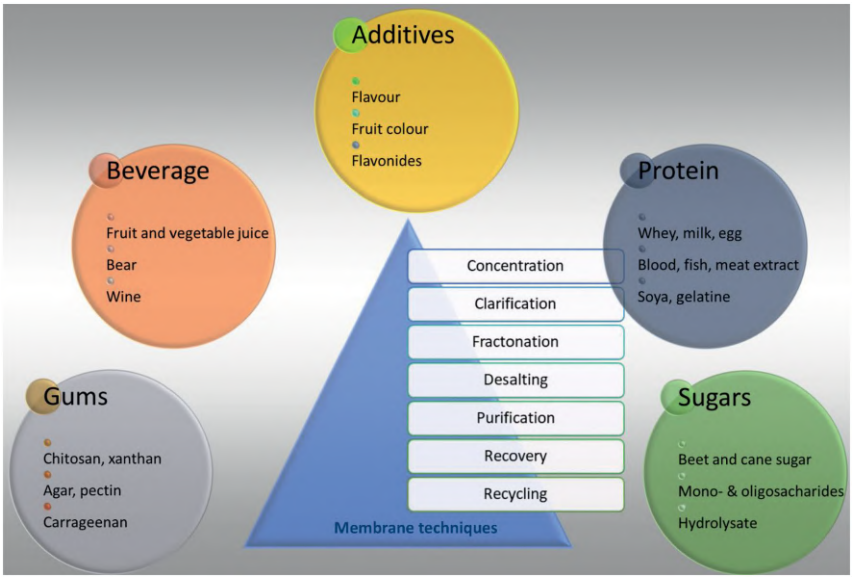

Figure 3.1: Membrane techniques in food industry.

security and nutrition. It mentions aspects such as aiming for zero hunger, realizing food security, removing malnutrition in all its forms and promoting sustainable agriculture. In addition, paragraph 12 (SDG-12) points to the need for responsible production and consumption. Thus, both producers and consumers should focus on achieving these goals through changes in food production, global nutrition and health [5]. On the other hand, producers expect the technologies used to be efficient and low-cost. If the need to adapt to increasingly stringent environmental requirements is taken into account [6], membrane techniques can be also and are an interesting alternative to many conventional methods of food production and waste water treatment [7–9].

Especially in food production it is important to maintain sterile production conditions [10], hence the food industry has been a driving force for the development of non-polymeric membranes such as ceramic ones. These membranes ensure that they can be sterilized at high temperatures and with a range of chemical reagents [11]. The introduction of ceramic membranes has, in many cases, allowed a significant expansion of the use of these membranes in the food industry.

The aim of this work is to present research directions and applications of membrane techniques in such agro-food industries as sugar production, dairy products and recovery of valuable components from fermentation broths. Furthermore, the issue of post-production waste water treatment will be discussed.

3.2 Sugar industry

Despite the existing trend to reduce sugar consumption, this product is widely used by food manufacturers and consumers (Figure 3.2). The current level of sugar production worldwide is estimated at 166.2 m t per year, with total annual consumptions worldwide on the level about 177.8 m t [12]. Of course, depending on the region, the source of the product may be different, but mainly sugarcane or sugar beet.

In general, the sugar production stage consists of cleaning the harvested crop and extracting the sugar from the cells to obtain the raw juice. Here, depending on the source of origin, the sugar is washed out with hot water or pressed out of the cells for beet and cane, respectively. The next stage is purification and clarification (to about 17–21 °Brix) of the raw juice to the thin juice and its concentration and finally crystallization. Schematically these processes, depending on the origin of the sugar (cane or beets), can be illustrated as in Figure 3.3 [13]. Sugar production is one of the most energy-intensive processes in the food industries, of which water evaporation accounts for the largest share of energy consumption, approximately 50% [14]. Therefore, novel solutions with reduced energy requirements are constantly being sought. Membrane techniques, known for their energy saving advantages, as well as for their ability to concentrate, are an excellent option. Work in this area appeared as early as the 1980s and 1990s, mainly on the application of membrane filtration to the purification of raw juice [15, 16].

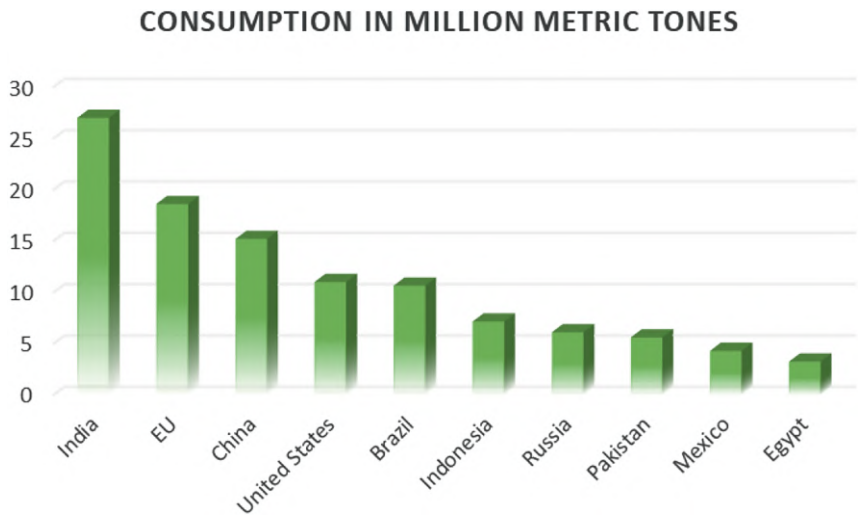

Figure 3.2: Consumption of sugar in 2020 (https://www.statista.com/statistics/887349/india-sugar-consumption-volume/).

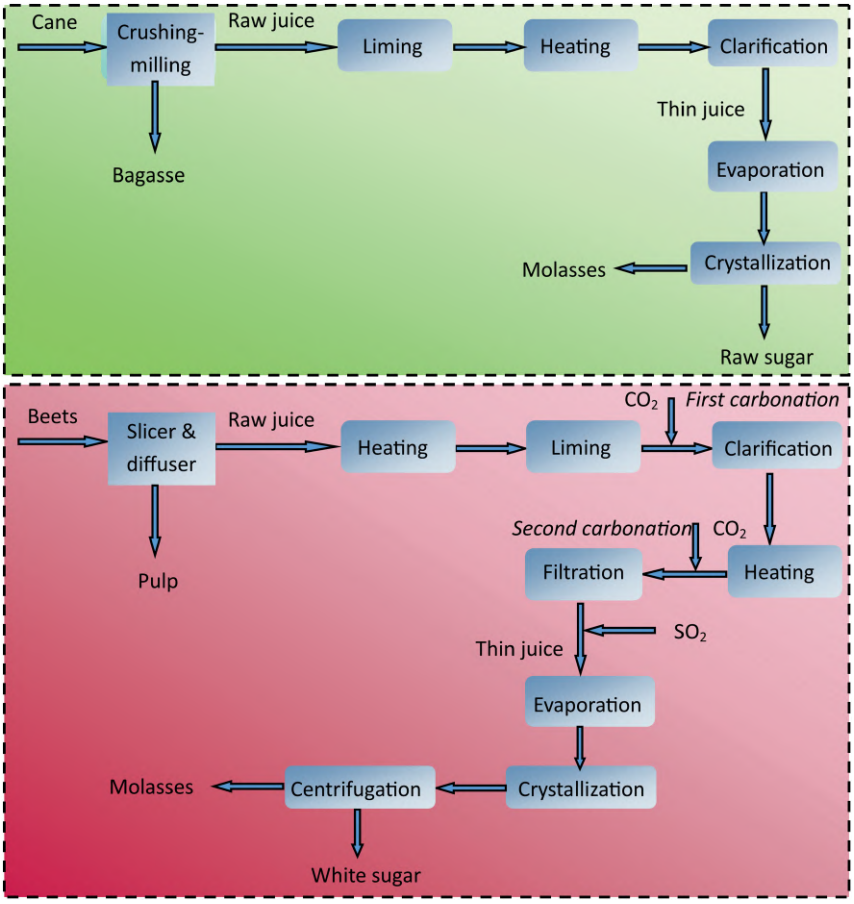

Figure 3.3: Schema of sugar production.

Membrane processes are especially recommended, as is presented in Figure 3.4, for sugar juice clarification as well concentration where the expensive evaporation step (the conventional technology) is omitted. However, a major limiting factor for the use of membranes in sugar production is the high osmotic pressure and high viscosity of the raw juices. In this case, a very interesting alternative to evaporation is membrane distillation (MD) due to the lower operating temperatures in comparison to the conventional distillation and consequently a reduction in energy consumption. This makes the method particularly suitable for heat-sensitive foods. As was presented by Nene and co-workers [17] it is possible to use MD concentration of raw cane-sugar syrup obtained from the sugar mill directly after Dorr filtration (clarified solution with 20°Brix) using polypropylene membrane. Despite obtaining satisfactory performance of sugar juice concentration at laboratory and semi-technical scale, there are still some

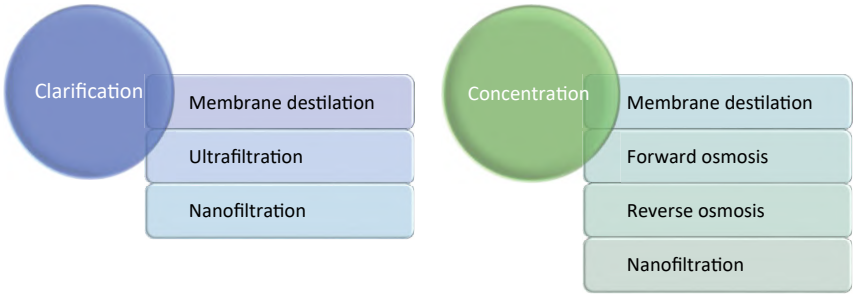

Figure 3.4: Membrane techniques in the sugar industry.

serious drawbacks limiting the use of membrane distillation technique in industrial practice [18]. These are mainly temperature polarization and membrane fouling. Both phenomena significantly limit the efficiency of the process by decreasing the flux due to a decrease of the driving force of the process (differences in temperature at the membrane surface and in bulk phase in case of polarization) and mechanical fouling of the membrane (decrease in permeability). Therefore it is important to find membranes with long-lasting wetting resistance, hence the proposals for membranes made not only of polymers. Additionally a pre-treatment is possible in order to remove e.g. suspended solids. Unfortunately, this makes it necessary to invest in further treatment processes, such as micro- and ultra-filtration. To solve the problem of membrane durability, especially of polymeric membranes, besides ceramic membranes, metal membranes e.g. made of alumina are proposed for sucrose concentration. Base on vacuum membrane distillation (VMD) process hydrophobic alumina hollow fibre membranes allow to sucrose concentrate from 10 to 50°Brix.

For the purification of raw sugar juice, membrane filtration processes, including micro- and ultra-filtration using ceramic membranes, are the most modern solution both in the laboratory and in pilot plants. As was shown by Hinkova and co-workers juice treated in MF and NF processes achieved such quality that directs crystallisation was possible [14]. To avoid the fouling process many authors proposed modification of membrane materials. For example functionalization of ceramic ultrafiltration membranes by lanthanum phosphate coating allow to sugarcane juice clarification [19]. Such membrane has got hydrothermal stability, as well as chemical resistance. Also the combination of UF and NF achieves the desired clarification, decolouration, and pre-concentration of raw sugarcane juice targets. Proposition of Leo and co-workers based on integrated membrane process consisting of a tubular loose UF, a spiral-wound tight UF and a spiral-wound NF at pilot-plant scale [20]. As was presented by the Authors such solution allow to obtain about 96.5% reduction of colour and 99.99% of turbidity with 45 days of stable installation work.

A relatively new proposal for membrane techniques used in practice is forward osmosis (FO). Some examples are presented in Table 3.1. There are several factors

Table 3.1: Forward osmosis applications in sugar production.

Operation conditions	Results	Ref.
Feed: UF pre-treated (clarified) raw sugarance juices (11.4°Brix, turbidity 5.5 NTU) Membrane: Aquaporin HF FO, polyamide active layer with integrated aquaporin proteins, 13,000 fibres Conditions: Juice in shell side, draw solution (NaCl 100 or 200 g/L) in lumen side, temp 25 °C, flow rate: feed 25 L/h, draw 25–45 L/h	– 7% higher water flux in counter-current flow configuration in comparison to co-current between FS and DS was – In optimal conditions (both flow rate 25 L/h and DS concentration 100 g/L) concentration up to 60% of initial concentration in 12 min	[24]
Feed: Sugarcane juices (up to 1.65 M sucrose) Membrane: Flat sheet of cellulose acetate or aromatic polyamide membranes Conditions: Counter current crossflow (both solution run in a closed loop), draw solution ($NaCl_2$ or 4 M), temp 20 or 30 °C, flow rate: 1 L/min	– –Concentration factor of 5.7 (2.5 higher in comparison to RO) – Final concentration up to 56.4°Brix – Effect of salt concentration and temperature is observed	[25]
Feed: Raw sugarcane juice, filtered before through 100 mesh size sieve Membrane: Aquaporin polycarbonate HF FO Conditions: Draw solution (NaCl 100 g/L) with flow rate 25, 35, 45 L/h, feed solution 25 L/h, co-current and counter-current mode	– Parameters, such as draw solution flow rate, sugarcane concentration, flow configuration between DS and FS influence the process efficiency	[26]

supporting the use of FO for the concentration of sugar juices or other juices (fruit, vegetable). First, FO can be an alternative to pressure-based processes including reverse osmosis (RO). This is particularly important when the osmotic pressure of the solution is very high (e.g. >80 bar). In this case, the use of classical RO, in which the operating pressure must be higher than the osmotic pressure, would be very expensive. The use of lower pressure also results in significantly lower energy consumption [21]. On the other hand, it should be noted that the cost of an FO-based plant currently exceeds the capital expenditure compared to conventional thermal processes. This is mainly due to the cost of the furnaces themselves. Additionally, studies have also shown that the fouling problem due to organic contamination in FO is comparable to NF/RO [22]. However, it should be kept in mind that this is a relatively new technique and the currently high costs should be significantly reduced with the development of commercial FO membrane production [23]. Such a trend is observed for each of the membrane techniques used in industrial applications. For example, the now commonly used RO for desalination water was considered a very expensive technique in the 1980s.

Numerous patents also point to the possibility of recovering sugar from molasses using membrane filtration. In US Patent [27] inventors from Tate & Lyle, Inc.

demonstrated the usefulness of nanofiltration in process for purification of low grade sugar syrups, such as molasses (composition sucrose and no less than 2% w/w invert sugars or no less than about 3% w/w embodiments). In this solution NF with 150–300 Da membrane shall be preceded by preliminary purification using microfiltration or ultrafiltration. The permeate form these processes could be directly filtrated in NF, while retentate contains about 50% of colloids, polysaccharides and colour-forming materials. Optionally, diafiltration process can be also used. In NF through membrane invert sugars permeated, whereas retentate contains sucrose which can be crystalized. Similar solutions with combination of UN and NF process for production sucrose from sugar beets and sugarcane are presented in patents [28] and [29], respectively.

In addition to supporting membrane technology for the direct production of sugar from raw sugarcane solutions, the extraction of sugars from other sources is an interesting proposition. An excellent example of this is the recovery of sugars from the conversion process of lignocellulosic biomass into chemicals and fuels by nanofiltration [30]. By using NF process to remove sugar and possible hydrolysis degradation products (i.e. acetic acid, furfural, 5-(hydroxymethyl)furfural), it is possible to run the biomass hydrolysis process continuously. From the lignocellulosic materials fermentable sugars for ethanol production can be obtained in acid-hydrolysation process [31]. In this process, it is necessary to separate these inhibitors from sugars or to reduce their concentration before the fermentation process. The removal of acetic acid while thickening the sugar is proposed in this process in contrast to the process above. The authors compared NF and RO membranes showing a much higher potential of RO membranes. For this process, a combination of NF modules with three RO modules was also proposed [32]. After remove the lignin by adsorption using activated carbon, multistage NF and RO allowed obtaining increase in total sugar concentration from 48 to 227 g/L in NF process (volume reduction factor 5, pH 4.3 and 500 psi) and acid concentration from 10 to 50 g/L in RO process (pH 4.3 and 500 psi). As presented in Ghazali and Razak review [33], membrane techniques, especially nanofiltration, are a promising alternative for the detoxification and purification of lignocellulosic hydrolysate from undesirable inhibitors. In conclusion, the authors pointed out that the efficiency and selectivity of the NF process depends mainly on the membrane material as well as on the process conditions (pressure, temperature, feed concentration and pH). The problem of membrane fouling was also pointed out.

It is worth emphasising that the use of membranes in the purification and concentration of sugarance juice is no longer just laboratory or semi-technical research. Ready-made solutions are already available on the market. This shows that the laboratory work, which started in the 1980s, was an excellent basis for the industrial solutions that have already been developed and are still being modified. For example, a Chinese company Jiangsu Jiuwu Hitech CO., LTD [34] offers a set of ceramic ultrafiltration and nanofiltration membranes (total length: 500–1200 mm, pore size: 500/200/100/50 nm) for purification, concentration and decolouration.

3.3 Dairy industry

Because the dairy industry, like all food industries, requires sterility, membrane techniques are a perfect fit in these needs. It is assumed that most membranes in the food industry are used in the dairy industry, mainly for separating components such as lactose, proteins, fat and salts from milk and its intermediate products [1]. Today membrane techniques in the food industry are already well-stablished supporting methods. For example, as early as the 1970s, ultrafiltration was used in New Zealand to concentrate whey proteins and produce whey protein concentrates (WPC) [35]. Particular attention should be paid to membrane filtration techniques, including microfiltration, MF. These techniques are textbook methods for the membrane separation of microorganisms and bacteria. Moreover, the membrane techniques are an alternative to the classical methods of preserving dairy products, such as pasteurization. Very detailed data on the experimental milk filtration results, including process parameters and properties of the obtained milk fractions, are presented in the paper [36] and stored in the INRAE public repository (https://www6.inrae.fr/cati-icat-atweb/Ontologies/Microfiltration) [37].

MF allows to reduction of bacteria and spore in fresh milk and to production extended shelf life milk, known as ELS milk [38]. This milk is characterized on the one hand by the taste of fresh milk, but has a longer shelf life of around 20–25 days. This is considerably longer than the shelf life of ordinary pasteurized milk, which is around 4–8 days. The use of the microfiltration process makes it possible to effectively reduce the number of bacteria as well as ensures stable operating conditions. As was presented in work [39] using ceramic membranes it is possible to minimalize the amount of microorganism per millilitre from 160,000 to less than 10, with 20 h working time without any intermediate cleaning procedure. Authors of citied work also concluded that the cost of MF process is lower in comparison to the UHT unit in production of ELS milk. Investment costs: 600,000–1,000,000 EUR for the same capacity 25,000 L/h; running costs (emerging, cleaning, etc.) 0.1–0.7 ct/L with similar maintenance costs (25,000 EUR/year). In summary, the total cost of ESL milk production is 0.15–0.4 ct/L for MF process and 0.9–1.5 ct/L for UHT process. Microfiltration support in ELS milk production is already a firmly established practice in dairy processing companies. Ready-made filter sets have been available on the market for several years, for example SYNELCO LTD Technical and Commercial Company [40], REDA Food Processing Plants [41], ELIQUO protect [42]. Moreover, in industrial practice microfiltration is commonly used to fractionate of milk proteins: casein micelles (as retentate) and serum proteins (as permeate) [36]. After the MF process retentate is applied to enrich vat milk for cheese production, while permeate (with the composition serum proteins, lactose and minerals) could be used for the production of protein-rich concentrate for infants and seniors (mainly using ultrafiltration).

Bacteria and spore reduction is necessary also in cheese production. Thus cheese production today cannot do without membrane techniques. An excellent example is Iranian cheese, which even in the aisle has reference to membrane techniques – Iranian ultrafiltration Feta cheese. It is the most widely consumed cheese in Iran, made from bovine milk with 3.8% fat [43, 44]. The milk is retarded to 35% total solids and then rennet is supplemented. The end product is a soft cheese with a content of 60% moisture, 16–22% fat, and 1–3% salt. As was presented by Jalilzadeh et al. [45] typical ultrafiltration conditions were: membrane with nominal molecular weight cut-off of 20 kg/mol, temperature 50 °C, inlet and outlet pressures of 530 and 170 kPa, respectively. It should be noted that UF is commonly used in the production of other cheeses as well. Ultrafiltration, thanks to its ability to remove water, lactose and certain minerals from milk, allows concentrated retentate to be obtained. It has thus become possible to standardise cheese production by uniformity the composition of the milk, creating a firmer gel structure. Moreover, by supporting ultrafiltration, it is possible to reduce the loss of casein to whey and, overall, to increase the efficiency of the process of cheese production [46]. This method has a long dairy tradition. It was first investigated by Maubois, Mocquot and Vassal in the 1960s and was named after its inventors "MMV process" [47].

In summary, depending on the membrane filtration technique used, other dairy products can be obtained. A summary of the most important ones is shown in Figures 3.5 and 3.6. As is presentenced in schemas, both UF and MF reserve the possibility to obtain a widely range of dairy products and their derivatives. Very detailed data on microfiltration of milk are available at website [37] a described at the work [36].

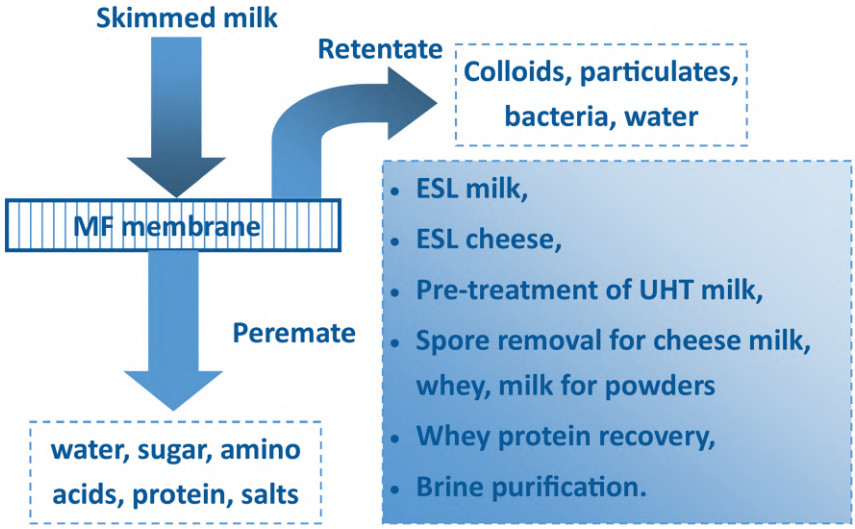

Figure 3.5: Microfiltration process in dairy industry.

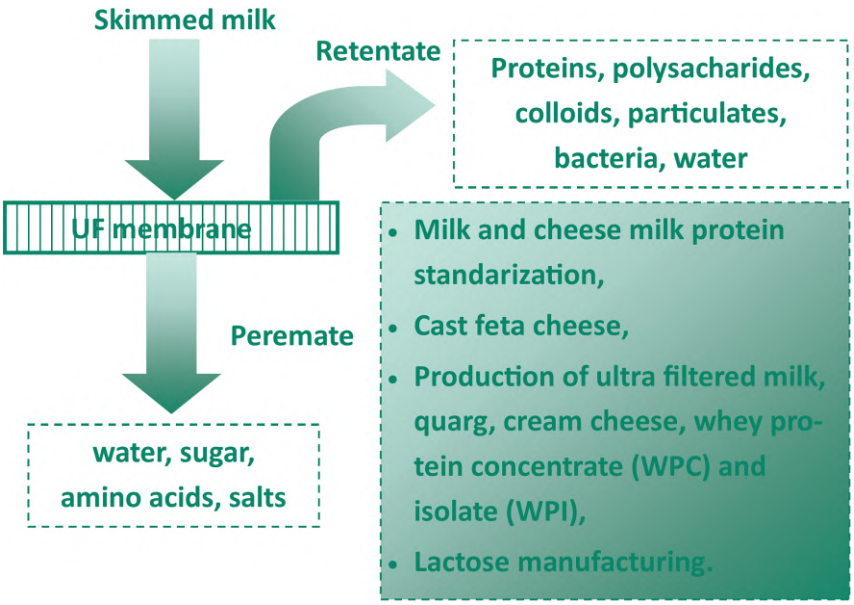

Figure 3.6: Ultrafiltration process in dairy industry.

In the dairy industry, however, the most common solution is to use different membrane techniques as a process sequence, as shown in Figure 3.7. Such combinations allow to obtain several product, for example milk for drink (i.e. ELS milk), concentrated and powder milk, as well as whey, whey protein concentrate and isolate, lactose. This shows how technologically important membrane techniques are in the dairy industry.

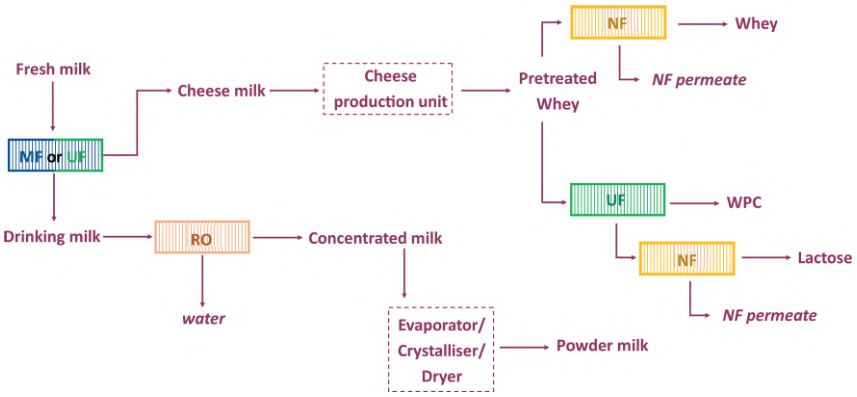

Figure 3.7: Exemplary schema of membrane techniques allied in diary industry.

The most important problem when using membranes in lactic acid applications is their fouling due to the presence of large quantities of both organic and inorganic foulants. Because skim milk contains high amount of protein, during ultrafiltration (see Figure 3.5) the concentration polarization layer forms within seconds [48]. Moreover biofouling due to the aggregation of microorganisms is observed [49]. Therefore, in industrial practice it is necessary to interrupt the filtration process in order to implement the clean-in-place (CIP) procedure. Numerous sources indicate that the cleaning process is usually carried out after 2–8 h of operation [1, 50–52]. Consequently, the main focus in improving performance of dairy production is to develop membranes with antifouling properties. Barclay et al. [1] successfully proposed polyzwitterionic antifouling coating of polyethersulfone membranes. However, the authors pointed out that the stability of the membrane should be improved. Moreover, because fouling problem is so important, a great deal of research is being conducted into cleaning methods, including the selection of suitable cleaning agents and process conditions [51–53]. Additionally, as Rabiller-Baudry et al. work shows [51], the degree of fouling depends to a large extent on the age of the marina as well as the way it is used. Here the use of chlorine deserves special attention as it can contribute significantly to a faster ageing of membranes. As was noted in work [52] the problem of fouling could be solved by adjusting appropriate filtration conditions. For example the filtrate flux of skim milk strongly depends on the temperature, and it is higher at 42 °C in comparison to 12 °C (probably due to lower filtrate viscosity).

It should be noted that in addition to classical filtration methods, membrane distillation is also proposed for the dairy industry [54]. Such solution allows obtaining good separation between protein and lactose, with a relatively high protein content and low lactose retention. Membrane distillation could be also applied in milk powder production [55]. In this case, the use of MD is supported by the well-known lower energy consumption compared to conventional pre-concentration methods before powder production (reverse osmosis and evaporation). It should be noted here that the production of milk powder is highly energy intensive and accounts for about 15% of the total energy consumption in the dairy industry [56]. The same MD method is proposed also for skim milk and whey processing [57]. Moreover, with the recent development of forward osmosis, the literature also proposes the use of this technique in dairy processing, mainly as a concentration process [58–61] or for treatment of effluents from the process [62, 63]. For comparison purposes, the paper [59] discusses the differences between forward osmosis (FO), reverse osmosis (RO) and pressure-assisted forward osmosis (PAFO) in the concentration of skim milk in the lab scale. The results presented indicated that intensity of protein fouling increased in the order FO<PAFO<RO, while critical fluxes for FO and RO were similar (regardless of the nature of pressure – hydraulic or osmotic). As the results obtained and described in the literature indicate the high potential of FO, in addition to laboratory studies, work on a much larger scale can also be found. Pilot forward osmosis filtration system (maximum volume capacity 250 L, spiral-wound cellulose triacetate membrane with 24 m^2 total active surface area

of filtration) was successfully tested in concentration of cheese whey: concentration factor 2.7, change the total solids content of whey from 6.5 to 18% [61]. In lab scale it is possible to obtain much higher concentration factor, up to four for sweet whey samples [60]. As the results of FO application in diary industry are encouraging, a response is expected from dairy companies. As described, a Fonterra company from New Zealand is considering replacing UF with FO in milk concentration [64]. This aspect is very important due to the peculiarities of New Zealand. Due to the relatively low population density, dairies are usually located at a considerable distance from milk producers. Thus, increasing the concentration of milk at source significantly reduces transport costs.

3.4 Recovery of valuable components from fermentation broths

Conversion of organic molecules by fermentation is now a desirable method, and its implementation particularly relates to the production of antibiotics, enzymes, bioethanol and organic acids. Production sector in which biotechnological processes are strongly developed is distillery. In the chapter "Membrane techniques in the production of beverages", membrane solutions for dealcoholisation were presented, while fermentation broths can also be a source of other important components. The bioethanol can be produced from renewable materials such as corn, sorghum, cellulose, and algae biomass. However, for starch and lignocellulose biomass pre-treatment is a necessary step to make the carbohydrates in the biomass accessible for conversion. The production of bioethanol from lignocellulosic biomass requires an additional step to separate the cellulosic component from hemicelluloses and lignin (e.g. treatment with water at high temperature and pressure, hydrolysis with ammonia, organosolv process). In such form, the biomass can be subjected to enzymatic hydrolysis. In the lignocellulosic biomass, the pre-treatment biomass is hydrolysed into glucose by *cellulases*, and after that the remaining lignin is separated from the mash and transported to the high gravity fermentation [65–68]. In this process, accumulated glucose reduces the activity of *β-glucosidases* and, consequently, causes the accumulation of *cellobiosis*. Moreover, the bioethanol production by cellulose, lignocellulose or starch fermentation is a process in which various inhibitors create during the pre-treatment stage, especially at high temperature hydrolysis or after contact with reactive chemicals. The amount and the type of inhibitor depends on the used biomass e.g. organic acids are products of hemicellulose degradation, while glycolaldehyde, furfural, and hydroxymethylfurfural are formed, when pentose and hexose sugars degrade. The aromatic compounds (i.e. vanillin, vanillic acid, syringaldehyde and ferulic acid) and aliphatic carboxylic acids (i.e. acetic, formic and levulinic acids) mainly occur when lignin degrades. Also, the low concentration of sugars in the pre-hydrolysates and

hydrolysates may not only reduce the ethanol concentration, but also increase the operating costs in the subsequent purification process. Interestingly, although high concentrations of furfural and hydroxymethylfurfural strongly inhibit the fermentation process and limit ethanol production, their low concentrations can improve sugar bioconversion. In the case of the ethanol fermentation from starch-based biomass, after liquefaction, the mash is cooled and, if necessary, supplemented with *glucoamylases* to hydrolyse the dextrin to fermentable sugars. If sufficient sugars are released during liquefaction, the process does not require pre-saccharification. In this conversion, the ethanol inhibitory effect is mainly observed [69, 70]. The use of a preparatory stage enabling the fermentation process to be carried out makes the bioconversion following two process paths: separate or simultaneous pre-treatment and fermentation [65–68, 71–74]. The sequential production system has a greater potential for membrane systems. This process flow has also the great advantage that both hydrolysis and fermentation can be optimized independently, while the inhibitory effect of the by-products is easily eliminated when the processes work together.

Microfiltration, ultrafiltration, nanofiltration and reverse osmosis are the most often tested membrane systems for detoxification of hydrolysates and concentration of sugar due to their unique ability to separate and purify process streams. The nanofiltration technique was tested for their ability to separate monosaccharides from furfural [75]. Earlier studies also indicated that nanofiltration technology can effectively concentrate sugars in the hydrolysates. Liu et al. [76] applied membrane with a molecular weight cut-off of 100 g/mol. In addition, to the concentration of sugars and polysaccharides, the removal of inhibitory compounds such as furfural, acetic acid, methanol, and formic acid from the sugar stream was carried out. Sjöman et al. [77] tested membranes with a molecular weight cut-off of 150–300 g/mol for xylose separation from glucose in different hemicellulose hydrolysates. Moreover, the results indicated that using the membranes glucose and other hexoses were retained more than the pentose and xylose. Weng et al. also tested the Desal-5 DK NF membrane and they showed that at the optimum temperature the membrane could effective concentrate sugars in the hydrolysate [78]. Nguyen et al. [79] also showed that nanofiltration membranes are more suitable for detoxification of lignocellulosic hydrolysates than reverse osmosis membranes. The semi-aromatic piperazine amide type membranes produced by Dow FilmTec and DK were particularly effective in detoxification, exhibited high sugar rejection and inhibitors carryover up to 80%. For example using NF270-2540 module the rejection of glucose, xylose and arabinose was 97, 87 and 92%, respectively. This module gave also high transmission of formic acid (90%), acetic acid (88%), furfural 98%, hydroxymethylfurfural (96%) and vanillin in 89%. The research has also shown that the hydrophilicity of sugars is partly responsible for their rejection, and the hydrophobicity for the aromatics transmission. Nguyen et al. also tested RO membrane (SUL-G10), which revealed higher sugar rejection of 99% but inhibitor removal was lower than expected (formic acid in 55%, acetic acid in 50%, furfural in 55%, hydroxymethylfurfural in 26% and vanillin in 16%) [79]. Further works aimed at

pre-industrial tests [80]. The tests have shown that the NF270-2540 membrane allowed satisfactory glucose rejection but less detoxification, e.g. vanillin passed up to 15% more than in preliminary tests. Diafiltration, regardless of the type of the tested membrane, allowed reducing the concentration of inhibitors below the critical level. The fermentation products confirmed that the overall glucose and xylose consumption rate in the diafiltered retentate was consistent with the process assumptions. Conversely, the conversion of glucose to ethanol was much more efficient than indicated by preliminary experiments. The tests have shown that the NF270-2540 membrane allowed satisfactory glucose rejection but less detoxification, e.g. vanillin passed up to 15% more than in preliminary tests. These studies were carried out using the pilot plant which scheme is illustrated on Figure 3.8. In another tests commercial NF (Desal-5

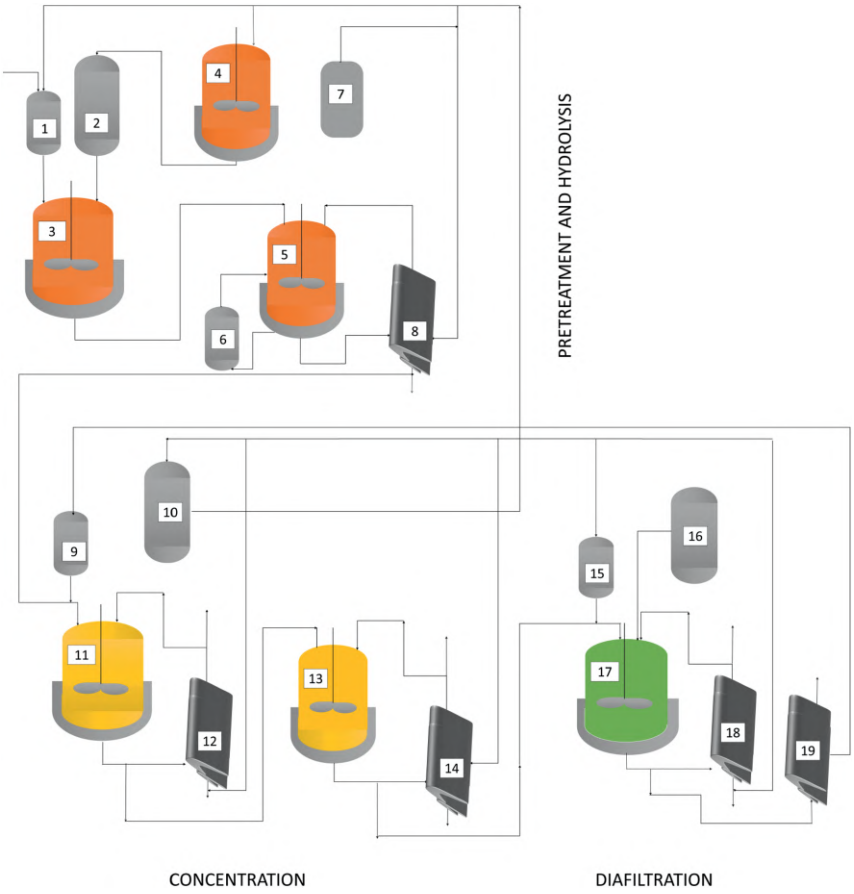

Figure 3.8: Bioethanol production from lignocellulosic hydrolysate: (1) Enzyme storage vessel, (2) biomass storage tank, (3) enzymatic hydrolysis reactor, (4) tank with acid pretreatment, (5), (11), (13), (17) feed tanks, (6) solid–liquid fraction separator, (7) cleaning solution, (8) MF/UF module, (9), (15) soluble anionic polymer vessel, (10) recycle water tanks, (12) NF module, (14), (18) RO module, (16) RO water tank, (19) UF module.

DK and Alfa Laval-NF) and RO (RO98pHt and RO99) membranes were considered for the separation furfural and hydroxymethylfurfural from hydrolysate solutions containing also glucose and xylose during sugar concentration process [81]. These results indicated that for removal of furfural and hydroxymethylfurfural significantly better nanofiltration compared to reverse osmosis was found. However, sugar loss was much higher during NF, which is unacceptable due to the low sugar concentration in the hydroxylates. The comparable results Lyu et al. obtained using the two-stage nanofiltration process to fractionate hydrolysates into glucose concentrate, monophenols and cyclopentenones concentrate, and acetic acid permeate [82]. Microfiltration is not a recommended technique for such system; however it can be used as pre-treatments before nanofiltration process to increase the separation performance of sugars from inhibitors [83]. Another option is forward osmosis, however, this type membrane was more adequate for concentration of the sugars than the NF membrane but less efficient for inhibitors [84]. Qi et al. [85] demonstrated the feasibility of recycling cellulase and concentrating glucose from lignocellulosic hydrolysate by a two-stage membrane process with combination of UF and NF. It was indicated that recycling of *cellulase* by ultrafiltration could reduce the costs of enzymatic hydrolysis of biomass, while the use of nanofiltration immediately after this stage to concentrate sugars could effectively improve the fermentation efficiency.

Membrane distillation has also been used to concentrate sugar solutions and remove inhibitors. The rejection of sugar can almost achieve 100%, also the furfural can be removed completely [86]. However the most interesting results obtained using vacuum membrane distillation (VMD). This technique has higher rejection for non-volatile components and can be carried out at low temperature; therefore it was tested for the glucose rejection [87]. In the case of acetic acid and furfural as temperature increased to 70 °C, the removal with VMD increased to 76 and 96%, respectively [88]. A more environmentally friendly membrane technique is pervaporation. Energy consumption for pervaporation was at least 70% lower than for classical distillation. This technique is characterized by high detoxification property. For example, the polydimethylsiloxane membrane with flux of 3223 g/m^{2}h allowed to achieve permeate with concentration of furfural 62.4 wt% [89]. In another study Cai et al. [90] implemented polydimethylsiloxane membrane for furfural removal from sweet sorghum hydrolysate pre-treated with dilute acetic acid. The process was quite effective, at 65 °C furfural is removed with flux of 1057 g/m^{2}h and with selectivity of 66, while at 37 °C, the selectivity was 39 and the furfural flux reached value of 116 g/m^{2}h. Finally, the 6.5 h pervaporation led to the decrease in the furfural concentration from 10.4 to 0.6 g/L, and the permeate concentration reached 138 g/L. The separation of toxic components such as phenols and furfural from biomass hydrolysates via pervaporation was also studied by Ghosh et al. [91]. However, in the case of furfural the modified polyurethaneurea membrane was found as a selective but with average efficiency material (selectivity 284 with flux of 41.5 g/m^{2}h). In another study the ultrafiltration with vinyl-modified polydimethylsiloxane membrane at 65 °C exhibited a furfural flux of 738 g/m^{2}h and

separation factor of 49 [92]. In order to improve the separation efficiency, another technique was proposed which was a compilation of gas stripping and vapour permeation (GSVP). In this the polydimethylsiloxane membrane was found to achieve not only very high permeate concentration (71 wt%) and furfural flux of 4.1×10^3 g/m^{2}h, but also separation index 2×10^5. Moreover, GSVP is less energy-consuming than PV [93].

After fermentation, bioethanol can be separated from the fermentation broth by various methods. Among the membrane technologies, pervaporation was most often studied for the separation, purification and dehydration of ethanol [94, 95]. Moreover, it has been shown that pervaporation with high selectivity in the water–ethanol system and effective solvent dewatering can significantly reduce the costs of bioethanol production. The selectivity and production cost of the membrane depend on its type. In the separation of ethanol–water azeotrope, a low cost hydrophobic membrane (polymeric) leads to obtain ethanol permeate, while hydrophilic membrane (e.g. ceramic) allows for selective water penetration [96]. Kang et al. [97] compared the pervaporation processes with molecular sieves and with hydrophilic PV membrane (e.g. BW30XLE, Dow Filmtec). The results showed that molecular sieves with a high potential for the production of anhydrous ethanol (>99.5%), can be successfully replaced by the membrane system saving 0.5 kg steam/kg ethanol. The expected purification was achieved at a feed temperature of 65 °C, permeate flow of 3002 kg/h and a membrane unit of 100 m^2.

The example of the bioconversion process in which the concentrated ethanol was purified by pervaporation is illustrated on Figure 3.9 [98]. The analysis of the energy

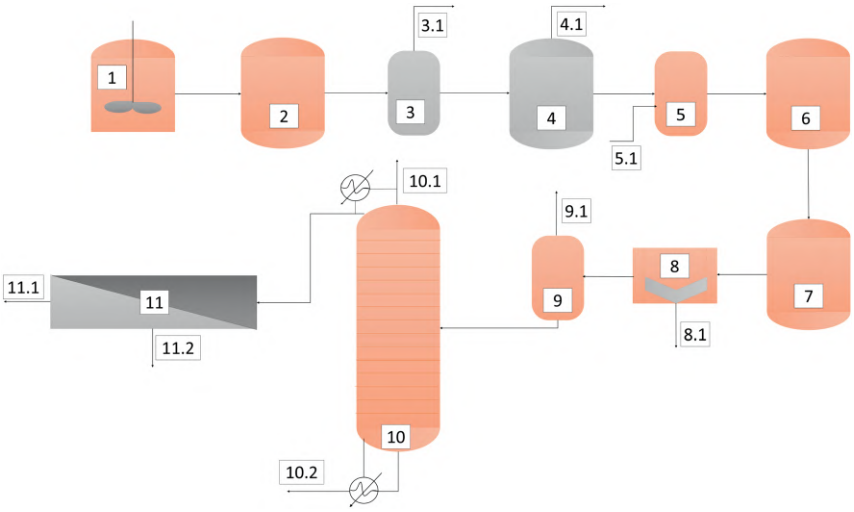

Figure 3.9: Bioethanol production-fermentation and separation process (1) mixer, (2) pretreatment stage, (3) solide separation (3.1. released solide), (4) adsorption on activated carbon (4.1. released furfural and 5-hydroxymethyl furfural), (5) neutralization with NaOH (5.1), (6) hydrolysis, (7) fermenter, (8) filtration (8.1 insoluble solides), (9) flash (9.1 CO_2, O_2), (10) Distillation column (10.1 CO_2, O_2), (11) pervaporation module (11.1 ethanol, 11.2 waste water) [98].

consumption of the process and its environmental impact showed that the use of pervaporation meets the expectations in both aspects. It can be seen that in this process the corn stover feed is first treated at 158 °C with diluted sulphuric acid to convert hemicellulose to the fermentable sugars. After separation of insoluble solids, the feed is then transported to the detoxification stage. Here the inhibitors such as furfural and 5-hydroxymethyl furfural are removed in 92–97% using activated carbon. The compound feed is then treated with an enzyme to convert the cellulose into fermentable sugars. The obtained hydrolysates with the fermentable sugars are then subjected to fermentation tank. After this step, the fermentation broth is filtered through a bed of activated carbon to remove suspended solids. Then, flash operation is applied to remove CO_2 from the ethanol-CO_2 phase (mixture having a specific boiling point and vapour pressure). Then the liquid product is sent to the distillation column to concentrate the ethanol to the azeotrope level, and dehydration is achieved by pervaporation [98].

Figure 3.10 shows an example of a bioethanol production using starch-base biomass with membrane modules [99]. Microfiltration and ultra- or nano-filtration modules, also in combination with a decanter, effectively clean the raw material after enzymatic hydrolysis and before fermentation. The combination of nanofiltration and reverse

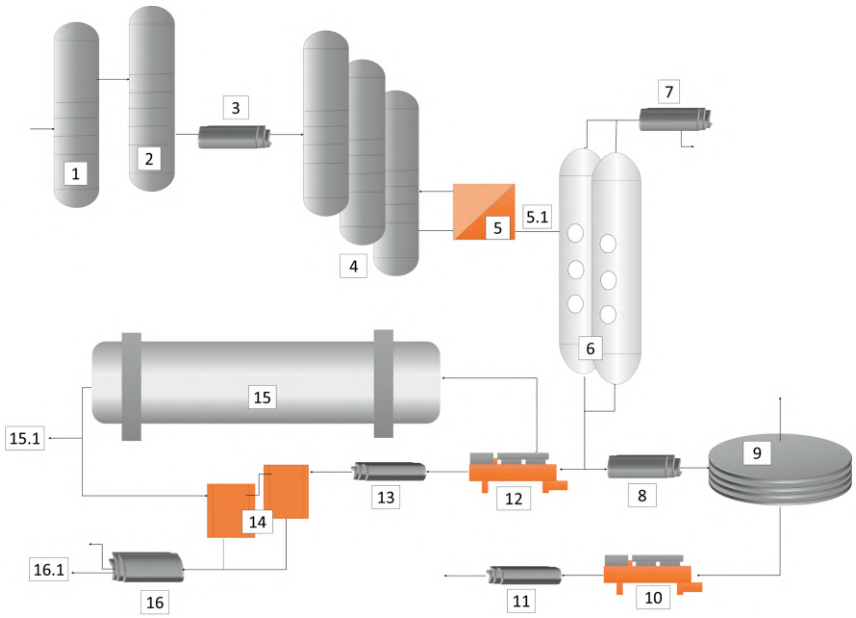

Figure 3.10: SHF process for starch-based bioethanol production: (1) Liquefaction, (2) saccharification, (3) MF/UF system, (4) fermentation, (5) MF/UF/PV system (5.1 ethanol removed), (6) distillation, (7) PV module (7.1 99% ethanol), (8), (11), (13) MF/UF systems, (9) digester (9.1 biogas), (10), (12) sludge decanters, (14) Evaporation, (15) RO (15.1 purified concentrate), (16) dryer (16.1 DGGS) [99].

osmosis system can be used to concentrate sugars prior to fermentation. As mentioned above, it is very important to eliminate the inhibitory effect of ethanol, and here the membrane processes find an effective solution. The appropriate module enables the continuous removal of ethanol from the fermenter, thus reducing the inhibition of the yeast product by ethanol.

The membrane unit can either be immersed directly in the fermenter or operated in a side stream (bleed stream). The efficiency of the membrane process can also be further improved by using a so-called membrane cascade, for example by using microfiltration as a pre-treatment step upstream of the hydrophobic pervaporation unit. Wangpor et al. [100] showed cascade module systems for separating ethanol from fermentation broth. The first module was microfiltration (membrane model M-M1812PS20), from which the permeate solution with a transmembrane pressure of 2 bar was transported to the nanofiltration module with transmembrane M-N1812A9, where ethanol was recovered at a pressure of 6 bar. A total reducing sugar rejection was also achieved; however, purification on level 92% required pressure of 5 bar. Another approach to reduce the inhibition of ethanol is performing the conversion process in a very high gravity fermenter (fermentation at concentration of sugars >250 g/L) are loaded into the fermenter when compared to classical fermentation. In this type of fermenter, pervaporation effectively lowers the ethanol concentration to a safe level (below the inhibition threshold limit of about 12 vol%). After exiting the fermenter by the ethanol rich stream and pre-concentration and pre-purification, the ethanol concentration is further increased by distillation of membrane technique such as pervaporation. After exiting the fermenter, the ethanol-rich stream is pre-treated (partially concentrated and purified), and next its concentration is increased by classical distillation and the final dehydration is achieved pervaporation.

Pervaporation coupled with laccase treatment to get well detoxification efficiency was also proposed as a promising way to industrial production of bio-butanol and furfural from sweet sorghum bagasse hydrolysate [101]. In the proposed fermentation and purification system furfural in 138 g/L and butanol in 202 g/L were separated. Generally, the production of biobutanol by acetone–butanol–ethanol (ABE) fermentation using *Clostridium species* (e.g. *Clostridium acetobutylicum*), is one of the least developed bioconversion methods [102–104]. However, several drawbacks still detract from the economic feasibility of this process, e.g. the high cost of feedstock, low butanol efficiency, and toxicity of the product [105, 106]. The ABE fermentation is a complex metabolic process with a large network of metabolic reactions; therefore the newest separation solutions are developed at each stage of the process. Furthermore, previous analysis of bioethanol production indicates that the use of membrane techniques has the greatest justification. Considering pervaporation and butanol recovery a ceramic hollow fibre supported polydimethylsiloxane composite membrane was found as efficient material with flux of 1.3×10^3 g/m^{2}h and separation factor of 43 [107]. Other membranes were applied to recover solvents from dilute aqueous solution. Moreover the further studies indicated that the optimized module consisting of seven bundles of HF

membranes (560 m^2/m^3) revealed ideal filtration properties and stability in 2 h continues test at fermentation conditions (separation factor for butanol, acetone and ethanol was 22, 29 and 6, respectively, F = 1000 g/m^2h) [108]. In another process polydimethylsiloxane membrane was used, revealing its butanol productivity (0.21 g/Lh) with butanol concentration in permeate of 71 g/L and selectivity of 10.3 [109]. Coupling pervaporation using silicalite-1 filled *poly*(dimethylsiloxane)-polyacrylonitrile with real fermentation process resulted in a reassimilation of the produced acid, as well as a higher total yield (0.37 g/g), which ultimately led to condensate containing mixture of solvents (89–160 g/L ABE) [110]. Researchers also tested a two-stage gas stripping-pervaporation process integral element in the ABE process. It was shown that using the highly hydrophobic carbon nanotubes filled polydimethylsiloxane membrane the fermentation process resulted in the high selectivity towards butanol and simultaneously with low selectivity towards other solvents [111]. It was also indicated that the butanol and total fluxes, as well as selectivity of the pervaporation step strictly dependent on the butanol and acetone concentrations in the retentate. As ethanol had a low diffusivity through the membrane, its flux was stable throughout the PV process (~15 g/m^2h). In the case of butanol and acetone, the reduction of fluxes caused the water flux to increase to a level significantly deteriorating the selectivity. Knozowska et al. presented both microfiltration and vacuum pervaporation as support for the fermentation process. The results showed that dehydration using polymeric or ceramic membranes (Pervap®4060, Pervap®4100, PEBAX, POMS) gave 80 wt% of butanol. While in the dehydrating step the permeate contains more than 90 wt% water and 10 wt% of the mixture of all solvents produced in the process. Higher purification of butanol was possible due to hydrophobic pervaporation [112].

Biorefineries not only convert biomass into biofuels but also into starting chemicals such as organic acids (e.g. fumaric, succinic, and malic acids can replace the synthetic maleic anhydride). Multi-stage separation and purification processes are often necessary to obtain a marketable product. Therefore the selection of the most appropriate techniques depends mainly on various parameters such as the concentration of the desired product, its form and the composition of the fermented stream. In the form of salt, organic acids can be recovered using a narrow group of methods, in which membrane processes are effective in reducing the number of recovery steps, e.g. by eliminating the neutralization stage. The organic acid salt produced in the fermentation broth usually is in concentration of 1–15%, so conventional electrodialysis (ED) is often used to make mixture more concentrated [113]. Compared to conventional processes, ED is a more economical technique as it consumes less energy and does not require the use of a diluent. However, this method is not proposed as a single method due to the low purity of the isolated product [114]. To improve the purification efficiency of ED, several investigators either compiled the ED with another method or used a new method that was a modification of ED (e.g. electrometathesis [EMT], electroions substitution [EIS], electro-electrodialysis [EED], bipolar membrane electrodialysis [BMED]). Using ED large molecules and solutes with opposite charge or no charge at all

are retained, but using a bipolar membrane, calcium salts, magnesium and unreacted glucose can be recycled to the fermentation process. The bipolar membrane electrodialysis method was tested to recover citric [115, 116], galacturonic [117], gluconic [118], lactic [119], malic [120], succinic [121], xylonic [122], and salicylic acids [123, 124] from fermented broth. An example is recovery of L-malic acid from the real waste solution prepared from the final concentrate of various fermentation batches. In this separation process a two-stage electrodialysis consisting modules ED and BMED was tested [120]. It was shown that the two-step process increased the purity of malic acid almost eightfold. The ED module allows increasing the concentration of organic acids and reduces the amount of mineral salts, while the MBED module can increase the concentration of malic acid even to the expected concentration of 300 g/L. The results also showed that the specific energy consumption was closely related to the presence of anionic impurities in the feed. This confirmed the legitimacy of using the ED module as the first purification step. Unfortunately, experiments on real fermentation wastes showed much higher energy consumption than obtained for model solutions (1.9 kWh/kg instead of 1.3 kWh/kg), which confirmed that the presence of organic and mineral anionic impurities of feed solutions has a decisive influence on the energy consumption of the process. Module BMED was also tested as two-electrode compartment with cationic or anionic ED membrane, as well as the three-module system arranged bipolar, cation exchange, and anion exchange membranes. As expected, the use of the three-modular system resulted in the production of both NaOH and organic acid with a high degree of purification. For instance, the results obtained for lactate recovery from fermentation broth using the three-electrode module indicated the 69.5% efficiency of the process (current density – 40 mA/cm^2) and production NaOH and lactic acid streams with net end concentration 1.3 and 1.5 mol/L, respectively [125–127]. Electrodialysis with bipolar membrane has been also tested for protein, amino-acids and phospholipids [128–136]. Especially important is high protein recovery yield and possibility of fractionation of soybean proteins [129, 133, 137, 138]. In the case of amino-acids, the electrodialysis with alternating cation-exchange and bipolar membranes were suggested to a final stage in the industrial synthesis e.g. in the production of high-purity methionine through the hydantoin pathway (efficiency 75% at a current density of 150 A/m^2) [129–132]. BMED was ale proposed for simultaneous methionine recovery and capturing CO_2 [128]. On industrial scale, conventional electrodialysis is used in the *γ*-aminobutyric acid production. In this process the used membrane enabled for removal of electrolyte in 99% and the amino acid loss below 3%, while the cumulative energy consumption for dry *γ*-aminobutyric was less than 500 kWh/t of the product [139]. Electro-electrodialysis (EED) is another method that, thanks to the ion exchange membrane and water splitting into H_2 and O_2, enables the conversion of carboxylates into the appropriate acid forms. This method was applied for the production of formic acid with a current efficiency of more than 100% [140]. In this process the formate ions pass through the anion exchange membrane to the electrolyte sphere where they contact the anodic H^+. EED was also proposed to remove tartaric [141], lactic [142], citric

[143], and acetic acids [144]. In order to improve the efficiency of the electric current at a higher concentration, consider the much larger difference between acid content in the feed, and in the concentrated product. Then this method is economically profitable. The latest reports also indicated the EDI technique, which takes full advantage of the ion exchange and classical electrodialysis processes. The EDI module in its design includes diluted compartments, concentrated compartments and electrodes. The diluted space is an ion exchange resin which supports the transport of ionic components towards the ion exchange membranes under the influence of direct current force. EDI module can be treated as an ion exchange column with continuous regeneration, which enables complete deionization of the feed solution (effect commonly used in water purification) [145]. EDI was tested for the recovery of citric acid, lactic acid and amino acids [139, 146–150]. However, only for citric acid the EDI was tested on pilot scale (see Table 3.2) [148].

Table 3.2: Example applications of electro-membrane processes.

Product	Operation conditions	Results	Ref.
Butanol (PV)	Feed: Real ABE fermentation, butanol conc. in fermenter 7.7–14.2 g/L Membrane: CNTsPDMS MMM (carbon nanotubes [CNTs] filled polydimethylsiloxane [PDMS] mixed matrix membrane [MMM]) Conditions: Two-stage gas stripping-pervaporation process, total flux 655 g/m^{2}h	Condensate consisting butanol – 521.3 g/L (with selectivity factor – 98), acetone – 93.4 g/L, ethanol – 10.1 g/L	[111]
Citric acid (BMED)	Feed: Sodium citrate conc. = 0.5–1 mol/L Membrane: (Commercial modules) Cation exchange membrane – sulphonated poly(phenylene oxide), anion exchange membrane brominated ammonium poly-(phenylene oxide), bipolar membrane-CuPc-mCMC/mCS, ion exchange capacity 1.6–2.1 mmol/g, effective surface area 20 cm^2 Conditions: Current density – 100 mA/cm^2, 0.5 M Na_2SO_4, recirculation time – 200 min	Overall current efficiency 70%, energy consumption 5 kWh/kg acid at current density of 100 mA/cm^2, acid concentrate 30 g/L	[148, 149]
Citric acid (EDI)	Feed: Pre-filtered (MF) fermentation broth, citrate conc. = 2 g/L Membrane: Barriers (cation-exchange MC-3470 and anion-exchange MA-3475 membranes), filler (strong acid cation-exchange resin C-100E and strong base anion exchange resin A-400) effective surface area 50 cm^2	Overall current efficiency 40–96% (depends on feed concentration and current density), acid concentrate 60 g/L, energy consumption 1.16 kWh/t acid	[150]

Table 3.2: (continued)

Product	Operation conditions	Results	Ref.
	Conditions: Current density – 50 A/cm^2, feed flow rate 10 L/H Total cation- and anion-exchange membrane area 123.5 m^2		
L-malic acid (ED-BMED)	Feed: Real solution after ED (K^+ 14 g/L, Na^+ 2.7 g/L, Mg^{2+} and Ca^{2+} <0.003 g/L), organic salts (malate 23.9 g/L, lactate 4.5 g/L, acetate and citrate – 0.4 g/L), pH 5.9 Membrane: (ED) NEOSEPTA, (MBED) BP-1E (seven cells) with total effective area 0.14 m^2 Conditions: Current density – 100 mA/cm^2, electrolyte – 1.5 M NaOH, circulation flow rates of acids and bases – 300 L/h, flow rate electrolyte – 400 L/h	Efficiency up to 97% L-malic acid recovery 97% energy consumption 1.9 kWh/kg	[120]
Lactic acid BMED/ CED/AED	Feed: Lactate solution – 0.075 mol/L, electrolyte – 1 M NaOH Membrane: Anion-exchange FAS-PET-130, cation-exchange JCM-II-05, bipolar BPM-I, total effective area 0.004 m^2 Conditions: Current density – 40 mA/cm^2, electrode rinsing solution 0.3 M Na_2SO_4, feed flow rate – 0.24 L/h	Lactate recovery from fermentation broth – 69.5% molar quantity for lactic acid – 1.46 mol/L, molar quantity for OH – 1.32 mol/L	[127]
Amino acids BMED	Feed: Real solution, industrial plant Membrane: Three-BPM-I system, total effective area – 540 m^2 Conditions: Time of production 8000 h/year	Net concentration of amino acids: 4–6 M	[114]

A thermo-driven membrane process such as pervaporation is another technique that can separate organic compounds from fermentation broth [151]. This technique competes with azeotropic distillation, which, as a result of the addition of an acid dehydration component, generates operational and environmental problems. The separation of azeotropic mixture such as acetic acid-water with pervaporation is also very energy-intensive. Unfortunately only a narrow group of membranes have been proposed for the dewatering of pre-treated feed solution, and much less for the separation of anhydrous acid from the fermentation broth. However, those, that were proposed showed low selectivity and can be used in the final purification step [151, 152]. Simulations showed that in a hybrid system consisting of a pervaporation module equipped with a commercial hydrophilic membrane coupled to a distillation column,

the results of the water–acetic acid separation are the most promising [152]. Other membrane methods such as microfiltration (MF), ultrafiltration (UF) and nanofiltration (NF) are often used as a pretreatment process e.g. UF is used for the separation of cell-debris and proteins as a first step, while NF is used to concentrate the permeates generated in UF module.

3.5 Conclusions

The presented above considerations indicate the high application potential of membrane techniques in the food industry. In addition to the already widely used commercial solutions, new solutions are still being sought to improve process efficiency and effectiveness. Modifications of already used membrane techniques are proposed, mainly by modification of membrane material, as well as the application of well-known lab-scale membrane techniques. Alternative solutions, although so far mainly tested on a small scale, are an interesting proposal and can support the development of the food industry.

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4 Membrane techniques in the production of beverages

Abstract: The most important developments in membrane techniques used in the beverage industry are discussed. Particular emphasis is placed on the production of fruit and vegetable juices and nonalcoholic drinks, including beer and wine. This choice was dictated by the observed consumer trends, who increasingly appreciate healthy food and its taste qualities.

Keywords: beverage; brewing process; clarification; dealcoholization; juice; membrane techniques.

4.1 Introduction

For years, the World Health Organization (WHO) has been highlighting lifestyle as a determinant of human health, including diet, alcohol consumption, lack of physical activity, or smoking [1–3]. This began in 2004 with the issuance of "Global Strategy on Diet, Physical Activity, and Health" [4]. The strategy developed involved, among other things, increased awareness as well as a better understanding of the impact of diet and physical activity on human health. Furthermore, there is a strong correlation between quality of diet and number of deaths [5]. This objective appears to have been partially achieved. For example, according to research from 1999 to 2016, the diet quality of US youth had been improving slightly, although more than half were still eating low-quality food [6]. In work of Orr et al. [7] indicated, based on data from 1999 to 2014, that diet quality of US adults also has increased over the years. At the same time, the results also indicate an increasing disparity in the quality of food consumed between people with high and low socioeconomic status. Moreover, observing global trends based on a Google search in the years 2004–2019, one can see the great popularity of various types of diets, in the order veganism, vegetarianism, gluten-free, low-carbohydrate, ketogenic, Atkins, Paleolithic, low-fat, South Beach, high-protein diets [8]. Interestingly, interest in most diets falls in December but rises markedly in January, probably as part of New Year's resolutions. Current trends in nutritional consumption have emphasized reducing meat intake and increasing consumption of plant-based foods as a dietary

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strategy, with both health and environmental profits [9, 10]. Thus, in addition to health issues [11, 12], this trend also results from concern for the environment (so-called sustainable consumption) [13, 14].

In today's increasingly diet-conscious society, fruit and vegetable drinks, as well as those that do not contain alcohol, are becoming increasingly popular. This is no longer an isolated trend, but a general tendency, that helps improve dietary habits and lifestyle. Just take a look at the supermarket shelves. The range actually includes fruit and vegetable juices, but also smoothies, fruit cocktails etc. [15, 16]. On the other hand, low-alcoholic or nonalcoholic wine and especially beer is becoming an interesting alternative for many consumers [17]. Moreover, market analysis indicates that the global fruit and vegetable processing market is on the rise. According to the valuation, it was at USD 230.96 Billion in 2016 with a projection of USD 346.05 Billion by 2022 [18].

This trend would not have been possible without the use of membrane techniques [19]. In fact, it can be said that membranes have accompanied beverage production since the time of the Egyptians. This is the first documented example of the use of simple ceramic membranes for wine clarification [20]. And although the real development of membrane techniques was definitely in the second half of the twentieth century, it is worth keeping in mind their thousand year old tradition. Of course, for industrial applications, various parameters should be taken into account, such as technological, economic, and environmental ones. Thus such parameters as permeate flux, yields, and rejections have to be considered and evaluated.

The aim of this study is to introduce the reader to the latest trends in the beverage production with the membrane support, both in terms of innovative developments on the laboratory scale and also in the industrial one.

4.2 Juice

A typical procedure for obtaining fruit and vegetable juices is illustrated in Figure 4.1. Membrane techniques are increasingly being used in several stages, such as clarification, concentration, and pasteurization. They are displacing classical methods such as, for example clarification using membrane filtration instead of long time sedimentation. In addition, membranes can support beverage production by extracting valuable compounds, regulating sugar levels, and stabilizing pH. Significantly, the production of juices using membrane technology produces high-quality, additive-free juice with a natural, fresh taste. The main progress and achievements in this field will be discussed below.

4.2.1 Clarification

Generally, after grinding and crushing, the removal of suspended particles from juices (i.e., pectin, starch, and cells from the juice) is essential, especially for the

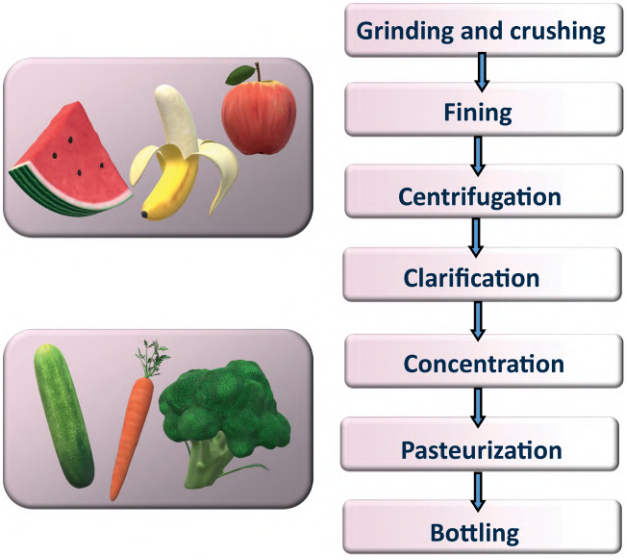

Figure 4.1: General scheme for juice production.

production of clear beverages (cold teas, natural aromatic waters, and alcoholic beverages), pastries (translucent fruit sauce and natural essences), and candies (melting products) [16]. In this situation, proposing membrane filtration, including ultrafiltration (UF) and microfiltration (MF), are among the first choices (from the late 1970s in the industry applications). Depending on the membrane type, in particular the pore size and the associated molecular weight cut-off (MWCO) parameter, it is possible to retain particles of a defined size. Membrane filtration processes allow the separation of juice components without the support of additional substances or heat application. The juice is separated into the desired permeate stream, which contains the components that have permeated the membrane, i.e., low molecular compounds such as sucrose, acids, salts, aroma, and flavor compounds, and the concentrated pulp (retentate). In addition, there are no spoilage microorganisms in the permeate, which makes it stable and therefore the juice is sterilized at the same time as being clarified. In this process, mainly UF and MF techniques are applied with different types of membranes. Industrial solutions use both polymeric membranes (i.e., cellulose acetate [21, 22], polyethersulfone [23], polypropylene, polysulfone [23, 24], polytetrafluoroethylene, polyacrylonitryle [25, 26] and poly(vinylidene fluoride) [27, 28], and the more robust ceramic membranes [29–31]). However, in the case of ceramic membranes, it should be noted that the durability of these membranes translates into a much higher cost of their production, which is about 4.5 times more expensive (per square meter) compared to polymeric membranes [32]. In terms of

solutions, tubular [29, 33, 34], capillary membranes, mainly Hollow fiber [25, 35, 36], as well as flat configurations [21, 23, 27] are offered. A detailed analysis of the conditions under which the clarification process with membrane is carried out is given in paper [37]. The authors have demonstrated, on the basis of about 50 process data, that the UF and MF are carried out over a range of transmembrane pressures TMP: 0.2–10.4 MPa, temperature: 20–55 °C (mainly 20–25 °C), feed flowrate: 1–800 L/h.

Membrane processes are an alternative to traditional juice clarification methods, such as enzymatic treatment, cooling, flocculation (gelatin, silica sol, bentonite, and diatomaceous), decanting, and filtration. The disadvantages of these methods are that they often require the use of additives and, in many cases; they are labor- and time-consuming processes. On the other hand, one of the main problems with using membranes for juice clarification is the low permeate flux achieved resulting mainly from fouling. Here it should be noted that the fouling depends intensely on the age and varieties of the fruit used. The more flocculent the juice components, the higher the fouling is observed. Therefore, finding the optimal process conditions is crucial. Of course, the simplest solution would be to increase the membrane pore size (MWCO, cut-off) but of course the consequence of this would be to reduce the retention of undesirable components. On the other hand, an obvious solution is also to clean the membrane surface during the process, e.g., by backward flushing and forcing a turbulent stream e.g., by pulsing (physical cleaning) or by using chemicals (chemical cleaning) [38]. Commercially available membranes are also in the form of dynamic filter modules, which have the ability to produce high shear rates on the membrane by using special rotating discs, or by rotating or vibrating the membranes [39]. Since this is only a temporary solution and requires stopping the plant or shutting down part of the membrane modules, many solutions propose to be supported by additional techniques. Different solutions are proposed, for example enzymatic pretreatment (as degradation of pectic substances by pectinases) [40–42] and adsorption [43] or superior filter-aid using bentonite [44], increase of temperature [21]. It should be noted that pretreatment procedures combined with filtration may result in a reduction of important juice components such as anthocyanins. Moreover, the removal of pectin and protein, which are natural components of juice, avoids the growth of bacteria and consequent spoilage of the juice [45]. For example, the work [42] showed a reduction of about 50% anthocyanin concertation in the case of depectinization by pectinolytic enzymes. On the other hand, the process significantly shortened the duration of UF, by about 20 min. From a practical point of view, in industrial solutions, this can be an excellent compromise between production time and nutrient loss in juices. Therefore lot of coupled depectinization of juices and subsequent membrane separation processes are proposed. Some examples are presented in Table 4.1. What is important in combining membrane filtration with enzyme applications besides the obvious advantages of improving juice clarification and increasing the permeate flux obtained is that the amount of enzymes for pretreatment can be reduced and can be recycled and reused. It has been observed that even after pretreatment with enzymes, pectin

residues are the main factor that limits permeate flux during juice clarification [46]. An interesting comparison of the pretreatment steps is summarized in the paper [47]. Domingues et al. indicated that of the three methods (centrifugation, enzymatic liquefaction, and chitosan coagulation), the last method was the best, providing the highest permeate flux. It should be noted, however, that the pretreatment method had no effect on the characteristics of the permeate obtained in the NF process.

Since the issue of fouling, although important, is already mastered in industrial practice (e.g., backwashing, appropriate selection of membrane material, etc.) it can be assumed that membrane filtration is a continuous and automated process. As a result, considerable labor savings are possible. According to literature reports [32], a plant for processing 20 t of fruit concentrate could save up to 6.3% of raw material, 93.5% of support material, 4.2% of energy, and 16.6% of labor input. This is due to several aspects. The use of membrane filtration does not require additives such as clarification or filtration media (e.g., diatomaceous earth and bentonite). In addition, the absence of these supplementary means that no associated waste is generated.

Among the commercial juice clarification solutions the PVDF UF membranes with a cut-off of 200,000 Da (FPA20 or FPS20) and MF membranes with a nominal

Table 4.1: Enzymatic support of membrane filtration for juice clarification and concentration.

Fruit juice	Enzyme treatment procedure	Membrane filtration procedure	Main results	Ref.
Cranberry juice	Klerzyme® 150, conc. 0.04% v/v at 50 °C for 1 or 2 h	PVDF flat-sheet UF membrane, cut-off: 50, 100, and 500 kDa	Depectinization treatment decreased time of UF clarification and enhanced the permeate fluxes, while concentrations of polyphenol and anthocyanins decreased.	[42]
Passion fruit	Pectinex 3 XL, conc. 0.1% v/v, at 44 °C, 90 min	MF polieterimide Hollow fiber membrane, pore diameter of 0.40 μm, TMP = 1 bar	MF reduced color and turbidity of fruit juice, enzymatic treatment lower the cake formation.	[47]
Blackcurrant juice	Panzym Super E and Trenolin Rot DF, conc. 0.04% v/v at 25 °C for 12 or 24 h, respectively	RO polyamide tubular membrane, TMP = 60 bar	Pretreatment with PSE enzyme allow obtaining higher permeate flux.	[48]
Lemon juice	*Penicillium occitanis* pectinase, conc. 0–1200 U/L, at 25–50 °C, 0–90 min	UF tubular mineral CARBOSEP M2 membrane, cut-off: 15 kDa, 20 °C, TMP = 0.3 MPa	Product without molds, aerobes, coliforms, enterobacteriaceae; microbiologically stable after 12 weeks storage.	[49]

separation of 0.2 μm (LM02) for dark juice and wine clarification could be mentioned, from PCI membranes. Based on this solution among others, there is a plant for the production of black currant juice [50]. Also Alfa Laval proposed UF membrane for industrial juice clarification [51].

4.2.2 Concentration

As transport and storage costs are one of the components that determine the final cost of a product, it is common industrial practice to concentrate juices. This concentration can be done for example by vacuum evaporation or with the support of membrane techniques. The biggest disadvantage of thermal evaporation is often the problem of maintaining juice quality in terms of flavor and color due to the Maillard reaction. In addition, because the process requires a high temperature of around 90 °C it involves a large amount of energy. Membrane processes that normally require mild low-temperature conditions should therefore consume less energy retain flavor and color, nutrients, and bioactive compounds. It would seem that reverse osmosis (RO) would be the best solution here. Unfortunately, in this case, the issue of fouling and lack of durability practically rules out this technique in industrial practice. Therefore, among the membrane techniques (RO), nanofiltration (NF),UF, MF and membrane distillation (MD), and osmotic distillation (OD) are used to concentrate beverages. The most popular one, which has been used in industry for about 40 years, is RO [52]. Industrial RO membranes for juice concentration offer i.e., Alfa Laval Company [51]. Due to its frequent use for desalinating water, it is a mature technique and manufacturers offer many interesting solutions. On the other hand, a serious limitation is that the final concentration in RO is limited to about 30°Brix. Hence, RO is often used as pre-concentration step and support for other methods [53, 54]. NF, on the other hand, thanks to the process being carried out at a much lower pressure, allows energy consumption to be reduced by around 21%, while at the same time the taste qualities, that are sometimes impaired by high pressures, are often better [37]. Among membrane processes, forward osmosis (FO) is also mentioned. Its use is supported by low energy consumption, low hydraulic pressure, high water recovery, and low tendency to fouling. These gentle operating conditions make it possible to maintain the taste and nutritional qualities of the juice during concentration [55, 56]. A process similar to traditional evaporation, MD can also be used for juice concentration. The advantage is that the process can be carried out at atmospheric pressure and a much lower temperature than the boiling point, resulting in lower energy consumption and preservation of valuable juice components during the process. This method, as well as RO, has been known and proposed in the food industry for more than 30 years [57]. Another solution, prosed in literature is OD. In this case, despite the many advantages of the process in terms of low-temperature and low pressure, and the consequent maintenance of the initial organoleptic and sensory characteristics and the high level of

soluble solids, it often requires preliminary treatment (clarification). Thus, OD process is usually preceded by MF or UF processes [58]. It is worth quoting here a very interesting overview of the costs of the OD process in comparison to the costs of evaporation provided by Roozitalab and co-workers [59]. The analysis indicates that both processes are economically viable, but due to the much higher equipment costs for OD (74,446$–34,499$.) the overall profit would be lower compared to evaporation (internal rate of return on investment (IRR): OD – 66.47%, Ev – 68.09%). In addition, a combination of OD and MD [60], so-called osmotic membrane distillation (OMD), is proposed as more effective [61] (see Table 4.2).

4.2.3 Sterilization

Sterilization of beverages is a key element when preparing products for sale. The removal of microorganisms maintains product safety and increases shelf life. While thermal sterilization techniques can be used, as typical in the home, industry is increasingly turning to nonthermal methods. This is because thermal sterilization can lead to chemical changes. Therefore, in line with its basic application, MF is proposed in this case. What is more, this method can and is used in the food industry in many stages, including clarification and sterilization at the same time without changing the juice components as was presented for apple juice [74] or mulberry juice [75] using UF ceramic membranes. An excellent example is also the use of membranes in the removal of *Alicyclobacillus acidoterrestris* (thermophilic and acidophilic bacilli species) from apple juice [76]. This microorganism causes a decline in quality of apple juice and show a high resistance to classical sterilization procedures. The antibacterial capacity of the membrane was achieved by grafting nisin as a natural food preservative onto the PVDF MF membrane via a multistage surface modification.

4.2.4 Supporting

The support of membrane techniques in beverage production, in addition to the processes mentioned above, is associated with a number of juice enrichment and stabilization methods. For example, the use of pervaporation allows the recovery of aromas [77–81]. It is often the case that aroma compounds can be lost during production, and since they influence the taste of the juice, their addition (after recovery) to the final product greatly improves the taste of the juices. It should be noted here that flavors are a broad group of chemicals compounds, including short-chain alkanes and alkenes and their derivatives (with or without nitrogen, oxygen, and sulfur), alcohols, esters, ketones, and organic acids, i.e., terpenoids, phenylpropanoids/benzenoids [82, 83]. Recovery methods therefore need to take account of their diversity. The advantages of pervaporation over conventional aroma recovery methods (thermal evaporation and

Table 4.2: Selected membrane processes used in juice concentration.

Process	Conditions	Results	Ref.
RO	– Apple juice, – Multistage RO industrial full-scale plant-based on the MSCB 2521 RE99 spiral-wound membrane module.	Configuration of 12 elements (1.03 m^2 area) enhanced juice concentration by about 142% in comparison to one element (up to 25°Brix).	[62]
	– Blackcurrant (*RibesnigrumL.*) juice, – Polyamide flat-sheet RO membrane, – Temperature 30 °C, TMP 30–50 bar.	Concentration of juice from 8–10 to 22–25°Brix. Over 99% retention of anthocyanins, phenols, and acids.	[63]
	– Grape juice, – Pilot plant equipment, built by the Hidrofilt Ltd.	In optimal conditions (40 °C, 50 bar) concentration up to 23°Brix. There is no significant difference in the permeate fluxes for the concentration of white and red grape juices in lab and pilot scale RO modules.	[64]
FO	– Jaboticaba (*Myrciaria jaboticaba*) juice, – Membrane: cellulose triacetate selective layer, polyester fibers coated with polyethylene, thickness between 30 and 50 µm.	Slightly lower anthocyanin content and antioxidant activity, but definite increase of sodium content from 1.7 to 12.9 mg/L in concentrated juice compared to fresh juice.	[65]
	– Sugarcane juice, – Polyamide HF membrane, – Specific reverse salt: 0.05 M NaCl, TMP 0.2 bar.	The sugar content in concentration juice: 53–60%. Fresh juice without pretreatment procedure (UF ceramic membrane with 0.1 µm mean pore size) caused high membrane fouling and additional washing with 0.1 M NaOH was necessary.	[66]
NF	– Strawberry (*Fragaria X ananassa* Duch cv. Oso Grande) juice fresh or pretreatment by MF – MF membrane: polyamide with pore diameter of 0.4 µm; NF membrane: PVDF, cut-off 150 or 300 Da.	No significant changes in bioactive compound content were observed.	[67]
	– Apple and pear juices, – Two tubular and two flats membranes, – Temperature 25–35 °C, TMP 8–12 bar.	The juices could be concentrated, retention in the range 54–75%.	[68]
MD	– Orange juice, – Polypropylene HF membrane, 50 fibers, porosity 49%, – Feed temperature ranged from 30 to 50 °C.	Two-fold concentration of juice (up to 35°Brix) with minimal nutrient loss (higher in higher temperature). Doubled membrane area caused three-fold increase of juice concentration with less than 5 and 7% reduction of the vitamin C and phenolic compound concentration.	[69]

Table 4.2: (continued)

Process	Conditions	Results	Ref.
OD	– Pomegranate juice, – Nanofibrous polyether-block-amid membrane, – Stripping solution: $CaCl_2$ (c = 3.62, 4.62, and 5.4 M), – Temperature difference (0, 15 and 30 °C, while the temp. of the osmotic solution = 20 °C).	Concentrate obtained with OD shows better quality (aroma and phenolic compounds retention) in comparison to thermal evaporation. Optimal conditions: conc. $CaCl_2$ = 5.43 mol/L, temperature difference = 0 °C, membrane thickness = 60 µm.	[59]
	– Black mulberry juice after clarification and pasteurization, – HF membrane module with 40 polypropylene capillaries, – Stripping solution: 65% w/w $CaCl_2$ dihydrate, – Temperatures of both, juice and stripping solution = 25 ± 1 °C.	Concentrate obtained with OD shows better quality (anthocyanin content and volatile components) in comparison to thermal evaporation. No 5-hydroxymethylfurfural (HMF) (mutagenic compounds) is observed in OD concentrate.	[70]
	– Pomegranate juice after clarification, – HF membrane module with 7400 polypropylene fibers, – Stripping solution: 6 M $CaCl_2$, – Temperatures of both, juice and stripping solution = 25 ± 1 °C.	Juice was concentrated from 13.0 to 52.0°Brix, contain of total sugars (as sucrose) was change from 11 to 46.73%, while acidity (as citric acid) from 1.18 to 3.88%.	[71]
OMD	– Cactus pear juice, – 0.45 and 0.20 µm polytetrafluoroethylene (PTFE) and 0.10 µm polypropylene (PP) membranes, – Stripping solution: 43 wt% $CaCl_2$, – Temperature: 20, 30, and 35 °C.	Higher permeate flux and more concentrated juice for PTFE membranes. Higher concentration was obtained with pretreatment of juice by filtration, longer process time and higher temperature. OM process is allowed to obtain a semi-concentrate juice, with a concentration of 23.4°Brix, and with a high content of antioxidants compounds.	[72]
	– Apple or beet juice, – PTFE, PVDF, and PP membranes with pore sizes: 0.10, 0.20, and 0.45 µm, – Stripping solutions: 25% w/w NaCl or 50% w/w $CaCl_2$, – Room temperature.	Better stripping solution: $CaCl_2$, The highest juice concentration (~20%): apple juice/$CaCl_2$ and the 0.45 µm PVDF membrane. No deterioration in total polyphenol content and antioxidant activity.	[73]

distillation) are high selectivity, low energy consumption due to moderate operating temperatures, no need to add other compounds and a separation mechanism based on a physical mechanism without chemical changes of the compounds. Work on this topic appeared in the 1980s, starting with model solutions, e.g., model flavor compound of apples (*trans*-2-hexenal) [84], grapes (methyl anthranilate) [85]. Investigations on both

model and real solutions were also carried out in subsequent years to assess the suitability of the membranes and to establish appropriate process conditions. In conclusion, the authors have always pointed out the promising nature of these studies and the high application potential. However, in the case of model solutions, the selectivity of the process was found to decrease with increasing amounts of components in the model solution [78]. The interesting comparison was done by Pereira and coworkers [77]. In their work pervaporation tests were carried out with binary or quaternary synthetic aqueous solutions of typical aroma components (oct-1-en-3-ol and esters: ethyl acetate, ethyl butanoate, ethyl hexanoate) and single strength and clarified pineapple juices. The authors showed that, whether a synthetic solution or juice is analyzed, pervaporation allows for the enrichment of the most volatile components and that the lower the miscibility of organic solvents in water, the higher the overall mass transfer coefficient was obtained. Unfortunately the paper did not compare the performance of the process for the systems considered (model and real).

Another proposition is to recover valuable ingredients from juice or byproducts (peals) such as **carotenoids** [86–90], **phenolic compounds** [91–94] (see Table 4.3). It is worth noting that the proposed solutions make it possible to use many of the valuable ingredients present in fruit and vegetables. Additional researchers are proposing solutions that can significantly improve the health benefits of plant-based products. In addition, the proposals to reduce sugar levels make them suitable for diabetics [88]. Presented examples show that there is still problem with precise separation of phenolic compound, mainly caused by the complicated components of feed liquids and the limited selection membranes. One of the supporting solutions may be to integrate additional separation techniques to increase the purity of polyphenols (Table 4.3).

It should also be noted that vegetable or fruit juices can only be a byproduct. One such example is potato juice, which is produced during the manufacture of potato starch. It is assumed that the processing of one tone of potatoes yields up to 500 kg of such juice, which contains both mineral compounds and organic substances (mainly proteins), such as vitamins (B1, B2, B3, B6, C, and E), antinutritional (phytates), as well as toxic substances (glycoalkaloids) [100]. Kowalczewski et al. [101] showed the possibility of utilizing this juice by membrane filtration-assisted enzymatic hydrolysis. Both enzymatic hydrolysis of potato juice in a membrane reactor, as well as membrane filtration systems (UF (polyethersulfone spiral-wound membrane, cut-off 1 kDa) and then NF (polyamide thin film composite NF membrane, cut-off 300–500 Da) to proteins concentration) allow to obtain product with higher antioxidant activity, cytotoxicity of the product against cancer cells and concentration of polyphenolic compounds in comparison to the raw materials. This research, although still at the lab stage, shows a very interesting direction for juice management. Also UF membranes are proposed for bioactive compound recovery (polyphenols and a nutrient-rich stream) from potato peels with sequential hydrothermal extraction [102]. The recovery of mentioned above compounds from beverage industrial products and byproducts not only could add economic value but also reduce the environmental burden.

Table 4.3: Exemplary of studies on the recovery of value compounds from beverage industry.

Procedure	Main results	Ref.
	Carotenoids	
From cashew apple (*Anacardium occidentale L.*) using cross-flow MF (tubular ceramic membrane with 0.2 µm pore diameter) with diafiltration of carotenoids.	Concentration step: 19-fold increase in carotenoid content, diafiltration stage: five-fold increase in carotenoid purity.	[86]
From *Dunaliella salina* using lab-scale membrane unit (asymmetric polysulfone [PS] capillary membrane, cut-off: 100 and 500 kDa), pilot scale – capillary membrane (asymmetric PS, cut-off 100 kDa).	Proposed solution: pre-concentration of carotenoid-rich ("orange") *D. salina* culture by membrane filtration, final concentration using low-shear centrifugation. Results: *D. salina* reached a concentration factor of 10 and a flux of 21 L/m^2 h.	[87]
From clementine/pink grapefruit juice using cross-flow MF (tubular ceramic membrane with pore diameter of 0.2 µm).	8-10-fold increase in final products in provitamin A carotenoids (33 mg/kg), lycopene (43 mg/kg), hesperidin (3.2 g/kg) and pectin (5.5 mg/kg), reduction of sugar content by three in the diafiltration process.	[88]
From watermelon juice using integrated enzymatic maceration, cross-flow MF (four tubular α-alumina membranes with average pore diameter of 0.2, 0.5, 0.8, and 1.4 µm), diafiltration and centrifugation processes.	41-fold increase of lycopene concentration and 34 ford purer. Lycopene is completely retained in MF with membrane pore diameters of up to 1.4 µm with reducing of cis-isomerization of lycopene during the process.	[90]
	Phenolic compounds	
From pomegranate juice using UF and NF flat-sheet membranes (cut-off: 1000–4000 Da) in cross-flow pilot unit.	Yields: polyphenols 84.8%, anthocyanins 90.7% in the retentate, glucose 90%, fructose 93% in the permeate (diafiltration step).	[92]
From strawberry (*Fragaria X ananassa Duch*) juice using MF as a pretreatment for removal of the suspended solids and juice clarification (polyamide membrane with pore diameter of 0.4 µm) and NF (PVDF membrane, cut-off: 150 and 300 Da).	Two options: (1) NF of in natural juice and (2) NF of microfiltered juice. 1.2-fold increase in the concentration factors of total phenolic content and 1.5-fold in anthocyanin content in comparison to *in natura* juice, for both options. Antioxidant activity of concentrates: 99% (1) and 51% (2) increase, with the maintenance of the red color and phenolic compounds.	[93]
From press liquors obtained by **pigmented orange peels** using spiral-wound NF membranes (cut-off: 250–1000 Da) and polymeric material (polyamide, polypiperazine amide, and polyethersulphone).	Yields: anthocyanins 89%, flavonoids 70%.	[95]
From camu-camu (*Myrciaria dubia*) using ultrasound assisted extraction and reverse osmosis (RO) (polyamide membrane, cut-off: 500 Da).	3.3-fold increase in total phenolics, six-fold in anthocyanins, four-fold in antioxidant activity, seven-fold in vitamin C, 4.5-fold in cyanidin-3-glucoside In concentrate than the initial extract.	[96]
From pequi (*Caryocar brasiliense Camb.)* fruit extract using MF (cellulose esters membrane, pore size: 0.22 µm), UF (polyethersulfone	MF reduced 65% of lipid and 50% of solid contents. UF allows to obtain a clear extract (58 NTU). NF retained 95% of *p*-coumaric acid.	[97]

Table 4.3: (continued)

Procedure	Main results	Ref.
membrane, cut-off: 5 kDa), and NF (polypropylene membrane, cut-off: 500–600 Da).	Combination of UF and NF retained almost all phenolic compounds.	
From artichoke brines using NF (polyethersulphone or polyamide membrane, cut-off: 200–1000 Da).	Higher than 92% rejection of caffeoylquinic acids, flavonoids, chlorogenic acid, and cynarin, low rejection of the dry residue (14–18%).	[98]
From cranberry juice using electrodialysis (ED, Microflow type electrodialysis cell with one and one anionic cationic membrane) with filtration (polyethersulfone membrane, cut-off: 500 kDa). Filtration step: transport of the polyphenolic antioxidants due to its cut-off; ED step: prevents transports of polyphenolic antioxidants and mixing juice with the electrode rinsing solutions.	Yields: 19.4% increase of anthocyanin concentration and 23.7% of antioxidant capacity. Disadvantage: decrease of sour taste intensity duo to 7.3% decrease of citric and 4.7% malic acid concentrations.	[99]

4.3 Beer and wine production

4.3.1 Beer

Both in the case of beer as well as wine the consumption depends on consumers' demographic, their socioeconomic characteristics and cultural convergences. For example in 2019 the largest world beer consumer is Chine, the US is in second place, Brazil was ranked third, next Mexico, Russia, and Germany. This relationship was also characteristic of production. The data per capita are slightly different, first location was taken by Czech Republic, second Austria, next Romania, Germany, and Poland. Most of listed countries have very long history in beer production, however, cultural differences influence on the diversity of processes, and kinds of beer produced. Demand for free-alcohol beverages is increasing due to newer consumption practices that limit alcohol consumption for a variety of reasons: healthier lifestyle, driving restrictions, or religious considerations. Tradition of brewing and significant sensitivity of quality and taste of the final product has resulted so far in an unwillingness to introduce changes in the production process. Technological innovations are unfortunately necessary and concern on saving energy, increasing quality of known product and in creation new catalog products. The traditional beer brewing process has a series of stages, which lead to conversion the starch source into the wort, and in the next into alcohol through the alcoholic fermentation. These stages are mashing, boiling, cooling, fermentation, maturation, separation, and clarification (Figure 4.2) [103, 104].

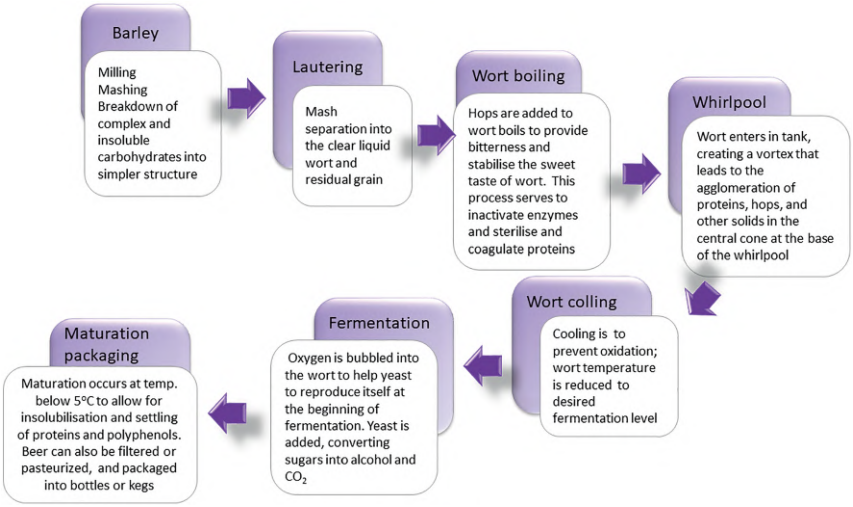

Figure 4.2: General scheme of brewing process [105].

Most of these steps require the use of filtration methods, including membrane processes. The first stage that requires the participation of this type of method is brew water treatment. Water quality has a significant influence on almost every stage of beer production. Especially the chemical composition of the water is of great importance for the quality and nature of the end product. For example ions such as iron, chlorides, and sulfates can affect the taste of beer, a pH value above seven can inhibit enzymes, fermentation disturbances can be caused by too high concentration of nitrate ions, while too low pH, and chloride ions can cause corrosion. The expected water demineralization is ensured by RO (water is transported through semi-permeable membrane and contaminant is removed as concentrate with desalination rate of 90–99%) or combination RO with saturation system e.g., EUWA LIQUICK® and processes (Figure 4.3). The pretreatment of water in RO system guarantees that the plant will be work trouble-free. The use of polishing filters, sand filters or activated carbon filters should eliminate any factors that can cause an irreversible damage of the membrane. Preventing, it is also applied anti-scalants or scale inhibitors. The supporting of RO by other technique positively influences on the desalination rate of particles larger than 5 μm, reduction pressure to 10 bar, and energy consumption. The RO system also prevents secondary contamination of water. The potential of poly(ether)sulphone or cellulose triacetate HF membranes (HF-Hollow Fiber) were also tested in dead-end or cross-flow technology. But despite the fact that the materials showed significant filtration properties, the solution was cost-intensive. Less costly method is NF, which requires much lower pressure than 15 bar. However, this system is not effective as expected for monovalent ions (Na^+, Cl^-). Therefore, NF has not been used in brewing process so far [106, 107]. This type of filtration can be used successfully for wastewater recycling.

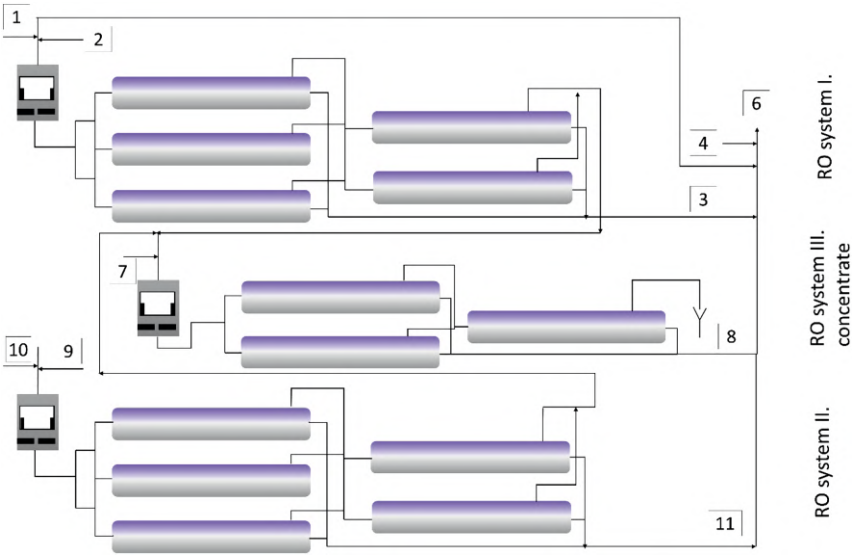

Figure 4.3: Scheme of pure water production (RO with saturation system): 1., 10. raw water, 2., 6., 8. inhibitor, 3.,7., 10. permeate, 4. Calmix to rise calcium level, 6. Brew water.

Filtration is also conducted after mashing process, after which the barley husks are removed from wort. On this stage two solution are used: mash filter or a lauter tun. The lauter tun is a two-unit operation, which eliminates the suspension from the wort and enables removal of soluble compounds from the extract. Wort separators mainly rely on the solid components in the mash as filter material. Mash filtering results in higher filtration efficiency in terms of wort clarity and filtration efficiency. The alternatives are a system with flexible membranes, between which the distance is regulated. Unfortunately this is a yield-limiting stage in the brewery, because the removed suspension must be disposed each time. Commercially available filter membranes can provide uninterrupted one unit filtration, however, this system was recommended for small brewing system. Another alternative is a system with flexible membranes, between which the distance is regulated by inflating with compressed air to squeeze the mash against a permeable polypropylene cloth [108, 109]. Schneider et al. [110] compared lauter tun and membrane filtration efficiencies in wort filtration. The research indicated that the final quality of beer produced was not depended on type of filtration technology. Using lauter tun and membrane filtration, the beer characteristics were comparable, but in some aspects such as the foam collapse time, were worse in the case of the membrane filtration process. The effectiveness of the membrane filtration of the wort was indicated as dependent on the hydrophobicity of the materials. The hydrophobic PTFE membrane showed higher permeability than the hydrophilic polyamide membrane. Moreover, the selectivity of the membrane filtration towards high

molecular weight substances did not depend on the pore size, but on the formation of the sediment layer. It is worth mentioning that high molecular weight polysaccharides lead to fouling in contrast to low molecular weight sugars [111–114]. In another works the mash separation were conducted using cross-flow MF. Daufin et al. [115] indicated that using MF more than 90% of the spent grains can be removed from the wort. Unfortunately to high amount of suspended particles required conducting filtration minimum in two-stages. The optimum fluxes is possible to applied using membrane with a pore size of 70–80 μm and after that using membrane with pore size 10 μm and higher. Cross-flow MF can also be assisted by centrifugal decanting to separate particles larger than 15 μm. This solution allows the use of milling malt and other milled grains in brewing [116]. Blanpain–Avet et al. [117] tested polycarbonate membranes and alumina with a pore size of 0.2 μm. As expected, using a cross-flow MF system, the sludge layer leaded to the protein separation through internal contamination of the pores in the initial stages of filtration, followed by external contamination of the surface. This problem could be solved operating at lower and constant pressures. However, even when a constant pressure condition will be applied, a decrease in the jet velocity will be observed [118].

Brewer's spent grain (BSG) is a major by-product of the brewing process, which can be used as a source of protein. Here, the membrane process has also found an application, e. g. for the purification of proteins by UF [119]. However, alkaline extraction and protein precipitation with ethanol and ammonium sulfate [120] or by acidification to pH 3 [121] are commonly employed for proteins separation. BSG can also be enzymatically treated using proteolytic enzymes or can be pretreated with carbohydrases followed by direct hydrolysis with enzymes *Alcalase* and *Flavourzyme* [120, 122, 123]. Tang et al. [119] studied the application of UF for recovery of proteins from BSG preprepared by ultrasound assisted extraction using the carbonate–bicarbonate buffer. In this system, more than 92% proteins were retained by the UF membrane with MWCO of 5 kDa.

The presence of components of potential in nutritional value enables BGS to be considered not only as animal feed but also as an attractive adjunct for human food [124]. The most attractive perspective is production of dietary fiber-rich and protein-rich flours but for this purpose BGS must be properly dried. In the technology proposed by Carvalho and coworkers, drying of BSG to moisture of 20% can be obtained after fresh BSG being mixed with water, filtered, water-washed, membrane-squeezed, and vacuum-dried. The developed conditions were also confirmed by the pilot plant testing. The obtained cake, after filtration at feed pressure of 3–5 bar, was dewatered by membrane squeezing using water of 65 °C to moisture of 51%. The followed vacuum hot cake drying enabled to the moisture decrease to ~20% [125]. Much better results the same team obtained using modified technology considering mainly construction changes [126]. In this study the PP membrane was circulated by water of 85–95 °C at the squeezing pressure of 2–3 bar, while vacuum drying was carried out over the hot cakes at 50–110 mbar. Further, modification concerned on applying stainless steel Rollfit®

plates® plates, using which cold water circulated through the membrane, while Rollfit® plates were heated with hot water 85–95 °C. The carried out experiments indicated that regardless used membrane plates the BSG can be dewatered to moisture of 15%.

4.3.1.1 Clarification

The clarification of rough beer must comply with the haze specification of the beer to produce a clear, bright beer according to the European Brewery Convention (EBC) norms. Filtration through kieselguhr or a diatomaceous earth rock, has been successfully used for many years to meet this specification. However, clarifiers and other agents used in this filtration can be considered as hazardous materials such that further use may conflict with the handling/disposal regulations in many countries. Filtration is generally used to clarify of the green beer and to remove turbidity formers, which could lead to visible changes, occur in the long storage of the final product.

4.3.1.2 Sterilization

Membrane techniques are recommended for the so-called cold sterilization. Then, the selection of the appropriate filters will allow even the complete removal of bacteria, yeasts, and molds, which results in a microbiologically stable beer with an extended shelf life [127]. These are general assumptions, while research in this area indicates that filtration efficiency depends on various factors. For example, filtration is influenced by the viscosity of beer, which is closely related to its composition, e.g., the presence of arabinoxylan, β-glucanβ-glucan, polyphenols. The interaction of the components with the membrane is also important, which results in fouling of internal pores at the initial stage of filtration or finally surface fouling. The fouling can also be limited by the appropriate selection of the membrane construction material [128]. For example, membranes with greater porosity, e.g., cellulose acetate membranes, are more sensible to fouling than polycarbonate membranes.

4.3.1.3 Dealcoholization

The low-alcohol beer (alcoholic residue less than 1.2% vol) can be effectively produced by fermentation limited by an appropriate low consisting of carbohydrates, or by a limited yeast metabolism (Figure 4.4). Unfortunately, using this procedure produced beer is devoid of expected by consumers flavors and sensory attributes such as bitterness [129]. Until quite recently beer has been dealcoholized by distillation. This method was effective but the heat treatment adversely changed the beer flavor. Even the using of much softer thermal methods such as vacuum rectification and evaporation did not eliminate losses of high volatile compounds.

Vacuum techniques, whose conditions are much milder, are seen with hope in limiting thermal damage to components, such as loss of smell and taste. The thermal

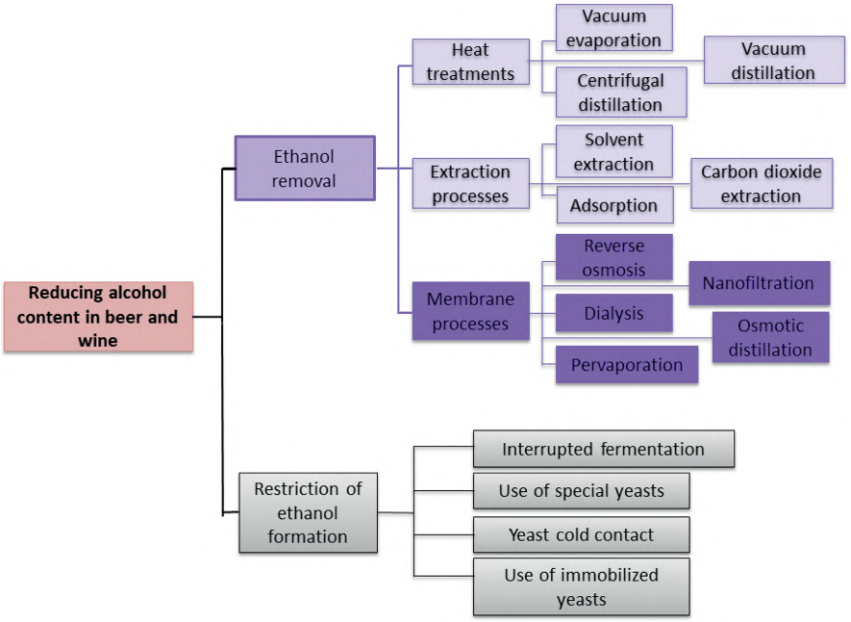

Figure 4.4: Methods used to reduce alcohol in beer and wine.

constituents degradation can be easily limited by using membrane-based methods. Membrane filtration is also less energy-intensive. The main membrane techniques used in the production of low-alcohol and nonalcoholic beer are dialysis, RO, and pervaporation. Less are osmotic evaporation, MD, and NF [130]. Selection of technique used and the effectiveness of the separation of ethanol or flavors depends on the composition of the material to be treated, e.g., molecular size, volatility, solubility, threshold, and taste value, which vary depending on the production method used.

4.3.1.3.1 Dialysis

Dialysis is based on the use of semipermeable membrane, in which, in the countercurrently system flow, low molecular weight ethanol passes through a membrane to a dialyzate at a pressure differential of less than 0.5 bar. Dealcoholization consists of passing the permeable alcohols molecules through the membrane into the aqueous phase (dialyzate fluid) in order to achieve an equilibrium concentration (Figure 4.5). The alcohol-enriched dialyzate is then sent to a stripper column to remove ethanol by evaporation. Next regenerated dialyzate is send back to the dialysis unit to remove remaining portion ethanol [131]. Due to the risk of CO_2 loss, the process requires pressure to the beer side even 0.1 bar, or as dialyzate a carbon dioxide-containing fluid is used. Using this technology, the beer in the dealcoholization process is processed at low-temperatures; therefore there are no thermal degradation products [132].

Moreover, this technique lowers the bitter units and the pH, but the level is positively identified by the consumer. Other parameters, such as color, total nitrogen, and polyphenol content are as identified at the predealcoholization level. The evaporation stage, supporting the dialysis process, also does not cause changes the taste values e.g., by the formation of caramel or bread notes. However, the sensitivity of the final beer composition depends on the used procedures [133–135].

4.3.1.3.2 Reverse osmosis

Another membrane technique is RO, which also works with semi-permeable membranes of asymmetric structure (from cellulose acetate, polyimide, or polyamide composite) at a pressure of up to 60 bar. In the dealcoholization process, ethanol together with water is transported through a membrane into a region of higher solute concentration – in the opposite direction to the osmotic pressure. It was why using RO dealcoholization below 0.45 vol% is economically not feasible, but it allow to obtain beer with a more complete but slightly acidic taste, with a greater loss of bitter substances and an increase in turbidity [137, 138] (Table 4.4). Higher pressures results in higher permeate flux but this condition can also increase aroma rejection causing loss of flavor. Ethanol and aroma components rejection also increases with elevated temperature. The membranes used for beer dealcoholization are usually of asymmetric

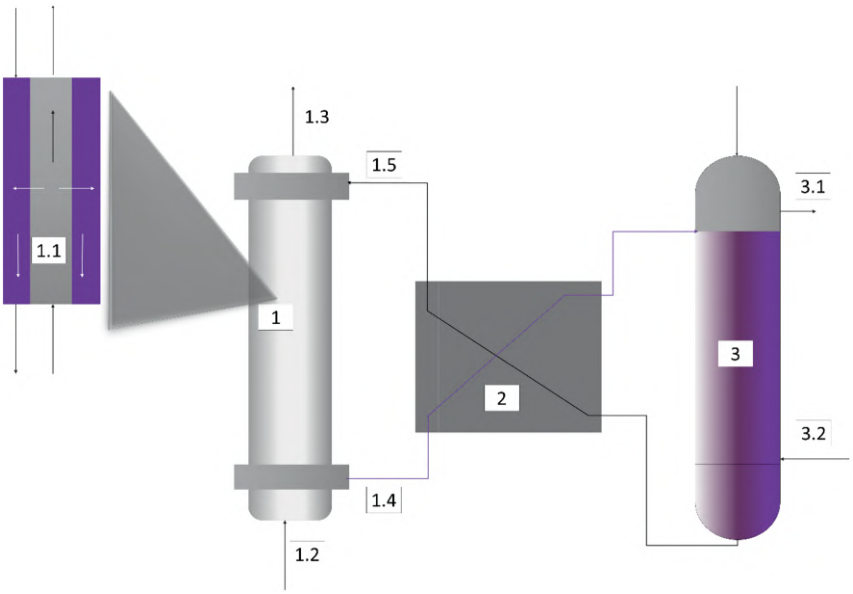

Figure 4.5: Flow diagram of dealcoholization by dialysis: 1. dialysis module 1.1 capillary membrane, 1.2 fresh beer, 1.3 dealcoholized beer, 1.4 alcohol-reach dialyzate, 1.5 alcohol-free dialyzate, 2. heat exchanger, 3. stripper column, 3.1 alcoholic condensate, 3.2 stripping steam [136].

structure, with the active layer made of cellulose acetate, polyamide, polysulfone. The life of acetate membranes depends on pH and temperature. Because both factors can affect the hydrolysis of the acetate group optimal pH at 0 °C is 4.5–5.0. Due to the large water losses, redilution of the alcohol-reduced retentate or continuous procedure in the diafiltration mode are necessary. In the case of diafiltration, the required alcohol concentration is adjusted by replenishing the removed water, but not exceeding the original beer volume. This type of operation also requires a carbonation step.

4.3.1.3.3 Membrane distillation

MD is a thermally controlled separation process in which only vapor molecules are transported through the micropores of the membrane. The driving force behind the process is the difference in partial vapor pressure caused by the temperature gradient across the membrane. According to the mechanism, the liquid compounds evaporate on the hot side of the membrane feed, then diffuse through the pores of the membrane

Table 4.4: Exemplars of using membrane processes in brewing process.

Brewing stage	Type of filtration	Filtration conditions	Main results	Ref.
Wort filtration	Vibrating membrane filtration	Membrane – PTFE Pore size – 0.45 μm filtrate flow – 10 hl/m^{2}h Δp = < 7 bar	Removing large molecules, such as proteins and β-glucans substances responsible for foam enhancement and protein complexes	[110]
Brewer's spent grain (BSG) treatment	Ultrafiltration	Membranes – polyethersulfone MWCO – 5 kDa Surface area 0.05 m^2 TMP 10–45 at cross-flow rate 0.9–2.7 L/h	Protein was retained in 92% leading to protein content in permeate 20.1%	[123]
	Membrane squeezing by circulating hot water	US Filter J-VAP membrane with PP filter plates T of water – 65 °C p = 6–7 bar. Vacuum drying at p = 0.048 bar	Dewatering to moisture of 20%	[125]
	Membrane squeezing by circulating cold water	US Filter J-VAP membrane with stainless steel filter plates T of water heated plates – 85–95 °C p = 6–7 bar. Vacuum drying at p = 0.05–0.1 bar	Dewatering to moisture of 15%	[126]

and eventually condense on the permeate side. The same mechanism controls the dealcoholization process. Ethanol has a higher vapor pressure than water; therefore the rate of penetration of ethanol is also higher. Unfortunately, although the water–ethanol separation process takes place without change in a flavor profile, this technique has not found industrial application. It has been proposed also modifications to this solution, e.g., vacuum MD, however the increase of feed and vacuum pressure not only improves the membrane flux, but also reduces the membrane selectivity [139, 140]. Ultimately, the changes in the membrane flux do not affect the effectiveness of the dealcoholization. The conduction of vacuum MD for 6 h reduced the alcohol content of the beer from five to just 2.25 vol%.

4.3.1.3.4 Osmotic distillation

OD is another membrane process in which the dealcoholization is carried out by using the difference in ethanol vapor pressure between the two sides of the hydrophobic microporous membrane. Even though in this process temperature gradient is not applied, membranes of high thermal conductivity such as polypropylene, polytetrafluoroethylene, and polyvinylidene fluoride are common used. In OD the evaporated alcohol is transferred through the membrane pores and condenses in the stripper. The stripper side states a concentrated solution of an electrolyte of high osmotic activity e.g., calcium chloride, sodium chloride, potassium acetate, however in the dealcoholization process water is the most recommended stripper. This recommendation was based on the low back transport of water with the simultaneously high ethanol flow [141]. The disadvantage of using water as a stripper is significant reduction of CO_2 and oxygenation of the dealcoholized beer. Here the solution is to use an intermediate cycle permeate as was confirmed by Russo et al. [142]. Moreover, the use of permeate maintains pH, polyphenols content, and antioxidant activity on the level before dealcoholization. However, the changes in bitterness, foam stability, turbidity, and aroma are also indicated and they have a negative impact on the final beer taste.

4.3.1.3.5 Pervaporation

Pervaporation is another membrane technology which enables to the production of nonalcoholic or low-alcoholic beer maintaining its characteristic flavors and aromas. The transport of alcohol molecules through the semipermeable hydrophobic membrane is due to the difference in chemical potential of alcohol/water in the feed and permeate side, which can be highlighted by vacuum. The permeate is condensed and transferred into the low concentrated alcoholic fluid and the retentate keeps rest of compounds determining the aroma profile of the original beer [130, 143]. This membrane technology enables to alcohol content reduction to ~1% (longue time duration), therefore it has been proposed as technique for partial dealcoholization of beverages [144] (Table 4.4). Another applicability is aroma extraction from beer, e.g., iso-amyl and isobutyl and alcohol, ethyl and iso-amyl acetate, as well as aldehydes [145–147]. And in most industrial solutions, this applicability complements more efficient

dealcoholization techniques such as centrifugal distillation [143] or by using two different PV systems, thanks to which the dealcoholized beer is enriched with the extracted in another unit aroma compounds (see Table 4.5).

Table 4.5: Exemplars of using membrane processes in dealcoholization stage.

	Filtration conditions	Main results	Ref.
D	Membrane: Cuprophan® (cellulose regenerate) hollow fiber module (d = 200 μm) surface area = 1.3 m^2 thickness = 8 μm V = 2–3.5 cm/s RT = 7.5–12.5 s T = 5 °C; Re = $3{\cdot}10^4$–$4.8{\cdot}10^4$ p = 20–40 kPa	Beer dealcoholization products up to 0.79 vol % Series of modules is required to achieve the desired low-alcohol content	[133]
	Flat film or tubular-film membranes of surface area of 1.3 m^2 T = 10 °C p below 0.5 bar V = 30 l/h m^2	Removing of alcohol partially through the use of dialysis membranes in series of modules US 4,664,918 US 5,075,123	[129, 130]
RO	Two spiral-wound acetate cellulose membranes T = 0 °C P = 35–50 bar Homemade beer	P = 45–50 bar Turbidity 0.4–0.6 pH – 4.7 Carbohydrates 81–85% Salts and minerals 0.7–1.1% C_E > 0.5 vol%	[137]
	Membrane DSS-CA995P (acetate cellulose) with area of 155 cm^2 Qf – 2–7 L/min P = 20–40 bar T = 5–20 °C	P increase causes 5% increase in aroma rejection, T decrease from 20 to 5 °C results in increase of aroma and ethanol rejection C_E – 0.47 vol%	[138]
	Circular dealcoholization p = 30–40 bar T = 5–15 °C sugar degree = 9.75	Color (EBC) = 11.7 CO_2 content = 0.3–0.6% C_E – 0.1 vol%	[148]
	Membrane filtration unit P = 80–276 bar T = 0–15 °C $C_{E,0}$ = 3–25%	Ethanol rejection up to 99% C_E – 0.1 vol%	[149]
FO	cellulose triacetate membrane	pH – 4.6 Elect. conduct. –2.5 mS/m Turbidity – 12.7 Color (EBC) – 6.9 C_E – 0.5 vol%	[150]
OD	Liqui-Cel polypropylene membrane surface area 1.8 m^2	Low-alcohol Bitter beer pH – 4.1	[151]

Table 4.5: (continued)

	Filtration conditions	Main results	Ref.
	porosity 40% Pore diameter 0.03 m Flow rates of feed 70 mL/min Flow rates of stripping (diluted beer up to 0.5% vol) 140 mL/min Number cycles – 5	Turbidity (EBC) – 5.1 Color (EBC) – 44.5 $C_E \leq 0.7$ vol% low-alcohol Weiss beer pH – 4.2 Turbidity (EBC) – 10.5 Color (EBC) – 10.7 $C_E \leq 1$ vol%	
PV	Commercial membranes with polydimethylsiloxane active layers: Pervatech 030705 and Pervap 4060 with polyvinylalcohol as separating layer At feed side $T = 25$ °C $p = 0.9$ bar At permeate side $p = 9$–13 mbar Feed flow – 3.8–4.2 L/min duration – 6 h, $C_{E,0} = 5\%$	Pervatech 030705-muh more efficient membrane Mass recovery of Ethyl acetate 33–35% Iso-amyl acetate 32–35% Isobutyl alcohol up to 10% 2-methyl butanol and 3-methylbutanol up to 10%	[147]
	PDMS–polyimide–polyethylene terephthalate composite membrane $T = 35$–65 °C (dealcoholization) $T = 10$–30 °C (aroma recovery) downstream pressure = 14–30 mbar feed flow rate – 100 L/h total flux – 0.52 kg/m^2 h, at 20 °C and 14 mbar	The optimal conditions: $T = 65$ °C $p = 14$ mbar overall ethanol removal up to ~0.05% first cycle ethyl acetate recover – 50% overall ethyl acetate 29.7% overall iso-amyl acetate 31.9%	[152]

4.4 Wine

As in the case of beer, wine is also dealcoholized. Also, the process may include activities in the fermentation stage of winemaking [153] as well as post-production physical activities [132]. However, it should be remembered that the wine brand itself imposes a specific composition and the reduction of alcohol to a level below 8.5% means that the beverage cannot be called "wine [154]. Comparable to the beer dealcoholization the removal of ethanol from wine can be conducted by using conventional heat techniques as well membrane systems. However, only membrane systems can be selective enough to ensure that the taste and bouquet of the wine meet consumer expectations [155].

Slight changes in the sensory qualities of wines are ensured by processes that remove up to 2% of ethanol or by using multi-stage processes based on membrane processes such as RO, pervaporation, OD. For example using RO phenolic substances and polysaccharides are almost completely preserved. Changes in aroma composition depend on membrane construction. The 70% loss occurs with a polyamide membrane,

Table 4.6: Exemplars of using membrane processes in wine dealcoholization.

Filtration conditions	Main results	Ref.
Circular dealcoholization using two RO unit CDRCM60S1 and MSD625W6 (membrane integrally bonded to a plastic separator support screen) p = 30–40 bar T = 5–15 °C sugar degree = 9.75	Color (EBC) = 11.7 CO_2 content = 0.3–0.6% C_E – 0.01 vol%	[157]
RO units consisting flat sheets of semipermeable membrane Qf – 20 L/h P = 35–50 bar T = 0–20 °C	P increase allows effective ethanol permeation, T increase causes increase of aroma and ethanol rejection C_E <0.5 vol% at 50 bar	[159]
Membrane filtration unit P = 80–276 bar T = 0–15 °C $C_{E,0}$ = 3–25%	Ethanol rejection up to 99% C_E – 0.1 vol%	[160]

while a 10% removal occurs with a cellulose acetate membrane [156]. Double RO process enable to produce not only wines composes less than 11–13% of alcohol but also nonalcoholic wines (alcohol content below 0.01%) with the unchanged polysaccharide composition [157]. In another solution the using two-stage membrane pervaporation enables to produce simultaneously grape spirit, such as brandy, and alcohol-free wine [158]. Moreover, the obtained brandy exhibited better smell and taste than traditional distilled liquor. In the case of rice wine, both the bentonite and RO treatment could be appropriate to prepare nonalcoholic takju [158] (see Table 4.6).

4.5 Conclusions

An analysis of recent literature reports clearly shows the continuous development of membrane techniques, which are used in the production of a wide range of food beverages. It has been shown that membranes can not only support production, but in many elements can effectively replace traditional processing methods.

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5 Polymeric membranes for biomedical applications

Abstract: The rapid development of nanotechnology paved the way for further expansion of polymer chemistry and the fabrication of advanced polymeric membranes. Such modifications allowed enhancing or adding some unique properties, including mechanical strength, excellent biocompatibility, easily controlled degradability, and biological activity. This chapter discusses various applications of polymeric membranes in three significant areas of biomedicine, including tissue engineering, drug delivery systems, and diagnostics. It is intended to highlight here possible ways of improvement the properties of polymeric membranes, by modifying with other polymers, functional groups, compounds, drugs, bioactive components, and nanomaterials.

Keywords: biomedicine; membrane technology; nanomaterials; nanoparticles; polymer membranes.

5.1 Introduction

Polymeric materials have been studied and developed for multiple biomedical applications to enhance the quality of human life [1–3], ranging from polymer membranes that improve the functionality of organs, such as bio-artificial kidney, pancreas, and lungs, to applications as implants, drug delivery systems, or diagnostic assays [4–12]. The physicochemical, mechanical, and surface properties of membranes vary in terms of specific applications or their placement within the body. For instance, membrane material applied as an implant can be exposed to high mechanical stress or aggressive chemical conditions [13–15]. Thus, the requirements in the selection of polymer material depend on the intended use of designed membranes. The examples of biomedical applications of membranes are presented in Figure 5.1.

Generally, the polymeric membranes can be applied in three main areas including, but not limited to: (i) tissue engineering, with purification procedure to restore functions of organs (e.g. removal of toxins from the blood, its oxygenation), as well as fabrication of artificial organs or scaffolds to stimulate cell growth and differentiation, (ii) drug delivery system allowing to transport various drugs, biologically active substances or even genes, and finally (iii) diagnosis allowing to detect several diseases

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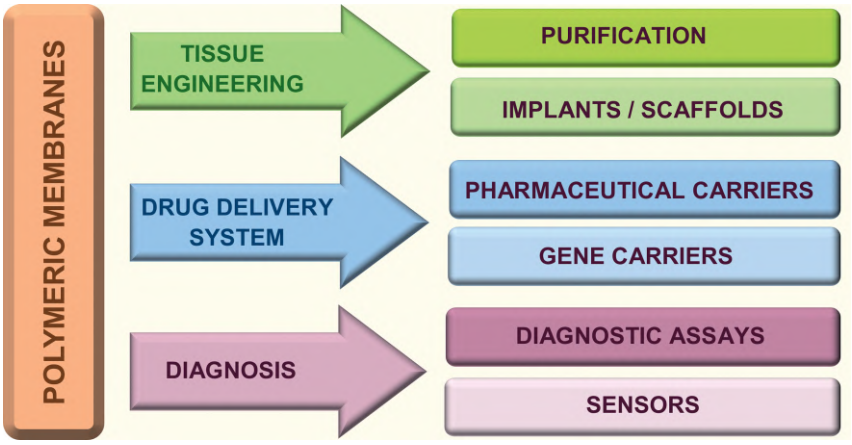

Figure 5.1: Biomedical application of polymeric membranes.

based on sensitive and selective membrane sensors or pre analytical processes on blood samples analysis.

There are three main concerns associated with the medical application of membranes: biofouling, uncontrollable degradation of the membrane, and immune reaction caused by the membrane. The contact of the membrane with biological fluids is the main cause of all of these problems. Various approaches come together to deal with these limitations, such as (i) modification of membrane surface properties, (ii) improvement their physicochemical, mechanical, and biological properties by attachment of bioactive molecules, targeting agents, or nanomaterials, (iii) modification of membranes production technology to easily control their morphology and final properties, and (iv) modification of polymer materials intended to impute new properties, such as biocompatibility, degradability, and biological resistance. Nanotechnology takes a special place in overcoming all of these limits [16–18]. This chapter discusses various applications of polymeric membranes in the field of biomedicine, pointing the weakness of membrane materials and possible ways of improvement their properties.

5.1.1 Restoration of organs function

Dialysis is one of the oldest examples of using membrane technology in the medical field [19]. The first dialysis treatment involving humans was reported in 1925 by Georg Haas [20]. However, the first scientific description of dialysis procedures dates back to 1856 and comes from Thomas Graham (Scottish chemist) [21]. The Haas dialyzer module was made of collodion tubes (materials based on cellulose nitrate) [22]. Over the next 50 years, most studies focused on the modification of membrane modules to

improve the diffusive mass transfer efficiency and reduce high blood compartment volumes. A turning point was the fabrication of the first hollow-fiber module in 1960 [19]. This module consisted of an array of narrow fibers enclosed in a pressure vessel (Figure 5.2). The hollow-fiber module geometry provided the highest membrane surface area (volume ratio in the blood compartment), as well as improved blood rheology and mass transfer.

There are three different types of dialysis applied for people with renal diseases: hemodialysis (HD), peritoneal dialysis (PD), and continuous renal replacement therapy (CRRT) [23–27]. Hemodialysis uses an "artificial kidney" to remove waste and extra fluid from the blood. Additionally, it helps to control the blood pressure and miner balance (including the level of potassium, sodium, and calcium). The blood is taken out of the body, filtered through the special dialysis module, and returned to the body (Figure 5.3a). Peritoneal dialysis involves pumping special sterile fluids into the abdomen through a permanent tube (catheter) placed in the peritoneal cavity, to remove waste products from surroundings blood vessels (Figure 5.3b). CRRT is applied for critically ill patients with acute kidney injury, whose bodies cannot tolerate regular dialysis. It mimics the kidney functions such as regulating electrolytes, acid/base, water, drugs, and toxins by a continuous and slow removal of fluids (24 h a day). The blood passes through a double-lumen venovenous catheter, an extracorporeal circuit, and a semipermeable membrane (hemofilter) that removes the fluids and impurities. At the same time, the replacement fluid replenishes the volume and electrolytes removed (Figure 5.3c) [28].

Dialysis membranes can be divided into cellulosic and synthetic groups, as well as a low or high flux (depending on pore sizes), according to the oldest classification based on material composition and water permeability, respectively. However, the development of polymer chemistry opened new frontiers in the production of advanced

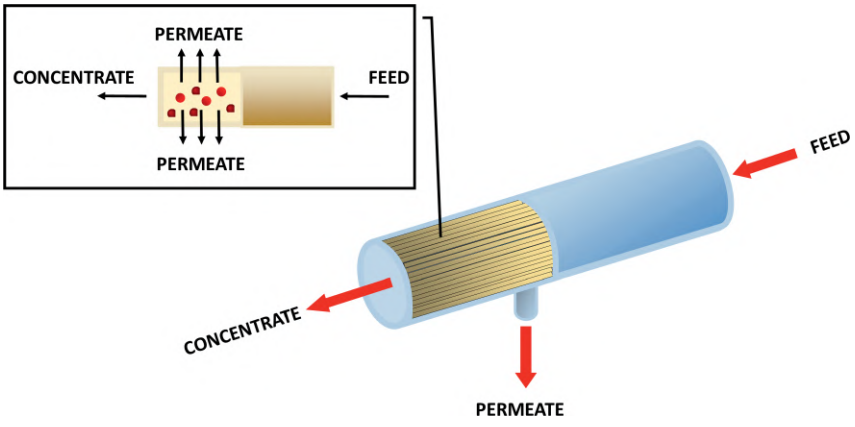

Figure 5.2: The hollow-fiber module.

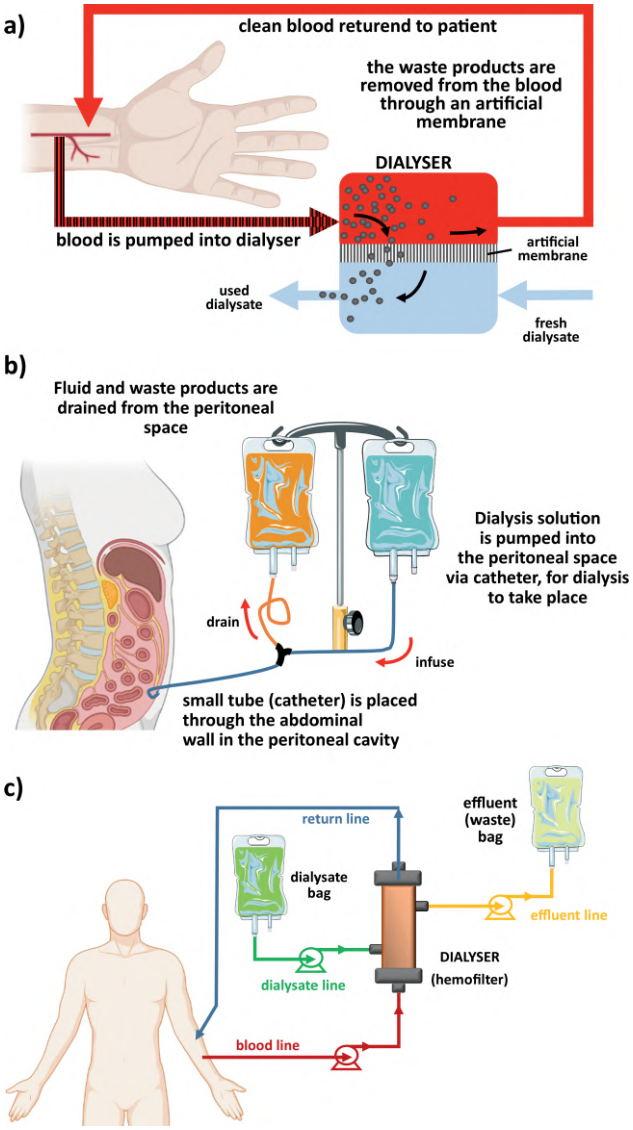

Figure 5.3: Three different dialysis systems: (a) hemodialysis, (b) peritoneal dialysis, and (c) continuous renal replacement therapy.

polymeric membranes with unique features. Thus, traditional classification requires a reconsideration to include other properties, such as the surface potential of membranes, their adsorption capacity, and their hydrophilic/hydrophobic nature. An early generation of cellulose-based membranes, such as Cuprophan®, Cuprammonium Rayon, Saponified Cellulose Ester (SCE®), or FIN-type, was extremely polar and

hydrophilic [29]. Additionally, cellulosic membrane exhibited a thin-walled structure, with favorable diffusive transport properties for low-weight molecules (500–1000 Da), which classified them to the low flux groups [30]. However, due to low biocompatibility, they contributed to the inflammatory response induced by the production of cytokine (e.g. interleukin IL-1) and tumor necrosis factor (TNF) [31]. Furthermore, the interaction between blood proteins and membrane surface may initiate a blood coagulation cascade, infections, and various allergic reactions [32]. In recent 30 years, cellulosic membranes were modified by partial substitution of hydroxyl groups by acetylation to improve hemocompatibility and make large molecule and water removal more efficient [33]. Such membranes are commonly called modified cellulose, substituted cellulose, or semisynthetic membranes. Depending on the degree of substitution, modified membranes can contain various amounts of cellulose acetate (CA), diacetate, or triacetate [34]. These modifications resulted in increased membrane pore size, yielding a higher water and high-weight molecules (>5000 Da) permeability. The esterification of cellulose reduced the inflammatory response; nevertheless, the biocompatibility issue remained. However, extensive research performed over the past few decades indicated that immune response is also associated with material hydrophobicity, their charge, number of hydroxyl groups, as well as the roughness of membrane surface [35–37]. Moreover, the hydrophobicity and surface roughness are involved in the activation of platelets, which may initiate the blood coagulation cascade [36].

Takouli and coworkers fabricated vitamin E-coated dialysis cellulose membrane to improve its biocompatibility [38]. The use of vitamin E-modified CA membrane significantly suppressed oxidative stress and inflammation. The authors concluded that liposoluble vitamin E on the blood surface allowed to direct free radical scavenging at the membrane site. The latest research improved also that polyethylene glycol (PEG) additives in CA influenced the pore size, permeate flux, and hydrophilic properties of membranes [39, 40]. Idris and Yet investigated the effect of different molecular weight polyethylene glycol (PEG) additives and on the performance and morphology of CA membrane [40]. It was shown that different molecular weight PEG influenced the formation of the various asymmetric layers as a result of different diffusion rates. For instance, high molecular weight PEG (e.g. PEG 600) revealed a low diffusion rate and promoted the formation of the thick dense asymmetric membrane [40]. Das et al. modified CA membrane with titanium oxide nanoparticles (TiO_2 NPs). This CA-TiO_2 hybrid membrane was fabricated using the electrospinning technique, commonly applied for the production of polymer fibers. The presence of TiO_2 NPs distributed within the CA matrix improved the roughness, affected its surface charge, and caused a uniform decline in average CA fiber diameter [41]. Nanoparticles might be also incorporated into the cellulose-based matrix to enhance antimicrobial properties. De Faria and coworkers presented fabrication of antimicrobial membranes made of CA modified with graphene oxide–silver nanocomposite. The authors improved that NPs-functionalized membrane exhibited larger surface pores and increased water flux.

Moreover, it revealed excellent antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* [42].

Synthetic membranes offer better biocompatibility in comparison with cellulose membranes [43]. They are made of polyamide (PA), polymethylmethacrylate (PMMA), polyacrylonitrile (PAN), and polysulfone (PS) [34]. Generally, synthetic membranes consist of a thin inner layer and a thicker outer layer. The outer layer provides mechanical support for a selective active inner layer. They can be classified as high-flux or low-flux, depending on the molecular weight cut-off (MWCO) [44–46]. The synthetic membranes are strongly hydrophobic and thick-walled (due to the presence of a thick support layer). The hydrophobicity of membranes is responsible for some side effects associated with the fouling of membranes caused by the adhesion of plasma proteins (mainly albumin, globulin, and hemoglobin) on the membrane surface. It can lead to platelet aggregation, adhesion, and coagulation [47, 48]. However, to minimize the membrane fouling, a hydrophobic matrix can be modified by the addition of hydrophilic polymers, such as polyvinylpyrrolidone (PVP), or PEG. This modification can be made through the blending method, plasma treatment, or surface modification, such as chemical reaction and grafting, or coating through adsorption or electrostatic interactions [49]. For example, Kim et al. improved hydrophilicity and stability of polysulfone membrane by entrapping of sulfonated poly(ethylene glycol) acrylate deblock copolymer into PS matrix [50]. Wang and coworkers enhanced hydrophilicity and hemocompatibility of polyethersulfone membrane by blending with a pore-forming agent, i.e. PVP. The authors demonstrated that PVP-modified polyethersulfone (PES) membranes exhibited higher water flux and lower water contact angle in comparison with pristine PES. Additionally, the PVP additive caused a reduction in plasma protein adsorption and prolonged blood coagulation time [51]. Improvement of anticoagulation performance of PES-based membranes can be achieved by immobilization of biologically active compounds or drugs. Ren et al. demonstrated immobilization of heparin onto PES surface by using low-temperature plasma treatment (LPT) and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide/*N*-hydroxysuccinimide (EDC/NHS) activation mechanism. It was shown that LPT immobilization methods retained the activity of heparin and improved the hydrophilic properties of PES membrane [52]. Another interesting report presented Zhao and coworkers. The authors improved hydrophilicity by immobilisation of single-strand DNA onto PES surface. Therefore, the adsorption of protein onto DNA-modified membranes significantly decreased, as a result of interactions between proteins and DNA [53].

To reduce the fouling phenomena, pristine polymeric membranes can be modified with nanoparticles. Said et al. improved the hydrophilicity of polysulfone (PS) hollow fiber membranes by incorporation of hydrophilic iron oxide nanoparticles (IONP). It was shown that the surface of IONP-modified membranes displayed less roughness, in comparison with pure PS membranes. Smother surface provided a smaller attractive area to proteins adsorption, thus reduced the fouling of the PS–IONP hollow fiber membranes [54]. The effect of PEG/Al_2O_3 nanoparticles on PES membrane structure

and its antifouling properties was investigated by Garcia–Ivars et al. The PES membrane was modified by UV irradiation (UV photographing technique) in the presence of PEG and Al_2O_3 nanoparticles. Both components had a high affinity to the polar environment, causing high permeability for pure water and thus, high rejection of hydrophobic proteins or macromolecules [55]. Chemical functionalization of aminated PES membranes with silver nanoparticles was demonstrated by Heider et al. The presence of silver nanoparticles attached to the surface of PES provided antibacterial properties against *E. coli*. In addition, the prolonged silver ions release extended the lifetime of the membrane [56].

Polymer materials are commonly applied in blood oxygenators to remove carbon dioxide and add oxygen during cardiopulmonary bypass surgery (Figure 5.4). The first experimental description of membrane oxygenator was published in 1956. The main component of this oxygenator device was a nonporous flat sheet gas permeable membrane made of ethylcellulose, which was highly hydrophilic, exhibited poor mechanical properties, and its sterilization was complicated [57]. Furthermore, the damage and breakdown of erythrocytes and platelets, due to the direct contact of blood with the membrane, substantially shortened its lifetime.

To enhance the mechanical properties of gas permeable membranes, the hydrophilic polymers were replaced by hydrophobic ones, such as polyethylene (PE) or polytetrafluoroethylene (PTFE, Teflon®). However, these polymers are characterized by the low velocity of oxygen and carbon dioxide transport [58]. The introduction of hydrophobic membranes based on polyorganosiloxanes, especially polydimethylsiloxane (PDMS) membranes, partially solved the low permeability problem (the permeability of O_2 and CO_2 for PDMS is around sixfold higher than other hydrophobic polymers) [59]. Polymeric membranes can be also used to oxygenate blood in longer-term life to perform

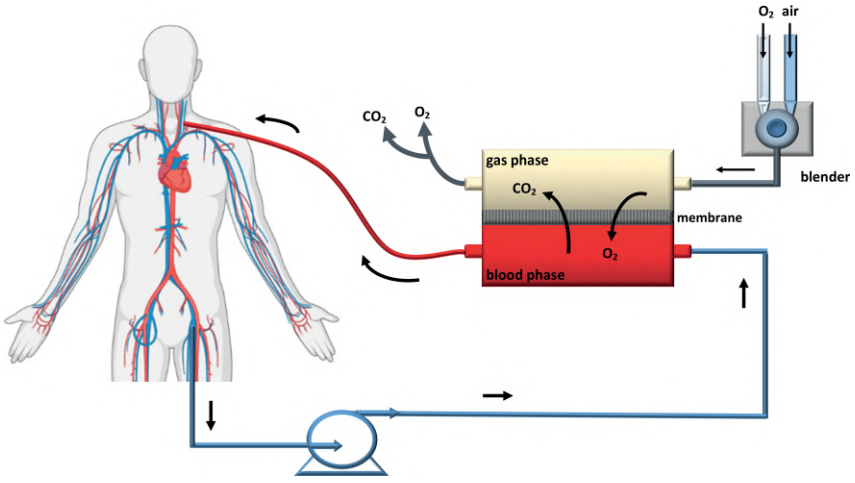

Figure 5.4: Membrane oxygenator.

extracorporeal blood oxygenation (ECMO) for patients with acute respiratory failure. The cylindrical Kolobow oxygenator equipped with spirally wound silicone rubber membrane was used for the first neonatal ECMO case in 1979 [60]. However, as with the dialysis process, an important finding was oxygenator based on hollow-fiber membranes [57]. This oxygenator was introduced in 1972 and quickly achieved more than 50% of the oxygenator market share. Moreover, hollow-fiber oxygenators become a standard of cardiopulmonary care from the 1970s to the present. The first hollow-fiber oxygenators consisted of a large number of microporous membranes made of polypropylene (PP) or silicone fiber [61, 62]. The main drawback of these devices was the tendency to leak blood plasma through the micropores of membranes, thus degrading gas transfer capability and markedly decreasing their service life. To prevent the blood plasma component's leakage, the outer surface of the hollow-fiber membrane was coated by hydrophilic polymers, such as hydrophilic silicones and siloxanes, alkoxyalkyl (meth)acrylate, or block copolymer of silicone and polyarylate [63–65]. This problem led also to the development of polymethylpentene (PMP) microporous hollow-fiber membranes, which provided almost complete physical separation between gases and circulated blood [66]. And, importantly, the oxygenator equipped with PMP hollow-fiber membranes can be applied for ECMO for periods beyond 60 days. However, due to some areas allowing limited blood plasma leakage, as well as gas emboli formation, the Food and Drug Administration (FDA or USFDA) approved the usage of PMP-based oxygenators for a maximum of 4–6 h [67].

Another way to enhance oxygenation efficiency is the application of nanoporous polymer materials in blood oxygenators. Nanoporous membranes may serve as a more efficient barrier to water influx, thus improving long term pulmonary support in ECMO procedures. Ambravaneswaran and coauthors fabricated a silicon nitride membrane via a combination of bulk micromachining and ion-beam drilling. The designed membranes exhibited mechanical properties enough to withstand pressures typically experienced for blood oxygenators. The initial studies showed that dimensions of the blood channels permitted the red cell shape changes, thereby enhanced the exchange of gas in the pulmonary capillary [68]. The PP and PMP membranes commonly applied in commercial ECMO systems suffer from low biocompatibility, which usually led to blood coagulation or hemolysis. Park et al. presented a new generation of blood oxygenation membranes based on amphipathic fluoropolymers [69]. The authors fabricated polyvinylidenefluoride-co-hexafluoropropylene (PVDF-co-HFP) using non-solvent induced phase separation method (NIPS). To reduce the interaction with blood components and pore wetting, the flat sheet nanoporous hexafluoropropylene (HPF) membrane was coated with Hyflon AD60X (amorphous perfluorinated copolymer of tetrafluoroethylene (TFE) and 2,2,4-trifluoro-5-trifluorometoxy-1,3-dioxole (TTD)). The *ex vivo* studies carried out using sheep blood indicated that the PVDF-co-HFP membrane was more effective in blood oxygenation than commercial PMP membranes [69].

Membrane technology can be applied in the artificial extracorporeal liver assist devices to temporarily support the failing organ before transplantation or until it will be

able to regenerate [70]. These extracorporeal devices use various membrane operations (e.g. hemodialysis, hemofiltration, and hemoperfusion) integrated with other separation techniques, including column purification, sorbents (such as cation-/anion-exchange resins, charcoal) or bioreactors containing immobilized enzymes [71–73]. For instance, hemoperfusion can be integrated with charcoal sorbent to adsorb water-soluble toxins in the low and middle molecular weight [74]. Single-pass albumin dialysis (SPAD) is another membrane-based support system to treat liver failure. The albumin is added to dialysate to improve the capturing of protein-bound toxins, such as nonceruloplasmin-bound copper, which is involved in Wilsonian liver disease. The blood flows across the high-lux dialysis membrane, while the albumin solution is transported in opposite direction to the dialysis membrane, to detoxicate the blood plasma [75]. However, the high cost associated with albumin concentration caused that this therapy was not often used in clinical practice.

Nowadays, there are only two artificial extracorporeal liver support system, based on the concept of albumin dialysis, applied in the clinic (Figure 5.5): Molecular

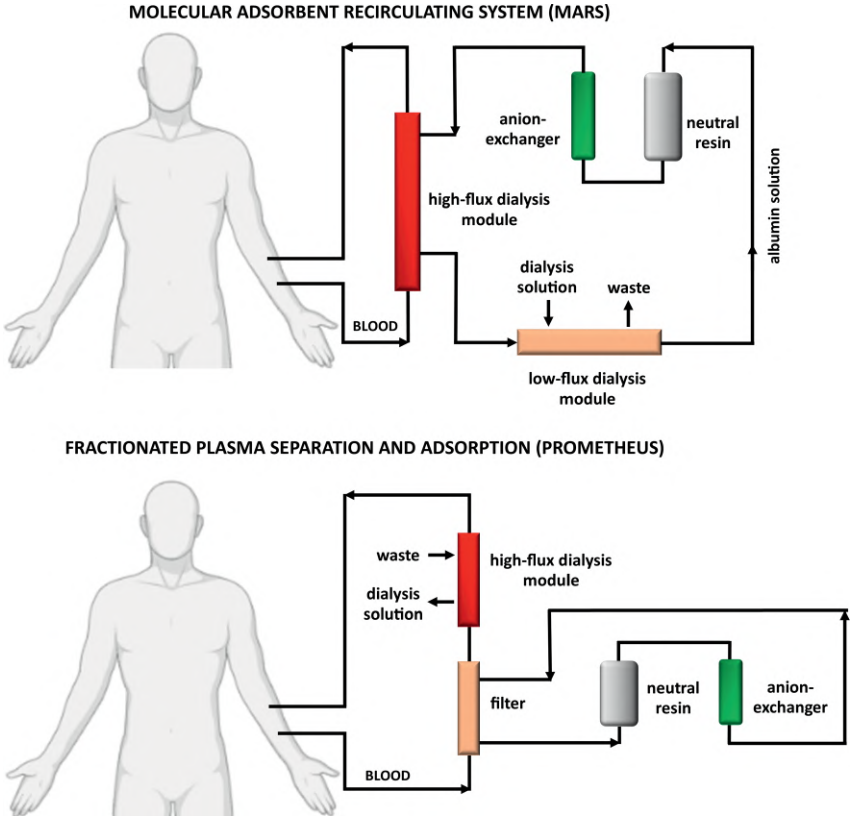

Figure 5.5: Artificial extracorporeal liver support systems: molecular adsorbents recirculating system (MARS) and Prometheus [78].

adsorbents recirculating system (called MARS®) and fractionated plasma separation and adsorption system (FPSA, commercialised as Prometheus®) [76]. MARS is consisting of three main components: (i) a conventional dialysis system equipped with PS membranes (50 kDa) to guide the extracorporeal blood circuit, and albumin containing dialysate to induce the dissociation of protein-bounded toxins, (ii) adsorption column filled with charcoal to retain high weight molecules (such as bilirubin, creatinine, and urea), and anion-exchange resin cholestyramine to retain negative-charged molecules, and (iii) single-pass dialyzer. Moreover, the dialysate albumin is restored passing to the adsorption columns and can be applied for the new cycle [77].

The Prometheus combines fractionated plasma separation with high-flux hemodialysis to remove albumin-bounded and water-soluble toxins. The clearance of toxins is achieved in several steps: (i) in the FPSA circuit, the albumin is separated from blood by a capillary dialyzer made of PS hollow-fibers (250 kDa), which allows free toxins and plasma albumin-bounded toxins to pass through the membrane, reaching the neutral resin's column and anion-exchange adsorber, (ii) in the high-flux dialyzer, the water-soluble toxins are removed from the albumin-free blood using hollow-fiber membranes [79].

Both MARS and Prometheus support devices can eliminate the water-soluble and albumin-bounded hepatic toxins. However, Prometheus exhibits higher clearances for the most bounded-proteins and water-soluble markers in comparison with MARS [80]. The main goal of the application of these systems is to grant patients a substantial survival benefit. Unfortunately, the use of artificial extracorporeal systems still faces several technical problems and high production costs. Moreover, clinical data regarding MARS and FPSA systems are conflicting [81].

5.1.2 Scaffolds fabrication

The development of membrane technology along with the evolution of regenerative medicine contributed to the application of polymer materials as scaffolds and/or implants to substitute or integrate the function of impaired tissues and organs. Scaffolds can be defined as three-dimension porous biomaterials fabricated to perform the following functions: (i) promote cell adhesion, proliferation, differentiation and cell-biomaterials interactions, (ii) allow transporting of nutrients and regulatory factors required for cell survival, and (iii) biodegradable at a controllable rate with minimal cytotoxicity [82]. The criteria for selecting scaffold materials are based on their chemistry, molecular weight, shape/form and structure, porosity, surface properties (hydrophilicity or hydrophobicity), mechanical properties, wettability, biocompatibility, and degradation rate [83]. Polymer-based materials due to their unique properties, such as high porosity with pores in varying sizes, the mechanical characteristic or degradation time, can be adapted for use in tissue engineering or fabrication of artificial organs. Both, synthetic and natural polymers (or combination of both) can be

considered as membrane materials to mimic the function of damaged tissues. However, synthetic polymers exhibit physiochemical and mechanical properties that are more predictable and reproducible than natural ones [84]. Among synthetic polymers used for the production of membranes, PDMS, polycaprolactone (PCL), polyglycolic acid (PGA), poly (L-lactic-co-glycolic acid) (PLGA), PTFE, PS, polyethersulfone, PEG, or PVP are the most relevant. Some of the examples of natural polymers are collagen, elastin, chitin, chitosan, silk, fibronectin, or cellulose [85].

For instance, the ultrathin, porous PCL membrane can be applied as prosthetic Bruch's membrane in the treatment of retinal degeneration [86]. Bruch's membrane is a thin, five-layered extracellular matrix located between metabolically active retinal pigment epithelium (RPE) and choriocapillaris. It serves as a molecular sieve, to maintain the metabolic exchange between the vasculature and outer retina, as well as tissue scaffold for the cells, providing sufficient mechanical strength [87]. Tan et al. demonstrated that the PCL membrane can mimic the Bruch's membrane functions. The fabricated scaffold improved the proliferation of adult retinal pigment epithelial (ARPE-19) cells (human retinal pigmented epithelial cells) and enhanced the formation of the monolayer by ARPE-19 cells, which is essential for fluid transport and creation of the blood–retinal barrier [86]. In turn, poly(lactic acid) (PLA) nanofibrous membrane modified with silver nanoparticles (Ag NPs) and cellulose nanofibrils (CNF) may prompt the treatment of eye infections. The modified PLA scaffold showed excellent biocompatibility to ocular epithelial cells and antimicrobial properties against *E. coli*, *S. aureus*, and *Fusarium* spp. The ocular cells formed a multilayered structure and retained the undifferentiated stem cells on the surface of the PLA scaffold, making it suitable for ocular bandages in controlling corneal and conjunctival infections [88].

Quiros–Solano et al. investigated the application of porous PDMS membranes for organs-on-chips, i.e. multichannel 3D microfluidic cell culture chip (a type of artificial organ) that simulates activities and physiological response of organs. The authors emphasized that the porous membrane characteristic influences the cell mechanisms (e.g. transmigrations of cells and their ability to form a monolayer), which might help to better understand or regulate the cellular responses in human physiology and pathology studies using organs-on-chips [89]. PTFE-based membranes can serve as mechanical support and osteoconductivity to the growing cells in bone and cartilage regeneration. Park et al. designed the PTFE/PEO porous membranes by a combination of electrospinning and sintering techniques (Figure 5.6). It was proven that the chemical composition of PTFE/PEO membranes affected the proliferation of mouse calvaria preosteoblast cell (MC3T3-E1), their osteoblastic differentiation and bone mineralization (*in vitro* studies) [90].

PCL nanofiber membranes are one of the ideal candidates for mimicking the extracellular matrix in bones. Pristine PCL nanofibers enhance the attachment and proliferation of osteoblast, osteoclast, osteocytes and chondrocytes, which are crucial for the regeneration of hard tissues [91]. Baylan et al. designed an injectable 3D cell encapsulated scaffold consisting of PCL nanofibers interspersed with collagen type I

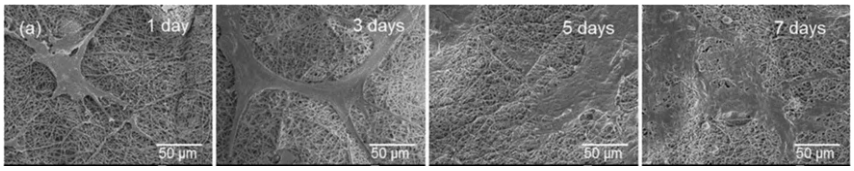

Figure 5.6: Scanningelectronmicroscope(SEM) micrographs of the MC3T3-E1 cells grown on polytetrafluoroethylene (PTFE) nanofibrous membranes for different durations. Reprinted with permission from [81].

microfibers for augmentation of bones. Based on *in vitro* studies, it was shown that PCL-collagen scaffold promoted the osteoblast cells proliferation, differentiation and formation of mineralized bone matrix [92]. The effect of plasma-treated PCL nanofibers modified with hydroxyapatite nanoparticles (HAP) on cell proliferation was also reported by Stastna et al. The plasma treatment of HAP-modified PCL scaffold resulted in a completely wettable surface. Both, the hydrophilicity of fibrous scaffold, and modification with HAP nanoparticles, improved cell proliferation by 30% compared to control [93].

Hollow-fiber membranes can also serve as bio-hybrid constructs to replace the damaged organs and tissues, especially for tissues that required a tubular shape, such as blood vessel, nerves, intestine, urethra or cartilage. They can be fabricated using various materials, either synthetic or natural, however, polyesters, such as PCL, PLA and PLGA are prefered [94]. For instance, the PLLA hollow-fiber membrane can mimic artificial vasculature. Based on *in vitro* static and dynamic mouse premyoblast cell (C2C12) culturing, it was shown that PLLA hollow-fiber membrane can improve the delivery of nutrients to the cells when integrated with tissue-engineered scaffold [95]. The examples of PLLA hollow-fiber membranes are presented in Figure 5.7.

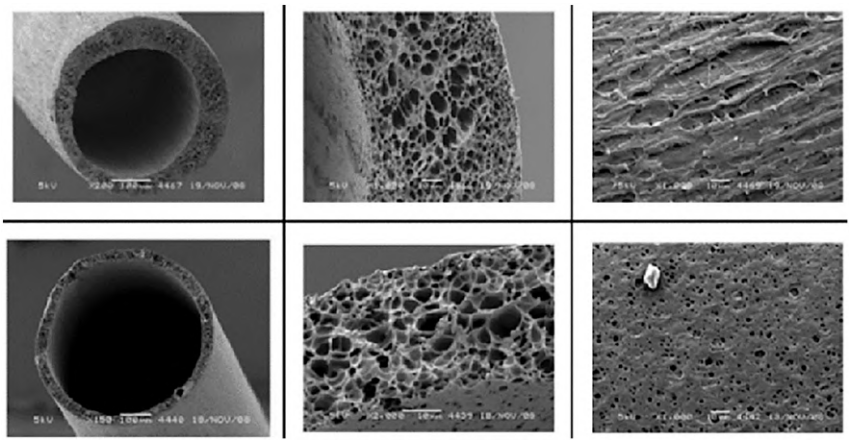

Figure 5.7: SEM micrographs of PLLA hollow-fiber membranes. Reprinted with permission from [83].

Mohammadzadeh and coworkers modified synthetic PCL with natural biopolymers to fabricate biomimetic scaffolds for cutaneous regeneration. This scaffold was composed of blend PCL, silk fibroin, aloe vera, and eggshell membrane and applied as a support for differentiation of human cutaneous basal cells toward keratinocyte-like cells. The authors observed an increased basal cell proliferation after 14 days in differentiation medium and formation of integrated cell-to-cell connection after cell seeding on the hybrid scaffold [96]. Wei et al. investigated the application of a 3D-printed PCL scaffold modified with insulin-like growth factor-1 (IGF-1)-loaded PLGA nanoparticles coated by polydopamine (PDA) for cartilage tissue engineering. It was shown that PCL-based scaffold enhanced the synthesis of collagen type II and provided a suitable environment for the proliferation and differentiation of chondrocytes, which are essential in stimulating cartilage regeneration [97].

Polymer materials exhibit sufficient biocompatibility to make them an available candidate for application as implants in tissue engineering. Ficek et al. demonstrated a novel strategy for anterior cruciate ligament (ACL) reconstruction using a tube-shaped perforated PLA stent with a porosity of 45% to improve the healing process. The implantation of PLA stent facilitated the osteointegration of the tendon graft after reconstruction (*in vivo* studies). This effect was likely associated with osteogenic and osteoconductive properties of PLA polymers [98]. Song and co-authors reported the bioartificial pancreas devices (BAP) based on silicon nanopore membrane (SNM) [99] (Figure 5.8). Commonly applied BAP devices exhibit poor islet viability and functionality, due to the low mass transfer. Based on the *in vivo* studies (porcine model) it was

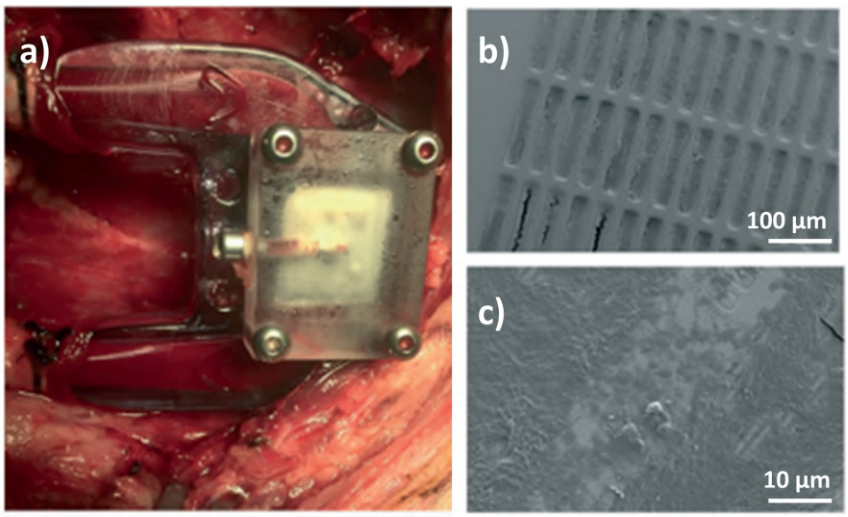

Figure 5.8: (a) The explanted bioartificial pancreas devices based on silicon nanopore membrane (*in vivo* studies); (b) SEM micrographs of the diffusion-side of implanted membrane, (c) SEM micrographs of the convection-side membrane coated with proteins and cells. Reprinted with permission from [99].

shown that intravascular SNM BAP revealed significant higher islet viability (>85%) than polymer-based BAP. However, a full-scale SNM BAP system must be developed to investigate the long-term hemocompatibility, and cell functionality in large diabetic animals before clinical trials involve diabetes patients [99].

Microporous polymer membranes can be used for the reconstruction of three-dimensional functional liver tissue [100]. Kasuya and Tanishita constructed 3D liver tissue by stacking two-dimensional (2D) tissues (composed of hepatic plate-like tissue, microvascular networks and intrahepatic bile ducts) on biodegradable microporous PLGA membranes. The 3D liver tissue was formed by controllable degradation of PLGA scaffolds after implantation (*in vitro* and *in vivo*) [101]. Another interesting approach is the recovery of nerve functions with the use of polymer membranes. PLGA membrane coated with PLL (poly(L-lysine)), PGA (poly(D-glutamic acid)) and nerve growth factor (NGF) was tested to investigate the nerve regeneration after a crush injury in rats. The NGF-loaded membrane was entirely biocompatible and enhanced the regeneration process throughout the first month after the lesion. However, the rate and dose of NGF released from the membranes were unknown [102]. Modified polymer membranes can promote guided bone and muscle regeneration. Liu et al. coated PCL fibrous membranes by mussel-inspired poly norepinephrine (pNE) to improve the regeneration of impaired rat skeletal muscle (rectus abdominal muscle, *in vivo*) [103]. The pNE-functionalized PCL membrane provided a better environment for cell adhesion and proliferation. It was well-integrated with regenerated muscle and achieved mechanical properties similar to native tissue. Polymer materials play a crucial role in guided bone regeneration (GBR). In the GBR procedure, the membrane prevents the in-growth of soft tissue to the bone defects and provides the defect space during tissue regeneration. Thus, membrane material should prevent epithelial cells migration, and ensure a proper mechanical property and resorption time after regeneration [104]. Among synthetic and natural materials, crosslinked collagen-based polymers, silk, ePTFE, or aliphatic polyesters (e.g. PLA, PGA, poly(ε-caprolactone), polydioxanone) are representative GBR membrane. However, due to the high production cost and limited mechanical properties, the development of new advanced polymers is vital for public health care [104]. Modification of polymeric membranes with bioactive compounds and/or stem cells can be useful for the regeneration of tissues in periodontal therapy [105]. Goncalves and coworkers designed a novel pol(isosorbide-succinate-co-L-lactide) (PisPLLA) membranes combined with collagen, hydroxyapatite and bone morphogenetic protein-7 (BMP7) growth factor to promote the periodontal regeneration, as well as bone formation in fenestration defects in rat jaws. The authors indicated that functionalized PisPLLA membranes exhibited osteoconductive capacity and increased extracellular mineralization (*in vivo* and *in vitro* studies). Therefore, this advanced membrane is a promising material for guided tissue regeneration. Da Cunha et al. fabricated chitosan/carbon nanotube membranes and chitosan/nanotube membrane mineralized with hydroxyapatite as alternative implants for the regeneration of cranial defects in rats. The carbon nanotubes significantly improved the mechanical properties of chitosan scaffolds. The *in vivo*

studies showed that designed implants were biocompatible, but did not indicate a considerable osteoregenerative capacity for the stimulation of bone repair [106].

5.1.3 Controlled drug delivery

Polymer membranes can serve as a vehicle for the delivery of drugs, proteins, or nucleic acids [107–110]. The main concept of all drug delivery systems is the controlled and sustained release of bioactive compound to enhance the absorption of hydrophilic or hydrophobic drugs at a specific site of the human body [107]. Among various routes, oral drug delivery is recognized as the most preferred for drug administration. However, when administrated orally, the therapeutic substances should be protected from degradation into physiological fluids, induced mainly by the gastrointestinal tract and first-pass liver effects [109, 110]. In this context, polymeric membrane-based delivery systems play an integral role in the advancement of drug delivery technology. A therapeutic substance can be coupled to polymers or encapsulated in the membrane structure to allow passive or active targeting and improve drug release kinetics. Various polymers are commonly used for drug encapsulation, but only biodegradable and non toxic ones are suitable for application as carriers. The most commonly applied are polyesters, acrylic polymers and polyamides. In the form of microcapsules, nanoparticles or thin films, they can act as a vehicle in cancer therapy (including targeted therapy), antibiotic therapy, analgesic therapies, etc. [111, 112]. The examples of various polymers used for the encapsulation of therapeutic agents were presented in Table 5.1.

Table 5.1: Polymers applied for drug encapsulation.

Polymer	Encapsulated drug	Therapy	References
Gelatin-co-PLA-DPPE	Doxorubicin	Cancer therapy	[113]
PLGA	Paclitaxel and vitamin E	Cancer therapy	[114]
PLA	Retinoic acid	Cancer therapy	[115]
PCL	Vitamin E	Antioxidant therapy	[116]
PLGA	Olanzapine	Antipsychotic therapies	[117]
PCL	Articaine	Anaesthesia	[118]
PLGA	Naproxen	Arthritis rheumatoid	[119]
Eudragit RSPO	Ibuprofen	Analgesic therapy	[120]
Starch	Heparin	Anticoagulation therapy	[121]
PLGA-lipid	Rifamycin, kanamycin, ampicillin, amoxicillin	Antibiotic therapy	[122]
mPEG-PLGA	Bedaquiline, vancomycin	Antibiotic therapy	[123]

Current cancer therapies include chemotherapy, radiation therapy (or the combination of chemotherapy with radiation), immunotherapy, hormone therapy, targeted therapy, or surgical intervention [124]. However, most chemotherapeutics leading to elevated toxicity in normal cells, thereby increasing adverse side effects. To enhance the therapeutic efficacy of cancer therapy, chemotherapeutics can be targeted to the tumor cell using various vehicles, including polymer microcapsules, scaffolds, hydrogels, or polymer nanoparticles. Polymer nanoparticles can be made form (i) synthetic polymers, such as PCL, PLA, or poly(styrene-maleic anhydride) copolymer, and (ii) natural polymers, e.g. gelatin, starch, and collagen [125]. For instance, Han and co-worker fabricated a drug delivery system based on amphiphilic copolymer nanoparticles consisting of gelatin, PLA and 1,2- dipalmitoyl-sn-glycero-3-phospho-ethanolamine (DPPE) to encapsulate doxorubicin (DOX) [113]. The DOX-loaded gelatin-co-PLA-DPPE delivery system exhibited anticancer efficacy against human lung carcinoma cells (*in vitro* studies) [113]. The release of drug from polymeric systems can be controlled by hydrolytic or enzymatic biodegradation. Kumar et al. reported the release of dexamethasone from the PLA composite films (i.e. PLA-calcium carbonate and PLA-ferric chloride) in the presence and absence of an enzyme. The inorganic salts were embedded in PLA matrix to provide a particular pH of media and regulate the biodegradation process. The biodegradation of PLA composite films in the presence of enzyme reached 20% and the release of dexamethasone achieved around 80% (after three days of the experiment). The authors showed that inorganic salts significant influenced the enzymatic biodegradation of PLA. Metal salts alter the pH of the medium, thus regulate the rate of biodegradation of polyesters [126].

Polymer nanocapsules may help to reduce the side effect associated with the administration of drugs. Campos et al. encapsulated the articaine into PCL nanocapsules to reduce unwanted symptoms during dental procedures, e.g. paresthesia or nerve injury [118]. The articaine-loaded PCL nanoparticles showed high encapsulation efficiency and colloidal characteristics optimal for the intrathecal administration of local anesthetic drugs. These findings open the way for future clinical studies using encapsulated drug formulations [118].

Microspheres made of natural polymers, such as starch, chitin or gelatin may protect the active substance from the harsh environment of physiological fluids. The rate of drug release depends on the size of the capsules. Larger microspheres release encapsulated drug more slowly and over a longer period than smaller ones [121, 127, 128]. Bajpai et al. presented studies dealing with the delivery of heparin encapsulated in swellable crosslinked starch microspheres to reduce its degradation when administrated orally. It was shown that the highest release of heparin was achieved in intestinal fluid (pH 7.5). At pH close to neutral starch microspheres showed enhanced swelling properties, thus increased the heparin release. Under acidic conditions, i.e. in gastric juice (pH 1.0), the microspheres did not swell sufficiently and the release of heparin was reduced accordingly [121]. The results indicated that encapsulation of drugs into starch microspheres may help to protect them from degradation into biological fluids.

Polymer-based membranes can provide optimal conditions for wound healing [129]. The moist environment promotes cell regrowth and can result in a reduction of scar formation [130]. Additionally, due to its occlusive properties, polymer dressing (called an occlusive dressing), can act as a barrier to harmful contaminants, such as bacteria and viruses [131]. Lopez-Calderon et al. designed bilayer membranes consisting of PVP-gelatin (hydrophilic layer), and CA (hydrophobic layer), loaded with gentamicin to improve the healing of infected wounds. The authors highlighted that those excellent antibacterial properties are associated with the bilayer composition of the fabricated wound dressing (*in vitro* studies). The hydrophilic layer in direct contact with injured tissue reduced bacterial biofilm formation and inhibited bacterial proliferation. On the other hand, the hydrophobic layer served as a physical barrier to reduce bacterial colonisation until solubilization [132]. Tong et al. fabricated a wound dressing made of cellulose nanocrystals film loaded with curcumin. Nanocellulose-based wound dressing caused a significant reduction of wound area from day 7 with the topical treatment of curcumin-loaded film (*in vivo* studies, diabetic rat models). The examination of skin sample excised from the animal model also showed a reduction in bacteria growth of 99.99%, and regeneration of hair follicles and sebaceous glands n the dermis layer of the skin [133]. Vimala et al. loaded curcumin into chitosan–PVA–silver nanoparticles film to enhance its antibacterial properties. The prepared nanocomposite films revealed well mechanical properties and superior antimicrobial activity against common bacteria and fungi found on burn wounds, i.e. *E. coli*, *Pseudomonas*, *Staphylococcus*, *Candida albicus*, and *Pseudomonas aeruginosa* (*in vitro*) [134].

Polymer materials can also act as carriers or recognition systems to facilitate cytoplasmic delivery of therapeutics, based on nucleic acids [108]. Various natural and synthetic polymers can be employed for the delivery of DNA, e.g. poly(D,L-lactide-co-glycolide) (PLG), polyanhydrides, PEG, collagen, or hyaluronic acid (HA). The release of DNA occurs usually through desorption, diffusion, polymer degradation, or a combination of these variants [135]. Yun and coauthors reported the incorporation of plasmid DNA (pDNA) into hyaluronan microspheres (5–20 μm) crosslinked by adipic dihydrazine as a novel gene delivery system (Figure 5.9). Around 60% of DNA released from HA microspheres after two months, due to degradation of crosslinked HA. Moreover, the released DNA was able to transfect the cell and skeletal muscle of rat (*in vitro* and *in vivo* studies) [136].

Plasmid DNA can be also encapsulated into biodegradable porous PLG microspheres. The incorporated DNA retained its integrity and released from PLG spheres within 24 h. The authors highlighted that pDNA-loaded PLG microspheres can be used in tissue regeneration to allow cell seeding and facilitate the transport of nutrients [137]. Polymer-based drug delivery systems are an interesting and promising option for DNA vaccination. Denis–Mize et al. fabricated DNA vaccine formulation consisting of pDNA attached to the microparticles made of PLG and cetyltrimethylammonium bromide (CTAB, cationic surfactant) to study the transfection of dendritic cell *in vitro* and *in vivo* [138]. Dendritic cells play a crucial role in the generation of the immune response

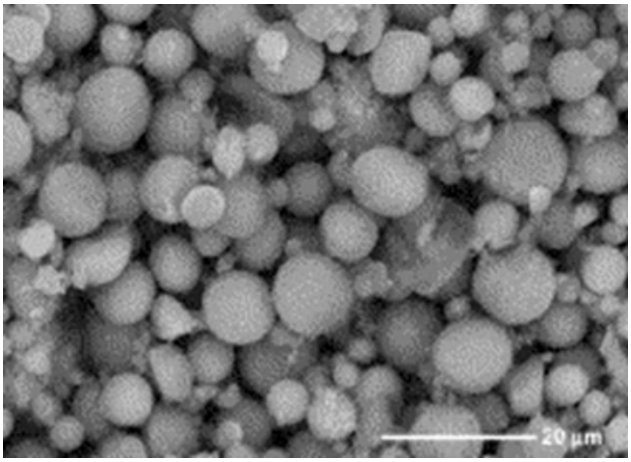

Figure 5.9: SEM micrograph of HA-DNA microspheres with a size ranged from 5 to 15 µm. Reprinted with permission from [136].

and demonstrate clinical efficiency in several types of cancer, e.g. melanoma, lung, prostate, etc. [139]. It was reported that the presence of cationic surfactant (CTAB) improved the transfection of dendritic cells, due to its interaction with DNA molecules. The results indicate that modification of polymers may imply a cellular response, which is essential for the efficacy of the vaccine [138].

One of the promising methods of gene delivery is adenoviral vectors [140]. However, adenovirus may lead to the infection of various cells, limiting the targeting to the specific tissues and organs. In order to reduce the possible interaction of the virus with healthy cells and provide its high uptake in a specific site, the adenovirus can be encapsulated into polymer microcapsules [141]. Sailaja et al. demonstrated encapsulation of human adenovirus type 5 (HAd5) into alginate microspheres with a size ranging from 5 to 10 µm. The size of microspheres allows them to be easily taken up by macrophages and dendritic cells. Based on *in vivo* studies (mice model) it was shown that mice immunization resulted in the development of virus-specific antibodies. However, encapsulation of adenovirus caused effectively circumvented the vector-specific immune response [142]. Modification of adenoviruses with polymers permits the incorporation of various targeting molecules, such as tumors antigen, enzymes, and proteins. Fisher and coworkers modified the surface of adenovirus by poly-[N-(2-hydroxypropyl) methacrylamide] (pHPMA)-based copolymer to protect it from antibodies action and incorporate of targeting ligands, i.e. fibroblast growth factor and vascular endothelial growth factor. This simple and cost-effective modification effectively changed the cell tropism and interaction with the immune system (*in vitro* and *in vivo* studies) [143].

5.1.4 Sensors and diagnostic assays

Detecting analytes with high selectivity, sensitivity, and low detection limits is of great interest in clinical diagnostics. Currently, two classes of polymer materials are the topic of intensive studies for the construction of sensors: artificial polymer vesicles (polymersomes, Figure 5.10), and planar polymer membranes (Figure 5.11) [144].

Polymersomes can be defined as 3D nanosized compartments surrounded by a stable synthetic membrane made of amphiphilic block copolymers. Hydrophilic biomolecules can be encapsulated into the inner cavity of polymersomes, hydrophobic biomolecules can be entrapped into membrane matrix and both of these bioactive compounds can be attached to the external surface of polymersomes (usually by chemical modification of their surface) [145]. The planar membranes are commonly made of copolymers, polymer composite or organic–inorganic hybrid materials. The active components are usually immobilized into a polymer porous membrane structure to improve the sensitivity of the sensor through improved signal transduction [146].

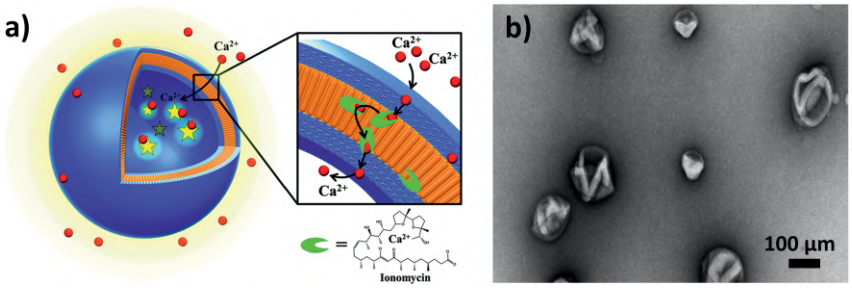

Figure 5.10: (a) Ca^{2+}-selective polymerosomes structure, (b) transmission electron microscope (TEM) micrograph of Ca^{2+}-selective polymerosomes. Reprinted with permission from [145].

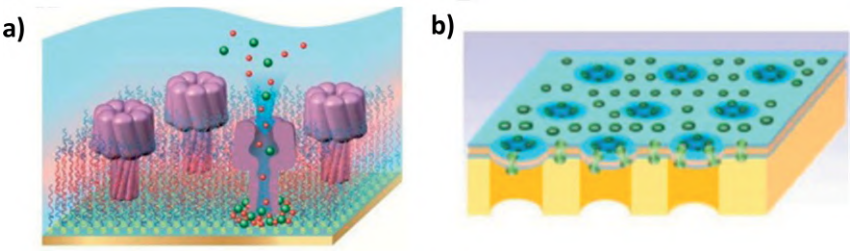

Figure 5.11: (a) Schemes of solid-supported planar membranes, and (b) pore-solid-supported membranes. Reprinted with permission from [146]. Copyright 2014 American Chemical Society.

Polymer based-nanosensor allow sensing of various biological and chemical analytes, from simple ions or inorganic particles to more complex ones, such as nucleic acid, proteins, oligonucleotides, enzyme or even cells [147–150].

An important class of advanced materials in the development of sensors is conducting polymers (CPs). CPs are polyconjugated polymers that possess mechanical properties of synthetic polymers (i.e. strength, plasticity, or flexibility) with excellent electrical conductivity. The most commonly applied conducting polymers include polypyrrole, polythiophene, or polyaniline [151]. CPs are suitable for application in electrochemical sensors, especially nucleic acids sensors because they can convert the hybridization event into an electrical signal. A typical scheme of DNA electrochemical sensor was presented in Figure 5.12. A DNA probe (e.g. specific oligonucleotides) was attached to the conducting polymer surface connected with the transducer (e.g. platinum or gold electrode). When the targeted DNA was captured by a specific probe, a recognition signal was generated at the CP/electrolyte interface and passed to the transducer through the CP layer [152].

A pivotal role in sensor application plays a special type of membranes known as ion-exchange, ion-selective, or sometimes conductive membranes. They are key components of potentiometric and chemical nanosensors. Ion-exchange membranes consist of highly swollen polymers carrying fixed positive or negative charges. There are three types of ion-exchange membranes: (i) cation-exchange membranes, which contain negatively charged groups (e.g. $-SO_3^-$, $-COO^-$, $-PO_3^{2-}$) fixed to the polymer matrix, (ii) anion-exchange membranes, which contain positively charged groups,

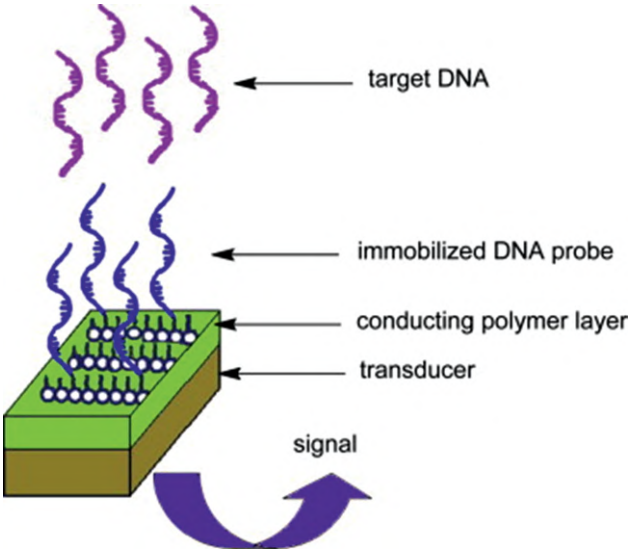

Figure 5.12: The scheme of DNA sensor based on conductive polymers. Reprinted with permission from [152].

such as $-^{+}NH_2R$, $-^{+}NR_3$, $-^{+}PR_3$, $-^{+}SR_2$, and (iii) bipolar membranes composed of cation- and anion-exchange layers [153]. The ion-selectivity of these membranes is associated with the presence of ion-exchange salts. The salts contain lipophilic ion enabling the exchange of only its hydrophilic counter ion with ions of the same charge. Senapati and coworkers designed an ion-exchange nanosensor made of divinylbenzene/polystyrene particles embedded into a polyethylene-polyamide/polyester matrix for nucleic acid detection using the charge inversion phenomenon. The negatively charged DNA oligoprobes were covalently attached to the positively charged surface of membranes. The hybridization of targets with specific oligoprobes caused significant changes in current–voltage characteristics, allowing identifying and quantifying nucleic acid molecules. This ion-exchange membrane-based nanosensor was able to specifically detect RNA associated with oral cancer, as well as RNA of dengue virus, *Brucella* and *E. coli* bacteria strains [154]. Jiang et al. designed a polymeric ion-selective electrode (ISE) for the detection of Ca^{2+} ions. The surface of polyvinyl chloride (PVC)-based polymeric membrane ISE was modified with polydopamine to improve its hydrophilic properties. The proposed modification of the sensor surface significantly reduced the adhesion of blood components from blood samples, and thus enhanced its biocompatibility [155]. The class of conducting polymers can be also used for the production of nanometer scale field effect transistor (FET) [156]. In order to prepare FET, a thin film of conducting polymer is deposited on the nanoelectrodes to comprise the channel of the transistor. Then, to create a FET biosensor, specific receptor molecules are attached to the sensing transistor channel. Zhang and coauthors demonstrated FET nanobiosensor for detection of single cells. The designed sensor consisted of polypyrrole thin film deposited on dual carbon nanoelectrodes. The sensing properties was achieved by modification of polypyrrole with hexokinase (adenosine triphosphate (ATP)-detecting enzyme). It is well-known that various cells release ATP as a result of hypoxia or osmotic stress, and its detection at a single cell may help to understand cancer cell metabolism. The resulting FET-sensor was capable to monitor the real-time changes of ATP concentration to cancer cells and cardiomyocytes (*in vitro*) down to 10 mM [157].

Polymer membranes can be also employed for the production of *in vitro* diagnostic test, such as lateral flow test strip assay (Figure 5.13) [159]. These assays are made for the detection of various analytes, i.e. hormones, enzymes, drugs, but also bacteria and viruses, including SARS-CoV-2 [160–163]. The main role of polymer membranes in these lateral flow tests is to provide support for the immobilization of labeled bioactive molecules. Test most of the test strips are made of modified porous nitrocellulose-based membranes. The sensitivity and selectivity of these assays can be improved by modification with targeting agents, as well as fluorescent and/or metallic nanoparticles [158]. The analytes migrate on the test strip (polymer membrane) by capillary force and are captured by immobilized molecules. These interactions result in colored spots or line, pointing to the targeted analyte. Additionally, these assays are fast, sensitive, and require no special equipment [164].

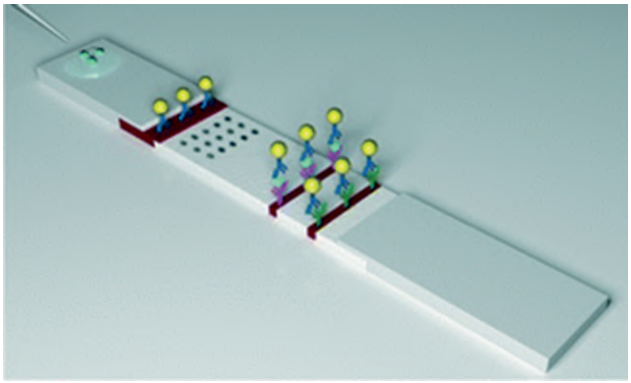

Figure 5.13: Examples of lateral flow assays. Reprinted with permission from [158].

5.2 Conclusions

Future progress in polymer membrane technology has a significant impact on the clinical success of tissue engineering strategies. Polymeric membranes have a huge potential for biomedical application, however, there are still many studies necessary to improve their final properties and many questions remaining to be answered. The major limitations lie in the time and cost spent in the production of 3D biocompatible constructs while maintaining their mechanical strength and surface properties. Another barrier is associated with advanced fabrication techniques, which may hider for a cost-effective upscaling of the membrane technology. In addition, the regulatory safety aspects and membrane life cycle should be intensively investigated before any of these membrane systems may be used in the clinic. In this context, the aspects related to interactions of polymeric materials with body fluids are particularly relevant. Important issues to consider are the influence of polymer-based systems on cell adhesion, proliferation, and differentiation, as well as their degradation in the human body. The modification of polymer membranes with nanomaterials to improve their physicochemical properties and biological activity may cause various adverse effects on the immune system or oxidative stress-related disorders. Accumulations of nanomaterials/nanoparticles in tissues and organs may induce mutagenesis and carcinogenesis. Furthermore, advanced preclinical studies in large animals will be indispensable in translating *in vivo* studies into medical applications within human care diagnostics and treatments.

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6 Liquid membranes for separation of metal ions from wastewaters

Abstract: The paper reviews application of various liquid membranes (LM), particularly of emulsion and supported liquid membranes, for metal separation from model and industrial wastewaters. A variety of carriers and separation systems is shown. Not only model solutions on a laboratory scale are presented but also some examples of real wastewater separation with LM are reported.

Keywords: emulsion liquid membranes; liquid membranes; metal ion carriers; metal separation; supported liquid membranes; wastewaters.

6.1 Introduction

In recent years, membrane techniques have become widely investigated and applied for many separation processes due to the possibility of using this technology to remove contaminants (especially metal ions) from waste solutions. The observed increase in the use of membrane techniques is related to their continuous development, increased environmental awareness and the fact that they can be used in processes where commonly known methods are not efficient or selective.

The chapter focuses on a review of the composition of various liquid membranes (LM) and their use (particularly of emulsion and supported liquid membranes) for metal separation from model and industrial wastewaters. A variety of carriers and separation systems is shown. Not only model solutions on a laboratory scale are presented but also some examples of real wastewater separation with LM are reported.

6.2 Classification of liquid membranes

Membrane operations are considered environmentally friendly and are recommended as best available techniques by the European Union because they are simple in concept

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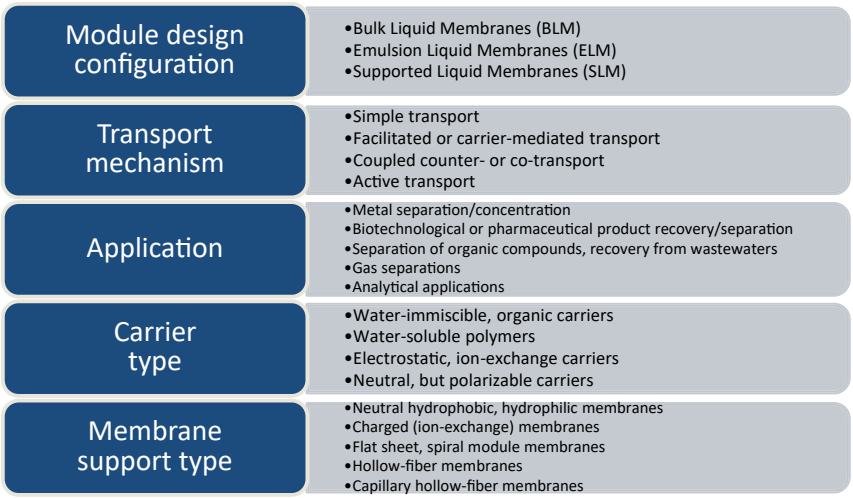

Figure 6.1: Classification of liquid membranes [1, 3, 4].

and operation, modular, easy to scale-up and low-energy consuming with a remarkable potential for an environmental impact, and energetic aspects [1, 2]. A membrane is a barrier between two phases that enables a solute to be transported across the barrier. Among various membranes, LM involve liquid immiscible with the feed (donor phase) and receiving (acceptor) phases that serves as a semipermeable barrier between these two liquid or gas phases. LMs are classified according to a module configuration, transport mechanism, application, type of carrier, and type of membrane support, as it is shown in Figure 6.1. Module design configuration, transport mechanism, and membrane support type are considered in detail in the further part of the chapter.

Many carriers typically applied in LM are used as commercial extractants, and some examples of the compounds used in a membrane phase are given in Table 6.1.

There are three main types of carriers [1, 5, 75–78]:

- *Acidic* (chelating and nonchelating): The transport is based on the reaction of a metal cation with an acidic extractant; a neutral complex is formed, here mainly hydroxyoximes and alkylphosphoric acids are used,
- *Basic*: The transport is mainly based on the addition or ion exchange reaction; an ion pair is formed, basic carriers include quaternary ammonium or phosphonium salts (many of them are classified as ionic liquids, ILs), tertiary amines, pyridine, and its derivatives,
- *Solvating (neutral)*: The transport is based on solvation; a solvate or adduct is formed; they include trialkylphosphine oxides or phosphoric acid esters.

An important specific group of carriers includes macrocyclic and macromolecular compounds – calixarenes, resorcinarenes, crown and lariat ethers [79, 80]. Transport

Table 6.1: Types and examples of commonly used extractants [1, 5, 6].

Chemical name	Trade name or abbreviation	Application in LM	Ref.
Acidic, chelating			
β-diketone	LIX 54	**ELM**: Cu(II) transport	[7]
2-hydroxy-5-nonylbenzophenone oxime	LIX 64N	**ELM**: Cu(II) transport	[8, 9]
Mixture of 5-nonylsalicylaldoxime and 2-hydroxy-5-nonylacetophenoneoxime	LIX 984N	**BLM**: Cu(II) transport	[10]
2-hydroxy-5-nonyl benzaldoxime with modifiers	ACORGA P50, ACORGA 5640, LIX 860	**SLM**: Cu(II) transport	[11, 12]
Acidic, nonchelating			
bis(2-ethylhexyl)phosphoric acid	HDEHP, D2EHPA, DEHPA	**BLM**: Cu(II) transport, Cu(II), Ni(II) and Zn(II) transport, Co(II), Cd(II) transport **SLM**: Co(II), Eu(III), Y(III), Nd(III), Dy(III) transport **SLM**: Zn(II) separation from Ni(II), **ELM**: Cu(II) and Zn(II) from wastewater, Cd(II), Pb(II), Ce(III), Hg(II), Ni(II) transport	[13–30]
bis(2,4,4-trimethylpentyl)phosphinic acid	Cyanex 272	**SLM**: Zn(II) and Fe(III) separation from Cr(III) **ELM**: Co(II) from waste	[31–33]
bis(2,4,4-trimethylpentyl)dithiophosphinic or *bis*(2,4,4-trimethylpentyl)-monothiophosphinic acids	Cyanex 301, Cyanex 302	**SLM**: Ge(IV) transport **ELM**: Ag(I) from waste, Pd(II) transport	[34–37]
2-ethylhexyl 2-ethylhexylphosphinate	PC88A	**SLM**: Dy(III), Nd(III) transport, **ELM**: Co(II) from wastewater, Cr(III) transport	[38–42]
Basic			
A mixture of trioctylamine and tridecylamine	Alamine 336	**ELM**: U(VI) from ore leach solution	[43]
methyltrioctylammonium chloride	Aliquat 336/TOAC	**BLM**: Cd(II) transport, Au(III), Ag(I), Pt(IV) and Pd(II) from waste **SLM** and PIM: Pt(IV) transport **ELM** and **SLM**: Cd(II), Cr(III) transport	[44–52]

Table 6.1: (continued)

Chemical name	Trade name or abbreviation	Application in LM	Ref.
		BLM and **SLM**: Cr(VI) transport	
trialkylamine, trioctylamine	Adogen 364, TOA	**BLM**: Hg(II) transport **SLM**: Zn(II) separation from Ni(II), V(V) transport	[21, 53, 54]
trihexyl(tetradecyl)phoshonium salts	Cyphos ILs	**BLM**: separation of Fe(III) from Ni(II) **PIM**: Zn(II), Fe(III), Cd(II), PGM, V(V) transport	[55–60]
Solvating			
Mixture of trialkylphosphine oxides	Cyanex 923, Cyanex 925	**SLM**: Ge(IV) transport	[61, 62]
trioctylphosphine oxide	TOPO	**ELM**: Ga(III) from wastewater, U(VI) transport	[63, 64]
tributylphosphate	TBP	**BLM**: Cr(VI) transport **SLM**: Zn(II), Fe(II) separation, **ELM**: Zn(II) from wastewater	[65–68]
diglycolamide derivatives, e.g. *N,N,N′,N′*-tetra-n-octyl diglycolamide	TODGA	**SLM**: Am(III), Np(IV), Pu(IV) transport	[69, 70]
Macrocyclic and macromolecular			
calix[4]resorcinarene derivatives	–	**PIM**: Zn(II), Cd(II) transport	[71]
calix[4]pyrroles	–	**SLM**: Ag(I) transport	[72]
4,4′(5′)di-t-butyl-cyclohexano-18-crown-6 ether	DtBuCH18C6	**SLM**: Sr(II) transport	[73]
dibenzyldiaza-18-crown-6 ether and derivatives	DBzDA18C6, DC18C6, DB18C6, B18C6	**SLM**: Ag(I) transport	[74]

with macrocyclic carriers is based on the size-selective complexation of a specific metal ion, especially the alkali and alkaline ones. For examples, these carriers have been reported to be applied for the selective removal of Sr-90 from nuclear waste solutions with little cotransport of other ions [73]. Although LMs need smaller amounts of carriers than the conventional extraction, the application of macrocyclic and macromolecular extractants is strongly limited by high cost of the macrocycle carriers and their difficult use in a membrane module. Another approach to affect the extraction in LM is a synthesis of various derivatives of common extractants which improves the selectivity of transport of selected metal species. As an example multiple diglycolamide

DGA-based extractants can be given, i.e. tripodal DGA (three DGA units pivoted on a C-atom) or TREN-DGA/TRPN-DGA (three DGA units pivoted on a N-atom) [69, 70]. The application of ionic liquids (ILs) as metal ion carriers in LM is also a part of the search for improvement in the stability and effectiveness of the membranes [55–60].

These various carriers are applied in LM to separate diverse metal ions, including alkali and alkaline metals (Cs^+, Sr^{2+}) [73], heavy metals (Pb(II), Zn(II), Co(II), Ni(II), Cr(III), Cd(II), Cu(II), Hg(II)) [7, 13, 15, 16, 21, 30, 53, 78], rare Earth elements (Dy(III), Nd(III), Eu(III), Y(III)) [18–20, 38], noble metals (Ag(I), Au(III), Pd(II), Pt(IV), Ru(III)) [35–37, 46, 59], Ge(IV), Ga(III), or actinides (U(VI), Am(III), Np(IV), Pu(IV)) [34, 43, 61–64, 69, 70] from model solutions and wastewaters.

A good carrier should be selective for the desirable solute, nonflammable, nontoxic, biodegradable, cheap, stable, soluble in the organic phase and poorly soluble in water, and easy to regenerate [81].

Metal species are transported from the feed phase (**F**) across the liquid membrane (**M** or **LM**) to the receiving (stripping) phase (**R**) according to various mechanisms (Figure 6.2). A solute (**S**) can be transported passively or the transport can be facilitated by other compounds called carriers [1, 82]. An efficient transfer of the solute is achieved in the following steps: (i) Transfer of S from the feed phase to the LM as a result of partitioning (passive transport) or chemical reaction (facilitated transport), (ii) diffusion-driven transport across the membrane of S or its hydrophobic complex/ion pair with the carrier (driven by concentration gradient of S at both sides of the

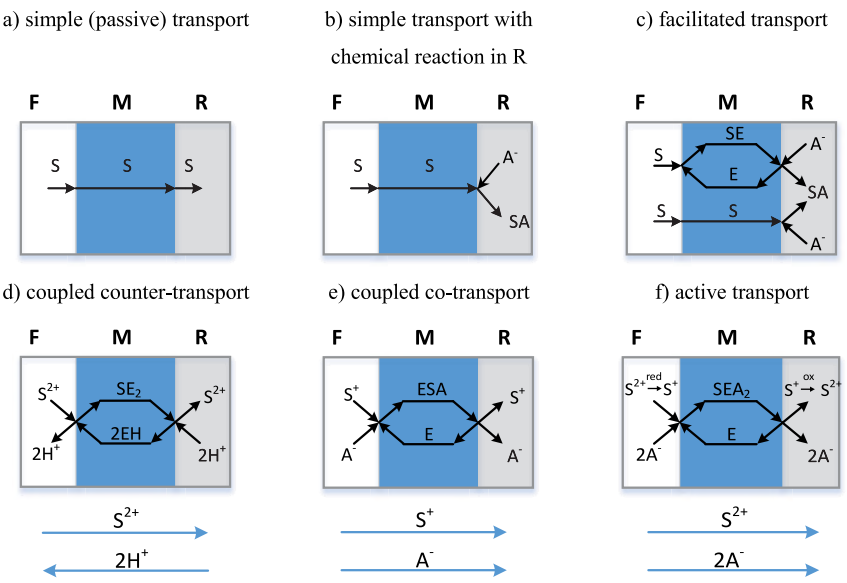

Figure 6.2: Schematic mechanisms of solute (S) transport in liquid membranes [1, 82, 83]. (F, M, R – stand for feed, membrane and receiving phases, respectively).

membrane), and (iii) transfer of S from the LM phase to the receiving phase and regeneration of the carrier (if present). Maintaining high driving force in LM systems is one of the main problems therefore various methods are applied to minimize solute concentration in the receiving phase [82], e.g. (i) converting S transferred to the receiving phase into another chemical species (complexation reactions or metal ion reduction by electrolysis), (ii) inducing convective mass transfer (mechanical stirring or flow), and (iii) combining the mentioned approaches. Some methods to intensify the transfer of S are shown in Section 3.2 (Table 6.5).

The passive transport (Figure 6.2a and b) corresponds to typical partition in solvent extraction, while the facilitated transport (Figure 6.2c), like in reactive extraction, is more selective and effective due to the carrier presence in the organic phase which is responsible for the transfer of some specific solutes. Because of higher selectivity, the facilitated transport mechanism is more common in the LM systems and is based on a reversible chemical reaction between the solute and the carrier. As a result of the reaction, only species forming a complex with the carrier are transferred from the feed to the receiving phase, while other species (not reacting with the carrier) do not enter the LM phase and stay in the feed [1, 84].

The facilitated transport can be realized by the mobile carrier according to carrier-mediated systems: the mobile carrier (MC) or the fixed site carrier (FSC). The mobile carrier freely diffuses across the liquid membrane (e.g. SLM, some of PIM), while in FSC the carrier is bound with the polymeric matrix and its ability to move (to diffuse) is limited. Some researchers report that the transport of the solute, for example in PIM, is realized by "fixed-site jumping" [85, 86]. The complex formed by S and the carrier after diffusion across the LM decays at the LM-R interface resulting in the release of S to the receiving phase. Facilitated transport accelerates and positively influences the selectivity of the transport.

Coupled counter-transport mechanism (Figure 6.2d) means the transport of metal ions (e.g. Co(II), Zn(II) [17, 87]) accompanied by the transport of other chemical species (e.g. protons as counterions) from the receiving to the feed phase (in the opposite direction to the metal ion transport), which offers the possibility of transporting a component against its concentration gradient. For example, lariat ethers transport metal ions simultaneously with back transport of H^+ ions and thus a pH gradient provides the potential for metal ion permeation across the LM [79]. Fakhari et al. [87] proposed 5,6,14,15-dibenzo-1,4-dioxa-8,12-diazacyclopentadeca-5,14-diene azacrown ether (DBDA15C4) with two ionizable protons as a carrier for Zn(II) in BLM. It was observed that pH of the feed decreased (from pH 7 to 3.5) during Zn(II) transport and the receiving phase (containing histidine donating H^+ to the carrier) pH increased to pH above 7. This proton counter-transport mechanism is based on a protonation–deprotonation cycle of azacrown ether at the membrane interfaces of the receiving phase and the feed, respectively. This cooperative effect enhances the proton driven selective Zn(II) transport.

In the co-transport (Figure 6.2e), for example for high feed acidity, anions can be transported together with metal cations in the same direction. In both cases, fluxes of metal ions, protons, and anions are stoichiometrically coupled [1].

Active transport (Figure 6.2f) is driven mostly by irreversible reactions, e.g. oxidation–reduction, catalytic reactions, and biochemical conversions on the membrane interfaces [1]. Thanks to specific reactions this type of transport is highly selective.

6.2.1 Bulk liquid membranes (BLM)

Bulk liquid membranes (BLM) consist of a bulk aqueous feed and receiving phase separated by a bulk organic, water-immiscible liquid phase. The phases may be separated by microporous support or the phases may contact directly without microporous support (then such a configuration is called a layered BLM – see Figure 6.3). BLMs are most often configured in U-shaped vessels or vessels with cylindrical partitions (Figure 6.3). Such geometry of the vessels used requires that the organic phase has a higher density than the aqueous phases. Due to the large thickness of the membrane phase, the amount of a transported substance is small. For this reason, BLMs are of no practical (industrial) importance and are used mainly to study transport mechanisms and the influence of a carrier structure on the efficiency and selectivity of transport [50].

6.2.2 Emulsion liquid membranes (ELM)

6.2.2.1 First industrial plants

Emulsion liquid membrane was invented by Li [89] in 1968 for separating hydrocarbons (a mixture of heptane and toluene, octane and isooctane, or octane and octene). Since ELMs were invented, they have begun to be used in many separation processes (recovery and/or separation of metal ions and organic compounds, dyes, and drugs).

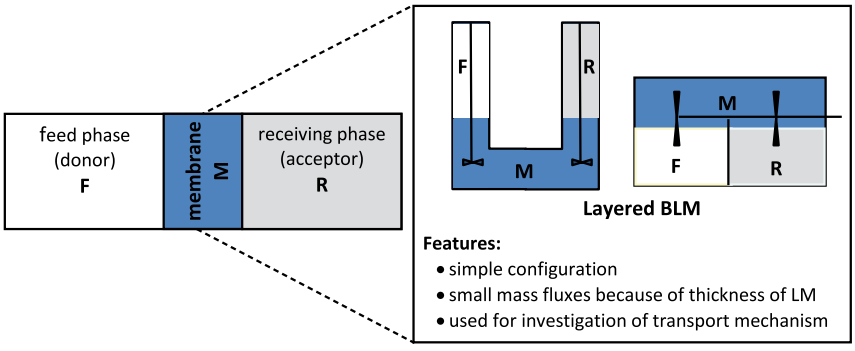

Figure 6.3: Scheme of bulk liquid membranes [1, 3, 82, 88].

The first liquid membrane industrial plant for Zn(II) removal from wastewater in the viscous fiber industry was opened in 1986 at Lenzing, AG (Austria). The capacity was 75 m^3/h. The concentration of zinc ions in the wastewater was reduced from 500 to 3 ppm. Plants of much higher capacity (200–700 m^3/h) using ELM to remove Zn(II) from industrial wastewater were opened at Glanzstoff AG in Austria, CFK Schwarz in Germany and AKZO Ede in the Netherlands [1, 90].

In 1986 for the first time on an industrial scale phenol was removed from wastewater using ELM plant at the Nachung Plastic Factory in Guangzhou in China. Phenol was reduced from 1000 to 0.5 ppm (extraction efficiency >99.95%). ELM on an industrial scale was used also for cyanide removal from wastewater in gold processing (Huang-Hua Mountain Gold plant, China) and extraction efficiency of 99.6% [1].

6.2.2.2 The composition of ELM

ELMs, also called surfactant liquid membranes, are generally multiple emulsions formed by emulsifying two immiscible phases, i.e. oil-in-water-in-oil (O/W/O) system or vice versa water-in-oil-in-water (W/O/W). Two main types of multiple emulsions are presented in Figure 6.4. As in the case of other liquid membranes, the difference of the chemical potentials between the external feed phase and the internal receiving (acceptor) phase is the main driving force of the solute transport through the membrane.

ELM consists of three phases [1]:

- Feed phase (external, aqueous phase),
- Organic membrane phase,
- Receiving phase (internal, aqueous phase).

The ELM stability depends on the stability of interfacial film whose stability depends on the various factors such as the emulsion droplet size, method of emulsion preparation, surfactant adsorption–desorption kinetics, intensity of mixing, concentration of ELM

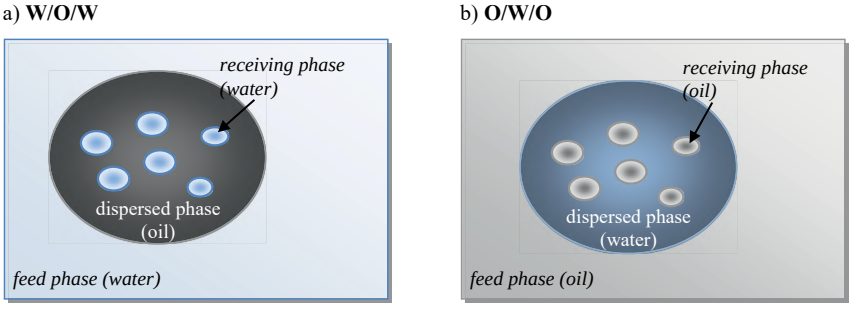

Figure 6.4: Types of emulsions: a) Water-in-oil-in-water (W/O/W), b) oil-in-water-in-oil (O/W/O) [91].

components, concentration of the receiving phase, pH of the feed phase, phase volumes, type of the used surfactant, carrier, and diluent [92, 93]. The size of the droplets dispersed in the oil or water phase is an important parameter influencing the ELM stability. It is reported that small droplets result in better breakage resistance and enhance rapid extraction while large droplets reduce membrane stability and extraction efficiency. Generally, the average droplet sizes favorable in ELM are in the range of 1–10 μm. However, also nanoemulsion liquid membranes (NELM) with the droplet size range of 20–200 nm, in some research up to 600 nm, have been reported for Ag(I) extraction [94] or Pd(II) transport followed by formation of palladium nanoparticles [95]. Droplets smaller than 0.98 μm are produced by ultrasounds and provide membranes with high stability, large surface area, uniform droplet distribution, low-energy, and low-surfactant consuming. However, too small droplets cause that it is very difficult to break the emulsion mechanically. In addition, too many of small droplets packed into each organic globule result in too thin membrane and is easily broken.

Liquid membrane usually consists of three components: extractant (or carrier) which transfers e.g. the valuable metal ions from external to internal phase, organic solvent, and stabilizer (mainly surfactant) [4]. In the case of ELMs, emulsion W/O/W is most common. Three steps for the ELM process are presented in Figure 6.5. In the first step (preparation of ELM), the receiving aqueous phase is emulsified in the organic phase (liquid membrane). This emulsion is dispersed in the aqueous feed phase. As a result, the two aqueous phases are separated by the liquid membrane and there is no direct contact between those two aqueous phases. The organic phase contains a hydrophobic surfactant which stabilizes the emulsion [4, 96].

In the second step, the solute is transported from a feed phase through the membrane to a receiving phase. In comparison to liquid–liquid extraction, where extraction and stripping are two different steps, in ELMs the extraction and stripping occur simultaneously. As a result, the number of intermediate steps in the separation process is reduced. The last step is separation of the external feed from emulsion 1 and de-emulsification to recover the organic membrane phase [1, 96].

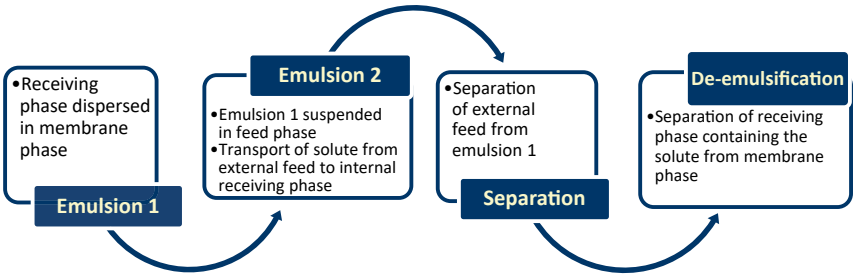

Figure 6.5: Three steps of the ELM process [96].

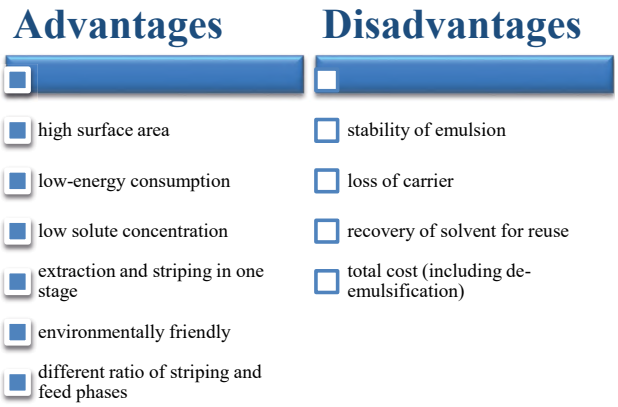

Figure 6.6: The main advantages and disadvantages of ELM [1, 51].

6.2.2.3 Advantages and disadvantages of ELM

The main advantages and disadvantages of ELM are presented in Figure 6.6. The most important advantage of ELM is a large interfacial surface which guarantees a high rate of mass transport. ELM can be used not only for separation and removal but also for a concentration of solutes in the receiving solutions (when the volume of a receiving phase is smaller than the volume of the feed). Also, the use of ELM is recommended when the solute concentration is quite low, and other methods (e.g. extraction) cannot be applied. As mentioned before, in ELM extraction and stripping are carried out in one stage which is favorable from an economic and ecological point of view. Moreover, the transport efficiency is high and the obtained products are of good purity and quality. In comparison to other membrane techniques (e.g. pressure-driven membrane techniques), ELMs are characterized by low-energy consumption [1, 51].

The main disadvantage of ELM process is maintaining stability of the emulsion. For this reason, it is necessary to use emulsion stabilizers, e.g. surfactants. When the size of a drop of the receiving phase is too large, the membrane can break during agitation. Moreover, the membrane can swell due to the osmotic transport of water from the continuous phase to the receiving phase and as a result the receiving phase becomes diluted. In some cases, a slight loss of the carrier is possible due to its transport from the organic to the aqueous phase [1, 51].

6.2.2.4 Surfactants

The desirable features from a good surfactant are the following: (i) membrane stabilization during mixing of the emulsion in the reactor, (ii) reduction of the osmotic transport of water between the phases, (iii) supporting the extraction of a component

Table 6.2: Types and examples of surfactants [1].

Type of surfactant	Examples
Anionic	sodium dodecyl sulfate (SDS), ammonium lauryl sulfate, fatty acid salts
Cationic	cetyltrimethylammonium bromide (CTAB)
Amphoteric	dodecylbetaine, dodecyldimethylamine oxide, cocamidopropylbetaine, cocoamphoglycinate
Nonionic	alkylpoly(ethylene oxide), copolymers of poly(ethylene oxide) and poly(propylene oxide), alkylpolyglucosides, sorbitan monooleate (Span 80)

from the feed phase to the receiving phase, and (iv) chemical stability [1]. Surfactants are mainly organic compounds that consist of two elements:

- A hydrophobic group (a *tail*),
- A hydrophilic group (a *head*).

A hydrophilic group is soluble in the water phase, while a hydrophobic group is soluble in the organic phase. Surfactants reduce the interfacial tension between the organic and aqueous phases by adsorbing at the interface of both phases [1]. The classification and some examples of surfactants are presented in Table 6.2.

6.2.2.5 Carriers/extractants used in ELM

As mentioned before, an extractant (or carrier) is mainly responsible for the selective diffusion transport of the solute from one phase, through the membrane, to the other phase [97]. The types of extractants and examples of the transported metal species are presented in Table 6.1. Two types of ELM are identified as type I – without a carrier and type II – with a carrier. The separation mechanisms responsible for the solute transport are as follows [1]:

a) *Simple permeation mechanism* – based on the transport of a solute from one aqueous phase to another aqueous phase through a liquid organic membrane which separates these two phases (Figure 6.2a). The driving force of the process is the concentration gradient of solute on both sides of the membrane. In the case of type I, a component is soluble in all three phases: External feed phase, organic membrane phase, and internal stripping phase. Solute diffuses from the feed through the membrane into the stripping phase where it reacts and forms the insoluble in the organic phase product (Figure 6.2b). This system is used for the extraction of weak acids or bases from wastewater e.g. removal of phenol by NaOH and removal of ammonia by H_2SO_4 [1].
b) *Facilitated transport mechanism* – ELM type II is based on the transport of the solute through the membrane by a selective carrier (Figure 6.2c). The carrier is

soluble only in the organic phase (membrane phase). The carrier reacts with the solute at the membrane-external phase interface and forms a membrane-soluble product. The product is transported through the membrane to the membrane-internal phase interface and dissociates. This type of transport is especially applicable to the separation or recovery of metal ions from wastewater [1, 24, 32, 33, 40].

6.2.2.6 Diluents

The diluent (or solvent) is a liquid or homogeneous mixture of liquids in which extractant and possible modifier (e.g. a surfactant) may be dissolved [97]. The most common diluents used in the ELM are n-hexane, kerosene, cyclohexane, benzene, toluene, chloroform, and carbon tetrachloride. A good diluent should dissolve the extractant well, has low volatility, high flash point, low surface tension, be insoluble in the aqueous phase, cheap and readily available, and cannot form a third phase with extracted compounds [1, 98].

6.2.3 Supported liquid membranes

Supported liquid membrane (SLM) consists of the polymeric porous support and liquid membrane (an organic phase containing a carrier) placed in micropores of the support fixed between two aqueous phases (F and R). SLM transport is limited by the concentration gradient between the feed and the receiving phase.

Typical configurations of SLM, a) sandwich module with flat sheet membrane and b) tubular module with hollow fiber (HF) capillary membranes, are shown in Figure 6.7.

The stability of a long term operation of LM is an important issue considered when these membranes are to be applied for metal ion transport. The long term performance is affected by the chemical nature and textural characteristics of the polymeric support,

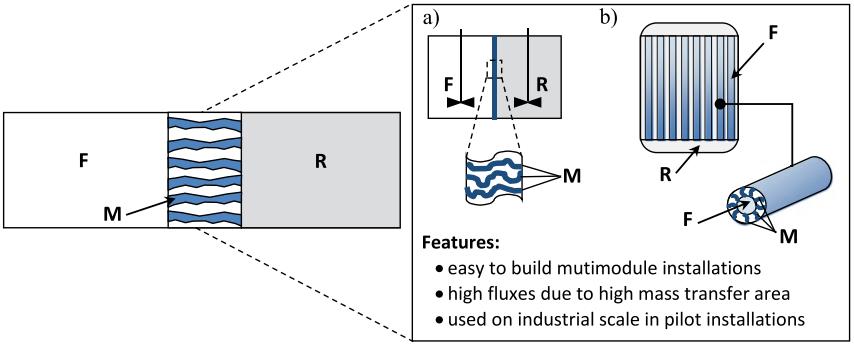

Figure 6.7: Scheme of supported liquid membranes [1, 82, 83, 88, 99].

nature of the organic membrane phase, and method of the preparation of the membranes [74]. Flat sheet membranes (used in sandwich-type modules) are impregnated by immersing for some time (e.g. 12 or 24 h [21]) a membrane in an organic phase containing a carrier, sometimes under pressure or vacuum. The drawback of this impregnation method is lack of control of the carrier penetration into pores of the polymeric support. It can be enhanced by ultrasounds which cause mechanical vibrations and acoustic streaming. Acoustic cavitation generated by ultrasounds helps to release dissolved in the organic phase gaseous nuclei and thus increase the amount of the carrier present in pores of the membrane support [13]. Although in some systems ion permeability values change marginally with time even in three weeks showing very good stability [73], in most reported systems after a long time of working or several cycles of transport experiments, a decrease in fluxes of the transported species is observed [13, 55, 70]. The loss of the organic phase from the membrane pores is indicated as a drawback of the impregnated flat sheet membranes and appears to be due to weak interactions (capillary forces) between a carrier and the support material [2, 55]. The poor stability limits the long term use of SLM, especially in a flat sheet configuration [70]. To overcome the instability of the impregnated SLMs, polymer inclusion membranes (PIM) – considered a special type of SLM – have been developed.

In PIM a carrier itself is built into the structure of the membrane and included in a polymer matrix (mainly cellulose triacetate (CTA), poly(vinyl chloride) (PVC), or poly(vinylidene fluoride-co-hexafluoropropylene) (PVDF-HFP)) with the addition of a plasticizer or a modifier (Figure 6.8) [55, 57–60]. Good stability of PIM, limited loss of carriers [44], high selectivity, and transport efficiency [71] compared to other types of liquid membranes are the most important advantages which result in great interest among various research groups investigating metal ion transport through LM. Also, a small amount of a carrier is required which opens the possibility to use also expensive extractants as ion carriers such as macromolecules or macrocyclic carriers (Table 6.1). However, it must be emphasized that small values of fluxes and low diffusion coefficients cause the transport long lasting what disqualifies PIM from being used on a large industrial scale for metal ion transport. At the same time, some researchers report new and prospective use of PIMs on a laboratory scale for analytical applications [102–104].

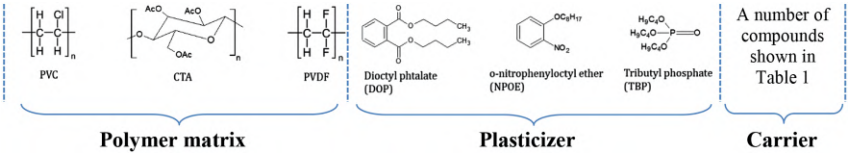

Figure 6.8: Composition of polymer inclusion membranes [1, 76, 77, 100, 101].

Generally, loss of the organic phase from the membrane pores is indicated as a drawback of not only impregnated flat sheet membranes but also of hollow fiber membranes. Various causes are reported to affect the leakage of the organic phase out of the membrane material [2]: (i) improper pressure difference between the organic and aqueous phases, (ii) solubility of an organic phase in a feed and/or receiving phases, (iii) wetting of membrane pores by the aqueous phases (F or R), (iv) blocking of the membrane pores by precipitation of a carrier or by water, and (v) emulsion formation by the organic phase in the aqueous phases by lateral sheer forces.

Nondispersive solvent extraction (**NDSX**) – contrary to a classical liquid–liquid extraction called also dispersive solvent extraction, is realized in membrane modules/contactors, preferentially *hollow fiber* (**HF**) ones, and the mass transfer occurs without dispersion of one phase in another [105]. HF modules offer a large mass transfer area due to their construction including a number (~10,000) of very thin (capillary) fibers gathered around a central tube. HF modules are considered a good technical solution because of the large area of mass exchange in a unit volume which means a small footprint. Generally, the organic phase containing an extractant reacting with the transported species flows in the *shell (outer) side*, while the aqueous feed in the *lumen (tube) side*. As the membrane is hydrophobic, the organic phase wets the pores of the fibers very well, however, a transmembrane pressure of 0.15–0.3 atm (0.015–0.03 MPa) in the lumen side must be applied to avoid leakage of the organic phase to the aqueous feed [67, 106]. In such a configuration (with circulated organic phase) one HF contactor is used for extraction, while the other one is necessary to strip extracted species to a receiving phase and regenerate the organic phase. Some authors have proposed the recycling of the organic phase after NDSX as a batch stripping operation. For example, after Nd(III) extraction the loaded 0.3 M DNPPA and 0.13 M TOPO was contacted with 5.5 M H_2SO_4 in separating funnels to receive Nd(III) [106]. The stripping was effective and the organic phase could be recycled to NDSX and showed excellent reproducibility of extraction. Another operating mode of NDSX is impregnating the membrane pores with the organic phase (LM) and circulating of the feed and receiving phases at both sides of the porous support in the lumen and shell side of one HF module [39, 107].

Another technical solution of the extraction-stripping process is *pseudo emulsion based hollow fiber strip dispersion* (**PEHFSD**), called also *emulsion pertraction technology* (**EPT**), which combines in one HF module extraction of the solute to an organic phase and stripping to a receiving phase dispersed in the organic phase forming pseudo emulsion [108, 109]. Similarly to PEHFSD, works *supported dispersion liquid membrane* (**SDLM**) with flat sheet poly(vinylidene fluoride) (PVDF) diaphragm [18]. A schematic representation of the transport applying pseudo emulsion is shown in Figure 6.9.

The stripping phase dispersed in the organic phase enables surface renewal and thus, such a membrane system has increased stability compared to a classical SLM, simplicity of operation, and very efficient stripping of the target species from the organic phase which leads to high flux and high concentration of the recovered

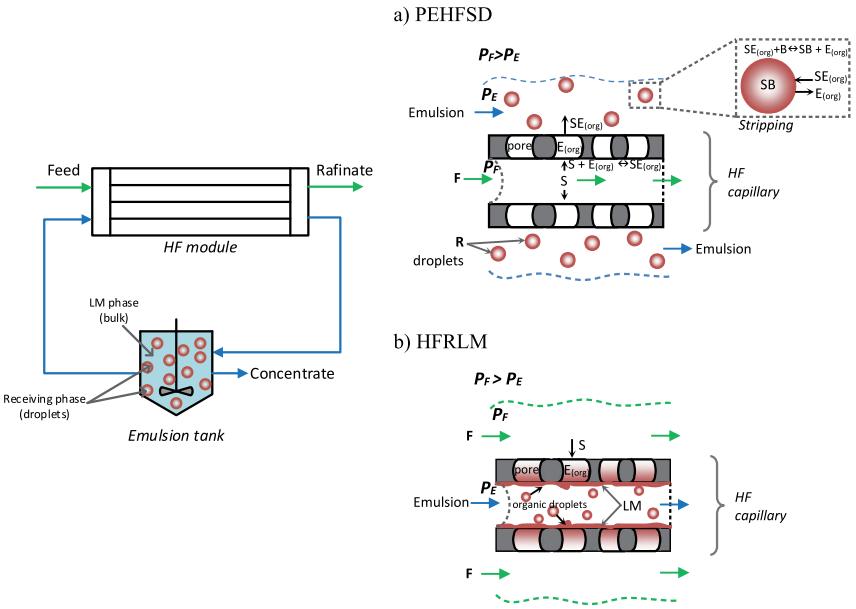

Figure 6.9: Transport of a solute (S) in extraction-stripping emulsion pertraction technology (EPT) in two configurations.
a) Pseudo emulsion based hollow fiber strip dispersion (PEHFSD), b) hollow fiber renewal liquid membranes (HFRLM) [18, 75, 108–110].

species. In the case when the stirred mixture of the organic and stripping phases flows at a high aqueous/organic volume ratio through the lumen side of the HF module, the technique is called *hollow fiber renewal liquid membrane* (**HFRLM**) [110–112]. While flowing through the lumen side of HF, the dispersion of the organic droplets in the stripping phase forms a thin organic film in the internal (lumen) side of fibers. The sheer force causes the film liquid to form microdroplets on the surface of the liquid membrane layer, which enter into the lumen side fluid after peeling off from the surface of the LM layer. Simultaneously, the organic droplets fill the surface of the liquid film and thus the renewal of the LM is continuously proceeding. HFRLM is reported to enhance the mass transfer rate and reduce the diffusion resistance across the aqueous boundary layer within the HF lumen side [110, 112].

The transport of metal ions through EPT (with strip dispersion) involves various steps [18, 109]: a) diffusion of metal species from the feed phase to the membrane interface embedded in the pores of the hydrophobic support, b) reaction with a carrier and extraction of metal species on the feed-membrane interface, c) metal-carrier complex diffusion through the membrane to the interface between the organic and the droplets of the receiving phase, d) stripping (back-extraction) reaction of the extracted metal ions from the liquid membrane phase to the dispersed receiving solution, and

e) back diffusion of the carrier to the feed-membrane interface. The transported metal ions are recovered from the aqueous receiving phase after pseudo emulsion settling. It was proven that EPT configuration overcomes NDSX in terms of zinc and iron separation kinetics [67], although separation selectivity was higher for NDSX configuration, $\alpha_{Zn/Fe} = 22$, compared to EPT process $\alpha_{Zn/Fe} = 15$.

The choice of polymeric support type influences the permeability, stability, and lifetime of the SLM. Some commonly used supports are characterized in Table 6.3.

Table 6.3: Characterization of the membranes used as a support.

Type of membrane	Parameters	Producers	Ref.
Flat sheet hydrophobic PVDF (polyvinylidene difluoride)	Thickness 120–125 μm Pore size 0.22 μm Porosity 60–75%	Millipore Durapore	[13, 48, 62]
Flat sheet hydrophobic PTFE (polytetrafluoroethylene)	Thickness 30 ÷ 50 μm Pore size 0.45 μm Porosity 85%	Millipore Durapore	[34, 61, 62]
	Thickness 80 μm Pore size 0.45 μm Porosity 72%	Sartorius	[69, 70]
Flat sheet hydrophobic PP (polypropylene)	Thickness 25 μm Pore size 0.02 μm Porosity 38%	Celgard 2400	[113]
	Thickness 38 μm Pore size 0.05 μm Porosity 60%	Celgard K-256	[72, 74]
PP (polypropylene) hollow fiber (Fiber X50)	Module length 20.3–28 cm Module diameter 6.3–7.7 cm Effective fiber length 15–15.6 cm Fiber inside diameter 214–240 μm Fiber outisde diameter 300 μm Pore size 0.03 μm Porosity 25–40% Tortuosity 2.6 Active interfacial area 1.13–1.4 m^2 Area per unit volume 28–29.3 cm^2/cm^3 Number of fibers 9950–10,800	Liqui Cel, Celgard, G501, Celgard	[7, 11, 31, 38, 49, 65, 67, 106–108, 114]

6.3 Application of liquid membranes for separation of metal ions from model or real wastewaters

In this section, several examples of metal ion separation from the model or real wastewaters with ELM or SLM are presented in Tables 6.4 and 5. Applications of BLM are not shown here because these systems have only cognitive goal realized on a laboratory scale and the results from BLM are then transferred to a large scale into SLM systems. Extraction-stripping of metal ions in membrane modules is indicated as a very promising technique for waste treatment within urban mining [2]. PIM applications are not discussed in the chapter because, in spite of a large number of publications in this field, PIMs seem not to have perspectives for an industrial application for wastewater treatment, except analytical uses. Applications of the LM techniques are presented in Figure 6.10.

6.3.1 ELM applications

ELMs have great potential especially for the recovery and removal of various metal ions, dyes, or organic compounds, such as citric acid transport [135], lactic acid recovery [136], and removal of acetic acid [137] from wastewater when the other techniques cannot be applied. The use of ELM in biomedical and biochemical industries (recovery of fermentation products, purification of antibiotics, e.g. penicillin [138]) has the great potential [90]. ELM can be also used to neutralize wastewater from industries e.g. for phenol removal (an industrial installation built in China in the late 80s) [88, 90].

Various examples of ELM application for the separation of metal ions are presented in Table 6.4. The most commonly used surfactant, stabilizing the emulsion, is Span 80, and kerosene is the most commonly used solvent. The main focus of various researches is on the selection of various extractants depending on the metal ions that were to be separated. ELMs were successfully used in the removal of numerous types of metal ions: Cu(II), Zn(II), Cd(II), Co(II), Mn(II), Ni(II), Cr(III) and Cr(IV), Ce(IV), Hg(II), U(VI), Ag(I), Pd(II), Ga(III) both from model solutions and wastewater (Table 6.4).

Not only a carrier and a surfactant but also a diluent play a very important role in the transport with ELM. Kerosene is the most commonly used as an organic diluent but with harmful to humans and not environmentally friendly. Therefore some vegetable oils (such as palm oil, sunflower oil, soyabean oil, sesame oil, and corn oil [51, 91]) have been investigated and shown to have great potential for use in chemical processes and could be an alternative to the commonly used kerosene. Palm oil was used for the extraction of heavy metals [51, 139], dyes [140], and phenol [141].

Table 6.4: ELM applications for metal ion transport.

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
Synthetic mixed cyanide solutions: CuCN and NaCN	6% LIX 7950 (trialkylguanidine)	5% Span 80 (sorbitan monooleate)	Kerosene with 2% 1-dodecanol (modifier)	0.05 M KOH	$E_{Cu(II)} > 90\%$	[115]
a) Synthetic solution: 100 ÷ 300 ppm $ZnSO_4$ or $CuSO_4$, b) Real solution: 100 ÷ 300 ppm Cu(II) from electroplating effluent, collected from industry	DEHPA	Span 80	Kerosene	1 M H_2SO_4	Recoveries from: a) From synthetic solutions: $E_{Cu(II)} = 84\%$ and $E_{Zn(II)} = 86\%$, b) Synthetic solution; recovery of Cu(II) electroplating effluent was 8–17% less than from synthetic solution	[22, 23]
Natural copper mine water: 1.0 g/dm^3 Cu(II), 0.15 g/dm^3 Fe, 0.20 g/dm^3 Al(III)	3–8.5% LIX-860 N-IC (5-nonylsalicylaldoxime)	2–5% Span 80	Kerosene	200 g/dm^3 H_2SO_4	$E_{Cu(II)} = 64 \div 99.5\%$	[24]
$ZnSO_4$	3% DEHPA	4% Span 80, cosurfactant 0.5 M Tween 80 and 2.5% butanol	Vegetable oil: **palm oil**, sunflower oil, soyabean oil, sesame oil	1 M H_2SO_4	$E_{Zn(II)} > 62\%$	[91]
100 ÷ 1000 ppm $ZnSO_4 \cdot 7H_2O$ in 0.5 M H_2SO_4	2 ÷ 8% DEHPA	Span 80	Isododecane	0.5 ÷ 2 M H_2SO_4	$E_{Zn(II)} = 90 \div 99\%$ (using hollow-fiber contactor)	[25]
150 ppm $CdCl_2$ in HCl	10% Aliquat 336	3% Span 80	Vegetable oils: Sunflower, **corn** and palm oil	0.1 M ammonia solution	$E_{Cd(II)} = 98.6\%$	[51]
$Cd(NO_3)_2$	5% DEHPA	5% Span 80	Paraffin oil	3 M HNO_3	Not determined	[116]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
0.001 ÷ 0.1 M Cd(II) ($CdCl_2 \cdot 2.5H_2O$)	DEHPA	2% Span 80	Kerosene	2 M HCl	$E_{Cd(II)} = 80 \div 99\%$	[26]
Sulfate salt dissolving in deionized water: 125 ppm Cd(II), 50 ppm Cu(II), 25 ppm Zn(II), and 25 ppm Fe(II)	3% DEHPA	1.7% Sodium dodecyl sulphonate	Kerosene	1 ÷ 4 M H_2SO_4	$E_{Cd(II)} \sim 98\%$ $E_{Cu(II)} = 60 \div 80\%$ $E_{Zn(II)}$ and $E_{Fe(III)} = 20 \div 40\%$	[117]
273.96 g of $ZnSO_4$ and 1.80 g of $CdSO_4$ in 1 dm^3 of water (simulate the chemistry of a zinc hydrometallurgy plant)	3% 3,5-diisopropylsalicylic acid (DIPSA) and 3% triisobutylphosphine sulfide (TIBPS)	ENJ-3209 or Span 80 and 1% LMA-1	Kerosene 6.0% n-octyl alcohol and 4.0% liquid paraffin	H_2SO_4	$E_{Cd(II)} \sim 98\%$ $E_{Zn(II)} < 6\%$	[118]
0.01 ÷ 0.1 g/dm^3 Cd(II) in 0.01 M KI and 0.01 M HCl, with 0.01 ÷ 0.1 g/dm^3 Zn(II), Fe(II), Co(II), Ni(II), Mn(II), and Cr(III)	0.015 M TOA	3% Span 80	oxylene	0.025 M NaOH	$E_{Cd(II)} = 96\%$ (method can be applied for the separation of Cd(II) from Zn(II), Fe(II), Co(II), Ni(II), Mn(II) and Cr(III) or as a preconcentrating step for measuring Cd(II)	[119]
50 mg/cm^3 Cd(II) in 0.01 M KI and 0.025 M HCl with Cu(II), Zn(II), Fe(II), Co(II), Ni(II), Mn(II), Cr(III) and Al(III)	0.02 M TIOA	3% Span 80	dimethylbenzene	0.05 M NaOH	$E_{Cd(II)} \sim 99\%$, feasible to separate Cd(II) from other cations, specifically from Zn(II)	[120]
Leaching of lithium ion batteries (from cell phone batteries) using 4 M HCl, amount of Co(II) in battery powder is 11.09% w/w.	0.7 M Cyanex 272	10% Span 80	Kerosene	H_2SO_4	$E_{Co(II)} = 55 \div 85\%$	[32]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
Leaching of lithium ion batteries (from cell phone batteries) using 4 M HCl: 8219 ppm Co(II) and 3889 ppm Mn(II)	0.7 M Cyanex 272	10% Span 80	Kerosene	0.1 M H_2SO_4	Leaching efficiency: $E_{Co(II)} = 88.5\%$, $E_{Mn(II)} = 89.3\%$ ELM: $E_{Co(II)} \sim 85\%$, $E_{Mn(II)} \sim 85\%$	[33]
a) The zinc plant purification cake: 20% Zn, 10% Cu, 1% Pb, 0.1% Fe, 2.2% Co, 3.1% Ni, 3.0% Cd, and 1% Al, was leached with 2 M HCl, b) Except for Cd(II), Co(II) and Ni(II), the other metal ions in the acidic leach solution were gradually precipitated by adding various reagents and adjusting the pH of the solution (100 mg/dm^3 Co(II) in feed: 100 mg/dm^3)	10% PC88A for Co(II), TOA for Cd(II)	2.5% ECA 4360J	Kerosene	0.5 M HCl, H_2SO_4 or HNO_3	a) Cd(II) from leaching solutions was extracted by using trioctylamine (TOA), b) Co(II) from the acidic leach solutions was extracted by ELM using PC-88A: $E_{Co(II)} = 90 \div 99\%$, $E_{Ni(II)} < 3\%$	[40]
a) The zinc plant copper cake: 15% Zn, 10% Cu, 8% Fe, 2.5% Cd, 0.2% Co, and 0.6% Ni was leached with a 2 M HCl, leach solution	3.5% TBP	5% Span 80	Kerosene	6 M NH_3	$E_{Co(II)} = 99\%$	[68]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
contained: Zn(II), Cu(II), Fe(III), Cd(II), Co(II), and Ni(II), b) Cd(II) was separated by solvent extraction, final leach solution contained: 525 ppm Co(II) and 1080 ppm Ni(II), 0.5 or 0.75 M SCN^-						
10 ppm Ni(II)	2% DEHPA	6% Span 80	toluene	H_2SO_4	$E_{Ni(II)} \sim 98\%$	[27]
300 ppm Ni(II)	7.2% Cyanex 301	2% Span 80	Kerosene	0.5 M H_2SO_4	$E_{Ni(II)} \sim 99\%$	[121]
0.16 g/dm^3 Co(II), 0.16 g/dm^3 Ni(II)	5 ÷ 60 mol/m^3 PC88A	10 ÷ 70 mol/m^3 PX 100 and Span 80	n-Heptane	0.1 ÷ 0.5 M, H_2SO_4	$E_{Co(II)} = 98\%$, $E_{Ni(II)} < 1\%$	[41]
0.002 M Cr(III) in HNO_3	0.5 M PC88A	2% Span 80	Kerosene	0.1–1 M $(NH_4)_2S_2O_8$	$E_{Cr(III)} = 94\%$	[42]
100 ppm Cr(VI)	10% Aliquat 336	5% Span 80	Kerosene and 5% n-heptane	1 M NaOH	$E_{Cr(IV)} \sim 95\%$	[52]
200 ppm Pb(II)	4% DEHPA	2% Span 80	Kerosene in the presence of magnetic 0.3% α-Fe_2O_3 particles	0.2 M H_2SO_4	$E_{Cr(III)} < 97.2\%$	[28]
327 ppm Ce(III)	0.1 M Cyanex 301	3% Span 80	Kerosene	0.5 M HCl	$E_{Cr(III)} \sim 99\%$	[29]
Ce(IV)	12% DEHPA	2–3% Span 80	Kerosene	4 ÷ 5 M HCl with 0.02 M H_2O_2	$E_{Ce(IV)} = 97 \div 99\%$, $E_{Re(II)} < 1\%$	[122]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
50 ppm Hg(II)	DEHPA	2% Span 80, 0.5% glycerol monostearate as co-surfactant	Toluene	1.0 M H_2SO_4 with 0.5 M thiourea (CH_4N_2S)	a) Small scale: $E_{Hg(II)}$ = 92% b) Scale up: $E_{Hg(II)}$ = 88%	[30]
50 ÷ 100 µg/cm^3 Hg(II) in 0.025 M HCl, 0.01 M KCl	0.015 M TOA	3% Span 80	Toluene	0.05 M NaOH	Hg(II) could be completely separated from Cu(II), Zn(II), Fe(III), Co(II), Ni(II), Pb(II), Mn(II) and Cd(II) ($E_{Hg(II)}$ ~ 99%, other metal ions <3%)	[123]
a) U(VI) from Industrial Leach Solutions synthetic leach liquor uranyl sulfate (0.5 g/dm^3) b) Leach Liquor of Jaduguda Ore uranium concentration of 0.32 g/dm^3 U(VI) along with other co ions: 0.47 g/dm^3 Fe(III), 0.062 g/dm^3 Ca(II), 0.45 g/dm^3 Mg(II), 2.55 g/dm^3 Mn(II)	3 ÷ 5% Alamine 336	3% Span 80	Light and heavy paraffins	1 M Na_2CO_3	a) Synthetic: $E_{U(VI)}$ < 81% (3.8% Fe, 4.6% Ca, 2% Mg, and 1.6% for Mn(II), b) 2.2 g/dm^3 U(VI), 0.025 g/dm^3 Fe(III), 0.01 g/dm^3 Ca(II), 0.004 g/dm^3 Mg(II), and 0.012 g/dm^3 Mn(II) in a stripping phase	[43]
The waste: 600 ppm U(VI), 360 ppm Fe(III), 325 ppm	TOPO	Span 80	Light and heavy paraffins	0.5 M Na_2CO_3	The final stripping phase: U(VI) = 1250 ppm, Fe(III) = 14 ppm,	[63]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
Ca(II), 390 ppm Mg(II) in 1.2 M HNO_3					Ca(II) = 10 ppm and Mg(II) = 4 ppm	
Ag(I)	0.02 ÷ 0.05 M Cyanex 302	5% Montane-80 (sorbitan monooleate)	MIPS, an industrial solvent contains paraffinic and naphthenic hydrocarbons (C_{10-14})	0.3 M HNO_3	$E_{Ag(I)}$ = 95 ÷ 99%	[124]
Real photographic waste solution: 2490 ppm Ag(I), 3630 ppm Na(I), 6240 ppm K(I), 1480 ppm Fe(II), 249 ppm Cl^-, 2202 ppm NO_3^-, 3712 ppm SO_4^{2-}, 62 ppm F^-	0.05 M Cyanex 302	5% Span 80	Kerosene	1 M thiourea in 1 M H_2SO_4	$E_{Ag(I)}$ ~ 99% $E_{K(I)}$, $E_{Na(I)}$, $E_{Fe(II)}$ < 25%	[35]
Real photographic wastes solution: 2490 ppm Ag(I), 3630 ppm Na(I), 6240 ppm K(I), 1480 ppm Fe(II), 0.38 ppm Zn(II), 0.17 ppm Cu(II), 1.36 ppm Pb(II), 0.29 ppm Cr(III), 0.24 ppm Cd (II)	0.05 M Cyanex 302	3% Span 80	**Kerosene**, *n*-dodecane, or toluene	1.0 M thiourea in 1 M H_2SO_4	$E_{Ag(I)}$ ~ 99% $E_{K(I)}$, $E_{Na(I)}$, $E_{Fe(II)}$ < 25%	[36]
Ag(I) recovery from deactivated Ag/alumina catalysts, leaching solution:	10% mixture of MEHPA and DEHPA	6% P5000	Paraffinic and naphthenic hydrocarbons	0.6 M HNO_3	$E_{Ag(I)}$ ~ 97%, $E_{Ca(II)}$ < 25%, $E_{Si(IV)}$ < 5%, $E_{Al(III)}$ < 22%, $E_{Ti(IV)}$ < 10%, $E_{K(I)}$ < 10%	[125]

Table 6.4: (continued)

Feed phase - metal ion(s)	Membrane			Receiving phase (stripping phase)	Efficiency	Ref.
	Carrier	Surfactant	Diluent			
5782 ppm Ag(I), 3053 ppm Al(III), 1.3 ppm K(I), 12 ppm Ti(IV), 225.5 ppm Si(IV), 11.9 ppm Ca(II)			without aromatic components			
10 ppm Pd(II)	0.1 M Cyanex 302	1 ÷ 7% Span 80	Kerosene	1 M thiourea in 1 M H_2SO_4	$E_{Pd(II)} \sim 85\%$	[37]
100 ppm Pt(IV), 50 ppm Pd(II) in 1000 mol/m^3 HCl	–	Span 80, PX 100	n-Heptane	1 ÷ 3 M $HClO_4$	Pt(IV) were selectively extracted from Pd(II) and concentrated	[126]
Rotary filter cake of the zinc plant residue: 12% Zn, 15% Pb, 7% Fe, 0.06% Co, 0.10% Ni, 0.15% Cd, 0.19% Cu, 4% Al and 380 ppm Ga(III) on mass basis, leached with HCl, leach solution contained 100 mg/dm^3 Ga(III), 8715 mg/dm^3 Fe(III), 60 mg/dm^3 Co(II), 80 mg/dm^3 Ni(II), 265 mg/dm^3 Cd(II), 24.02 mg/dm^3 Zn(II), 6592 mg/dm^3 Pb(II), 315 mg/dm^3 Cu(II), and 3100 mg/dm^3 Al(III) in 7 M HCl	6% TOPO	2% ECA 4360J	Kerosene, **STA90 NS** (is an isoparaffinic mixture and contains no aromatics)	0.1 M H_2SO_4	It was possible to selectively extract 99% of Ga(III) from the acidic leach solutions, containing Fe(III), Co(II), Ni(II), Zn(II), Cd(II), Pb(II), Cu(II), and Al(III)	[64]

Table 6.5: SLM applications for metal ion transport.

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
SLM					
Sr(II) from nitrate nuclear waste solution	**FP:** Synthetic nuclear waste solution containing Sr(II), Zr(IV), Cs(I), Ba(II), Mo(VI), Ce(III), Eu(III), Sm(III), Fe ions, Na(I), Ni(II), Co(II), Al.(III), Cr(III) in 0.5 ÷ 8 M HNO_3 **RP:** distilled water $V_{FP} = V_{RP}$	PTFE/sandwich (membrane area: 3.16 cm^2)	0.01 ÷ 0.05 M DtBuCH18C6 in 1-octanol	Sr(II) transport with DtBuCH18C6 is slow. $R_{Sr(II)} > 95\%$, $R_{Ba(II)} \sim 13\%$	[73]
Cr(VI) in model solution	**FP:** 100 mg/dm^3 Cr(VI) in water **RP:** 0.03 M Na_2-EDTA, pH 6.5 $V_{FP} = V_{RP} = 130$ cm^3	PVDF/sandwich (membrane area: 11.3 cm^2)	1 vol.% Aliquat 336 in **vegetable oil**	$E_{Cr(VI)} = 80\%$ $R_{Cr(VI)} = 73\%$	[50]
Ag(I) from model solution	**FP:** $5{\cdot}10^{-5}$ M Ag(I) in $8.0{\cdot}10^{-3}$ M picric acid **RP:** 0.015 M sodium thiosulfate $V_{FP} = V_{RP} = 150$ cm^3	PP/sandwich (membrane area: 10 cm^2)	Calix[4]pyrrole derivatives in kerosene	Depending on the derivative $R_{Ag(I)} = 39 \div 97\%$ High selectivity in Ag(I) transport over Pb(II), Zn(II), Fe(II), Fe(III), Ni(II), Co(II), Ca(II), Mg(II), Cu(II), Cd(II), Al(III), Cr(III)	[72]
Ag(I) from model solution	**FP:** 2 ppm Ag(I) in $4.0{\cdot}10^{-3}$ M picric acid **RP:** 0.02 ÷ 0.7 M sodium thiosulfate $V_{FP} = V_{RP} = 150$ cm^3	PP/sandwich (membrane area: 10 cm^2)	10^{-3} M dibenzyl-diaza-18-crown-6 ether and derivatives in **supramolecular solvent** (stable suspension of decanoic acid and Bu_4NOH mixture in distilled water)	$R_{Ag(I)} = 98.3\%$ (to thiosulfate RP at pH 5.4) High selectivity in Ag(I) transport over Pb(II), Ni(II), Co(II), Cu(II), Cd(II), Mn(II), Cr(III)	[74]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
Ag(I) from model solution	**FP:** $5{\cdot}10^{-5}$ M Ag(I) in 10^{-3} M picric acid **RP:** 10^{-5} M sodium thiosulfate $V_{FP} = V_{RP} = 150$ cm^3	PP/sandwich (membrane area: 10 cm^2)	**DES:** L-menthol and salicylic acid (4:1 M ratio), salicylic acid plays a role of a carrier	$R_{Ag(I)} > 90\%$ High selectivity in Ag(I) transport over Pb(II), Ni(II), Cu(II), Cd(II), Mn(II), Fe(III)	[127]
Au(III) from HCl solutions	**FP:** 0.01 g/dm^3 Au(III) in 1 M HCl **RP:** 0.01 M sodium thiosulfate $V_{FP} = V_{RP} = 200$ cm^3	PVDF/sandwich (membrane area: 11.3 cm^2)	IL ($A324H^+Cl^-$) in Solvesso 100	Au(III) is separated from Cu(II), Fe(III), Ni(II). Gold is recovered from the receiving solution as metallic gold nanoparticles.	[128]
REE from the fluorescent lamp leach solution	**FP concentrations in g/dm^3:** 6.8 Ca(II), 0.04 Fe ions, 0.311 Ba(II), 0.236 Sr(II), 0.152 Mn(II), 0.132 Si(IV), 0.116 Al(III), 0.09 Na^+, 0.064 Mg(II), 0.056 K^+, 0.02 Sb(IV), **0.49** Y(III), 0.04 Eu(III), 0.016 La(III) in 1 M HNO_3 **RP:** 0.05 M Na_2EDTA $V_{FP} = V_{RP} = 250$ cm^3	PTFE/sandwich (membrane area: 11.4 cm^2)	– 0.9 M Cyanex 923 in kerosene – Cyanex 572 in kerosene	Permeability coefficients with Cyanex 923 for Eu and Y: $4.9{\cdot}10^{-6}$ and $3.6{\cdot}10^{-6}$ m/s	[129]
Ge(IV) from model solution	**FP:** 10 ÷ 40 mg/dm^3 Ge(IV) in 1.5 ÷ 5 pH **RP:** 100 ÷ 400 mg/dm^3 H_2SO_4 solution $V_{FP} = V_{RP} = 250$ cm^3	PTFE/sandwich (membrane area: 9.62 cm^2)	10 ÷ 40 vol.% Cyanex 301 in kerosene	$J_{Ge(IV)} = 11.4{\cdot}10^{-7}$ mol/cm$^2{\cdot}$s	[34]
Ge(IV) from model solution	**FP:** 100 mg/dm^3 Ge(IV) in oxalic acid **RP:** 0.01 ÷ 0.04 M NaOH solution $V_{FP} = V_{RP} = 220$ cm^3	PTFE/sandwich (membrane area: 11 cm^2)	5 ÷ 30 vol.% (0.126–0.757 M) Cyanex 923 in kerosene	Ge(IV) diffusion coefficients: $8.50{\cdot}10^{-4} \div 2.09{\cdot}10^{-5}$ cm^2/s for 0.126–0.757 M Cyanex 923 $R_{Ge(IV)}$ up to 87%	[61, 62]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
Ge(IV) from model fly ash leachate	**FP:** 100 mg/dm^3 Ge(IV), Ni(II), Cd(II), Co(II) and 1 g/dm^3 Zn(II) with 2.76·10^{-3} M tartaric acid **RP:** 1 M HCl solution $V_{FP} = V_{RP} = 220$ cm^3	PTFE or PVDF/sandwich (membrane area: 11 cm^2)	5 vol.% Alamine 336 in kerosene and 1-decanol	Ge(IV) transport efficiency and rate across PTFE membrane ($R_{Ge(IV)} = 96\%$) is larger than across PVDF ($R_{Ge(IV)} = 75\%$). Ge(IV) transport through flat sheet SLM is slower than with HF. Selectivity coefficients: $\alpha_{Ge(IV)/Zn(II)} = 287$, $\alpha_{Ge(IV)/Cd(II)} = 290$, $\alpha_{Ge(IV)/Co(II)} = \infty$, $\alpha_{Ge(IV)/Ni(II)} = 287$	[114]
Zn(II) from waste discharge liquor of galvanizing plant	**FP:** four waste discharge liquors from galvanizing plants in Pakistan containing 0.130 ÷ 0.190 g/dm^3 Zn(II), 0.0014 ÷ 0.009 g/dm^3 Co(II), 0.0039 ÷ 0.013 g/dm^3 Cu(II), 0.010 ÷ 0.116 g/dm^3 Cd(II), 0.0015 ÷ 0.0062 g/dm^3 Mn(II), 0.0075 ÷ 0.038 g/dm^3 Cr(III), 0.003 ÷ 0.017 g/dm^3 Fe ions, 2 M HCl **RP:** 2 M NaOH $V_{FP} = V_{RP} = 300$ cm^3	PP/sandwich (membrane area: 23.79 cm^2)	0.8 M TDDA in xylene	$R_{Zn(II)} = 93 \div 99.37\%$, high selectivity over other metal ions: $R_{Co(II)} = 0.08\%$, $R_{Cu(II)} = 0.23\%$, $R_{Cd(II)} = 0.15\%$, $R_{Mn(II)} = 0.36\%$, $R_{Cr(III)} = 0.06\%$, $R_{Fe\ ions} = 0.28\%$	[113]
Am(III), from nitrate model solutions	**FP:** $10^{-6} \div 10^{-7}$ M Am(III) in 1 ÷ 6 M HNO_3 **RP:** 0.01 M HNO_3, 1 M α-HIBA, 0.01 M EDTA $V_{FP}=V_{RP} = 20$ cm^3	PTFE/sandwich (membrane area: 3.14 cm^2)	10^{-3} M multiple DGA-based extractants in 95% dodecane and 5% isodecanol	Diffusion coefficients for Am(III) transport to 1 M α-HIBA with TRPN-DGA $D_{eff} = 6.58 \cdot 10^{-8}$ cm^2/s or with iPr3-TREN-DGA $D_{eff} = 3.03 \cdot 10^{-7}$ cm^2/s.	[69]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
Np(IV), Pu(IV) from nitrate model solutions	**FP:** 10^{-12} M and 10^{-6} M Np(IV) and Pu(IV) in 1–6 M HNO_3 **RP:** 0.5 M HNO_3 + 0.5 M oxalic acid $V_{FP} = V_{RP} = 20$ cm^3	PTFE/sandwich (membrane area: 3.14 cm^2)	10^{-3} M multiple DGA-based extractants in 95% dodecane and 5% isodecanol	Lower pertraction of Pu(IV) than of Np(IV). Diffusion coefficients for Np(IV) transport to 0.5 M HNO_3 + 0.5 M oxalic acid with TRPN-DGA $D_{eff} = 7.13 \cdot 10^{-8}$ cm^2/s or with iPr3--TREN-DGA $D_{eff} = 8.71 \cdot 10^{-8}$ cm^2/s.	[70]
NDSX					
Dy(III) from NdFeB magnetic scrap (model and real solutions)	**FP model**: 1 g/dm^3 Dy(III) in HNO_3 **FP real**: 0.200, 0.438, 0.385 g/dm^3 Dy(III), Nd(III), and Pr(III) in 0.1 or 0.3 M HNO_3 **FP:** Counter currently in lumen side at 100 cm^3/min **OP**: Counter currently in shell side at 100 cm^3/min **RP**: 1.5 M HNO_3 at 100 cm^3/min $V_{FP}/V_{OP}/V_{RP} = 1$	PP/HF	0.5 M PC88A in heavy normal paraffin	Two cycles 1st cycle: Dy(III) concentration from 20 to 83% 2nd cycle: raising Dy(III) purity>97%	[38]
Nd(III) model HNO_3 solution	**FP:** pH 4.5, counter currently in lumen side at 100 cm^3/min **RP:** 1 M H_2SO_4 counter currently in shell side at 100 cm^3/min $V_{FP} = V_{RP} = 5$ dm^3	PP/HF	0.5 M PC88A in octane	$E_{Nd(III)} = 91.5\%$ $R_{Nd(III)} = 88.1\%$	[39]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
Nd(III) model HNO_3 solution	**FP**: 0.03 ÷ 1.6 g/dm^3 Nd(III) in 0.1 ÷ 0.7 M HNO_3, in lumen side, 100 cm^3/min **OP**: Circulated in shell side, 50 ÷ 150 cm^3/min $V_{FP} = V_{OP} = 300$ cm^3	PP/HF	0.3 M DNPPA and 0.13 M TOPO in petrofin	$R_{Nd(III)} > 99.9\%$ in 30 min	[106]
Nd(III), Dy(III), Pr(III) from waste permanent magnet (WPMs) leach liquor	**FP real after leaching**: 6 g/dm^3 Fe, 2.7 g/dm^3 Nd(III), 0.155 g/dm^3 Dy(III), 0.857 g/dm^3 Pr(III) at pH 2, in lumen side, 200–250 cm^3/min **OP**: Circulated in shell side, 250 ÷ 300 cm^3/min **RP:** 2 M HNO_3 $V_{FP} = V_{OP} = 300$ cm^3	PP/HF	1 M DEHPA in Isopar L	The REE transport follows the order: Nd > Pr > Dy. $E_{Nd(III)} = 58.62\%$, $E_{Dy(III)} = 98.46\%$, $E_{Pr(III)} = 85.59\%$, $R_{Nd(III)} = 63.13\%$, $R_{Dy(III)} = 15.21\%$, $R_{Pr(III)} = 56.29\%$	[130]
Ta(V) and Nb(V) in model HF solutions	**FP**: 10 mg/dm^3 of Ta(V) or Nb(V) in lumen side **RP**: 0.2 M $NaClO_4$, or 0.1 M thiourea, or 0.1 M HCl counter-currently in shell side	PP/HF	3 vol.% Aliquat 336 in kerosene	Ta(V) extracted and separated from Nb(V)	[107]
EPT					
Cu(II) in sulfate solution	**FP model:** 0.1 ÷ 1.0 g/dm^3 Cu(II) in pH 1.4, circulation in lumen side at 280 cm^3/min **FP simulated real:** 1.0 g/dm^3 Cu, 40 g/dm^3 Zn(II), 13 g/dm^3 Fe(III), pH 1.4	PP/HF	10 vol.% Acorga M5640 in Shellsol D70	**PEHFSD compared to ELM** $R_{Cu(II)} = 91 \div 97\%$ for ELM, $R_{Cu(II)} = 96 \div 97\%$ for PEHFSD	[11]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
	RP: 180 g/dm^3 H_2SO_4 or 25 g/dm^3 Cu(II) + 180 g/dm^3 H_2SO_4 **R + OP:** Circulation in shell side at 320 cm^3/min $V_F = 2 \div 8$ dm^3, $V_{R+OP} = 0.8$ dm^3 ($V_O/V_R = 1$)				
Eu(III) in model nitrate solution	**FP:** $1 \cdot 10^{-4}$ M Eu(III) pH 5 **RP:** 4 M HNO_3 $V_{FP} = 60$ cm^3	PVDF/sandwich	0.16 M DEHPA in kerosene	**SDLM** 94.2% Eu(III) separation from the feed	[18]
Y(III)	**FP:** 0.01 ÷ 0.5 g/dm^3 Cr(III), 0.1 M NaOH, in lumen side **RP:** 0.5 M H_2SO_4 solution **R + OP:** In shell side $V_F = 3$ dm^3, $V_{R+OP} = 0.8$ dm^3 ($V_O/V_R = 1$)	PP/HF	DEHPA	**PEHFSD**	[19]
Cr(III) in alkaline solutions	**FP:** 0.01 ÷ 0.5 g/dm^3 Cr(III), 0.1 M NaOH, in lumen side **RP:** 0.5 M H_2SO_4 solution **R + OP:** In shell side $V_F = 3$ dm^3, $V_{R+OP} = 0.8$ dm^3 ($V_O/V_R = 1$)	PP/HF	1–20 vol.% TOMACl in decanol and decane	**PEHFSD** Aqueous and membrane mass transfer coefficients: $9.3 \cdot 10^{-4}$ and $1.2 \cdot 10^{-8}$ cm/s	[49]
Ge(IV) from model fly ash leachate	**FP:** 100 mg/dm^3 of Ge(IV), Ni(II), Cd(II), Co(II) and 1 g/dm^3 of Zn(II) with $2.76 \cdot 10^{-3}$ M tartaric acid in shell side at 28 dm^3/h **RP:** 1 M HCl solution	PP/HF	5 vol.% Alamine 336	**PEHFSD** Ge(IV) transport through HF is faster than through flat sheet SLM, HF transport is comparable to dispersive extractions.	[114]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
	R + OP: Circulation in lumen side at 23 dm^3/h $V_F = 2\ dm^3$, $V_{R+OP} = 0.5\ dm^3$			No transport of Ni(II), Cd(II), Co(II) and Zn(II).	
Zn(II) and Fe(II) from model and real spent pickling solution	**FP synthetic:** 150 g/dm^3 Zn(II), 120 g/dm^3 Fe(II) in 1 M HCl **FP real:** 122 g/dm^3 Zn(II), 93 g/dm^3 Fe(II) in 1.1 M HCl **RP**: Tap water	PP/HF	50 vol.% TBP in Shellsol D70	**PEHFSD** Separation factor Zn/Fe = 15	[67]
Zn(II) and Fe(III) from real Cr(III) passivation baths	**FP:** 6 g/dm^3 Zn(II), 0.45 g/dm^3 total Fe, 6 g/dm^3 Cr(III) nitrates in pH 1.8 circulation in shell side at 220 dm^3/h flow rate **RP**: 4 M H_2SO_4 solution **R + OP:** Circulation in lumen side at 70 dm^3/h flow rate $V_F = 2\ dm^3$ $V_{R+OP} = 1\ dm^3$ ($V_O/V_R = 4$)	PP/HF	15 vol.% Cyanex in Shellsol D70	**PEHFSD** Slower Zn(II) and iron separation rates observed at 10 °C in comparison with those at 20–40 °C, attributed to a shift in the driving force due to an endothermic change of the interfacial extraction reaction	[31]
Zn(II) and Fe(III) from real Cr(III) passivation baths	**FP:** 3 < Cr(III) < 7 g/dm^3, 11 < Zn(II) < 20.5 g/dm^3, 0.015 < Fe(III) < 0.100 g/dm^3, 0.3 g/dm^3 W in pH < 3 **RP**: 4 M H_2SO_4 solution $V_O/V_R = 4$ Laboratory scale: $V_F = V_{R+OP} = 1\ dm^3$ Industrial scale: $V_F = 690\ dm^3$ $V_{R+OP} = 67.5\ dm^3$	PP/HF – Membrane area 1.4 m^2 – laboratory – Membrane area 40 m^2 – industrial	Cyanex in Shellsol D70	**PEHFSD** Laboratory results easily scaled-up to an industrial scale; Zn, Fe and W fluxes: 4.49, $2.2 \cdot 10^{-2}$, $2.5 \cdot 10^{-2}$ g/m^2h	[131]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
Zn(II) in model HCl solution	**FP**: 0.3 ÷ 5 g/dm^3 Zn(II) in 1 M HCl, in lumen side **R + OP**: Circulated in shell side at 300 cm^3/min **RP**: 5% Na_2SO_4 or water $V_{FP} = V_{R+OP}$ = 800 cm^3	PP/HF	– 0.1 M 3PC10 in toluene – 2.9 M TBP in Shellsol D70	**PEHFSD**	[108]
Zn(II), Fe(II), Fe(III) in model HCl solution	**FP**: 0.3 ÷ 5 g/dm^3 Zn(II) in 1 ÷ 3 M HCl, in lumen side at various flow rates **R + OP**: Circulated in shell side at various flow rates **RP**: Na_2SO_4 $NaNO_3$, HCl solutions, water $V_{FP} = V_{R+OP}$ = 800 cm^3	PP/HF	0.05 or 0.1 M D-3EI in Shellsol D70	**PEHFSD** separation factor Zn/Fe(III) = 50 ÷ 80	[132]
SLM integrated with other operations					
Co(II) in model acetate solution	**FP**: 0.010 ÷ 0.200 M Co(II) in 0.2 M acetate buffer, pH from 3 to 7 **RP**: 0.005 and 1 M H_2SO_4 $V_{FP} = V_{RP}$ = 250 cm^3	PVDF/sandwich (membrane area: 15 cm^2)	DEHPA	**U-SLM** – ultrasound enhanced impregnation of the support with the carrier	[13]
Ni(II), Zn(II) from model wastewater	**FP**: 20 ÷ 100 mg/dm^3 Ni(II) and Zn(II) at pH 5 **RP**: 0.1 M H_2SO_4, NH_4Cl and NaCl	PVDF/sandwich (membrane area: 7.07 cm^2)	3 vol.% DEHPA or 5 vol.% TOA in **vegetable oil**	**SLM-EW** – directly in the receiving phase EW unit (4 cm distance between electrodes) reduces metal ions to metallic form at cathode electrode;	[21]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
	solutions $V_{FP} = V_{RP} = 140$ cm^3			85% total metal deposition at TOA in SLM, 75.98% total metal deposition at TOA in SLM	
Cd(II) in model wastewater	**FP**: 25 ÷ 100 mg/dm^3 Cd(II) in 0.5 ÷ 2 M HCl circulated at 80 cm^3/min **RP**: 0.01 M HCl circulated at 80 cm^3/min $V_{FP} = V_{RP} = 1$ dm^3	PVDF/sandwich	0.01 M Aliquat 336 in toluene	**SLM-ED** – receiving phase from SLM was transferred to ED in 3 compartment microflow laboratory-scale ED module with Pt/Ti electrodes (Electrocell) and Nafion117 as CEM, Neosepta as AEM, flow rate: 200 cm^3/min, Electrolyte solution 0.05 M NaCl, voltage: 40 V, EA: 10 cm^2 $S_{Cd(II)} = 55\%$ in SLM, $S_{Cd(II)} = 70\%$ in ED	[48]
Zn(II), Fe(II), Fe(III) from model HCl spent-pickling wastewater	**FP**: 95 g/dm^3 Fe(II), 80 g/dm^3 Zn(II), 1.3 M HCl in lumen side circulated at 30 dm^3/h **OP**: In shell side concurrently circulated at 35 dm^3/h **RP**: Water in lumen side circulated at 30 dm^3/h $V_{FP} = V_{RP} = 1$ dm^3	PP/HF	pure TBP	**NDSX-ED** Receiving phase was transferred to ED with 3 compartments, electrodes: Titanium coated with ruthenium oxide, commercial Ralex AEM and CEM, 5 membrane units in the stack to provide 0.1 m^2 membrane area, electrolyte solution 1.0 M H_2SO_4	[65]

Table 6.5: (continued)

Metal ion(s)	Media	Membrane		Remarks	Ref.
		Support/ configuration	Carrier		
SLM hybrid systems					
Zn(II) from model nitrate solution	**FP**: Zn(II), Cu(II), Ca(II), Mg(II), Na^+, K^+ as nitrates in deionized water **RP**: 1 M H_2SO_4 solutions V_{RP} = 30 cm^3	Neosepta CEM/ sandwich (membrane area: 12.56 cm^2)	0.1 M DEHPA in kerosene	**MHS** Selectivity order of DEHPA extraction in the system: $Zn(II)>Ca(II)>Cu(II)>>Mg(II)>K^+>Na^+$	[133]
Cd(II) from acidic solution	**FP**: 50 ppm Cd(II) in 0.01 M KI at pH 1.8 **RP**: NaOH solution pH 13 $V_{FP} = V_{RP}$ = 90 cm^3	PES-based porous AEM	0.05 M TIOA in kerosene	**HLM** Cd(II) transfer coefficient for PES-based AEMs compared to nonionic PES membranes increases from 0.0068 to 0.017 1/min	[134]

α-HIBA, *α*-hydroxyisobutyric acid; AEM, anion exchange membrane; Bu_4NOH, tetrabutylammonium hydroxide; CEM, cation exchange membrane; Cyanex 572, a mixture of phosphinic and phosphonic acids; D-3EI, N-decoxy-1-(pyridin-3-yl)ethaneimine; DNPPA, dinonylphenylphosphoric acid; EA, effective area of the membrane; ED, electrodialysis; EDTA, ethylenediamine-*N,N,N′N′*-tetraacetic acid; FP, feed phase; HLM, hybrid liquid membrane; MHS, membrane hybrid systems; OP, organic phase; PES, polyethersulfone; R, recovery; R + OP, pseudoemulsion phase; RP, receiving phase; S, separation performance; TDDA, tri-n-dodecylamine.

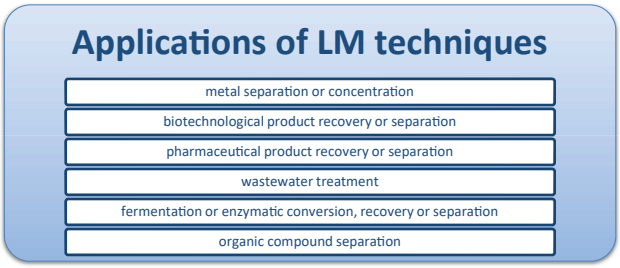

Figure 6.10: Applications of the LM techniques [90].

6.3.2 SLM applications

Examples of the variety of SLM systems applied for metal ion transport either from the model or real waste solutions are presented in Table 6.5. Typically kerosene or VOCs (volatile organic compounds) are applied as solvents to prepare the liquid (organic) phase for LM; however, novel solvents are also investigated to make the LM more environmentally friendly, more stable and/or more efficient. Among the novel systems are supramolecular solvents (SUPRAS) characterized by high water-immiscibility, low vapor pressure and high tendency to dissolve the carrier, and its metal ion complex and high wettability of the polymeric support. SUPRAS composed of vesicles of decanoic acid in the presence of tetrabutylammonium ion (Bu_4N^+) was applied as a solvent for dibenzyl-diaza-18-crown-6 (DBzDA18C6) for Ag(I) transport across flat sheet SLM [74]. SURPAS is considered easily tunable due to a variety of hydrophobic or polar groups of the surfactant components. Also, SUPRAS contain high concentrations of amphiphiles with many binding sites and ensures high extraction efficiencies at low extractant volumes.

Deep eutectic solvents (DES) are considered a new generation of green and sustainable solvents. They possess the advantages of ionic liquids (low vapor pressure, tunability, high chemical and thermal stability), and overcome some limitations of ILs. They are reported to be less toxic, more biodegradable, cheaper, and have a lower environmental impact than ILs. Thanks to the mentioned properties SUPRAS and DES stabilize LM in PP support and ensure SLM operation for a couple of cycles [74, 127].

Sunflower oil has been selected among other tested vegetable oils (i.e. coconut oil, mustard oil, sesame oil, and soybean oil) as a green solvent for organic phase preparation. This oil is a low cost, immiscible with the aqueous phase, has low volatility, and low viscosity, these properties ensure environmental and physiological benignity of the LM separation with vegetable oil-based organic phases. Sunflower and coconut oils were proven to be good solvents in LM containing basic carriers (Aliquat 336, TOA) for the transport of Ni(II), Zn(II), Cr(VI) in SLM or Pb(II), and Cd(II) in BLM [21, 50, 142].

EPT (PEHFSD) has been proven to be an efficient technology to remove and recover selectively zinc from wastewaters produced by the surface treatment industry,

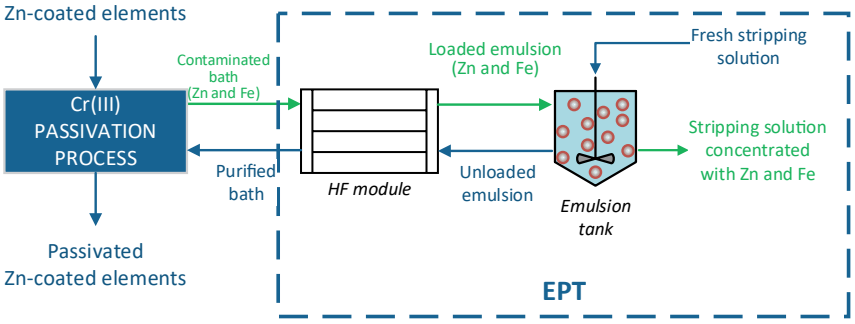

Figure 6.11: Integration of EPT and passivation step in the Zn electroplating process [131].

e.g. spent pickling solution generated in the hot-dip galvanizing process or spent chromium-based passivation baths [109].

An integration of EPT to the passivation step of the Zn electroplating process on an industrial scale has been implemented in a company and reported to be an efficient operation to purify the real Cr(III) including baths from the Zn(II) and Fe ions (Figure 6.11). The process is flexible and is applicable for passivation baths of various compositions [131].

Different mathematical models for metal ion transport have been developed [61, 62, 84, 137]. They are not considered in this chapter, however, it is noteworthy that many of them assume that the complexation reaction between metal ions and ligands at the aqueous-membrane interface is instantaneous and diffusion of the metal–ligand complex through the pores of the membrane (membrane thickness) into the bulk of the organic phase or across the LM to the receiving phase is the rate-determining step [106, 107].

Additional operations are employed or follow the membrane process to overcome diffusion limitations and increase the driving force, and thus the effectiveness, of the separation processes. Strip dispersion in the liquid membrane phase forming pseudo emulsion (PEHFSD, described in Section 2.3) can be considered as such an approach. Another proposal to improve the solute transfer is further processing of the receiving phase. For example, electrodialysis (ED) prevents the increase in metal ion concentration in the receiving solution, thus preventing the decrease in the membrane separation driving force [48]. Also, an electrodeposition (electrowinning, EW) of metal ions (e.g. nickel and zinc) stripped to the receiving phase makes it possible to keep constant driving force and, additionally, both to separate toxic heavy metals from wastewater and to obtain valuable metallic products [21]. The idea of the integrated LM and EW is shown in Figure 6.12.

NDSX with ED configuration provides recovery of all the possible valuable products present in wastewaters, e.g. from model spent pickling wastewater: coagulant

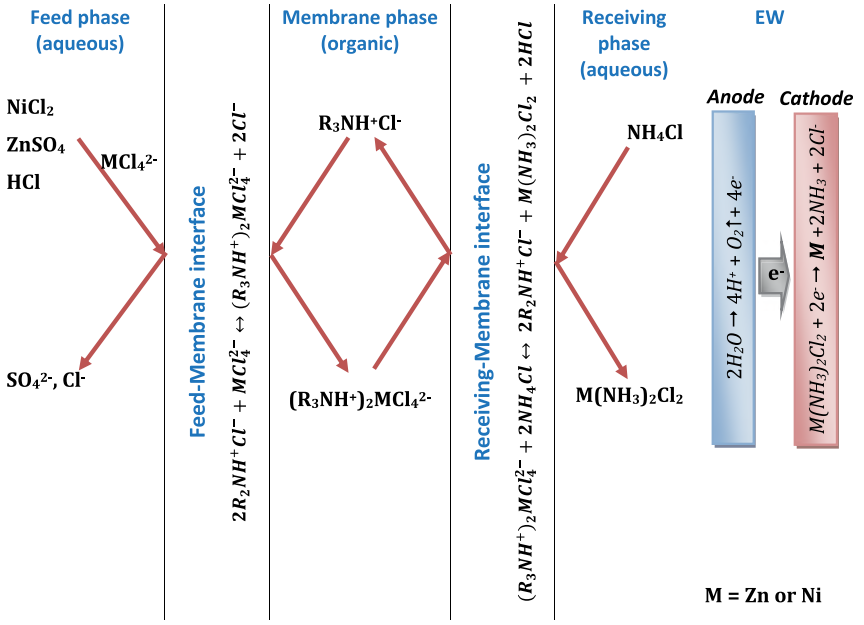

Figure 6.12: Integrated liquid membrane – electrowinning (LM-EW) system for metal ion transport [21].

$FeCl_3$ diluted electrolyte for zinc electrowinning and recyclable HCl solution [65]. The role of ED lies in selective separation of Zn(II) from concentrated HCl solution.

Another approach to improve LM performance on a large scale and overcome low stability, leakage of the organic phase in the aqueous phases, as well as a small contact area, is called a multimembrane hybrid system (MHS) or hybrid liquid membrane (HLM). The MHS combines some properties of the ion-exchange and liquid membranes and consists of a liquid membrane containing a selective carrier, two cation-exchange membranes placed at the interfaces of the LM, aqueous feed and receiving phases. MHS is a beneficial membrane system due to mechanical stability in a long-time continuous operation and protection LM from direct contact between the aqueous and organic solutions. Placing LM between two CEMs makes it possible to use carriers with significant solubility in water [133]. In such a system an increase in the removal efficiency of metal ions and mass transfer flux results from the enhancement in overall mass transfer rate, which is considered as an effect of positive fixed charges in the pores of the charged supporting membranes [134].

Hollow fiber renewal liquid membrane (HFRLM, mentioned in Section 2.3) has been considered as a scale-up for an industrial process instead of a flat sheet SLM [111]. SLM has been proposed as an additional step preventing loss of REE in the leaching of YOX fluorescent lamp wastes and improving recovery of the valuable metals, especially Eu(III) and Y(III) [129]. A scheme of the process is shown in Figure 6.13. After the first

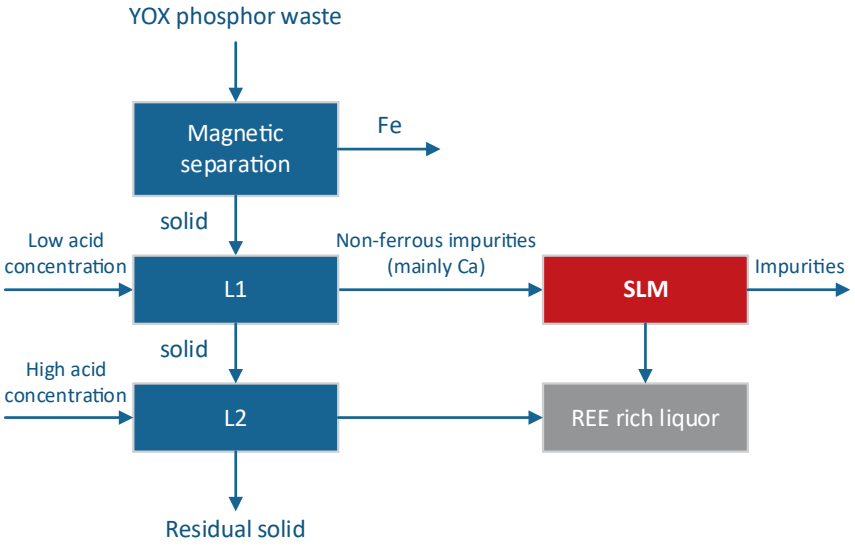

Figure 6.13: A flowsheet of REE recovery from YOX fluorescent lamp wastes including SLM step [129]. (L1, L2 – leaching steps).

step of metal leaching from waste fluorescent lamps, the leach solution contained a large amount of Ca(II) and a small quantity of REE. To avoid loss of REE, a recovery by flat sheet SLM (Cyanex 923 as REE carrier) from the leach solution was incorporated into the flowsheet of the waste treatment. The scale-up from laboratory SLM to industrial process with HFRLM assumed 95% REE recovery from 1 m^3 of a solution after leaching 100 kg of the fluorescent lamp waste with 33 m^2 membrane area at permeability coefficient near $4{\cdot}10^{-6}$ m/s [129].

6.4 Summary

Low operating and investment costs, minimum product contamination, no phase separation requirement, selectivity; flexibility; and easy modularization, and low energy consumption are the reported advantages of SLM [74]. Extraction and stripping are carried out in one stage which is favorable from an economic and ecological point of view. They are characterized by no back mixing/flooding and theoretically no loss of organic carriers if a support membrane is used [2, 18], high mass transport fluxes resulting from high diffusion coefficients in LM, possibility to use expensive and selective carriers because small volumes of organic phase as a membrane phase. SLMs show high separation coefficients and opportunity to concentrate the transported solute. Although LMs (ELM, SLM) are perceived as more environmentally friendly than traditional separation techniques (liquid–liquid extraction) due to many advantages,

they are not still widely applied on an industrial scale. Despite the LMs are considered a promising technique for the recovery of metal ions or organic compounds, they still have not been adopted on large scale in industrial processes due to their drawbacks such as problems with long-term stability, difficulty in operation of emulsification and de-emulsification in ELM and strip dispersion (pseudo emulsion) techniques, and large membrane resistance in HFSLM [18].

New carriers and solvents (e.g. vegetable oils as natural diluents) are proposed to improve selectivity of the solute transport and environmental friendliness of the separation systems. To improve stability and performance of the LM, especially of SLM, new membrane materials, new configurations of membrane operations and/or integration of LM with other operations to increase or keep constant the driving force, are investigated which might be interesting both for researchers and industry. Some examples of ELM on a large scale for removal of organic compounds indicate that these liquid membranes have the greatest potential of industrial application also for metal ion removal from wastewaters.

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7 Membrane-based processes in essential oils production

Abstract: Essential oils are compounds extracted from plants which are usually utilized to produce perfumes, soaps, lotions, and flavorings as well as other well-being or aromatherapy products with antioxidant and antimicrobial properties. Membrane technology has been proposed as a method for purification of essential oils extract from waxes fats, lipids, or chlorophyll to avoid the formation of precipitate in finished essential oil-based products. Furthermore, nanofiltration processes have been recommended for fractionation and concentration of essential oils raw materials to enhance their valuable properties.

Keywords: aromatic materials; essential oils; membranes.

7.1 Essential oils

Essential oils are aromatic materials of vegetable origin. They are complex mixtures of over 100 components synthesized through secondary metabolic pathways of plants as communication and defence molecules. Commonly, essential oils play crucial roles in direct and indirect plant defences against herbivores and pathogens, in plant reproduction processes through attraction of pollinators and seed disseminators, and in plant thermotolerance. They occur in various parts of plants [1]. For example, vetiver oil has been extracted from roots, cinnamon oil was detected in bark, sandalwood oil has been obtained from heartwood, bay oil has been found from leaves, peppermint oil has been achieved from herbs, nutmeg oil has been obtained from seeds, while lavender oil has been produced from flowers. Following the ISO standards 4720:2018 and 9235:2013 rules

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they are classified as the product gained by steam distillation of plant parts (leaves, flowers, branches), by mechanical cold-pressing of the peels of citrus fruits, or by dry distillation, after separation of the aqueous phase (when exists) by physical means. The global essential oils market size is expected to reach a value of 16.0 billion USD by 2026 comparing, while in terms of volume, the market is expected to reach at 345.4 kT by 2026. Essential oils are typically used to create perfumes, soaps, lotions, and flavorings. Essential oils have also been used as antimicrobial additives in food due to their antioxidant and antimicrobial properties, which attract interest as preservative in the nutrition sector. Moreover, due to their antiseptic properties, they have been wildly applied in traditional and folklore remedies. Besides, their proved capacity as nematocidal, antibacterial, antifungal, insecticidal or, even, herbicidal as well as insect repellent have attracted high interest from agriculture industry, especially from organic farming. Indeed, Tylkowski and co-inventor in the patent application WO/2022/029238A1 disclosed encapsulation of essential oils in hybrid organic–inorganic capsules shells for consumer good products and agriculture applications. Currently the knowledge and know-how on essential oils encapsulation, protected in the WO/2022/029238A1 patent application has been applied in BioHortiTech – "Improved bio-inocula and living mulching technologies for integrated management of horticultural crops" project. According to European regulations, in organic agriculture, farmers are only allowed to use naturally derived pesticides, made from plants, animals, microorganisms, or minerals. It is important to underline that the most essential oils are reasonably nontoxic to mammals and aquatic life, and they can be categorized as low-risk pesticides. It means that they could present low toxicity against non-target organisms. This aspect is important to remark for environmental-friendly agricultural production following the Horizon Europe strategy launched under Challenges: "Food Security, Sustainable Agriculture and Forestry, Marine and Maritime and Inland Water Research, and the Bioeconomy". Therefore, various essential oils can be considered for the development of innovated plant protection products. Moreover, additional factors such as improvements in the standard of living along with increase in demand for aromatherapy are some of the driving points to the growth of the market for essential oils. Indeed, aromatherapy is a form of complementary and alternative therapy. In order to improve the essential oil delivery in consumer good products, development of biodegradable and non-toxic capsules is required. Encapsulation of essential oils in a main aim of GreenCap project, financed by Spanish Government, which the pursue is to improve the leadership and excellence of the Spanish company in the development of detergents and cleaning products that do not generate microplastics.

7.2 Purification of essential oils

Essential oils are complex substances which contain multiple high value chemical species, most of them with organoleptic properties useful in the food and beverage industry, and the flavor and fragrance industry, for example.

These oils are isolated from plant materials through two main procedures: hydrodistillation or extraction with an appropriate hydrophobic solvent depending on the oil properties and where they are located in the plant (petals, bud/leaf, stem or root). In all cases the technique used generates a multicomponent solution. Valuable chemicals of the oil must often be further isolated to obtain the product of interest. Many applications require the removal of these natural and synthetic impurities [2].

Patents EP3677328A1, US10934501B2, EP1003537B1 describes that the impurities present in the crude solution may be natural or synthetic ones, such as: environmental pollutants, agrochemical residues, extractable compounds from packaging additives, plant sterols, lipophilic hormones, waxes, colored components, oxidation products, vitamins, and components that create undesired odor and taste in the oil, such as aldehydes and/or ketones. In at least one embodiment, while the removal of colored substances result in enhances the color of the oil, the removal of components responsible for undesired odor and taste enhance the organoleptic profile of the oil. Regarding the environmental pollutants they could include: polycyclic aromatic hydrocarbons (PAHs), polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), non-ortho-PCBs, dichlorodiphenyltrichloroethane (DDT), hexachlorocyclohexanes (HCHs), dioxins, furans, or heavy metals. Finally, agrochemical residues are mainly composed by pesticides, mostly organochloride-based compounds used widely in intensive agriculture for decades. Among them, there are: aldrin, cis-chlordane, trans-chlordane oxy-chlordane, dieldrin, endosulfan-1, endrin, heptachlor, heptachlor-endo-epoxide, heptachlor-exo-epoxide, isodrin, lindane, or mirex. When processing the crudes the first step is focused on the elimination of waxes, fats, lipids, or chlorophyll to avoid the formation of any precipitate in final essential oil-based products. For example, the process to eliminate waxes is known as dewaxing or winterization and it is described in patent applications EP0278693 and EP0278693A2 and in [3]. It is expected that dewaxed material can stand stable at 4 °C for a prolonged period. During dewaxing the crude essential oil is refrigerated to temperatures between –10 °C. and –40 °C, letting waxes to crystallize. Then wax crystals are settled under gravity. Because of the slow velocity of crystallization and the low-density difference between the solid wax and crude oil, this process may require several weeks. Additionally, obtained semi-product of the winterization process can also be centrifuged to remove any remaining wax. Despite of fact that high energy consumption for refrigerating and time consuming makes expensive dewaxing process, this have been widely studied for vegetable oil applications and in biodiesel production for its excellent results as a purification method [4, 5].

Finn and Gabelman in the European Patent EP2205710 and US Patent 9422506 disclosed a method of dewaxing a citrus oil by a filtration process. This technology consists in flowing the citrus oil parallelly to a porous membrane surface at a temperature of less than 11 °C. According to the inventors, a suitable membrane should be composed by ceramic, metal, graphite, or a combination of polymer on ceramic, zirconia on graphite, titanium dioxide on stainless, or polymer on a different polymer support. Those inventors recommend using membranes for the ultrafiltration (with a

molecular weight cut-off in the range 2000 Da to 2,000,000 Da) or microfiltration (with a pore diameter of 0.2 μm and larger). Well-known commercial products suitable for this process include the FICL filter of Doulton USA and the Membralox™ membranes of Pall Corp., USA. Moreover, all such membranes and any associated supporting apparatus are generally available in modular form for easy installation and replacement.

As mentioned before, processing many essential oils for reducing the content of impurities present in the crude may require several separation methods. Due to the heterogeneity of impurities, they cannot be reduced with just one unit operation. The current state-of-the-art for removing the synthetic ones is employing different unit operations that may include use of adsorbents or washing the oil with aqueous solutions. As a matter of example, contaminant residues frequently identified in essential oils extracted from Sicilian citrus are generally: imazalil, ortophenylphenol, thiabendazole, parathion, or malathion, which could be classified as antifungal or phosphorated pesticides products, respectively. These pesticides are characterized by a very low water solubility and high solubility in citrus essential oils; thus, these active compounds are not removed from the peel with the process water and remain in the essential oil owing to their low polarity and physicochemical properties. Consequently, conventional purification techniques, although capable to remove pesticides from citrus essential oils, could determine significant modification of their composition making them unsuitable for commercial purposes. Therefore, research efforts are required to decrease the pesticide content of essential oils without modifying their chemical and organoleptic characteristics. Cassano and co-workers [6] reported that the use of polyacrylonitrile hollow fiber membranes loaded with triacetyl-β-cyclodextrin can be proposed as a viable method to reduce the content of some pesticides from mandarin, orange and lemon essential oils. The authors demonstrated that the used membrane did not modify the organoleptic and physicochemical characteristics of the tested essential oil. They also reported that on the contrary, the treatment of orange essential oil with ceramic membranes having a molecular weight cut-off between 750 and 1000 Da produced a removal of 5–10% of the volatile fraction, a removal of the non-volatile fraction in the range of 10–50% (especially in terms of cumarines) and a removal of carotenoids higher than 90%.

United States Patent 10202562 describes the process based on membrane technology for (i) reducing the content of impurities, i.e., undesirable natural components or other from synthetic origin; or (ii) fractionation of natural components present in an essential oil using at least one selective membrane. The inventors of this patent showed that removal of pesticides can be achieved by applying the lower molecular weight cut-off membrane DuraMem™ S XP2. They demonstrated the potential of the process disclosed to remove agrochemical residues from essential oil. Additionally, they put into evidence the potential benefits of applying sequentially selectively permeable membranes. According to the United States Patent 5234579, the dewaxed oils can be additionally purified by separating elastomer membrane with a non-porous separating

membrane layer. Peev et al. [7] disclosed the use of organic solvent nanofiltration membranes for the concentration of a rosmarinic acid extract from lemon balm. The authors reported that no membrane fouling has been observed and satisfying flux has been realized at pressure of 30 bar up to retentate concentration near to rosmarinic acid solubility. During these studies the authors carried out the dead-end nanofiltrations experiments using a nanofiltration equipment provided by Evonik Membrane Extraction Technology, UK, shown in Figure 7.1.

This setup is based on a 270 mL stirred cell with a pressure regulator and an effective membrane area of 54 cm^2. During the experiments the stirrer revolutions were kept constant at 350 rpm, in order to minimize the concentration polarization.

By employing the same setup, Tylkowski and co-workers [8] reported the application of organic solvent nanofiltration membranes for concentrating an aqueous ethanolic extract of propolis or Sideritis ssp. L [9, 10]. These disclosures pertain the fact that free fatty acids are easier dissolved in ethanol than triglycerides to produce an ethanol extract enriched in free fatty acids. Afterward, the membrane is used for separation of free fatty acids from the ethanolic extract. Both, Peev and co-workers as well as Tylkowski *et al.* during the experiments used DuraMem® membranes. They are solvent-resistant polymeric membranes designed to be used in Organic Solvent Nanofiltration (OSN) applications. These membranes perform best filtrations in polar

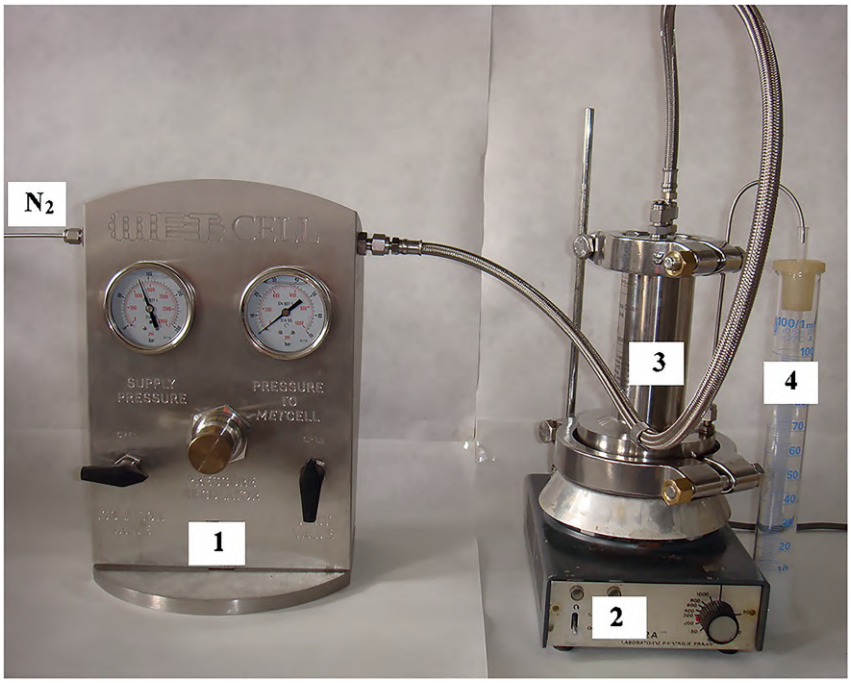

Figure 7.1: Experimental set-up: (1) pressure regulator, (2) magnetic stirrer, (3) nanofiltration METcell, and (4) measuring cylinder.

and polar aprotic solvents and have a wide cutoff range, from 150 to 900+ Da. DuraMem® membranes are typically used in flat sheet format for lab-scale membrane screening tests and in spiral wound format for pilot and commercial processes. The OSN technology has been designed to recovery of some aroma raw materials from plant extracts instead of the whole essential oil. It means that such plant extracts cannot be compared to feedstocks consist of the whole essential oil, *i.e.*, all components of the essential oil. It is well known that some of these components may be vulnerable to thermal degradation. Processes involving the membrane technologies may be carried out at near-ambient or sub-ambient temperature conditions while many of the other known methods of purification involve higher temperatures, which could be damaging to the thermally sensitive compounds, *i.e.*, the thermally-sensitive compounds are converted to different chemical molecules which decreases their yield and may also modify the organoleptic or physicochemical properties of the essential oil.

The use of reverse osmosis membrane combined supercritical carbon dioxide seems to be an excellent alternative to traditional methods of separation and purification. Indeed, Araus and Temelli [11] demonstrated that by using this system triacylglycerol and α-tocopherol/β-sitosterol can be separated from oleic acid. The authors reported that the use of cross-flow regime can reduce effectively the accumulation of solutes on the membrane surface and competently help to mitigate the reduction on the flux. Sarmento et al. [12] also showed that the reverse osmosis membranes can be used to concentrate essential oils from supercritical carbon dioxide. The authors used commercial reverse osmosis membranes supplied by Osmonics USA for the separation of lemongrass, orange, and nutmeg essential oils from supercritical mixtures with CO_2. The extraction and separation pilot plant employed by the authors is schematically represented in Figure 7.2.

Carlson and co-workers [13, 14] as well used this process to separate supercritical carbon dioxide from limonene. The authors demonstrated the membrane application for recovery and concentration of essential oils from a solvent matrix. Dupuy and coworkers [15, 16] also disclosed the application of membrane technologies to deliver emulsion-free extraction of essential oil raw materials from lemon oil by using aqueous ethanolic solutions. It is important to highlight that in this protocol the quality of separation was regulated by the aqueous ethanolic extraction solvent and not by the film properties. The film was utilized to stabilize the interface between the aqueous ethanolic solution and the lemon oil. Recovery of raw material compounds from essential oil from solid/liquid matrices by employing membrane-based processes is also well-known. Pervaporation can be applied to recuperate aroma raw materials under mild conditions. The pervaporation can be considered as a separation process due to its significant potential to purify thermolabile compounds (that degrade/decompose in high temperatures) or mixtures that form azeotropes. The process is based on application of dense (non-porous) hydrophobic film, which possesses a higher affinity to the volatile compounds, capable to separate e from a liquid mixture selected aromatic raw materials such as: ketones or aldehydes. The separation process

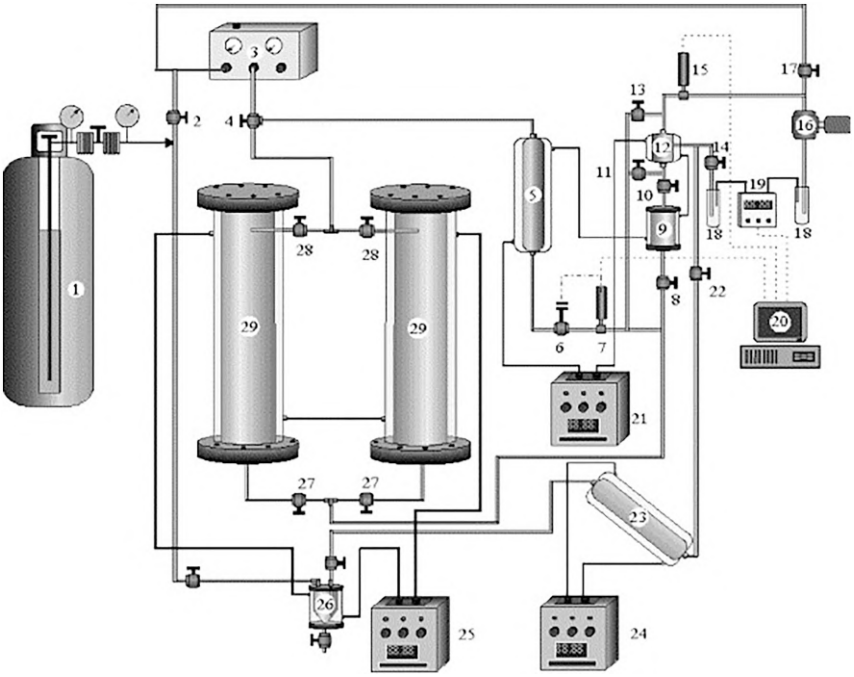

Figure 7.2: Extraction and separation pilot unit: (1) CO2 cylinder; (3) gas booster; (5) surge tank; (6) pneumatic control valve; (7) and (15) pressure transducers; (9) essential oil cell; (12) membrane cell; (16) back pressure regulator; (18) oil separators; (19) flow meter; (20) personal computer; (21), (24) and (25) thermostatic water baths; (23) separator of waxes; (26) essential oil separator; (29) extractors (2, 4, 8, 10, 11, 13, 14, 17, 22, 27 and 28) valves. Reprinted with permission from Elsevier [12].

occurs due to the differentiation of individual components in the membrane (sorption) and the differences depending on their diffusion through the membrane. Indeed, it is an alternative technology to reverse osmosis. It does not require pressure reduction on the permeate side; however, it is often reduced to improve the process. Though the pervaporation is already applied in some segments of essential oil industry, the growth of pervaporation membranes to fractionate or/and separate organic compounds still requires a technological improvement that permits the direct pervaporation of raw essential oil (without the necessity of aqueous or hydroalcoholic mixtures) to replace the vacuum fractional distillation. The two main challenges of pervaporation membrane technology are:

- the development & commercialization of improved films which are durable, chemically resistant, and with appropriated selectivity to the compounds of interest.
- the employment of the pervaporation in hybrid technologies in order to, improve the overall efficiency of various 'traditional' separation and purification technologies [17].

Du et al. [18] applied pervaporation technology by using poly(ether-block-amide) (PEBA) and polydimethylsiloxane (PDMS) membranes for separation limonene, linalool, and perillaldehyde from perilla essential oil. Yi and Wan [19] investigated recovery of volatile organic compounds from aqueous solutions via pervaporation with vinyltriethoxysilane-grafted-silicalite-1/polydimethylsiloxane mixed matrix membrane. Actually, more than 70 various types of aromatic raw materials which include esters, ketones, aldehydes, alcohols, and hydrocarbons have already been fractionated or concentrated from different sources by means of pervaporation membranes [20].

Since pervaporation does not involve any chemical solvents and operates at moderate temperatures, it provides a green process for extracting valuable volatile compounds. According to inventors of US Patent Application 20090191309 on "Process for recovering aroma from tea", pervaporation or reverse osmosis can be used for concentration of aroma. However, the processes can be appreciated when the aroma condensate comprising less than 0.1% by weight of solids allows concentration of aroma while substantially reducing the fouling of membranes.

Silvestre and co-workers [21] have proposed a use of chitosan membranes in pervaporation technologies for aroma compounds separation/concentration. However, following the current state of art, it is challenging to find some scientific papers which describe the use of chitosan-based membranes in the separation/fractionation of essential oil components in a feed stream composed by pure essential oil, a method that, if effective, could lead to novel and outstanding products, covering different brands focused on innovation in food, pharmaceuticals cosmetics, and chemical sectors. Up to now, chitosan and its derivatives have been applied to protect the essential oils from degradation in contact oxygen or light by means of encapsulation technology. Applications of chitosan-based carrier as an encapsulating agent in food industry was investigated by Maleki et al. [22] while Zhang and co-workers [23] reported anti-bacterial activity of chitosan-loaded plant essential oil against multidrug-resistant *K. pneumoniae*.

Figoli and co-workers [24] highlighted that pervaporation is one of the most investigated and implemented membrane technology for the fractionation, separation of recovery of aroma raw materials from fruit juices, as well as from industrial mixtures or from alcoholic beverages. The authors studied application of polysulfone, poly(vinylidene fluoride-co-hexafluoropropylene), polystyrene-block-polybutadiene-block-polystyrenecellulose and polyamide membranes for the concentration and isolation of bergamot essential oil volatile compounds having potential applicability in aromatherapy. The authors demonstrated that the presence in the polysulfone and cellulose structure of functional groups which contain oxygen atoms, make them more polar and in the case of cellulose membrane highly hydrophilic. According to the authors, these 2 polymeric membranes are able to reject yclic and acyclic oxygenated monoterpenes (linalool, linalyl acetate, 4-terpineol, α-terpineol).

7.3 Conclusions

The global essential oils market size is expected to reach a value of 16.0 billion USD by 2026 comparing, while in terms of volume, the market is expected to reach at 345.4 kT by 2026. Numerous techniques have been recommended for the extraction, fractionation. Separation or concentration aroma raw materials from natural sources. Traditional processes involve distillation, solvent extraction, gas stripping and supercritical fluids. Different membranes based on polymers, inorganic or ceramic composed materials have been applied; however, further development of new materials is mandatory for the process improvement. Comparing to the traditional processes, membrane ones show numerous advantages which permit concentration and isolation/fractionation of aroma raw materials at mild temperature conditions which do not involve additional extracting agents. Thus, membrane technology can be considered as a very competitive one from the energetic point of view.

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