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# Biomimetic membranes: A critical review of recent progress

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## Abstract

A membrane material that can concurrently provide commercially acceptable levels of water permeability, high salt rejection, and of sufficient stability to withstand mechanical and chemical stresses seems to be necessary to guarantee the energy and environmental sustainability of desalination systems and other membrane separation processes. Recent developments in desalination have shown that bio-inspired membranes are moving steadily in this direction. Sustainable desalination via aquaporin-based bio-inspired membranes is elucidated in this paper in terms of recent commercialization exploitation and progress towards real operations. Current large-scale applications, viable opportunities, remaining challenges and sustainability of operations, in terms of comparison with established technologies, are discussed in this paper. The major drawback of aquaporin-based membranes, which has been highlighted repeatedly in recent studies, is the stability of the membranes during real operations. This review is focused on recent solutions provided by scientists towards the mitigation of these problems and commercialization of aquaporin-based membranes.

*Keywords:* Aquaporins; bio-inspired membranes; sustainable desalination; separation processes; commercialization.

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## **1. Energy requirement as a major barrier to sustainable desalination**

### *1.1 Current status of desalination energy requirements*

The Earth's surface is composed of 71% water, of which only 1% accounts for accessible fresh water and 97% is seawater. The most threatening challenges of the 21<sup>st</sup> century are water

scarcity, climate change and accelerated population growth. The latter two challenges only exacerbate the former: water scarcity is an alarming threat to our sustainability and requires immediate action. According to data obtained by UNICEF and WHO, about 1.1 billion people are without access to clean drinking water [1]. The demand for potable drinking water is increasing with the global population (Fig. 1), leading to a decrease in the available freshwater resources per capita.

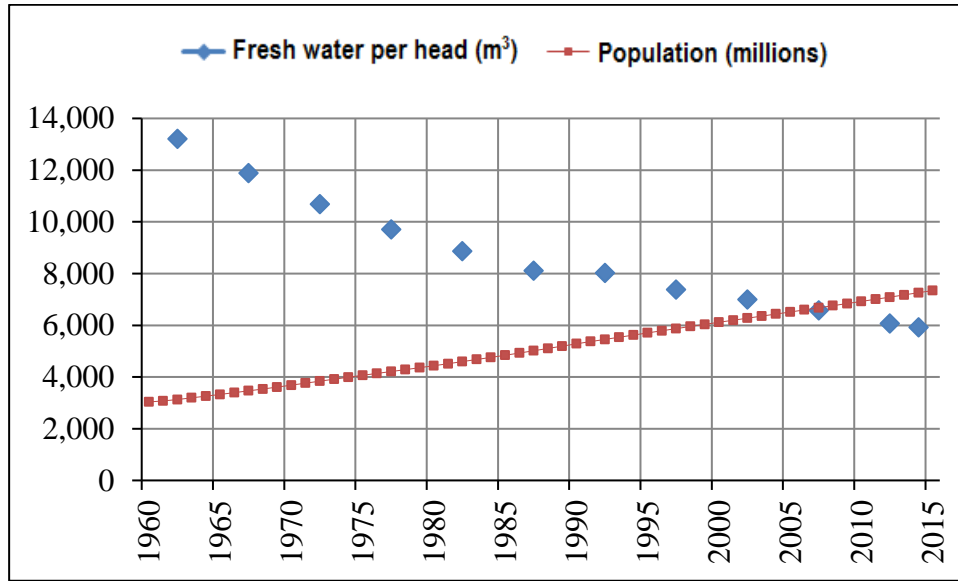


Fig. 1. Decreasing available fresh water resources per head and rising total population [2].

For improved water sustainability, new purification methods and increased water resources are urgently required. Water desalination is one way to provide potable drinking water. Thermal processes and membrane desalination are the most common methods of modern desalination. Thermal processes, such as multi-stage flash, multi-effect distillation, vapor compression, and humidification dehumidification, usually follow the concept of evaporation and condensation of water. Membrane desalination technologies, such as reverse osmosis (RO), forward osmosis (FO), electrodialysis (ED), and nanotechnology-based processes, use membranes as salt rejection barriers to desalinate water. Membrane technology is advantageous compared to thermal processes because of comparatively low energy usage [3].

Energy is the single biggest cost component in desalination, accounting for up to half of the total cost of fresh water production [4,5]. The increasing trend in energy demand for desalination will continue into the future if necessary steps are not taken (Fig. 2). Therefore, this major problem will result in a drastic increase in global energy usage as a result of surging desalination capacity.

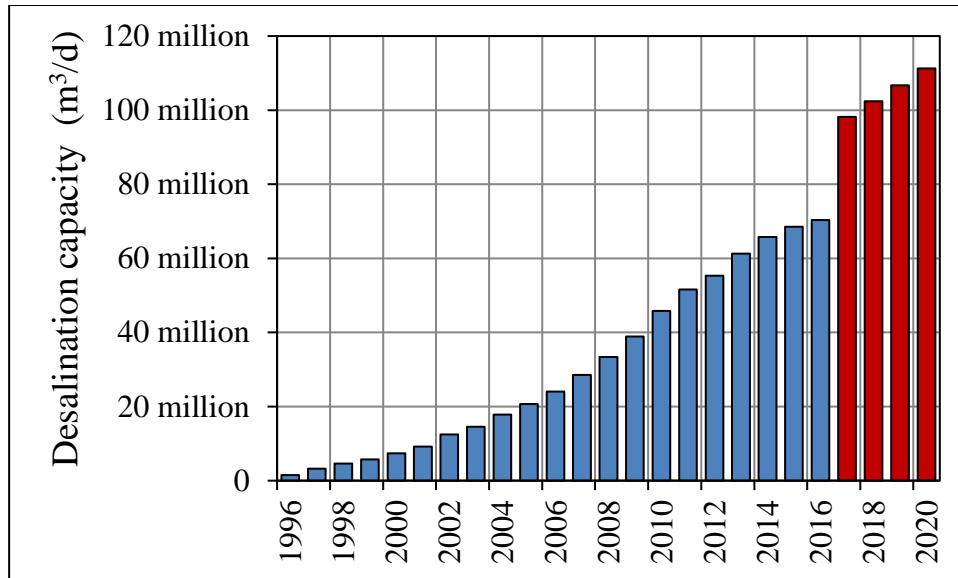


Fig. 2. Annual online desalination capacity (in blue color) and total predicted contracted capacity for 2017 – 2020 (in red color) [6].

The energy required for desalination has considerably decreased in recent years as a result of development of energy recovery devices, more efficient pumps and membranes, and development of improved configurations [7,8]. However, when the magnitude of the world's total desalination capacity is taken into consideration the total energy cost is still considerable. For the desalination step alone, high-performance membranes which are capable of desalinating seawater through an RO process at an energy level of 1.8 kWh/m<sup>3</sup> (just above the thermodynamic minimum) and 50% freshwater recovery have been demonstrated [9]. The question to ask is: which step in the overall desalting system requires the most attention in order to optimize energy efficiency? The various steps that contribute to the energy costs of desalination are outlined below.

(1) Intake step:

The energy required for the feed intake to the pretreatment step depends on the feed quality, source and geographical location. Intake sources may include open surfaces, subsurfaces, such as underground wells, and effluents from power plants [10]. The energy required for feed intake may become higher if there are regular impingements and entrainments of biological species from the source in the intake system [7]. However, this energy cost can be minimized if the sharing of intakes between new and existing plants is encouraged.

(2) Pre-treatment step:

The pre-treatment step prevents regular membrane fouling and unnecessary process shut-downs by removing particulate matter, organic substances, inorganic salts, and turbidity from the feed water. Current commercial desalination processes would not run smoothly and flow channels would become plugged in minutes if they are not fed with pretreated water. However, the pre-treatment step requires a large amount of energy and materials [11].

### (3) Desalination step:

The hypothetical lowest energy required by the desalination step is the Gibbs free energy of mixing or energy required to achieve salt rejection via thermodynamic reversibility [12]. This energy is ensured by the osmotic pressure of the feed solution and it is highly dependent on the feed salinity and fresh water recovery. However, the actual energy required for the desalination step is higher than the thermodynamic minimum of about 1.06 kWh/m<sup>3</sup> because of pressure losses [9], which are due to friction to flow contributed by the membrane channels and their tortuosity, layer of foulants on membrane, frictional losses in the pipelines, concentration polarization, and inefficiencies of inflow pumps [13–16]. Therefore, the water permeability of the membrane is the ultimate determinant of the actual hydraulic pressure required to achieve a particular recovery at standard process conditions.

To reduce the gap between the actual energy and the theoretical minimum energy required for the desalination step, the following approaches have been suggested: the use of multi-stage systems to recover residual energy from the concentrates; use of energy recovery devices, hybridization of two desalination technologies to utilize the comparative advantages; use of waste heat from boiler blowdown or cooling water effluent for thermal distillation; and utilization of salinity gradient power [17].

### (4) Post-treatment:

Post-treatment involves disinfection, adjustment of pH and hardness, removal of some trace pollutants such as boron and chlorides, and re-mineralization so that the final product water can be able to provide some health benefits. Post-treatment consumes a considerable amount of energy in current large-scale desalination plants because in many cases, membranes, pumps and other mechanical equipment are involved [10,18].

### (5) Concentrate management:

The reject brine from desalination is a critical environmental issue because of its huge volume [19,20]. This is due to the residual pre-treatment chemicals and high salinity and temperature of the disposed brine. Also, the heavy metal content in the reject brine due to pipe corrosion constitutes serious environmental risks. The characteristics of the reject brine depends on the quality of the supplied and generated water, the techniques used for pre-treatment, and the desalination process employed [21]. The energy required for the concentrate treatment depends on the deployed technology, as thermal crystallizers and brine concentrators are known to use a considerable amount of energy [22]. However, this may be effectively controlled by mixing concentrate streams with low-salinity effluents such as cooling water to ensure safe discharge to a water body, optimizing fresh water recovery through a multi-stage desalination step and recovery of valuable products from the concentrate [17,23–25]. In addition, the generation of electric power from the osmotic potential of reject brine could open another vista of opportunities for renewable energy generation via pressure-retarded osmosis (PRO) [26].

Of all the steps in a desalination system, pre- and post- treatment account for the highest proportion of energy, most especially for seawater desalination [18], with intake, pre- and post-treatment, and brine management normally consuming more than 1 kWh/m<sup>3</sup> [27]. Thus, the actual overall energy usage for desalination is 1.5-2 times higher than what is calculated by theoretical thermodynamics [28]. In fact, the energy requirements of some recent plants are 3-4 times more than the theoretical minimum [9]. Some RO plants (using seawater as feed) are now

operating at applied pressure that is only about 10 – 20% greater than what is thermodynamically required for the desalination step [8,9]. From these estimations, suggestions that research focus should be directed towards pre- and post- treatment steps mainly have been made because inefficiencies in these steps might double the thermodynamic energy requirement.

However, the desalination step influences the energy requirements of the pre- and post- treatment steps. An efficient desalination step that is highly resistant to fouling and scaling from feed contaminants and can provide high water flux and salt rejection with high quality permeate would significantly reduce pre- and post- treatment energy costs. A lot of work has been done with regards to improving membranes and desalination stages to tolerate the harsh conditions of the feed saline water with minimal fouling [29–32].

Between 2016 and 2020, an estimated 18.4 million m<sup>3</sup>/d is expected to be added to the world's contracted desalination capacity [6]. In Spain alone, the average CO<sub>2</sub> emission of desalination plants was 6.99 kg/m<sup>3</sup> [33]. However, using a value of 1.8 kg/m<sup>3</sup> as the CO<sub>2</sub> emission from recent plants with improved performance [9], one-third reduction in CO<sub>2</sub> emission would lead to 4 Mt CO<sub>2</sub> saving every year between 2016 and 2020.

### *1.2 Reduced energy requirements through novel aquaporin containing membranes*

Many membrane materials have been used for the desalination step [34]. However, it is often impracticable to obtain excellent flux, high salt rejection, and superb membrane stability simultaneously. The challenge, therefore, is to develop membranes that exhibit all of these properties in order to significantly reduce the energy requirements of desalination systems and ensure energy efficiency.

A very promising candidate to produce a very high water permeability, salt rejection, and stability are aquaporin-based membranes [35]. Aquaporins are transport proteins in living cell membranes, acting as selective water channels through the membrane, that are capable of transporting up to one billion water molecules per second with a permeability that is 5 to 1,000 times greater than those of conventional membranes, based on recent studies [36,37]. The selectivity of aquaporins is also superb, as aquaporins can reject virtually everything apart from water, including protons, dissolved gases, and very small molecules such as boric acids, urea, and chlorides, depending upon the particular aquaporin under study [38–41]. These interesting properties of aquaporins present aquaporin-based membranes as a low-energy option for desalination. In this regard, the use of aquaporins as bio-inspired membranes for highly efficient widespread commercial desalination would be a breakthrough for the world of desalination [42]. Before now, the most challenging obstacle to widespread application of aquaporin-based membranes in the industry is their lack of stability due to non-compatibility with porous supports capable of withstanding high pressures. However, impressive results have been obtained recently in this regard. Aquaporin-based membranes fabricated via interfacial polymerization have now shown stable performance for several weeks and months [41], and have now been commercialized.

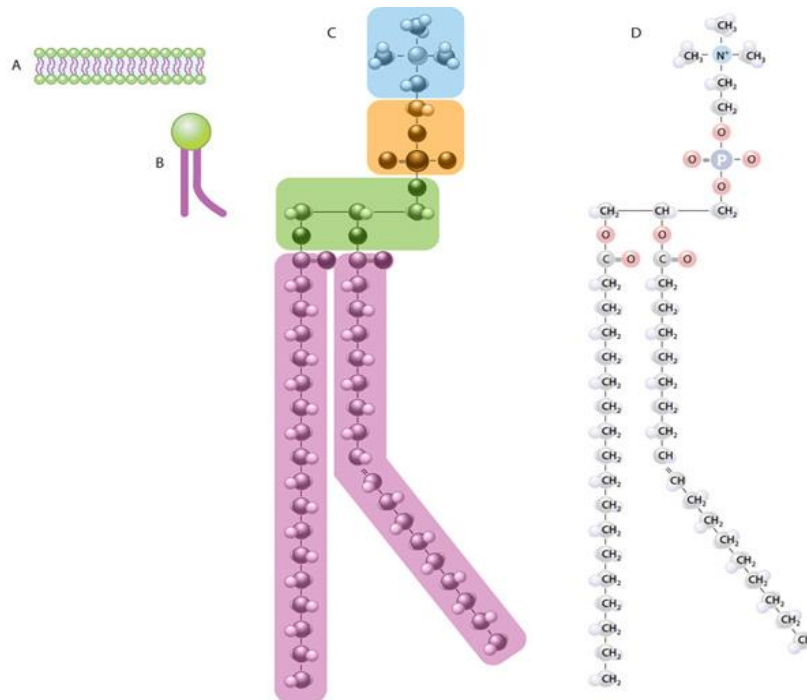
Sustainable desalination via bio-inspired aquaporin-based membranes is described in this paper in terms of recent developments and progress, viable opportunities, current challenges, operating conditions, and sustainability. The major challenge of aquaporin-based membranes, which has been highlighted repeatedly in recent articles, are stability problems, due to aquaporins

embedded on lipid bilayers being fragile assemblies which are and difficult to handle. This review is focused on recent solutions provided by scientists towards the mitigation of these challenges and commercialization of aquaporin-based membranes.

## **2. The cell membrane as a great separation medium**

The contents of a biological cell are protected by an enclosure known as cell membrane, which regulates traffic between the cytoplasm and external environment. Eukaryotes, unlike the simpler procaryotes, also have internal membranes which allow internal compartmentalisation and enclose cell organelles [43–45]. Most cellular plasma membranes are made up of two important components: (1) a lipid bilayer consisting of glycerophospholipids, mixed with other lipids such as cholesterol, and (2) proteins embedded into or inserted through the bilayer [44,46]. The lipid bilayer is the main structural element of the membranes and as a result imparts mechanical properties to the membrane providing resistance to [47–49]. The thickness of the lipid bilayer is in the nanometer range. Lipids are any of a group of organic compounds including fats, oils, waxes, sterols, and triglycerides [50,51]. To a large extent, glycerophospholipids are the most common lipids in cell membranes and they self-assemble into bilayers without any input of energy [52,53]. By convention, a glycerophospholipid molecule consists of glycerol, two fatty acid chains, and one phosphate group [54]. Since glycerol consists of three carbon atoms, it serves as the backbone and two of its carbon atoms are attached to the two fatty acid chains at its hydrophobic tail while its third carbon atom is attached to the phosphate group at its hydrophilic head. The phosphate group consists of phosphate attached to several possible head groups, such as choline to form phosphatidylcholine (Fig. 3). The hydrophilic phosphate groups in the bilayer are directed towards the water-based cell cytoplasm and exterior of the cell while the hydrophobic tails face the interior of the bilayer [55,56]. Although a glycerophospholipid molecule is cylindrical in shape, several molecules can form broad sheets when they are horizontally aligned [44,57,58].

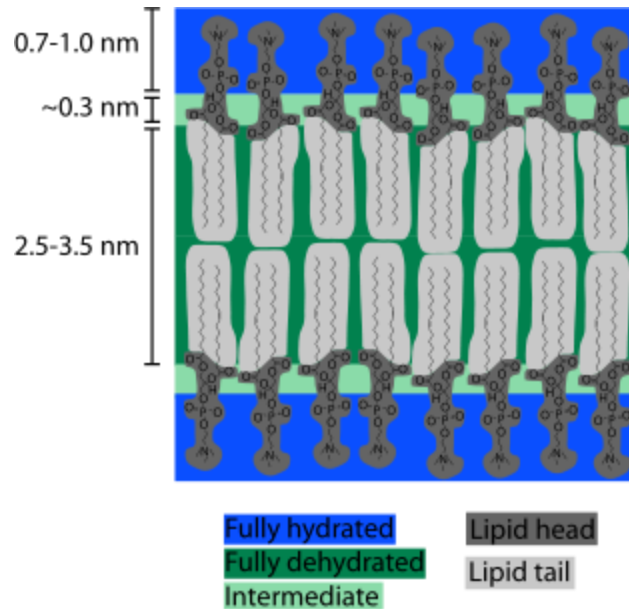




*Fig. 3. A glycerophospholipid molecule with its different components [59].*

(A) A broad sheet of glycerophospholipid molecules in a cell's plasma membrane. (B) A glycerophospholipid molecule (phosphatidylcholine) consisting of a hydrophilic head (green) and hydrophobic tails (purple). One of the tails appears bent because of the double bond between the two carbon atoms in glycerol connected to the lipids (C) The glycerophospholipid molecule's hydrophilic subregions.

Water is forced away from the hydrophobic side of the hydrophilic head into the bulk aqueous solution. This activity is aided by noncovalent interactions between hydrophobic molecules known as the hydrophobic effect [55,60,61]. In this hydrophobic region, the surface tension of water is increased (i.e. there is enhanced free bonding of water molecules to one another) and the system's entropy is increased. The different regions of the lipid bilayer are illustrated in Fig. 4.

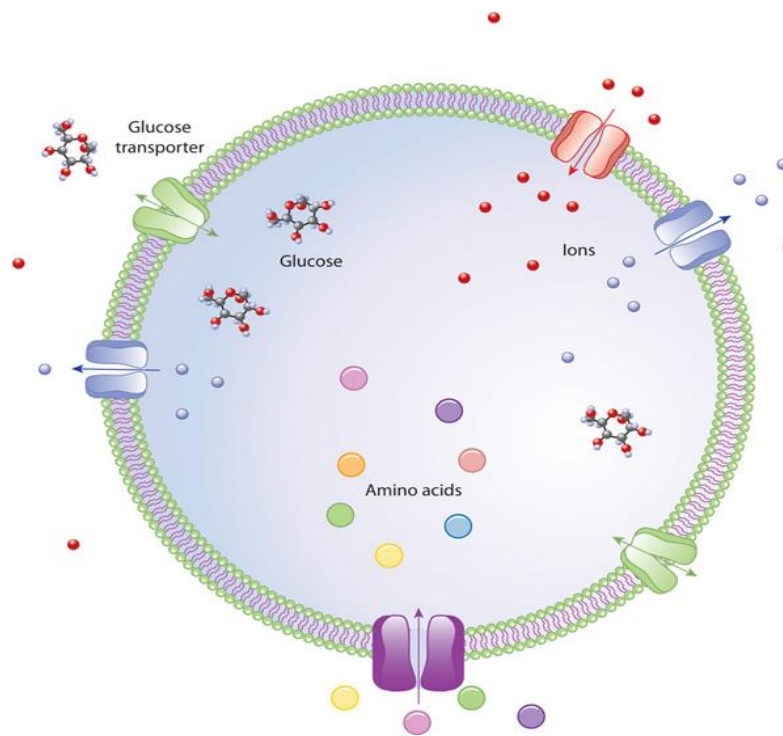


*Fig. 4. The three regions of a lipid bilayer: (1) fully hydrated head (in blue); (2) fully dehydrated or hydrophobic core (in dark green); and (3) an intermediate region with incomplete hydration [62].*

Proteins are another important component of cell plasma membranes and they are responsible for a significant fraction of the entire mass of a cell membrane [63,64]. A portion of these proteins is directed outwards from both sides or from layers of the cell membrane while the other portion is located at the lipid tails. These proteins are also attached to the interior and exterior of cell membranes by tethers, cytoskeletal elements or lipid shell [64–66].

### *2.1 Bio-inspiration from cell membrane functionality for fabrication of desalination membranes*

Cell membranes are semi-permeable barriers that can permit the transport of only very small molecules and reject ions and large molecules, such as carbohydrates and amino acids. Transport across the membrane is mostly facilitated by embedded proteins [59,67,68], as illustrated in Fig. 5. The functionality of cell membranes can be adapted to the fabrication of biomimetic or bio-inspired membranes for desalination. The concept of these membranes is not new, as many articles have been published in recent years on their applicability for water treatment [40,41,69–75]. The missing link is that the applicability of these membranes for sustainable desalination needs to be emphasized and accorded due attention. Recent efforts aimed at tackling membrane stability under high pressure and harsh feed conditions have also been sparsely discussed in most of the reviews on this technology. This paper has focused on these crucial issues.



*Fig. 5. Semi-permeable cell membrane with specialized proteins that selectively reject the transport of molecules across the membrane [59]. Glucose, amino acids and ions are present in the interior of the cell with the permeating water. The intracellular components are permeated via transporters while rejected salts are shown with colored shapes outside the cell membrane.*

Meanwhile, one common area of confusion in the fundamental understanding of these membranes for desalination is the distinction between the terms ‘biomimetics’ and ‘bioinspiration’. Biomimetics or biomimicry involves the study of the production, processing, morphology, working mechanisms, characterization and application of natural biological matter and substances such as proteins, enzymes and others for the sole purpose of artificially producing or simulating similar materials that could mimic these biological materials [76–78]. Therefore, biomimicry is the direct imitation of natural techniques and processes in biological applications and it represents a paradigm shift in focus from the chemical composition of molecular species to the structure and application of these species [78]. Bioinspiration is the indirect imitation of natural principles, activities and processes in non-biological applications to provide solutions to human problems. However, the concept of biomimicry and bioinspiration overlap in many ways. For example, the knowledge of the pathway for the biosynthesis of natural products so that this pathway can be adapted for use in vitro systems could also be termed as biomimicry [78]. Therefore, for the purpose of the discussions in this paper, ‘biomimetic’ and ‘bio-inspired’ can be used interchangeably. Bioinspired membranes have previously found applications in biosensing and biocatalytic applications, medical implants, and microfluid devices [79–82].

Natural lipid membranes are composed in part of phosphatidylcholine. Phosphatidylcholine possesses biointerfacial properties and is able to form various self-assembled structures because of its amphiphilicity. These structures include supported artificial membranes, micelles, and

liposomes as supports for immobilization of biological species, such as proteins [83,84]. Phosphatidylcholine consists of an anionic phosphate group and a cationic choline which make it compatible with materials that impart handling properties. Bio-inspired membrane assembly mechanism can be likened to the building blocks principle of polymer design. The contrast between the monomeric molecules of synthetic macroscopic polymers and self-assembled building blocks of biopolymers can be used to explain this mechanism. Like synthetic polymer production, which involves the action of nucleus formation and a growing polymer chain resulting from repetitive addition of monomers, biomimetic reactions involve templated polymerization of thermodynamically energetic bio-based monomers in self assemblies [85,86]. Biopolymers are responsive to light and heat stimuli, which are comparable to transport mechanisms in synthetic polymers [78]. These biomimetic reactions are mostly polycondensation reactions. However, synthetic polymers are mostly produced from highly reactive intermediates such as ions, radicals, or through polycondensation at conditions that vary widely from those of natural systems.

## *2.2 Aquaporin-based membranes for bio-inspired membrane desalination: Current commercialization efforts*

Aquaporins are protein channels that permit the transport of up to a billion water molecules per second, if a sufficiently high osmotic potential exists across the membrane [87,88]. They constitute a large family of proteins that transport water across cell membranes. Thus, they are promising building blocks for efficient bio-inspired membranes for desalination. In a recent analysis in the field of membrane nanotechnology, aquaporin-based membranes were considered to provide the best solution to most challenges associated with current desalination practices (low productivity, membrane fouling, high cost as compared to water reuse etc.) and were observed to be highly efficient [41,89]. They are present in natural membrane structures and they consist of channels that are capable of transporting water molecules and rejecting all types of solutes like salts, ions, bacteria and other impurities [40,41]. Aquaporins are abundant throughout nature, but are particularly abundant in, for instance, mangrove plants (which are also salt-tolerant), mammalian kidneys and bacteria [90]. The major advantage of aquaporin-based membranes is that they offer no compromise between selectivity and water permeability. Because of these advantages, researchers' interest in this technology is growing rapidly. Shen et al. reviewed the structure of biological membranes along with the operating mechanism in complete detail [89]; Zhao and his co-authors studied the formation and applications of both biological and bioinspired membranes [72]; Neilson et al. wrote a book chapter on biomimetic application in sensors and separation process [80]; and Schuster et al. reviewed surface layer proteins for biological membrane fabrication [91].

Recent efforts geared towards the fabrication of commercial aquaporin-based membranes have shown the viability of using these protein channels for water treatment. A company known as Aquaporin based in Copenhagen, Denmark have incorporated aquaporin proteins into a thin bilayer film supported by a porous membrane. After several years of research, this company has commenced the commercial production of these membranes based on its patented technology known as Aquaporin Inside™ [92]. This technology has been featured in “Quest Means Business” show of Cable News Network (CNN, USA) in the series known as “Make, Create, Innovate”. Aquaporin Inside™ patented technology is based on novel dynamic simulations used

by a scientist, Morten Østergaard Jensen, to simulate the movement of water through biomembrane systems [93]. Jensen himself was inspired by the initial discovery of aquaporins in living cells by Peter Agre, which earned Agre the 2003 Nobel prize in Chemistry [93,94]. In Aquaporin Inside™ technology, aquaporin proteins are hosted by a thin film coating which ensures that the natural activity of such proteins are preserved during water treatment. Flat sheet and hollow fiber membranes can contain this coating [92]. Aquaporin Inside™ hollow fiber modules can be used in forward osmosis (FO) process and these modules contain proteins on the fiber's lumen side. For pilot scale operations, hollow fiber modules with active area of 0.6 m<sup>2</sup>, which can also reject very small molecules, have been manufactured by the company. Flat sheet FO membranes with a width of up to 40 cm, which can be rolled into the required length, have also been produced. The other kinds of flat sheet membranes manufactured by the company for FO and RO applications include: AQUAPORIN INSIDE™ AIM60 apx. 5.5 cm x 11 cm (fitted to a Sterlitech CF042-chamber), AQUAPORIN INSIDE™ AIM256 apx. 13.5 cm x 19 cm (fitted to a Sterlitech SEPA CFII), and customized sizes (currently up to 20 cm x 25 cm). Sterlitech's CF042 and SEPA CF chambers can withstand pressures of up to 69 bar and temperatures that are more than three times the average ambient temperatures of many tropical countries. These Aquaporin membranes have been reported to have an initial salt rejection of 99.99%, initial water flux of more than ~ 10 kg/m<sup>2</sup>, and osmotic gradient of 30 bar in draw solutions. All the company's products are expected to comply with both EU & US legislations for Food Contact Materials (No 1935/2004, No 10/2011 & FDA 21 CFR 177.2550) with ISO 9001:2015 certification applied for. Currently, the company is constructing new Group Headquarters and large-scale production lines in Denmark, and venturing into China's household water purification market through its Chinese subsidiary known as Aquapoten. Aquaporin Inside™ hollow fibers and flat sheet modules are shown in Fig. 6.



(a)



(b)

*Fig. 6. Aquaporin-embedded membranes in (a) hollow fiber and (b) flat sheet configurations produced by Denmark-based company known as Aquaporin [92].*

Most of this company's products are currently used for FO treatment of low-salinity feed water in pilot-scale units but efforts are underway to upscale this technology for the treatment of various streams in industrial spiral-wound settings. Currently, the company has 61 granted patents including three granted US patents and three granted European patents. It also has patents in Singapore, Japan, South Korea, China, and Australia. The list of its US patents is provided in Table 1. This company has won the Frost & Sullivan's "2009 European Biomimetic Membranes Technology Innovation Award", European Patent Office's "Inventor of the Year 2014 (category SME)" and 2015 Singapore Water Technology New Product Innovation Award [92].

Table 1. Aquaporin's US patents and patent applications [95].

Product	US patent and patent application
Any Aquaporin Inside™ membrane or module, when used in pressure retarded osmosis for the production of salinity power or salinity energy	US 8,123,948 B2
A power plant for the production of salinity power using an Aquaporin Inside™ membrane	US 8,123,948 B2
AQPFOFS60 - Aquaporin Inside™ AIM 60 flat sheet FO membrane	WO2015166038 (A1) designating USA
AQPFOFS256 - Aquaporin Inside™ AIM 256 flat sheet FO membrane	WO2015166038 (A1) designating USA
AQPROLP - Aquaporin Inside™ flat sheet LPRO membrane and SW module	WO2015166038 (A1) designating USA
AQPROTW-1812/150 – Aquaporin Inside™ RO Tap Water SW Module	WO2015166038 (A1) designating USA
AQPFOHF-200/25-116cm <sup>2</sup> - Aquaporin Inside™ Medium Hollow Fiber FO module	US2015144553 (A1) and WO2015166038 (A1) designating USA
AQPFOHF-265/55-0.6m <sup>2</sup> - Aquaporin Inside™ Large hollow fiber FO module	US2015144553 (A1) and WO2015166038 (A1) designating USA

Another Danish company, Applied Biomimetic, is embedding aquaporin proteins into a polymer matrix for the purpose of manufacturing biomimetic membranes [96]. A subsidiary of Applied Biomimetic known as Mangrove Membranes, Inc. has used coating techniques to stack and cross-link multiple layers of aquaporin proteins on a polymer support [97]. The support is an ultrafiltration membrane with dextran molecular weight cut-off (MWCO) of about 10 kDa and the aquaporin-based membranes produced are commercially available for applications such as dairy processing, wastewater treatment, and treatment of low-salinity feed. These membranes are available in flat sheet and spiral-wound forms. Spiral-wound forms of Mangrove membranes are shown in Fig. 7. These forms contain elements with diameters of 3.8, 6.3, and 7.9 in. According to the company, Mangrove membranes' technology would have the capacity to substantially increase the efficiency of transmembrane flow by a factor of 5-10, thereby reducing the energy consumption and economic footprint of water treatment process. The first commercial application of this technology was launched in 2014.



*Fig. 7. Spiral-wound Mangrove membranes produced by Mangrove Membranes Inc [97].*

In initial investigations on biomimetic membranes carried out by a team at Sandia National Laboratory in the United States, a nanoporous polypeptide biomimetic membrane fabricated via atomic layer deposition and constructed on a porous ceramic support was compared with the widely known Dow FILMTEC SW30HR [98,99]. It was estimated that the reduction in transmembrane flow resistance offered by this biomimetic membrane would lead to 88% lowering of excess energy requirement and savings of \$1.45 million per year for a desalination plant operating at 100 million L per day. These estimations were based on single-pass flow across the membrane. For double pass flow, 63% reduction in excess energy requirement was obtained when compared with the best competitor at the time of this investigation – Dow SW30ULE. However, this study was not a pilot or industrial-scale investigation and the applied pressure was only up to 10.3 bar. This was only a preliminary study and more flexible supports, such as thin film supports, will be needed before the biomimetic membrane can withstand higher pressures. Meanwhile, efforts are underway to scale-up this approach.

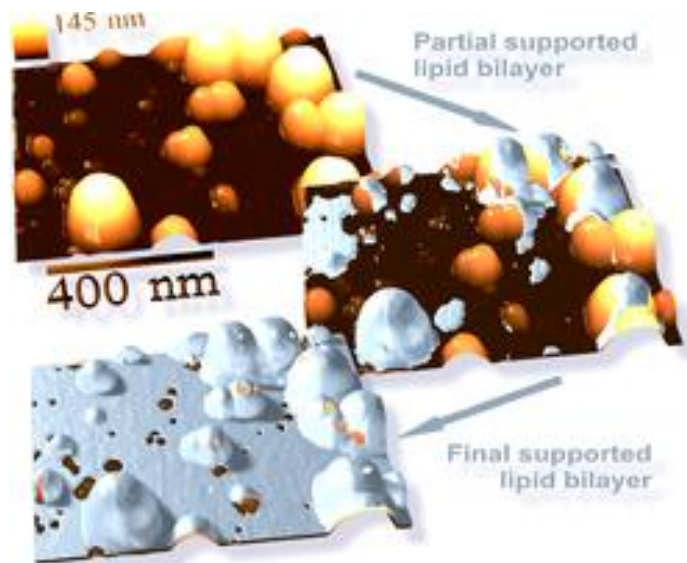
A research team at the National University of Singapore (NUS) Environmental Research Institute has also produce an aquaporin-based membrane that could reduce water purification costs by 30% [90]. The design of the membrane was made to mimic cell layers on the roots of mangrove trees because mangrove trees can basically reject 90 - 95% of salt around their roots. The team produced this biomimetic membrane by incorporating nano-sized aquaporin-embedded vesicles onto an ultrafiltration membrane. According to the team, the fabricated membrane is mechanically stable and can be used for desalination and industrial water treatment. Currently, the team is in discussion with a US-based company for the fabrication of pilot-scale modules in the next 2 years.

### *2.3 Fabrication approaches for the lipid bilayer*

The fabrication of an aquaporin-embedded lipid bilayer is a complicated task because the bilayer is fragile [40,100,101]. In addition, the characterization of the bilayer requires advanced techniques such as atomic force microscopy (AFM) [102,103]. AFM uses a sharp probe tip that physically interacts with the sample surface allowing a 3-dimensional topography of the membrane surface to be visualized at high resolution. AFM has been used to measure the



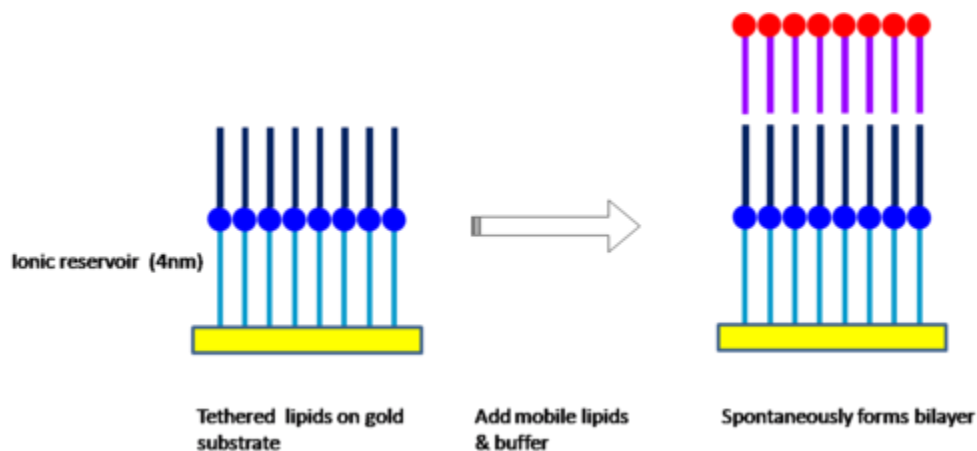
existence of pores in the bilayer and transitions of phases in supported bilayers and characterize their physical properties [103]. The authors added the lipid bilayer to a support covered in silver nanoparticles. For nanoparticles with diameters less than 22nm the bilayer formed pores around them, but for larger nanoparticles the bilayer was continuous over the nanoparticles. When the particles were removed the smaller nanoparticles left pores in the bilayer (Fig. 8).



*Fig. 8. AFM scan showing the transmembrane pores in a lipid bilayer. Initially, the surface of the virgin substrate was covered with silver nanoparticles and then the silver-colored lipid bilayer was formed over the surface. The support was removed to produce the final supported lipid bilayer with mixed 5-140 nm silica particles. Removal of nanoparticles of sizes <22nm left pores, seen as dark patches in the final image [104].*

When natural lipid bilayers are not available, synthetic lipid bilayers can be fabricated. Synthetic lipid bilayers are referred to as model lipid bilayers and they can be fabricated using both natural and synthetic lipids [105]. Many types of synthetic lipid bilayers exist, including black lipid membranes (BLM), supported lipid bilayer (SLB), tethered bilayer lipid membranes (t-BLM), and model vesicles [106]. BLM is the oldest synthetic system which is fabricated by making a small opening with a diameter in the micrometer range in Teflon or another hydrophobic polymer [107,108]. A lipid solution is then dissolved in a viscous hydrophobic solvent and this mixture is applied across the opening to obtain a thin lipid bilayer. The “Black” in BLM means that the bilayer becomes dark in reflected light as a result of the destructive interference between the light reflections from both sides. SLB is a bilayer supported by a solid support. As a result of the support, only one face of the bilayer is in contact with the feed. The presence of this support imparts mechanical stability to SLB which makes it relatively easy for SLB to be characterized; therefore, operations running into months can be carried out using SLB [109].

The stability of SLB can be further enhanced by anchoring the lipids to a substrate chemically to produce what is known as t-BLM [110]. Gold is applicable for use in t-BLM because of its chemical inertness and good covalent bonding, most especially with thiolipids [111,112]. A diagrammatic representation of the anchoring of lipids on gold substrate to form a t-BLM is shown in Fig. 9. Vesicles are lipid bilayers that are rolled up in lamellar or spherical enclosures or shells in such a way as to shown fundamental similarity with the functionality of a cell membrane [113]. Therefore, most studies on model lipid bilayers have been carried out on vesicles. In addition, they are relatively easy to fabricate because a dehydrated lipid suddenly forms a vesicle when it is exposed to water. Also, vesicles can be isolated from the cultures of cells and tissues instead of artificially producing them. These natural vesicle offer greater real-life compatibility to the biological phenomena of membrane separation and they consist of a consortium of complex natural lipids.

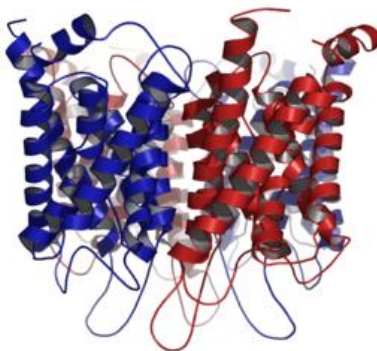


*Fig. 9. The production of t-BLM through the anchoring of lipids on gold substrate. Lipids are chemically tethered to inert gold substrate (with yellow shade). A bilayer is formed by exposing the anchored lipids to the lipids at the outer layer. The mobility of the lipids is enhanced by a 4 nm hydrophilic spacer (shown in blue color as ionic reservoir).*

Water transport through the lipid bilayer is much slower than through aquaporin channels leading water transport through cell membranes to be mediated via water diffusion through aquaporins embedded in the lipid bilayers [114,115]. Some aquaporins, referred to as aquaglyceroporins, also allow the transmembrane transport of uncharged small solutes, such as glycerol and urea [116,117]. However, all aquaporins prevent the transport of charged protons due to the membrane's electrochemical activity. The quest to explain the mechanism of water selectivity through the cell membrane was fulfilled by the discovery of special a protein pallet in red blood cells by Peter Agre. This pallet was named by Agre as Aquaporin 1 [118]. Aquaporin belongs to a large family of proteins consisting of more than 800 integral proteins. Aquaporins are alternately named major intrinsic protein (MIP). Aquaporin monomer has an hourglass structure with the narrowest pore constriction of 2.8 Å [119,120].

Water permeation through aquaporins is modulated by three different mechanisms. Firstly, mass transport of water occurs as a result of its rheological properties, such as kinetic flux from cell metabolism and gravitational potential. The second mechanism is charge repulsion which restricts the invasion of ions and other solute. For example, the arginine residue in aquaporin is positively charged at physiological pH values, thereby restricting the flow of cations due to electrostatic repulsion while repulsion of anions is due to Donnan exclusion phenomena in order to maintain charge balance [121]. Thirdly, there is breakage of hydrogen bonds as a result of reorientation of water molecules across the membrane, thereby leading to improvement in water flux and further decrease in ion permeation [122]. The hydrogen bond is broken by the reorientation of water molecule due strong dipole interaction by two short helices present at the end of the protein channel.

Aquaporin consists of 6 transmembrane  $\alpha$ -helices which are organized in bundle. The amino and carboxylic terminals are both located on the cell membrane's cytoplasmic surface [123,124]. This sequence is shown in Fig. 10. Aquaporin protein sequences form tertiary structures, each of four monomer units (tetramers) in the cell membrane, and each monomer serves as a water conducting channel [125]. These proteins are present in almost all living organisms and classified into three categories on the basis of their specific functionalities. These categories include 1) orthodox aquaporin, which allows water only to pass and restricts flow of all other solutes; 2) aquaglyceroporins which permits the passage of both water and glycerol and 3) subcellular aquaporin which are confined in the cell [126,127]. Meanwhile, all aquaporins allow efficient transport of water. These aquaporins have been recognized in almost all living organisms from mammals to plants and in microorganisms. In mammals, almost 13 aquaporins have been recognized so far in organs and cell tissues [68]. Six of these can be found in the kidney [128]. Aquaporin 1, Aquaporin 2, Aquaporin 3, Aquaporin 4, and Aquaporin Z are some of the most extensively studied Aquaporins. Aquaporins 1 to 4 are found in the cell membranes in the kidney. Aquaporin 1 assists in water reabsorption; Aquaporin 2 assists in water reabsorption in response to antidiuretic hormone; Aquaporin 3 assists in water reabsorption and glycerol transport; and Aquaporin 4 assists in water reabsorption but is mainly found in basolateral cell membranes.



*Fig. 10. A crystallographic representation of 6 transmembrane  $\alpha$ -helices aquaporin 1 sequence containing amino and carboxylic terminals located on the cell membrane's cytoplasmic surface.*

Aquaporins have also been identified in many unicellular organisms. The yeast *Saccharomyces cerevisiae* and *Escherichia coli* contain water facilitator aquaporins [129]. Aquaporin Z (AqpZ) is found in bacteria such as from the cell membrane of *E. coli*. Successful AqpZ synthesis (up to 12.2 mg/L) can be carried out by using *E. coli* BL21(DE3) host strain through the addition of 0.1 mM isopropyl-b-D-thiogalactoside and a post induction time of 5 h [130]. The characterization of this recombinant protein can be done via sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) combined with western blot analysis.

Plants have about 38 putative aquaporin genes. Examples of aquaporins found in the plasma and vacuolar membranes of plants include plasma membrane intrinsic protein, tonoplast intrinsic protein, small basic intrinsic protein, X intrinsic protein, and nodulin-26 like intrinsic protein. These aquaporins have been extensively studied and detailed information about them can be found elsewhere [131–135].

## *2.4 Fabrication approaches for biomimetic membranes*

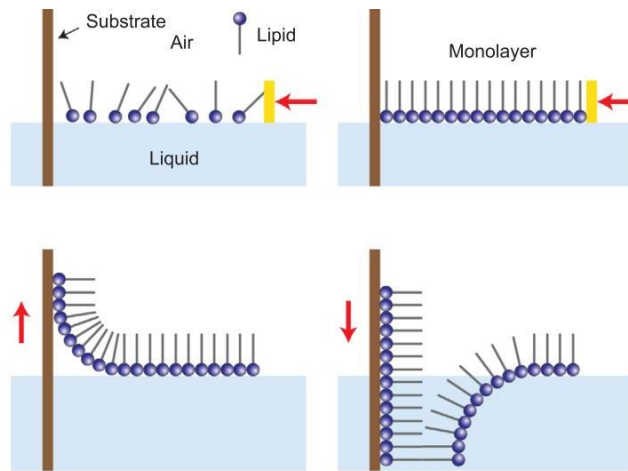
The major component of the biomimetic membranes are: (1) Aquaporins; (2) amphiphilic polymers called block copolymers or lipids that incorporate these proteins; and (3) porous support for membrane stability. Aquaporin arrays in biomimetic membranes have the potential to provide a water flux of around 16000 LMH but this does not seem achievable during large scale operations [136]. However, as suggested by Kumar et al., an aquaporin membrane configuration should be able to show a flux of 11,000 LMH if it is scaled up [42]. The fabrication procedure of biomimetic membranes can be broadly assigned into two categories in accordance with membrane structure: 1) membranes with planar biomimetic structures and 2) membranes with vesicular biomimetic structures.

### *2.4.1 Biomimetic membranes with planar structures*

#### *2.4.1.1 Stability problems with planar biomimetic structures*

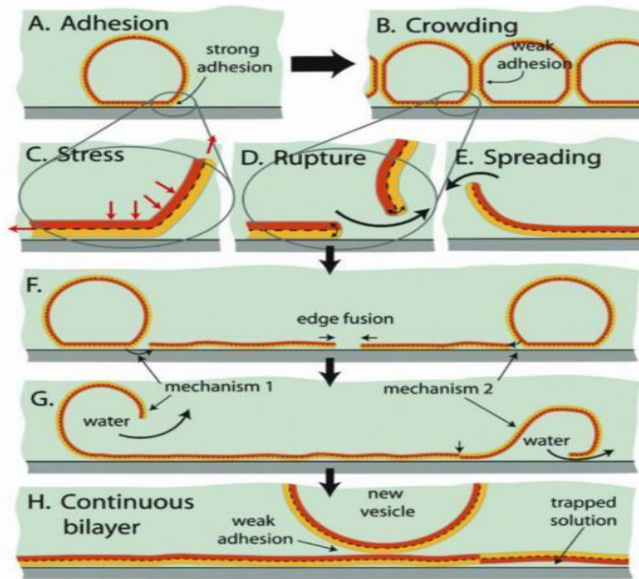
A planar structure is formed when the aquaporin-embedded lipid bilayer is deposited onto a solid porous support [137–139]. The Langmuir-Blodgett method is the oldest technique for fabrication of planar amphiphilic membrane whereby a thin film was first fashioned over an air-liquid surface and then transferred to a moving substrate [89,140,141], as shown in Fig. 11. Blodgett and Schafer used the same principle, except that the substrate deposition was prepared horizontally in their method, as opposed to vertically using the Langmuir-Blodgett method [142].

However, this method was not comprehensively studied, as the process involved excessive use of the amphiphile (detergent in this case) which disturbed the formed monolayer possibly by causing formation of defects during monolayer deposition and possible de-activation of proteins at the air-liquid interface. A high ratio of detergent to protein concentration was thought to be responsible for the defects. Later, Sun et al. utilized a modified method using a minimal detergent to protein concentration with the aid of bio-beads [143].



*Fig. 11. Schematic of Langmuir-Blodgett Method. Monolayers of lipids were systematically arranged on a vertically moving substrate over an air-liquid interface [89].*

Nonetheless, the membrane produced still contained defects, leading to other fabrication methods being favored, such as the rupture or fusion of vesicles on porous supports or through spin coating [137,138,144]. The solid supports improve the stability of the structures by ensuring that they are not hydrated from both sides, as is the case with freestanding vesicles [138]. Vogel et al. [145] and Wang et al. [146] developed freestanding lipid membranes but their studies reported no data on the permeability or selectivity of the membranes. Meanwhile, these studies also investigated the use of membrane supports as a comparative approach. The vesicular rupture method is the most widely used method for biomimetic membrane fabrication [142,147]. The process is simple and can be easily scaled up without any complicated equipment and has thus become quite popular. The process involves three stages: vesicle adsorption to a substrate; rupture of vesicles; and spreading to form a bilayer. The process involves electrostatic, steric, hydration and Van der Waals forces and double layer interactions [142,148]. The substrate and vesicles are generally of opposite charges, which result in the creation of attractive forces that enhance vesicle adhesion to the substrate. After adhesion, they form a disk-like shape and then when the vesicle concentration over substrate reaches a threshold value they rupture and self-assemble on the substrate [142]. Fig. 12 shows the pictorial presentation of the process.

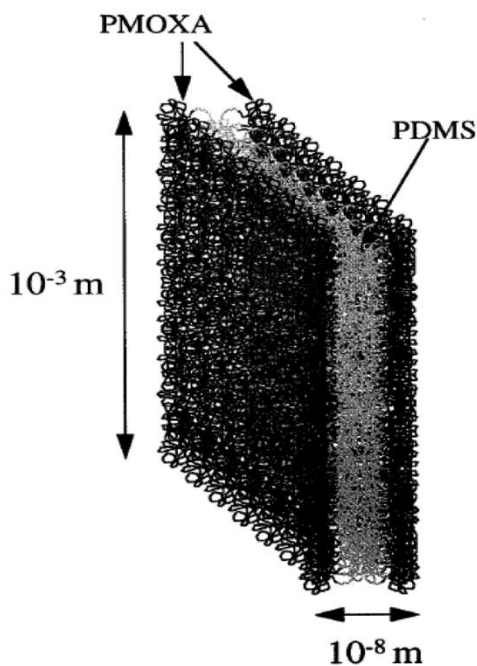


*Fig. 12. Schematic representation of vesicle rupturing and spreading [142]. A: strong vesicle adhesion to the substrate; B: Crowding of adhered vesicles on the substrate, with weak adhesion between them; C, B, D, E: bilayer rupture and spreading arising from stressed edges of crowded vesicles; F: amalgamation of edges ensured by their high energies; G: release of bound water and surplus lipid; H: the continuous lipid bilayer formed. A weak adhesion would arise from the introduction of another vesicle and rupture would not occur.*

To impart strength to the biological component, a solid support is essential, as has been successfully applied for biosensors. However, the water impermeability of many solid supports restricts their use in desalination [106,149]. To address this problem, Kaufman et al. fabricated a supported lipid bilayer over a commercial nanofiltration membrane [150]. This was the first attempt in which aquaporins were incorporated within a planar membrane and the membrane was able to withstand a pressure of around 10 bar. The water permeability for this membrane was too low but it opened the door for planar biomimetic membrane in desalination. It was also observed that appropriate selection of membrane support, deposition method and lipid characteristics would help to obtain a biomimetic membrane with better performance.

Early supported lipid planar membranes still showed fragility due to direct contact between the membrane proteins and supports [137]. Aluminum oxide, gold, mica and silica have been tested as supports, with gold showing the superior performance [151–155]. Almost none of these initial supported lipid planar membranes were tested for desalination and most of them were not even embedded with aquaporins because of two reasons. Firstly, the planar membranes were fragile and lacked mechanical stability, and thus aquaporin embedding and performance tests in desalination environment was challenging. Secondly, there was high probability of defect formation when aquaporins were coupled with a rough surface. Subsequently, Kaufman et al. prepared a solid supported biomimetic membrane (SBM) over silica through a thread-like micelle fusion process instead of vesicles from bolaamphiphile GLH-20 and incorporated

spinach aquaporin in it [155]. It was observed that SBM can incorporate aquaporin which can be deposited on different surfaces, not including from lipid vesicles, depending on the specific requirements. However, although membrane stability was improved, no desalination experiment was performed using this strategy to investigate the actual potential. Currently, amphiphilic block copolymers are being tested instead of lipids in order to improve membrane stability [138]. These block copolymers are large enough to prevent direct contact between the aquaporin proteins and solid supports, therefore they can be altered in order to control membrane permeability, thickness, and stability [156,157]. In this regard, vesicles of poly(2-methyloxazoline)-block-poly(dimethylsiloxane)-block-poly(2-methyloxazoline) i.e. PMOXA-PDMS-PMOXA block copolymers have been mostly studied because they have been found to be compatible with many aquaporin proteins [137]. A planar biomimetic structure fabricated from PMOXA-PDMS-PMOXA block copolymers is shown in Fig. 13.



*Fig. 13. Planar biomimetic structure made from PMOXA-PDMS-PMOXA block copolymers [139]. 10 nm-thick PDMS is overlaid on both sides of the 1 mm-long structure by PMOXA.*

#### *2.4.1.2 Recent advances towards improving the stability of planar membrane structures*

The recent advances aimed at improving the stability of planar membrane structures include: the incorporation of a cushion, the use of pore spanning technique, and the use of polymeric support with higher dissociation constant of surface charged groups [74,75,140,146,148,158]. The incorporation of a cushion can help to maintain the structural properties of protein and generate a high-performance separation improving the mechanical strength or performance of the substrate



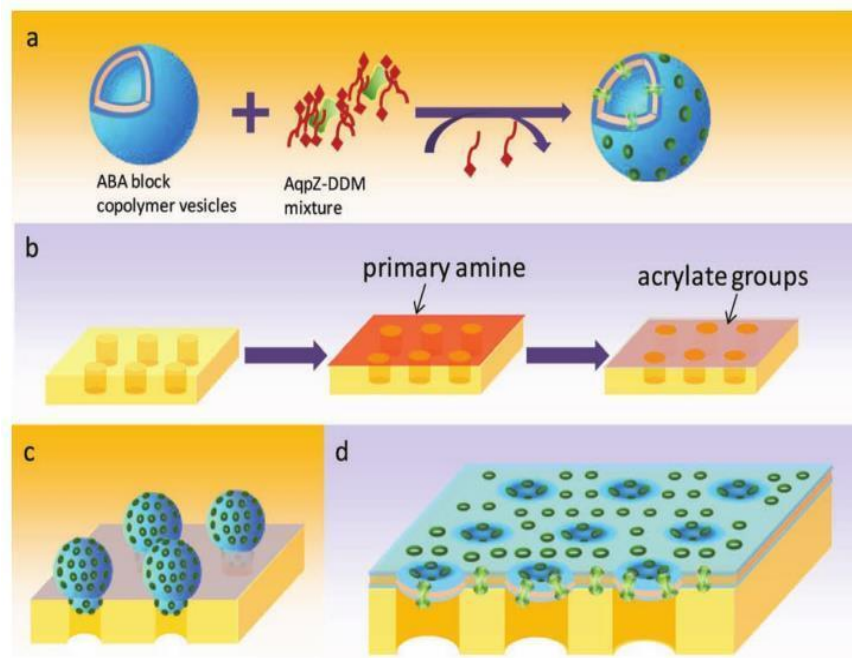
of the biomimetic membrane [80]. A carboxylated polyethylene glycol polymer is one cushion that has been shown to improve membrane flexibility when used over a porous alumina substrate, as demonstrated by Wang et al [146]. AqpZ was embedded in 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) using a lipid to protein molar ratio of 2000:1 and the aquaporin-embedded bilayer was ruptured on the cushioned support in such a way that the pores of the proteoliposomes (with an average size of 109.8 nm) were suspended on porous alumina (with pore sizes less than 100 nm). The biomimetic membrane produced from the cushioned support exhibited more flexibility and mechanical stability than that produced from the pristine substrate.

A new design was proposed by Wang et al. to form a planar pore-spanning membrane [75]. A pore-spanning membrane is a membrane in which the pores of the support are seamlessly covered by the proteoliposomes. Proteoliposomes are liposomes (lipid vesicles) into which proteins have been inserted. Liposomes have been produced in the lab from materials including DMPC, 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 2-dimyristoyl-sn-glycero-3-phosphate (DMPA), and 1,2-dimyristoyl-3-trimethylammonium-propane (DMTAP) [73,148]. Zhao et al. studied the effect of lipid type and protein-lipid ratio (PLR) on the water permeability and salt rejection of AqpZ-embedded liposomes and concluded that DOPC-based proteoliposomes are the most effective in terms of NaCl rejection and water permeability [159]. However, not all known lipids were tested; the duration of investigation of this comparative study cannot be verified; and it was not stated whether the reported results are the stable values.

A common method for producing liposomes is the film rehydration method, while proteoliposomes have been produced using the dialysis method, size exclusion chromatography or mixing in organic phase [159–161]. Proteoliposomes are referred to as proteopolymersomes when triblock copolymers are used in lieu of liposomes as the vesicle. In the improved work of Wang et al. [75], AqpZ were first embedded in PEOXA-PDMS-PEOXA proteopolymersomes end functionalized with acrylate triblock copolymers i.e. PMOXA<sub>12</sub>-PDMS<sub>54</sub>-PMOXA<sub>12</sub>. The aquaporin-embedded proteopolymersomes were placed over a polycarbonate tracked-etched (PCTE) substrate coated with a layer of gold (Fig. 14a and 14b). Pressure assisted adhesion of the proteopolymersomes on the cushioned support was carried out. A minimum pressure of 84 mbar was required to ensure that a cushioned support with a pore size of 100 nm was seamlessly covered by the proteopolymersomes. The vesicles were then ruptured by smooth extrusion over the substrate (Fig. 14c). The proteopolymersomes were thereafter immobilized through UV polymerization and covalent bonds were formed between the methacrylate head groups of the triblock copolymer and acrylate residues on the porous PCTE support (Fig. 14d). The biomimetic membrane produced showed good performance in a FO investigation with salt flux below  $1 \times 10^{-2} \text{ kg/m}^2\text{h}$  - much lower than that obtained from an efficient polymeric membrane. The inspiration for this concept of proteoliposome vesicles was obtained from a patent registered by Montemagno et al. [162]. This approach of using cushioned substrates was also adopted by Zhong et al. who used cellulose acetate as substrate and functionalized it with methacrylate end groups to make it porous. The surface modification of the cellulose acetate was carried out by functionalizing or silanizing the polymer substrate with 3-(trimethoxysilyl)propyl methacrylate and ethanol. Methacrylate end functionalized poly(2-methyloxazoline-b-dimethylsiloxane-b-2-methyloxazoline), i.e. PMOXA<sub>1000</sub>-b-PDMS<sub>4000</sub>-PMOXA<sub>1000</sub> (ABA), was used to form the triblock copolymer vesicles. AqpZ was embedded in the vesicles using AqpZ:ABA ratios of 1:200 and 1:50 and the proteopolymersomes obtained were tested for nanofiltration.



Nanofiltration membranes prepared from AqpZ:ABA at a ratio of 1:50 showed a remarkable flux of 34 LMH, although further improvements were recommended.



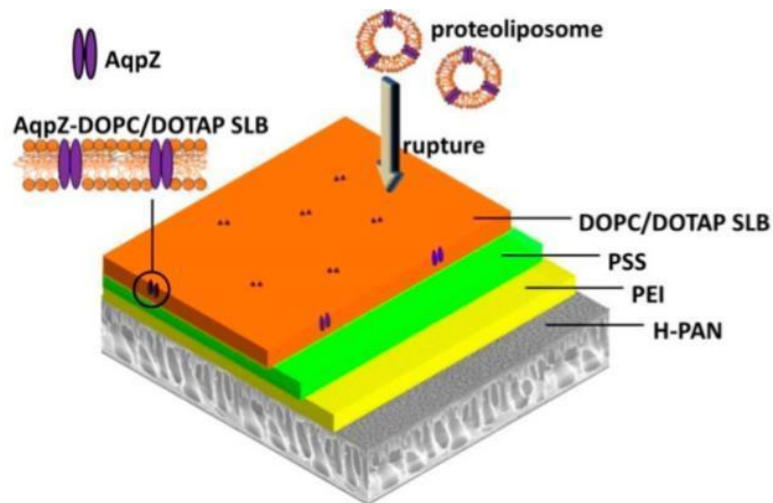
*Fig. 14. Fabrication techniques for pore-spanning planar biomimetic membrane [75]. The aquaporin-embedded proteopolymersomes were placed over a polycarbonate tracked-etched (PCTE) substrate coated with layer of gold (Fig. 14a and 14b). Pressure assisted adhesion of the proteopolymersomes on the cushioned support was carried out. A minimum pressure of 84 mbar was required to ensure that a cushioned support with a pore size of 100 nm was seamlessly covered by the proteopolymersomes. The vesicles were then ruptured by smooth extrusion over the substrate (Fig. 14c). The proteopolymersomes were thereafter immobilized through UV polymerization and covalent bonds were formed between the methacrylate head groups of the triblock copolymer and acrylate residues on the porous PCTE support (Fig. 14d).*

To produce good planar biomimetic membranes, Kaufman et al. [148] proposed to form a dense layer over permeable non-porous polymeric NF membranes. The motive behind using polymer-based NF membranes as the substrates was to impart mechanical strength to the biomimetic membranes and to reduce the chance of lipid leakage under pressure-driven flow. Two negatively charged NF membranes namely NF-270 (polyamide layer with carboxylic surface charges) and NTR-7450 (sulfonated polyethersulfone with sulfonic charges) were used. GLH-20 bolaamphiphile was used as the lipid as it has two hydrophilic (amine) headgroups that can be covalently linked to membrane supports [163], thereby improving their mechanical adhesion to the membranes [148]. The adhesion of the lipid to NTR-7450 was greater in comparison to NF-7450 possibly as a result of the dissociation of the strong sulfonic acid group. Therefore the lipid

coverage on the sulfonated support was higher because the double layer interactions which influenced the adhesion were improved. AqpZ aquaporins were embedded in the lipid. Spinach aquaporin (PM-28) was also used which gave an improved water flux. However, this study was only focused on improving the flux and stability of the biomimetic membranes and no significant contribution was made towards the production of membranes with high selectivity.

All techniques discussed above regarding the fabrication of SLB biomimetic membranes involve the use of chemical forces. Another approach was presented by Sun et al. [164] in which he suggested the use of electrostatic forces instead of chemical forces to form a lipid bilayer. Utilization of electrostatic forces has already been employed in various fields to incorporate protein, DNA, enzymes, nanoparticles, liposome etc. on a surface [165,166]. The rationale behind the electrostatic layer-by-layer (LBL) fabrication approach is to provide stability and mechanical strength to a SLB [167]. LBL film is formed by alternatively depositing polycations and polyanions onto a charged substrate. The general scheme of the method investigated by Sun et al. [164] was to deposit positively charged proteoliposomes (coated with poly-L-lysine PLL) onto a negatively charged membrane of polyelectrolyte through electrostatic force. The poly-lysine is a gentle polyelectrolyte and proteoliposomes are encapsulated into it to induce mechanical and chemical stability [164]. AqpZ-incorporated proteoliposomes were stabilized with PLL and then deposited on a bilayer of polycation and polyanion. The polycation layer contained PAH. A mix of polyacrylic acid PAA and polystyrene sulfonate PSS was used to form a polyanion layer. ABM was then fabricated by encapsulating the proteoliposome on the LBL matrix. The greatest advantage of this approach is that membrane properties can be controlled as required by varying the amount and type of polyelectrolyte and lipid. The aquaporin biomimetic membrane (ABM) demonstrated a water permeability of 6 LMH and salt rejection of 95%.

In order to improve the efficiency of biomimetic membranes produced using the electrostatic fabrication method, magnetic forces can be employed to enhance the amount of Aqpz-embedded liposomes on the substrate. The whole electrostatic fabrication method is the same except for application of magnetic forces at the bottom of the membrane [168]. The function of the magnetic forces is to increase the quantity of vesicles deposited on the surface because leading to an improvement in membrane permeability [140,168–170]. However, high salt flux through the membrane might occur, predicted from the presence of defects around the membrane [168]. Following the same approach, Wang et al. [167] fabricated a biomimetic membrane using the LBL method and tested its performance in a nanofiltration setup at a pressure of 4 bar for 36 hours. As can be seen in Fig. 15, a positive layer of polyethyleneimine (PEI) was deposited on a porous substrate of hydrolyzed polyacrylonitrile (H-PAN), followed by a negative layer of PSS. Thereafter, vesicle rupture method was used to immobilize positively charged DOPC/1,2-dioleoyl-3-trimethylammoniumpropane (DOPC/DOTAP) proteoliposomes on the anionic layer. From the experiments, a linear relationship between flux and applied pressure was observed, with no considerable effect on salt rejection. Thus, the attractive force of interaction between the cationic lipid mixture bilayer and anionic LbL polyelectrolyte has been able to and can be further modified to improve stability of the membrane's active layer.



*Fig. 15. Layer-by-layer aquaporin biomimetic membrane fabrication. PEI was deposited on H-PAN substrate as a polycation layer [167]. PSS was formed as the polyanion layer to complete the LbL membrane. Then, the deposition of positively-charged AqpZ-embedded DOPC/DOTAP proteoliposome on the membrane was carried out through vesicle rupture.*

A similar strategy was carried out by Wang et al. [169] with minor modifications. A double-skinned ABM membrane was fabricated and its performance was evaluated using a FO process. Electrostatic LBL method was used to form polycation and polyanion layers. The vesicle rupture method was used to deposit and mix DOPC/DOTAP proteoliposomes on the top surface to form SLB. The results of the FO test were compared with those of a single-skinned membrane. The single-skinned FO membrane had better water permeability in comparison to the double-skinned membrane. However, the salt permeability of the double-skinned membrane was also lower compared to that of the single-skinned membrane. The second advantage of the double-skinned membrane is that it was less susceptible to fouling.

Ding et al. [171] proposed further modifications to the above method. ABM was fabricated by forming an amide bond between the substrate and lipid bilayer. A polydopamine (PDA) layer was first deposited on polysulfone (PSF) support, then an amidation reaction was carried out in the presence of a catalyst between PDA and amino groups of AqpZ-embedded 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) bilayer. A water flux of 19.2 LMH was achieved when the fabricated membrane was used in the FO process. When positively charged DOTAP was blended with the DOPE bilayer, a lower reverse salt flux and at the same time, a higher flux of 23.1 LMH was reached.

Lipid mobility is an important performance parameter for aquaporin-based membranes [148,150,172]. Monoolein, a relatively simple lipid molecule, has also been suggested to be a viable polymorph for the fabrication of biomimetic membranes because of its ability to maintain its stability and self-assemble into various crystalline structures under different temperature and solvent compositions [173]. The incorporation of monoolein into proteoliposomes in SLBs might

improve mobility and reduce inactivity of proteins [174]. Wang et al. [174] reported that lipid mobility in AQP1-embedded SLB can be successfully tuned through the addition of monoolein. The nanofiltration performance of AQP1-embedded membranes was studied by using 2,000 ppm NaCl as the feed solution in a nanofiltration setup at an applied pressure of 4 bar. Monoolein is a non-toxic and biocompatible monoglyceride which, when added to a lipid bilayer, can improve molecular mobility in a bilayer because it can provide additional free volume through its *cis*-double bond [174,175]. Meanwhile, to evaluate the real impact of monoolein integration with lipid bilayers on membrane water permeability and salt rejection, further investigations at higher applied pressures are required.

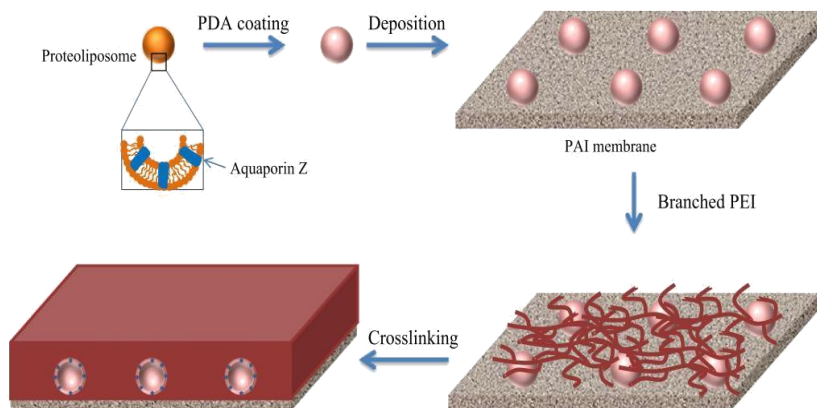
#### *2.4.2 Biomimetic membranes with vesicular structures*

Recently, immobilization of aquaporin-containing vesicles in a dense polymer layer has been investigated in order to preserve the original properties of the vesicles and to maintain their integrity [167]. UV polymerization, polymer cross-linking and interfacial polymerization, and the surface imprinting method are mostly used in this approach to produce defect-free structures [73,159,164,167,168,172,176–180]. In this approach, aquaporin-incorporated vesicles can also be sealed by a polymeric layer that protects the fragile biological structure and protects it from environmental degradation. Zhao et al. [73] used this approach to produce a biomimetic membrane by soaking a microporous polysulfone substrate in an aqueous mixture of *m*-phenylene-diamine (MPD) and AqpZ-based DOPC proteoliposomes. This substrate was then exposed to trimesoylchloride (TMC) so that a cross-linked polyamide layer which has already been embedded with the proteoliposomes can be formed. This aquaporin-embedded thin film composite membrane produced by interfacial polymerization was used for cross-flow RO desalination of feed solution containing 10 mM NaCl. This membrane was able to withstand a pressure of up to 10 bar. Performance results from the fabricated membrane were compared with those from commercially available RO membranes for brackish water BW30 and sea water SW30HR and it was concluded that biomimetic membrane was almost 40% more superior in comparison to BW30 and slightly better than SW30HR. The membrane was able to achieve a very high water permeability of 4 LMH/bar and comparable NaCl rejection of 97% at an applied pressure of 5 bar.

Zhao et al. [159] has also suggested that an additional polymeric layer can be used to protect aquaporin-embedded lipid bilayers. The reduction of pore defects in a biomimetic membrane prepared through the incorporation of cholesterol in DOPC bilayer was presented in this work. In this case, the advantages and drawbacks of both the proteoliposomes and their polymeric ‘protector’ would be shared i.e. the water permeability of the ‘protector’ might be less than that of the proteoliposomes while the reverse might be the case for their salt rejection capabilities. The addition of cholesterol to lipids has also been shown to seal defects and improve water permeability [159,181]. A ring-ring stacking might be formed between the rings of cholesterol and the aromatic residues on the surface of protein, thereby improving the stability of aquaporins in biomimetic membranes [182]. The sealing effect of cholesterol in a lipid bilayer was also suggested by other researchers, as cholesterol is an anti-pore former and can regulate the bilayer properties through bilayer bending [183,184]. However, more research is needed in fabricating biomimetic membranes integrated with cholesterol, as no recent work has been carried in this regard for real-life desalination. In general, the incorporation of proteoliposomes in a dense polymer matrix can protect the active sites of a biomimetic membrane by isolating them from the

external environment: however, the selection of matrix is critical to have efficient performance [73,185].

As aforementioned, the concept of interfacial polymerization has been shown to produce defect-free and reproducible large-scale biomimetic membranes. However, the excessive amount of chemical usage and gas sweeping in this process can reduce aquaporin activity [172]. To solve this problem, cross-linking via other polymers, apart from the well-known cross-linking for thin film polyamide fabrication, is a viable approach. PDA has been tested for this purpose. The rationale behind using PDA is to improve the affinity of proteoliposomes to the substrate as it is a polymer that is biologically compatible and can cling to liposomes through covalent and non-covalent bonding [186]. Li et al. [172] used polymer crosslinking in order to overcome the shortcomings of interfacial polymerization, by minimizing chemical usage and retaining activity of special protein pallets. Proteoliposomes encapsulated in a polyelectrolyte were first decorated with PDA and then incorporated onto a porous substrate of PAI through polyelectrolyte crosslinking. The polyelectrolyte used was polyethylenimine (PEI) because PEI can form an efficient selective layer with minimum defects and can withstand high temperature [179,187,188]. Fig. 16 clearly illustrates this membrane fabrication mechanism.



*Fig. 16 Incorporation of PDA-coated proteoliposomes on PAI porous substrate via crosslinking with branched PEI [172].*

Wang et al. [180] also prepared AqpZ-embedded polymersomes which were cross-linked with disulfide anchors to prevent the leaching of the proteopolymersomes during desalination. The polymersomes are ABA triblock copolymer vesicles prepared by blending PMOXA<sub>1000</sub>-PDMS<sub>4000</sub>-PMOXA<sub>1000</sub> containing acrylate ends with PMOXA<sub>1600</sub>-PDMS<sub>5500</sub>-PMOXA<sub>1600</sub> containing disulfide ends. The proteopolymersomes were then immobilized on a gold-coated polycarbonate track-etched support membrane through covalent bonding i.e. through vesicle extrusion at a critical pressure of 900 – 925 mbar to ensure disulfide-gold conjugation and good vesicle coverage. The structure was then stabilized by the PDA coating layer. The role of the PDA layer was to seal the defects between the pore wall and surface of the vesicles since PDA is a bio-compatible glue [180,189]. The membrane was tested at different FO conditions, and it showed high mechanical robustness with a sufficiently high flux of 17.6 LMH and salt rejection

of 91.8% when 6,000 ppm NaCl was used as feed and 0.8 M sucrose was used as the draw solute. However, further investigations of this fabrication method were suggested so that the long-term performance of the membrane in real-life desalination can be evaluated.

This method clearly gave a membrane with better performance compared with previous pore-spanning membrane fabrication techniques and it was observed that vesicle characteristics, coverage, and mechanical supports are the important parameters to be studied in order to make high-performance biomimetic membranes. Wang and co-authors [190] later carried out mathematical modelling of the water transport mechanism through this membrane in order to study the effect of vesicles on membrane performance. It was concluded that the size, permeability and geometry of vesicles and the concentration of feed solution (and draw solution in FO) play an important role on the performance and stability of the biomimetic membrane [190].

The positive aspect of the polymer crosslinking approach is that it can be optimized easily by varying operating conditions such as temperature and type of polyelectrolyte [179]. Sun et al. used methacrylate monomers to crosslink [176]. Firstly, porous polyacrylonitrile (PAN) substrate was coated with PDA. Amine-functionalized AqpZ proteoliposomes were then prepared and stabilized through UV polymerization. The UV illumination prevented the rupture of vesicles to planar structures. Without UV polymerization, the vesicles would not be able to tolerate hydraulic stresses and thus would only prevent 10% of salt leakage. With the aid of pressure, the vesicles were then adsorbed over the coated substrate. The membrane was further cross-linked with glutaraldehyde (GA) to improve vesicle stabilization and prevent external interferences. The interesting point here is that although GA would stabilize the membrane, cross-linking may denature the protein by, if care is not taken. Therefore, research efforts should be directed towards alternatives to GA so as to decrease the probability of protein malfunction. The fabricated biomimetic membrane with AqpZ-to-lipid weight ratio of 1:100 increased the water flux by 65% and improved NaCl and MgCl<sub>2</sub> rejections to 66.2% and 88.1%, respectively, when compared with the membrane without AqpZ.

Another method that has been used to produce relatively stable biomimetic membranes is surface imprinting technology [90,172,177,191,192]. Xie et al. [177] has used this method to overcome membrane fragility by ‘imprinting’ protein vesicles on a porous substrate [177]. This surface imprinting technology is not a new method, but has been applied in many fields such as catalysis, bio-sensing, drug delivery etc. because it is able to produce chemically, thermally and physically strong imprinted polymers [193–195]. The surface imprinting technique involves the coating of a dense layer of immobilized proteoliposomes on a porous substrate [172,177]. AqpZ vesicles were immobilized on a porous substrate by Xie et al. [177] via covalent bonding and surface imprinting polymerization was performed to form a dense protective layer. The top layer restricted the flow of solute, permitted the transport of water only and provided stable to fragile AqpZ that was able to withstand mechanical and shear stresses during filtration.

Recently, Li et al. [178] gave a unique modification to the concept of surface imprinting by employing a polyethersulfone hollow fiber substrate for the preparation of an ABM. Aquaporin-embedded proteoliposomes were immobilized on the hollow-fiber substrate by soaking and flushing the membrane with MPD solution containing the proteoliposomes. The modified hollow fiber membrane was then soaked in trimethylsilyl (TMS) group in order to encapsulate a proteoliposome-embedded polyamide layer through non-gas assisted interfacial polymerization.

The rationale behind employing a hollow fiber substrate is to avoid a gas sweeping process, thermal-driven process for layer deposition and to minimize chemical consumption, which are the inherent advantages of the non-gas assisted polymerization [178]. In addition, proteoliposome losses and aquaporin malfunction can be circumvented by avoiding gas sweeping [172,196]. Easy scale-up for industrial operation is another crucial advantage of this method. The mechanical strength and anti-fouling stability were checked and it was found that membrane produced by this process has the potential to tolerate the harsh environment created by foulants and cleaning chemicals. Moreover, FO and RO tests have revealed that the membrane was able to show 200% higher flux performance than a commercial RO membrane (BW30) i.e. it showed a flux of 40 LMH. This membrane also showed higher salt rejection than BW30. However, it was only tested using a pressure of 5 bar and more work needs to be carried out to investigate the performance of the membrane at higher operating pressures.

### **3 Results from desalination studies using biomimetic membranes**

Different biomimetic membrane strategies have been evaluated by different groups of researchers to fulfill the current membrane requirement of the industry. The ideal aquaporin biomimetic membrane should allow good water permeability with maximum rejection of solute. It should be mechanically stable to withstand the harsh environmental conditions of desalination processes and be easy to scale-up. The techniques tested so far are somewhat able to generate good performance membranes, but long-term stability is required for practical applications.

#### *3.1 Reported results from desalination studies on RO/NF processes*

At present, about half of the world's desalination capacity is dependent on RO [34]. This technology is present in water stressed regions due to its simplicity and energy efficiency in comparison with thermal desalination. The technological improvements of RO processes are continuous, with much research aimed at minimizing due largely to high pressure requirements, membrane fouling and scaling issues [11,197]. Aquaporin-based membranes are more permeable than commercial RO membranes by two orders of magnitude [174]. Thus, the implementation of biomimetic membranes in the RO process could help to attain good water flux using low pressure and thus save hundreds of millions of dollars by reducing annual electrical energy expenses. On the other hand, NF has been employed for a good number of pre- and post-treatment operations in desalination [11,198]. Table 2 shows the recent developments in RO/NF technology using biomimetic membranes for desalination. The water permeability and salt rejection of biomimetic membranes reported so far for RO desalination are also summarized in Table 2.

Table 2. Performance results reported in RO and NF desalination studies.

Biomimetic membrane fabrication strategy	Water permeability	Salt rejection	Remarks	Pressure	Reference
Rupture of triblock copolymer (ABA) vesicles and UV polymerization of substrate of cellulose acetate (NF)	34.19 LMH/bar	32.86% NaCl	Mechanically stable; comparable performance to qualified nanofiltration membrane	5 bar	[74]
Vesicles incorporated in polymerized PA layer	2 LMH/ bar	94% NaCl rejection	High chances of scale formation	50 bar	[41]
Amine functionalized proteoliposomes vesicles deposited on the PDA layer	3.8 LMH/bar	66.2% NaCl, 88.1% MgCl <sub>2</sub>	Chances of protein de-activity because of the use of GA	5 bar	[176]
AqpZ-implanted liposomes on a PDA coated microporous membrane (NF)	8.5 LMH (using NaCl solution) and 8 LMH (using MgCl <sub>2</sub> solution)	66.2% NaCl and 88.1% MgCl <sub>2</sub>	Properties of membrane can be controlled according to requirement	5 bar	[164]
Aquaporin-embedded through pressure assisted sorption on gold-coated polycarbonate substrates	4.3 LMH/bar	65.8% NaCl	Better performance than other pore spanning membranes.	1 bar	[190]
Electrostatic layer by layer assembly, with AqpZ-embedded DOPC/DOTAP	22 LMH	97% MgCl <sub>2</sub> and 75% NaCl	Excellent separation under high pressure environment	4 bar for at least 36 h	[167]
AqpZ/ABA on gold coated porous alumina membrane (NF)	16.1 LMH/bar	45.1% NaCl	Good performance but some defects were found	5 bar	[137]



Polymer crosslinking using polyamide as substrate	36.6 LMH	95% MgCl <sub>2</sub>	Easily scalable; less fouling; ability to tolerate high temperature of 343 K for 2 hours	1 bar	[172]
Thin film composite aquaporin biomimetic membrane by interfacial polymerization	4 LMH	90%	Able to withstand pressure till 10 bar; higher permeability than seawater SW30 and brackish water BW30 membrane	5 bar	[73]
AqpZ embedded membrane on cellulose acetate using surface imprinting technology	22.9 LMH/bar	61% NaCl, 75% MgCl <sub>2</sub>	High strength membrane; presence of defects in membrane decreases salt rejection	5 bar in two stages	[177]
Hollow fiber composite ABM	40 LMH	97.5% NaCl	Unique design; robust and easily scalable; might be applied in PRO and NF modes; good for FO and RO processes	5 bar	[178]
LBL adsorption ABM	6 LMH/bar	95% MgCl <sub>2</sub> (not tested for NaCl)	Easy to scale up	4 bar	[164]
Membrane using gramicidin	8.31 LMH	97% NaCl			[100]
SLB membrane on NF membrane using vesicle fusion and Spin coating vesicle fusion with the aid of pressure	3.6 LMH/bar	20% NaCl rejection	Presence of large number of defects; pressure required to deposit vesicles over commercial NF membrane	1 bar	[199]

### 3.2 Reported results from desalination studies on FO process

FO has gained researchers' attention recently because of its energy efficient behavior (when the energy required for the draw solution regeneration step is regulated) and scientists' work to develop high performance membranes suitable for the process [75,168,169,180,200–204].

Moreover, appropriate draw solution and fouling behavior of membranes are also areas of interest [200,205]. FO has two solutions that play crucial roles: one is the feed solution and the other is the draw solution, which is an osmotic agent that draws fresh water from the feed solution through a semi-permeable membrane. The advantage of the FO process, compared with RO, is that hydraulic pressure is not the driving force but an osmotic pressure gradient across the membrane resulting from the chemical potentials of the feed and draw solutions. The performances of various FO desalination studies involving the use of aquaporin biomimetic membranes are summarized in Table 3.

Table 3. Performance results reported in FO desalination studies.

Membrane fabrication method	Water flux	Salt rejection	Draw solution	Remarks	Reference
Magnetic aided ABM	21.8 LMH	Selectivity of 47,987	0.3M sucrose as DS; 200 ppm MgCl <sub>2</sub> as FS	Presence of minor defects; stable membrane; salt flux of 2.4 GMH of MgCl <sub>2</sub>	[168]
Magnetic aided ABM	83.5 LMH	< 47,987	Ultra-pure water as feed; 1.5 M MgCl <sub>2</sub> as DS	Vesicle embedment was enhanced; salt flux of ~30 GMH of MgCl <sub>2</sub>	[168]
Pressure aided vesicular adsorption on gold-coated PCTE support with AqpZ-ABA block copolymer	17.6 LMH	91.8% using 6,000 ppm NaCl	0.8 M sucrose as DS; 6000 ppm NaCl FS	Improved results than commercially available HTI membranes	[180]
Pressure-assisted vesicle adsorption of AqpZ into amphiphilic matrix with AQPZ:ABA of 1:100	16.4 LMH	98.8% NaCl	0.3 M sucrose DS; 200 ppm NaCl FS	Able to retain Aquaporin Z functionality	[75]
AqpZ-incorporated membrane on cellulose acetate using surface imprinting technology	5.58 LMH	50% NaCl rejection	0.3 M sucrose DS; 200 ppm NaCl FS	Low salt rejection because of defects	[177]
AqpZ-double skinned membrane formed from electrostatic LbL method	13.2 LMH	Salt flux of 3.2 GMH	2M MgCl <sub>2</sub> DS; DI water as FS	Better salt rejection and less fouling but lower water permeability than single-skinned membranes	[169]

Aquaporin-incorporated LbL membrane with covalent bond between lipid bilayer and microporous support	23.1 LMH	Salt flux of 3.1 GMH; 90% salt rejection	MgCl <sub>2</sub> DS	Large membrane area of about 36 cm <sup>2</sup>	[171]
Aquaporin-based hollow fiber composite via interfacial polymerization	55.2 LMH	Salt flux of 4.5 LMH	0.5 M NaCl	Higher water flux than bare FO composite membranes	[178]

<sup>1</sup>GMH means g/m<sup>2</sup>h; DS means draw solute; FS means feed solution

### 3.3 Performance results for other separation processes

Aquaporin-based biomimetic membranes possess a huge potential but to date these membranes have been mostly studied for desalinating water, although they can also be applied to other separation processes and energy generation. Other potential areas of research for these aquaporin-based biomimetic membranes include removal of trace pollutants, alcohol recovery, recrystallization, and energy production from salinity gradients.

#### 3.3.1 Trace pollutant removal

To meet the world's water demand and bridge the gap between water consumption and availability, water reuse is an important factor. The contamination of wastewater with trace pollutants is a serious challenge that needs to be tackled for optimum water usage. Membrane-based removal processes are a remedy that can be adopted to decrease the concentration of these pollutants to acceptable limits. Conventional RO and FO membrane technologies have been tested for removal of trace contaminants from wastewater [206–211]. The concentrations of these trace components are usually very low and removal of such low-concentration organics require high pressure when using the RO process which makes it uneconomic to operate in many places. As compared to RO, the rejection of small neutral organics by the FO process is found to be low [212]. Biomimetic membranes offer a less expensive choice for the removal of trace organic contaminants because they can ensure higher levels of fresh water permeability and permit low pressure usage. Thus, a unique biomimetic removal mechanism can help to remove even small concentrations of organics efficiently. Recently, Madsen et al. [213] studied biomimetic membrane performance in a FO test for the removal of trace organics such as atrazine, 2,6-dichlorobenzamide and desethyl-desisopropyl-atrazine found in ground water, achieving 97% rejection of all trace organics with higher water permeability than that provided by a standard cellulose acetate FO membrane. FO has gained huge attention by researchers for the removal of these neutral organic pollutants, but this is the first reported use of biomimetic membrane in this regard. This research opened the door for biomimetic membranes in the area of rejection of trace organic contaminants, thereby providing another huge opportunity for biomimetic membranes.

Another interesting application of biomimetic membranes is in the removal of boron from seawater. According to the World Health Organization, the boron concentration in potable water should be less than 0.5 mg/L, which is difficult to achieve by current RO approaches [214].

Boron exists mostly as boric acid in water. Conventional RO technology is not able to achieve more than 50% boron rejection; thus, there is a need to improve this technology so that boron content of RO permeates can meet the regulatory standard [215–217]. Biomimetics can play an important role in the improvement of this technology because bioinspired membranes have the potential to reject everything except water at a high water permeability rate. Recently, a patent has been published in this regard, which claimed that 60 - 85% removal of boron is possible via FO and  $50\% \pm 8\%$  via RO with the aid of biomimetic membranes [218]. In both FO and RO tests, a feed solution comprising of 5 mg/mL of boron in the form of boric acid in tap water was used. This patent is also applicable for the removal of other trace components in water, especially for the removal of dilute nutrients and arsenic present in agricultural and drinking water.

### *3.3.2 Alcohol recovery*

Massive generation of biomass from different sources for the production of biofuels and biochemicals through fermentation reactions has spurred great research interest [219,220]. These fermentation reactions are product-inhibitory and thus continuous removal of the product(s) is required so that the reactions can proceed effectively. Moreover, excessive amounts of water in a stream make the recovery process difficult and costly. Pervaporation, which is the partial vaporization of liquid streams through a semi-permeable membrane, is an attractive technique for the removal of these products as it is less energy intensive, simple, easy to be integrate with a biochemical reactor and gives no harm to the fermentation environment [221]. Biomimetic membranes can also become effective candidates for the recovery of these valuable chemicals and can be employed in pervaporation. Ethanol recovery through pervaporation using membranes made from di- and tri- block copolymers has been investigated by various researchers and the potential of biomimetic membranes in this area has justified its potential [222,223]. Thus, the use of aquaporin biomimetic membranes is crucial in this area because more positive results will not only strengthen the concept of biomimicry but also result in the widespread use of biomimetic membranes in the sustainable biorefinery industry.

### *3.3.3 Crystallization*

Crystallization is an important separation method widely employed in the chemical and pharmaceutical industries. Conventional crystallization methods such as evaporation, seeding, solvent extraction etc. are not able to produce high quality (pure) crystals. Moreover, they are not even reproducible because of the non-controlled supersaturation of solution [224]. Membrane-assisted crystallization has been introduced to create reproducible crystals with appropriate sizes and shapes in an energy efficient way without compromising quality [225,226]. The second advantage of membrane crystallization is that renewable energy sources can be used to supply energy to the process and this can contribute to sustainable development [227]. Biomimetic FO membranes have been tested for the crystallization of  $\text{Na}_2\text{CO}_3$  from aqueous solution of NaOH in the scenario of carbon capture from flue gases [227]. The advantage of using this biomimetic membrane was the production of high purity crystals, with minimum energy consumption and minimum blockage. Crystals of a purity of 99.94% were obtained and the water permeability of the FO process was 46 LMH. Thus, crystallization via biomimetic membrane separation is a reasonable alternative to conventional crystallization techniques. There are also other alternatives available for carbon capture, such as amine-based adsorbents, but they are associated with high

regeneration energy [228,229]. Biomimetic membranes can help to reduce the overall energy consumption of a carbon capture system [230].

### *3.3.4 Energy production from salinity gradient power*

Salinity gradient can be used to generate electrical energy due to the difference in salinity in a process called Pressure Retarded Osmosis (PRO). In this process, feed water permeates to a pressurized high-salinity draw solution from a low salinity feed solution with the aid of its osmotic pressure and power is produced by depressurizing the water through a hydro-turbine. The global power production of this technology is around 2,000 TWh/yr [231]. A patent which shows the potential of biomimetic membranes for energy generation from salinity gradient power has been published [232]. Through this invention, several lipid bilayers and block copolymers can be used to enhance electric power production from PRO technology. High water permeability values of aquaporin-based membranes may lead to a high osmotic pressure driving force and this force can be used in electric power generation [232]. Salinity power is an environmentally friendly way of generating power and countries such as Japan and Canada have engaged “Aquaporin” company (which produces “Aquaporin Inside™” membranes) for the production of biomimetic membranes that can be applied for salinity power generation in their countries. However, little research has been done in the area of improved salinity power utilization via aquaporin biomimetic membranes, but current and recent work has shown the potential of these membranes for energy extraction from saline solutions.

## **4. Current challenges associated with biomimetic membranes and future perspectives**

Taking inspiration from nature to provide high water flux with the aid of natural protein pallets is a remarkable innovation in the field of water treatment. The interest in this field is growing and the promising results obtained so far shows that the practical application of biomimetic membranes for water treatment is feasible. However, this technology still faces some crucial challenges that need to be attended to in order to ensure successful widespread commercialization. The major challenges include technical difficulties encountered during the extraction of aquaporin and production of biomimetic aquaporin membranes, concerns over the durability and long-term stability of these membranes during desalination of feed containing high salinity, such as seawater, and the need for specially designed cleaning chemicals that are different from conventional anti-fouling or anti-scaling chemicals because of the delicate nature of biomimetic membranes.

The up-scaling of biomimetic aquaporin membranes for large-scale seawater desalination is a challenge since the aquaporin proteins are not commercially available in large quantities. Generally, the production of membrane proteins is a complicated task because very careful details are required. Protein generation from parent organisms is significantly dependent on intracellular movement, and transportation and modification of existing pathways which is complex to manage. If there is over-expression of protein from a living cell membrane, it may affect the basic function of the cell membrane and might prove detrimental to the parent organism [233]. Meanwhile, for the widespread commercialization of this technology, large quantities of aquaporin are required: this is not a trivial task. Ultra-centrifugation and affinity

labeling, among others, are the techniques that have been used for the purification of the proteins, but both methods are difficult to scale up [120,234,235]. Another challenge faced in the upscaling of biomimetic membranes is the nature of the host membrane. The host membrane must be hydrophobically compatible with the proteins. This puts a limitation on the thickness of the host membrane i.e. the host membrane must not exceed a thickness of only a few nanometers so that it can be compatible with an appropriate support material [236]. Keeping these limitations in focus and from the production point of view, wide-scale application of aquaporin membrane technology requires high permeability, adequate mechanical stability, high selectivity and elevated strength in order to withstand design pressure for impactful market applications. One of the recent technological advancements aimed at providing solutions to aquaporin design limitations is the use of yeast-based systems [237,238]. Substantial increase in the membrane density of Aquaporin 1 has been expressed in a yeast host [237]. These expression systems also enabled cheap production of significant quantities of the functional protein. However, the feasibility of using the synthesized aquaporin for desalination of saline water has not been investigated. Another technique might be the use of cell-free expression systems [239,240]. These systems exhibit relatively enhanced efficiency since they are designed to remove the toxic and detrimental effects of recombinant proteins on the physiology of host cells and can also cater for complications in the transportation and translocation of synthesized proteins. The major focus of research at this point should be on the identification of specific type of proteins present in biological materials that can be easily expressed in large quantities. The discovery and incorporation of new proteins in a suitable matrix would also help to improve the membrane system and achieve efficiencies close to those of real biological systems. These system modifications would also be useful for other water separation processes apart from desalination and this approach can help to further strength the biomimetic membrane platform.

The extended lifetimes of biomimetic membranes are also questionable. Biological membranes undergo incessant exchange of proteins and lipids. So, the forecasting of membrane lifespan for long-term applications is a challenge. A large amount of work has been done on biomimetic membrane fabrication, including patents and pilot or demonstration-scale investigations, but until now, no one has studied the lifetime stability of biomimetic membranes because the concept of biomimetics for commercial water production and chemical processing is fairly new. Intensive work is required in this area in order to analyze the stability of these membranes throughout the lifetime of a commercial operation. Doing this would ensure significant market switch from conventional to biomimetic membranes.

Chemical cleaning of biomimetic membranes is another major issue. Organic acids, such as EDTA and citric acid, are quite effective for the removal of metal oxides and scaling compounds from conventional membranes during membrane cleaning. However, the efficiency of cleaning is dependent on cleaning time, hydrodynamic conditions, concentration and temperature. All of these parameters and operating conditions would need to be incorporated in an extensive testing system for biomimetic membranes. Due to the amphiphilic nature of biomimetic membranes, not all commercial detergents can be used. Green chemicals and specially designed detergents, which may not be available commercially in bulk amounts, are required in order to preserve the biochemical properties of aquaporin-based membranes. The cost associated with the use of compatible anti-fouling chemicals need to be investigated and accessed in order to ensure rapid industrial scale-up of biomimetic membrane technology.

The intrusion of a new process or technology into an established market is always fraught with problems. Therefore, there is an immense need to take into account all the risks associated with it. The commercial application of biomimetic membrane technology is relatively new and is in its cradle stage. Also, since there is no five year reference commercial data (at least), the best way to minimize these risks is to carry out extensive testing. To ensure credibility of this new technology and acceptance by market operators, irrefutable and comprehensive testing systems are required, using optimized membranes. These systems should not only test the membrane stability in terms of working under different operating parameters and conditions, such as high temperature and pressure, they must also measure the membrane performance after extensive exposure to these operating conditions. More efforts should now be directed towards pilot testing and full-scale industrial plant operations by using actual process parameters and authentic real-life feed water in order to demonstrate the efficiency of the technology under real operating conditions.

When considering the introduction of a new membrane technology into an existing market and planning its upscale and widespread commercial production, the main parameter to consider is that the investment cost must satisfy the revenue and profit margin. In the commercial market of desalination, the new product must be profitably advantageous and competent enough to stand its ground as compared to the current existing technologies in the market. The fundamental key for successful commercialization is that the quality and value of the product is not compromised and is at par with the end user's expectations. Hence, there is a great potential for this new technology in the water treatment business, because it promises high productivity and high-quality product. However, the current challenges still need to be tackled. Currently, there is insufficient information regarding the unit cost of water production through biomimetic membranes and thus, convincing the market to adapt the novel technology is a challenging task. However, it is important to build credibility and integrity for great future prospects. A well sought dialogue and meeting with market operators would be significant to address any concerns raised or any reservations made regarding the deficiencies of conventional water treatment approaches so that works on biomimetic membrane technology would be directed towards filling the gaps.

Currently, biomimetic membranes are able to hold pressures of 10 bar and above with appreciable water flux. However, the technology has mostly been applied successfully for the desalination of brackish water, reuse of wastewater and tap water purification. Most applications of biomimetic membrane technology for water treatment have been carried out using FO. For seawater generally, 50 bar pressure and above are required for RO processes and no biomimetic membrane fabricated until now is able to withstand this pressure. However, the performance of biomimetic membranes for seawater separation is comparable to that of current RO membranes at the laboratory level but stability of these membranes for long-term commercial seawater desalination is still a challenge. Certainly, the replacement of conventional membranes with biomimetic membranes can help to save money as biomimetic membranes can function in low-pressure environments. Technological advancements in membrane fabrication methods to ensure that biomimetic membranes are applicable for long-term seawater desalination would help to save even larger amounts of money.

## References

- [1] WHO, UN, Progress on drinking water and sanitation. Joint monitoring programme update, 2012.
- [2] The World Bank, Data, (2015). data.worldbank.org (accessed April 20, 2017).
- [3] U.K. Kesieme, N. Milne, H. Aral, C.Y. Cheng, M. Duke, Economic analysis of desalination technologies in the context of carbon pricing, and opportunities for membrane distillation, *Desalination*. 323 (2013) 66–74. doi:10.1016/j.desal.2013.03.033.
- [4] Y. Zhou, R.S.J. Tol, Evaluating the costs of desalination and water transport, *Water Resour. Res.* 41 (2005) 1–10. doi:10.1029/2004WR003749.
- [5] A. Al-Karaghoul, L.L. Kazmerski, Energy consumption and water production cost of conventional and renewable-energy-powered desalination processes, *Renew. Sustain. Energy Rev.* 24 (2013) 343–356. doi:10.1016/j.rser.2012.12.064.
- [6] DesalData, Desalination data, (2016).
- [7] National Research Council of the National Academies, *Desalination: A National Perspective*, National Academies Press, Washington, DC, 2008. doi:10.17226/12184.
- [8] M. Busch, W.E. Mickols, Reducing energy consumption in seawater desalination, *Desalination*. 165 (2004) 299–312. doi:10.1016/j.desal.2004.06.035.
- [9] M. Elimelech, W. Phillip, The Future of Seawater Desalination: Energy, Technology, and the Environment, *Science* (80-. ). 333 (2011) 712–717. doi:10.1126/science.1200488.
- [10] N. Ghaffour, T.M. Missimer, G.L. Amy, Technical review and evaluation of the economics of water desalination: Current and future challenges for better water supply sustainability, *Desalination*. 309 (2013) 197–207. doi:10.1016/j.desal.2012.10.015.
- [11] S. Jamaly, N.N. Darwish, I. Ahmed, S.W. Hasan, A short review on reverse osmosis pretreatment technologies, *Desalination*. 354 (2014) 30–38. doi:10.1016/j.desal.2014.09.017.
- [12] R.W. Stoughton, M.H. Lietzke, Calculation of Some Thermodynamic Properties of Sea Salt Solutions at Elevated Temperatures from Data on NaCl Solutions., *J. Chem. Eng. Data*. 10 (1965) 254–260. doi:10.1021/je60026a016.
- [13] M. Amokrane, D. Sadaoui, C.P. Koutsou, A.J. Karabelas, M. Dudeck, A study of flow field and concentration polarization evolution in membrane channels with two-dimensional spacers during water desalination, *J. Memb. Sci.* 477 (2015) 139–150. doi:10.1016/j.memsci.2014.11.029.
- [14] B.J. Feinberg, G.Z. Ramon, E.M. V Hoek, Thermodynamic analysis of osmotic energy recovery at a reverse osmosis desalination plant., *Environ. Sci. Technol.* 47 (2013) 2982–9. doi:10.1021/es304224b.
- [15] T. Nguyen, F.A. Roddick, L. Fan, Biofouling of water treatment membranes: A review of



- the underlying causes, monitoring techniques and control measures, *Membranes (Basel)*. 2 (2012) 804–840. doi:10.3390/membranes2040804.
- [16] R. Holdich, S. Kosvintsev, I. Cumming, S. Zhdanov, Pore design and engineering for filters and membranes., *Philos. Trans. A. Math. Phys. Eng. Sci.* 364 (2006) 161–174. doi:10.1098/rsta.2005.1690.
- [17] R. Semiat, Energy issues in desalination processes, *Environ. Sci. Technol.* 42 (2008) 8193–8201. doi:10.1021/es801330u.
- [18] D.L. Shaffer, N.Y. Yip, J. Gilron, M. Elimelech, Seawater desalination for agriculture by integrated forward and reverse osmosis: Improved product water quality for potentially less energy, *J. Memb. Sci.* 415–416 (2012) 1–8. doi:10.1016/j.memsci.2012.05.016.
- [19] N. Afrasiabi, E. Shahbazali, RO brine treatment and disposal methods, *Desalin. Water Treat.* 35 (2011) 39–53. doi:10.5004/dwt.2011.3128.
- [20] G. Al Bazed, R.S. Ettouney, S.R. Tewfik, M.H. Sorour, M. a. El-Rifai, Salt recovery from brine generated by large-scale seawater desalination plants, *Desalin. Water Treat.* (2013) 1–9. doi:10.1080/19443994.2013.810381.
- [21] P. Chelme-Ayala, D.W. Smith, M.G. El-Din, Membrane concentrate management options: a comprehensive critical review A paper submitted to the *Journal of Environmental Engineering and Science.*, *Can. J. Civ. Eng.* 36 (2009) 1107–1119. doi:10.1139/L09-042.
- [22] J. Morillo, J. Usero, D. Rosado, H. El Bakouri, A. Riaza, F.J. Bernaola, Comparative study of brine management technologies for desalination plants, *Desalination*. 336 (2014) 32–49. doi:10.1016/j.desal.2013.12.038.
- [23] H. Geng, J. Wang, C. Zhang, P. Li, H. Chang, High water recovery of RO brine using multi-stage air gap membrane distillation, *Desalination*. 355 (2015) 178–185. doi:10.1016/j.desal.2014.10.038.
- [24] A. Pérez-González, A.M. Urtiaga, R. Ibáñez, I. Ortiz, State of the art and review on the treatment technologies of water reverse osmosis concentrates, *Water Res.* 46 (2012) 267–283. doi:10.1016/j.watres.2011.10.046.
- [25] D.H. Kim, A review of desalting process techniques and economic analysis of the recovery of salts from retentates, *Desalination*. 270 (2011) 1–8. doi:10.1016/j.desal.2010.12.041.
- [26] C. Feng Wan, T.-S. Chung, Osmotic power generation by pressure retarded osmosis using seawater brine as the draw solution and wastewater retentate as the feed, *J. Memb. Sci.* 479 (2015) 148–158. doi:10.1016/j.memsci.2014.12.036.
- [27] C. Fritzmann, J. Löwenberg, T. Wintgens, T. Melin, State-of-the-art of reverse osmosis desalination, *Desalination*. 216 (2007) 1–76. doi:10.1016/j.desal.2006.12.009.
- [28] W.R. Bowen, Biomimetic separations - learning from the early development of biological

- membranes, *Desalination*. 199 (2006) 225–227. doi:10.1016/j.desal.2006.03.053.
- [29] N.L. Le, S.P. Nunes, Materials and membrane technologies for water and energy sustainability, *Sustain. Mater. Technol.* 7 (2016) 1–28. doi:http://dx.doi.org/10.1016/j.susmat.2016.02.001.
- [30] D. Rana, T. Matsuura, Surface modifications for antifouling membranes, *Chem. Rev.* 110 (2010) 2448–2471. doi:10.1021/cr800208y.
- [31] R. Yang, H. Jang, R. Stocker, K.K. Gleason, Synergistic prevention of biofouling in seawater desalination by zwitterionic surfaces and low-level chlorination, *Adv. Mater.* 26 (2014) 1711–1718. doi:10.1002/adma.201304386.
- [32] N. Misdan, A.F. Ismail, N. Hilal, Recent advances in the development of (bio)fouling resistant thin film composite membranes for desalination, *Desalination*. 380 (2016) 105–111. doi:10.1016/j.desal.2015.06.001.
- [33] J. Melgarejo, B. Montano, The power efficiency of the Tajo-Segura transfer and desalination, *Water Sci. Technol.* 63 (2011) 536–541. doi:10.2166/wst.2011.254.
- [34] A. Giwa, N. Akther, V. Dufour, S.W. Hasan, A critical review on recent polymeric and nano-enhanced membranes for reverse osmosis, *RSC Adv.* 6 (2016) 8134–8163. doi:10.1039/C5RA17221G.
- [35] P. Agre, G.M. Preston, B.L. Smith, J.S. Jung, S. Raina, C. Moon, et al., Aquaporin CHIP: the archetypal molecular water channel., *Am. J. Physiol.* 265 (1993) F463–F476. doi:10.1085/jgp.79.5.791.
- [36] S. Phongphananee, N. Yoshida, F. Hirata, On the proton exclusion of aquaporins: A statistical mechanics study, *J. Am. Chem. Soc.* 130 (2008) 1540–1541. doi:10.1021/ja077087+.
- [37] H. Ma, C. Burger, B.S. Hsiao, B. Chu, Highly permeable polymer membranes containing directed channels for water purification, *ACS Macro Lett.* 1 (2012) 723–726. doi:10.1021/mz300163h.
- [38] I. Petrinić, N. Bajraktari, C. Hélix-Nielsen, Membrane technologies for water treatment and reuse in the textile industry, in: A. Basile, A. Cassano, N.K. Rastogi (Eds.), *Adv. Membr. Technol. Water Treat.*, Woodhead Publishing Series in Energy, 2015: pp. 537–550.
- [39] A.F. Ismail, M. Padaki, N. Hilal, T. Matsuura, W.J. Lau, Thin film composite membrane — Recent development and future potential, *Desalination*. 356 (2015) 140–148. doi:10.1016/j.desal.2014.10.042.
- [40] C. Tang, Z. Wang, I. Petrinić, A.G. Fane, C. Hélix-Nielsen, Biomimetic aquaporin membranes coming of age, *Desalination*. 368 (2015) 89–105. doi:10.1016/j.desal.2015.04.026.
- [41] C.Y. Tang, Y. Zhao, R. Wang, C. Hélix-Nielsen, A.G. Fane, Desalination by biomimetic

- aquaporin membranes: Review of status and prospects, *Desalination*. 308 (2013) 34–40. doi:10.1016/j.desal.2012.07.007.
- [42] M. Kumar, M. Grzelakowski, J. Zilles, M. Clark, W. Meier, Highly permeable polymeric membranes based on the incorporation of the functional water channel protein Aquaporin Z., *Proc. Natl. Acad. Sci. U. S. A.* 104 (2007) 20719–24. doi:10.1073/pnas.0708762104.
- [43] D. Devos, S. Dokudovskaya, F. Alber, R. Williams, B.T. Chait, A. Sali, et al., Components of coated vesicles and nuclear pore complexes share a common molecular architecture, *PLoS Biol.* 2 (2004). doi:10.1371/journal.pbio.0020380.
- [44] G. van Meer, D.R. Voelker, G.W. Feigenson, Membrane lipids: where they are and how they behave., *Nat. Rev. Mol. Cell Biol.* 9 (2008) 112–124. doi:10.1038/nrm2330.
- [45] J.G. Black, *Microbiology : Principles and Explorations*, in: *Microbiol. Princ. Explor.*, 2002: pp. 292–293. doi:978-1-118-12923-4.
- [46] S. Suetsugu, S. Kurisu, T. Takenawa, Dynamic shaping of cellular membranes by phospholipids and membrane-deforming proteins, *Physiol. Rev.* 94 (2014) 1219–1248. doi:10.1152/physrev.00040.2013.
- [47] A. Anishkin, S.H. Loukin, J. Teng, C. Kung, Feeling the hidden mechanical forces in lipid bilayer is an original sense., *Proc. Natl. Acad. Sci. U. S. A.* 111 (2014) 7898–905. doi:10.1073/pnas.1313364111.
- [48] S.A. Olaf, Roger E. Koeppe II, Bilayer Thickness and Membrane Protein Function: An Energetic Perspective, *Annu. Rev. Biophys. Biomol. Struct.* 36 (2007) 107–130. doi:10.1146/annurev.biophys.36.040306.132643.
- [49] M.F. Brown, Curvature forces in membrane lipid-protein interactions, *Biochemistry*. 51 (2012) 9782–9795. doi:10.1021/bi301332v.
- [50] L.P. Cunico, A.S. Hukkerikar, R. Ceriani, B. Sarup, R. Gani, Molecular structure-based methods of property prediction in application to lipids: A review and refinement, *Fluid Phase Equilib.* 357 (2013) 2–18. doi:10.1016/j.fluid.2013.04.004.
- [51] S.-C. Liang, R.D. Orlandi, Purification of triglyceride oil from microbial sources using short path distillation, 9,040,730, 2015.
- [52] D. Lingwood, K. Simons, Lipid rafts as a membrane-organizing principle., *Science*. 327 (2010) 46–50. doi:10.1126/science.1174621.
- [53] E. Fahy, S. Subramaniam, H.A. Brown, C.K. Glass, A.H. Merrill, R.C. Murphy, et al., A comprehensive classification system for lipids., *J. Lipid Res.* 46 (2005) 839–861. doi:10.1194/jlr.E400004-JLR200.
- [54] Y.-M. Zhang, C.O. Rock, Thematic review series: Glycerolipids. Acyltransferases in bacterial glycerophospholipid synthesis., *J. Lipid Res.* 49 (2008) 1867–1874. doi:10.1194/jlr.R800005-JLR200.

- [55] P.L. Yeagle, *The membranes of cells*, Academic Press, 2016.
- [56] A. Bruce, A. Johnson, J. Lewis, M. Raff, K. Roberts, P. Walter, The lipid bilayer, in: *Mol. Biol. Cell*, 4th editio, 2002.
- [57] A.I.P.M. De Kroon, P.J. Rijken, C.H. De Smet, Checks and balances in membrane phospholipid class and acyl chain homeostasis, the yeast perspective, *Prog. Lipid Res.* 52 (2013) 374–394. doi:10.1016/j.plipres.2013.04.006.
- [58] P. Blasi, S. Giovagnoli, A. Schoubben, M. Ricci, C. Rossi, Solid lipid nanoparticles for targeted brain drug delivery, *Adv. Drug Deliv. Rev.* 59 (2007) 454–477. doi:10.1016/j.addr.2007.04.011.
- [59] C. O'Connor, J.U. Adams, *Essentials of Cell Biology*, Nat. Educ. (2010) 1–100. doi:10.1145/634067.634339.
- [60] M.M. Kozlov, F. Campelo, N. Liska, L. V. Chernomordik, S.J. Marrink, H.T. McMahon, Mechanisms shaping cell membranes, *Curr. Opin. Cell Biol.* 29 (2014) 53–60. doi:10.1016/j.ceb.2014.03.006.
- [61] M. Luckey, *Membrane structural biology: With biochemical and biophysical foundations*, 2008. doi:10.1080/09687680802375451.
- [62] A. Mashaghi, P. Partovi-Azar, T. Jadidi, N. Nafari, P. Maass, M.R.R. Tabar, et al., Hydration strongly affects the molecular and electronic structure of membrane phospholipids., *J. Chem. Phys.* 136 (2012) 114709. doi:10.1063/1.3694280.
- [63] H. Nikaido, M. Vaara, Molecular basis of bacterial outer membrane permeability, *Microbiol Rev.* 49 (1985) 1–32.
- [64] B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, P. Walter, Membrane Proteins, in: *Mol. Biol. Cell*, 4th editio, 2002.
- [65] P.H.M. Lommerse, H.P. Spink, T. Schmidt, In vivo plasma membrane organization: Results of biophysical approaches, *Biochim. Biophys. Acta - Biomembr.* 1664 (2004) 119–131. doi:10.1016/j.bbamem.2004.05.005.
- [66] Z. Peng, X. Li, I. V Pivkin, M. Dao, G.E. Karniadakis, S. Suresh, Lipid bilayer and cytoskeletal interactions in a red blood cell., *Proc. Natl. Acad. Sci. U. S. A.* 110 (2013) 13356–61. doi:10.1073/pnas.1311827110.
- [67] W. Stein, *Transport and diffusion across cell membranes*, Academic Press, 1986.
- [68] P. Gena, M. Pellegrini-Calace, A. Biasco, M. Svelto, G. Calamita, Aquaporin Membrane Channels: Biophysics, Classification, Functions, and Possible Biotechnological Applications, *Food Biophys.* 6 (2011) 241–249. doi:10.1007/s11483-010-9193-9.
- [69] S.S. Shenvi, A.M. Isloor, A.F. Ismail, A review on RO membrane technology: Developments and challenges, *Desalination.* 368 (2015) 10–26. doi:10.1016/j.desal.2014.12.042.

- [70] K.P. Lee, T.C. Arnot, D. Mattia, A review of reverse osmosis membrane materials for desalination-Development to date and future potential, *J. Memb. Sci.* 370 (2011) 1–22. doi:10.1016/j.memsci.2010.12.036.
- [71] A. Subramani, M. Badruzzaman, J. Oppenheimer, J.G. Jacangelo, Energy minimization strategies and renewable energy utilization for desalination: a review., *Water Res.* 45 (2011) 1907–20. doi:10.1016/j.watres.2010.12.032.
- [72] J. Zhao, X. Zhao, Z. Jiang, Z. Li, X. Fan, J. Zhu, et al., Biomimetic and bioinspired membranes: Preparation and application, *Prog. Polym. Sci.* 39 (2014) 1668–1720. doi:10.1016/j.progpolymsci.2014.06.001.
- [73] Y. Zhao, C. Qiu, X. Li, A. Vararattanavech, W. Shen, J. Torres, et al., Synthesis of robust and high-performance aquaporin-based biomimetic membranes by interfacial polymerization-membrane preparation and RO performance characterization, *J. Memb. Sci.* 423–424 (2012) 422–428. doi:10.1016/j.memsci.2012.08.039.
- [74] P.S. Zhong, T.S. Chung, K. Jeyaseelan, A. Armugam, Aquaporin-embedded biomimetic membranes for nanofiltration, *J. Memb. Sci.* 407–408 (2012) 27–33. doi:10.1016/j.memsci.2012.03.033.
- [75] H. Wang, T.S. Chung, Y.W. Tong, K. Jeyaseelan, A. Armugam, Z. Chen, et al., Highly permeable and selective pore-spanning biomimetic membrane embedded with aquaporin Z, *Small.* 8 (2012) 1185–1190. doi:10.1002/smll.201102120.
- [76] J.M. Benyus, Biomimicry: Innovation Inspired by Nature, *Innovation.* (1997) 308. doi:10.2307/4450504.
- [77] A. Lakhtakia, R.J. Martín-Palma, W. Banzhaf, Engineered Biomimicry, *Eng. Biomimicry.* (2013) 429–447. doi:10.1016/B978-0-12-415995-2.00017-9.
- [78] G.F. Swiegers, Bioinspiration and Biomimicry in Chemistry: Reverse-Engineering Nature, 2012. doi:10.1002/9781118310083.
- [79] T. Kubik, K. Bogunia-Kubik, M. Sugisaka, Nanotechnology on duty in medical applications., *Curr. Pharm. Biotechnol.* 6 (2005) 17–33. doi:http://dx.doi.org/10.2174/1389201053167248.
- [80] C.H. Nielsen, Biomimetic membranes for sensor and separation applications, *Anal. Bioanal. Chem.* 395 (2009) 697–718. doi:10.1007/s00216-009-2960-0.
- [81] E. Stratakis, A. Ranella, C. Fotakis, Biomimetic micro/nanostructured functional surfaces for microfluidic and tissue engineering applications, *Biomicrofluidics.* 5 (2011) 13411. doi:10.1063/1.3553235.
- [82] M.M. Stevens, Exploring and Engineering the Cell-Surface Interface, *Science* (80-. ). 310 (2005) 1135–1138. doi:10.1016/j.bpj.2010.12.1248.
- [83] A. Valkov, F. Nakonechny, M. Nisnevitch, Polymer-immobilized photosensitizers for continuous eradication of bacteria, *Int. J. Mol. Sci.* 15 (2014) 14984–14996.

doi:10.3390/ijms150914984.

- [84] F. Nakonechny, A. Pinkus, S. Hai, O. Yehosha, Y. Nitzan, M. Nisnevitch, Eradication of gram-positive and gram-negative bacteria by photosensitizers immobilized in polystyrene, *Photochem. Photobiol.* 89 (2013) 671–678. doi:10.1111/php.12022.
- [85] M. Sarikaya, C. Tamerler, A.K.-Y. Jen, K. Schulten, F. Baneyx, Molecular biomimetics: nanotechnology through biology., *Nat. Mater.* 2 (2003) 577–585. doi:10.1038/nmat964.
- [86] C. Sanchez, H. Arribart, M.M.G. Guille, Biomimetism and bioinspiration as tools for the design of innovative materials and systems., *Nat. Mater.* 4 (2005) 277–288. doi:10.1038/nmat1339.
- [87] F. Chaumont, F. Barrieu, E. Wojcik, M.J. Chrispeels, R. Jung, Aquaporins constitute a large and highly divergent protein family in maize, *Plant Physiol.* 125 (2001) 1206–1215. doi:10.1104/pp.125.3.1206.
- [88] P.W. Kuchel, G. Benga, Why does the mammalian red blood cell have aquaporins?, *Biosystems.* 82 (2005) 189–196. doi:10.1016/j.biosystems.2005.07.002.
- [89] Y. Shen, P.O. Saboe, I.T. Sines, M. Erbakan, M. Kumar, Biomimetic membranes: A review, *J. Memb. Sci.* 454 (2014) 359–381. doi:10.1016/j.memsci.2013.12.019.
- [90] T.Y. Wah, Nature-inspired membrane set to reduce purification costs, *Membr. Technol.* 2016 (2016) 7. doi:10.1016/S0958-2118(16)30105-7.
- [91] B. Schuster, D. Pum, U.B. Sleytr, S-layer stabilized lipid membranes (Review), *Biointerphases.* 3 (2008) FA3. doi:10.1116/1.2889067.
- [92] AQUAPORIN Asia, AQUAPORIN Inside™ membranes: Higher productivity and higher rejection in a wide range of applications, (2016). <http://aquaporin.asia/> (accessed July 15, 2016).
- [93] M.Ø. Jensen, Molecular dynamics simulations of proteins, biomembrane systems, and interfaces, Technical University of Denmark (supervised by Günther Peters and Ole G. Mouritsen), 2002.
- [94] P. Agre, Aquaporin water channels (nobel lecture), *Angew. Chemie - Int. Ed.* 43 (2004) 4278–4290. doi:10.1002/anie.200460804.
- [95] AQUAPORIN, Current Aquaporin virtual patent marking, (2016). <http://aquaporin.dk/patents/> (accessed July 15, 2016).
- [96] APPLIED BIOMIMETIC, Trans-membrane protein platform, (2016). [http://www.appliedbiomimetic.com/?page\\_id=707](http://www.appliedbiomimetic.com/?page_id=707) (accessed July 15, 2016).
- [97] APPLIED BIOMIMETIC, Mangrove Membranes, (2016). <http://www.mangrovemembranes.com/> (accessed July 10, 2016).
- [98] S. Rempe, C.J. Brinker, D.M. Rogers, Y.-B. JIANG, S. Yang, US9486742, 2016.

- [99] S.B. Rempe, C.J. Brinker, Y.-B. Jiang, Biomimetic membranes for water purification, New Mexico, USA, 2011. <http://bit.ly/2pBw2Gz>.
- [100] D. Saeki, T. Yamashita, A. Fujii, H. Matsuyama, Reverse osmosis membranes based on a supported lipid bilayer with gramicidin A water channels, *Desalination*. 375 (2015) 48–53. doi:10.1016/j.desal.2015.07.030.
- [101] L. Liu, C. Yang, K. Zhao, J. Li, H.-C. Wu, Ultrashort single-walled carbon nanotubes in a lipid bilayer as a new nanopore sensor., *Nat. Commun.* 4 (2013) 2989. doi:10.1038/ncomms3989.
- [102] S. Morandat, S. Azouzi, E. Beauvais, A. Mastouri, K. El Kirat, Atomic force microscopy of model lipid membranes, *Anal. Bioanal. Chem.* 405 (2013) 1445–1461. doi:10.1007/s00216-012-6383-y.
- [103] S.J. Attwood, Y. Choi, Z. Leonenko, Preparation of DOPC and DPPC supported planar lipid bilayers for atomic force microscopy and atomic force spectroscopy, *Int. J. Mol. Sci.* 14 (2013) 3514–3539. doi:10.3390/ijms14023514.
- [104] Y. Roiter, M. Ornatska, A.R. Rammohan, J. Balakrishnan, D.R. Heine, S. Minko, Interaction of nanoparticles with lipid membrane, *Nano Lett.* 8 (2008) 941–944. doi:10.1021/nl080080l.
- [105] R.H. Müller, V. Jennings, K. Mader, A. Lippacher, Lipid particles on the basis of mixtures of liquid and solid lipids and method for producing same, US8663692 B1, 2014.
- [106] E.T. Castellana, P.S. Cremer, Solid supported lipid bilayers: From biophysical studies to sensor design, *Surf. Sci. Rep.* 61 (2006) 429–444. doi:10.1016/j.surfrep.2006.06.001.
- [107] K. Funakoshi, H. Suzuki, S. Takeuchi, Lipid bilayer formation by contacting monolayers in a microfluidic device for membrane protein analysis, *Anal. Chem.* 78 (2006) 8169–8174. doi:10.1021/ac0613479.
- [108] M. Winterhalter, Black lipid membranes, *Curr. Opin. Colloid Interface Sci.* 5 (2000) 250–255. doi:10.1016/S1359-0294(00)00063-7.
- [109] O. Purrucker, H. Hillebrandt, K. Adlkofer, M. Tanaka, Deposition of highly resistive lipid bilayer on silicon-silicon dioxide electrode and incorporation of gramicidin studied by ac impedance spectroscopy, *Electrochim. Acta.* 47 (2001) 791–798. doi:10.1016/S0013-4686(01)00759-9.
- [110] R.L.C. Naumann, A. Jonczyk, R. Kopp, J. Van Esch, H. Ringsdorf, W. Knoll, et al., Incorporation of Membrane Proteins in Solid-Supported Lipid Layers, *Angew. Chem. Int. Ed.* 34 (1995) 2056–2058. doi:10.1002/anie.199520561.
- [111] L. He, J.W.F. Robertson, J. Li, I. Kärcher, S.M. Schiller, W. Knoll, et al., Tethered bilayer lipid membranes based on monolayers of thiolipids mixed with a complementary dilution molecule. 1. Incorporation of channel peptides, *Langmuir*. 21 (2005) 11666–11672. doi:10.1021/la051771p.

- [112] R. Naumann, S.M. Schiller, F. Giess, B. Grohe, K.B. Hartman, I. Kärcher, et al., Tethered lipid bilayers on ultraflat gold surfaces, *Langmuir*. 19 (2003) 5435–5443. doi:10.1021/la0342060.
- [113] R.B. Gennis, *Biomembranes: molecular structure and function*, Ed., 2013.
- [114] J. Heo, F. Meng, S.Z. Hua, Contribution of aquaporins to cellular water transport observed by a microfluidic cell volume sensor, *Anal. Chem.* 80 (2008) 6974–6980. doi:10.1021/ac8008498.
- [115] T.J. Jentsch, VRACs and other ion channels and transporters in the regulation of cell volume and beyond, *Nat. Rev. Mol. Cell Biol.* 17 (2016) 293–307. doi:10.1038/nrm.2016.29.
- [116] J. Héning, E. Tajkhorshid, K. Schulten, C. Chipot, Diffusion of glycerol through *Escherichia coli* aquaglyceroporin GlpF., *Biophys. J.* 94 (2008) 832–839. doi:10.1529/biophysj.107.115105.
- [117] D. Gomes, A. Agasse, P. Thiébaud, S. Delrot, H. Gerós, F. Chaumont, Aquaporins are multifunctional water and solute transporters highly divergent in living organisms, *Biochim. Biophys. Acta - Biomembr.* 1788 (2009) 1213–1228. doi:10.1016/j.bbamem.2009.03.009.
- [118] P. Agre, L.S. King, M. Yasui, W.B. Guggino, O.P. Ottersen, Y. Fujiyoshi, et al., Aquaporin water channels--from atomic structure to clinical medicine., *J. Physiol.* 542 (2002) 3–16. doi:10.1113/jphysiol.2002.020818.
- [119] B.L. De Groot, H. Grubmüller, The dynamics and energetics of water permeation and proton exclusion in aquaporins, *Curr. Opin. Struct. Biol.* 15 (2005) 176–183. doi:10.1016/j.sbi.2005.02.003.
- [120] B.L. De Groot, T. Frigato, V. Helms, H. Grubmüller, The mechanism of proton exclusion in the aquaporin-1 water channel, *J. Mol. Biol.* 333 (2003) 279–293. doi:10.1016/j.jmb.2003.08.003.
- [121] J. Masin, A. Osickova, A. Sukova, R. Fiser, P. Halada, L. Bumba, et al., Negatively charged residues of the segment linking the enzyme and cytolysin moieties restrict the membrane-permeabilizing capacity of adenylate cyclase toxin, *Sci. Rep.* 6 (2016) 29137. doi:10.1038/srep29137.
- [122] a S. Verkman, More than just water channels: unexpected cellular roles of aquaporins., *J. Cell Sci.* 118 (2005) 3225–3232. doi:10.1242/jcs.02519.
- [123] T. Gonen, T. Walz, The structure of aquaporins., *Q. Rev. Biophys.* 39 (2006) 361–96. doi:10.1017/S0033583506004458.
- [124] D. Fu, M. Lu, The structural basis of water permeation and proton exclusion in aquaporins., *Mol. Membr. Biol.* 24 (2015) 366–74. doi:10.1080/09687680701446965.
- [125] M. Parisi, R.A. Dorr, M. Ozu, R. Toriano, From membrane pores to aquaporins: 50 years



- measuring water fluxes, *J. Biol. Phys.* 33 (2007) 331–343. doi:10.1007/s10867-008-9064-5.
- [126] J.M. Carbrey, D.A. Gorelick-Feldman, D. Kozono, J. Praetorius, S. Nielsen, P. Agre, Aquaglyceroporin AQP9: solute permeation and metabolic control of expression in liver., *Proc. Natl. Acad. Sci. U. S. A.* 100 (2003) 2945–50. doi:10.1073/pnas.0437994100.
- [127] K. Ishibashi, Aquaporin subfamily with unusual NPA boxes, *Biochim. Biophys. Acta - Biomembr.* 1758 (2006) 989–993. doi:10.1016/j.bbamem.2006.02.024.
- [128] S. Nielsen, J. Frøkiær, D. Marples, T.-H. Kwon, P. Agre, M.A. Knepper, Aquaporins in the Kidney: From Molecules to Medicine, *Physiol. Rev.* 82 (2002) 205–244. doi:10.1152/physrev.00024.2001.
- [129] A. Tanghe, P. Van Dijck, J.M. Thevelein, Why do microorganisms have aquaporins?, *Trends Microbiol.* 14 (2006) 78–85. doi:10.1016/j.tim.2005.12.001.
- [130] S.-J. Kim, J. Lee, H.-W. Yu, I.S. Kim, Study on mass production of aquaporinZ for biomimetic water purification membrane, *Desalin. Water Treat.* 51 (2013) 6370–6377. doi:10.1080/19443994.2013.780998.
- [131] R.K. Vandeleur, G. Mayo, M.C. Sheldon, M. Gilliam, B.N. Kaiser, S.D. Tyerman, The role of plasma membrane intrinsic protein aquaporins in water transport through roots: diurnal and drought stress responses reveal different strategies between isohydric and anisohydric cultivars of grapevine., *Plant Physiol.* 149 (2009) 445–60. doi:10.1104/pp.108.128645.
- [132] S. Gattolin, M. Sorieul, L. Frigerio, Tonoplast intrinsic proteins and vacuolar identity., *Biochem. Soc. Trans.* 38 (2010) 769–773. doi:10.1042/BST0380769.
- [133] C. Maurel, L. Verdoucq, D.-T. Luu, V. Santoni, Plant aquaporins: membrane channels with multiple integrated functions., *Annu. Rev. Plant Biol.* 59 (2008) 595–624. doi:10.1146/annurev.arplant.59.032607.092734.
- [134] I.S. Wallace, W.G. Choi, D.M. Roberts, The structure, function and regulation of the nodulin 26-like intrinsic protein family of plant aquaglyceroporins, *Biochim. Biophys. Acta - Biomembr.* 1758 (2006) 1165–1175. doi:10.1016/j.bbamem.2006.03.024.
- [135] B. Pommerrenig, T.A. Diehn, G.P. Bienert, Metalloido-porins: Essentiality of Nodulin 26-like intrinsic proteins in metalloid transport, *Plant Sci.* 238 (2015) 212–227. doi:10.1016/j.plantsci.2015.06.002.
- [136] H.-J. Choi, C. Montemagno, Recent Progress in Advanced Nanobiological Materials for Energy and Environmental Applications, *Materials (Basel)*. 6 (2013) 5821–5856. doi:10.3390/ma6125821.
- [137] P.H.H. Duong, T.S. Chung, K. Jeyaseelan, A. Armugam, Z. Chen, J. Yang, et al., Planar biomimetic aquaporin-incorporated triblock copolymer membranes on porous alumina supports for nanofiltration, *J. Memb. Sci.* 409–410 (2012) 34–43. doi:10.1016/j.memsci.2012.03.004.

- [138] J. Kowal, X. Zhang, I.A. Dinu, C.G. Palivan, W. Meier, Planar biomimetic membranes based on amphiphilic block copolymers, *ACS Macro Lett.* 3 (2014) 59–63. doi:10.1021/mz400590c.
- [139] Y.R. Kim, S. Jung, H. Ryu, Y.E. Yoo, S.M. Kim, T.J. Jeon, Synthetic biomimetic membranes and their sensor applications, *Sensors (Switzerland)*. 12 (2012) 9530–9550. doi:10.3390/s120709530.
- [140] R. Sengur-Tasdemir, S. Aydin, T. Turken, E.A. Genceli, I. Koyuncu, Biomimetic Approaches for Membrane Technologies, *Sep. Purif. Rev.* 45 (2015) 122–140. doi:10.1080/15422119.2015.1035443.
- [141] K. Ariga, Y. Yamauchi, T. Mori, J.P. Hill, 25th Anniversary Article: What Can Be Done with the Langmuir-Blodgett Method? Recent Developments and its Critical Role in Materials Science, *Adv. Mater.* 25 (2013) 6477–6512. doi:10.1002/adma.201302283.
- [142] G.J. Hardy, R. Nayak, S. Zauscher, Model cell membranes: Techniques to form complex biomimetic supported lipid bilayers via vesicle fusion., *Curr. Opin. Colloid Interface Sci.* 18 (2013) 448–458. doi:10.1016/j.cocis.2013.06.004.
- [143] G. Sun, H. Zhou, Y. Li, K. Jeyaseelan, A. Armugam, T.S. Chung, A novel method of AquaporinZ incorporation via binary-lipid Langmuir monolayers, *Colloids Surfaces B Biointerfaces*. 89 (2012) 283–288. doi:10.1016/j.colsurfb.2011.09.004.
- [144] K. Norrman, A. Ghanbari-Siahkali, N.B. Larsen, Studies of spin-coated polymer films, *Annu. Reports Sect. "C" (Physical Chem.* 101 (2005) 174–201. doi:10.1039/b408857n.
- [145] J. Vogel, M. Perry, J.S. Hansen, P.-Y. Bolinger, C.H. Nielsen, O. Geschke, A support structure for biomimetic applications, *J. Micromechanics Microengineering*. 19 (2009) 25026. doi:10.1088/0960-1317/19/2/025026.
- [146] H. Wang, T.-S. Chung, Y.W. Tong, W. Meier, Z. Chen, M. Hong, et al., Preparation and characterization of pore-suspending biomimetic membranes embedded with Aquaporin Z on carboxylated polyethylene glycol polymer cushion, *Soft Matter*. 7 (2011) 7274. doi:10.1039/c1sm05527e.
- [147] S.P. Nunes, Block Copolymer Membranes for Aqueous Solution Applications, *Macromolecules*. 49 (2016) 2905–2916. doi:10.1021/acs.macromol.5b02579.
- [148] Y. Kaufman, S. Grinberg, C. Linder, E. Heldman, J. Gilron, Y. xiao Shen, et al., Towards supported bolaamphiphile membranes for water filtration: Roles of lipid and substrate, *J. Memb. Sci.* 457 (2014) 50–61. doi:10.1016/j.memsci.2014.01.036.
- [149] W. Knoll, R. Naumann, M. Friedrich, J.W.F. Robertson, M. Lösche, F. Heinrich, et al., Solid supported lipid membranes: new concepts for the biomimetic functionalization of solid surfaces., *Biointerphases*. 3 (2008) FA125. doi:10.1116/1.2913612.
- [150] Y. Kaufman, A. Berman, V. Freger, Supported lipid bilayer membranes for water purification by reverse osmosis, *Langmuir*. 26 (2010) 7388–7395. doi:10.1021/la904411b.

- [151] K. Tawa, K. Morigaki, Substrate-supported phospholipid membranes studied by surface plasmon resonance and surface plasmon fluorescence spectroscopy., *Biophys. J.* 89 (2005) 2750–8. doi:10.1529/biophysj.105.065482.
- [152] E.S. Karp, J.P. Newstadt, S. Chu, G.A. Lorigan, Characterization of lipid bilayer formation in aligned nanoporous aluminum oxide nanotube arrays, *J. Magn. Reson.* 187 (2007) 112–119. doi:10.1016/j.jmr.2007.04.004.
- [153] R.F. Roskamp, I.K. Vockenroth, N. Eisenmenger, J. Braunagel, I. K??per, Functional tethered bilayer lipid membranes on aluminum oxide, *ChemPhysChem.* 9 (2008) 1920–1924. doi:10.1002/cphc.200800248.
- [154] J.A. Jackman, W. Knoll, N.J. Cho, Biotechnology applications of tethered lipid bilayer membranes, *Materials (Basel).* 5 (2012) 2637–2657. doi:10.3390/ma5122637.
- [155] Y. Kaufman, S. Grinberg, C. Linder, E. Heldman, J. Gilron, V. Freger, Fusion of bolaamphiphile micelles: A method to prepare stable supported biomimetic membranes, *Langmuir.* 29 (2013) 1152–1161. doi:10.1021/la304484p.
- [156] K. Kita-Tokarczyk, J. Grumelard, T. Haefele, W. Meier, Block copolymer vesicles - Using concepts from polymer chemistry to mimic biomembranes, *Polymer (Guildf).* 46 (2005) 3540–3563. doi:10.1016/j.polymer.2005.02.083.
- [157] R. Rodríguez-García, M. Mell, I. López-Montero, J. Netzel, T. Hellweg, F. Monroy, Polymersomes: smart vesicles of tunable rigidity and permeability, *Soft Matter.* 7 (2011) 1532. doi:10.1039/c0sm00823k.
- [158] A. Janshoff, C. Steinem, Mechanics of lipid bilayers: What do we learn from pore-spanning membranes?, *Biochim. Biophys. Acta - Mol. Cell Res.* 1853 (2015) 2977–2983. doi:10.1016/j.bbamcr.2015.05.029.
- [159] Y. Zhao, A. Vararattanavech, X. Li, C. H??lixnielsen, T. Vissing, J. Torres, et al., Effects of proteoliposome composition and draw solution types on separation performance of aquaporin-based proteoliposomes: Implications for seawater desalination using aquaporin-based biomimetic membranes, *Environ. Sci. Technol.* 47 (2013) 1496–1503. doi:10.1021/es304306t.
- [160] M.J. Borgnia, D. Kozono, G. Calamita, P.C. Maloney, P. Agre, Functional reconstitution and characterization of AqpZ, the *E. coli* water channel protein., *J. Mol. Biol.* 291 (1999) 1169–1179. doi:10.1006/jmbi.1999.3032.
- [161] J. Habel, M. Hansen, S. Kynde, N. Larsen, S.R. Midtgaard, G.V. Jensen, et al., Aquaporin-Based Biomimetic Polymeric Membranes: Approaches and Challenges., *Membranes (Basel).* 5 (2015) 307–51. doi:10.3390/membranes5030307.
- [162] C.D. Montemagno, Biomimetic membrane formed from a vesicle-thread conjugate, US20110259815 A1, 2011.
- [163] A. Gliozzi, A. Relini, P.L.G. Chong, Structure and permeability properties of biomimetic membranes of bolaform archaeal tetraether lipids, *J. Memb. Sci.* 206 (2002) 131–147.

doi:10.1016/S0376-7388(01)00771-2.

- [164] G. Sun, T.-S. Chung, K. Jeyaseelan, A. Armugam, A layer-by-layer self-assembly approach to developing an aquaporin-embedded mixed matrix membrane, *RSC Adv.* 3 (2013) 473–481. doi:10.1039/C2RA21767H.
- [165] M.F. Bédard, B.G. De Geest, A.G. Skirtach, H. Möhwald, G.B. Sukhorukov, Polymeric microcapsules with light responsive properties for encapsulation and release, *Adv. Colloid Interface Sci.* 158 (2010) 2–14. doi:10.1016/j.cis.2009.07.007.
- [166] F. Meyer, V. Ball, P. Schaaf, J.C. Voegel, J. Ogier, Polyplex-embedding in polyelectrolyte multilayers for gene delivery, *Biochim. Biophys. Acta - Biomembr.* 1758 (2006) 419–422. doi:10.1016/j.bbamem.2005.11.015.
- [167] M. Wang, Z. Wang, X. Wang, S. Wang, W. Ding, C. Gao, Layer-by-layer assembly of aquaporin z-incorporated biomimetic membranes for water purification, *Environ. Sci. Technol.* 49 (2015) 3761–3768. doi:10.1021/es5056337.
- [168] G. Sun, T.-S. Chung, N. Chen, X. Lu, Q. Zhao, Highly permeable aquaporin-embedded biomimetic membranes featuring a magnetic-aided approach, *RSC Adv.* 3 (2013) 9178–9184. doi:10.1039/c3ra40608c.
- [169] S. Wang, J. Cai, W. Ding, Z. Xu, Z. Wang, Bio-inspired aquaporin z containing double-skinned forward osmosis membrane synthesized through layer-by-layer assembly, *Membranes (Basel)*. 5 (2015) 369–384. doi:10.3390/membranes5030369.
- [170] H. Ye, A. Curcuro, Vesicle biomechanics in a time-varying magnetic field, *BMC Biophys.* 8 (2015) 2. doi:10.1186/s13628-014-0016-0.
- [171] W. Ding, J. Cai, Z. Yu, Q. Wang, Z. Xu, Z. Wang, et al., Fabrication of an aquaporin-based forward osmosis membrane through covalent bonding of a lipid bilayer to a microporous support, *J. Mater. Chem. A.* 3 (2015) 20118–20126. doi:10.1039/C5TA05751E.
- [172] X. Li, R. Wang, F. Wicaksana, C. Tang, J. Torres, A.G. Fane, Preparation of high performance nanofiltration (NF) membranes incorporated with aquaporin Z, *J. Memb. Sci.* 450 (2014) 181–188. doi:10.1016/j.memsci.2013.09.007.
- [173] C. V. Kulkarni, W. Wachter, G. Iglesias-Salto, S. Engelskirchen, S. Ahualli, Monoolein: a magic lipid?, *Phys. Chem. Chem. Phys.* 13 (2011) 3004–3021. doi:10.1039/C0CP01539C.
- [174] Z. Wang, X. Wang, W. Ding, M. Wang, X. Qi, C. Gao, Impact of monoolein on aquaporin1-based supported lipid bilayer membranes, *Sci. Technol. Adv. Mater.* 16 (2015) 45005. doi:10.1088/1468-6996/16/4/045005.
- [175] Y. Corvis, G. Brezesinski, R. Rink, A. Walcarius, A. Van der Heyden, F. Mutelet, et al., Analytical investigation of the interactions between SC3 hydrophobin and lipid layers: Elaborating of nanostructured matrixes for immobilizing redox systems, *Anal. Chem.* 78 (2006) 4850–4864. doi:10.1021/ac0602064.

- [176] G. Sun, T.S. Chung, K. Jeyaseelan, A. Armugam, Stabilization and immobilization of aquaporin reconstituted lipid vesicles for water purification, *Colloids Surfaces B Biointerfaces*. 102 (2013) 466–471. doi:10.1016/j.colsurfb.2012.08.009.
- [177] W. Xie, F. He, B. Wang, T.-S. Chung, K. Jeyaseelan, A. Armugam, et al., An aquaporin-based vesicle-embedded polymeric membrane for low energy water filtration, *J. Mater. Chem. A*. 1 (2013) 7592. doi:10.1039/c3ta10731k.
- [178] X. Li, S. Chou, R. Wang, L. Shi, W. Fang, G. Chaitra, et al., Nature gives the best solution for desalination: Aquaporin-based hollow fiber composite membrane with superior performance, *J. Memb. Sci.* 494 (2015) 68–77. doi:10.1016/j.memsci.2015.07.040.
- [179] S.P. Sun, T.A. Hatton, T.S. Chung, Hyperbranched polyethyleneimine induced cross-linking of polyamide-imide nanofiltration hollow fiber membranes for effective removal of ciprofloxacin, *Environ. Sci. Technol.* 45 (2011) 4003–4009. doi:10.1021/es200345q.
- [180] H.L. Wang, T.S. Chung, Y.W. Tong, K. Jeyaseelan, A. Armugam, H.H.P. Duong, et al., Mechanically robust and highly permeable AquaporinZ biomimetic membranes, *J. Memb. Sci.* 434 (2013) 130–136. doi:10.1016/j.memsci.2013.01.031.
- [181] J. Tong, M.M. Briggs, D. Mlaver, A. Vidal, T.J. McIntosh, Sorting of lens aquaporins and connexins into raft and nonraft bilayers: Role of protein homo-oligomerization, *Biophys. J.* 97 (2009) 2493–2502. doi:10.1016/j.bpj.2009.08.026.
- [182] J.W. O'Connor, J.B. Klauda, Lipid membranes with a majority of cholesterol: Applications to the ocular lens and aquaporin 0, *J. Phys. Chem. B*. 115 (2011) 6455–6464. doi:10.1021/jp108650u.
- [183] Z. Chen, R.P. Rand, The influence of cholesterol on phospholipid membrane curvature and bending elasticity., *Biophys. J.* 73 (1997) 267–276. doi:10.1016/S0006-3495(97)78067-6.
- [184] H.G.L. Coster, The Physics of Cell Membranes, in: *J. Biol. Phys.*, 2003: pp. 363–399. doi:10.1023/A:1027362704125.
- [185] G.M. Geise, H.S. Lee, D.J. Miller, B.D. Freeman, J.E. McGrath, D.R. Paul, Water purification by membranes: The role of polymer science, *J. Polym. Sci. Part B Polym. Phys.* 48 (2010) 1685–1718. doi:10.1002/polb.22037.
- [186] R. van der Westen, L. Hosta-Rigau, D.S. Sutherland, K.N. Goldie, F. Albericio, A. Postma, et al., Myoblast cell interaction with polydopamine coated liposomes, *Biointerphases*. 7 (2012). doi:10.1007/s13758-011-0008-4.
- [187] L. Setiawan, R. Wang, L. Shi, K. Li, A.G. Fane, Novel dual-layer hollow fiber membranes applied for forward osmosis process, *J. Memb. Sci.* 421–422 (2012) 238–246. doi:10.1016/j.memsci.2012.07.020.
- [188] L. Setiawan, R. Wang, K. Li, A.G. Fane, Fabrication and characterization of forward osmosis hollow fiber membranes with antifouling NF-like selective layer, *J. Memb. Sci.*

- 394–395 (2012) 80–88. doi:10.1016/j.memsci.2011.12.026.
- [189] H. Lee, J. Rho, P.B. Messersmith, Facile conjugation of biomolecules onto surfaces via mussel adhesive protein inspired coatings, *Adv. Mater.* 21 (2009) 431–434. doi:10.1002/adma.200801222.
- [190] H. Wang, T.S. Chung, Y.W. Tong, Study on water transport through a mechanically robust Aquaporin Z biomimetic membrane, *J. Memb. Sci.* 445 (2013) 47–52. doi:10.1016/j.memsci.2013.05.057.
- [191] I. Gehrke, A. Geiser, A. Somborn-Schulz, Innovations in nanotechnology for water treatment, *Nanotechnol. Sci. Appl.* 8 (2015). doi:10.2147/NSA.S43773.
- [192] P.S. Goh, A.F. Ismail, N. Hilal, Nano-enabled membranes technology: Sustainable and revolutionary solutions for membrane desalination?, *Desalination.* 380 (2016) 100–104. doi:10.1016/j.desal.2015.06.002.
- [193] C.J. Tan, Y.W. Tong, Molecularly imprinted beads by surface imprinting, *Anal. Bioanal. Chem.* 389 (2007) 369–376. doi:10.1007/s00216-007-1362-4.
- [194] J.T. Chau, G.C. Hong, H.K. Kwee, W.T. Yen, Preparation of bovine serum albumin surface-imprinted submicrometer particles with magnetic susceptibility through core-shell miniemulsion polymerization, *Anal. Chem.* 80 (2008) 683–692. doi:10.1021/ac701824u.
- [195] R.E. Fairhurst, C. Chassaing, R.F. Venn, A.G. Mayes, A direct comparison of the performance of ground, beaded and silica-grafted MIPs in HPLC and Turbulent Flow Chromatography applications, in: *Biosens. Bioelectron.*, 2004: pp. 1098–1105. doi:10.1016/j.bios.2004.01.020.
- [196] J.S. Hansen, A. Vararattanavech, I. Plasencia, P. Greisen, J. Bomholt, J. Torres, et al., Interaction between sodium dodecyl sulfate and membrane reconstituted aquaporins: A comparative study of spinach SoPIP2;1 and E. coli AqpZ, *Biochim. Biophys. Acta - Biomembr.* 1808 (2011) 2600–2607. doi:10.1016/j.bbamem.2011.05.021.
- [197] N. Misdan, W.J. Lau, A.F. Ismail, Seawater Reverse Osmosis (SWRO) desalination by thin-film composite membrane—Current development, challenges and future prospects, *Desalination.* 287 (2012) 228–237. doi:10.1016/j.desal.2011.11.001.
- [198] S. Daer, J. Kharraz, A. Giwa, S.W. Hasan, Recent applications of nanomaterials in water desalination: A critical review and future opportunities, *Desalination.* 367 (2015) 37–48. doi:10.1016/j.desal.2015.03.030.
- [199] X. Li, R. Wang, C. Tang, A. Vararattanavech, Y. Zhao, J. Torres, et al., Preparation of supported lipid membranes for aquaporin Z incorporation, *Colloids Surfaces B Biointerfaces.* 94 (2012) 333–340. doi:10.1016/j.colsurfb.2012.02.013.
- [200] N. Akther, A. Sodiq, A. Giwa, S. Daer, H.A. Arafat, S.W. Hasan, Recent advancements in forward osmosis desalination: A review, *Chem. Eng. J.* 281 (2015) 502–522. doi:10.1016/j.cej.2015.05.080.

- [201] D.L. Shaffer, J.R. Werber, H. Jaramillo, S. Lin, M. Elimelech, Forward osmosis : Where are we now ?, *Des.* 356 (2015) 271–284. doi:10.1016/j.desal.2014.10.031.
- [202] Y. Yu, S. Seo, I.C. Kim, S. Lee, Nanoporous polyethersulfone (PES) membrane with enhanced flux applied in forward osmosis process, *J. Memb. Sci.* 375 (2011) 63–68. doi:10.1016/j.memsci.2011.02.019.
- [203] Z.M. Darbari, A.A. Mungray, Synthesis of an electrically cleanable forward osmosis membrane, *Desalin. Water Treat.* (2014) 1–13. doi:10.1080/19443994.2014.978390.
- [204] F.J. Fu, S. Zhang, S.P. Sun, K.Y. Wang, T.S. Chung, POSS-containing delamination-free dual-layer hollow fiber membranes for forward osmosis and osmotic power generation, *J. Memb. Sci.* 443 (2013) 144–155. doi:10.1016/j.memsci.2013.04.050.
- [205] Z.Y. Li, V. Yangali-Quintanilla, R. Valladares-Linares, Q. Li, T. Zhan, G. Amy, Flux patterns and membrane fouling propensity during desalination of seawater by forward osmosis, *Water Res.* 46 (2012) 195–204. doi:10.1016/j.watres.2011.10.051.
- [206] N. Garcia, J. Moreno, E. Cartmell, I. Rodriguez-Roda, S. Judd, The application of microfiltration-reverse osmosis/nanofiltration to trace organics removal for municipal wastewater reuse, *Environ. Technol.* 34 (2013) 3183–3189. doi:10.1080/09593330.2013.808244.
- [207] S. Beier, S. Köster, K. Veltmann, H.F. Schröder, J. Pinnekamp, Treatment of hospital wastewater effluent by nanofiltration and reverse osmosis, *Water Sci. Technol.* 61 (2010) 1691–1698. doi:10.2166/wst.2010.119.
- [208] M.A. Barakat, New trends in removing heavy metals from industrial wastewater, *Arab. J. Chem.* 4 (2011) 361–377. doi:10.1016/j.arabjc.2010.07.019.
- [209] S. Jamaly, A. Giwa, S.W. Hasan, Recent improvements in oily wastewater treatment: Progress, challenges, and future opportunities, *J. Environ. Sci.* 37 (2015) 1–16. doi:10.1016/j.jes.2015.04.011.
- [210] B.D. Coday, B.G.M. Yaffe, P. Xu, T.Y. Cath, Rejection of trace organic compounds by forward osmosis membranes: a literature review., *Environ. Sci. Technol.* 48 (2014) 3612–24. doi:10.1021/es4038676.
- [211] A.A. Alturki, J.A. McDonald, S.J. Khan, W.E. Price, L.D. Nghiem, M. Elimelech, Removal of trace organic contaminants by the forward osmosis process, *Sep. Purif. Technol.* 103 (2013) 258–266. doi:10.1016/j.seppur.2012.10.036.
- [212] M. Xie, L.D. Nghiem, W.E. Price, M. Elimelech, Comparison of the removal of hydrophobic trace organic contaminants by forward osmosis and reverse osmosis, *Water Res.* 46 (2012) 2683–2692. doi:10.1016/j.watres.2012.02.023.
- [213] H.T. Madsen, N. Bajraktari, C. Høllix-Nielsen, B. Van der Bruggen, E.G. Søgaard, Use of biomimetic forward osmosis membrane for trace organics removal, *J. Memb. Sci.* 476 (2015) 469–474. doi:10.1016/j.memsci.2014.11.055.

- [214] N. Hilal, G.J. Kim, C. Somerfield, Boron removal from saline water: A comprehensive review, *Desalination*. 273 (2011) 23–35. doi:10.1016/j.desal.2010.05.012.
- [215] N. Kabay, M. Bryjak, Boron Removal From Seawater Using Reverse Osmosis Integrated Processes, in: *Boron Sep. Process.*, 2015: pp. 219–235. doi:10.1016/B978-0-444-63454-2.00009-5.
- [216] P. Dydo, M. Turek, A. Milewski, Removal of boric acid, monoborate and boron complexes with polyols by reverse osmosis membranes, *Desalination*. 334 (2014) 39–45. doi:10.1016/j.desal.2013.12.001.
- [217] A. Farhat, F. Ahmad, N. Hilal, H.A. Arafat, Boron removal in new generation reverse osmosis (RO) membranes using two-pass RO without pH adjustment, *Desalination*. 310 (2013) 50–59. doi:10.1016/j.desal.2012.10.003.
- [218] S. Mentzel, M.E. Perry, J. Vogel, S. Braekevelt, O. Geschke, M. Larsen, Systems for water extraction, WO 2014128293 A1, 2014.
- [219] A.J. Ragauskas, C.K. Williams, B.H. Davison, G. Britovsek, J. Cairney, C.A. Eckert, et al., The Path Forward for Biofuels and Biomaterials, *Science* (80-. ). 311 (2006) 484–489. doi:10.1126/science.1114736.
- [220] S.N. Naik, V. V Goud, P.K. Rout, A.K. Dalai, Production of first and second generation biofuels: a comprehensive review, *Renew. Sustain. Energy Rev.* 14 (2010) 578–597.
- [221] A. Thongsukmak, K.K. Sirkar, Extractive pervaporation to separate ethanol from its dilute aqueous solutions characteristic of ethanol-producing fermentation processes, *J. Memb. Sci.* 329 (2009) 119–129. doi:10.1016/j.memsci.2008.12.025.
- [222] A.K. Jha, S.L. Tsang, A.E. Ozcam, R.D. Offeman, N.P. Balsara, Master curve captures the effect of domain morphology on ethanol pervaporation through block copolymer membranes, *J. Memb. Sci.* 401–402 (2012) 125–131. doi:10.1016/j.memsci.2012.01.037.
- [223] A.K. Jha, L. Chen, R.D. Offeman, N.P. Balsara, Effect of nanoscale morphology on selective ethanol transport through block copolymer membranes, *J. Memb. Sci.* 373 (2011) 112–120. doi:10.1016/j.memsci.2011.02.043.
- [224] C. Charcosset, A review of membrane processes and renewable energies for desalination, *Desalination*. 245 (2009) 214–231. doi:10.1016/j.desal.2008.06.020.
- [225] D. Weckesser, A. König, Particle shape and purity in membrane based crystallization, *Chem. Eng. Technol.* 31 (2008) 157–162. doi:10.1002/ceat.200700190.
- [226] F. Macedonio, E. Drioli, E. Curcio, G. Di Profio, Experimental and economical evaluation of a membrane crystallizer plant, *Desalin. Water Treat.* 9 (2009) 49–53. doi:10.5004/dwt.2009.751.
- [227] W. Ye, J. Lin, H. Tækker Madsen, E. Gydesen Søggaard, C. Hélix-Nielsen, P. Luis, et al., Enhanced performance of a biomimetic membrane for Na<sub>2</sub>CO<sub>3</sub> crystallization in the scenario of CO<sub>2</sub> capture, *J. Memb. Sci.* 498 (2016) 75–85.



doi:10.1016/j.memsci.2015.09.010.

- [228] Q. Wang, J. Luo, Z. Zhong, A. Borgna, CO<sub>2</sub> capture by solid adsorbents and their applications: current status and new trends, *Energy Environ. Sci.* 4 (2011) 42–55. doi:10.1039/C0EE00064G.
- [229] D.V. Quang, N. El Hadri, M.R.M. Abu-zahra, Reduction in the regeneration energy of CO<sub>2</sub> capture process by impregnating amine solvent onto precipitated silica, *Esj.* 9 (2013) 82–102.
- [230] P. Luis, T. Van Gerven, B. Van der Bruggen, Recent developments in membrane-based technologies for CO<sub>2</sub> capture, *Prog. Energy Combust. Sci.* 38 (2012) 419–448. doi:10.1016/j.peccs.2012.01.004.
- [231] A. Achilli, T.Y. Cath, A.E. Childress, Power generation with pressure retarded osmosis: An experimental and theoretical investigation, *J. Memb. Sci.* 343 (2009) 42–52. doi:10.1016/j.memsci.2009.07.006.
- [232] P.H. Jensen, Biomimetic water membrane comprising aquaporins used in the production of salinity power, US20090007555 A1, 2012.
- [233] R. Kaldenhoff, A. Bertl, B. Otto, M. Moshelion, N. Uehlein, Characterization of plant aquaporins, in: 2007: pp. 505–531. doi:10.1016/S0076-6879(07)28028-0.
- [234] D.A. Gorelick, J. Praetorius, T. Tsunenari, S. Nielsen, P. Agre, Aquaporin-11: a channel protein lacking apparent transport function expressed in brain., *BMC Biochem.* 7 (2006) 14. doi:10.1186/1471-2091-7-14.
- [235] A. Nozawa, T. Ogasawara, S. Matsunaga, T. Iwasaki, T. Sawasaki, Y. Endo, Production and partial purification of membrane proteins using a liposome-supplemented wheat cell-free translation system., *BMC Biotechnol.* 11 (2011) 35. doi:10.1186/1472-6750-11-35.
- [236] M. Perry, S. Madsen, T. Jørgensen, S. Braekevelt, K. Lauritzen, C. Hélix-Nielsen, Challenges in commercializing biomimetic membranes, *Membranes (Basel).* 5 (2015) 685–701. doi:10.3390/membranes5040685.
- [237] J. Bomholt, C. Hélix-Nielsen, P. Scharff-Poulsen, P.A. Pedersen, Recombinant production of human aquaporin-1 to an exceptional high membrane density in *Saccharomyces cerevisiae*, *PLoS One.* 8 (2013) e56431. doi:10.1371/journal.pone.0056431.
- [238] K. Molbaek, P. Scharff-Poulsen, C. Helix-Nielsen, D.A. Klaerke, P.A. Pedersen, High yield purification of full-length functional hERG K<sup>+</sup> channels produced in *Saccharomyces cerevisiae*., *Microb. Cell Fact.* 14 (2015) 15. doi:10.1186/s12934-015-0193-9.
- [239] N. Altamura, G. Calamita, Systems for production of proteins for biomimetic membrane devices, in: *Biomim. Membr. Sens. Sep. Appl.*, 2011: pp. 233–250.
- [240] N.T. Hovijitra, J.J. Wu, B. Peaker, J.R. Swartz, Cell-free synthesis of functional aquaporin Z in synthetic liposomes, *Biotechnol. Bioeng.* 104 (2009) 40–49.

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