Chapter 9
Antibacterial Polymeric Membranes

Abstract Membranes have been typically defined as interfaces between two interfaces having as a major role to regulate the transport between two different compartment and act as selective barrier. Membranes are able to selectively allow the transport of one substance in the presence of other compounds without the use of additives or the use of elevated temperatures, thus reducing the energy consumption. They have found multiple applications in different areas ranging from separation processes but have also been employed in the fabrication of biomaterials, catalytic purposes, or even lab-on-chip devices.

Several major characteristics including the low operation cost, relatively small footprint, and complicity with environmental regulations have provoked that polymers have been extensively employed for the fabrication of membranes. Polymeric membranes do not require the use of additives. This permits these membranes to be active at low temperatures thus enabling a significant decrease of the energy employed for the separation in comparison with other processes. In addition, these membranes are easily formed and up-scaling and downscaling can be easily carried out.

This chapter will provide a brief description about polymeric membranes focusing on one of the major remaining issues, that is, their contamination by microorganisms and, in particular, by bacteria. Upon a concise analysis of the problem, the alternative approaches developed to produce antifouling/antibacterial membranes will be thoroughly analyzed. For detailed reviews on membrane fabrication and their applications, the reader is referred to the following publications.

9.1 Introduction to Polymer Membranes

Membranes have been typically defined as interfaces between two interfaces having as a major role to regulate the transport between two different compartment and act as a selective barrier [1]. As described by Ulbricht [2], membranes are able to

Table 9.1 Classification of membranes as a function of the material employed, the membrane cross-section, the preparation method, and the module configuration

Classifications	Description
Membrane materials	Organic polymers, inorganic materials (oxides, ceramics, metals), mixed matrix, or composite materials
Membrane cross-section	Isotropic (symmetric), integrally anisotropic (asymmetric), bi- or multilayer, thin layer or mixed matrix composite
Preparation method	Phase separation (phase inversion) of polymers, sol–gel process, interface reaction, stretching, extrusion, track-etching, micro-fabrication, electrospinning
Membrane module configuration	Flat sheet, hollow fiber, hollow capsule

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selectively allow the transport of one substance in the presence of other compounds without the use of additives or the use of elevated temperatures, thus reducing the energy consumption.

Membranes have found multiple applications in different areas ranging from separation processes but have also been employed in the fabrication of biomaterials, catalytic purposes, or even lab-on-chip devices [2].

Several properties are desired in a membrane including high and stable filtration flux and low filtration pressure but also, for instance, in the case of water filtration to produce a high-quality water produced without thorough pretreatments. In view of these requirements, a large variety of membranes suited for technical applications [2] have been designed in which several aspects have been considered in its design. As depicted in Table 9.1, membranes can be classified depending on the membrane materials, membrane cross-section, preparation method, and the membrane shape. In this context, polymers are probably the most extended material employed for the fabrication of membranes. This is without any doubt due to three major causes. First of all, polymeric materials permit a better pore-forming control. Secondly, polymeric membranes can be fabricated at a lower cost in comparison to inorganic counterparts. Finally, there exists a wide range of monomers with variable functionalities that allow the preparation of membranes suitable for different separation process [1].

Another interesting classification proposed by Ng et al. [1] is depicted in Table 9.2. This classification takes into account the structure of the membrane that varies from nonporous to microporous membranes. Different separation processes through passive transport membranes can be found depending on the driving force employed. As a result, membranes with different gradients (e.g., concentration or pressure or by an electrical field) have been reported.

As introduced above, several major characteristics including the low operation cost, relatively small footprint, and complicity with environmental regulations have provoked that polymers have been extensively employed for the fabrication of membranes. Polymeric membranes do not require the use of additives. This permits these membranes to be active at low temperatures thus enabling a significant decrease of

Table 9.2 Membrane classification for the separation processes via passive transport

Membrane barrier configuration	Transmembrane gradient		
	Concentration	Pressure	Electrical field
Nonporous	Pervaporation (PV)	Gas separation (GS)	Electrodialysis (ED)
		Reverse osmosis (RO)	
Microporous pore diameter dp ≤2 nm	Dialysis (D)	Nanofiltration (NF)	
Mesoporous pore diameter dp=2–50 nm	Dialysis	Ultrafiltration (UF)	Electrodialysis
Macroporous pore diameter dp=50–500 nm		Microfiltration (MF)	

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the energy employed for the separation in comparison with other processes. In addition, these membranes are easily formed and up-scaling and downscaling can be easily carried out [1, 2]. As a result, polymeric membranes have found interest in many different applications such as drug delivery [3] or whey protein fractionation using polyether sulfone (PES) [4, 5], polysulfone [4, 6], and cellulose [7, 8] membranes on a laboratory scale.

This chapter will provide a brief description about polymeric membranes focusing on one of the major remaining issues, that is, their contamination by microorganisms and, in particular, by bacteria. Upon a concise analysis of the problem, the alternative approaches developed to produce antifouling/antibacterial membranes will be thoroughly analyzed. For detailed reviews on membrane fabrication and their applications, the reader is referred to the following publications [2, 9–13].

9.2   Contamination of Polymeric Membranes

As mentioned above, polymers are among the most favorable membrane materials mainly because their unique film forming ability, their mechanical strength, chemical and thermal stability, as well as both corrosion and oxidation resistance. In spite of this, a critical aspect in the design of polymer membranes is related to their inherently hydrophobic character. Hydrophobic materials exhibit important drawbacks associated to their increase in resistance to water permeation and, therefore, the energy consumption. In addition, colloids, organics as well as microorganisms present in the solution tend to be absorbed onto the membrane surfaces and, in the case of porous membranes, into pore walls, leading to membrane fouling. In summary, several kinds of fouling may occur in membrane systems, such as organic fouling, particulate and colloidal fouling, crystalline fouling, and also microbial fouling [12]. The fouling materials introduced an additional barrier that may even block the membrane pores limiting or completely preventing the solvent to be transported

through the membrane. In this situation, the transmembrane pressure increasing while the permeate productivity is reduced. Fouling is, thus, an undesirable process that finally produces a degradation of the membranes or at least a significant reduction of the membrane performances [14, 15]. This is particularly common in water and wastewater treatment applications [16].

Membrane technologies are paying special attention to this phenomenon attempting to design and fabricate membranes able to remove contaminants without production of any harmful by-products, especially in water and wastewater treatment processes. Nevertheless, even after decades of development, fouling still remains one of the major limitations of polymeric membranes that decline the flux to a large extent, particularly, in industrial wastewater treatment processes [17]. It is worth mentioning that severe membrane fouling may either require extensive chemical cleaning processes or, in the worst case, membrane replacement increasing the operation costs.

As will be depicted, the main approach for minimizing polymeric membrane fouling requires the prevention of the undesired both adsorption and adhesion processes. This will, completely prevent or, at least to some extent, difficult the accumulation of colloids, particles, or microorganism at the membrane surface.

9.2.1 Membrane Biofouling

While fouling is a general problem when using membranes, membrane biofouling which referees to dynamic processes of microbial adhesion and colonization as well as growth at the membrane surface [18, 19] is present in almost all aqueous media [20]. Biofouling remains, for instance, the most technical challenges in the desalination industry, since microbial adhesion decreases the permeate flux, shortens the lifetime of the membrane and, as a consequence, increases the operational costs [14, 15]. Similar to other polymeric surfaces (see Chap. 5), when the microorganism is established at the surface, they start to produce extracellular polymeric secretions (EPS). EPS comprise many different biomolecules including proteins, glycoproteins, lipoproteins, and polysaccharides among others [13] and is at the origin of the biofilm formation [21–23]. A crucial step is, therefore, the initial adhesion. Many different research groups have focused their efforts in the prevention and/or reduction of undesired interactions between foulants and the membrane surface.

In order to avoid fouling, different strategies have been proposed that, otherwise, usually resorts to the chemical modification of the membrane to either render the surface hydrophilic or to incorporate functional groups with either/both antifouling and antimicrobial properties [24]. Equally, reduce membrane surface roughness or the modification of the membrane surface charge with molecules that have the same electrical charge as the foulants have also been explored [19]. Hence, the following paragraphs of this chapter will describe recent advances in the devel-

opment of either antifouling or antimicrobial membranes through surface modification.

9.3   Strategies for the Modification of Polymeric Membranes

Various technical solutions have been proposed in order to overcome biofouling. These include chemical and physical membrane cleaning, pretreatment process installation, or ultrasonic entrenchment. Also physical cleaning techniques have been employed to limit biofouling. For instance, relaxation and backwashing (when permeate is used to flush the membrane backwards) is nowadays standard strategies incorporation in the operating process [25]. Nevertheless, the surface modification of membranes is nowadays one of the most important research areas since (as will be depicted) many different studies demonstrated that biofouling can be significantly reduced by fabricating functionalized (mainly hydrophilic) membranes [26]. In this context, the most extended procedures to functionalize membrane surfaces are:

(a) Membranes produced from polymer blends

Blending different polymeric materials or polymer with inorganic compounds is a convenient way to avoid complicated synthetic steps to prepare membrane materials with precisely defined hydrophilicity. This strategy was employed by Wang et al. [27] to prepare ultrafiltration membranes with enhanced protein-adsorption-resistant ability. They employed as the first component branched amphiphilic copolymers P123-*b*-PEGs, prepared by reacting Pluronic P123 with PEG400 using PCl_3 as a conjugation reagent. The second component of the blend is polyethersulfone (PES). The authors evidenced an enrichment of PEG segments at blend membrane surface directly related to the PEG arm number in the P123-*b*-PEG copolymers. Moreover, they observed that the protein adsorption amount was significantly decreased.

PEG was also employed by Mural et al. [28] as one of the components in combination with different polymers such as amine-terminated grapheme oxide ($GO–NH_2$), in situ formed polyethylene-grafted GO (PE-g-GO) and their combinations with maleated PE (maleic anhydride-grafted PE) to produce antifouling membranes. Upon finding the best blends with improved mechanical properties having a uniform dispersion of PEG, selected membranes were also tested for their antibacterial properties. In particular, they inoculated *E. coli* culture with the membranes and imaging at different time scales. They concluded that the developed polymeric membranes do not support live bacteria or bacterial growth and can act as an antibacterial membrane.

Wu et al. [29] employed inherently antimicrobial natural polymers as one of the components to fabricate the membrane. They blended chitosan known for their antimicrobial properties and cellulose by casting films from trifluoroacetic acid. Two interesting properties were found in these membranes. On the one hand, they present low water vapor transpiration rate, which prevented excessive

dehydration of the wound. On the other hand, chitosan/cellulose blend membrane was effective against *E. coli* and *S. aureus* [30]. Later, they developed membranes based also on chitosan in which another antimicrobial component $Ca_3V_{10}O_{28}$ was added in order to provide a synergistic effect. These membranes were prepared by self-assembly of $V_{10}O_{28}^{6-}$ and chitosan using the Ca^{2+} ion linkers. The complex membranes exhibited larger antimicrobial activity in comparison to the individual components against *S. aureus* and *E. coli* [31].

(b) Application of surface coatings and surface functionalization of membranes

In order to decrease the high susceptibility to fouling in commercial polyvinylidene fluoride (PVDF) ultrafiltration membranes (UF), Asatekin et al. [32] fabricated membranes coated with the amphiphilic graft copolymer poly(vinylidene fluoride)-graft-poly(oxyethylene) methacrylate, PVDF-*g*-POEM to create thin-film composite (TFC) ultrafiltration membranes. Reversible fouling occurring typically during the first hours was observed in these membranes during the first 10 days. Thus, the fouling performances of the membrane and, in addition, the effluent water quality were significantly improved in comparison to the base PVDF membrane. By using the atomic force microscope (AFM) colloid probe technique, the authors evidenced the presence repulsive steric interactions, which is, most probably the cause of the low adhesion of foulants to the membrane.

Poly(ethyelene glycol) (PEG) is by large the most extensively employed for the preparation of antifouling coatings on membranes. Another example of the use of this polymer has been reported by Ju et al. [33] that prepared cross-linked poly(ethylene glycol) diacrylate materials via free-radical photopolymerization of poly(ethylene glycol) diacrylate (PEGDA) solutions in water. These materials were employed as fouling-resistant coating in UF membranes. By varying the chain length of the PEGDA as well as the amount of water introduced in the initial feed, the authors varied the permeability of the membranes between 0.5 and 150 L μm/(m^2 h bar). In addition to the permeability, the fouling resistance of the membranes was characterized via static protein adhesion experiments. The authors evidenced that the membrane surfaces are more hydrophilic in samples prepared with a larger amount of water in the initial feed and with longer PEGDA chains and, therefore, exhibit less BSA accumulation.

Another interesting example of the fabrication of surface antifouling coatings has been reported by Sagle et al. [11, 34]. Similarly to the previous example, PEG was introduced for their antifouling properties but in this case forming part of hydrogel networks. They initially prepared three series of hydrogel using PEGDA as cross-linking agent and varied the monomer employed: acrylic acid (AA), 2-hydroxyethyl acrylate (HEA), or poly(ethylene glycol) acrylate (PEGA) as comonomers [11]. By modifying the cross-link density, both water uptake and water permeability for materials of constant chemical composition could be finely tuned. In addition, they identified that the incorporation of a comonomer reduced hydrogel cross-link density, and therefore increased the water sorption accordingly. These preliminary work demonstrated based on contact angle measurements that *n*-decane in water, oil exhibited a low affinity

for the surfaces of these polymers. In a subsequent study, the authors applied these hydrogels to commercial reverse osmosis (RO) membrane and provided a thorough study of the fouling properties of these membranes [34]. In particular, they have shown by Zeta potential measurements that the hydrogel coating slightly reduced the negative surface charge of the RO membrane.

Moreover by applying an oil/water emulsions model, they described that the surfactant charge played a major role in membrane fouling. More precisely, a strong decline in water flux was observed when using a cationic surfactant (dodecyltrimethyl ammonium bromide (DTAB)). On the contrary, little or no flux decline was measured in the case of an anionic surfactant (sodium dodecyl sulfate (SDS)). In spite of these differences, the coated membranes experienced low fouling in oil/water emulsions. For example, in the case of emulsions prepared from DTAB and *n*-decane, the water flux of the commercial RO membrane decreased down to 26 % of its initial value after 24 h. On the contrary, in the case of PEGDA-coated RO membrane the water flux remains in values of 73 % of its initial value.

(c) Incorporation of nanoparticles in membranes

The incorporation of nanoparticles in polymeric membranes has been the center of a large number of studies during the last decade in order to produce membranes with improved antifouling properties. Several strategies have been proposed to incorporate nanoparticles in polymeric membranes being the two most common [1]:

– *Direct casting* from solutions containing both polymers and nanoparticles in the solvent in a precise ratio [35–40]. Nevertheless, in some cases, the use of dispersants is a requirement in order to produce homogeneous particle distributions [41, 42]. This strategy has been employed by Yu et al. [36] to fabricate poly(vinylidene fluoride) composite membranes filled with different weight fractions of SiO_2 nanoparticles.

– An alternative to the direct blending in a solution methodology is the wet *phase inversion method*. The membranes are, in this case, fabricated by immersion of a glass plate into a coagulation bath of water at room temperature [43–46]. A large variety of nanoparticles have been employed to prepare hybrid membranes by this methodology including TiO_2 [47–49], SiO_x [50], CdS [51] ZrO_2, [52] or Fe_3O_4 [53]. The particles incorporated provide unique properties that, together with those of the polymeric material can produce membranes with tailor-made characteristics. For instance, it has been demonstrated that inorganic nanoparticles finely dispersed in a polymeric matrix significantly improved the membrane performance, among others, for ultra and nanofiltration [54–57] as well as for pervaporation and gas separation processes [10, 58].

An illustrative example of the superior performance of hybrid membranes has been reported by Bottino et al. [56]. This group reported the fabrication of organic–inorganic membranes composed of silica nanoparticles dispersed in poly(vinylidene fluoride). According to the authors, by increasing the amount

of silica nanoparticles the resulting membranes exhibit both higher permeate flux and lower retention. In addition, the addition of silica increases the viscosity of the casting solutions that simplifies the casting processes when using nonwoven supports.

Finally, it is worth mentioning that, in addition to inorganic charges, also polymeric nanoparticles have incorporated on membranes. For instance, Xu et al. [59] prepared a series of pyromellitic dianhydride (PMDA)/oxydianiline (ODA) polyimide (PI) membranes filling with polystyrene (PS) and poly(styrene-*co*-4-vinylpyridine) (PSVP)-nanoparticles.

(d) Functionalization by *grafting-from* and *grafting-onto* membrane surfaces

Polymerization from surfaces having immobilized initiators (*grafting-from* methodology) and the covalent attachment of preformed polymer chains onto surfaces with complementary functional groups (*grafting-onto* approach) have also been investigated to produce nonadherent membranes. The *grafting-from* approach was employed by Zhang et al. [60]. They prepared polyamide membrane surfaces grafted with a zwitterionic poly(sulfobetaine methacrylate) (pSBMA) via surface-initiated atom transfer radical polymerization. In comparison to the untreated membranes, these functionalized membranes displayed a remarkable increase in water flux (~65 %) while the amount of irreversible proteins adsorbed was considerably reduced by ~97 %. A similar strategy, i.e., surface initiated polymerization was also recently employed by Meng et al. [61] to fabricate responsive thin-film composite reverse osmosis (TFC RO) membrane. These easy-cleaning membranes were obtained by anchoring a zwitterionic poly (4-(2-sulfoethyl)-1-(4-vinylbenzyl) pyridinium betaine) (PSVBP) onto the surface of a polyamide membrane. The PSVBP was effectively grafted via redox-initiated graft polymerization. The polyamide-grafted-PSVBP (PA-*g*-PSVBP) demonstrated a significant increase in the salt rejection. However, a cross-flow protein fouling experiment for about more than 4 days evidenced that the PA-*g*-PSVBP membrane exhibit greater antifouling properties in the short term but lost the benefit for long-term operation.

The *grafting-onto* approach has been employed by Li et al. [62] to prepare zwitterionic-catechol conjugates by modifying a catechol molecule to introduce an initiator. Atom transfer radical polymerization (ATRP) of *N*-(methacryloxyethyl)-*N*,*N*-dimethylammonium betaine monomers (SBMA) was employed to produce catechol-containing zwitterionic polymers with narrow molecular weight distributions and precise molecular weights as shown in Fig. 9.1. Then, mild de-protecting conditions (using tetrabutylammonium fluoride) were employed to remove the catechol protecting groups before covalently attach the pSBMA-catechol onto the modified surface. In order to control the amount of polymer anchored different binding experiments were carried out on surfaces, including methyl (CH$_3$), hydroxyl (OH), and amino (NH$_2$)-terminated self-assembled monolayers (SAMs) as well as unmodified gold. The authors observed that by optimizing the experimental conditions, the coated surfaces are extremely resistant to nonspecific protein adsorption independently of the complexity and variety of proteins present in the solution. In addition, the
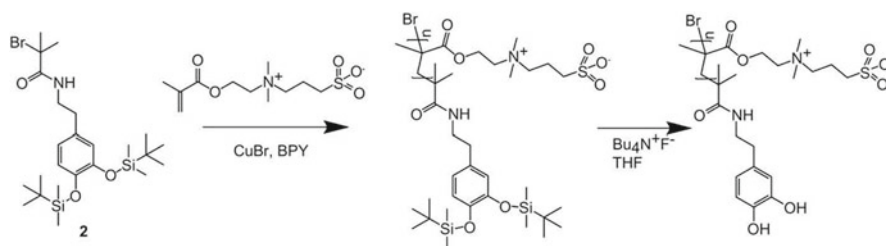
Fig. 9.1 Reaction steps for the grafting of pSBMA from the catechol initiator via ATRP and subsequent deprotection of hydroxyl groups before surface adhesion

authors explored the accumulation of *P. aeruginosa* during 3 days on the coated surfaces evaluating the amount of attached *P. aeruginosa* on the modified and non-modified surfaces. While, on the untreated glass surface, fast bacterial adhesion and subsequent biofilm formation of *P. aeruginosa* was observed, the adhesion of *P. aeruginosa* on the treated surface decreased by 99.6%.

9.4 Types of Antifouling/Antimicrobial Polymers Employed in the Fabrication of Membranes

9.4.1 Membrane Surface Modification with Anti-Adhesive Polymers

The most extended strategy to prepare antimicrobial/antifouling membranes involve the surface chemical modification introducing the appropriate functional groups [20]. Several functional groups can be attached to the surface to render the membrane surfaces anti-adhesive against bacteria.

(a) Incorporation of polyethylene glycol (PEG) at the membrane surface
   Polyethylene glycol is a highly hydrophilic and neutrally charged polymer well known for its extremely low-fouling ability that, among others, prevents the non-specific protein adsorption as well as significantly reduces cell adhesion [34, 63, 64]. In particular, this polymer forms hydrogen bonds in aqueous solutions that in addition to increase the surface hydrophilicity decreases the number of interactions with nonspecific proteins [63, 65]. The immobilization of PEG chains on surfaces, also known as PEGylation, has been explored to fabricate low fouling membranes by different research groups employing a variety of alternatives. In an exhaustive work, Gol et al. [65, 66] succeeded in the preparation of pegylated polyamides by in situ PEGylation of conventional poly(piperazineamide) thin-film composite nanofiltration (TFC NF) membranes. As depicted in Fig. 9.2, the authors explored three different alternatives to fabricate pegylated membranes

PEGylation of polyamide TFC NF membranes
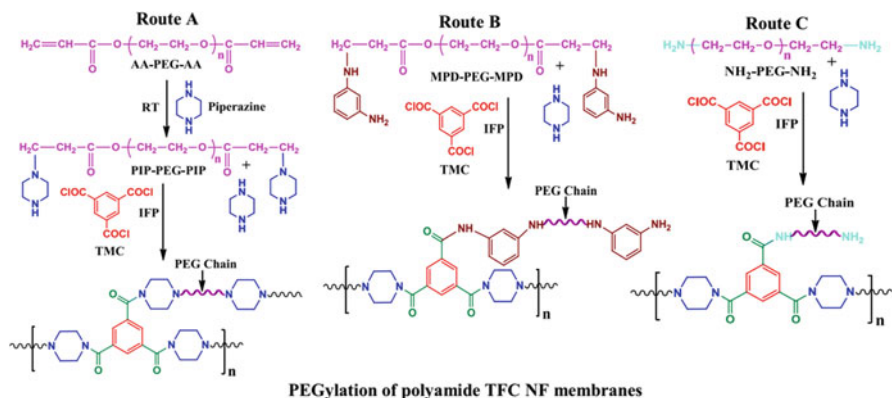
Fig. 9.2 PEGylation of TFC NF membrane via interfacial polymerization (IFP) between TMC and (**a**) PIP+PIP−PEG−PIP (in situ generated), (**b**) PIP+MPD−PEG−MPD, and (**c**) PIP+H$_2$N−PEG−NH$_2$ mixtures. Reproduced with permission from [65]

involving the interfacial polymerization between trimesoyl chloride (TMC) and (a) piperazine (PIP)+piperazine-terminated polyethylene glycol (PIP–PEG–PIP), (b) PIP+m-phenylenediamine-terminated PEG (MPD–PEG–MPD), and (c) PIP+alkyl amine-terminated-PEG (H$_2$N–PEG–NH$_2$) mixtures, respectively.

In comparison to the standard polyamide networks, these pegylated membranes significantly reduced the nonspecific protein adsorption probably due to the hydrophilization of the membrane network but also due, according to the authors, to two other important aspects. On the one hand, the authors reported a decrease of the surface roughness that limits the surface area and prevent the formation of any protein accumulation on eventually present micrometer size valleys. On the other hand, the steric hindrance of as a consequence of the incorporation of the PEG chains that is not present in the non-pegylated membranes [65, 66].

Microporous membranes prepared using the breath figures approach were reported by Martínez-Gómez et al. [67]. This approach permits the fabrication in one single step of hexagonally arranged porous surfaces with variable chemical composition by simply evaporating a polymer solution in a moist atmosphere. These authors prepared polyimide copolymers having pendant poly(ethylene oxide) (PEO) chains, that is, polyimide-g-PEO copolymers. The incorporation of PEO side chains enhanced the solubility of the polymers in chloroform (solvent employed for the breath figures approach due to the high volatility) and permits a particular orientation of these chains toward the inner part of the pores. As a result, PEO would work as antifouling compound to avoid the adhesion of microorganisms onto the porous films. The authors established that surface modified polyimide membranes exhibited a high resistance to biofouling against *S. aureus*. As depicted in Fig. 9.3, the antifouling performance is directly related to the amount of PEO chains within
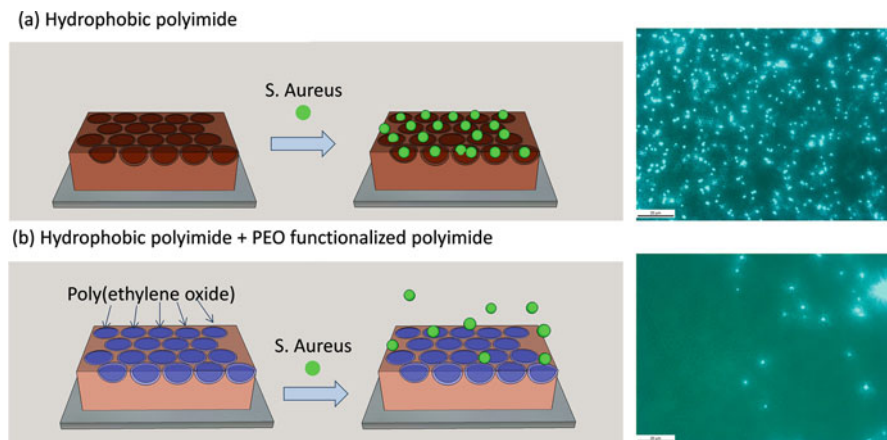
Fig. 9.3 Bacterial adhesion on honeycomb structured films. The presence of PEO groups reduced the amount of *S. aureus* that adhere to the porous films. Adapted from [67]

the pores. In particular, the authors evidenced an increase in the amount of PEO in the blend employed to prepare the porous films produced a reduction in the bacterial adhesion.

Nevertheless, serious limitations in the use of PEG are still trying to be resolved being the most relevance the effect of oxygen and transition metal ions on the PEG chains that oxidize the structure and finally degrade the polymer [64, 68, 69].

(b) Incorporation of natural hydrophilic polymers

Probably *sericin* is a natural, water-soluble protein bearing polar side groups: carboxyl, amino groups and hydroxyl [70, 71] extensively employed to functionalize polymeric membranes. For instance, *sericin* has been coated on the surface of commercial thin-film composite membrane for reverse osmosis (TFC-RO) membranes and covalently anchored by chemical cross-linking with glutaraldehyde (GA) [71]. The *sericin*-coated membrane presented reduced water permeability (as a result of the additional hydraulic resistance), but on the other hand improved salt rejection as a consequence of the enrichment of surface negative charge. More interestingly, the resistance of these membranes to BSA fouling was enhanced based on the combination of three important features: improved surface hydrophilicity, high surface negative charge, and smoothed surface morphology [71].

Also, Zhou et al. [70] employed *sericin* to, upon reaction with trimesoyl chloride (TMC) in an interfacial polymerization process, produce antifouling membranes. The fouling test confirmed that the sericin-TMC composite membrane has improved the fouling resistance to sodium alginate (SA) and BSA in comparison to homologous commercial membranes. In agreement with

other reports, the authors hypothesize that this phenomenon is basically due to the greater electrostatic repulsion between the *sericin*-TMC membrane (negatively charged) and the foulant molecules [70].

(c) Coating membranes with hyperbranched polymers

Polymers with a high density of hydrophilic end groups, hyperbranched polymers or dendritic, have also been employed to impart protein resistance to polymer membranes [72, 73]. For instance, Nikolaeva et al. [72] employed hydrophilic hyperbranched poly(amido amine) (PAMAM) to modify TFC membranes. PAMAM is a low cost material that can be produced in a simple one-pot polymerization step and can be easily purified. They fabricated RO membranes by interfacial polymerization (IP). More precisely, a thin polyamide separation layer was coated onto a porous poly(ether sulphone) support employing *m*-phenylenediamine (MPD) and trimesoyl chloride (TMC) as reactants for the IP. The acid chloride groups that remained non-converted during the interfacial polymerization are, in turn, employed to covalently anchor PAMAM to the PA layer forming amide bonds between TMC groups of the PA layer and amine groups of PAMAM dendrimer. The modification was achieved by spraying a solution of PAMAM onto the membrane surface either using methanol (PAMAM1) or water (PAMAM2). In contrast to the unmodified membranes, independently of the solvent employed both strategies led to membranes with a substantial increase in water flux. However, taking into account the required salt rejection and protein adsorption, PAMAM2 was preferred over the use of methanol (PAMAM1). This is mainly due to the creation of supplementary hydrophilic PAMAM layer, which behaves similar to a hydrogel layer when in contact with water (Fig. 9.4) [72].

(d) Surface membrane functionalization with zwitterionic polymers

Polymers bearing zwitterionic functional groups have gained special attention as a new group of fouling-resistant materials [60, 61, 74]. Zwitterionic functional groups incorporate both positive and negative charged units and are able to establish strong electrostatic interactions with water (even stronger than standard hydrophilic materials). Azari et al. [74], based on the unique adhesive proteins found in mussel, fabricated a zwitterionic amino acid, L-DOPA (3-(3,4-Dihydroxyphenyl)-L-alanine) that was effectively anchored on the membrane surface in order to resist protein fouling. Due to the functional groups contained in L-DOPA such as acid groups, carboxylate, hydroxyl, or amino [74] after L-DOPA immobilization a significant increase in membrane hydrophilicity was observed. The water flux increases accordingly to the surface hydrophilicity while the salt rejection remains unaffected. More interestingly, during filtration tests with BSA and alginic acid solution, the authors reported that in the unmodified membrane only 62 % of its initial flux was measured while the modified membrane retained about 82 % after 16 h [74].

Other zwitterionic groups employed as antifouling in membranes include poly(sulfobetaine methacrylate) (pSBMA) that was grafted onto the polyamide membrane surface via surface-initiated atom transfer radical polymerization [60, 75] or (4-(2-sulfoethyl)-1-(4-vinylbenzyl) pyridinium betaine) (PSVBP) anchored onto the polyamide surface [61].
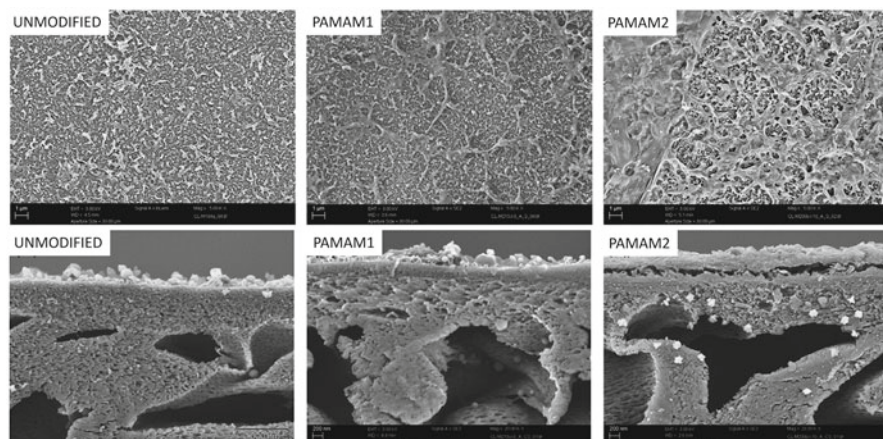
Fig. 9.4 SEM images of membrane surfaces (*above*) and cross-sectional profiles (*below*) of unmodified, TFC PAMAM1, and TFC PAMAM2
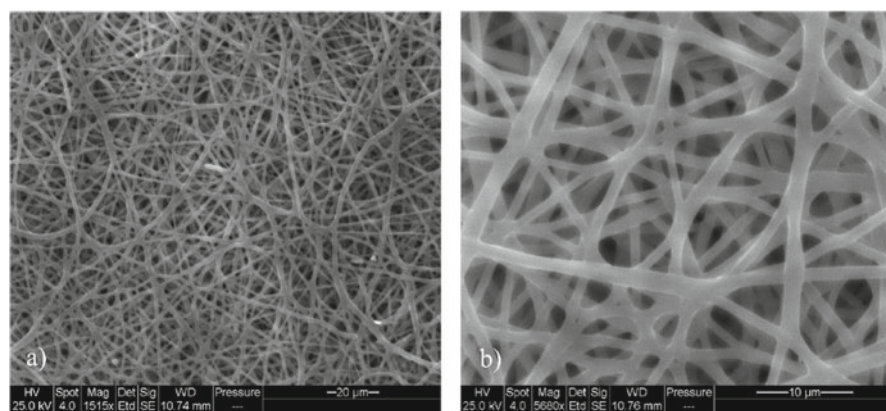
Fig. 9.5 Scanning electron micrographs of PSBMA electrospun membranes. Reproduced with permission from [75]

For instance, Lalani et al. [75] employed zwitterionic PSBMA known for its superhydrophilic and ultralow biofouling properties to fabricate water stable electrospun membranes (Fig. 9.5). They described a three-step involving a polymerization, an electrospinning step and finally a photo-cross-linking process. As a result, the electrospun membrane showed strong resistance to protein adsorption and cell attachment. Equally, bacterial adhesion studies using Gram-negative *P. aeruginosa* and Gram-positive *S. epidermidis* revealed that the PSBMA electrospun membrane was also highly resistant to bacterial adhesion. More interestingly, the authors fabricated Ag+-impregnated electrospun PSBMA membranes in order to confer antimicrobial properties to the membrane.

These membranes exhibit antimicrobial activity against both *S. epidermidis* and *P. aeruginosa*. According to the authors, such electrospun PSBMA-based membranes are excellent candidates for novel nonadherent, superabsorbent, and antimicrobial wound dressing.

Using a similar strategy Liu et al. [76] reported the preparation of antimicrobial fibers. Their strategy involves three consecutive steps, i.e., pre-polymerization, electrospinning, and finally photo-cross-linking process that leads to water-stable cross-linked electrospun zwitterionic PSBMA fiber. The fibers were employed to construct a membrane that exhibited strong resistance to protein adsorption as well as cell attachment. Moreover, as depicted in Fig. 9.6, 3 h bacterial incubation results evidenced that the PSBMA electrospun membrane exhibited small bacterial adhesion for both *P. aeruginosa* and *S. epidermidis* in comparison with other electrospun fibers such as polycaprolactone (PCL) or using standard supports such as tissue culture polystyrene (TCPS) or glass. Equally, bacterial adhesion tests carried out during 24 h show that the PSBMA electrospun membranes still exhibited the lowest bacterial adhesion for both species. In addition to the antifouling properties observed in the PSBMA fibers, the authors explored the antimicrobial activity of the silver-incorporated electrospun PSBMA membrane. $AgNO_3$ was incorporated into the electrospun PSBMA membrane by means of ionic interactions and the antimicrobial activity of the Ag^+-impregnated membrane was determined using a zone-of-inhibition method. The authors found that the electrospun PSBMA membranes infused with silver nitrate inhibit the growth of both *P. aeruginosa* and *S. epidermidis*. The zone of inhibition was 6.3 mm for *P. aeruginosa* and 3.6 mm for *S. epidermidis* after 24 h of incubation.

These membranes are promising materials among others for wound dressing purposes since they can prevent attachment and entry of the environmental pathogens to the wound. In addition to the protection capabilities, the dressing applied to the wound would not require often replacement, thus decreasing the probability of further contamination by introducing bacteria upon exposure of the wound site to the environment.

9.4.2 Antimicrobial Biocides and Polymers Incorporated in Polymeric Membranes

In addition to the use of microbial repellent molecules several groups have focused in the incorporation of biocidal groups able to kill those bacteria upon contact with the membrane surface. Some of the most relevant antimicrobials employed to functionalize membrane surfaces are depicted below:
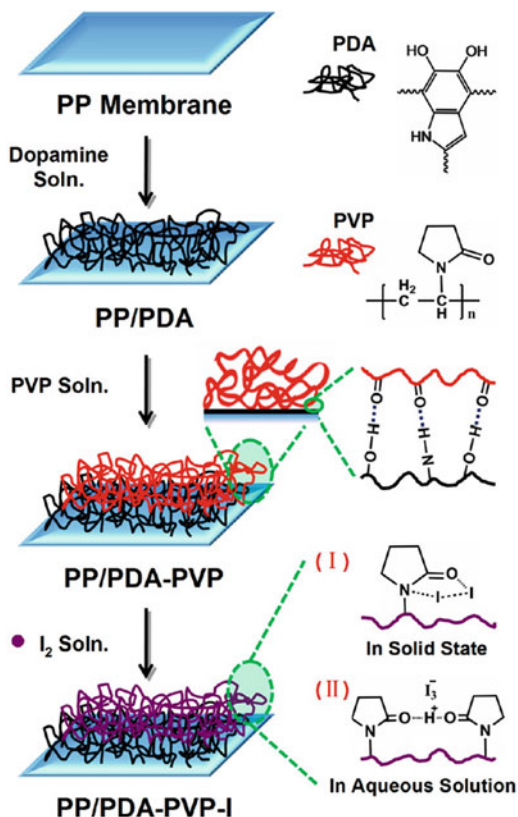
(a) Polydopamine
    Polydopamine (PDA) has been straightforwardly employed for the preparation of antimicrobial and antifouling membranes by a simple dip-coating process.
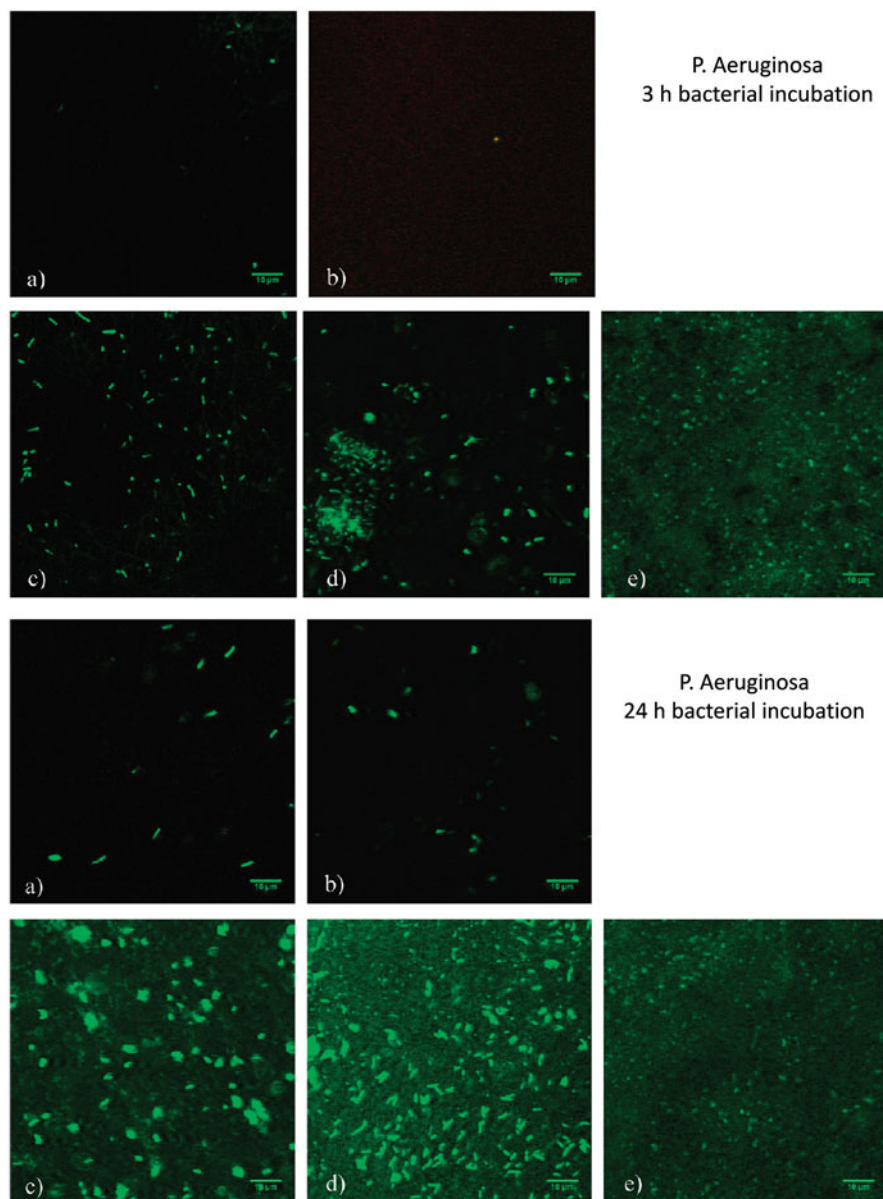
Fig. 9.6 Fluorescence microscopy images of *P. aeruginosa* immobilized onto electrospun PSBMA (**a**), PSBMA hydrogel (**b**), electrospun PCL (**c**), TCPS (**d**), and glass (**e**) at 3 and 24 h. Reproduced with permission from [76]

Fig. 9.7 Scheme of coating polydopamine (PDA) on a PP membrane as well as subsequent PVP and iodine complexation. Reproduced with permission from [24]

PDA forms strongly adherent PDA layer over an extensive variety of material surfaces by dipping the polymeric material on dopamine aqueous solution. Jiang et al. [24] employed this strategy (see Fig. 9.7) to coat hydrophobic poly-propylene (PP) porous membrane with a PDA layer that served, in turn, to via hydrogen-bonding interactions between PVP and PDA anchor poly(*N*-vinyl pyrrolidone) (PVP). The PVP layer anchored on the membrane surface exhibit long-term stability because of the strong non-covalent forces between PVP and PDA coating. As a result, and based on the well-known anti-adherent properties of PVP, the permeation fluxes and antifouling properties of the membranes were improved as evaluated in protein filtration, adsorption tests, and oil/water emulsion filtration.

Additional antimicrobial activity was achieved by iodine complexation with the PVP layer. In order to evaluate the activity against bacteria the authors employed *S. aureus* and found that the sum for viable colonies con-siderably diminished after contacting with PP/PDA-PVP-I membrane for 24 h. Moreover, the relative viability of the *S. aureus* was lower than 0.1 % and the log decrease achieved more than 3 for the PP/PDA-PVP-I membrane (99.9 % of the *S. aureus* were killed).
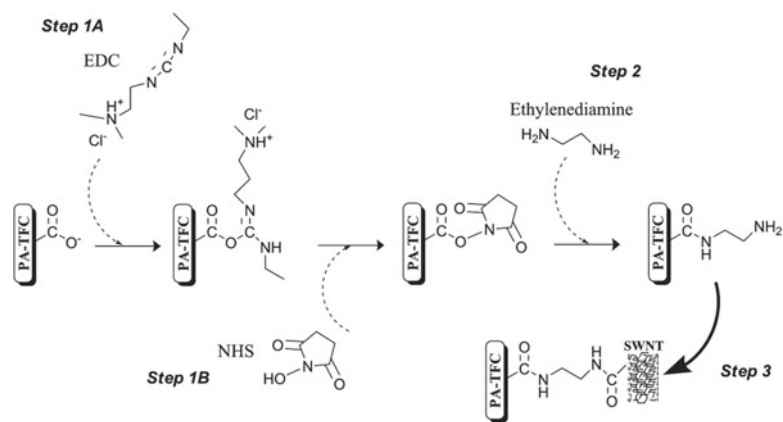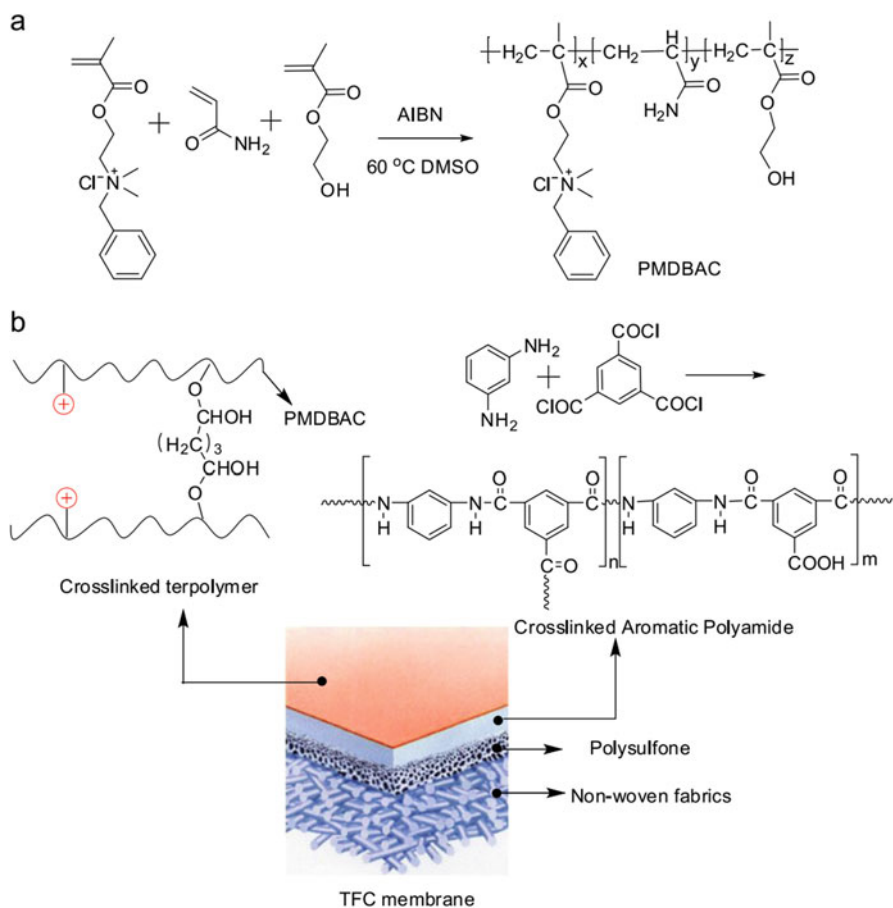
(b) Membranes bearing antimicrobial polymers

Antimicrobial polymers immobilized on the surface of TFC membrane surface have been employed to prevent both biofilm growth and (bio)fouling. A large variety of antimicrobial polymers have been explored including polylactams, polymers containing *N*-halamines [77, 78] or tertiary and/or quaternary ammonium groups, and polyamino acids [79].

Membrane degradations by biofouling and free chlorine oxidation are the main problems for the extensive applications of aromatic polyamide RO membranes. *N*-halamine precursors were employed by Wang et al. [77, 80] to fabricate TFC membrane with enhanced chlorine resistance and anti-(bio)fouling property. For that purpose, the authors employed a commercial RO polyamide membrane and modified the surface by free-radical graft polymerization of 3-allyl-5,5-dimethylhydantoin (ADMH). The ADMH-functionalized materials can be chlorinated and lead to the well-known antimicrobial *N*-halamines [77, 78]. The antimicrobial tests exhibited that the chlorinated membranes possessed better antimicrobial efficiencies than the non-treated membranes, and the antimicrobial functions could be successfully regenerated by chlorination. According to the author's findings, upon chlorination, the decrease *E. coli* present in at the surface of the grafted membrane was above 90 % in comparison to the unmodified membrane [77].

Quaternary ammonium groups are also recognized by their unique antimicrobial properties. For instance, Ni et al. [81] prepared hydrophilic random copolymers based on poly(methylacryloxyethyldimethyl benzyl ammonium chloride-r-acrylamide-r-2-hydroxylethylmethacrylate)   (P(MDBAC-*r*-Am-*r*-HEMA)) by simple free-radical copolymerization (Fig. 9.8). The terpolymer was later employed to coat a commercial RO membrane and anchored to the surface by glutaraldehyde (GA) cross-linking. The large hydrophilicity of the coated membranes considerably retains its flux under BSA filtration in comparison to that of pristine membranes. Interestingly, the coated membranes showed excellent antimicrobial activity to *E. coli* and inhibit bacterial growth [81].

(c) Covalent Binding of Single-Walled Carbon Nanotubes to Polymer Membranes

Single-walled carbon nanotubes (SWNTs) have been proposed to impart nanomaterial-specific properties to the surface of thin-film composite membranes. In particular, the immobilization of SWNTs at the membrane surfaces can provide additional biocidal properties. An illustrative example of the biocidal activity of SWNT on membranes has been reported by Tiraferri et al. [82]. Prior to the immobilization of the SWNTs, they first require the purification and modification (e.g., by ozonolysis) to provide the SWNT with sidewall functionalities. These functional groups will improve the cytotoxic properties and, simultaneously, improve the dispersion in aqueous solution. As depicted in Fig. 9.9, a three-step reaction protocol was established to create covalent amide bonds with the functionalized SWNTs. The first reaction step, involves the activation, with *N*-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride of the carboxylate groups of the membrane. In the second step, the carboxylic activated groups react with ethylenediamine to provide membranes surfaces reach

Fig. 9.8 Schematic diagram for (**a**) synthesis of the terpolymer P(MDBAC-r-Am-r-HEMA) and (**b**) surface modification of RO membranes. Reproduced with permission from [81]

Fig. 9.9 Procedure to covalently bind single-wall carbon nanotubes (SWNTs) to the membrane surface

in amine groups. Finally, the amine groups were employed to form amide bonds with the carboxylic acid functionalized SWNTs. The stability of the covalently anchored SWNTs was confirmed by sonication of the membranes. The authors confirmed the antimicrobial activity of the membrane surfaces against *E. coli* cells evidencing an enhanced bacterial cytotoxicity for the SWNT-coated membranes. The SWNT membranes achieved up to 60 % inactivation of bacteria anchored to the membrane within 1 h of contact time.

(d) Polymeric membranes impregnated with antibacterial nanoparticles

As has been mentioned above, the incorporation of nanoparticles in polymeric membranes increases the several membrane properties such as selectivity, permeability, mechanical strength, and, in some cases also the hydrophilicity [1, 35, 83, 84]. Examples of this behavior include the case of poly(vinylidene fluoride) membranes combined with silica nanoparticles that exhibit higher selectivity, higher diffusivity and higher temperature [36], or polysulfone membranes incorporating silica nanoparticles that showed improved gas permeability [85].

Together with these mentioned advantages, it is worth mentioning that the integration of nanoparticles into polymeric membranes has some drawbacks. Probably, the most important restrictive factor is the distribution of the nanoparticles within the polymers. Particularly difficult to disperse are nanoparticles with less than 100 nm in diameter due to the extremely large amount of surface interactions. Moreover, the causes of the agglomeration inside polymeric membranes remain controversial. Authors such as Yu et al. [86] proposed that an increase of the nanoparticle concentration favors their agglomeration. On the other hand, Benjamin et al. [87] remarked that, in addition to the nanoparticle concentration, pH and ionic strength of the solution clearly direct the agglomeration between nanoparticles.

Within this context, provided an appropriate nanoparticle dispersion and the required membrane properties (mechanical, permeability, etc.) different groups have focus on the fabrication of membranes with antibacterial properties by using, among others Ag, TiO_2, CuO, or ZnO nanoparticles.

Zodrow et al. [88] prepared polysulfone membranes (PSf) impregnated with silver-based nanoparticles (nAg) fabricated using the wet phase-inversion process [9]. For that purpose, silver nanoparticles (1–70 nm) were dispersed polysulfone membrane in the casting solution prior to the dissolution of the polysulfone resin. Zodrow et al. [88] found that polysulfone membranes with 0.9 wt% nAg (nAg–PSf) exhibit similar permeability and surface charges to the pure polysulfone membranes and did not significantly vary the membrane structure. However, the incorporation of nAg (0.9 % by weight) considerably reduced the amount of E. coli grown on the membrane surface upon filtration (Fig. 9.10). In spite of the improved properties exhibited by the membranes, some aspects still require improvement. The most important aspect is related to the leaching of Ag^+ out of the membrane with a lost about 10 % of total silver (i.e., the silver leached from the membrane mainly in ionic form). It is worth mentioning that the Ag^+ loss was mainly occurs from the surface, precisely in those areas where membrane-bacteria and membrane-virus interactions occur [88].
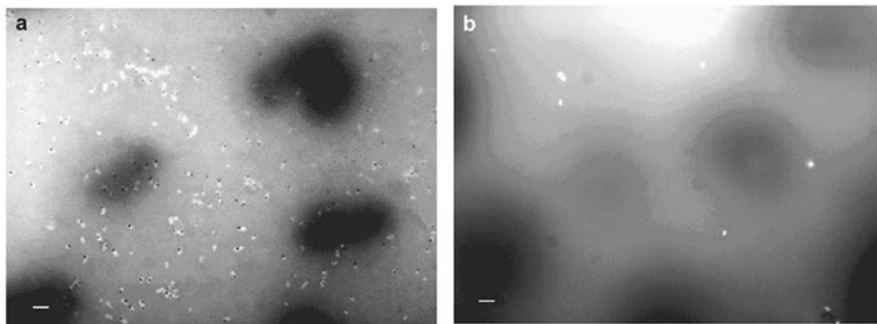
Fig. 9.10 Attachment of *E. coli* suspended in MD medium to membrane surface on (**a**) PSf and (**b**) nAg–PSf membranes. Cells were stained with DAPI and viewed with a fluorescence microscope. Scale bar indicates 5 μm. Reproduced with permission from [88]

This phenomenon has two major related drawbacks. On the one hand, leaching of silver from the membranes produced a significant decrease of the performances of the membranes as a function of time, and therefore they could be not appropriated to be used during long periods of time. On the other hand, leaching of silver nanoparticles might additionally pose the danger of water contamination if the membranes with silver nanoparticles are expected to be used in drinking water decontamination processes.

The synergistic effect of antimicrobial polymers and nanoparticles was explored by Li et al. [89] to produce chitosan/zinc oxide nanoparticles membrane displaying good mechanical properties and high antibacterial activities. The chitosan/ZnO nanoparticle (CS/nano-ZnO) composite membranes were fabricated by the sol-cast transformation method. The ZnO nanoparticles, homogeneously dispersed in the chitosan matrix, significantly improved the mechanical properties of CS/nano-ZnO composite membranes. Equally, the antibacterial activities of CS membranes against *B. subtilis*, *E. coli*, and *S. aureus* were largely enhanced by the incorporation of ZnO. In particular, composite membranes with as low as 6–10 wt% ZnO exhibited high antibacterial activities.

In addition, titanium dioxide (with similar band-gap and antibacterial activity than zinc oxide) alone or in combination with other nanoparticles has been equally employed for the fabrication of antimicrobial membranes. For example, Pant et al. [90] prepared silver-impregnated TiO_2/nylon-6 nanocomposite mats with exceptional characteristics as a filter media with simultaneously photocatalytic and antibacterial properties. For this purpose, silver nanoparticles (NPs) were incorporated in electrospun TiO_2/nylon-6 nanofibers by photocatalytic reduction of silver nitrate solution under UV-light irradiation. More importantly, the antibacterial activity of a TiO_2/nylon-6 composite mat bearing Ag NPs was evaluated against *E. coli*. In all cases, the authors evidenced that TiO_2/nylon-6 nanocomposite mats charged with Ag NPs exhibit a larger activity than those

mats without Ag NPs. Thus, the prepared material may find potential interest in the preparation of economically friendly photocatalyst and water filter media.

Finally, copper (II) oxide nanoparticles (CuO NPs) have also demonstrated notable antimicrobial properties. Yalcinkaya et al. [91] employed these Cu NPs to evaluate the antibacterial effectiveness of nanofiber composite yarns in order to potentially employ the composite nanomaterial in antibacterial filtration. The copper (II) oxide particles were immobilized at the polyurethane and polyvinyl butyral (PVB) nanofiber components of a composite yarn during the experimental tests. The antibacterial effectiveness was assessed against Gram-positive *S. gallinarum* bacteria as well as Gram-negative *E. coli.* The authors showed that the composite yarn with polyvinyl butyral nanofibers bearing CuO NPs exhibited better antibacterial efficiency compared to the yarn containing the polyurethane nanofibers. More precisely, with an amount of 5 % wt of CuO immobilized in PVB nanofibers displayed an antibacterial efficiency of 99.99 % at a production rate of 200 m/min.

9.5   Responsive Membranes

The possibility to control the membrane properties depending on the environmental conditions offers new potential alternatives to precisely control their behavior on demand.

An interesting example of responsive membranes was reported by Liu et al. [92] that employed biodegradable polymers, e.g., poly(lactic-*co*-glycolic acid) (PLGA) for the fabrication of bioresponsive membranes for wound-healing applications. Based on the PLGA/collagen wound dressing membranes that have been shown to accelerate wound healing, the authors studied the early stage open wound healing in rats. The results evidenced that electrospun PLGA/collagen membranes promoted early stage wound healing. The pictures of histological analysis showed that PLGA/collagen nanofiber revealed superior wound-healing influence in comparison to gauze and commercial dressing. After 1 week, there was no clear difference between histological sections of wounds treated by gauze, PLGA/collagen, and commercial dressing. All the tissues show inflammatory cell infiltration, granulation tissue formation, and ulcerated surface. However, after 3 weeks, the wound cured with PLGA/collagen nanofiber was almost healed, while the wounds treated with either gauze or commercial dressing, showed prominent inflammatory cell infiltration and incomplete re-epithelialization.

The salt-responsive property of polyelectrolyte membranes provides an interesting force to additionally force the release of protein foulants. Meng et al. [61] fabricated salt-responsive reverse osmosis (RO) membranes by tethering (by surface-initiated free-radical polymerization) a zwitterionic polymer poly (4-(2-sulfoethyl)-1-(4-vinylbenzyl) pyridinium betaine) (PSVBP) onto a commercially available RO membrane. Covalent grafting of PSVBP provides a negative charge to the membrane surface and, therefore, significantly improved membrane surface hydrophilicity and improved the rejection

from 98.0 to 99.7 %. The functionalized membranes exhibit higher antifouling response in the short term (less than 100 h) but lost the advantage for long-term operation. However, the PA-g-PSVBP membrane can recover 90 % of the initial flux by simply rinsing with a concentrated salt solution (brine). The salt-responsive property of the PSVBP membranes is assumed to be at the origin of the driving force for the release of protein foulants.

9.6   Conclusions

Microorganism biofouling and contamination, as well as biofilm formation, on polymeric membranes still currently a major issue limiting the use of these materials. In order to limit the adhesion of microorganism several strategies have been developed in which either antifouling or antimicrobial molecules have been incorporated within the membranes. Equally, the surface modification has been extensively explored. The incorporation of antifouling polymers such as polyethylene oxide, zwitterionic moieties, or even antimicrobial polymers such as polydopamine have significantly improved the efficiency of these membranes and enlarged their lifetime.

The incorporation of inorganic nanoparticles embedded in polymeric membranes is also a currently investigated alternative. Their incorporation has two interesting effects on the material. On the one hand, the improvement of the mechanical properties of the membrane and on the other hand the antimicrobial properties obtained when using, for instance, silver or TiO_2 nanoparticles. However, leaching still among the major problems to be faced in this case that both limits the antimicrobial activity of the membrane and could lead to the contamination of the membrane environment.

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