REVIEW ARTICLE

Membrane bioreactors for hospital wastewater treatment: recent advancements in membranes and processes

Yan Zhao[1], Yangbo Qiu[2], Natalie Mamrol[3], Longfei Ren[2], Xin Li[1], Jiahui Shao (✉)[2], Xing Yang (✉)[1],

Bart van der Bruggen (✉)[1]

1 Department of Chemical Engineering, KU Leuven, B-3001 Leuven, Belgium
2 School of Environmental Science and Engineering, Shanghai Jiao Tong University, Shanghai 200240, China
3 Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Abstract Discharged hospital wastewater contains various pathogenic microorganisms, antibiotic groups, toxic organic compounds, radioactive elements, and ionic pollutants. These contaminants harm the environment and human health causing the spread of disease. Thus, effective treatment of hospital wastewater is an urgent task for sustainable development. Membranes, with controllable porous and nonporous structures, have been rapidly developed for molecular separations. In particular, membrane bioreactor (MBR) technology demonstrated high removal efficiency toward organic compounds and low waste sludge production. To further enhance the separation efficiency and achieve material recovery from hospital waste streams, novel concepts of MBRs and their applications are rapidly evolved through hybridizing novel membranes (non hydrophilic ultrafiltration/microfiltration) into the MBR units (hybrid MBRs) or the MBR as a pretreatment step and integrating other membrane processes as subsequent secondary purification step (integrated MBR-membrane systems). However, there is a lack of reviews on the latest advancement in MBR technologies for hospital wastewater treatment, and analysis on its major challenges and future trends. This review started with an overview of main pollutants in common hospital wastewater, followed by an understanding on the key performance indicators/criteria in MBR membranes (i.e., solute selectivity) and processes (e.g., fouling). Then, an in-depth analysis was provided into the recent development of hybrid MBR and integrated MBR-membrane system concepts, and applications correlated with wastewater sources, with a particular focus on hospital wastewaters. It is anticipated that this review will shed light on the knowledge gaps in the field, highlighting the potential contribution of hybrid MBRs and integrated MBR-membrane systems toward global epidemic prevention.

1 Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory tract infection caused by a novel coronavirus (SARS-CoV-2). This disease has rapidly transmitted worldwide and has been declared a global pandemic by the World Health Organization (WHO) [1,2], and currently has already led to more than 3500000 deaths. Worldwide measures for treating and preventing COVID-19 spread have been enforced. Including intense epidemiology research, new political policies, and pandemic mitigation techniques, which have achieved initial success and slowed down the infection rate [3]. However, vaccine research efforts and patient hospitalization consume large quantities of disinfectants, drugs and other medical substances, leading to an enormous amount of discharged hospital wastewater that may ultimately transfer into the water system [4]. Generally, the hospital wastewater contains viruses/bacteria, pathogenic microorganisms, antibiotic groups, partially metabolized pharmaceutical substances, organic compounds, radioactive elements, and ion pollutants [5–7]. In fact, several case studies have reported fecal-oral transmission through wastewater as a possible vector of COVID-19 [8].

The byproduct pollutants from epidemic prevention, may lead to environmental issues and eventually deteriorate human health [9]. Therefore, effective treatment of

hospital wastewater is also an important step to prevent the spread of diseases. The traditional methods used in hospital wastewater treatment to destroy bacteria and viruses include disinfection (e.g., ozone and chlorine, sodium hypochlorite) and chlorine dioxide detoxification [10–13]. However, drugs, harmful ions, antivirals, antibacterial, and other toxic substances still remain in the hospital wastewater after the above disinfection steps. More aggressive approaches are adopted, such as high-temperature calcination, evaporation and precipitation, which may be helpful but come with high cost, environmental strain, and low efficiency. Thus, these drawbacks greatly limit the applications of these technologies in hospital wastewater treatment [14].

Membrane separation is an advanced technology in hospital wastewater treatment because of its high solute selectivity, relatively low energy consumption, easy scalability, and attractive process economics [15,16]. Membranes have been widely used in wastewater treatment to separate contaminants (such as bacteria and protozoa) or ions [17–19].

Membrane bioreactors (MBRs) mainly consist of the activated sludge process and microfiltration/ultrafiltration (UF/MF) membranes filtration for wastewater treatment and recycling. Compared to a conventional activated sludge treatment system, the secondary settling tank and sand filtration system are replaced by UF/MF membranes in the classical MBR processes. MBRs remove viruses from wastewater through a combined mechanism: steric removal, adsorption, and inactivation during biological treatment [20]. Consequently, MBRs have shown increased removal of enteric viruses in comparison to activated sludge treatment [21]. Also, MBR technology shows cost-effective with higher efficiency and low energy consumption [22], providing an advanced method to effectively separate complex contaminant mixtures and pathogenic microbes from wastewater [23].

Traditional MBRs can effectively remove activated sludge and some macromolecular organic substances [24]. However, this technology still faces challenges such as high membrane fouling propensity and low micromolecular rejection [25,26]. Many harmful microorganisms or ionic species are present in hospital wastewater, requiring thorough disinfection [27,28]. With a sustainable mindset, there is emerging interest to simultaneously remove harmful substances and recover valuable components (e.g., radioactive elements) [29]. These may require the further adaptation of the MBR units by hybridizing novel membranes (non hydrophilic UF/MF), namely hybrid MBRs; or the MBR as a pretreatment step and integrating other membrane processes as subsequent secondary purification step (e.g., nanofiltration (NF), reverse osmosis (RO), electrodialysis (ED)), namely integrated MBR-membrane systems [30,31]. With a particular interest on hospital wastewater treatment, tremendous efforts have been made to carefully design

the MBRs to achieve high separation efficiency and various purification purposes, by enhancing the solute selectivity (or rejection) and membrane flux, as well as reducing the fouling tendency [32,33].

However, there is a lack of reviews on the latest advancement in MBR technologies designed for hospital wastewater treatment, and analysis on its major challenges and future trends. This review starts with an overview of main pollutants in common hospital wastewater, follows by an understanding on the key performance indicators/criteria in MBR membranes (i.e., solute selectivity) and processes (e.g., fouling). Then, an in-depth analysis was provided into the recent development of the concepts on hybrid MBRs and integrated MBR-membrane systems, and applications correlated with wastewater sources, with a particular focus on hospital wastewaters. It is anticipated that this review will shed light on the knowledge gaps in the field, highlighting the potential contribution of hybrid MBRs and integrated MBR-membrane systems toward global epidemic prevention.

2 Components of hospital wastewater

Hospitals and medical activities use purified water every day, leading to the discharge of a high volume of hospital wastewater. This hospital wastewater contains complicated compounds from diagnostic activities, laboratory research, epidemic prevention/sanitation, and medicine excretion. Depending on a variety of toxic or persistent substances, the components of typical hospital wastewater include pathogenic microorganisms (e.g., coronavirus, enterovirus, hepatitis A virus, *Staphylococcus aureus*, sulfite-reducing anaerobes), antibiotic groups (e.g., enrofloxacin, ciprofloxacin, oxalinic, ofloxacin, norfloxacin, sulphapyridine, trimethoprim, metronidazole, and their metabolites), common organic compounds pollutants (e.g., pharmaceutical residues, carbohydrates, proteins, amino acids, generic drugs, esters, organic solvents), and ionic pollutants (e.g., heavy metals, contrast agents) [34], as shown in Fig. 1.

2.1 Pathogenic microorganisms

Viruses are composed of internal nucleic acids surrounded by a protective protein coating and typically have diameters between 20 and 300 nm (some filoviruses have a total length around 1400 nm). Due to their sizes, viruses are difficult to detect, isolate and classify [35]. However, they are the most abundant biological entities in our biosphere and play a significant role in genetic diversity [36]. Furthermore, viruses rely on a range of hosts to survive and repopulate and impart considerable reactions, sometimes averse to the host, called cytopathic effects [37]. Virus transmission in different organisms requires mobile media; for example, COVID-19 may spread
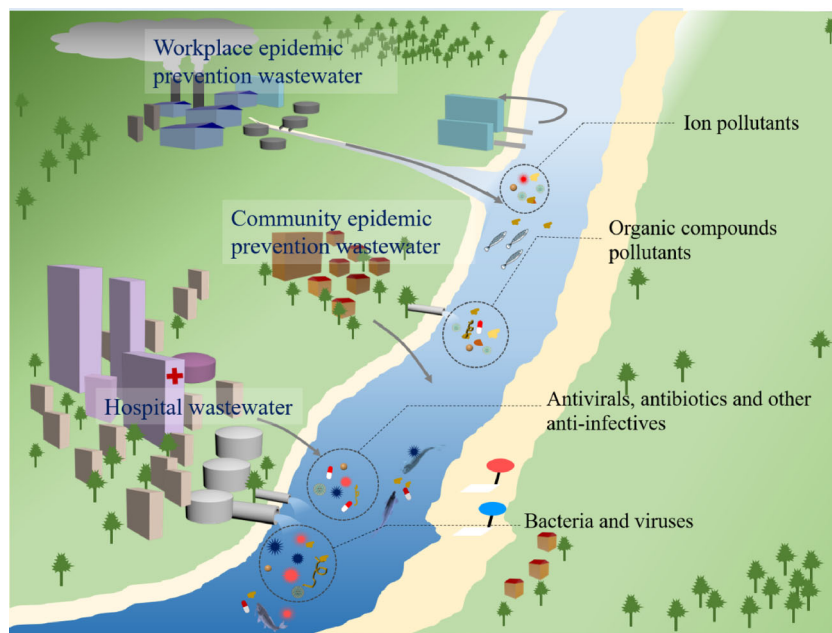
Fig. 1 The hospital wastewater, community epidemic prevention, and workplace epidemic prevention containing large amounts of water-borne bacteria and viruses, antivirals, antibacterial, and other anti-infectives, organic compounds, and ionic pollutants.

between humans through direct or indirect contact, respiratory droplets, and possibly, through fecal-oral transmission. A separate study revealed that coronavirus could remain infectious in wastewater for days to weeks [38] and contaminated water may also increase the risk of transmission.

Unlike viruses, bacteria are larger (typically several micrometers in length) and have a cellular structure. Bacteria can inhabit in water, soil, and gaseous environments and contribute to symbiotic and parasitic relationships with plants, animals, and humans [35]. Many of them are rendered harmless, but several species of bacteria are pathogenic and cause infectious diseases (e.g., *Staphylococcus aureus*, sulfite-reducing anaerobes) [39]. Due to the high concentration of viruses or bacteria in the hospital wastewater, the development of highly efficient methods or technologies to remove these viruses or bacteria enables fully effective transmission and infection control of contaminated water. Table 1 shows the many typical water-borne viruses and bacteria in hospital wastewater and their typical concentration range in various wastewater sources. Their upper concentration limits in the treated water defined by WHO, i.e., effluent from treatment plans, are also given in the table.

2.2 Antibiotic groups

Antibiotic groups, including antivirals, antibacterial, and other anti-infectives, are the most common medicines. When an infection is linked to an unidentified pathogen in clinical treatment, empiric therapies using large quantities of antivirals or antibacterial are used to treat the patients in

these emergencies, sometimes within a short period [72,73]. Recently, many hospitals and research facilities have been required to reduce the application of these medicines for several reasons. First, according to numerous studies, researchers confirmed these drugs have heavily leached into the environment in the past 20 years [74]. Secondly, the effluent from hospital wastewater has been regarded as the primary source for the spread of antiviral- and antibacterial-resistance genes [75]. Table 2 shows a list of discharged antivirals, antibacterial, antimycotics, and metabolites in hospital wastewater. For example, when antivirals, antibacterial, and other anti-infectives are not completely metabolized in patients, they are excreted via feces or urine, which enter the environment through wastewater discharge [76]. Sometimes, this wastewater comes from hospitals due to their high volume of care and is tainted with unmetabolized species due to high drug consumption [77]. Especially during the pandemic, the large loading and high concentration of antivirals, antibacterial, and other anti-infectives in wastewater enter rivers or lakes due to low-efficiency separation in WWTPs [78]. This kind of wastewater discharge may incur potential ecosystem alterations (including toxicity toward algae, daphnids, and fish) and the development of virus and bacteria resistant microbes (Fig. 1) [79]. Once released into the waterways, these drugs are consumed by birds, poultry, livestock, and other animals and even present in drinking water, thus posing a threat to human health [78,80]. The unmetabolized medicines in wastewater also represent a waste of hospital resources. Medicine's repurposing, in which the effective drug is extracted from the wastewater, may resolve the pollution

Table 1 Recently reported typical water-borne viruses and bacteria in hospital wastewater

Name	Molecular size	Hopstial wastewater treatment plant (WWTP) sample concentration	Ref.
Virus			
Adenovirus	Diameter: 70–100 nm	2.02×10^6 to 7.23×10^6 GC·mL^{-1} [a]	[40–42]
Astrovirus	Diameter: 28 nm	6.3% (of total influent samples)	[40,43,44]
Coronavirus (SARS-CoV-2)	Diameter: 60–140 nm	Confirmed, but not quantified	[40,45,46]
Enteroviruses (echovirus, coxsackie viruses, poliovirus)	Diameter: 25–30 nm	2.6×10^6 GC·mL^{-1}	[40,47,48]
Hepatitis A/E	Diameter: 27–30 nm	2.8×10^4 GC·mL^{-1}	[40,49]
Norovirus I/II	Diameter: 27–38 nm	3.1% (of total influent samples)	[40,44,50]
Rotavirus	Diameter: 75 nm	32.3% (of total influent samples)	[40,44,51]
Sapovirus	Diameter: 41–46 μm	29.4% (of total influent samples	[40,52,53]
Protozoa			
Cryptosporidium	Diameter: 3–14 μm	18.9% (of total influent samples)	[40,54,55]
Entamoeba histolytica	Diameter: 3–14 μm	59% (of total influent samples)	[40,56,57]
Giardia duodenalis	Diameter: 3–14 μm	27.4% (of total influent samples)	[40,55,58]
Bacteria			
Campylobacter	Diameter: 0.2–0.4 mm Length: 0.5–5 mm	87% (of total influent samples)	[59,60]
Escherichia coli	Diameter: 0.2–6.0 μm Length: 1.1–1.1 μm	4.6×10^6 CFU·mL^{-1} [b]	[40,61,62]
Legionella	Diameter: 0.3–0.9 μm Length: 1–3 μm	58% (of total influent samples)	[63,64]
Pseudomonas	Diameter: 0.6–1.2 μm Length: 2–3 μm	2 to 800 CFU·mL^{-1}	[40,65]
Salmonella	Diameter: 0.8–1.5 μm Length: 2–5 μm	71% (of total influent samples)/5.5×10^4 CFU·g^{-1}	[40,66–68]
Shigella	Diameter: 0.6–1.2 μm Length: 2–3 μm	62% (of total influent samples)/2.2×10^5 CFU·g^{-1}	[40,67–69]
Streptococcus	Diameter: 0.6–1.2 μm Length: 2–3 μm	1.6×10^5 CFU·g^{-1}	[40,68]
Vibrio cholera	Diameter: 0.6–1.2 μm Length: 0.5–3 μm	0.01 to 10 CFU·mL^{-1}	[40,70,71]

a) GC·mL^{-1}: genome copies per milliliter; b) CFU·mL^{-1}: colony-forming units per milliliter.

issue, and significantly reduce medication costs [81,82]. Therefore, a novel technology for highly efficient selective separation and extraction of the target medicines is needed.

2.3 Organic compounds

Hospital wastewater contains a large variety of small (100–1000 Da) organic compounds, including carbohydrates, proteins, amino acids, generic drugs, esters, and organic solvents, which are widely discharged into surface waters and drinking water sources [88,89]. These organic compounds pose a direct threat to human health through drinking or irrigation water. Another significant threat from these organic compounds is their large volume generated in wastewater, resulting in oxygen deficiency and

mutagenic properties in aquatic environments [90,91]. Some of the organic compounds are considered persistent pollutants due to their low biodegradability and high adsorption affinity in aquatic ecosystems, such as caffeine, tramadol, and iopromide [92]. These organic compounds in hospital wastewater have become one of the most extensively studied classes of emerging organic contaminants in aquatic environments. The common and persistent organic compounds in hospital wastewater are list in Table 3. Unfortunately, the traditional methods based on disinfection, flotation, and clarification do not effectively remove these organic micropollutants [93]. Only a very small fraction of these hospital organic compounds is removed from WWTPs [94]. Hence, efficient technologies to remove these persistent organic compounds including pharmaceuticals, from wastewater are highly desirable.

Table 2 Discharged antivirals, antibacterials, antimycotics, and metabolites in hospital wastewater

Name	Chemical formula	Size/(g·mol^{-1})	Hopstial WWTPs sample concentration/ (ng·L^{-1})	Ref.
Antibacterials				
Azythromycin	$C_{38}H_{72}N_2O_{12}$	748.98	20.1 ± 5.7	[83,84]
Carbamazpine	$C_{15}H_{12}N_2O$	236.27	14	[84]
Cefotaxime	$C_{16}H_{17}N_5O_7S_2$	455.5	143.7 ± 4.2	[83]
Ceftazidime	$C_{22}H_{22}N_6O_7S_2$	636.7	1200	[85]
Cefazolin	$C_{14}H_{14}N_8O_4S_3$	454.5	83.4 ± 3.6	[83]
Ciprofloxacin	$C_{17}H_{18}FN_3O_3$	331.34	8372.9 ± 67.8	[83,84,86]
Chlortetracycline	$C_{22}H_{23}ClN_2O_8$	478.88	8	[84]
Clarithromycin	$C_{38}H_{69}NO_{13}$	747.95	167.3 ± 10.7	[83,84]
Doxycycline	$C_{22}H_{24}N_2O_8$	444.44	18	[84]
Enrofloxacin	$C_{19}H_{22}FN_3O_3$	359.4	4	[84]
Erythromycin	$C_{37}H_{65}NO_{12}$	715.92	188 ± 297	[84,87]
Lomefloxacin	$C_{17}H_{19}F_2N_3O_3$	351.35	10	[84]
Metronidazole	$C_6H_9N_3O_3$	171.15	937.4 ± 111.8	[83]
Norfloxacin	$C_{16}H_{18}FN_3O_3$	319.33	5933 ± 3390	[84,86]
Ofloxacin	$C_{18}H_{20}FN_3O_4$	361.37	14377.8 ± 50.9	[83,84]
Oxytetracycline	$C_{22}H_{24}N_2O_9$	460.43	18	[84]
Roxithromycin	$C_{41}H_{76}N_2O_{15}$	837.05	23	[4]
Spiramycin	$C_{43}H_{74}N_2O_{14}$	843.1	1700	[85]
Sulfadiazine	$C_{10}H_{10}N_4O_2S$	250.28	1896 ± 4003	[87]
Sulfadimidine	$C_{12}H_{14}N_4O_2S$	278.33	59	[84]
Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	253.27	9800	[84,85]
Sulfapyridine	$C_{11}H_{11}N_3O_2S$	249.29	251	[87]
Tetracycline	$C_{22}H_{24}N_2O_8$	444.44	23	[84]
Trimethoprim	$C_{14}H_{18}N_4O_3$	290.32	7700	[84,85]
Antimycotics				
Fluconazole	$C_{13}H_{12}F_2N_6O$	306.1	3445 ± 1569	[87]
Antivirals				
Oseltamivir	$C_{16}H_{31}N_2O_8P$	410.4	25 ± 18	[87]
Ritonavir	$C_{37}H_{48}N_6O_5S_2$	720.9	108 ± 94	[87]
Metabolites				
N4-Acetylsulfamethoxazole	$C_{12}H_{13}N_3O_4S$	295.32	2394 ± 2261	[87]
Oseltamivir carboxylate	$C_{14}H_{24}N_2O_4$	284.35	151 ± 81	[87]

2.4 Radioactive elements and ionic pollutants

Radioactive elements and some ions are essential resources for hospital treatment and clinical diagnosis [96,97]. For instance, radiotherapy with heavy, charged particles (e.g., protons and carbon ions) is an established treatment option for many tumors [98]. For hospital testing and analysis, elements, and ions, are widely used in hospital imaging, anesthesia, and neuroprotection [6]. However, once these radioactive ions are released through wastewater into the environment, they may pose a high risk to the ecosystem and public health due to their carcinogenic and mutagenic characteristics. Specific ions in discharged hospital wastewater cause severe contamination of drinking water sources [99,100]. Furthermore, there are many valuable and essential ions in the hospital wastewater, which could be selectively separated or extracted for reuse such as Xe [101]. However, the coexistence of chemically similar ions in wastewater severely limits the extraction of these valuable ions [102,103]. Currently, the inevitability of environmental pollution and low-efficiency implementation of the traditional methodologies, including calcina-

Table 3 Persistent organic compounds found in hospital wastewater

Name	Chemical formula	Molecular weight /(g·mol^{-1})	Concentration upper limit /(µg·L^{-1})	Ref.
Anti-inflammatory preparations				
Diclofenac	$C_{14}H_{11}Cl_2N_1O_2$	295.0	0.833 ± 0.179	[87]
Ibuprofen	$C_{13}H_{18}O_2$	206.3	7.8	[95]
Indometacin	$C_{19}H_{16}ClNO_4$	357.07	0.069 ± 0.080	[87]
Mefenamic acid	$C_{15}H_{15}NO_2$	241.2	6.140 ± 1.779	[87]
Naproxen	$C_{14}H_{14}O_3$	230.1	< 5.6	[87]
Salicylic acid	$C_7H_6O_3$	138.1	45.3	[95]
Anti-neoplastics				
Cyclophosphamide	$C_7H_{15}Cl_2N_2O_2P$	260.0	0.161 ± 0.026	[87]
Ifosfamide	$C_7H_{15}Cl_2N_2O_2P$	260.0	0.895 ± 0.293	[87]
Cardiovascular system preparations				
Atenolol	$C_{14}H_{22}N_2O_3$	266.2	2.315 ± 0.632	[87]
Atenolol acid (metoprolol acid)	$C_{14}H_{21}N_1O_4$	267.1	9.840 ± 1.859	[87]
Bezafibrate	$C_{19}H_{20}ClNO_4$	361.1	0.063 ± 0.075	[87]
Clofibric acid	$C_{10}H_{11}ClO_3$	214.0	< 0.07	[87]
D617	$C_{17}H_{26}N_2O_2$	290.2	0.155 ± 0.114	[87]
Furosemide	$C_{12}H_{11}ClN_2O_5S$	330.0	2.037 ± 0.595	[87]
Hydrochlorothiazide	$C_7H_8ClN_3O_4S_2$	297.0	1.995 ± 0.547	[87]
Metoprolol	$C_{15}H_{25}NO_3$	267.2	1.325 ± 0.330	[87]
Propranolol	$C_{16}H_{21}NO_2$	259.2	0.116 ± 0.041	[87]
Sotalol	$C_{12}H_{20}N_2O_3S$	272.1	0.700 ± 0.551	[87]
Valsartan	$C_{24}H_{29}N_5O_3$	435.2	3.032 ± 1.282	[87]
Verapamil	$C_{27}H_{38}N_2O_4$	454.3	0.030 ± 0.022	[87]
Hormonal preparations				
Bisphenol A	$C_{15}H_{16}O_2$	228.3	0.833	[84]
Dexamethasone	$C_{22}H_{29}FO_5$	392.2	0.147 ± 0.013	[87]
17β-Estradiol	$C_{18}H_{24}O_2$	272.4	0.030	[84]
Estriol	$C_{18}H_{24}O_3$	288.4	0.092	[84]
Methylprednisolone	$C_{22}H_{30}O_5$	374.2	1.420 ± 0.768	[87]
Nervous system preparations				
4-Acetamidoantipyrine	$C_{13}H_{15}N_3O_2$	245.1	225 ± 89	[87]
4-Aminoantipyrine	$C_{11}H_{13}N_3O_1$	203.1	101 ± 44	[87]
Carbamazepine	$C_{15}H_{12}N_2O$	236.1	0.222 ± 0.118	[87]
Diazepam	$C_{16}H_{13}ClN_2O$	284.1	0.069	[87]
4-Dimethylaminoantipyrine	$C_{13}H_{17}N_3O$	231.1	< 0.14	[87]
Fluoxetine	$C_{17}H_{18}F_3NO$	309.1	< 0.03	[87]
Gabapentin	$C_9H_{17}NO_2$	171.1	19.40 ± 24.15	[87]
4-Formylaminoantipyrine	$C_{12}H_{13}N_3O_2$	231.1	47.88 ± 12.39	[87]
Levetiracetam	$C_8H_{14}N_2O_2$	170.1	11.02 ± 6.546	[87]
Lidocaine	$C_{14}H_{22}N_2O$	234.2	9.133 ± 8.071	[87]
4-Methylaminoantipyrine	$C_{12}H_{15}N_3O$	217.1	218 ± 208	[87]
Morphine	$C_{17}H_{19}NO_3$	285.1	3.679 ± 1.834	[87]
Oxazepam	$C_{15}H_{11}ClN_2O_2$	286.0	1.123 ± 0.335	[87]
Paracetamol (acetaminophen)	$C_8H_9N_1O_2$	151.1	107.0 ± 85.7	[87]

(*Continued*)

Name	Chemical formula	Molecular weight /(g·mol^{-1})	Concentration upper limit /(μg·L^{-1})	Ref.
Phenazone (antipyrine)	$C_{11}H_{12}N_2O$	188.1	0.162 ± 0.079	[87]
Primidone	$C_{12}H_{14}N_2O_2$	218.1	0.383 ± 0.390	[87]
Ritalinic acid	$C_{13}H_{17}NO_2$	219.1	0.295 ± 0.142	[87]
Thiopental	$C_{11}H_{18}N_2O_2S$	242.1	0.763 ± 0.860	[87]
Tramadol	$C_{16}H_{25}NO_2$	263.2	0.958 ± 0.264	[87]
Venlafaxine	$C_{17}H_{27}NO_2$	277.2	0.811 ± 0.316	[87]
Other organic compounds				
Caffeine	$C_8H_{10}N_4O_2$	194.2	25.8	[95]
Fenofibrate	$C_{20}H_{21}ClO_4$	360.8	0.6	[95]
Gemfibrozil	$C_{15}H_{22}O_{13}$	250.3	2.7	[95]
Disinfectant				
Triclosan	$C_{12}H_7Cl_3O_2$	289.5	–	[95]
X-ray contrast media				
Diatrizoate (diatrizoic acid)	$C_{11}H_9I_3N_2O_4$	613.8	348.7 ± 241.0	[87]
Iohexol	$C_{19}H_{26}I_3N_3O_9$	820.9	< 12	[87]
Iomeprol	$C_{17}H_{22}I_3N_3O_8$	776.9	439.0 ± 443.9	[87]
Iopamidol	$C_{17}H_{22}I_3N_3O_8$	776.9	2599 ± 1512	[87]
Iopromide	$C_{18}H_{24}I_3N_3O_8$	790.9	170.6 ± 156.3	[87]
Ioxitalamic acid	$C_{12}H_{11}I_3N_2O_5$	643.8	342.0 ± 197.0	[87]

tion, adsorption, precipitation, and salting, limit the use of these methods in wastewater treatment [104].

3   MBR in hospital wastewater treatment

Conventional MBR is a technology that combines biological treatment with membrane separation. It was first designed and applied in the food industry in the 1970s and then developed to treat various wastewaters during the last few decades [105]. Compared to conventional activated sludge systems, the sedimentation tank is replaced by a membrane process in an MBR. Consequently, numerous advantages, including high effluent quality, low sludge production, and enhanced contaminant removal capacity, are obtained [22]. In theory, MBR is suitable for hospital wastewater treatment: antibiotic groups and organic compounds can be degraded during biological treatment, meanwhile, due to the membrane pores, left pathogenic microorganisms, antibiotic groups, organic compounds, and ionic pollutants are further eliminated [106,107]. To further improve performance in hospital wastewater treatment, the advanced MBRs were developed including that hybridizing some novel membranes into MBR units (defined as hybrid MBRs) or integrating MBR with other membrane processes (defined as integrated MBR-membrane systems).

3.1   MBR technology

3.1.1   Types of membranes used in MBRs

Membranes are the core part of MBRs and have a critical influence on the rejection of pathogenic microbe and virus in hospital wastewater treatment. During the past 60 years, the rapid development of membrane materials has pushed the evolution of MBR technology from simple and laboratory-scale to complex and large-scale industrial applications. The current MF/UF membranes used in MBRs are made from polymeric, ceramic, and metallic materials (see Table 4).

Polypropylene (PP), polyethylene (PE), polytetrafluoroethylene (PTFE), polyvinylidene difluoride (PVDF), and polysulfone have been widely used in preparing polymeric membranes for MBRs [108]. The polymeric membrane exhibits controllable pore size (distribution), wettability, surface charge, functional groups, and excellent chemical, thermal, mechanical, and hydrolytic stability [109]. Polymeric membrane properties can be modified by polymer selection, polymer blending, and additives addition for different applications [110].

Ceramic membranes are fabricated using Al_2O_3, TiO_2, ZrO_2, SiO_2 and other inorganic materials. These membranes are reported to have a high chemical, thermal, and mechanical resistance, unique separation properties, and a

Table 4 Different types of membranes in the MBR process

Membrane type	Material	Membrane pore size/μm	Ref.
Polymeric membrane	PVDF	0.04	[118]
	PVDF	0.4	[119]
	PVDF	< 0.1	[120]
	PVDF	0.2	[121]
	Polyvinyl chloride	0.2	[122]
	PTFE	0.2	[123]
	PE	0.4	[124]
	PE	0.4	[125]
	PE	0.2	[126]
	High density polyethylene	0.2	[127]
	PP	0.03	[128]
Ceramic membrane	Ceramic	0.4	[129]
	Silicon carbide	0.6	[130]
	Ceramic	0.1	[131]
Metallic membrane	Flat stainless steel	0.2	[113]
	Flat stainless steel	0.2	[132]
	Flat stainless steel	0.4	[114]

long operational life. They are ideal for treating industrial wastewater and oil-water separation [111]. In the past 20 years, ceramic membranes have been widely studied in MBRs for wastewater treatment [112]. Notably, the placement of ceramic membranes allows the MBRs to operate at high mixed liquid suspended solids concentrations and high fluxes.

Metallic (e.g., Pd, Ag, alloys, and steel) membranes are also used in MBRs because they have a high resistance to extreme acidity or alkalinity, temperature, and high-pressure operations. Compare to ceramic membranes, metallic membranes show higher mechanical strength, conductivity and selectivity. Zhang et al. investigated the application of flat stainless steel membranes in aerated submerged MBR for treating synthetic domestic wastewater [113]. The metallic membrane showed a steady permeate flux of >17 L·m^{-2}·h^{-1} and an average chemical oxygen demand (COD) removal rate of 97%. Xie et al. also used a stainless-steel sheet membrane in MBR for synthetic domestic sewage treatment, which achieved mean removal efficiencies of 96.7% for COD and 32.1% for total nitrogen (TN), respectively [114]. Compared with polymeric membranes, ceramic and metallic membranes can be cleaned by high-pressure backwashing, thus reducing the use and impact of cleaning chemicals [115]. However, the main drawback of these membranes is the higher cost, which limits their widespread industrial applications.

Mixed matrix membranes as a novel membrane that hybrid in MBRs have been reported for wastewater treatment. These membranes are the incorporation of synthetic or natural inorganic compounds in a continuous polymer matrix to enhance their chemical and physical properties, including the charge, pore size and distribution, hydrophilicity, and surface roughness [116]. Recently, some highly porous and hydrophilic mixed matrix membranes have been developed and applied in MBRs. For example, Bilad et al. reported a polyvinyl chloride and silica-based mixed matrix membrane with the enhanced porosity, chemical and thermal stability, and used in the MBR [117].

3.1.2　Bioreactor

Microorganisms determine the biological treatment in MBRs. Generally, biological processes in MBRs for pharmaceutical removal include biosorption, bioaccumulation, biodegradation, volatilization, and photodegradation [24]. Compared with conventional activated sludge systems, more microorganisms even with a slow growth rate (e.g., nitrifying bacteria) and poor settling performance (e.g., filamentous bacteria) can be retained in the feedstock, and be successfully proliferated in MBR due to membrane rejection, which is beneficial for wastewater treatment [133,134]. For certain pollutants in hospital wastewater, the microbial community is mainly controlled by adjusting the ratio of nutrients, controlling dissolved oxygen, dosing chemicals, increasing sludge discharge, and increasing the hydraulic retention time.

3.2　MBR classification

3.2.1　Membrane configuration

MBRs are classified into submerged MBRs (Fig. 2(a)) and external MBRs (Fig. 2(b)) based on their membrane

modules inside/outside the bioreactor. In external MBRs, the membrane module and bioreactor are independent, giving easy operation and management advantages. Furthermore, membrane fouling is controlled by using the shearing effect of the high-speed water flow generated by the circulation pump. External MBRs can be worked at constant pressure with different permeate fluxes, while submerged MBRs usually always works at a constant flow with variable transmembrane pressures. However, external MBRs are usually more expensive than submerged MBRs due to their relatively complex operation and maintaining [24].

3.2.2   Aerobic and anaerobic biological processes

Conventional MBRs also can be classified as aerobic MBR (Fig. 3(a)) and anaerobic MBR (Fig. 3(b)), depending on whether aeration is used in the bioreactor [136]. Aerobic MBR has been widely used in the treatment of hospital wastewater, landfill leachate, and aquaculture wastewater. Aerobic MBR is easier to operate, but it usually suffers from poor sludge settling, low activated sludge concentration, and low stability under sudden changed wastewater conditions. Compared to aerobic MBR, the anaerobic MBR process has a higher organic load, lower energy consumption, and higher stability to resist the sudden changed wastewater conditions. Besides, anaerobic MBR can be used to recover energy in the form of biogas from wastewater [137]. These attributes make the anaerobic MBR more promising in treating refractory organic

wastewater, however, these attributes also make it more difficult to operate than aerobic MBR [138].

3.3   Hybrid MBRs and integrated MBR-membrane systems

Currently, increasingly stringent standards and lower-cost processing requirements limit the broad application of MBRs for hospital wastewater treatment. Hence, the hybrid MBRs, which combine the biological treatment with other novel membranes like NF membrane, forward osmotic membrane, and extractive membrane, show high separation efficient for specific inorganic or organic compounds removal. Besides, the integrated MBR-membrane systems, which integrating MBRs and other membrane processes (e.g., RO, NF, and ED), are also promising in hospital wastewater treatment [139]. The following section reviews the application of hybrid MBRs (aeration MBR (AMBR), extractive MBR (EMBR), NF MBR (NMBR) and osmotic MBR (OMBR)) and integrated MBR-membrane systems (integrated MBR-RO process, MBR-NF process, MBR-ED process, and MBR-forward osmosis (FO) process).

3.4   Critical performance indicators of MBRs

3.4.1   Solute selectivity

Some compounds in hospital wastewater, such as waterborne viruses and bacteria, pose a significant threat to humans and require selective separation by the membrane
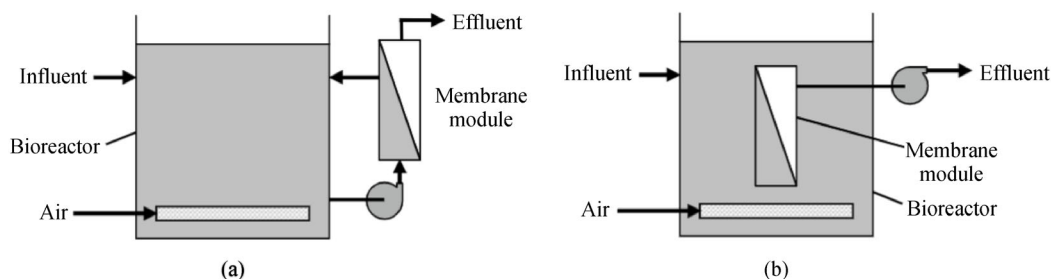

Fig. 2   (a) External MBR and (b) submerged MBR. Reprinted with permission from ref. [135], copyright 2007, Elsevier.
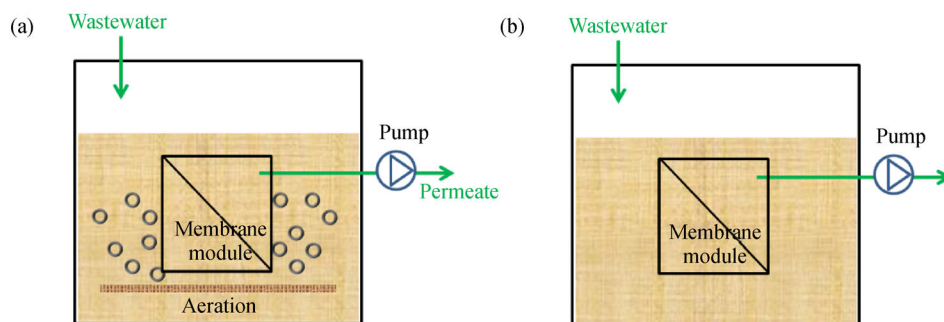

Fig. 3   (a) Aerobic MBR and (b) anaerobic MBR.

process. Meanwhile, some species such as antivirals, antibacterial, and some radioactive ions may cause serious water pollution when discharged into rivers or lakes. These compounds also require selective separation for removal. Compared with conventional activated sludge systems, membranes used in conventional MBRs exhibit the advantage to achieve a high rejection of suspended solids, macromolecules such as proteins and pathogens, and yield a better effluent quality [140]. However, a low removal rate of pathogenic microbes, ions, and other micromolecules was observed in MF and UF operations due to the large pore sizes [141].

Hybrid MBRs or integrated MBR-membrane systems, such as the RO membranes used in an MBR or a conventional MBR system integrated with NF/ED processes, show a high removal rate or selectivity due to its membrane pore sizes (< 2 nm). The main principle of membrane selectivity in wastewater treatment is the size sieving of the membrane, and membrane electrostatic interaction between membrane and solutes. Size sieving is accomplished through tuning the pore size of the membrane structure. During the separation process for hospital wastewater, molecules larger than the membrane pore size are rejected; otherwise, they will pass through the membranes (Fig. 4(a)).

During hospital wastewater treatment, membrane separation technologies are impeded by a trade-off between flux and retention [142]. To overcome this phenomenon, most membranes are developed using advanced composite materials. For example, many new nanomaterials (from zero-dimensional to three-dimensional) are designed and prepared as membranes with controllable structures (pore size and shape) [143,144]. Nanospheres or nanoparticles have large specific surface areas and are fabricated as functional layers with enhanced membrane flux or selectivity [145–147]. One-dimensional nanomaterials such as nanowires, nanotubes, and nanofibers have high mechanical strength, stability, and selectivity and have been widely used for membrane separation [148–150]. Graphene oxide, MXene, and MoS_2 nanosheets are advanced two-dimensional nanomaterials and have nanoscale thickness and controllable interlayer sizes to yield membranes for molecular separations and wastewater treatment [151]. Recently, metal-organic frameworks (MOFs) and covalent organic frameworks based membranes have attracted significant attention for separation processes due to their precisely tunable micro/mesopores, composition, and functionality [152,153]. For example, there are some works on composite NF membranes with controllable structures that use MOFs (such as ZIF-8 and UiO-66-NH_2) [154–157]. With the development of these novel membranes, hybrid MBRs or integrated MBR-membrane systems have a high potential to remove hazardous compounds or recycle values selectively.

Another effect giving membrane selectivity is the electrostatic interaction (either electrostatic attraction or repulsion), which depends on the interaction force between the charged membrane surface/pores and the target compounds/ions in solution (Fig. 4(b)). During hospital wastewater treatment, membrane surface/pores have opposite charges from target compounds/ions, leading to attractive driving forces for the transport of these materials. Zhang et al. created an artificial solid-state ion pump in the membrane to mimic the delicate ion transport behavior of a biological protein-based ion pump for transport of a target ion from the membrane [158]. Therefore, this membrane type is auspicious for extracting valuable antivirals, antibacterial, other anti-infectives, ions, or elements from hospital wastewater and recycling them for epidemic prevention. Otherwise, when the membrane surface/pores and target compounds/ions show the same charge or repulsive interaction, the retention rate of these target compounds/ions is enhanced. For example, a membrane surface layer constructed by zwitterionic and polycationic components may display high antibacterial properties and rejects viruses and bacteria during hospital wastewater treatment [159]. In this way, by designing the membranes based on the purpose of separation, MBRs can be carefully designed and utilized for simultaneously remove harmful
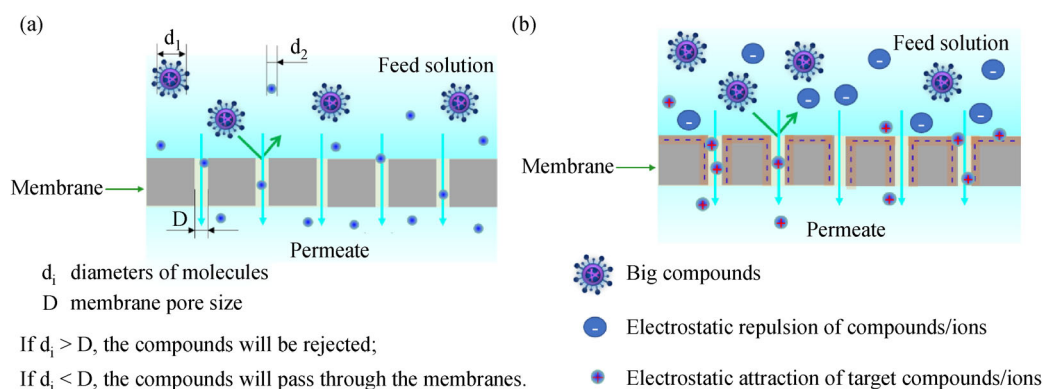

Fig. 4 (a) Membrane pore size sieving for different sized compounds/ions; (b) electrostatic interaction for charged compounds/ions.

materials and extract valuable materials during hospital wastewater treatment.

3.4.2 Membrane fouling mechanisms in MBR

Membrane fouling is a significant issue, especially during the separation of hospital wastewater loaded with viruses, bacteria, antivirals, antibacterial, and other compounds. They build-up of cake layers or gel layers and pore blockages, leading to reduced flux or retention rate, and increased energy consumption [160]. Ways to mitigate fouling or reverse flushing are increasing the sludge filterability or physical cleaning during long-term operation. However, sometimes the effects of fouling cannot be reversed (irreversible fouling) [161]. Membrane fouling in MBR processes is classified as biofouling, colloidal fouling, organic fouling, and scaling [162].

Biofouling is caused by bacteria and viruses and leads to the formation and growth of a biofilm. It is considered the most ubiquitous and recalcitrant fouling type. Hospital wastewater contains harmful viruses and bacteria, prompting removal before deposition onto the membrane surface and formation of biofilms [163]. Biofilms form when microorganisms grow on the membrane surfaces [164]. In that context, biofouling during hybrid MBRs or integrated MBR-membrane systems operations may be attributed to the adsorption of organics or toxins generated by microorganisms (Fig. 5(a)). Methods directed at biofouling prevention include feed pretreatment, rinsing or flushing of the membrane surface, and air-sparging and cleaning with different chemical agents [165]. However, these methods have only a temporary effect and cannot prevent membrane biofouling after multiple exposures to pollutants [166]. Antifouling membrane layers have been employed as an efficient method to solve fouling issues. To prevent attachment of these biofouling agents, the membrane surface is usually modified to have high hydrophilicity, low surface roughness, and negative charge, e.g., by incorporating nanomaterials [167–169].

Colloids are non-dissolved suspended solids ranging from 1 nm to 2 μm in size and are abundant in hospital wastewater, including inorganic colloids (such as hydroxides of heavy metals, etc.), organic macromolecules (such as proteins, etc.) and biocolloids (such as viruses and bacteria, etc.) [170]. Colloidal fouling profoundly limits membrane separation performance and may even lead to a complete failure of the membrane separation process [171]. This fouling occurs due to interactive forces between colloidal particles and the membrane surface (Fig. 5(b)) [172,173], including London-van der Waals forces, electrical double layer forces, solvation or hydration forces, hydrophobic forces, and steric forces [174], as described by the Derjaguin, Landau, Verwey, Overbeek theory. Based on this theory, membrane surfaces are usually modified with hydrophilic groups and charged

bactericide materials to minimize undesired interactions and prevent or reduce colloidal fouling [175,176].

Organic fouling materials are dissolved into the solution and maintained by covalent bonds, and these bonds lead to interactions with membrane surfaces [177]. These organic foulants originate from large quantities of disinfectant agents, pesticides, organic solvents, alginate, proteins, and other aromatic substances used and discharged into the rivers, leading to a heavy organic matter load in the environment. For instance, a gel layer accumulates in hybrid MBRs or integrated MBR-membrane systems due to continuous organic fouling under sub-critical flux operation [178,179]. Especially, humic acids and alginate are significant organic foulants during MBRs operation. These organic substances stick easily to the membrane surface or cause blockages inside to membrane structure during separation (Fig. 5(c)) [180]. The mechanisms of organic fouling are related to the interaction between the organics and membrane surface such as electrostatic and hydrophobic interactions [181].

In hospital wastewater treatment, scaling or inorganic fouling on membranes may occur when ions in wastewater are concentrated and exceed the threshold for solubility of sparingly soluble salts [182], e.g., Al^{3+}, Mg^{2+}, Ca^{2+}, Ba^{2+}, SO_4^{2-} and CO_3^{2-}, often exceed the solubilities of sparingly soluble salts. Some metal cations (e.g., Ca^{2+}, Mg^{2+} and Al^{3+}) react with functional organics groups to form organic-inorganic compounds (Fig. 5(d)) [183]. For example, alginate forms a severe gel layer when Ca^{2+} is present in wastewater. Inorganic fouling in MBRs processes is due to the precipitation of inorganic crystals on the membrane surface [110]. The metal ions (e.g., Ca^{2+}, Mg^{2+}, and Al^{3+}) and some anions (e.g., OH^-, SO_4^{2-} and CO_3^{2-}) react and lead to chemical precipitation on the membrane surface [177]. Likewise, scaling occurs when saturation concentrations of some insoluble salts ($CaSO_4$) are exceeded in the concentrate solution. Inorganic crystals existing in the MBRs processes may accumulate in the membrane channels and then block membrane pores. Conventionally, two main factors affecting the scaling formation on membrane surfaces; one is the characteristics of the filtered solution (including concentration of ions, pH of solutions and temperature of solutions), and the other is the characteristics of the membrane (including membrane structure, and the charge of the membrane surface) [182].

4 MBR advancements for potential hospital wastewater treatment

4.1 Hybrid MBRs

As analyzed in Section 3.4.2, the hydrophilic UF/MF membranes commonly employed in the conventional MBR units are subject to severe fouling and hence rapid
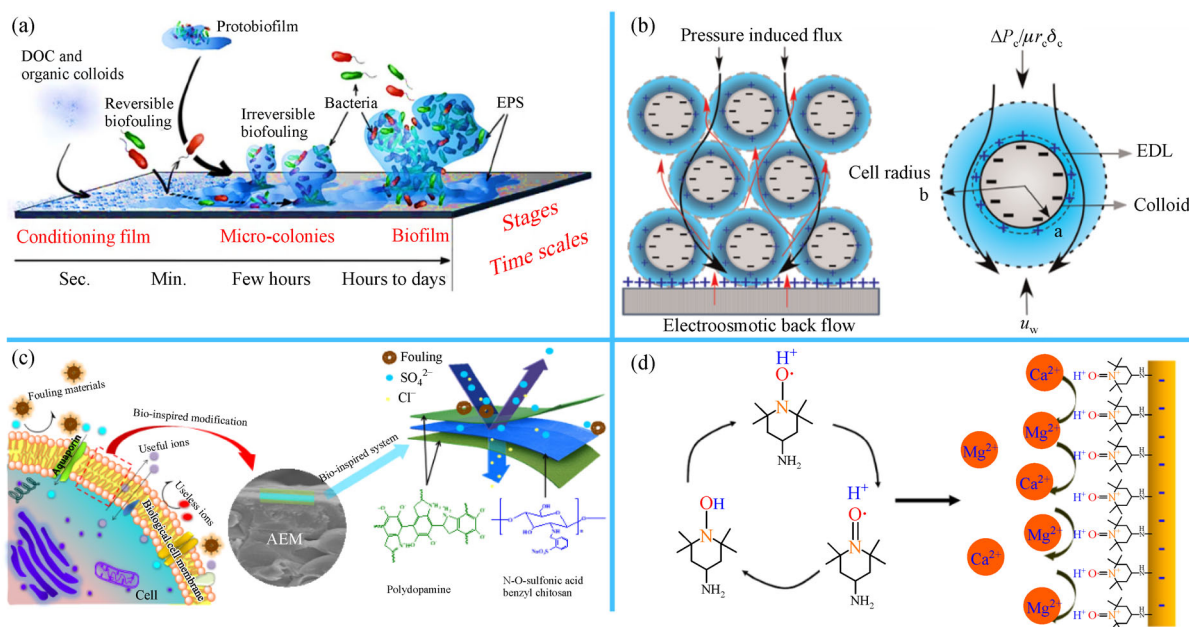
Fig. 5 The mechanism of four main fouling types in membrane processes used in wastewater treatment. (a) Biofouling by bacteria, viruses, the formation, and growth of biofilm. Reprinted with permission from ref. [165], copyright 2017, Elsevier. (b) Colloidal fouling mechanism. Reprinted with permission from ref. [172], copyright 2015, Elsevier. (c) Organic fouling. Reprinted with permission from ref. [180], copyright 2016, Springer Nature. (d) Scaling resistance. Reprinted with permission from ref. [183], copyright 2021, Elsevier.

flux decline. In recent years, there is a surge of interest to adapt the use of MBRs for achieving various separation purposes, depending on the main aim of purification, e.g., volatile removal, extraction of valuable components. Thus, novel concepts of hybrid MBRs have evolved by employing other types of membranes such as hydrophobic or non-UF/MF membranes. In this part, the use of hybrid MBRs in hospital wastewater treatment, including AMBR, EMBR, NMBR, OMBR and ED MBR (EDMBR) are reviewed.

4.1.1 AMBR

In AMBR, a dense permeable membrane or a microporous membrane with high hydrophobicity is used for aeration rather than wastewater separation and thus adopted in volatile removal, which exhibits a larger membrane surface and oxygen transfer area than the previous aeration method (Fig. 6). In AMBR, O_2 could be supplied directly to the biofilm on membrane surface, and bubble-free air improves the aeration efficiency. These characteristics make AMBR more suitable for treating wastewater containing volatile organic compounds such as xylene, acetonitrile, and perchloroethylene. In this way, no bubbles are generated during reactor operation, reducing the pollution generated by volatile organics. Li et al. reported that the AMBR was applied in the treatment of acetonitrile wastewater, and the removal rates of total organic carbon and TN approached 98.6% and 83.3%, respectively [184]. Furthermore, Tian et al. demonstrated the high efficiency

for *o*-aminophenol removal by applying a two-stage AMBR process [185], which confirmed the advantages of AMBR in removing COD, biochemical oxygen demand, turbidity, NH_4^+-N, and TN.

4.1.2 EMBR

EMBR is a novel membrane-based process, which employs a selectively permeable membrane (usually hydrophobic-organophilic membrane) to replace the MF/UF membrane in conventional MBR [187]. In EMBR, the membrane has tailored pore structure to selectively separate the targeted organic compounds from inorganic compounds, rather than acting as a physical barrier to separate wastewater from microorganisms. Inorganic compounds (salts, metals, charges ions) are rejected by the membrane, freeing microorganisms from underlying inhibitory effects with high bioactivity [188]. Thus, the toxic organic compounds in wastewater are permeated into the bioreactor and subsequently biodegraded by microorganisms [189]. Ongoing biodegradation is helpful to maintain the concentration gradient between membrane sides. Thus the continuous separation and biodegradation of targeted organic compounds is achieved [190]. EMBR exhibits several advantages during the treatment of wastewaters: no need for high pressure in conventional MBR and pre-treatment, low secondary waste stream production (less than 1%), low demands for post-treatment and waste disposal, and low operational cost [191].
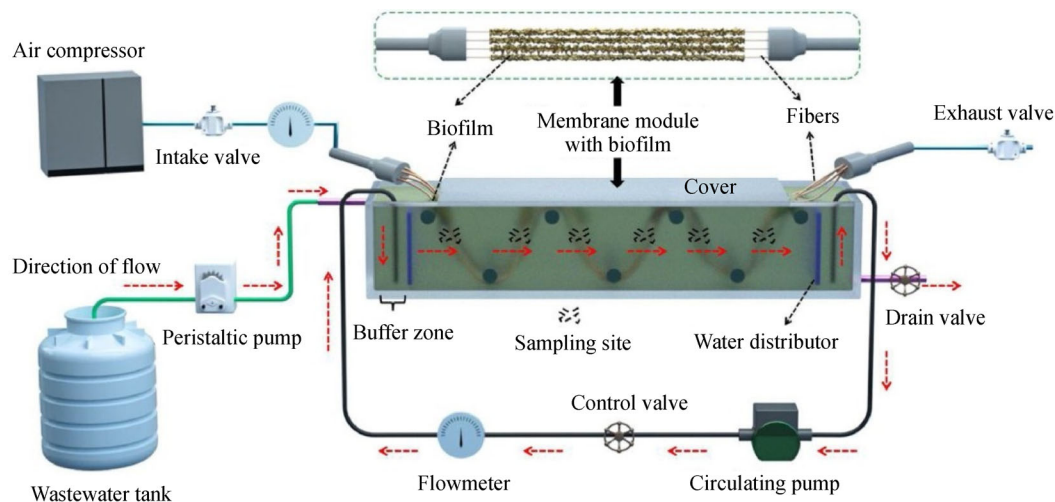
Fig. 6 Schematic diagram of AMBR system. Reprinted with permission from ref. [186], copyright 2020, Elsevier.

Commercial non-porous polydimethylsiloxane (PDMS) tubular membranes [192,193] were initially used in EMBRs. An EMBR using silicone rubber tube membrane (non-porous PDMS) was designed by Xiao et al., and found to be effective in treating phenol saline wastewater (5000–5500 mg·L^{-1} phenol, 25–300 g·L^{-1} NaCl) with a phenol removal efficiency above 95% under optimized conditions [194]. Afterwards, specifically designed non-porous PDMS flat-sheet membranes [195,196] and non-porous thin PDMS flat-sheet membranes with porous support [197,198] were developed to improve the separation efficiency of organic compounds. Liao et al. employed a dry phase inversion method to coat the thin film PDMS layer (with the thickness range of 3–22 µm) on the top of an electrospun layer (Fig. 7) [197]. Compared with non-porous PDMS tubular membranes, the thickness of the non-porous PDMS layer on a substrate was decreased significantly, and resultant phenol mass transfer coefficients significantly increased to 4.1–6.5 m·s^{-1} [197,198]. These findings make EMBR suitable to treat inorganic-organic composite wastewater [199–201].

4.1.3 NMBR

Compared with conventional MBR with UF/MF membranes, MBR with NMBR (Fig. 8) can further improve solute rejection and enhance the quality of produced water. NF membranes effectively retain organic contaminants with low molecular weight, increase the bioreactor retention time, and achieve better biodegradation [202]. They also effectively reject the hydrophilic and/or charged antibiotic groups and organic compounds (molecule weight >200 Da) via membrane adsorption, size exclusion, and electrostatic exclusion [203]. The permeate flux of conventional MBR is usually in the range of 10–150 L·m^{-2}·h^{-1}, depending on operating pressures and
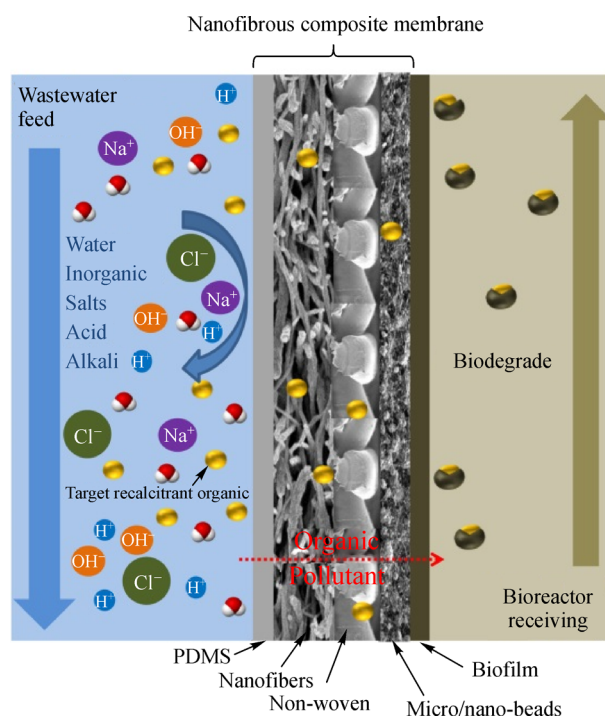

Fig. 7 Schematic diagram of EMBR system. Reprinted with permission from ref. [197], copyright 2018, Elsevier.

membrane structures [202]. In comparison, the permeate flux of NMBR is relatively lower. A submerged MBR using cellulose acetate NF membrane was developed by Choi et al. to treat domestic wastewater [204]. Results showed that dissolved organic carbon concentration in the effluent was 0.5–2.0 mg·L^{-1}, and salt rejections (Cl$^-$, Na$^+$, SO$_2^-$ and Ca^{2+}) were between 40%–90% during operation. Zaviska et al. also investigated an MBR system using ceramic NF multitubular membrane to treat antibiotic groups (cyclophosphamide and ciprofloxacin) [205]. This
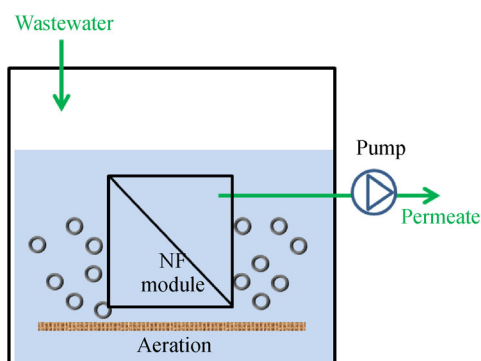
Fig. 8   Schematic diagram of NMBR system.

ceramic membrane further retained antibiotic groups and accumulated them in a bioreactor. Consequently, high remove efficiencies of COD, total suspended solids, and color were observed.

In addition to the low water permeate flux, the membrane biofouling is another limitation of NMBR. To alleviate membrane fouling in NMBR, a high cross-flow velocity and suitable permeate recovery are usually used to minimize the cake layer formation on the membrane surface. Besides, it is essential to develop a novel NF membrane with high fouling resistance, chemical stability, and water permeates flux [206].

Depending on whether aeration is used in MBR system, NMBR can be classified as aerobic NMBR and anaerobic NMBR. The aerobic NMBR is equipped with bio-carriers, and the dissolved oxygen is maintained by aeration rate. An air pump is used to aerate NMBR system for biological growth and provide a constant air flow rate to reduce fouling. Aerobic NMBR process presents excellent biodegradation efficiency and organic removal. Ming

et al. reported a high organic removal (>97%) and ammonia removal (>98%) for the treatment of municipal wastewater via aerobic NMBR [207]. The anaerobic NMBR can be used to prepare chemicals such as glycerol through fermentation, and NF membrane played an important role in nutrition rejection [208]. Especially, the external anaerobic NMBR system was proposed by Snowdon et al., which the high-strength starch-based wastewater was treated by anaerobic MBR system, then NF membranes were applied to treat the anaerobic MBR effluent [209]. Compare to aerobic NMBR, the anaerobic NMBR can decrease operation costs and sludge yields.

4.1.4   OMBR

OMBR is a relatively new concept that was first proposed in 2008 by combining the MBR and FO processes, as shown in Fig. 9, which simultaneously achieves the organic compounds removal by biological treatment and physicochemical separation of produced water by FO [210,211]. Compared to conventional MBR with MF/UF membranes, produced water in OMBR can spontaneously pass through the FO membrane driven by the osmotic pressure difference [212]. The OMBR has several advantages, including high produced water quality, low membrane fouling tendency, and potentially low energy demands [213,214]. An OMBR system was set up by Lay et al. using cellulose triacetate membrane to investigate its performance in the removal of pharmaceuticals from wastewater, and the results showed that removal efficiencies of carbamazepine, diclofenac and ibuprofen were above 96% with a stable water flux of 2.7 L·m^{-2}·h^{-1} [215]. Alturki et al. further demonstrated the performance of OMBR for the removal of 50 trace organic compounds [216]. For trace organic compounds with molar weight
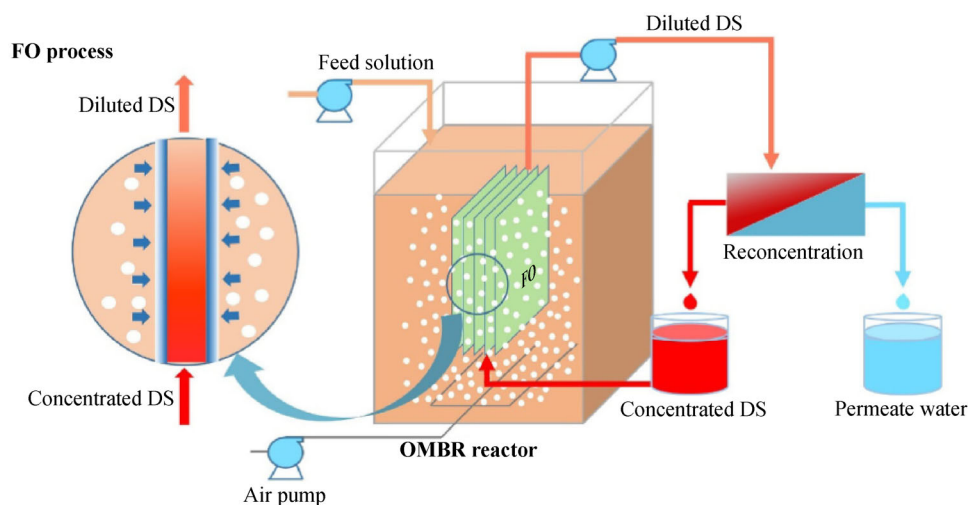

Fig. 9   Schematic diagram of OMBR system integrated with an ED unit to regenerate the draw solution. Reprinted with permission from ref. [220], copyright 2019, Elsevier.

above 266 Da, the obtained removal efficiencies were above 80%, while for a molar weight below 266 Da, the removal efficiencies were scattered.

The draw solution is another crucial factor in OMBR. The most widely used draw solution is an inorganic salt solution (especially NaCl solution) [217]. Salt concentrations gradually increase in the bioreactor during OMBR operation, which reduces the effective draw from the bioreactor to the draw solution, affects microorganism bioactivity, and inhibits biological treatment efficiency [213]. Simultaneously, the elevated salt concentration promotes the release of soluble microbial products and extracellular polymers in the bioreactor, which aggravates the membrane fouling in OMBR [218]. Besides, the main inherent problem of OMBR for hospital wastewater treatment is the inevitable dilution of the draw solution resulting in reduced process driving force. Thus, other membrane separation processes (NF, RO) are needed to reconcentrate and replenish the draw solution. For example, Lu and He studied a system incorporating OMBR and ED process for wastewater treatment and waste salt recovery [219]. Results indicated that the hybrid OMBR-ED system could achieve a stable water flux of about 6.23 $L \cdot m^{-2} \cdot h^{-1}$ and salt recovery of 1.26 $kg \cdot m^{-3}$. Figure 9 showed a diagram of OMBR system integrated with an ED unit to regenerate the draw solution [220].

4.1.5   EDMBR

EDMBR is a novel reactor that integrates ED into the MBR process. Geng et al. used EDMBR for enhanced biological phosphorus removal (EBPR) sludge treatment for the recovery of energy and phosphorus resource [221]. Results indicated that over 90% of the phosphorus in the EBPR sludge is released, while about 50% of the phosphorus is concentrated to 4 $mmol \cdot L^{-1}$ as a relatively pure phosphate solution. Nitrogen can be removed from EBPR sludge by desalination and denitrification processes. Wang et al. developed a novel ion selective EDMBR for source-separated urine treatment and resource recovery by integrating selective ED into the EMBR [222]. Results showed that 97.4% of the NH_4^+, 76.7% of the PO_4^{3-}, and 94.5% of the SO_4^{2-} was removed, while 65% of the phosphate and 54.9% of the sulfate (based on their amounts in urine after stripping) were recovered as a concentrated solution. The minerals in the wastewater stream (e.g., NaCl) were selectively retained as brine.

4.2   Integrated MBR-membrane systems

The following sections review the integrated MBR-membrane systems, where MBR is used as a pretreatment step and other membrane processes are used for the subsequent purification. Such integrated systems provide clear advantages toward an efficient wastewater treatment,

such as high operational flexibility, stability, and treatment versatility. Also, it may help to reduce the membrane fouling issues compared to what was observed in the hybrid units (as discussed in Section 4.1).

4.2.1   Integrated MBR-RO system

Integrated MBR-RO systems combine an MBR treatment system with a high-pressure RO membrane treatment system. The MBR serves as a pretreatment process to remove large solids and organic matter from the wastewater. Then, the RO process removes the remaining contaminants, including more than 90% of monovalent ions, 95% of divalent ions, and nutrient ions. Compared to NF, UF, and MF membranes, RO membranes offer much higher rejection and thus their integration with MBR demonstrated great potential in water purification and reuse. The other main advantages for integrated MBR-RO systems are the greater removal efficiency of pharmaceuticals and endocrine-disrupting chemicals [84,223–226]. In 2010, Beier et al. created the first full-scale integrated MBR-RO system for hospital wastewater treatment and effectively removed all pharmaceutical residues [227]. Since then, other researchers have built and tested MBR-RO systems to remove contaminants including viruses, bacteria, pharmaceuticals, and organic compounds from wastewater sources in municipal and domestic sewage WWTPs, where hospital wastewater is normally directed toward.

The removal of viruses, bacteria, and pathogens is essential in treating hospital wastewater for reuse applications and avoiding reinfection. Several studies used an integrated MBR-RO system to filter various pathogens from municipal wastewater and sewage. For example, Tam et al. investigated the feasibility of an MBR-RO system to reclaim treated effluent for potable and non-potable reuse applications [228]. Their MBR unit removed organic matter and nitrogen to an acceptable level. Then, RO membrane filtration improved the treated water quality in terms of turbidity, organic content, ammonia, nitrate, hardness, and *Escherichia coli* and virus requirements. Comerton et al. developed an integrated MBR-RO system to filter water-borne pathogens, disinfection byproducts, and nitrate from municipal wastewater. They found the filtered water was suitable for non-potable use and passed the California Title 22 reuse regulation and US EPA drinking eater limits for viruses and chlorite (1.0 $mg \cdot L^{-1}$) [229]. Prado et al. compared the virus removal efficiency from WWTPs by tertiary or advanced sewage treatment processes, such as sedimentation, sand-anthracite filters, MBR-RO system, and disinfection by chlorination. They found the highest virus removal for MBR-RO system approached 2.9 log10 [230]. In another study, this group found MBR-RO system completely removed noroviruses from WWTPs and are more suitable for applications

requiring high-quality produced water [231]. Plevri et al. reported a compact MBR-RO system and sewer mining technique with a treatment capacity greater than the total consumption for 100000 population equivalents. Sewer mining is the direct treatment of raw wastewater from the sewage network, on-site treatment, and immediate water reuse. Their system achieved water quality with no *E. coli* detectable and heavy metals to concentrations below the detection limit, and thus meeting the Greek legislative requirements [232,233].

Antibiotics groups, pharmaceuticals, and other organic compounds are another category of hospital wastewater contaminant [234]. Several studies explored the removal of these contaminants from municipal and industrial wastewater in the past six years. Li et al. published a review detailing the applications of MBR-RO system in pharmaceutical micropollutant removal before 2015 [234–236]. While the recent advancement in the past six years have not been reviewed. Racar et al. investigated the feasibility of the raw municipal wastewater reclamation by an integrated MBR-NF/RO system. The MBRs achieved a high removal efficiency of methiocarb (>99.9%), triallate (>99.9%), clothianidin (>88.0%), and clarithromycin (71.9%–74.2%). Further treatment with RO XLE (a commercial RO membrane, Dow FilmTec., USA.) and NF90 membranes showed very high removal rates (>99%) for all compounds [224]. Wang et al. applied MBR-RO system to achieve a deep removal of pharmaceuticals and personal care products (PPCPs) in municipal wastewater. The results showed that the removal rate of PPCPs by the traditional MBR system ranged from 41.08% to 95.41%; while the removal rate of most PPCPs by integrated MBR-RO/NF system could reach more than 95% [84]. Mamo et al. also achieved over 99% removal of 13 pharmaceuticals, 20 metabolites, and transformation products using an MBR-RO system at a permeate flux of 18 L·m^{-2}·h^{-1} [223]. Aziz and Ojumu treated domestic wastewater using an MBR-RO system to remove natural steroid hormones 17β-estradiol and testosterone, and they found excellent removal rates >95% for both compounds [237].

However, the emergence of membrane fouling is still an inevitable problem. Díaz et al. found that organic fouling, mainly polysaccharides and proteins, is the predominant issue when using RO as a secondary step after the MBR pretreatment. Also, inorganic foulants consisted of calcium, phosphorus, and iron [225]. Wu et al. observed the membrane fouling propensities of RO membranes in two parallel MBR-RO systems with varying food to microorganism (F/M) ratios (Fig. 10). The results show that more organic matter in the high F/M (0.50 g·g^{-1}·d^{-1}) MBR permeate led to higher RO scaling rates (>4.5-fold) compared to the low F/M (0.17 g·g^{-1}·d^{-1}) MBR scenario [238].

Overall, integrated MBR-RO systems have demonstrated to be the most effective in treating pathogens, pharmaceuticals, and other organic compounds from hospital and municipal WWTPs. But fouling and high energy requirements remain significant limitations to this technology. While there is much evidence that MBR-RO systems can thoroughly disinfect wastewater, it is still
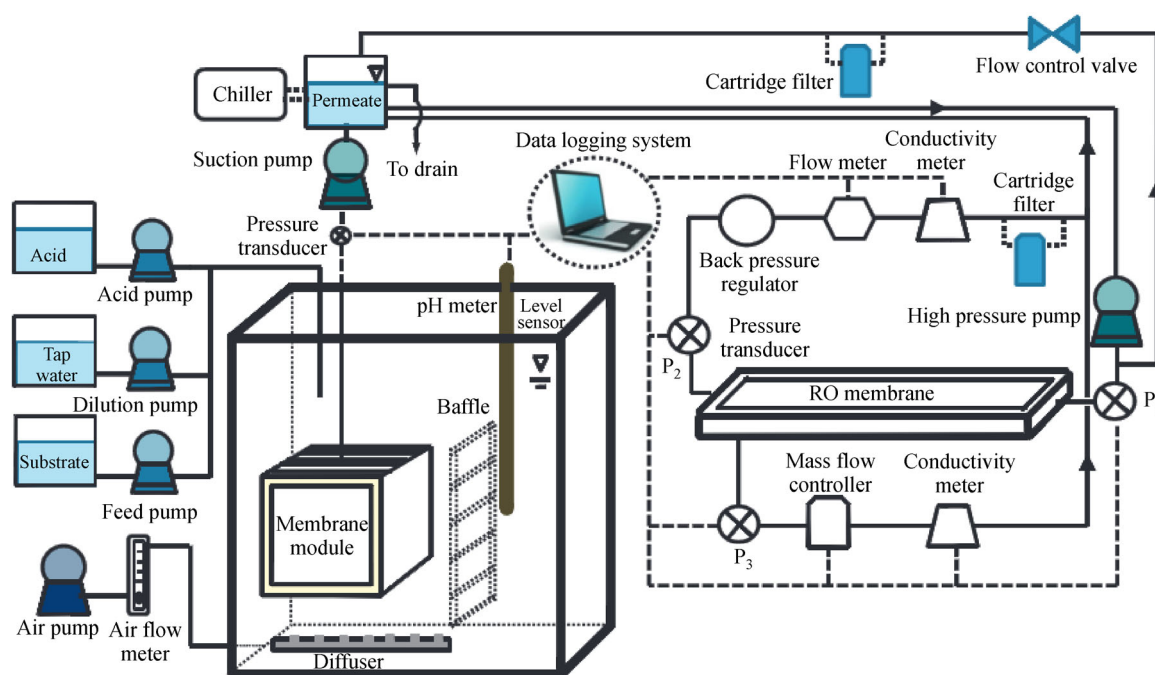

Fig. 10 The scheme of integrated MBR-RO systems. Reprinted with permission from ref. [238], copyright 2013, Elsevier.

recommended to include an additional filtration step for high-quality water and drinking water applications.

4.2.2 Integrated MBR-NF system

Integrated MBR-NF systems combine a MBR treatment system with a high-pressure NF membrane treatment system. In this case, the MBR serves as a pretreatment system and limits the number of biodegradable compounds and organic matter in the hospital wastewater for the subsequent NF treatment. The effectiveness of the MBR-NF system has been studied extensively for treating municipal landfill leachate, saltwater and brackish water for desalination, and industrial and pharmaceutical wastewater [239–242]. Recently, researchers have explored MBR-NF systems for hospital wastewater because MBRs alone are insufficient at removing all pharmaceuticals, disinfectants, metabolites, and particularly iodinated contrast media (Fig. 11) [87]. Therefore, an additional NF filtration acts the purification step to remove bio-refractory micropollutants, hardness salts, and heavy metals from hospital wastewater thoroughly and enable its sustainable reuse and recycling.

There are several advantages to treating hospital wastewater with intreated MBR and NF treatment systems, as the synergy promotes the treatment efficiency. First, compared to using an NF system alone, an MBR pretreatment step significantly improves an integrated NF treatment system's efficiency and stability/lifespan [243]. Second, based on the application, NF membrane treatment is preferable to other integrated MBR-membrane treatment systems. For water softening applications, NF systems allow the passage of monovalent ions and retain multivalent ions. NF membranes are also very effective at bacteria elimination, pharmaceuticals, personal care products, and organic compound removal [84,244]. Moreover, NF membranes have smaller pore sizes (1–2 nm) than UF and MF membranes to reject smaller viruses and maintain microbial quality in wastewater systems for high residence time. Compared to RO, NF systems use lower operating pressures, have higher fluxes, and lower implementation and operation costs [226]. However, MBR-NF systems are not able to produce high quality water, i.e., drinking water, which is only possible when coupled with additional post-treatment steps for complete disinfection or desalination.

Despite these advantages, fouling and irreversible membrane scaling remain a significant disadvantage of MBR-NF systems, limiting their greater implementation for hospital wastewater treatment. Fouling occurs when colloidal-sized substances and soluble inorganic compounds such as silica, metal oxides, and microorganisms pass through the MBR and deposit and stick onto the NF membrane surface, leading to a decline in flux, increased energy demand and operation costs, and conception of cleaning chemicals.

To create a fouling and scaling control strategy for MBR-NF systems, Lan et al. conducted a study to optimize the permeate flux using wastewater from Purpan, a hospital in Toulouse, France, and found critical flux, threshold flux, and limiting flux [245]. The critical flux is the flux below which no fouling occurs and permeate drag forces overcome repulsive membrane forces, inducing foulant deposition on the membrane surface. The threshold flux is the flux below which a low constant fouling rate occurs; while above it, the fouling rate increases rapidly. The limiting flux represents the maximum stationary flux at a transmembrane pressure with a given solution, and above it, an increase in transmembrane pressure does not increase flux. The corresponding values for these fluxes were 70 L·h^{-1}·m^{-2} at 3.4 bar and 33 L·h^{-1}·m^{-2} for the limiting flux at 10–35 bar. The exact threshold flux was not found but occurred around 3.4 to 10 bar. By optimizing these parameters, they could correlate flux behavior and fouling mechanisms for MBR-NF systems.

However, these correlated mechanisms are highly susceptible to the MBR efficiency and effluent composition. Therefore, Lan et al. proposed a follow-up study to correlate fouling mechanisms and foulant compositions in an MBR-NF medical wastewater treatment system [246]. They used the same MBR effluent and NF membrane system from the previous study and altered the transmembrane pressures to find a stable flux filtration [245]. Then, they used surface morphology and chemical composition analysis to establish a quantitative link between stable flux and calcium phosphate concentration in MBR effluents and found a specific range of pH values reasonable for the irreversible fouling of calcium phosphate on the NF membrane.

Despite the fouling issue, other studies have shown excellent separation performance for integrated MBR-NF systems. In a study by Tran et al., an integrated MBR-NF system was evaluated for treating medical wastewater from the Military hospital 175 in Ho Chi Minh City, Vietnam. For organic loading rates of 2.5 kg COD m^{-3}·d^{-1}, the performance of the integrated system showed a consistently high COD removal average of 92.7%, nitrogen removal rate of 83%, log removal rate for *E. coli*, and coliform bacteria four times higher than the average. Overall, this integrated system produced grade A effluent according to the Vietnamese water quality standards. Likewise, Beier et al. confirmed using MBR technology followed by an advanced NF post-treatment step [227]. They used wastewater from Waldbröl hospital in Germany and achieved excellent performance for separating compounds with a molar weight greater than 200 g·mol^{-1}. Besides these studies on hospital wastewater, several other MBR-NF systems have been used to purify wastewater from pharmaceutical industry containing trace organic compounds, antibiotic groups, and other micropollutants [223,224,240,247–249].

Overall, the MBR-NF systems have demonstrated

potential in treating hospital wastewater on-site to prevent the pollution of aquatic ecosystems and offer many advantages compared to other integrated systems. Significant progress has been made on fouling control strategies. Nevertheless, MBR-NF systems are less effective in solute rejection and should only be used in applications with lower water quality.

5 Conclusions and outlook

Given the rapid spread of emerging infectious diseases during the global epidemics, urgent preventative actions should be taken. During epidemic treatment, large amounts of hospital wastewater from hospitals and related medical activities are discharged into our waterways, posing high risks to human health and may contribute to the failure in pandemic control. Meanwhile, despite the growing concern over the hospital waste management, there is still a lack of attention on treatment technologies for hospital wastewater.

Membrane technology possesses distinct advantages in achieving selective separation, significantly less chemical consumption, less byproducts as secondary pollutants, and higher energy efficiency. Based on current advancement in membrane technology for hospital wastewater treatment, the future trends of their applications are discussed as follows:

1) By applying MBRs, pharmaceuticals can be effectively removed from hospital wastewater via the integration biodegradation/adsorption and membrane filtration. Other than conventional UF/MF hydrophilic membranes, the evolution of novel MBR concepts is emerging by employing other types of membranes to achieve different separation purposes, such as volatile removal, selective extraction of particular microorganisms of interests. The tailoring of high-performance membranes for the MBR applications has created new research avenue, including the incorporation of functional materials such as nanoparticles to enhance selectivity and permeability, and reduce fouling.

2) MBRs play an essential role in removing viruses from hospital wastewater in large-scale WWTPs. However, the different removal efficiencies of the same virus through different types of MBRs are not compared or rationalized; the reasons for the widely scattering data (of removal efficiency) for different virus is not well understood. Therefore, more investigation is still required to processing viral pathogens with the different capabilities of MBRs.

3) The mitigation strategies to reduce irreversible membrane fouling need to be further investigated. Further control strategies such as the use of pretreatment methods and membranes surface modification should be comprehensively studied to improve antifouling properties. The equilibrium model of fouling extends and operating conditions need to be optimized. Furthermore, the MBR cleaning reagents and versatile cleaning procedure need to be explored to ensure sustainable operation. Attempts to translate the technology from laboratory to industry-scale should aim to achieve a balance between sustainability and energy consumption.

4) The energy evaluation and techno-economic analysis are essential but lacking for large-scale MBR applications. In general, micropollutants generated from the pharmaceutical industries experience low removal efficiency with traditional MBRs and hence should be improved. The choices of membrane types, integration of separation units and operating conditions will significantly affect the removal efficiency of contaminants in hospital wastewater treatment. The two levels of integration have greatly
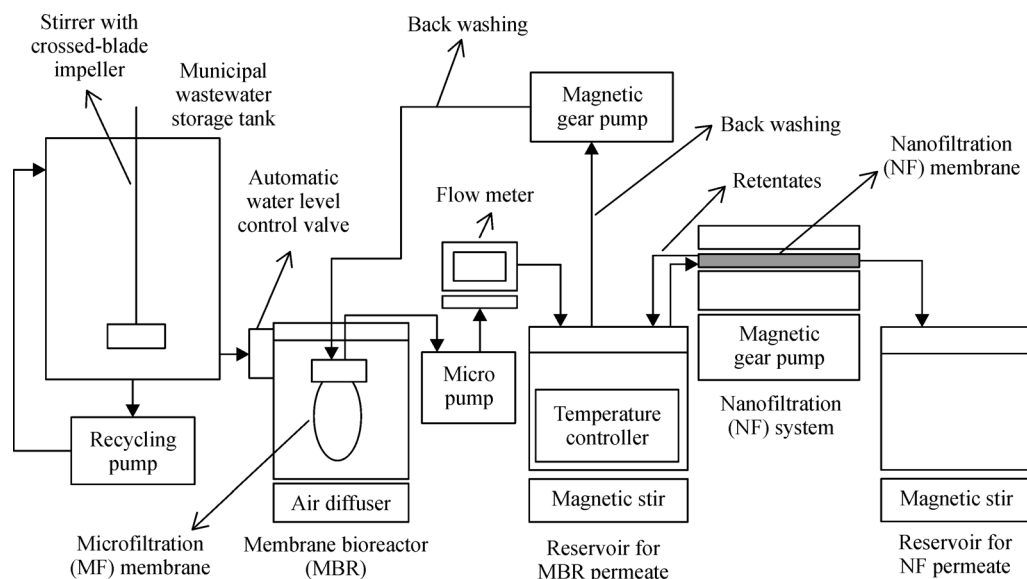

Fig. 11 The scheme of integrated MBR-NF systems. Reprinted with permission from ref. [250], copyright 2011, Elsevier.

extended the applications of MBR systems, i.e., hybridizing novel membranes into the MBR units (namely hybrid MBRs), or MBR as a pretreatment step and integrating other membrane processes as a purification step (namely integrated MBR-membrane systems). The latter offers more flexibility and process stability, and lower operation cost, thus better scalability for industrial applications.

Through this review, it believes that the advancement in MBR concepts and systems exhibit great potential in assisting hospital wastewater treatment and hence contributing toward epidemic prevention.

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