Chemical Engineering Journal 358 (2019) 1421–1437

Contents lists available at ScienceDirect

Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Review

The effect of bioelectrochemical systems on antibiotics removal and antibiotic resistance genes: A review

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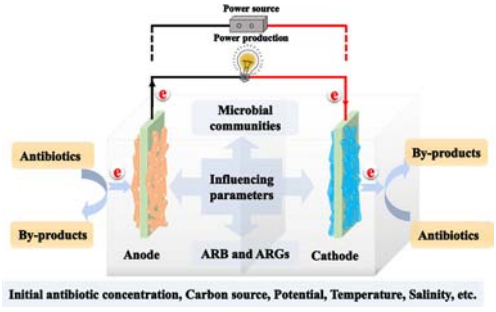
HIGHLIGHTS

- Removal mechanisms and degradation pathways of antibiotics are elucidated.
- Effect of parameters on antibiotics removal in BESs is systematically reviewed.
- Predominant microbes and effect of parameters on them are elaborated.
- Effect of BESs on ARB and ARGs during antibiotics removal is discussed.
- Challenges and future researches for BESs development are proposed.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Bioelectrochemical system
Antibiotic
Antibiotic resistance gene
Microbial community
Environmental factor

ABSTRACT

Increasing human activities, a great demand for animal protein and intensive use of antibiotics, are responsible for the persistent emergence of antibiotic contaminants in the environment. Increased attention has been paid to this pollution because it possibly exacerbates the appearance of antibiotic resistance bacteria and antibiotic resistance genes. Hence, the effective removal of antibiotic pollutants has become a hot topic in environmental research. Bioelectrochemical systems (BESs) coupled with microbial metabolisms and electrochemical redox reactions are considered to be promising alternatives for the degradation of antibiotics contaminants. In this review, state-of-the-art BESs for enhanced antibiotics removal are described and antibiotics removal mechanisms based on BESs are reviewed. The effects of typical parameters, such as the electrochemical properties and initial concentration of antibiotics, applied potential, electrode material, carbon source, temperature, and salinity, on the overall performance of such systems are elaborated. Degradation pathways and metabolic byproducts of antibiotics related to BESs processes are also reported. Additionally, predominant microbes responsible for several representative antibiotics are demonstrated and their evolution factors are tabulated and discussed. Furthermore, the effect of the temperature, salinity, initial antibiotic concentration, and potential applied in BESs on the fate of antibiotic resistance genes is disclosed. Finally, an outlook on future applications and challenges is provided, which is conducive to the development of BESs for the treatment of wastewater containing antibiotics.

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https://doi.org/10.1016/j.cej.2018.10.128
Received 30 July 2018; Received in revised form 6 October 2018; Accepted 14 October 2018
Available online 15 October 2018
1385-8947/

Nomenclature

BES	bioelectrochemical system
MEC	microbial electrolysis cell
WWTP	waste water treatment plant
ARG	antibiotics resistance gene
CV	cyclic voltammetry
CAP	chloramphenicol
NFZ	nitrofurazone
3A5MI	3-amino-5-methylisoxazole
AMH	[(5-hydroxyamino-2-furyl)-methyl]-hydrazinecarboxamide
AMN	[(5-amino-2-furyl)-methylene]-hydrazinecarboxamide
NFF	(5-nitro-2-furyl)-methanamine
MFC	microbial fuel cell
SBBR	sequencing batch biofilm reactor
PCR	polymerase chain reaction
ARB	antibiotic resistant bacteria
SHE	standard hydrogen electrode
SMX	sulfamethoxazole
SDZ	sulfadiazine

1. Introduction

Nowadays antibiotic contaminants extensively enter many environment matrixes and are considered as emerging contaminants of concern [1–3]. This issue raises serious concerns for public health because the ecological balance is endangered and it poses a persistent pressure on antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARGs) [4–8]. Moreover, because of human activities, ARB and ARGs move around the globe at an unprecedented scale compared to the past billion years [9]. Hence, the worldwide occurrence of antibiotics contamination requires effective and economical treatments to eliminate these pollutants, which has become a hot topic in environmental research.

Different treatments with considerable removal efficiencies with respect to antibiotic residuals were developed in recent years. Advanced oxidation processes (AOPs) attract attentions due to their robust removal efficiencies [10,11]. But they are cost-prohibitive for full mineralization of antibiotics and possibly produce sub-active toxic byproducts [12]. The antibiotics removal efficiencies of adsorption processes and membrane technologies are satisfying [13,14]. But these techniques are unable to ultimately degrade antibiotics and are markedly impaired by the presence of other organic contaminants [14]. Biological methods catch attentions mainly with respect to their high versatile performance for *in situ* application, but they are usually time-consuming techniques [15–17].

Bioelectrochemical systems (BESs), including microbial fuel cells (MFCs) and microbial electrolysis cells (MECs), coupled with microbial metabolisms and electrochemical redox reactions are considered to be promising alternatives for the degradation of biorefractory contaminants [18–21]. Compared with the aforementioned techniques, BESs show the following advantages: (1) cost-effective operation: without additional reductant usage in biocathodes and any external power input, BESs exhibit high antibiotics removal efficiencies (Table 1); (2) eco-friendliness: 3-amino-5-methylisoxazole (3A5MI), a highly biotoxic intermediate of sulfamethoxazole (SMX), is further degraded in MFCs [22]. The use of biocathodes also circumvents the production of highly toxic byproducts from chloramphenicol (CAP) and nitrofurazone (NFZ) [23,24]; (3) versatile treatment of solid-phase matrixes: Zhang *et al.* reported good performances of three-dimensional biofilm electrode reactors for the antibiotics removal in solid-phase environments [25]; and (4) integration possibilities with other technologies: MFCs coupled with AOPs, adsorption methods, and constructed wetlands for various antibiotics removal were investigated, which are illustrated in Fig. 1.

The objective of this paper is to give a comprehensive review about the effect of BESs on antibiotics pollutants and ARGs. Therefore, this review firstly focuses on the application of BESs to seven classes of antibiotics degradation, which are tabulated in Table 1. Based on illustrating the antibiotics removal mechanisms of BESs, the effect of various operating parameters on the performance of BESs are elaborated. Degradation pathways and representative metabolic products of antibiotics are disclosed. Additionally, predominant microbes responsible for several representative antibiotics are demonstrated and their evolution is tabulated and discussed. The effect of BESs on the fate of ARB and ARGs during antibiotics removal is also addressed. Finally, challenges and outlooks are discussed, which aids the acquisition of knowledge about biocatalyst mechanisms and contributes to the development of BESs in different matrixes.

2. Antibiotics removal mechanisms based on BESs

Considering the different operation modes of BESs used to degrade antibiotics, the removal mechanisms can be divided into the following three categories:

In category A (Fig. 2A), mostly MFCs are operated, which consist of a biological anode and abiotic cathode. Potassium ferricyanide (operated as two-chamber MFC) or oxygen (operated as single-chamber air cathode MFC) are usually used as electron acceptors in the abiotic cathode [50]. In biological anodes, antibiotics serve as electron donors and carbon sources. Exoelectrogenic microbes and degrading antibiotic bacteria, which attach to the anodes to form biofilms within extracellular polymeric substances, are responsible for the reduction of an overpotential of biorefractory antibiotic parents and their metabolites. Anaerobic biodegradation coupled with electrical stimulation is a key mechanism in MFCs, contributing to the mineralization of antibiotics. Persistent electrical stimulation can provide electrons to the microenvironment and stimulate the microbial metabolism through direct or indirect electron transfer to bacterial cells [51]. The stimulated microorganisms metabolize antibiotics quickly by secreting enzymes, for example, SMX and its byproduct 3A5MI [22].

In category B (Fig. 2B), the systems are usually operated as biocathodes, that is, an MEC with external energy supply, because the reduction potentials of antibiotics are always higher at the biological anode [52]. The anodes of this system are always operated as microbial anodes to reduce the overall power consumption. The degradation mechanism of antibiotics in this system mainly involves direct electrochemical reduction and biodegradation reactions. Antibiotics accept electrons from the cathode and are directly reduced through electrochemical reduction. Additionally, microbes flourishing in cathode electrodes as biocatalysts accelerate the reduction of antibiotics by reducing their overpotential. Representative examples include CAP and NFZ [23,24]. The systems can also be operated as a biocathode without external power supply if the antibiotics have a higher reduction potential than the biological anode.

In category C (Fig. 2C), modified materials are often used in the BES cathode to generate radical species, which attack and degrade target antibiotics. This process mainly involves the following reactions: (i) electrons generated by bioanode transfer to the surface of the cathodic material through an external circuit; (ii) cathodic material accepting electrons to reduce dissolved oxygen or air from pumps for the production of H_2O_2, i.e. $O_2 + 2e^- + 2H^+ \rightarrow H_2O_2$; and (iii) H_2O_2 under ultraviolet light or cathodic material can generate radical species, such as hydroxyl radicals (·OH), which oxidize and destroy antibiotics parents, i.e. $H_2O_2 + h\nu \rightarrow 2OH\cdot$ and Antibiotic + $OH\cdot \rightarrow$ Degradation products.

Table 1
Researches using bioelectrochemical systems for antibiotics removal.

Antibiotics	Classes of Antibiotics	Configuration	Inoculation	HRT	Initial Concentration	Removal Efficiency/%		Refs.
						Experiment	Control	
cefazolin sodium	cephalosporins	Air-cathode single-chambered MFC	aerobic activated sludge	31 ± 3.7 h	50 mg/L	> 70	~40	[26]
metronidazole	nitroimidazoles	two-chamber MFC	anaerobic sludge	24 h	10 mg/L	85.4	35.2	[27]
nitrofurazone	nitrofurans	biocathode with applied voltage of 0.8 V (vs. SHE)	nitrofurazone- reducing consortium	1 h	50 mg/L	70.60 ± 4.21	53.82 ± 1.80	[23]
penicillin	*β*-lactam	air–cathode single-chambered MFC	another MFC in group	24 h	50 mg/L	98	N.M	[28]
ceftriaxone sodium	*β*-lactam	air–cathode single-chambered MFC	another MFC in group	24 h	50 mg/L	91	51	[29]
cefuroxime	*β*-lactam	SBBR with electrodes	activated sludge	12 h	0.5 mg/L	> 90	30–40	[30]
tetracycline	tetracyclines	three-dimensional biofilm-electrode reactors with applied voltage of 0.8 V (vs. N.M)	anaerobic sludge	40 h	200 μg/L	89.3–95.6	21.8–60.2	[25]
tetracycline	tetracyclines	three-dimensional biofilm-electrode reactors with applied voltage of 0.8 V (vs. N.M)	anaerobic sludge	40 h	200 μg/L	82.61–95.80	~76–82	[31]
tetracycline	tetracyclines	MFC coupled with photo-electrochemical catalysis	N.M	2 h	100 mg/L	70	10	[32]
tetracycline	tetracyclines	MFC coupled with constructed wetlands	anaerobic sludge	2.5 d	800 μg/L	> 99	N.M	[33]
tetracycline	tetracyclines	MFC coupled with membrane bioreactor	*Shewanella* sp.	17 h	90 mg/L	99.5	N.M	[34]
tetracycline	tetracyclines	two-chamber MFC	Anaerobic activated sludge	7 d	50 mg/L	79.1	14.90	[35]
oxytetracycline	tetracyclines	two-chamber MFC	pig manure	78 h	10 mg/L	99	58.26	[36]
sulfamethoxazole	sulfonamides	two-chamber MFC	anaerobic sludge	48 h	20 mg/l	> 99	65	[37]
sulfamethoxazole	sulfonamides	two-chamber MFC	sulfamethoxazole acclimatized culture	48 h	0.08 mmol/L	83.3	63.3	[38]
sulfamethoxazole	sulfonamides	two-chamber MEC with applied voltage of 0.2 V (vs. Ag/ AgCl)	municipal wastewater	7 d	6 μg/L	100	N.M	[39]
sulfamethoxazole	sulfonamides	three-dimensional biofilm-electrode reactors with applied voltage of 0.8 V (vs. N.M)	anaerobic sludge	40 h	200 μg/L	88.9–93.5	23.3–64.2	[25]
sulfamethoxazole	sulfonamides	three-dimensional biofilm-electrode reactors with applied voltage of 0.8 V (vs. N.M)	anaerobic sludge	40 h	200 μg/L	72.20–93.52	~63–82.5	[31]
sulfamethoxazole	sulfonamides	MFC coupled with constructed wetlands	anaerobic sludge	2.5 d	800 μg/L	> 99	N.M	[33]
sulfanilamide	sulfonamides	two-chamber MFC	anaerobic sludge	96 h	30 mg/L	90	60	[40]
choramphenicol	choramphenicols	two-chamber MFC	anaerobic sludge	12 h	50 mg/L	84	48	[41]
choramphenicol	choramphenicols	two-chamber MFC	anaerobic sludge	48 h	30 mg/L	83.7	60.5	[42]
choramphenicol	choramphenicols	biocathode with applied voltage of 0.5 V (vs. SHE)	activated sludge	24 h	30 mg/l	99.98 ± 0.10	94.65 ± 4.26	[43]
choramphenicol	choramphenicols	biocathode with applied voltage of 0.5 V (vs. SHE)	activated sludge	24 h	32 mg/L	96.0 ± 0.9	62.0	[24]
choramphenicol	choramphenicols	biocathode with applied voltage of 0.5 V (vs. SCE)	activated sludge	24 h	30 mg/L	86.3	62.9	[44]
choramphenicol	choramphenicols	biocathode with applied voltage of 1.5 V (vs. SHE)	anaerobic sludge from a bioreactor	72 h	50 mg/L	92.50	N.M	[45]
choramphenicol	choramphenicols	biocathode with applied voltage of 1.5 V (vs. SHE)	anaerobic sludge	72 h	50 mg/L	> 90	N.M	[46]
choramphenicol	choramphenicols	two-chamber MEC with applied voltage of 0.3 V	a bioelectrochemical reactor effluent	24 h	32 mg/L	100	< 7.8	[47]

Notes: HRT: hydraulic retention time; SHE: standard hydrogen electrode; SCE: saturated calomel electrode; N.M: not mentioned.

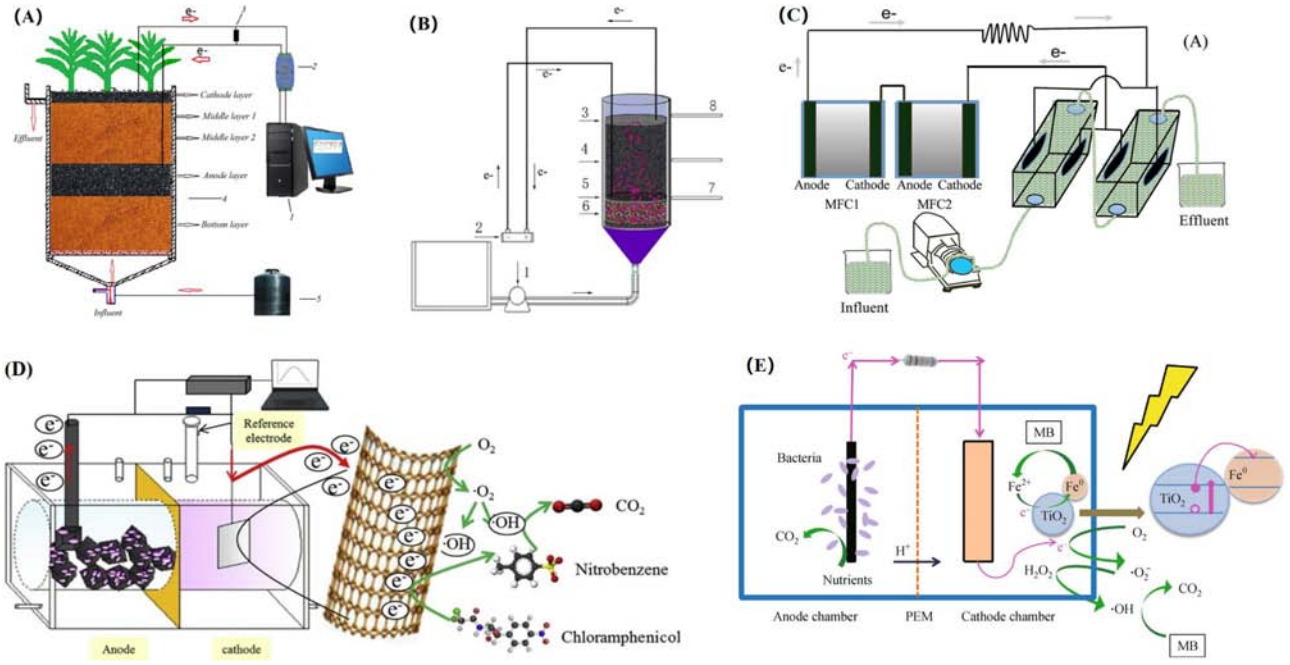


Fig. 1. Schematic diagrams of combination of bioelectrochemical systems and other treatment process for antibiotics removal. (A) Schematics of constructed wetlands-MFCs (1 computer; 2 data acquisition module; 3 resistance; 4 constructed wetlands-MFC; 5 peristaltic pump and tank). Reproduced with permission from ref [48]. Copyright 2017 Elsevier. (B) Schematics of the three-dimensional biofilm-electrode reactors: (1 peristaltic pump; 2 DC regulated power supply; 3 active carbon fiber/Ti mesh anode; 4 granular activated carbon; 5 active carbon fiber/Ti mesh cathode; 6 gravel; 7 cathode effluent; 8 anode effluent.). Reproduced with permission from Ref. [25]. Copyright 2016 Elsevier. (C) Schematics of MFC-sorption apparatus. Reproduced with permission from Ref. [49]. Copyright 2015 Royal Society of Chemistry. (D) Schematics of BESs coupled with advanced oxidation process (with novel metal foam electrodes). Reproduced with permission from ref [47]. Copyright 2017 Elsevier. (E) Schematics of BESs coupled with advanced oxidation process (with Fe0/TiO2 cathode). Reproduced with permission from ref [32]. Copyright 2016 SpringerLink.

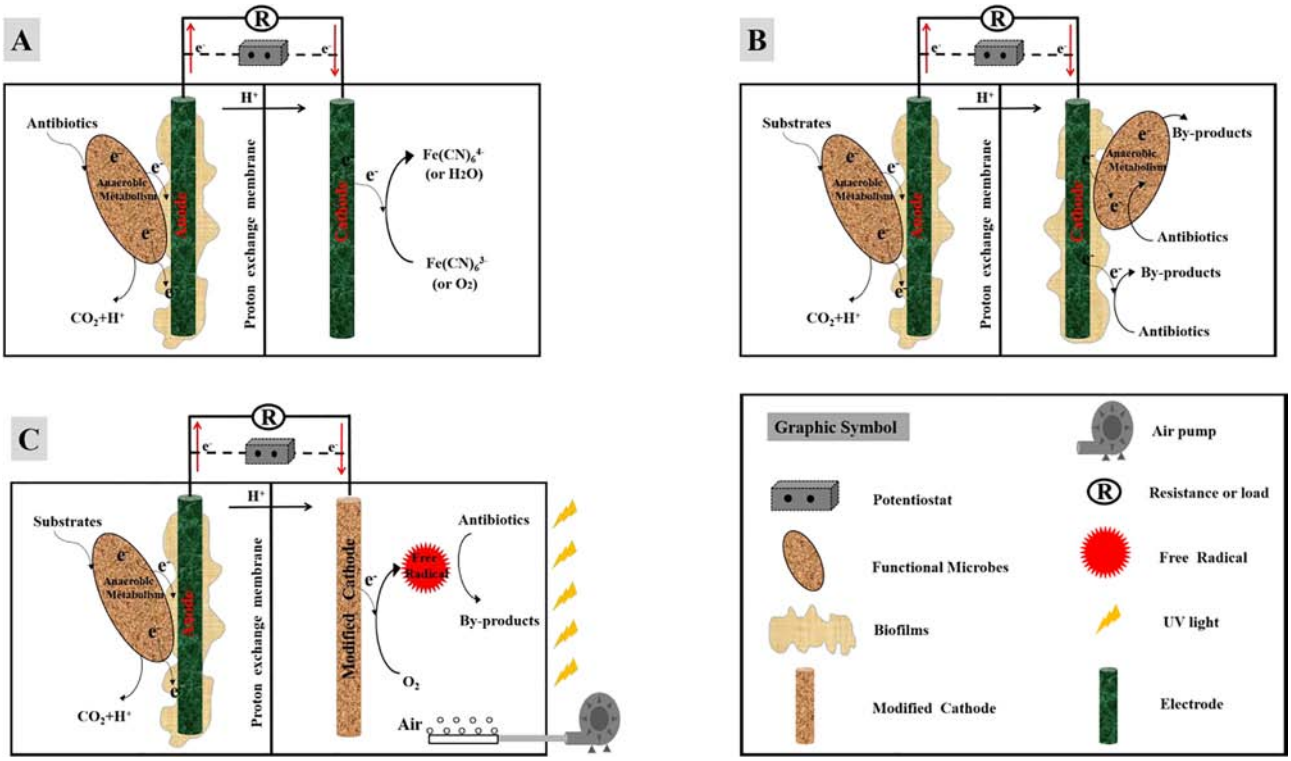


Fig. 2. Antibiotics removal mechanisms based on bioelectrochemical systems. (A) A biological anode on antibiotic oxidation coupled to an abiotic cathode. (B) A biological anode coupled to biological cathode to reduce antibiotics. (C) A biological anode coupled to a cathode compartment with destroying antibiotics through AOPs.

Wu *et al.* rapidly degraded CAP in a copper foam cathode with *in situ* produced hydroxyl radicals and direct electrochemical reduction affecting the cathode (Fig. 1D) [47]. In addition, Jiang *et al.* reported that the cathode modified by photo- and electrochemical catalysis materials ($Fe0/TiO_2$) effectively produced ·OH radicals under visible light and electrons from the bioanode to achieve a rapid degradation of tetracycline (Fig. 1E) [32].

3. Effect of parameters on BESs during antibiotics removal

Studies on the removal of contaminants in BESs showed that the performance of BESs is affected by many parameters [52–55]. Hence, it is essential to discuss the effects of parameters in detail to optimize and apply the systems in the future. Several parameters, such as the flow rate, additives, source of inoculation, pH, and buffer solution have been addressed in several reviews [56,57]. Here, properties of contaminants themselves, such as electrochemical properties of antibiotics and their initial concentration; system determiners, such as the applied potential and electrode material; and environmental factors, such as the carbon source, temperature, and salinity, are discussed. Their effects on the performance of BESs are elaborated, mainly involving the power generation capacity, removal efficiency of antibiotics, and transformation of degradation byproducts.

3.1. Electrochemical properties of antibiotics

The roles of the molecular structure and functional groups of pollutants have been proven to notably affect the performance of bioelectrochemical or electrochemical reduction [58,59]. With respect to BESs treating antibiotics, the electrochemical properties of target antibiotics are important parameters because they provide a theoretical basis to determine if the target antibiotics in the BES anode or cathode are suitable for removal.

Cyclic voltammetry (CV), linear sweep voltammetry and chronoamperometry are powerful electrochemical techniques and CV is often performed to elucidate the possible redox reactions of target antibiotics under different potentials [60,61]. The CV results from Kong *et al.* showed that NFZ has three reduction peak potentials at approximately –0.35 V, –0.60 V, and –0.95 V (Fig. 3A; peaks a1, a2, and a3, respectively) [59]. This indicates that NFZ can be reduced on the cathode and three cathodic reactions will occur under different cathode potentials. Further investigation showed that the three cathode potentials 0.2 V, 0.5 V, and 0.8 V notably influence the bio-electro degradation efficiency and byproduct formation of NFZ [23].

Another representative antibiotic is CAP, which is widely reduced in biocathodes. Its electrochemical properties were revealed by Kong *et al.* and Liang *et al.* using CV (Fig. 3A, peaks c1 and c2, and Fig. 3B, peaks a' and c) [24,59]. The reduction potential of CAP was observed close to -0.55 V and 0 V, suggesting that different cathode potentials lead to different transformation reactions and metabolites of CAP. Guo *et al.* provided experimental evidence that confirmed this conclusion [46]. They pointed out that the degradation efficiency of CAP at -1.25 V is higher than that at –0.5 V and $AMCl_2$, a typical byproduct of CAP, dechlorinates more easily.

3.2. Initial concentration of antibiotics

The effect of the initial concentration of antibiotics on the removal efficiencies in BESs is rather complicated, because prior studies provided contradictory conclusions. Several studies showed that the higher the concentration of the antibiotics is, the lower is the removal capacity of BESs. Several studies reported an improvement in the removal efficiencies with increasing antibiotics concentration, while other work demonstrated that the initial concentration of antibiotics has no notable effect.

It is easily understandable that the pollution load of the systems ascends with increasing initial concentration of antibiotics. Therefore, more time is required to remove them. Guo *et al.* pointed out that the degradation efficiency of CAP in the biocathode decreases with increasing concentration [46]. Wang *et al.* obtained a similar result; with the increase of the SMX concentration from 20 mg/L to 200 mg/L, the half-life of SMX removal in MFCs showed a greater extension from 24 h to 72 h [37]. These results show that the degradation efficiencies of antibiotics depend on the original concentration to some extent.

Nevertheless, other studies offered contradictory experimental results, that is, it was reported that the higher the antibiotics concentration is, the better is the BES performance. Wen *et al.* found that the removal rate of 50 mg/L ceftriaxone sodium is much higher than that of 30 mg/L ceftriaxone sodium in single-chamber MFCs [29]. Based on electrochemical impedance spectroscopy and the anode discharge performance, they revealed that ceftriaxone sodium indirectly influences the redox enzymes of microbes, which leads to the overall decline of the internal MFC resistance. In another MFC study, similar results were obtained [28]. It was observed that the electricity generation of MFC increases with increasing penicillin concentration.

Additionally, some researchers reported that the performances of BESs remain constant with increasing initial concentration of

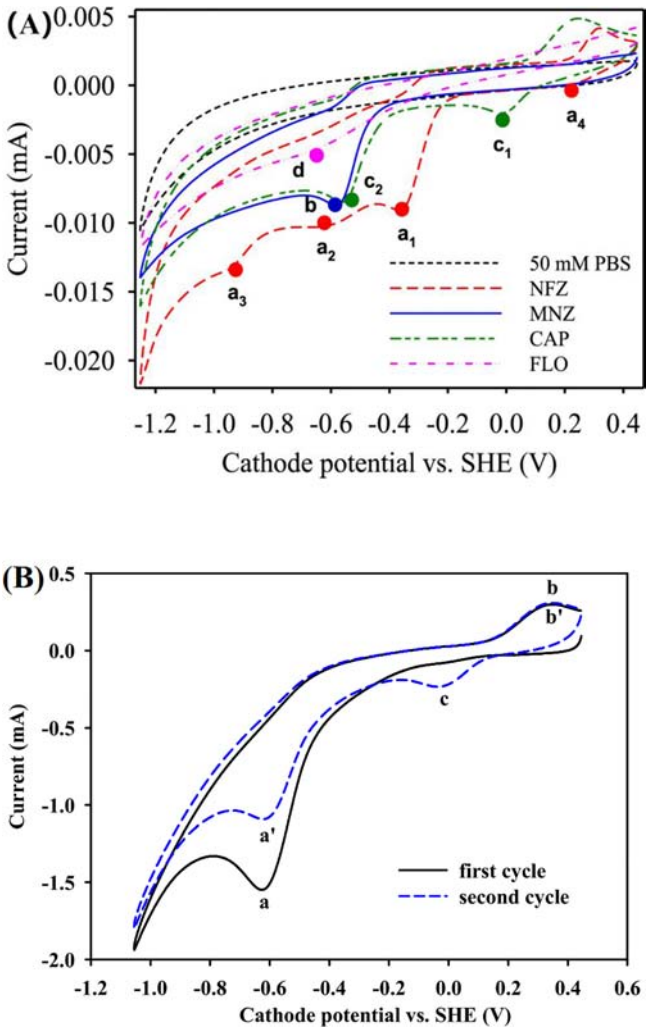


Fig. 3. Cyclic voltammograms of nitrofurazone and chloramphenicol. (A) Cyclic voltammograms of 50 mg/L nitrofurazone (NFZ) and chloramphenicol (CAP) in the 50 mmol/L phosphate buffered solution (PBS); Scan rate: 5 mV/s. Reproduced with permission from ref [59]. Copyright 2015 Elsevier. (B) Cyclic voltammograms of 32 mg/L chloramphenicol reduction on the bare cloth cathode. Scan rate: 5 mV/s. Reproduced with permission from ref [24]. Copyright 2013 American Chemical Society.

antibiotics. Zhang *et al.* showed an excellent tolerance of anodic biofilms to cefazolin sodium [26]. The anodic biofilms were continuously exposed to increasing cefazolin sodium concentrations (from 50 to 450 mg/L) and a reduction of voltages over 1200 h during MFC operation was not observed. Extracellular polymeric substances and the thickness of biofilms may be responsible for quenching the toxin of those antimicrobial compounds. Another example was reported in Wu *et al.* [62]; with the addition of tobramycin at the μg/L to mg/L level, the voltage outputs in MFCs remained relatively high but steady. These studies exhibited a prominent tolerance to the shock load, providing a scientific reference for the treatment of highly concentrated pharmaceutical wastewater containing antibiotics in BESs.

3.3. Applied potential

The change of applied potentials leads to the electrochemically active biofilm having a variety of degrees of electrical stimulation and provides different numbers of electron donors to affect the mineralization of antibiotics [63,64]. A clear conclusion was drawn based on previous studies; more negative applied potentials notably enhance the removal efficacy of antibiotics and sharply shorten the hydraulic retention time (HRT) of biocathodes.

Kong *et al.* determined NFZ reduction rate constant of $0.677 \pm 0.069\ h^{-1}$ and reduction efficiency of 42.25 ± 1.35% at 1 h when applying a voltage of -0.2 V, whereas these constants increased to $1.202 \pm 0.124\ h^{-1}$ and 70.60 ± 4.21%, respectively, at a cathode potential of -0.8 V [23]. In addition, the more negative cathode voltage was applied, the faster transformation rates of degradation intermediates were achieved. In $NaHCO_3$-fed biocathodes, [(5-amino-2-furyl)-methylene]-hydrazinecarboxamide (AMN), and (5-nitro-2-furyl)-methanamine (NFF) products notably accumulated within 72 h at -0.2 V, but they both further degraded and disappeared quickly within 48 h at -0.8 V.

Similar results were reported in other studies. The increase of the applied voltage leads to a higher degradation efficiency and removal degree of CAP. Guo *et al.* demonstrated that the CAP removal efficiency increases with increasing cathode potential (from −0.5 V to −1.25 V; vs. standard hydrogen electrode (SHE)) [46]. The amine product of the CAP reduction ($AMCl_2$) could be further degraded at −1.25 V but not at −0.5 V. Wu *et al.* found that by increasing the applied voltage from 0.3 V to 0.5 V with a nickel foam electrode, the CAP degradation started directly because of breaking of the bond of the terminal carbon instead of hydroxylation of the head-end carbon with a nitrato nitro group [47].

The increment of cathode potentials is tightly associated with higher removal rates; however, when the externally applied potential is too low, the overall energy consumption will increase. Therefore, the optimization of the applied potential to reduce the energy consumption while keeping a high degradation efficiency of antibiotics needs to be studied in the future.

3.4. Electrode material

Electrode materials are fundamental for the overall performance of BESs because microbes flourish in the electrode as biocatalysts to form biofilms for electron transfer [65–68]. Numerous researchers have used carbon felts as electrode materials (Table 1). However, the studies that documented the performance of different electrode materials for the treatment of wastewater containing antibiotics are limited. There is only one study from Wu *et al.* who investigated the degradation efficacy of three metal foams as cathode electrodes for CAP treatment in BESs [47].

Wu *et al.* compared the use of carbon rods, copper foam, and nickel foam as cathodic electrodes and found that copper foam exhibits the best CAP removal performance (Fig. 1D) [47]. Using a copper foam electrode, 32 mg/L CAP was removed within 12 h, which is more than that based on the carbon rod (after 24 h) and nickel foam (> 120 h). In addition, electrode materials also affect the formation of final degradation products. The CAP is completely mineralized to CO_2 and H_2O with the copper foam electrode, while the main products based on the use of carbon rod and nickel foam electrodes are nitrobenzene and 4-nitrobenzyl alcohol, respectively. They revealed the materials reduction current based on the results from CV. Based on the comparison of the carbon rod with nickel foam electrodes, the highest reduction current was obtained with the copper foam electrode.

With the goal of sustainable development of BESs, some low-cost and environment-friendly electrode materials, such as biochar and modification materials, can be developed to promote the redox reaction rate. More attention needs to be paid on the investigation of the interaction between electrodes and microbes and the mutual effect between electrodes and antibiotic pollutants. For example, whether modified electrodes can cause an increase in expression of genes related to electron transfer and further to enhance electron transfer rates involving the redox reaction of antibiotic degradation warrants further studies.

3.5. Carbon source

The carbon source plays an important role in the balance between competition and commensalism of the microbial community and metabolic activities of microbes [69,70]. Research in this area mainly focuses on the performance of BESs without additional carbon sources (antibiotic acting as sole carbon source) and with inorganic and organic carbon sources.

Wang *et al.* proved the feasibility and effectiveness of anodic oxidation of SMX in MFCs in an oligotrophic environment [22]. Without additional carbon sources, the SMX, as the sole nitrogen and carbon source, is deeply mineralized to CH_4 (final degradation product). This indicates that the metabolic capacity of microbial communities, which utilized antibiotics as sole carbon sources, is greatly improved after acclimation. Another study about the effect of the inorganic carbon source $NaHCO_3$ on the biocathodic metabolism for NFZ removal was conducted by Kong *et al.* [23]. They demonstrated that the rate constant and removal efficiency of NFZ reduction in $NaHCO_3$-fed biocathodes are a little bit lower than that with the addition of glucose but markedly higher than those of the abiotic cathode. This implies that the $NaHCO_3$-fed biocathode still has a significant biocatalytic capacity. Based on the studies of Wang *et al.* and Kong *et al.*, antibiotic pollutants can be metabolized by functional microbes under oligotrophic conditions. However, this generally takes longer time.

Additionally, a lot of researches are based on easily biodegradable carbon sources, such as glucose and acetate, as cosubstrates to enhance the antibiotics treatment. Wen *et al.* demonstrated that the power output of MFCs, which use glucose and penicillin as cosubstrates, is nearly 48-fold that of MFCs only containing penicillin as substrate [28]. This observation indicates that the addition of cosubstrates provides sufficient carbon sources and more electron donors to enhance the metabolism of microbial communities. Similar evidence supporting this conclusion was found in another study about ceftriaxone sodium degradation in MFCs [29]. The role of an easily biodegradable cosubstrate was discussed by Liang *et al.* [24]. With the addition of glucose, the cathodic current of the biocathode notably increased at a more positive potential, suggesting that certain cathodic reactions occur and the electron transfer rate enhances in the presence of glucose.

Organic cosubstrates, often used as additional electron donors, promote the growth and metabolic activities of microbes. It is difficult to achieve a desired removal efficiency in a short time when using antibiotics as sole carbon sources due to their complex structures. However, do antibiotics directly co-metabolize with additional carbon sources or are they indirectly degraded through the secretion of enzymes and electronic shuttles from the microbial metabolism of additional carbon sources? These questions remain and need to be addressed in further research.

3.6. Temperature

Many studies have proven that the temperature greatly impacts the bacterial growth, metabolic activity, and further biochemical reactions related to antibiotics treatment [71–73].

Zhang *et al.* designed a single-factor experiment to explore the effect of the temperature (20 °C, 30 °C, and 40 °C) [41]. They obtained a higher CAP removal efficiency (75.13%) at 40 °C compared with 20 °C (68.11%). Guo *et al.* investigated CAP removal efficiencies in BESs at 10 °C, 15 °C, and 30 °C, respectively [45]. The CAP removal efficiencies sharply decreased from above 95% to below 10% as the temperature decreased from 30 °C to 10 °C. Interestingly, the temperature did not notably affect the performance of BESs with 2% salinity. Although the reaction temperature varied from 30 °C to 10 °C, the BESs maintained CAP removal efficiencies above 75%. Their results indicate the interaction of environmental factors and that the effect of the salinity on BESs is more influential than that of the temperature.

Kong *et al.* and Liang *et al.* reported the effect of a temperature switchover on the CAP removal by biocathodes [43,74]. Kong *et al.* showed that the CAP reduction rate significantly decreases when temperature decreases from 25 °C to 10 °C, but the biocathodes still have a larger reduction rate in contrast to the abiotic cathode at 10 °C. This is in accordance with the CAP reduction reaction current they revealed *via* CV. Based on GeoChip and Illumina sequencing approaches employing 16S rRNA genes, Liang *et al.* determined relevant microbes and functional genes responding to a temperature change from 10 °C to 25 °C. The main difference of the key genes responding to a 15 °C temperature increase is that the genes involve nitroreductase and heat shock protein but no electron transfer genes. The good catalytic stability of the biocathode exposed to a continuous low temperature of 10 °C is mainly based on: (i) enriching two dominant cold-adapted nitroreductase-carrying microbes, that is, *Aeromonas* and *Vagococcus*; and (ii) maintaining the relative abundance of key electron transfer genes such as unique cytochrome *c* genes and hydrogenase genes. Their investigation provided new insight into the development of cold-adapted biocatalytic systems.

It is necessary to assess the operation of large-scale BESs degrading antibiotics at different temperatures in the future. Hence, more experimental studies are required to understand the metabolic activities and stress mechanisms of electrode biofilms exposed to environments with temperature fluctuation.

3.7. Salinity

A high salinity has an adverse effect on the biological treatment and influences the conductivity of wastewater, which involves redox reaction rates in BESs [75–77]. Up to now, however, only one study by Guo *et al.* focused on the effect of the salinity on the removal efficiency of CAP by BESs [45].

The CAP degradation rates and formation of degradation products under different salinities (0, 0.5%, 2%, and 6%) were evaluated. Approximately 92.5% of the CAP removal efficiency was obtained at a salinity of 0.5%, which is higher than those without salinity (88.3%) and with a salinity of 6% (49.5%), indicating that the CAP removal efficiency can be enhanced under low salinity but not under high salinity. Furthermore, the trends of $AMCl_2$ and AMCl formation are consistent with the above-mentioned conclusion. The $AMCl_2$ concentration increases within 24 h and then is transformed to AMCl at salinities of 0.5%. In contrast, the content of $AMCl_2$ ascends continuously up to 58 h at a salinity of 6%, but almost no AMCl is generated. This suggests that the low salinity of pharmaceutical wastewater accelerates the transformation rate of CAP to $AMCl_2$ and the dechlorination of $AMCl_2$ to AMCl, but an inhibition effect occurs under higher salinity.

Based on the poor degradation of traditional biological treatment due to the high salt content and limited removal of AOPs because of high total dissolved solids, BESs are considered to be alternative treatments for high-salinity wastewater containing antibiotics. Previous studies on antibiotics removal by BESs have paid more attention to municipal wastewater and simulative artificial sewage. However, given the high diversity of antibiotics pollutants and universality of high-salinity pharmaceutical wastewater, more attentions are required to study the removal dynamics of a broad range of antibiotics using BESs under pressure of salinity. Additionally, more focus should be placed on the effect of operating parameters on the long-term stability of electroactive biofilms exposed to high salinity.

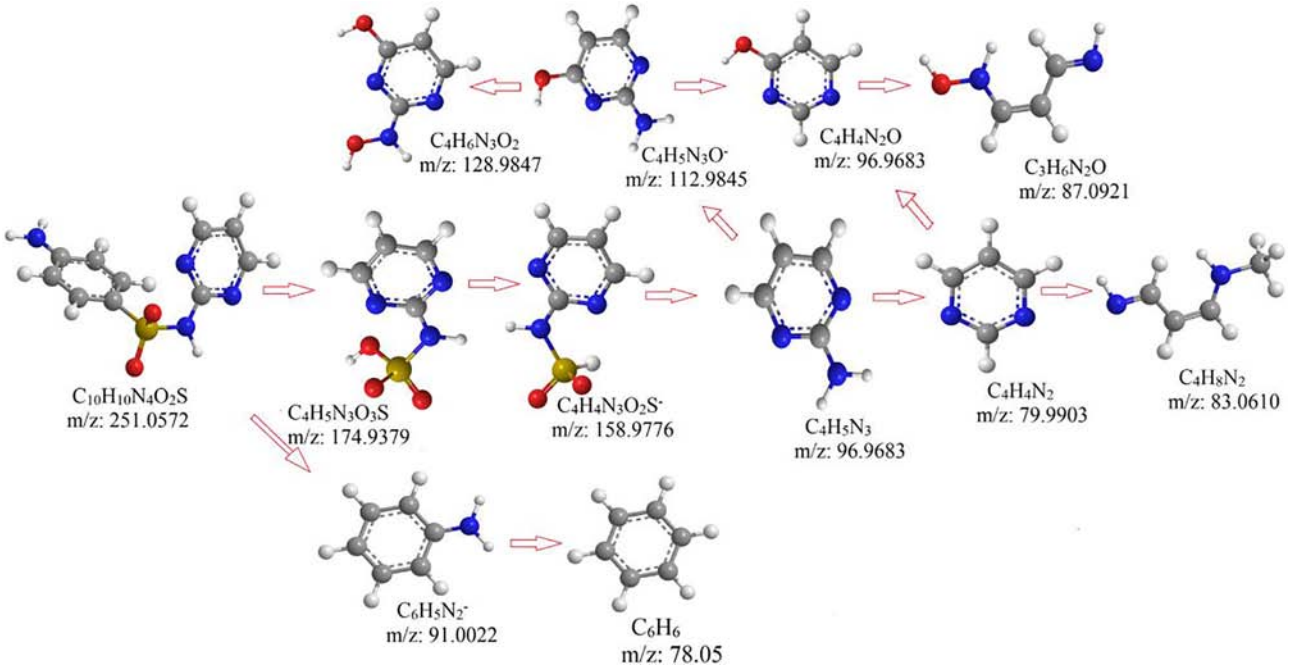
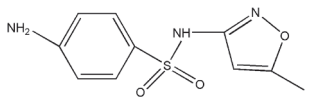
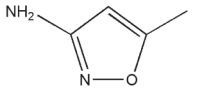
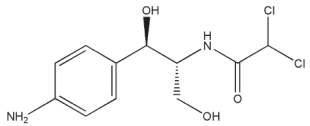
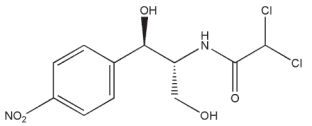
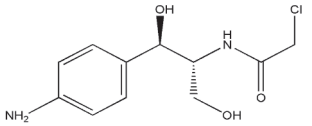
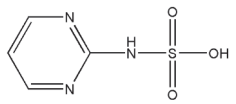
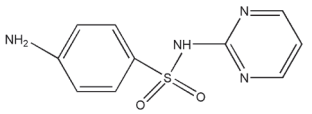
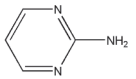
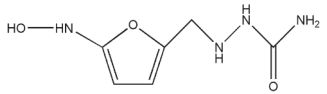
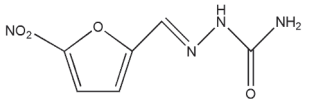
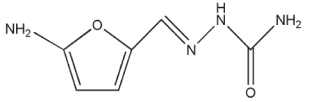
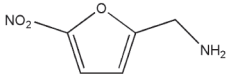


Fig. 4. Degradation pathways of sulfadiazine. Reproduced with permission from ref [82]. Copyright 2018 Elsevier.

Table 2
Intermediate degradation products of representative antibiotics.

Antibiotic	Byproducts	Exacted *m/z*	Proposed formula	Molecular weight	Proposed structure	Refs.
	3A5MI	99.10 $[M+H]^+$	$C_4H_6N_2O$	98.10		[22]
	$AMCl_2$	291.0351 $[M-H]^-$	$C_{11}H_{14}Cl_2N_2O_3$	292.03		[24]
	AMCl	257.0702 $[M-H]^-$	$C_{11}H_{14}ClN_2O_3$	258.70		
	pyrimidin-2ylsulfamic acid	174.9379 $[M-H]^-$	$C_4H_5N_3O_3S$	175.17		[82]
	aniline	96.9683 $[M+H]^+$	$C_4H_5N_3$	95.11		
	AMH	209.0630 $[M+Na]^+$	$C_6H_{10}N_4O_3$	186.17		[23]
	AMN	191.0526 $[M+Na]^+$	$C_6H_8N_4O_2$	168.15		
	NFF	164.9287 $[M+Na]^+$	$C_5H_6N_2O_3$	142.04		

Notes: 3A5MI: 3-amino-5-methylisoxazole; AMH: [(5-hydroxyamino-2-furyl)-methyl]-hydrazinecarboxamide; AMN [(5-amino-2-furyl)-methylene]-hydrazinecarboxamide; NFF: (5-nitro-2-furyl) methanamine.

Table 3
Effect of factors on microbial communities in bioelectrochemical systems.

Antibiotic	Condition	Value	Predominant microbial community	Refs.
chloramphenicol	salinity	0% 0.5% 2% 6%	*Methylophilus, Methyloversatilis, Chryseobacterium* and *Comamonas* *Proteiniphilum, Candidatus_Methangranum* and *Ornatilinea* *Halomonas, Haliangium, Byssovorax* and *Methylophaga* *Lysinibacillus* and *Pseudomonas*	[45]
chloramphenicol	temperature	10 °C 15 °C 30 °C	*Leptolinea*, *Longilinea* and *Acinetobacter* *Terrimonas* and *Erysipelothrix* *Methylophilus* and *Candidatus_Methanogranum*	[45]
chloramphenicol	temperature	10 °C 10 °C to 25 °C	*Aeromonas* and *Vagococcus* *Raoultella* and *Enterococcus*	[74]
chloramphenicol	antibiotics concentration	10 mg/L 20 mg/L 50 mg/L	*Brevundimonas*, *Pseudomonas Saccharibacteria* and *Methylobacillus* *Methylobacillus* *Methylobacillus, Pseudomonas* and *Methylophilus*	[46]
chloramphenicol	applied potentials	−1.25 V −1 V −0.5 V	Phylum: Proteobacteria Genus: *Alkaliphilus* and *Acinetobacter* Phylum: Proteobacteria Genus: *Flavobacterium* and *Acholeplasma* Phylum: Proteobacteria Genus: *Halomonas, Methylophaga*	[46]
nitrofurazone	applied potentials	−0.2 V −0.5 V −0.8 V	Phylum: Proteobacteria Genus: *Klebsiella* Phylum: Proteobacteria Genus: *Klebsiella* Phylum: Firmicute Genus: *Enterococcus*	[23]

4. Degradation pathways and metabolic byproducts of antibiotics

The exploration of antibiotics byproducts and degradation pathways was mainly carried out by HPLC, LC-MS/MS and LC-QToF/MS [78–80]. From a scientific and rigorous perspective, the identification of metabolic products should also be verified by their corresponding commercial reference standards if they can be bought and testified in combination with other techniques such as nuclear magnetic resonance, if needed. With respect to the detection procedure of degradation byproducts, Helbling *et al.* developed an effective technique as guidance [81]. They provided a detailed description of high-throughput identification of biodegradation products of micropollutants, mainly through target and non-target screenings of full-scan MS data and the proposition of structures according to the interpretation of MS spectra and MS/MS fragments.

The degradation pathway of sulfadiazine (SDZ) in biofilm-electrode reactors is depicted in Fig. 4. Based on the results from a Q-Exactive Hybrid Quadrupole-Orbitrap mass spectrometer, Yang *et al.* proposed twelve potential degradation byproducts [82]. The split of the S–N bond between the aniline ring and sulfonic group of SDZ generates two main byproducts, that is, pyrimidin-2ylsulfamic acid and aniline. Subsequently, two degradation pathways of SDZ along with these two primary intermediates were proposed by the authors. In addition, Kong *et al.* conducted a comprehensive byproduct analysis of NFZ based on the HPLC peak and mass/charge rates from HPLC-QTOFMS and found three furan ring-containing products of AMH, AMN, and NFF as main metabolites [23]. Their chemical structures are presented in detail in Table 2. The main NFZ degradation reaction involved in the nitro group reduction, cleavage of C-N unsaturated bond, and split of N-N bond are shown.

Note that degradation pathways of CAP have been proposed in many studies on biocathodes or MFCs and $AMCl_2$ and AMCl are mainly considered to be representatives for amine and dechlorinated products of CAP (Table 2). Based on HPLC-MS/MS, LC-QTOFMS, and IC analysis, Liang *et al.* firstly put forward that the nitro group of the CAP molecule is converted to an amine group with the production of $AMCl_2$ and then $AMCl_2$ is further transformed to AMCl through dichlorination, likely due to dehalogenase secreted from microbes (Fig. 5A) [24]. Their results were also confirmed by other studies on biocathodes [45,46]. Additionally, Zhang *et al.* identified four probable metabolites, that is, CAP-acetyl, AMCl2, AMCl2-acetyl, and *Mc*-AMCl2, based on the results of ESI-Q-TOF-MS [41]. They revealed that the acetylation, nitroreduction, hydrolysis, and *meta*-cleavage pathways as the basic reactions in MFCs (Fig. 5B). Different from processes with microorganism participation, Wu *et al.* conducted CAP degradation under pure chemical reactions and proposed a different degradation pathway (Fig. 5C) [47]. Electrons from anode microbes and hydroxyl radicals generated in the cathode collaboratively enhanced the CAP reduction.

Interestingly, although the degradation of SMX in MFCs has been investigated, two different degradation pathways of SMX were proposed by Wang *et al.* and Miran *et al.* (Fig. 6) [22,38]. Wang *et al.* provide a comprehensive byproduct analysis according to HPLC detection of 3A5MI, the metabolite representative for biodegradation of SMX, and the UPLC-QTOF-MS chromatogram. The split of the S-N bond of SMX is a step to generate 3A5MI. Subsequently, amidogen of 3A5MI as nitrogen source was further metabolized by microorganisms. Additionally, Miran *et al.* elucidated two main degradation pathways of SMX based on different mass-to-charge ratios from LC-TOF-MS/MS. One of the degradation routes involves the degradation of N-[(4-aminophenyl)sulfonyl]carbamimidic acid to 4-aminobenzenesulfonamide, while the other one concerns the transformation of N-(4-sulfamoytphenyl)acetamide to 4-aminobenzenesulfonamide. The difference of the SMX degradation pathways might be due to the distinction of the functional microbes in these two MFC systems, which are provided in detail in Table 4.

5. Predominant microbes for antibiotics degradation in BESs

Microbial communities play a significant role as biocatalysts in the overall performances of BESs. Rapid development of high-throughput sequencing technology helps to explore the predominant microbes in BESs for antibiotics degradation and to understand the changes of microbial communities responding to environmental factors. Similar to the initial antibiotic concentration, applied potential, temperature, and

salinity, their effects on microbes were investigated in previous studies (Table 3). These effective factors prominently alter the diversity and richness of microbial communities. Yan *et al.* reported that with the prolongation of acclimation, the Chao1, Simpson, and Shannon indices of microbial communities in MFCs sharply decline and *Eubacterium* spp. flourishes in MFCs as sole dominating genus [36]. The factors enrich the corresponding specific functional microbes. For example, based on the temperature change to 10 °C, biocathodes significantly enrich *Aeromonas* and *Vagococcus* with cold-adapted ability [74]. Nonetheless, the effect of the factors varies from pharmaceutical to pharmaceutical

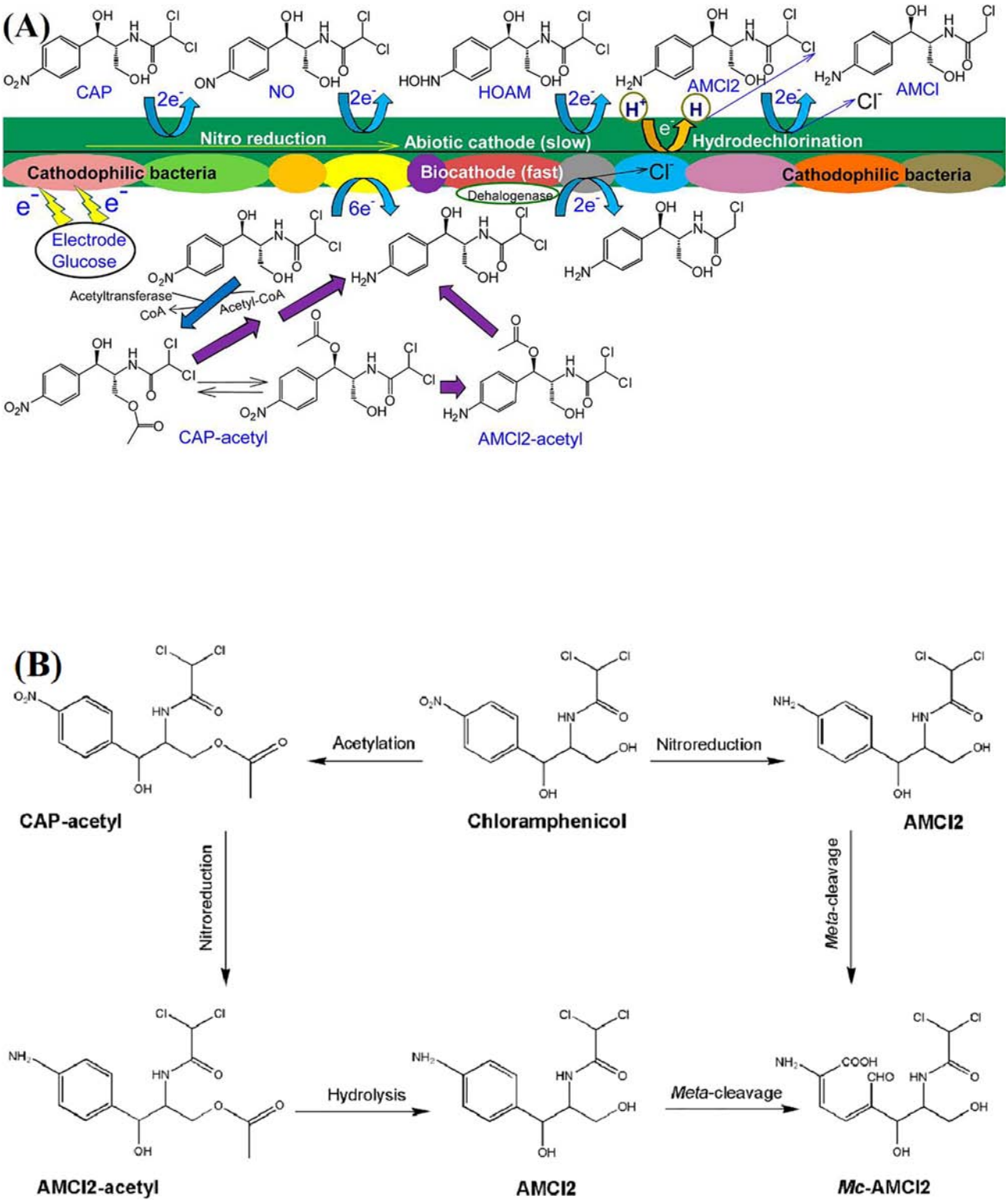


Fig. 5. Degradation pathways of chloramphenicol. (A) The cathodic CAP reduction in biocathodes; Green bar represents the abiotic cathode and biocathode, the occurred reduction was indicated purple arrows. Reproduced with permission from ref [24]. Copyright 2013 American Chemical Society. (B) degradation pathway of CAP in MFCs; Reproduced with permission from ref [41]. Copyright 2017 Elsevier. (C) degradation pathways of CAP with AOPs; Reproduced with permission from ref [47]. Copyright 2017 Elsevier. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

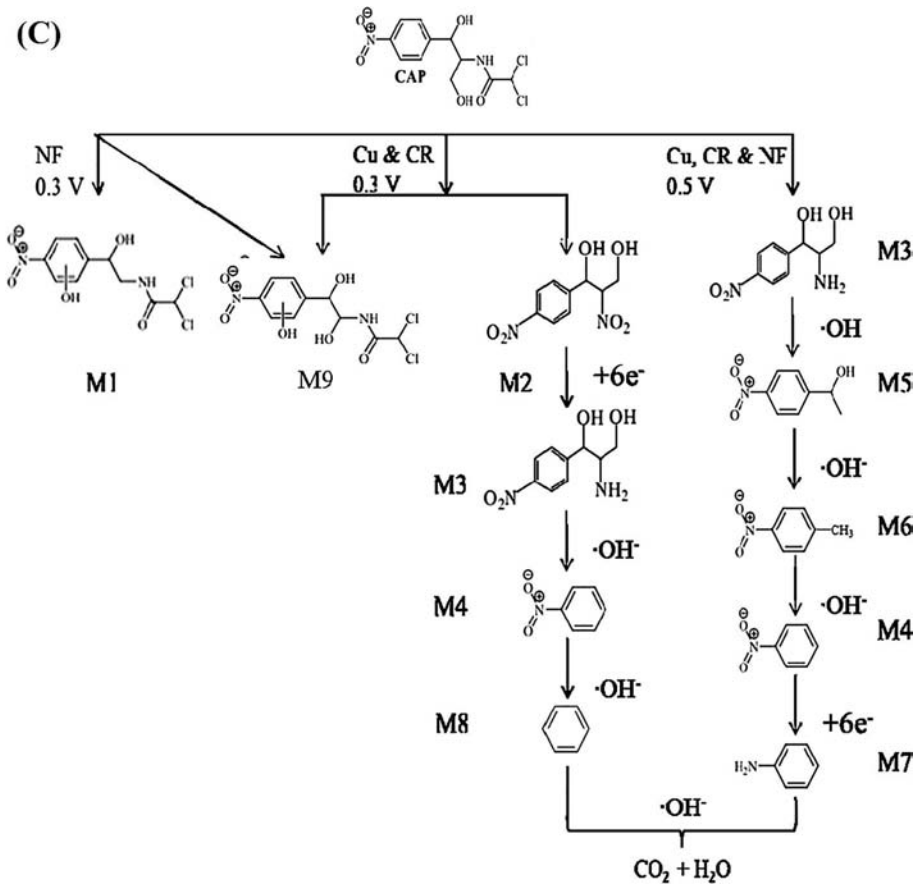


Fig. 5. (*continued*)

and causes clear differences between microbial communities. For instance, in biocathodes, the abundance of Proteobacteria increases with a more negative potential for CAP treatment [46], while Firmicute enriches to 60.07% based on a 0.8 V group treating NFZ [23].

The predominant microbes, which may be responsible for the degradation of antibiotics, are listed in Table 3. At the phylum level, the three dominant microbes belonging to Proteobacteria, Firmicutes and Bacteroidetes occur in most BES reactors. At the genus level, the functional microorganisms vary from system to system and from pharmaceutical to pharmaceutical. For SMX, *Thauera* capable of degradation of aromatic hydrocarbons flourishes in MFCs inoculating SMX-acclimatized cultures [38]. In another study, Wang *et al.* pointed out that the increment of the abundance of *Methanobacterium, Methanosaeta, Treponema,* and *Achromobacter* is responsible for the degradation of highly concentrated SMX in MFCs [37]. For CAP, the electrochemically active bacterium *Pseudomonas* occurs in all biocathodes, possessing the ability of reducing nitroaromatics. For NFZ, *Klebsiella* plays an important role as dominant genus (62.54% under −0.2 V and 56.96% under −0.5 V, respectively) in biocathodes [23]. *Klebsiella* not only has the ability of reducing nitroaromatics, but also is electrochemically active. For oxytetracycline, the functional bacteria *Eubacterium* spp. are extremely enriched (up to 91.69% ± 0.27%) in MFCs [36]. Previous studies showed that some members of *Eubacterium* spp. anaerobically transform oxygen-containing heterocyclic aromatic compounds or secrete enzymes to catalyze metabolic processes of complex compounds [83–85]. For cefazolin sodium, *Geobacter*, *Acinetobacter*, *Stenotrophomonas*, *Dysgonomonas*, and *Lysinibacillus* were observed and are responsible for its degradation in single-chamber MFCs through commensalism [26].

Further understanding of functional microbes will contribute to the rapid development of BESs to treat wastewater containing antibiotics. Isolation of pure functional bacterium, genetic engineering and genome-scale metabolic modeling might yield functional species that possess excellent degradation capacities [57]. Inoculation of these functional species will contribute to the quick start-up of biofilms and the good operation of BESs degrading antibiotics in practice.

6. Effect of BESs on the fate of ARB and ARGs during antibiotics removal

The increasing appearance of ARB and more extensive proliferation of ARGs are of concern [87,88]. These pollutants raise serious concerns with respect to the public health due to the increase in the use of last-resort antibiotic drugs [89–91]. For biological treatments, long-term antibiotics treatment exerts persistent and selective pressure on microbes to increase the transmission of ARGs, which is a common and unavoidable challenge. Hence, it is of great importance to investigate the effect of BESs on the fate of ARB and ARGs during antibiotics removal.

6.1. Do BESs facilitate or reduce the transmission of ARB and ARGs?

The question if BESs facilitate or reduce the transmission of ARGs remains unanswered because the experimental evidences in the literarure results provided contradictory conclusions. In some pure ARB model bacteria, current and electron shuttles are unbeneficial to the removal of ARB and ARGs in BESs. In contrast, BESs contribute to the removal of ARB and ARGs in other cases compared with other biological treatment processes.

Yuan *et al.* used a tetracycline and SDZ resistant *E. coli* strain carrying *intI1*, *sulI,* and *tet(E)* genes as a model bacterium and incubated it into BESs [92]. Independent of the systems operated in the MFC or MEC

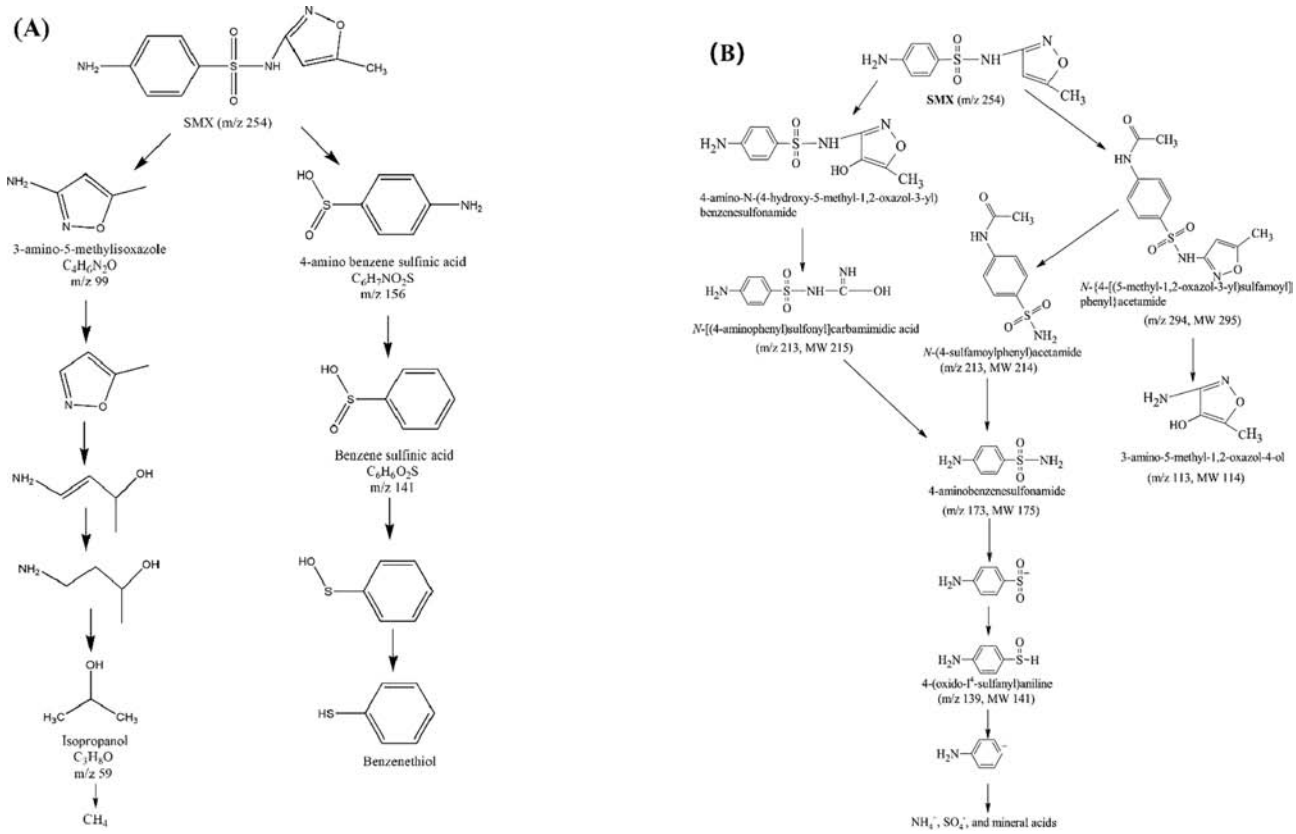


Fig. 6. Degradation pathways of sulfamethoxazole. (A) Reproduced with permission from ref [22]. Copyright 2016 Elsevier. (B) Reproduced with permission from ref [38]. Copyright 2018 Elsevier.

mode, both the abundances of *E. coli* and the aforementioned three ARGs enrich with increasing current. Correlation analysis revealed that a higher current is advantageous for the survival of *E. coli*, which determines the persistence of ARGs in BESs. Additionally, the availability of the anode electrode and electron shuttles is tightly associated with the survival of *E. coli.*, indicating that indigenous electron acceptors in the BESs are favorable to the existence of ARGs. Similar to the results obtained with another SDZ-resistant bacterium, Li *et al.* investigated the viability and ARGs expression of *Klebsiella* spp. exposed to direct-current stimulation in BESs [93]. A higher current (7–28 mA) accelerates the growth rate of *Klebsiella* spp. and causes an upregulation of the *sulII* and *int1* expressions. The strong correlation between *int1* and the current reveals that a higher current may promote the horizontal transfer of ARGs. Based on the combination of the results from Yuan *et al.* and Li *et al.*, there is a potential risk in applying BESs to the treatment of antibiotics with respect to the transmission of ARB and ARGs.

On the contrary, some researchers believe that the BES has its own advantage over traditional biological processes with respect to the minimization of the appearance and proliferation of ARB and ARGs. For example, based on the results of high-throughput quantitative polymerase chain reaction (PCR), Yan *et al.* found that the normalized copy numbers of total ARGs and mobile genetic elements in MFC biofilms were markedly lower after long-term acclimation than those of microbial controls representing conventional anaerobic treatments [36]. Compared with the long-term treatment of low concentrations of cefuroxime in conventional sequencing batch biofilm reactors, BESs can reduce three representative *β*-lactam ARGs, that is, *OXA-1*, *OXA-2*, and *OXA-10* [30]. Compared with the used of only constructed wetlands in previous reports [94], Zhang *et al.* found that the lowest abundances of *tet(E)* and *sulI* in the effluent were observed in integrated systems, that is, MFCs coupled with constructed wetlands [48]. This indicates that treatments coupled with BESs are more favorable for the reduction of ARGs in the effluent. Additionally, Guo *et al.* found that both the richness of ARB and the relative expression of *floR* and *cmlA* genes decline with subsequent complete degradation of CAP [46]. This implies that the selective pressure of CAP to ARGs would be relieved during the removal and the discharge of ARB is not enriched. Compared with conventional WWTPs, where ARB and ARGs are enriched during the sludge treatment process, the abundances of ARB and ARGs can be efficiently controlled in BESs [46].

It is worth noting that the initial experimental conditions of the aforementioned experiments were different and those experimental conditions may cause different conclusions. For example, Yuan *et al.* and Li *et al.* used antibiotics-resistant but not antibiotics-degrading bacteria as mode microorganisms. Hence, the questions are if ARGs in antibiotics-degrading bacteria are upregulated as functional genes when the bacteria metabolize the antibiotics as the growth substrate and if they are downregulated when the antibiotics are completely degraded. These questions about the effect of the current on antibiotics-degrading bacteria and interaction of ARGs remain unanswered and further investigation is needed. It is the opinion of the authors that BESs have the potential to reduce the risk of ARB and ARGs because: (i) BESs are constructed based on anaerobic biotechnologies because previous studies confirmed that anaerobic treatment processes can efficiently remove ARB and ARGs [95,96]; and (ii) BESs produce extremely low excess biomass and less residual sludge compared with conventional aerobic methods[97], which reduce the ARG carriers to some extent. Hence, it seems that BESs are beneficial to the reduction of ARGs compared with traditional biological treatments, but more research is needed to obtain a more scientific conclusion.

6.2. Effect of the applied potential, initial antibiotic concentration, salinity, and temperature on the ARB and ARGs

Based on the aforementioned evaluation of the environmental effect on microbial communities mainly belonging to the hosts of ARGs, the

Table 4
Predominant microbes in bioelectrochemical systems for degrading antibiotics.

Antibiotics	Phylum	Class	Family	Genus	Refs.
chloramphenicol	Proteobacteria (> 60.48%) Actinobacteria (15.40%) Bacteroidetes (8.00%)	β-proteobacteria (47.61%) Actinobacteria (15.40%) α-proteobacteria (9.35%) Flavobacteriia (8.00%) Sphingobacteriia (5.05%) γ-proteobacteria (3.52%)	N.M.	*Azonexus* (19.94%) *Comamonas* (19.41%) *Nitrososphaera* (12.15%) *Chryseobacterium* (8.86%) *Gaiella* (5.45%)	[41]
chloramphenicol	Proteobacteria Firmicutes Bacteroidetes	N.M.	N.M.	*Methylobacillus* *Pseudomonas* *Brevundimonas*	[46]
chloramphenicol	Proteobacteria Firmicutes	N.M.	N.M.	*Lysinibacillus* *Pseudomonas*	[45]
chloramphenicol	Proteobacteria (82.48%) Bacteroidetes Firmicutes Synergistetes	δ-proteobacteria (71.61%) α-proteobacteria β-proteobacteria γ-proteobacteria Clostridia Bacteroidia Flavobacteria		*Geobacter* (67.55%) *Rhodopseudomonas* (4.83%) *Desulfovibrio* (3.49%) *Pseudomonas* (2.29%) *Dysgonomonas* (1.70%) *Petrimonas* (1.54%) *Cloacibacillus* (1.24%)	[86]
chloramphenicol	Bacteroidetes Proteobacteria	Flavobacteriia α-Proteobacteria β-Proteobacteria γ-Proteobacteria		*Salmonella bongori* *Clavibacter michiganensis* *Enterobacter* *Pseudomonas* *Dechloromonas denitrificans*	[24]
tetracycline	Proteobacteria (62.4%) Firmicutes (26.1%) Bacteroidetes (8.1%)	N.M.	N.M.	*Achromobacter* (14.9%), Burkholderia–Paraburkholderia (12.3%) *Alcaligenes* (9.4%) *Geobacter* (5.01%) *Stenotrophomonas* (4.4%) *Enterobacter* (4%).	[35]
oxytetracycline	Firmicutes (94.70%) Proteobacteria (60–80%)	Clostridia α-Proteobacteria β-Proteobacteria γ-Proteobacteria	N.M.	*Eubacterium* spp. (91.8%)	[36]
sulfadiazine	N.M.	N.M.	N.M.	*Methylococcus capsulatus,* *Dechloromonas* *Byssovorax cruenta* *Longilinea arvoryzae* *Malikia spinose*	[82]
sulfamethoxazole	Proteobacteria Euryarchaeota Bacteroidetes Planctomycetes Firmicutes Spirochaetes synergistetes	N.M.	N.M.	*Methanobacterium* *Methanosaeta* *Treponema* *Achromobacter*	[37]
sulfamethoxazole	Proteobacteria Firmicutes Bacteroidetes	β-proteobacteria Clostridia Bacteroidia		*Thauera* (56.4%)	[38]

(*continued on next page*)

Table 4 (*continued*)

Antibiotics	Phylum	Class	Family	Genus	Refs.
sulfamethoxazole and tetracycline	Proteobacteria (45.93%) Bacteroidetes (20.16%) Chloroflexi (4.23%)	N.M.	N.M.	*Dechloromonas* (31.47%) *Bacteroidetes* (23.70%) *Nitrospira* (4.63%) *Crenothrix* (4.54%)	[31]
Sulfamethoxazole and tetracycline	Proteobacteria (47.3%) Bacteroidetes (18.6%) Chloroflexi (4.2%)	N.M.	N.M.	N.M.	[25]
cefuroxime	Proteobacteria (60–80%)	N.M.	Xanthomonadaceae, Propionibacteriaceae Alcaligenaceae	N.M.	[30]
cefazolin sodium	Proteobacteria (> 38.89%) Bacteroidetes (20.1%) Spirochaetae (7.05%) Firmicutes (4.28%)	N.M.	N.M.	*Geobacter* (18.71%) *Acinetobacter* (15.82%) *Dysgonomonas* (5.36%) *Lysinibacillus* (3.22%) *Stenotrophomonas* (2.85%)	[26]
nitrofurazone	Proteobacteria (84.81%)	γ-proteobacteria (81.09%)	N.M.	*Klebsiella* (62.54%)	[23]

Notes: The percentage in brackets are the abundance of microbes according to previous references. And the order in one excel blank is reflected by their abundances, that is, the highest abundance of microbes was placed in the top of the same blank; N.M: Not mentioned.

environmental factors also affect the ARB and ARGs in BESs. However, the studies of the effect of environmental factors on the ARB and ARGs during antibiotics removal in BESs are limited. Apart from the conclusion about the effect of the higher current on the ARB and ARGs in Section 6.1, only Guo *et al.* evaluated the effect of the applied potential, initial antibiotic concentration, salinity, and temperature on the fate of ARB and ARGs [45,46]. Hence, the effects of other environmental factors on ARB and ARGs, mainly including the *cmlA*, *floR*, *tetC, sul1*, and *intI1* genes, are debated in detail in the following section based on the results from Guo and her co-workers.

The cathode potential affects the abundances of ARB and ARGs. Except for *tetC*, the relative abundances of the *cmlA*, *floR*, *sul1*, and *intI1* genes are the lowest at −1 V in BESs with 2% salinity compared with those at −1.25 V and −0.5 V (the result that the current induces the persistence of ARGs to some extent contradicts the conclusions of Yuan *et al.* and Li *et al.*). The abundances of ARB are similar to that of ARGs, that is, the lowest richness of ARB carrying *floR* and *cmlA* genes occurs in BESs with an applied voltage of −1 V. These phenomena may contribute to the fact that the applied electrical field changes the cell membrane permeability and speeds up the death of bacteria without resistance under the poison of antibiotics. These results imply that the appearance of ARB and transmission of ARGs can be controlled at −1 V and that it would be a good choice to apply a voltage of - −1 V for CAP wastewater treatment.

A higher initial antibiotic concentration contributes to a higher selection pressure for the propagation of the ARB and enrichment of ARGs. As the CAP concentration increases from 10 to 50 mg/L, the abundance of ARB increases more quickly and the relative expression of the *floR* gene is induced more profoundly. A similar increase was also obtained by ARB carrying the *cmlA* gene. Compared with 10 mg/L, the CAP concentrations of 20 and 50 mg/L result in a striking rise in ARB carrying the *cmlA* gene.

A low salinity, especially a salinity of 0.5%, facilitates the expression of *cmlA*, *floR*, *sul1*, and *intI1* compared with salinities of 0.2% and 6%. The higher abundance of *cmlA*, *floR*, *sul1*, and *intI1* at a salinity of 0.5% implies that not only the spread of ARGs is enhanced, but horizontal gene transfer of ARGs is promoted by the lower salinity. However, the effect of the salinity on the *tetC* gene is completely opposite to that of the other ARGs and its abundance increases with increasing salinity from 0% to 6%. This indicates that the role of the salinity to different ARGs is diverse.

A low temperature of 10 °C accelerates the proliferation of ARGs and further enhances affected by the salinity. In BESs without salinity, the relative abundances of ARGs and *intI1* affected by 15 °C and 10 °C are similar and both notably higher than those at 30 °C. However, at a salinity of 2%, the highest relative expression of ARGs and *intI1* occurs at 10 °C and the abundance of ARGs and *intI1* remains relatively low at 15 °C and 30 °C. The strong correlation between ARGs and *intI1* reveals that a 2% salinity has a stronger environmental impact than the temperature, which is conducive to the horizontal transfer of ARGs.

It is important to note that discussion about effect of these factors on ARB and ARGs are based on limited results from Guo and her coworkers, hence more investigations are required to get a more scientific conclusion. Additionally, previous studies have confirmed positive correlations between different ARGs and between ARGs and mobile genetic elements [98–101]. But the existing literatures are mostly limited to individual ARGs relevant to antibiotics. Hence, it needs more attention to investigate the fate of a broad range of ARGs under different operating conditions in BESs.

7. Challenges and outlook

Through combined integration of microbial metabolism and electrochemical redox reduction, BESs are regarded as emerging environment-benign and promising treatments for emerging pollutants, especially antibiotics. In this review, the effect of various environmental

factors on the performance of BESs, functional microbes, and ARGs has been addressed. However, the existing literatures paid more attention to search functional bacteria but not further to reveal biocatalyst mechanism about functional genes. And previous studies focused on the removal capacity of traditional BESs for wastewater containing antibiotics but not contribute to the development of BES systems to treat antibiotics contaminants concentrated in solid matrixes. Hence, given the diversity of antibiotics pollutants and the complexity of realistic pollutant environments, several challenges with respect to the improvement of the removal capacity, revelation of biocatalyst mechanism, development of BES systems, and ARGs investigation remain to be addressed and need more attention.

7.1. Capacity improvement

Despite the major advances, the removal capacities of antibiotics in BESs are relatively low considering their future application in realistic polluted environments. Improving the electron transfer capacity is a key to solve this issue. Electrodes are the habitats of exoelectrogens and determine the activity of microorganisms and overall performance of BESs. Therefore, low-cost and durable electrode materials with excellent conductivity and biocompatibility should be developed. Biochar and its modification materials as well as other cost-effective carbon based electrodes may be good choices. The comparison of different electrodes with respect to their influence on microbial community and electron transfer should be studied in the future. Furthermore, the addition of electron transfer mediators might enhance the removal capacity and the interplay of electrochemically active microbes, electrodes, and electron transfer mediators warrants further studies.

7.2. Biocatalyst mechanism

The functional species corresponding to several representative antibiotics were revealed in the Section 5. Nevertheless, the mechanism involved in the electron transfer between microbes and electrodes and among mixed bacteria remains obscure and the metabolic pathways of functional genes for antibiotics detoxification need to be revealed in the future. Omics technologies, such as metagenomics, metaproteomics, and metabolomics, might be conducive for the exploration of functional genes concerning the electron transfer and metabolic pathways of antibiotics to illustrate the potential proteins mediating electron transport and to identify the potential enzymes catalyzing metabolic reactions of antibiotics. Moreover, how to efficiently control the formation of functional biofilms and to enhance the expression of relevant functional genes under different operating parameters should be paid more efforts in future researches.

7.3. ARG investigation

Given the diversity of ARGs and the dissimilarity of environmental factors of different ARGs, more investigations of more types of ARGs and their interaction in BESs are required. High-throughput quantitative PCR is a powerful technique that can be used to simultaneously measure nearly 300 types of ARGs. In addition, functional metagenomics play an indispensable role in discovering unknown ARGs. Hence, high-throughput quantitative PCR and functional metagenomics are expected to illuminate scientific issues concerning biofilms in BESs including the abundance and diversity of ARGs, mechanism of horizontal gene transfer, and differences of ARG expression under single- and multi-antibiotics during long-term operation. Co-existence of antibiotics and other emerging contaminants, such as pharmaceuticals and personal care products, should be noticed in the realistic environment. Therefore, besides the feasibility of BESs for removing co-existent contaminants, the effect of co-existent contaminants on ARGs in electroactive biofilms should be considered.

7.4. System development

Previous studies were performed in simulative aquatic environments, but the emerging contaminants of antibiotics are ubiquitous and often found to be easily concentrated in solid matrixes such as sediments, sludge, and soil. The emergence of sediment MFCs and plant MFCs or other solid BESs might be a good basis to study these troublesome issues. Specific BESs should be developed for different surroundings involving the investigation of the removal capacity and critical factors of antibiotics-containing solid matrixes. Additionally, the coexistence of antibiotics pollutants and other contaminants, such as heavy metals, is pervasive. Heavy metals pose a co-selective pressure on ARGs. Biocathodes have proven to be a good platform for the reduction of metals and antibiotics. Hence, it needs to be studied if biocathodes are a good choice for the treatment of matrixes containing both antibiotic pollutants and heavy metals and for the release of the co-selective pressure through rapid transformation.

Acknowledgments

This study was supported by grants from the National Natural Science Foundation of China (51478451) and the Youth Innovation Promotion Association of Chinese Academy of Sciences (2018344).

References

[1] M.J. Blaser, Antibiotic use and its consequences for the normal microbiome, Science 352 (2016) 544–545.
[2] N.H. Tran, M. Reinhard, K.Y.-H. Gin, Occurrence and fate of emerging contaminants in municipal wastewater treatment plants from different geographical regions-a review, Water Res. 133 (2018) 182–207.
[3] M. Ashfaq, Y. Li, Y. Wang, W. Chen, H. Wang, X. Chen, W. Wu, Z. Huang, C.P. Yu, Q. Sun, Occurrence, fate, and mass balance of different classes of pharmaceuticals and personal care products in an anaerobic-anoxic-oxic wastewater treatment plant in Xiamen, China, Water Res. 123 (2017) 655–667.
[4] Y. Wang, R. Zhang, J. Li, Z. Wu, W. Yin, S. Schwarz, J.M. Tyrrell, Y. Zheng, S. Wang, Z. Shen, Z. Liu, J. Liu, L. Lei, M. Li, Q. Zhang, C. Wu, Q. Zhang, Y. Wu, T.R. Walsh, J. Shen, Comprehensive resistome analysis reveals the prevalence of NDM and MCR-1 in Chinese poultry production, Nat. Microbiol. 2 (2017) 16260.
[5] S. Atashgahi, I. Sánchez-Andrea, H.J. Heipieper, J.R. van der Meer, A.J.M. Stams, H. Smidt, Prospects for harnessing biocide resistance for bioremediation and detoxification, Science 360 (2018) 743–746.
[6] S. Baker, N. Thomson, F.-X. Weill, K.E. Holt, Genomic insights into the emergence and spread of antimicrobial-resistant bacterial pathogens, Science 360 (2018) 733–738.
[7] C.M. Manaia, J. Rocha, N. Scaccia, R. Marano, E. Radu, F. Biancullo, F. Cerqueira, G. Fortunato, I.C. Iakovides, I. Zammit, I. Kampouris, I. Vaz-Moreira, O.C. Nunes, Antibiotic resistance in wastewater treatment plants: tackling the black box, Environ. Int. 115 (2018) 312–324.
[8] Y.G. Zhu, Y. Zhao, B. Li, C.L. Huang, S.Y. Zhang, S. Yu, Y.S. Chen, T. Zhang, M.R. Gillings, J.Q. Su, Continental-scale pollution of estuaries with antibiotic resistance genes, Nat. Microbiol. 2 (2017) 16270.
[9] Y.G. Zhu, M. Gillings, P. Simonet, D. Stekel, S. Banwart, J. Penuelas, Microbial mass movements, Science 357 (2017) 1099–1100.
[10] L. Feng, E.D. van Hullebusch, M.A. Rodrigo, G. Esposito, M.A. Oturan, Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced oxidation processes: a review, Chem. Eng. J. 228 (2013) 944–964.
[11] O.M. Rodriguez-Narvaez, J.M. Peralta-Hernandez, A. Goonetilleke, E.R. Bandala, Treatment technologies for emerging contaminants in water: a review, Chem. Eng. J. 323 (2017) 361–380.
[12] R.F. Dantas, S. Contreras, C. Sans, S. Esplugas, Sulfamethoxazole abatement by means of ozonation, J. Hazard. Mater. 150 (2008) 790–794.
[13] S. Kim, K.H. Chu, Y.A.J. Al-Hamadani, C.M. Park, M. Jang, D.H. Kim, M. Yu, J. Heo, Y. Yoon, Removal of contaminants of emerging concern by membranes in water and wastewater: a review, Chem. Eng. J. 335 (2018) 896–914.
[14] F. Mansour, M. Al-Hindi, R. Yahfoufi, G.M. Ayoub, M.N. Ahmad, The use of activated carbon for the removal of pharmaceuticals from aqueous solutions: a review, Rev. Environ. Sci. Bio. 17 (2018) 109–145.
[15] X. Shi, K.Y. Leong, H.Y. Ng, Anaerobic treatment of pharmaceutical wastewater: a critical review, Bioresour. Technol. 245 (2017) 1238–1244.
[16] D. Cheng, H.H. Ngo, W. Guo, Y. Liu, S.W. Chang, D.D. Nguyen, L.D. Nghiem, J. Zhou, B. Ni, Anaerobic membrane bioreactors for antibiotic wastewater treatment: performance and membrane fouling issues, Bioresour. Technol. 267 (2018) 714–724.
[17] B. Tiwari, B. Sellamuthu, Y. Ouarda, P. Drogui, R.D. Tyagi, G. Buelna, Review on fate and mechanism of removal of pharmaceutical pollutants from wastewater using biological approach, Bioresour. Technol. 224 (2017) 1–12.

[18] G. Zhen, X. Lu, G. Kumar, P. Bakonyi, K. Xu, Y. Zhao, Microbial electrolysis cell platform for simultaneous waste biorefinery and clean electrofuels generation: Current situation, challenges and future perspectives, Prog. Energ. Combust. 63 (2017) 119–145.

[19] C. Santoro, C. Arbizzani, B. Erable, I. Ieropoulos, Microbial fuel cells: from fundamentals to applications. A review, J. Power Sources 356 (2017) 225–244.

[20] M. Kronenberg, E. Trably, N. Bernet, D. Patureau, Biodegradation of polycyclic aromatic hydrocarbons: using microbial bioelectrochemical systems to overcome an impasse, Environ. Pollut. 231 (2017) 509–523.

[21] R. Ilamathi, J. Jayapriya, Microbial fuel cells for dye decolorization, Environ. Chem. Lett. 16 (2018) 239–250.

[22] L. Wang, Y. Liu, J. Ma, F. Zhao, Rapid degradation of sulphamethoxazole and the further transformation of 3-amino-5-methylisoxazole in a microbial fuel cell, Water Res. 88 (2016) 322–328.

[23] D. Kong, H. Yun, D. Cui, M. Qi, C. Shao, D. Cui, N. Ren, B. Liang, A. Wang, Response of antimicrobial nitrofurazone-degrading biocathode communities to different cathode potentials, Bioresour. Technol. 241 (2017) 951–958.

[24] B. Liang, H.Y. Cheng, D.Y. Kong, S.H. Gao, F. Sun, D. Cui, F.Y. Kong, A.J. Zhou, W.Z. Liu, N.Q. Ren, W.M. Wu, A.J. Wang, D.J. Lee, Accelerated reduction of chlorinated nitroaromatic antibiotic chloramphenicol by biocathode, Environ. Sci. Technol. 47 (2013) 5353–5361.

[25] S. Zhang, H.L. Song, X.L. Yang, K.Y. Yang, X.Y. Wang, Effect of electrical stimulation on the fate of sulfamethoxazole and tetracycline with their corresponding resistance genes in three-dimensional biofilm-electrode reactors, Chemosphere 164 (2016) 113–119.

[26] E. Zhang, Q. Yu, W. Zhai, F. Wang, K. Scott, High tolerance of and removal of cefazolin sodium in single-chamber microbial fuel cells operation, Bioresour. Technol. 249 (2018) 76–81.

[27] H. Song, W. Guo, M. Liu, J. Sun, Performance of microbial fuel cells on removal of metronidazole, Water Sci. Technol. 68 (2013) 2599–2604.

[28] Q. Wen, F. Kong, H. Zheng, D. Cao, Y. Ren, J. Yin, Electricity generation from synthetic penicillin wastewater in an air-cathode single chamber microbial fuel cell, Chem. Eng. J. 168 (2011) 572–576.

[29] Q. Wen, F. Kong, H. Zheng, J. Yin, D. Cao, Y. Ren, G. Wang, Simultaneous processes of electricity generation and ceftriaxone sodium degradation in an air-cathode single chamber microbial fuel cell, J. Power Sources 196 (2011) 2567–2572.

[30] Z. Cheng, X. Hu, Z. Sun, Microbial community distribution and dominant bacterial species analysis in the bio-electrochemical system treating low concentration cefuroxime, Chem. Eng. J. 303 (2016) 137–144.

[31] H.L. Song, S. Zhang, X.L. Yang, T.Q. Chen, Y.Y. Zhang, Coupled effects of electrical stimulation and antibiotics on microbial community in three-dimensional biofilm-electrode reactors, Water Air Soil Poll. 228 (2017) 83.

[32] C. Jiang, L. Liu, J.C. Crittenden, An electrochemical process that uses an Fe0/TiO2 cathode to degrade typical dyes and antibiotics and a bio-anode that produces electricity, Front. Env. Sci. Eng. 10 (2016) 15.

[33] S. Zhang, H.L. Song, X.L. Yang, Y.L. Yang, K.Y. Yang, X.Y. Wang, Fate of tetracycline and sulfamethoxazole and their corresponding resistance genes in microbial fuel cell coupled constructed wetlands, RSC Adv. 6 (2016) 95999–96005.

[34] Y. Li, L. Liu, F. Yang, Destruction of tetracycline hydrochloride antibiotics by FeOOH/TiO2 granular activated carbon as expanded cathode in low-cost MBR/MFC coupled system, J. Membrane Sci. 525 (2017) 202–209.

[35] J. Wang, M.F. He, D. Zhang, Z. Ren, T.S. Song, J. Xie, Simultaneous degradation of tetracycline by a microbial fuel cell and its toxicity evaluation by zebrafish, RSC Adv. 7 (2017) 44226–44233.

[36] W. Yan, Y. Guo, Y. Xiao, S. Wang, R. Ding, J. Jiang, H. Gang, H. Wang, J. Yang, F. Zhao, The changes of bacterial communities and antibiotic resistance genes in microbial fuel cells during long-term oxytetracycline processing, Water Res. 142 (2018) 105–114.

[37] L. Wang, Y. Wu, Y. Zheng, L. Liu, F. Zhao, Efficient degradation of sulfamethoxazole and the response of microbial communities in microbial fuel cells, RSC Adv. 5 (2015) 56430–56437.

[38] W. Miran, J. Jang, M. Nawaz, A. Shahzad, D.S. Lee, Biodegradation of the sulfonamide antibiotic sulfamethoxazole by sulfamethoxazole acclimatized cultures in microbial fuel cells, Sci. Total Environ. 627 (2018) 1058–1065.

[39] F. Harnisch, C. Gimkiewicz, B. Bogunovic, R. Kreuzig, U. Schröder, On the removal of sulfonamides using microbial bioelectrochemical systems, Electrochem. Commun. 26 (2013) 77–80.

[40] W. Guo, H. Song, L. Zhou, J. Sun, Simultaneous removal of sulfanilamide and bioelectricity generation in two-chambered microbial fuel cells, Desalin. Water Treat. 57 (2016) 24982–24989.

[41] Q. Zhang, Y. Zhang, D. Li, Cometabolic degradation of chloramphenicol via a meta-cleavage pathway in a microbial fuel cell and its microbial community, Bioresour. Technol. 229 (2017) 104–110.

[42] W. Guo, M. Geng, H. Song, J. Sun, Removal of chloramphenicol and simultaneous electricity generation by using microbial fuel cell technology, Int. J. Electrochem. Sci. 11 (2016) 5128–5139.

[43] D. Kong, B. Liang, D.J. Lee, A. Wang, N. Ren, Effect of temperature switchover on the degradation of antibiotic chloramphenicol by biocathode bioelectrochemical system, J. Environ. Sci. 26 (2014) 1689–1697.

[44] F. Sun, H. Liu, B. Liang, R. Song, Q. Yan, A. Wang, Reductive degradation of chloramphenicol using bioelectrochemical system (BES): a comparative study of abiotic cathode and biocathode, Bioresour. Technol. 143 (2013) 699–702.

[45] N. Guo, Y. Wang, T. Tong, S.G. Wang, The fate of antibiotic resistance genes and their potential hosts during bio-electrochemical treatment of high-salinity pharmaceutical wastewater, Water Res. (2018).

[46] N. Guo, Y. Wang, L. Yan, X. Wang, M. Wang, H. Xu, S. Wang, Effect of bio-electrochemical system on the fate and proliferation of chloramphenicol resistance genes during the treatment of chloramphenicol wastewater, Water Res. 117 (2017) 95–101.

[47] D. Wu, F. Sun, Y. Zhou, Degradation of chloramphenicol with novel metal foam electrodes in bioelectrochemical systems, Electrochim. Acta 240 (2017) 136–145.

[48] S. Zhang, H.L. Song, X.L. Yang, S. Huang, Z.Q. Dai, H. Li, Y.Y. Zhang, Dynamics of antibiotic resistance genes in microbial fuel cell-coupled constructed wetlands treating antibiotic-polluted water, Chemosphere 178 (2017) 548–555.

[49] W. Yang, H. Han, M. Zhou, J. Yang, Simultaneous electricity generation and tetracycline removal in continuous flow electrosorption driven by microbial fuel cells, RSC Adv. 5 (2015) 49513–49520.

[50] H. Yuan, Y. Hou, I.M. Abu-Reesh, J. Chen, Z. He, Oxygen reduction reaction catalysts used in microbial fuel cells for energy-efficient wastewater treatment: a review, Mater. Horiz. 3 (2016) 382–401.

[51] X. Dominguez-Benetton, J.C. Varia, G. Pozo, O. Modin, A. Ter Heijne, J. Fransaer, K. Rabaey, Metal recovery by microbial electro-metallurgy, Prog. Mater Sci. 94 (2018) 435–461.

[52] T. Jafary, W.R.W. Daud, M. Ghasemi, B.H. Kim, J. Md Jahim, M. Ismail, S.S. Lim, Biocathode in microbial electrolysis cell; present status and future prospects, Renew. Sust. Energ. Rev. 47 (2015) 23–33.

[53] M. Hasany, M.M. Mardanpour, S. Yaghmaei, Biocatalysts in microbial electrolysis cells: a review, Int. J. Hydrogen Energ. 41 (2016) 1477–1493.

[54] A. Kadier, M.S. Kalil, P. Abdeshahian, K. Chandrasekhar, A. Mohamed, N.F. Azman, W. Logroño, Y. Simayi, A.A. Hamid, Recent advances and emerging challenges in microbial electrolysis cells (MECs) for microbial production of hydrogen and value-added chemicals, Renew. Sust. Energ. Rev. 61 (2016) 501–525.

[55] D. Recio-Garrido, M. Perrier, B. Tartakovsky, Modeling, optimization and control of bioelectrochemical systems, Chem. Eng. J. 289 (2016) 180–190.

[56] R.G. Saratale, G.D. Saratale, A. Pugazhendhi, G. Zhen, G. Kumar, A. Kadier, P. Sivagurunathan, Microbiome involved in microbial electrochemical systems (MESs): a review, Chemosphere 177 (2017) 176–188.

[57] S. Venkata Mohan, G. Velvizhi, J. Annie Modestra, S. Srikanth, Microbial fuel cell: critical factors regulating bio-catalyzed electrochemical process and recent advancements, Renew. Sust. Energ. Rev. 40 (2014) 779–797.

[58] J. Shen, Y. Zhang, X. Xu, C. Hua, X. Sun, J. Li, Y. Mu, L. Wang, Role of molecular structure on bioelectrochemical reduction of mononitrophenols from wastewater, Water Res. 47 (2013) 5511–5519.

[59] D. Kong, B. Liang, H. Yun, H. Cheng, J. Ma, M. Cui, A. Wang, N. Ren, Cathodic degradation of antibiotics: characterization and pathway analysis, Water Res. 72 (2015) 281–292.

[60] J. Hoyos-Arbeláez, M. Vázquez, J. Contreras-Calderón, Electrochemical methods as a tool for determining the antioxidant capacity of food and beverages: a review, Food Chem. 221 (2017) 1371–1381.

[61] M. Alagiri, P. Rameshkumar, A. Pandikumar, Gold nanorod-based electrochemical sensing of small biomolecules: a review, Microchim. Acta 184 (2017) 3069–3092.

[62] W. Wu, K.L. Lesnik, S. Xu, L. Wang, H. Liu, Impact of tobramycin on the performance of microbial fuel cell, Microb. Cell Fact. 13 (2014) 1–7.

[63] R. Moscoviz, J. Toledo-Alarcón, E. Trably, N. Bernet, Electro-fermentation: how to drive fermentation using electrochemical systems, Trends Biotechnol. 34 (2016) 856–865.

[64] A.S. Commault, G. Lear, M.A. Packer, R.J. Weld, Influence of anode potentials on selection of Geobacter strains in microbial electrolysis cells, Bioresour. Technol. 139 (2013) 226–234.

[65] L. Yu, S. Ruan, X. Xu, R. Zou, J. Hu, One-dimensional nanomaterial-assembled macroscopic membranes for water treatment, Nano Today 17 (2017) 79–95.

[66] P.Y. You, S.K. Kamarudin, Recent progress of carbonaceous materials in fuel cell applications: an overview, Chem. Eng. J. 309 (2017) 489–502.

[67] Z. Jiang, D. Zhang, L. Zhou, D. Deng, M. Duan, Y. Liu, Enhanced catalytic capability of electroactive biofilm modified with different kinds of carbon nanotubes, Anal. Chim. Acta 1035 (2018) 51–59.

[68] P. Champigneux, M.-L. Delia, A. Bergel, Impact of electrode micro- and nano-scale topography on the formation and performance of microbial electrodes, Biosens. Bioelectron. 118 (2018) 231–246.

[69] F. Chen, Z.L. Li, J.Q. Yang, B. Liang, X.Q. Lin, J. Nan, A.J. Wang, Effects of different carbon substrates on performance, microbiome community structure and function for bioelectrochemical-stimulated dechlorination of tetrachloroethylene, Chem. Eng. J. 352 (2018) 730–736.

[70] S. Mateo, P. Cañizares, M.A. Rodrigo, F.J. Fernandez-Morales, Driving force behind electrochemical performance of microbial fuel cells fed with different substrates, Chemosphere 207 (2018) 313–319.

[71] S.I. Mulla, H. Wang, Q. Sun, A. Hu, C.-P. Yu, Characterization of triclosan metabolism in *Sphingomonas* sp. strain YL-JM2C, Sci. Rep. 6 (2016) 21965.

[72] L.J. Pan, J. Li, C.X. Li, X.D. Tang, G.W. Yu, Y. Wang, Study of ciprofloxacin biodegradation by a *Thermus* sp. isolated from pharmaceutical sludge, J. Hazard. Mater. 343 (2018) 59–67.

[73] A.G. More, S.K. Gupta, Evaluation of chromium removal efficiency at varying operating conditions of a novel bioelectrochemical system, Bioproc. Biosyst. Eng. 41 (2018) 1547–1554.

[74] B. Liang, D. Kong, J. Ma, C. Wen, T. Yuan, D.J. Lee, J. Zhou, A. Wang, Low temperature acclimation with electrical stimulation enhance the biocathode functioning stability for antibiotics detoxification, Water Res. 100 (2016) 157–168.

[75] M. Grattieri, S.D. Minteer, Microbial fuel cells in saline and hypersaline environments: advancements, challenges and future perspectives, Bioelectrochemistry 120 (2018) 127–137.

[76] A. Vijay, S. Arora, S. Gupta, M. Chhabra, Halophilic starch degrading bacteria isolated from Sambhar Lake, India, as potential anode catalyst in microbial fuel cell: a promising process for saline water treatment, Bioresour. Technol. 256 (2018) 391–398.
[77] K.K. Ng, X. Shi, H.Y. Ng, Evaluation of system performance and microbial communities of a bioaugmented anaerobic membrane bioreactor treating pharmaceutical wastewater, Water Res. 81 (2015) 311–324.
[78] X. Liu, Y. Zhou, J. Zhang, L. Luo, Y. Yang, H. Huang, H. Peng, L. Tang, Y. Mu, Insight into electro-Fenton and photo-Fenton for the degradation of antibiotics: mechanism study and research gaps, Chem. Eng. J. 347 (2018) 379–397.
[79] J. Wang, S. Wang, Microbial degradation of sulfamethoxazole in the environment, Appl. Microbiol. Biot. 102 (2018) 3573–3582.
[80] Y. Deng, Y. Mao, B. Li, C. Yang, T. Zhang, Aerobic degradation of sulfadiazine by Arthrobacter spp.: kinetics, pathways, and genomic characterization, Environ. Sci. Technol. 50 (2016) 9566–9575.
[81] D.E. Helbling, J. Hollender, H.-P.E. Kohler, H. Singer, K. Fenner, High-throughput identification of microbial transformation products of organic micropollutants, Environ. Sci. Technol. 44 (2010) 6621–6627.
[82] X.L. Yang, S. Zhang, H. Li, L.M. Zhang, H.L. Song, Y.W. Wang, Effects of voltage on sulfadiazine degradation and the response of sul genes and microbial communities in biofilm-electrode reactors, Ecotox. Environ. Safe. 151 (2018) 272–278.
[83] G. Qiu, Y.H. Song, P. Zeng, L. Duan, S. Xiao, Characterization of bacterial communities in hybrid upflow anaerobic sludge blanket (UASB)–membrane bioreactor (MBR) process for berberine antibiotic wastewater treatment, Bioresour. Technol. 142 (2013) 52–62.
[84] H. Schneider, M. Blaut, Anaerobic degradation of flavonoids by *Eubacterium* ramulus, Arch. Microbiol. 173 (2000) 71–75.
[85] L.Q. Wang, M.R. Meselhy, Y. Li, N. Nakamura, B.-S. Min, G.W. Qin, M. Hattori, The heterocyclic ring fission and dehydroxylation of catechins and related compounds by *Eubacterium* sp. strain SDG-2, a human intestinal bacterium, Chem. Pharm. Bull. 49 (2001) 1640–1643.
[86] H. Yun, D. Kong, B. Liang, M. Cui, Z. Li, A. Wang, Response of anodic bacterial community to the polarity inversion for chloramphenicol reduction, Bioresour. Technol. 221 (2016) 666–670.
[87] G.C.A. Amos, S. Ploumakis, L. Zhang, P.M. Hawkey, W.H. Gaze, E.M.H. Wellington, The widespread dissemination of integrons throughout bacterial communities in a riverine system, ISME J. 12 (2018) 681–691.
[88] Y. Xue, H. Chen, J.R. Yang, M. Liu, B. Huang, J. Yang, Distinct patterns and processes of abundant and rare eukaryotic plankton communities following a reservoir cyanobacterial bloom, ISME J. 12 (2018) 2263–2277.
[89] E. Meyer, P. Gastmeier, M. Deja, F. Schwab, Antibiotic consumption and resistance: data from Europe and Germany, Int. J. Med. Microbiol. 303 (2013) 388–395.
[90] E.I. Broughton, T. Chitashvili, K. Hill, E. Cherkezishvili, N. Shengelia, Antibiotic use worldwide, Lancet Infect. Dis. 14 (2014) 1179.
[91] F. Megraud, S. Coenen, A. Versporten, M. Kist, M. Lopez-Brea, A.M. Hirschl, L.P. Andersen, H. Goossens, Y. Glupczynski, Helicobacter pylori resistance to antibiotics in Europe and its relationship to antibiotic consumption, Gut (2012).
[92] H. Yuan, J.H. Miller, I.M. Abu-Reesh, A. Pruden, Z. He, Effects of electron acceptors on removal of antibiotic resistant *Escherichia coli*, resistance genes and class 1 integrons under anaerobic conditions, Sci. Total Environ. 569–570 (2016) 1587–1594.
[93] H. Li, X.L. Yang, H.-L. Song, S. Zhang, X.Z. Long, Effects of direct current on *Klebsiella* spp. viability and corresponding resistance gene expression in simulative bio-electrochemical reactors, Chemosphere 196 (2018) 251–259.
[94] X. Huang, C. Liu, K. Li, J. Su, G. Zhu, L. Liu, Performance of vertical up-flow constructed wetlands on swine wastewater containing tetracyclines and *tet* genes, Water Res. 70 (2015) 109–117.
[95] S. Ghosh, S.J. Ramsden, T.M. LaPara, The role of anaerobic digestion in controlling the release of tetracycline resistance genes and class 1 integrons from municipal wastewater treatment plants, Appl. Microbiol. Biot. 84 (2009) 791–796.
[96] B. Christgen, Y. Yang, S.Z. Ahammad, B. Li, D.C. Rodriquez, T. Zhang, D.W. Graham, Metagenomics shows that low-energy anaerobic − aerobic treatment reactors reduce antibiotic resistance gene levels from domestic wastewater, Environ. Sci. Technol. 49 (2015) 2577–2584.
[97] B.E. Logan, B. Hamelers, R. Rozendal, U. Schröder, J. Keller, S. Freguia, P. Aelterman, W. Verstraete, K. Rabaey, Microbial fuel cells: methodology and technology, Environ. Sci. Technol. 40 (2006) 5181–5192.
[98] Y.G. Zhu, T.A. Johnson, J.Q. Su, M. Qiao, G.X. Guo, R.D. Stedtfeld, S.A. Hashsham, J.M. Tiedje, Diverse and abundant antibiotic resistance genes in Chinese swine farms, Proc. Natl. Acad. Sci. U.S.A. 110 (2013) 3435–3440.
[99] L.G. Li, Y. Xia, T. Zhang, Co-occurrence of antibiotic and metal resistance genes revealed in complete genome collection, ISME J. 11 (2016) 651.
[100] W.Y. Xie, S.P. McGrath, J.Q. Su, P.R. Hirsch, I.M. Clark, Q. Shen, Y.G. Zhu, F.J. Zhao, Long-term impact of field applications of sewage sludge on soil antibiotic resistome, Environ. Sci. Technol. 50 (2016) 12602–12611.
[101] Q. Chen, X. An, H. Li, J. Su, Y. Ma, Y.G. Zhu, Long-term field application of sewage sludge increases the abundance of antibiotic resistance genes in soil, Environ. Int. 92–93 (2016) 1–10.