RSC Advances

REVIEW

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Cite this: *RSC Adv.*, 2026, **16**, 25787

Biological treatment strategies for antibiotic contamination: mechanisms, applications, and future perspectives

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The persistence of antibiotic residues in aquatic environments poses significant environmental and health risks. Biological treatment technologies, owing to the cost-effectiveness and environmental benefits, represent a crucial strategy for addressing this challenge. This review systematically elucidates the degradation mechanisms centered on microbial cometabolism, which involves a series of biochemical reactions mediated by functional microorganisms, including hydrolysis, oxidation, reduction, and side-chain modification and cleavage. It also provides a comprehensive evaluation of treatment systems ranging from conventional processes to emerging enhanced technologies such as bioaugmentation, immobilization, and biomaterial coupling. Two major challenges in this field are clearly identified: the inhibitory effects of antibiotics on functional microorganisms, and the secondary dissemination risk of antibiotic resistance genes (ARGs) dissemination. In response, the paper further summarizes recent advances in frontier approaches, such as process intensification, novel material coupling, synthetic biology tools, resource recovery, and intelligent model-based control. These strategies collectively aim to synergistically improve treatment efficiency and mitigate environmental risks. This review aims to provide a valuable reference for developing more efficient and safer biological treatment technologies for antibiotic-containing wastewater.

Received 15th January 2026
Accepted 1st May 2026

DOI: 10.1039/d6ra00375c

rsc.li/rsc-advances

1 Introduction

Antibiotics, as one of the greatest medical discoveries of the 20th century, have significantly reduced the mortality rate of infectious diseases and have safeguarded global public health security. However, the success has also led to the overuse and misuse of antibiotics on a global scale.[1] Not only in human medicine, but also in livestock farming and aquaculture, antibiotics are widely used as growth promoters and therapeutic agents.[2] By 2030, the consumption of antibiotics in developing countries is expected to reach 105.5 kt.[3] This extensive use has resulted in significant amounts of antibiotics and their metabolites entering water and soil environments through pharmaceutical wastewater, hospital sewage, agricultural runoff, and domestic sewage.[4,5] It is reported that approximately 53.80 kt of antibiotics or their degradation products are discharged into aquatic environments each year, thereby emerging as a new type of global environmental pollutant.[6]

Residual antibiotics are frequently detected in various water bodies at concentrations ranging from ng L^{-1} to mg L^{-1}, and in soil from μg kg^{-1} to mg kg^{-1}.[7,8] In the influent and effluent of urban wastewater treatment plants in China, average concentrations can reach 786.2 μg L^{-1} to 186.8 μg L^{-1}.[9] In aquaculture wastewater, concentrations are approximately 25.2–267.3 μg L^{-1}, while pharmaceutical wastewater can contain concentrations as high as 8–22.4 mg L^{-1}.[10,11] These residual antibiotics can enter the human body through the accumulation effects of the food chain and pose a potential threat to human health, including triggering allergic reactions and disrupting the balance of intestinal flora.[12,13] Additionally, it can also damage the microbial community structure within ecosystems.[12,14] Long-term exposure to these antibiotics can have potential toxic effects on aquatic and terrestrial ecosystems and exert strong selective pressure.[15] This selective pressure is a key driver behind the generation and spread of antibiotic resistance genes (ARGs).[16] Microorganisms in the environment will acquire and disseminate ARGs through mutations or horizontal gene transfer (HGT) to survive, leading to the enrichment of antibiotic-resistant bacteria (ARB).[17] These ARGs and ARB in the environment can eventually re-enter human society through food chains, drinking water, or direct contact, making previously treatable infections difficult to treat and constituting one of the most severe global public health crises of this century.[18,19] Previously, a report from the United States indicated that in

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2016, 23 000 people died from antibiotic resistance-related treatment failures.[20] And projections estimate that by 2050, this issue could cause 10 million deaths worldwide.[15,21] The World Health Organization (WHO) has classified antibiotic as one of the "Top Ten Global Health Threats."

Currently, the commonly used methods for removing antibiotics from water include physical, chemical, and biological approaches. Physical methods, including activated carbon adsorption and membrane separation, primarily transfer pollutants from one phase to another and do not achieve degradation. This can result in the production of high-concentration concentrated waste liquid or waste activated carbon, potentially leading to secondary pollution.[22] Chemical methods, such as Advanced Oxidation Processes (AOPs), can effectively degrade and even mineralize antibiotics.[23] However, AOPs often face challenges such as high costs, excessive energy consumption, harsh operating conditions, and the potential generation of unknown toxic by-products.[24] Plant remediation technology, including artificial wetlands, utilizes plants to absorb pollutants while root-associated microorganisms degrade antibiotics. However, this method has limitations, including long remediation cycles, low efficiency, and the risk of plant toxicity.[25] Biological treatment technology leverages the metabolic capabilities of microorganisms to degrade or transform antibiotic pollutants in the environment.[26] This approach is often more cost-effective, environmentally friendly, and produces less secondary pollution. Furthermore, biological treatment technology has the potential to completely mineralize contaminants into CO_2 and H_2O. As such, it presents an extremely attractive alternative or supplementary solution for antibiotic removal. Lou *et al.*[27] employed a laccase–syringaldehyde mediator system to degrade sulfanilamide in real aquaculture wastewater. Enzyme kinetics analyses indicated that Novozym 51003 laccase exhibited strong catalytic activity toward sulfonamide compounds, achieving an actual degradation efficiency of 94.84%. Mousavi *et al.*[28] investigated the degradation of tetracycline (TC) and ciprofloxacin (CIP) during composting using organic waste, rice husk, and returned activated sludge as microbial sources. The results showed that after 92 days, the removal rates of TC reached 85%, 90%, and 92.5%, while those of CIP were 75%, 77.5%, and 82.5%, respectively. These findings demonstrated that the use of microbial sources during composting can effectively degrade antibiotics in contaminated environments. Wang *et al.*[29] reported that, in a continuous-flow reactor for TC degradation, biological degradation was the dominant pathway, accounting for 88.9% of total removal. The continuous-flow reactor provided a more favorable environment for the enrichment and proliferation of functional microorganisms. However, antibiotics are originally designed to inhibit or kill microorganisms, and their inherent biological toxicity poses significant challenges to biological treatment technology.[30] The degradation efficiency is highly dependent on factors such as antibiotic type and concentration, microbial community structure, and environmental operating parameters.[31] Moreover, whether biological treatment systems may accelerate the dissemination of ARGs while removing the parent antibiotic compounds remains a critical issue that must be clarified prior to their widespread environmental application.

Although numerous studies have reported the degradation of antibiotics by strains or the removal efficiencies achieved by particular treatment processes, a systematic framework for biological treatment technologies is still lacking, and critical perspectives on the key challenges and future research directions remain insufficient. Therefore, this review systematically summarizes and critically evaluates recent advances in antibiotic biotreatment. It aims to provide an in-depth analysis of the core mechanisms of antibiotic biodegradation, including cometabolism, hydrolysis, oxidation, reduction, side-chain modification and cleavage (SMC); comprehensively review the performance and application efficiency of various bioremediation processes, ranging from conventional activated sludge systems to emerging biotechnologies; and particular emphasis on the fate and transmission risks of ARGs during bioremediation. Based on the current state of knowledge, this review further identifies the key challenges in this field and indicates future research directions.

2 Mechanism of antibiotic biodegradation

2.1 Cometabolism

Cometabolism is a fundamental biological pathway by which microorganisms degrade refractory organic pollutants, particularly emerging contaminants such as antibiotics. When microorganisms metabolize easily degradable substrates, which induce the production of non-specific enzymes. These enzymes catalyze the metabolism of the primary substrates. At the same time, they can accidently attack and transform antibiotic molecules that cannot serve as carbon or energy sources for the microorganisms. In the cometabolism process, the enzyme systems produced by microorganisms facilitate the degradation of antibiotics. However, the antibiotics do not provide the carbon or energy necessary to support microbial growth. Cometabolism significantly enhances the degradation efficiency of refractory antibiotics and is considered a key mechanism for breaking down persistent antibiotic. Furthermore, different microbial groups with unique metabolic networks have evolved diverse cometabolic pathways (Fig. 1). These pathways form the functional core for antibiotic degradation within treatment systems.

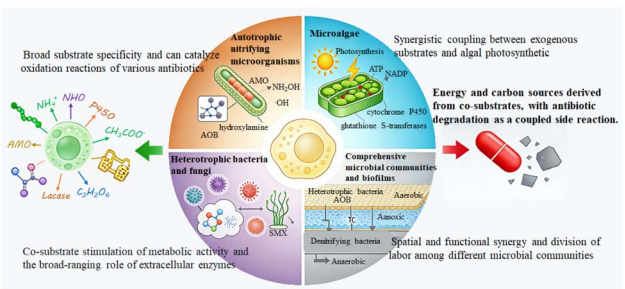

Fig. 1 Cometabolism mechanism of antibiotic biodegradation.

2.1.1 Autotrophic nitrifying microorganisms. Autotrophic nitrifying microorganisms, represented by ammonia-oxidizing bacteria (AOB), are key participants in the wastewater denitrification process and the co-metabolic degradation of antibiotics. The core enzyme of these microorganisms, ammonia monooxygenase (AMO), exhibits broad substrate specificity and can catalyze oxidation reactions of various antibiotics.[32] When AOB using ammonia nitrogen as the electron donor and energy source, AMO not only oxidizes ammonia to hydroxylamine but also inserts oxygen atoms into the inert chemical bonds of various antibiotics.[33] For instance, AMO can directly catalyze the cleavage of the piperazine ring in fluoroquinolones (such as CIP) and the deamination reaction of sulfonamide antibiotics.[34] Studies have shown that in moving bed biofilm reactors (MBBR) with nitrifying bacteria, AOB-mediated cometabolism plays a dominant role in the removal of CIP, while heterotrophic bacteria contributing only about 9%.[35] Moreover, intermediates such as hydroxylamine generated during AOB metabolism can be converted into hydroxyl radicals in subsequent reactions, and further transform antibiotics through an indirect oxidation pathway.

2.1.2 Microalgae. Microalgae, such as *Chlorella* and *Chlamydomonas*, offer an efficient cometabolic pathway for antibiotic degradation. The addition of organic substrates such as acetate and yeast extract to microalgal cultures containing antibiotics significantly enhances the degradation capacity. The underlying mechanism involves a synergistic coupling between the boosted metabolic activity fueled by the exogenous substrates and the algal photosynthetic apparatus.[36] On the one hand, the light reaction stage of photosynthesis provides the cell with abundant reducing power (NADPH) and energy (ATP).[37] On the other hand, the energy and reducing power markedly upregulate the activities of phase I and phase II metabolic enzymes, including cytochrome P450 and glutathione *S*-transferases.[38,39] Such a metabolic enzyme–photosynthesis coupling system efficiently drives a series of reactions such as hydroxylation, decarboxylation, and ring-opening of antibiotics. For example, *Chlorella pyrenoidosa* under acetate cometabolism can achieve 100% removal of TC within the concentration range of 1–50 mg L^{-1}. Furthermore, this process effectively reduced the total concentration of 18 antibiotics in actual reclaimed water from 495.54 ng L^{-1} to 221.80 ng L^{-1}.[40]

However, before intracellular uptake and enzymatic transformation occur, antibiotics may first interact with the extracellular polymeric matrix surrounding microalgal cells. Besides intracellular enzymatic metabolism, microalgal extracellular polymeric substances (EPS) can contribute significantly to antibiotic removal by acting as an extracellular interception layer.[41] Rich in polysaccharides, proteins, and reactive functional groups, EPS can interact with antibiotics through biosorption, electrostatic attraction, hydrogen bonding, hydrophobic interaction, and complexation, thereby reducing their dissolved concentration and buffering direct cellular toxicity.[42] At the same time, EPS-bound antibiotics may accumulate near the algal surface, facilitating subsequent uptake and intracellular transformation. By restricting the rapid influx of reactive antibiotic molecules into the cytosol, EPS complexation significantly mitigates intracellular oxidative stress and physiological toxicity, thereby preserving the structural integrity and metabolic vitality required for subsequent intracellular enzymatic degradation.[43] Thus, antibiotic removal by microalgae should be viewed as a coupled process of EPS-mediated extracellular retention and intracellular biodegradation.

2.1.3 Heterotrophic bacteria and fungi. Heterotrophic bacteria and fungi can utilize various easily degradable organic substrates, such as methanol, acetate, ethanol, and glucose as growth substrates. During the metabolism of these substrates, microorganisms induce the production of a range of enzymes, including oxidoreductases (such as dehydrogenases), hydrolases (such as esterases, amidases), and peroxidases (such as lignin peroxidase, laccase).[44] These non-specific enzymes are capable of attacking specific bonds within antibiotic molecules. For example, the cometabolic degradation of sulfamethoxazole by heterotrophic bacteria was significantly enhanced by acetate addition, which can increase the relative oxygen uptake rate by nearly 10-fold.[45] Extracellular laccases secreted by fungi effectively oxidize pharmaceuticals such as sulfamethoxazole, carbamazepine, ampicillin, and TC.[46–48] Furthermore, specific functional microorganisms, such as *Arthrobacter* and *Pseudomonas*, drive the transformation of sulfadiazine and sulfamethoxazole through hydroxylation and acetylation reactions under conditions with abundant co-substrates.[49]

2.1.4 Comprehensive microbial communities and biofilms. In practical biological treatment systems, antibiotic degradation is rarely the function of a single microbial species. Instead, it results from the spatial and functional synergy and division of labor among different microbial communities. Within activated sludge flocs, AOB may initiate the preliminary oxidation of antibiotics. This process generates intermediates that are more readily degradable. These intermediates are subsequently mineralized by surrounding heterotrophic bacteria. In biofilms, a unique stratified structure exists. It ranges from aerobic outer layers to anoxic or anaerobic inner layers. The structure provides ideal microenvironments for microorganisms with different metabolic requirements. As a result, complex symbiotic networks are established. AOB and heterotrophic bacteria in the aerobic layer conduct oxidative cometabolism, while denitrifying bacteria and other microbes in the anoxic layers may utilize alternative electron acceptors to further transform the intermediates. The sequential microbial action enables the degradation of various antibiotics, including TC and fluoroquinolones.[50,51] In photocatalysis coupled with constructed wetland microbial fuel cells (PCW-MFC), *Pseudomonas acidovorans* and *Pseudomonas aeruginosa* work synergistically to convert TC intermediate degradation product acetamide into acetyl groups.[52]

Although many biological treatment systems can effectively reduce the concentration of parent antibiotics, such removal often results from partial biotransformation rather than complete mineralization. For instance, sulfamethoxazole is frequently converted into N4-acetylsulfamethoxazole, which can be chemically or biologically de-acetylated back to its parent form, acting as a temporary reservoir of toxicity.[53] Similarly, the

degradation of CIP often results in the formation of several piperazine-ring-opened products.[34] The formation of these intermediate metabolites introduces complex dynamics within the wastewater microbial community. These transformation products may still retain antibacterial activity or exert selective pressure on wastewater functional microbes such as AOB and NOB.[54] Furthermore, the persistence of these intermediates in the effluent may continue to promote the HGT of ARGs. Therefore, the evaluation of antibiotic removal in biological systems should not be limited to parent-compound disappearance, but should also consider transformation product formation and the residual toxicity of these metabolites.

2.1.5 Kinetic basis and factors influencing enzymatic degradation. Enzyme activity is a key determinant of antibiotic degradation efficiency and is affected by multiple factors, including substrate structure, enzyme specificity, pH, temperature, redox conditions, cofactor availability, and competing substrates. To better reflect this point, we added a kinetic perspective based on the Michaelis–Menten equation, where K_m and V_{max} are used to characterize substrate affinity and catalytic capacity, respectively. For example, the macroscopic degradation rates such as the pseudo-first-order rate constant K_{obs} for TC reaching 3.62×10^{-3} min^{-1} are fundamentally governed by the enzyme's affinity for the K_m and its overall catalytic efficiency.[55] While the wild-type enzyme exhibits a substrate affinity (K_m) of 5.34 ± 1.9 μM, specific mutations (*T331I*) can increase the overall catalytic efficiency (K_m/K_{cat}) from 6.60 ± 1.7 to 21.37 ± 0.3 μM^{-1} h^{-1}.[56] These results underscore that the specificity constant (K_{cat}/K_m), rather than substrate concentration alone, dictates the kinetic limit of antibiotic removal in complex matrices. However, because most published studies on antibiotic removal report reactor-scale or community-level degradation rather than purified enzyme kinetics, directly comparable K_m and V_{max} values for different antibiotic-degrading enzymes remain scarce. We therefore discuss enzyme kinetics as an important mechanistic framework while identifying the lack of harmonized kinetic constants as a current research gap.

2.2 Biochemical reactions

2.2.1 Hydrolysis reaction. The antibiotic biochemical reactions include hydrolysis, oxidation, reduction, and SMC (Fig. 2). Hydrolysis plays a pivotal role in the biodegradation of antibiotics. Hydrolysis directly cleaves the core chemical bonds of antibiotic molecules through specific enzymes, such as β-lactamases, esterases, and amidases. Consequently, the antibiotics rapidly lose antimicrobial activity. β-Lactamases hydrolyze the β-lactam rings present in drugs like penicillins and cephalosporins.[57] Esterases and amidases are responsible for breaking the lactone rings of macrolide antibiotics and the amide bonds of sulfonamide antibiotics, respectively. Biological aerated filter can achieve removal efficiencies exceeding 90% for sulfonamides and TCs. The primary removal mechanisms include biodegradation and adsorption. Within the biological component, hydrolytic and photolytic degradation contributed to concentrations of 0.01–2.69 mg L^{-1} for sulfonamides and 1.53–2.68 mg L^{-1} for TCs.[58] Similarly, in the anaerobic zone of a hybrid aerated biofilter, hydrolytic enzymes directly attack the piperazine ring of enrofloxacin, cleaving the C–N bond and causing its detachment. The intermediate 1-ethylpiperazine ($C_6H_{14}N_2$, *m*/*z* 115) then migrates to the anoxic zone, where it undergoes *N*-dealkylation mediated by hydrolytic enzymes, followed by ring-opening and further degradation in the aerobic zone.[59]

2.2.2 Oxidation reaction. Oxidation reactions involve the loss of electrons and are typically catalyzed by oxidases. It is crucial for attacking the recalcitrant structures of antibiotic and achieving deep transformation. Common oxidases include monooxygenases, dioxygenases, and peroxidases, which generally require cofactors such as NADH and $FADH_2$.[60] Cytochrome P450 enzymes and laccases play important roles in microalgae and fungi by catalyzing hydroxylation and dealkylation. For instance, the hydroxylation of the benzene ring in sulfonamide, which introduces a hydroxyl group to alter electron distribution, facilitates subsequent ring-opening reactions.[61] Oxidases are instrumental in directly cleaving aromatic rings of TC intermediates, a critical step toward complete mineralization.[62] Versatile peroxidase, a type of heme peroxidase, catalyzes two-electron transfers through the formation of unstable compound I and compound II intermediates. The intermediates facilitate the direct oxidation of substrates.[63] Notably, under cometabolic conditions, the activity of cytochrome P450 enzymes in microalgae can increase by 20–50%, driving both hydroxylation and ring-opening of TCs.[38]

2.2.3 Reduction reaction. Reduction reactions is the dominant pathway for antibiotic biotransformation in anoxic or anaerobic environments. Nitroreductases can reduce the nitro groups on antibiotics such as chloramphenicol to amino groups, significantly decreasing toxicity.[64] Dehalogenases catalyze the removal of fluorine atoms from fluoroquinolone.[65,66] These reductive transformations are particularly crucial in anaerobic digestion and the anoxic zones of constructed wetlands. The redox processing is exemplified in aerated biofilters, where enrofloxacin is first converted to an aldehyde intermediate by reductases in the anoxic zone. Subsequently, in the aerobic zone, dioxygenases catalyzed epoxidation of the quinoline ring, resulting in break of the C2–C3 bond and formation of aniline compounds.[59] Notably, the microalga *Chlamydomonas reinhardtii* demonstrates a distinct mechanism for degrading TC, oxytetracycline, and doxycycline effectively.

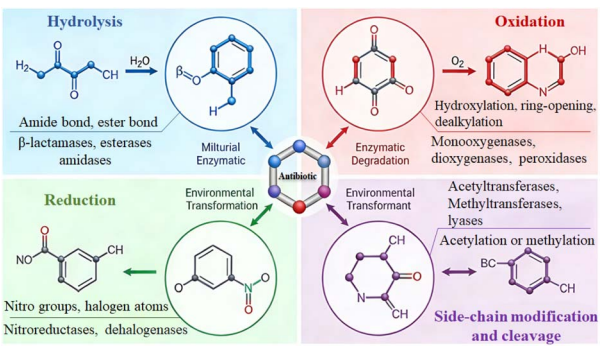

Fig. 2 Biochemical reactions of antibiotic biodegradation.

Interestingly, neither cytochrome P450 enzymes nor primary amine oxidases in *Chlamydomonas reinhardtii* appear to be essential for oxytetracycline degradation. Instead, *Chlamydomonas reinhardtii* utilizes a novel tropinone reductase I (TRI) to mediate oxytetracycline demethylation, resulting in a removal rate of 93.10% within 24 h.[67] This observation provides an important mechanistic insight into algal antibiotic metabolism. This result suggests that oxytetracycline biotransformation in microalgae can proceed through a distinct cytochrome P450-independent pathway, highlighting the metabolic diversity and specificity of algal responses to antibiotic contaminants.

2.2.4 Side-chain modification and cleavage. The complex side chains of antibiotic often serve as the initial targets for microbial attack. Enzymes such as acetyltransferases and methyltransferases inactivate antibiotics by adding acetyl or methyl groups, simultaneously increasing their water solubility.[68,69] Concurrently, specific lyases cleave the side chains that connect the aromatic rings to the pharmacophore in antibiotics with complex structures, breaking down large molecules into simpler fragments. This initial cleavage facilitates subsequent oxidative or ring-opening reactions. For instance, sulfamethoxazole is initially degraded by C–N lyase to generate 4-aminobenzenesulfonamide. Then further converted to *p*-aminophenol by oxidases acting on sulfur-containing donors.[53] Furthermore, ring-opening reactions represent a hallmark step toward the complete mineralization of antibiotics, typically catalyzed by dioxygenases or monooxygenases. These enzymes directly attack and cleave aromatic structures such as benzene and naphthalene rings, generating linear aliphatic compounds. For example, the ultimate degradation of TC and sulfonamide antibiotics relies on the successful cleavage of their aromatic rings.[62]

3 Technology of antibiotic biodegradation

3.1 Traditional biological treatment technology

3.1.1 Activated sludge process. The activated sludge process, as a classical wastewater treatment technology, features highly standardized equipment, low operational and maintenance technical requirements, without expensive chemical reagents. It primarily relies on microbial metabolic activity.[70] Compared to advanced oxidation and membrane separation technologies, it offers lower operational costs and mitigating secondary pollution risks. However, conventional activated sludge exhibits significant limitations in the removal of most antibiotics. The removal efficiencies for TC and quinolone generally less than 80%, while some recalcitrant antibiotics show removal rates below 50% and can even manifest negative removal.[71,72] For example, Chen *et al.*[73] reported negative removal efficiencies of −664.0% and −959.3% observed in the A^2/O and AB processes, respectively. Performance declines markedly under complex conditions such as low temperature and high salinity. Low temperatures inhibit the activity of functional microorganisms, while metal ions can form complexes with antibiotics, reducing adsorption and degradation efficiency.[74,75] Antibiotic-selective pressure often leads to sludge performance deterioration. High antibiotic concentrations inhibit nitrifier bacteria growth, causing total nitrogen and ammonium nitrogen removal efficiencies to drop below 40%.[76] Sufficient aeration is essential for biodegradation. However, high dissolved oxygen levels (around 8 mg L^{-1}) induce reactive oxygen species generation, which drives the enrichment of ARGs. Therefore, precise DO control (2–4 mg L^{-1}) is necessary to balance treatment efficacy and resistance risks.[77] Prolonged antibiotic exposure can also suppress the microbial community, leading to simplified community structures, reduced system resilience, and potential sludge bulking. Currently, parameter optimization and physical enhancement strategies can significantly improve the removal efficiency of antibiotics in activated sludge systems. For instance, the application of a static magnetic field has been shown to enable complete TC removal while reducing treatment time.[78] In sequencing batch reactor systems, the impact of CIP was found to be highly dependent on the carbon source. Specifically, the addition of glucose stimulated microbial abundance, which subsequently enhanced CIP removal efficiency by 18% to 24%. This improvement was attributed to the positive role of key bacterial genera, such as *Dyella* and *Microbacterium*.[79]

3.1.2 Biofilm process. Biofilm processes exhibit significant advantages in treating antibiotic-contaminated wastewater due to their unique internal stratified structure and diverse microbial ecology. Within the biofilm, a natural gradient of oxygen concentration from aerobic on the outside to anoxic and anaerobic conditions toward the interior. The heterogeneous microenvironment provides ideal niches for microorganisms with varying metabolic requirements, enabling the enrichment of slow-growing yet functionally critical microbial communities. Degradation is achieved through synergistic microbial metabolism and cometabolism. Aerobic microbes in the outer layer initiating the cometabolic oxidation of low-concentration antibiotics.[33] Subsequently, microbes in the anoxic and anaerobic layer complete reduction, ring-opening, and other transformations. This spatially sequential degradation pathway simplifies the molecular structure of final products and markedly reduces their antibacterial activity. For example, the integrated fixed-film activated sludge (IFAS) improves the biotransformation efficiency of trimethoprim by 30% to 50% compared to conventional activated sludge, achieving sulfamethazine removal rates of 69.5% to 90%.[80,81] In full-scale applications, IFAS attains 50% to 90% removal efficiencies for antibiotics such as amoxicillin and azithromycin.[82] Mobile bed biofilm reactors (MBBR) treated hospital wastewater achieve approximately 80% removal of antibiotics including roxithromycin and metronidazole.[83] Oxygen-based membrane biofilm reactors (MBfR) degraded sulfamethazine and sulfathiazole at rates of 77% and 87%, respectively, while hydrogen-based MBfR synchronously removed 96% of chlortetracycline and 99% of nitrate.[84,85] Furthermore, biological aerated filters (BAF) demonstrate high removal efficiencies of high-strength swine wastewater ranging from 79.6% to 100% for multiple antibiotics, including sulfamonomethoxine and norfloxacin.[86,87]

3.1.3 Anaerobic biological treatment. Anaerobic biological treatment holds significant potential for treating antibiotic-containing wastewater due to its advantages in handling high organic loads and energy recovery through methane production.[88] The synergistic metabolism of anaerobic microbial communities under anoxic conditions, enabling the transformation and partial degradation of various antibiotics. The treatment efficacy is significantly influenced by antibiotic type, available electron acceptors, and process configuration. For example, continuous-flow anaerobic digestion systems achieve approximately 45% overall removal of TC. In these systems, biodegradation was identified as the predominant removal mechanism, accounting for 88.9% of this total removal, with the remaining proportion attributed to adsorption.[29] In contrast, the degradation pathway of sulfamethoxazole is highly dependent on the presence of coexisting electron acceptors. Under sulfate-reducing conditions, its degradation rate can reach 72.72% within 8 days. It is significantly higher than the 35.65% observed under nitrate-reducing conditions.[89] Implementing an expanded granular sludge bed (EGSB) reactor for anaerobic co-digestion enhances the removal of amoxicillin and erythromycin from real pharmaceutical wastewater to 78% and 72%, respectively.[90] Furthermore, coupling anaerobic processes with membrane separation substantially improves treatment efficiency and stability. For instance, anaerobic membrane bioreactors exhibit excellent removal of COD and multiple sulfamethoxazole antibiotics, while anaerobic dynamic membrane bioreactors achieved simultaneous high removal efficiencies for COD, sulfamethoxazole, and heavy metals in swine wastewater, with sulfamethoxazole removal exceeding 94%.[91,92] Compared to conventional single-stage processes, anaerobic co-digestion system achieved a sulfadiazine removal efficiency of 47.5% at a total solids concentration of 450 mg kg^{-1}.[93]

3.2 Emerging and coupled biotechnologies

3.2.1 Bioaugmentation. Bioaugmentation involves introducing naturally selected, domesticated, or genetically engineered high-efficiency microbial strains into existing biological treatment systems to enhance the degradation of antibiotics.[94] For example, the addition of the aerobic denitrifying bacterium *Achromobacter sp. JL9* achieved an 85.16% removal rate of sulfamethoxazole along with a total nitrogen removal efficiency of 91.83%, demonstrating synergistic potential for simultaneous denitrification and pollutant degradation.[95] Similarly, augmentation with *Pseudomonas* strains resulted in a cefalexin degradation rate of 92.1%.[96] Strains such as *Glutamicibacter sp. S2* and *Herbaspirillum sp. S8* isolated from activated sludge, achieved over 82% degradation of amoxicillin under optimized conditions, with mechanisms involving β-lactamase production and bio-adsorption.[97] Additionally, *strain JWJ-09* efficiently degraded quinoline under methanol co-metabolism. When combined with activated sludge to treat actual coking wastewater, the quinolone degradation reached 90.75% total organic carbon removal within 24 h.[98] However, the practical stability of augmented strains poses a significant challenge, as their survival and activity are highly dependent on environmental conditions. For instance, isolated *Rhizobium* and *Klebsiella* strains effectively removed cefalexin. In contrast, *Pseudomonas* strains exhibited a strong dependence on multi-substrate mixed cultures. Severe inhibition was observed when exposed to high concentrations or single-substrate conditions of cefalexin.[96,99] Moreover, the periodic addition of functional sludge, such as anammox sludge, to restore the community structure and functionality of systems stressed by antibiotics is also an effective bioaugmentation strategy.[100]

Although engineered bacteria may show high antibiotic degradation efficiency in laboratory studies, their application in wastewater systems is often limited by poor ecological fitness, unstable colonization, and rapid loss of niches. To enhance their persistence, strategies such as carrier-assisted immobilization, biofilm-based retention, pre-acclimation to wastewater conditions, synthetic consortium design, metabolic burden reduction, and microenvironment optimization should be considered.[101,102] Thus, successful deployment of engineered strains depends not only on degradative capability, but also on their ability to establish stable ecological interactions and persist under complex environmental conditions.

3.2.2 Immobilized microorganism technology. Immobilized microbial technology involves anchoring functional microbial strains or microalgae onto specific carriers and represents a key strategy to overcome challenges in bioaugmentation, such as biomass washout and poor stability. The technology significantly enhances the concentration of functional microbes within reactors, improves its resilience to environmental stress, and enables the recovery and reuse of biocatalysts. For instance, encapsulating *Chlorella* within a semi-permeable, double-network hydrogel created a microalgal gel system that achieved TC removal efficiencies exceeding 99%. The hydrogel effectively shielded the algal cells from direct antibiotic stress and prevented biomass leakage.[103] Combining *Pseudomona* spp. with graphene composite hydrogels to create a functionally enhanced system (MC + Pseu-BGH). MC + Pseu-BGH optimized carrier conductivity, modulated microbial communities, and upregulated key enzymes such as nitroreductase, thereby increasing chloramphenicol and sulfamethoxazole removal rates to 99.89% and 94.7%, respectively.[104] Furthermore, immobilizing *Raoultella ornithinolytica CC12* on magnetic biochar derived from corn straw not only enhanced microbial loading but also enhanced the degradation capacity for cyclophosphamide to 305.29 mg g^{-1} d^{-1}.[105] Moreover, *Bacillus* strains embedded within an active sponge formed a bacterium-microalgae consortium co-immobilized filter (BMCCF) have removed 98.54% of 82 mg L^{-1} lincomycin within 7 days.[106] Additionally, composite immobilized forms such as algae–bacteria symbiotic granules also demonstrate promising potential for removing antibiotics like TC.[107]

3.2.3 Coupling of biology and materials. Coupled biomaterial systems, which incorporate functional materials such as modified biochar, graphene, and composite adsorbents into biological treatment processes, represent a promising strategy for enhancing antibiotic removal through the synergy of physicochemical interactions and microbial metabolism.[108] In these

coupled systems, materials transcend their conventional roles as mere adsorbents to concentrate pollutants or simple physical carriers; they actively reconstruct the biological microenvironment through advanced micro-interfacial mechanisms. Specifically, a dynamic adsorption-bioregeneration loop is established, where materials overcome mass-transfer limits by concentrating trace antibiotics, while continuous localized biodegradation naturally regenerates the adsorption sites.[109] Concurrently, high-affinity materials provide critical toxicity buffering by rapidly sequestering toxic parent compounds to safeguard sensitive indigenous microbiota.[110] Furthermore, functioning as extracellular electron-transfer mediators, conductive materials facilitate direct interspecies electron transfer, which significantly lowers the activation energy required for the cleavage of recalcitrant antibiotic structures and accelerates the overall transformation kinetics. For instance, the addition of $FeCl_3$-modified biochar in anaerobic digesters provided a porous refuge for functional microbes such as *Clostridia*, facilitated interspecies electron transfer. And simultaneously enhanced methane production and TC removal efficiency, while effectively reducing the relative abundance of ARGs such as tetA.[111] Similarly, the fabrication of nitrogen-doped graphene nanosheets anchored with graphene or carbon nanotubes can respectively enhance methane production and antibiotic degradation rates by 20–30%, and achieve 92% TC degradation within 20 minutes.[112,113] In aerobic or hybrid systems, adsorption–biological coupling reactors constructed with coke or bamboo charcoal was also highly efficient. The removal rates of sulfadiazine and sulfamethoxazole in reactors can reach 88.29% and 96.76%, respectively.[49] Bamboo charcoal strongly adsorbed TC and sulfamethoxazole through pore retention, π–π interactions, and hydrogen bonding. Its abundant pore structure provided an ideal habitat for functional microorganisms such as nitrifiers, denitrifying bacteria, and *Pseudomonas*.[114] In addition, the addition of composite materials such as granular activated carbon and zero-valent iron has also been proven to simultaneously increase the methane production and the antibiotic metabolic activity.[115]

3.2.4 Combined treatment technologies. Combined treatment technologies, which integrate or couple different treatment units, aim to overcome the limitations of individual methods by achieving synergistic pollutant removal, toxicity reduction, and resource recovery. For high-concentration and highly toxic wastes, the integration of thermal hydrolysis pretreatment and anaerobic digestion process can thoroughly degrade residual antibiotics and produce biogas, thereby realizing harmless treatment and resource recovery.[116] For complex antibiotic-containing wastewater, combinations of different biological processes significantly improve removal efficiencies. For example, the "AAO + AAO + MBR" system demonstrated superior and more stable comprehensive antibiotic removal performance compared to the "AB + AAO" system.[117] More advanced coupling strategies involve the deep integration of biological treatment with physicochemical or electrochemical processes. For instance, the hybrid system integrating a reticulated polyurethane foam biological trickling filter with vertical-flow constructed wetlands achieved over 94% synchronous

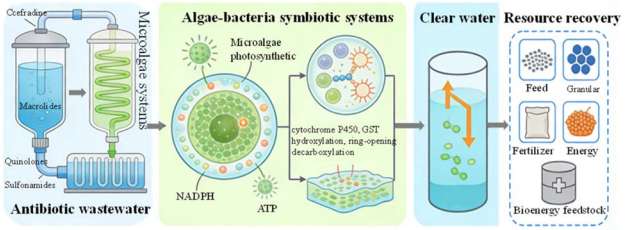

Fig. 3 Process flow of microalgae technology.

removal of antibiotics and heavy metals *via* synergistic adsorption, microbial metabolism, and phytoremediation.[114,118] The combination of photocatalysis and constructed wetland microbial fuel cells enhanced TC removal to 77.65% through subsequent biological deamination and mineralization of photocatalytic products.[52] Furthermore, the biogenic manganese oxide-polishing MBBR process substantially increased sulfamethoxazole removal from 24% to 80% through catalytic oxidation by biogenic manganese oxides.[119]

3.2.5 Microalgae technology. Microalgal technology has attracted increasing attention in antibiotic wastewater treatment due to its environmental friendliness and resource recovery potential (Fig. 3).[16] By leveraging the photosynthetic and metabolic activities of microalgae to efficiently degrade or transform antibiotics, and accumulating high-value biomass.[120,121] For example, microalgae can achieve a chloramphenicol removal rate of 94.27% in aquaculture wastewater.[122] *Rhodococcus rhodochrous* exhibited removal efficiencies ranging from 60% to 100% for ten antibiotics including sulfonamides, macrolides, and quinolones within 40 days.[123] The underlying mechanisms extend beyond microalgal biosorption and degradation to include synergistic effects generated by constructing algae-bacteria symbiotic systems. For example, an artificial wetland system integrating algae–bacteria consortia with gravel substrate exhibited optimal comprehensive performance in the simultaneous removal of COD, nitrogen, phosphorus, and multiple pollutants such as cefradine.[124] The harvested microalgal biomass can be further utilized as feed, biofertilizer, or bioenergy feedstock. Thereby enhancing the economic viability and sustainability of the technology. Consequently, microalgae-based technology represents an advanced biological treatment strategy that integrates deep pollutant removal, carbon fixation, and resource recovery.

4 Challenges and innovation

4.1 Challenges and obstacles

A detailed comparison of traditional and emerging antibiotic bioremediation technologies is shown in Table 1. To facilitate comparison among treatment technologies, Table 2 provides a side-by-side summary of the removal efficiencies of major antibiotic classes, including sulfonamides, TCs, and quinolones, under different treatment systems. Although biological treatment technologies show considerable promise for antibiotic removal. The practical application of biological treatment for antibiotic-remediation is primarily bottlenecked by the

Table 1 Comparative of antibiotic biodegradation technology

Biodegradation	Technology	Key mechanism	Removal efficiency	Challenges	References
Traditional biological treatment technology	Activated sludge process	Activated sludge metabolism, lower costs and mitigating secondary pollution	Tetracycline and quinolone generally less than 80%; optimization such as magnetic field, carbon source regulation can be further enhanced	Antibiotics inhibit the functional bacteria; high dissolved oxygen induce the emergence of ARGs; performance is affected by low temperatures, high salinity	70–79
	Biofilm process	Aerobic/anoxic/anoxic conditions within the biofilm, functional bacteria are enriched, synergistic metabolism	The removal rates of IFAS, MBBR, MBfR, and BAF are usually between 70% and 100%	Parameters (HRT, DO) need to be optimized; high concentrations may damage the biofilm	33, and 80–87
	Anaerobic biological treatment	Synergistic metabolism of anaerobic, converting organic substances into methane, energy recovery	Degradation rate of tetracycline is approximately 45% (mainly through biodegradation); SMX is significantly affected by the electron acceptor	High concentrations inhibit methane production; competition for electron acceptors affects the degradation pathway	29, and 88–93
Emerging and coupled biotechnologies	Bioaugmentation	Introduce high-efficiency microbial strains, enhance degradation capacity	SMX and cephalexin have a degradation rate of over 80% to 90%	Difficulty in establishing colonies and compete with the indigenous bacteria; strong substrate dependence; ecological safety risk	94–100
	Immobilized microorganism technology	Anchoring functional microbial strains onto carriers, enhance stability and recoverability	*Bacillus* strains embedded within an active sponge resulted in a 7 days removal rate of 98.54% for lincomycin	Carriers have high costs; mass transfer limitations; long-term operational stability	103–107
	Coupling of biology and materials	The material serves as an adsorbent, carrier and electronic medium, synergy between physicochemical and microbial metabolism	Coke or bamboo – biological coupling achieved the removal rates of sulfadiazine and sulfamethoxazole reach 88.29% and 96.76%	High cost of functional materials; complex mechanism of multiphase interfaces	111–115
	Combined treatment technologies	Multiple technical units are connected in series to achieve deep removal and risk control	Pretreatment + biodegradation, physicochemical treatment + biodegradation can achieve removal of antibiotics and heavy metals (more than 90%)	System complex, design and control challenging; investment and operation costs increase	52, 114, and 116–119
	Microalgae technology	Microalgae perform photosynthesis to degrade pollutants and convert resources into biomass	Removal rate of chloramphenicol can reach 94.27%; synergistic purification of algal-bacterial system	Efficiency is greatly affected by environmental factors; high cost of biomass recovery	16, and 120–124

Table 2 Comparative removal of major antibiotic classes in different treatment systems

Antibiotic class	Representative compound	Treatment system	Removal efficiency	Key operating conditions	References
Sulfonamides	Sulfamethoxazole	Anaerobic degradation	20–60%	Sulfate as electron acceptor	89
	Sulfadiazine	Laccase–syringaldehyde system	94.84%	30 °C; pH 5.32; laccase 0.5 mL L^{-1}; syringaldehyde 0.15 mM	27
	Sulfamethazine	Fixed-film activated sludge membrane bioreactor	87%	HRT 10 h; SRT 80 days	81
	Sulfamethazine/ sulfathiazole	Oxygen-based membrane biofilm reactor	77%/87%	32 hollow-fiber membranes	84
	Sulfadiazine/ sulfamethazine	Anaerobic membrane bioreactor	80.1–54.33%/74.12–47.66%	0.5 g L^{-1} biochar; monitored from day 73 to day 86	91
	Sulfamethoxazole/ sulfadiazine/ sulfamethazine	Anaerobic dynamic membrane bioreactor	94.2%/51.2%/52.8%	HRT 40 h; 1.5 mg L^{-1} Cu^{2+}/Zn^{2+}	92
	Sulfamethoxazole	Moving bed biofilm reactor	85.16%	Ammonia-N or nitrate-N as nitrogen source	95
	Sulfamethoxazole	Microbial-graphene hydrogel	94.7%	Graphene oxide, *Pseudomonas*, pH 7.0; 10 mg L^{-1} initial conc.	104
	Sulfamethoxazole	Biogenic manganese oxides-moving bed biofilm reactors	80%	Mn(II); COD 165 mg L^{-1}; ammonia 50 mg L^{-1}	119
Tetracyclines	Tetracycline	Continuous-flow reactors	1.4 mg per g VSS per d	35 °C; 24 h reaction cycle	29
	Tetracycline	Static magnetic field-activated sludge process	100%	Sludge loading 3 mg TC per g MLSS per d; static magnetic field 5 mT and 25 mT	78
	Tetracycline	Immobilized bacteria + algae	93.87%	*Alcaligenes faecalis* strain R1 + *Tetradesmus obliquus*	103
	Tetracycline	Nonradical process	92%	N-doped graphene nanosheets; carbon nanotubes	112
	Tetracycline/ sulfamethoxazole	Polyurethane foam biological trickling filter with vertical-flow constructed wetlands	>94%	HRT 72 h; HLR 0.050 m^3 m^{-2} day^{-1}; *Canna indica* L.	114
	Chlortetracycline	H_2 – membrane biofilm reactors	96%	5 h HRT; 2 psi H_2 pressure	85
Quinolones	Ciprofloxacin	Aerobic activated sludge	39.69%	25 °C; HRT 11 h; glucose as co-substrate	79
	Ciprofloxacin	Submerged attached biofilter	95%	Dextrose 500 mg L^{-1}	87
	Ciprofloxacin	Partial nitritation-moving bed biofilm reactor	98%	FNA level 0.056 mg N L^{-1}	34
	Ciprofloxacin	Moving bed biofilm reactor	27.11%	Ammonia-N or nitrate-N as nitrogen source	95
	Enrofloxacin	Microbial	80.8%	*Nitrobacter* sp.; initial enrofloxacin 5 mg L^{-1}	66
	Quinoline	*Achromobacter* sp. strain JWJ-09	99.39%	100 mg L^{-1} methanol	98
Others	Chloramphenicol	Cyanobacteria	94.27%	*Synechocystis* sp.	123
	Chloramphenicol	*Raoultella ornithinolytica* CC12	99.32%	Magnetic biochar	105
	Amoxicillin/ erythromycin	Expanded granular sludge bed	78%/72%	30 °C, HRT 24 h	90
	Lincomycin	Bacterium–algae consortium	98.54%	*Bacillus subtilis* strain	106

inherent bacteriostatic or bactericidal nature of these compounds. The response of biological systems is strictly concentration-dependent and often exhibits hormetic behavior. At trace levels (ng L^{-1} to low μg L^{-1}), antibiotics may undergo partial removal through sorption and biotransformation without causing measurable inhibition.[125] However, as concentrations rise to high μg L^{-1} or mg L^{-1} levels, systemic toxicity emerges through the disruption of key metabolic enzymes and cell membrane integrity. The sensitivity of different biological processes varies considerably, making toxicity thresholds highly process-specific. For instance, sulfonamides at concentrations above 100 μg L^{-1} have been shown to disrupt amino acid synthesis, cofactor production, and purine/pyrimidine metabolism in anammox bacteria, eventually leading to community collapse and performance deterioration. In addition to direct metabolic inhibition, antibiotics can also reshape microbial community composition.[126] Exposure to sulfamethoxazole may suppress conventional heterotrophic denitrification such as *Phycisphaera* and *Winogradskyella* while enriching sulfur-autotrophic denitrifiers such as *Sediminicola* and *Thiogranum*.[127] In contrast, CIP and amoxicillin have been reported to inhibit *Proteobacteria* and promote *Bacteroidetes* and fungi in denitrification systems.[128] Such community shifts often occur at the expense of original treatment functions, including nitrogen and phosphorus removal, thereby threatening the long-term stability and efficiency of biological processes. Therefore, the toxicity turning point of antibiotics should be understood not as a fixed value, but as a process-dependent concentration range closely linked to microbial ecology, antibiotic type, and operational conditions.[129] This constitutes one of the fundamental challenges in the biological treatment of antibiotic-containing wastewater.

The dissemination of ARGs driven by antibiotic residues and the associated secondary risks represent one of the most severe environmental challenges for biological treatment technologies.[51] Antibiotics in the environment exert strong selective pressure on microbial communities. Biological treatment systems, especially wastewater treatment plants, serve as hotspots for ARG enrichment and HGT. Due to their high microbial density and frequent exposure to antibiotics.[6,70] A more complex and concerning issue is that many key degradation enzymes, such as hydrolases and modifying enzymes, are encoded by specific genes. These genes are often located on mobile genetic elements (MGEs), including plasmids, transposons, or integrons. Importantly, these MGEs frequently co-carry ARGs.[58] It implies that a bacterium may simultaneously acquire the capability to degrade a particular antibiotic and resist other antibiotics through the acquisition of one plasmid. Consequently, biological treatment processes may inadvertently select for microorganisms harboring multifunctional enzymes alongside ARGs. These processes can also enrich such microorganisms. As a result, the treatment systems may effectively transform into amplifiers and dissemination of ARGs. Studies have demonstrated that antibiotics such as sulfamethoxazole and TC can induce the expression of integrons. Thereby accelerating the dissemination of multiple ARGs within bacterial populations, including *intI1*, *sul1*, *dfrA12*, *mexB*, and *mexF*. Moreover, ARGs are often associated with MGEs, including transposons, insertion sequences, integrons, and plasmids, which can disseminate resistance determinants among bacteria through HGT pathways, mainly conjugation, transformation, and transduction.[128] The induction of MGEs by antibiotics, coupled with the efficient operation of these HGT pathways, creates a powerful engine for ARG dissemination.[130,131]

Transitioning from laboratory validation to engineering application represents a critical leap for biological treatment technologies for a process often hindered by multiple practical obstacles. The primary challenge arises from the interference present in actual water bodies. Coexisting contaminants such as organic matter and heavy metals may exhibit synergistic or antagonistic effects with antibiotics, competing for microbial metabolic resources or directly inhibiting the activity of key enzymes. Consequently, treatment efficiency in real systems is often significantly lower than those achieved under laboratory conditions.[132,133] Introduced high-efficiency degrading bacteria or enzymes frequently undergo rapid inactivation in dynamic natural environments. This instability is caused by difficulties in adapting to fluctuations in pH, temperature, and other environmental factors. Additionally, these bacteria or enzymes face competitive disadvantages compared to indigenous microorganisms. They are also vulnerable to predation by protozoa. All of these factors prevent sustained, long-term degradation function. Although many enhanced materials and novel processes can improve treatment efficacy, their high preparation and operational costs limit large-scale implementation. Collectively, these factors constitute significant bottlenecks for the efficient, stable, and safe application of biological treatment technologies in complex real environments.

4.2 Frontier countermeasures and innovative

4.2.1 Process intensification and stress-resistance regulation. To proactively mitigate the inhibitory effects of antibiotics on biological treatment systems, various strategies have been developed. The focus is on process intensification and stress-resistance regulation. Micro-electric field stimulation is a promising physical intensification method. For example, applying a low-intensity voltage of 0.3–1.5 V has been shown to effectively alleviate the inhibitory effects of sulfamonomethoxine on anammox systems. The underlying mechanism involves stabilizing microbial cell membrane structure, promoting the synthesis of key cofactors such as cytochrome *c*, and enhancing purine and pyrimidine metabolism, thereby shortening the recovery time of inhibited systems by more than one week.[134] Quorum sensing regulation is achieved by adding or interfering with signaling molecules. This regulation can coordinate microbial community behavior and enhance collective stress response. Furthermore, it improves the cooperative degradation capability.[135] Meanwhile, the addition of trace elements and cometabolic substrates, such as iron and sodium acetate, supplies essential cofactors or extra energy for functional enzyme synthesis. As a result, it directly promotes antibiotic degradation pathways dominated by cometabolism.[136] These

strategies optimize microbial survival environments and metabolic states through external interventions. As a result, it improves the tolerance, resilience, and degradation performance of biological treatment systems under antibiotic stress. Additionally, it offers diversified technical options to ensure stable operation.

The efficiency of antibiotic degradation is intrinsically tied to the precision of electron transfer efficiency (ETE). However, ETE does not automatically guarantee selective antibiotic degradation, because electrons may also be consumed by competing pathways such as methanogenesis and sulfate reduction. Therefore, stabilization of electron flow is essential for maintaining selective antibiotic transformation. Practical strategies include optimizing redox potential and electron donor dosage, limiting competing electron acceptors, enriching target functional microorganisms, and using conductive carriers or redox-active materials to direct electron transfer toward antibiotic-transforming pathways.[137,138]

Residual sub-inhibitory levels may still impose selective pressure on wastewater microorganisms and induce ARG expression. Functional microbes, including nitrifiers, may serve as ARG hosts can spread to indigenous microbiota through HGT.[139] Therefore, the risk mechanism involves not only microbial inhibition, but also residual antibiotic selection, ARG maintenance, and HGT-mediated dissemination. Control strategies should extend beyond operational regulation and include quorum quenching, phage therapy, improving sludge management, integrating polishing technologies for ARG and extracellular DNA removal, and adopting monitoring frameworks that couple antibiotic removal with ARGs and MGEs.[140]

4.2.2 Synergistic treatment using novel materials and coupling technologies. The development of multifunctional materials and the integration of different technological processes represent a significant trend for achieving synergistic enhancement. The advancement of novel functional materials, such as modified biochar and gel-immobilized carriers, extends beyond traditional adsorption functions. These materials can provide refuges for microorganisms to against antibiotic stress and serve as electron mediators to activate catalytic processes. For example, the addition of biochar has been shown to increase the removal rates of various sulfonamide antibiotics by 53% to 88%.[141] Nano zero-valent iron and granular activated carbon significantly enhanced system stability and tolerance.[88] The deep integration of materials with biological processes can generate synergistic enhancements. In anaerobic digestion systems, the application of modified biochar or granular activated carbon not only adsorbed antibiotics but also enriched functional microbial communities and promotes interspecies electron transfer through porous structures. This dual function synchronously enhanced methane production and inhibited the proliferation of resistance genes like *tetA*.[142] Additionally, incorporating physical field regulation into biological systems could activate microbial oxidative phosphorylation and electron mediator synthesis, resulting in a 1.46-fold increase in the degradation of sulfamethoxazole.[53] Phosphorus-modified biochar-MoS_2/alginate hydrogel beads could efficiently adsorb and concentrate antibiotics. It also activated persulfate to generate reactive oxygen species, enabling *in situ* advanced oxidation degradation of pollutants and material regeneration. Collectively, these advances highlight that interdisciplinary integration aimed at optimizing materials and multi-technology processes is a key pathway to advancing water treatment technologies toward higher efficiency, intelligence, and sustainability.

4.2.3 Synthetic biology and precise biological tools. The application of synthetic biology and precise biological tools has introduced breakthrough paradigms of green catalysis and intelligent bioremediation for antibiotic pollution control. Researchers have identified highly active and specific enzymes from nature, such as nitroreductase, and employed protein engineering to enhance the performance.[143] Furthermore, one representative example is the FerTiG complex, a modular protein assembly that integrates Tet(X4) for TC decomposition, glucose dehydrogenase for cofactor regeneration, and ferritin for enzyme protection, with the aim of improving catalytic efficiency and operational stability. The biomimetic design significantly enhanced catalytic efficiency, environmental stability, and operational safety.[122] The artificial design and synthesis of novel biocatalysts also demonstrate great potential. For instance, $Co_{0.5}Fe_{0.5}Fe_2O_4$ with enzyme-like activity has been developed to efficiently catalyze the degradation of various antibiotics under mild conditions. This process achieved deep mineralization while preventing the accumulation of toxic intermediates.[144] Moreover, intelligent engineered strains or synthetic microbial consortia have been constructed through metabolic pathway editing and the introduction of genetic circuits. The modifications endow microorganisms with high and specific degradation capabilities. Additionally, it confers intelligent sensing–response regulatory functions that respond to specific pollutant concentrations in the environment.

4.2.4 Resource recovery and turning waste into wealth. Advancing biological treatment from simple pollutant removal toward resource recovery and recycling represents a forward-looking strategy for addressing antibiotic pollution and improving process sustainability. Pollutants in wastewater are increasingly regarded as misplaced resources, and emerging technologies seek to achieve both contaminant removal and value recovery. Under light-driven conditions, microalgal systems can effectively degrade antibiotics while assimilating nutrients such as nitrogen and phosphorus into biomass enriched in lipids and proteins, which can be further utilized as feed, fertilizer, or converted into biodiesel.[121] Anaerobic digestion and related enhanced processes not only contribute to antibiotic removal but also convert organic pollutants into biogas, while optimization through functional materials such as biochar can further improve methane yield and treatment performance.[111] In addition, anaerobic fermentation can produce short-chain fatty acids, and specific microorganisms may further convert antibiotic degradation intermediates into bio-based chemicals. Beyond these conventional recovery pathways, biological treatment processes may also enable the recovery of high-value products such as EPS-derived biopolymers. As EPS contains polysaccharides, proteins, and other macromolecular components with diverse functional groups, it

has potential for valorization in bio-based materials, flocculants, adsorbents, and related polymeric applications.[145,146] In antibiotic treatment systems, this pathway could further enhance sustainability by coupling pollutant removal with the recovery of value-added biomaterials. However, its practical implementation remains constrained by EPS heterogeneity, extraction efficiency, and possible contamination by residual antibiotics, resistance genes, or related transformation products, highlighting the need for further evaluation of product safety and process feasibility.[147] Collectively, these strategies support a green circular model that integrates pollution control, energy recovery, and material valorization, thereby enhancing both the economic and environmental sustainability of wastewater treatment processes.

4.2.5 Process control and models. To achieve stable, efficient, and low-risk operation of antibiotic bioprocessing, the development of advanced process control and predictive model strategies is essential. Comprehensive risk management throughout the entire process is the central guiding principle. It is essential to establish a continuous risk assessment system that uses the abundance, transmission potential, and driving factors of ARGs as key indicators for evaluating process success or failure. This foundation enables the development of targeted regulatory strategies to suppress ARGs dissemination. To achieve the goal, the in-depth application of multi-omics technologies including metagenomics, meta transcriptomics, and metabolomics is critical. These approaches allow precise identification of key functional microorganisms and degradation enzyme genes, elucidation of complete metabolic pathways, and systematic revealing of ARGs transmission networks.[148,149] Building upon this knowledge, advanced control based on mathematical model and artificial intelligence offers a means to achieve precise regulation. Given the highly nonlinear of biological systems, emerging dissipation-based control methods can better coordinate internal processes. Meanwhile, machine learning algorithms such as random forests, support vector machines, and neural networks can be employed to mine stress-response markers from multi-omics big data. The algorithms can also be used to construct predictive models that link antibiotic concentration, process parameters, and nitrogen removal performance. It facilitates risk early-warning and parameter optimization.[150,151] Furthermore, tools like graph neural networks can decode complex microbial interaction networks and identify core microbial communities and critical ecological niches that maintain system functional stability.[30] In summary, through the deep integration of mechanistic knowledge and artificial intelligence, biological treatment systems can be propelled toward a more intelligent, precise, and predictive-controlled.

5 Conclusions

Biological treatment technologies are considered a central strategy for addressing antibiotic pollution due to cost-effectiveness and environmental friendliness. The biological removal of antibiotics is primarily driven by microbial cometabolism, involving complex microbial communities composed of AOB, microalgae, heterotrophic bacteria. These communities collaboratively execute a series of biochemical transformations such as hydrolysis, oxidation, reduction, and SMC. Emerging enhancement technologies including bioaugmentation, immobilization, bio-material coupling, and integrated processes have demonstrated significant advantages in improving removal efficiency and operational stability. However, the inherent inhibitory effects of antibiotics on functional microorganisms can disrupt microbial community structures and treatment performance. What's more, the treatment processes may become hotspots for the proliferation and dissemination of ARGs, posing serious secondary environmental risks. Therefore, there is a pressing need to shift from mere contaminant removal toward resource recovery, such as microalgal biomass production and biogas energy. Concurrently, advancing the deep integration of multi-omics technologies with mechanistic knowledge and artificial intelligence, ARGs process control and predictive model is essential. These approaches will lay the foundation for developing next-generation sustainable biological treatment technologies that are intelligent, efficient, and capable of simultaneously mitigating resistance risks.

Author contributions

Xiangtao Zhao: writing – original draft, and conceptualization. Enhui Xie: writing – original draft. Huina Xie: writing – review & editing, supervision, funding acquisition.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

Acknowledgements

This project has received funding from Gansu Youth Science and Technology Fund (23JRRA888), Tianyou Youth Talent Lift Program of Lanzhou Jiaotong University.

References

1 T. Zhuo, L. He, B. Chai, S. Zhou, Q. Wan, X. Lei, Z. Zhou and B. Chen, Micro-pressure promotes endogenous phosphorus release in a deep reservoir by favouring microbial phosphate mineralisation and solubilisation coupled with sulphate reduction, *Water Res.*, 2023, **245**, 120647.
2 K. A. Alrefaey, N. A. Sallam, E. M. ElZayat, A. F. A. Youssef, I. S. Fahim, H. Hosney and P. N. L. Lens, A comprehensive review of techniques for removal of antibiotics from wastewater, *Environ. Sci. Water Res. Technol.*, 2025, **11**, 2782–2809.

3 T. T. H. Van, Z. Yidana, P. M. Smooker and P. J. Coloe, Antibiotic use in food animals worldwide, with a focus on Africa: pluses and minuses, *J. Glob. Antimicrob. Resist.*, 2020, **20**, 170–177.
4 K. Liu, C. Gan, Y. E. Peng, Y. Gan, J. He, Y. Du, L. Tong, J. Shi and Y. Wang, Occurrence and source identification of antibiotics and antibiotic resistance genes in groundwater surrounding urban hospitals, *J. Hazard. Mater.*, 2024, **465**, 133368.
5 L. Lei, N. Chen, Z. Chen, Y. Zhao, H. Lin, X. Li, W. Hu, H. Zhang, J. Shi and Y. Luo, Dissemination of antibiotic resistance genes from aboveground sources to groundwater in livestock farms, *Water Res.*, 2024, **256**, 121584.
6 Z. Lu, G. Liu, H. Xie, Y. Zhai and X. Li, Advances and solutions in biological treatment for antibiotic wastewater with resistance genes: A review, *J. Environ. Manage.*, 2024, **368**, 122115.
7 P. Sharma, M. Sharma, D. Nimesh and R. Gupta, Exploring the potential of hydrogel adsorbents for antibiotic removal from water: A review, *J. Mol. Liq.*, 2025, **426**, 127383.
8 Y. Xu, D. Li, Y. Yuan, F. Fang and B. Xi, Antibiotic resistance occurrence and ecological impact in landfill leachate: A review on compound effect of antibiotics and non-antibiotics, *Emerging Contam.*, 2025, **11**, 100508.
9 X. Zhou, Y. Shi, Y. Lu, S. Song, C. Wang, Y. Wu, R. Liang, L. Qian, Q. Xu, X. Shao and X. Li, Ecological risk assessment of commonly used antibiotics in aquatic ecosystems along the Coast of China, *Sci. Total Environ.*, 2024, **935**, 173263.
10 B. Shi, X. Cheng, H. Chen, J. Xie, Z. Zhou, S. Jiang, X. Peng, Y. Zhang, D. Zhu and Z. Lu, Occurrence, source tracking and removal of antibiotics in recirculating aquaculture systems (RAS) in southern China, *J. Environ. Manage.*, 2022, **324**, 116311.
11 L. Liu, K. Lei, X. Gao, M. Zhang, H. Wang, S. Shan, S. D. Joseph and J. Fang, Aeration-assisted removal of tetracycline from wastewater by biochar: mechanisms and cost-benefit analysis, *Environ. Res.*, 2025, **285**, 122407.
12 T. Cherian, C. Ragavendran, S. Vijayan, S. Kurien and W. J. Peijnenburg, A review on the fate, human health and environmental impacts, as well as regulation of antibiotics used in aquaculture, *Environ. Adv.*, 2023, 100411.
13 S. Li, C. Zhang, F. Li, T. Hua, Q. Zhou and S. Ho, Technologies towards antibiotic resistance genes (ARGs) removal from aquatic environment: a critical review, *J. Hazard. Mater.*, 2021, **411**, 125148.
14 C. L. Gregory, E. L. Bradford, R. D. Fell, D. C. Haak and L. K. Belden, Utilizing a novel fecal sampling method to examine resistance of the honey bee (Apis mellifera) gut microbiome to a low dose of tetracycline, *PLoS One*, 2025, **20**, e0317129.
15 W. Wang, W. Yang, L. Jiang, C. Yao, Z. Zhang, M. Xu, X. Yan and X. Qian, Applications of Oxford Nanopore Technology in the analysis of antibiotic resistance genes: A review, *J. Hazard. Mater.*, 2025, **498**, 139824.
16 Z. Gasana, A. Kayiranga, J. C. Nizeyimana, S. Tian, J. Rugema, L. You and J. Su, Removal of antibiotics and antibiotic resistance genes using microalgae-based wastewater treatment system: A bibliometric review and mechanism analysis, *J. Water Process Eng.*, 2025, **72**, 107496.
17 S. Zhang, T. Xu, C. Zhang, H. Zhou and H. Song, A review of antibiotic resistance generation and control in wastewater and solid waste system, *J. Environ. Chem. Eng.*, 2025, **13**, 118014.
18 A. Wang, M. Ding, Y. Cai, L. Wang, Y. Guo, Y. Guo and W. Zhan, Ultra-efficient Ru and Nb co-modified CeO_2 catalysts for catalytic oxidation of 1,2-Dichloroethane, *Environ. Sci. Technol.*, 2024, **58**, 20300–20312.
19 S. O. Rab, F. M. A. Altalbawy, L. Baldaniya, A. Kumar, R. M. M, M. Kundlas, G. C. Sharma, K. K. Joshi, S. Saydaxmetova and M. K. Abosaoda, A comprehensive review of bismuth-based photocatalysts and antibiotic pollution degradation: Recent trends and challenges, *Inorg. Chem. Commun.*, 2025, **174**, 114067.
20 T. M. Uddin, A. J. Chakraborty, A. Khusro, B. Zidan, S. Mitra, T. B. Emran, K. Dhama, M. K. H. Ripon, M. Gajdács, M. U. K. Sahibzada, M. J. Hossain and N. Koirala, Antibiotic resistance in microbes: history, mechanisms, therapeutic strategies and future prospects, *J. Infect. Public Health*, 2021, **14**, 1750–1766.
21 A. Raichur and N. Sinha, Narrow spectrum nano-antibiotic for selective removal of ARB from contaminated water: new insights into stimuli response based on cellular attachment, lysis, and excretion, *J. Hazard. Mater.*, 2024, **472**, 134475.
22 S. Moosavi, C. W. Lai, O. Akbarzadeh and M. R. Johan, Recycled activated carbon-based materials for the removal of organic pollutants from wastewater, in *Waste Recycling Technologies for Nanomaterials Manufacturing*, ed. A. S. H. Makhlouf and G. A. M. Ali, Springer International Publishing, Cham, 2021, pp. 513–539.
23 H. R. Ahmed, Heterogeneous catalysts in advanced oxidation processes: A comprehensive review on antibiotic removal from wastewater, *Sep. Purif. Technol.*, 2025, **374**, 133670.
24 X. Zhang, T. Cai, S. Zhang, J. Hou, L. Cheng, W. Chen and Q. Zhang, Contamination distribution and non-biological removal pathways of typical tetracycline antibiotics in the environment: a review, *J. Hazard. Mater.*, 2024, **463**, 132862.
25 M. W. Nugraha, S. Kim, F. Roddick, Z. Xie and L. Fan, A review of the recent advancements in adsorption technology for removing antibiotics from hospital wastewater, *J. Water Process Eng.*, 2025, **70**, 106960.
26 S. Y. Cai, X. Y. Zhang, S. Y. Chen, S. A. Peng, T. Sun, Y. Zhang, P. Yang, H. X. Chai, D. S. Wang and W. J. Zhang, Solid-liquid redistribution and degradation of antibiotics during hydrothermal treatment of sewage sludge: interaction between biopolymers and antibiotics, *Water Res.*, 2024, **258**, 121759.
27 Q. Lou, Y. Wu, H. Ding, B. Zhang, W. Zhang, Y. Zhang, L. Han, M. Liu, T. He and J. Zhong, Degradation of sulfonamides in aquaculture wastewater by laccase–

syringaldehyde mediator system: response surface optimization, degradation kinetics, and degradation pathway, *J. Hazard. Mater.*, 2022, **432**, 128647.
28 S. F. Mousavi, M. A. Zazouli and F. Gholami-Borujeni, Biodegradation of tetracycline and ciprofloxacin in aerobic composting using different microbial sources, *Waste Biomass Valoriz.*, 2024, **15**, 4761–4772.
29 Y. Wang and G. Wu, Leveraging anaerobic biodegradation of tetracycline in anaerobic digestion systems with different operational modes, *Environ. Technol. Innov.*, 2023, **32**, 103373.
30 X. Xu, M. Zhang, J. Wu, S. Wang, W. Chen, C. Dong, B. Hu, P. Zheng and D. Qu, Big data analytics of antibiotic toxicity and inhibition in anammox systems: A review, *Bioresour. Technol.*, 2026, **441**, 133656.
31 L. Jin, C. Li, A. M. Addou, Y. Huang and H. Li, Remediation of antibiotic pollution in the global environment by iron-based materials activating advanced oxidation processes: A systematic review, *J. Environ. Manage.*, 2025, **384**, 125519.
32 B. Wang, Y. Wang, J. Fang, Z. Feng, H. Hu, H. Zhong, S. Chen and J. Li, Exogenous C6-HSL enhanced the cometabolic removal of sulfadiazine by an enriched ammonia oxidizing bacteria culture, *Environ. Pollut.*, 2025, **364**, 125396.
33 N. Wang, L. Peng, Y. Gu, C. Liang, R. W. M. Pott and Y. Xu, Insights into biodegradation of antibiotics during the biofilm-based wastewater treatment processes, *J. Clean. Prod.*, 2023, **393**, 136321.
34 Y. Xu, X. Wang, Y. Gu, C. Liang, W. Guo, H. H. Ngo and L. Peng, Optimizing ciprofloxacin removal through regulations of trophic modes and FNA levels in a moving bed biofilm reactor performing sidestream partial nitritation, *Water Res.:X*, 2024, **22**, 100216.
35 Y. Xu, Y. Gu, L. Peng, N. Wang, S. Chen, C. Liang, Y. Liu and B. Ni, Unravelling ciprofloxacin removal in a nitrifying moving bed biofilm reactor: Biodegradation mechanisms and pathways, *Chemosphere*, 2023, **320**, 138099.
36 C. Zhang, Q. Zhang, S. Dong and D. Zhou, Could co-substrate sodium acetate simultaneously promote Chlorella to degrade amoxicillin and produce bioresources?, *J. Hazard. Mater.*, 2021, **417**, 126147.
37 A. D. S. Vidotti, D. M. Riaño-Pachón, L. Mattiello, L. A. Giraldi, F. V. Winck and T. T. Franco, Analysis of autotrophic, mixotrophic and heterotrophic phenotypes in the microalgae Chlorella vulgaris using time-resolved proteomics and transcriptomics approaches, *Algal Res.*, 2020, **51**, 102060.
38 X. Qi, L. Yang and J. Xiong, Cometabolism enhanced removal of enrofloxacin by Chlamydomonas Mexicana for sustainable water remediation with simultaneous production of fatty acids, *Chem. Eng. J.*, 2025, **525**, 169858.
39 S. Li, Y. Chu, N. Ren and S. H. Ho, Cytochrome P450 enzyme-based biotransformation of pharmaceuticals and personal care products (PPCPs) by microalgae in the aquatic environment, *Chem. Eng. J.*, 2023, **476**, 146557.
40 X. Qi, J. Xiong, C. Zhao and S. Ru, Unraveling the key driving factors involved in cometabolism enhanced aerobic degradation of tetracycline in wastewater, *Water Res.*, 2022, **226**, 119285.
41 Q. Cheng, J. Ma, Y. Yang, J. Ma, H. Grossart, L. Xu and H. Lin, Enrichment of vitamin B12-producing Porphyrobacter in the phycosphere microbiome promotes microalgal stress adaptation to antibiotic exposure, *Microbiome*, 2025, **13**, 240.
42 S. Li, G. Duan, Y. Xi, Y. Chu, F. Li and S. Ho, Insights into the role of extracellular polymeric substances (EPS) in the spread of antibiotic resistance genes, *Environ. Pollut.*, 2024, **343**, 123285.
43 W. Gong, L. Guo, C. Huang, B. Xie, M. Jiang, Y. Zhao, H. Zhang, Y. Wu and H. Liang, A systematic review of antibiotics and antibiotic resistance genes (ARGs) in mariculture wastewater: Antibiotics removal by microalgal-bacterial symbiotic system (MBSS), ARGs characterization on the metagenomic, *Sci. Total Environ.*, 2024, **930**, 172601.
44 D. M. Kennes-Veiga, L. González-Gil, M. Carballa and J. M. Lema, Enzymatic cometabolic biotransformation of organic micropollutants in wastewater treatment plants: A review, *Bioresour. Technol.*, 2022, **344**, 126291.
45 A. Bezsenyi, G. Sági, M. Makó, G. Palkó, T. Tóth, L. Wojnárovits and E. Takács, The effect of combined cometabolism and gamma irradiation treatment on the biodegradability of diclofenac and sulfamethoxazole, *Radiat. Phys. Chem.*, 2020, **170**, 108642.
46 I. Akrout, K. Staita, H. Zouari-Mechichi, B. Ghariani, M. Khmaissa, D. Navarro, A. Doan, Q. Albert, C. Faulds, G. Sciara, E. Record and T. Mechichi, Valorizing fungal diversity for the degradation of fluoroquinolones, *Heliyon*, 2024, **10**, e30611.
47 B. Ghariani, A. H. Alessa, I. Ben Atitallah, I. Louati, A. A. Alsaigh, T. Mechichi and H. Zouari-Mechichi, Fungal bioremediation of the β-lactam antibiotic ampicillin under laccase-induced conditions, *Antibiotics*, 2024, **13**, 407.
48 H. Tan, D. Kong, Q. Ma, Q. Li, Y. Zhou, X. Jiang, Z. Wang, R. E. Parales and Z. Ruan, Biodegradation of tetracycline antibiotics by the yeast strain Cutaneotrichosporon dermatis M503, *Microorganisms*, 2022, **10**, 565.
49 X. Dai, C. Su, R. Nong, X. Huang, Y. Xie, B. Liang, S. Gao and M. Chen, Performance, microbial community, and metabolism pathway in adsorption-biological coupling reactor treating sulfonamide antibiotics wastewater: Effect of influent frequency and aeration rate, *J. Water Process Eng.*, 2023, **53**, 103732.
50 C. Yang, C. Liu and B. Chang, Biodegradation of amoxicillin, tetracyclines and sulfonamides in wastewater sludge, *Water*, 2020, **12**, 2147.
51 I. Hamid and W. A. Khanday, Recent advances in antibiotic removal methods from wastewater: A comprehensive review, *Sep. Purif. Technol.*, 2026, **381**, 135478.
52 R. Gan, J. Chen, H. Luo and K. Zhang, Photocatalysis and CW-MFC coupling to enhance antibiotic wastewater treatment and biological mechanisms, *Chem. Eng. Res. Des.*, 2025, **224**, 408–419.

53 K. Shi, W. Xu, H. Cui, L. Zhang, J. He, W. Ben, C. Su, S. Gao, A. Wang and B. Liang, Regulating community redox metabolism for systematic mitigation of antibiotic chemical and biological risks, *Water Res.*, 2025, **285**, 124147.

54 Z. Tang, H. Liu, Y. Wang, Q. Wang, L. Zhang, F. An and Y. Chen, Impacts of cefalexin on nitrite accumulation, antibiotic degradation, and microbial community structure in nitrification systems, *J. Hazard. Mater.*, 2024, **478**, 135430.

55 K. He, C. Sun, S. Yang, H. Liu, H. Fu and X. Qu, Peroxidase-like activity of widely-used commercial inorganic pigments induces oxidative stress and antibiotic degradation: Implications for health risks, *Sci. Total Environ.*, 2025, **958**, 177979.

56 L. Ali, S. Karki, G. D. Boorgula, A. Mekakda, B. Cagle-White, S. Bhattarai, R. Beaudoin, A. Blakeney, S. Singh, S. Srivastava and M. H. Abdelaziz, A mechanistic understanding of the effect of Staphylococcus aureus VraS histidine kinase single point mutation on antibiotic resistance, *Microbiol. Spectr.*, 2025, **13**, 631495.

57 Y. Pang, Y. Zhai, Y. Fu, H. Lin and J. Wang, A review of antibiotic effects on wastewater denitrification: From process inhibition to microbial resistance mechanism, *Process Saf. Environ. Prot.*, 2025, **201**, 107590.

58 X. Li, Z. Lu, B. Wu, H. Xie and G. Liu, Antibiotics and antibiotic resistance genes removal in biological aerated filter, *Bioresour. Technol.*, 2024, **395**, 130392.

59 D. Xia, W. Dou, Y. Tian, L. Zhang, C. Wang, Y. Wang, J. Zhang, Y. Han, Y. Xiao, X. Mei and X. Yang, Efficient removal of nitrogen, phosphorus and antibiotics in freshwater aquaculture wastewater using a novel hybrid aeration biological filter, *J. Environ. Manage.*, 2025, **396**, 128079.

60 S. Xu, X. Chen, X. Wang, H. Sun, Z. Hou, J. Cheng and Y. Yuan, Artificial microbial consortium producing oxidases enhanced the biotransformation efficiencies of multi-antibiotics, *J. Hazard. Mater.*, 2022, **439**, 129674.

61 L. Yang, B. Qiao, Q. Xu, S. Liu, Y. Yuan and J. Cheng, Biodegradation of sulfonamide antibiotics through the heterologous expression of laccases from bacteria and investigation of their potential degradation pathways, *J. Hazard. Mater.*, 2021, **416**, 125815.

62 Q. Li, Y. Zheng, L. Guo, Y. Xiao, H. Li, P. Yang, L. Xia, X. Liu, Z. Chen, L. Li and H. Zhang, Microbial Degradation of Tetracycline Antibiotics: Mechanisms and Environmental Implications, *J. Agric. Food Chem.*, 2024, **72**, 13523–13536.

63 R. Zhuo and F. Fan, A comprehensive insight into the application of white rot fungi and their lignocellulolytic enzymes in the removal of organic pollutants, *Sci. Total Environ.*, 2021, **778**, 146132.

64 X. Jiang, H. Li, J. Kong, Y. Li, X. Xin, J. Zhou, R. Zhang, K. S. Lee, B. R. Jin and Z. Gui, Comprehensive analysis of biotransformation pathways and products of chloramphenicol by Raoultella Ornithinolytica CT3: Pathway elucidation and toxicity assessment, *J. Hazard. Mater.*, 2024, **480**, 136199.

65 Y. Xiang, S. Li, E. R. Rene, X. Lun, P. Zhang and W. Ma, Detoxification of fluoroglucocorticoid by Acinetobacter pittii C3 *via* a novel defluorination pathway with hydrolysis, oxidation and reduction: Performance, genomic characteristics, and mechanism, *J. Hazard. Mater.*, 2023, **452**, 131302.

66 C. Xu, Y. Li, J. Lu, X. Zhu, S. Li, N. Bai, J. Zhang, H. Zhang and W. Lv, Efficient biodegradation of enrofloxacin by Citrobacter sp. SAASenr-X1: Characteristics, performance, pathways, risk assessment, and practical applications, *Chem. Eng. J.*, 2025, **517**, 164355.

67 X. Qi, Z. Chen, X. He and J. Xiong, Unveiling the role of tropinone reductase I in biodegradation of oxytetracycline: Identifying antibiotic deactivation enzymes to enhance engineering feasibility of microalgae-based biotechnologies, *Chem. Eng. J.*, 2025, **519**, 165234.

68 J. Chen and S. Xie, Overview of sulfonamide biodegradation and the relevant pathways and microorganisms, *Sci. Total Environ.*, 2018, **640–641**, 1465–1477.

69 Y. Deng, Y. Mao, B. Li, C. Yang and T. Zhang, Aerobic degradation of sulfadiazine by Arthrobacter spp.: kinetics, pathways and genomic characterization, *Environ. Sci. Technol.*, 2016, **50**, 9566–9575.

70 P. Sharma, N. Pal, M. Kumawat, S. Singh, D. Das, A. Tilwari, A. Prakash, R. R. Tiwari and M. Kumar, Investigating the antibiotic resistance genes and mobile genetic elements in water systems impacted with anthropogenic pollutants, *Environ. Res.*, 2025, **269**, 120814.

71 J. Wang and S. Wang, Microbial degradation of sulfamethoxazole in the environment, *Appl. Microbiol. Biotechnol.*, 2018, **102**, 3573–3582.

72 M. Zou, W. Tian, J. Zhao, M. Chu and T. Song, Quinolone antibiotics in sewage treatment plants with activated sludge treatment processes: A review on source, concentration and removal, *Process Saf. Environ. Prot.*, 2022, **160**, 116–129.

73 T. Chen, Y. Li, C. Mo, P. Gao, X. Wu and X. Qu, Screening of sulfonamide and fluroquinolone antibiotics in wastewater of sewage treatment plants in Guangzhou, South China, *Environ. Sci. Technol.*, 2010, **33**, 144–147.

74 S. Aydin, M. E. Aydin, A. Ulvi and H. Kilic, Antibiotics in hospital effluents: occurrence, contribution to urban wastewater, removal in a wastewater treatment plant, and environmental risk assessment, *Environ. Sci. Pollut. Res.*, 2019, **26**, 544–558.

75 L. Tian, G. Li, L. Li, M. Yang, H. Li, Q. Li and Y. Mao, Environmentally relevant low metal concentrations drive co-selection of antibiotic and metal resistance genes in activated sludge, *Environ. Res.*, 2025, **287**, 123042.

76 X. Fan, Z. Zhang, N. Li and X. Li, Molecular ecological insights into the synergistic response mechanism of nitrogen transformation, electron flow and antibiotic resistance genes in aerobic activated sludge systems driven by sulfamethoxazole and/or trimethoprim stresses, *Water Res.*, 2025, **270**, 122853.

77 S. Manna, X. Zhou and N. Singhal, ROS-induced stress promotes enrichment and emergence of antibiotic

resistance in conventional activated sludge processes, *Water Res.*, 2025, **277**, 123366.
78 Y. Zhu, Y. Chen, H. Lu, K. Jin, Y. Lin, H. Ren and K. Xu, Simultaneous efficient removal of tetracycline and mitigation of antibiotic resistance genes enrichment by a modified activated sludge process with static magnetic field, *Water Res.*, 2024, **262**, 122107.
79 Y. Cai, Z. Yan, Y. Ou, B. Peng, L. Zhang, J. Shao, Y. Lin and J. Zhang, Effects of different carbon sources on the removal of ciprofloxacin and pollutants by activated sludge: Mechanism and biodegradation, *J. Environ. Sci.*, 2022, **111**, 240–248.
80 K. J. Murray, W. J. Parker, L. M. Bragg and M. R. Servos, Fate of selected pharmaceutically active compounds in the integrated fixed film activated sludge process, *Water Sci. Technol.*, 2017, **75**, 2680–2691.
81 H. Hou, L. Duan, B. Zhou, Y. Tian, J. Wei and F. Qian, The performance and degradation mechanism of sulfamethazine from wastewater using IFAS-MBR, *Chin. Chem. Lett.*, 2020, **31**, 543–546.
82 M. J. Shreve and R. A. Brennan, Trace organic contaminant removal in six full-scale integrated fixed-film activated sludge (IFAS) systems treating municipal wastewater, *Water Res.*, 2019, **151**, 318–331.
83 A. Mousaab, C. Claire, C. Magali and D. Christophe, Upgrading the performances of ultrafiltration membrane system coupled with activated sludge reactor by addition of biofilm supports for the treatment of hospital effluents, *Chem. Eng. J.*, 2015, **262**, 456–463.
84 J. Kim, I. Song, S. Lee, P. Kim, H. Oh, J. Park and Y. Choung, Decomposition of pharmaceuticals (sulfamethazine and sulfathiazole) using oxygen-based membrane biofilm reactor, *Desalination*, 2010, **250**, 751–756.
85 E. Aydın, M. Şahin, E. Taşkan, H. Hasar and M. Erdem, Chlortetracycline removal by using hydrogen based membrane biofilm reactor, *J. Hazard. Mater.*, 2016, **320**, 88–95.
86 J. Chen, Y.-S. Liu, J.-N. Zhang, Y.-Q. Yang, L.-X. Hu, Y.-Y. Yang, J.-L. Zhao, F.-R. Chen and G.-G. Ying, Removal of antibiotics from piggery wastewater by biological aerated filter system: treatment efficiency and biodegradation kinetics, *Bioresour. Technol.*, 2017, **238**, 70–77.
87 V. Arya, L. Philip and S. Murty Bhallamudi, Performance of suspended and attached growth bioreactors for the removal of cationic and anionic pharmaceuticals, *Chem. Eng. J.*, 2016, **284**, 1295–1307.
88 Y. Song, Z. Zhang, Y. Liu, F. Peng and Y. Fen, Enhancement of anaerobic treatment of antibiotic pharmaceutical wastewater through the development of iron-based and carbon-based materials: A critical review, *J. Hazard. Mater.*, 2024, **479**, 135514.
89 X. Su, F. Sun, J. Zhang, D. Xing, X. Li, Z. Song, L. Feng, Z. Huang and A. Li, Characterization and shifting of microbial community to denitrification for anaerobic sulfamethoxazole biodegradation with different electron acceptors, *J. Clean. Prod.*, 2023, **387**, 135870.
90 H. Vistanty, B. Budiyono, M. A. Budihardjo, R. A. Malik, A. Mukimin and N. I. Setianingsih, Enhanced antibiotic removal by anaerobic co-digestion in an Expanded Granular Sludge Bed (EGSB) reactor treating real pharmaceutical wastewater: From lab-scale to pilot-plant application, *Bioresour. Technol. Rep.*, 2025, **31**, 102286.
91 D. Cheng, H. H. Ngo, W. Guo, S. W. Chang, D. D. Nguyen, Q. A. Nguyen, J. Zhang and S. Liang, Improving sulfonamide antibiotics removal from swine wastewater by supplying a new pomelo peel derived biochar in an anaerobic membrane bioreactor, *Bioresour. Technol.*, 2021, **319**, 124160.
92 Y. Sun, Q. Guo, F. Sun, W. Rao, J. Zhang, L. Song and S. Liang, Anaerobic dynamic membrane bioreactor treating swine wastewater: Fate of sulfonamide antibiotics and heavy metals with their effect on filtration performance, *J. Hazard. Mater.*, 2025, **489**, 137718.
93 J. Liang, Y. Zhang, J. Zhang, Z. Xie, H. Chen, K. Koch, A. Hu and L. Luo, Biodegradation of sulfadiazine in anaerobic co-digestion of swine manure and food waste, *Bioresour. Technol.*, 2025, **429**, 132518.
94 H. Ma, Y. Zhao, K. Yang, Y. Wang, C. Zhang and M. Ji, Application oriented bioaugmentation processes: mechanism, performance improvement and scale-up, *Bioresour. Technol.*, 2022, **344**, 126192.
95 D. Liang, Y. Hu, R. Huang, J. Cheng and Y. Chen, Effects of various antibiotics on aerobic nitrogen removal and antibiotic degradation performance: mechanism, degradation pathways, and microbial community evolution, *J. Hazard. Mater.*, 2022, **422**, 126818.
96 B. Lin, J. Lyu, X. Lyu, H. Yu, Z. Hu, J. C. W. Lam and P. K. S. Lam, Characterization of cefalexin degradation capabilities of two Pseudomonas strains isolated from activated sludge, *J. Hazard. Mater.*, 2015, **282**, 158–164.
97 X. Shan, Z. Shan, H. Guo and F. Ma, Biodegradation of cephalexin in wastewater by Glutamicibacter sp. S2 and Herbaspirillum sp. S8: Performance, pathway, genomes and synergistic bio-augmentation, *Chem. Eng. J.*, 2025, **507**, 160783.
98 M. Deng, F. Yu, J. Wang, J. Yu and W. Jin, Bio-augmentation effect of Achromobacter sp. strain JWJ-09 on quinoline and real coking wastewater under methanol co-metabolism, *J. Water Process Eng.*, 2023, **53**, 103611.
99 J. Tian, C. Chen, G. Lartey-Young and L. Ma, Biodegradation of cefalexin by two bacteria strains from sewage sludge, *R. Soc. Open Sci.*, 2023, **10**, 220442.
100 Q. Zhang, Y. Bai, J. Wu, L. Xu, W. Zhu, G. Tian, P. Zheng, X. Xu and R. Jin, Microbial community evolution and fate of antibiotic resistance genes in anammox process under oxytetracycline and sulfamethoxazole stresses, *Bioresour. Technol.*, 2019, **293**, 122096.
101 M. Zhao, S. Jiang, D. Wu, H. Xue, W. Zhang, X. Wu, Q. Yu, Y. He and J. Geng, Microbial remediation as a key pathway for pollutant removal in constructed wetlands: Mechanisms, bioaugmentation strategies, and perspectives, *Bioresour. Technol.*, 2026, **441**, 133570.

102 F. Eghbalpoor, M. Gorji, M. Zamani Alavigeh and M. Taati Moghadam, Genetically engineered phages and engineered phage-derived enzymes to destroy biofilms of antibiotics resistance bacteria, *Heliyon*, 2024, **10**, e35666.

103 J. Wang, X. Chen, H. Sun, X. Li, Q. Lu, P. Qin, Y. Yang, D. Lai, L. Luo, X. Peng, Y. Yang and Z. Wu, Accelerated removal and mechanism of tetracycline from water using immobilized bacteria combined with microalgae, *J. Environ. Chem. Eng.*, 2025, **13**, 115424.

104 H. Chen, L. Tang, Z. Hua, M. Wu, Z. Jia and J. Fu, Synergistic bioaugmentation of microbial-graphene hydrogel for enhanced antibiotic degradation: Insights into material-microbe interactions, *J. Environ. Chem. Eng.*, 2025, **13**, 119680.

105 J. Zhou, Y. Liu, S. Liu, L. Zhao, S. Zhao, F. Huang and J. Qu, Biotransformation of chloramphenicol by free and biochar-immobilized Raoultella ornithinolytica CC12: Performance, immobilization feasibility, and mechanistic insights, *Chem. Eng. J.*, 2025, **523**, 168795.

106 Y. Li, L. Feng, G. Li, J. Wang and K. Li, Removing high strength lincomycin in pharmaceutical wastewater by a bacteria microalgae consortium co-immobilized filter, *Bioresour. Technol.*, 2025, **415**, 131704.

107 Y. Zhou, X. Li, J. Chen and F. Wang, Treatment of antibiotic-containing wastewater with self-suspended algae-bacteria symbiotic particles: removal performance and reciprocal mechanism, *Chemosphere*, 2023, **323**, 138240.

108 C. Hou, Q. Wang, Q. Liu, Z. Li, C. Ke, X. Wang and K. Huang, Review: Development and application of porous materials to antibiotic drug adsorption and removal, *J. Water Process Eng.*, 2025, **69**, 106583.

109 Z. Yang, X. Wan, Y. Chen, X. Chen, Z. Wang, C. Zhang, V. Kumar, C. Varrone, X. Xiao, P. Yu and W. Huang, A review of lignin-based adsorbent materials: Synthesis and applications in the remediation of heavy metal/antibiotic-containing wastewater, *J. Environ. Chem. Eng.*, 2025, **13**, 119080.

110 R. Singh, C. Lim, H. Kim, S. Kang and K. Kim, Sustainable material platforms for multi-log removal of antibiotic-resistant bacteria and genes from wastewater: A review, *Int. J. Biol. Macromol.*, 2025, **321**, 146561.

111 C. Ding, J. Liu, J. Wang, J. Le, B. Lu, N. Qu, S. Zhao, H. Zhang, J. Su, Y. Li and Q. Liu, Modified biochar effectively removes tetracycline and antibiotic resistance genes to enhance anaerobic digestion performance, *J. Environ. Chem. Eng.*, 2025, **13**, 120076.

112 C. Fu, G. Sun, C. Wang, B. Wei, G. Ran and Q. Song, Fabrication of nitrogen-doped graphene nanosheets anchored with carbon nanotubes for the degradation of tetracycline in saline water, *Environ. Res.*, 2021, **206**, 112242.

113 P. Wang, Y. Zheng, P. Lin, J. Li, H. Dong, H. Yu, L. Qi and L. Ren, Effects of graphite, graphene, and graphene oxide on the anaerobic co-digestion of sewage sludge and food waste: Attention to methane production and the fate of antibiotic resistance genes, *Bioresour. Technol.*, 2021, **339**, 125585.

114 A. Ameen, Y. Zheng, Q. Wang, Y. Li, S. U. Saleem, M. A. Saleem, W. Niaz, H. A. Anjum and F. Li, Sustainable hybrid constructed wetland-biological trickling filter system for simultaneous removal of antibiotics and heavy metals: Performance, mechanisms, and microbial insights, *J. Water Process Eng.*, 2025, **79**, 108979.

115 N. Aryal, T. Kvist, F. Ammam, D. Pant and L. D. M. Ottosen, An overview of microbial biogas enrichment, *Bioresour. Technol.*, 2018, **264**, 359–369.

116 Y. Sun, H. Luo, R. Iboleon and Z. Wang, Fate of antibiotic resistance genes and class 1 integrons during sludge treatment using pilot-scale anaerobic digestion with thermal hydrolysis pretreatment, *Bioresour. Technol.*, 2022, **364**, 128043.

117 M. Pu, N. Ailijiang, A. Mamat, J. Chang, Q. Zhang, Y. Liu and N. Li, Occurrence of antibiotics in the different biological treatment processes, reclaimed wastewater treatment plants and effluent-irrigated soils, *J. Environ. Chem. Eng.*, 2022, **10**, 107715.

118 A. Ameen, Y. Zheng, Q. Wang, Y. Li, S. F. Javaid, M. Salah and F. Li, Integrating constructed wetlands with maize cobs biological trickling filter for antibiotic removal: An innovative waste-to-treatment approach, *J. Environ. Manage.*, 2025, **391**, 126382.

119 G. Wang, A. C. Hambly, Y. Dou, G. Wang, K. Tang and H. R. Andersen, Polishing micropollutants in municipal wastewater, using biogenic manganese oxides in a moving bed biofilm reactor (BioMn-MBBR), *J. Hazard. Mater.*, 2022, **427**, 127889.

120 X. Xu, Y. Cao, S. Zhi, K. Phyu, H. Wang, J. Liu, C. M. Cordeiro, E. Sindhøj, K. Zhang and R. Zhao, Current perspectives on microalgae and extracellular polymers for reducing antibiotic resistance genes in livestock wastewater, *Bioresour. Technol.*, 2025, **431**, 132622.

121 X. Zhang, X. Hou, X. Jiang, D. Chen, S. Ge, L. Wang and J. Shen, Development of a microalgal (Chlorella)-bacterial (Paracoccus) symbiotic system for pyridine biodegradation under photosynthetic oxygenation, *ACS ES&T Water*, 2021, **1**, 356–365.

122 Q. Zhong and J. Xiong, A globally distributed cyanobacterial nitroreductase capable of conferring biodegradation of chloramphenicol, *Research*, 2025, **8**, 0692.

123 C. Kiki, A. Rashid, Y. Wang, Y. Li, Q. Zeng, C. P. Yu and Q. Sun, Dissipation of antibiotics by microalgae: kinetics, identification of transformation products and pathways, *J. Hazard. Mater.*, 2022, **387**, 121985.

124 Y. Wang, P. Chen, X. Yu and J. Zhang, Algae-bacteria symbiotic constructed wetlands for antibiotic wastewater purification and biological response, *Front. Microbiol.*, 2022, **13**, 1044009.

125 J. Zhang, S. Li, H. Lu, L. Zhu and F. Wu, Lighting strategy drives removal of ammonia nitrogen and phosphate in microalgae-bacteria consortia under tetracycline hydrochloride exposure, *Algal Res.*, 2025, **88**, 103989.

126 Z. He, G. Fan, Z. Xu, S. Wu, J. Xie, W. Qiang and K.-Q. Xu, A comprehensive review of antibiotics stress on anammox systems: Mechanisms, applications, and challenges, *Bioresour. Technol.*, 2025, **418**, 131950.

127 Y. Zhu, Y. Zhao, J. Liu, Y. Chen, M. Gao, L. Guo and P. Mupindu, Rapid conversion of heterotrophic denitrification to autotrophic denitrification in mariculture wastewater treatment: denitrification performance and microbial communities under antibiotic stress, *J. Water Process Eng.*, 2024, **62**, 105391.

128 Z. Li, R. Cheng, F. Chen, X. Lin, X. Yao, B. Liang, C. Huang, K. Sun and A. J. Wang, Selective stress of antibiotics on microbial denitrification: inhibitory effects, dynamics of microbial community structure and function, *J. Hazard. Mater.*, 2021, **405**, 124366.

129 Y. Hu, N. Gai, Z. Yuan, B. Zhou, R. Hou, R. Yuan and H. Chen, Ecological effects of antibiotics on aquatic microbial communities: Structure-function response dynamics and multifactorial drivers, *Chem. Eng. J.*, 2025, **525**, 169822.

130 N. Fan, Y. Bai, Q. Chen, Y. Shen, B. Huang and R. Jin, Deciphering the toxic effects of antibiotics on denitrification: process performance, microbial community and antibiotic resistance genes, *J. Environ. Manage.*, 2020, **262**, 110375.

131 T. Li, Y. Li, M. Li, N. Wang, Z. Sun, X. Li and B. Li, Effects of sulfamethoxazole on nitrogen transformation and antibiotic resistance genes in short-cut nitrification and denitrification process treating mariculture wastewater, *Chem. Eng. J.*, 2023, **454**, 140517.

132 Y. Xiao, Y. Qin, X. Jiang and P. Gao, Effects of polypropylene microplastics on digestion performance, microbial community, and antibiotic resistance during microbial anaerobic digestion, *Bioresour. Technol.*, 2024, **411**, 131358.

133 Q. Niu, K. Li, H. Yang, P. Zhu, Y. Huang, Y. Wang, X. Li and Q. Li, Exploring the effects of heavy metal passivation under Fenton-like reaction on the removal of antibiotic resistance genes during composting, *Bioresour. Technol.*, 2022, **359**, 127476.

134 Z. Wang, B. Yang, J. Cao, D. Wang, X. Zhang and M. Li, Molecular insights into anammox inhibition induced by environmentally relevant sulfamonomethoxine and functional recovery *via* voltage stimulation, *Bioresour. Technol.*, 2025, **436**, 133018.

135 H. Xu, Y. Yang, T. Xia, Y. Feng, X. Liu, N. J. D. Graham, K.-H. Choo, S. Takizawa, H. Y. Ng and L. A. Hou, Overlooked interference of antibiotics on quorum sensing inhibitors for membrane biofouling mitigation by affecting AHLs and PQS pathway, *Sep. Purif. Technol.*, 2025, **363**, 132116.

136 L. Tang, J. Li, Z. Yu, J. Meng and J. Li, Improving antibiotic resistance removal from piggery wastewater by involving zero-valent iron within an integrated anoxic-aerobic biofilm reactor, *Chem. Eng. J.*, 2024, **493**, 152688.

137 J. Chen, Y. Tang, X. Chen, J. Chen, Z. Yan, X. Yao, H. Zhang, Y. Pei and Z. Jiang, Enhanced methanogenesis and efficient ciprofloxacin degradation *via* nZVI@LDH in an electricity-driven anaerobic bioreactor: A biotic-abiotic hybrid system for ROS regulation and ARGs mitigation, *J. Hazard. Mater.*, 2025, **488**, 137348.

138 J. Wang, Y. Hu, L. An, J. Wang, F. Wu, J. Gu, X. Wang and J. M. Tiedje, An efficient strategy for BDD electrode drive electro-catalysis triggering active species on lincomycin and antibiotic resistance genes removal: Electron transfer based on calculation modeling, *J. Hazard. Mater.*, 2025, **491**, 137915.

139 Y. Liu, X. Song, X. Hou, Y. Wang and X. Cao, Effect of Mn-HA on ARGs and MRGs in nitrogen-culturing sludge, *J. Environ. Manage.*, 2024, **365**, 121615.

140 A. R. Nava, L. Daneshian and H. Sarma, Antibiotic resistant genes in the environment-exploring surveillance methods and sustainable remediation strategies of antibiotics and ARGs, *Environ. Res.*, 2022, **215**, 114212.

141 D. Cheng, H. H. Ngo, W. Guo, S. W. Chang, D. D. Nguyen, J. Li, Q. V. Ly and T. A. H. Nguyen, Applying a new pomelo peel derived biochar in microbial fell cell for enhancing sulfonamide antibiotics removal in swine wastewater, *Bioresour. Technol.*, 2020, **318**, 123886.

142 V. A. Burboa-Charis and L. H. Alvarez, Methane production from antibiotic bearing swine wastewater using carbon-based materials as electrons conduits during anaerobic digestion, *Int. J. Energy Res.*, 2020, **44**, 10996–11005.

143 H. Ren, M. Qin, L. Zhang, Z. Li, Y. Li, Q. He, D. Zhao, X. Lian, H. Jiang, X. Liao and J. Sun, Modular engineering of a synthetic biology-based platform for sustainable bioremediation of residual antibiotics in aquatic environments, *Engineering*, 2025, **53**, 231–244.

144 S. Ghasemi and F. Nabizadeh Chianeh, Synthesis of iron and cobalt oxide nanocatalysts with various molar ratios and their application for antibiotic removal from aqueous solutions, *J. Cluster Sci.*, 2025, **36**, 21.

145 C. Miranda, S. I. A. Pereira, A. S. S. Sousa, P. Wilfert, M. van Loosdrecht, A. Martins, P. M. L. Castro and C. L Amorim, Valorization of wastewater-derived biopolymers for use as soil amendments in agriculture, *Environ. Sci. Pollut. Res.*, 2025, **32**, 25944–25958.

146 W. Mo, C. Jian, A. Deng, J. Xu, L. Liu, Y. Bai and S. Li, Sustainable biosynthesis of exopolysaccharides derived from agricultural byproducts with effective antioxidant properties, *Bioproc. Biosyst. Eng.*, 2026, **49**, 559–569.

147 G. Sharma, N. Babbar, A. Sharma, H. Setia and R. Bhatia, Extremophilic exopolysaccharides: diversity, biosynthesis, and industrial applications, *Environ. Technol. Rev.*, 2026, **15**, 1–10.

148 C. Bu, S. Wang, B. Yu, F. Pfaender, T. Zhu, Y. Li and J. Liu, Intelligent FA/FNA alternating strategy for nitrite-oxidizing bacteria inhibition: Data-driven prediction and process control, *J. Environ. Manage.*, 2025, **386**, 125688.

149 Z. Li, Y. Wu, T. Chen, B. Yan and C. Wei, Deciphering organic substrate impacts in Anammox systems: a machine learning driven framework for predictive classification and process mechanism analysis, *Environ. Int.*, 2025, **202**, 109637.

150 S. Ismail, M. Elsamadony, M. Fujii and A. Tawfik, Evaluation and optimization of anammox baffled reactor (AnBR) by artificial neural network modeling and economic analysis, *Bioresour. Technol.*, 2019, **271**, 500–506.
151 A. Almuntashiri, J. Jiang, A. Hosseinzadeh, U. Badeti, A. H. Navidpour, P. Dorji, N. Ghaffour, H. K. Shon and S. Phuntsho, Removal of antibiotics from a biologically nitrified human urine using granular activated carbon adsorption for a safe nutrient recovery in a circular economy, *Process Saf. Environ. Prot.*, 2025, **201**, 107516.