Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Risks, characteristics, and control strategies of disinfection-residual-bacteria (DRB) from the perspective of microbial community structure

Hao-Bin Wang, Yin-Hu Wu, Li-Wei Luo, Tong Yu, Ao Xu, Song Xue, Gen-Qiang Chen, Xin-Ye Ni, Lu Peng, Zhuo Chen, Yun-Hong Wang, Xin Tong, Yuan Bai, Yu-Qing Xu, Hong-Ying Hu

ABSTRACT

The epidemic of COVID-19 has aroused people’s particular attention to biosafety. A growing number of disinfection products have been consumed during this period. However, the flaw of disinfection has not received enough attention, especially in water treatment processes. While cutting down the quantity of microorganisms, disinfection processes exert a considerable selection effect on bacteria and thus reshape the microbial community structure to a great extent, causing the problem of disinfection-residual-bacteria (DRB). These systematic and profound changes could lead to the shift in regrowth potential, biofouling potential, as well as antibiotic resistance level and might cause a series of potential risks. In this review, we collected and summarized the data from the literature in recent 10 years about the microbial community structure shifting of natural water or wastewater in full-scale treatment plants caused by disinfection. Based on these data, typical DRB with the most reporting frequency after disinfection by chlorine-containing disinfectants, ozone disinfection, and ultraviolet disinfection were identified and summarized, which were the bacteria with a relative abundance of over 5% in the residual bacteria community and the bacteria with an increasing rate of relative abundance over 100% after disinfection. Furthermore, the phylogenetic relationship and potential risks of these typical DRB were also analyzed. Twelve out of fifteen typical DRB genera contain pathogenic strains, and many were reported of great secretion ability. Pseudomonas and Acinetobacter possess multiple disinfection resistance and could be considered as model bacteria in future studies of disinfection. We also discussed the growth, secretion, and antibiotic resistance characteristics of DRB, as well as possible control strategies. The DRB phenomenon is not limited to water treatment but also exists in the air and solid disinfection processes, which need more attention and more profound research, especially in the period of COVID-19.

1. Introduction

Biosafety is of vital importance in water treatment, storage, distribution, and usage (Ruiz et al., 2000; Sedlak and von Gunten, 2011). Therefore, disinfection units are essential in all kinds of water treatment facilities (Rutala and Weber, 2016; Shannon et al., 2008). Due to the wide applicability and technological economy, chlorine-containing disinfectants (mainly including free chlorine, chloramine, and chlorine dioxide), ultraviolet (UV) disinfection, and ozone disinfection became the three most commonly-used disinfection technologies (Sedlak and von Gunten, 2011). The COVID epidemic, beginning in 2019, has increased people’s concern for microbial risks. As a consequence, more...
demand of disinfectants was generated (Bogler et al., 2020), and some authorities began to apply higher dosages of disinfectants in wastewater treatment processes (Lu and Guo, 2021; Peng et al., 2021; Wang et al., 2020a). Nevertheless, scarcely any of the disinfection methods could inactivate all microorganisms in water in full-scale applications (Proctor and Hammes, 2015). Disinfection possesses a significant selection effect on different kinds of bacteria in water (Lopez et al., 2019; Luo et al., 2021), and the residual part usually contains undesirable bacteria, which could cause various hazards under diverse scenarios (Garner et al., 2018; Yu et al., 2018). Hence, the residual part of microorganisms remaining the capacity of growth or virulence after disinfection, which could be defined as the disinfection-residual-bacteria (DRB), deserves special attention in water disinfection processes. It is not only the total amount of DRB that needs to be considered, but also the composition and characteristics of them.

Most of commonly-used microbial assessment methods in water treatment are based on plate culture. These methods can only reveal the level of bacterial quantity, rather than microbial community structure, which is vital for comprehensive evaluation of microbial risk of the water (Szewzyk et al., 2000). In addition, only a small fraction of microorganisms in the water are culturable (Van Nevel et al., 2017; Ward et al., 1990). Therefore, it is hard to acquire a comprehensive understanding of microbial risk levels via heterotrophic plate counts (HPC).

Up to now, there have been many studies on the resistance of pure strains towards disinfection (Luo et al., 2021). However, research aimed at relative resistance of bacteria in water from full-scale treatment plants is more meaningful for microbial risk control. Since the beginning of the 21st century, high-throughput sequencing, or next-generation sequencing (NGS) has been continuously developed and applied to the analysis of water samples (Hirai et al., 2017; Tan et al., 2015). A number of studies have found that the disinfection processes, such as chlorine and chloramine disinfection (Bellila et al., 2016; Chiao et al., 2014; Jia et al., 2015), UV disinfection (Li et al., 2020; Liu et al., 2019b; Pullerits et al., 2020), and ozone disinfection (Alexander et al., 2016; Chen et al., 2019; Li et al., 2020), have a significant effect on the microbial community structure. However, there has not been a systematic and logical evaluation of DRB.

The present study aimed at establishing a systematic analysis of DRB, and proposing criteria for identification of DRB from the perspective of microbial community structure. Herein, we recognized typical DRB at phyla and genera levels, and analyzed the growth, secretion, and antibiotic resistance characteristics of DRB. Several promising approaches for DRB control were also discussed. In general, this study provided a novel perspective towards aquatic microbial risk analysis and control.

2. Risks of DRB

DRB refers to the residual part of microorganisms which remain their growing ability or virulence after disinfection. DRB could bring about a series of potential risks, which could not be evaluated by the amount of bacteria in water, and in some cases, are even greater than that of undisinfected microbiome (Flemming, 2020; Wang et al., 2019b). The risks of DRB could be divided into three categories, which are health, ecological, and process risks (Fig. 1).

2.1. Health risks

One of the primary aims of disinfection is to reduce pathogens and opportunistic pathogens. Nevertheless, it has been reported that pathogens and opportunistic pathogens could regrow, and their relative abundance might be higher among DRB in drinking water and treated wastewater, posing threats to human and animal health (Gui et al., 2020; Pang et al., 2016).

Furthermore, it is possible for DRB in water to be spread to other phases and trigger additional hazards during water distribution and usage. DRB colonized in water distribution systems could form a biofilm, which is a shelter providing durable high-level tolerance against disinfectants for pathogens and other unfavorable bacteria (Flemming, 2020; Garner et al., 2018; Zhu et al., 2014). DRB within irrigation water could migrate onto the surface of crops, posing a threat to food safety (Gu et al., 2020; Truchado et al., 2018).

2.2. Process risks

Process risk means harm to facilities caused by DRB in water treatment, distribution, storage, and usage. In many scenarios, though, the disinfection units reduce the amount of microorganism and improve the quality of the effluent, DRB also sometimes bring more risks to water treatment facilities, especially when the growth and metabolic characteristics of DRB rather than their quantity play a more important role. In particular, most process risks are associated with biofilm formation and growth.

One of the significant process risks of DRB is the fouling of the...
separation membranes in water purification processes. Membrane fouling is usually caused by polysaccharides and proteins in extracellular polymeric substances (EPS) of bacteria rather than bacteria themselves (Khan et al., 2015; Wang et al., 2019b). Commonly-used separation membranes in water treatment include microfiltration, ultrafiltration, nanofiltration, and reverse osmosis (RO). RO is an essential process in seawater desalination and high-quality reclaimed water production (Bai et al., 2001). Unlike micro- and ultra-filtration membranes, the current market-dominating polyamide thin-film composite RO membrane has poor tolerance of oxidant (Yao et al., 2020). Therefore, it is hard to apply disinfectants on the membrane surface directly, increasing the difficulty of controlling the growth and EPS secretion of DRB. Membrane fouling is a serious expense for water treatment plants, especially high-quality water reclamation plants. It was estimated that the costs of membrane fouling accounted for 30% of the operating costs at Water Factory 21, which is one of the most famous water reclamation projects (Flemming, 2011).

Pipe corrosion in water distribution systems is another typical and costly risk of DRB. Iron and steel pipes are the most frequently-used materials in water distribution systems (Mohebbi and Li, 2011). Though most of the water was disinfected before distribution, corrosion of the pipe network was still unavoidable. Pipe corrosion is more related to the microbial community structure and function of the microbiome than the number of organisms (Zhang et al., 2018a). The abundances of four kinds of bacteria related to sulfur and iron biotransformation play the main roles, which are iron-oxidizing bacteria, iron-reducing bacteria, sulfate-reducing bacteria, and sulfur-oxidizing bacteria (Wang et al., 2012). The corrosion of pipes results in tremendous costs. For instance, in China, the cost of pipe corrosion was estimated to be 10 billion RMB in 2014 (Hou et al., 2017).

Except for membrane fouling and pipe corrosion, biofouling also cause significant hazards and cost in many other industries. Tough thousands of tons of disinfectants are applied every day in power plants around the world, cost of biofouling still accounts for about 20% of overall fouling costs in heat exchangers (Cloete, 2003; Murthy and Venkatesan, 2009). Azis et al. (2001) estimated that cost caused by biofouling in seawater desalination systems was about 15 billion dollars per year over world.

2.3. Ecological risks

The ecological risks of DRB consist of two aspects: dominant species shifting and abundance variation of functional genes. Since disinfection exerts a selection effect on the microbiome, dominant species of DRB are frequently different from that before disinfection, leading to a prominent shift of metabolism, adaptability and resistance of microbiome (Cui et al., 2020; Pang et al., 2016).

Similar problems also took place in terms of the abundance of functional genes. Higher antibiotic resistance level of DRB is a crucial ecological risk causing by disinfection processes (Chen et al., 2020c). There has been plenty of evidence of abundance increasing of antibiotic resistance genes after disinfection (Alexander et al., 2016; Guo et al., 2013; Meckes, 1982). Furthermore, ubiquitous horizontal transfer of antibiotic resistance genes might aggravate this risk (Khan et al., 2016).

3. Research methods and recognition criteria of typical DRB

The risks of DRB are mainly derived from the characteristics shift of microbiome causing by the selection effect of disinfection. These changes mainly include microbial community shifting, growth characteristics shifting, secretion characteristics shifting, and antibiotic resistance characteristics shifting (Fig. 2). The shift of microbial community structure is the most critical aspect, as all of other changes have inevitable relation with the microbial community structure changes (Wang et al., 2019c; Chen et al., 2020b). Therefore, a deep insight into microbial community shift is foremost. Typical DRB at phyla (classes) and genera levels were recognized from the literature in this review.

3.1. Research methods of microbial community shifting

Up to now, NGS is the most effective method for comprehensive analysis of microbial communities (Tan et al., 2015). The processing methods and sequencing platforms applied by previous researchers are listed in Table S1. Illumina and Roche 454 are the two most widely-used platforms. 454 pyrosequencing is better for investigating microbial communities, while Illumina high-throughput sequencing is more suitable for metagenomic analysis (Hirai et al., 2017; Huang et al., 2014).

As the concentration of bacteria in water samples, especially DRB, is relatively low, bacteria must be effectively enriched prior to DNA extraction and sequencing. Membrane filtration enrichment has been widely adopted by researchers due to its feasibility and little effect on microbial community structure. Typically, 1–10 L water sample was filtered through 0.2/0.22 μm membrane filters. Then the filters were preserved at –80°C until DNA extraction and amplification. The volume of the water sample could be roughly determined according to HPC (Wang et al., 2013). We recommend to process the liquid samples as fast as possible once sampling is done in order to maintain the original microbial community structure, and the filters should be frozen immediately after the filtration process. Regrettably, only a few researchers indicated the time consume from sampling to processing in their research articles.

Data quality control is of great significance in the testing and analysis of environmental samples (Ju and Zhang, 2015). A larger sample number brings about larger statistical significance and stronger persuasion. To ensure the reliability of the data, at least three biological replicates are essential. Furthermore, we suggest that the number of replicates in the experimental group and the control group remain similar to make a better comparison.

3.2. Recognition criteria of DRB

DRB does not refer to several specific strains, it is a summary of a series of phenomena. Nevertheless, it is of great significance to summarize the regularity of these phenomena and identify typical DRB for future research. We recognized typical DRB from two perspectives, the bacteria becoming dominant in the microbial community after disinfection, and the bacteria with a drastically increasing of relative abundance after disinfection. The results of high-throughput sequencing are
mainly presented at the phyla level and genera level. The thresholds of dominant phylum in previous studies are quite different, from 0.01% to more than 10% (Liu et al., 2021; Qiao et al., 2021; Shahi et al., 2016; Yan et al., 2021; Zha et al., 2021). Among these thresholds, 5% is a typical one for microbial community structure of water and wastewater (Wu et al., 2019; Zhang et al., 2019). Proteobacteria was usually separated into α-β-, γ-, δ-, and other Proteobacteria, as it is a rather rich phylum (Becerra-Castro et al., 2016; Ling et al., 2018; Wang et al., 2017, 2014). Considering that there are about 20–30 phyla (or classes belonging to Proteobacteria) commonly found in water (Li et al., 2017a), the average relative abundance of each phylum is about 3–5%. Thus, a low threshold is not applicable for distinguishing dominant phyla. On the other hand, if the threshold is too high, only a few of most dominant phylum (classes), such as Firmicutes, β- and γ-Proteobacteria could be recognized (Bal Krishna et al., 2020; Chen et al., 2020a). Therefore, we used the threshold of 5% of relative abundance to identify dominant phyla. As for genera level, the threshold of dominant genera was set at 1% (Alexander et al., 2016; Campbell et al., 2011; Numberger et al., 2019; Yuan et al., 2020; Zhang et al., 2018b; Zhao et al., 2020).

The bacteria whose relative abundance significantly increased after disinfection were also considered as DRB. Though the microbial community structure of influents and seasonal fluctuations have effects on the microbial community structure of the effluents, disinfection processes stronger impact on it (Ma et al., 2020; Potgieter et al., 2018). In addition, the microbial communities of influents of different water plants vary greatly, while the disinfection processes are relatively similar. Hence, it is necessary to conduct an investigation on the relative abundance changes of bacteria during disinfection to find out several typical DRB. In our study, the threshold for typical DRB was set as "relative abundance increases over 100% after disinfection and reported by more than two research articles". For most commonly-used chlorine-containing disinfectants, the threshold of the number of reports is increased to three, as research articles about disinfection using chlorine-containing disinfectants are much more than that on UV and ozone disinfection.

4. Microbial community characteristics of DRB

4.1. DRB at phyla level

According to the aforementioned identification criteria, dominant phyla before and after disinfection reported previously are listed in Table S2, and the occurrence frequency of dominant phyla in DRB were summarized in Fig. 3a. α-, β-, and γ-Proteobacteria frequently presented as dominant classes in DRB under all three commonly-used disinfection processes (chlorine-containing disinfectants, UV, and ozone).
disinfection). This might be attributed to wide metabolic versatility and adaption of the adverse environment of Proteobacteria (Becerra-Castro et al., 2016). α-Proteobacteria, having a wide range of general stress responses (Francez-Charlot et al., 2015), occurred most frequently in DRB of disinfection by chlorine-containing disinfectants.

The changes of relative abundance of the top 10 most common phyla are shown in Fig. 3b-d. Firmicutes was not the most frequent dominant phylum, but performed a clear regularity of higher relative abundance in DRB. Spore production is an ineluctable reason for Firmicutes to survive from disinfection. The proportion of γ-Proteobacteria increased in all three kinds of disinfection processes, especially in ozonation. A comparative study showed that no matter how the water quality fluctuated, the relative abundance of γ-Proteobacteria was consistently higher in DRB (Becerra-Castro et al., 2016). A number of well-known fecal-oral pathogens are from γ-Proteobacteria, including Legionella, Acinetobacter, Salmonella, and so on (Blaschke et al., 2021; Santos 2014; Yunana et al., 2021). Combined with the results of analysis of the dominant phyla, γ-Proteobacteria deserves distinctive attention in terms of the harmful microorganisms after disinfection. Verrucomicrobia displayed a long box in Fig. 3c, which is similar for Chloroflexi in ozone. That means these phyla showed an extensive variability in microbial community structure of DRB, implying that bacteria in these phyla from different water samples might possess greatly difference of resistance toward disinfection. Hence, analysis at lower level, such as genera level, is necessary.

Types of water samples were listed in Table S2. We divided all data into three categories: drinking water, wastewater (including secondary effluent and reclaimed water), and other (including seawater, cooling water, irrigation water, and domestic hot water) to perform a sub-analysis of water source effect. The results of sub-analysis basically met those regardless of water sources. In wastewater, α-, β-, and γ-Proteobacteria were more likely to become dominant phylum among DRB. The relative abundance increasement of γ-Proteobacteria and Firmicutes were more obvious in drinking water than other types of water source.

4.2. DRB at genera level

Dominant genera (>1%) before disinfection and in DRB were listed in Table S3. Dominant genera of effluents were largely affected by that of influents, having a great deal of uncertainty. Hence, we mainly concentrated on relative abundance changes of genera. A total of 15 genera were recognized as typical DRB genera according to the criteria mentioned above (Fig. 4). Ten of them were DRB of disinfection using chlorine-containing disinfectants, including Mycobacterium, Bacillus, Legionella, Pseudomonas, and Sphingomonas, which have been reported as chlorine-resistant bacteria (Le Dantec et al., 2002; Luo et al., 2021). There were three and five typical DRB genera under UV and ozone disinfection, respectively.

Resistance of bacteria is the major reason for relative abundance changes of DRB. Cell resistance might be derived from protective secretions, special resistant structures and a series of stress responses. Certain Proteobacteria, such as Pseudomonas, were known for strong secretion ability of EPS, which could act as a shelter against disinfectants (Freitas et al., 2011). Furthermore, persister formation is a universal reaction against adversity existing in almost all bacteria (Maisonneuve and Gerdes, 2014). This process is motivated by a ubiquitous bacterial stress alarmone guanosine pentao- and tetra-phosphate ((p)ppGpp), offering a considerable high resistance level for persisters.

We used type strains of each genus to figure the phylogenetic relationship of typical DRB genera (Fig. 5). Typical DRB were distributed in three phyla, which are Proteobacteria, Actinobacteria, and Firmicutes. These three phyla are also the main home of chlorine-resistant bacteria (Luo et al., 2021). Though ozone has a more similar disinfection mechanism with chlorine-containing disinfectants, we found that typical DRB of UV and ozone disinfection were more phylogenetic.
closely. It implied that similar resistance mechanisms against UV and ozone might exist, and different bacteria might possess various resistance mechanisms to chlorine-containing disinfectants.

Disinfection processes might also have a selection effect on Gram-positive/negative bacteria. Most species in typical DRB of UV and ozone disinfection were Gram-negative (Fig. 5). Experiments of drinking water have also found that the proportion of Gram-negative bacteria increased in DRB of UV disinfection (Chen et al., 2020a). Though the Gram-positive bacteria have thicker cell walls, Gram-negative bacterial cell walls consisting of two layers. Lipopolysaccharides are the main component of the outer layer, while a thin layer of peptidoglycan resides in the inner plasma membrane (Yusof et al., 2019). Multiple barriers allow Gram-negative bacteria to withstand more adverse conditions. Types of water samples were listed in Table S3.

A sub-analysis of water source effects conducted with the same methods as Section 4.1 showed basically the same result.

Pathogens and opportunistic pathogens belonging to typical DRB genera was listed in Table S4. 12 of 15 typical DRB genera contain pathogenic species, and some of them are known to possess multi-drug resistance, such as 
*Acinetobacter baumannii* and 
Pseudomonas aeruginosa
(Blaschke et al., 2021; Tarazi et al., 2021). In addition to pathogenicity, biofouling is also an essential risk of DRB. Among typical DRB genera, 
Pseudomonas and 
Sphingomonas are known to secrete sticky polysaccharides, which enhance the adhesion between cell and surface and facilitate the formation of biofilm (Freitas et al., 2011).

4.3. Multiple disinfection resistance in DRB

We applied the Venn diagram to depict the multiple disinfection resistance characteristics of typical DRB in Fig. 6. It was found that 
*Acinetobacter* has resistance against UV and ozone disinfection, and 
Pseudomonas possesses resistance against all three commonly-used disinfection methods. Both of them belong to the order 
Pseudomonadales in class 
γ-Proteobacteria. Except for the perspective of relative abundance, similar results were found in the study of pure strains under mono and synergistic disinfection (Jung and Park, 2015; Liu et al., 2019b; Wei et al., 2020). Therefore, 
Pseudomonas and 
Acinetobacter could be considered as model genera in subsequent studies of DRB, especially researches in multiple disinfection resistance and evaluations of novel disinfection technologies.

4.4. Microbial diversity of DRB

Microbial diversity plays a dual role in microbial risk control. Higher microbial diversity generally means a more stable microbiome as well as its functional characteristics. On the other hand, the high diversity of unfavorable bacteria in DRB, such as pathogenic bacteria, means microbial risks are more difficult to cope with (Huang et al., 2014). Variations of the five most commonly-used Alpha diversity indexes of DRB were listed in Table S5. Among them, OTUs, ACE, and Chao1 index reflect the richness of the microbial community, and Shannon index and Simpson index comprehensively consider the evenness as well as the richness of species in the water samples. A higher Shannon index or lower Simpson index indicates higher microbial evenness. It is easily accepted that DRB has lower total bacteria numbers, as well as lower microbial diversity. However, microbial diversity did not always decline after disinfection (Fig. 7). There have been some cases of higher microbial diversity of DRB (Li et al., 2017a; Liu et al., 2019b; Ma et al., 2020). Therefore, there has not been a consensus on whether DRB possess lower microbial diversity than microorganisms before disinfection. The changes of microbial diversity and corresponding functions and risks of the microbiome need to be profoundly investigated.
Fig. 7. Statistics of Alpha diversity indexes shift during disinfection. Data were taken from the field investigation of 54 different water treatment plants in 31 research articles.

5. Growth, secretion, and antibiotic resistance characteristics of DRB

5.1. Growth characteristics

Regrowth of DRB is a pervasive problem existing in all of disinfection processes (Nocker et al., 2020). UV and ozone have little continuous disinfection effect (Wang et al., 2021). Free chlorine is much better than them, but still facing the problem of decay (Wang et al., 2019a). Chloramine and chlorine dioxide have a relatively low rate of decay (Chen et al., 2020b). For all that, few disinfection methods can prevent bacterial regrowth problems. Furthermore, disinfection processes could alter the growth characteristics of the bacteria, complicating the regrowth process (Miettinen et al., 1998). Cases of growth characteristics of DRB and potential risks were listed in Table 1.

The shift of microbial community structure may lead to the change of growth characteristic, as different strains possess various growth rates. The regrowth process could collaborate with the selection effect of disinfection to further promote the dominance of certain harmful bacteria. Some pathogens and opportunistic pathogens, such as *Salmonella* and *Pseudomonas*, have been reported of higher levels of regrowth after disinfection than indicator bacteria (Li et al., 2013; Ribas et al., 2000). As a consequence, the relative abundance of these undesirable bacteria would increase and hide corresponding risks behind the ostensible decrease in numbers of total bacteria or indicator bacteria (Ling et al., 2018).

DRB might also have a different growth cycle from bacteria before disinfection. The growth process of bacteria could be divided into lag phase, exponential phase, plateau phase, and dead phase. Disinfection processes could expand the lag phase and faster the growth rate of bacteria during the exponential phase, which means a higher regrowth potential of DRB (Chen et al., 2020b). Disinfection processes also impact quorum sensing signals secretion, which may cause more serious biofouling (Wang et al., 2021). In addition, DRB could be induced into the viable but non-culturable (VBNC) state by disinfection processes (Chen et al., 2018; Lin et al., 2017; Zhang et al., 2015). VBNC state is a way for bacteria to resist the stress of the adverse environment. Under VBNC state, bacteria retain their metabolic activity and pathogenicity but not culturability (Liu et al., 2010). Accordingly, it is hard for water plant operators to tell the true microbial risk level of water by HPC and other plating methods, which are commonly-used in full-scale water treatment facilities.

Disinfectants interact not only with microorganisms, but also with organic substances in the water, which act as nutrients for bacterial growth. Assimilable organic carbon (AOC), which means the assimilable part of biodegradable dissolved organic carbon, is a widely-used indicator to evaluate the biological stability of water during storage and distribution (Nescerecka et al., 2018; Prest et al., 2016; Zhao et al., 2014a). Oxidative disinfectants, such as chlorine and ozone, could convert biological recalcitrant natural organic matter to AOC, providing more nutrients for the bacteria and creating a higher potential of DRB regrowth (Chen et al., 2018b; Huang et al., 2020; Kim et al., 2016; Zhao et al., 2014a). Therefore, the evaluation of a disinfection method should not only be limited to the effect of microbial inactivation, but also include the influence on AOC level.

### Table 1

| Disinfectant | Types of water samples | Characteristics of DRB | Potential risks | References |
|--------------|------------------------|------------------------|----------------|------------|
| Chlorine Reclaimed water | *Enterococcus* and *Salmonella* grew much faster than indicator bacteria | Higher risks of disease | (Ribas et al., 2000) |
| Chlorine Reclaimed water | *Pseudomonas* grew much faster than average | Higher risks of disease | (Li et al., 2013) |
| Chlorine Drinking water | Higher abundance of opportunistic pathogens | A threat to human health | (Ling et al., 2018) |
| Chloramine Drinking water | Shorter generation time and higher regrowth potential | High probability of biofilm growth and a threat to human health | (Chen et al., 2020b) |
| Chlorine Pure bacteria in dilute LB medium | More quorum sensing signals secretion | Higher probability of biofilm growth and membrane fouling | (Bai et al., 2020b) |
| Chlorine Pure bacteria in buffered saline | Containing bacteria in VBNC state | Higher persistence to antibiotics and latent health risks hard to detect | (Lin et al., 2017) |
| UV Pure bacteria in saline | Containing bacteria in VBNC state | Higher probability of biofilm growth and latent health risks hard to detect | (Chen et al., 2020a) |
| Chlorine UV Drinking water | Higher regrowth rate caused by AOC increase | Higher risks of disease | (Huang et al., 2020) |
| Ozone Drinking water | Higher regrowth rate caused by AOC increase | Higher risks of disease | (Kim et al., 2010) |
| Ozone Reclaimed water | Higher regrowth rate caused by AOC increase | Higher risks of disease and higher probability of biofilm growth | (Zhao et al., 2014a) |

5.2. Secretion characteristics

The secretion characteristics of DRB might be drastically different from that before disinfection. The shift of secretion characteristics contains two aspects. One is linked to the changes of microbial community structure, and the other is accounted for the responses of bacteria towards disinfectants (Chen et al., 2021). Soluble microbial products (SMP) and EPS are the microbial products worthy of special attention in water treatment (More et al., 2014; Ni et al., 2011). SMP comprise the majority of soluble organic material in biological treatment effluents and might bring about additional toxicity compared to original organic compounds, which show ecological risk towards native
microorganism (Barker and Stuckey, 1999). EPS plays a crucial role in biofilm formation, which is the key factor of biofouling and disinfectant tolerance in a wide variety of scenarios (Flemming 2020; Meng et al., 2009; Xue et al., 2012; Yu et al., 2018; Yu et al., 2021). Cases of secretion characteristics of DRB and corresponding risks were summarized in Table 2.

Secretion characteristics of different strains are significantly different (Yu et al., 2018). Therefore, the reshaping of microbial community structure by disinfection contributes to the difference of secretion characteristics of DRB. Disinfection processes usually select bacteria with higher EPS secretion ability, as one of the major functions of EPS is protecting bacteria from disinfectants (Sheng et al., 2010). Wang et al., found that long-term usage of free chlorine selected four genera of bacteria with high EPS secretion ability, which are Methylobacterium, Pseudomonas, Sphingomonas, and Acinetobacter (Wang et al., 2019b). After chlorine disinfection, the DRB dominated by these bacteria secreted more EPS with a higher proportion of high-molecular-weight matter. A similar phenomenon also appeared in DRB of UV. There has been evidence that the EPS amount of DRB increased with UV dose (Wu et al., 2021). As a consequence, long-term applications of a single disinfection pre-treatment might aggravate biofouling rather than alleviate it.

The acute responses to oxidative stress also attribute to the shift of secretion characteristics of the microbiome. Disinfectants could accelerate intracellular reactive oxygen species (ROS) production of bacteria and dramatically alter bacteria metabolism and secretion ability (Han et al., 2017).

In addition, some disinfectants react with secreta directly (Xue et al., 2014). Sacrificial reactions of EPS matrix with disinfectants are not only an effective protection mechanism for bacteria (Xue et al., 2012), but might also lead to more release of organic matters and ambiguous biofouling potential alteration (Wang et al., 2019c; Yu et al., 2017).

5.3. Antibiotic resistance characteristics

Antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs) have received particular attention in public health in recent years (Hoffman et al., 2015; Takeuchi and Tanaka, 2020). It is possible for ARGs to be either destroyed or selected during disinfection (Xu et al., 2020), and the ultimate antibiotic resistance level of DRB results from these two aspects competitively. Cases of growth characteristics of DRB and potential risks were summarized in Table 3.

Similar to growth and secretion characteristics, the variation of antibiotic resistance characteristics of DRB could also be induced by microbial community shift. There has been evidence that the microbial community shift made a significant contribution to the shift of antibiotic resistance characteristics in drinking water, rather than mobile genetic elements reproduction or transfer (Jia et al., 2015). ARB have a greater ability to cope with the selection pressures of disinfectants (Munir et al., 2011). Hence, the inactivation rate of some ARB was significantly lower than the total level of bacteria in water, leading to an increase in the relative abundance of ARB and a selection effect of ARGs in the disinfection process (Czekalski et al., 2016; Guo et al., 2013).

Drug efflux pump is one of the mechanisms of antibiotic resistance of cells. Oxidative stress generated by oxidative disinfectants induces the overexpression of the efflux pump genes, leading to a higher antibiotic resistance level of DRB (Hou et al., 2019). Furthermore, low doses of disinfectants could aggravate this process, as the expression of the efflux pump is stronger, while the inactivation effect of ARGs and ARB is dissatisfactory. Unfortunately, the doses of ozone added into water is usually low (Czekalski et al., 2016). When ammonia nitrogen content is high in water, part of free chlorine transfer to chloramine, which possesses a worse removal efficiency of ARG (Yoon et al., 2017).

Disinfection processes also have an impact on the horizontal transfer of antibiotic resistance genes in DRB. The horizontal transfer includes conjugation, transduction, and transformation, in which bacteria acquire ARG from donor bacterial, phage, and foreign DNA, respectively (Chen et al., 2020c; Qiu et al., 2012). Horizontal transfer of antibiotic resistance genes facilitates the recombination of various risks. For

### Table 2

Secretion characteristics of DRB and corresponding risks reported in literature.

| Disinfectant Types of water samples | Characteristics of DRB | Potential risks | References |
|------------------------------------|------------------------|-----------------|------------|
| Chlorine Reclaimed water | Bacteria secreting more EPS became dominant in DRB | Aggregate the fouling of membrane | (Wang et al., 2019b) |
| UV Reclaimed water | Higher EPS secretion ability | Aggregate the fouling of membrane | (Wu et al., 2021) |
| Chlorine MBR effluent | Higher EPS secretion ability | Higher biofouling potential | (Han et al., 2017) |
| Chlorine Seawater | Higher proportion of biofilm formation bacteria and stronger biogenic material synthetic ability | Aggregate the fouling of membrane | (Khan et al., 2015) |
| Chlorine Drinking water | Higher EPS secretion ability | High probability of biofilm formation in distribution systems and threat to human health | (Liu et al., 2017) |
| Chlorine Pure bacteria in dilute LB medium | Higher EPS secretion ability | Aggregate the fouling of membrane | (Wang et al., 2020) |

### Table 3

Antibiotic resistance characteristics of DRB and corresponding risks reported in literature.

| Disinfectant Types of water samples | Characteristics of DRB | Potential risks | References |
|------------------------------------|------------------------|-----------------|------------|
| Chlorine Drinking water | Higher relative abundance of ARBs | Higher persistence to antibiotics | (Xu et al., 2020) |
| Chlorine Drinking water | Higher relative abundance of bacteria with persistence of antibiotics | Higher persistence to antibiotics | (Jia et al., 2015) |
| Chlorine UV Wastewater | Higher relative abundance of ARB | Higher persistence to antibiotics | (Munir et al., 2011) |
| Ozone Wastewater | Higher relative abundance of ARGs | Higher persistence to antibiotics | (Czekalski et al., 2016) |
| UV Wastewater | Higher relative abundance of ARB | Higher persistence to antibiotics | (Guo et al., 2013) |
| Ozone Wastewater | Higher relative abundance of ARB | Higher persistence to antibiotics | (Czekalski et al., 2016) |
| ChlorineUV Wastewater | ARGs damage was slower than the loss of cell culturability | Higher persistence to antibiotics | (Yoon et al., 2017) |
| Chlorine UV Wastewater | More frequent horizontal transfer | Higher ratio of ARG in pathogens | (Guo et al., 2015) |
| Chlorine Wastewater | More frequent horizontal transfer | Higher ratio of ARB in pathogens | (Cheng et al., 2021) |
instance, certain pathogens may turn to ARB via this process (Salyers and Shoemaker, 2006). Guo et al. (2015) found that chlorine disinfection significantly amplified the cell permeability and led to a high frequency of conjugative transfer. Cheng et al., (2021) reported that chlorine could reduce the relative abundance of ARGs but simultaneously broaden the host range.

6. Challenges and prospects

6.1. Possible control strategies against DRB

A number of novel disinfection strategies have been developed and might be applicable for eliminating DRB, including synergic disinfection, secondary disinfection, and novel disinfection technologies.

Synergistic disinfection could effectively cope with bacterial resistance to a single disinfectant. Ding et al. reported that ozone achieved a inactivation rate of 99.9% for chlorine-resistant Bacillus cereus spore (Ding et al., 2019). Similar results were found in the synergistic disinfection of UV and chlorine (Cho et al., 2018). However, some other studies showed that synergistic disinfection was unsatisfactory. Cui et al. found that Pseudomonas, one of typical DRB genus, became dominant genera after ozone disinfection, and its relative abundance did not decrease after subsequent UV disinfection (Cui et al., 2020). Another study of drinking water manifested that the relative abundance of Mycobacterium was higher in the effluent of synergistic disinfection of ozone and chlorine (Li et al., 2017a). Therefore, whether synergistic disinfection could solve the problem of DRB is not sure, the result might vary with water samples.

Secondary disinfection is an effective strategy for long-distance delivery of water (Wang et al., 2014). Secondary disinfection includes two steps of chlorine or chloramine dosing, preventing high initial chlorine concentration. The original intention of secondary disinfection was to control disinfection by-products (DBPs) (Seidel et al., 2005). Recent studies indicated that secondary disinfection could achieve higher disinfection efficiency and causing severer damages to the cells, preventing bacterial regrowth and biofilm formation in water distribution systems (Li et al., 2017b; Zhao et al., 2020).

Lots of novel disinfection methods have been developed in the recent decade. Novel disinfection methods differ from traditional ones in terms of mechanisms, and were developed to overcome the drawbacks of traditional disinfection methods. Ferrate is a novel disinfectant with a two-step disinfection mechanism. The combination of strong oxidizing ability of ferrate and coagulation initiated by its reduction product makes ferrate an effective disinfectant for a wide range of bacteria and virus (Sharma et al., 2015). Ferrut could inactivate total coliform and chlorine-resistant spore-forming bacteria with an efficiency of more than 3 log at a dosage about 2–3 mg/L (Sharma et al., 2005). Studies have also shown that ferrate was effective for damaging harmful genes and preventing bacteria regrowth (Wang et al., 2020b; Yan et al., 2020). Electric disinfection is an environmentally benign disinfection technology. Either electroporation induced by the enhanced electric field (Huo et al., 2016; Zhou et al., 2020a; Zhou et al., 2020b) or direct oxidation of the anode (Liu et al., 2019b; Ni et al., 2020a; Ni et al., 2020b) could achieve a high inactivation rate up to 6 log without regrowth. Nanomaterials are also alternatives for DRB control (Elbourne et al., 2019; Huo et al., 2020). Nanomaterials can be made from a variety of materials, involving diverse inactivation mechanisms such as ROS generation and mechanical cell damage (Alvarez et al., 2018; Qu et al., 2015). The main advantages of nanomaterials are the avoidance of regrowth and low DBPs formation (Huo et al., 2020). Nanomaterials could achieve complete disinfection (no culturable bacteria detected) within one minute, especially in the flow-through reactor. Nevertheless, any novel method of disinfection might also have its own DRB, which has not been deeply studied.

DRB could also be controlled together with other hazards in the water. Advanced oxidation processes (AOPs) are effective methods to remove lots of refractory contaminants in water. Hydroxyl radical (·OH) generated by AOPs has great disinfection ability due to its strong oxidizing property (Fan and Song, 2020). For instance, photo-Fenton reached a considerable inactivation efficiency of ARG in real hospital wastewater (Serna-Galvis et al., 2019).

In addition to the choice of disinfection technologies, the determination of the dosage of disinfectants should also be meticulously considered. High-, mid-, and low- dose of disinfectants might have completely different effects on bacterial regrowth potentials of DRB and AOC level (Chen et al., 2020a; Kim et al., 2010). Over dosage of disinfectants seemingly reduce the total amount of DRB in short term. However, it might cause more severe problems of DRB (Wang et al., 2019d), as well as increase the generation of DBPs. Therefore, the appropriate dosage is beneficial for the balance between microbial control and the costs.

Moreover, it is necessary to exploit a series of monitoring methods that can effectively reflect the microbial community structure characteristics in water on time. Culture-based methods could not provide sufficient information on time (Ward et al., 1990), while the applications of microfluidics provide the possibility for the rapid detection of some key microorganisms (Bridle et al., 2014).

6.2. Extended concept of DRB in other treatment processes

Disinfection is not the only unit in water treatment that changes the composition of microorganisms. Other units, such as filtration, also reshape the microbial community structure and might also have residual bacteria problems (Kristian Stevik et al., 2004). For instance, the increase in AOC levels after coagulation led to a higher microbial growth potential of reclaimed water than secondary effluent (Chen et al., 2018b; Zhao et al., 2014b). For microbial risk control through the whole flow path of a water plant, attention of engineers and researchers should not be limited to disinfection units, but also on other processes having effect on the microbial community structure (Greay et al., 2019).

The concept of DRB indicates that the quantity control of microorganisms in water treatment has been developed to the consideration of the microbial community structure. Meanwhile, DRB problems might also exist in disinfection possesses in the air and solid phase. Harmful microorganisms existing in bioaerosols and on food surfaces pose a threat to human health through breathing and eating (Masotti et al., 2019). In commonly-used disinfection processes for air and solid surface, disinfectants cannot remain in the air or on solid surfaces for too long, which might also cause DRB problem similar to water treatment.

7. Conclusions

- Disinfection-residual-bacteria (DRB) is a ubiquitous problem and a great challenge in water treatment and reuse, which could bring about various risks in the aspects of health, process, and ecology.
- On the phyla (classes) level, α, β, γ-Proteobacteria and Bacteroidetes were the top four most common dominant phyla (classes) after disinfection, and Firmicutes showed a clear regularity of relative abundance rising up after disinfection.
- On the genera level, Pseudomonas, Mycobacterium, Legionella, Sphingomonas, and Bacillus were the top five most common genera of great increase in relative abundance after disinfection using chlorine-containing disinfectants. Pseudomonas, Acinetobacter, and Limnobacter were the top three typical DRB genera after UV disinfection, and those for ozone disinfection were Pseudomonas, Acinetobacter, and Rheinheimera.
- Pseudomonas and Acinetobacter could be considered as model bacteria in further disinfection research as they possess multiple disinfection resistance and various hazards.
- Except for disinfection, other water treatment processes might also face the problems of residual bacteria, which have not received enough attention and need to be further investigated.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (No. 52001114) and the Key Program of the National Natural Science Foundation of China (No. 51738005).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.watres.2021.117606.

References

Alexander, J., Knopp, G., Dötsch, A., Wieland, A., Schwartz, T., 2016. Ozone treatment of conditioned wastewater selects antibiotic resistance genes, opportunistic bacteria, and induce strong population shifts. Sci. Total Environ. 559, 103–112.

Alvarez, F.J., Chan, C.K., Elimelech, M., Halas, N.J., Villagran, M., 2018. Emerging opportunities for nanotechnology to enhance water security. Nat. Nano. 13 (8), 634–641.

Aziz, P.K.A., Al-Tisan, I., Sasikumar, N., 2001. Biofloating potential and environmental factors of seawater at a desalination plant intake. Desalination 135 (1–3), 69–82.

Bai, Y., Shan, F., Zhu, Y.Y., Xu, J.Y., Wu, Y.S., Luo, X.G., Wu, Y.H., Hu, H.Y., Zhang, B.L., 2020. Long-term performance and economic evaluation of full-scale MF and RO process – a case study of the changing NE water project phase 2 in Singapore. Water Cycle 1, 128–135.

Bai, Y., Wu, Y.H., Wang, Y.H, Tong, X., Zhao, X.H., Ikuno, N., Hu, H.Y., 2020b. Membrane fouling potential of the denitrification filter effluent and the control mechanism by ozonation in the process of wastewater reclamation. Water Res. 173, 115561.

Bal Krishna, K.C., Sathasivam, A., Listowski, A., 2020. Influence of treatment processes and disinfectants on bacterial community compositions and opportunistic pathogens in a full-scale recharged water distribution system. J. Clean. Prod. 274, 123034.

Barker, D.J., Stuckey, D.C., 1999. A review of soluble microbial products (SMP) in wastewater treatment systems. Water Res. 33 (14), 3063–3082.

Becerra-Castro, C., Macedo, G., Silva, A.M.T., Manaia, C.M., Nunes, O.C., 2016. Proteobacteria become predominant during regrowth after water disinfection. Sci. Total Environ. 573, 313–323.

Belila, A., El-Chakhtoura, J., Otaibi, N., Muyzer, G., Gonzalez-Gil, G., Saikaly, P.E., van Ootsch, A., Wieland, A., Schwartz, T., 2016. Ozone treatment of drinking water bacterial populations to monochloramine disinfection. Environ. Sci. Technol. 50 (21), 11862–11871.

Chen, Z., Yu, T., Ngo, H.H., Lu, Y., Li, G., Wu, Q., Li, K., Bai, Y., Liu, S., Hu, H.Y., 2018b. Assimilable organic carbon (AOC) variation in reclaimed water: insight on biological stability evaluation and control for sustainable water reuse. Bioreesour. Technol. 254, 403–409.

Cheng, X., Xu, J., Smith, G., Zhang, Y., 2021. Metagenomic insights into dissemination of antibiotic resistance across bacterial genera in wastewater treatment. Chemosphere 242, 125190.

Chen, Y., Ji, Q., Zhang, G., Liu, H., Qu, J., 2020c. Synergistic metabolic disturbance with oxidative damage amplifies cell membrane destructive stresses and enables rapid sterilization. Angew. Chem. Int. Ed. 60 (14), 7744–7751.

Chen, Z., Yu, T., Ngo, H.H., Lu, Y., Li, G., Wu, Q., Li, K., Bai, Y., Liu, S., Hu, H.Y., 2018b. Assimilable organic carbon (AOC) variation in reclaimed water: insight on biological stability evaluation and control for sustainable water reuse. Bioreesour. Technol. 254, 403–409.

Cheng, X., Xu, J., Smith, G., Zhang, Y., 2021. Metagenomic insights into dissemination of antibiotic resistance across bacterial genera in wastewater treatment. Chemosphere 242, 125190.

Chiao, T.H., Clancy, T.M., Pinto, A., Xi, C., Raskin, L., 2014. Differential resistance of drinking water bacterial populations to monochloramine disinfection. Environ. Sci. Technol. 48 (7), 4038–4047.

Cho, S., Jeong, D., Lee, S., Rae, H., 2018. Chlorination caused a shift in marine biofilm niches on microfiltration/ultrafiltration and reverse osmosis membranes and UV irradiation effectively inactivated a chlorine-resistant bacterium. Appl. Microbiol. Biotechnol. 102 (16), 7183–7194.

Cloete, T.E., 2003. Biofouling control in industrial water systems: what we know and what we need to know. Mater. Corros. Werkst. Korros. 54 (7), 520–526.

Cui, Q., Liu, H., Yang, H.W., Lu, Y., Chen, Z., Hu, H.Y., 2020b. Bacterial removal performance and community changes during advanced treatment process: a case study at a full-scale reclamation plant. Sci. Total Environ. 705, 3.

Czekalski, N., Imming, S., Salhi, E., Veljkovic, M., Killefl, K., Drissner, D., Hammes, F., Burgmann, H., von Gunten, U., 2016. Inactivation of antibiotic resistant bacteria and resistance genes by ozone: from laboratory experiments to full-scale wastewater treatment. Environ. Sci. Technol. 50 (21), 11862–11871.

Ding, W.Q., Jin, W.B., Cao, S., Zhou, X., Wang, C.P., Jiang, Q.J., Huang, H., Tu, R.J., Han, S.F., Wang, Q.L., 2019. Oxidation disinfection of chlorine-resistant bacteria in drinking water. Water Res. 160, 339–349.

Elborne, R., Chapman, J., Gelmi, A., Corzinnol, D., Crawford, R.J., Truong, V.K., 2019. Bacterial-nanostructure interactions: the role of cell elasticity and adhesion forces. J. Colloid Interface Sci. 546, 192–210.

Fan, X., Song, Y., 2020. Advanced oxidation process as a postharvest decontamination technology to improve microbial safety of fresh produce. J. Agric. Food Chem. 68 (46), 12916–12926.

Flemming, H.C., Fleeming, H.C.W.J., Szewczyk, U., 2011. Biofilm Highlights. Springer Berlin Heidelberg Berlin, Heidelberg, pp. 81–109.

Fleeming, H.C., 2020. Biofouling and me: my stockholm syndrome with biofilms. Water Res. 173, 115576.

Fleming, H.C., Fleeming, H.C.W.J., Szewczyk, U., 2011. Biofilm Highlights. Springer Berlin Heidelberg Berlin, Heidelberg, pp. 81–109.

Flemming, H.C., Fleeming, H.C.W.J., Szewczyk, U., 2011. Biofilm Highlights. Springer Berlin Heidelberg Berlin, Heidelberg, pp. 81–109.

Garner, E., McLain, J., Bowers, J., Engelthaler, D.M., Edwards, M.A., Pruden, A., 2016. Microbial ecology and water chemistry impact regrowth of opportunistic pathogens in full-scale reclaimed water distribution systems. Environ. Sci. Technol. 52 (16), 9056–9068.

Grey, T.L., Gofton, A.W., Zahedi, A., Paparini, A., Linge, L.J., Joll, C.A., Ryan, U.M., 2019. Evaluation of 16S next-generation sequencing of hypervariable region 4 in wastewater samples: an unsuitable approach for bacterial enteric pathogen identification. Sci. Total Environ. 670, 1111–1124.

Gu, Y., Fierro, A., Ridereau, S., Nui, X., 2020. Microbiome convergence following sanitizer treatment and identification of sanitizer resistant species from spinach and lettuce raw water. Int. J. Food Microbiol. 318, 108458.

Guo, M.T., Yuan, Q.B., Yang, J., 2013. Microbial selectivity of UV treatment on antibiotic-resistant heterotrophic bacteria in secondary effluents of a municipal wastewater treatment plant. Water Res. 47 (16), 6388–6394.

Guo, M.T., Yuan, Q.B., Yang, J., 2015. Distinguishing effects of ultraviolet exposure and chlorination on the horizontal transfer of antibiotic resistance genes in municipal wastewater. Environ. Sci. Technol. 49 (9), 5771–5778.

Han, X., Wang, Z., Chen, M., Zhang, X., Tang, C.Y., Wu, Z., 2017. Acute responses of microorganisms from membrane bioreactors in the presence of NaOCl protective mechanisms of extracellular polymeric substances. Environ. Sci. Technol. 51 (6), 3233–3241.

Hirai, J., Nagai, S., Hidaka, K., 2017. Evaluation of metagenetic community analysis of planktonic copepods using illumina MiSeq comparisons with morphological classification and metagenetic analysis using Roche 454. PLoS One 12 (7), e0181452.

Hoffman, S.J., Calo, G.M., Daumert, S., Nettles, S., Johnson, G., Johnson, G., 2018. Evaluation of the environmental impact of disinfection byproducts on aquatic bacteria in surface water. Environ. Sci. Technol. 52 (20), 11862–11871.

Horn, H., Negev, I., Zucker, I., Bar-Or, I., Moran-Gilad, J., Balcazar, J.L., Bibby, K., Hill, C., Vaizel-Ohayon, D., Morgenroth, E., Bertuzzo, E., Wells, G., Kiperwas, H.R., Burgmann, H., von Gunten, U., 2016. Inactivation of antibiotic resistant bacteria and resistance genes by ozone: from laboratory experiments to full-scale wastewater treatment. Environ. Sci. Technol. 50 (21), 11862–11871.

Huang, K., Zhang, X.X., Shi, P., Wu, B., Ren, H., 2014. Comprehensive insight into bacterial virulence in drinking water using 454 pyrosequencing and illumina high-throughput sequencing. Environ. Toxicol. Environ. Saf. 101, 15–21.
H.-B. Wang et al.

Water Research 204 (2021) 117606

Jung, J., Park, W., 2015. Acinetobacter species as model microorganisms in water treatment. Water Res. 87, 135-147.

Huo, Z.Y., Du, Y., Chen, Z., Wu, Y.H., Hu, H.Y., 2020. Evaluation and prospects of nanomaterial-enabled innovative processes and devices for water disinfection: a review for the future of the art. React. Funct. Polym. 153, 113501.

Moehbi, H., Li, C.Q., 2011. Experimental investigation on corrosion of cast iron pipes. Int. J. Corros. 506501, 506501.

More, T.T., Yadav, J.S.S., Yan, S., Tyagi, R.D., Surampalli, R.Y., 2014. Extracellular polymeric substances of biofilms and their potential environmental applications. J. Environ. Manage. 144, 1-25.

Munir, M., Hong, K., Zagarolami, L., 2011. Release of antibiotic resistant bacteria and genes in the effluent and biosolids of five wastewater utilities in Michigan. Water Res. 45 (12), 681-693.

Murthy, P.S., Venkatesan, R., Fleming, H.C., Murthy, P.S., Venkatesan, R., Cooksey, K., 2009. Marine and Industrial Biofouling. Springer Verlag Berlin, Berlin, pp. 65-101.

Neschina, A., Juliana, T., Hames, F., 2018. Identifying the underlying causes of biological instability in a full-scale drinking water supply system. Water Res. 135, 1-11.

Ni, B.J., Rittmann, B.E., Yu, H.Q., 2011. Soluble microbial products and their implications in mixed culture biotechnology. Trends Biotechnol. 29 (9), 454-461.

Ni, X.Y., Liu, H., Wang, C., Wang, W.L., Chen, Z., Wu, Y.H., Hu, H.Y., 2020a. Comparison of carbonized and graphitized carbon fiber electrodes under flow-through electrode system (FES) for high-efficiency bacterial inactivation. Water Res. 165, 115505.

Ni, X.Y., Liu, H., Xin, L., Xu, Z.B., Wang, Y.H., Peng, L., Chen, Z., Wu, Y.H., Hu, H.Y., 2020b. Disinfection performance and mechanism of the carbon fiber-based flow-through electrode system (FES) towards gram-negative and gram-positive bacteria. Electrochim. Acta 341, 139030.

Nocker, A., Schulte-Illingen, M., Huhn, A., Zimmermann, G., Gaba, A., 2020. Microbiological changes along a modular wastewater reuse treatment process with a special focus on antibiotic resistance gene transfer. J. Water Reuse Desalin. 10 (4), 380-393.

Numerator, D., Ganzert, L., Zoccarato, L., Muller, S., Sauer, S., Grossberg, B.H., Greenwood, A.D., 2019. Characterization of bacterial communities in wastewater with enhanced taxonomic resolution by full-length 16S rDNA sequencing. Sci. Rep. 9 (1), 15664.

Pang, Y.C., Xi, X.J., Yu, H.Z., Hu, Y.O., 2016. Shifts of live bacterial community in secondary effluent by chlorination disinfection revealed by MetaIqen high-throughput sequencing combined with propidium monoazide treatment. Appl. Microbiol. Biotechnol. 100 (14), 6435-6446.

Peng, L., Wang, F., Zhang, D., Fang, C., van der Hoek, J.P., Chu, W., 2021. Effect of ozonation and disinfection with citric acid and persulfate. Water Res. 161, 354-367.

Qiu, Z., Yu, Y., Chen, Z., Jin, M., Yang, D., Zhao, Z., Wang, J., Shen, Z., Wang, X., Qian, D., Huang, A., Zhang, B., Li, J.W., 2012. Nanocellulose promotes the horizontal transfer of multisResistance genes mediated by plasmids across genera. Proc. Natl. Acad. Sci. 109 (13), 4944.

Qiu, X., Brame, J., Li, Q., Alvarez, P.J., 2013. Nanotechnology for a safe and sustainable water supply: enabling integrated water treatment and reuse. Acc. Chem. Res. 46 (3), 834-843.

Ribas, F., Perramon, J., Terradillos, A., Frias, J., Lucena, F., 2000. The pseudomonas group as an indicator of potential regrowth in water distribution systems. J. Appl. Microbiol. 88 (4), 704-716.

Ruiz-Muguiro, T., Kob, D.C., Drake, L.A., Mullady, T., Hua, A., Colwell, R.R., 2000. Global spread of microorganisms by ships - ballast water discharged from immigrant vessels a coastal and continental pathway. Nature 408 (6808), 48-50.

Rutala, W.A., Weber, D.J., 2016. Disinfection and sterilization in health care facilities: an overview and current issues. Infect. Dis. Clin. N. Am. 30 (3), 609-637.

Salyers, A., Shiookave, R.B., 2006. Reservoirs of antibiotic resistance genes. Annu. Rev. Biotechnol. 17 (2), 137-146.

Santos, R.L., 2014. Pathobiology of salmonella, intestinal microbiota, and the host innate immune response. Front. Immunol. 5, 252.

Sedlak, D.L., von Gunten, U., 2011. The chlorine dilemma. Science 331 (6013), 42-46.

Sedlak, D.L., McGuire, M.J., 2016. Chlorine use and treatment chemistries. Water Res. 93, 153-168.

Serna-Galvis, E.A., Velaz-Pena, E., Osorio-Vargas, P., Jimenez, J.N., Salazar-Ospina, L., Mejias, J.L., Gonzalez, Y.M., Torres-Palma, R.A., 2019. Inactivation of carbenicillin-resistant klebsiella pneumoniae by photo-Fenton: residual effect, gene evolution and modifications with citric acid and persulfate. Water Res. 161, 354-363.

Shabi, A., Aydin, S., Ince, B., Ince, O., 2016. Reconstruction of bacterial community sequence and variation by chlorination disinfection by chlorination disinfection. J. Environ. Sci. 36, 60-66.

Miettinen, I.T., Vartiainen, T., Nissinen, T., Tukkuniemi, T., Martikainen, P.J., 1998. Microbial growth in drinking waters treated with ozone, ozone/hydrogen peroxide and hydrogen peroxide. Ozoni Sci. Eng. 20 (4), 303-317.

11
Shannon, M.A., Bohn, P.W., Elimelech, M., Georgiadis, J.G., Marinas, B.J., Mayes, A.M., 2008. Science and technology for water purification in the coming decades. Nature 452 (7189), 30–38.

Sharma, V.K., Kazama, F., Jiangyong, H., Ray, A.K., 2005. Ferrates (Iron (IV) and Iron (V))—environmentally friendly oxidants and disinfectants. J. Water Health 3 (1), 45–59.

Sharma, V.K., Zboril, R., Varma, R.S., 2015. Ferrates: greener oxidants with multimodal action in water treatment technologies. Acc. Chem. Res. 48 (2), 182–191.

Sheng, G.P., Yu, H.Q., Li, X.Y., 2010. Extracellular polymeric substances (EPS) of microbial aggregates in biological wastewater treatment systems: a review. Biotechnol. Adv. 28 (6), 882–894.

Szewzyk, U., Szewzyk, R., Manz, W., Schleifer, K.H., 2000. Microbiological safety of drinking water. Annu. Rev. Microbiol. 54 (1), 81–127.

Tafei, H., Tan, H.S., 2021. Regrowth of bacteria after light-initiated disinfection. Front. Microbiol. 12, 1027.

Tan, B., Ng, C., Nshimyimana, J., Loh, L.L., Gin, K., Thompson, J., 2015. Next-generation decay model of reclaimed water using chemical chlorine demands. Chem. Eng. J. 280, 626–635.

Tan, B., Hu, X., 2019a. Quantifying chlorine-reactive substances to establish a chlorine conversion model for cast iron pipes in a reclaimed water distribution system. Water Res. 144 (4), 1070–1078.

Wang, X., Ma, J., Wu, Z., Wang, Z., 2020. Stimulatory effects on bacteria induced by chemical cleaning cause severe biofouling of membranes. Journal of Water Reuse and Desalination 10 (1), 82–94, https://doi.org/10.1177/2151585919872397.

Wang, H., Proctor, C.R., Edwards, M.A., Pryor, M., Santo Domingo, J.W., Ryu, H., Sharma, V.K., Zboril, R., Varma, R.S., 2015. Ferrates: greener oxidants with multimodal action in water treatment technologies. Acc. Chem. Res. 48 (2), 182–191.

Wang, Y., Xu, C., Chen, F., Yin, H., Sun, H., Cheng, L., Bi, X., 2021. Microcoagulation improved the performance of the UF-RO system treating the effluent from a coastal municipal wastewater treatment plant: a pilot-scale study. J. Water Reuse Desalin. 11 (2), 177–188.

Yu, W., Zhang, D., Graham, N.J.D., 2017. Membrane fouling by extracellular polymeric substances after ozone pre-treatment: variation of nano-particles size. Water Res. 120, 146–155.

Zhang, Y., Zhao, X., Hu, H.Y., Yu, T., Xu, C., Chen, F., Yin, H., Sun, H., Cheng, L., Bi, X., 2021. Microcoagulation significantly promotes cast iron corrosion in reclaimed drinking water. Water Res. 172, 12277–12289.

Zhang, S., Zhou, Z., Liu, B., Chen, G.Q., Nozomu, I., Chen, Z., Hu, H.Y., 2021. Metagenomics analysis of the key functional genes related to biofouling aggravation of reverse osmosis membranes. J. Haz. Mat. 124602, https://doi.org/10.1016/j.jhazmat.2020.124602.

Zhou, J.F., Yu, C., Xie, X., 2020b. Development of nanowire-modified ZnO catalysts as stabilizing agent and their antibacterial properties against gram-positive and gram-negative bacteria. Int. J. Biol. Macromol. 124, 1132–1139.

Zhou, J.F., Yu, C., Wang, T., Xie, X., 2020a. Development of nanowire-modified ZnO catalysts as stabilizing agent and their antibacterial properties against gram-positive and gram-negative bacteria. Int. J. Biol. Macromol. 124, 1132–1139.

Zhao, X., Hu, H.Y., Yu, T., Su, C., Jiang, H., Liu, S., 2014a. Effect of different molecular chlorine pre-treatment and disinfectant on microbial community structure and opportunistic pathogen occurrence. Water Res. 47 (15), 5760–5773.

Zhao, L., Liu, Y.W., Li, N., Fan, X.Y., Li, X., 2020. Response of bacterial regrowth, susceptibility of multidrug-resistant pseudomonas aeruginosa isolated from drinking water patients in Jordan. Acta Trop. 217, 105859, 105859.

Zhao, L., Liu, Y.W., Li, N., Fan, X.Y., Li, X., 2020. Response of bacterial regrowth, susceptibility of multidrug-resistant pseudomonas aeruginosa isolated from drinking water patients in Jordan. Acta Trop. 217, 105859, 105859.