Trends in
Microbiology

Review

Importance of Bacteroidetes in host–microbe interactions and ecosystem functioning

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Bacteroidetes are prevalent in soil ecosystems and are associated with various eukaryotic hosts, including plants, animals, and humans. The ubiquity and diversity of Bacteroidetes exemplify their impressive versatility in niche adaptation and genomic plasticity. Over the past decade, a wealth of knowledge has been obtained on the metabolic functions of clinically relevant Bacteroidetes, but much less attention has been given to Bacteroidetes living in close association with plants. To improve our understanding of the functional roles of Bacteroidetes for plants and other hosts, we review the current knowledge of their taxonomy and ecology, in particular their roles in nutrient cycling and host fitness. We highlight their environmental distribution, stress resilience, genomic diversity, and functional importance in diverse ecosystems, including, but not limited to, plant-associated microbiomes.

Highlights

Bacteroidetes can adapt to physicochemically and (micro)biologically diverse niches ranging from aquatic to terrestrial environments.

Bacteroidetes actively participate in global nutrient cycling.

Less attention has been given to Bacteroidetes in plant microbiomes compared to their counterparts associated with human and animal guts.

By facilitating nutrient uptake and defense against various (a)biotic stress, Bacteroidetes significantly contribute to host fitness.

Bacteroidetes' genomes harbor a rich repertoire of enzymes and biosynthetic gene clusters that allow versatile lifestyles.

Introduction

Microorganisms living on and inside plant tissues are key to plant growth and fitness, similar to the functional importance of gut microbiota for animal and human wellbeing [1,2]. Changes in the community structure of gut and plant microbiomes typically coincide with dysbiosis and alterations in host performance. Among the bacterial members of the microbiomes of eukaryotes, Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria are the dominant phyla [3,4]. Although Bacteroidetes are well studied as an important member of the human intestinal tract [5], their functional roles in plant microbiomes remain largely elusive. Their wide distribution and diverse lifestyles suggest high adaptability to various environments and coevolution with host species, yet little is known about their ecology and natural functions [6,7]. In this review, we summarize current knowledge of the taxonomic diversity of members of the phylum Bacteroidetes and give insights into their functional roles in interactions with hosts in diverse ecosystems.

Taxonomy and ecology of Bacteroidetes

The first Bacteroidetes studies date back to the 1890s with the isolation of anaerobic *Bacteroides* species in postoperative infections [8]. The advances in cultivation techniques boosted more frequent isolations of Bacteroidetes from human gastrointestinal tracts in the 1970s [9]. The introduction of molecular techniques and genomics in the early 2000s marked a turning point in the field of Bacteroidetes research with new insights in their taxonomic and functional diversity [8]. From a historical perspective, these different steps in our fundamental knowledge of Bacteroidetes align with several technological leaps (Figure 1, Key figure).

Classification of the Gram-negative Bacteroidetes has proved to be challenging, yet recent whole-genome sequence data improved their phylogenetic delineation (Figure 2A) [10]. With over 32,000 genomes sequenced and assembled, the Bacteroidetes (Bacteroidota) phylum is now divided into six main classes: Bacteroidia, Cytophagia, Flavobacteriia, Chitinophagia, Sphingobacteriia, and Saprospiria (NCBI, August 2022, https://www.ncbi.nlm.nih.gov/data-hub/taxonomy/976/).

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Key Figure

Representation of ecology and history of Bacteroidetes

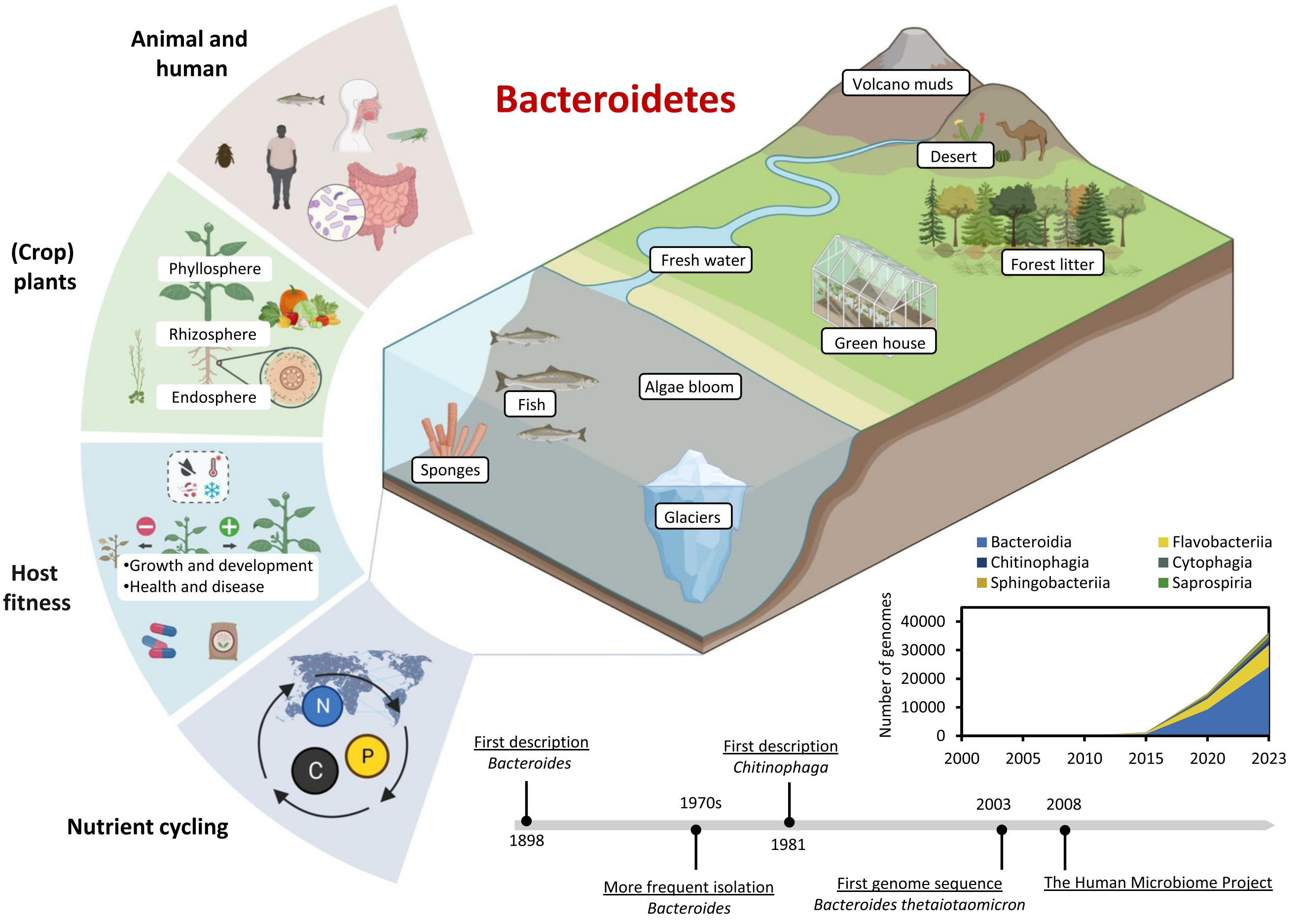

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Figure 1. Bacteroidetes colonize a variety of natural ecosystems, including aquatic and terrestrial habitats. Some Bacteroidetes can tolerate extreme environments such as desert soil and glacier ice. While environmental Bacteroidetes are widely distributed and participate in global nutrient cycling, those recovered from animal and human guts provide important functions for host fitness. Bacteroidetes can colonize all plant compartments, including phyllosphere (above-ground plant parts), rhizosphere (soil–root interface), and root endosphere (internal root tissue). The history of Bacteroidetes research dates back to 1890s when the first *Bacteroides* member was described. Advances in molecular and (bio)chemical technologies have resulted in an exponential growth of available Bacteroidetes genomes that have expanded our fundamental knowledge of this bacterial phylum. The number of genomes listed in the graph represents the cumulative number of published genomes in the NCBI database per year. Figure designed with BioRender (biorender.com).

They show ample variation in morphologies and physiology, with cell shape ranging from long filaments to short rods. Bacteroidetes taxa do not form spores or endospores, whereas members of the Chitinophagaceae family have been reported to produce spherical bodies (myxospores) upon aging without developing into fruiting bodies [11]. Bacteroidetes species move via gliding motility resulting in spreading colonies that typically exhibit a yellow-orange to pink-red color due to the production of carotenoids and flexirubin-like pigments that serve as antioxidants [12].

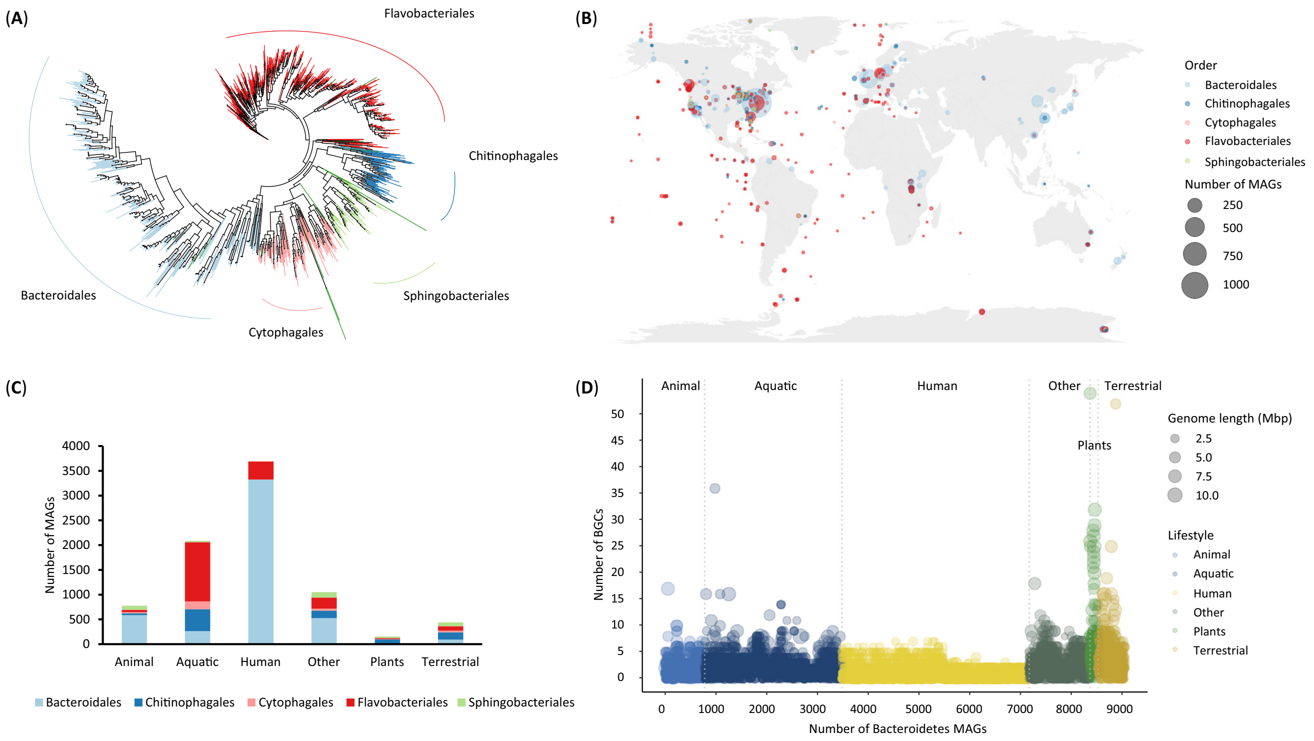

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Figure 2. Phylogeny, distribution, and biosynthetic potential of Bacteroidetes. (A) Phylogenetic tree of 1,173 Bacteroidetes reference genomes from the NCBI database created by PhyloPhlAn 3.0 [123]. Bacteroidetes mainly consist of five orders: Bacteroidales, Flavobacteriales, Chitinophagales, Cytophagales, and Sphingobacteriales. (B) The geographic distribution of Bacteroidetes based on metagenome data. Point sizes represent the number of metagenome-assembled genomes (MAGs). Notably, the Flavobacteriales order is widely distributed in the aquatic environment. Bacteroidales are commonly detected in human and animal microbiomes. The number of MAGs and their corresponding lifestyles are summarized in the bar plot (C). (D) Scatter plot showing the number of biosynthetic gene clusters (BGCs) predicted per Bacteroidetes MAG. Point sizes reflect the genome sizes and are color-coded according to the lifestyles of reconstructed MAGs. The number of Bacteroidetes MAGs on the X axis is the cumulative number. Terrestrial and plant-associated Bacteroidetes contain relatively larger biosynthetic potential despite their small sample sizes. Figure 2B–D constructed from data retrieved from [7].

While strictly anaerobic *Bacteroides* species from the Bacteroidia class are well-known members in gut microbiota of humans and animals, aerobic Flavobacteriia is the largest class found in a wide range of ecosystems [6]. The isolation of *Flavobacterium* species has been reported for soil and aquatic environments, ranging from freshwater to seawater, and notably cold environments [13]. In addition to traditional culture-based approaches, the emergence of **culturomics** (see Glossary) has further provided a high-throughput method to identify novel bacterial species via the optimization of culturing conditions and combination with multi-omics for rapid identification [14,15]. Moreover, the latest advances in sequencing have enabled more accurate insight into the underestimated distribution and diversity of Bacteroidetes worldwide (Figure 2B). Recently, more than 10,000 environmental **metagenomes** have been obtained by large-scale microbiome analyses to help build a comprehensive catalogue of the Earth's microbiomes [7]. In this project, the authors reconstructed 52,515 **metagenome-assembled genomes (MAGs)**, among which over 9,000 Bacteroidetes MAGs were identified [7]. Although metagenomic approaches can uncover part of the uncultured microbial communities, it remains challenging to resolve complete and accurate genomes due to the gaps and local assembly errors [16]. In spite of the limitations, these MAGs were mainly classified as Bacteroidales, Flavobacteriales, and Chitinophagales. The origins of these samples indicated that Bacteroidetes members are often found in human, aquatic, and terrestrial ecosystems (Figure 2C). In particular the Flavobacteriales order appeared to be widely distributed in a variety of natural and agricultural ecosystems (Figure 2B). Certain members of the Bacteroidetes phylum are competent colonizers of extreme environments, such as some *Flavobacterium* strains in glacier ice [17], *Salinibacter* in desert soil [18–20] and hypersaline environments [21]. Their tolerance to cope with a wide range of environmental stresses make them abundant members of soil microbiomes [22,23] and forest litter [24–26]. In addition, Bacteroidetes members are abundant in aquatic habitats, either as free-living or attached to particles and other surfaces [27–29]. In particular, marine Bacteroidetes are reported to increase in abundance during and following phytoplankton blooms [30,31].

In addition to these aquatic and terrestrial environments, Bacteroidetes are important residents of the human microbiome and are typically recovered from the oral cavity, respiratory and gastrointestinal tracts [32,33]. Together with Firmicutes, the phylum Bacteroidetes (primarily *Bacteroides*, *Alistipes*, *Parabacteroides*, *Prevotella*) represents the majority of the bacterial community found in the human gut [34,35]. Gut colonization starts immediately after birth and then undergoes successional dynamics driven by changes in abiotic conditions and interactions with other gut (micro)organisms [36]. Despite the variations in nutrient status, pH, and other physiological parameters, the Bacteroidales order is reported to colonize all gut compartments including ileum, cecum, and colon in mice [33]. To unravel their biochemistry and ecology, *Bacteroides* has become the model genus of human gut Bacteroidetes as it is highly abundant, culturable, and genetically tractable [5,37].

Compared with Bacteroidetes in the mammalian gut, their counterparts associated with other hosts such as sponges [38], fish [39], insects [40], and plants [41] are much less studied. Bacteroidetes can colonize the model plant species *Arabidopsis thaliana* [42] and various agriculturally important crops [43–46]. They can be found in different plant compartments, including the **phyllosphere** (above-ground plant parts), **rhizosphere** (soil–root interface), and root **endosphere** (internal root tissue) [19,47,48] as well as the fruit surface [49]. For instance, the relative abundance of Bacteroidetes species was shown to increase in the arabidopsis rhizosphere along with plant growth and reached the highest level at flowering [50]. *Flavobacterium* species are dominant in both rhizosphere and phyllosphere of wheat, especially in the earlier growth stages [51]. Interestingly, Bacteroidetes were reported to have a higher relative abundance in wild crop species compared to their domesticated counterparts [52]. This pattern was observed across various plant species including *Arabidopsis*, sugar beet, lettuce, barley, and common bean [52]. It was shown that Bacteroidetes – mainly Chitinophagaceae and Cytophagaceae – were enriched in the rhizosphere of wild relatives of common bean that have a lower root density and higher specific root length (i.e., root length per unit of root dry mass) [53]. Additionally, it is worth noting that many Bacteroidetes members can degrade complex polysaccharides such as cellulose, the major component of plant cell walls [54]. Difference in root architecture and exudate profile between wild and modern plants at different developmental stages may play a key role in structuring the root microbiome [55] and the differential recruitment of Bacteroidetes. These findings exemplify how plant development and domestication affected the composition and abundance of the Bacteroidetes.

Functional roles of Bacteroidetes

Role in global nutrient cycling

Soil harbors a rich reservoir of complex organic materials that serve as a food source for millions of microorganisms. Specialized in the decomposition of high-molecular-weight polymers, soil Bacteroidetes species significantly contribute to carbon recycling and aboveground biodiversity (reviewed in [23]). Enhanced ability in the breakdown of plant-derived glycans enables the

Glossary

Biosynthetic gene cluster (BGC): two or more physically clustered genes in a genome that, together, encode a biosynthetic pathway for (primary or) secondary metabolites. Typical secondary metabolites include antibiotics and pigments that are not needed for the organism's growth or reproduction but provide diverse functions in its survival and interactions with the surrounding environment.

Comparative genomics: the comparison of genomic features of various (micro)organisms to pinpoint their similarity and difference.

Culturomics: a culturing approach that uses multiple culture conditions, MALDI-TOF mass spectrometry, and 16S rRNA sequencing for the identification of bacterial species.

Endosphere: the internal plant tissue that is colonized by distinct microbial communities.

Genomic diversity: the total difference of genetic makeup of a species that provides a basis for genetic variation and enables the population to adapt to changing environments.

Genomic plasticity: the alterable nature of prokaryotic genomes that enables the fluid DNA exchange, which allows rapid adaptations to environmental changes and colonization of novel niches.

Metagenome: the collective set of genomic sequences of microorganisms in a sample. It is a culture-independent approach typically used in the functional analysis of microbial communities present in environmental and gut samples.

Metagenome-assembled genomes (MAGs): individual microbial genomes reconstructed from metagenome data. The process of MAG reconstruction is commonly called binning; MAGs are also known as bins.

Niche adaptation: in ecology and evolution, niche describes the range of conditions under which an organism can survive and reproduce. Various strategies, such as altering cellular structures and metabolic patterns, have emerged to meet the environmental constraints and in response to surrounding changes. The process in which an organism adapts itself to colonize the different niches is called niche adaptation.

Phyllosphere: a region that encompasses the above-ground parts of a plant colonized by microorganisms.

genus *Flavobacterium* to reach high relative abundance in terrestrial ecosystems and to actively participate in global carbon cycling [22]. Also the *Chitinophaga* genus is a key player in carbohydrate turnover in soil and especially abundant in the soil leaf litter layer which is often rich in plant and fungal biomass [11,56]. Soil Bacteroidetes also actively participate in underground phosphorus (P) dynamics and either contribute to or compete with plant P acquisition [41,57]. It was shown that plant-associated *Flavobacterium* species exhibited constitutive phosphatase activity that potentially allows them to overcome competition with other rhizobacteria and improve plant P uptake [41]. Moreover, Bacteroidetes may contribute to the regulation of soil nitrogen cycling, as several genera/species possess the *nosZ* gene that encodes the nitrous oxide reductase, an enzyme that can help to reduce the potent greenhouse gas nitrous oxide (N_2O) and expand the soil N_2O-sink capacity [58]. A recent study used a removal-by-dilution approach to manipulate microbial communities of barley [58]. More specifically, a serial dilution of soil suspension was inoculated to sterile soil in which higher dilution resulted in lower microbial diversity [58]. They found that some orders of Bacteroidetes, namely Chitinophagales, Cytophagales, Flavobacteriales and Sphingobacteriales, were enriched in the barley root microbiome, irrespective of the overall decrease in soil microbial diversity [58]. As nitrous oxide reducers, Bacteroidetes presented stable relative abundance and might play a key role in soil N-cycling [58]. Despite the role of these functional traits in nitrogen cycling and microbiome assembly, Bacteroidetes generally show strong negative responses to large input of nitrogen fertilizers in intensive agriculture [58,59]. For example, nitrogen addition leads to the decreased relative abundance of Bacteroidetes with exception of the order Sphingobacteriales [59].

Plant-growth-promoting rhizobacteria (PGPR): bacteria that live in the rhizosphere and enhance plant growth and/or protect plants from (a) biotic stresses through various mechanisms.

Plant-microbiome breeding programs: microbiome-based plant-breeding strategies that rationally select and manipulate plant genetic traits that recruit specific microbiomes and facilitate beneficial interactions to improve crop growth and resilience.

Rhizosphere: the narrow zone adjacent to plant roots directly influenced by root chemistry and associated microorganisms.

Association with host growth and development

In the past years, ‘the food connection’ or ‘one health’ concept has been coined to connect environmental, plant and animal microbiomes [60,61]. For aquatic and terrestrial environments, Bacteroidetes are found to be strongly associated with animal hosts such as human, fish, and insects [35,39,62]. Gut Bacteroidetes can have an impact on host growth by facilitating food digestion and nutrient acquisition. Various reviews have summarized the impact of diet on recruitment of certain microbiota, including Bacteroidetes [63,64]. Alike their environmental relatives, gut-associated Bacteroidetes have the ability to degrade complex polymers, thereby facilitating food digestion and nutrient acquisition, in particular constituents of vegetarian and vegan meals [65]. For example, Bacteroidetes are reported to be significantly enriched in the gut microbiota of African children from rural regions who consume fiber-rich diets [66]. Among gut Bacteroidetes, *Bacteroides thetaiotaomicron* was shown to employ a so-called ‘selfish’ strategy to keep the released sugar away from its competitors by secreting endo-acting enzymes consuming yeast mannan [67]. In addition, gut Bacteroidetes are generally considered less motile than their soil relatives, as they can attach to the mucosal layer and harvest passing glycans, while the latter are required to actively ‘hunt for food’ in the nutrient-heterogeneous soil environment [23]. Aquatic Bacteroidetes are abundant in the intestinal microbiome of some carp species that mainly feed on aquatic plants [39,68]. Remarkably, they were significantly enriched in the gut of Asian seabass under starvation [69]. This observation is likely due to the competitive advantages of Bacteroidetes in spite of limited nutrient sources, as they may outcompete other phyla due to their large enzymatic capacities in polysaccharide degradation for additional energy [69]. Within insects, Bacteroidetes have been described to act as symbionts, engaging in nutritional mutualism. The best-studied example encompasses Blattabacteriaceae as symbionts in specialized cells of the fat bodies of cockroaches [70]. These endosymbionts are vertically transmitted from mother to offspring and play an important role in nitrogen cycling for their hosts [70–72]. Interestingly, a recent study reported the distribution patterns of *Blattabacterium* among wild and pest cockroach species and speculated this endosymbiont may participate in nitrogen metabolism differently due to the different diets and lifestyles of their respective hosts [73]. The closely related obligate endosymbiont *Sulcia muelleri*, which is found in many sap-feeding insects, exchanges nutrients with the host and undergoes a symbiotic coevolutionary history of about 300 million years [62,74]. Bacteroidetes also live closely with plants, but their functions remain largely unknown. Bacteroidetes members, primarily Flavobacteria, Sphingobacteria and Cytophagia, displayed high relative abundance in the root endosphere of maize plants from organic fertilizer sites and exhibit beneficial effects on plant growth [75]. Bacteroidetes can degrade plant and fungal residues in the soil and convert them into more easily available forms, thereby providing necessary nutrients for plant growth and development. In this context, several publications have indicated that they contribute to the acquisition of carbon [22], nitrogen [58], and phosphate [41,57] (discussed in detail in the sections about nutrient cycling and enzymatic potential).

Association with host health and disease

The functional roles of Bacteroidetes in various infections and human metabolic health have been first explored in studies on the Bacteroidia class. For example, *B. fragilis* is an anaerobic pathogen, most frequently isolated in the abdominal cavity [76]. Members of *Prevotella*, *Tannerella* and *Porphyromonas* spp. can colonize the oral cavity, causing caries and periodontal diseases [77]. *Prevotella*, recognized as one of the core genera in the oral microbiome, also plays a role in health and disease of the respiratory and digestive tracts [32]. Although Bacteroidetes relative abundance is reported to be decreased in obese animals and subjects along with the compensation of Firmicutes [78], the Firmicutes/Bacteroidetes ratio is still under debate as a relevant marker for obesity [79]. Intriguingly, Bacteroidetes were relatively more abundant in the gut microbiota of children with autism spectrum disorder (ASD), although the observations were inconsistent across different studies [80–82]. It should be noted that these findings are mostly correlative and associative that do not necessarily imply causation [83]. Follow-up experimental work will give additional information to validate the causative dynamics and establish underlying molecular mechanisms. For example, it was shown that some Bacteroidetes species produce short-chain fatty acids that influence gut and brain functions [84]. These microbial-derived metabolites may induce biochemical changes such as increased oxidative stress and trigger autism-like behaviors including hyperactivity [80,85]. In addition to the impacts on human health, several Bacteroidetes members, especially *Flavobacterium* species, were shown to be pathogenic to fish. For instance, *Flavobacterium psychrophilum*, *F. branchiophilum*, and *F. columnare* are reported to cause cold-water disease, gill disease, and columnaris disease, respectively [86–89].

Bacteroidetes, and in particular the *Flavobacterium* genus, have recently received attention for their potential role as **plant-growth-promoting rhizobacteria (PGPR)** [45,48,52,90]. Metagenomic analysis of the tomato rhizosphere highlighted the involvement of *Flavobacterium* sp. TRM1 in disease suppression against the bacterial root pathogen *Ralstonia solanacearum* [45]. In another independent study, compelling evidence was presented for the role of endophytic Chitinophagaceae and Flavobacteriaceae in controlling fungal root infections of sugarbeet seedlings [48]. Moreover, metagenomic and transcriptomic analyses revealed enrichment for chitinase genes and a large number of yet unknown **biosynthetic gene clusters (BGCs)** encoding nonribosomal peptide synthetases (NRPSs) and polyketide synthases (PKSs) [48]. In addition, *Flavobacterium johnsoniae* GSE09 was shown to contribute to protection of pepper against *Phytophthora capsica*; the proposed underlying mechanism was the production of indolic compounds, biosurfactants, and biofilm formation [91]. Besides biotic stress alleviation, *Flavobacterium* can enhance tolerance to drought and salt stress in arabidopsis [92]. The treatment of *Flavobacterium crocinum* HYN0056^T led to the induction of stomatal closure, upregulation of stress-responsive genes, and development of lateral roots [92]. These induced physiological changes may facilitate more efficient and effective acquisition of water and nutrients for arabidopsis to survive the drought/salt stress conditions. In addition, members of the genus *Flavobacterium* are capable of producing growth-stimulating phytohormones like gibberellin, cytokinin, and auxin [93], which are considered to be signal molecules involved in root architecture alteration under abiotic stresses [94]. However, the relative importance of these bacterial metabolites in their interactions with plants is yet to be explored. In addition, *Flavobacterium* has been selected as a member of the simplified model system involving three bacterial species co-isolated from field-grown soybean roots to study community-level interactions [95,96]. Recent investigation showed that the dynamics and functions of this synthetic community may be modulated by and contribute to the regulation of secondary metabolism of the consortium members including *Flavobacterium* [97]. The expression of putative saccharide and/or fatty acid BGCs in *Flavobacterium* was significantly affected in the coculture, whereas other members were observed to be less responsive towards *Flavobacterium* alone [97].

Exploring the untapped genomic potential of Bacteroidetes

The **niche adaptations** and diverse (but largely putative) functions of Bacteroidetes are consistent with their **genomic diversity** and **genomic plasticity**. For example, the insect endosymbiont *S. muelleri* has a small genome of only 0.2 Mbp, comprising highly specialized metabolic functions, in particular the biosynthesis of essential amino acids [70,98]. In contrast, environmental Bacteroidetes tend to have larger genomes equipped with more broad metabolic traits to cope with higher fluctuations in the ecosystems [99].

Here we summarize genomic features of Bacteroidetes recovered from a range of ecosystems (Table 1) and highlight their enzymatic and biosynthetic potential.

Enzymatic potential

Notably in Bacteroidetes, polysaccharide utilization loci (PULs) – gene clusters encoding carbohydrate-active enzymes (CAZymes) – enable metabolism of complex glycans derived from plants, fungi, or plankton. In addition, PULs are often connected to the phylum-exclusive gliding motility, allowing the rapid secretion and release of CAZymes into the environment (reviewed in [23,54]). The gliding machinery stabilizes and energizes the secretion encoded by the type IX protein secretion system (T9SS) representing a unique molecular signature of intertwining cell movement and secretion [100]. Involved in cell movement and nutrient uptake, these molecular traits are vital for Bacteroidetes' survival and growth.

Bacteroidetes are abundant in aquatic environment and dominate during phytoplankton blooms [101]. Microalgae provide various polysaccharides (e.g., laminarin) as food resource to bacterioplankton during and after the bloom events. Their ability to degrade the algae-derived complex organic matter, using PULs with efficient SusC/D-like uptake systems, may play a pivotal role in the competitiveness of marine Bacteroidetes. Using time-series metagenome analyses, it was shown that an increased frequency and diversity of CAZymes along with the high abundance of Flavobacteriia during coastal spring algal blooms between 2009 and 2012 in the North Sea [101]. Among these Flavobacteriia, two *Formosa* strains were identified as specialized polysaccharide degraders. Following genome sequencing (2 Mbp and 2.7 Mbp, respectively), the laminarin-specific PULs were identified [30]. Interestingly, *Formosa* cells use laminarin not only as a major energy source, but also as a signal molecule to induce transporters and peptidases that boost the utilization of amino acids [30]. This uptake strategy leads to a balanced carbon–nitrogen diet that provides a competitive advantage for *Formosa* species in the algal blooms. In another study based on extended metagenomic and metaproteomic analyses, it was demonstrated that there was an association of marine Bacteroidetes and glycan utilization during algal blooms [31].

Table 1. Summary of genomic features of Bacteroidetes recovered from a range of ecosystems

Origin	Taxonomic lineage	Lifestyles	Physiological features	Genetic features	Refs
Soil	*Flavobacterium johnsoniae*	Free-living in soil or fresh water	Polysaccharide utilization (chitin and hemicelluloses), gliding motility	Large genome size (6.1 Mbp), 138 predicted glycoside hydrolases (GHs) and nine predicted polysaccharide lyases. The type IX secretion system (T9SS): Gld motors (encoded by *gld* genes) and cell surface adhesins (encoded by *sprB* genes)	[117,118]
	Cytophaga hutchinsonii	Free-living in soil	Cellulose utilization (digest insoluble crystalline cellulose), gliding motility	Large genome size (4.4 Mbp), periplasmic and cell-surface endoglucanases and novel cellulose-binding proteins. Core T9SS genes and motility-related genes	[119]
	Chtinophaga spp.	Plant litter	Chitin utilization	Large genome size (9.1 Mbp), 169 glycoside hydrolases belonging to 49 different GH families	[56]
Aquatic	*Flavobacterium columnare*	Fish pathogen	Anaerobic growth, nitrate respiration and biofilm formation	3.0–3.2 Mbp (including 1 plasmid pFB1)	[89,120]
	Flavobacterium psychrophilum	Fish pathogen	Pathogen of salmonid fish, psychrotrophic, gliding motility	2.8 Mbp (including 1 plasmid pCP1), stress response mediators, gliding motility proteins, adhesins and many putative secreted proteases are probably involved in colonization, invasion, and destruction of the host tissues	[86]
	Flavobacterium branchiophilum	Fish pathogen	Fastidious growth, nongliding, strictly aerobic, do not produce flexirubin-type pigments but produce carotenoid-type pigments	3.5 Mbp, *gld* and *spr* genes present (may actually be motile, but experimental conditions used so far failed to mimic natural conditions where gliding motility is expressed), 23 predicted GHs, presence of pigment biosynthesis gene cluster	[87]
	Flavobacteriace family: *Gramella*, *Polaribacter*, *Dokdonia*, and *Leeuwenhoekiella*	Free-living in oceans, abundant during and following algal blooms	Attachment to particles and degradation of polymers	Small genome size (around 3.0 Mbp), large number of GHs, peptidases and adhesion proteins, some use proteorhodopsin (PR) to obtain energy from light	[104]
	Candidatus *Sulcia muelleri*	Obligate symbiont of sap-feeding insect, tripartite symbiosis with coresident symbiont *Baumannia cicadellinicola* (Gammaproteobacteria)	Very likely cannot be cultured outside of the host	Very small genome (0.3 Mbp), complementarity of *Sulcia* and *Baumannia* in metabolic capabilities, lacks most genes for membrane synthesis and cell division control	[121]
Human/animals	Flavobacteria class: *Blattabacterium*	Cockroach endosymbiont	Key involvement in nitrogen metabolism and excretion in the cockroach host	Very small genome (0.6 Mbp), highly compact, strong reduction of gene numbers, presence of a complete urea cycle	[70,72]
	Bacteroidia class: *Bacteroides* spp.	Animal gut commensal and pathogen	Anaerobic. Degrade host-derived carbohydrates	Small and varying genome size. Polysaccharide utilization locus (PUL)	[122]

Chitinophaga genomes are well known for genes encoding chitinase and β-glucanases [102]. The large number of enzymatic capabilities of *Chitinophaga* makes it a promising bacterium for biotechnological purposes. Specific and rapid polysaccharide degradation is facilitated by PUL-encoded digestive enzymes in Bacteroidetes. Based on 13 537 PULs from 964 Bacteroidetes genomes, it was shown that Bacteroidetes can use thousands of enzyme combinations to break down glycans [103]. The authors proposed that functional profiling of CAZymes and PULs is instructive to predict the presence of specific polysaccharides as carbon sources for Bacteroidetes to aid in the next-generation prebiotics and symbiotics. More specifically, Bacteroidetes and other microorganisms may respond differently to specific glycans. Therefore, molecular characterization of the PULs and enzyme systems will shed light on microbial nutrient-uptake strategies and ecological interactions that can be engineered for novel enzyme discovery and tailored microbial therapies.

Comparative genomics studies showed that *Flavobacterium* have the functional capacity adapt to terrestrial environments by encoding a diverse group of glycoside hydrolases (GHs), whereas higher peptidase/GH ratios are found in the aquatic clade of the Bacteroidetes phylum [22,104]. Taking advantage of the rapidly growing number of sequenced (meta)genomes, large-scale comparative analyses could provide more information about the functional roles of enzymes in the host-associated lifestyles of environmental Bacteroidetes. For example, a recent comparative genomic study showed that plant-associated *Flavobacterium* is specialized in phosphorus (P) metabolism [41,57]. *Flavobacterium* strains were isolated from the rhizosphere of field-grown oilseed rape and all isolates showed constitutive phosphatase activity [41]. Together with outer membrane SusCD-like complexes and TonB-dependent transporters, several novel phosphatases were identified with inducible activity during orthophosphate (Pi)-starvation [41]. This may allow *Flavobacterium* to surpass other species in competition for P in the rhizosphere. More importantly, some of these proteins, such as the phosphatase PhoX, appear to be conserved across plant-associated *Flavobacterium* isolates. Hence, the phosphorus acquisition ability was proposed as an adaptive genomic signature in plant-associated Bacteroidetes [41].

Biosynthetic potential

The bioactivity and biosynthesis of diverse secondary metabolites isolated from Bacteroidetes have been recently reviewed by Brinkmann *et al*., providing an excellent summary and urge to revisit the Bacteroidetes phylum for future natural product discovery [105]. For example, biosynthesis of the pigment zeaxanthin has been shown to be involved in tolerance of glacial *Flavobacterium* isolates to extreme cold and high UV radiation [17].

In the work on genome-resolved metagenomics of the Earth's microbiomes, a total of 104,211 putative BGCs were predicted, among which 16,222 BGCs were associated with Bacteroidetes (Figure 2D), ranking second after Proteobacteria (37,888 BGCs) [7]. Most of the Bacteroidetes BGCs were predicted to encode PKSs and terpenes. In a recent genome mining study, it was revealed that Chitinophagia class has high biosynthetic potential encoding diverse BGCs [106]. By analyzing 600 publicly available Bacteroidetes genomes, they found hot spots of natural product biosynthesis in *Chitinophaga* with 15.7 BGCs per strain on average and discovered new nonribosomally synthesized cyclic lipopeptides (CLPs) referred to as chitinopeptins [106]. These bioactive compounds show iron-chelating properties and antimicrobial activity at 4–8 μg/ml against *Candida* species [106]. Collectively, these initial genomic and biochemical analyses are beginning to give more fundamental insights into the genomic traits underlying the adaptive capacity and functional diversity of Bacteroidetes associated with various environments and hosts. The yet unknown functional potentials of Bacteroidetes also pave the way for novel biotechnological exploitation in medical, industrial, and agrochemical applications.

Potential biotechnological applications of Bacteroidetes

Bacteroidetes is a phylum with a wide range of applications in different fields ranging from medicine to industry to agriculture. Hence, several genera and species are considered as a yet untapped resource for next-generation prebiotics and symbiotics for gut health [107,108]. Some strains are promising candidates in targeting infections and antibiotic-associated diarrhea. For instance, a non-toxic *Bacteroides fragilis* strain ZY-312 was shown to protect cell morphology from damage caused by pathogenic bacteria [109], and restore the dysbiotic gut microbiota composition by increasing the relative abundance of commensal microbiota [110]. Potential safety risks should be taken into consideration next to the beneficial traits of Bacteroidetes. Considering the animal pathogens among Bacteroidetes, especially the fish pathogenic *Flavobacterium* species, research on the virulence factors and mechanism underlying infection can give insights into the precaution and treatment for controlling severe disease outbreaks in aquaculture.

To date, polymer-degrading enzymes (e.g., protease, lipase, xylanase, amylase, cellulase, chitinase) produced by *Chitinophaga*, *Cytophaga*, and *Flavobacterium* are a major focus of biotechnological applications. In particular, the cold-active enzymes produced by Bacteroidetes receive much attention [111]. For example, psychrophilic Bacteroidetes could be employed for biodegradation of wastes at low temperature or for the production of anti-freezing compounds for food preservation and cryo-surgery. A recent report on *B. vulgatus* has pointed its promising function in H_2 production via dark fermentation [112].

Bacteroidetes has been proposed as an ecologically important player in soil functioning and are therefore recommended as a biological indicator of agricultural soil health [113,114]. More specifically, metagenomic analysis revealed that the abundance of Bacteroidetes was significantly affected by agricultural practices in arable soils [113]. In addition, to serve as a biological indicator, Bacteroidetes are potential candidates for microbial inoculants to replace traditional fertilizers and pesticides. For example, several *Flavobacterium* strains show promising effects on plant growth and stress alleviation of drought, salt and various bacterial or fungal diseases [45,48,92]. It remains challenging to establish and maintain single strains in competition with the indigenous microbiomes [115]. The intra- and inter-phylum interactions between Bacteroidetes and other microbial residents are worthy of further research to disentangle their role in plant microbiome assembly. The unique nutrient utilization strategies and motility patterns of Bacteroides members provide a basis of their active participation in these community interactions. Moreover, the importance and central roles of Bacteroidetes in natural or synthetic communities suggest their great yet understudied potential in managing soil health and promoting plant growth [48,97]. Unraveling the plant genes, phenotypic traits and chemical cues involved in the recruitment of beneficial Bacteroidetes will greatly contribute to the design of so-called **plant-microbiome breeding programs** aimed at selecting specific traits that enrich for beneficial Bacteroidetes and other plant-associated microbes [44,116].

Concluding remarks and future perspectives

Bacteroidetes species greatly vary in morphology, physiology, diversity, and niche distribution and can perform highly diverse functions, ranging from global nutrient cycling (including carbon, nitrogen, and phosphate) to positive or adverse effects on host growth and development. With this review we intended to draw more attention to environmental Bacteroidetes, especially those living in close association with plants and food crops, and highlight their role in (a)biotic stress tolerance. Bacteroidetes is trending in microbiology research due to their exceptional adaptive capacity to proliferate in diverse environments, whereas genetic determinants underlying the various lifestyles are not yet clear. Moreover, the mechanistic understanding of their functional roles in interkingdom interactions remains largely elusive (see Outstanding questions).

Outstanding questions

What are the functional differences and commonalities between Bacteroidetes from animal, plant, and environmental origin?

What are the genetic determinants of the different lifestyles of Bacteroidetes?

Are there specific genes involved in pathogenic and/or beneficial activities in Bacteroidetes?

To what extent do Bacteroidetes contribute to the protection of plants exposed to (a)biotic stresses?

How do Bacteroidetes interact with other members of the plant microbiome, and what are the underlying mechanisms of plant domestication on the observed depletion of Bacteroidetes in the plant microbiome?

How to explore and exploit the yet untapped functional potential of Bacteroidetes?

Deciphering the large, yet unexplored genomic diversity and functional potential of host-associated Bacteroidetes will uncover the molecular dialogues with various hosts which in turn will aid in the development of novel biotechnological, medical, and environmental applications of this understudied bacterial phylum.

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Declaration of interests

No interests are declared.

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