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Review

Exchange or Eliminate: The Secrets of Algal-Bacterial Relationships

Bertille Burgunter-Delamare [1,*], Prateek Shetty [1,2], Trang Vuong [1] and Maria Mittag [1,2,*]

[1] Matthias Schleiden Institute of Genetics, Bioinformatics and Molecular Botany, Friedrich Schiller University Jena, 07743 Jena, Germany; prateek.shetty@uni-jena.de (P.S.); trang.vuong@uni-jena.de (T.V.)
[2] Cluster of Excellence Balance of the Microverse, Friedrich Schiller University Jena, 07743 Jena, Germany
* Correspondence: bertille.burgunter-delamare@uni-jena.de (B.B.-D.); m.mittag@uni-jena.de (M.M.)

Abstract: Algae and bacteria have co-occurred and coevolved in common habitats for hundreds of millions of years, fostering specific associations and interactions such as mutualism or antagonism. These interactions are shaped through exchanges of primary and secondary metabolites provided by one of the partners. Metabolites, such as N-sources or vitamins, can be beneficial to the partner and they may be assimilated through chemotaxis towards the partner producing these metabolites. Other metabolites, especially many natural products synthesized by bacteria, can act as toxins and damage or kill the partner. For instance, the green microalga *Chlamydomonas reinhardtii* establishes a mutualistic partnership with a *Methylobacterium*, in stark contrast to its antagonistic relationship with the toxin producing *Pseudomonas protegens*. In other cases, as with a coccolithophore haptophyte alga and a *Phaeobacter* bacterium, the same alga and bacterium can even be subject to both processes, depending on the secreted bacterial and algal metabolites. Some bacteria also influence algal morphology by producing specific metabolites and micronutrients, as is observed in some macroalgae. This review focuses on algal-bacterial interactions with micro- and macroalgal models from marine, freshwater, and terrestrial environments and summarizes the advances in the field. It also highlights the effects of temperature on these interactions as it is presently known.

Keywords: antagonism; brown algae; diatoms; dinoflagellates; green algae; haptophytes; mutualism; primary metabolites; red algae; secondary metabolites

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Citation: Burgunter-Delamare, B.; Shetty, P.; Vuong, T.; Mittag, M. Exchange or Eliminate: The Secrets of Algal-Bacterial Relationships. *Plants* **2024**, *13*, 829. https://doi.org/10.3390/plants13060829

Academic Editor: Stefano Accoroni

Received: 20 February 2024
Revised: 9 March 2024
Accepted: 11 March 2024
Published: 13 March 2024

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1. Introduction

1.1. Definition, Phylogeny, Distribution, and Relevance of Algae

'Algae' refers to a heterogeneous polyphyletic group of photosynthetic eukaryotes excluding land plants (Embryophyta). Characterized by the absence of typical plant organs such as leaves, stems, or roots [1,2], they are derived from primary and secondary endosymbiosis [3], which can be succeeded by higher-order—tertiary, quaternary—endosymbioses [4]. In primary endosymbiosis, a cyanobacterium was engulfed by a eukaryotic cell, while in secondary endosymbiosis, a green or red alga was engulfed by a eukaryotic cell. Algae derived by primary endosymbiosis include the green and red algae, as well as the glaucophytes [2,3,5]. Secondary endosymbionts of the green lineages comprise the Chlorachniophytes and the Euglenoids. The red lineage includes the Cryptophytes, Haptophytes, Dinoflagellates, and Stramenopiles. The Stramenopiles are the most species-rich clade, including diatoms, brown algae, xanthophytes, and other ochrophytes [2,3,5]. Through repeated endosymbiotic events, plastids spread through the eukaryotic tree of life, spanning more than 1.6 billion years of evolution [4].

Algae are also grouped into micro- and macroalgae. Their sizes can range from extremely small, such as the picoalga *Ostreococcus* (0.8 µm) [6], to giant kelps with fronds up to 60 m in length [7]. The number of algal species has been estimated to exceed one million, with most of them being microalgae [8,9]. Algae are prominent in bodies of water, such as oceans, rivers, and lakes [7,10], and are also common in terrestrial environments [11,12]. Algae can be found on snow and ice [13], and even in the desert [14].

Algae play a significant role in global annual primary production; together with cyanobacteria, they contribute to about 50% of CO_2 fixation on Earth [15]. As primary producers, algae are at the base of food webs [16]. Algal activities also affect biogeochemical processes, as observed with the accelerated melting of the Greenland ice sheet [17]. In the ocean, they participate in nutrient [18], carbon [19–21], and sulfur cycles [22,23]. Macroalgae and kelps, in particular, are ecosystem engineers and habitat builders that shelter various forms of life [24–26].

Algae are strongly affected by climate change; along with the increased temperatures, there is a decrease in natural populations of kelp, such as *Saccharina latissima* [27,28], and there is coral reef bleaching due to the loss of the algal symbiont (see Section 3.3). Climate-driven shifts in algal-bacterial interactions were also reported over ten years [29].

Algae are used as food [30,31] and feed [32,33], as texture agents [34,35], in biomaterial [36,37], in medicine [38,39], as fertilizer in agriculture [40–42], in biofuel and hydrogen production [43–45], and in pollution control and bioremediation [46,47].

1.2. The Phycosphere and Algal-Microbial Interactions

The phycosphere is the region immediately surrounding an algal cell within a phytoplankton or in soil. It is enriched in organic molecules exuded by the cell into the surrounding water [48,49]. In this microenvironment, organisms interact via chemical compounds, such as signaling molecules, nutrients, toxins, morphogens, defense compounds, and quorum-sensing signals [50–53]. These infochemicals can reach significantly higher concentrations than those measured in bulk seawater, generating chemical gradients that can be detected by marine microbes [48,54].

Bacteria can detect and navigate towards favorable chemical gradients in their immediate surroundings through a process known as chemotaxis. This involves the utilization of transmembrane chemoreceptors, which enable bacteria to measure concentrations of chemicals. Subsequently, signal transduction systems process this information, allowing bacteria to precisely modulate their motility in response to perceived chemical gradients [48,55,56]. Algae, especially flagellate ones, also react to chemicals by tactic processes [57,58].

The algal host and its associated microbiota are collectively called holobiont [25,59–61], and biotic interactions within such a system are drivers of algal evolution [62]. Host-microbe interactions are grouped into "positive", "neutral", and "negative" interactions, called mutualism, commensalism, and antagonism, respectively [63–65].

Mutualism refers to a symbiotic relationship between bacteria and microalgae, in which both organisms gain advantages, irrespective of which partner receives greater benefits. This natural symbiosis typically evolves gradually over an extended period, remaining relatively stable across several generations [66].

Commensalism describes a relationship in which only one symbiotic partner benefits, while the other is unaffected. Algal-bacterial associations can transition between mutualism and commensalism, depending on environmental factors [67].

A relationship marked by **antagonism** occurs when one partner adversely affects or harms the other. Presently, limited research is dedicated to the algal antagonism on bacterial partners. One bulk of research studies focuses on the detrimental effects of extracellular degrading enzymes produced by interacting bacteria, which induces lysis of algal cell walls [68,69], but knowledge about algicidal bacteria that use secondary metabolites as toxins also emerges (e.g., [70,71]).

Partners of algae include viruses [72–75] and bacteria [12,25,76], as well as eukaryotic organisms such as fungi [77–80] or even sloths [81]. For this review, we will focus on the bacterial partners of algae. While algae and bacteria have coexisted since the early stages of evolution, we still have limited knowledge about their detailed modes of interaction. Here, we have selected exemplary model species of micro- and macroalgae from terrestrial, freshwater, and marine environments and will present the current knowledge about their relationships with bacteria (Figure 1). We are aware that more model species have emerged; however, these are beyond the scope of this review (e.g., [2,82,83]).

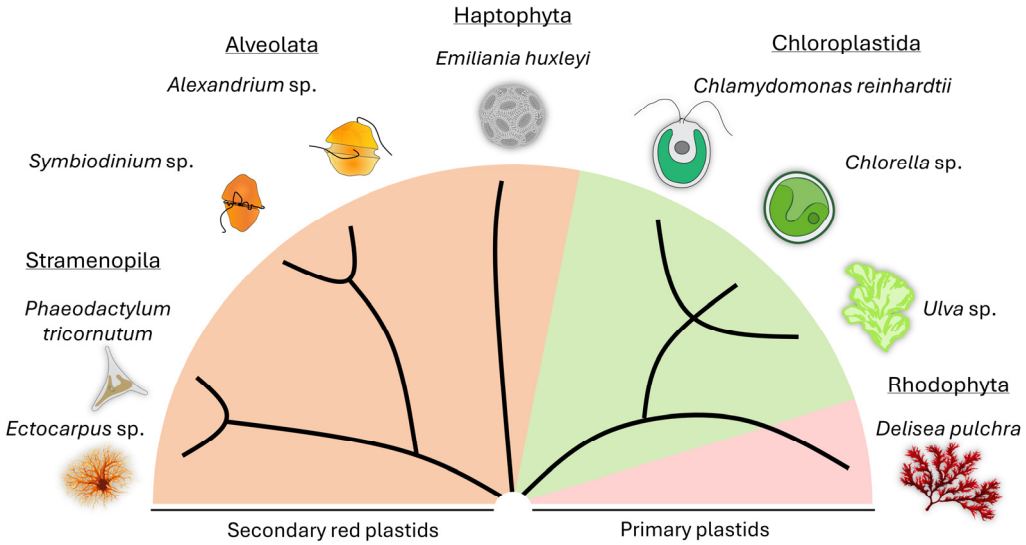

Figure 1. Representative micro- and macroalgal models used for studying algal-bacterial interactions are highlighted, along with their phylogenetic background. A simplified cladogram scheme derived from a phylogenetic tree [84] was taken as a basis.

2. Terrestrial and Freshwater Microalgae

2.1. The Green Microalga Chlamydomonas reinhardtii Emerges as a Soil Model

For decades, the biflagellate microalga *C. reinhardtii* has been used as a model for specific biological processes, including, for example, photosynthesis, cilia formation and function, and light-driven processes [85]. The alga can be genetically manipulated, its genome is annotated, and many molecular tools and large-scale mutant libraries are available [86–89]. Moreover, genetic crosses can be easily performed [90]. Although it is usually grown in liquid culture in the laboratory, in nature, it is mostly found in inhomogeneous wet soil [91]. It was originally isolated from a potato field in Massachusetts, USA [90].

In the past years, this microalga emerged as a model for studying microbial interactions [12,63,92], including algal-bacterial relationships. Its phycosphere was comprehensively studied by cultivating *C. reinhardtii* in soil [49], and this approach allowed for the identification of the diverse bacterial partners selected by the algal host. The algal phycosphere microbiome was then compared against the rhizosphere microbiome associated with roots of *Arabidopsis thaliana*. Surprisingly, the analysis revealed a notable overlap in the microbiome between the land plant and the chlorophyte alga, despite their evolutionary distinctiveness. Both host-associated bacterial microbiomes were dominated by Proteobacteria (Pseudomonodata), along with members of the Actinobacteria (Actinomycetota), Bacteroidetes (Bacteroidota), and Firmicutes (Bacillota) phyla [49]. These data provide an important insight into the complexity of the algal rhizosphere and reveal common bacterial communities compared to land plants.

In many investigations, dual interactions of *C. reinhardtii* and a specific bacterium were studied; mutualistic, as well as antagonistic, interactions were hereby in focus, and examples for both will be presented. In mutualistic interactions, *C. reinhardtii* has been reported to offer carbon sources in exchange for bacterial metabolites [12]. Cobalamin (vitamin B_{12}) is a critical metabolite required for many cellular processes [93]. Most eukaryotic algae are cobalamin auxotrophs and must receive cobalamin exogenously or through bacterial cooperation. *C. reinhardtii* requires vitamin B_{12} for the B_{12}-dependent methionine synthase called METH. As *C. reinhardtii* also encodes METE, a B_{12}-independent methionine synthase, wild-type algae do not necessarily require exogenous B_{12}; however, *metE* mutants must obtain vitamin B_{12} [94]. A recently evolved B_{12}-dependent *C. reinhardtii* strain, *metE7*, thus establishes a mutualism with some bacteria, one of them being the rhizobium *Mesorhizobium loti* [95]. Heat stress represses *METE* gene expression; consequently, vitamin B_{12} is essential for heat-treated algal cells [96]. *C. reinhardtii* becomes thermally tolerant via a mutualistic

interaction with vitamin B_{12}-producing bacteria such as *Ensifer meliloti*. In this context, it is also interesting that *C. reinhardtii* synthesizes mimics of *N*-acyl-1-homoserine lactones (AHL) that stimulate quorum sensing in *E. meliloti* [97]. By quorum sensing, bacteria sense cell population numbers and react to them.

In addition to vitamins, *C. reinhardtii* profits from nitrogen sources provided by N-fixing bacteria or through N-mineralizing bacteria. For example, the diazotroph *Azotobacter chroococcum* and other *Azotobacter* species establish a mutualism with *C. reinhardtii* when any C- and N-sources are omitted in the growth media (reviewed in [12]). While *C. reinhardtii* can grow on nitrate, nitrite, ammonium, and certain amino acids, it cannot metabolize proline, hydroxyproline or peptides bearing these amino acids [98]. In coculture with *Methylobacterium* spp., the algae can grow on these substrates by establishing a mutualistic relationship with the bacterium and offering glycerol. Indole-3-acetic acid (IAA, also known as auxin) is synthesized by the algal cells via an extracellular enzyme; it inhibits algal growth, while *Methylobacterium aquaticum* degrades auxin in the presence of the alga. Thus, auxin mediates the mutualism between both microorganisms [99]. Recently, it was shown that *Microbacterium forte* sp. nov. also forms a mutual relationship with *C. reinhardtii* and even promotes algal hydrogen production [100].

Besides mutualistic interactions, antagonistic interactions with bacteria also emerged for *C. reinhardtii*. Among three examined species of the genera, *Flavobacterium*, *Xanthomonas*, and *Pseudomonas*, *P. protegens* (Pf-5) turned out to act algicidal [70]. A cocktail of toxic natural products of *P. protegens* is involved in the bacterial attack on the algae (Table 1) [70,101–103]. They all change the algal cell morphology, or even lyse the cells (in the case of protegencin) and influence algal growth; some secondary metabolites immobilize the algal cells (Table 1). The cyclic lipopeptide orfamide A causes the strongest immobility of algal cells with the lowest IC_{50} value [102]. Orfamide A triggers an increase in cytosolic Ca^{2+} that results in the deflagellation of the algal cells and thus renders them immotile [70,103]. Remarkably, this reaction takes place within a minute. In contrast to other cyclic lipopeptides, orfamide A does not seem to cause membrane pores [70]. The action of orfamide A depends on Ca^{2+} channels of the transient receptor potential (TRP)-type, including TRP5, TRP11, TRP15 (also known as ADF-1), and TRP22 [104]. For its activity, the N-terminal amino acids of the linear part and the terminal fatty acid tail of orfamide A are highly important [104]. One of the most potent toxins of *P. protegens* is the polyyne protegencin [101]. Protegencin acts within several hours; it blinds the cells by destroying their eyespot and lyses them [101]. This rather unstable toxin could be identified by Raman microspectroscopy, as such triple-bond-containing compounds appear in the silent region of the Raman spectrum [101].

Table 1. Bacterial toxins from *P. protegens* and their effects on *C. reinhardtii*.

Toxin	Nature of Chemical Compound	Effect
Orfamide A [70,102,103]	Cyclic lipopeptide	Inhibits algal growth on plates and in liquid culture Changes cell morphology Inhibits algal motility (IC_{50} 4.1 µM) Deflagellates algal cells
Protegencin [101]	Polyyne	Inhibits algal growth in liquid culture Destroys the algal eyespot Lyses the algal cells
Pyoluteorin [102]	Natural antibiotic (hybrid stemming from a nonribosomal peptide synthase and a polyketide synthase [105])	Inhibits algal growth on plates and in liquid culture Changes cell morphology Inhibits algal motility (IC_{50} 95 µM) Deflagellates algal cells

Table 1. *Cont.*

Toxin	Nature of Chemical Compound	Effect
Pyrrolnitrin [102]	Phenylpyrrole compound	Inhibits algal growth on plates and in liquid culture Changes cell morphology Inhibits algal motility (IC_{50} 20 µM) Deflagellates algal cells
Rhizoxin S2 [102]	16-membered lactone ring connected to an oxazole ring by a long unsaturated chain [106]	Inhibits algal growth on plates and in liquid culture Changes cell morphology
2,4-Diacetylphloroglucinol [102]	Phenol compound	Inhibits algal growth on plates and in liquid culture Changes cell morphology Inhibits algal motility (IC_{50} 350 µM)

Recently, another algicidal bacterium, *Paenibacillus polymyxa* MEZ6, was detected in soil samples. It acts against *C. reinhardtii* and other microalgae, including *Haematococcus pluvialis* and *Chlorella ellipsoidea* [107]. In this context, it should also be mentioned that orfamide A from *P. protegens* deflagellates not only *C. reinhardtii* but also a marine *Chlamydomonas* sp., as well as *Haematococcus pluvialis* and *Gonium pectorale* from the Chlorophyceaea, but not selected members from the Pedinomonaceae and Euglenophyceae [70].

Another bacterium that is antagonistic against *C. reinhardtii* is *Streptomyces iranensis*, which secretes the algicidal marginolactone azalomycin F when co-cultivated with the algal cells [108]. In tripartite cultures with the fungus *Aspergillus nidulans*, the algal cells get shielded from the bacterial toxin. These data emphasize the influence of additional partners in algal-bacterial interactions. An azalomycin F resistant fungus is needed to protect the alga [71]. The alga uses an alternative strategy when no fungus is present. In this case, a specific type of palmelloid, called a gloeocapsoid, is formed [108]. It has been postulated that the margolactone-triggered formation of such cell aggregates may have contributed to the evolution of multicellular colony-forming algae such as *Eudorina* or *Volvox* [108].

2.2. The Freshwater Green Alga Chlorella sp. and Its Potential for Biotechnology via Bacterial Interactions

Chlorella is a unicellular, non-motile green alga found in freshwater environments. The genomes of several species, including *C. vulgaris* [109], *C. sorokiniana* [110,111], and *C. variablis* [112] have been completely sequenced and characterized. Unlike *Chlamydomonas*, *Chlorella* cannot reproduce sexually; however, various transformation techniques exist to simplify genetic manipulation. The first successful attempt to genetically transform *C. vulgaris* used the electroporation technique; however, the rigid cell wall of *Chlorella* can hinder the efficiency of electroporation-based transformations [113]. Thus, cellulase was used to degrade the cell walls of *C. ellipsoidea*, facilitating the exogenous DNA uptake and leading to transformation [114]. More recently, *Agrobacterium* [115] and CRISPR-Cas9 [116] systems have been effectively employed to transform *C. sorokiniana* and *C. vulgaris*.

Members of the genus *Chlorella* have found utility across a wide array of biotechnology fields, including human and animal nutrition, bioremediation, and the production of antimicrobial compounds. Thus, there has been a persistent search for bacterial partners capable of improving either the macromolecule properties of *Chlorella* or nutrient uptake by algal-bacterial consortia.

The foremost study into the *Chlorella* phycosphere identified 29 distinct bacterial isolates from non-axenic *C. sorokiniana* cultures. These bacterial strains encompassed various genera, including *Pseudomonas*, *Acinetobacter*, *Flavobacterium*, and *Bacillus* [117]. Recent studies have investigated the effect of pairwise cocultivation on algal growth and utilized xenic *Chlorella* cultures to further explore the diversity of bacteria coexisting with *Chlorella*. Cocultivation with *Ralstonia* sp. has been shown to promote the development

of *C. sorokiniana* [118], while *Brevundimonas* sp. has been found to stimulate the growth of *C. ellipsoidea* [119] and *C. vulgaris* [120]. Additionally, pairwise cultivation with *Bacillus pumilus* promotes the growth of *C. vulgaris* [121]. However, the precise mechanism of growth promotion still needs to be discovered for these pairwise combinations.

One of the most well-studied associations is between *Chlorella* and *Azospirillum brasilense*. *A. brasilense* is a well-established plant growth-promoting diazotrophic bacteria, capable of increasing the growth of 113 plant species [122]. The earliest report of *A. brasilense*-induced algal growth promotion comes from a study involving the co-immobilization of *A. brasilense* and *C. vulgaris* within alginate beads. The co-immobilization increased the total number of algal cells and pigments [123]. Subsequent research confirmed that the exudation of auxin by *A. brasilense* played a crucial role in promoting the growth of *C. vulgaris* [124]. Furthermore, transcriptomic investigations identified that IAA exudation also induces the Type 6 secretion system (T6SS1) of *A. brasilense* [125]. The T6SS is a complex multi-protein machinery crucial for modulating bacterial competition, fostering symbiotic relationships, and discerning between bacteria of the same or different species. Structurally similar to a phage tail, it enables the host bacteria to translocate effector molecules and proteins into both prokaryotic and eukaryotic cells. T6SS1 plays a pivotal role in promoting attachment between *A. brasilense* and *C. sorokiniana*, forming a physical bond between the algae and the bacterium consortium [126]. Mutants lacking T6SS1 genes exhibited reduced IAA exudation, indicating a reciprocal relationship between IAA biosynthesis and the T6SS gene cluster. While the mutant *A. brasilense* could promote algal growth, it could not induce the accumulation of carbohydrates, lipids, and proteins like the wild type, suggesting that the effector molecules and IAA were essential for these processes. However, the specific effector molecules released from T6SS1, which lead to the physiological changes observed in *C. sorokiniana*, remain elusive.

Interestingly, coculturing is not essential to promote the growth of *Chlorella*, as *A. brasilense* can release a whole collection of volatile organic compounds (VOCs). When exposed to these VOCs, *C. sorokiniana* exhibited enhanced growth and accumulation of total carbohydrates, lipids, and chlorophyll. This enhancement can be attributed to the presence of known plant growth-promoting VOCs such as 2,3-butanediol and acetoin, which are released by *A. brasilense* [121].

Chlorella finds immense utility as a phytoremediation agent, even though the comparatively low abundance of micro-nutrients such as iron and vitamins can hinder sustained phytoremediation. Also, algae cannot secrete chelating agents to solubilize inorganic iron [127]. In contrast, heterotrophic bacteria can produce low molecular weight chelating agents or siderophores. Siderophore-mediated iron chelation enhances the formation of bioavailable iron complexes, which algae can then absorb through plasma membrane-bound ferrireductase [128]. Consequently, the introduction of siderophore-producing *Ralstonia pickettii* establishes a mutualistic relationship whereby the bacteria benefit from the photosynthetically fixed algal exopolysaccharides while reciprocally enhancing the growth and degradation of complex azo dyes by *C. sorokiniana* [129].

It is essential to highlight that not all interactions mutually benefit both partners. In 1972, Gromov and Mamkaeva first described *Vampirovibrio chlorellavorus*, a predatory cyanobacterium with a distinct evolutionary path compared to other cyanobacteria [130]. Unlike its counterparts, *V. chlorellavorus* has completely lost its photosynthetic apparatus and instead adapted into an obligate parasite of *Chlorella*. Upon attachment to the cell wall of *Chlorella*, it uses a type 4 secretion system to form a conjugative apparatus. It can then release over 100 different hydrolytic enzymes, including proteases and peptidases, to digest its prey. Subsequently, the bacterium ingests algal lysates to aid in bacterial binary fission and plasmid replication, and finally, bacterial offsprings are released from the algal host cells to continue the cycle [131].

3. Marine Microalgae

Phytoplankton communities can be found in the photic zones of the oceans and are characterized by the interactions of microalgae and bacteria that coevolved and shaped the planktonic microbiome [64]. Chemical mediators, such as sulfur metabolites exchanged between the algae and bacteria, play an important role [132–134].

3.1. Phaeodactylum tricornutum: A Phytoplankton Diatom Model for Microbial Interactions

Diatoms, prominent microalgae in the oceans, are a key population of phytoplankton. Bacteria have the capacity to either promote or inhibit their growth and proliferation [135,136], and diatoms can also change their metabolic profile in response to bacteria [137]. Among these microalgae, the pennate *Phaeodactylum tricornutum*, with its diverse morphotypes, alongside the centric *Thalassiosira pseudonana*, has emerged as a model for diatom research [10,138,139]. The focus here will be on *P. tricornutum,* as it was used as a model in many algal-bacterial interactions. Its genome is known [140], it can be transformed biolistically and by electroporation, and many molecular tools are available [10,141–143]. Ten isolates from nine different geographic locations (seashores, estuaries, rock pools, and tidal creeks) worldwide, spanning from sub-polar to tropical latitudes, have been accessioned and well-described for this diatom [144].

The effect of different bacteria on *P. tricornutum* was investigated through algal-bacterial cocultures, identifying the presence of both mutualistic and antagonistic bacteria. The algal-bacterial interactions influenced intracellular lipids, as well as extracellular metabolites [145]. Phytoplankton-derived dissolved organic matter (DOM) is dependent on the algal strain [146]. Thus, DOM from some studied photosynthetic bacteria and the diatoms *Thalassiosira* and *Phaeodactylum* revealed a high complexity and strain dependence. It was also shown that the micro-environment plays an essential role in the bacterial interaction of *Phaeodactylum.* Introducing a polymer-based porous microtiter plate increased algal cell abundance and spatially influenced algal-bacterial interactions [147]. Moreover, exometabolites from *P. tricornutum* can influence bacterial communities, as they can act as selective bacterial growth substrates [148]. Exopolysaccharides were found to represent the largest fraction of microalgal exudates. In a coculture of *P. tricornutum* and the bacterium *Pseudoalteromonas haloplanktis*, the exo-environment described by exo-monosaccharide profiles varied depending on the culture condition [149]. This bacterium can utilize diatom-released compounds [150]. Algal-derived dissolved organic carbon and nitrogen and bacterial incorporation of these remineralized compounds were studied with *P. tricornutum* and several different bacteria. These studies defined three groups: macromolecule remineralizers, macromolecule users, and small-molecule users [151]. The relevance of dissolved organic nitrogen compounds was also shown with *Rhodobacteriaceae*-type strains that interact with *P. tricornutum* and can degrade such compounds [152].

Some bacteria act algicidal on *P. tricornutum*, such as *Kordia algicida*, which releases an algicidal protease [69]. Moreover, there are also secondary metabolites that act antagonistic. For example, the release of 2-heptyl-4-quinolone from marine bacteria causes inhibition of the cytochrome b_6f complex in *P. tricornutum* and inhibition of its respiration [153].

3.2. The Coccolithophore Emiliania huxleyi: An Algal Chameleon

Coccolithophore haptophyte algae such as *E. huxleyi* are key contributors to global carbon fluxes and are essential for biogeochemistry [154]. *E. huxleyi* is ecologically highly relevant; it can form large blooms that are even visible from space. The pangenome of the *E. huxleyi* reference strain CCMP 1516 and of 13 additional isolates has been sequenced [155]. A transformation method via electroporation based on a virus approach was also established [156].

One of the first fascinating reports dealt with the interaction of *E. huxleyi* with a Roseobacter clade bacterium named *Phaeobacter gallaeciensis*, also known as *P. inhibens* [157]. The bacterium supports algal growth via an algal growth promotor, phenylacetic acid, and an antibiotic that protects the host from bacterial pathogens called tropodithietic acid

(TDA). In return, the algal cells provide dimethylsulfoniopropionate (DMSP), as C- and S-sources, and a biofilm surface to the bacteria [158,159]. It was also found that auxin plays a role in both the growth promotion of *E. huxleyi* by *P. inhibens* and the ultimate death of the algae [160]. *E. huxleyi* cells exude tryptophan in normal conditions, increasing the bacterial production of IAA and attachment to the algae. When high concentrations of IAA are reached, the algal cell will enter a senescence stage and produce *p*-coumaric acid, which initiates the synthesis of bacterial roseobacticides. These secondary metabolites are algicidal. Thus, the aging algae convert *P. inhibens* into a pathogen [158] (Figure 2). Interestingly, the synthesis of the roseobacticides is based on algal and bacterial precursor biomolecules [159]. Moreover, the genes required for TDA synthesis are also necessary for producing roseobacticides. Here, one gene cluster synthesizes two biomolecules that differ in structure and function [161].

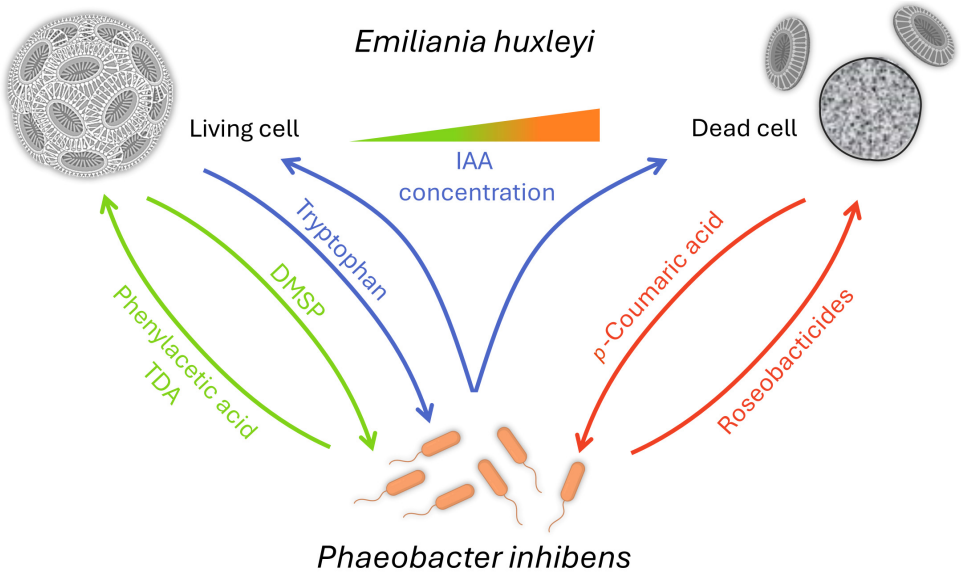

Figure 2. How bacterial friends turn into foes—from mutualism to antagonism [158,159,162]. *E. huxleyi* cells provide a biofilm surface and DMSP for its bacterial partner *P. inhibens* in healthy conditions. In return, the bacteria will provide the growth factor phenylacetic acid and the antibiotic TDA. In normal conditions, *E. huxleyi* cells also exude tryptophan, increasing the bacterial production of IAA and attachment to algae. When high concentrations of IAA are reached, the algal cell will enter a senescence stage and produce *p*-coumaric acid, triggering the production of the algicidal roseobactericides by *P. inhibens*.

Remarkably, associated bacterial communities can protect *E. huxleyi* from the pathogen, such as the helper bacteria *Sulfitobacter pontiacus* [163]. *P. inhibens* can also influence the production of algal alkenone lipids that play a role in estimating sea surface temperature. Unsaturated alkenones are increased in algal-bacterial cocultures, leading to changes in growth temperature up to 2 °C compared to axenic cultures [162]. A bacterial lifestyle switch with *E. huxleyi* was also observed with *Sulfitobacter* D7 [164], where algal DMSP is involved in the switch to pathogenicity. Notably, algal-produced benzoate promotes the growth of the bacterium and hinders the DMSP-caused switch [164]. The diversity of bacterial communities present in an *E. huxleyi* bloom was also studied, and the initial inoculum plays a major role in shaping the microbiome community [165]. These data emphasize that algal-bacterial relationships can transition between mutualistic and antagonistic states within the algal lifespan. Furthermore, they highlight the relevance of the surrounding bacterial microbiome as present in nature.

3.3. Dinoflagellate Symbiotic Symbiodiniaceae and Toxic Alexandrium sp.

Dinoflagellates are found in freshwater and oceans as a significant part of phytoplankton. They are distinguished by their enormous genome sizes, which can be attributed to the presence of hundreds of gene copies. This includes, for example, the gene encoding the luciferin-binding protein found in *Gonyaulax polyedra* [166], nowadays called *Linguludinium polyedra*. The genomic and transcriptomic characterization of a dinoflagellate genome from the toxic *Alexandrium ostenfeldii* revealed tandem repeats covering more than half of the genome [167]. Some of these microalgae are bioluminescent [168,169], and others live in symbiosis with cnidarians in reef-building corals [170]. Coral reef symbionts include mainly members from the dinoflagellate family of Symbiodiniaceae [171], whose genomes have been analyzed [172,173]. Interestingly, the associated bacterial microbiomes are distinct across symbiotic states [174].

Coral reefs are very susceptible to ocean warming, and the loss of the dinoflagellate symbiont due to climate change results in coral bleaching [170]. There is evidence that bacterial communities that are associated with Symbiodiniaceae react to heat selection and may contribute to coral adaptation to altered temperatures [175]. Increased temperature also affects the bacterial microbiome of the red tide-causing *Alexandrium minutum* [176], highlighting that global temperature increases will perturb dinoflagellate ecology significantly.

As already indicated above, some dinoflagellates, including the *Alexandrium* species, are highly toxic and dominate harmful algal blooms, also known as red tides [177]. Bacteria are usually associated with these toxic species of *Alexandrium*, such as *Pseudosulfitobacter koreense* sp. nov., together with *A. pacificum* [178] or *Haliea alexandrii* with *A. catenella* [179]. *A. catenella* produces saxitoxin and is related to shellfish poisoning, which is also highly dangerous for human consumption [180]. It was found that some marine lytic bacteria from the Proteobacteria and Cytophaga group are closely associated with this dinoflagellate. Interestingly, a change from a high-nutrient medium to a medium without organic nutrients turns them into symbiotic partners [180]. Harmful algal blooms with *A. fundyense* influence the relative abundances of bacteria and phytoplankton by repressing and promoting different taxa [181]. Microbiome stability was also investigated with an axenic strain of *A. tamarense*, to which the intact microbiome was reintroduced. Interestingly, the original microbiome was not restored; instead, a bacterial community shift to the Roseobacter clade was observed [182]. These studies show that understanding dinoflagellate-bacterial interactions is the key to understanding the biology and ecology of these fascinating, but often also highly dangerous microalgae.

4. Marine Macroalgae

Bacteria also colonize marine macroalgae, and these bacterial communities are not fixed and can change temporally and spatially across seasons, lifespans, life stages, and tissue types, and are shaped by biotic and abiotic factors [25,183,184]. The following section describes three macroalgal models: the red, green, and brown algae.

4.1. The Rhodophyceae Delisea pulchra and Its Bacterial Enemies

The red macroalga *Delisea pulchra* (Rhodophyta, Bonnemaisonales) is a widely distributed, shallow-subtidal red alga occurring throughout Southern Australia, New Zealand, Japan, and Antarctica [185–187]. It is one of the best-studied models for the interactions between macroalgae, bacteria, and the environment in the context of disease [188].

Bleaching disease is one of the few well-characterized examples of disease in macroalgae. A bacterial infection causes this disease [189,190], leading to the loss of photosynthetic pigments along the thallus, resulting in tissue necrosis, reduced fecundity, and increased herbivory [191]. The occurrence of bleaching disease is highly correlated with increased seawater temperatures in the summer months, which is thought to reduce the algae's natural chemical defenses and render it more susceptible to microbial infections [192]. These infections lead to a downregulation of genes coding for predicted protein metabolism, stress response, energy generation, and photosynthesis functions. The rapid repression of genes

coding for core cellular processes will likely interfere with the macroalgal antipathogen response, leading to infection, tissue damage, and bleaching symptoms [193].

Furthermore, 16S rRNA gene library analysis showed that *D. pulchra* bacterial communities contained seven phyla, including 79 species. Alpha-, Delta-, and Gammaproteobacteria are well-represented, and Planctomycetes and Bacteroidetes are relatively common in healthy *D. pulchra* [194]. Bleached *D. pulchra* microbiota is enriched in *Rhodobacteraceae*, *Saprospiraceae,* and *Flavobacteriaceae* [195]. *Colwelliaceae* and *Rhodobacteraceae* families and *Thalassomonas* and *Parvularcula* genera were the most impacted taxa between healthy and bleached communities [196]. Also, comparative metagenomics showed changes in functions associated with transcriptional regulation, cation/multidrug efflux, and nonribosomal peptide synthesis [196]. Several bacterial strains are responsible for bleaching symptoms, e.g., *Alteromonas* sp. BL110, *Aquimarina* sp. AD1 and BL5, and *Agarivorans* sp BL7 [190].

In response to the pathogen, *D. pulchra* will produce a range of secondary metabolites based on brominated furanones [189,192,197]. These molecules antagonize the same receptor as AHL—a group of widespread intercellular communication signals among bacteria. Halogenated furanones compete with and inhibit bacterial cell-to-cell communication and thus interfere with critical bacterial communication-regulated processes, such as biofilm formation and virulence [188]. They will also help the alga to shape its associated bacterial community by selecting specific groups [198]. Halogenated furanones are localized in the central vesicle of gland cells in *D. pulchra* [199]. Quantitative variations of *D. pulchra* furanones are driven by small-scale variations in environmental factors (nutrients and light) and genetic differences among individuals [200,201]. These cells release furanone onto the alga's surface, and furanones levels on the thallus were highest near the apical tips and decreased towards the base of the alga. Variation in furanone levels within the plant and the number of gland cells followed a similar pattern [199]. These brominated furanones covalently modify and inactivate the LuxS enzyme, which produces autoinducer-2, molecules involved in bacterial quorum-sensing [202]. Furanones can also modulate the cellular concentration of the LuxR protein responsible for the reception of and response to AHLs [203,204]. In parallel to the algal chemical defense, the already established algal microbiota can prevent the pathogenicity of other bacteria, such as *Phaeobacter* sp. BS52. That bacterial strain, isolated from healthy *D. pulchra*, was antagonistic towards bleaching pathogens by significantly increasing the proportion of healthy individuals, suggesting a protective activity by preventing dysbiosis rather than direct pathogen inhibition [205].

4.2. The Chlorophyceae Ulva sp. Needs Its Bacteria to Get in Shape

The marine green macroalga *Ulva* (Chlorophyta, Ulvales), also named sea lettuce or gut weeds, is a model organism for morphogenesis studies, seaweed-bacteria interactions, and chemical ecology. The whole-genome sequence of *U. mutabilis* is available [206], and its genome contains genes encoding enzymes involved in the production and transformation of DMSP. A gene sequence homologous to the DMSP lyase Alma [207] enables *Ulva* to convert DMSP to dimethyl sulfide under axenic conditions [208], making this alga an essential component of the marine sulfur cycle because of its rapid growth and high DMSP content. DMSP can play multiple roles as an osmolyte and cryoprotectant in the thallus [209,210], as well as a chemoattractant [208].

In natural populations, *Ulva*-associated bacterial composition is strongly structured by both salinity and host species [211]. The bacterial communities are mainly composed of Alphaproteobacteria and Bacteroidete members, especially within the *Rhodobacteriaceae*, *Sphingomonadaceae*, *Flavobacteriaceae,* and *Sapropiraceae* families [212]. Several of these marine bacteria will have an impact on the morphologies and polymorphisms of various *Ulva* species, such as *U. clathrata* [213], *U. fasciata* [214], *U. intestinalis* [215], *U. linza* [216], *U. mutabilis* [215,217], or *U. pertusa* [218].

The first step in the interaction between *Ulva* and marine bacteria occurs during the settlement of zoospores, the motile reproductive stage of *Ulva*. Biofilms that release AHLs attract zoospores [219]. The swimming rate is reduced when zoospores detect AHLs,

resulting in the accumulation of cells at the source of the AHLs. AHLs probably act as cues for the settlement of zoospores, rather than being directly involved as a signaling mechanism [50].

One of the most described interactions of *Ulva* with bacteria is the tripartite interaction *Ulva-Maribacter-Roseovarius* (Figure 3; [220,221]). *U. mutabilis* provides a substrate layer enriched with glycerol, a carbon source for *Roseovarius* sp., supporting biofilm formation [52]. The macroalga also releases DMSP to attract *Roseovarius* sp. [208,222], which secretes an unknown cytokinin-like growth factor promoting cell division and growth [217]. The tripartite interaction is completed with *Maribacter* sp., which is mainly found attached to the rhizoidal zone of the alga [223]. *Maribacter* sp. produces thallusin, a differentiation inducer that promotes rhizoid and cell wall formation [224]. Thallusin was isolated from the epiphytic marine bacterium YM2-23 (Cytophaga-Flavobacteria-Bacteroides group) of the green alga *Monostroma* sp. [225,226]. *Ulva* can also acquire iron from associated bacterial communities [227,228], as its genome contains iron uptake genes coding for putative transporter [206]. *Ulva* can get iron by importing a 2:1 thallusin-Fe(III)-complex [224]. The role of the Fe(III)-complex remains to be defined, as the cellular uptake of iron facilitated by thallusin derivatives was independent of their morphogenic activity [229]. These results also suggest their active import via siderophore transporters as a shuttle system.

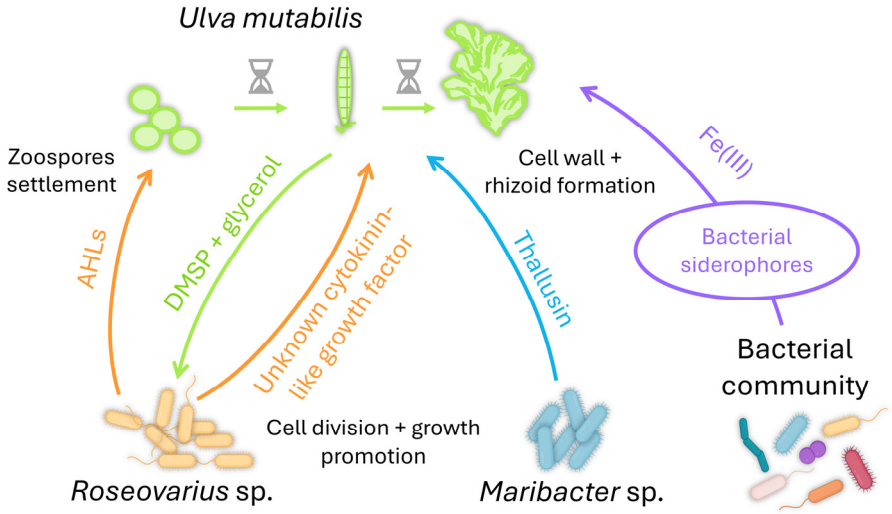

Figure 3. The beneficial tripartite interaction *Ulva-Roseovarius-Maribacter* (reviewed in [221]). *Roseovarius* sp. secrete AHLs that act as cues for the zoospores' settlement. *U. mutabilis* also provides a surface enriched in glycerol and DMSP for biofilm formation by *Roseovarius* sp. This bacterial partner promotes cell division and growth by producing an unknown cytokinin-like factor. The third partner, *Maribacter* sp., induces cell wall and rhizoid formation via the production of thallusin. *Ulva* can also acquire iron from its associated bacterial communities via siderophores.

4.3. The Phaeophyceae Ectocarpus sp. Needs Bacteria for Its Shape, Sex, Fitness, and Environmental Adaptation

The brown filamentous macroalga *Ectocarpus* (Ochrophyta, Ectocarpales) is a cosmopolitan genus that occurs worldwide across temperate and subtropical regions and has been sampled on all continents except Antarctica [230].

Ectocarpus sp. is a genetic and genomic model for brown algae [231]. The genome [232], corresponding metabolic network [233], and transformation protocol by CRISPR-Cas9 [234] are available. *Ectocarpus* is currently being used as a laboratory model to study several aspects of brown algal biology, including the implementation of in silico approaches to understand brown algal metabolism [233,235,236] and biophysical approaches to study brown algal growth and morphology [237,238]. *Ectocarpus* is also used to study interactions between brown algae and other organisms, such as symbiotic bacteria [239–241] or pathogens [242]. Most studies on the host-bacteria interactions in *Ectocarpus* use a screening

approach by first identifying the macroalgae-associated microorganisms and characterizing potential beneficial or pathogenic effects, then creating synthetic communities and testing in vitro their effects on algal biological parameters.

It has been shown that *Ectocarpus* depends on its microbiota for its morphology, reproduction, fitness, and adaptation to a changing environment. When cultured under axenic conditions, *Ectocarpus* sp. loses its branched morphology and grows with a small ball-like appearance [240,243]. Similarly, bacterial isolates significantly promoted the production of new germlings in *Ectocarpus* [243]. Additionally, adaptation to a salinity gradient is only possible in the presence of an associated bacterial community. *Ectocarpus* relies on bacteria to facilitate the transition from low to high salinity, and cultures deprived of their associated microbiome fail to survive a transfer to freshwater. However, restoring their microflora also restores their capacity to acclimate to this change [244]. While there are compositional differences in bacterial communities associated with algal hosts, there were no functional differences, suggesting functional redundancy in the associated bacterial community [244].

The microbiota composition of lab-cultured *E. subulatus* was assessed with isolation techniques and 16S rRNA metabarcoding [239]. The identified isolates belong to 33 genera, with *Halomonas* (Gammaproteobacteria), *Bosea* (Alphaproteobacteria), and *Limnobacter* (Betaproteobacteria) being the most abundant [239]. Metabarcoding sequences data clustered into 48 operational taxonomic units. The genus *Alteromonas* represents 41.6% of the reads, making Gammaproteobacteria the most abundant class. The microbiota of *Ectocarpus subulatus* natural populations from Australia was also characterized by 16S rRNA metabarcoding [245]. The bacterial communities were dominated by Alphaproteobacteria (25% of reads), Bacteriodetes (20%), Gammaproteobacteria (8%), Planctomycetes (8%), and Actinobacteria (8%) [245].

Following the characterization of *Ectocarpus* microbiota, Karimi et al. annotated the draft genomes of seventy-two cultivable *Ectocarpus*-associated bacteria [246]. Gene clusters related to secondary metabolites production revealed that terpene, bacteriocin, nonribosomal peptide synthetases, polyketide synthases type 1 and type 3, siderophore, and homoserine lactone clusters were abundant in these genomes. Moreover, detoxification and provision of vitamin B pathways have been observed, highlighting potential contributions of bacterial metabolism toward host fitness and survival [246]. Also, coculture experiments with specific bacteria showed a significant increase in algal growth [240,241]. Seven metabolites predicted to be producible by the algae only through metabolic exchanges with specific bacteria [236,247] were selected for targeted metabolite profiling: L-histidine, putrescine, beta-alanine, nicotinic acid, folic acid, auxin, and spermidine. In several cases, these key metabolites were detected only in the inoculated cocultures [240].

5. Conclusions and Futures Directions

This review highlights the importance of bacteria associated with micro- and macroalgae. Bacteria can not only promote or even enable algal growth, but they are also essential for the development of some algae, shaping their morphology, as exemplified with *Ulva* and *Ectocarpus* in Sections 4.2 and 4.3. Moreover, bacteria can be detrimental to algae, ultimately leading to their death. Often, primary and secondary metabolites are involved in these interactions. Beneficial primary metabolites include N- and C-sources or vitamins, and toxins compromise many natural products such as, for example, cyclic lipopeptides, polyynes, or phenolic compounds (see Table 1). Some metabolites are altered depending on the age of the algal culture, thus triggering the change from a mutualistic lifestyle to an antagonistic one (see Figure 2). Abiotic factors such as structured surfaces can influence microbial interactions. Moreover, temperature can play a critical role, as emphasized by coral bleaching due to the loss of the algal symbiont caused by climate change-induced heat waves. All these examples demonstrate how the bacterial microbiome associated with algae profoundly shapes their growth and life, consequently influencing their photosynthetic capacities that are necessary for sustaining life on Earth.

Currently, two major approaches are used for studying algal-microbial interactions, both with pros and cons. On one side, the entire microbiome associated with an alga is characterized, encompassing all microorganisms and their potential effects on algal life. However, such a microbiome is complex, and it is hard to understand the detailed roles of single partners and enemies in the consortium; "-omics" approaches are often used to get a first overview. Genomic and metabolomic tools are being developed to assess these interactions in silico. On the other side, individual bipartite are often examined by coculturing a single alga and a bacterium together. One alga and one bacterium are often put together in coculture. In this case, all exchanged metabolites can be studied; it can usually be predicted from which microorganism they are produced. However, this laboratory scenario does not reflect the natural environment, as we see in the case of those tripartite systems studied so far, where a third partner can already significantly change an alga's interplay with a bacterium. In the future, it is desirable that we continuously increase the number of microorganisms in cocultures to study the influence of further partners, opportunistic pathogens, and enemies. Ultimately, we should aim to find out if new members may change their positive or negative behavior once confronted with further partners. It is also evident that the interaction of algae with bacteria is just a first step in understanding algal holobionts, as viruses, fungi, and other microorganisms will also be potential partners in the natural ecological environment.

Author Contributions: Conceptualization, B.B.-D. and M.M.; writing—original draft preparation, B.B.-D., P.S. and M.M.; writing—review and editing, B.B.-D., P.S., T.V. and M.M.; figures and table, T.V., B.B.-D. and M.M.; funding acquisition, M.M. All authors have read and agreed to the published version of the manuscript.

Funding: P.S. and T.V. had fellowships from the Carl-Zeiss Foundation under the umbrella of the Jena School for Microbial Communication (JSMC). M.M. received funding from the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) within the collaborative research center SFB1127/2 ChemBioSys—Project ID 239748522, subproject A02. M.M. and P.S. received funding from DFG within Germany's Excellence Strategy—EXC 2051—Project-ID 390713860.

Data Availability Statement: The used information in this review has been referenced.

Acknowledgments: We thank Volker Wagner for valuable comments on the manuscript and Alsatia Lohr for proofreading. The figures were prepared with the help of Biorender.com (accessed 12 February 2024). We thank the funding agencies mentioned above.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

AHL	*N*-acyl-homoserine lactones
DMSP	Dimethylsulfoniopropionate
DOM	Dissolved organic matter
IAA	Indole-3-acetic acid
T6SS	Type 6 secretion system
TDA	Tropodithietic acid
TRP	Transient receptor potential
VOC	Volatile organic compounds

References

1. Parker, M.S.; Mock, T.; Armbrust, E.V. Genomic insights into marine microalgae. *Annu. Rev. Genet.* **2008**, *42*, 619–645. [CrossRef] [PubMed]
2. Coelho, S.M.; De Clerck, O. Embracing algal models. *Semin. Cell Dev. Biol.* **2023**, *134*, 1–3. [CrossRef] [PubMed]
3. Gentil, J.; Hempel, F.; Moog, D.; Zauner, S.; Maier, U.G. Review: Origin of complex algae by secondary endosymbiosis: A journey through time. *Protoplasma* **2017**, *254*, 1835–1843. [CrossRef]
4. Strassert, J.F.H.; Irisarri, I.; Williams, T.A.; Burki, F. A molecular timescale for eukaryote evolution with implications for the origin of red algal-derived plastids. *Nat. Commun.* **2021**, *12*, 1879. [CrossRef] [PubMed]
5. Coelho, S.M.; Cock, J.M. Brown algal model organisms. *Annu. Rev. Genet.* **2020**, *54*, 71–92. [CrossRef] [PubMed]

6. Courties, C.; Vaquer, A.; Troussellier, M.; Lautier, J.; Chrétiennot-Dinet, M.J.; Neveux, J.; Machado, C.; Claustre, H. Smallest eukaryotic organism. *Nature* **1994**, *370*, 255. [CrossRef]
7. Van Den Hoek, C.; Mann, D.G.; Jahns, H.M. *Algae: An Introduction to Phycology*; Cambridge University Press: Cambridge, MA, USA; New York, NY, USA, 1995; ISBN 978-0-521-30419-1.
8. Barsanti, L.; Gualtieri, P. *Algae: Anatomy, Biochemistry, and Biotechnology*, 3rd ed.; CRC Press: Boca Raton, FL, USA; Taylor & Francis Group: Abingdon, UK, 2022; ISBN 978-1-03-203512-3.
9. Guiry, M.D. How many species of algae are there? *J. Phycol.* **2012**, *48*, 1057–1063. [CrossRef] [PubMed]
10. Falciatore, A.; Jaubert, M.; Bouly, J.-P.; Bailleul, B.; Mock, T. Diatom molecular research comes of age: Model species for studying phytoplankton biology and diversity. *Plant Cell* **2020**, *32*, 547–572. [CrossRef]
11. Hawksworth, D.L.; Grube, M. Lichens redefined as complex ecosystems. *New Phytol.* **2020**, *227*, 1281–1283. [CrossRef]
12. Calatrava, V.; Tejada-Jimenez, M.; Sanz-Luque, E.; Fernandez, E.; Galvan, A.; Llamas, A. *Chlamydomonas reinhardtii*, a reference organism to study algal-microbial interactions: Why can't they be friends? *Plants* **2023**, *12*, 788. [CrossRef]
13. Krug, L.; Erlacher, A.; Markut, K.; Berg, G.; Cernava, T. The microbiome of alpine snow algae shows a specific inter-kingdom connectivity and algae-bacteria interactions with supportive capacities. *ISME J.* **2020**, *14*, 2197–2210. [CrossRef] [PubMed]
14. Treves, H.; Siemiatkowska, B.; Luzarowska, U.; Murik, O.; Fernandez-Pozo, N.; Moraes, T.A.; Erban, A.; Armbruster, U.; Brotman, Y.; Kopka, J.; et al. Multi-omics reveals mechanisms of total resistance to extreme illumination of a desert alga. *Nat. Plants* **2020**, *6*, 1031–1043. [CrossRef] [PubMed]
15. Field, C.B.; Behrenfeld, M.J.; Randerson, J.T.; Falkowski, P. Primary production of the biosphere: Integrating terrestrial and oceanic components. *Science* **1998**, *281*, 237–240. [CrossRef] [PubMed]
16. Steele, J.H. Marine food webs. In *The Structure of Marine Ecosystems*; Harvard University Press: Cambridge, MA, USA, 1974; pp. 2–98, ISBN 978-0-674-59251-3.
17. McCutcheon, J.; Lutz, S.; Williamson, C.; Cook, J.M.; Tedstone, A.J.; Vanderstraeten, A.; Wilson, S.; Stockdale, A.; Bonneville, S.; Anesio, A.M.; et al. Mineral phosphorus drives glacier algal blooms on the Greenland Ice Sheet. *Nat. Commun.* **2021**, *12*, 570. [CrossRef] [PubMed]
18. B-Béres, V.; Stenger-Kovács, C.; Buczkó, K.; Padisák, J.; Selmeczy, G.B.; Lengyel, E.; Tapolczai, K. Ecosystem services provided by freshwater and marine diatoms. *Hydrobiologia* **2023**, *850*, 2707–2733. [CrossRef]
19. Chung, I.K.; Oak, J.H.; Lee, J.A.; Shin, J.A.; Kim, J.G.; Park, K.-S. Installing kelp forests/seaweed beds for mitigation and adaptation against global warming: Korean Project Overview. *ICES J. Mar. Sci.* **2013**, *70*, 1038–1044. [CrossRef]
20. Van Oostende, N.; Moerdijk-Poortvliet, T.C.W.; Boschker, H.T.S.; Vyverman, W.; Sabbe, K. Release of dissolved carbohydrates by *Emiliania huxleyi* and formation of transparent exopolymer particles depend on algal life cycle and bacterial activity. *Environ. Microbiol.* **2013**, *15*, 1514–1531. [CrossRef]
21. Hartnett, H.E. Dissolved Organic Matter (DOM). In *Encyclopedia of Engineering Geology*; Bobrowsky, P., Marker, B., Eds.; Encyclopedia of Earth Sciences Series; Springer International Publishing: Cham, Switzerland, 2018; pp. 1–3, ISBN 978-3-319-12127-7.
22. González, J.M.; Simó, R.; Massana, R.; Covert, J.S.; Casamayor, E.O.; Pedrós-Alió, C.; Moran, M.A. Bacterial community structure associated with a dimethylsulfoniopropionate-producing North Atlantic algal bloom. *Appl. Environ. Microbiol.* **2000**, *66*, 4237–4246. [CrossRef]
23. Durham, B.P.; Sharma, S.; Luo, H.; Smith, C.B.; Amin, S.A.; Bender, S.J.; Dearth, S.P.; Van Mooy, B.A.S.; Campagna, S.R.; Kujawinski, E.B.; et al. Cryptic carbon and sulfur cycling between surface ocean plankton. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 453–457. [CrossRef]
24. Jones, C.G.; Lawton, J.H.; Shachak, M. Positive and negative effects of organisms as physical ecosystem engineers. *Ecology* **1997**, *78*, 1946–1957. [CrossRef]
25. Egan, S.; Harder, T.; Burke, C.; Steinberg, P.; Kjelleberg, S.; Thomas, T. The seaweed holobiont: Understanding seaweed-bacteria interactions. *FEMS Microbiol. Rev.* **2013**, *37*, 462–476. [CrossRef] [PubMed]
26. Steneck, R.S.; Graham, M.H.; Bourque, B.J.; Corbett, D.; Erlandson, J.M.; Estes, J.A.; Tegner, M.J. Kelp forest ecosystems: Biodiversity, stability, resilience and future. *Environ. Conserv.* **2002**, *29*, 436–459. [CrossRef]
27. Araújo, R.M.; Assis, J.; Aguillar, R.; Airoldi, L.; Bárbara, I.; Bartsch, I.; Bekkby, T.; Christie, H.; Davoult, D.; Derrien-Courtel, S.; et al. Status, trends and drivers of kelp forests in Europe: An expert assessment. *Biodivers. Conserv.* **2016**, *25*, 1319–1348. [CrossRef]
28. Diehl, N.; Li, H.; Scheschonk, L.; Burgunter-Delamare, B.; Niedzwiedz, S.; Forbord, S.; Sæther, M.; Bischof, K.; Monteiro, C. The sugar kelp *Saccharina latissima* I: Recent advances in a changing climate. *Ann. Bot.* **2024**, *133*, 183–212. [CrossRef] [PubMed]
29. González-Olalla, J.M.; Medina-Sánchez, J.M.; Lozano, I.L.; Villar-Argaiz, M.; Carrillo, P. Climate-driven shifts in algal-bacterial interaction of high-mountain lakes in two years spanning a decade. *Sci. Rep.* **2018**, *8*, 10278. [CrossRef] [PubMed]
30. MacArtain, P.; Gill, C.I.R.; Brooks, M.; Campbell, R.; Rowland, I.R. Nutritional value of edible seaweeds. *Nutr. Rev.* **2008**, *65*, 535–543. [CrossRef]
31. Koyande, A.K.; Chew, K.W.; Rambabu, K.; Tao, Y.; Chu, D.-T.; Show, P.-L. Microalgae: A potential alternative to health supplementation for humans. *Food Sci. Hum. Wellness* **2019**, *8*, 16–24. [CrossRef]
32. McHugh, D.J. *A Guide to the Seaweed Industry*; FAO Fisheries Technical Paper; Food and Agriculture Organization of the United Nations: Rome, Italy, 2003; ISBN 978-92-5-104958-7.
33. Yaakob, Z.; Ali, E.; Zainal, A.; Mohamad, M.; Takriff, M.S. An overview: Biomolecules from microalgae for animal feed and aquaculture. *J. Biol. Res.* **2014**, *21*, 6. [CrossRef]

34. Bernaerts, T.M.M.; Gheysen, L.; Foubert, I.; Hendrickx, M.E.; Van Loey, A.M. The potential of microalgae and their biopolymers as structuring ingredients in food: A review. *Biotechnol. Adv.* **2019**, *37*, 107419. [CrossRef]
35. Indergaard, M.; Ostgaard, K. Polysaccharides for food and pharmaceutical uses. In *Seaweed Resources in Europe: Uses and Potential*; Guiry, M.D., Blunden, G., Eds.; John Wiley & Sons: Hoboken, NJ, USA, 1991; pp. 169–183, ISBN 0-471-92947-6.
36. Onen Cinar, S.; Chong, Z.K.; Kucuker, M.A.; Wieczorek, N.; Cengiz, U.; Kuchta, K. Bioplastic production from microalgae: A review. *Int. J. Environ. Res. Public. Health* **2020**, *17*, 3842. [CrossRef]
37. Schmidtchen, L.; Roleda, M.Y.; Majschak, J.-P.; Mayser, M. Processing technologies for solid and flexible packaging materials from macroalgae. *Algal Res.* **2022**, *61*, 102300. [CrossRef]
38. Karuppusamy, S.; Rajauria, G.; Fitzpatrick, S.; Lyons, H.; McMahon, H.; Curtin, J.; Tiwari, B.K.; O'Donnell, C. Biological properties and health-promoting functions of laminarin: A comprehensive review of preclinical and clinical studies. *Mar. Drugs* **2022**, *20*, 772. [CrossRef]
39. Borowitzka, M.A. Microalgae in medicine and human health. In *Microalgae in Health and Disease Prevention*; Elsevier: Amsterdam, The Netherlands, 2018; pp. 195–210, ISBN 978-0-12-811405-6.
40. Blunden, G. Agricultural uses of seaweeds and seaweed extracts. In *Seaweed Resources in Europe*; Guiry, M.D., Blunden, G., Eds.; John Wiley & Sons: Chichester, UK, 1991; pp. 65–81.
41. Castro, J.D.S.; Calijuri, M.L.; Ferreira, J.; Assemany, P.P.; Ribeiro, V.J. Microalgae based biofertilizer: A life cycle approach. *Sci. Total Environ.* **2020**, *724*, 138138. [CrossRef] [PubMed]
42. Sæther, M.; Diehl, N.; Monteiro, C.; Huiru, L.; Niedzwiedz, S.; Burgunter-Delamare, B.; Scheschonk, L.; Bischof, K.; Forbord, S. The sugar kelp *Saccharina latissima* II: Recent advances in farming and applications. *J. Appl. Phycol.* **2024**. [CrossRef]
43. Khetkorn, W.; Rastogi, R.P.; Incharoensakdi, A.; Lindblad, P.; Madamwar, D.; Pandey, A.; Larroche, C. Microalgal hydrogen production—A review. *Bioresour. Technol.* **2017**, *243*, 1194–1206. [CrossRef] [PubMed]
44. Branco-Vieira, M.; San Martin, S.; Agurto, C.; Freitas, M.A.V.; Martins, A.A.; Mata, T.M.; Caetano, N.S. Biotechnological potential of *Phaeodactylum tricornutum* for biorefinery processes. *Fuel* **2020**, *268*, 117357. [CrossRef]
45. Kouhgardi, E.; Zendehboudi, S.; Mohammadzadeh, O.; Lohi, A.; Chatzis, I. Current status and future prospects of biofuel production from brown algae in North America: Progress and challenges. *Renew. Sustain. Energy Rev.* **2023**, *172*, 113012. [CrossRef]
46. Broch, O.; Ellingsen, I.; Forbord, S.; Wang, X.; Volent, Z.; Alver, M.; Handå, A.; Andresen, K.; Slagstad, D.; Reitan, K.; et al. Modelling the cultivation and bioremediation potential of the kelp *Saccharina latissima* in close proximity to an exposed salmon farm in Norway. *Aquac. Environ. Interact.* **2013**, *4*, 187–206. [CrossRef]
47. Leong, Y.K.; Chang, J.-S. Bioremediation of heavy metals using microalgae: Recent advances and mechanisms. *Bioresour. Technol.* **2020**, *303*, 122886. [CrossRef]
48. Bell, W.; Mitchell, R. Chemotactic and growth responses of marine bacteria to algal extracellular products. *Biol. Bull.* **1972**, *143*, 265–277. [CrossRef]
49. Durán, P.; Flores-Uribe, J.; Wippel, K.; Zhang, P.; Guan, R.; Melkonian, B.; Melkonian, M.; Garrido-Oter, R. Shared features and reciprocal complementation of the *Chlamydomonas* and *Arabidopsis* microbiota. *Nat. Commun.* **2022**, *13*, 406. [CrossRef] [PubMed]
50. Joint, I.; Tait, K.; Wheeler, G. Cross-kingdom signalling: Exploitation of bacterial quorum sensing molecules by the green seaweed *Ulva*. *Philos. Trans. R. Soc. B Biol. Sci.* **2007**, *362*, 1223–1233. [CrossRef] [PubMed]
51. Goecke, F.; Labes, A.; Wiese, J.; Imhoff, J. Chemical interactions between marine macroalgae and bacteria. *Mar. Ecol. Prog. Ser.* **2010**, *409*, 267–299. [CrossRef]
52. Alsufyani, T.; Weiss, A.; Wichard, T. Time course exo-metabolomic profiling in the green marine macroalga *Ulva* (Chlorophyta) for identification of growth phase-dependent biomarkers. *Mar. Drugs* **2017**, *15*, 14. [CrossRef] [PubMed]
53. Adouane, E.; Mercier, C.; Mamelle, J.; Willocquet, E.; Intertaglia, L.; Burgunter-Delamare, B.; Leblanc, C.; Rousvoal, S.; Lami, R.; Prado, S. Importance of quorum sensing crosstalk in the brown alga *Saccharina latissima* epimicrobiome. *iScience* **2024**, *27*, 109176. [CrossRef] [PubMed]
54. Seymour, J.R.; Amin, S.A.; Raina, J.-B.; Stocker, R. Zooming in on the phycosphere: The ecological interface for phytoplankton-bacteria relationships. *Nat. Microbiol.* **2017**, *2*, 17065. [CrossRef] [PubMed]
55. Wadhams, G.H.; Armitage, J.P. Making sense of it all: Bacterial chemotaxis. *Nat. Rev. Mol. Cell Biol.* **2004**, *5*, 1024–1037. [CrossRef]
56. Stocker, R.; Seymour, J.R. Ecology and physics of bacterial chemotaxis in the ocean. *Microbiol. Mol. Biol. Rev.* **2012**, *76*, 792–812. [CrossRef]
57. Amsler, C.D. *Algal Chemical Ecology*; Springer: Berlin/Heidelberg, Germany, 2008; ISBN 978-3-540-74180-0.
58. Govorunova, E.G.; Sineshchekov, O.A. Chemotaxis in the green flagellate alga *Chlamydomonas*. *Biochemistry* **2005**, *70*, 717–725. [CrossRef]
59. Bordenstein, S.R.; Theis, K.R. Host biology in light of the microbiome: Ten principles of holobionts and hologenomes. *PLoS Biol.* **2015**, *13*, e1002226. [CrossRef]
60. Rosenberg, E.; Zilber-Rosenberg, I. The hologenome concept of evolution after 10 years. *Microbiome* **2018**, *6*, 78. [CrossRef] [PubMed]
61. Dittami, S.M.; Arboleda, E.; Auguet, J.-C.; Bigalke, A.; Briand, E.; Cárdenas, P.; Cardini, U.; Decelle, J.; Engelen, A.H.; Eveillard, D.; et al. A community perspective on the concept of marine holobionts: Current status, challenges, and future directions. *PeerJ* **2021**, *9*, e10911. [CrossRef] [PubMed]

62. Brodie, J.; Ball, S.G.; Bouget, F.; Chan, C.X.; De Clerck, O.; Cock, J.M.; Gachon, C.; Grossman, A.R.; Mock, T.; Raven, J.A.; et al. Biotic interactions as drivers of algal origin and evolution. *New Phytol.* **2017**, *216*, 670–681. [CrossRef] [PubMed]
63. Hom, E.F.Y.; Aiyar, P.; Schaeme, D.; Mittag, M.; Sasso, S. A chemical perspective on microalgal-microbial interactions. *Trends Plant Sci.* **2015**, *20*, 689–693. [CrossRef]
64. Cirri, E.; Pohnert, G. Algae-bacteria interactions that balance the planktonic microbiome. *New Phytol.* **2019**, *223*, 100–106. [CrossRef] [PubMed]
65. Tirichine, L.; Piganeau, G. Editorial: Algal symbiotic relationships in freshwater and marine environments. *Front. Plant Sci.* **2023**, *14*, 1155759. [CrossRef] [PubMed]
66. Chomicki, G.; Kiers, E.T.; Renner, S.S. The evolution of mutualistic dependence. *Annu. Rev. Ecol. Evol. Syst.* **2020**, *51*, 409–432. [CrossRef]
67. Mathis, K.A.; Bronstein, J.L. Our current understanding of commensalism. *Annu. Rev. Ecol. Evol. Syst.* **2020**, *51*, 167–189. [CrossRef]
68. Wang, X.; Li, Z.; Su, J.; Tian, Y.; Ning, X.; Hong, H.; Zheng, T. Lysis of a red-tide causing alga, *Alexandrium tamarense*, caused by bacteria from its phycosphere. *Biol. Control* **2010**, *52*, 123–130. [CrossRef]
69. Paul, C.; Pohnert, G. Interactions of the algicidal bacterium *Kordia algicida* with diatoms: Regulated protease excretion for specific algal lysis. *PLoS ONE* **2011**, *6*, e21032. [CrossRef]
70. Aiyar, P.; Schaeme, D.; García-Altares, M.; Carrasco Flores, D.; Dathe, H.; Hertweck, C.; Sasso, S.; Mittag, M. Antagonistic bacteria disrupt calcium homeostasis and immobilize algal cells. *Nat. Commun.* **2017**, *8*, 1756. [CrossRef] [PubMed]
71. Krespach, M.K.C.; García-Altares, M.; Flak, M.; Schoeler, H.; Scherlach, K.; Netzker, T.; Schmalzl, A.; Mattern, D.J.; Schroeckh, V.; Komor, A.; et al. Lichen-like association of *Chlamydomonas reinhardtii* and *Aspergillus nidulans* protects algal cells from bacteria. *ISME J.* **2020**, *14*, 2794–2805. [CrossRef] [PubMed]
72. Schroeder, D.C.; McKeown, D.A. Viruses of seaweeds. In *Studies in Viral Ecology*; Hurst, C.J., Ed.; Wiley: Hoboken, NJ, USA, 2021; pp. 121–138, ISBN 978-1-119-60836-3.
73. Lauritano, C.; Galasso, C. Microbial interactions between marine microalgae and fungi: From chemical ecology to biotechnological possible applications. *Mar. Drugs* **2023**, *21*, 310. [CrossRef] [PubMed]
74. Schleyer, G.; Kuhlisch, C.; Ziv, C.; Ben-Dor, S.; Malitsky, S.; Schatz, D.; Vardi, A. Lipid biomarkers for algal resistance to viral infection in the ocean. *Proc. Natl. Acad. Sci. USA* **2023**, *120*, e2217121120. [CrossRef] [PubMed]
75. Walde, M.; Camplong, C.; De Vargas, C.; Baudoux, A.-C.; Simon, N. Viral infection impacts the 3D subcellular structure of the abundant marine diatom *Guinardia delicatula*. *Front. Mar. Sci.* **2023**, *9*, 1034235. [CrossRef]
76. Amin, S.A.; Parker, M.S.; Armbrust, E.V. Interactions between diatoms and bacteria. *Microbiol. Mol. Biol. Rev.* **2012**, *76*, 667–684. [CrossRef]
77. Zuccaro, A.; Mitchell, J. Fungal communities of seaweeds. In *The Fungal Community: Its Organization and Role in the Ecosystem*; Dighton, J., White, J.F., Eds.; CRC Press: New York, NY, USA, 2005; pp. 533–580, ISBN 978-0-429-11640-7.
78. Vallet, M.; Strittmatter, M.; Murúa, P.; Lacoste, S.; Dupont, J.; Hubas, C.; Genta-Jouve, G.; Gachon, C.M.M.; Kim, G.H.; Prado, S. Chemically-mediated interactions between macroalgae, their fungal endophytes, and protistan pathogens. *Front. Microbiol.* **2018**, *9*, 3161. [CrossRef]
79. Tourneroche, A.; Lami, R.; Hubas, C.; Blanchet, E.; Vallet, M.; Escoubeyrou, K.; Paris, A.; Prado, S. Bacterial-fungal interactions in the kelp endomicrobiota drive autoinducer-2 quorum sensing. *Front. Microbiol.* **2019**, *10*, 1693. [CrossRef]
80. Tourneroche, A.; Lami, R.; Burgaud, G.; Domart-Coulon, I.; Li, W.; Gachon, C.; Gèze, M.; Boeuf, D.; Prado, S. The bacterial and fungal microbiota of *Saccharina latissima* (*Laminariales*, *Phaeophyceae*). *Front. Mar. Sci.* **2020**, *7*, 587566. [CrossRef]
81. Pauli, J.N.; Mendoza, J.E.; Steffan, S.A.; Carey, C.C.; Weimer, P.J.; Peery, M.Z. A syndrome of mutualism reinforces the lifestyle of a sloth. *Proc. R. Soc. B Biol. Sci.* **2014**, *281*, 20133006. [CrossRef]
82. Carrasco Flores, D.; Fricke, M.; Wesp, V.; Desirò, D.; Kniewasser, A.; Hölzer, M.; Marz, M.; Mittag, M. A marine *Chlamydomonas* sp. emerging as an algal model. *J. Phycol.* **2021**, *57*, 54–69. [CrossRef] [PubMed]
83. Mock, T. Algal model species for advancing biological sciences. *J. Phycol.* **2023**, *59*, 1–3. [CrossRef] [PubMed]
84. Burki, F.; Roger, A.J.; Brown, M.W.; Simpson, A.G.B. The new tree of Eukaryotes. *Trends Ecol. Evol.* **2020**, *35*, 43–55. [CrossRef] [PubMed]
85. Findinier, J.; Grossman, A.R. *Chlamydomonas*: Fast tracking from genomics. *J. Phycol.* **2023**, *59*, 644–652. [CrossRef] [PubMed]
86. Merchant, S.S.; Prochnik, S.E.; Vallon, O.; Harris, E.H.; Karpowicz, S.J.; Witman, G.B.; Terry, A.; Salamov, A.; Fritz-Laylin, L.K.; Maréchal-Drouard, L.; et al. The *Chlamydomonas* genome reveals the evolution of key animal and plant functions. *Science* **2007**, *318*, 245–250. [CrossRef]
87. Li, X.; Patena, W.; Fauser, F.; Jinkerson, R.E.; Saroussi, S.; Meyer, M.T.; Ivanova, N.; Robertson, J.M.; Yue, R.; Zhang, R.; et al. A genome-wide algal mutant library and functional screen identifies genes required for eukaryotic photosynthesis. *Nat. Genet.* **2019**, *51*, 627–635. [CrossRef]
88. Fauser, F.; Vilarrasa-Blasi, J.; Onishi, M.; Ramundo, S.; Patena, W.; Millican, M.; Osaki, J.; Philp, C.; Nemeth, M.; Salomé, P.A.; et al. Systematic characterization of gene function in the photosynthetic alga *Chlamydomonas reinhardtii*. *Nat. Genet.* **2022**, *54*, 705–714. [CrossRef]

89. Craig, R.J.; Gallaher, S.D.; Shu, S.; Salomé, P.A.; Jenkins, J.W.; Blaby-Haas, C.E.; Purvine, S.O.; O'Donnell, S.; Barry, K.; Grimwood, J.; et al. The *Chlamydomonas* Genome Project, version 6: Reference assemblies for mating-type plus and minus strains reveal extensive structural mutation in the laboratory. *Plant Cell* **2023**, *35*, 644–672. [CrossRef]
90. Harris, E.H. *The Chlamydomonas Sourcebook: A Comprehensive Guide to Biology and Laboratory Use*; Academic Press Inc.: San Diego, CA, USA, 1989; ISBN 978-1-4832-8860-4.
91. Sasso, S.; Stibor, H.; Mittag, M.; Grossman, A.R. From molecular manipulation of domesticated *Chlamydomonas reinhardtii* to survival in nature. *eLife* **2018**, *7*, e39233. [CrossRef]
92. Cooper, M.B.; Smith, A.G. Exploring mutualistic interactions between microalgae and bacteria in the omics age. *Curr. Opin. Plant Biol.* **2015**, *26*, 147–153. [CrossRef]
93. Croft, M.T.; Lawrence, A.D.; Raux-Deery, E.; Warren, M.J.; Smith, A.G. Algae acquire vitamin B_{12} through a symbiotic relationship with bacteria. *Nature* **2005**, *438*, 90–93. [CrossRef] [PubMed]
94. Helliwell, K.E.; Collins, S.; Kazamia, E.; Purton, S.; Wheeler, G.L.; Smith, A.G. Fundamental shift in vitamin B_{12} eco-physiology of a model alga demonstrated by experimental evolution. *ISME J.* **2015**, *9*, 1446–1455. [CrossRef] [PubMed]
95. Bunbury, F.; Deery, E.; Sayer, A.P.; Bhardwaj, V.; Harrison, E.L.; Warren, M.J.; Smith, A.G. Exploring the onset of B_{12}-based mutualisms using a recently evolved *Chlamydomonas* auxotroph and B_{12}-producing bacteria. *Environ. Microbiol.* **2022**, *24*, 3134–3147. [CrossRef] [PubMed]
96. Xie, B.; Bishop, S.; Stessman, D.; Wright, D.; Spalding, M.H.; Halverson, L.J. *Chlamydomonas reinhardtii* thermal tolerance enhancement mediated by a mutualistic interaction with vitamin B_{12}-producing bacteria. *ISME J.* **2013**, *7*, 1544–1555. [CrossRef] [PubMed]
97. Teplitski, M.; Chen, H.; Rajamani, S.; Gao, M.; Merighi, M.; Sayre, R.T.; Robinson, J.B.; Rolfe, B.G.; Bauer, W.D. *Chlamydomonas reinhardtii* secretes compounds that mimic bacterial signals and interfere with quorum sensing regulation in bacteria. *Plant Physiol.* **2004**, *134*, 137–146. [CrossRef] [PubMed]
98. Calatrava, V.; Hom, E.F.Y.; Llamas, Á.; Fernández, E.; Galván, A. OK, thanks! A new mutualism between *Chlamydomonas* and methylobacteria facilitates growth on amino acids and peptides. *FEMS Microbiol. Lett.* **2018**, *365*, fny021. [CrossRef] [PubMed]
99. Calatrava, V.; Hom, E.F.Y.; Guan, Q.; Llamas, A.; Fernández, E.; Galván, A. Genetic evidence for algal auxin production in *Chlamydomonas* and its role in algal-bacterial mutualism. *iScience* **2024**, *27*, 108762. [CrossRef] [PubMed]
100. Fakhimi, N.; Torres, M.J.; Fernández, E.; Galván, A.; Dubini, A.; González-Ballester, D. *Chlamydomonas reinhardtii* and *Microbacterium forte* sp. nov., a mutualistic association that favors sustainable hydrogen production. *Sci. Total Environ.* **2024**, *913*, 169559. [CrossRef]
101. Hotter, V.; Zopf, D.; Kim, H.J.; Silge, A.; Schmitt, M.; Aiyar, P.; Fleck, J.; Matthäus, C.; Hniopek, J.; Yan, Q.; et al. A polyyne toxin produced by an antagonistic bacterium blinds and lyses a Chlamydomonad alga. *Proc. Natl. Acad. Sci. USA* **2021**, *118*, e2107695118. [CrossRef]
102. Rose, M.M.; Scheer, D.; Hou, Y.; Hotter, V.S.; Komor, A.J.; Aiyar, P.; Scherlach, K.; Vergara, F.; Yan, Q.; Loper, J.E.; et al. The bacterium *Pseudomonas protegens* antagonizes the microalga *Chlamydomonas reinhardtii* using a blend of toxins. *Environ. Microbiol.* **2021**, *23*, 5525–5540. [CrossRef]
103. Bando, Y.; Hou, Y.; Seyfarth, L.; Probst, J.; Götze, S.; Bogacz, M.; Hellmich, U.A.; Stallforth, P.; Mittag, M.; Arndt, H. Total synthesis and structure correction of the cyclic lipodepsipeptide Orfamide A. *Chem. Eur. J.* **2022**, *28*, e202104417. [CrossRef] [PubMed]
104. Hou, Y.; Bando, Y.; Carrasco Flores, D.; Hotter, V.; Das, R.; Schiweck, B.; Melzer, T.; Arndt, H.; Mittag, M. A cyclic lipopeptide produced by an antagonistic bacterium relies on its tail and transient receptor potential-type Ca^{2+} channels to immobilize a green alga. *New Phytol.* **2023**, *237*, 1620–1635. [CrossRef] [PubMed]
105. Gross, H.; Loper, J.E. Genomics of secondary metabolite production by *Pseudomonas* spp. *Nat. Prod. Rep.* **2009**, *26*, 1408. [CrossRef] [PubMed]
106. Iwasaki, S.; Kobayashi, H.; Furukawa, J.; Namikoshi, M.; Okuda, S.; Sato, Z.; Matsuda, I.; Noda, T. Studies on macrocyclic lactone antibiotics. VII Structure of a phytotoxin "rhizoxin" produced by *Rhizopus chinensis*. *J. Antibiot.* **1984**, *37*, 354–362. [CrossRef] [PubMed]
107. Zhao, N.; Yi, L.; Ren, S.; Yin, Q.; Xiang, W.; Zhang, X.; Xie, B. Algicidal interaction between *Paenibacillus polymyxa* MEZ6 and microalgae. *J. Appl. Microbiol.* **2022**, *133*, 646–655. [CrossRef] [PubMed]
108. Krespach, M.K.C.; Stroe, M.C.; Flak, M.; Komor, A.J.; Nietzsche, S.; Sasso, S.; Hertweck, C.; Brakhage, A.A. Bacterial marginolactones trigger formation of algal gloeocapsoids, protective aggregates on the verge of multicellularity. *Proc. Natl. Acad. Sci. USA* **2021**, *118*, e2100892118. [CrossRef] [PubMed]
109. Cecchin, M.; Marcolungo, L.; Rossato, M.; Girolomoni, L.; Cosentino, E.; Cuine, S.; Li-Beisson, Y.; Delledonne, M.; Ballottari, M. *Chlorella vulgaris* genome assembly and annotation reveals the molecular basis for metabolic acclimation to high light conditions. *Plant J.* **2019**, *100*, 1289–1305. [CrossRef]
110. Hovde, B.T.; Hanschen, E.R.; Steadman Tyler, C.R.; Lo, C.-C.; Kunde, Y.; Davenport, K.; Daligault, H.; Msanne, J.; Canny, S.; Eyun, S.; et al. Genomic characterization reveals significant divergence within *Chlorella sorokiniana* (*Chlorellales*, *Trebouxiophyceae*). *Algal Res.* **2018**, *35*, 449–461. [CrossRef]
111. Wu, T.; Li, L.; Jiang, X.; Yang, Y.; Song, Y.; Chen, L.; Xu, X.; Shen, Y.; Gu, Y. Sequencing and comparative analysis of three *Chlorella* genomes provide insights into strain-specific adaptation to wastewater. *Sci. Rep.* **2019**, *9*, 9514. [CrossRef]

112. Blanc, G.; Duncan, G.; Agarkova, I.; Borodovsky, M.; Gurnon, J.; Kuo, A.; Lindquist, E.; Lucas, S.; Pangilinan, J.; Polle, J.; et al. The *Chlorella variabilis* NC64A genome reveals adaptation to photosymbiosis, coevolution with viruses, and cryptic sex. *Plant Cell* **2010**, *22*, 2943–2955. [CrossRef]
113. Chow, K.-C.; Tung, W.L. Electrotransformation of *Chlorella vulgaris*. *Plant Cell Rep.* **1999**, *18*, 778–780. [CrossRef]
114. Liu, L.; Wang, Y.; Zhang, Y.; Chen, X.; Zhang, P.; Ma, S. Development of a new method for genetic transformation of the green alga *Chlorella ellipsoidea*. *Mol. Biotechnol.* **2013**, *54*, 211–219. [CrossRef] [PubMed]
115. Sharma, P.K.; Goud, V.V.; Yamamoto, Y.; Sahoo, L. Efficient *Agrobacterium tumefaciens*-mediated stable genetic transformation of green microalgae, *Chlorella sorokiniana*. *3 Biotech* **2021**, *11*, 196. [CrossRef] [PubMed]
116. Lin, W.-R.; Ng, I.-S. Development of CRISPR/Cas9 system in *Chlorella vulgaris* FSP-E to enhance lipid accumulation. *Enzyme Microb. Technol.* **2020**, *133*, 109458. [CrossRef] [PubMed]
117. Litchfield, C.D.; Colwell, R.R.; Prescott, J.M. Numerical taxonomy of heterotrophic bacteria growing in association with continuous-culture *Chlorella sorokiniana*. *Appl. Microbiol.* **1969**, *18*, 1044–1049. [CrossRef] [PubMed]
118. Watanabe, K.; Takihana, N.; Aoyagi, H.; Hanada, S.; Watanabe, Y.; Ohmura, N.; Saiki, H.; Tanaka, H. Symbiotic association in *Chlorella* culture. *FEMS Microbiol. Ecol.* **2005**, *51*, 187–196. [CrossRef]
119. Park, Y.; Je, K.-W.; Lee, K.; Jung, S.-E.; Choi, T.-J. Growth promotion of *Chlorella ellipsoidea* by co-inoculation with *Brevundimonas* sp. isolated from the microalga. *Hydrobiologia* **2008**, *598*, 219–228. [CrossRef]
120. Thi Vu, H.; Otsuka, S.; Ueda, H.; Senoo, K. Cocultivated bacteria can increase or decrease the culture lifetime of *Chlorella vulgaris*. *J. Gen. Appl. Microbiol.* **2010**, *56*, 413–418. [CrossRef]
121. Amavizca, E.; Bashan, Y.; Ryu, C.-M.; Farag, M.A.; Bebout, B.M.; de-Bashan, L.E. Enhanced performance of the microalga *Chlorella sorokiniana* remotely induced by the plant growth-promoting bacteria *Azospirillum brasilense* and *Bacillus pumilus*. *Sci. Rep.* **2017**, *7*, 41310. [CrossRef]
122. Pereg, L.; de-Bashan, L.E.; Bashan, Y. Assessment of affinity and specificity of *Azospirillum* for plants. *Plant Soil* **2016**, *399*, 389–414. [CrossRef]
123. Gonzalez, L.E.; Bashan, Y. Increased growth of the microalga *Chlorella vulgaris* when coimmobilized and cocultured in alginate beads with the plant-growth-promoting bacterium *Azospirillum brasilense*. *Appl. Environ. Microbiol.* **2000**, *66*, 1527–1531. [CrossRef] [PubMed]
124. De-Bashan, L.E.; Antoun, H.; Bashan, Y. Involvement of indole-3-acetic acid produced by the growth-promoting bacterium *Azospirillum* spp. in promoting growth of *Chlorella vulgaris*. *J. Phycol.* **2008**, *44*, 938–947. [CrossRef] [PubMed]
125. Van Puyvelde, S.; Cloots, L.; Engelen, K.; Das, F.; Marchal, K.; Vanderleyden, J.; Spaepen, S. Transcriptome analysis of the rhizosphere bacterium *Azospirillum brasilense* reveals an extensive auxin response. *Microb. Ecol.* **2011**, *61*, 723–728. [CrossRef] [PubMed]
126. Cassan, F.D.; Coniglio, A.; Amavizca, E.; Maroniche, G.; Cascales, E.; Bashan, Y.; de-Bashan, L.E. The *Azospirillum brasilense* type VI secretion system promotes cell aggregation, biocontrol protection against phytopathogens and attachment to the microalgae *Chlorella sorokiniana*. *Environ. Microbiol.* **2021**, *23*, 6257–6274. [CrossRef] [PubMed]
127. Qiu, Y.; Wang, Z.; Liu, F.; Wu, Z.; Chen, H.; Tang, D.; Liu, J. Effect of complex iron on the phosphorus absorption by two freshwater algae. *Environ. Technol.* **2021**, *42*, 4125–4133. [CrossRef]
128. Amin, S.A.; Green, D.H.; Hart, M.C.; Küpper, F.C.; Sunda, W.G.; Carrano, C.J. Photolysis of iron-siderophore chelates promotes bacterial-algal mutualism. *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 17071–17076. [CrossRef] [PubMed]
129. Rawat, D.; Sharma, U.; Poria, P.; Finlan, A.; Parker, B.; Sharma, R.S.; Mishra, V. Iron-dependent mutualism between *Chlorella sorokiniana* and *Ralstonia pickettii* forms the basis for a sustainable bioremediation system. *ISME Commun.* **2022**, *2*, 83. [CrossRef]
130. Gromov, B.V.; Mamkaeva, K.A. Electron microscopic study of parasitism by *Bdellovibrio chlorellavorus* bacteria on cells of the green alga *Chlorella vulgaris*. *Tsitologiia* **1972**, *14*, 256–260.
131. Soo, R.M.; Woodcroft, B.J.; Parks, D.H.; Tyson, G.W.; Hugenholtz, P. Back from the dead; the curious tale of the predatory cyanobacterium *Vampirovibrio chlorellavorus*. *PeerJ* **2015**, *3*, e968. [CrossRef]
132. Landa, M.; Burns, A.S.; Durham, B.P.; Esson, K.; Nowinski, B.; Sharma, S.; Vorobev, A.; Nielsen, T.; Kiene, R.P.; Moran, M.A. Sulfur metabolites that facilitate oceanic phytoplankton–bacteria carbon flux. *ISME J.* **2019**, *13*, 2536–2550. [CrossRef]
133. Moran, M.A.; Durham, B.P. Sulfur metabolites in the pelagic ocean. *Nat. Rev. Microbiol.* **2019**, *17*, 665–678. [CrossRef] [PubMed]
134. Deng, Y.; Vallet, M.; Pohnert, G. Temporal and spatial signaling mediating the balance of the plankton microbiome. *Annu. Rev. Mar. Sci.* **2022**, *14*, 239–260. [CrossRef] [PubMed]
135. Amin, S.A.; Hmelo, L.R.; van Tol, H.M.; Durham, B.P.; Carlson, L.T.; Heal, K.R.; Morales, R.L.; Berthiaume, C.T.; Parker, M.S.; Djunaedi, B.; et al. Interaction and signalling between a cosmopolitan phytoplankton and associated bacteria. *Nature* **2015**, *522*, 98–101. [CrossRef] [PubMed]
136. Branscombe, L.; Harrison, E.L.; Choong, Z.Y.D.; Swink, C.; Keys, M.; Widdicombe, C.; Wilson, W.H.; Cunliffe, M.; Helliwell, K. Cryptic bacterial pathogens of diatoms peak during senescence of a winter diatom bloom. *New Phytol.* **2024**, *241*, 1292–1307. [CrossRef] [PubMed]
137. Shibl, A.A.; Isaac, A.; Ochsenkühn, M.A.; Cárdenas, A.; Fei, C.; Behringer, G.; Arnoux, M.; Drou, N.; Santos, M.P.; Gunsalus, K.C.; et al. Diatom modulation of select bacteria through use of two unique secondary metabolites. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 27445–27455. [CrossRef] [PubMed]
138. Bowler, C.; Falciatore, A. *Phaeodactylum tricornutum* . *Trends Genet.* **2019**, *35*, 706–707. [CrossRef] [PubMed]

139. Russo, M.T.; Rogato, A.; Jaubert, M.; Karas, B.J.; Falciatore, A. *Phaeodactylum tricornutum*: An established model species for diatom molecular research and an emerging chassis for algal synthetic biology. *J. Phycol.* **2023**, *59*, 1114–1122. [CrossRef] [PubMed]
140. Bowler, C.; Allen, A.E.; Badger, J.H.; Grimwood, J.; Jabbari, K.; Kuo, A.; Maheswari, U.; Martens, C.; Maumus, F.; Otillar, R.P.; et al. The *Phaeodactylum* genome reveals the evolutionary history of diatom genomes. *Nature* **2008**, *456*, 239–244. [CrossRef]
141. Apt, K.E.; Grossman, A.R.; Kroth-Pancic, P.G. Stable nuclear transformation of the diatom *Phaeodactylum tricornutum*. *Mol. Gen. Genet.* **1996**, *252*, 572–579. [CrossRef]
142. De Riso, V.; Raniello, R.; Maumus, F.; Rogato, A.; Bowler, C.; Falciatore, A. Gene silencing in the marine diatom *Phaeodactylum tricornutum*. *Nucleic Acids Res.* **2009**, *37*, e96. [CrossRef]
143. Xie, W.-H.; Zhu, C.-C.; Zhang, N.-S.; Li, D.-W.; Yang, W.-D.; Liu, J.-S.; Sathishkumar, R.; Li, H.-Y. Construction of novel chloroplast expression vector and development of an efficient transformation system for the diatom *Phaeodactylum tricornutum*. *Mar. Biotechnol.* **2014**, *16*, 538–546. [CrossRef]
144. De Martino, A.; Meichenin, A.; Shi, J.; Pan, K.; Bowler, C. Genetic and phenotypic characterization of *Phaeodactylum tricornutum* (*Bacillariophyceae*) accessions. *J. Phycol.* **2007**, *43*, 992–1009. [CrossRef]
145. Chorazyczewski, A.M.; Huang, I.; Abdulla, H.; Mayali, X.; Zimba, P.V. The influence of bacteria on the growth, lipid production, and extracellular metabolite accumulation by *Phaeodactylum tricornutum* (Bacillariophyceae). *J. Phycol.* **2021**, *57*, 931–940. [CrossRef] [PubMed]
146. Becker, J.W.; Berube, P.M.; Follett, C.L.; Waterbury, J.B.; Chisholm, S.W.; DeLong, E.F.; Repeta, D.J. Closely related phytoplankton species produce similar suites of dissolved organic matter. *Front. Microbiol.* **2014**, *5*, 111. [CrossRef] [PubMed]
147. Kim, H.; Kimbrel, J.A.; Vaiana, C.A.; Wollard, J.R.; Mayali, X.; Buie, C.R. Bacterial response to spatial gradients of algal-derived nutrients in a porous microplate. *ISME J.* **2022**, *16*, 1036–1045. [CrossRef]
148. Brisson, V.; Swink, C.; Kimbrel, J.; Mayali, X.; Samo, T.; Kosina, S.M.; Thelen, M.; Northen, T.R.; Stuart, R.K. Dynamic *Phaeodactylum tricornutum* exometabolites shape surrounding bacterial communities. *New Phytol.* **2023**, *239*, 1420–1433. [CrossRef] [PubMed]
149. Daly, G.; Decorosi, F.; Viti, C.; Adessi, A. Shaping the phycosphere: Analysis of the EPS in diatom-bacterial co-cultures. *J. Phycol.* **2023**, *59*, 791–797. [CrossRef] [PubMed]
150. Daly, G.; Perrin, E.; Viti, C.; Fondi, M.; Adessi, A. Scaling down the microbial loop: Data-driven modelling of growth interactions in a diatom-bacterium co-culture. *Environ. Microbiol. Rep.* **2021**, *13*, 945–954. [CrossRef] [PubMed]
151. Mayali, X.; Samo, T.J.; Kimbrel, J.A.; Morris, M.M.; Rolison, K.; Swink, C.; Ramon, C.; Kim, Y.-M.; Munoz-Munoz, N.; Nicora, C.; et al. Single-cell isotope tracing reveals functional guilds of bacteria associated with the diatom *Phaeodactylum tricornutum*. *Nat. Commun.* **2023**, *14*, 5642. [CrossRef] [PubMed]
152. Zecher, K.; Hayes, K.R.; Philipp, B. Evidence of interdomain ammonium cross-feeding from methylamine- and glycine betaine-degrading *Rhodobacteraceae* to diatoms as a widespread interaction in the marine phycosphere. *Front. Microbiol.* **2020**, *11*, 533894. [CrossRef]
153. Dow, L.; Stock, F.; Peltekis, A.; Szamosvári, D.; Prothiwa, M.; Lapointe, A.; Böttcher, T.; Bailleul, B.; Vyverman, W.; Kroth, P.G.; et al. The multifaceted inhibitory effects of an alkylquinolone on the diatom *Phaeodactylum tricornutum*. *ChemBioChem* **2020**, *21*, 1206–1216. [CrossRef] [PubMed]
154. Brownlee, C.; Langer, G.; Wheeler, G.L. Coccolithophore calcification: Changing paradigms in changing oceans. *Acta Biomater.* **2021**, *120*, 4–11. [CrossRef] [PubMed]
155. Read, B.A.; Kegel, J.; Klute, M.J.; Kuo, A.; Lefebvre, S.C.; Maumus, F.; Mayer, C.; Miller, J.; Monier, A.; Salamov, A.; et al. Pan genome of the phytoplankton *Emiliania* underpins its global distribution. *Nature* **2013**, *499*, 209–213. [CrossRef] [PubMed]
156. Cai, W.; Wang, X.; Su, J.; Li, J.; Zeng, J.; Li, G.; Liu, J. Transformation of coccolithophorid *Emiliania huxleyi* harboring a marine virus (Coccolithoviruses) serine palmitoyltransferase (SPT) gene by electroporation. *J. Oceanol. Limnol.* **2021**, *39*, 693–704. [CrossRef]
157. Frank, O.; Pradella, S.; Rohde, M.; Scheuner, C.; Klenk, H.-P.; Göker, M.; Petersen, J. Complete genome sequence of the *Phaeobacter gallaeciensis* type strain CIP 105210T (= DSM 26640T = BS107T). *Stand. Genomic Sci.* **2014**, *9*, 914–932. [CrossRef] [PubMed]
158. Seyedsayamdost, M.R.; Case, R.J.; Kolter, R.; Clardy, J. The Jekyll-and-Hyde chemistry of *Phaeobacter gallaeciensis*. *Nat. Chem.* **2011**, *3*, 331–335. [CrossRef] [PubMed]
159. Seyedsayamdost, M.R.; Wang, R.; Kolter, R.; Clardy, J. Hybrid biosynthesis of roseobacticides from algal and bacterial precursor molecules. *J. Am. Chem. Soc.* **2014**, *136*, 15150–15153. [CrossRef]
160. Segev, E.; Castañeda, I.S.; Sikes, E.L.; Vlamakis, H.; Kolter, R. Bacterial influence on alkenones in live microalgae. *J. Phycol.* **2016**, *52*, 125–130. [CrossRef]
161. Wang, R.; Gallant, É.; Seyedsayamdost, M.R. Investigation of the genetics and biochemistry of roseobacticide production in the *Roseobacter* clade bacterium *Phaeobacter inhibens*. *mBio* **2016**, *7*, e02118-15. [CrossRef]
162. Segev, E.; Wyche, T.P.; Kim, K.H.; Petersen, J.; Ellebrandt, C.; Vlamakis, H.; Barteneva, N.; Paulson, J.N.; Chai, L.; Clardy, J.; et al. Dynamic metabolic exchange governs a marine algal-bacterial interaction. *eLife* **2016**, *5*, e17473. [CrossRef]
163. Beiralas, R.; Ozer, N.; Segev, E. Abundant *Sulfitobacter* marine bacteria protect *Emiliania huxleyi* algae from pathogenic bacteria. *ISME Commun.* **2023**, *3*, 100. [CrossRef]
164. Barak-Gavish, N.; Dassa, B.; Kuhlisch, C.; Nussbaum, I.; Brandis, A.; Rosenberg, G.; Avraham, R.; Vardi, A. Bacterial lifestyle switch in response to algal metabolites. *eLife* **2023**, *12*, e84400. [CrossRef] [PubMed]

165. Câmara dos Reis, M.; Romac, S.; Le Gall, F.; Marie, D.; Frada, M.J.; Koplovitz, G.; Cariou, T.; Henry, N.; De Vargas, C.; Jeanthon, C. Exploring the phycosphere of *Emiliania huxleyi*: From bloom dynamics to microbiome assembly experiments. *Mol. Ecol.* **2023**, *32*, 6507–6522. [CrossRef] [PubMed]
166. Lee, D.H.; Mittag, M.; Sczekan, S.; Morse, D.; Hastings, J.W. Molecular cloning and genomic organization of a gene for luciferin-binding protein from the dinoflagellate *Gonyaulax polyedra*. *J. Biol. Chem.* **1993**, *268*, 8842–8850. [CrossRef] [PubMed]
167. Jaeckisch, N.; Yang, I.; Wohlrab, S.; Glöckner, G.; Kroymann, J.; Vogel, H.; Cembella, A.; John, U. Comparative genomic and transcriptomic characterization of the toxigenic marine dinoflagellate *Alexandrium ostenfeldii*. *PLoS ONE* **2011**, *6*, e28012. [CrossRef]
168. Fogel, M.; Hastings, J.W. Bioluminescence: Mechanism and mode of control of scintillon activity. *Proc. Natl. Acad. Sci. USA* **1972**, *69*, 690–693. [CrossRef] [PubMed]
169. Hastings, J.W. Chemistries and colors of bioluminescent reactions: A review. *Gene* **1996**, *173*, 5–11. [CrossRef]
170. Jacobovitz, M.R.; Hambleton, E.A.; Guse, A. Unlocking the complex cell biology of coral–dinoflagellate symbiosis: A model systems approach. *Annu. Rev. Genet.* **2023**, *57*, 411–434. [CrossRef]
171. Dougan, K.E.; González-Pech, R.A.; Stephens, T.G.; Shah, S.; Chen, Y.; Ragan, M.A.; Bhattacharya, D.; Chan, C.X. Genome-powered classification of microbial eukaryotes: Focus on coral algal symbionts. *Trends Microbiol.* **2022**, *30*, 831–840. [CrossRef]
172. Liu, H.; Stephens, T.G.; González-Pech, R.A.; Beltran, V.H.; Lapeyre, B.; Bongaerts, P.; Cooke, I.; Aranda, M.; Bourne, D.G.; Forêt, S.; et al. *Symbiodinium* genomes reveal adaptive evolution of functions related to coral-dinoflagellate symbiosis. *Commun. Biol.* **2018**, *1*, 95. [CrossRef]
173. González-Pech, R.A.; Stephens, T.G.; Chen, Y.; Mohamed, A.R.; Cheng, Y.; Shah, S.; Dougan, K.E.; Fortuin, M.D.A.; Lagorce, R.; Burt, D.W.; et al. Comparison of 15 dinoflagellate genomes reveals extensive sequence and structural divergence in family Symbiodiniaceae and genus *Symbiodinium*. *BMC Biol.* **2021**, *19*, 73. [CrossRef] [PubMed]
174. Wuerz, M.; Lawson, C.A.; Oakley, C.A.; Possell, M.; Wilkinson, S.P.; Grossman, A.R.; Weis, V.M.; Suggett, D.J.; Davy, S.K. Symbiont identity impacts the microbiome and volatilome of a model cnidarian-dinoflagellate symbiosis. *Biology* **2023**, *12*, 1014. [CrossRef] [PubMed]
175. Maire, J.; Deore, P.; Jameson, V.J.; Sakkas, M.; Perez-Gonzalez, A.; Blackall, L.L.; Van Oppen, M.J.H. Assessing the contribution of bacteria to the heat tolerance of experimentally evolved coral photosymbionts. *Environ. Microbiol.* **2023**, *25*, 3298–3318. [CrossRef] [PubMed]
176. Deschaseaux, E.; O'Brien, J.; Siboni, N.; Petrou, K.; Seymour, J.R. Shifts in dimethylated sulfur concentrations and microbiome composition in the red-tide causing dinoflagellate *Alexandrium minutum* during a simulated marine heatwave. *Biogeosciences* **2019**, *16*, 4377–4391. [CrossRef]
177. Anderson, D.M. Bloom dynamics of toxic *Alexandrium* species in the northeastern U.S. *Limnol. Oceanogr.* **1997**, *42*, 1009–1022. [CrossRef]
178. Jiang, Y.; Li, Z. Identification and genomic analysis of *Pseudosulfitobacter koreense* sp. nov. isolated from toxin-producing dinoflagellate *Alexandrium pacificum*. *Arch. Microbiol.* **2023**, *205*, 245. [CrossRef] [PubMed]
179. Yang, Q.; Jiang, Z.; Zhou, X.; Zhang, R.; Xie, Z.; Zhang, S.; Wu, Y.; Ge, Y.; Zhang, X. *Haliea alexandrii* sp. nov., isolated from phycosphere microbiota of the toxin-producing dinoflagellate *Alexandrium catenella*. *Int. J. Syst. Evol. Microbiol.* **2020**, *70*, 1133–1138. [CrossRef]
180. Amaro, A.M.; Fuentes, M.S.; Ogalde, S.R.; Venegas, J.A.; Suárez-Isla, B.A. Identification and characterization of potentially algal-lytic marine bacteria strongly associated with the toxic dinoflagellate *Alexandrium catenella*. *J. Eukaryot. Microbiol.* **2005**, *52*, 191–200. [CrossRef]
181. Hattenrath-Lehmann, T.K.; Gobler, C.J. Identification of unique microbiomes associated with harmful algal blooms caused by *Alexandrium fundyense* and *Dinophysis acuminata*. *Harmful Algae* **2017**, *68*, 17–30. [CrossRef]
182. Choi, C.J.; Jauzein, C.; Erdner, D.L. High-resolution phylogenetic analysis reveals long-term microbial dynamics and microdiversity in phytoplankton microbiome. *J. Eukaryot. Microbiol.* **2023**, *70*, e12966. [CrossRef]
183. Hollants, J.; Leliaert, F.; De Clerck, O.; Willems, A. What we can learn from sushi: A review on seaweed-bacterial associations. *FEMS Microbiol. Ecol.* **2013**, *83*, 1–16. [CrossRef] [PubMed]
184. Burgunter-Delamare, B.; Rousvoal, S.; Legeay, E.; Tanguy, G.; Fredriksen, S.; Boyen, C.; Dittami, S.M. The *Saccharina latissima* microbiome: Effects of region, season, and physiology. *Front. Microbiol.* **2023**, *13*, 1050939. [CrossRef] [PubMed]
185. Ricker, R.W. *Taxonomy and Biogeography of Macquarie Island Seaweeds*; British Museum (Natural History): London, UK, 1987; ISBN 978-0-565-00998-4.
186. Bonin, D.R.; Hawkes, M.W. Systematics and life histories of New Zealand *Bonnemaisoniaceae* (*Bonnemaisoniales*, *Rhodophyta*): II. The genus *Delisea*. *N. Z. J. Bot.* **1988**, *26*, 619–632. [CrossRef]
187. Millar, A. Marine red algae of the Coffs Harbour region, northern New South Wales. *Aust. Syst. Bot.* **1990**, *3*, 293. [CrossRef]
188. Harder, T.; Campbell, A.H.; Egan, S.; Steinberg, P.D. Chemical mediation of ternary interactions between marine holobionts and their environment as exemplified by the red alga *Delisea pulchra*. *J. Chem. Ecol.* **2012**, *38*, 442–450. [CrossRef]
189. Case, R.J.; Longford, S.R.; Campbell, A.H.; Low, A.; Tujula, N.; Steinberg, P.D.; Kjelleberg, S. Temperature induced bacterial virulence and bleaching disease in a chemically defended marine macroalga: Temperature, disease and algal chemical defense. *Environ. Microbiol.* **2011**, *13*, 529–537. [CrossRef] [PubMed]
190. Kumar, V.; Zozaya-Valdes, E.; Kjelleberg, S.; Thomas, T.; Egan, S. Multiple opportunistic pathogens can cause a bleaching disease in the red seaweed *Delisea pulchra*. *Environ. Microbiol.* **2016**, *18*, 3962–3975. [CrossRef]

191. Campbell, A.H.; Vergés, A.; Steinberg, P.D. Demographic consequences of disease in a habitat-forming seaweed and impacts on interactions between natural enemies. *Ecology* **2014**, *95*, 142–152. [CrossRef]
192. Campbell, A.H.; Harder, T.; Nielsen, S.; Kjelleberg, S.; Steinberg, P.D. Climate change and disease: Bleaching of a chemically defended seaweed. *Glob. Chang. Biol.* **2011**, *17*, 2958–2970. [CrossRef]
193. Hudson, J.; Deshpande, N.; Leblanc, C.; Egan, S. Pathogen exposure leads to a transcriptional downregulation of core cellular functions that may dampen the immune response in a macroalga. *Mol. Ecol.* **2022**, *31*, 3468–3480. [CrossRef]
194. Longford, S.; Tujula, N.; Crocetti, G.; Holmes, A.; Holmström, C.; Kjelleberg, S.; Steinberg, P.; Taylor, M. Comparisons of diversity of bacterial communities associated with three sessile marine eukaryotes. *Aquat. Microb. Ecol.* **2007**, *48*, 217–229. [CrossRef]
195. Zozaya-Valdés, E.; Roth-Schulze, A.J.; Egan, S.; Thomas, T. Microbial community function in the bleaching disease of the marine macroalgae *Delisea pulchra*. *Environ. Microbiol.* **2017**, *19*, 3012–3024. [CrossRef] [PubMed]
196. Fernandes, N.; Steinberg, P.; Rusch, D.; Kjelleberg, S.; Thomas, T. Community structure and functional gene profile of bacteria on healthy and diseased thalli of the red seaweed *Delisea pulchra*. *PLoS ONE* **2012**, *7*, e50854. [CrossRef] [PubMed]
197. De Nys, R.; Wright, A.D.; König, G.M.; Sticher, O. New halogenated furanones from the marine alga *Delisea pulchra* (cf. *fimbriata*). *Tetrahedron* **1993**, *49*, 11213–11220. [CrossRef]
198. Steinberg, P.D.; De Nys, R.; Kjelleberg, S. Chemical cues for surface colonization. *J. Chem. Ecol.* **2002**, *28*, 1935–1951. [CrossRef]
199. Dworjanyn, S.A.; De Nys, R.; Steinberg, P.D. Localisation and surface quantification of secondary metabolites in the red alga *Delisea pulchra*. *Mar. Biol.* **1999**, *133*, 727–736. [CrossRef]
200. Wright, J.T.; Zuccarello, G.C.; Steinberg, P.D. Genetic structure of the subtidal red alga *Delisea pulchra*. *Mar. Biol.* **2000**, *136*, 439–448. [CrossRef]
201. Wright, J.; De Nys, R.; Steinberg, P. Geographic variation in halogenated furanones from the red alga *Delisea pulchra* and associated herbivores and epiphytes. *Mar. Ecol. Prog. Ser.* **2000**, *207*, 227–241. [CrossRef]
202. Zang, T.; Lee, B.W.K.; Cannon, L.M.; Ritter, K.A.; Dai, S.; Ren, D.; Wood, T.K.; Zhou, Z.S. A naturally occurring brominated furanone covalently modifies and inactivates LuxS. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6200–6204. [CrossRef]
203. Manefield, M.; de Nys, R.; Naresh, K.; Roger, R.; Givskov, M.; Peter, S.; Kjelleberg, S. Evidence that halogenated furanones from *Delisea pulchra* inhibit acylated homoserine lactone (AHL)-mediated gene expression by displacing the AHL signal from its receptor protein. *Microbiology* **1999**, *145*, 283–291. [CrossRef]
204. Manefield, M.; Rasmussen, T.B.; Henzter, M.; Andersen, J.B.; Steinberg, P.; Kjelleberg, S.; Givskov, M. Halogenated furanones inhibit quorum sensing through accelerated LuxR turnover. *Microbiology* **2002**, *148*, 1119–1127. [CrossRef] [PubMed]
205. Li, J.; Weinberger, F.; Saha, M.; Majzoub, M.E.; Egan, S. Cross-host protection of marine bacteria against macroalgal disease. *Microb. Ecol.* **2022**, *84*, 1288–1293. [CrossRef] [PubMed]
206. De Clerck, O.; Kao, S.-M.; Bogaert, K.A.; Blomme, J.; Foflonker, F.; Kwantes, M.; Vancaester, E.; Vanderstraeten, L.; Aydogdu, E.; Boesger, J.; et al. Insights into the evolution of multicellularity from the sea lettuce genome. *Curr. Biol.* **2018**, *28*, 2921–2933.e5. [CrossRef] [PubMed]
207. Alcolombri, U.; Ben-Dor, S.; Feldmesser, E.; Levin, Y.; Tawfik, D.S.; Vardi, A. Identification of the algal dimethyl sulfide–releasing enzyme: A missing link in the marine sulfur cycle. *Science* **2015**, *348*, 1466–1469. [CrossRef]
208. Kessler, R.W.; Weiss, A.; Kuegler, S.; Hermes, C.; Wichard, T. Macroalgal-bacterial interactions: Role of dimethylsulfoniopropionate in microbial gardening by *Ulva* (*Chlorophyta*). *Mol. Ecol.* **2018**, *27*, 1808–1819. [CrossRef] [PubMed]
209. Karsten, U.; Kirst, G.O.; Wiencke, C. Dimethylsulphoniopropionate (DMSP) accumulation in green macroalgae from polar to temperate regions: Interactive effects of light versus salinity and light versus temperature. *Polar Biol.* **1992**, *12*, 603–607. [CrossRef]
210. Van Alstyne, K.L.; Puglisi, M.P. DMSP in marine macroalgae and macroinvertebrates: Distribution, function, and ecological impacts. *Aquat. Sci.* **2007**, *69*, 394–402. [CrossRef]
211. Van Der Loos, L.M.; D'hondt, S.; Engelen, A.H.; Pavia, H.; Toth, G.B.; Willems, A.; Weinberger, F.; De Clerck, O.; Steinhagen, S. Salinity and host drive *Ulva*-associated bacterial communities across the Atlantic-Baltic Sea gradient. *Mol. Ecol.* **2022**, *32*, 6260–6277. [CrossRef]
212. Burke, C.; Thomas, T.; Lewis, M.; Steinberg, P.; Kjelleberg, S. Composition, uniqueness and variability of the epiphytic bacterial community of the green alga *Ulva australis*. *ISME J.* **2011**, *5*, 590–600. [CrossRef]
213. Gemin, M.; Peña-Rodríguez, A.; Quiroz-Guzmán, E.; Magallón-Servín, P.; Barajas-Sandoval, D.; Elizondo-González, R. Growth-promoting bacteria for the green seaweed *Ulva clathrata*. *Aquac. Res.* **2019**, *50*, 3741–3748. [CrossRef]
214. Singh, R.; Mantri, V.; Reddy, C.; Jha, B. Isolation of seaweed-associated bacteria and their morphogenesis-inducing capability in axenic cultures of the green alga *Ulva fasciata*. *Aquat. Biol.* **2011**, *12*, 13–21. [CrossRef]
215. Ghaderiardakani, F.; Coates, J.C.; Wichard, T. Bacteria-induced morphogenesis of *Ulva intestinalis* and *Ulva mutabilis* (Chlorophyta): A contribution to the lottery theory. *FEMS Microbiol. Ecol.* **2017**, *93*, fix094. [CrossRef]
216. Vesty, E.F.; Kessler, R.W.; Wichard, T.; Coates, J.C. Regulation of gametogenesis and zoosporogenesis in *Ulva linza* (*Chlorophyta*): Comparison with *Ulva mutabilis* and potential for laboratory culture. *Front. Plant Sci.* **2015**, *6*, 15. [CrossRef] [PubMed]
217. Spoerner, M.; Wichard, T.; Bachhuber, T.; Stratmann, J.; Oertel, W. Growth and thallus morphogenesis of *Ulva mutabilis* (*Chlorophyta*) depends on a combination of two bacterial species excreting regulatory factors. *J. Phycol.* **2012**, *48*, 1433–1447. [CrossRef] [PubMed]
218. Nakanishi, K.; Nishijima, M.; Nishimura, M.; Kuwano, K.; Saga, N. Bacteria that induce morphogenesis in *Ulva pertusa* (*Chlorophyta*) grown under axenic conditions. *J. Phycol.* **1996**, *32*, 479–482. [CrossRef]

219. Tait, K.; Joint, I.; Daykin, M.; Milton, D.L.; Williams, P.; Camara, M. Disruption of quorum sensing in seawater abolishes attraction of zoospores of the green alga *Ulva* to bacterial biofilms. *Environ. Microbiol.* **2005**, *7*, 229–240. [CrossRef]
220. Wichard, T. Exploring bacteria-induced growth and morphogenesis in the green macroalga order Ulvales (*Chlorophyta*). *Front. Plant Sci.* **2015**, *6*, 86. [CrossRef] [PubMed]
221. Wichard, T. From model organism to application: Bacteria-induced growth and development of the green seaweed *Ulva* and the potential of microbe leveraging in algal aquaculture. *Semin. Cell Dev. Biol.* **2023**, *134*, 69–78. [CrossRef]
222. Kessler, R.W.; Crecelius, A.C.; Schubert, U.S.; Wichard, T. In situ monitoring of molecular changes during cell differentiation processes in marine macroalgae through mass spectrometric imaging. *Anal. Bioanal. Chem.* **2017**, *409*, 4893–4903. [CrossRef]
223. Vallet, M.; Kaftan, F.; Grabe, V.; Ghaderiardakani, F.; Fenizia, S.; Svatoš, A.; Pohnert, G.; Wichard, T. A new glance at the chemosphere of macroalgal-bacterial interactions: In situ profiling of metabolites in symbiosis by mass spectrometry. *Beilstein J. Org. Chem.* **2021**, *17*, 1313–1322. [CrossRef]
224. Alsufyani, T.; Califano, G.; Deicke, M.; Grueneberg, J.; Weiss, A.; Engelen, A.H.; Kwantes, M.; Mohr, J.F.; Ulrich, J.F.; Wichard, T. Macroalgal-bacterial interactions: Identification and role of thallusin in morphogenesis of the seaweed *Ulva* (*Chlorophyta*). *J. Exp. Bot.* **2020**, *71*, 3340–3349. [CrossRef] [PubMed]
225. Matsuo, Y.; Suzuki, M.; Kasai, H.; Shizuri, Y.; Harayama, S. Isolation and phylogenetic characterization of bacteria capable of inducing differentiation in the green alga *Monostroma oxyspermum*. *Environ. Microbiol.* **2003**, *5*, 25–35. [CrossRef]
226. Matsuo, Y.; Imagawa, H.; Nishizawa, M.; Shizuri, Y. Isolation of an algal morphogenesis inducer from a marine bacterium. *Science* **2005**, *307*, 1598. [CrossRef] [PubMed]
227. Wichard, T. Identification of metallophores and organic ligands in the chemosphere of the marine macroalga *Ulva* (*Chlorophyta*) and at land-sea interfaces. *Front. Mar. Sci.* **2016**, *3*, 131. [CrossRef]
228. Comba González, N.; Ramírez Hoyos, M.; López Kleine, L.; Montoya Castaño, D. Production of enzymes and siderophores by epiphytic bacteria isolated from the marine macroalga *Ulva lactuca*. *Aquat. Biol.* **2018**, *27*, 107–118. [CrossRef]
229. Wienecke, P.; Ulrich, J.F.; Morales-Reyes, C.F.; Dhiman, S.; Wichard, T.; Arndt, H. Enantioselective total synthesis of the morphogen (−)-thallusin and mediated uptake of Fe(III) into the green seaweed *Ulva*. *Chem. Eur. J.* **2024**, e202304007. [CrossRef]
230. Charrier, B.; Coelho, S.M.; Le Bail, A.; Tonon, T.; Michel, G.; Potin, P.; Kloareg, B.; Boyen, C.; Peters, A.F.; Cock, J.M. Development and physiology of the brown alga *Ectocarpus siliculosus*: Two centuries of research. *New Phytol.* **2007**, *177*, 319–332. [CrossRef]
231. Coelho, S.M.; Peters, A.F.; Müller, D.; Cock, J.M. *Ectocarpus*: An evo-devo model for the brown algae. *EvoDevo* **2020**, *11*, 19. [CrossRef]
232. Cock, J.M.; Sterck, L.; Rouzé, P.; Scornet, D.; Allen, A.E.; Amoutzias, G.; Anthouard, V.; Artiguenave, F.; Aury, J.-M.; Badger, J.H.; et al. The *Ectocarpus* genome and the independent evolution of multicellularity in brown algae. *Nature* **2010**, *465*, 617–621. [CrossRef]
233. Prigent, S.; Collet, G.; Dittami, S.M.; Delage, L.; Ethis de Corny, F.; Dameron, O.; Eveillard, D.; Thiele, S.; Cambefort, J.; Boyen, C.; et al. The genome-scale metabolic network of *Ectocarpus siliculosus* (EctoGEM): A resource to study brown algal physiology and beyond. *Plant J.* **2014**, *80*, 367–381. [CrossRef]
234. Badis, Y.; Scornet, D.; Harada, M.; Caillard, C.; Godfroy, O.; Raphalen, M.; Gachon, C.M.M.; Coelho, S.M.; Motomura, T.; Nagasato, C.; et al. Targeted CRISPR-Cas9-based gene knockouts in the model brown alga *Ectocarpus*. *New Phytol.* **2021**, *231*, 2077–2091. [CrossRef] [PubMed]
235. Prigent, S.; Frioux, C.; Dittami, S.M.; Thiele, S.; Larhlimi, A.; Collet, G.; Gutknecht, F.; Got, J.; Eveillard, D.; Bourdon, J.; et al. Meneco, a topology-based gap-filling tool applicable to degraded genome-wide metabolic networks. *PLoS Comput. Biol.* **2017**, *13*, e1005276. [CrossRef] [PubMed]
236. Frioux, C.; Fremy, E.; Trottier, C.; Siegel, A. Scalable and exhaustive screening of metabolic functions carried out by microbial consortia. *Bioinformatics* **2018**, *34*, i934–i943. [CrossRef] [PubMed]
237. Le Bail, A.; Billoud, B.; Kowalczyk, N.; Kowalczyk, M.; Gicquel, M.; Le Panse, S.; Stewart, S.; Scornet, D.; Cock, J.M.; Ljung, K.; et al. Auxin metabolism and function in the multicellular brown alga *Ectocarpus siliculosus*. *Plant Physiol.* **2010**, *153*, 128–144. [CrossRef] [PubMed]
238. Rabillé, H.; Billoud, B.; Tesson, B.; Le Panse, S.; Rolland, É.; Charrier, B. The brown algal mode of tip growth: Keeping stress under control. *PLOS Biol.* **2019**, *17*, e2005258. [CrossRef]
239. KleinJan, H.; Jeanthon, C.; Boyen, C.; Dittami, S.M. Exploring the cultivable *Ectocarpus* microbiome. *Front. Microbiol.* **2017**, *8*, 2456. [CrossRef] [PubMed]
240. Burgunter-Delamare, B.; KleinJan, H.; Frioux, C.; Fremy, E.; Wagner, M.; Corre, E.; Le Salver, A.; Leroux, C.; Leblanc, C.; Boyen, C.; et al. Metabolic complementarity between a brown alga and associated cultivable bacteria provide indications of beneficial interactions. *Front. Mar. Sci.* **2020**, *7*, 85. [CrossRef]
241. Karimi, E.; Dittami, S.M. Maintaining beneficial alga-associated bacterial communities under heat stress: Insights from controlled co-culture experiments using antibiotic-resistant bacterial strains. *FEMS Microbiol. Ecol.* **2023**, *99*, fiad130. [CrossRef]
242. Strittmatter, M.; Grenville-Briggs, L.J.; Breithut, L.; Van West, P.; Gachon, C.M.M.; Küpper, F.C. Infection of the brown alga *Ectocarpus siliculosus* by the oomycete *Eurychasma dicksonii* induces oxidative stress and halogen metabolism. *Plant Cell Environ.* **2016**, *39*, 259–271. [CrossRef]
243. Tapia, J.E.; González, B.; Goulitquer, S.; Potin, P.; Correa, J.A. Microbiota influences morphology and reproduction of the brown alga *Ectocarpus* sp. *Front. Microbiol.* **2016**, *7*, 197. [CrossRef]

244. Dittami, S.M.; Duboscq-Bidot, L.; Perennou, M.; Gobet, A.; Corre, E.; Boyen, C.; Tonon, T. Host-microbe interactions as a driver of acclimation to salinity gradients in brown algal cultures. *ISME J.* **2016**, *10*, 51–63. [CrossRef]
245. Dittami, S.M.; Peters, A.F.; West, J.A.; Cariou, T.; KleinJan, H.; Burgunter-Delamare, B.; Prechoux, A.; Egan, S.; Boyen, C. Revisiting Australian *Ectocarpus subulatus* (Phaeophyceae) from the Hopkins River: Distribution, abiotic environment, and associated microbiota. *J. Phycol.* **2020**, *56*, 821579. [CrossRef]
246. Karimi, E.; Geslain, E.; KleinJan, H.; Tanguy, G.; Legeay, E.; Corre, E.; Dittami, S.M. Genome sequences of 72 bacterial strains isolated from *Ectocarpus subulatus*: A resource for algal microbiology. *Genome Biol. Evol.* **2020**, *12*, 3647–3655. [CrossRef]
247. Dittami, S.M.; Eveillard, D.; Tonon, T. A metabolic approach to study algal-bacterial interactions in changing environments. *Mol. Ecol.* **2014**, *23*, 1656–1660. [CrossRef]

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