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**Bioinformatics of Corals:
 Investigating Heterogeneous
 Omics Data from Coral
 Holobionts for Insight into
 Reef Health and Resilience**

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Abstract

Coral reefs are home to over two million species and provide habitat for roughly 25% of all marine animals, but they are being severely threatened by pollution and climate change. A large amount of genomic, transcriptomic, and other omics data is becoming increasingly available from different species of reef-building corals, the unicellular dinoflagellates, and the coral microbiome (bacteria, archaea, viruses, fungi, etc.). Such new data present an opportunity for bioinformatics researchers and computational biologists to contribute to a timely, compelling, and urgent investigation of critical factors that influence reef health and resilience.

1. INTRODUCTION

Corals are important natural resources that are key to the oceans' vast biodiversity and provide economic, cultural, and scientific benefits. While coral reefs cover only 0.1% of the ocean floor, they are home to the largest density of animals on earth, rivaling rainforest habitats in species diversity (1). Coral colonies are comprised of clonal cnidarian polyps that depend on a symbiotic relationship with single-celled algae in the family Symbiodiniaceae (2), belonging to the broader group of unicellular algae known as dinoflagellates. The endosymbiotic algae harvest light and synthesize carbon in exchange for shelter and nitrogen sources (3). This nutritional symbiosis, which was originally thought to primarily include endosymbiotic algae, is now known to extend to a much more complex community than anticipated, with thousands of bacteria, bacteriophages, viruses, and fungi (4, 5) in addition to the Symbiodiniaceae. The entirety of this community is referred to as a holobiont (6), or metaorganism (7) (**Figure 1**). Thus, these reef-building, scleractinian coral holobionts are more like cities than individual animals, as they provide factories,

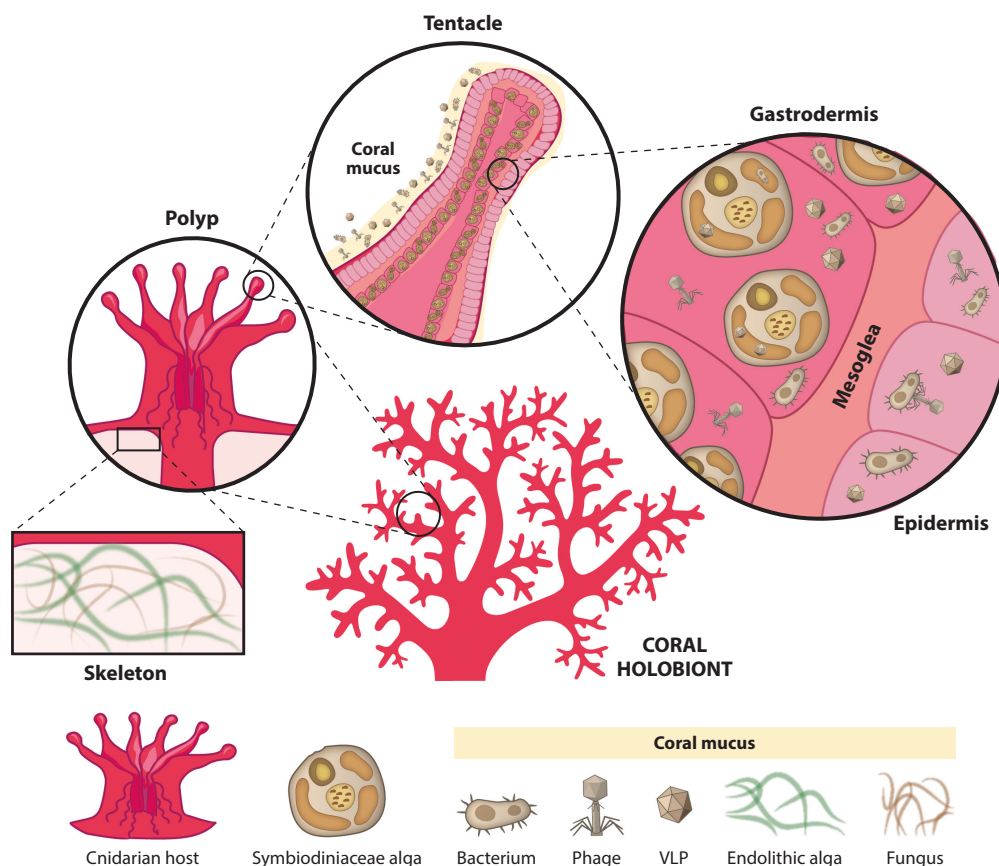


Figure 1

The coral holobiont is comprised of the cnidarian host; single-celled endosymbiotic algae in the family Symbiodiniaceae; and a variety of bacteria, archaea, viruses, virus-like particles (VLPs), endolithic algae, and fungi. The coral forms the base unit of a polyp with tentacles and mouth. The coral body has two tissue layers, the ectodermis and the gastrodermis. The gastrodermis houses the symbiotic algae. The coral microbiome can be found both on the coral surface in a coral mucus layer and within the cells, gastrovascular cavity, and skeleton.

housing, restaurants, nurseries, and more for an entire ecosystem, both at microscopic and macroscopic levels.

While the symbiotic biological complexity of corals provides the power to thrive in nutrient-poor waters, it also leaves the holobiont vulnerable to the limitations of all of the component partners. This makes it very challenging to understand the myriad factors that influence the environmental sensitivity and resilience of local coral reef systems (8). The extreme vulnerability of reef-building corals to warming oceans and ocean acidification has led to an acute coral reef crisis (9). For example, a 2017 study estimated that coral reefs are likely to decline by 70–90% relative to their current abundances by mid-century, even if ocean temperatures increase only by 2°C, in accordance with the Paris Climate Accords' target (1). This estimate preceded the marine heatwave that led to the most recent mass bleaching events of the Great Barrier Reef (10). Because of a constellation of factors from human-generated climate change in the Anthropocene, the frequency and duration of heatwaves (11) leading to coral mass bleaching events and coral habitat loss are only projected to accelerate (12).

In light of the complexity and sensitivity of corals and the urgency of the coral reef crisis under climate change, bioinformatics approaches are emerging as critical tools to help illuminate the external and internal mechanisms and biological pathways involved in coral stress response and disease. Building on the foundation of knowledge and tools accumulated in the study of human disease and other model organisms, we can enhance the critical analysis of a vast array of omics data that are being generated from reef-building corals (e.g., 13). Of particular interest in biomedical and restoration contexts is whether we can discover supportive interventions or treatments for stressed or diseased corals (14). For example, could a bioinformatics-informed understanding of coral biology help us to design diagnostics and treatments for bleaching?

It is still early in our understanding of how bioinformatics approaches can help, given that much about the coral holobiont is still unknown. However, we are finding that there is overlap between human and coral biological pathways (15, 16), as well as between those of the endosymbiotic algae and those of humans and plants (17), which is perhaps surprising given their evolutionary distance. We refer to such comparative genomics approaches, which leverage knowledge of related genes and pathways found to be somewhat conserved even in quite distant species, as remote homology approaches (16). As an additional benefit, our study of these commonalities, and how we can leverage them for corals, may help provide a roadmap and a toolbox for bioinformatic and biomedical investigations of other nonmodel organisms.

We focus here on describing the emerging omics approaches, data availability, and state of the field in corals in Section 2; we further discuss computational advances and additional challenges for our understanding of the coral holobiont in Section 3, where we have provided the interested reader with some contextual background on basic coral holobiont biology in the **Supplemental Appendix**. In Section 4, we highlight the role of bioinformatics in elucidating pathways of coral dysbiosis, which are particularly important in light of the massively destructive effects of coral bleaching (Section 4.1) and disease (Section 4.2). In Section 5, we highlight the roles bioinformatics approaches have already played in molecular diagnostics of coral health amid the growing call for human interventions in coral reef systems. We then look to the future, identifying grand challenges that could be addressed with modified and novel computational tools in support of diagnostics and interventions for reef-building corals under stress (Section 6).

Improving our molecular understanding of coral holobiont biology has taken on increasing urgency, as coral reefs are declining rapidly due to the consequences of climate change. Coral biologists are generating vast amount of genomic, transcriptomic, and other omics data from different species of reef-building corals (13, 15, 18–23), the unicellular dinoflagellates (24–26), and the highly diverse coral microbiome (4, 19). This growing omics momentum (13, 27) has

Supplemental Material >

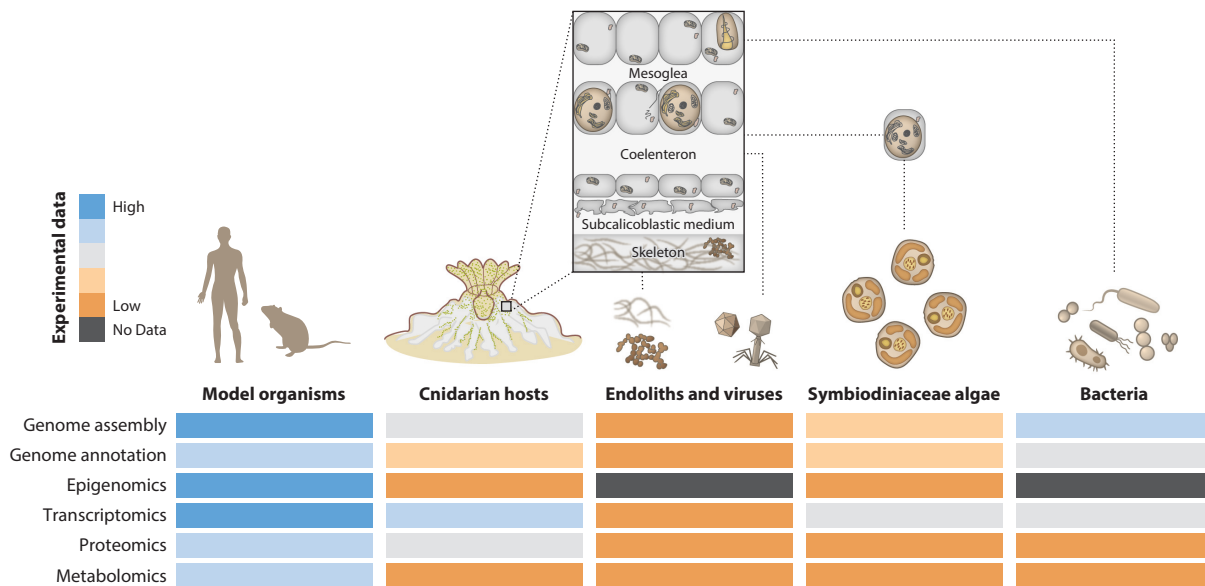


Figure 2

Based on the literature, a qualitative snapshot of the relative differences in the amount of omics data of various types that have been collected across the holobiont partners, as compared to what is available for model organisms.

already allowed coral biologists to make some progress in identifying key genes and biological pathways. We briefly review the state of knowledge of important coral biological pathways (from biomineralization to host–symbiont communication, early development, and stress response) in the **Supplemental Appendix**. New omics data provide a terrific opportunity for bioinformatics researchers and computational biologists to harness this data revolution and contribute to a timely, compelling, and urgent investigation of critical factors that influence reef health, resistance, and resilience (28).

2. EMERGING CORAL OMICS INFORMATION

The amount of various omics data available for the coral holobiont has vastly increased over the past decade. With the pace of data generation massively accelerating, there are genomic, epigenomic, transcriptomic, proteomic, and metabolomic data available (see **Figure 2**), much of which has been made open access (e.g., <http://www.reefgenomics.org>) and is often publicly available even prior to publication. In this section we outline current availability of omics data across the holobiont partners and highlight bioinformatics studies that have used different types of omics data to understand crucial aspects of genotype-to-phenotype linkages in the coral holobiont.

2.1. Coral Animal Genomes

The first-draft genome of a reef-building coral animal was the Okinawan staghorn coral *Acropora digitifera* in 2011 (29). The *A. digitifera* genome was assembled from short-read technology (454 shotgun and Illumina Genome Analyzer IIx paired-end and mate pair reads). There is now a growing list of draft genomes, with the greatest number of genomes from the genus *Acropora*, followed by *Montipora*, *Pocillopora*, and *Orbicella* (**Table 1**).

More recent genome sequencing efforts have included a combination of long-read scaffolds, short-read error correction, and sometimes proximity ligation approaches, which together have

Table 1 Published coral animal genomes by family, species, and genome size

Family	Species	Clade	Genome size (Mb) ^a	Reference
Acroporidae	<i>Acropora digitifera</i> ^b	Complex	416	18
Acroporidae	<i>Acropora millepora</i>	Complex	475	20
Acroporidae	<i>Acropora millepora</i>	Complex	387	30
Acroporidae	<i>Astreopora myriophthalma</i>	Complex	384	18
Acroporidae	<i>Montipora cactus</i>	Complex	653	29
Acroporidae	<i>Montipora capitata</i>	Complex	885	31
Acroporidae	<i>Montipora capitata</i>	Complex	614	32
Acroporidae	<i>Montipora efflorescens</i>	Complex	643	18
Poritidae	<i>Porites lutea</i>	Complex	552	19
Poritidae	<i>Porites rus</i>	Complex	470	33
Agariciidae	<i>Pachyseris speciosa</i>	Robust	984	34
Euphylliidae	<i>Galaxea fascicularis</i>	Robust	334	35
Fungiidae	<i>Fungia</i> spp.	Robust	606	35
Merulinidae	<i>Orbicella faveolata</i> ^c	Robust	486	36
Merulinidae	<i>Goniastrea aspera</i>	Robust	764	35
Montastraeidae	<i>Montastraea cavernosa</i>	Robust	448	19
Pocilloporidae	<i>Pocillopora acuta</i>	Robust	404	37
Pocilloporidae	<i>Pocillopora damicornis</i>	Robust	234	38
Pocilloporidae	<i>Pocillopora verrucosa</i>	Robust	380	39
Pocilloporidae	<i>Stylophora pistillata</i>	Robust	400	40

^aReported genome sizes are sequence and assembly based. Further statistics describing assembly quality appear in **Supplemental Table 1**, including scaffold number, estimated gene number, and the BUSCO (41) completeness score.

^bIn addition to *A. digitifera*, Reference 18 also contains similar quality assemblies for the following *Acropora* spp.: *acuminata*, *awi*, *cytherea*, *digitifera*, *echinata*, *florida*, *gemmaifera*, *hyacinthus*, *intermedia*, *microphthalma*, *muricata*, *nasta*, *selago*, *tenuis*, and *yongei*.

^cReference 36 also has some genome information for two other *Orbicella* spp.

improved assembly metrics. We now have chromosome-level assembly of a handful of genomes including *Acropora millepora* (20), *Astrangia poculata* (K. Stankiewicz, unpublished data), and *Montipora capitata* (42). Two recent studies have enhanced our analytical capacity through the sequencing of large numbers of corals species (18), or large sample sizes within a single species (20). First, a comparative genomics approach analyzed 18 closely related coral genomes (15 from *Acropora* and 3 additional taxa), further strengthening our phylogenetic understanding in this family via whole-genome analysis (18). Second, using a long-read sequencing technology (from Pacific Biosciences) combined with gap filling and error correcting with short reads (from Illumina), Fuller et al. (20) produced a high-quality chromosome-level genomic sequence for *A. millepora*. The quality of the *A. millepora* assembly was high enough that Fuller et al. were able to perform the first genome-wide association study (GWAS) on corals, comparing individual corals for statistically significant mutations that linked to stress-tolerant phenotype.

While the number of coral genomes and their quality are increasing, there are still bioinformatic challenges remaining that would further enable functional studies if solved or improved. These include challenges in assembly due to repetitive regions and genome heterozygosity and in functional annotation, particularly of those genes that are coral specific, unknown, or so-called dark genes (28).

2.2. Algal Symbiont Genomes

For the symbiont, emerging genomic information has triggered a recent revolution in taxonomy (2): Before the era of genomics, symbionts were classified primarily by morphology. In fact, it

Supplemental Material >

was initially erroneously believed that all of the coral algal symbionts were from or were closely related to the same the species, *Symbiodinium microadriaticum* (43). Based on initial sequencing of marker gene regions such as the nr28S (44), ITS2 (45), cp23S (46), and psbA (47), and further supported by recent genomic resources, we now know there is a vast diversity of genera and species. Initial genetic studies partitioned the symbionts into clades, where the clades were assumed to roughly correspond to species-level boundaries. However, with the emerging sequenced genomes of several symbiont species (48), it has been found that what were previously identified as clades can have differences that are on the order of taxa-level differences in other organisms, with less than 20% orthologous gene loci between clades (2), and that many clades have subclades that are as diverse as different species. Thus, LaJeunesse et al. (2) revised the taxonomy to assign separate genera to the previous clade level and refer to the union of all the species formerly classified as part of the *Symbiodinium* genus as the family Symbiodiniaceae. This revision has placed the former clade A as *Symbiodinium*; clade B as *Breviolum*; clade C, *Cladocopium*; clade D, *Durudinium*; clade E, *Effrenium*; clade F, *Fugacium*; and clade G, *Gerakladium*, with clades A–D including the species typically found in symbiosis with corals. The genomic evidence strongly supports this reclassification (25, 49). However, since all but the most recent published literature uses the older, “clade” nomenclature, for the remainder of this article we will use new nomenclature with the old nomenclature following in parentheses.

The family Symbiodiniaceae are part of the broader class of Dinophyceae, whose genomes are particularly massive for single-celled organisms (49), contain unusual structural organization and repetitive elements (48), and, thus, are very difficult to assemble computationally (48). While Symbiodiniaceae have smaller genomes relative to other dinoflagellates (49), the repetitive elements make assembly of short reads extremely challenging. Symbiodiniaceae can survive free-living, or apart from their animal host, while others have been found nearly impossible to culture apart from their animal hosts (e.g., 50), adding an additional level of difficulty to isolating the material needed to generate draft genomes for many critical symbiont taxa [e.g., *Cladocopium*, C15 (50)]. Additionally, without the capacity to more cheaply and rapidly sequence, assemble, and analyze at the whole-genome level for Symbiodiniaceae, it is unclear how cultured and *in hospite* symbionts may be evolving differently. For example, *Breviolum minutum* (subclade B1) was one of the first species of *Symbiodinium* cultured, though it is mostly known to be associated with a noncoral animal host (the jellyfish *Cassiopea xamachana*), but recently, Ros et al. (51) reported a sample of *B. minutum* recovered from the torch coral, *Euphyllia glabrescens*. To what extent are these instances of *B. minutum* identified by marker genes as a single species the same? In the case of the particular strain of *B. minutum* from which the genome was derived, in attempting to answer this question, we also run into some of the same issues that one has when comparing cell lines in the lab to strains of organisms in the wild. In particular, while the sample of *B. minutum* that was sequenced was taken from a jellyfish, it was attractive to sequence because it had been able to be cultured and survive apart from any host for multiple generations in the lab. The fact that it was able to be cultured successfully outside the animal, along with the fact that the genome was smaller in size than most symbionts (50), made *B. minutum* in many ways a great first model organism for the study of coral symbionts. However, it has not yet been established how different the genome of this lab-cultured *B. minutum* might be from the symbiont that shares the same marker gene sequence cultured from the torch coral. In general, whole-genome measures of diversity, rather than just marker genes, are preferable to design species boundaries (52). Recent hybrid assemblies containing both short-read Illumina and long-read PacBio data generate more contiguous assemblies than short-read data alone, and will enable high-quality symbiont genomes going forward (25). **Table 2** (and **Supplemental Table 2**) give a catalog of current published algal symbiont genomes.

Table 2 Published algal symbiont genomes, by family, species, and genome size^a

Family	Species	Genome size (Mb)	Reference
Symbiodiniaceae	<i>Breviolum minutum</i>	616	17
Symbiodiniaceae	<i>Cladocopium</i> spp. C92	705	53
Symbiodiniaceae	<i>Cladocopium goreau</i>	1,028	48
Symbiodiniaceae	<i>Durusdinium trenchii</i>	670	54
Symbiodiniaceae	<i>Fugacium kawagutii</i> (V3)	937	55
Symbiodiniaceae	<i>Symbiodinium fitti</i>	602	56
Symbiodiniaceae	<i>Symbiodinium microadriaticum</i>	808	55
Symbiodiniaceae	<i>Symbiodinium microadriaticum</i> CassKB8	1,120	25
Symbiodiniaceae	<i>Symbiodinium microadriaticum</i> 04-503SCI.03	1,053	25
Symbiodiniaceae	<i>Symbiodinium tridacnidorum</i> CCMP2592 ^b	1,287	25
Symbiodiniaceae	<i>Symbiodinium linucheae</i> CCMP2456	915	25
Symbiodiniaceae	<i>Symbiodinium necroappetens</i> CCMP2469	1,007	25
Symbiodiniaceae	<i>Symbiodinium natans</i> CCMP2548 ^b	740	25
Symbiodiniaceae	<i>Symbiodinium pilosum</i> CCMP2461	1,994	25
Symbiodiniaceae	<i>Symbiodinium tridacnidorum</i>	767	53

^aFor further details describing assembly quality and estimated number of genes, we refer the reader to Reference 25.

^bThese are hybrid short-/long-read assemblies, whereas the others in Reference 25 are all based on only short reads.

Particularly noteworthy, given the need for improved assemblies and increasing the number of genomes available for comparative genomics, are several recent Symbiodiniaceae studies. First, González-Pech et al. (57) generated a new, higher-quality assembly of the *Symbiodinium tridacnidorum* genome (isolated from the *Heliofungia actiniformis* stony coral from the Coral Sea) using a combination of short- and long-read sequencing technologies. Furthermore, multiple genomes are now available for comparative analyses, such as the generation of seven de novo genomes of *Symbiodinium* spp. (clade A) and the comparison of these seven with genomes from *Breviolum* (clade B, $n = 1$), *Cladocopium* (clade C, $n = 2$), and *Fugacium* (clade F, $n = 1$) (25). Genome-level analyses have also been completed by examining single-nucleotide polymorphism (SNP) differences in *Symbiodinium* spp. (clade A, $n = 3$) across three different *Acropora* spp. of corals that are adapted to different light and temperature gradients (56). Additionally, new chromosome-scale scaffolds for *S. microadriaticum* have been constructed with the help of Hi-C data (26). Given the novel organization of the Symbiodiniaceae genome, it is exciting that the first Hi-C studies of 3D genome organization have recently been published for both *B. minutum* (58) and *S. microadriaticum*, a species in symbiosis with a reef-building coral (26). It is estimated that these species have 91 and 94 chromosomes, respectively, with a gene density lower than that of bacteria, but substantially higher than that of the human genome (59).

Because of the difficulty of sequencing symbiont species that cannot be cultured outside of the host (50, 57), the ongoing revision of taxonomic classifications, and the difficulty in genome annotation for symbiont genomes (60), a full characterization of how symbiont species membership affects bleaching tolerance remains an ongoing subject of research. A major paradigm in the field is that corals with *Durusdinium* (clade D) symbionts appear more heat tolerant and resistant to bleaching than corals that host *Cladocopium* (clade C) symbionts (61–63), but this is not universally tested. Determining the genes or genomic features for gene expression regulation that differ between Symbiodiniaceae genera and species is an important open research topic. Initial progress along these lines appears in References 25, 55, and 57. We note that there are

computational challenges in dinoflagellate bioinformatics that go beyond assembly for repetitive sequences, where gene prediction also seems uniquely challenging (60). This is partially due to a different organization and regulation of genes than in other eukaryotes, including noncanonical intron splicing, the existence of unusual promoter regions for many genes, and a greater reliance on translational, rather than transcriptional, regulation (55). Baumgarten et al. (64) have also suggested a role of microRNAs in symbiont gene regulation.

2.3. Holobiont Microbiome

Technically, the symbiotic algae are also members of the coral microbiome, but they are often called out separately because of their importance to the holobiont in carbon generation via photosynthesis and translocation of carbon products to the coral host (3). The remainder of the microbiome includes bacteria, viruses, fungi, and coral-associated archaea (19) and is among the most diverse discovered (65). Just like humans, where the gut microbiome, skin microbiome, etc. form distinct communities, there are multiple niche habitats in the coral holobiont; principally the coral gut, mucus, and skeleton microbiomes have been documented (66–68). This microbial symbiosis can provide benefits to both the bacteria and the holobiont; for example, microbiome inhabitants of the coral mucus receive a constant supply of organic nutrients, carbon, and energy, as well as perhaps a partial shield against protozoan predators and bacteriophages (69). However, the coral benefits from natural antibiotics and complex polysaccharides produced by the microbiome, which also could produce supplementary nutrients, fix nitrogen, or possibly scavenge for trace metals in the surrounding water (5, 67, 69).

Most microbiome studies of bacterial species diversity in corals have used 16S ribosomal RNA (rRNA) gene sequencing to characterize the presence/absence of certain bacterial species (70, 71). The composition of the coral microbiome can be either stable or variable across different species and environmental conditions (4–6, 72–75). One particularly abundant bacterium in corals that also associates with many other marine organisms is *Endozoicomonas* (75, 76), whose genome has been sequenced (77). The extent to which the bacterial microbiome can explain stress tolerance can vary by coral taxa, or can vary for the same species under a variety of conditions (78, 79). Certainly, it can change as the coral bleaches and dies (67).

The study of the coral microbiome has become more urgent as several devastating coral bacterial diseases, including white band and black band diseases and the recent stony coral tissue loss disease (SCTLD), have devastated reefs. There has been a concerted effort to index the cultured bacterial fraction of the coral holobiont from past studies into a centralized database (80), which provides a comprehensive overview of 3,055 isolates from 52 studies conducted before 2022, including 1,045 with full-length 16S rRNA gene sequences spanning 138 known and 12 potentially novel bacterial genera across the *Proteobacteria*, *Firmicutes*, *Bacteroidetes*, and *Actinobacteria* phyla (80), sampled from 84 coral species. The researchers behind this effort additionally matched these 16S sequences to available full genomes for 36 species, and themselves constructed genomes for 38 more. This represents roughly 2.5% of the 3,055 isolates that can now be mapped to full bacterial genomes and identifies the need for further metagenomic sequencing of the holobiont.

The functional roles of additional members of the coral microbiome including viruses, fungi, and endolithic algae cannot be overlooked (e.g., 81, 82). Due to their microscopic and cryptic nature, there is a relatively smaller (Figure 2) but growing amount of omics information for these taxa. We point the reader to comprehensive reviews and seminal work in these areas highlighted in the **Supplemental Appendix**. Clearly there is a diversity of microbiota with particularly important functional roles that will benefit from additional sequencing and multiomics approaches and the essential computational tools to deal with such data.

3. COMPUTATIONAL ADVANCEMENTS AND CHALLENGES FOR UNDERSTANDING THE CORAL HOLOBIONT

3.1. Genomics

Once new genomes have been sequenced, a primary goal for functional understanding of the genome is to identify protein-coding regions and to annotate these genes based on their predicted function and broader role in biological pathways. Prior to the increase in sequenced genomes for many coral species, studies have compared orthologous groups between several genomes (e.g., 40) using a combination of expressed sequence tag and genomic data across multiple species of corals in Reference 15. Early comparative studies of protein domains have found a wealth of transmembrane transporters among the genes of the symbiont, including specific sequence signatures for transporters of bicarbonate, ammonium, phosphate, lipids, glycerol, amino acids, choline, sugars, and sulfates, as well as the more general ABC and ion transporters (55).

More recently, for the coral animal, we are finding that remote homology approaches can help recover a surprising amount of information from mapping the statistical sequence signal of genes that evolved from a common ancestor to various well-studied vertebrate genes and pathways, ranging from membrane receptor proteins (16, 83) to the biomineralization processes and primitive portions of the immune system. As vertebrate relatives are too divergent for simple BLAST-based sequence approaches to work, we have found that profile–profile hidden Markov model methods [e.g., HHblits (84)] are necessary to identify distant mammalian homologs to coral animal genes. For the symbiont, some of the same strategies can be employed using plants as a model organism, but in corals and Symbiodiniaceae we also find a tremendous amount of genes that seem very different from studied genes and pathways in other species, termed the dark genes, or genes of yet unknown function (28). Recently, there has been some notable initial success in setting up CRISPR/Cas9 pipelines (85, 86) for gene-knockout experiments in the coral animal; an efficient CRISPR pipeline would help with functional genomic studies of, for example, genes that could be implicated in coral stress response (28). Another novel approach to try to organize the genes into functionally coherent clusters and pathways from just gene sequence information is via predictions of protein–protein interactions [e.g., D-SCRIPT (87)].

3.2. Holobiont Metagenomics

Given the complexity of the microbiome and the holobiont more broadly, the need to characterize the community dynamics and interactive functions of these partners is paramount. Metagenomic studies are on the rise for corals (e.g., 88–92). One of the most comprehensive metagenomic sequencing studies has been completed using the massive and dominant reef-building coral *Porites lutea*, including the host coral, its alga symbiont *Cladocopium* C15 (clade C, type C15), and 52 bacterial and archaeal groups (19), further clarifying the genomic basis of holobiont functionality. In addition, shotgun metagenomic sequencing has been used to characterize benthic cyanobacterial mats adjacent to reef corals in Bonaire, Caribbean Netherlands (93). The need for additional metagenomic analyses is clear with respect to coral holobiont function, as climate continues to change in tandem with increasing local anthropogenic impacts (e.g., nutrients, sewage, and sedimentation).

3.3. Transcriptomics

Using short-read Illumina technology, transcriptomes are much easier to produce and analyze than genomes. Analysis of coral gene expression data generated via RNA sequencing (RNA-seq) (94) and TagSeq (95, 96) methods currently makes up the bulk of published studies in holobiont gene

expression. Most commonly, coral researchers are interested in differential gene expression between species, time points, or environmental conditions [e.g., 57, 97–102; although note that such studies are improved by taking into account individual colony variation (37, 103)]. Gene expression studies start with raw RNA-seq reads that must be assembled into gene-level transcripts and then quantified on a gene-by-gene basis into counts tables for statistical analyses. In most cases, the multiple holobiont partners contribute reads that must be then separated into coral animal or symbiont reads, while screening out reads from the bacterial microbiome—exceptions are sequencing studies of host sperm (31) or aposymbiotic larvae for the cnidarian, or separate symbiont cell cultures (17) for the Symbiodiniaceae, which deliberately remove this complication. Typical analysis pipelines require a reference genome (104), but tools that can make use of a reference transcriptome constitute an alternative (105). While these methods provide capacity to generate gene expression counts to calculate differentially expressed genes, there remain unknowns in (a) the robustness and accuracy of transcript assignments based on the assembly quality of the draft genomes or transcriptomes, (b) tools to separate the holobiont data, and (c) the many genes with generic or unknown functional annotations.

Reference quality can be quantified to address some of these limitations via BUSCO (benchmarking universal single-copy orthologs) scores of the related genomes or transcriptomes (41, 106, 107), which will inform the choice of more rigorous draft references. When the expression data span the holobiont partners (e.g., 108), there is a need for data separation. Here, genomic and transcriptomic references of known origin [e.g., host sperm or aposymbiotic larvae for the cnidarian (31) and in vitro symbiont cultures for the Symbiodiniaceae (17)] can be bootstrapped to generate *k*-mer-level sequence-based profiles of the component species to classify and segregate reads—see, for example, psytrans (<https://github.com/sylvainforet/psytrans>), a popular support vector machine-based tool for this purpose used in the community. Furthermore, the use of single-cell RNA-seq (scRNA-seq) can help to provide context for functional annotation. The first scRNA-seq studies in corals have just recently been published (22, 23). Hu et al. (22) generated a chromosome-level draft genome for the soft coral *Xenia* spp. and used scRNA-seq to identify 16 cell types via their expression profiles. Their focus on the function of endosymbiotic cells has provided an enhanced working model of genes involved in the maintenance of symbiosis. The first scRNA-seq study for a reef-building coral built a coral cell expression atlas for adults, larvae, and polyps for *Stylophora pistillata* (23). Levy et al. (23) were able to identify 37 transcriptionally distinct cell types in adult *S. pistillata*, 13 types in primary polyps, and 17 types in swimming larvae. Collectively these studies provide both proof of concept for scRNA-seq and the opportunity to generate testable hypotheses for further identification of remaining dark genes (28).

3.4. Epigenomics

While transcriptomic studies have provided a wealth of knowledge on coral function under differing environmental conditions, epigenetic mechanisms are an understudied and critical means by which environmental signals can influence the regulation of gene expression and, therefore, phenotype. Epigenetics can be defined as the change in gene expression outcomes in the absence of changes in DNA bases (109). The most well-studied epigenetic mechanism in corals to date is that of DNA methylation, or the addition of a methyl group to the 5C of a cytosine base in a CpG motif. A role for DNA methylation in corals was first proposed following the in silico calculation of historical methylation using transcriptomic data from a variety of coral species (110, 111) that revealed higher methylation in essential housekeeping genes and lower methylation in environmentally responsive genes. Putnam et al. (112) first demonstrated that DNA methylation is inducible in corals experiencing environmental stress (low pH), and this change in methylation was linked to cellular (metabolomic) and organismal (growth) phenotypes. This linkage is also

supported by DNA methylation sequencing and phenotyping in other coral taxa (113). Furthermore, whole-genome bisulfite sequencing analysis of DNA methylation in *S. pistillata* exposed to low pH (114) revealed a positive correlation between gene expression and methylation, as well as a negative correlation between methylation and variation in gene expression, supporting a role for gene body methylation in expression regulation and the reduction of spurious transcription, respectively.

Additional comparative work has begun to benchmark methods for the quantification of DNA methylation in corals (115, 116). At single-base-pair resolution, a recent study by Trigg et al. (116) compared the methylomes generated from two reef-building coral species with contrasting environmental sensitivities using three methods (whole-genome bisulfite sequencing, reduced-representation bisulfite sequencing, and methyl-binding domain bisulfite sequencing). All methods reveal substantially greater methylation in the more environmentally robust *M. capitata* (11.4%) than the more sensitive *Pocillopora acuta* (2.9%). As has been shown in other marine invertebrates (109) and corals (114), the majority of CpG methylation in both species occurs in gene bodies and flanking regions (116). Other recent studies have quantified differential DNA methylation responses to coral stress based on nutrient exposure (117), transplantation (118), and symbiont type (119), and have identified a role for DNA methylation in epigenomic inheritance (120). In related cnidarians (Aiptasia), there have also been initial investigations of chromatin dynamics via ChIP-seq (chromatin immunoprecipitation and sequencing) (121) and ATAC-seq (assay for transposase-accessible chromatin sequencing) (122), but much remains to be advanced in this area as well.

We are still in the early days of our understanding of epigenetics in nonmodel organisms such as corals, but there is support for a role of epigenetic processes, which are unlikely to be a single mechanism, but instead a temporally dynamic interplay that results in mitotically and meiotically derived inherited gene expression regulation (123) that facilitates acclimatization to the rapidly changing marine environment (109).

3.5. Proteomics

Proteomic analyses are also rapidly emerging, with a focus on several key areas of coral biology, including biomineralization and symbiosis/dysbiosis. For example, the protein composition of the skeletal organic matrix has been described in several species [e.g., *S. pistillata* (124), *A. millepora* (125), and *A. digitifera* (126), among others], including fossil taxa (127). In terms of symbiosis, proteomic analysis of bleaching in *Acropora* spp. (128, 129) further supports a breakdown of photosynthesis and an increase in oxidative stress and resulting proteolysis. At the symbiotic interface, a recent examination of the cell wall proteins for multiple Symbiodiniaceae species provides a foundation for our understanding in the areas of molecule transporters and translocases, as well as catalytic hydrolases (130). Proteomics has been used to describe the function of coral tissue in growth anomalies (131). In terms of environmental responsiveness, protein analysis has identified different molecular phenotypes of corals due to reciprocal nearshore (poorer water quality) to offshore (higher water quality) transplantation (132). We note that coral proteomic studies need to be done with an awareness that they can be sensitive to the extraction protocol (133). Additionally, annotation remains an issue, as the majority of the proteins identified have no homologs in existing reference databases.

3.6. Metabolomics

Metabolomic studies have shown that environmental stressors elicit differences in lipid and primary metabolite composition (134), and that the metabolome shows a statistical

correspondence to both the algal symbiont and bacterial microbiome communities (135). Using untargeted metabolomic analysis, Stien et al. (136) studied the impact of 10 ultraviolet filters commonly used in sunscreen products on the coral *Pocillopora damicornis* in order to better understand coral stress response to emerging pollutants introduced by human populations (during, for example, recreational swimming). Hillyer et al. (137, 138) used ^{13}C metabolomics to document widespread differences in carbon fate between healthy and bleached corals. Matthews et al. (139–141) investigated the effect of symbiont type on the metabolome in *Aiptasia* and in corals. Andersson et al. (142) used metabolomic approaches to study coral growth anomalies. Of particular interest are three very recent studies that measured metabolomic signatures associated with thermal stress in the coral holobiont (21, 143, 144), including the effect of thermal stress on hormones involved in coral reproduction (144).

3.7. Other Omics Data and Multiomics Integration

With the capability to collect different types of omics data across the holobiont, integrative multi-omics analyses are becoming increasingly possible and useful. For example, Czieleski et al. (145) simultaneously compared transcriptome- and proteome-wide responses to heat stress in the anemone *Aiptasia*, which is a model for corals. They found correlations, but the correspondence was imperfect, similar to the uncoupling of transcription and translation in symbiont gene expression found in previous studies (145). Multiomics integrative analyses have also been applied in corals (144) to map gene expression levels to global modules and pathways, taking a systems-level approach by considering the network of coexpressed genes and decomposing this network into modules. One strength of this approach is that it can help generate hypotheses about the dark genome of holobiont-specific gene families of unknown function (28). In particular, linking genes of unknown function to other genes in known biological pathways via similarities in patterns of co-expression can help generate hypotheses about such unknown genes and their functions. Furthermore, such network analyses can improve our understanding of the roles of the symbiotic partners and develop hypotheses about how responses are shared and communicated across the different members of the holobiont. If we are to uncover novel holobiont biology, there is a pressing need for new analytical approaches and tools for multiomics integration across biological scales and the holobiont partners, making this an exciting frontier for the development of new useful tools for multiomics integration, analysis, and visualization.

4. CORAL HOLOBIONT DYSBIOSIS

As discussed above and contextualized in the **Supplemental Appendix**, the coral–dinoflagellate symbiosis is a powerful yet fragile relationship, which can range on the symbiotic spectrum from mutualism to parasitism. Here we discuss two increasingly common disruptions to the symbiosis: coral bleaching and disease. This symbiotic dysbiosis, or imbalance in the microbe–coral community and their interactions, is of great concern for the future of reef-building corals and, thus, coral ecosystems.

4.1. Coral Bleaching

Coral coloration is primarily due to the pigmentation of endosymbiotic dinoflagellates, which are found on the coral surface at densities on the order of $10^6/\text{cm}^2$. More importantly, these algal symbionts can translocate more than 90% of their photosynthetically generated carbon to the coral host (146), which can provide the majority of the carbon necessary for the daily metabolic

needs of the cnidarian host (147). The loss of these dinoflagellates and their pigments can be triggered by warming seawater temperatures of only 1–2°C above summer maxima (148, 149). This breakdown in the coral–algal symbiotic relationship is termed coral bleaching. Mass bleaching events have been occurring with increasing (9) and alarming frequency, and they correlate directly with warming oceans and marine heatwaves (9). Coral bleaching can be reversible if the conditions revert to normal (for example, a heatwave subsides) (150–152). Corals can then be repopulated with algal symbiont from the cells remaining in the tissues, or from uptake from the environment, and recover their pigmentation and function. However, since the coral is dependent on its algae for its primary metabolic carbon supply, prolonged bleaching often results in mass coral mortality (153). Given the distressing occurrence of mass bleaching events of corals in the Great Barrier Reef (154) and worldwide (9) and predicted intensification of thermal stress under a warming climate (11), omics tools for human and model systems are now commonly being applied to corals with the goal of understanding the molecular pathways and players in dysbiosis and recovery.

It is urgent to use all emerging omics data being collected for corals to better understand the mechanisms of vulnerability and resilience to bleaching in reef-building corals. Certainly, different species of coral animal have different levels of sensitivity to different stressors; the growing number of genomes and the decreasing cost of whole-genome sequencing will allow comparative genomics approaches to pinpoint specific genes and pathways involved [e.g., GWAS (20)]. Gene expression studies have already started to document some of the pathways and genes that are differentially expressed when corals are exposed to warming temperatures or other stressors (see Section 3.3 above), and we expect this to continue as an area of active research. Together, these approaches will also benefit from dynamic and stakeholder-driven metadata tools [e.g., MEDFORD (155)] to track and share experimental conditions for future large integrative omics comparisons and meta-analyses not yet imagined or articulated.

It is also now well documented that the different species of symbiont can influence the thermal stress tolerance of corals (61–63, 156, 157). There have been some initial bioinformatics studies of potential differences at the gene or pathway level in important processes in these species (25, 55, 57). This raises the questions of whether the coral itself can adjust the variety or proportion of different symbiont species to respond to changing environmental conditions (158) and, even if not, of whether artificial transplantation of different symbiont species could improve coral resilience (159–161). Whether corals can even accept different species of symbiont seems to be highly species dependent (62, 63, 162).

Recovery from bleaching events also appears to differ among different species of coral animal. For example, some species of coral have been shown to better recover from temporary bleaching events by switching to increased heterotrophic feeding rates. The branching *M. capitata* was found to shift over 100% of its energy needs from feeding, whereas both the branching *Porites compressa* and the mounding *Porites lobata* instead tried to survive with existing energy reserves and did not increase feeding when bleached (163). The molecular basis for these climate change winners and losers is not yet fully clear from a host perspective.

The role of bacterial species (and, indeed, the entire rest of the microbiome) in bleaching remains an open question. It has already been documented that there are huge microbiome shifts that accompany adverse environmental conditions (164). There is at least one documented case where a bacterial species appears implicated as a causative agent of bleaching (69), but it would greatly revise our understanding the field if this was found to be the usual case. Instead, there seem to be particular bacterial taxa that are more beneficial and protective against bleaching (165) (see Section 5.3 below).

4.2. Coral Diseases

There is an extensive number of coral diseases that have been documented, including the various so-called band diseases, named for the visible lesions on the affected corals, including white band disease, black band disease, yellow band disease, and brown band disease. Many of these coral diseases respond to topical antibiotics (e.g., painting corals with a base substance plus amoxicillin), suggesting a bacterial origin (166). However, it has also been noted that coral disease lesions are also associated with several species of ciliates, which are hypothesized in most instances to be opportunistic organisms eating the bacteria in the dead and dying tissue or the bacteria that are colonizing the bare skeleton (167). For the bacterial diseases, in some cases, the exact species of pathogenic bacteria that is the causative agent of the disease has been identified; in others it is unknown. For space reasons, we do not include everything known about coral bacterial disease in this article but instead point to reviews of the field (168–171). However, the newly identified SCTLD has become an issue only so recently that it is not well covered by recent reviews; below we discuss what is known about it in more depth.

Since 2014, SCTLD has been devastating corals in the Caribbean (172, 173). It affects over two dozen different coral species, and it has spread extremely rapidly. It is believed that the cause is bacterial, but the precise species of bacteria that causes SCTLD has not yet been definitively identified. Studies have identified enrichment of the bacterial orders Flavobacteriales, Clostridiales, Rhodobacterales, Alteromonadales, and Vibrionales in the disease lesions compared to the apparently healthy areas of the same colonies, or of healthy neighboring colonies (174). A similar study identified sequences belonging to Rhodobacterales and Rhizobiales in disease tissue that matched those in the surrounding sediment, suggesting an environmental reservoir for at least some of these lesion-associated bacteria (175).

The successful treatment of some coral diseases by antibiotics raises a natural question: Do corals already get some natural antibiotic protection from benign denizens of their microbiome? For example, Ritchie (176) found some natural antibiotics being produced in coral mucus microbiomes. Indeed, since coral diseases can also be caused by opportunistic, and not just primary, pathogens, there is some worry that overuse of antibiotics could kill off portions of the microbiome that could provide a buffer against stressors (177). Certainly, bleached and stressed corals have been found to be vulnerable to opportunistic pathogens that cannot typically attack their healthy counterparts (67, 178, 179).

5. CORAL DIAGNOSTICS AND INTERVENTIONS

Human-assisted coral evolution (180) and additional interventions (181) have been proposed as possible human support of coral reef resilience and adaptation in response to climate change, reviewed in a recent report from the National Academy of Sciences (14). Some of the proposed interventions, while essential to mitigate reef loss (e.g., ameliorating underlying environmental stressors, such as those that are the consequences of carbon emissions), do not have bioinformatics aspects. Several of the proposed interventions, however, will benefit greatly from guidance from omics data and novel bioinformatics tools. We describe some of these interventions below.

In the dynamic cities of the coral reef ecosystem, one emerging biomedical data science approach could be to diagnose and treat the holobiont partners as individual patients via targeted therapies (e.g., drugs, nutritional supplements, probiotics; see below). Such diagnostic tools could be applied in a coral “hospital” setting, where diseased or stressed corals are transferred to controlled coral husbandry environments for diagnosis and treatment and then possibly retransplanted back to their original reef once they recover (182). Alternatively, it is possible to take a more public health approach to improving overall performance of the coral population

through acclimatory and adaptive means (183). Below we discuss diagnostics, targeted treatments, and population-level interventions to sustain and improve coral health.

5.1. Diagnostic Toolkit: Coral Biomarkers of Disease and Stress

The first step to effective coral treatment is to recognize when corals are stressed. In particular, one focus of research is to determine reliable gene expression signatures, termed gene expression biomarkers (184), of early coral stress before there are clinically measurable symptoms (184–187). The reliability of different biomarkers could vary with different species of coral (animal or symbiont) (188), which may exhibit different rates of adaptation (189), so it would be important to quantify natural ranges of variability of any proposed biomarkers (190).

5.2. Stress-Priming

Corals are sessile organisms that settle and fix themselves to the benthos in their first several days and weeks of life, and as such they depend on acclimatory mechanisms for resistance and resilience to environmental change (191). Studies of acclimatization in corals support the existence of coral stress memory and, therefore, the application of stress-priming for enhanced coral stress tolerance. For example, Brown et al. (192) published a foundational study of acquired tolerance through stress-priming that showed that portions of coral colonies that experienced aerial exposure and solar irradiance-driven bleaching were protected from subsequent thermal stress bleaching, whereas adjacent previously unbleached portions of colonies were not protected. Furthermore, this thermal tolerance was retained for at least 10 years (193), indicating that the corals exhibited stress memory. Such memory could be derived from a hormetic response and hormetic priming (8), where exposure to sublethal stressors may enhance the organism's tolerance to subsequent or different stressors. This stress-priming has been documented in a variety of corals both within (194, 195) and across (196, 197) a generation. Furthermore, it has been suggested that stress-priming has an epigenetic component in corals (8, 196, 198), where changes in gene expression [e.g., frontloading (101)] could be driven by changes in DNA methylation (114), for example, which may also be heritable across a generation (120). Thus, there is a clear need for bioinformatic approaches to clarify the epigenetic and genetic molecular underpinnings of plasticity and acclimatization and the consistency of these in stress-priming across multiple coral taxa.

5.3. Beneficial Microorganisms for Corals

Coral injuries and disease seemingly predispose the coral microbial community to shift its composition toward higher ratios of potentially pathogenic and opportunistic bacteria, including *Vibrio* spp., Cyanobacteria, Rhodobacteraceae, and Bacteroidetes (199). Conversely, species in the coral microbial community can protect against these shifts. For example, mucus from healthy samples of the elkhorn coral *Acropora palmata* displayed antibiotic activity and could inhibit the growth of potentially invasive microbes by up to 1-fold. However, mucus samples collected during a summer bleaching event were dominated by problematic *Vibrio* spp. and had lost any sort of antibiotic properties (176). The coral probiotic hypothesis (200) maintains that the coral holobiont adapts to changing environmental conditions by shifting the composition of its microbiome. The term “beneficial microorganisms for corals” was subsequently coined by Peixoto et al. (201). The natural next step was to consider microbiome transplants of helpful bacterial species (5), which has opened up the entire field of coral probiotics (5, 202, 203).

The recent first tests of coral probiotics have tried to enhance coral heat tolerance by transplantation with beneficial bacteria (204). The field remains in its early stages, but a better

understanding of the natural defenses in the coral microbiome through metagenomic analysis, for example, will help us know where to start. Other suggested coral interventions include phage therapy (205), vitamins, antioxidants, and nutritional supplements. Other possible interventions look beyond the holobiont to the surrounding ecosystem. For example, Lamb et al. (206) showed in field studies that reef-building corals located adjacent to seagrass meadows showed twofold reductions in disease levels compared to corals at paired sites without adjacent seagrass meadows, but the involvement of the microbiome is not fully clear.

5.4. Selective Breeding

Manipulation of genetic stocks is a longstanding human intervention used in agriculture and aquaculture. The breeding for specific traits can enhance stocks for desired outcomes. This has become particularly germane in terms of the need for increased thermal tolerance of reef corals due to frequent mass bleaching. Initial work breeding corals from warmer and cooler areas on the Great Barrier Reef indicates the potential for thermal adaptation across a single generation (207). Selective breeding experiments in *Acropora* scanning for SNPs support the efficacy of selection even in a relatively small number of crosses (208). Subsequently, corals from the world's hottest reefs in the Persian gulf showed a greater than 80% increase in survival under heat stress due to breeding of heat-tolerant mothers (209). Fuller et al. (20) recently conducted a GWAS of whole-genome sequence data from 237 coral samples with known thermal tolerance and identified selection for the gene *sacs1n*, a key heat-shock cochaperone. The increase of genomic data will, therefore, further improve our capacity to test such genome-wide associations with other key traits such as growth, fecundity, and disease resistance for use in subsequent selective breeding.

6. DISCUSSION AND FUTURE DIRECTIONS

In this review, we have endeavored to describe existing bioinformatics tools and omics data that have enabled significant insights into the coral holobiont, along with newer approaches that have furthered our understanding of the diagnosis and treatment of coral stress, sickness, and disease. As these omics data continue to proliferate, we call attention in **Figure 3** to areas across biological scales where novel bioinformatics methods and analytical tools could close current holobiont knowledge gaps. Development of some of the tools suggested is clearly tractable (e.g., better symbiont gene models), whereas others may be extremely difficult to design (e.g., cross-species gene regulatory network modeling). To summarize our call to action for advanced analytical resources to study the coral holobiont, in this section we outline the state of the field and realistic near-term goals and point toward next steps to better understand this critical symbiotic system.

The explosion in the number and variety of coral animal and symbiont genomes presents an opportunity for evolutionary biologists to get a more precise view into ancient species' biology. On the macroscopic scale, taking into account the fossil record of corals and related species such as soft corals, sponges, and deep-sea cold-water relatives of corals, researchers could use new genomic data to revisit past debates about corals' era of origin. On the microscopic scale, new models of coevolution could be built that incorporate cross-talk between the animal and the symbiont in their evolutionary trajectories, with resulting insights into varieties of corals that might be most suitable for coral farming and reef revival efforts.

The coral animal has many more crucial pathways in common with vertebrates than scientists had previously expected from looking at fly and worm genomics: It appears that many complex processes and pathways, including biomineralization and sensory pathways in vertebrates, evolved earlier than we knew, where some of those genes were lost in fly and worm and did not evolve

	CHALLENGES	DRIVERS OF RESPONSE	MEASUREMENTS	BIOINFORMATICS TOOLS	
BIOLOGICAL SCALE	Population and ecosystem dynamics: changing holobionts	• Environmental factors • Biotic interactions	• Surveys of reef composition abundance, population genomics, metagenomics, physiology, and energy budgets	• Multiomics biomarkers • Systems biology modeling approaches • Multispecies gene regulatory network tools • Phylogenetic models incorporating coevolution of holobiont partners	EXISTING TOOLS
	Genotype-to-phenotype linkages	• Host and symbiont species • Individual SNPs and genomic variants • Microbiome composition • Interacting networks of holobiont partners	• Organismal physiology, transcriptomics, proteomics, metabolomics, and epigenomics • Microbiome community inventories • Network analysis • Gene-knockout experiments	• Systems biology tools • PPI predictors • Gene community predictor tools • Gene regulatory network models • Multiomics biomarkers • Stress resistance gene identification tools • Model organism information transfer tools • Cross-species multiomics analysis tools	
	Genomic information and organization	• Natural selection • Genetic drift	• Genomic and metagenomic sequencing • GWAS • Genomic assembly • Genomic organization maps • Chromatin structure maps	• Reference genomes and pathway annotations • Remote homology tools • Multiomics biomarkers • Gene models for unusual symbiont genomes • Whole-genome sequence comparison tools • In silico separation of holobiont partners	

Figure 3

A grand challenge facing coral reefs is the need for a greater understanding of biological function in corals, from microscopic to macroscopic scales. There is currently a greater number of tools to address problems on the microscopic scales, but there are major gaps and specific bioinformatics tools needed at all scales. Here, we outline major challenges in the field, drivers of coral response, measurements and assays needed to gather multiomics and physiological phenotypic data, and bioinformatics tools needed to advance the field. Abbreviations: GWAS, genome-wide association studies; PPI, protein–protein interaction; SNP, single-nucleotide polymorphism.

more recently in mice and humans. Thus, remote homology approaches will enable functional genomic insights into the genes and pathways involved in coral biological function.

However, bootstrapping by homology will only go so far and will not help with coral-specific genes. This limitation underlines the need for better genome annotation for the coral animal, where new computational approaches to gene-finding will be needed that are adapted specifically for corals. In the case of the symbiotic algae, this need is even more pressing, as the structure of the symbiont genome makes it hard to sequence and assemble, there is evidence that genome organization is quite different, and there are many unique genes.

Transcriptomic analyses will continue to be crucial in understanding important pathways and processes relevant to coral stress and disease. Single-cell transcriptomic studies of corals (23) could shed light on host–symbiont communication and on early stages of coral development, among other critical processes. The recent success of CRISPR in corals (85, 86) means that we may soon be able to confirm or validate functional genomics predictions using gene-knockdown experiments. Further computational advances in deep learning methods for protein–protein interactions (87) will enable the prediction of protein–protein interactions de novo and genome wide, which could be a powerful lens for identifying important genes in key pathways and functional modules.

Proteomics and metabolomics will become increasingly important, not just for studying the coral skeleton and coral energy budgets but also for understanding posttranslational modification as a means of (epi)genetic gene regulation in the holobiont partners and as a regulation of symbiosis.

Metagenomic studies are poised to help researchers pin down the exact agents responsible for some of the devastating bacterial coral diseases, understand environmental factors that lead to outbreaks, and suggest mechanisms for control of disease spread. Protective probiotics for corals is an emerging field, but with great promise for reducing dysbiosis during thermal stress.

Multionics studies of resilient reefs may help researchers understand how to best support and influence the healthy coral holobiont. Genetic and functional characterization of the core resistant taxa, as well as of opportunistic taxa that flourish when corals are sick or bleached, will help us understand strategies that can ameliorate or reverse coral decline.

Bioinformatics approaches will continue to help in the development of important diagnostic assays to proactively monitor the state of holobiont partner members that are integral components of a local reef ecosystem. Furthermore, they can help us uncover novel treatments to support corals prior to and during times of stress.

These are only some of the ways that various rich omics data will help us understand, and ultimately treat or support, threatened corals. Bioinformatics researchers have a deep and useful toolbox to draw from in the fight to save our coral reefs.

DISCLOSURE STATEMENT

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Errata

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