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The Role of Symbioses in the Adaptation and Stress Responses of Marine Organisms

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Abstract

Ocean ecosystems are experiencing unprecedented rates of climate and anthropogenic change, which can often initiate stress in marine organisms. Symbioses, or associations between different organisms, are plentiful in the ocean and could play a significant role in facilitating organismal adaptations to stressful ocean conditions. This article reviews current knowledge about the role of symbiosis in marine organismal acclimation and adaptation. It discusses stress and adaptations in symbioses from coral reef ecosystems, which are among the most affected environments in the ocean, including the relationships between corals and microalgae, corals and bacteria, anemones and clownfish, and cleaner fish and client fish. Despite the importance of this subject, knowledge of how marine organisms adapt to stress is still limited, and there are vast opportunities for research and technological development in this area. Attention to this subject will enhance our understanding of the capacity of symbioses to alleviate organismal stress in the oceans.

> If you think about the coral that survived, those are the most robust genotypes. So that means what doesn't kill you makes you stronger.
>
> —Ruth Gates (quoted in Kolbert 2016)

Adaptation: a modification in the structure, physiology, immunology, development, or behavior of a species or population in response to changed conditions

Symbiosis: persistent interactions between different organisms

1. INTRODUCTION

Marine organisms are some of the most genetically, morphologically, metabolically, and behaviorally diverse life forms on Earth, and many of them also provide substantial services to humans and to the ecosystems they inhabit (Costello et al. 2010, Duarte 2000). Marine organisms have developed complex and innovative solutions for living within the dynamic ocean environment. For example, pelagic migrating animals are able to survive daily movements across steep gradients in temperature, pH, pressure, and prey or nutrient availability at different ocean depths. Adaptations have also played a role in the survival of sessile benthic organisms, which may experience diverse abiotic conditions, especially within intertidal and coastal habitats, but also need to find ways to obtain adequate nutrition, avoid predators, and/or prevent overgrowth of their benthic territory.

Symbiosis has contributed to some of the innovative solutions needed to reside in these ocean environments and has provided opportunities for adaptations to occur over timescales much shorter than those of traditional mutation- and competition-driven adaptations. Marine organisms are currently facing unprecedented climate-based and other anthropogenically induced environmental changes (Burrows et al. 2011, Doney et al. 2012, Hughes et al. 2018), and as these pressures persist and strengthen, symbiosis may become an even more important mechanism for driving organismal adaptation in the ocean.

There are multiple definitions of symbiosis. The term derives from the Greek *sym-*, meaning "together," and *bios*, meaning "life," and is generally used to describe dissimilar organisms living together (de Bary 1879). It can also refer to solely mutualistic associations (van Beneden 1873). Another interpretation considers the evolutionary aspect of relationships and refers to symbioses as long-term interactions that lead to novel capabilities (Douglas 1994). Not surprisingly, many scientists in the field of symbiosis have their own definitions for this term, but most investigators do agree that symbioses span a diverse range of organismal interactions, behaviors, and types of physical associations.

The main types of symbiotic interactions are mutualism, commensalism, parasitism, and amensalism (**Figure 1*a***). Mutualism involves interactions that benefit both organisms; for example, clownfish receive protection from anemones, and anemones in turn gain nutrients and protection from the clownfish. Commensalism is beneficial to one or more organisms but has little or no impact on the other partner. An example of this is barnacles, which settle on whales and thereby receive a substrate, but their presence does not affect the whale. Parasitism occurs when one organism is harmed and another organism benefits, such as an isopod feeding on the tissues of fish. Amensalism is a less examined type of symbiosis in which one organism is harmed but the other receives no benefit. An example of amensalism is a human-driven vessel that transits over a coral reef: The people on the ship gain no particular benefit from its location over the reef, but the ship produces sounds that mask the natural communication of reef organisms, which can negatively affect reef animals (Holles et al. 2013, Simpson et al. 2016). It may seem odd to include humans in an example of marine symbiosis; however, our species has a global and growing impact on ocean ecosystems and organisms (Halpern et al. 2008), and our activities have the potential to play a role in driving organismal evolution in the ocean.

Symbioses vary in their level of dependency and physical association. In obligate symbioses (**Figure 1*b***), the survival of one partner depends on the symbiosis. The relationship between corals

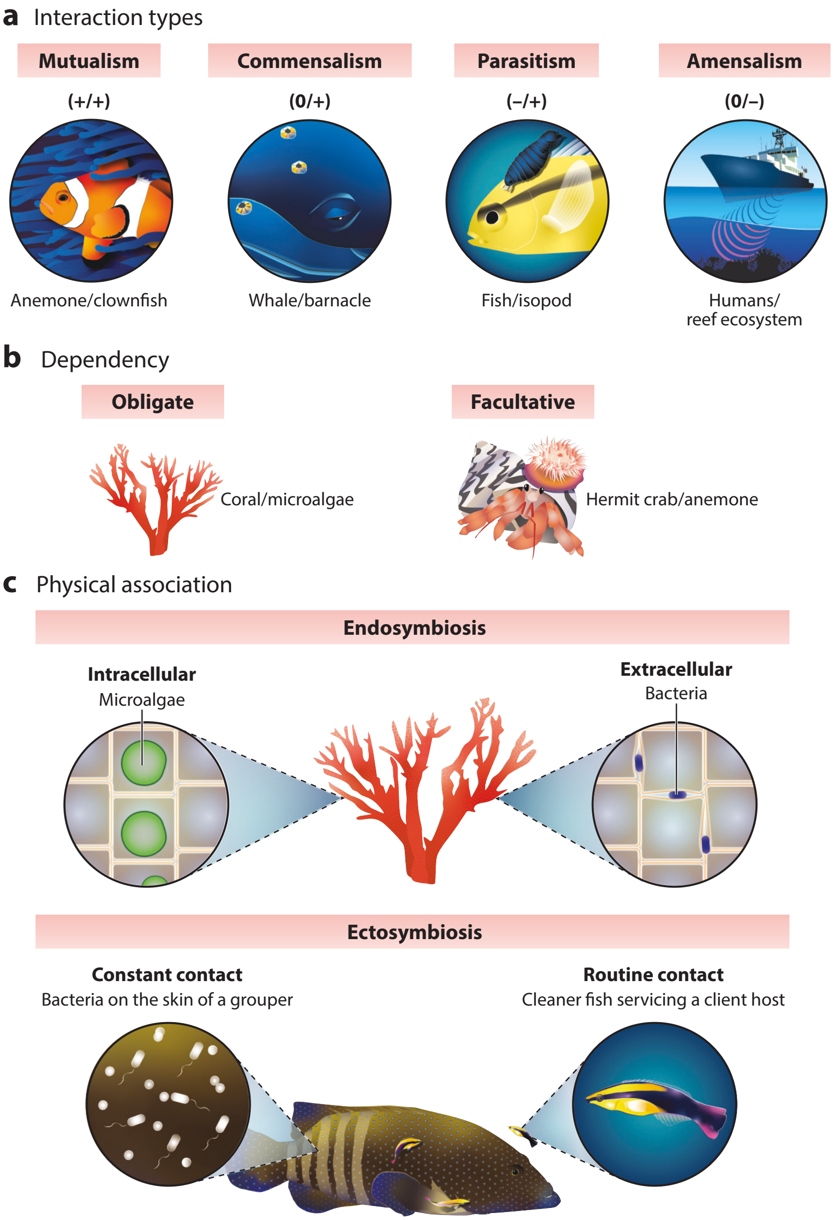

Figure 1

Examples of the diverse types of interactions between organisms that constitute symbiosis, along with the various types of associated dependencies and physical associations. (*a*) The four types of symbiotic interactions, along with examples. A plus (+) indicates a benefit, a zero (0) indicates no benefit or harm, and a minus (−) indicates harm from the interaction. (*b*) The two types of symbiotic dependencies: obligate (necessary for the survival of at least one species) and facultative (in which both organisms can survive independent of the partnership). (*c*) Physical associations between symbiotic partners. In endosymbiosis, symbionts live either intracellularly within host cells (such as microalgae in corals) or extracellularly within the cavities surrounding host cells (such as some bacteria within corals). In ectosymbiosis, the partners may have consistent contact (such as bacteria on the surface of fish) or less consistent but routine contact (such as a cleaner fish interacting with a client host).

and their microalgae is an illustrative example of an obligate association: When corals lose their microalgal symbionts, a substantial source of their diet is gone, and this nutritional loss threatens their survival. By contrast, organisms within facultative host–symbiont associations are able to survive without their partner, as in the symbiosis between anemones and hermit crabs (**Figure 1*b***). The type of physical association between the organisms is also useful for describing symbiotic interactions. Endosymbiosis refers to symbionts residing within the body of another organism, such as intracellular microalgae living within the gastrodermal cells of corals, or extracellular bacteria residing between the cells of the coral (**Figure 1*c***). Ectosymbiosis describes symbionts residing outside the body of the host. In this case, the symbiont may be in constant contact, as when an organism resides on the surface of a host (**Figure 1*c***). In the marine environment, there are also examples of hosts and symbionts displaying routine external contact, such as the association between cleaner fish and client fish.

Stress: a phenomenon that is brought on by biotic or abiotic factors that cause a temporary or permanent disruption of homeostasis and can have negative fitness consequences if unmitigated

Stress is a phenomenon that is brought on by biotic or abiotic factors that cause a temporary or permanent disruption of homeostasis and can have negative fitness consequences if unmitigated. Organisms routinely contend with environmental and organismal stressors and have adopted means to combat them (**Figure 2**). In today's ocean, organisms are also experiencing novel stressors that were not encountered in the geologic past, related largely to anthropogenic activities (**Figure 2**). Climate change, for example, is one of the global stressors that ocean organisms are facing. Earth's average temperature has risen by nearly 1°C since 1880, and recent global temperatures have been the warmest ever recorded (Ciais et al. 2013). Human development of coastal areas is another novel stressor to marine organisms. Coastal development often delivers elevated levels of nutrients, pharmaceuticals, and sounds to the ocean environment, and whether and (if so) how marine organisms will be able to overcome these stressors and adapt to the new conditions are major questions that have implications for the stability and fate of the coastal ecosystems. This is also an important topic for human society, due to the sizable economic value

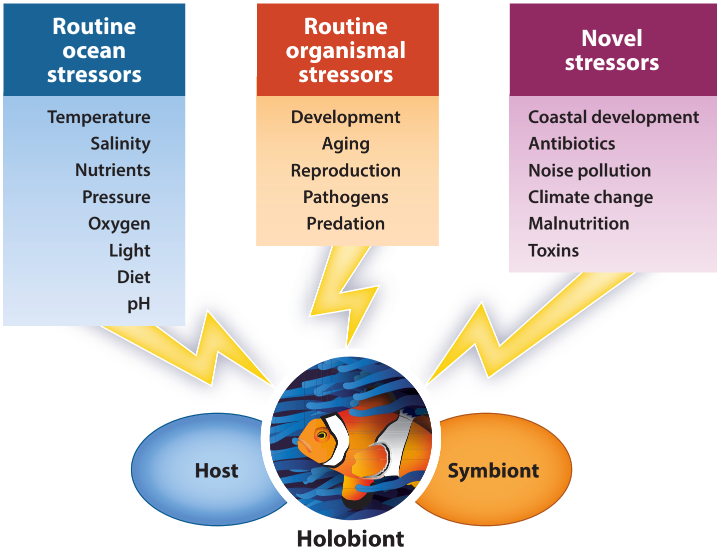

Figure 2

Examples of stressors in the ocean. Host and symbiont partnerships (holobionts) routinely experience a variety of environmental and organismal stressors, and today are more commonly exposed to novel stressors that are often related to human activities.

of our ocean's resources (Costanza 1999) and our need to understand and predict the fate of these resources.

Below, I review the evolutionary theory of symbiosis in biological innovation and consider the role of routine environmental and organismal stress as mechanisms facilitating symbiosis and adaptations. I present four well-studied yet diverse coral reef symbioses and provide examples of stress and adaptations in these systems. The review concludes with an overview of the plentiful opportunities available to expand our knowledge of this topic.

Holobiont: the combination of two or more organisms that form a unique ecological unit

Hologenome: the combined genetic information of a host and symbiont(s) that acts as an independent subject of selection in evolution

Symbiogenesis: the role of symbiosis in major evolutionary innovation, most commonly used to refer to the origin of eukaryotic cells by symbiosis with prokaryotes

2. THE ROLE OF SYMBIOSIS IN ORGANISMAL ADAPTATIONS

2.1. Symbiosis and Evolution

Symbiosis is increasingly recognized as a selective force behind evolution. The mitochondria and chloroplast organelles within modern eukaryotic cells are one of the most illustrative examples of how bacterial cells became intracellular symbionts and provided novel respiration and photosynthesis capabilities to eukaryotic cells (Margulis 1970). These symbioses enabled the development and expansion of eukaryotic taxa, which occurred over 2 billion years (Margulis & Sagan 1997). Lichen is a particularly good example of extracellular symbioses leading to biological innovation. In lichen, cyanobacterial cells reside within the physical matrix provided by the hyphae of fungi. In this mutualistic symbiosis, the fungi gain adequate nutrition from the cyanobacteria, and the cyanobacteria receive protection within the branching network of the fungi. Together, these organisms form a holobiont, or a combination of a host and symbiont(s) together as one organism (Margulis 1991). The holobiont concept is not restricted to mutualistic associations.

One major advantage of utilizing symbioses to advance biological innovation is that the time frame for the development of a new functional trait or behavior can be quite rapid compared with standard evolutionary events (Margulis 1991). This idea has led to the concept of the hologenome, or the combined genetic information of the host and symbiont(s) that may act as an independent level of selection in evolution (Rosenberg et al. 2007). The holobiont concept most commonly refers to hosts with microbial symbionts. This concept is sometimes viewed as controversial because holobionts "do not meet the criteria for being organisms, evolutionary individuals, or units of selection" (Skillings 2016, p. 875). Despite the disagreement about the concept, the popularity of the term reflects a wider appreciation for the role of symbiosis in driving biological and ecological innovation on Earth (Gilbert et al. 2010, Kiers & West 2015, Sudakaran et al. 2017).

Persistent interactions between organisms are not spontaneous and are the cumulative result of many fine-tuned and tested strategies by the partners. Therefore, knowledge about the evolution of symbiotic interactions will advance our understanding of the origin of specific adaptations (Carrapiço 2010). The term symbiogenesis refers to the role of symbiosis in major evolutionary innovation, including new behaviors, morphologies, metabolic pathways, and taxa (Margulis 2010). The term was popularized by Lynn Margulis but was first introduced in the early 1900s (Mereschkowsky 1910, Wallin 1927). Symbiogenesis is most commonly used to refer to microbial endosymbiosis events (Margulis 1970). Several lines of evidence support this type of event; the most noteworthy is that the mitochondria and chloroplasts of eukaryotes still have their ancestral genomes, which are distinct from the nuclear genome of the eukaryotic cell (Gray & Doolittle 1982). Insect symbioses are studied in regard to symbiogenesis (reviewed in Guerrero et al. 2013), including complex interactions such as the contribution of flagellate gut protists and fungi in the eusociality of termites (Aanen & Eggleton 2017). Some studies have suggested that symbiogenesis also occurs in marine organisms—for example, in the intracellular *Prochloron* photosymbionts of didemnid ascidians (Lewin 1981, Wallin 1927) and as the origin of cnidarian cnidocysts (Shostak 1993).

The term symbiogenesis is generally reserved for major evolutionary events (Cavalier-Smith 2013), and researchers prefer to use the terms coevolution and phylosymbiosis to describe lesser events within host–symbiont evolution. Some studies have suggested evidence for coevolution or cospeciation patterns between two or more partners, which refers to the reciprocal evolution of one lineage in response to another (Ehrlich & Raven 1964). The relationship between the Hawaiian bobtail squid (*Euprymna scolopes*) and the bacterium *Vibrio fischeri* (also known as *Aliivibrio fischeri*) is one of the best-studied examples of a simplistic host–symbiont association. Both partners have coevolved specific signaling and recognition traits to form a successful and mutualistic relationship (McFall-Ngai et al. 2012). More recently, molecular studies have reported patterns of phylosymbiosis, or relationships between a host and a larger symbiont community (such as the community of microorganisms associated with a host). These relationships are generally defined by similarity in the host phylogeny and community structure of the associated microorganisms (O'Brien et al. 2019, Wallin 1927). In the marine realm, reports have emerged of phylosymbioses between microorganisms and sponges (Reveillaud et al. 2014), corals (Pollock et al. 2018), and reef fish (Chiarello et al. 2018).

2.2. Mechanisms Used by Symbioses to Adapt

A variety of mechanisms enable symbiotic species to coevolve. These mechanisms may also play a role in longer-term adaptation of organisms to stress in the marine environment. Genetic mutations are undoubtedly a key process leading to genetic variation and novel traits within a species. Horizontal gene transfer, or the transfer of genetic elements between nonmating species, also leads to genetic differentiation and adaptive evolution (Goldenfeld & Woese 2007). For example, the genome of the sponge *Astroclera willeyana* contains a gene involved in the expression of spherulite-forming cells that is of bacterial origin. The transfer of this gene may have led to the biocalcification process of the sponge (Jackson et al. 2011). The genome of the starlet sea anemone (*Nematostella vectensis*) includes bacterial genes involved in the shikimic acid pathway, which may offer protection from ultraviolet radiation for this sessile salt-marsh-residing organism (Starcevic et al. 2008). In most cases, genomes provide evidence of the transferred genes. Critically, few gene expression studies have been conducted to examine whether the horizontally acquired genes are transcribed (reviewed in Boto 2014).

Genome erosion—the minimization of genetic information within a genome—is another mechanism that promotes coevolution between a host and symbiont. It is most commonly observed for genes that were used in the lifestyle of a free-living organism and are no longer needed when that organism becomes a symbiont for another organism (Moran 2003). By minimizing its genome, the organism reduces its energy demands for cell maintenance and replication. Illustratively, the genomes of many obligate microbial symbionts are indeed much smaller than those of microbes in facultative symbiotic relationships. For example, the genomes of intracellular, obligate bacterial symbionts of *Calyptogena okutanii* hydrothermal vent clams are only 1.02 Mb. Comparatively, *V. fischeri*, the symbiont of the bobtail squid that includes a free-living life stage, harbors a genome more than four times that size (4.28 Mb) (reviewed in Duperron 2017). In keeping with this theme, the genes necessary for symbiotic interactions in many organisms are quite small and are limited to a handful of genes necessary to initiate and facilitate the symbiosis (Hoffmeister & Martin 2003). Often these symbiosis genes are housed in plasmids, small circular DNA molecules that are distinct from a cell's DNA. Thus, they are highly mobile genetic elements ripe for exchange and sharing (Christie & Gordon 2014).

Strain specificity is also emerging as a feature in many symbiotic relationships, which could lead to host–symbiont adaptations. Strain-level genetic differences can exist in symbionts and are particularly common for bacteria (Bongrand & Ruby 2019, Bongrand et al. 2016). For example, the bacterium *Lactobacillus reuteri* is a gut symbiont of various terrestrial vertebrate hosts, and genomic data suggest that some strains have adapted to specific hosts (Duar et al. 2017). An experimental comparison of 11 *V. fischeri* strains identified one particular genetically distinct strain that dominated colonization of the Hawaiian bobtail squid's light organ (Bongrand et al. 2016).

With the reduced cost and increased accuracy of genome sequencing, host–symbiont strain specificity appears to be a relatively ripe area for examination and discovery in marine symbioses. However, understanding the costs and benefits of each strain may be challenging for complex symbiotic communities (Bongrand & Ruby 2019). In host–microbiome relationships, the growth, reduction, and acquisition of novel microorganisms from the environment are also thought to lead to longer-term adaptations in a symbiotic relationship. These scenarios are most commonly documented as microbial community changes and are widespread in the marine environment in relation to a host or environmental feature (discussed further in Section 5). Observations supporting the host acceptance of these novel microbes or strains and the long-term nature of the relationship are often lacking, leaving uncertainties about the ability of these changes to reflect adaptation.

Vertical transmission: the direct transmission of symbionts from a parent to an offspring

Horizontal transmission: the acquisition of symbionts from the surrounding environment

3. ROUTINE STRESS IN SYMBIOSIS: PAVING THE WAY FOR ADAPTATION TO NOVEL STRESSORS?

Stress is routinely experienced in most symbiotic relationships. In the ocean, changes in environmental conditions can present considerable stress to organisms, and symbiotic organisms have evolved traits or phenotypes to overcome many of these stressors (**Figure 2**). Holobionts residing in tidal environments experience daily or twice-daily desiccation stress and must transition between periods when they are submerged in the water and periods when they are completely out of the water and exposed to the air, during which they also experience extreme changes in temperature, salinity, and light (including ultraviolet light). In polar environments, resident organisms transition each year between sea and ice-dominated environments, with variations in temperature, visible and ultraviolet light, and prey availability. Pressure could be another routine stress for holobionts such as deep-diving sperm whales and their microbial symbionts, which tolerate pressure changes of more than 9,000 kPa between the surface and depths of 1 km. In less extreme temperate coastal environments, there are still routine diurnal changes in oxygen, CO_2, and pH in addition to seasonal changes in temperature and light intensity.

Holobionts can also experience routine stress from the symbiosis itself (**Figure 2**). From the onset of the symbiosis, the developmental period of most symbiotic interactions involves some type of stress. When microbial symbionts are transferred from a parent to an offspring (vertical transmission), the microorganisms must tolerate extreme transitions in pH, nutrients, and trace metals as well as osmotic and oxidative stress in response to changes in host developmental hormones, host diet, and host habitat. The onset of symbiosis may be even more stressful for organisms acquiring symbionts from the environment (horizontal transmission) or for the horizontally transmitted symbionts. In this common mode of microbial symbiont transmission in the marine environment (Russell 2019), the symbiont must transition from a free-living state to one within a host body cell or cavity. These transitions are also stressful to the host, whose immune system must recognize, accept, and incorporate a foreign cell and who needs to activate the genes and subsequent chemical or physical alterations to accommodate the symbiont (reviewed in Douglas 2010). In the mutualistic association between the Hawaiian bobtail squid and *V. fischeri*, five or more *V. fischeri* cells transition from a flagellated, free-living state in the coastal waters of Hawaii to become resident intracellular symbionts within the epithelial tissues of specialized crypts within the juvenile squid's light organ. The squid, in turn, provide chemical signals to attract the bacteria, utilize specialized ciliary currents and mucus to move the squid into the crypts, and must recognize these cells as nonforeign bodies. The bacteria then induce developmental changes to the light organ (McFall-Ngai 1999, Nyholm & McFall-Ngai 2004). Thus, both the hosts and the symbionts experience, tolerate, and respond to these dramatic changes, which results in a successful endosymbiotic relationship. Hosts and symbionts undergoing major transitions, such as from a free-living state to a symbiotic state, routinely experience many phenotypic variations, in which distinct phenotypes are expressed that facilitate the symbiotic partnership (Cao & Goodrich-Blair 2017). Demands on this phenotypic flexibility may continue throughout the lifetime of the host and symbiont due to natural fluctuations in the host, including diel, circadian, and reproductive cycles; stress hormone production caused by predator avoidance; and aging-related changes (**Figure 2**).

Phenotypic variation: the expression of distinct phenotypes that provide an adaptive advantage

Beneficial priming effect: a phenomenon in which the establishment of a symbiosis leads to a more efficient activation of host defense mechanisms

Acclimation: the process by which an organism or partnership becomes accustomed to changed conditions, but the resulting trait is not shared over generations

Holobionts that have evolved with a routine need for phenotypic plasticity may have an advantageous ability to acclimate and adapt to novel sources of stress or change (**Figure 2**). These novel stressors may stem directly from human activities or may be a consequence of these activities, such as climate change affecting a species' prey supply (Hazen et al. 2013). There is limited experimental evidence that microbes might be able to anticipate changes in a host environment. In *Escherichia coli* bacteria transitioning from lactose to maltose environments within the mammalian gut, some cells predictably express genes for growth on maltose prior to maltose exposure, suggesting anticipatory behavior for an upcoming environmental change (Mitchell et al. 2009). There is evidence from mycorrhizal symbioses, or relationships between plants and soil fungi, that the development of the symbiosis can lead to a beneficial priming effect in which the establishment of the symbiosis leads to a more efficient activation of host defense mechanisms (Grube et al. 2010, Pozo & Azcón-Aguilar 2007). This priming effect may mediate tolerance to novel stressors (Grube et al. 2010), resulting in acclimation of the host organism to particular conditions.

Whether and how an organism acclimates or ultimately adapts to stressors depend on the duration, severity, and frequency of stressors. Combinations of stressors may additionally accelerate the effect or the need for adaptation. In coral reef ecosystems, both the time frame and the origin of stressors are diverse (**Figure 3**). Natural climate-related changes can affect this ecosystem over

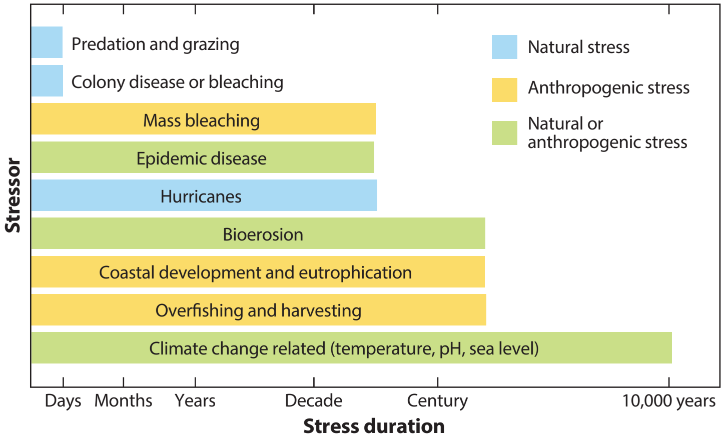

Figure 3

The general duration of natural and anthropogenic stressors that affect coral reef ecosystems. Bioerosion is the erosion of calcifying organisms and is a stress specific to these organisms. Figure adapted from Stambler (2010) with permission, with additional data from Jackson (1991) and Nyström et al. (2000).

thousands of years, although anthropogenic activities have accelerated the rate of change (Doney et al. 2012). This results in a novel stress that affects the entire coral reef ecosystem: mass coral bleaching (Hughes et al. 2017) (**Figure 3**). Bioerosion, or the erosion of calcified organisms (e.g., coral skeletons) by boring animals, is another natural stress to reefs, but the rates of erosion have been accelerated by ocean acidification, and the impacts of this stress on reef ecosystems could span century-long time frames (DeCarlo et al. 2015, Wisshak et al. 2012) (**Figure 3**). Overfishing and coastal development are anthropogenic stressors with impacts that may last months to centuries, depending on their extent and severity (**Figure 3**). Coral disease epidemics appear to be increasing in severity, partially due to accelerated climate change, and the effects of these outbreaks can stress reef ecosystems over decades (Harvell et al. 2007) (**Figure 3**). There are also short-term natural stressors to reefs, including individual colonies experiencing bleaching or disease, as well as predation and grazing, which ultimately have played a large role in the symbiotic adaptations within coral reef ecosystems (**Figure 3**). Diverse micro- and macroorganismal symbioses common to coral reef ecosystems are reviewed below in the context of specific stressors, stress effects, and adaptations.

Coral bleaching: the loss of algal symbionts or their pigmentation from corals, generally caused by a stress event

4. CORAL–ALGAE SYMBIOSES

The relationship between tropical and subtropical corals and their endosymbiotic algae is one of the most iconic examples of a symbiosis that responds to conditions of stress. Scleractinian or stony corals secrete calcium carbonate skeletons that form the structural basis of reefs. Stony corals harbor microscopic dinoflagellates belonging to the family Symbiodiniaceae (recently expanded from the single genus *Symbiodinium*) (LaJeunesse et al. 2018) that photosynthesize within host-derived membranes (symbiosomes) in the host gastrodermal cells and transfer up to 90% of their fixed carbon to the host (Muscatine & Cernichiari 1969, Trench 1971) (**Figure 4*a*,*b***). In exchange, the symbionts receive a constant light environment, protection from predators, and access to micronutrients that are often scarce on oligotrophic coral reefs. This symbiosis is believed to have originated approximately 140–200 million years ago, coinciding with the adaptive radiation of calcifying corals and spread of reefs during the Jurassic period (LaJeunesse et al. 2018).

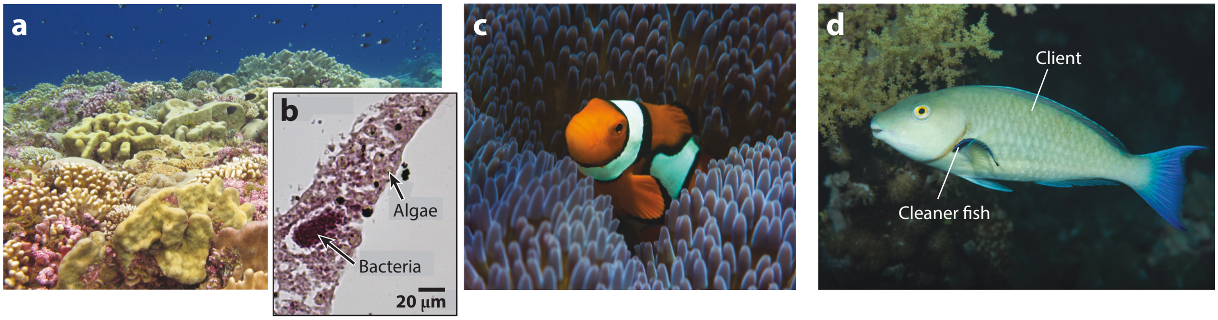

Figure 4

Symbioses common within coral reef ecosystems. (*a*) A coral reef on the island of Nukuoro, Federated States of Micronesia. Photo by Alyson Santoro. (*b*) Light microscopy image of the hematoxylin- and eosin-stained gastrodermis from a *Pocillopora verrucosa* colony sampled in the Federated States of Micronesia, with arrows indicating an aggregate of bacterial cells and microalgae. Photo by Liping Xun. (*c*) Clownfish (*Amphiprion percula*) and anemone (*Stichodactyla* sp.) in Kimbe Bay, Papua New Guinea. Photo by Simon Thorrold. (*d*) Cleaner wrasse (*Labroides dimidiatus*) servicing a parrotfish client (*Hipposcarus harid*) at the Farasan Banks, Saudi Arabia. Photo by Simon Thorrold.

4.1. Coral Stress and Bleaching

The coral–algae relationship is highly sensitive to several stressors, and stress frequently results in a breakdown of the symbiosis. This breakdown can happen in response to changes in temperature, salinity, visible and ultraviolet light, sedimentation, and pollution, among other factors (reviewed in Brown 1997, Lesser 2011). It is most commonly attributed to elevated seawater temperatures that remain anomalously elevated for periods of time, such as 1–2°C increases above historical mean summer maximum temperatures for several weeks. This elevation in temperature causes the release of the pigmented algal symbionts from the coral or in situ degradation of cells, and the result is an overall paling or whitening of the coral colony. When bleaching occurs on a large scale, such as across the Great Barrier Reef, it is visible from airplanes and even spacecrafts. Thus, coral bleaching is among the largest and most visible examples of how stress affects symbiosis on Earth. While some corals can repopulate their tissues with algal symbionts and recover from bleaching, many colonies die or develop symptoms of disease (Baird & Marshall 1998). Future projected atmospheric emissions of CO_2 are expected to result in even greater rates of warming (IPCC 2013), and whether corals can survive this change is a major question plaguing coral reef scientists, managers, and economists (Carpenter et al. 2008, Hughes et al. 2018).

A body of research has investigated how coral bleaching occurs in response to stress. This still limited research suggests that the overproduction of oxygen radicals under stress conditions damages the photosystem, including the thylakoid membrane or proteins such as D1, causing photoinhibition of the algal symbionts (reviewed in Stambler 2010). Antioxidants produced by algal symbionts (e.g., superoxide dismutase, ascorbate, and peroxidase) can dissipate the impact of radicals, and bleaching is believed to occur when antioxidant production cannot keep up with the production of radicals, thus resulting in oxidative stress (reviewed in Lesser 2011). At this point, the algal symbionts either degrade within host tissues or are expelled from the host, primarily through apoptosis and necrosis processes, although exocytosis and host cell detachment processes have also been seen in stressed corals (Weis 2008).

4.2. Adaptive Bleaching Hypothesis

Coral bleaching disrupts the mutualistic association between corals and their algal symbionts and threatens the survival of corals and reef ecosystems. The algal symbionts are genetically diverse (Rowan & Powers 1991), and this evidence combined with the persistence of corals over geologic time initially sparked the controversial idea that bleaching may be an adaptive response to environmental stress (Buddemeier & Fautin 1993). The adaptive bleaching hypothesis posits that changes in environmental conditions may lead to a loss of algal symbionts, which are replaced by symbionts more suited to the new conditions (Baker 2001, Buddemeier & Fautin 1993). This idea fueled a flurry of research designed to understand the genetic, phenotypic, and physiological properties of algal symbionts in response to thermal stress. Some of the key findings from this effort are that clade D symbionts (*Durusdinium* spp.) can exhibit enhanced thermal tolerance and can dominate the symbiont community in a coral following bleaching (Berkelmans & van Oppen 2006, Cunning et al. 2018, Jones et al. 2008, Sampayo et al. 2008). The basis of this enhanced thermotolerance includes their differential production of the reactive oxygen species hydrogen peroxide and expression of antioxidant enzymes such as superoxide dismutase (Lesser 2011). However, there is also contrary evidence that suggests symbiont genotype is not the central component dictating thermal tolerance in some coral species. For example, some thermally sensitive and thermally tolerant coral species harbor genetically similar symbionts (reviewed in Baird et al. 2009). Additionally, studies have questioned whether stressful conditions are even experienced by the algae prior to bleaching, as many expelled symbionts appear to be healthy and photosynthetically active (Bhagooli & Hidaka 2004, Nielsen et al. 2018).

There is also evidence that the coral host may possess adaptive mechanisms to resist the heated conditions on reefs. As such, some coral colonies show evidence for heat-resistant alleles (Bay & Palumbi 2014). Similarly, coral genomes appear to be selected for specific environmental conditions (van Oppen et al. 2018). Recent work has shown that epigenetic mechanisms, specifically epigenetic programming via DNA methylation, may be a rapid avenue for plasticity in corals (Dixon et al. 2016, Putnam et al. 2016). As these mechanisms are environmentally inducible and potentially heritable, this is a promising area of research for corals (Torda et al. 2017).

There is a need to bring the symbiosis back into the study of coral–algae relationships, as many investigations focus on either the symbionts or the hosts, rather than the collective relationship. Baird et al. (2009) suggested that coral bleaching is best regarded as a breakdown in the communication between the host and symbiont. Indeed, the temperatures causing bleaching do not result in the death of phytoplankton, seagrass, or other animals on the reef. Rather, only corals engaged in mutualism with algae are undergoing dysbiosis, or a breakdown in symbiosis. While there is evidence that each partner may have acclimation strategies for heat tolerance, the potential for the symbiosis itself to play a role in adaptation to higher temperature still requires study. From the known mechanisms of symbiosis-driven adaptations and innovations, it is plausible that environmentally tolerant super-corals may emerge over time. The current studies on assisted evolution (van Oppen et al. 2015) and other synthetic systems (Damjanovic et al. 2017) will greatly inform our understanding of the capacity of corals and reef ecosystems to survive climate change impacts as well as other novel stressors.

5. CORAL–BACTERIA SYMBIOSES

In addition to hosting microalgae, corals engage in relationships with other microorganisms, including other protists, endolithic algae, bacteria, archaea, fungi, and viruses (Ainsworth et al. 2017, Knowlton & Rohwer 2003, Kwong et al. 2019, Rohwer et al. 2002). Of these microorganisms, bacteria are thought to play a critical role in the cycling and regeneration of nutrients for the coral holobiont (Rohwer et al. 2001, 2002) (**Figure 4*b***). There is also evidence that coral-associated bacteria are capable of producing antibiotic and other secondary metabolite compounds, which could help protect the coral against pathogens (Kelman 2004, Ritchie 2006). Stony corals host some of the most phylogenetically diverse bacterial communities of any animal, with representatives from up to 69 described and candidate phyla (Huggett & Apprill 2019, Pollock et al. 2018). The composition of the bacterial community varies across the major life stages of corals (Apprill et al. 2009, Sharp et al. 2010) and among the distinct mucus, tissue, and skeletal features of adult corals (Sweet et al. 2011), which explains some of this high phylogenetic diversity. For example, the Caribbean coral *Porites porites* contains *Tumebacillus* within the mucus and "*Candidatus* Amoebophilus" within the tissues (Apprill et al. 2016). The stability of these types of specific coral–bacteria associations appears to vary widely across coral species, environments, and stress-related conditions (Bourne et al. 2016, McDevitt-Irwin et al. 2017, Morrow et al. 2018, Zaneveld et al. 2016).

5.1. The Role of Bacteria in Coral Stress and Stress Response

In addition to bacteria possibly providing protection for corals, the concept of bacteria causing coral bleaching has been a target of considerable research attention. In the eastern Mediterranean Sea, bleaching of the coral *Oculina patagonica* generally occurred each summer under elevated water temperatures and was attributed to an infection by toxin-producing *Vibrio shiloi* bacteria (Kushmaro et al. 1996, Rosenberg & Falkovitz 2004). However, after approximately 10 years of study on this *V. shiloi*/*O. patagonica* system of coral bleaching, the corals were resistant to the pathogen (Reshef et al. 2006), and the pathogens were also not readily identifiable in the hosts (Ainsworth et al. 2007). Whether the corals developed immunity, the pathogen perished, or there were other factors involved in this bleaching scenario has not been investigated. This finding led to the development of the coral probiotic hypothesis, which posits that "a dynamic relationship exists between symbiotic microorganisms and environmental conditions which brings about the selection of the most advantageous coral holobiont" (Reshef et al. 2006, p. 2068). Advancements in descriptions of coral bacteria combined with the demise of corals resulted in a similar hypothesis released more than a decade later. The beneficial microorganisms for corals hypothesis (Peixoto et al. 2017) suggests that certain coral microbes play a beneficial role in coral health and that a probiotic cocktail may be a useful way for humans to assist in the acclimation and adaptation of corals to environmental conditions, including rising seawater temperature.

Field and laboratory investigations generally identify alterations in the coral-associated bacteria with natural thermal stress, and often with an increase in the occurrence of *Vibrio* bacteria (reviewed in Morrow et al. 2018). A common theme across studies is that coral microbiomes become more diverse (enhanced alpha-diversity) and exhibit more variation across colonies (enhanced beta-diversity) as thermal stress increases (reviewed in McDevitt-Irwin et al. 2017, Morrow et al. 2018). Results from a thermal stress experiment with *Acropora hyacinthus* corals suggest that long-term exposure to elevated temperature enhances the heat tolerance of both corals and coral bacteria (Ziegler et al. 2017). Similarly, thermal stress experiments with *Pocillopora damicornis* corals suggest that some bacteria may assist in mitigating coral bleaching (Rosado et al. 2018).

A key missing factor in understanding whether coral bacteria may be able to enhance the resilience of corals to ocean warming is underlying knowledge about the functional role of the bacteria in residence with corals, and whether and (if so) how this role changes with elevated temperatures. Very few studies have addressed the functional changes in the coral-associated bacterial community during thermal stress. In aquarium experiments, Vega Thurber et al. (2009) observed an altered bacterial community with thermally stressed corals and used early metagenomic techniques to demonstrate the enhanced presence of genes associated with nitrogen metabolism, membrane transport, motility and chemotaxis, stress response, and virulence, among others. In the above-mentioned study by Ziegler et al. (2017), predictive metagenomic analysis suggested enrichment of genes involved in the sugar transport system, nitrogen fixation, the reactive oxygen species scavenger ferredoxin, and the chaperonin protein GroES, which may play a role in intracellular signaling. While these studies suggest possible beneficial changes to the microbiome under thermal stress, several studies have seen a reduction of the antibacterial activity of bacteria residing within the mucus of corals, which is likely less beneficial for the holobiont (Rypien et al. 2010, Shnit-Orland & Kushmaro 2009). Overall, there is considerable speculation about the ability of the coral bacteria to provide added resistance and resilience to corals under warmer ocean conditions (Ainsworth & Gates 2016, Damjanovic et al. 2017, Morrow et al. 2018, Peixoto et al. 2017, van Oppen et al. 2015, Webster & Reusch 2017), and more research is needed.

6. ANEMONE–CLOWNFISH SYMBIOSES

The relationship between anemones and their clownfish is a behavioral and nutritional mutualistic symbiosis on Pacific and Indian Ocean reefs (**Figure 4*c***). Thirty species of clownfish (also called anemonefish, genus *Amphiprion* and *Premnas*) form specific relationships with anemones, which comprise 10 species (Litsios & Salamin 2014, Ollerton et al. 2006). The anemones provide protection to the clownfish from predators, which is especially important during the vulnerable juvenile stage of the fish and for the eggs, which are laid near the anemone (Fautin 1992). This protection results in the clownfish life span being approximately six times that of similarly sized nonsymbiotic fish (Buston & García 2007). The clownfish exhibit specificity to the host and are immune to the stinging cells within the anemone tentacles (reviewed in Mebs 2009). In return for this protection, the anemone and its algal symbionts benefit from the waste products excreted by the clownfish (Roopin et al. 2008). These symbioses occur in oligotrophic regions, primarily coral reefs; these areas have only trace levels of nitrogen, and thus nitrogen is an especially important resource that the clownfish provides for the anemone and its endosymbiotic algae.

6.1. Adaptive Evolution of Anemone–Clownfish Partnerships

Molecular evidence suggests that the anemone–clownfish mutualistic symbiosis is uniquely responsible for the adaptive radiation of clownfish. Adaptive radiation is the process by which an ancestral species diversifies into many descendants that are adapted to specific habitats. A genomic and morphological study suggested that the evolution of symbiotic traits in clownfish occurred much more quickly than evolution in their closest relatives, which are nonsymbiotic fish (Litsios et al. 2012). Specifically, this acceleration occurred through an increase in the rates of species diversification and morphological evolution and resulted in the clownfish radiating to reef habitats across the Indian Ocean and western Pacific Ocean, which is unique for a settling reef fish (Litsios et al. 2012). Part of the clownfish diversification is attributed to hybridization, or the process of two species hybridizing to form a new species (Litsios & Salamin 2014).

The clownfish coloration is also thought to have arisen from the mutualism with anemones. Ancestral clownfish were thought to harbor more stripes, which provided camouflage among the long tentacles of the host. Speciation toward more toxic anemones with generally shorter tentacles coincided with the more distinctive, bright, and visible coloration that arose to advertise the toxicity of the anemones to potential predators (Merilaita & Kelley 2018). This adaptive shift in the coloration of the clownfish associated with the different anemone species illustrates the evolutionary and ecological history of the partnership.

6.2. Impacts of Stress on the Anemone–Clownfish Partnership

As with corals, thermal stress causes endosymbiotic algae hosted by the anemones to leave the host cells, resulting in a similar bleaching response. The bleaching of anemones leads to negative repercussions for the clownfish symbionts. Clownfish residing in the bleached anemones lay fewer and less viable eggs compared with fish in unbleached anemones (Beldade et al. 2017, Saenz-Agudelo et al. 2011). When exposed to the bleached anemones, clownfish also show decreased growth rates, higher oxygen uptake rates, and higher concentrations of the stress hormone cortisol, as well as significantly lower levels of reproductive hormones (testosterone and estrogen) (Beldade et al. 2017, Norin et al. 2018). Settling clownfish preferentially recognize healthy (unbleached) anemones over bleached anemones, through the use of olfactory cues (Scott & Dixson 2016). There is some evidence that substitution, or switching between hosts, could be an adaptive behavior that the fish use to cope with bleached hosts. Host substitution, where fish switch between multiple hosts, has been observed in juvenile clownfish (Miyagawa-Kohshima et al. 2014), offering them choices during the short settlement period when a preferred host is not available. Host substitution as an adaptive mechanism still relies on some species of anemones surviving thermal stress, possibly through the acquisition of more thermotolerant endosymbiotic algae. Studies suggest that the clownfish possess significant potential to acclimate to heat stress by maintaining high levels of the heat shock protein Hsp70, and do so without decreasing survival (Madeira et al. 2017). Thus, the adaptation of the anemone–clownfish symbiosis to elevated ocean temperature, and possibly other stressors, may ultimately depend on the adaptability of the anemone–microalgae symbiosis.

7. CLEANER FISH–CLIENT FISH SYMBIOSES

One of the first observations of symbiosis in the ocean was the discovery of the mutually beneficial relationship between small fish known as cleaner fish and their host clients, which are generally larger fish (Limbaugh 1961). The cleaner fish occupy a specific territory on a reef known as a cleaning station, where they inspect clients for parasites (often gnathiid isopods) as well as dead or infected tissue on their body surfaces, mouths, and gill chambers and remove and ingest the material (Côté 2000, Grutter 1999, Losey 1972) (**Figure 4*d***). Both the cleaners and the clients benefit from this interaction. The cleaners receive a consistent food source from the clients, with some obligate cleaners dependent exclusively on client-sourced parasite and tissue removal (Grutter 1999). The clients generally span a spectrum of larger fish species (e.g., groupers and surgeonfish), and the benefits to them include enhanced longevity and reproductive success and lower rates of ectoparasite infection (Grutter et al. 2018). There are also additional benefits to the reef ecosystem, as cleaner fish can enhance fish diversity on the reefs they service (Grutter et al. 2003).

7.1. Adaptive Evolution of Cleaner Fish–Client Fish Traits

Convergent evolution has contributed to the development and success of cleaner fish on tropical reefs, spanning both shallow and mesophotic depths. Cleaning gobies (*Elacatinus* spp., part of the Labridae family) in the Caribbean and cleaner wrasse (*Labroides* spp., part of the Gobiidae family) in the Indian and Pacific Oceans service a similar spectrum of larger fish clients. Despite the geographic separation and species differences, these cleaner fish have converged on several similar traits. They possess similar color patterns, with both species harboring a dark median lateral stripe that is typically blue or black (Arnal et al. 2006, Potts 1968), which makes them easily recognizable to many species of clients (Cheney et al. 2009). Additionally, both species are relatively small, with mouths adept at parasite removal, and advertise their presence using an oscillating dance behavior (Feder 1966, Potts 1968). Cleaning is a coevolved interspecies interaction between cleaner fish and clients. An evolutionary examination of the wrasse lineages using phylogenetic analysis showed that the cleaning symbiosis feeding mode is the most recently derived of the 11 wrasse feeding modes (Cowman et al. 2009). Cleaning first appeared during the late Miocene (9.5 Mya) in a lineage of specialized coral-feeding fish with small mouths and long intestines modified to handle the digestion of corals.

The clients of cleaner fish have evolved specific behaviors to encourage interactions with the cleaners. While some of the predatory client fish are certainly capable of ingesting the cleaners, this is rarely documented (reviewed in Gingins et al. 2017). Instead, clients often reduce predation near cleaning stations. Even though cleaners have less need to escape from predators than other fish, at least one species of cleaner (*Labroides dimidiatus*) has maintained fast-start escape performance similar to that of closely related noncleaner wrasse species, suggesting that mutualistic symbiosis and a lack of predation pressure have not reduced this trait (Gingins et al. 2017). In fact, it is possible that the cleaners have continued to need the fast-start escape to escape reprimands when cheating—that is, eating client mucus (often a preferred food for cleaners) instead of ectoparasites or dead or damaged tissue (Grutter 1997, Grutter & Bshary 2003). The clients use partner control strategies against cheating cleaner fish, including partner switching (in which the client switches cleaners if dissatisfied with the service) and punishment (in which the client chases the cleaner to ram or bite it) (Grutter & Bshary 2003). Overall, cleaners appear to cheat less with predatory clients (Soares et al. 2011).

7.2. Stress and the Cleaner Fish–Client Fish Symbiosis

In contrast to the other symbioses discussed, stress research in the cleaner fish–client fish symbiosis has focused less on environmental stress and more on understanding conflict-related stress.

Stress-related hormones and molecules play a major role in regulating natural behavioral responses within the cooperative cleaner–client symbiosis. Cleaning gobies (*Elacatinus* spp.) experience enhanced cortisol levels in the presence of predatory clients, which results in them approaching the clients more rapidly and cleaning them for longer compared with exposure to nonpredatory (herbivorous) clients (Soares et al. 2007, 2012). Thus, the cleaner may respond to the increased stress level by becoming more proactive, thereby diverting predation risk by enhancing attention to their client. Serotonin also modulates cooperative behavior between the Indo-Pacific cleaner wrasse *L. dimidiatus* and client fish, with enhanced serotonin causing the cleaners to become more engaged in cleaning behavior and more likely to provide tactile stimulation to the clients (Paula et al. 2015). Similarly, dopamine, a neurotransmitter involved in animal behavior and cognition, plays a role in the negotiation skills of cleaner wrasse and the avoidance of negative consequences during potentially conflicting interactions (Messias et al. 2016). Thus, cleaner fish and client fish have routine stress-reduction mechanisms that are under hormonal and neurotransmitter control, which play a major role in this cooperative symbiosis. While thermal stress has not been investigated in cleaner fish–client fish relationships, it is possible that the routine stress experienced by the symbiosis plays a role in their ability to acclimate to warmer conditions, as well as other stressors.

Ocean acidification–related stress has been found to impact a common client fish, the coral trout (*Plectropomus leopardus*). In ocean acidification conditions caused by high atmospheric CO_2 emissions (700 and 960 μatm CO_2), juvenile *P. leopardus* fish substantially alter their sensory function and behavior and become more attracted to the odor of potential predators than fish reared in conditions with lower CO_2 emissions (490 and 570 μatm CO_2) (Munday et al. 2013). In other coral reef fish, this change in behavior and olfactory response is caused by the interference of acid–base-related ions (HCO_3^- and Cl^-) with the functioning of GABA-A neurotransmitters, a major inhibitory neurotransmitter in the vertebrate brain (Nilsson et al. 2012). Altered behaviors associated with high-CO_2 scenarios also affect the survival and energy budgets of the fish (Munday et al. 2013). To my knowledge, the effects of ocean acidification and GABA-A functioning have not been examined in any cleaner fish–client fish symbiosis. Understanding how ocean acidification–related olfactory impairment affects these symbioses is an important area of future research.

8. OPPORTUNITY KNOCKS FOR STUDYING SYMBIOSES, STRESS, AND ADAPTATIONS IN THE OCEANS

8.1. Advancing Observations of Marine Symbioses

There is a tremendous opportunity to learn from symbioses in the ocean and to enhance our understanding of the possible role of symbiosis and adaptation in tolerating stress. There are nearly 2 million known species of marine animals in the ocean (Mora et al. 2011), and symbiotic interactions in most of these organisms are unstudied. These animals most certainly engage in partnerships with microorganisms, and the extent to which they host persistent or routine microbial symbionts will require survey-based molecular and microscopic investigations. Similarly, understanding macroorganism interactions also requires observations, surveys, and knowledge of these organisms during their typical behaviors, such as hunting, feeding, mating, and cleaning. It is not surprising that most of the examples used in this review are from coral reef habitats—an ecosystem that has benefited from countless underwater observational hours by scientists, curious naturalists, and recreationalists. Hydrothermal vents are also a relatively well-studied habitat for symbioses, which are observed and accessed by scientific teams using manned and unmanned vehicles, and in which life is concentrated near vent fluids.

The areas of least observation are the twilight zone and greater depths of the ocean, which still hold countless uncharacterized marine organisms. While samples of these animals can be obtained using net tows and trawls, there are also modern technologies that will advance discovery in this area. The REMUS (Remote Environmental Monitoring Units) autonomous robot can be used to follow tagged animals, such as sharks and turtles, throughout their habitats (Dodge et al. 2018, Skomal et al. 2015). The Mesobot, a new autonomous robot designed to study mesopelagic animals (Yoerger et al. 2018), can follow animals as they undertake diel vertical migrations and utilizes a camera and video system to record animal behaviors. An autonomous system capable of swabbing the surfaces of these animals has not yet been developed, but this type of instrument could provide invaluable access to the genomes of both hosts and surface microbial symbionts, providing a window into host–symbiont evolution and the potential for symbiont interactions and adaptations.

8.2. Sophisticated Aquarium Facilities Will Promote Experimental Research

Mesocosm and aquarium-based manipulative experiments will also play a major role in advancing our knowledge of stress, acclimation, and marine symbioses. Systems that enable the tuning of various environmental conditions, such as temperature, light, pH, and nutrients, will be particularly informative regarding the role of symbioses in stress responses. The Australian Institute of Marine Science's National Sea Simulator (SeaSim) and the Red Sea Simulator are examples of state-of-the-art facilities that offer fine-level control of environmental conditions. Dozens of marine field laboratories throughout the world offer access to seawater aquarium systems, which can be modified for a variety of investigations. Additionally, some scientists have developed portable experimental devices or chambers that allow investigations in remote areas. There is still a need for a research vessel to carry state-of-the-art aquarium facilities onboard the ship. This development would expand the geographic spectrum of manipulative marine symbiosis research.

8.3. Knowledge of Marine Symbioses Will Impact Diverse Fields

Expanding knowledge of symbioses in marine animals will inform diverse fields. Knowledge of animal symbioses can be used to further our understanding of fundamental concepts in biology, such as host–symbiont recognition, which is based largely on a few model organisms. Marine biotechnology is another area of potential growth from enhanced knowledge of marine symbioses. For example, harnessing the vast array of microbial symbionts of marine animals could greatly expand the discovery of antimicrobial peptides from marine bacteria. Additionally, biofouling is a $200-billion-per-year problem facing the United States, as well as other countries (Bîrluţiu et al. 2017). Toxic substances are used to prevent marine species from colonizing ship hulls, yet many marine organisms resist such colonization naturally, possibly through the contributions of surface-associated microorganisms. There are countless other examples where humans utilize harmful chemicals to prevent microbial colonization, yet marine animals, faced with orders of magnitude more microbes in the surrounding water, are able to resist colonization by these cells. Bioengineering or synthetic biology could benefit from enhanced knowledge of marine symbioses, specifically by advancing knowledge of how relationships among multiple species can contribute to new system traits (Porcar et al. 2013).

The vast diversity of life in the ocean combined with the potential for innovation via symbiosis creates an exciting, interdisciplinary area of research that remains virtually unexplored. Enhanced research in this area will undoubtedly boost our understanding of the connections between symbiosis adaptation and environmental stressors in our oceans.

SUMMARY POINTS

1. Symbiosis has played a major role in the evolution of marine organisms and may have driven biological innovation on timescales that are shorter than those of traditional evolutionary responses.
2. Marine organisms involved in symbiotic interactions experience routine stressors in their lifestyles and under normal ocean conditions, and the phenotypic variations that they develop to acclimate to these conditions may prime them for tolerance and adaptations to novel stressors.
3. Elevated ocean temperatures are causing routine breakdowns of the mutualistic coral–microalgae symbiosis. There is some evidence that this relationship may be undergoing an adaptive response to warming ocean conditions by switching from less to more thermotolerant symbionts. Coral-associated bacteria are hypothesized to play a beneficial, probiotic-type role in corals exposed to or overcoming heat stress.
4. There is evidence for adaptive radiation and mutualism-driven traits in the anemone–clownfish symbiosis. Thermal stress is also a major stress affecting this relationship, and host substitution may be one mechanism used to prolong interactions under these conditions.
5. The mutualistic cleaner fish–client fish symbiosis has evolved specific coloration, morphology and behavior traits. While environmental stress is not well studied in this system, the cleaners and clients have an established capacity for mitigating routine stress in the partnership.
6. Numerous opportunities are available for research and technological developments in marine symbiosis. Attention toward this subject will enhance our understanding of the capacity of symbioses to alleviate organismal stress in the oceans.

FUTURE ISSUES

1. Most symbiotic studies focus on partnerships between a single host and a single symbiont, and there is still a limited understanding of more complex, multimember symbioses.
2. Molecular clock dating is needed to inform the acquisition of specific traits within diverse marine symbiotic associations. This will advance our understanding of the timescales and rates of adaptations in symbiotic systems.
3. Understanding failures in symbiosis, or scenarios of dysbiosis and extinction, will inform the field about the limitations of symbiotic relationships for specific acclimations and adaptations.
4. Technological advancements in imaging and chemical tracing are needed to better understand organismal functions and interactions while in the symbiosis. This is especially necessary when the symbionts (e.g., obligate endosymbiotic bacteria) are not able to grow without the host.
5. Studying marine symbiosis requires integrating marine science with nearly all biological and biogeochemical disciplines. Funding sources are needed to bring together large

interdisciplinary teams with diverse expertise, including isotope tracers, microscopy, genomics, genetics, bioinformatics, biochemistry, physical oceanography, and fossil records, among many others.

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