CellPress

Current Biology
Review

The Vulnerability and Resilience of Reef-Building Corals

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http://dx.doi.org/10.1016/j.cub.2017.04.047

Reef-building corals provide the foundation for the structural and biological diversity of coral-reef ecosystems. These massive biological structures, which can be seen from space, are the culmination of complex interactions between the tiny polyps of the coral animal in concert with its unicellular symbiotic algae and a wide diversity of closely associated microorganisms (bacteria, archaea, fungi, and viruses). While reef-building corals have persisted in various forms for over 200 million years, human-induced conditions threaten their function and persistence. The scope for loss associated with the destruction of coral reef systems is economically, biologically, physically and culturally immense. Here, we provide a micro-to-macro perspective on the biology of scleractinian corals and discuss how cellular processes of the host and symbionts potentially affect the response of these reef builders to the wide variety of both natural and anthropogenic stressors encountered by corals in the Anthropocene. We argue that the internal physicochemical settings matter to both the performance of the host and microbiome, as bio-physical feedbacks may enhance stress tolerance through environmentally mediated host priming and effects on microbiome ecological and evolutionary dynamics.

Introduction

Coral reefs are among the most biodiverse ecosystems on the planet, the persistence of which depends upon the reef-building capacity of scleractinian corals. Coral reefs thrive in oligotrophic tropical waters due to the intricate symbiosis between the coral host, its single-celled algal endosymbionts, *Symbiodinium* spp., and its diverse microbiome (Figure 1A,B). Coral symbiosis with *Symbiodinium* algae allows the coral animal to harness energy from sunlight via photosynthesis, as fixed organic carbon is transferred to the host while the algae receive inorganic nutrients recycled from the host's metabolism (e.g. ammonium and carbon dioxide) [1]. This exchange is critical for biomineralization, the formation of the coral skeleton via the precipitation of calcium carbonate ($CaCO_3$) around an extracellular organic matrix [2], which contributes to reef accretion rates of up to 10,000 g $CaCO_3$ m^{-2} yr^{-1} [3]. The complex physical structures built by corals are the foundation of coral reef ecosystems (Figure 1 C–E), providing habitat for the incredible biodiversity typical of a healthy coral reef [4], and supporting ecosystem services (e.g. fishing, tourism and shoreline protection) that are valued at hundreds of billions of dollars annually (for more on marine ecosystem services, see the primer by Barbier in this issue) [5].

Coral reef ecosystems are at the forefront of concern for persistence in the Anthropocene, as corals, their keystone species, are sensitive to a variety of anthropogenic disturbances ranging from local (e.g. overfishing, coastal development and pollution) to global in scope (e.g. climate change and ocean acidification). While pollution and development can be managed at the regional level, the impact of rising CO_2 levels in the atmosphere is now apparent across the world's oceans and is causing international concern. Anthropogenic CO_2 has led to a global rise in sea surface temperatures and ocean acidification, as atmospheric CO_2 taken up by surface waters drives changes in seawater carbonate chemistry resulting in lower pH. This acidification of the ocean has negative effects on marine calcifiers such as corals, inhibiting growth and calcification through direct effects of pH on biochemistry and carbonate ion limitations for calcification [6]. Furthermore, ocean acidification is predicted to reduce reef accretion rates and increase bioerosion and susceptibility to breakage and destruction during storms [3].

Rising sea surface temperatures are of paramount and imminent concern for coral reef survival given the detrimental effect of increased temperature on the stability of the coral–algal symbiosis. While this symbiosis underlies the geologic success of coral reefs, it is also their Achilles heel because it is sensitive to seemingly slight increases in temperature. For example, temperatures over 1°C above long-term summer maxima can result in breakdown of the symbiosis and loss of the symbiotic algae from the host [1]. This phenomenon is referred to as 'coral bleaching' due to the stark white appearance of corals lacking the pigmented *Symbiodinium* cells (Figure 2B–D). Unless corals regain their nutritional partners, the animal eventually starves to death, leading to colony mortality and reef degradation (Figure 2A). Repeated bleaching and mass mortality of scleractinian corals, such as on the Great Barrier Reef during 2015–2017 [7], is predicted to become an annual event for many reefs by the mid-century [8]. Future reefs may thus become structures dominated by algae and other non-calcifying, non-coral constituents [9], drastically eliminating many ecosystem goods and

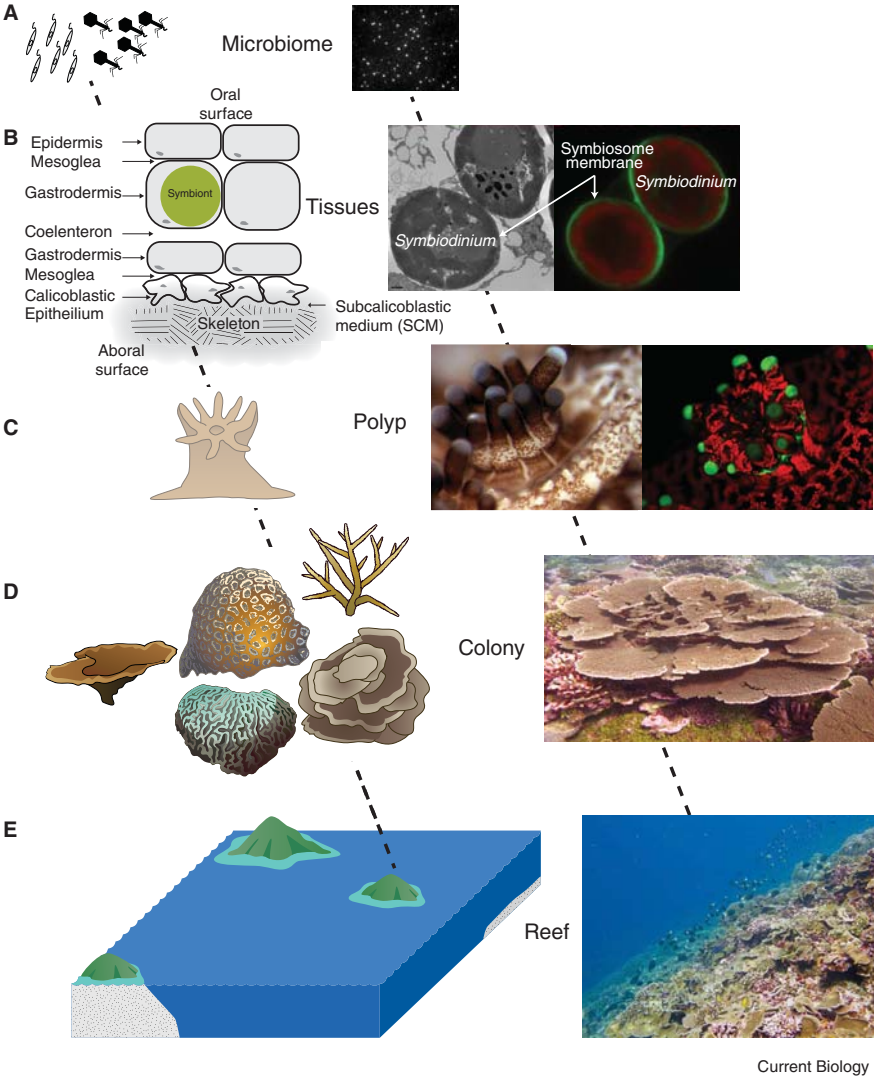

Figure 1. Coral scaling from cells to reefs.
Corals are complex meta-organisms whose cellular level interactions generate tissues, polyps, and colonies that engineer the coral reef ecosystem. (A) At the smallest scale is the coral microbiome, comprised of bacteria, archaea, eukaryotic microbes, and viruses. (B) Diagram of the coral tissue layers (left). *Symbiodinium* reside within the symbiosome, an organelle inside coral gastrodermal cells. Transmission electron micrograph of *Symbiodinium* within the host (center; image: Katie Barott); fluorescence image of a coral cell housing two *Symbiodinium* (red: chlorophyll; green: lysosensor green, which stains the symbiosome lumen; image: Katie Barott). (C) The coral polyp: diagram (left); image of *Pocillopora damicornis* polyps (center, bright field and fluorescence; red: chlorophyll; green: endogenous green fluorescent protein; image: Hollie Putnam and Katie Barott). (D) Examples of colony level morphological differences (photo: Katie Barott). (E) The cellular to colony levels of complexity culminate to build the most diverse marine ecosystems known (photo: Katie Barott).

services. Despite this bleak scenario, there are rays of hope for the persistence of corals and coral reefs into the future. During severe bleaching events, there are corals that retain their symbionts (Figure 2D), and bleached corals that survive the stress and recover their symbionts over time (Figure 2A) [10]. Such resilience is likely due to a combination of host and symbiont-derived factors [11,12]. Understanding the mechanisms that underpin resilience will help us assess the acclimatization and adaptation potential of reef-building corals in the face of continued and intensifying anthropogenic perturbation.

Our ability to assess and project the response of corals to environmental change requires an understanding of the fundamental cellular biology of reef-building corals. Coral reefs are ultimately the result of cellular level processes within the coral animal that rely on intricate exchanges between prokaryotic and eukaryotic organisms. The scientific task is to untangle this complexity and identify unifying themes that allow us to make biological models and projections that inform policy and conservation actions aimed at protecting these threatened ecosystems. In this review, we detail the anatomy of the coral meta-organism (i.e. the coral animal and all associated microorganisms; Box 1), highlight the variation in physicochemical micro- and macro-habitat created by interaction of coral cells with skeletal and seawater features, explore the functional and evolutionary implications of microbiome flexibility and fidelity, discuss how microhabitat variation and symbiotic dynamism contribute to the acclimatization and adaptation potential of corals and identify promising research foci for future study.

Coral Cellular Diversity Generates Complex Micro-Environments

The predecessors to reef-building corals are present in the fossil record dating back ~400 million years, with reef-building corals arising in the last ~250 million years [13]. There are hundreds of scleractinian coral species known, exhibiting a variety of shapes (e.g. branching, mounding, plating, encrusting; Figure 1D), colony sizes (centimeters to meters) and life spans (years to centuries). These features provide an array of habitats for larger reef residents, such as fish, molluscs or custaceans, yet much remains to be learned about the microhabitat variability within the coral animal itself and how that micro-scale diversity shapes the diversity and resilience of symbiotic microbial communities (e.g. *Symbiodinium*, bacteria, fungi, viruses; Figure 1A).

Coral Cellular Architecture

As colonial marine cnidarians, corals are comprised of an interconnected network of polyps that share a continuous epithelial surface and internal gastrovascular system (Figure 1B,C). Corals are diploblastic, with two distinct tissue layers: the epidermis and the gastrodermis (from the ectoderm and endoderm, respectively). Each of the coral's tissue layers contain numerous cell types, the total number and physiological function of which are not entirely known [14]. The cells in the oral ectoderm shape coral interactions with the external environment, including the

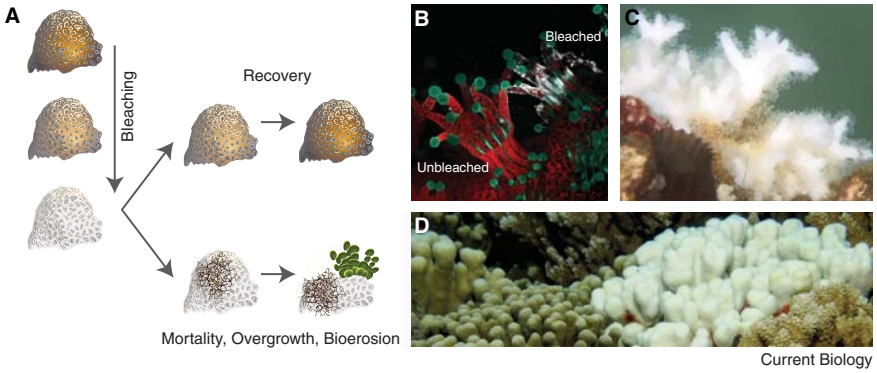

Figure 2. Coral bleaching and recovery.
(A) Coral bleaching is the gradual loss of symbionts over time, which can be followed by recovery if the stressor ceases. If not, bleaching will lead to colony mortality, followed by overgrowth by seaweeds and erosion of the carbonate skeleton. (B) Fluorescence image of a partially bleached *Pocillopora damicornis* colony (image: Amy Eggers). The polyp on the left still contains a full complement of *Symbiodinium*, whose endogenous chlorophyll fluorescence is shown in red. The neighboring polyp on the right has lost the majority of its symbionts. Green fluorescence is due to endogenous coral green fluorescent protein. (C) Completely bleached *P. damicornis* colony *in situ* (photo: Hollie Putnam). (D) Bleached *Porites compressa* colony neighbored by a conspecific colony that appears healthy (photo: Raphael Ritson-Williams).

production of the surface mucus layer by mucocytes, clearance of mucus and sediment by ciliated cells as well as prey capture and defense by nematocysts. Beneath the oral ectoderm is the oral gastroderm, where *Symbiodinium* algae reside within specialized cells called 'symbiocytes' [14]. *Symbiodinium* initially enter host cells via phagocytosis, and are acquired either from the parent during gametogenesis (vertical transmission) or taken up from the seawater (horizontal transmission). Each algal cell is contained within a membrane-bound organelle, the symbiosome, which occupies most of the symbiocyte (Figure 1B) [15]. *Symbiodinium* are also found in the aboral gastroderm, though at much lower abundance. Below the aboral gastroderm lies the aboral ectoderm, referred to as the 'calicoblastic epithelium' due to its role in promoting coral calcification. Desmocytes within the calicoblastic epithelium anchor the tissue to the skeleton [16], forming a network of fluid pockets, the sub-calicoblastic medium, the chemistry of which is actively modified by calicoblasts to promote biomineralization [2,17]. One consequence of this cell type diversity is the generation of distinct intra- and extracellular physicochemical gradients within the colony. This is the result of cell-specific physiological activities, such as photosynthesis, calcification or respiration, which are strongly influenced by conditions in the surrounding environment, such as light, temperature or nutrients.

Light as a Driver of Physical and Biological Variability

The physicochemical gradients within the coral colony are both spatially and temporally variable. Light is the most pronounced driver of these dynamics. Light stimulates *Symbiodinium* photosynthesis, which subsequently promotes rapid daytime calcification by the coral (light-enhanced calcification [2]). The mechanisms of light-enhanced calcification are not fully understood, and the role of *Symbiodinium* in this process may include provisioning of energy to the host via translocation of sugars, synthesis and transfer of precursors for the skeletal organic matrix required for aragonite biomineralization and removal of the inhibitory protons generated during calcification [2]. Further elucidation of the mechanisms underlying these processes needs to consider the internal physical variability within the colony and the spatial arrangement of the *Symbiodinium* cells. For example, in an apparent paradox, rapidly calcifying tissues are spatially separated from photosynthetically active regions [18], despite the need for photosynthetically derived energy and the benefit of pH buffering from photosynthetic activity mentioned above. Spatial structuring is also present within the tissues, as carbon fixation by individual algal cells decreases with increasing tissue depth due to the attenuation of light within the tissues from symbiont self-shading (Figure 3A) [19,20]. Furthermore, coral tissues can become anoxic in the dark (<2% air saturation; Figure 3B) [21]. Thus, in the same way physical conditions at the reef scale influence niche partitioning, we assert that variable microenvironments within the coral tissue can lead to spatial structuring of microbial ecotypes and regions of the colony dominated by distinct physiology and chemistry (e.g. calcification vs. photosynthesis) that support distinct microbial communities and host functions.

Endosymbiosis and Biomineralization Require Active Regulation

Increasing concern regarding the effect of ocean acidification on marine life [6] has placed an emphasis on understanding intracellular pH regulation of calcifying marine organisms. The shift in carbonate chemistry due to ocean acidification reduces the saturation state of aragonite (the mineral form of calcium carbonate precipitated by corals), which increases the energetic cost of biomineralization. In addition, ocean acidification increases the cost of intracellular acid–base homeostasis, a process critical for cellular function. The sensitivity of coral physiology to pH requires the ability to sense and compensate for changes in acid–base equivalents (e.g. H^+, HCO_3^-) and we are just beginning to scratch the surface of these mechanisms in corals [14]. Coral cells maintain stable intracellular pH across the day–night cycle, except cells containing *Symbiodinium* become more alkaline in the light due to photosynthesis (Figure 3C,D) [17,22,23]. The presence of *Symbiodinium* buffers the coral host cell during acute external acidification [22], likely due to the consumption of CO_2 by photosynthesis. Encouragingly, corals exposed to chronic low pH maintain normal acid–base homeostasis and calcification rates at seawater acidification far more severe than that expected from climate change (pH 7.4 vs. pH 7.9–8.0, respectively), but coral buffering capacity is eventually exhausted [24]. Calcification at such low external pH is sustained through elevation of the sub-calicoblastic medium pH by a combination of coral ion channels and active transporters, thereby maintaining high aragonite saturation states favorable for biomineralization [14]. However, we do not yet understand the energetic tradeoffs required to maintain sub-calicoblastic medium or

Box 1. Glossary

Aragonite: The form of calcium carbonate mineral produced during coral calcification.
Biomineralization: The production of crystalline carbonate minerals (e.g. aragonite) by living organisms.
Coral bleaching: The disruption of the symbiotic relationship between the coral host and *Symbiodinium*, resulting in symbiont pigment and cell loss and paling and transparency of the coral tissue color, making visible the underlying white skeleton. Bleaching is an increasingly common global problem that can lead to coral mortality and widespread reef habitat loss.
Carbon concentrating mechanism: Cellular enzymes that promote the accumulation of carbon dioxide for carbon fixation by RuBisCo in carbon-limited environments (e.g. carbonic anhydrase).
Diffusive boundary layer: A thin layer of low-velocity seawater above the surface of the coral tissue, the thickness of which is dictated by flow and colony structure. Metabolic byproducts such as oxygen and carbon dioxide accumulate in this layer and their removal is limited by the rate of diffusion.
Dissolved inorganic carbon (DIC): The combined total of the species of inorganic carbon dissolved in seawater: carbonate, bicarbonate, carbonic acid, and aqueous carbon dioxide.
Environmentally-mediated priming hypothesis: Extreme fluctuations of the physicochemical internal environment generated within thick coral tissues preconditions these corals to potential external perturbations, thus decreasing sensitivity to environmental change.
Holobiont: The community formed by a macroorganism and all associated symbiotic microbiota, both stable and transient, that create a biotic (ecological) unit, synonymous to meta-organism.
Hormesis (Hormetic priming): Exposure to mild, sublethal stressors can improve an organism's ability to tolerate subsequent or different stressors.
Microhabitat: A distinct microenvironment that provides a habitat niche for microbes.
Microbiome: The community of microbes associated with a macroorganism.
Perturbation: A temporary or long-term change in environmental conditions that leads to a physiological or community response.
Resilience: The ability of an ecosystem (or holobiont) to tolerate disturbance and retain the same or similar state.
Sub-calicoblastic medium: The extracellular fluid between the coral calicoblastic epithelium and the skeleton in which aragonite formation occurs.
Surface mucus layer: The external mucus layer lining the oral epithelium; location of the greatest abundance of coral-associated bacteria. Produced by coral mucocytes and occasionally shed by ciliary action along the epithelium.
Symbiocyte: A specialized cnidarian cell that contains intracellular *Symbiodinium* algae.
***Symbiodinium*:** Dinoflagellate algae capable of forming intracellular symbioses with corals and a variety of marine organisms. Some strains are found only in a free-living state.

intracellular pH at optimal levels in the face of these challenges. Furthermore, the interaction of multiple stressors, such as high temperature and low pH, can exacerbate cellular perturbation. Additional thermal stress reduces coral acid–base regulation capacity relative to acidification alone [25]. It is imperative to characterize the responses of corals to perturbation and the interactive effects of stressors, particularly as cellular processes dictate colony survival.

In addition to calcification and host metabolism, acid–base regulation by the coral is critical for maintaining physiological function of *Symbiodinium.* Because *Symbiodinium* are spatially sequestered away from seawater, corals must supply the algae with dissolved inorganic carbon, as metabolic CO_2 and passive diffusion of CO_2 from seawater are insufficient to meet photosynthetic demands [26]. Since most dissolved inorganic carbon in seawater is HCO_3^-, active transport across the plasma membrane by the coral is required. DIC must then be actively concentrated, as *Symbiodinium* express form II ribulose bisphosphate carboxylase oxygenase (RuBisCo), which cannot well discriminate between CO_2 and O_2. Two major carbon-concentrating mechanisms have been described in corals: carbonic anhydrases that catalyze the conversion of HCO_3^- to CO_2 are abundant in *Symbiodinium* and the surrounding coral cells, and are necessary for maximal photosynthetic activity [27]; a second mechanism involves host vacuolar H^+-ATPases in the symbiosome membrane, which acidify the symbiosome to pH 4 via energy-dependent proton translocation [15]. This acidification promotes *Symbiodinium* photosynthesis, likely by facilitating accumulation of CO_2 [15]. These studies provide insights into the mechanism and significance of pH regulation in coral, and highlight the need for a mechanistic understanding if we are to project how different coral species will respond to stressors such as climate change.

Tissue and Skeletal Interactions Drive Functional Variation in the Colony

Internal variation in pH, light and oxygen on the cellular level also manifests on the colony scale. For example, skeletal morphology is linked to the generation of diverse physicochemical environments due to the effect of colony shape on the flow of water across the surface of the colony. By altering water motion, coral morphology directly influences the thickness of the diffusive boundary layer (DBL), which impacts rates of nutrient delivery and export of metabolic byproducts. Finely branched shapes, for example, promote flow across branch interstices, thinning the DBL and promoting physiological performance [28,29]. In addition, the thickness of the DBL influences the ability of microbes to colonize the coral surface, potentially affecting the success of corals facing competition with other benthic organisms [30]. Variation in DBL properties has also been

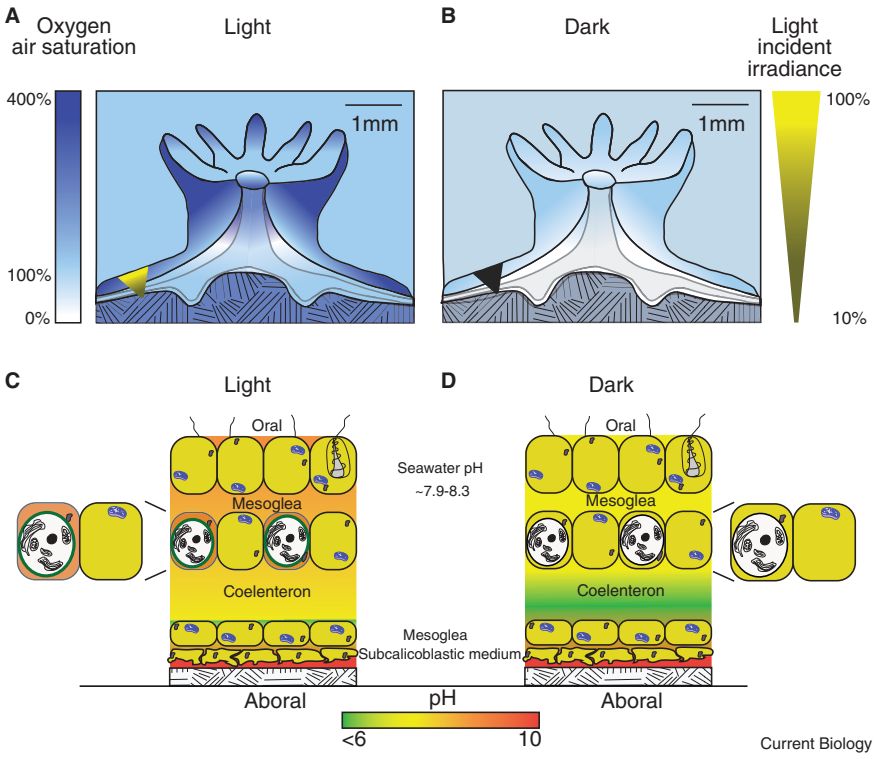

Figure 3. Microhabitat variability of oxygen, light, and pH in coral cells and tissues.
(A) Diagram of contrasting light and oxygen levels within a coral polyp between light and dark. Light irradiance is highest at the surface of the tissue, and decreases with increasing tissue depth. Oxygen is significantly elevated in coral tissues relative to the surrounding seawater during the day, reaching as high as 250–400% air saturation [111,112]. In the coelenteron (interior gut cavity), daytime oxygen levels are elevated near the mouth of the polyp, coinciding with the highest density of *Symbiodinium*, but plummet to near anoxia within the lower reaches of the coelenteron [113]. (B) In the dark, the tissues become nearly anoxic (2% air saturation [21]). Diagram of the pH of coral cells and compartments in the (C) light versus (D) dark. Coral cells without *Symbiodinium* remain at a constant pH across light and dark conditions (pH ~7.0–7.4), while symbiocytes undergo alkalinization of ~0.5 pH units in the light due to photosynthesis [23]. The pH of the coelenteron and the sub-calicoblastic medium also increases in the light, with the coelenteron ranging from pH ~6.6–8.5 from dark to light, and a thin band of acidic pH lining the aboral end in the light. The pH of the sub-calicoblastic medium is significantly elevated over that of seawater (pH ~8.6–10 vs. pH ~7.8–8.1) [114], while the pH of the symbiosome compartment is acidic (pH ~4) in both light and dark conditions [15].

hypothesized to underlie differential coral bleaching susceptibility, as increased buildup of reactive oxygen species at high temperatures in corals with a thicker DBL results in greater cellular damage [31]. Differences in DBL thickness may also contribute to the range of sensitivity to ocean acidification observed in corals, as it results in substantially different pH conditions along the coral surface [32].

Microscale variation may help explain variation in coral responses to stress events, as it results in different levels of exposure for individual cells and polyps. For example, colonies adjacent to each other experiencing the same seawater temperature may be completely bleached or apparently healthy (Figure 2D) [10], and even different regions within the same colony can show different bleaching severities (Figure 2B). Species-level differences in bleaching susceptibility are often attributed to host characteristics such as tissue biomass and tissue thickness, with greater tissue thickness conferring greater bleaching resistance [31]. This positive relationship may be explained by several hypotheses. First, thick tissues provide greater energy reserves, generating a temporal buffer against starvation during bleaching [31]. Second, the pronounced heterogeneity within thick tissues may lead to selection for symbionts with improved physiological performance, thus promoting host survival during times of stress. Given the importance of microhabitats in other systems (e.g. root nodules of legumes that harbor nitrogen-fixing bacteria and thus facilitate plant growth in nitrogen-limited environments [33]), we predict that physicochemical variability at the cellular and tissue scales provide habitats for novel microbe–coral symbioses that can underlie the success of corals as reef-builders in nutrient limited environments. In addition, the greater physical habitat provided by thick tissues is associated with higher *Symbiodinium* density, causing self-shading within the tissues that may reduce light stress and damage to the understory symbionts during bleaching events. The remaining symbiont community may then repopulate the bleached tissues [34], promoting more rapid coral recovery.

Third, the diversity and magnitude of physicochemical gradients within coral cells and tissues corresponds positively with tissue thickness (Figure 4) [21]. Here, we propose the hypothesis that the environmental fluctuations, such as pH, light, O_2 or temperature, within thick host tissues may provide environmental hardening [35], or environmentally-mediated priming (Box 2). We predict that thick tissue corals are thus better acclimated to environmental variability due to their extreme internal milieu. Acquired environmental tolerance has been documented in corals [35], and is also observed in other organisms, such as oysters [36], plants [37] and *Drosophila melanogaster* [38]. The within-tissue bio-physical feedback mechanism we posit here with environmentally-mediated priming is likely to work in combination with the other benefits of thick tissues (Box 2) to achieve the enhanced environmental tolerance documented in thick-tissue corals to a variety of stressors including ocean acidification [39] and thermal stress [31].

Contribution of the Microbiome to Coral Performance

The concept of multicellular organisms as meta-organisms is now well established [40] and refers to the totality of any multicellular organism. The concept specifically recognizes the essential roles that microbes (both prokaryotic and eukaryotic) play in an organism's phenotype. Importantly, meta-organisms are considered 'polygenomic' in that the phenotype of the meta-organism is the product of the transcriptomic, proteomic and metabolic responses of all the symbiotic partners. Corals were one of the first meta-organisms to be considered in this way,

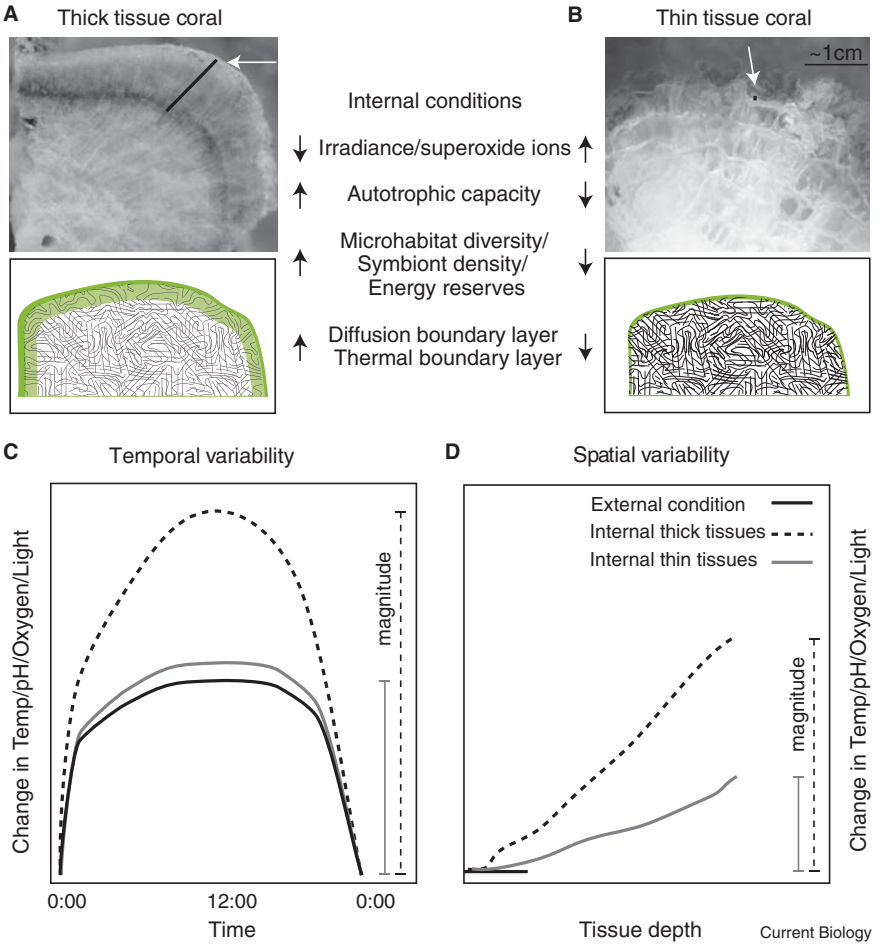

Figure 4. Tissue thickness affects coral physicochemical microenvironments.
Images and schematics of the tissue thickness and tissue skeletal interface for (A) thick tissue and (B) thin tissue corals, with contrasting features listed between. White arrows indicate the position of black lines showcasing different tissue thicknesses. Tissue thickening promotes both (C) temporal and (D) spatial variability in physicochemical parameters, with a greatly enhanced magnitude of change within thick tissues relative to the external environment potentially generating environmentally-mediated priming and enhanced tolerance to future exposure. (Photos: Peter Edmunds, Hollie Putnam.)

predominantly due to the research focus on the photosynthetic algal endosymbiont and its influence on host physiology. While coral ecology was initially studied with a focus on *Symbiodinium* [41], more recently the contribution of diverse prokaryotes interacting with corals has been recognized [42–44]. The role of the coral microbiome in organism performance is an important albeit underexplored one. Below, we focus on two groups with undeniable links to coral function: bacteria and *Symbiodinium*, although similar processes are likely for the fungi, archaea and viruses [45,46].

The bacterial community can be divided into 'core' microbiome that is stable across space and time, and a more dynamic, sporadic community (Box 3). There is much debate over how to define 'core' taxa [43], but this group provides a breadth of candidates for obligate, physiologically significant bacterial symbioses for corals. One such candidate is *Endozoicomonas*, a γ-proteobacterium, which is closely associated with corals from around the world across a range of habitats. In several coral species, this taxon makes up most of the community (e.g. *Porites* spp. [47–49]; *Stylophora pistillata* [50]; *Pocillopora verrucosa* [44]). However, persistently associated core bacterial taxa are also commonly found in low abundance, highlighting the danger of inferring physiological significance from relative abundance [51]. Further work is needed to fully identify the functional roles of the core microbiome, which include nitrogen fixation, sulfur cycling and competitive exclusion of pathogens [42,43,52,53]. Genomic characterization of coral symbionts is promising to greatly expand our understanding of the coral meta-organism [54,55].

The function of bacterial communities may be dictated by their location within the meta-organism [56], as they are likely to be adapted to the specific microenvironments of the host. The coral surface mucus layer, for example, is a dynamic, heavily colonized environment replete with photosynthetically fixed carbon. This layer is analogous to the soil environment of a plant root, forming a diffusion gradient within which microbes utilize waste and alter the biochemical properties of the host-derived mucus. The surface mucus layer is further impacted by the broader habitat in which the coral resides due to re-suspension and connection to the sediment, water column and benthic organisms [57]. Furthermore, other microhabitats within the body of the coral provide niches for microbial interactions with the host, such as the gut, the skeleton (which is exposed to the seawater and sediment environment) and the various coral tissues [56,58,59].

With regards to the symbiotic dinoflagellate *Symbiodinium*, the core microbiome is not a unified concept. While *Symbiodinium* were thought of as one global species, *Symbiodinium microadriaticum* [60], they have since been genetically characterized to comprise nine clades (clades A–I) and hundreds of sequence types [61]. *Symbiodinium* are found in association with a variety of organisms, such as ciliates, foraminifera, giant clams, nudibranchs, sponges and acoelomate worms [62], but the cnidarian–*Symbiodinium* symbiosis is dominated by *Symbiodinium* clades A, B, C and D [63]. *Symbiodinium* host-specificity varies between coral species. The exemplar high fidelity symbiont is the consistent presence of specific C types (e.g. C15) with massive *Porites* and other thick-tissued, stress-tolerant corals [61,64]. Clades C, D and A contain generalists and have been shown to shuffle and switch between hosts during thermal stress [62,65,66]. There are functional differences between clades [67,68] and between types within a clade [69], but there are potentially hundreds of types for which we have

Box 2. Thick tissues, physicochemical extremes, and the environmentally-mediated priming hypothesis

Coral tissue thickness ranges from micrometers to centimeters, and thicker tissue corals have been reported to be less susceptible to bleaching [31]. Comparison of thick-tissue corals (e.g., massive *Porites*) with thin-tissue corals (e.g., *Pocillopora*) highlights the variation in a number of physical factors. Thick tissues can be intercalated as deep as 1 cm into the skeleton (Figure 4A), forming a profoundly different internal microenvironment [21,115], whereas thin tissues that reside on the surface of the skeleton mirror more closely the external environment (Figure 4B).

The idea that coral tissue thickness contributes to resilience is prevalent in the literature, but the mechanistic underpinnings have yet to be fully elucidated. Exposure to fluctuating conditions generates different phenotypic responses than exposure to stable conditions [116,117]. This is not surprising as biochemical processes are highly sensitive to the physical milieu within cells and the enzymatic reactions underpinning basic cellular processes are strongly sensitive to pH and temperature [118]. We posit that exposure to extreme spatial and temporal internal physicochemical fluctuations may pre-condition thick tissue corals to withstand environmental perturbation (Figure 4), through what we call 'environmentally-mediated priming'.

Exposure to environmental stressors in sub-lethal doses can provide acclimatization [119–122]. A coral's internal *Umwelt* at the level of the cells within the tissue layers is undeniably modulated by tissue thickness with respect to external conditions [21,123,124]. Cells in thicker tissue corals thus experience a wider range of conditions, with the potential for hormetic priming to promote tolerance to future stressors [120,121]. In thin tissue corals, the internal environment does not change as much and more closely reflects external conditions. Therefore, environmental perturbations elicit strong responses — thin tissue, branching coral taxa are for instance highly prone to bleaching. Conversely, the internal fluctuations of thick tissue corals occur over a wider range, thus preparing the coral for a wider range of external changes and reducing the response to external environmental perturbations. Environmentally-mediated priming can therefore provide acclimatization in thick tissue corals, with prior extreme experience culminating in reduced environmental sensitivity. This mechanism is likely one of several benefits of thick tissues that together reduce susceptibility to environmental perturbations and contribute to their ecological success.

no functional information. A recent investigation has linked differences in metabolite profiles with the abundance of distinct, yet genetically related, types [70], reinforcing the need for innovative culturing efforts [71] and more importantly *in situ* tracking of symbiont identity and function. Issues with the primary genetic marker used in the field, the internal transcribed spacer region of nuclear rDNA (ITS2), such as the presence of diverse copies within a single genome [72], have precluded species level identification of *Symbiodinium* [72,73]. The sequencing of additional *Symbiodinium* genomes will provide new markers [74–76], improving characterization of *Symbiodinium* community diversity and dynamics.

Microbial interactions with a coral can range from mutualistic, to neutral, to pathogenic and can change over time and in response to environmental stimuli [42,77] (Box 3). Coral bleaching events cause such shifts in coral bacteria, including an increase in potentially pathogenic *Vibrio* spp.; however, corals can subsequently recover their initial microbial communities [78]. This pattern highlights two important properties of the coral microbiome: first that it is resilient and second that it is dynamic. We do not know if increases in certain species during times of stress indicate disease, opportunistic colonization of a compromised host that may lead to disease if the stress is sufficiently prolonged in duration, or even which microbes cause the majority of observed coral diseases [42,79]. Stress induces changes in the taxonomic and functional composition of the coral microbiome, with a rise in disease-associated taxa and genes [80] and loss of potentially beneficial intracellular bacterial symbionts [81]. Thermal stress can also induce shifts in *Symbiodinium*, with switching from clade C to D leading to increased thermal tolerance [82] but decline in growth [67]. We therefore need to decipher the specific bacterial and *Symbiodinium* types that closely interact with the coral (core microbiome), the environmental conditions that influence these interactions and the capacity for the coral host to shape these interactions to optimize performance.

Coral Complexity Enables Acclimatization and Adaptation

The complexity from cell to organism and microbe to host provides the fodder for buffering and acclimatization, plasticity and evolution, and thus resilience, conservation and restoration of reef ecosystems. It is clear there is a great amount of biological variation in the response of corals to environmental perturbation, where survivors are found even during mass bleaching events [7] and some coral colonies bleach completely, while their neighbors hardly pale (Figure 2) [10]. We have discussed how cellular to colony scale variation in physical environment and symbiotic interactions generates contrasting biological responses or emergent properties of the meta-organism. We now consider how these mechanisms contribute to the acclimatization and adaptation of coral reefs to the novel environments generated by anthropogenic climate change.

The most pressing large-scale stressor on reefs today is thermal stress from global warming [7]. Its rapid pace potentially limits the ability of corals to respond via adaptive evolution. Thermal tolerance in corals is related to both host and symbiont physiology [83–85]. Coral larvae that have not yet acquired *Symbiodinium* are a useful system for testing host genetic adaptation, as studies can be conducted in the absence of influence from *Symbiodinium* or intracolony genetic variability [84–86]. Quantitative genetic experiments using coral larvae have demonstrated that there is heritable host variation even within a small number of families [84,86], and rapid adaptation may be possible in corals depending on standing genetic variation and connectivity between populations [86]. Connectivity between reefs can lead to increased environmental tolerance and potentially genetic rescue through the immigration of new

Box 3. Ecological and evolutionary dynamics within the coral microbiome

Symbiotic microbial community dynamics are shaped by two differing adaptive strategies: symbiont fidelity and sporadic opportunism. Both occur within the coral microbiome, each with distinct selective pressures that together may provide advantages to the meta-organism when responding to perturbation.

Symbiont fidelity and coevolution in the core microbiome

The core microbiome is operationally defined as taxa that are associated with the host across space and time. Evolution of obligate symbiosis is predicted to be strengthened through vertical transmission, promoting coevolution and genetic exchange between host and symbiont, and enhancing adaptive capacity of the meta-organism. Interestingly, the majority of coral species do not vertically transmit *Symbiodinium*; instead, ~80% of coral species acquire their algal symbionts from the environment [125]. How bacteria are transmitted is only known for a few coral species, and there is evidence for both vertical and horizontal transmission [126]. In persistent associations, the community is predicted to respond to novel environments by acclimatization and evolution. As microbes have short generation times, adaptive functions can evolve fast. As such, the holobiont may successfully acclimatize to a rapidly changing environment despite the long generation times (decades to centuries) of the coral host. Furthermore, genomic streamlining between host and symbiont would be expected to occur during the evolution of obligate symbioses [127], and corals acquire genes from bacteria and *Symbiodinium* [93]. This genetic exchange within the coral meta-organism may promote functional and energetic efficiency.

Symbiont promiscuity and ecology

A subset of the coral microbiome is only transiently associated with individual colonies. Ecological dynamics drive adaptation, as horizontal exchange of microbes with the surrounding environment leads to acquisition of novel, potentially beneficial functions. Horizontal acquisition has been documented in corals for both bacteria and *Symbiodinium* [126,128]. The transient microbiome may undergo rapid changes in response to perturbation as novel strains colonize the host or members of the microbial community increase in abundance. Bacterial community shifts have been documented in response to a wide variety of parameters, including season [58], thermal stress [78,89], depth and geographic distance [129], as well as intracolony habitat [56,58,112]. Intriguingly, the transient members of the community are commonly among the most abundant phylotypes [51], but their physiological importance for the holobiont remains unknown. Ecological switching also occurs among *Symbiodinium*. For example, thermal stress can lead to a shift in the dominant *Symbiodinium* clade, a process termed 'adaptive bleaching' [62]. However, some coral species are highly specific in their associations and have limited capacity for shuffling (e.g. *Porites* spp. [64]). Furthermore, acquisition of new *Symbiodinium* strains is not always adaptive; some strains release little to no nutrients to the host, suggesting the evolution of 'cheaters' or a parasitic relationship [77].

Finally, genetic exchange between microbes via horizontal gene transfer blurs the line between ecological and evolutionary avenues, providing a route for the core microbiome to acquire novel functions from the transient community without shifts in composition. This dynamic has been observed in bacterial communities associated with the surface boundary layer of corals and other benthic reef organisms, whereby the functional genetic repertoire changes in response to the abiotic environment, while the taxonomic composition remains specific to the host [130].

genotypes [87], but current connectivity estimates remain limited for many reef locations globally. Further, the necessity for evolutionary rescue [88], or enhancement of novel adaptive alleles to reverse the current trajectory of reef decline is becoming a reality. However, fine scale oceanographic models for connectivity, species dispersal potential and the rates of environmental change of source and sink populations are largely unknown. The potential to reduce levels of maladaptation and increase the matching of the phenotype to the environment through evolutionary rescue may therefore be limited by both connectivity and, in some connected locations, by contrasting thermal histories.

It is not surprising that genetic variability corresponds to phenotypic variability, but the mechanisms by which this is accomplished in a complex meta-organism are less clear. Adaptation of the coral meta-organism can clearly be facilitated by the symbiotic microbiome (Box 3) [62,89]. Evolutionary adaptation through natural selection on the microbiome across generations under different conditions can also drive drastic differences in coral performance. For example, local adaptation of *Symbiodinium* has led to increased thermal tolerance in corals. *Symbiodinium* populations from a warmer northern Great Barrier Reef locale displayed more efficient photosynthetic function, both in symbiosis and in culture, when exposed to a high temperature of 32°C [90]. In contrast, corals inoculated with *Symbiodinium* from the cooler central locale displayed bleaching and mortality at the same temperature, highlighting the role of the microbiome in thermal tolerance [90].

Recent genome sequencing of coral [91], *Symbiodinium* [74,75,76] and symbiotic bacteria [55,92] has provided a wealth of data. The first published coral genome (~420 million base pairs) has just under 24,000 genes, and showed that core functions have been lost in the host and are now carried out by the symbiont (e.g., enzymes necessary for amino acid biosynthesis [91]). Analyses of the existing genomic and transcriptomic resources to date (20 coral taxa as of 2016) have outlined genes

involved in symbiosis, including complex ion trafficking, biomineralization and immune response, as well as their conservation across coral clades [93]. *Symbiodinium* genome architecture remains more of a mystery, despite draft genome assemblies for several species (*S. minutum*, clade B [75], *S. kawagutii*, clade F [74], and *S. microadriaticum*, clade A [76]). *Symbiodinium* have some of the largest eukaryotic genomes (1.1–1.5 billion base pairs), yet there is nearly a total lack of conservation between some genomes (~2% for *S. kawagutii* to *S. minutum*, and ~6% in the reciprocal BLAST analyses [76]). This divergence in gene number and content enables researchers to link variation in physiological performance to genetic features. Comparative genomics of coral-associated bacteria have revealed potential symbiotic functions (e.g. amino acid production [54]). However, the top candidate for obligate bacterial symbiosis in corals, the intracellular *Endozoicomonas* spp., have large genomes that do not show the streamlining expected of an obligate endosymbiont [54]. Advances in sequencing coverage across the taxonomic range of both host and its diverse microbiome will provide the capacity to test for genomic exchange and streamlining within the meta-organism (Box 3), and will help link genes to traits.

The rapid improvement of sequencing technology and establishment of a reef genomics consortium promises to provide genomic enlightenment through sequencing the hologenomes (i.e., genomes of all meta-organism constituents) of ten coral species (ReFuGe2020) [94]. For example, genomic resources will provide references for resequencing projects, mapping of DNA methylation, annotation of proteomics work, as well as identification of genes under selection in resilient taxa or individuals. Furthermore, these efforts will aid in the elucidation of the role of a wider variety of genomic regions (e.g., miRNAs, lncRNAs, transposable elements) in coral stress response and resilience, and will provide a baseline for genomically-informed conservation and restoration efforts.

A growing body of work focuses on gene expression. It is clear that gene-expression plasticity is an important mechanism by which corals cope with environmental fluctuation. Gene-expression dynamics can be responsible for environmentally dependent acquisition of heat sensitivity following transplantation that can be as strong as or stronger than adaptive gains due to selection [95]. While transcriptomics have also provided direct insights into coral stress response pathways [96,97], gene expression does not always correlate with enzymatic activity [98]. Furthermore, the diversity of cell and tissue types within the coral colony make bulk analyses of any parameter (e.g. transcript or protein abundance) difficult to interpret as changes in one tissue may be masked by contrasting changes in another compartment [99].

One of the major challenges for symbiotic systems, and coral biology in particular, is developing the tools necessary for characterizing the cellular mechanisms responsible for physiological variability. To date, much headway has been made in genomics, symbiotic regulation and microbiome linkages to meta-organism function using the model system of *Aiptasia*/*Exaiptasia* [100–102], but in the absence of the calcification process. Currently, there has been no application of genetic manipulation in corals (e.g., CRISPR), there are only a few published coral genomes [94], there are no stable cell cultures or coral inbred lines, and tools for characterizing cellular mechanisms (e.g. antibodies, morpholinos) are largely missing. Coral biology needs to overcome these limitations and move towards cell-type-specific analyses through single-cell genomics [54] and transcriptomics [99], to sub-cellular localization of proteins [15,103] and symbionts [59] within the context of surrounding microhabitats. By filling these gaps in our basic understanding of coral cell biology, we will better understand the ability of corals to respond to stress.

An area of intensifying research in coral biology is the possible role of epigenetic changes in rapid acclimatization. Epigenetics refers to the potential to generate multiple phenotypes from a single genotype through differential gene expression [104]. An initial examination of the link between DNA methylation and physiological plasticity in corals shows species-specific differences in bulk coral DNA methylation, with variability in DNA methylation documented in a phenotypically plastic and environmentally sensitive species [105]. A role for DNA methylation in coral plasticity is further suggested by data from *in silico* studies showing that strong gene-body methylation is associated with genes with housekeeping functions, whereas weak methylation is associated with those with responsiveness to environmental changes [106,107]. While epigenetics has been hailed as a new frontier with great promise as a mechanism of environmental memory with a role in intra- and trans-generational plasticity and acclimatization to climate change [105,108], it is critical to ensure that no genetic changes have taken place to truly understand its role in corals [104]. Much remains to be discerned regarding the exact roles of, for instance, DNA methylation, including the genetic or epigenetic origin of changes, the timing of exposure necessary to induce plasticity and the temporal stability of any resulting phenotypes (e.g. intra-generational or trans-generational [108]). It is important to clearly understand mechanisms of acclimatization and adaptation to determine how generally they are used by different coral species and in response to different environmental perturbations.

The Future of Coral Biology

It is undeniable that anthropogenic pressures on coral reef ecosystems are driving their decline [7]. Mass coral bleaching, a consequence of climate change, is now commonplace and occurring every year, for instance in Hawaii in 2014 and 2015, and on the Great Barrier Reef in 2016 and 2017. We must cut emissions globally to preserve reefs and the goods and services they provide to humans. In the most comprehensive analysis of repeat coral bleaching to date, the overwhelming impacts of thermally-induced coral bleaching were identified, even in areas with high water quality and rigorous reef management [7]. This powerful message reinforces the call for reductions in carbon emissions as a primary mechanism to combat coral-reef decline. In this review, we have advocated the need for a better understanding of fundamental coral biology and micro-complexity (e.g., symbiotic dynamism, cell-specific responses) to incorporate the full range of potential coral responses into resilience estimates, ecological and evolutionary models, as well as conservation strategies [109,110].

We now have techniques in place to better understand the biology of corals at the cellular level. The discovery and characterization of physical complexity and dynamics within cells and

tissues highlights the necessity to conduct both organismal approaches as well as detailed reductionist experiments in single cells. The complexity of coral biology makes assigning definitive regional or global response patterns or conservation and management solutions challenging. Studies focused on the integration of cellular structure and cellular function in combination with the environmental setting will provide essential mechanistic insights in critical areas such as stress response, symbiosis and biomineralization. Single-cell approaches and improved genomic isolation from small samples, as well as advances in *Symbiodinium* and bacterial culturing, are likely to provide some of the most useful avenues to overcoming the limitations imposed by the tightly-coupled and highly diverse eukaryote–prokaryote symbiosis of the coral meta-organism. The future challenge will then be applying the information generated within laboratory scenarios, or model species, to the environmental complexity of the reef habitat and diversity of reef-building corals.

The meta-organism and its symbiotic, genetic, and epigenetic complexity may provide corals with adaptive avenues. It is critical to now examine the scope for rapid acclimatization through microbiome switching, shuffling and host epigenetic and genetic adaptation to generate a temporal buffer to help maintain pace with increasing environmental change. Genomic and metagenomic research on corals is still in its infancy, with most known about small bacterial genomes, a growing body of host coral studies, and limited information on large and complex *Symbiodinium* genomes. Genomic sequencing, annotation and analysis of genetic architecture are key, as they provide resources for understanding phenotypic responses and the adaptive capacity of the meta-organism. The complexity of the coral meta-organism provides a variety of evolutionary trajectories we have yet to fully explore.

AUTHOR CONTRIBUTIONS

Conceptualization, H.M.P., K.L.B., T.D.A., R.G.D.; writing – original draft, H.M.P., K.L.B., T.D.A.; writing – review & editing, H.M.P., K.L.B., R.D.G.; visualization, H.M.P., K.L.B.

ACKNOWLEDGEMENTS

K.L.B. was supported by funds from the PGA Family Foundation. We would like to thank many of our colleagues for stimulating discussions that have contributed to the articulation of these ideas. Further, the constructive comments of two anonymous reviewers are greatly appreciated. This is SOEST contribution #10005 and HIMB contribution #1685.

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