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Is Ocean Acidification Really a Threat to Marine Calcifiers? A Systematic Review and Meta-Analysis of 980+ Studies Spanning Two Decades

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Ocean acidification is considered detrimental to marine calcifiers, but mounting contradictory evidence suggests a need to revisit this concept. This systematic review and meta-analysis aim to critically re-evaluate the prevailing paradigm of negative effects of ocean acidification on calcifiers. Based on 5153 observations from 985 studies, many calcifiers (e.g., echinoderms, crustaceans, and cephalopods) are found to be tolerant to near-future ocean acidification (pH ≈ 7.8 by the year 2100), but coccolithophores, calcifying algae, and corals appear to be sensitive. Calcifiers are generally more sensitive at the larval stage than adult stage. Over 70% of the observations in growth and calcification are non-negative, implying the acclimation capacity of many calcifiers to ocean acidification. This capacity can be mediated by phenotypic plasticity (e.g., physiological, mineralogical, structural, and molecular adjustments), transgenerational plasticity, increased food availability, or species interactions. The results suggest that the impacts of ocean acidification on calcifiers are less deleterious than initially thought as their adaptability has been underestimated. Therefore, in the forthcoming era of ocean acidification research, it is advocated that studying how marine organisms persist is as important as studying how they perish, and that future hypotheses and experimental designs are not constrained within the paradigm of negative effects.

1. Ocean Acidification Caused by CO_2 Emissions

Since the beginning of the Industrial Revolution in the 18th century, anthropogenic CO_2 emissions have escalated due to intensified combustion of fossil fuels. In fact, atmospheric CO_2 concentrations surged from ≈280 to ≈400 ppm in the last 250 years.[1] By the end of this century, atmospheric CO_2 concentrations are forecast to range from ≈580 ppm (RCP4.5) to ≈1000 ppm (RCP8.5), depending on the strength of measures taken to mitigate CO_2 emissions.[2,3] The unprecedented upward trend of CO_2 emissions has raised global concern about the future of marine ecosystems because oceans will absorb more atmospheric CO_2 that leads to ensuing pH reduction in seawater (i.e., ocean acidification),[4] following a series of chemical reactions:

$$CO_{2(g)} \rightleftharpoons CO_{2(aq)} + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^- \rightleftharpoons 2H^+ + CO_3^{2-} \quad (1)$$

When atmospheric CO_2 dissolves in seawater, carbonic acid (H_2CO_3) is formed. Being unstable in seawater, H_2CO_3 undergoes dissociation into bicarbonate (HCO_3^-) and carbonate (CO_3^{2-}) ions by losing hydrogen ions (H^+), accounting for pH reduction in seawater. Since the preindustrial period, global seawater pH has declined by 0.1 units on average. Subject to CO_2 emission scenarios, a further reduction by about 0.15 (RCP4.5), 0.20 (RCP6.0), or 0.30 units (RCP8.5) is predicted to occur by the end of this century.[1,2] Given the projected future increase in CO_2 concentrations, the equilibrium of the seawater carbonate system will be altered, especially for the concentrations of HCO_3^- and CO_3^{2-}.[4] Under the business-as-usual scenario in the year 2100, the concentration of CO_3^{2-} is estimated to decrease by ≈50%,[5,6] causing the carbonate saturation state (Ω) in seawater to decline. Based on the dissolution kinetics, the reduced seawater Ω is expected to affect the formation and dissolution rates of calcium carbonate ($CaCO_3$)—a key ingredient in calcareous shells or skeletons produced by many marine organisms.

$$\Omega = [Ca^{2+}][CO_3^{2-}]/K_{sp} \quad (2)$$

where solubility product K_{sp} depends on temperature, salinity, pressure, and mineral type.

It is proposed that the formation of $CaCO_3$ minerals is favored when $\Omega > 1$, whereas dissolution occurs when $\Omega < 1$ (i.e., undersaturation). Seawater in cold, high-latitude regions

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is more prone to carbonate undersaturation than in warm, equatorial regions according to the solubility of $CaCO_3$.[5] Comparing the two most common $CaCO_3$ minerals, namely calcite and aragonite, the latter has higher solubility and thus becomes undersaturated sooner in the acidifying ocean.[6]

Acidified seawater at pH levels predicted by the end of this century can already be found in some natural marine habitats influenced by CO_2 emissions from underwater volcanic vents (e.g., Aeolian Islands, Italy;[7] Island of Ischia, Italy;[8] the Canary Islands, Spain;[9] Tutum Bay, Papua New Guinea;[10] North Sulawesi, Indonesia;[11] White Island, New Zealand;[12] Nikko Bay, Japan;[13] Levante Bay, Italy;[14]). Analogous to ocean acidification driven by anthropogenic CO_2 emissions, seawater in these habitats can be persistently acidified, but the degree of acidification can vary from mild to extreme that creates a pH gradient.[7,8,12]

Compared to open oceans, seawater in coastal regions is more prone to acidification driven largely by hydrodynamic processes and human activities, which can lead to rapid and extreme pH reduction.[15] For example, wind-driven upwelling of CO_2-rich deep seawater can rapidly and considerably acidify the surface seawater in coastal regions (e.g., Biobío River Basin, Chile;[16] California Current Large Marine Ecosystem, USA;[17] Bahía Culebra, Costa Rica;[18] Cape Byron Marine Park, Australia;[19] Western Arabian Sea[20]). Eutrophication due to agricultural runoff can also result in serious coastal acidification because boosted nutrient levels (e.g., nitrate and phosphate) in seawater can trigger algal blooms, eventually increasing bacterial decomposition of organic matter where CO_2 is released.[21] Freshwater input, particularly from streams and rivers, is another major cause of coastal acidification because it directly reduces seawater total alkalinity, carbonate saturation, and buffering capacity to pH change.[22,23] Hydrodynamic processes and human activities are considered more influential than anthropogenic CO_2 emissions to determine the acidity of coastal waters as extreme levels of coastal acidification (pH ≈ 7.0) have been globally observed.[15,23]

2. Potential Impacts of Ocean Acidification on Marine Organisms

As oceans are forecast to be acidified at an unprecedented rate in the future, the substantial concern is raised by marine scientists about the potential impacts of ocean acidification on marine organisms. Those building calcareous structures (i.e., marine calcifiers) are considered particularly susceptible because calcification is expected to be hindered by reduced seawater Ω.[6] In addition, acidified seawater is considered "corrosive" and can cause the dissolution of $CaCO_3$ minerals.[24] Consequently, net calcification (i.e., gross calcification minus gross dissolution) decreases and calcareous structures become more fragile. Apart from impaired calcification, ocean acidification can also elicit acidosis (i.e., increased acidity in body fluids) that can undermine many vital physiological processes, such as aerobic metabolism.[25] Metabolic depression in turn retards energy production that supports calcification and many other biological processes and activities. Although CO_2-induced acidosis can be compensated through acid-base regulation, energy is required to activate the related ion transporters and exchangers,[25] suggesting an energy trade-off against calcification. In short, reduced seawater Ω, intensified $CaCO_3$ dissolution and impaired physiology are regarded as the major factors limiting the capacity of calcifiers to build calcareous structures under ocean acidification.

Whether calcifiers can construct durable and functional calcareous structures is fundamental to their fitness and survival because these structures (e.g., shells or skeletons) not only provide protection but also support growth. If calcification is retarded by ocean acidification, survival of calcifiers would be diminished and hence functioning of marine ecosystems tremendously disrupted since calcifiers are highly diverse and abundant in oceans (e.g., coccolithophores, coralline algae, corals, bivalves, gastropods, sea urchins, crustaceans, etc.), contributing to various ecological processes (e.g., trophic dynamics, global geochemical cycles, and habitat formation). Apart from ecological impacts, ocean acidification could also incur socioeconomic costs if the production of shelled seafood plummets, such as mussels and oysters maricultured in coastal waters.

Given the serious concern about the fate of calcifiers in the acidifying ocean, a plethora of early studies were conducted to decipher the potential impacts of ocean acidification on calcifiers rather than noncalcifiers (e.g., fish). In concordance with the prevailing paradigm based on seawater carbonate chemistry, ocean acidification was shown to pose negative effects, especially for growth and calcification, on a variety of calcifiers (c.f. the contemporary level at pH ≈ 8 or ≈400 ppm CO_2). For example, ocean acidification not only hinders calcite production in coccolithophores *Emiliania huxleyi* and *Gephyrocapsa oceanica*, but also leads to an increased proportion of malformed coccoliths and incomplete coccospheres;[26] reducing seawater CO_3^{2-} concentration by 50% suppresses skeletal growth in four scleractinian corals (*Acropora verweyi*, *Galaxea fascicularis*, *Pavona cactus* and *Turbinaria reniformis*), possibly caused by impaired crystallization of $CaCO_3$ minerals;[27] gastropod *Strombus luhuanus* as well as sea urchins *Echinometra mathaei* and *Hemicentrotus pulcherrimus* have retarded growth after 26 week exposure to seawater with an additional 200 ppm CO_2.[28] Although growth and calcification are the key variables expected to be compromised by ocean acidification, many other variables can also be impacted. For instance, mussel *Mytilus galloprovincialis* suffers from permanent reduction in hemolymph pH when exposed to acidified seawater (pH 7.3) for 8 d, thereby resulting in metabolic depression, protein degradation, reduced growth, and shell dissolution;[29] oyster *Pinctada fucata* reared at pH 7.6 produces more fragile shells with the nacreous layer showing signs of malformation and dissolution;[30] foraminifera *Marginopora vertebralis* as well as calcifying algae *Halimeda macroloba* and *Halimeda cylindracea* have reduced photosynthetic efficiency, chlorophyll content, and calcification at pH 7.7, indicating their vulnerability to ocean acidification;[31] polychaete *Hydroides elegans* produces softer shells of lower structural integrity at pH 7.4, which may be associated with the increased calcite to aragonite ratio and increased content of amorphous calcium carbonate in shells.[32]

Many marine organisms have a biphasic life cycle, alternating between larval and adult stages. Owing to the differences in size, morphology, physiology, mobility, and mode of life, larvae often differ from adults in terms of their response to ocean acidification. Understanding the response of calcifiers in both life stages is critical to evaluate their fitness and survival in the acidifying ocean. Despite the technical difficulty to obtain and rear larvae in the laboratory, studies on the early development of calcifiers under ocean acidification are not lacking. For instance, fertilization success, larval size, and larval development of sea urchins *Echinometra mathaei* and *Hemicentrotus pulcherrimus* generally decrease with increasing CO_2 concentrations, implying that their populations would sharply decline in the future;[33] reduced larval growth and impaired skeletal development are observed in brittlestar *Ophiothrix fragilis* with 100% mortality after 8 d exposure to slightly acidified seawater (ambient pH -0.2), suggesting a devastating impact of ocean acidification on the population of this keystone species;[34] larval size and larval survival are dramatically reduced in clam *Mercenaria mercenaria* and scallop *Argopecten irradians* with delayed metamorphosis at 650 ppm CO_2, indicating their extreme sensitivity to increased CO_2 concentrations;[35] oysters *Saccostrea glomerata* and *Crassostrea gigas* suffer from reduced fertilization success, retarded embryonic development, decreased larval size and increased abnormal larval development at 1000 µatm CO_2.[36] Given the evidence from many early studies, we generally realize the detrimental effects of ocean acidification on multifarious traits of calcifiers across life stages,[37,38] which would cause a decline in their populations and eventually ecosystem collapse in future oceans.

3. Controversy Arisen Due to Increased Observations of Non-Negative Effects

The pessimistic view that ocean acidification would jeopardize the survival of calcifiers in the near future appears to become a common belief among marine scientists as it is widely written in textbooks and disseminated in media.[39] However, this view seems to focus disproportionately on the studies showing negative effects, while those showing neutral or positive effects are rarely emphasized. Negative results (i.e., showing minimal or no effects) are also less likely to be published than positive results. These reasons would create a perception bias about the effects of ocean acidification on calcifiers. On the other hand, some early studies infer the ecological consequences of ocean acidification from the biological responses shown at extreme CO_2 levels.[29,33,40,41] Despite being not quite ecologically relevant, the implications made in these studies would generate a very negative perception of ocean acidification. When considering the plausible RCP6.0 scenario (≈700 ppm atmospheric CO_2), or even less plausible RCP8.5 scenario (≈1000 ppm atmospheric CO_2) by the year 2100, the impacts of ocean acidification on calcifiers may be less deleterious than initially thought. Furthermore, short-term experiments of only a few days to weeks using unrealistic methods, such as the addition of hydrochloric acid or manipulation of total alkalinity to lower seawater pH, are often conducted in early studies,[26,27,42] which tend to elicit stress responses of the tested organisms and thus create a negative perception of ocean acidification. Instead, these short-term experiments may better represent pulse acidification events that occur in coastal ecosystems.

In fact, growing evidence shows that calcifiers can maintain growth and calcification under near-future ocean acidification. For example, shell weight and shell diameter of foraminifera *Baculogypsina sphaerulata*, *Calcarina gaudichaudii* and *Amphisorus hemprichii* can be maintained or even boosted at 770 µatm CO_2 following 12 week exposure;[43] mussel *Mytilus edulis* reared at pH 7.7 for 7 weeks has normal somatic growth and shell growth without shell dissolution;[44] calcification of corals *Stylophora pistillata* and *Acropora muricata* is unaffected by ocean acidification at pH 7.8;[45] sea urchin *Echinometra* sp. has enhanced growth after 17 month exposure at natural volcanic CO_2 vents (pH 7.73), indicating its capacity to persist in the acidifying ocean.[46] Apart from growth and calcification, non-negative responses to near-future ocean acidification have been observed in various traits. For example, photosynthetic efficiency, symbiont density, and chlorophyll content of corals *Acropora digitifera*, *Montipora digitata*, and *Porites cylindrica* are unaffected by acidified seawater (1000 µatm CO_2) after 26 day exposure;[47] calcifying algae *Halimeda cuneata*, *Padina gymnospora*, and *Tricleocarpa cylindrica* cultured at pH 7.85 for 24 d can maintain carbonic anhydrase activity and photosynthetic efficiency;[48] sea urchin *Paracentrotus lividus* can maintain the mechanical strength of tests at pH 7.78 under both laboratory and field conditions;[49] gastropod *Austrocochlea concamerata* upregulates respiration rates at 940 ppm CO_2, whereas shell organic matter content, mechanical strength, crystallinity and body condition are maintained.[50] The above examples unequivocally show that some calcifiers are tolerant to acidified seawater, which not only implies their adaptability to near-future ocean acidification, but also draws concerns over experimental confirmation of prevailing negative effects.

The capacity of some calcifiers to sustain calcification under ocean acidification seems counter-intuitive and is contradictory to the early paradigm,[5,6] suggesting that seawater carbonate chemistry is not strongly associated with calcification. Indeed, calcification is a physiological process where calcifiers per se can create an optimal alkaline condition for precipitating $CaCO_3$ minerals at the calcification site. It is also important to note that CO_3^{2-} in seawater is not directly utilized, but HCO_3^- or metabolically-produced CO_2, by calcifiers for calcification,[51,52] implying that seawater Ω is not the key driver of calcification. This concept can help explain why some calcifiers can maintain or even enhance calcification under carbonate undersaturated conditions.[53] Given the increased observations of non-negative effects as well as rapid development of ocean acidification research in the last decade, time has come to reassess the effects of ocean acidification on calcifiers systematically, which can be achieved by conducting a meta-analysis that identifies the key traits, taxa and life stages that are sensitive or resistant to ocean acidification. By being open to non-negative effects, which conflicts the widely recognized paradigm of negative effects, this systematic review and meta-analysis can offer new directions for the advancement of knowledge and progress in ocean acidification research.

4. Meta-Analysis on the Effects of Ocean Acidification on Calcifiers

4.1. Data Collection and Selection Criteria for the Meta-Analysis

To gather the data from relevant studies assessing biological responses of calcifiers to ocean acidification, an exhaustive literature review was performed using the search engine Google Scholar, where keywords "carbon dioxide," "marine organism," "calcification" and "ocean acidification" were input for each search per year from 1998 to 2020 using custom range function. A total of 1000 search results, sorted by relevance, were obtained per year (i.e., a total of 23 000 search results for 23 years). A two-step screening process for all search results was performed to include relevant studies for the meta-analysis (Figure S1, Supporting Information for the PRISMA flow diagram). First, we only considered peer-reviewed journal articles and excluded those without reporting biological responses of calcifiers to ocean acidification after reading the abstract. Then, we checked the details of all the studies passing the first screening step and excluded those studies if they fail to meet the selection criteria for the meta-analysis, which are described as follows. Studies were excluded if variance (e.g., standard deviation, standard error, and 95% confidence interval) was not reported in the main text or Supporting Information, or could not be obtained through calculation. Since not all marine algae are able to produce $CaCO_3$ minerals, we only included calcifying algae for the meta-analysis by checking the biology of species in the literature when necessary. Some crustaceans, such as krill and copepods, do not produce $CaCO_3$ as the structural material; therefore, we only included those crustaceans which can produce heavily calcified structures (e.g., shrimps, crabs, and lobsters). Field studies were included for the meta-analysis if the seawater conditions were mainly influenced by CO_2 concentrations, whereas other environmental variables (e.g., salinity, temperature, and dissolved oxygen concentrations) were comparable to the ambient levels. As for laboratory studies, we included those using either CO_2 aeration or acid–base addition method to manipulate seawater pH.[54] For those studies employing a factorial design with variables in addition to pH or CO_2 concentration (e.g., salinity, temperature, light intensity, dissolved oxygen concentration, food availability, and nutrient concentration), we only included the treatments with these variables maintained at the ambient level so that the selected data are only subject to pH or CO_2 concentration. When the ambient food/nutrient concentration was not reported, we chose the fed/high nutrient treatment as the experimental organisms can be stressed by starvation or malnutrition that confounds interpretation. For those laboratory studies exploring the effects of ocean acidification on multiple species and their interactions (e.g., predator–prey interaction, intra- and interspecific competition), we excluded the treatments influenced by species interactions. Some studies examined biological responses to ocean acidification using the same species collected from different locations or populations. The data from each location or population were included in the meta-analysis because they are independent. For those laboratory studies with time-series measurements, we collected the data from the last time point unless severe mortality was observed (either control or acidified treatment) that can cause large errors for comparisons. In this case, we chose the time point that is the closest to the nominal end point without severe mortality for both control or acidified treatments. A few studies investigated the effect of pH fluctuations on biological responses. We only selected the data from the treatments with static pH level. We included studies on carry-over effect and transgenerational effect, but only the data from treatments with seawater conditions maintained across life stages or generations were chosen. While data extraction was done by the first author, all authors were involved in the initial step of this process by extracting data from the same papers (n = 20) and cross-checking the results. This step can ensure that the same protocol was used to minimize extractor bias.

In the meta-analysis, we compared the biological responses of calcifiers caused by pH reduction, which allows best standardized comparisons among studies,[37] despite the inevitable differences in total alkalinity and pCO_2 (Supporting Information). Besides, pH is a sensible indicator of the impact of ocean acidification on calcifiers because pH (a measure of H^+ concentration) rather than pCO_2 can directly affect the acid–base balance of calcifiers for calcification. Four categories of seawater acidity with a pH range were used: current (pH 8.2– 7.91), near-future (pH 7.90– 7.61), far-future (pH 7.60–7.21) and extreme (pH ≤ 7.20). These pH ranges were commonly used in the literature to represent the respective category, where the near-future and far-future levels are based on the prediction models.[1] Coastal acidification can particularly be represented by the far-future and extreme levels. In each study, we also checked the difference in seawater pH between control (i.e., ambient pH level) and acidified treatments to ensure correct categorization. The ambient pH level was designated by authors, but we excluded those studies using abnormally low pH (or high CO_2 level) for the control, which possibly results from the impact of upwelling in field sites or acid sulfate soils in coastal areas. To ensure more accurate comparisons of biological responses, we did not mix plausibly related variables to create response categories because the direction of change among these variables is not always the same. For example, we did not create a category "photosynthesis" by pooling the data of photosynthetic rate and photosynthetic efficiency for the meta-analysis. Instead, we reported these responses separately. Similarly, "growth" was classified into two types based on 1) change in body size and 2) change in body weight because they do not necessarily show the same direction of change. Concerning the change in body size, we chose the variable with the largest number of dimensions (i.e., volume > area > length) as possible to better reflect growth in body size. Only one of these growth variables was included for the meta-analysis to avoid pseudo-replication (e.g., length data excluded when area data included). Change in shell or skeletal size may not perfectly indicate calcification as mineral density or porosity should be taken into account; therefore, we defined calcification based on the weight change in $CaCO_3$ minerals. We did not include mortality (or survival) of juveniles/adults in the meta-analysis because it depends strongly on experimental duration and is difficult to standardize this duration with the life span of organisms among studies. Yet, larval mortality was included and converted to survival given by: 1—mortality.

4.2. Data Analysis

To estimate the effect of ocean acidification on the biological responses of calcifiers, we calculated Hedges' *g*, which is the bias-corrected standardized mean difference between the control (i.e., ambient pH level) and treatment (i.e., reduced pH level). Hedges' *g* is widely used as a measure of effect size in academic research and calculated using the following formula:[55]

$$g = \frac{\overline{x_t} - \overline{x_c}}{\sqrt{\frac{(n_t - 1)s_t^2 + (n_c - 1)s_c^2}{n_t + n_c - 2}}} \times J \quad (3)$$

where $\overline{x}_t$ and $\overline{x}_c$ are the mean in treatment and control, respectively; n is the sample size; s is the standard deviation; J is a correction factor for the bias due to small sample size and is given by:

$$J = 1 - \frac{3}{4(n_t + n_c - 2) - 1} \quad (4)$$

To account for the inequality in study variance, effect sizes were weighted by the inverse of the sampling variance, where the variance for each effect size (V_g) is calculated using the following formula:[56]

$$V_g = \frac{n_t + n_c}{n_t n_c} + \frac{g^2}{2(n_t + n_c)} \quad (5)$$

Meta-analysis was conducted to estimate the effects of ocean acidification on the commonly measured biological responses of calcifiers using software JASP 0.15 (University of Amsterdam, Netherlands), which is based on the metafor package for R. Since experimental design and species vary across studies, random-effect model was used to enable heterogeneity of true effect sizes among the studies.[57] The pooled effect sizes with the associated 95% confidence intervals were shown in a forest plot for each biological response. Effect sizes are generally interpreted as follows: $|g| < 0.2$ (small); $0.2 \leq |g| < 0.5$ (medium); $0.5 \leq |g| < 0.8$ (large); $|g| \geq 0.8$ (very large).[56] Effect sizes are significant when their 95% confidence intervals did not overlap with zero.

Publication bias, caused by selective publication of articles reporting significant effects over those reporting nonsignificant effects, may distort meta-analysis results.[56] To identify potential publication bias, funnel plots were used to visualize the outliers among studies and Egger's regression test was applied to evaluate funnel plot asymmetry. While it is suggested to remove the outliers causing funnel plot asymmetry, careful judgment was made because the heterogeneity among studies can be true, especially considering the differences in physiology among species. Thus, funnel plot asymmetry does not necessarily indicate publication bias and inappropriate use of funnel plots can even worsen the meta-analysis results.[58] After considering the outliers shown in funnel plots and checking the quality control of the associated studies, we only removed those outliers that can substantially drive funnel plot asymmetry (typically $|g| \geq 7$ due to large treatment effect, but unusually small standard deviations within each group).

4.3. Results

Our meta-analysis comprises 985 studies with a total of 5153 observations (68 outliers excluded) from various calcifiers in different life stages, where bivalves, corals, sea urchins, gastropods, and calcifying algae are the five most studied taxa (Supporting Information). According to mobility and mode of life, calcifiers are classified into five groups, including 1) planktonic calcifiers, 2) sessile photosynthetic calcifiers, 3) sessile filter-feeding calcifiers, 4) benthic calcifiers of low mobility, and 5) highly mobile calcifiers.

4.3.1. Planktonic Calcifiers

Coccolithophores are the most studied planktonic calcifiers. Their growth, PIC (i.e., an indicator of $CaCO_3$ production) and coccolith size are reduced by near-future ocean acidification (pH 7.90–7.61), but cell density, photosynthetic rate, POC, and PON are promoted (**Figure 1**a). The reduction in growth and PIC is slightly intensified by far-future ocean acidification (pH 7.60–7.21). Regarding foraminifera, only $CaCO_3$ production is impaired by ocean acidification, whereas other variables (e.g., growth, respiration rate, and photosynthetic rate) remain unchanged (Figure 1b). Pteropods appear to be susceptible to ocean acidification in view of the reduced growth in size and calcification (Figure 1c). However, the reduction in calcification is insignificant due to the large variation among the few numbers of observations.

4.3.2. Sessile Photosynthetic Calcifiers

Sponges are rarely studied in ocean acidification research. Based on the few numbers of observations, sponges are found to be generally insensitive to ocean acidification, except that their spicules can be eroded by acidified seawater at a higher rate (**Figure 2**a). Calcifying algae appear to be vulnerable to ocean acidification in view of the decrease in growth, calcifying fluid pH, $CaCO_3$ production, skeletal Ca^{2+} content, and chlorophyll a content (Figure 2b). Ocean acidification at the far-future level further reduces $CaCO_3$ production, and lowers respiration rate and photosynthetic efficiency in terms of Fv/Fm. Carbonic anhydrase activity, nitrogen content, and C/N ratio remain unchanged under ocean acidification.

Corals are intensively studied in ocean acidification research, but studies on their early life stages are scant. Based on the few numbers of observations, only larval settlement and survival rate are reduced by ocean acidification, whereas other variables (e.g., fertilization rate, developmental success, larval growth, respiration rate, and symbiont density) remain unaltered (Figure 2c). Adult corals are sensitive to ocean acidification as many variables, including growth, calcifying fluid pH, $CaCO_3$ production, skeletal density, and symbiont density, are negatively affected especially at the far-future level of acidification

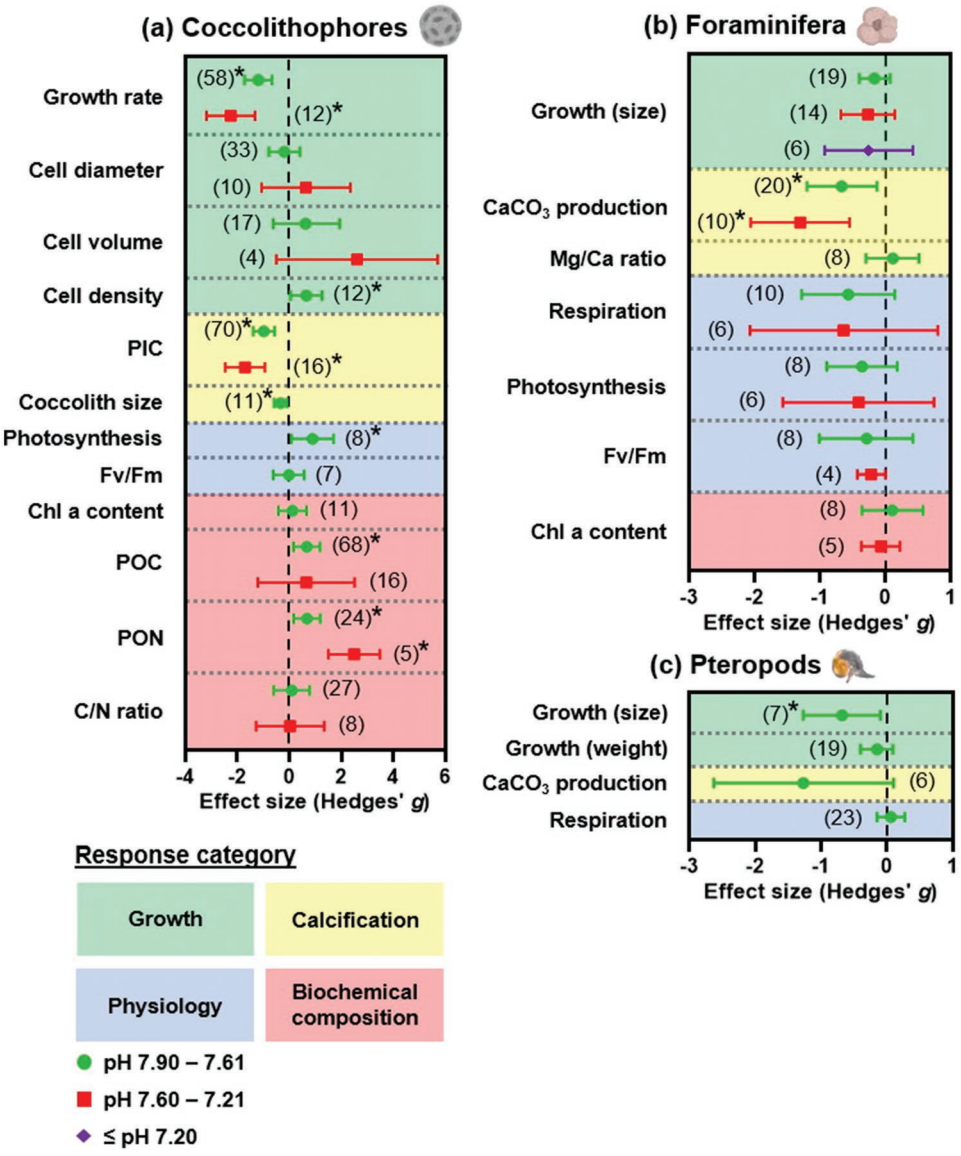

Figure 1. Effects of ocean acidification on different biological traits of a) coccolithophores, b) foraminifera, and c) pteropods, indicated by Hedges' *g* (mean ± 95% confidence interval). The number of observations for each trait is shown in parentheses. The vertical dashed line at zero indicates no effect. Significant difference is indicated by an asterisk when the 95% confidence interval does not overlap the vertical dashed line. PIC: particulate inorganic carbon; POC: particulate organic carbon; PON: particulate organic nitrogen; Chl a: chlorophyll a; Fv/Fm: maximum quantum efficiency of photosystem II.

(Figure 2d). Yet, several physiological variables (e.g., respiration and photosynthesis) and chlorophyll a content are generally unaffected by ocean acidification.

4.3.3. Sessile Filter-Feeding Calcifiers

Bryozoans are seldom used as the study organism for ocean acidification research. Based on the currently available observations in the literature, bryozoans are found to be tolerant to ocean acidification (**Figure 3**a). Barnacles are also resistant to ocean acidification since no variable is negatively affected (Figure 3b). Instead, $CaCO_3$ production is boosted by ocean acidification at the far-future level.

Bivalves (e.g., oysters, mussels, clams and scallops; brachiopods included given the similar biological features as bivalves) are the most studied group of calcifiers in ocean acidification research. Bivalve embryos/larvae are susceptible to pH reduction because many variables, such as fertilization success, hatching rate, larval development rate, growth, metamorphosis and survival, are reduced even by near-future ocean acidification (Figure 3c). Their vulnerability generally increases with the degree of acidification. In contrast, juvenile/adult bivalves are quite tolerant to near-future ocean acidification as many

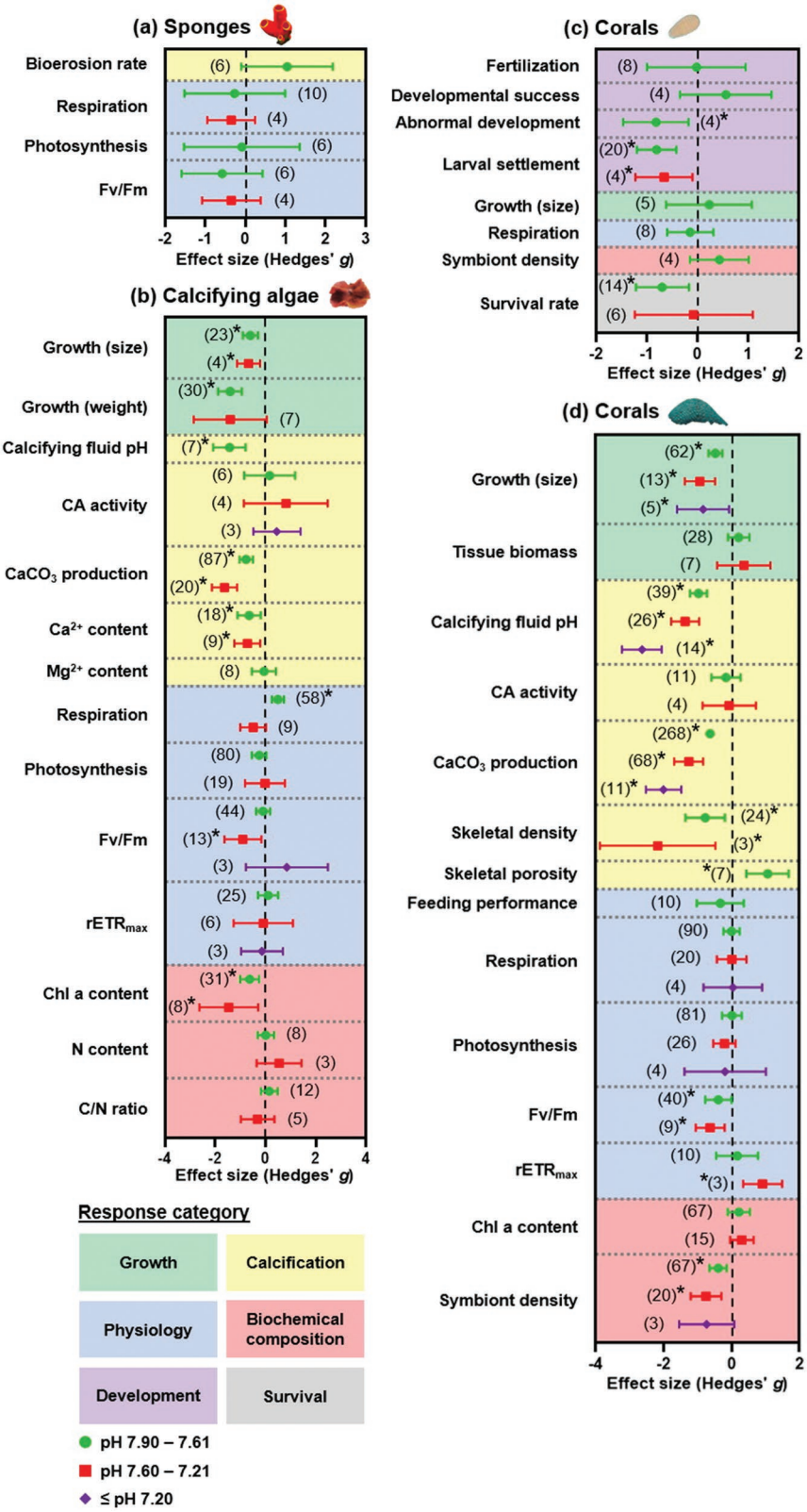

Figure 2. Effects of ocean acidification on different biological traits of a) sponges, b) algae, c) coral embryos/larvae, and d) juvenile/adult corals, indicated by Hedges' *g* (mean ± 95% confidence interval). The number of observations for each trait is shown in parentheses. The vertical dashed line at zero indicates no effect. Significant difference is indicated by an asterisk when the 95% confidence interval does not overlap the vertical dashed line. Fv/Fm: maximum quantum efficiency of photosystem II; CA activity: carbonic anhydrase activity; $rETR_{max}$: maximum relative electron transport rate; Chl a: chlorophyll a.

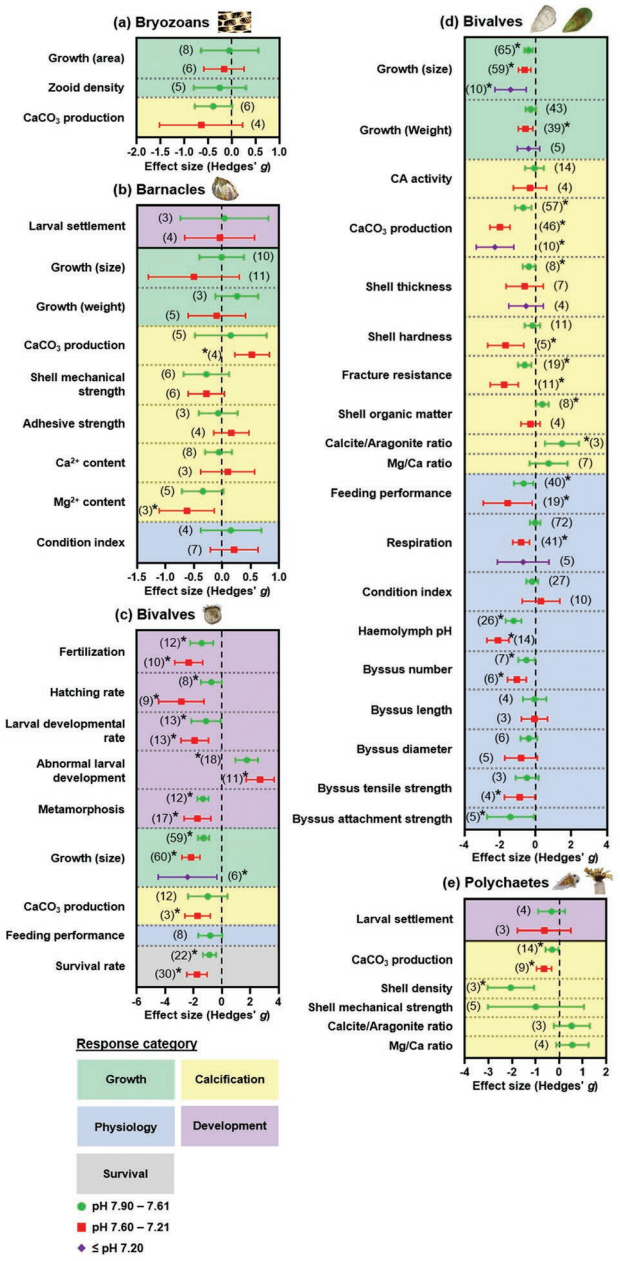

Figure 3. Effects of ocean acidification on different biological traits of a) bryozoans, b) barnacles, c) bivalve embryos/larvae, d) juvenile/adult bivalves, and e) polychaetes, indicated by Hedges' *g* (mean ± 95% confidence interval). The number of observations for each trait is shown in parentheses. The vertical dashed line at zero indicates no effect. Significant difference is indicated by an asterisk when the 95% confidence interval does not overlap the vertical dashed line. CA activity: carbonic anhydrase activity.

variables remain unaffected, such as respiration, condition index and byssus parameters (Figure 3d). Yet, slight reduction is observed in growth, $CaCO_3$ production, feeding performance, and fracture resistance of shells. Ocean acidification at the far-future level can usually exacerbate these adverse effects. Shell organic matter and calcite to aragonite ratio are slightly elevated by near-future acidification.

Polychaetes are rarely studied in ocean acidification research and thus the number of observations is rather low. $CaCO_3$ production and shell density of polychaetes are reduced by ocean acidification (Figure 3e).

4.3.4. Benthic Calcifiers of Low Mobility

Gastropod embryos/larvae are sensitive to near-future ocean acidification, indicated by the decreased hatching rate, larval developmental rate, growth, metamorphosis success, feeding performance and survival, as well as increased hatching time and abnormal larval development (**Figure 4**a). These negative effects are often aggravated by the far-future level of acidification. In contrast, juvenile/adult gastropods are more tolerant to near-future ocean acidification, despite the mild reduction in growth and $CaCO_3$ production (Figure 4b). Ocean acidification at the far-future level can undermine growth, $CaCO_3$ production and shell thickness. Shell organic matter, calcite to aragonite ratio and Mg/Ca ratio tend to be elevated by ocean acidification.

Echinoderms (typically sea stars, brittle stars, and sea cucumbers included in this meta-analysis) are generally tolerant to near-future ocean acidification as only growth in weight and coelomic fluid pH are slightly reduced (Figure 4c). However, ocean acidification at the far-future level can pose obvious negative effects on fertilization success, larval growth, and coelomic fluid pH. Sea urchins are separated from the group "Echinoderms" not only because they are more frequently used than other echinoderms for ocean acidification research, but also because they have to build solid calcareous structures to cover their whole body, which differs from other echinoderms. Sea urchin embryos/larvae are vulnerable to near-future ocean acidification that poses adverse effects on many variables, such as fertilization success, larval developmental rate, growth, $CaCO_3$ production, and survival (Figure 4d). Increased abnormal embryonic and larval development due to increased arm asymmetry are also observed. All these negative effects are usually intensified by a higher degree of acidification. In contrast, juvenile/adult sea urchins are more resistant to ocean acidification as only few variables are negatively affected, such as growth in weight, test thickness, spine mechanical strength, and feeding performance (Figure 4e).

4.3.5. Highly Mobile Calcifiers

Crustaceans (e.g., amphipods, shrimps, crabs, and lobsters) are very tolerant to near-future ocean acidification in both life stages since no variable is adversely affected (**Figure 5**a,b). However, crustacean larvae have reduced hatching rate, growth, and shell Ca^{2+} content at the far-future level of acidification. Similarly, juvenile/adult crustaceans are only impacted by far-future ocean acidification in few variables, including growth in size, shell Ca^{2+} and Mg^{2+} contents (Figure 5b). Interestingly, $CaCO_3$ production is facilitated by ocean acidification. Cephalopods are rarely examined in ocean acidification research. Based on the limited number of observations, cephalopods appear to be very resistant to near-future level of acidification

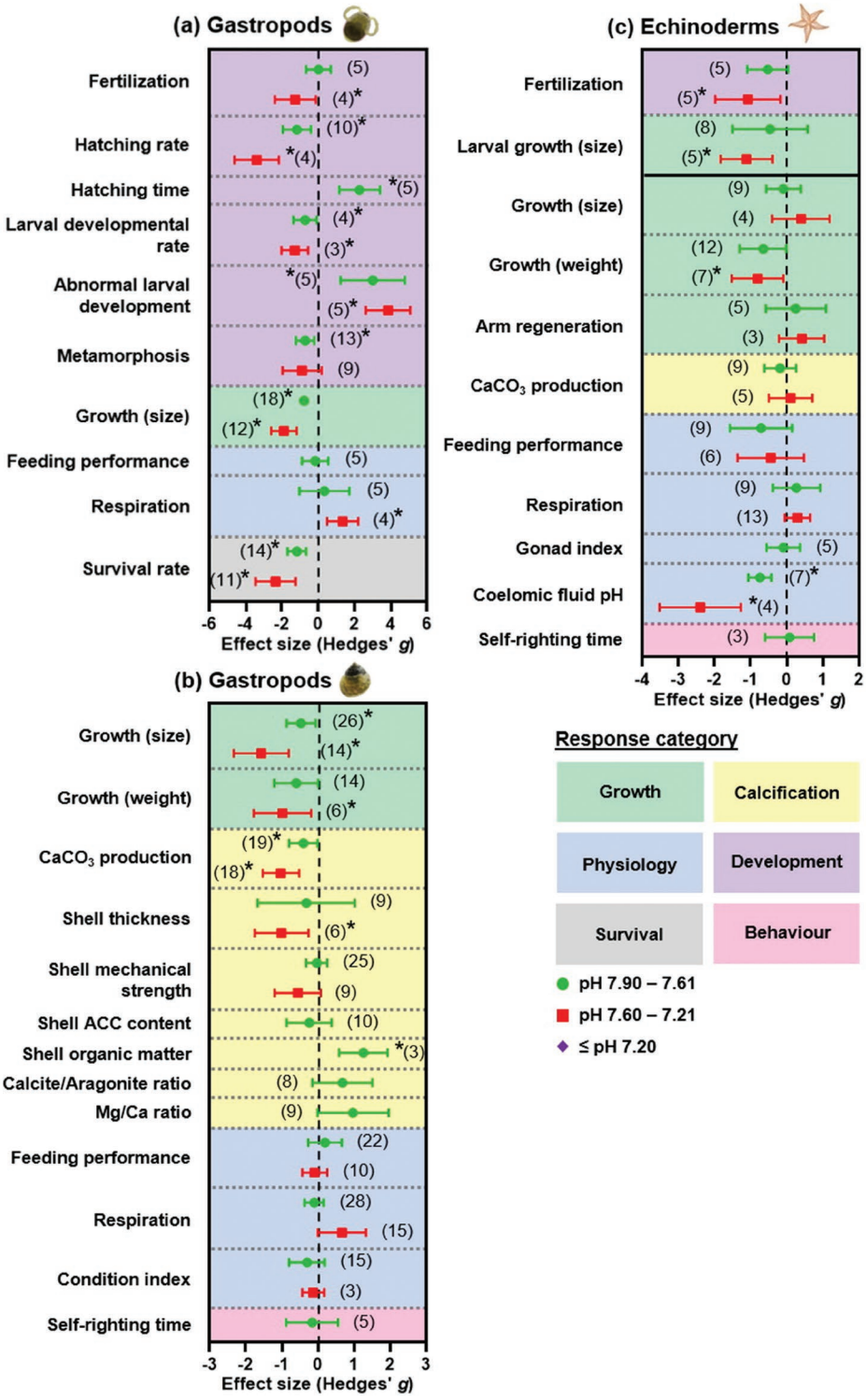

Figure 4. Effects of ocean acidification on different biological traits of (a) gastropod embryos/larvae, (b) juvenile/adult gastropods, (c) echinoderms, (d) sea urchin gastropod embryos/larvae and (e) juvenile/adult sea urchin, indicated by Hedges' g (mean ± 95% confidence interval). The number of observations for each trait is shown in parentheses. The vertical dashed line at zero indicates no effect. Significant difference is indicated by an asterisk when the 95% confidence interval does not overlap the vertical dashed line. ACC: amorphous calcium carbonate.

as no variable is seriously impacted (Figure 5c). Under far-future ocean acidification, however, negative effects are observed in embryonic growth, perivitelline fluid pH, juvenile growth, and respiration rate. Same as crustaceans, $CaCO_3$ production in juvenile cephalopods is enhanced by ocean acidification.

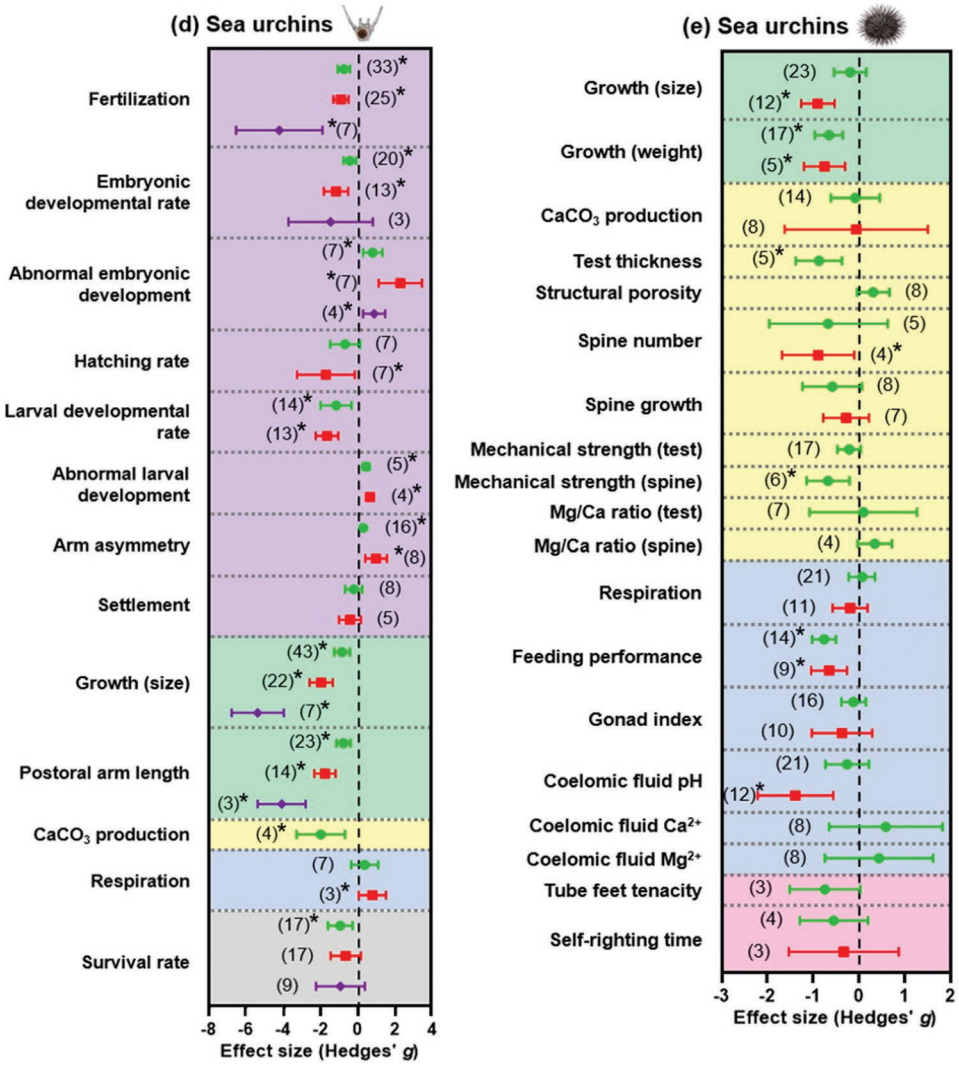

Figure 4. Continued.

4.4. Effects of Near-Future Ocean Acidification on Growth and Calcification

For calcifiers, growth and calcification are regarded as the two key variables impacted by ocean acidification. However, this notion is partially influenced by the results of previous studies using extreme pH levels, which would have overestimated the negative effects of ocean acidification. As such, we gathered the data from studies that evaluate the effects of near-future level of acidification (pH 7.90–7.61) on calcification, juvenile/adult growth, and larval growth in various taxa of calcifiers. In each study, *t*-test was used to compare these responses between the control and acidified treatment (i.e., ambient pH vs near-future pH) at a significance level of $p \leq 0.05$. Considering the observations across all taxa, only 29.6% of calcifiers respond negatively to ocean acidification in calcification, while 66.4% of them have a neutral response (**Figure 6**a). Negative responses are not frequently observed in many taxa (<20%), including bryozoans, barnacles, polychaetes, echinoderms, sea urchins, crustaceans, and cephalopods. Similar observations as calcification are found in juvenile/adult growth, where 26.1% and 67.4% of calcifiers across all taxa show a negative response and neutral response, respectively (Figure 6b). Many taxa have a high percentage of non-negative responses (>70%), particularly for barnacles, crustaceans, sea urchins, echinoderms, and bryozoans. Despite the high susceptibility of larvae to ocean acidification shown in the meta-analysis, only 39.9% of them respond negatively in growth, while 57.3% exhibit a neutral response (Figure 6c). Coral and echinoderm larvae are more resistant to ocean acidification that only 20% and 25% of them show a negative response, respectively.

5. Mechanisms Allowing Calcifiers to Resist Ocean Acidification

By reanalyzing the data in the literature, we found that both growth and calcification of many calcifiers are unaffected by near-future ocean acidification. Understanding the compensatory mechanisms enabling calcifiers to counter ocean

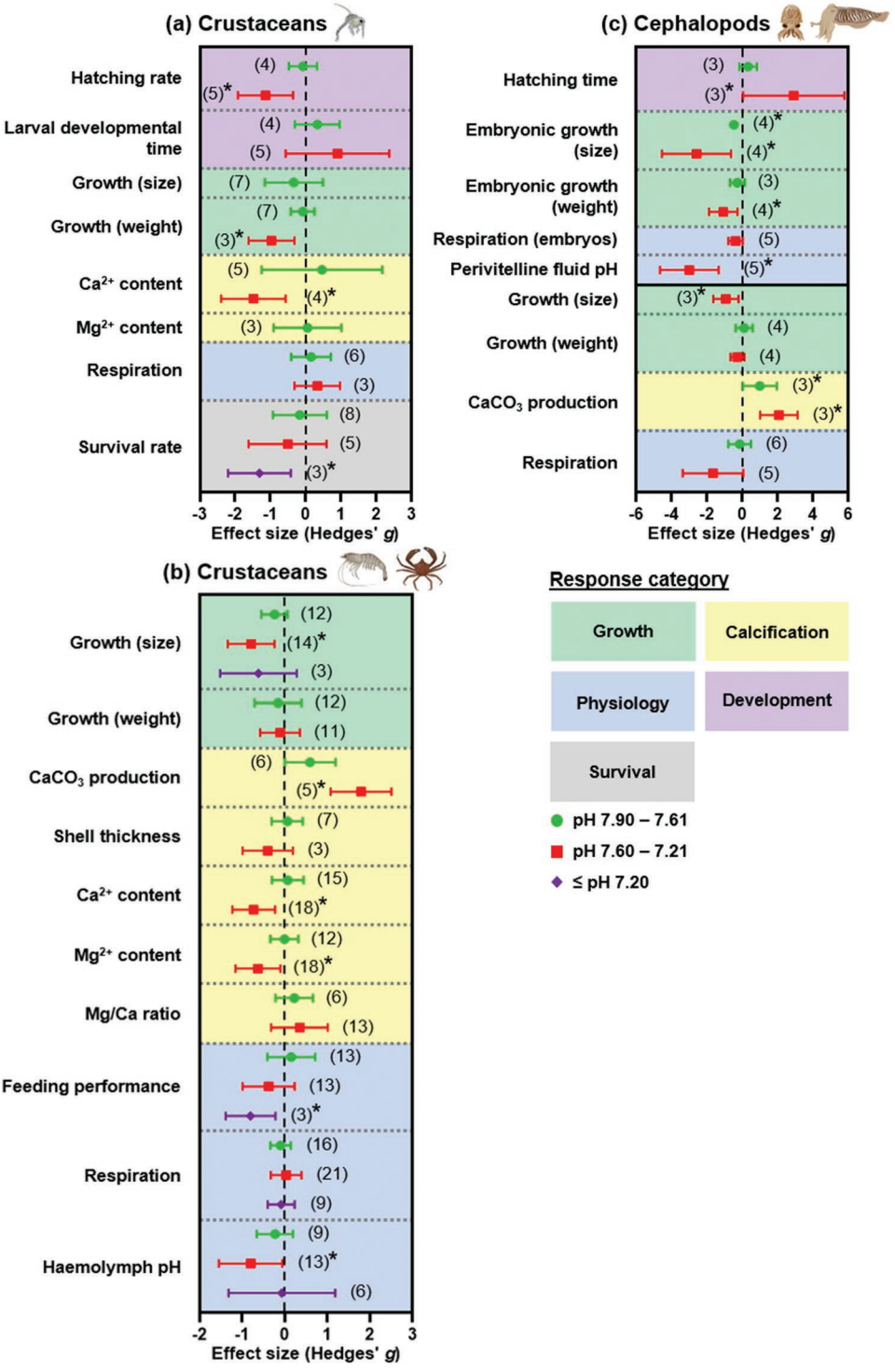

Figure 5. Effects of ocean acidification on different biological traits of a) crustacean embryos/larvae, b) juvenile/adult crustaceans, and c) cephalopods, indicated by Hedges' *g* (mean ± 95% confidence interval). The number of observations for each trait is shown in parentheses. The vertical dashed line at zero indicates no effect. Significant difference is indicated by an asterisk when the 95% confidence interval does not overlap the vertical dashed line.

acidification is critical to shed light on their fate in future marine ecosystems. In recent years, several compensatory mechanisms have been proposed to explain why calcifiers can be more resistant to ocean acidification than initially thought.

5.1. Compensatory Feeding by Calcifiers

It is important to recognize that calcification is a physiological process, where specific proteins and ion transporters are

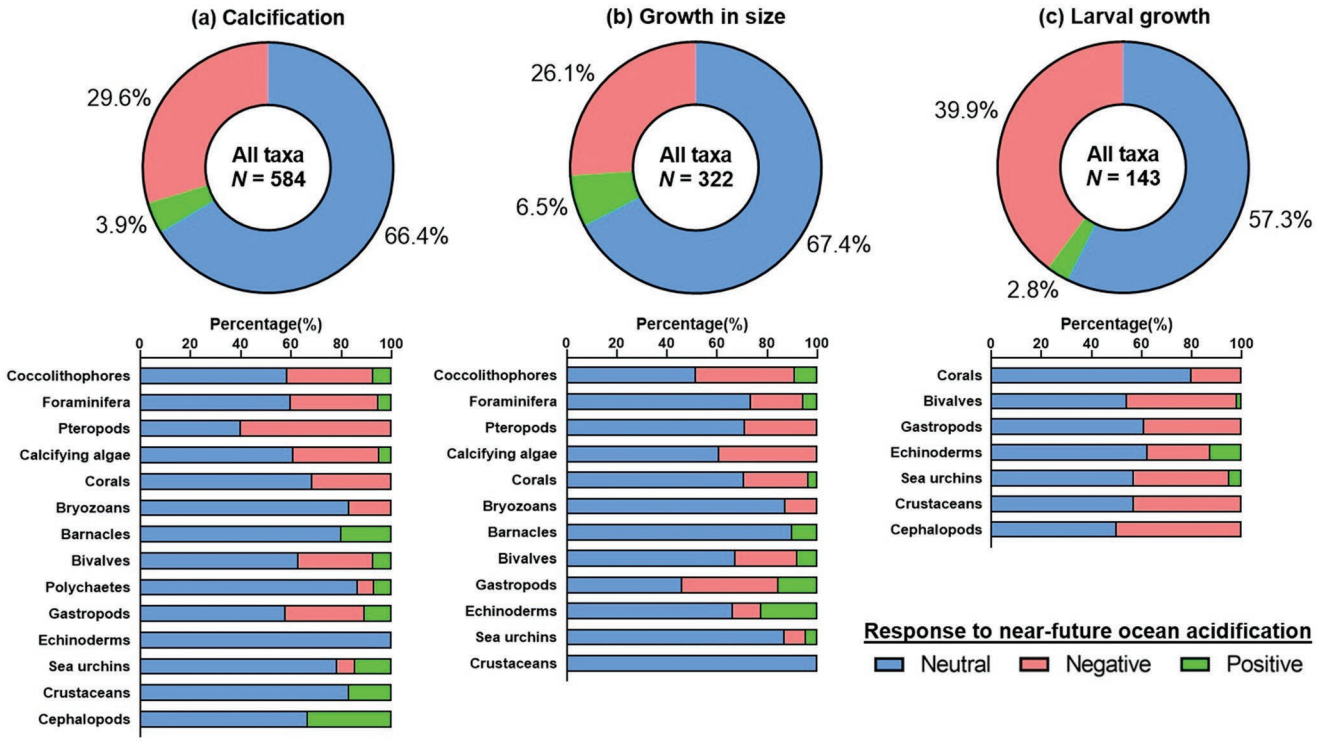

Figure 6. Effects of near-future ocean acidification on a) calcification, b) juvenile/adult growth in size, and c) larval growth of various taxa of calcifiers, indicated by the percentage of positive, negative, and neutral responses (c.f. ambient pH). *N*: number of observations.

involved.[59] Therefore, energy is required to fuel calcification, especially for the synthesis of organic matrix to precipitate $CaCO_3$ minerals and maintain shell integrity.[60] Given the changes in seawater carbonate chemistry, it is estimated that the energy cost of calcification is raised by ≈10% under ocean acidification, which may retard the precipitation of $CaCO_3$ minerals.[61] Indeed, energy availability is strongly linked to both quality and quantity of calcareous structures produced. For example, gastropod *Austrocochlea concamerata* has faster shell growth and produces more durable shells when energy budget is boosted.[50] Based on this concept, calcifiers could maintain or even enhance calcification under ocean acidification when they increase their food intake. Such compensatory feeding has been reported in some calcifiers, such as coral *Acropora cervicornis* which increases feeding rates under ocean acidification (800 ppm CO_2), resulting in elevated lipid content and sustained growth rates after 8 weeks.[62] Scallop *Argopecten purpuratus* increases ingestion rates at pH 7.60, resulting in enhanced growth and calcification.[63] Similarly, gastropod *Phasianella australis* consumes turf algae at a higher rate under ocean acidification (1000 ppm CO_2) so that growth can be maintained.[64] The importance of energy availability to calcification can be further manifested by the reduction in shell growth under energy-limiting conditions (e.g., starvation and hypoxia[65–67]), where seawater carbonate chemistry is not perturbated by elevated CO_2 concentrations. Since energy budget is primarily determined by nutrient or food intake, the slightly increased energy cost of calcification under ocean acidification can be offset when calcifiers raise their feeding rates so that calcification can be maintained or even enhanced (**Table 1**).

5.2. Regulation of pH and Ionic Composition in the Extracellular Calcifying Fluid

At the cellular level, precipitation of $CaCO_3$ minerals occurs at the calcifying tissue–mineral interface, where calcifying fluid pH is adjusted to a slightly alkaline level with the aid of ion transporters and exchangers to favor calcification.[68] When $CaCO_3$ is precipitated, the H^+ released needs to be constantly removed from the calcifying fluid by ion transporters or exchangers (e.g., Ca^{2+} ATPase[69,70] and V-type H^+ ATPase[52]). Efflux of H^+ can also be mediated via H^+ channels on the plasma membrane, such as voltage-gated H^+ channels.[71] $CaCO_3$ precipitation would be hampered by H^+ accumulation in the calcifying fluid, which can be worsened by ocean acidification.[72] Nevertheless, many calcifiers can actively regulate acid–base balance of their calcifying fluid, which can be achieved by H^+ extrusion or HCO_3^- accumulation via ion transporters or exchangers so that acidosis induced by ocean acidification can be fully or partially compensated.[73] For instance, corals *Porites compressa* and *Montipora capitata* can upregulate calcifying fluid pH under ocean acidification (pH 7.71) to sustain calcification.[74] Similar observations are found in massive *Porites* corals colonized at a CO_2 seep site (pH 7.9), which can maintain normal calcifying fluid pH.[75] Bivalve *Mytilus edulis* reared at pH 7.7 has an increased Na/Ca ratio in shells, implying its ability to sustain an optimal pH condition for calcification via Na^+/H^+ exchanger.[76] Indeed, acid–base regulation to buffer the impacts of acidified seawater has been demonstrated in various calcifiers,[77] even at the larval stage.[78,79] Maintaining acid–base homeostasis is also conducive to mitigating the potential

Table 1. Compensatory mechanisms to ocean acidification by adjusting physiological performance and regulating acid-base balance of body fluids.

Taxon	Species (life stage)	pH/pCO_2 level	Exposure duration	Compensatory mechanism	Beneficial effect	Refs.
Sea urchin	*Strongylocentrotus droebachiensis* (juveniles)	pH 7.66	45 d	Enhancing protein metabolism to support ion homeostasis and accumulating bicarbonate to offset extracellular pH changes	~ Somatic growth ~ Calcification ~ Reproductive growth ~ Feeding rate ~ Metabolism	[78]
Crab	*Petrolisthes cinctipes* (larvae and juveniles)	pH 7.58	6 d (larvae); 33 d (juveniles)	Enhancing acid–base regulatory mechanism to compensate for extracellular pH changes	~ Larval growth ~ Juvenile growth	[218]
Gastropod	*Cyclope neritea*; *Nassarius corniculus* (juveniles/adults)	pH 7.2	N/A (from the field)	Reducing body size (Lilliput effect)	↑ Mass-specific energy consumption ↓ Metabolic energy demand ~ Calcification	[114]
Coral	*Porites cylindrica* (adults)	pH 8.24–7.74	6 months	Upregulating calcifying fluid pH	~ Skeletal extension rate ~ Skeletal density	[219]
Coral	*Acropora cervicornis* (adults)	800 ppm	8 weeks	Increasing feeding rates	↑ Lipid content ~ Growth rate	[62]
Coral	*Lophelia pertusa* (juveniles)	982 µatm	6 months	Upregulating calcifying fluid pH	~ Wall thickness ~ Skeletal arrangement	[220]
Mussel	*Mytilus edulis* (larvae)	pH 7.85	48 d	Shifting energy budget to calcification	~ Larval growth ~ Larval development ~ Larval survival	[221]
Coral	*Pocillopora damicornis* (adults)	pH 7.63	8 weeks	Increasing dissolved inorganic carbon concentration in the calcifying fluid	~ Calcification	[70]
Mussel	*Mytilus edulis* (larvae)	1250 µatm	40 h	Increasing pH and carbonate saturation of the calcifying fluid	~ Calcification	[79]
Coral	*Montipora capitata*; *Porites compressa* (adults)	pH 7.71	14 weeks	Upregulating calcifying fluid pH	~ Calcification	[74]
Coral	*Pocillopora damicornis* (adults)	pH 7.63	8 weeks	Increasing calcium ion concentration in the calcifying fluid	~ Calcification	[80]
Coccolithophore	*Ochrosphaera neapolitana*	750 ppm	2 weeks (10–15 generations)	Maintaining constant pH at the calcification site and utilizing carbon from a single internal dissolved inorganic carbon pool for both calcification and photosynthesis	~ Calcification ~ Photosynthesis	[222]
Brachiopod	*Magellania venosa* (adults)	pH 7.35	>2 years	Regulating calcifying fluid pH between the epithelial mantle and the shell	~ Shell growth	[223]
Sea urchin	*Paracentrotus lividus* (adults)	pH 7.8	N/A (from the field)	Increasing total antioxidant capacity, phagosome proteins and enzymatic activity of ammonium metabolism, and amino-acid degradation in immune cells	~ Coelomic fluid pH ~ Immune cell composition ~ Metabolic rate ~ Nitrogen excretion ~ Skeletal mineralogy	[224]
Sea urchin	*Paracentrotus lividus* (adults)	pH 7.63	N/A (from the field)	Regulating acid-base of extracellular fluid and maintaining expression of biomineralization genes	~ Shell integrity ~ Shell strength	[14]
Calcifying alga	*Lithothamnion proliferum*; *Melyvonnea madagascariensis*	1160 ppm	24 d	Maintaining the capacity of carbon concentrating mechanism	~ Growth ~ Photochemical efficiency	[225]
Coral	*Pocillopora damicornis*; *Stylophora pistillata* (adults)	2800 ppm	30 d	Increasing calcifying fluid pH	↑ Calcification	[226]

impacts of acidosis on physiological performance, especially metabolism so that the fitness of calcifiers can be sustained (Table 1).

Apart from CO_3^{2-}, calcium ion (Ca^{2+}) is another major ingredient of $CaCO_3$ minerals and therefore calcifiers may increase their internal Ca^{2+} to boost calcification. The importance of

Ca^{2+} to calcification is often overlooked because the prevailing paradigm does not consider Ca^{2+}, but CO_3^{2-} as the limiting factor for calcification under ocean acidification. Given that most calcifiers utilize HCO_3^- rather than CO_3^{2-} as the substrate for $CaCO_3$ precipitation,[51] Ca^{2+} would more likely be the limiting factor for calcification due to plenty of HCO_3^- in seawater. Indeed, a recent study found that coral *Pocillopora damicornis* can elevate Ca^{2+} in the calcifying fluid (≈25% above seawater) to maintain calcification under near-future ocean acidification, whereas coral *Acropora youngei* that exhibits less control over Ca^{2+} suffers from a decline in calcification.[80] It is noteworthy that energy is required to activate ion transporters and exchangers for acid-base and ionic regulation,[73] which further substantiates the critical role of energy in calcification.

5.3. Mineralogical Adjustments

In addition to retarded calcification, dissolution of $CaCO_3$ minerals is another major concern raised by ocean acidification because increased H^+ in seawater can lead to corrosion on calcareous structures, which has been observed in some calcifiers.[9,81,82] To reduce dissolution of $CaCO_3$ minerals, changing carbonate polymorphs is a possible way, which can particularly be achieved by bimineralic calcifiers that are able to produce both calcite and aragonite—the predominant carbonate polymorphs. Since calcite is generally less soluble than aragonite, bimineralic calcifiers may precipitate more calcite than aragonite (i.e., higher calcite to aragonite ratio) under ocean acidification to reduce the solubility of calcareous structures. Some bimineralic calcifiers indeed exhibit this kind of mineralogical adjustment even after short-term exposure to ocean acidification. For instance, gastropod *Austrocochlea constricta* has an increased calcite to aragonite ratio in shells following 10 week exposure at pH 7.85, which not only helps reduce shell solubility, but also facilitates shell growth.[83] A similar observation is found in the shell of limpet *Patella rustica* collected from a natural CO_2 seep site at pH 7.73.[84] Enhanced precipitation of calcite over aragonite is also exhibited in calcifying polychaetes following short-term exposure to acidified seawater,[32,85] indicating their rapid acclimation capacity. The adaptive value of changing carbonate polymorphs is recognized on the geological time scale, when the physicochemical conditions of seawater shifted between "aragonite sea" and "calcite sea" due to the changes in temperature and CO_2 concentrations.[86,87] If the carbonate polymorph of calcifiers mismatches the physicochemical conditions of seawater (e.g., producing aragonite in the "calcite sea"), severe mortality may ensue.[87] Given the short life cycle of most calcifiers relative to the rate of ocean acidification, calcifiers would have sufficient time to adaptively change the carbonate polymorph of their shells or skeletons so that the "corrosive" effect of acidified seawater can be minimized (**Table 2**).

Apart from calcite and aragonite, some coralline algae can produce a certain amount of dolomite, which can greatly reduce skeletal porosity and solubility through dolomite infilling in $CaCO_3$ minerals.[88] Although the mechanism driving intracellular dolomite formation is unclear, it is evident that this process is unlikely impacted by ocean acidification.[89] For instance, a twofold increase in dolomite concentration is observed in the skeleton of coralline alga *Porolithon onkodes* after 2 month exposure to future seawater conditions, which is regarded as a

Table 2. Compensatory mechanisms to ocean acidification by adjusting mineralogical or structural properties of calcareous structures.

Taxon	Species (life stage)	pH/pCO_2 level	Exposure duration	Compensatory mechanism	Beneficial effect	Refs.
Cidaroid	*Phyllacanthus imperialis* (adults)	pH 7.6	3 weeks	Increasing skeletal density and lowering Mg concentration of the cortex	↓ Shell dissolution	[227]
Mussel	*Mytilus edulis* (adults)	1000 µatm	6 months	Increasing calcite growth	~ Shell growth	[125]
Limpet	*Patella caerulea* (adults)	pH 6.46–6.51	N/A (from the field)	Increasing thickness of aragonitic shell layers	↓ Shell dissolution	[228]
Calcifying alga	*Lithophyllum* sp.; *Titanoderma* sp.; *Phymatolithon* sp.	pH 7.8	14 months	Maintaining control of skeletal mineralogy	~ Growth (algal area) ~ Skeletal Mg content	[229]
Pteropod	*Limacina helicina* (juveniles)	800 µatm	4 d	Secreting additional aragonite internally to maintain and repair shells	↓ Shell dissolution	[230]
Gastropod	*Austrocochlea constricta* (adults)	1000 ppm	10 weeks	Increasing calcite precipitation	↑ Shell growth ↑ Shell hardness	[83]
Pteropod	*Limacina helicina* (juveniles)	pH 8.0 (ambient level: pH 8.35)	N/A (from the field)	Thickening inner shell walls	~ Shell integrity	[112]
Brachiopod	*Liothyrella uva* (adults)	pH 7.54	7 months	Producing thicker shells by increasing inner secondary layer thickness	↓ Shell dissolution	[111]
Gastropod	*Nucella ostrina* (juveniles)	pH 7.4	6 months	Changing microstructural arrangements of shell layers	~ Shell growth ~ Shell strength	[109,110]
Gastropod	*Eatoniella mortoni* (adults)	pH 7.76	N/A (from the field)	Increasing nanotwin density and organic matter content; reducing porosity and crystal thickness	↑ Mechanical resilience ↓ Crack propagation caused by physical damage	[12]

protective mechanism against ocean acidification.[90] Whether other calcifiers can produce dolomite and incorporate it into their calcareous structures to counter the "corrosive" effect of acidified seawater remains largely unexplored.

Unlike aragonite, a tiny amount of magnesium can incorporate into the lattice structure of calcite, thereby increasing its solubility. In fact, high Mg-calcite (>8 mol% $MgCO_3$) is even more soluble than aragonite;[85] therefore, it has been proposed that high Mg-calcite may dissolve and reprecipitate as low Mg-calcite under ocean acidification,[91] whereby the structural stability and resistance of calcite to acidified seawater can be enhanced. Previous studies indeed demonstrated that some calcifiers, such as coralline algae,[92,93] can construct calcite of reduced Mg content when exposed to acidified seawater, suggesting their potential capacity to regulate magnesium incorporation in response to ocean acidification. Many calcifiers, however, do not exhibit this kind of mineralogical adjustment.[85,89,94,95] In view of the limited and inconsistent results, it remains uncertain whether calcite-producing calcifiers can adjust magnesium incorporation to counter ocean acidification, especially when the underlying mechanism is not fully understood.

Calcareous structures are chiefly composed of crystalline calcium carbonate that originates from amorphous calcium carbonate (ACC)—a highly unstable, disordered form of $CaCO_3$. ACC often exists in mineral-containing vesicles,[96] which are transported to the mineralization site of specialized cells for nucleation and crystallization with the aid of matrix proteins (e.g., glycoproteins[97]). Many calcifiers use ACC as the precursor to build their calcareous structures, such as sea urchins and bivalves.[98,99] After crystallization, a tiny amount of ACC is present in the mature $CaCO_3$ minerals (i.e., no 100% crystallinity[96]) that can reflect the "quality" of crystallization. Ocean acidification has been shown to compromise crystallographic control during $CaCO_3$ precipitation, which could eventually undermine structural integrity and increase solubility due to the disrupted growth pattern of $CaCO_3$ crystals.[100] As such, higher ACC content is considered undesirable because it reflects an increased effort for structural repair and weakens mechanical strength.[94,101] However, crystallinity of gastropod shells appears to be less influenced by ocean acidification,[95] and some gastropods can even produce more crystalline $CaCO_3$ minerals, which are more resistant to acidified seawater. For example, gastropod *Eatoniella mortoni* can build more crystalline and durable shells at natural CO_2 vents.[102] The reason for the enhanced crystallization of ACC is enigmatic, but it may result from an increased energy allocation to the synthesis of specific proteins for stabilizing ACC so that uncontrolled crystallization can be averted.[97] Crystallinity of $CaCO_3$ minerals is rarely examined in ocean acidification research; therefore, more mechanistic studies are needed to elucidate how ocean acidification affects crystallization of ACC and how the properties of $CaCO_3$ minerals are related to ACC content.

5.4. Structural Modifications

From a structural perspective, calcareous shells or skeletons are made of hierarchically arranged $CaCO_3$ crystals embedded in organic matrix.[12,103] Acidified seawater is expected to dissolve and weaken these structures, rendering them more fragile due to the looser package of $CaCO_3$ crystals (i.e., lower density or higher porosity[104–106]). Contrary to this expectation, structural integrity and mechanical strength of $CaCO_3$ minerals remain unchanged in some calcifiers inhabiting the natural CO_2-acidified environment,[14,107,108] implying their adaptability to ocean acidification. As mechanical strength of materials is largely associated with structural integrity, calcifiers may modify structural properties to augment durability and reduce solubility. For example, gastropod *Eatoniella mortoni* produces less porous shells at natural CO_2 vents (pH 7.76), which is correlated with greater mechanical resilience;[12] shell breaking force of gastropod *Nucella ostrina* is minimally affected by ocean acidification because it produces a thick, homogeneous calcitic layer made of closely packed grainy crystals, which can also reduce shell dissolution;[109,110] brachiopod *Liothyrella uva* builds a thicker inner shell layer at pH 7.54, which can counter shell dissolution induced by acidified seawater.[111] Similarly, pteropod *Limacina helicina* can maintain shell integrity by thickening inner shell wall after mechanical and dissolution damage.[112] When constructing thicker or denser $CaCO_3$ minerals is not possible due to energy constraint, altering structural morphology can be beneficial to reduce mechanical failure, such as fracture. For example, mussel *Mytilus edulis* reared at 1000 µatm CO_2 builds rounder shells, which provide stronger physical defense against predator attacks.[113] Diminished body size is generally considered unfavorable because of the reduced competitiveness of organisms for food and space in the community, but it can be advantageous for survival in the acidifying ocean. For instance, gastropods *Cyclope neritea* and *Nassarius corniculus* living in shallow-water CO_2 seeps (pH 7.2) have reduced shell size, which enormously lowers energy demand for metabolism and hence allows maintenance of calcification.[114] Indeed, many survivors in oceans after mass extinction events caused by elevated CO_2 concentrations, such as volcanism, tend to have reduced body size.[115]

Organic matrix (e.g., proteins and polysaccharides) plays a crucial role in initiating nucleation and controlling crystallization to form crystalline structures of $CaCO_3$.[116,117] Despite only contributing to a small proportion of weight (≈5%), the organic matrix occluded in calcareous structures is vital for maintaining structural integrity that affects mechanical strength. For example, the mechanical strength of pearls (i.e., biogenic $CaCO_3$) is raised by more than 3000 times than that of pure $CaCO_3$ without organic matrix.[118] A recent study also found that the shell of gastropod *Eatoniella mortoni* is more durable and resistant to crack propagation at natural CO_2 vents due to greater organic matter content, which is in turn pertinent to the thinner $CaCO_3$ crystals produced.[12] Apart from improving structural integrity and mechanical resilience, organic matrix is resistant to dissolution and therefore calcareous structures are typically coated with a thin layer of organic matter (e.g., periostracum of molluscs) to reduce solubility.[119] When this organic coating is damaged, shell or skeletal dissolution may occur due to the direct contact of $CaCO_3$ minerals with acidified seawater,[120] depending on the shell repairing capacity of calcifiers. Although production of organic matrix for biominerals can be biologically regulated and beneficial to counter ocean

acidification,[102,121] whether calcifiers tend to produce thicker organic coatings to resist "corrosive" seawater remains elusive, especially considering the high energy demand for synthesizing organic matrix.

Technically, structural properties of biominerals are mostly observed under scanning electron microscopes (SEM), which enable reliable analyses of structures at the microscale. While this powerful equipment is widely used for structural analyses, some structures are minuscule that can only be seen and quantified at the nanoscale under transmission electron microscopes (TEM). For instance, a recent study found that crystal size and nanotwin thickness (or nanotwins density) of gastropod shells can be altered by ocean acidification.[12] Despite being nanoscopic, nanotwins can greatly affect the mechanical strength of materials since nanotwin boundaries act as the barrier against physical force and thus resist structural deformation.[103] The importance of nanotwins to mechanical properties is well acknowledged in materials science, but marine scientists are likely at the beginning to appreciate how this nanostructure may influence the fitness of calcifiers. Indeed, structural and mechanical properties of $CaCO_3$ minerals are rarely studied in ocean acidification research (c.f. physiology and mineralogy, Table 2) and thus more interdisciplinary studies are required to explore whether calcifiers can modify their calcareous structures to cope with ocean acidification.

5.5. Molecular Adjustments

As briefly mentioned above (see Section 5.2), calcification is favored under slightly alkaline conditions at the calcifying tissue–mineral interface, maintained by active ion transport. Ocean acidification can disrupt the acid–base balance of the calcifying fluid in calcifiers and thus compromise calcification. Nevertheless, transcriptomic evidence unravels that the activity of ion transporters and exchangers (e.g., V-type H^+ ATPase, Na^+/K^+ ATPase, and Cl^-/HCO_3^- exchanger[122]) can be promoted under ocean acidification to maintain acid–base balance of the calcifying fluid. For example, coral *Pocillopora damicornis* upregulates the genes associated with Ca^{2+} and HCO_3^- transporters that can help sustain calcification under ocean acidification.[123] Upregulation of genes involved in ionic and acid–base regulation is also observed in oyster *Pinctada fucata* reared at pH 7.8,[124] suggesting a compensatory response to counter ocean acidification. Apart from obtaining optimal alkaline conditions, cellular CO_2 needs to be converted to HCO_3^- for $CaCO_3$ precipitation and this conversion process is catalyzed by carbonic anhydrase.[51] Crystallographic control and growth of $CaCO_3$ minerals would be disturbed if the activity of carbonic anhydrase is inhibited by ocean acidification.[125] Based on the results of previous studies, the activity of carbonic anhydrase appears to be unaffected or even promoted by ocean acidification in many calcifiers,[126–128] meaning that the conversion of CO_2 to HCO_3^- is unlikely a rate-determining step in calcification.

Organic matrix is responsible for nucleation, crystallization, and growth of biominerals. Some studies showed that the capacity of calcifiers to synthesize this important component can be undermined by ocean acidification,[129,130] possibly weakening structural integrity and mechanical strength of $CaCO_3$ minerals. However, some calcifiers are able to maintain or enhance the synthesis of organic matrix in response to ocean acidification. For instance, pteropod *Clio pyramidata* upregulates the gene expression of shell proteins, including C-type lectins and collagens, when exposed to acidified seawater (800 ppm CO_2) for 10 h.[131] Mussel *Mytilus edulis* reared at 4000 µatm CO_2 for 8 weeks substantially upregulates the gene expression of tyrosinase, an enzyme involved in periostracum formation, which represents an adaptive response to prevent shell dissolution.[132] Despite the critical role of organic matrix in calcification, it is rarely studied in ocean acidification research. Whether the quality and quantity of organic matrix produced would be affected by ocean acidification remains unclear due to the inconsistent results in the literature.

Changes in gene expression due to environmental stress, including ocean acidification, can also be mediated by epigenetic modifications that usually elicit rapid plastic responses.[133,134] DNA methylation is one of the most recognized epigenetic mechanisms of gene regulation in response to environmental stress. Instead of altering the original DNA sequence, DNA methylation involves the addition of a methyl group to the 5-position of cytosine,[134] thereby modulating gene activity often expressed in the functional molecules (e.g., proteins). In this regard, DNA methylation may act as a rapid compensatory mechanism allowing calcifiers to exhibit phenotypic plasticity to buffer the impacts of ocean acidification. For example, the larvae of oyster *Crassostrea hongkongensis* cultured at pH 7.4 have 130 genes differentially methylated, which is related to growth maintenance and increased metamorphosis rates;[135] DNA methylation can fine-tune the expression of genes associated with cell growth in coral *Stylophora pistillata* when exposed to ocean acidification (pH 7.2), resulting in facilitated cell growth.[136] Epigenetic modifications are regarded as the critical mechanism responsible for phenotypic plasticity and adaptation (**Table 3**), but whether this mechanism allows calcifiers to persist in the acidifying ocean remains largely unknown due to a paucity of studies thus far.

5.6. Transgenerational Plasticity

It is noteworthy that the effects of ocean acidification on marine organisms are typically examined by exposing them to CO_2-enriched seawater for a relatively short period of time (e.g., few weeks or months). Although this experimental design can reveal the responses of calcifiers to reduced seawater pH, it cannot truly represent ocean acidification in view of the rate of pH change driven by anthropogenic CO_2 emissions over time. Indeed, ocean acidification is a slow process during which calcifiers, especially those with short life cycles, may modify their phenotypes across generations to adapt to the changing environment. Such transgenerational plasticity is a non-genetic inheritance process, where parents experienced environmental stress can alter the phenotypes of their offspring without modifying DNA sequence.[137] As genetic modifications are not required, transgenerational plasticity may enable calcifiers to rapidly adjust to ocean acidification, mediated possibly by parental provisioning where the stressed parents invest

Table 3. Compensatory mechanisms to ocean acidification through molecular adjustments, such as change in gene expression and epigenetic modification.

Taxon	Species (life stage)	pH/pCO_2 level	Exposure duration	Compensatory mechanism	Beneficial effect	Refs.
Sea urchin	*Paracentrotus lividus* (larvae)	pH 7.7	69 hours	Increasing expression of genes involved in development and biomineralization	~ Larval growth ~ Postoral arm growth ~ Larval symmetry	[231]
Sea urchin	*Strongylocentrotus purpuratus* (larvae)	900 µatm	17 d	Altering expression of genes involved in biomineralization, lipid metabolism, ion homeostasis, and pH regulation	~ Larval growth ~ Calcification	[232]
Coral	*Desmophyllum dianthus* (adults)	pH 7.70	8 months	Upregulating expression of genes involved in cellular stress, immune defense, and skeletal synthesis	~ Calcification ~ Respiration rate	[233]
Sea urchin	*Strongylocentrotus purpuratus* (larvae)	800 µatm	14 d	Increasing protein synthesis and ion transport rates	~ Larval growth ~ Metabolism	[234]
Coral	*Siderastrea siderea* (adults)	604 µatm	95 d	Increasing transcription of genes associated with H^+ transporter	~ Calcification	[235]
Oyster	*Pinctada fucata* (juveniles)	pH 7.7	42 d	Maintaining expression of genes involved in biomineralization	~ Shell length ~ Calcium content ~ Shell hardness ~ Shell integrity	[171]
Coral	*Stylophora pistillata* (cell cultures)	700 ppm	9 d	Upregulating gene expression of carbonic anhydrase and increasing pH at calcification sites	↑ Calcification	[236]
Sea urchin	*Stongylocentrotus purpuratus* (larvae)	pH 7.7	5 d	Increasing SpSlc4a10 expression for intracellular pH regulation and biomineralization	~ Calcification	[237]
Coral	*Stylophora pistillata* (adults)	pH 7.2	2 years	Epigenetic modification by DNA methylation to reduce spurious transcription	↑ Cell size ↑ Polyp size	[136]
Pteropod	*Limacina retroversa* (adults)	1200 ppm	14 d	Increasing expression of genes related to metabolism and biomineralization	↑ Growth rate ↑ Calcification	[238]
Oyster	*Crassostrea virginica* (larvae)	1000 ppm	48 hours	Upregulating expression of biomineralization-related and calcium-binding protein genes	~ Larval mortality ~ Larval shell growth	[239]
Coral	*Balanophyllia elegans* (adults)	pH 7.4	29 d	Upregulating expression of genes involved in calcium ion binding and ion transport for pH homeostasis and calcification	~ Respiration rate ↑ Protein and lipid content	[240]
Sea urchin	*Strongylocentrotus purpuratus* (larvae)	pH 7.8	10 d	Changing expression levels of midgut acid-base transporters to maintain midgut pH	~ Larval growth ~ Respiration rate ~ Feeding rate	[241]
Coral	*Lophelia pertusa* (adults)	pH 7.6	6 months	Upregulating expression of genes related to proton transport as well as formation of microtubules and organic matrix	~ Calcification	[242]
Oyster	*Crassostrea gigas* (adults)	pH 7.5	60 d	Regulating expression of genes associated with calcium homeostasis and stimulating transcription of calcium signal pathways	↑ Ca^{2+} in serum ~ H_2O_2 in serum ~ ROS level in hemocytes	[243]
Oyster	*Crassostrea hongkongensis* (larvae)	pH 7.4	21 d	Epigenetic modification via DNA methylation i n genes related to metamorphosis, oxidative stress as well as cytoskeletal and signal transduction	~ Larval growth ↑ Larval settlement	[135]
Oyster	*Crassostrea hongkongensis* (juveniles)	pH 7.4	4.5 months	Maintaining expression of key biomineralization-related genes, such as carbonic anhydrase and alkaline phosphatase	~ Shell growth ~ Shell hardness ~ Crystal orientation	[244]

more energy for reproductive growth to improve the fitness of their offspring. For example, mussel *Musculista senhousia* reared at pH 7.7 produces larger eggs, resulting in increased larval growth, survival, metamorphosis, and energy budget of the offspring.[138] The advantage of parental provisioning is also observed in sea urchin *Sterechinus neumayeri* after long-term exposure at pH 7.7.[139] Transgenerational plasticity can also be mediated by epigenetic inheritance (e.g., DNA methylation), as discussed above (see Section 5.5).

Given the adaptive value of transgenerational plasticity, calcifiers with their parents exposed to acidified seawater usually have a greater capacity to cope with ocean acidification through various compensatory mechanisms summarized above (i.e., acid–base regulation, mineralogical adjustment, etc.). For instance, adult oyster *Saccostrea glomerata* with a history of transgenerational exposure to acidified seawater has a greater capacity to regulate acid-base homeostasis and their offspring have faster larval development and shell growth than those

without parental exposure to ocean acidification;[140] clam *Ruditapes philippinarum* with parents exposed to ocean acidification has an improved capacity to regulate carbonate chemistry of the calcifying fluid by preferentially extracting metabolic carbon rather than actively transporting seawater DIC, resulting in enhanced calcification.[141] By analyzing transcriptome, Goncalves et al.[142] showed that the positive transgenerational effect observed in oyster *Saccostrea glomerata* is driven by upregulating the expression of genes associated with cellular homeostasis, antioxidant defense, and energy metabolism, thereby conferring resilience to ocean acidification. Bimineralic mussel *Mytilus edulis* with parents exposed to acidified seawater (1000 μatm CO_2) no longer produces aragonite but calcite in shells, which is favorable to resist shell dissolution.[100] Apart from the above examples, many recent studies also clearly illustrate that calcifiers can respond differently to ocean acidification across generations (**Table 4**). If transgenerational plasticity is not taken into consideration (as found in most previous studies), it is premature to make a general conclusion that ocean acidification is detrimental to calcifiers.

Positive transgenerational effect to counter ocean acidification is well recognized, but it can be subject to the duration of parental exposure. For instance, sea urchin *Strongylocentrotus droebachiensis* sourced from parents exposed to acidified seawater (1200 μatm CO_2) for 4 months suffers from reduced larval settlement and juvenile survival under ocean acidification, but these negative effects disappear if the parents have acclimated to ocean acidification for 16 months.[143] Similarly, sea urchin *Psammechinus miliaris* has increased body size under ocean acidification only for those with parents reared in acidified seawater (1000 μatm CO_2) for 72 d (but not for 28 d), highlighting the importance of parental exposure duration to transgenerational plasticity.[144] To provide a more realistic evaluation of the transgenerational effect, we recommend examining the responses of organisms across at least three consecutive generations (F_0, F_1, and F_2) or those that can persist in naturally CO_2-acidified habitats for generations.

5.7. Indirect Effect through Trophic Transfer

Based on the discussion above, we realize that many compensatory mechanisms to ocean acidification are fuelled by energy. Therefore, whether calcifiers can maintain a sufficient energy budget is critical to determine their fitness in the acidifying ocean.[50,145] For heterotrophs, energy is acquired by food consumption, suggesting the importance of food availability to the fitness of calcifiers. Among different types of heterotrophs, herbivores are less likely subject to food deprivation under ocean acidification because CO_2 can act as a resource for primary producers (e.g., algae and plants) to carry out photosynthesis.[146,147] Consequently, their productivity can be raised by CO_2 enrichment, indirectly favoring the survival of herbivorous calcifiers due to increased food availability. In fact, the adverse effects of ocean acidification on calcifiers are often eradicated when sufficient food is provided. For example, the zooids of bryozoan *Jellyella tuberculata* not only have a higher growth efficiency under ocean acidification (1050 μatm CO_2), but also have a lower proportion of skeletal dissolution when more food is offered.[148] The beneficial effect of increased food supply is also manifested in the larvae of oyster *Ostrea angasi*, which have higher developmental rates and lower abnormality than those with half diet at pH 7.79.[149] It appears that increasing food availability can consistently result in boosted growth and calcification irrespective of seawater carbonate chemistry (**Table 5**), which underpins the proposition that calcification is primarily driven by the energetics of calcifiers. It is also important to highlight that many previous studies did not provide food for the tested organisms,[37] and therefore the observed negative effects of ocean acidification are probably overestimated.

Apart from boosting the productivity of primary producers, CO_2 enrichment can also promote their nutritional value, indicated by energy and macronutrient contents (i.e., proteins, carbohydrates, and lipids). Many primary producers indeed have improved nutritional quality (i.e., increased energy content or decreased C/N ratio) under CO_2-enriched conditions, which could be attributed to increased nitrogen assimilation or enhanced photosynthetic efficiency.[147,150,151] For example, the energy, protein, and carbohydrate contents of turf algae are boosted by CO_2 enrichment at natural CO_2 vents, and consumption of this energy-enriched food allows gastropod *Eatoniella mortoni* to produce thicker, more durable, and more crystalline shells.[102] As nitrogen is often the limiting nutrient for herbivores,[152] the increased protein content (or reduced C/N ratio) in primary producers can elevate their feeding rates,[64,153–155] which is favorable to offset their increased energy demand under ocean acidification. Among different types of compensatory mechanisms to ocean acidification, increase in food availability clearly provides the strongest compensatory effect that usually enhances growth and calcification regardless of seawater pH and carbonate saturation (Table 5). As such, calcifiers can likely prevail in the acidifying ocean as long as they are able to access food sources and maintain feeding performance.

5.8. Indirect Effect through Species Interactions

Marine ecosystems are complex and dynamic, comprising various biotic and abiotic components. Thus, calcifiers are constantly interacting with these components in the natural environment rather than exist in isolation. Most previous studies, however, did not include species interactions and environmental fluctuations in the experimental design. Oversight of these factors would lead to erroneous conclusions about the impacts of ocean acidification on calcifiers because the results have limited ecological relevance. Habitat-forming primary producers, such as macroalgae and seagrasses, are of particular research interest because they may ameliorate the impacts of ocean acidification via their photosynthetic ability to fix CO_2 and raise seawater pH.[156–158] Diffusive boundary layers are then created surrounding primary producers, where the seawater carbonate chemistry differs from that of bulk seawater.[159] As such, habitats formed by primary producers (e.g., kelp forests and seagrass meadows) can act as refugia for calcifiers under ocean acidification.[160,161] For example, Wahl et al.[162] found that macrophytes can elevate seawater pH by up to 0.3 units and calcification of mussel *Mytilus edulis* is enhanced with increasing macrophyte biomass, suggesting that habitats with dense macrophytes can

Table 4. Compensatory mechanisms to ocean acidification via transgenerational plasticity.

Taxon	Species (Life stage)	pH/pCO_2 level	Exposure duration	Parental exposure duration and possible adaptive transgenerational mechanism	Beneficial effect on the offspring	Refs.
Oyster	*Saccostrea glomerata* (F1 larvae)	856 µatm	19 d	5 weeks. Elevating standard metabolic rate of parents and increasing parental provisioning	↑ Larval growth ↑ Larval development ~ Larval survival	[245]
Sea urchin	*Psammechinus miliaris* (F1 larvae)	1000 µatm	17 d	70 d. Improving gamete quality and increasing fertilization success	↑ Larval growth ↑ Larval development ↑ Larval settlement	[144]
Oyster	*Saccostrea glomerata* (F1 adults; F2 larvae and spat)	856 µatm	5 weeks (adults); 19 d (larvae); 6 d (spat)	5 weeks for F1 adults and 2 generations for F2 larvae and spat. Increasing capacity to regulate extracellular pH, epigenetic inheritance, and natural selection of genotypes	↑ Adult pH regulation capacity ↓ Abnormal larval development ↑ Larval developmental rate ↑ Larval and spat shell growth ↑ Spat heart rate	[140]
Coral	*Pocillopora damicornis* (F1 larvae)	805 µatm	5 d	1.5 months. Epigenetic inheritance	~ Metabolic rate	[246]
Mussel	*Mytilus edulis* (F2 larvae)	1120 µatm	21 d	2 generations for F2 larvae. Increasing maternal provisioning	~ Shell growth rate ~ Larval survival	[247]
Clam	*Ruditapes philippinarum* (F1 juveniles)	pH 7.7	30 d	70 d. Increasing active removal of excessive H^+ through Na^+/H^+ exchanger	↑ Growth rate	[248]
Sea urchin	*Strongylocentrotus purpuratus* (F1 embryos)	1100 µatm	30 hpostfertilization	4.5 months. Downregulating genes related to protein breakdown to conserve energy; epigenetic modification via DNA methylation.	↑ Embryonic growth	[249]
Clam	*Ruditapes philippinarum* (F1 juveniles)	pH 7.7	6 months	70 d. Preferentially extracting internal metabolic carbon to reduce calcification cost	↑ Shell growth rate ↑ Condition index ↓ Metabolic rate	[141]
Mussel	*Musculista senhousia* (F1 embryos/larvae/juveniles)	pH 7.7	1 d (embryos); 15 d (larvae); 6 months (juveniles)	40 d. Increasing maternal provisioning to eggs and energy availability to improve fitness via metabolic plasticity	↑ Egg size ↑ Larval shell length ↑ Larval survival ↑ Metamorphosis ~ Juvenile growth ~ Juvenile feeding rate ~ Juvenile respiration rate	[138]
Calcifying alga	*Hydrolithon reinboldii* (F5)	pH 7.7	At the end of each generation	5 generations. Increasing levels of organic matrix proteins and use of Ca^{2+} and CO_3^{2-} during calcification	~ Growth ~ Calcifying fluid pH ~ Mg content	[250]
Oyster	*Crassostrea hongkongensis* (F1 larvae and F1 juveniles)	pH 7.4	14 d (larvae); 10 months (juveniles)	4 weeks. Increasing acid-base and ion regulatory capacity as well as the synthesis of proteins through improved metabolism	~ Larval survival ↑ Larval growth ~ Metamorphosis ↑ Juvenile survival ↑ Juvenile growth	[251]
Calcifying alga	*Hydrolithon reinboldii* (F5)	pH 7.70	At the end of each generation	5 generations. Prioritizing energy allocation to reproduction	↑ Reproductive output (conceptacle abundance)	[252]

buffer the impacts of ocean acidification. Likewise, the negative effects of ocean acidification on the growth and calcification of epiphytic foraminifera *Marginopora vertebralis* are alleviated by the presence of alga *Laurencia intricata*.[163] Apart from creating a more desirable microenvironment, primary producers can also take advantage of CO_2 enrichment to increase areal coverage that can indirectly benefit calcifiers if they rely on these primary producers as habitats. This can be exemplified by the expansion of turf algae at natural CO_2 vents, which accounts for the increased abundance of the turf-associated gastropod *Eatoniella mortoni*.[164]

Diel pH fluctuations in seawater generated by primary producers are also critical for calcifiers to accommodate and persist in the acidifying ocean. Instead of being stable as manipulated in most studies, seawater pH can greatly fluctuate in the natural environment, especially in the presence of primary producers

Table 5. Compensatory mechanisms to ocean acidification by increasing food availability or species interactions.

Taxon	Species (Life stage)	pH/pCO_2 level	Exposure duration	Compensatory mechanism	Beneficial effect	Refs.
Coral	*Porites* spp. (juveniles)	pH 7.74	1 month	Providing *Artemia* spp. (1.6×10^4 nauplii L^{-1}) as food for 1 hour every second day	↑ Biomass ↑ Calcification ↑ Symbiont density	[253]
Mussel	*Mytilus edulis* (juveniles)	pH 7.70	7 weeks	Increasing food availability from 350 algal cells mL^{-1} to 2000 algal cells mL^{-1}	↑ Somatic growth ↑ Calcification ↑ Shell length ↓ Shell dissolution	[44]
Coral	*Porites rus* (adults)	700 µatm	3 weeks	Providing zooplankton as food for 1 h every other day	~ Calcification ~ Biomass	[254]
Coral	*Balanophyllia elegans* (juveniles)	pH 7.60	3 months (adults); 8 months (juveniles)	Increasing food availability (nauplii larvae of *Artemia*) from once every 21 d to once every 3 d	↑ Number of larvae released ↑ Juvenile survival ↑ Juvenile skeletal weight ↑ Juvenile skeletal volume	[255]
Coral	*Favia fragum* (juveniles)	1311 µatm	3 weeks	Providing *Artemia* nauplii as food for 3 h every night for 2 weeks and every other night for the third week	↑ % Spat with tertiary septa ↑ Primary septa diameter ↑ Corallite weight	[256]
Oyster	*Ostrea lurida* (larvae)	1000 µatm	11 d	Increasing food availability from 10 000 algal cells mL^{-1} to 100 000 algal cells mL^{-1}	↑ Larval growth ↑ Dry weight ↑ Metamorphosis	[257]
Mussel	*Mytilus edulis* (juveniles)	1120 µatm	7 weeks	Increasing food availability from 4000 algal cells mL^{-1} to 40 000 algal cells mL^{-1}	↑ Growth ↑ Calcification	[258]
Barnacle	*Amphibalanus improvisus* (juveniles)	1120 ppm	20 weeks	Increasing food availability (microalgae or *Artemia* nauplii) by five times	↑ Size ↑ Condition index ↑ Reproduction ↑ Shell strength ~ Calcification	[259]
Sea urchin	*Strongylocentrotus fragilis* (adults)	pH 7.6	140 d	Providing sufficient kelp as food	↑ Growth ↑ Gonadosomatic index	[260]
Sea urchin	*Strongylocentrotus purpuratus* (larvae)	800 µatm	14 d	Providing alga *Rhodomonas lens* at 30 000 cells mL^{-1} daily as food	↑ Body length ↑ Metabolic rate ↑ Protein synthesis rate	[234]
Coral	*Acropora cervicornis* (adults)	800 ppm	8 weeks	Providing dried zooplankton powder as food twice a week	↑ Growth ↑ Lipid content ~ Chl a content ~ Symbiont density	[62]
Oyster	*Ostrea angasi* (larvae)	pH 7.79	4 d	Increasing food availability from 25 000 algal cells mL^{-1} to 50 000 algal cells mL^{-1}	~ Larval shell length ↑ Larval development ↓ Abnormal larvae ~ Larval survival	[149]
Scallop	*Argopecten purpuratus* (juveniles)	pH 7.60	30 d	Increasing food availability (phytoplankton suspension) from 0.1% to 5% dry weight individual per day	↑ Growth ↑ Calcification ↑ Oxygen consumption ↑ Feeding rate	[63]
Sea urchin	*Echinometra* sp. (adults)	pH 7.73	17 months	Increasing algal productivity and hence food availability at CO_2 vents	↑ Growth rate ~ Metabolic rate ~ Calcification	[46]
Coral	*Lophelia pertusa* (adults)	800 µatm	6 months	Increasing food availability from 0.305 nauplii mL^{-1} to 3.05 nauplii mL^{-1} twice a week	~ Growth ↑ Fitness (RNA/DNA ratio)	[261]
Gastropod	*Eatoniella mortoni* (adults)	pH 7.67	N/A (from the field)	Increasing habitat-forming turf from 1.16 to 2.66 g per quadrat	↑ Population size	[164]
Coral	*Pocillopora verrucose* (adults)	1200 µatm	8–14 d	Increasing conspecific aggregations from 133 to 400 colonies m^{-2} that creates small-scale refugia	~ Calcification ~ Net photosynthesis	[196]
Sea star	*Acanthaster planci* (juveniles)	pH 7.6	6 weeks	Consuming food (coralline algae) of enhanced palatability and nutritional quality	↑ Consumption rate ↑ Growth rate	[155]

Table 5. Continued.

Taxon	Species (Life stage)	pH/pCO_2 level	Exposure duration	Compensatory mechanism	Beneficial effect	Refs.
Bryozoan	*Jellyella tuberculata* (adults)	1050 µatm	8 weeks	Increasing food availability from 50 to 200 algal cells mL^{-1}	↑ Growth efficiency ↓ Skeletal dissolution	[148]
Rhodolith	*Sporolithon australe*	1500 µatm	40 d	Altering microbe–host interaction (stable rhodolith microbiome) to provide host resilience to elevated pCO_2	↑ Photosynthesis ~ $CaCO_3$ biomass	[262]
Coral	*Pocillopora verrucose* (adults)	pH 7.7	21 d	Interacting with ectosymbiotic crustaceans	~ Calcification	[263]
Coral	*Favia fragum* (juveniles)	pH 7.78	3 weeks	Providing *Artemia* nauplii as food for 3 h on alternating nights	↑ Skeletal weight ↑ Skeletal size	[264]
Gastropod	*Phasianella australis* (juveniles)	1000 ppm	6 months	Increasing nutritional quality of food (turf algae) due to CO_2 enrichment	↑ Feeding rate ↑ Energy budget ~ Biomass ~ Body condition	[64]
Coral	*Pocillopora damicornis* (larvae)	pH 7.7	24 h	Host–symbiont interaction where the symbiont upregulates ion transport genes that may help maintain holobiont homeostasis	~ Larval growth ~ Total protein ~ Symbiont density	[265]
Mussel	*Mytilus edulis* (juveniles)	1120 µatm	3 months	Interacting with a high biomass of brown alga *Fucus vesiculosus* and seagrass *Zostera marina*, which create pH fluctuations and offer temporal refugia	~ Calcification	[162]
Calcifying alga	*Halimeda cuneata*	822 ppm	10 d	Interacting with seagrass *Halodule wrightii* which provides refuges	↑ Calcification ↑ Gross primary production	[266]
Gastropod	*Eatoniella mortoni* (adults)	pH 7.76	N/A (from the field)	Increasing nutritional quality of food (proteins, carbohydrates, and energy content of turf algae) at CO_2 vents	↑ Shell thickness ↑ Shell crystallinity ↑ Mechanical resilience ↑ Shell organic matter	[102]
Foraminifera	*Rosalina* sp.	pH 7.7	17 d	Interacting with seagrass *Posidonia oceanica* that creates diel pH fluctuations	↑ Net population growth rate	[167]
Foraminifera	*Marginopora vertebralis*	1000 µatm	15 d	Interacting with alga *Laurencia intricata* that creates diffusive boundary layers	~ Growth ~ Calcification ↑ Net photosynthetic production ↑ Respiration	[163]
Sea urchin	*Arbacia lixula* (larvae)	pH 7.80	24 h	Increasing food availability and pH fluctuations at CO_2 vents	↑ Total arm length	[190]
Calcifying alga	*Ellisolandia elongata*	pH 7.8	44 d	Interacting with noncalcifying epiphytic algae that create diffusive boundary layers as refugia	↑ Net photosynthesis ↑ Calcification	[267]
Sea urchin	*Pseudechinus huttoni* (larvae and juveniles)	pH 7.5	51 hours (larvae); 4 days (juveniles)	Interacting with coralline algae which create diffusive boundary layers as refugia	~ Larval settlement ~ Spine length ~ Test diameter	[191]
Coral Calcifying alga Sponge	*Corallium rubrum* (adults) *Phymatolithon* sp. *Hemimycale columella*	pH 7.84	86 d	Increasing diversity of the associated coralligenous assemblages that act as food resources and offer healthy microbe–host associations	↑ Biomass (corals) ↑ Areal coverage (algae and sponges)	[268]
Mussel	*Mytilus edulis* (adults)	1000 µatm	4 months	Increasing food availability from 5 mL to 10 mL microalgae every day	↑ Metabolic carbon uptake for shell growth	[269]

because they can take up seawater DIC for photosynthesis during daytime and release CO_2 by respiration that dominates during night time.[160,165] For instance, seagrass meadows (*Posidonia oceanica*) can create diel pH fluctuations of 0.24 units in summer,[157] whereas large diel pH fluctuations of 0.94 units have been observed in kelp forests (*Macrocystis pyrifera*).[156] Similarly, diel pH range up to 0.46 units can be observed in coral reef ecosystems due to reef metabolism, which is in turn driven by temperature and water depth.[166] Constant exposure to pH fluctuations can confer calcifiers with resilience to ocean acidification, which has been illustrated in foraminifera *Rosalina* sp. that can maintain net population growth rates under ocean acidification when exposed to diel pH fluctuations of 0.3 units, but not to stable pH.[167] The recruits of coral

Seriatopora caliendrum exposed to ecologically relevant pH fluctuations calcify at higher rates than those exposed to static pH, highlighting the benefit of pH fluctuations on coral survival.[168] Compared to subtidal organisms, intertidal organisms are naturally subject to greater pH fluctuations with extreme pH values,[165] which possibly make them more robust to ocean acidification.[95] More detailed studies are needed to confirm this hypothesis.

5.9. Limits and Trade-Offs of compensatory mechanisms

While compensatory mechanisms can help calcifiers resist and acclimate to ocean acidification, most of them are fuelled by energy, meaning that these mechanisms would collapse when energy budget of calcifiers becomes insufficient (e.g., under stressful or food-limiting conditions). This explains why the performance of calcifiers can be maintained under mild acidification, but deteriorate under extreme acidification as shown in our meta-analysis. For example, coral *Stylophora pistillata* can upregulate pH in the subcalicoblastic medium at pH 7.8 to maintain calcification, but this regulation fails at pH 7.2, resulting in reduced crystal cross-sectional area and colony growth.[72] Similarly, coralline alga *Neogoniolithon* sp. can upregulate calcifying fluid pH at pH 7.91, but this regulatory capacity is undermined at pH 7.49, leading to retarded calcification.[169] Changes in transcriptome can account for the success or failure of acid–base regulation, which can be exemplified by the upregulation of genes associated with acid-base homeostasis and energy metabolism in crab *Hyas Araneus* reared at 1120 µatm CO_2, but not at 1960 µatm CO_2.[170] Likewise, coral *Pocillopora damicornis* can sustain calcification at pH 7.8 by upregulating the genes involved in calcium and carbonate transport, carbonic anhydrase activity, and organic matrix synthesis, but this molecular adjustment fails at pH 7.2 in order to conserve energy for defense response.[123] Shell growth, hardness, and calcium content of oyster *Pinctada fucata* can be sustained at pH 7.7, but decrease at pH 7.4 due to downregulation of biomineralization-related genes *nacrein*, *aspein*, and *n16*.[171] Structural plasticity also has a limit, which can be illustrated by gastropod *Eatoniella mortoni* that can produce more durable shells at pH 7.76 by reducing shell porosity, nanotwin thickness and crystal thickness; however, these adaptive adjustments are compromised at pH 6.63, leading to production of more fragile shells.[12] Overall, an enormous amount of energy is usually required to support compensatory mechanisms, particularly synthesizing organic matrix and activating ion transporters; therefore, energy budget is the key factor that sets the limit of compensatory mechanisms and determines the fitness of calcifiers under ocean acidification.

It is noteworthy that the impacts of mild acidification on calcifiers can often be fully offset by compensatory mechanisms, but at the expense of other processes. For example, shell growth of gastropod *Austrocochlea constricta* is enhanced at pH 7.85 owing to the increased precipitation of calcite, but inner shell density is reduced as the trade-off.[83] Alga *Lithothamnion glaciale* exhibits a similar response after 10 month exposure to acidified seawater at 1024 µatm CO_2, where its growth rate is maintained at the expense of cell wall thickness, suggesting an adaptive response via reallocation of energy budget.[172] For oyster *Saccostrea glomerata*, exposure to ocean acidification (1000 ppm CO_2) for 4 weeks increases the expression of genes involved in protein synthesis and biomineralization (e.g., carbonic anhydrase and alkaline phosphatase), but those genes involved in cilia and flagella function are downregulated as the trade-off.[173] In short, calcifiers have an innate capacity to adaptively modify their phenotypes in response to ocean acidification, but their compensatory mechanisms through phenotypic plasticity have a limit and may incur trade-offs against other physiological processes.

Marine organisms are expected to gradually acclimatize to the changing environment over generations according to the concept of natural selection; however, few studies revealed that transgenerational effect can be non-positive. For instance, larval settlement rates of sea urchin *Strongylocentrotus droebachiensis* are reduced when the parents experienced ocean acidification (1200 µatm CO_2) for 4 months.[143] Increased mortality of clam and scallop larvae (*Mercenaria mercenaria* and *Argopecten irradians*) with reduced growth and metamorphosis is observed when their parents were exposed to acidified seawater at 2500 µatm CO_2, implying increased sensitivity of the offspring to ocean acidification.[174] Amphipod *Gammarus locusta* with a history of parental exposure to acidified seawater at 800 µatm CO_2 has increased mortality due to the reduced investment to reproduction by parents.[175] A majority of studies show that the negative transgenerational effects of ocean acidification manifested in the early life stages (i.e., embryonic and larval stages) are caused by reduced parental provisioning (e.g., reduced fecundity and lipid content of eggs), underpinning the notion that sufficient energy budget is fundamental to survival under adverse environmental conditions.

Habitat-forming primary producers are recognized for their ability to modify seawater carbonate chemistry and create diffusive boundary layers that possibly ameliorate the impacts of ocean acidification.[160,161] However, the buffering effect created by primary producers is subject to environmental conditions. Cornwall et al.[159] found that thick diffusive boundary layers formed under slow flows can protect coralline alga *Arthrocardia corymbosa* from skeletal dissolution and enable calcification at pH 7.65, but those layers formed under high flows become too thin to provide protection from acidified seawater. This implies that the effectiveness of diffusive boundary layers as refugia highly depends on hydrodynamic conditions. On the other hand, pH fluctuations generated by photosynthesis and respiration of primary producers do not necessarily improve the performance of calcifiers due to the additional energy demand potentially created. For instance, coral *Pocillopora damicornis* exposed to ocean acidification (pH 7.82) with fluctuating pH for 7 d has lower asexual budding rates and skeletal weight because of the higher energy expenditure on calcification (c.f. static pH), indicated by the upregulation of Ca-ATPase and Mg-ATPase.[176] To date, how indirect effects via species interactions influence the fitness of calcifiers remains largely unexplored. Future studies employing more realistic experimental designs that mimic natural marine ecosystems are needed to ascertain whether habitat-forming primary producers can indirectly allow calcifiers to prevail in the acidifying ocean.

6. Implications for the Fate of Calcifiers in the Acidifying Ocean

Ocean acidification is considered as a calamity in the future since reduced seawater Ω is predicted to retard calcification by calcifiers,[5,6] which not only diminishes their survival, but also impacts the functioning of marine ecosystems. This gloomy prediction is supported by many early studies and thus appears to become a consensus among marine scientists. Nevertheless, this common belief has been increasingly challenged due to experimental artifacts in many early studies, especially for short-term exposure that excludes the potential acclimation of calcifiers. For example, calcification of coral *Lophelia pertusa* is greatly reduced at pH 7.76 after 1 week exposure, but slightly enhanced after 6 month exposure,[177] which could be mediated by adaptive molecular changes.[178] Publication bias in the early development of this research field may also strengthen the negative public perception of ocean acidification.[39,179] Indeed, our meta-analysis reveals that some of the adverse effects supposed to be triggered by ocean acidification are not widely observed. For example, hypercapnia is expected to cause metabolic depression, leading to serious consequences on the health of marine organisms.[25] Yet, we found that metabolism is not depressed (or even elevated) by ocean acidification in many calcifiers, even though extracellular pH is reduced in the less mobile taxa. This can be illustrated by oyster *Saccostrea glomerata* that has a drop in extracellular pH, but a rise in oxygen consumption after 7 week exposure to seawater at pH 7.8.[180] Since the early studies often used extreme pH levels to represent ocean acidification (e.g., pH 7.3[29]), the causation between ocean acidification and metabolic depression is likely overstated, or reassessment using more realistic near-future pH levels is needed.

Dissolution of calcareous structures is commonly believed to occur when Ω is less than 1.[4,24] This "rule" is, however, broken by many calcifiers which not only have maintained or enhanced net calcification when Ω is less than 1, but also reduced net calcification when CO_3^{2-} is highly saturated.[53] The mixed responses among calcifiers simply invalidate the prevalent notion in the ocean acidification literature that calcification or dissolution is driven by Ω.[181] To illustrate dissolution by ocean acidification, some early studies exposed empty shells or skeletons to acidified seawater and measured their weight change after a certain period of time.[81,182] However, this method is inappropriate because the ability of calcifiers to maintain and repair calcareous structures is ignored, thereby overestimating the degree of dissolution.[73] In the ocean acidification literature, dissolution due to reduced seawater pH or Ω appears to be overused as the only reason to account for any damage or increased porosity in calcareous structures, as suggested in the early paradigm.[6,24] In view of dissolution kinetics, pure $CaCO_3$ is practically insoluble in seawater even at pH 7.8 (weakly alkaline) due to its very low solubility ($K_{sp} = 4.39 \times 10^{-7}$),[183] which explains the persistence of calcareous structures in natural habitats over a geological time.[184] Instead of being directly "dissolved" by acidified seawater, substantially overlooked in the literature is shell or skeletal degradation by bacteria that consume organic matter (e.g., organic coatings or intercrystallite organic matrix) as the carbon source for oxidation. This microbial process creates an acidic microenvironment and eventually leads to carbonate dissolution and microboring on calcareous structures.[185,186] Since ocean acidification can alter microbial community structures,[187] whether it can accelerate bacterial-induced carbonate degradation and account for dissolution of calcareous structures deserves in-depth investigations.

Our meta-analysis shows that planktonic calcifiers, such as coccolithophores and larvae, are generally more susceptible than other groups of calcifiers to ocean acidification, possibly due to their larger surface area to volume ratio that makes them more prone to the direct contact with acidified seawater. Coccolithophores, especially *Emiliania huxleyi*, are important to geochemical cycles and trophic dynamics in oceans, but their growth and calcification would be impaired by ocean acidification based on the results of laboratory studies. However, a study using data from the Continuous Plankton Recorder revealed an optimistic finding that the occurrence of coccolithophores in the North Atlantic increased by up to 20% from 1965 to 2010, where increasing CO_2 concentrations is the best predictor of their facilitated growth.[188] In addition, the response of coccolithophores to ocean acidification is strain-dependent. For example, *E. huxleyi* with "over-calcified" strains is resistant to near-future ocean acidification with respect to growth and calcification performance.[189] As such, it is intriguing to examine whether this morphotype will become more dominant in the acidifying ocean so that the populations and ecological contributions of coccolithophores can be maintained. The higher vulnerability of larvae than adults to ocean acidification implies that larval stage would be the bottleneck for population persistence. Yet, more comprehensive investigations are still required to confirm this proposition because nearly all of the previous studies on larvae were conducted in the laboratory. The performance of larvae in the natural environment can be different, which can be demonstrated in a recent study that the larvae of sea urchin *Arbacia lixula* have reduced arm length at pH 7.8 under laboratory conditions, but those developed at natural CO_2 vents (pH 7.33– 7.99) have surprisingly longer arms.[190] On the other hand, most marine invertebrate larvae are highly mobile, meaning that they have opportunities to locate refugia (e.g., diffusive boundary layers) to avoid contact with acidified bulk seawater. Indeed, a recent study showed indiscernible effects of ocean acidification at pH 7.5 on larval settlement and juvenile growth of sea urchin *Pseudechinus huttoni* due to the presence of diffusive boundary layers created by coralline algae.[191] Without considering how larvae behave and interact with other components (e.g., biofilms, macroalgae, etc.) in natural habitats, the notion that ocean acidification is devastating to calcifiers in their early life stages can be wrong.

Corals are considered susceptible to ocean acidification, which can be underpinned by the reduced growth and calcification in our meta-analysis. These observations are also reported in a previous meta-analysis.[37] Indeed, it is forecast that global net carbonate production by coral reefs will be lowered by 156% under RCP8.5 by the end of this century, possibly driven by bleaching events.[192] Nevertheless, carbonate production can be subject to geographical locations as a recent meta-analysis shows that calcification of corals in the Caribbean region is unaffected by ocean acidification.[193] This unexpected resistance of corals to ocean acidification has also been shown in

some meta-analyses. For example, Wittmann and Pörtner[194] found that only 38.5% of extant coral species are sensitive to end-of-century CO_2 levels projected under RCP6.0; Klein et al.[195] detected only a 9.2% decline in calcification under the most pessimistic RCP8.5 scenario, and suggested that temperature plays a more important role than seawater pH in coral calcification. Regardless of the underlying mechanisms, these seemingly counter-intuitive findings further substantiate that seawater Ω is not a key factor driving calcification. The negative effect of ocean acidification on coral calcification observed in our and previous meta-analyses[37] can result from the predominant use of coral nubbins for experimentation, which may not reflect the response of corals in the natural environment. In fact, corals naturally exist in colonies that have a capacity to alleviate the impacts of ocean acidification. For instance, light calcification of coral *Pocillopora verrucose* is boosted by 23% under ocean acidification when densely aggregated to create a small-scale refugium.[196] This observation supports the results from an in situ experiment where maintaining high living coral cover can help mitigate skeletal dissolution caused by ocean acidification.[197] More studies are needed to ascertain whether corals and other calcifiers can increase their resilience to ocean acidification through conspecific or heterospecific aggregation.

Our meta-analysis is mainly sourced from short-term studies (typically less than 3 months) using simple experimental designs, which tend to inflate the negative effects of ocean acidification. Apart from this, the widespread use of the most extreme RCP scenario of CO_2 emissions (i.e., RCP8.5) for experimentation also increases the likelihood to observe negative effects. Nevertheless, non-negative effects to near-future ocean acidification are still dominant in terms of growth and calcification across various taxa. The proportion of non-negative effects would be higher when different types of compensatory mechanisms (see Section 5) are considered and included in the experimental design. Thus, we are cautiously optimistic to suggest that many calcifiers would be able to persist in the acidifying ocean since their short life cycles allow them to acclimatize to the gradual change in seawater carbonate chemistry caused by anthropogenic CO_2 emissions. Calcifiers are constantly experiencing large fluctuations of seawater pH in their habitats,[165] which can also promote their acclimation capacity to ocean acidification. As such, many calcifiers are "surprisingly" found to persist in the naturally CO_2-acidified environment without any defects.[102,164,198–202] Overall, we expect that calcifiers with limited acclimation capacity (e.g., some coccolithophores, coralline algae and corals[194,203,204]) could be substantially impacted or even eliminated by ocean acidification, but many calcifiers could evolve and survive in the changing ocean so that the stability and integrity of marine ecosystems are sustained.

Although this review brings greater optimism about the fate of calcifiers in future oceans, it is important to highlight that some of them (e.g., gastropods, bivalves, and crustaceans) live in coastal habitats, which are subject to coastal acidification. Unlike open oceans, seawater in coastal habitats can be severely acidified with large pH fluctuations due to intense biological and anthropogenic activities.[23,205] The highly acidified seawater can undermine the compensatory mechanisms of calcifiers and lead to adverse effects. For example, feeding performance of intertidal gastropod *Nassarius festivus* is maintained at pH 7.5, but greatly worsened at pH 7.0 possibly due to metabolic depression and impaired chemoreception;[206] estuarine acidification (≈pH 6.80) reduces shell strength of intertidal oyster *Saccostrea glomerata*, and hence increases its vulnerability to predation by gastropod *Morula marginalba*.[207] While coastal acidification is usually transient, calcifiers generally show intensified negative responses to extreme acidification, which can be supported by our meta-analysis. This suggests that the fitness of coastal calcifiers would be impacted if they cannot recover from the short-term exposure to coastal acidification. Therefore, conservation efforts should focus on those calcifiers impacted by coastal acidification due to their repeated exposure to extremely acidified seawater. Regulation of human activities (e.g., agricultural practices) can help reduce the degree of coastal acidification and hence its impacts on coastal organisms.

7. Future Directions for Ocean Acidification Research

The global concern raised over ocean acidification has galvanized a substantial number of studies over the last two decades. Most of them were conducted in the laboratory, where calcifiers were typically exposed to CO_2-manipulated seawater for a certain period of time, followed by measuring their biological responses. Physiological parameters, such as growth, calcification, photosynthesis, and respiration, were frequently measured to indicate the effects of ocean acidification. Despite the important insights offered, one of the major shortcomings of most previous studies is the lack of habitat complexity in the experimental design (e.g., only seawater and calcifiers included in the system), making the results less ecologically relevant. The static seawater pH manipulated in most previous studies is also unnatural and can elicit additional stress to marine organisms (see Section 5.8.). Furthermore, a majority of previous experiments were short-term (typically less than 3 months), possibly due to logistical and financial constraints. These short-term studies might have overstated the negative effects of ocean acidification as the acclimation capacity of calcifiers, especially via transgenerational plasticity, was overlooked. To evaluate the impacts of ocean acidification on calcifiers more realistically with broader perspectives, the experimental design in future studies should be improved to incorporate broader and more comprehensive sets of species, experimental duration, and environmental relevance:

- Coccolithophores, calcifying algae, corals, bivalves, and sea urchins have been intensively studied, whereas calcifiers that are considered tolerant to ocean acidification (e.g., barnacles, shrimps, crabs, and cephalopods) are underexplored by comparison. Without a more balanced number of observations across various taxa in the literature, it is premature to draw a general conclusion that ocean acidification is detrimental to calcifiers.[39,179] More studies on tolerant taxa are needed to shed light on the potential mechanisms offering calcifiers with resistance to ocean acidification.
- Results from short-term CO_2 perturbation experiments poorly represent the effects of ocean acidification because

calcifiers may be able to acclimate to the gradual change in seawater pH. Instead, these results indicate the shock response of calcifiers as their adaptive potential is neglected (e.g., via physiological or genetic adaptation). Although it is impractical to simulate the slow rate of pH change based on the predicted increase in CO_2 concentrations over time, the exposure duration of experiments should be lengthened (e.g., ≈50% life span of organisms) to ensure that the acclimation capacity of calcifiers is taken into consideration.

- Most marine organisms have a biphasic life cycle, switching between larvae and adults. Whether the environmental stress experienced in the early life stage can be carried over to the subsequent one (i.e., carry-over effect[208,209]) remains largely unexplored in ocean acidification research. Carry-over effect can occur in the natural environment due to diel/seasonal pH fluctuations. Unlike carry-over effect, studies on transgenerational effect are more available in the literature, but most of them work on bivalves and sea urchins. More taxa should be studied in the future to have an unbiased conclusion about the adaptive value of transgenerational plasticity.
- To make experimental designs more ecologically relevant, all factors in natural habitats (e.g., pH fluctuations, day-night cycles, substratum, habitat-forming species, etc.) should be incorporated into the system as possible to maximize habitat complexity.[210] This consideration is particularly important for studying coastal organisms, which are constantly exposed to environmental fluctuations that can affect their adaptive plasticity.[211] Field studies, such as using natural CO_2 vents, are highly recommended, but habitat characteristics in addition to seawater carbonate chemistry (e.g., seawater mineral composition, nutrient concentration, light intensity, turbidity, water flow rate, characteristics of substrates, macroalgae, or plants, etc.) should be quantified as possible to minimize the factors that may confound the results.
- A majority of previous studies investigated the effects of ocean acidification on marine organisms by choosing RCP8.5, which is commonly known as the "business-as-usual" scenario. However, this worst-case scenario is increasingly deemed implausible as it does not consider any mitigation policies to regulate CO_2 emissions,[3] and thus overstates the impacts of ocean acidification. To obtain more realistic results, plausible scenarios (e.g., RCP6.0 or RCP4.5) should be chosen for future research.
- Anthropogenic CO_2 emissions will not only cause ocean acidification in the future, but also global warming and more extreme weathers (e.g., heatwaves, heavy downpours, and hurricanes). While we generally realize that the combined effect between ocean acidification and warming on marine organisms is complex,[37,38] how extreme weathers modulate the impacts of ocean acidification on marine organisms remains largely unexplored. In addition, oceans are increasingly impacted by man-made pollutants, such as heavy metals, microplastics and organic pollutants. Whether ocean acidification can influence the toxicity and bioavailability of these pollutants may shed light on the fate of marine organisms; therefore, multiple-stressor research is needed to address this important issue.

Improving experimental designs is a critical step to ensure high quality and ecological relevance of future ocean acidification research. Then, more investigations in the emerging research areas at different levels of biological organization are required to delve into the potential fate of calcifiers as well as the functioning of marine ecosystems in the future (**Figure 7**):

- To date, studies on structural and mineralogical properties of calcareous structures are scant in ocean acidification research (c.f. physiological responses) probably because these studies require the knowledge and technique of other disciplines, especially materials science and geochemistry. Examining whether structural and mineralogical properties (e.g., nanostructures, crystallinity, mineral composition, and carbonate polymorphs) are altered by ocean acidification can shed light on the fitness of calcifiers; therefore, more interdisciplinary studies are needed to broaden the scopes of ocean acidification research.
- At the cellular level, examining molecular responses using multi-omics approaches is encouraged to elucidate the mechanisms accounting for the inconsistent responses of calcifiers to ocean acidification. In particular, shell properties are strongly related to shell proteins and therefore identifying and quantifying the proteins through proteomic analysis can provide novel insights into the shell formation process under ocean acidification.
- Environmental epigenetics is an emerging discipline deserving more investigations in ocean acidification research. Apart from DNA methylation, understanding how other pathways of epigenetic modifications (e.g., histone modification and gene regulation via noncoding RNA) are linked to phenotypic plasticity is of great interest.
- Most marine organisms are not solitary, but live in colonies or groups with conspecifics in their natural habitats. Most previous studies, however, determined the effects of ocean acidification on calcifiers without considering intraspecific interactions (e.g., only one or few individuals used in the system). Intraspecific interactions can modulate the physiology and behavior of calcifiers, possibly alleviating the impacts of ocean acidification.[196] Whether conspecific aggregations help calcifiers counter ocean acidification deserves more investigations.
- It is noteworthy that same species from different populations or geographical locations can respond differently to ocean acidification (i.e., intraspecific variability), subject to the environmental conditions of their habitats.[212–214] It is intriguing to understand if hybridization between populations can facilitate adaptation as gene flow is fundamental to adaptive evolution.[215] Studying hybridization along with transgenerational effect would be a new frontier in ocean acidification research.
- Studies on how species interactions modulate the effects of ocean acidification on calcifiers are recommended. One of the research focus areas is to ascertain whether macroalgal forests or seagrass meadows can act as refugia for calcifiers.[158,216] Predator–prey and microbe–host interactions have received limited attention thus far and more investigations are needed to have holistic insights into the potential

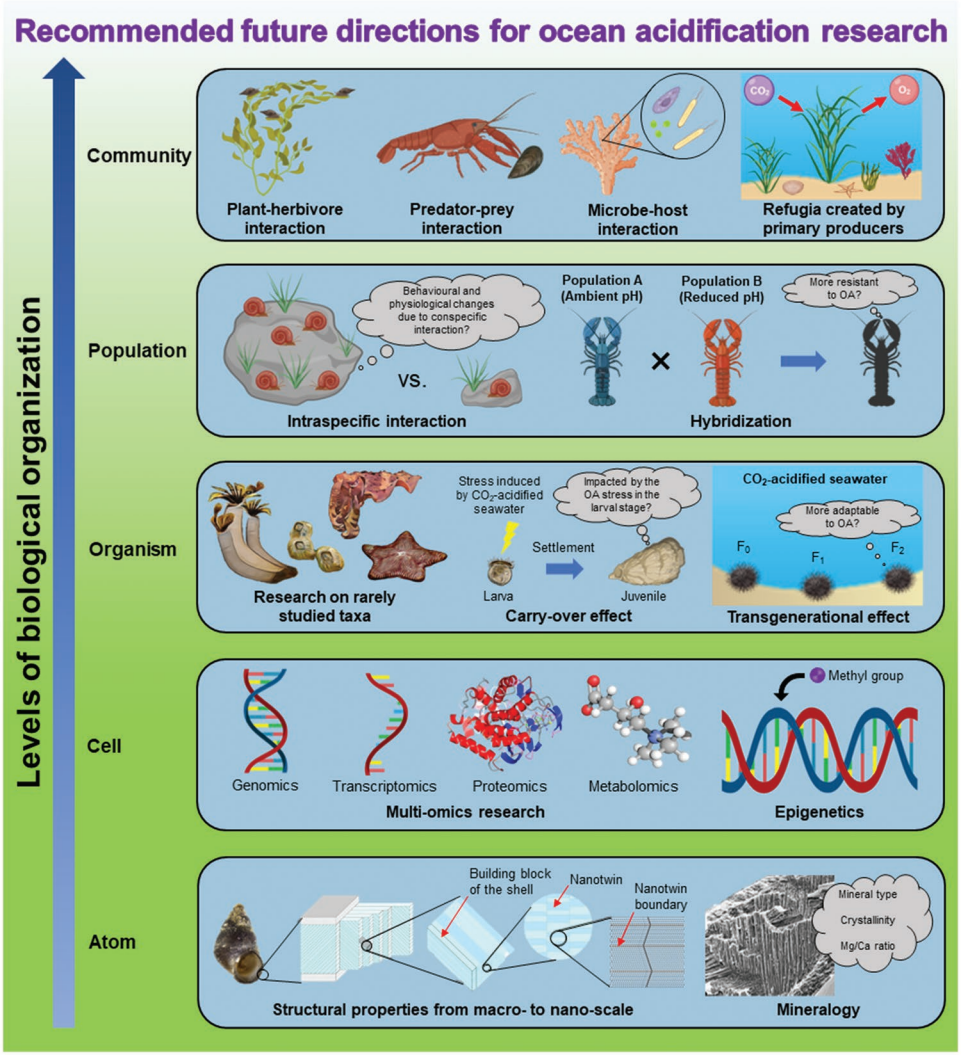

Figure 7. Recommended future directions for ocean acidification research across different levels of biological organization from atom to community.

changes in community structures and energy dynamics of future marine ecosystems.

8. Conclusion

Ocean acidification caused by anthropogenic CO_2 emissions has been regarded as a serious threat to marine organisms worldwide, especially for those constructing calcareous structures for growth and protection. Many early studies indeed demonstrated that ocean acidification can undermine the fitness of calcifiers; however, this notion has been increasingly challenged by evidence showing the persistence of calcifiers in the CO_2-acidified environment. In this regard, we conduct a meta-analysis of 985 relevant studies in the last two decades to re-evaluate the impacts of ocean acidification on calcifiers. Our meta-analysis shows that some taxa (e.g., coccolithophores, calcifying algae, and corals) are sensitive to near-future ocean acidification, whereas many of them appear to be tolerant (e.g., bryozoans, echinoderms, crustaceans, and cephalopods). Calcifiers are more susceptible to ocean acidification at the larval stage than adult stage in general. Furthermore, the observed negative effects of ocean acidification on biological responses are often intensified with an increasing degree of acidification. When near-future ocean acidification is considered, non-negative effects on growth and calcification are widespread among various taxa, implying that ocean acidification would be less deleterious on calcifiers than initially thought. Our take-home message differs from that conveyed in the earlier influential meta-analyses published nearly a decade ago,[37,38] which suggested that ocean acidification is detrimental to a variety of calcifiers. This difference is largely due to the fact that research on the adaptability of calcifiers to ocean acidification had not been the focus until the last 7–8 years;[217] therefore, early studies predominantly reported how calcifiers are stressed by ocean acidification. Apart from the much greater number of studies (985 herein vs 228 in the previous biggest meta-analysis[37]) and multiple acidity levels included, our meta-analysis is more informative and accurate by reporting the effect size of each response variable rather than using response categories

by mixing seemingly related variables (e.g., photosynthetic rate and photosynthetic efficiency).

The resistance of calcifiers to ocean acidification can be mediated by a variety of compensatory mechanisms, such as physiological plasticity, transgenerational adaptation, increased food availability, and species interactions, which highlight the adaptability of calcifiers and the importance of habitat complexity for surviving in the acidifying ocean. It appears to be a misconception in the literature that seawater Ω is the key predictor of calcification because it alone cannot account for the inconsistent responses of calcifiers to ocean acidification. As most of the compensatory mechanisms are fuelled by energy, we propose that calcification is primarily associated with energy budget of calcifiers, which is consistently manifested by the facilitated shell or skeletal growth through increased food availability. In other words, whether calcifiers can maintain energy surplus is fundamental to determining the limit of compensatory mechanisms and thus their fitness in the acidifying ocean.

While ocean acidification is a challenge to the survival of calcifiers, it also brings an opportunity for those with a great acclimation capacity to thrive in the community. Given the benefits of compensatory mechanisms, we are cautiously optimistic that a majority of calcifiers would be able to prevail in the acidifying ocean. The ever-increasing global awareness to mitigate anthropogenic CO_2 emissions in the near future also increases the likelihood of this scenario. We expect that calcifiers with a limited acclimation capacity would inevitably be eliminated by ocean acidification, but their ecological roles would be taken over by tolerant calcifiers so that the functioning of marine ecosystems can be sustained. Despite the research effort over the last two decades, there are still lots of uncertainties about the actual effects of ocean acidification on calcifiers as most previous studies were laboratory-based using simple experimental designs and focused on individual responses. In the future, studying individual responses is still necessary, but research on intra- and inter-specific interactions by employing ecologically relevant experimental designs should be emphasized more (see Section 7). This allows a more realistic, holistic evaluation of the fitness and survival of calcifiers under ocean acidification.

To date, literature and media disproportionately report the negative effects of ocean acidification by using emotive language (e.g., "rapid dissolution," "corrosive seawater," "evil twin," "deadly trio," "global calamity," "acidification apocalypse," etc.), which can draw public attention, but lead to perception bias. By increasingly acknowledging the results from studies using sophisticated experimental designs with realistic ecological complexity, we highlight the importance of considering mechanisms that allow calcifiers to accommodate ocean acidification. While this review draws attention to conflicting observations about the potential fate of calcifiers in the future, it represents a powerful set of observations for the advancement of knowledge into mechanisms of the persistence of calcifiers under ocean acidification. Furthermore, this review not only offers a critical re-evaluation of the types of hypotheses being tested, but also of the methods being used so that future research will not be constrained within the paradigm of negative effects. In the forthcoming era of ocean acidification research, therefore, studying how marine organisms persist is as important as studying how they perish.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] K. Caldeira, M. E. Wickett, *J. Geophys. Res.: Oceans* **2005**, *110*, C09S4.
[2] IPCC, *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*, (Eds: T. F. Stocker, D. Qin, G.-K. Plattner, M. Tignor, S. K. Allen, J. Boschung, A. Nauels, Y. Xia, V. Bex, P. M. Midgley), Cambridge University Press, Cambridge **2013**, pp. 1585.
[3] Z. Hausfather, G. P. Peters, *Nature* **2020**, *577*, 618.
[4] S. C. Doney, V. J. Fabry, R. A. Feely, J. A. Kleypas, *Annu. Rev. Mar. Sci.* **2009**, *1*, 169.
[5] R. A. Feely, C. L. Sabine, K. Lee, W. Berelson, J. Kleypas, V. J. Fabry, F. J. Millero, *Science* **2004**, *305*, 362.
[6] J. C. Orr, V. J. Fabry, O. Aumont, L. Bopp, S. C. Doney, R. A. Feely, A. Gnanadesikan, N. Gruber, A. Ishida, F. Joos, R. M. Key, K. Lindsay, E. Maier-Reimer, R. Matear, P. Monfray, A. Mouchet, R. G. Najjar, G. K. Plattner, K. B. Rodgers, C. L. Sabine, J. L. Sarmiento, R. Schlitzer, R. D. Slater, I. J. Totterdell, M. F. Weirig, Y. Yamanaka, A. Yool, *Nature* **2005**, *437*, 681.
[7] F. Prada, E. Caroselli, S. Mengoli, L. Brizi, P. Fantazzini, B. Capaccioni, L. Pasquini, K. E. Fabricius, Z. Dubinsky, G. Falini, S. Goffredo, *Sci. Rep.* **2017**, *7*, 40842.
[8] L. Porzio, M. C. Buia, V. Ferretti, M. Lorenti, M. Rossi, M. Trifuoggi, A. Vergara, C. Arena, *Sci. Total Environ.* **2018**, *628-629*, 375.
[9] S. Viotti, C. Sangil, C. A. Hernández, J. C. Hernández, *Mar. Environ. Res.* **2019**, *152*, 104789.
[10] T. Biscéré, M. Zampighi, A. Lorrain, S. Jurriaans, A. Foggo, F. Houlbrèque, R. Rodolfo-Metalpa, *Biol. Lett.* **2019**, *15*, 20180777.
[11] A. Oprandi, M. Montefalcone, C. Morri, F. Benelli, C. N. Bianchi, *Estuarine, Coastal Shelf Sci.* **2019**, *217*, 158.

[12] J. Y. S. Leung, Y. Chen, I. Nagelkerken, S. Zhang, Z. Xie, S. D. Connell, *Small* **2020**, *16*, 2003186.
[13] H. Kurihara, Y. Suhara, I. Mimura, Y. Golbuu, *Front. Mar. Sci.* **2020**, *7*, 581160.
[14] S. Di Giglio, D. Spatafora, M. Milazzo, S. M'Zoudi, D. Zito, P. Dubois, C. Costa, *Sci. Total Environ.* **2020**, *720*, 137443.
[15] S. G. Klein, A. Steckbauer, C. M. Duarte, *Global Change Biol.* **2020**, *26*, 355.
[16] C. A. Vargas, P. Y. Contreras, C. A. Pérez, M. Sobarzo, G. S. Saldías, J. Salisbury, *J. Geophys. Res.: Biogeosci.* **2016**, *121*, 1468.
[17] F. Chan, J. A. Barth, C. A. Blanchette, R. H. Byrne, F. Chavez, O. Cheriton, R. A. Feely, G. Friederich, B. Gaylord, T. Gouhier, S. Hacker, T. Hill, G. Hofmann, M. A. McManus, B. A. Menge, K. J. Nielsen, A. Russell, E. Sanford, J. Sevadjian, L. Washburn, *Sci. Rep.* **2017**, *7*, 2526.
[18] C. Sánchez-Noguera, I. Stuhldreier, J. Cortés, C. Jiménez, Á. Morales, C. Wild, T. Rixen, *Biogeosciences* **2018**, *15*, 2349.
[19] K. G. Schulz, S. Hartley, B. Eyre, *Front. Mar. Sci.* **2019**, *6*, 636.
[20] M. G. Sreeush, S. Rajendran, V. Valsala, S. Pentakota, K. Prasad, R. Murtugudde, *Mar. Chem.* **2019**, *209*, 14.
[21] A. L. Strong, K. J. Kroeker, L. T. Teneva, L. A. Mease, R. P. Kelly, *BioScience* **2014**, *64*, 581.
[22] G. G. Waldbusser, J. E. Salisbury, *Annu. Rev. Mar. Sci.* **2014**, *6*, 221.
[23] J. Carstensen, C. M. Duarte, *Environ. Sci. Technol.* **2019**, *53*, 4020.
[24] V. J. Fabry, B. A. Seibel, R. A. Feely, J. C. Orr, *ICES J. Mar. Sci.* **2008**, *65*, 414.
[25] H. O. Pörtner, *Mar. Ecol.: Prog. Ser.* **2008**, *373*, 203.
[26] U. Riebesell, I. Zondervan, B. Rost, P. D. Tortell, R. E. Zeebe, F. M. M. Morel, *Nature* **2000**, *407*, 364.
[27] F. Marubini, C. Ferrier-Pages, J. P. Cuif, *Proc. R. Soc. B* **2003**, *270*, 179.
[28] Y. Shirayama, H. Thornton, *J. Geophys. Res.* **2005**, *110*, C09S08.
[29] B. Michaelidis, C. Ouzonuis, A. Paleras, H. O. Pörtner, *Mar. Ecol.: Prog. Ser.* **2005**, *293*, 109.
[30] H. M. Welladsen, P. C. Southgate, K. Heimann, *Molluscan Res.* **2010**, *30*, 125.
[31] S. Sinutok, R. Hill, M. A. Doblin, R. Wuhrer, P. J. Ralph, *Limnol. Oceanogr.* **2011**, *56*, 1200.
[32] V. B. S. Chan, C. Li, A. C. Lane, Y. Wang, X. Lu, K. Shih, T. Zhang, V. Thiyagarajan, *PLoS One* **2012**, *7*, e42718.
[33] H. Kurihara, Y. Shirayama, *Mar. Ecol.: Prog. Ser.* **2004**, *274*, 161.
[34] S. Dupont, J. Havenhand, W. Thorndyke, L. Peck, M. Thorndyke, *Mar. Ecol.: Prog. Ser.* **2008**, *373*, 285.
[35] S. C. Talmage, C. J. Gobler, *Limnol. Oceanogr.* **2009**, *54*, 2072.
[36] L. M. Parker, P. M. Ross, W. A. O'Connor, *Mar. Biol.* **2010**, *157*, 2435.
[37] K. J. Kroeker, R. L. Kordas, R. Crim, I. E. Hendriks, L. Ramajo, G. S. Singh, C. M. Duarte, J. P. Gattuso, *Global Change Biol.* **2013**, *19*, 1884.
[38] B. P. Harvey, D. Gwynn-Jones, P. J. Moore, *Ecol. Evol.* **2013**, *3*, 1016.
[39] C. M. Duarte, R. W. Fulweiler, C. E. Lovelock, P. Martinetto, M. I. Saunders, J. M. Pandofi, S. Gelcich, S. W. Nixon, *BioScience* **2015**, *65*, 130.
[40] H. Kurihara, S. Kato, A. Ishimatsu, *Aquat. Biol.* **2007**, *1*, 91.
[41] E. Beniash, A. Ivanina, N. S. Lieb, I. Kurochkin, I. M. Sokolova, *Mar. Ecol.: Prog. Ser.* **2010**, *419*, 95.
[42] C. E. Cornwall, C. L. Hurd, *ICES J. Mar. Sci.* **2016**, *73*, 572.
[43] K. Fujita, M. Hikami, A. Suzuki, A. Kuroyanagi, K. Sakai, H. Kawahata, Y. Nojiri, *Biogeosciences* **2011**, *8*, 2089.
[44] F. Melzner, P. Stange, K. Trübenbach, J. Thomsen, I. Casties, U. Panknin, S. N. Gorb, M. A. Gutowska, *PLoS One* **2011**, *6*, e24223.
[45] T. Biscéré, R. Rodolfo-Metalpa, A. Lorrain, L. Chauvaud, J. Thébault, J. Clavier, F. Houlbrèque, *PLoS One* **2015**, *10*, e0122898.
[46] S. Uthicke, T. Ebert, M. Liddy, C. Johansson, K. E. Fabricius, M. Lamare, *Global Change Biol.* **2016**, *22*, 2451.
[47] J. Kavousi, J. D. Reimer, Y. Tanaka, T. Nakamura, *Mar. Environ. Res.* **2015**, *109*, 9.
[48] F. Scherner, C. M. Pereira, G. Duarte, P. A. Horta, C. B. Castro, J. B. Barufi, S. M. B. Pereira, *PLoS One* **2016**, *11*, e0154844.
[49] M. Collard, S. P. S. Rastrick, P. Calosi, Y. Demolder, J. Dille, H. S. Findlay, J. M. Hall-Spencer, M. Milazzo, L. Moulin, S. Widdicombe, F. Dehairs, P. Dubois, *ICES J. Mar. Sci.* **2016**, *73*, 727.
[50] J. Y. S. Leung, B. D. Russell, S. D. Connell, *Sci. Total Environ.* **2020**, *715*, 136939.
[51] M. Y. Roleda, P. W. Boyd, C. L. Hurd, *J. Phycol.* **2012**, *48*, 840.
[52] T. Toyofuku, M. Y. Matsuo, L. J. de Nooijer, Y. Nagai, S. Kawada, K. Fujita, G. J. Reichart, H. Nomaki, M. Tsuchiya, H. Sakaguchi, H. Kitazato, *Nat. Commun.* **2017**, *8*, 14145.
[53] J. B. Ries, A. L. Cohen, D. C. McCorkle, *Geology* **2009**, *37*, 1131.
[54] U. Riebesell, V. J. Fabry, L. Hansson, J. P. Gattuso, *Guide to Best Practices for Ocean Acidification Research and Data Reporting*, European Union, Luxembourg **2011**.
[55] M. Borenstein, L. V. Hedges, J. P. T. Higgins, H. R. Rothstein, *Introduction to Meta-Analysis*, John Wiley & Sons, Hoboken **2009**.
[56] J. Koricheva, J. Gurevitch, K. Mengersen, *Handbook of Meta-Analysis in Ecology and Evolution*, Princeton University Press, Princeton **2013**.
[57] M. Borenstein, L. V. Hedges, J. P. T. Higgins, H. R. Rothstein, *Res. Synth. Methods* **2010**, *1*, 97.
[58] J. Lau, J. P. A. Ioannidis, N. Terrin, C. H. Schmid, I. Olkin, *BMJ* **2006**, *333*, 597.
[59] M. S. Clark, L. S. Peck, J. Arivalagan, T. Backeljau, S. Berland, J. C. R. Cardoso, C. Caurcel, G. Chapelle, M. De Noia, S. Dupont, K. Gharbi, J. I. Hoffman, K. S. Last, A. Marie, F. Melzner, K. Michalek, J. Morris, D. M. Power, K. Ramesh, T. Sanders, K. Sillanpää, V. A. Sleight, P. J. Stewart-Sinclair, K. Sundell, L. Telesca, D. L. J. Vendrami, A. Ventura, T. A. Wilding, T. Yarra, E. M. Harper, *Biol. Rev.* **2020**, *95*, 1812.
[60] A. R. Palmer, *Proc. Natl. Acad. Sci. USA* **1992**, *89*, 1379.
[61] C. Spalding, S. Finnegan, W. W. Fischer, *Global Biogeochem. Cycles* **2017**, *31*, 866.
[62] E. K. Towle, I. C. Enochs, C. Langdon, *PLoS One* **2015**, *10*, e0123394.
[63] L. Ramajo, N. Marba, L. Prado, S. Peron, M. A. Lardies, A. B. Rodriguez-Navarro, C. A. Vargas, N. A. Lagos, C. M. Duarte, *Global Change Biol.* **2016**, *22*, 2025.
[64] J. Y. S. Leung, I. Nagelkerken, B. D. Russell, C. M. Ferreira, S. D. Connell, *Sci. Total Environ.* **2018**, *639*, 360.
[65] M. E. Blicher, S. Rysgaard, M. K. Sejr, *Mar. Ecol.: Prog. Ser.* **2010**, *407*, 71.
[66] A. Aguirre-Velarde, F. Jean, G. Thouzeau, J. Flye-Sainte-Marie, *J. Sea Res.* **2018**, *131*, 85.
[67] J. Y. S. Leung, N. K. M. Cheung, *Biogeosciences* **2018**, *15*, 3267.
[68] J. B. Ries, *Geochim. Cosmochim. Acta* **2011**, *75*, 4053.
[69] D. Zoccola, E. Tambutté, E. Kulhanek, S. Puverel, J. C. Scimeca, D. Allemand, S. Tambutté, *Biochim. Biophys. Acta* **2004**, *1663*, 117.
[70] S. Comeau, E. Tambutté, R. C. Carpenter, P. J. Edmunds, N. R. Evensen, D. Allemand, C. Ferrier-Pagès, S. Tambutté, A. A. Venn, *Proc. R. Soc. B* **2017**, *284*, 20161669.
[71] A. R. Taylor, A. Chrachri, G. Wheeler, H. Goddard, C. Brownlee, *PLoS Biol.* **2011**, *9*, e1001085.
[72] A. A. Venn, E. Tambutté, M. Holcomb, J. Laurent, D. Allemand, S. Tambutté, *Proc. Natl. Acad. Sci. USA* **2013**, *10*, 1634.
[73] F. Melzner, F. C. Mark, B. A. Seibel, L. Tomanek, *Annu. Rev. Mar. Sci.* **2020**, *12*, 499.
[74] V. Schoepf, C. P. Jury, R. J. Toonen, M. T. McCulloch, *Proc. R. Soc. B* **2017**, *284*, 20172117.
[75] M. Wall, J. Fietzke, G. M. Schmidt, A. Fink, L. C. Hofmann, D. de Beer, K. E. Fabricius, *Sci. Rep.* **2016**, *6*, 30688.

[76] L. Zhao, B. R. Schöne, R. Mertz-Kraus, F. Yang, *J. Exp. Mar. Biol. Ecol.* **2017**, *486*, 148.
[77] Y. W. Liu, J. N. Sutton, J. B. Ries, R. A. Eagle, *Sci. Adv.* **2020**, *6*, eaax1314.
[78] M. Stumpp, M. Y. Hu, F. Melzner, M. A. Gutowska, N. Dorey, N. Himmerkus, W. C. Holtmann, S. T. Dupont, M. C. Thorndyke, M. Bleich, *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 18192.
[79] K. Ramesh, M. Y. Hu, J. Thomsen, M. Bleich, F. Melzner, *Nat. Commun.* **2017**, *8*, 1709.
[80] T. M. DeCarlo, S. Comeau, C. E. Cornwall, M. T. McCulloch, *Proc. R. Soc. B* **2018**, *285*, 20180564.
[81] S. Nienhuis, A. R. Palmer, C. D. G. Harley, *Proc. R. Soc. B* **2010**, *277*, 2553.
[82] N. Bednaršek, G. A. Tarling, D. C. E. Bakker, S. Fielding, A. Cohen, A. Kuzirian, D. McCorkle, B. Lézé, R. Montagna, *Global Change Biol.* **2012**, *18*, 2378.
[83] J. Y. S. Leung, B. D. Russell, S. D. Connell, *Environ. Sci. Technol.* **2017**, *51*, 2652.
[84] A. Duquette, J. B. McClintock, C. D. Amsler, A. Pérez-Huerta, M. Milazzo, J. M. Hall-Spencer, *Mar. Pollut. Bull.* **2017**, *124*, 917.
[85] J. B. Ries, *J. Exp. Mar. Biol. Ecol.* **2011**, *403*, 54.
[86] E. M. Harper, T. J. Palmer, J. R. Alphey, *Geol. Mag.* **1997**, *134*, 403.
[87] M. Hautmann, *Facies* **2006**, *52*, 417.
[88] M. C. Nash, B. N. Opdyke, U. Troitzsch, B. D. Russell, W. H. Adey, A. Kato, D. I. Kline, *Nat. Clim. Change* **2013**, *3*, 268.
[89] M. C. Nash, S. Uthicke, A. P. Negri, N. E. Cantin, *Biogeosciences* **2015**, *12*, 5247.
[90] G. Diaz-Pulido, M. C. Nash, K. R. N. Anthony, D. Bender, B. N. Opdyke, C. Reyes-Nivia, U. Troitzsch, *Nat. Commun.* **2014**, *5*, 3310.
[91] A. J. Andersson, F. T. Mackenzie, N. R. Bates, *Mar. Ecol.: Prog. Ser.* **2008**, *373*, 265.
[92] H. Egilsdottir, F. Noisette, L. M. Noel, J. Olafsson, S. Martin, *Mar. Biol.* **2013**, *160*, 2103.
[93] F. Ragazzola, L. Foster, C. Jones, T. B. Scott, J. Fietzke, M. R. Kilburn, D. N. Schmidt, *Sci. Rep.* **2016**, *6*, 20572.
[94] V. B. S. Chan, V. Thiyagarajan, X. W. Lu, T. Zhang, K. Shih, *PLoS One* **2013**, *8*, e78945.
[95] J. Y. S. Leung, S. D. Connell, I. Nagelkerken, B. D. Russell, *Environ. Sci. Technol.* **2017**, *51*, 12097.
[96] S. Weiner, L. Addadi, *Annu. Rev. Mater. Res.* **2011**, *41*, 21.
[97] L. Addadi, D. Joester, F. Nudelman, S. Weiner, *Chem. - Eur. J.* **2006**, *12*, 980.
[98] E. Beniash, J. Aizenberg, L. Addadi, S. Weiner, *Proc. R. Soc. B* **1997**, *264*, 461.
[99] I. M. Weiss, N. Tuross, L. Addadi, S. Weiner, *J. Exp. Zool.* **2002**, *293*, 478.
[100] S. C. Fitzer, M. Cusack, V. R. Phoenix, N. A. Kamenos, *J. Struct. Biol.* **2014**, *188*, 39.
[101] S. C. Fitzer, P. Chung, F. Maccherozzi, S. S. Dhesi, N. A. Kamenos, V. R. Phoenix, M. Cusack, *Sci. Rep.* **2016**, *6*, 21076.
[102] J. Y. S. Leung, Z. A. Doubleday, I. Nagelkerken, Y. Chen, Z. Xie, S. D. Connell, *Proc. R. Soc. B* **2019**, *286*, 20190757.
[103] Y. A. Shin, S. Yin, X. Li, S. Lee, S. Moon, J. Jeong, M. Kwon, S. J. Yoo, Y. Kim, T. Zhang, H. Gao, S. H. Oh, *Nat. Commun.* **2016**, *7*, 10772.
[104] P. Fantazzini, S. Mengoli, L. Pasquini, V. Bortolotti, L. Brizi, M. Mariani, M. Di Giosia, S. Fermani, B. Capaccioni, E. Caroselli, F. Prada, F. Zaccanti, O. Levy, Z. Dubinsky, J. A. Kaandorp, P. Konglerd, J. U. Hammel, Y. Dauphin, J. P. Cuif, J. C. Weaver, K. E. Fabricius, W. Wagermaier, P. Fratzl, G. Falini, S. Goffredo, *Nat. Commun.* **2015**, *6*, 7785.
[105] S. Johnson, J. Harianto, M. Thomson, M. Byrne, *J. Exp. Mar. Biol. Ecol.* **2020**, *523*, 151250.
[106] E. Chatzinikolaou, K. Keklikoglou, P. Grigoriou, *Front. Mar. Sci.* **2021**, *8*, 645660.
[107] K. Stemmer, G. Nehrke, T. Brey, *PLoS One* **2013**, *8*, e70106.
[108] S. Milano, B. R. Schöne, S. Wang, W. E. Müller, *Mar. Environ. Res.* **2016**, *119*, 144.
[109] K. M. Barclay, B. Gaylord, B. M. Jellison, P. Shukla, E. Sanford, L. R. Leighton, *Mar. Ecol.: Prog. Ser.* **2019**, *626*, 109.
[110] K. M. Barclay, M. K. Gingras, S. T. Packer, L. R. Leighton, *Mar. Environ. Res.* **2020**, *162*, 105105.
[111] E. Cross, E. M. Harper, L. S. Peck, *Environ. Sci. Technol.* **2019**, *53*, 5016.
[112] V. L. Peck, R. L. Oakes, E. M. Harper, C. Manno, G. A. Tarling, *Nat. Commun.* **2018**, *9*, 264.
[113] S. C. Fitzer, L. Vittert, A. Bowman, N. A. Kamenos, V. R. Phoenix, M. Cusack, *Ecol. Evol.* **2015**, *5*, 4875.
[114] V. Garilli, R. Rodolfo-Metalpa, D. Scuderi, L. Brusca, D. Parrinello, S. P. S. Rastrick, A. Foggo, R. J. Twitchett, J. M. Hall-Spencer, M. Milazzo, *Nat. Clim. Change* **2015**, *5*, 678.
[115] R. J. Twitchett, *Palaeogeogr., Palaeoclimatol., Palaeoecol.* **2007**, *252*, 132.
[116] F. Marin, N. L. e Roy, B. Marie, *Front. Biosci.* **2012**, *4*, 1099.
[117] K. M. Kocot, F. Aguilera, C. McDougall, D. J. Jackson, B. M. Degnan, *Front. Zool.* **2016**, *13*, 23.
[118] A. P. Jackson, J. F. V. Vincent, R. M. Turner, *Proc. R. Soc. B* **1988**, *234*, 415.
[119] R. Rodolfo-Metalpa, F. Houlbrèque, É. Tambutté, F. Boisson, C. Baggini, F. P. Patti, R. Jeffree, M. Fine, A. Foggo, J. P. Gattuso, J. M. Hall-Spencer, *Nat. Clim. Change* **2011**, *1*, 308.
[120] V. Tunnicliffe, K. T. A. Davies, D. A. Butterfield, R. W. Embley, J. M. Rose, W. W. Chadwick, *Nat. Geosci.* **2009**, *2*, 344.
[121] L. Telesca, L. S. Peck, T. Sanders, J. Thyrring, M. K. Sejr, E. M. Harper, *Global Change Biol.* **2019**, *25*, 4179.
[122] K. Ramesh, T. Yarra, M. S. Clark, U. John, F. Melzner, *Ecol. Evol.* **2019**, *9*, 7157.
[123] J. Vidal-Dupiol, D. Zoccola, E. Tambutté, C. Grunau, C. Cosseau, K. M. Smith, M. Freitag, N. M. Dheilly, D. Allemand, S. Tambutté, *PLoS One* **2013**, *8*, e58652.
[124] S. Li, C. Liu, J. Huang, Y. Liu, S. Zhang, G. Zheng, L. Xie, R. Zhang, *Sci. Rep.* **2016**, *6*, 18943.
[125] S. C. Fitzer, V. R. Phoenix, M. Cusack, N. A. Kamenos, *Sci. Rep.* **2014**, *4*, 6218.
[126] L. C. Hofmann, G. Yildiz, D. Hanelt, K. Bischof, *Mar. Biol.* **2012**, *159*, 783.
[127] K. D. Hoadley, D. T. Pettay, A. G. Grottoli, W. J. Cai, T. F. Melman, V. Schoepf, X. Hu, Q. Li, H. Xu, Y. Wang, Y. Matsui, J. H. Baumann, M. E. Warner, *Sci. Rep.* **2015**, *5*, 18371.
[128] A. V. Ivanina, G. H. Dickinson, O. B. Matoo, R. Bagwe, A. Dickinson, E. Beniash, I. M. Sokolova, *Comp. Biochem. Physiol., Part A: Mol. Integr. Physiol.* **2013**, *166*, 101.
[129] P. Kaniewska, C. K. K. Chan, D. Kline, E. Y. S. Ling, N. Rosic, D. Edwards, O. Hoegh-Guldberg, S. Dove, *PLoS One* **2015**, *10*, e0139223.
[130] X. Yuan, T. Yuan, H. Huang, L. Jiang, W. Zhou, S. Liu, *Sci. Rep.* **2018**, *8*, 2787.
[131] A. E. Maas, G. L. Lawson, A. M. Tarrant, *Comp. Biochem. Physiol., Part D: Genomics Proteomics* **2015**, *16*, 1.
[132] A. Hüning, F. Melzner, J. Thomsen, M. A. Gutowska, L. Krämer, S. Frickenhaus, P. Rosenstiel, H. O. Pörtner, E. E. R. Philipp, M. Lucassen, *Mar. Biol.* **2013**, *160*, 1845.
[133] G. E. Hofmann, *Front. Mar. Sci* **2017**, *4*, 4.
[134] J. M. Eirin-Lopez, H. M. Putnam, *Annu. Rev. Mar. Sci.* **2019**, *11*, 335.
[135] Y. K. Lim, K. Cheung, X. Dang, S. B. Roberts, X. Wang, V. Thiyagarajan, *Mar. Environ. Res.* **2021**, *163*, 105214.

[136] Y. J. Liew, D. Zoccola, Y. Li, E. Tambutté, A. A. Venn, C. T. Michell, G. Cui, E. S. Deutekom, J. A. Kaandorp, C. R. Voolstra, S. Forêt, D. Allemand, S. Tambutté, M. Aranda, *Sci. Adv.* **2018**, *4*, eaar8028.
[137] P. M. Ross, L. Parker, M. Byrne, *ICES J. Mar. Sci.* **2016**, *73*, 537.
[138] L. Zhao, B. Liu, W. An, Y. Deng, Y. Lu, B. Liu, L. Wang, Y. Cong, X. Sun, *Sci. Total Environ.* **2019**, *689*, 322.
[139] C. C. Suckling, M. S. Clark, J. Richard, S. A. Morley, M. A. S. Thorne, E. M. Harper, L. S. Peck, *J. Anim. Ecol.* **2015**, *84*, 773.
[140] L. M. Parker, W. A. O'Connor, D. A. Raftos, H. O. Pörtner, P. M. Ross, *PLoS One* **2015**, *10*, e0132276.
[141] L. Zhao, F. Yang, S. Milano, T. Han, E. O. Walliser, B. R. Schöne, *Sci. Total Environ.* **2018**, *627*, 95.
[142] P. Goncalves, D. B. Jones, E. L. Thompson, L. M. Parker, P. M. Ross, D. A. Raftos, *Mol. Ecol.* **2017**, *26*, 5974.
[143] S. Dupont, N. Dorey, M. Stumpp, F. Melzner, M. Thorndyke, *Mar. Biol.* **2013**, *160*, 1835.
[144] C. C. Suckling, M. S. Clark, C. Beveridge, L. Brunner, A. D. Hughes, E. M. Harper, E. J. Cook, A. J. Davies, L. S. Peck, *Invertebr. Reprod. Dev.* **2014**, *58*, 161.
[145] I. M. Sokolova, M. Frederich, R. Bagwe, G. Lannig, A. A. Sukhotin, *Mar. Environ. Res.* **2012**, *79*, 1.
[146] S. D. Connell, K. J. Kroeker, K. E. Fabricius, D. I. Kline, B. D. Russell, *Philos. Trans. R. Soc., B* **2013**, *368*, 20120442.
[147] M. Koch, G. Bowes, C. Ross, X. H. Zhang, *Global Change Biol.* **2013**, *19*, 103.
[148] D. S. Swezey, J. R. Bean, A. T. Ninokawa, T. M. Hill, B. Gaylord, E. Sanford, *Proc. R. Soc. B* **2017**, *284*, 20162349.
[149] V. J. Cole, L. M. Parker, S. J. O'Connor, W. A. O'Connor, E. Scanes, M. Byrne, P. M. Ross, *Mar. Biol.* **2016**, *163*, 125.
[150] C. L. Hurd, C. D. Hepburn, K. I. Currie, J. A. Raven, K. A. Hunter, *J. Phycol.* **2009**, *45*, 1236.
[151] Z. Xu, G. Gao, J. Xu, H. Wu, *Biogeosciences* **2017**, *14*, 671.
[152] W. J. Mattson, *Annu. Rev. Ecol. Syst.* **1980**, *11*, 119.
[153] L. J. Falkenberg, B. D. Russell, S. D. Connell, *Mar. Ecol.: Prog. Ser.* **2013**, *492*, 85.
[154] G. Ghedini, S. D. Connell, *Ecology* **2016**, *97*, 2671.
[155] P. Z. Kamya, M. Byrne, B. Mos, L. Hall, S. A. Dworjanyn, *Proc. R. Soc. B* **2017**, *284*, 20170778.
[156] C. E. Cornwall, C. D. Hepburn, C. M. McGraw, K. I. Currie, C. A. Pilditch, K. A. Hunter, P. W. Boyd, C. L. Hurd, *Proc. R Soc. B* **2013**, *280*, 20132201.
[157] I. E. Hendriks, Y. S. Olsen, L. Ramajo, L. Basso, A. Steckbauer, T. S. Moore, J. Howard, C. M. Duarte, *Biogeosciences* **2014**, *11*, 333.
[158] A. M. Ricart, M. Ward, T. M. Hill, E. Sanford, K. J. Kroeker, Y. Takeshita, S. Merolla, P. Shukla, A. T. Ninokawa, K. Elsmore, B. Gaylord, *Global Change Biol.* **2021**, *27*, 2580.
[159] C. E. Cornwall, P. W. Boyd, C. M. McGraw, C. D. Hepburn, C. A. Pilditch, J. N. Morris, A. M. Smith, C. L. Hurd, *PLoS One* **2014**, *9*, e97235.
[160] C. L. Hurd, *J. Phycol.* **2015**, *51*, 599.
[161] L. J. Falkenberg, E. Scanes, J. Ducker, P. M. Ross, *Conserv. Physiol.* **2021**, *9*, coab077.
[162] M. Wahl, S. Schneider Covachã, V. Saderne, C. Hiebenthal, J. D. Müller, C. Pansch, Y. Sawall, *Limnol. Oceanogr.* **2018**, *63*, 3.
[163] S. S. Doo, A. Leplastrier, A. Graba-Landry, J. Harianto, R. A. Coleman, M. Byrne, *Ecol. Evol.* **2020**, *10*, 8465.
[164] S. D. Connell, Z. A. Doubleday, S. B. Hamlyn, N. R. Foster, C. D. G. Harley, B. Helmuth, B. P. Kelaher, I. Nagelkerken, G. Sarà, B. D. Russell, *Curr. Biol.* **2017**, *27*, R95.
[165] G. E. Hofmann, J. E. Smith, K. S. Johnson, U. Send, L. A. Levin, F. Micheli, A. Paytan, N. N. Price, B. Peterson, Y. Takeshita, P. G. Matson, E. D. Crook, K. J. Kroeker, M. C. Gambi, E. B. Rivest, C. A. Frieder, P. C. Yu, T. R. Martz, *PLoS One* **2011**, *6*, e28983.
[166] T. Cyronak, Y. Takeshita, T. A. Courtney, E. H. DeCarlo, B. D. Eyre, D. I. Kline, T. Martz, H. Page, N. N. Price, J. Smith, L. Stoltenberg, M. Tresguerres, A. J. Andersson, *Limnol. Oceanogr. Lett.* **2020**, *5*, 193.
[167] L. Ramajo, N. A. Lagos, C. M. Duarte, *Mar. Pollut. Bull.* **2019**, *146*, 247.
[168] A. M. Dufault, V. R. Cumbo, T. Y. Fan, P. J. Edmunds, *Proc. R. Soc. B.* **2012**, *279*, 2951.
[169] H. K. Donald, J. B. Ries, J. A. Stewart, S. E. Fowell, G. L. Foster, *Geochim. Cosmochim. Acta* **2017**, *217*, 240.
[170] L. Harms, S. Frickenhaus, M. Schiffer, F. C. Mark, D. Storch, C. Held, H. O. Pörtner, M. Lucassen, *BMC Genomics* **2014**, *15*, 789.
[171] W. Liu, Z. Yu, X. Huang, Y. Shi, J. Lin, H. Zhang, X. Yi, M. He, *Mar. Environ. Res.* **2017**, *130*, 174.
[172] F. Ragazzola, L. C. Foster, A. U. Form, J. Büscher, T. H. Hansteen, J. Fietzke, *Ecol. Evol.* **2013**, *3*, 3436.
[173] N. G. Ertl, W. A. O'Connor, A. N. Wiegand, A. Elizur, *Clim. Change Responses* **2016**, *3*, 6.
[174] A. W. Griffith, C. J. Gobler, *Sci. Rep.* **2017**, *7*, 11394.
[175] F. O. Borges, C. Figueiredo, E. Sampaio, R. Rosa, T. F. Grilo, *Mar. Environ. Res.* **2018**, *138*, 55.
[176] L. Jiang, Y. J. Guo, F. Zhang, Y. Y. Zhang, L. J. McCook, X. C. Yuan, X. M. Lei, G. W. Zhou, M. L. Guo, L. Cai, J. S. Lian, P. Y. Qian, H. Huang, *Front. Physiol.* **2019**, *9*, 1952.
[177] A. U. Form, U. Riebesell, *Global Change Biol.* **2012**, *18*, 843.
[178] A. Moya, L. Huisman, S. Forêt, J. P. Gattuso, D. C. Hayward, E. E. Ball, D. J. Miller, *Mol. Ecol.* **2015**, *24*, 438.
[179] H. I. Browman, *ICES J. Mar. Sci.* **2016**, *73*, 529.
[180] L. S. Stapp, L. M. Parker, W. A. O'Connor, C. Bock, P. M. Ross, H. O. Pörtner, G. Lannig, *Mar. Environ. Res.* **2018**, *135*, 103.
[181] T. Cyronak, K. G. Schulz, P. L. Jokiel, *ICES J. Mar. Sci.* **2016**, *73*, 558.
[182] J. McClintock, R. Angus, M. McDonald, C. Amsler, S. Catledge, Y. Vohra, *Antarct. Sci.* **2009**, *21*, 449.
[183] J. W. Morse, A. Mucci, F. J. Millero, *Geochim. Cosmochim. Acta* **1980**, *44*, 85.
[184] C. R. Clark, *Palaeogeogr., Palaeoclimatol., Palaeoecol.* **1999**, *149*, 305.
[185] C. P. Glover, S. M. Kidwell, *J. Geol.* **1993**, *101*, 729.
[186] A. Freiwald, *Palaios* **1995**, *10*, 337.
[187] P. A. O'Brien, K. M. Morrow, B. L. Willis, D. G. Bourne, *Front. Mar. Sci.* **2016**, *3*, 47.
[188] S. Rivero-Calle, A. Gnanadesikan, C. E. Del Castillo, W. M. Balch, S. D. Guikema, *Science* **2015**, *350*, 1533.
[189] M. N. Müller, T. W. Trull, G. M. Hallegraeff, *Mar. Ecol.: Prog. Ser.* **2015**, *531*, 81.
[190] S. A. Foo, D. A. Koweek, M. Munari, M. C. Gambi, M. Byrne, K. Caldeira, *Sci. Total Environ.* **2020**, *723*, 138003.
[191] E. P. Houlihan, N. Espinel-Velasco, C. E. Cornwall, C. A. Pilditch, M. D. Lamare, *Front. Mar. Sci.* **2020**, *7*, 577562.
[192] C. E. Cornwall, S. Comeau, N. A. Kornder, C. T. Perry, R. van Hooidonk, T. M. DeCarlo, M. S. Pratchett, K. D. Anderson, N. Browne, R. Carpenter, G. Diaz-Pulido, J. P. D'Olivo, S. S. Doo, J. Figueiredo, S. A. V. Fortunato, E. Kennedy, C. A. Lantz, M. T. McCulloch, M. González-Rivero, V. Schoepf, S. G. Smithers, R. J. Lowe, *Proc. Natl. Acad. Sci. USA* **2021**, *118*, e2015265118.
[193] C. B. Bove, J. Umbanhowar, K. D. Castillo, *Front. Mar. Sci.* **2020**, *7*, 127.
[194] A. C. Wittmann, H. O. Pörtner, *Nat. Clim. Change* **2013**, *3*, 995.
[195] S. G. Klein, N. R. Geraldi, A. Anton, S. Schmidt-Roach, M. Ziegler, M. J. Cziesielski, C. Martin, N. Rädecker, T. L. Frölicher, P. J. Mumby, J. M. Pandolfi, D. J. Suggett, C. R. Voolstra, M. Aranda, C. M. Duarte, *Global Change Biol.* **2022**, *28*, 1753.
[196] N. R. Evensen, P. J. Edmunds, *J. Exp. Biol.* **2017**, *220*, 1097.

[197] D. I. Kline, L. Teneva, D. K. Okamoto, K. Schneider, K. Caldeira, T. Miard, A. Chai, M. Marker, R. B. Dunbar, B. G. Mitchell, S. Dove, O. Hoegh-Guldberg, *Nat. Ecol. Evol.* **2019**, *3*, 1438.
[198] C. Jantzen, V. Häussermann, G. Försterra, J. Laudien, M. Ardelan, S. Maier, C. Richter, *Mar. Biol.* **2013**, *160*, 2597.
[199] K. E. F. Shamberger, A. L. Cohen, Y. Golbuu, D. C. McCorkle, S. J. Lentz, H. C. Barkley, *Geophys. Res. Lett.* **2014**, *41*, 499.
[200] L. H. Spencer, M. Horwith, A. T. Lowe, Y. R. Venkataraman, E. Timmins-Schiffman, B. L. Nunn, S. B. Roberts, *Comp. Biochem. Physiol., Part D: Genomics Proteomics* **2019**, *30*, 91.
[201] I. C. Enochs, N. Formel, D. Manzello, J. Morris, A. B. Mayfield, A. Boyd, G. Kolodziej, G. Adams, J. Hendee, *Coral Reefs* **2020**, *39*, 523.
[202] J. D. Reimer, H. Kurihara, T. Ravasi, Y. Ide, M. Izumiyama, H. Kayanne, *Mar. Biodiversity* **2021**, *51*, 19.
[203] J. Meyer, U. Riebesell, *Biogeosciences* **2015**, *12*, 1671.
[204] C. E. Cornwall, B. P. Harvey, S. Comeau, D. L. Cornwall, J. M. Hall-Spencer, V. Peña, S. Wada, L. Porzio, *Global Change Biol.* **2022**, *28*, 362.
[205] E. C. Shaw, B. I. McNeil, B. Tilbrook, R. Matear, M. L. Bates, *Global Change Biol.* **2013**, *19*, 1632.
[206] J. Y. S. Leung, B. D. Russell, S. D. Connell, J. C. Y. Ng, M. M. Y. Lo, *Anim. Behav.* **2015**, *106*, 223.
[207] V. Amaral, H. N. Cabral, M. J. Bishop, *Mar. Ecol.: Prog. Ser.* **2012**, *445*, 117.
[208] J. A. Pechenik, in *Evolutionary Ecology of Marine Invertebrate Larvae* (Eds: T. J. Carrier, A. M. Reitzel), Oxford University Press, Oxford, UK **2018**.
[209] J. Y. S. Leung, D. McAfee, *Sci. Total Environ.* **2020**, *700*, 134491.
[210] S. U. Goldenberg, I. Nagelkerken, E. Marangon, A. Bonnet, C. M. Ferreira, S. D. Connell, *Nat. Clim. Change* **2018**, *8*, 229.
[211] C. A. Vargas, N. A. Lagos, M. A. Lardies, C. Duarte, P. H. Manríquez, V. M. Aguilera, B. Broitman, S. Widdicombe, S. Dupont, *Nat. Ecol. Evol.* **2017**, *1*, 0084.
[212] C. Duarte, J. M. Navarro, K. Acuña, R. Torres, P. H. Manríquez, M. A. Lardies, C. A. Vargas, N. A. Lagos, V. Aguilera, *Estuaries Coasts* **2015**, *38*, 590.
[213] H. Kurihara, A. Takahashi, A. Reyes-Bermudez, M. Hidaka, *Mar. Biol.* **2018**, *165*, 38.
[214] J. Y. S. Leung, B. D. Russell, M. A. Coleman, B. P. Kelaher, S. D. Connell, *Sci. Total Environ.* **2021**, *771*, 145208.
[215] M. W. Kelly, J. S. Griffiths, *Biol. Bull.* **2021**, *241*, 30.
[216] B. Van Dam, C. Lopes, M. A. Zeller, M. Ribas-Ribas, H. Wang, H. Thomas, *Front. Mar. Sci.* **2021**, *8*, 729992.
[217] U. Riebesell, J. P. Gattuso, *Nat. Clim. Change* **2015**, *5*, 12.
[218] H. A. Carter, L. Ceballos-Osuna, N. A. Miller, J. H. Stillman, *J. Exp. Biol.* **2013**, *216*, 1412.
[219] L. Georgiou, J. Falter, J. Trotter, D. I. Kline, M. Holcomb, S. G. Dove, O. Hoegh-Guldberg, M. McCulloch, *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 13219.
[220] M. Wall, F. Ragazzola, L. C. Foster, A. Form, D. N. Schmidt, *Biogeosciences* **2015**, *12*, 6869.
[221] A. Ventura, S. Schulz, S. Dupont, *Sci. Rep.* **2016**, *6*, 23728.
[222] Y. W. Liu, R. A. Eagle, S. M. Aciego, R. E. Gilmore, J. B. Ries, *Nat. Commun.* **2018**, *9*, 2857.
[223] H. Jurikova, V. Liebetrau, M. Gutjahr, C. Rollion-Bard, M. Y. Hu, S. Krause, D. Henkel, C. Hiebenthal, M. Schmidt, J. Laudien, A. Eisenhauer, *Geochim. Cosmochim. Acta* **2019**, *248*, 370.
[224] O. Migliaccio, A. Pinsino, E. Maffioli, A. M. Smith, C. Agnisola, V. Matranga, S. Nonnis, G. Tedeschi, M. Byrne, M. C. Gambi, A. Palumbo, *Sci. Total Environ.* **2019**, *672*, 938.
[225] E. Bergstrom, A. Ordoñez, M. Ho, C. Hurd, B. Fry, G. Diaz-Pulido, *Mar. Environ. Res.* **2020**, *161*, 105107.
[226] M. Guillermic, L. P. Cameron, I. De Corte, S. Misra, J. Bijma, D. de Beer, C. E. Reymond, H. Westphal, J. B. Ries, R. A. Eagle, *Sci. Adv.* **2021**, *7*, eaba9958.
[227] A. Dery, V. Guibourt, A. I. Catarino, P. Compere, P. Dubois, *Invertebr. Biol.* **2014**, *133*, 188.
[228] G. Langer, G. Nehrke, C. Baggini, R. Rodolfo-Metalpa, J. M. Hall-Spencer, J. Bijma, *Biogeosciences* **2014**, *11*, 7363.
[229] N. A. Kamenos, G. Perna, M. C. Gambi, F. Micheli, K. J. Kroeker, *Proc. R. Soc. B* **2016**, *283*, 20161159.
[230] V. L. Peck, G. A. Tarling, C. Manno, E. M. Harper, E. Tynan, *Deep Sea Res., Part II* **2016**, *127*, 41.
[231] S. Martin, S. Richier, M. L. Pedrotti, S. Dupont, C. Castejon, Y. Gerakis, M. E. Kerros, F. Oberhansli, J. L. Teyssie, R. Jeffree, J. P. Gattuso, *J. Exp. Biol.* **2011**, *214*, 1357.
[232] M. H. Pespeni, E. Sanford, B. Gaylord, T. M. Hill, J. D. Hosfelt, H. K. Jaris, M. LaVigne, E. A. Lenz, A. D. Russell, M. K. Young, S. R. Palumbi, *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 6937.
[233] M. Carreiro-Silva, T. Cerqueira, A. Godinho, M. Caetano, R. S. Santos, R. Bettencourt, *Coral Reefs* **2014**, *33*, 465.
[234] T. C. Pan, S. L. Applebaum, D. T. Manahan, *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 4696.
[235] S. W. Davies, A. Marchetti, J. B. Ries, K. D. Castillo, *Front. Mar. Sci.* **2016**, *3*, 112.
[236] J. L. Drake, M. F. Schaller, T. Mass, L. Godfrey, A. Fu, R. M. Sherrell, Y. Rosenthal, P. G. Falkowski, *Limnol. Oceanogr.* **2018**, *63*, 107.
[237] M. Y. Hu, J. J. Yan, I. Petersen, N. Himmerkus, M. Bleich, M. Stumpp, *eLife* **2018**, *7*, e36600.
[238] A. E. Maas, G. L. Lawson, A. J. Bergan, A. M. Tarrant, *J. Exp. Biol.* **2018**, *221*, jeb164400.
[239] M. Richards, W. Xu, A. Mallozzi, R. M. Errera, J. Supan, *Front. Mar. Sci.* **2018**, *5*, 203.
[240] J. S. Griffiths, T. C. F. Pan, M. W. Kelly, *Mol. Ecol.* **2019**, *28*, 2715.
[241] H. G. Lee, M. Stumpp, J. J. Yan, Y. C. Tseng, S. Heinzel, M. Y. Hu, *Comp. Biochem. Physiol., Part A: Mol. Integr. Physiol.* **2019**, *234*, 87.
[242] A. Glazier, S. Herrera, A. Weinnig, M. Kurman, C. E. Gómez, E. Cordes, *Mol. Ecol.* **2020**, *29*, 1657.
[243] X. Wang, M. Wang, W. Wang, Z. Liu, J. Xu, Z. Jia, H. Chen, L. Qiu, Z. Lv, L. Wang, L. Song, *Sci. Total Environ.* **2020**, *741*, 140177.
[244] K. C. Rajan, Y. Meng, Z. Yu, S. B. Roberts, T. Vengatesen, *Global Change Biol.* **2021**, *27*, 3779.
[245] L. M. Parker, P. M. Ross, W. A. O'Connor, L. Borysko, D. A. Raftos, H. O. Pörtner, *Global Change Biol.* **2012**, *18*, 82.
[246] H. M. Putnam, R. D. Gates, *J. Exp. Biol.* **2015**, *218*, 2365.
[247] J. Thomsen, L. S. Stapp, K. Haynert, H. Schade, M. Danelli, G. Lannig, K. M. Wegner, F. Melzner, *Sci. Adv.* **2017**, *3*, e1602411.
[248] L. Zhao, B. R. Schöne, R. Mertz-Kraus, F. Yang, *Sci. Total Environ.* **2017**, *577*, 360.
[249] J. M. Wong, K. M. Johnson, M. W. Kelly, G. E. Hofmann, *Mol. Ecol.* **2018**, *27*, 1120.
[250] C. E. Cornwall, S. Comeau, T. M. DeCarlo, E. Larcombe, B. Moore, K. Giltrow, F. Puerzer, Q. D'Alexis, M. T. McCulloch, *Nat. Clim. Change* **2020**, *10*, 143.
[251] Y. K. Lim, X. Dang, V. Thiyagarajan, *Sci. Total Environ.* **2021**, *782*, 146704.
[252] B. Moore, S. Comeau, M. Bekaert, A. Cossais, A. Purdy, E. Larcombe, F. Puerzer, M. T. McCulloch, C. E. Cornwall, *Proc. R. Soc. B* **2021**, *288*, 20210130.
[253] P. J. Edmunds, *Limnol. Oceanogr.* **2011**, *56*, 2402.
[254] S. Comeau, R. C. Carpenter, P. J. Edmunds, *Mar. Biol.* **2013**, *160*, 1127.
[255] E. D. Crook, H. Cooper, D. C. Potts, T. Lambert, A. Paytan, *Biogeosciences* **2013**, *10*, 7599.
[256] E. J. Drenkard, A. L. Cohen, D. C. McCorkle, S. J. de Putron, V. R. Starczak, A. E. Zicht, *Coral Reefs* **2013**, *32*, 727.

[257] A. Hettinger, E. Sanford, T. M. Hill, J. D. Hosfelt, A. D. Russell, B. Gaylord, *Biogeosciences* **2013**, *10*, 6629.
[258] J. Thomsen, I. Casties, C. Pansch, A. Körtzinger, F. Melzner, *Global Change Biol.* **2013**, *19*, 1017.
[259] C. Pansch, I. Schaub, J. Havenhand, M. Wahl, *Global Change Biol.* **2014**, *20*, 765.
[260] J. R. Taylor, C. Lovera, P. J. Whaling, K. R. Buck, E. F. Pane, J. P. Barry, *Biogeosciences* **2014**, *11*, 1413.
[261] J. V. Büscher, A. U. Form, U. Riebesell, *Front. Mar. Sci.* **2017**, *4*, 101.
[262] G. S. Cavalcanti, P. Shukla, M. Morris, B. Ribeiro, M. Foley, M. P. Doane, C. C. Thompson, M. S. Edwards, E. A. Dinsdale, F. L. Thompson, *BMC Genomics* **2018**, *19*, 701.
[263] S. S. Doo, R. C. Carpenter, P. J. Edmunds, *Coral Reefs* **2018**, *37*, 997.
[264] E. J. Drenkard, A. L. Cohen, D. C. McCorkle, S. J. de Putron, V. R. Starczak, D. J. Repeta, *J. Exp. Mar. Biol. Ecol.* **2018**, *507*, 61.
[265] E. B. Rivest, M. W. Kelly, M. B. DeBiasse, G. E. Hofmann, *Front. Mar. Sci.* **2018**, *5*, 186.
[266] E. Bergstrom, J. Silva, C. Martins, P. Horta, *Sci. Rep.* **2019**, *9*, 1932.
[267] T. Guy-Haim, J. Silverman, M. Wahl, J. Aguirre, F. Noisette, G. Rilov, *Mar. Environ. Res.* **2020**, *161*, 105093.
[268] E. Rastelli, B. Petani, C. Corinaldesi, A. Dell'Anno, M. L. Martire, C. Cerrano, C. R. Danovaro, *Sci. Rep.* **2020**, *10*, 2948.
[269] T. H. Lee, R. A. McGill, S. Fitzer, *J. Exp. Mar. Biol. Ecol.* **2021**, *541*, 151562.

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Sean D. Connell coordinates multidisciplinary teams to solve the scientific dilemma of relating biological processes from atoms to ecosystems. His group discovered that organisms can make nanoscale adjustments (e.g., in shell-building) to maintain their ecological role (e.g., herbivory) and stabilize ecosystems (e.g., productivity) against climate change. This work has expanded to provide actionable solutions for environmental repair by using next-generation technology (e.g., acoustics) to rewild extinct ecosystems and repair failing commercial fisheries. He currently works with legal-scholars and policy-scholars to link these science-driven successes to bringing these benefits to the environment and humanity.