



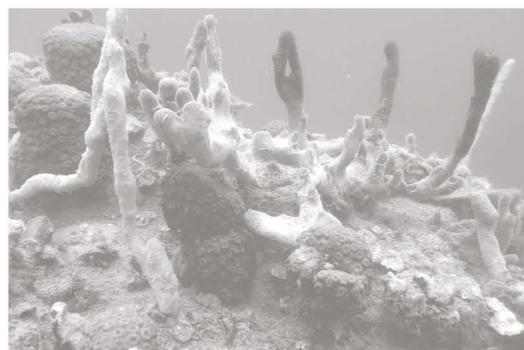
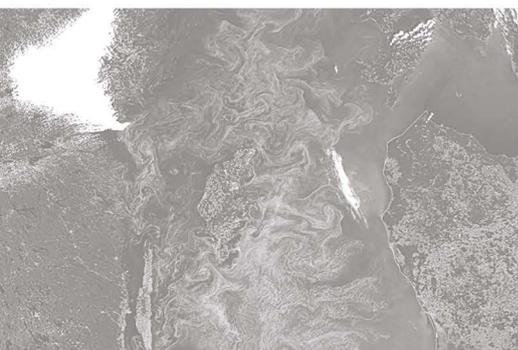
# Ocean deoxygenation: Everyone's problem

Causes, impacts, consequences and solutions

Edited by D. Laffoley and J.M. Baxter

## 6. Multiple stressors – forces that combine to worsen deoxygenation and its effects

Denise L. Breitburg, Hannes Baumann, Inna M. Sokolova and Christina A. Frieder



IUCN GLOBAL MARINE AND POLAR PROGRAMME





# Multiple stressors – forces that combine to worsen deoxygenation and its effects

# 6

Denise L. Breitburg<sup>1</sup>, Hannes Baumann<sup>2</sup>, Inna M. Sokolova<sup>3</sup> and Christina A. Frieder<sup>4</sup>

<sup>1</sup>Smithsonian Environmental Research Center, 647 Contees Wharf Road, Edgewater, MD 21037, USA

<sup>2</sup>Department of Marine Sciences, University of Connecticut, 1080 Shennecossett Road, Groton, CT 06340, USA

<sup>3</sup>Institute of Biological Sciences, University of Rostock, Albert-Einstein-Strasse 3, D-18057 Rostock, Germany

<sup>4</sup>Department of Civil and Environmental Engineering, University of California Irvine, 4130 Engineering Gateway, CA 92697, USA

## Summary

- Human activities have altered not only the oxygen content of the coastal and open ocean, but also a variety of other physical, chemical and biological conditions that can have negative effects on physiological and ecological processes. As a result, marine systems are under intense and increasing pressure from multiple stressors.
- The combined effects of ‘stressors’ can be greater than, less than, or different from the sum of each stressor alone, and there are large uncertainties surrounding their combined effects.
- Warming, acidification, disease, and fisheries mortality are important common stressors that can have negative effects in combination with low oxygen.
- Warming, deoxygenation, and acidification commonly co-occur because they share common causes. Increasing carbon dioxide (CO<sub>2</sub>) emissions simultaneously warm, deoxygenate, and acidify marine systems, and nutrient pollution increases the severity of deoxygenation and acidification.
- A better understanding of the effects of multiple stressors on ocean ecosystems should improve the development of effective strategies to reduce the problem of deoxygenation and aid in identifying adaptive strategies to protect species and processes threatened by oxygen decline.

Ocean hypoxia effect	Potential consequences
Oxygen decline occurs along with other changes to oceans and coastal waters caused by human activities. These changes include co-stressors such as warming, acidification, nutrient pollution and overfishing.	<ul style="list-style-type: none"> <li>• The combined effects of multiple stressors can differ from what would be predicted from simply summing their individual effects and can be difficult to predict.</li> <li>• Management actions may be less effective if co-occurring stressors are not considered.</li> </ul>
Oxygen is required by organisms to turn food into energy that can be used to escape from, adapt to, and repair damage caused by other stressors.	<ul style="list-style-type: none"> <li>• When oxygen is insufficient, an organism may not have the necessary energy to withstand other stressors.</li> </ul>
Increasing global temperature simultaneously worsens oxygen decline and increases oxygen requirements of organisms that rely on aerobic respiration.	<ul style="list-style-type: none"> <li>• Some species will become more temperature-sensitive at lower oxygen levels and more oxygen sensitive at higher temperatures.</li> <li>• Models predict shifts in global distributions and the sizes of fishes as result of the combined effects of decreased oxygen supply and increased temperatures.</li> </ul>
Low oxygen alone and in combination with other stressors can reduce the ability of an animal to fight pathogens and parasites.	<ul style="list-style-type: none"> <li>• Low oxygen can lead to increased intensity and prevalence of a number of diseases of marine animals.</li> <li>• Energy deficiency due to low oxygen can increase morbidity and mortality from diseases.</li> </ul>
Avoidance of low oxygen can result in altered spatial distributions.	<ul style="list-style-type: none"> <li>• Mobile species may experience higher fishing mortality if fishers target well-oxygenated areas that serve as a refuge for animals fleeing oxygen-depleted habitat.</li> <li>• Well-oxygenated habitat may not be suitable as a refuge from oxygen-depleted areas because of the presence of other stressors such as high temperatures.</li> </ul>

## 6.1 Introduction

Humans have wide-ranging effects on oceanic and coastal marine ecosystems that are critical to Earth's ecology, economies, and food security (Boyd et al., 2015; Breitburg et al., 2015a; Doney, 2010; Levin & Le Bris, 2015; Prichard & Granek, 2016; Wallace et al., 2014). We remove biomass through fishing; we warm, deoxygenate, and acidify waters through our release of carbon dioxide (CO<sub>2</sub>) and other greenhouse gases into the atmosphere; we deoxygenate and acidify coastal systems by releasing nitrogen and phosphorus from agriculture, human waste, and combustion of fossil fuels; and we have increased burdens of pollutants such as trace metals, pesticides, nanomaterials, pharmaceuticals, and microplastics. We refer to these drivers (e.g. fisheries removals) as 'stressors' when they cause undesirable changes to the physical environment, or to individual organisms, food webs or ecosystems (Breitburg et al., 2015a). Only 13% of the world's

ocean can be considered wilderness with only minor anthropogenic impact; much of the remainder and even some areas considered to be wilderness are affected by multiple stressors stemming from human activities (Jones et al., 2018).

The effects of multiple stressors that co-occur, occur sequentially, or affect the same organism or water parcel as it transits among locations, are often not additive. When two or more stressors affect the same organism or ecological process, their combined effects can be greater than (synergistic effects, Folt et al., 1999), less than (antagonistic effects, Folt et al., 1999), or qualitatively different from changes that would be predicted by simply summing up the independent effects of each stressor. For example, the toxicity of mercury pollution depends on the presence of anaerobic conditions that allow methanogens (microbes using anaerobic metabolic pathways) to transform elemental mercury to methyl mercury – the form that accumulates

in individuals and food webs (Gilmour et al., 2013). Heavy rainfall causes landslides where deforestation removes the underground root structure that would otherwise hold soil in place (Glade, 2003). Malnutrition can make humans more susceptible to disease (Rice et al., 2000). The cases of greatest concern are often those in which the combined effects of multiple stressors are substantially greater than or different from their additive effects; in such cases negative effects can be most severe and difficult to predict. Important stressors that have the potential to exacerbate or alter the effects of oxygen loss in marine systems manifest at both local and global scales (Breitburg & Riedel, 2005).

There are two broad categories of stressors – (1) those that combine to worsen the decline in oxygen or to create a multi-stressor environment that includes oxygen decline, and (2) those that alter the effects of low oxygen on organisms and ecological processes. We focus on human-caused stressors because these can be mitigated through management and policy actions to ultimately reduce or reverse oxygen decline, or to reduce its ecological and economic consequences. Considering the potential for other stressors to modulate the severity and effects of deoxygenation is important for the correct identification of causes and effects of deoxygenation in complex marine ecosystems and for the development of sound policy and management strategies.

### **6.1.1 Suboptimal oxygen supply can limit the ability of organisms to tolerate additional stressors**

The ability of an organism to tolerate stress is directly related to its ability to maintain an internally balanced physiological state (i.e. homeostasis) to counteract stressor-induced physiological perturbations (Sokolova et al., 2012, 2013). Increasing severity and duration of environmental stressors leads to elevated costs of the basal maintenance of an organism reflected in an increased basal metabolic rate (BMR) (Figure 6.1). This increase in the BMR reflects elevated energy demands of physiological mechanisms that re-establish cellular and organismal homeostasis, as well as the energy costs of cellular stress protection and damage repair. Cellular homeostasis and stress protection mechanisms are linked to an organism's immediate survival and thus typically prioritized over other energy expenditures.

In order to fuel most cellular processes, external energy (e.g. in the form of food) obtained by an organism must

be converted into adenosine triphosphate (ATP), a universal energy currency of the cell. Since the amount of energy available to an organism and its capacity to assimilate and convert energy into ATP is intrinsically limited, an increase in the BMR reduces the energy available for other fitness-related functions such as growth, reproduction, and defences against pathogens.

Oxygen is required for the production of ATP through aerobic respiration. Oxygen deficiency therefore exacerbates energy deficiency by reducing the capacity of mitochondria to produce ATP (Pamenter, 2014; Sokolova et al., 2011). As a result, the decline in oxygen in the open ocean and coastal waters is expected to increase the trade-off between basal maintenance and other functions. Exposure to low oxygen may also increase energy costs of basal maintenance due to escape behaviours, physiological adjustments to enhance oxygen delivery, or elevated expression of antioxidants that counteract hypoxia-induced oxidative stress (Bavis et al., 2007; Ivanina & Sokolova, 2016; Solaini et al., 2010). The impacts of low oxygen on energy balance may also be intensified by its negative effects on energy intake of an organism through, for example, suppressed feeding activity or food assimilation (Thibodeaux et al., 2009; Yang et al., 2013).

While the impact of each hypoxia-induced physiological and behavioural alteration on overall energy balance may be subtle, their cumulative effects exacerbate the potential mismatch between cellular ATP demand and capacity for ATP production. This can result in an earlier onset of suboptimal or bioenergetically unsustainable conditions in multiple stress exposure scenarios. As a result, declining oxygen in the open ocean and coastal waters can exacerbate the effects of other common stressors in marine and coastal environments acting as an overall 'stress enhancer' and limiting an organism's ability to deal with additional stressors.

Oxygen can be the dominant factor in multiple stressor interactions because low oxygen can limit an organism's ability to deal with additional stressors. Under optimal, well-oxygenated conditions (Figure 6.1), energy uptake and aerobic ATP production are sufficient to cover the energy costs of basal maintenance (maintaining homeostasis, cellular stress protection and damage repair), as well as the energy costs of other fitness-related functions such as growth, reproduction, immunity, locomotion, and storage of an energy buffer in the form of energy reserves (such as glycogen and

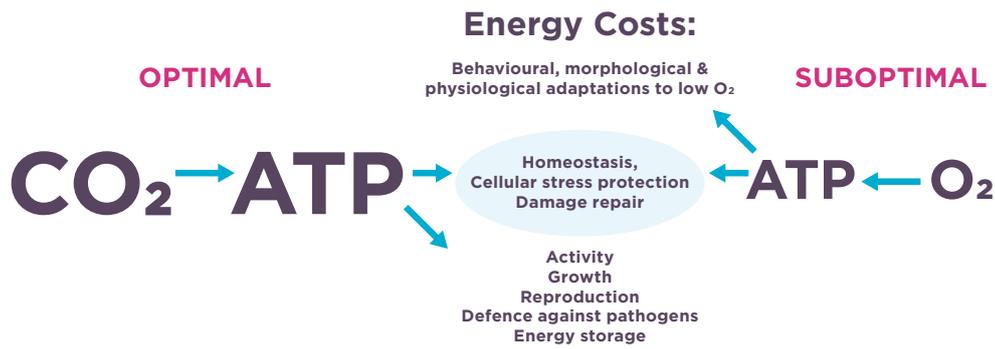


Figure 6.1 Energy-limited stress tolerance.

lipids). Under such conditions, energy is available to repair and reduce damage caused by the variety of natural and human-caused stressors that challenge an organism. As environmental oxygen conditions degrade into the suboptimal range (Figure 6.1), the energy demand for basal metabolism increases to counteract the stress-induced disturbances of homeostasis and cover the costs of stress protection and damage repair. This can result in a trade-off with other fitness-related functions such as growth, immune defence and reproduction. Furthermore energy reserves of the body may be tapped to buffer the increasing energy demand of basal maintenance. As conditions further deviate from optimal, an organism reaches a critical threshold where all available energy and metabolic capacity are used to support immediate survival. Commonly, anaerobic ATP-producing pathways become engaged to cover the elevated costs of basal maintenance. Under these conditions the organism can potentially survive a long time, but no growth or reproduction is possible and thus the population is bioenergetically non-sustainable. Some stress-adapted organisms can suppress their basal metabolic rate during suboptimal conditions; this metabolic strategy extends the survival time under stress but does not increase the energy available for other functions (Hochachka et al., 1996; Sokolova et al., 2011; Storey & Storey, 2004). Extreme stress in the lethal range occurs when the combined aerobic and anaerobic ATP production is insufficient for the basal maintenance; stress protection and damage repair mechanisms are overwhelmed, and cellular damage accumulates culminating in cell death and organ failure, and as a result, the death of the organism.

## 6.2 The causes of deoxygenation create a multi-stressor environment

Aerobic respiration uses  $\text{O}_2$  and releases  $\text{CO}_2$  and is the major driver of deoxygenation both in metabolically active coastal waters and in deeper, bathyal waters where respiration decreases the partial pressure of oxygen ( $p\text{O}_2$ ) and elevates the partial pressure of carbon dioxide ( $p\text{CO}_2$ ) over much longer time scales. As a result, dissolved oxygen concentrations,  $p\text{CO}_2$  and pH (a measure of acidity influenced by the amount of dissolved  $\text{CO}_2$ ) tend to correlate in many habitats including saltmarshes and eutrophic estuaries (Baumann et al., 2015; Cai et al., 2011; Wallace et al., 2014), oceanic oxygen minimum zones (Paulmier et al., 2011), and kelp forests (Frieder et al., 2012) (Figure 6.2). Drivers that increase respiration – especially warming and nutrient pollution – create a multi-stressor environment by simultaneously worsening oxygen depletion and acidification. In addition, the direct effects of high temperatures and nutrients, as well as the ecosystem processes that they alter, occur alongside low oxygen, leading to a complex combination of potentially stressful environmental conditions to which marine organisms are exposed. In a similar manner, harmful algal blooms, which can be caused or exacerbated by warming, nutrients and oceanographic conditions, not only lead to low oxygen, acidification and sometimes elevated  $p\text{CO}_2$  as they die off, but can also release toxins and damage gills of animals in affected areas (e.g. Glibert et al., 2018; Pitcher et al., 2018).

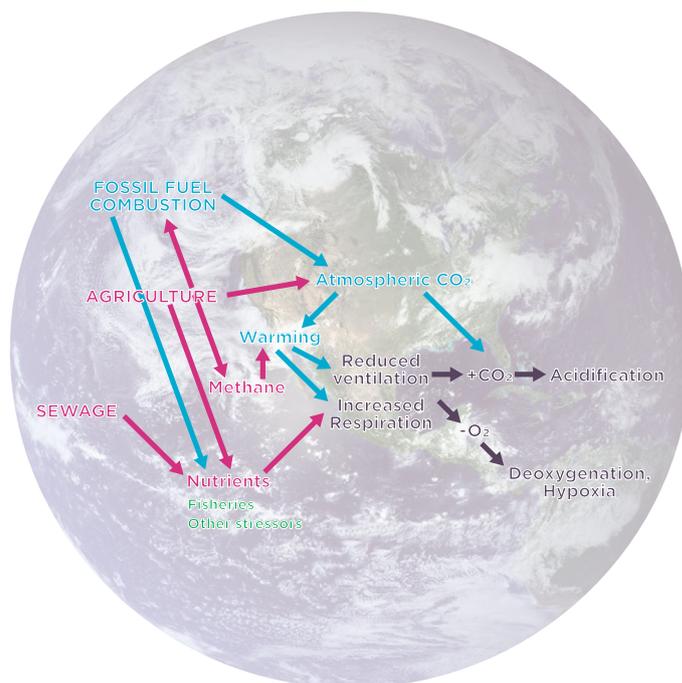


Figure 6.2 Global warming, acidification and deoxygenation are linked. Increasing carbon dioxide in the Earth's atmosphere results in higher ocean temperatures, more acidic conditions, and deoxygenation (Gattuso et al., 2015; Gruber et al., 2012). The warming caused by greenhouse gases, including  $\text{CO}_2$ , lowers oxygen solubility in sea water, increases respiration rates of organisms, and reduces mixing that could otherwise increase exchanges between subsurface waters and the oxygen-rich atmosphere. Respiration by microbes, plants, and animals depletes oxygen and produces  $\text{CO}_2$ , causing further acidification. Nutrients increase total respiration (the biological demand for oxygen) in water bodies by increasing the total production of organic biomass. There are also important feedbacks not illustrated in this figure. For example, extreme low oxygen and anoxic environments can release phosphorus bound to sediment, fuelling further primary production, and are also the sites of production of potent greenhouse gases. Red = major pathways for nutrient sources and effects; blue = major pathways for warming and  $\text{CO}_2$  enrichment; green = other stressors that can increase respiration, for example by altering food webs. (Note that the size of arrows does not indicate the relative importance of these processes.) Earth image: NASA.

### 6.2.1 Increased greenhouse gas emissions increase the severity of multiple interacting stressors

Increasing greenhouse gas concentrations in the atmosphere warm, deoxygenate, and acidify marine systems (Bopp et al., 2013; Gruber, 2011) (Figure 6.3). Models project a continuation of this trend, with temperature, oxygen, and acidification conditions all becoming more severe with increasing greenhouse gas (GHG) emissions to a degree that depends on future GHG emission rates (Bopp et al., 2013). Global warming reduces the oxygen content of the ocean through three primary mechanisms – by reducing ventilation (i.e. the introduction of oxygen to subsurface waters), by reducing oxygen solubility, and by altering the net balance between oxygen production and consumption (Chapters 3 and 4; Levin, 2018; Oschlies et al., 2018). As surface waters warm, the water column becomes more strongly stratified. In combination with changes in winds and ocean currents, this stratification reduces ventilation – the introduction of oxygen to subsurface waters. The solubility of oxygen in sea water declines

with rising temperature, so that the absolute amount of oxygen (e.g.  $\text{mg L}^{-1}$  dissolved oxygen) at full saturation is less in warmer water than in cooler water. Furthermore, elevated temperature increases the metabolic rates of marine bacteria and ectothermic (colloquially called cold-blooded) animals that constitute >99% of marine biodiversity and the vast majority of biomass (Pörtner, 2012). This increased respiratory demand can accelerate the rate of oxygen loss at the same time that reduced ventilation and solubility reduce oxygen re-supply.

### 6.2.2 High nutrients, high productivity and high temperatures combined

Coastal environments – estuaries, semi-enclosed seas and embayments – are among the most productive regions of the ocean (Cloern et al., 2016; Costanza et al., 1997). Temporal variation in ecosystem metabolism of these systems can cause large, co-occurring pH and oxygen fluctuations on diel, seasonal, and interannual timescales (Figure 6.4) (Baumann & Smith, 2018; Odum, 1961; Wootton et al., 2008). In shallow waters,

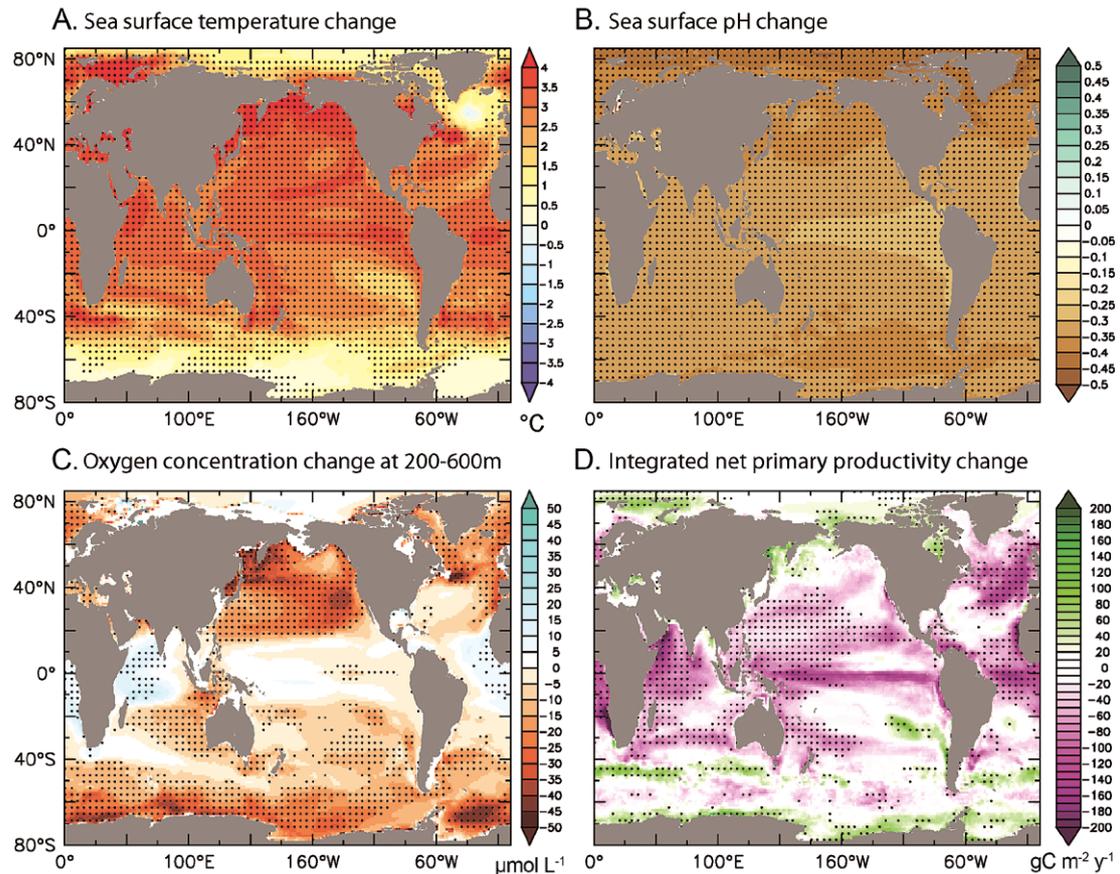


Figure 6.3 Projected changes in A) sea surface temperature, B) pH, C) dissolved oxygen concentration and D) primary production in 2090–2099 relative to 1990–1999 under the RCP8.5 “business-as-usual” model scenario (Bopp et al., 2013). Image reproduced from Bopp et al. (2013).

oxygen consumption and  $\text{CO}_2$  production by respiration are countered by photosynthesis by phytoplankton, macroalgae, and submerged aquatic vegetation that fixes  $\text{CO}_2$  while raising oxygen and pH levels in the water. The balance between heterotrophic (respiration) and autotrophic (photosynthesis) processes changes naturally between day and night, and between seasons of high and low productivity (e.g. summer vs. winter months), causing large correlated pH and oxygen fluctuations (Baumann et al., 2015; Baumann & Smith, 2018; Breitburg et al., 2015a; O’Boyle et al., 2013).

Human activity significantly alters and intensifies the natural dynamics of these systems. Coastal systems are warming more rapidly than average oceanic rates (Field et al., 2014). For nearshore environments, warming alone can exacerbate acidification and deoxygenation because ecosystem respiration increases more rapidly with temperature than photosynthesis (Baumann & Smith, 2018; Vaquer-Sunyer & Duarte, 2011; Yvon-Durocher et al., 2010).

Nutrient pollution (eutrophication) of coastal habitats causes or intensifies coastal hypoxia and acidification by stimulating phytoplankton production that in turn fuels high microbial respiration (Cai et al., 2011; Gobler & Baumann, 2016). Algal blooms and growth of epiphytes stimulated by nutrients can reduce light penetration, leading to altered benthic production (Cloern, 2001; Kemp et al., 2005). High nutrient loads also lead to changes in algal species composition and the efficiency of energy transfer to upper trophic levels (Cloern, 2001). As a result, hypoxia, acidification, altered benthic production, and other food web changes, as well as increasing temperatures, commonly co-occur.

Unlike many of the stressor combinations discussed above, anthropogenic nutrient loads can sometimes reduce potential negative consequences of hypoxia by enhancing productivity and food supply in coastal ecosystems (Breitburg et al., 2009; De Mutsert et al., 2016). Total fisheries landings can remain high, for example, even if demersal species in oxygen-depleted areas decline, because nutrients can stimulate prey

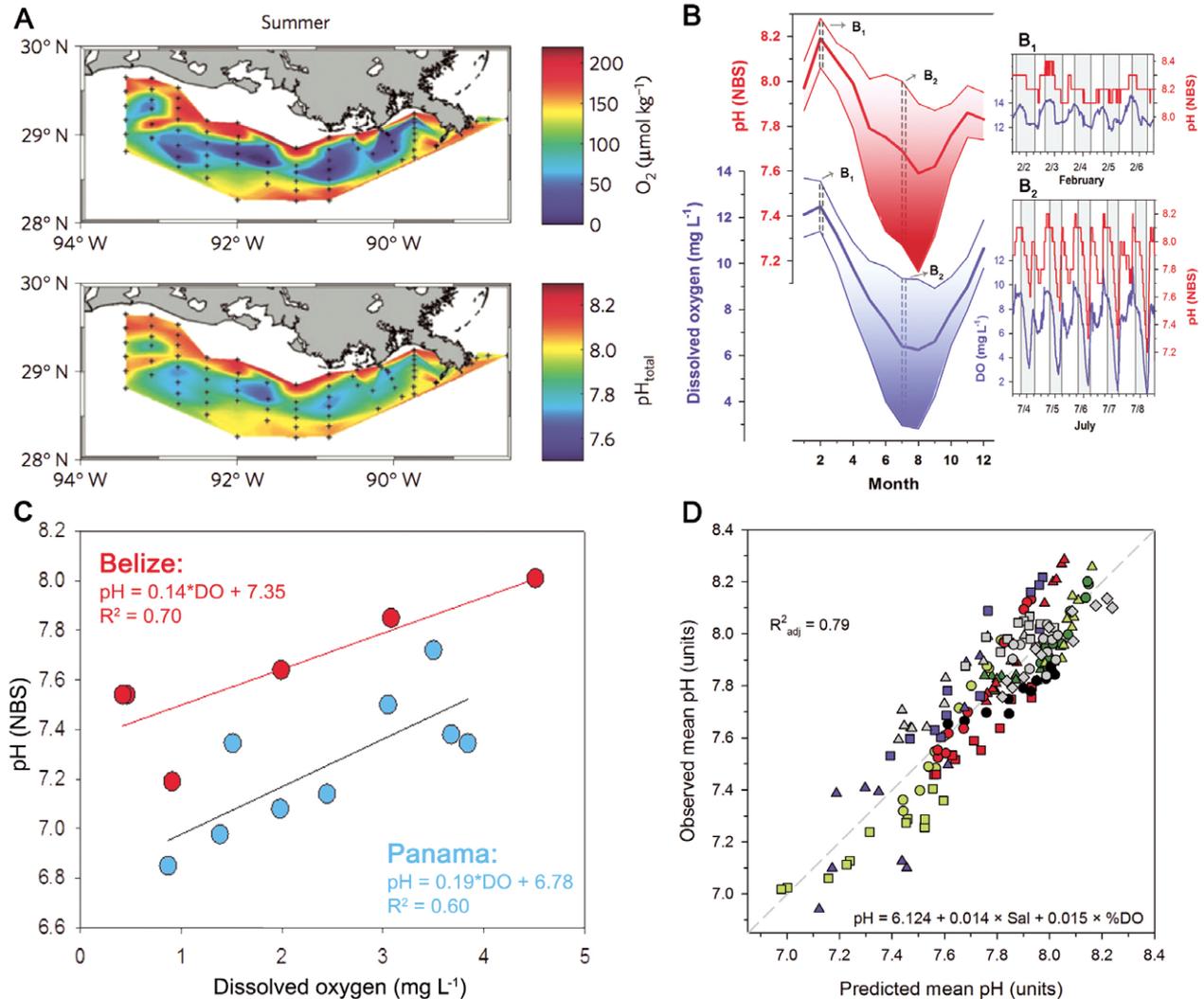


Figure 6.4 In coastal habitats, ecosystem metabolism commonly accounts for large, concurrent pH and oxygen fluctuations on diel and seasonal timescales. (A) Excessive respiration of organic material in the northern Gulf of Mexico consumes oxygen leading to hypoxia in bottom waters, while at the same time increasing CO<sub>2</sub> levels (decreasing pH), causing acidification (modified after Cai et al., 2011). (B) Average pH and oxygen levels decline seasonally in most coastal environments, as productivity and thus net oxygen demand increases during spring/summer months. This seasonal decline is associated with increasing diel fluctuations of pH and oxygen (B<sub>1</sub>, B<sub>2</sub> inserts) (modified after Baumann et al., 2015). (C) The correlation between minimum dissolved oxygen and pH can also be seen in saltwater ‘ponds’ that form within mangrove islands in the tropics, even in areas with minimal anthropogenic nutrient loads (modified from Gedam et al., 2017). (D) The metabolic pH-oxygen coupling is so strong in most coastal environments that average pH levels can be predicted by average oxygen and salinity conditions. Symbols in D depict predicted vs. observed monthly means of pH in 16 nearshore sites across the US Atlantic, Gulf of Mexico, and Pacific coasts (modified after Baumann & Smith 2017).

production in surface waters, shallow benthic habitats, and other well-mixed parts of a system (Breitburg et al., 2009; Nixon & Buckley, 2002). Abundant prey can also improve stress tolerance of organisms in nutrient-enriched habitats (Marigómez et al., 2017). However, system-wide compensation through enhanced productivity due to nutrient input has limits that can be reached as the volume of oxygen depleted habitat expands or critical habitats are affected (Breitburg, 2002).

### 6.3 Effects of multiple stressors

Synergistic negative effects have been proposed for a large number of stressors that co-occur with low oxygen. For example, the combination of low salinity in surface waters and low oxygen in bottom waters limits suitable habitat for development of cod (*Gadus morhua*) eggs in the deep basins of the Baltic Sea (Hansson et al., 2007). Avoidance of low oxygen can force aggregation of fish and mobile crustaceans in refuge habitats and increase fishing mortality where

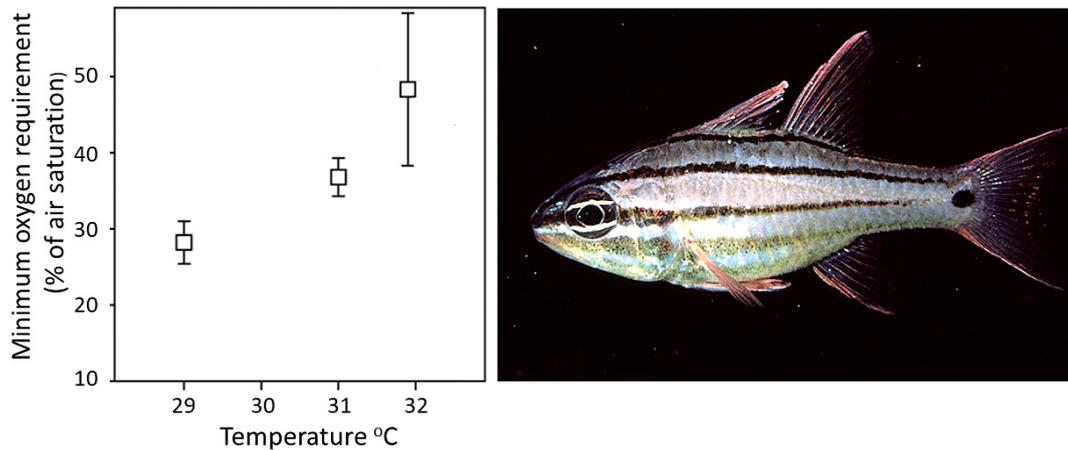


Figure 6.5 Oxygen requirements of fish increase with increasing temperatures. In the case of this coral reef cardinal fish, a 3 °C increase in temperature increased oxygen required to sustain life by 40%. Modified from Nilsson et al. (2010). Photo by JE Randall downloaded from fishbase.org.

these refuge locations are targeted, potentially increasing the likelihood of overfishing (Craig, 2012; Froehlich et al., 2017; Section 9.2). Habitat loss due to hypoxia may also make populations more susceptible to large-scale population declines due to overfishing by reducing resilience (Wainger et al., 2017). Low oxygen can sometimes increase the toxicity of contaminants, and contaminant exposure can increase sensitivity to low oxygen (Delorenzo, 2015). Here we focus on three stressors – temperature, acidification and disease – and consider the effects when they co-occur with low oxygen conditions. Warming, acidification, and disease can all increase energy requirements of organisms, while deoxygenation can limit its supply.

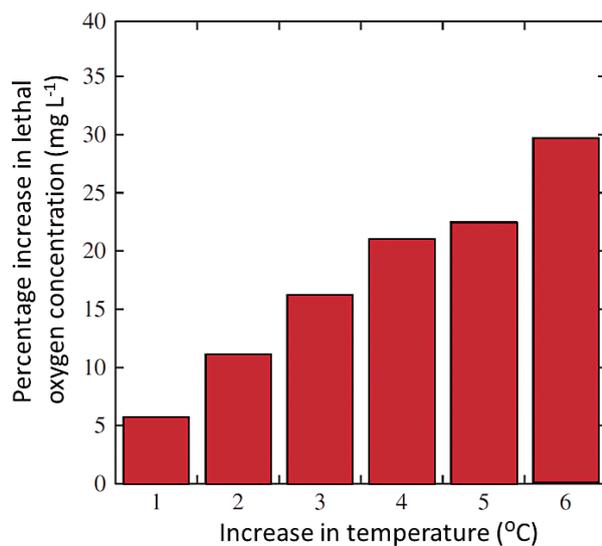


Figure 6.6 Percentage change in oxygen saturation leading to 50% mortality with temperature increases between 1 and 6 °C. Modified from Vaquer-Sunyer & Duarte (2011).

### 6.3.1 Deoxygenation and increasing temperature

Increasing GHG emissions, elevated anthropogenic nutrient loads (especially pronounced in coastal waters), and low ventilation rates strengthen the vertical structure of marine waters. Suitable habitat becomes limited by high temperatures in upper waters and by lower oxygen and elevated CO<sub>2</sub> in mid or bottom depths. This habitat compression can lead to altered distributions and reduced diversity of taxa most susceptible to these stressors in both the open ocean and in coastal waters (Coutant, 1985; Eby & Crowder, 2002; Stramma et al., 2012). Warming of surface waters can reduce the ability of vertical migrators to repay the oxygen debt (i.e. the additional energy costs of restoring homeostasis after periods of oxygen deficiency) they incur during time spent in oxygen minimum zones (OMZs; Rosa & Seibel, 2008). For species that do not migrate, the combination of warming surface waters and low oxygen in the mid or lower water column can reduce suitable habitat. High surface temperatures during summer combined with low bottom-layer oxygen conditions can limit suitable habitat in estuaries even in the absence of global warming (Coutant, 1985). In contrast to sensitive species, some hypoxia-tolerant species (e.g. some squid and jellyfish) may expand their population size and distribution areas under these conditions (Breitburg et al., 1997; Gilly et al., 2013).

Increased temperature elevates oxygen demand while simultaneously reducing oxygen supply, thus expanding the area of the ocean and coastal waters where oxygen is insufficient. Experiments on individual species often show large increases in oxygen requirements with only



Figure 6.7 European spider crab *Maja squinado* © WaterFrame / Alamy stock photo.

a few degrees centigrade increase in temperature (e.g. Figure 6.5).

An analysis of temperature effects on oxygen thresholds of benthic marine organisms (including demersal fishes), for example, found that a 4 °C increase in temperature decreased survival times for animals exposed to lethal oxygen saturation by 36% and increased the oxygen threshold leading to high mortality by 25% (Figure 6.6; Vaquer-Sunyer & Duarte, 2011). In this analysis, oxygen requirements of sessile species rose faster than those of motile species with increasing temperatures; and oxygen thresholds of crustaceans were more sensitive to temperature than other groups of animals.

In many aquatic ectotherms, thermal tolerance is limited by the capacity to meet oxygen demands of tissues as increasing temperatures lead to a progressive mismatch between the high oxygen demand for routine metabolism and supply of oxygen through gill ventilation and circulation (Pörtner, 2012; Pörtner et al., 2017). This mismatch between oxygen consumption by tissues and the capacity for oxygen delivery has been demonstrated in many fish and invertebrate species, e.g. *Maja squinado* (Figure 6.7) and *Littorina saxatilis* (Figure 6.8) (Bagwe et al., 2015; Frederich & Pörtner, 2000; Jensen et al., 2017; Sokolova & Pörtner, 2003; Sommer & Pörtner, 2004). Through this mechanism, ocean warming caused by elevated GHG emissions is predicted to result in shifts in the distribution of fishes and invertebrates poleward by 10s-100s km per decade, shifts into deeper, cooler waters, and local extinctions (Cheung et al., 2011; Deutsch et al., 2015; Nye et al., 2009). The mismatch is also predicted to reduce maximum sizes of many fish species (including those that support important fisheries), leading to a projected

14–24% reduction in assemblage-averaged body mass globally between 2000 and 2050 under a high GHG emission scenario (Cheung et al., 2013; Pauly & Cheung, 2017). Models project that warming combined with even modest deoxygenation (less than 10  $\mu\text{mol kg}^{-1}$ ) can cause declines in important fishery species that are sensitive to low oxygen (Stortini et al., 2017). This temperature-induced mismatch between oxygen supply and metabolic oxygen demand affects organisms at all depths including well-oxygenated surface waters but might be more pronounced at depths where the most severe deoxygenation is seen.

Some animals can, nevertheless, maintain oxygen uptake as temperatures rise by increasing heart and gill ventilation rates, or by other mechanisms (Brijs et al., 2015; Gräns et al., 2014; Verberk et al., 2016). For example, landlocked arctic char (*Salvelinus alpinus*) and Atlantic salmon (*Salmo salar*) tolerated lower oxygen saturation, and longer exposure to 13% oxygen saturation, respectively, when acclimated to 14.9 °C than when acclimated to 7.7 °C (Anttila et al., 2015). Acclimation to the higher temperature led to changes in cardiac tissue (in both studied species), capillary density within gill lamellae (in char), and lengthening of gill lamellae (in salmon) in response to hypoxia. Similarly, acclimation to elevated temperature led to increased gill lamellar surface area in mummichogs (*Fundulus heteroclitus*) (McBryan et al., 2016). All of these physiological and morphological adjustments can increase oxygen supply and delivery. This emphasizes an important role of oxygen delivery mechanisms for successful acclimation to warming and indicates that physiological plasticity of these mechanisms may provide cross-tolerance to warming and low oxygen (McBryan et al., 2016). In contrast to observed long-term temperature



Figure 6.8 Rough periwinkle *Littorina saxatilis* © Buiten-Beeld / Alamy stock photo.

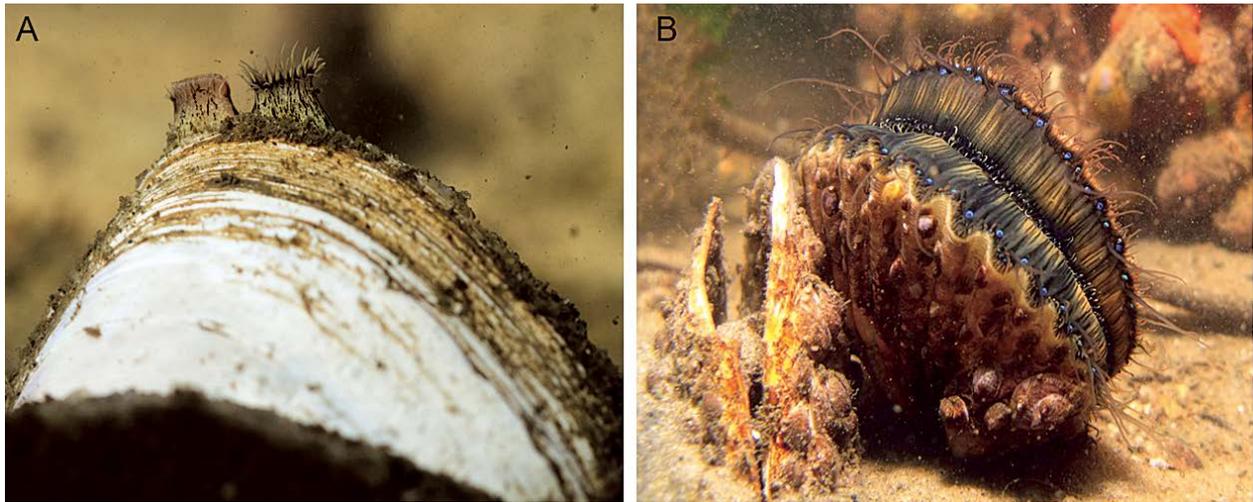


Figure 6.9 Effects of co-occurring hypoxia and acidification differ between (A) the northern quahog *Mercenaria mercenaria* and (B) bay scallop *Agropecten irradians* (Images by Christopher Paparo; provided by C. Gobler).

acclimation, acute high temperature exposure reduced hypoxia tolerance in mummichogs. McBryan et al. (2016) suggested that the magnitude of the effect indicated that the reduced hypoxia tolerance was caused by the negative effect of temperature on oxygen affinity of haemoglobin. Decreased haemoglobin affinity for oxygen with increasing temperatures has also been found for other fish species (Weber & Jensen, 1988).

Fluctuating environmental conditions sometimes modulate the combined effects of elevated temperature and low oxygen. Elevated temperature increased growth of newly settled Olympia oysters (*Ostrea lurida*) and partially offset the negative effect of diel cycling hypoxia (daily minima to 2.0 or 0.6 mg L<sup>-1</sup>) on growth (Cheng et al., 2015). The authors suggested that the combination of metabolic suppression during low oxygen, and temperature-accelerated feeding during high-oxygen periods, protected oysters from the more severe effects of low oxygen that would occur under constant low oxygen conditions and resulted in an additive rather than synergistic negative interaction between the stressors. Overall, the interactive effects of fluctuating oxygen and temperature conditions may be quantitatively and qualitatively different from those of chronic, stable conditions (Dowd et al., 2015; Kingsolver & Buckley, 2017; Kingsolver et al., 2016), and future experiments should be designed to more closely mimic environmentally realistic fluctuations.

### 6.3.2 Deoxygenation and acidification

The combined effects of hypoxia and acidification are important to understand because of their widespread

co-occurrence, and because of increasing evidence of the ecological threat of acidification (Williamson et al., 2017). The effects of hypoxia on marine organisms have been empirically studied for decades (Breitburg et al., 2009; Diaz & Rosenberg, 1995). In isolation, hypoxia may pose a more severe threat to most marine species than acidification (Gobler & Baumann, 2016). However, the combined effects of these stressors on organisms are not well studied and thus insufficiently understood; recent studies have found that the combined effects of hypoxia and acidification can sometimes be more severe than effects of either stressor alone (Gobler & Baumann, 2016).

In general, co-occurring hypoxia and acidification can have additive, antagonistic, or synergistic effects (Gobler & Baumann, 2016). A review of the still limited empirical evidence suggested that the majority of hypoxia × acidification effects across various traits (e.g. growth, survival, calcification rate), life stages, and taxa are additive (Gobler & Baumann, 2016). However, the same review also observed that every published study to date reported at least one instance of interactive effects on a specific trait, life stage or species. Synergistic negative effects of acidification and hypoxia, which were more common than antagonistic effects, comprise the most worrisome outcome, in part because they indicate that many species may be more sensitive to low oxygen conditions in the environment than experiments conducted at high pH conditions would suggest.

Studies of molluscs such as abalone (*Haliotis rufescens*), Baltic clam (*Macoma balthica*), and northern quahog (*Mercenaria mercenaria*) (Figure 6.9A), have found



Figure 6.10 Atlantic silversides *Menidia menidia* © Jacob Snyder.

evidence for synergistic negative effects of hypoxia  $\times$  acidification on growth, but mostly additive effects for survival (Gobler et al., 2014; Jansson et al., 2015; Kim et al., 2013). In contrast, in larval bay scallops (*Argopecten irradians*) (Figure 6.9B), low dissolved oxygen conditions reduced growth but not survival, whereas low pH conditions reduced survival but not growth (Gobler et al., 2014). This suggests that potential effect interactions may be highly species-specific. In addition, sensitivity to acidification and hypoxia, alone and in combination, is likely to differ between life stages. In early northern quahog juveniles (2 months), for example, low oxygen alone reduced survival but not growth, low pH conditions reduced growth but not survival, whereas the combined low oxygen-low pH treatment elicited additive reductions in both traits. In older quahog juveniles (4 months), on the other hand, survival and growth were unaffected by acidified and low oxygen conditions individually, but their combined effect on growth was synergistically negative (Gobler et al., 2014).

For fish, the current evidence of combined hypoxia  $\times$  acidification effects is even scarcer than for molluscs. It is not clear whether this reflects the need for additional experimental work or a tolerance to acidification. As highly mobile vertebrates, fish tend to be very sensitive to reduced oxygen conditions. In contrast, acidification tested at levels that currently occur or are projected by

the end of the 21st century in marine systems primarily affect early life stages and behaviours (Baumann et al., 2012; Cattano et al., 2018; Esbaugh, 2017; Ishimatsu et al., 2008). However, experiments indicate that acidification can increase the sensitivity of adult Atlantic (Figure 6.10) and inland silversides (*Menidia menidia*, *M. beryllina*, respectively) to hypoxia - a significant synergistic effect (Miller et al., 2016). High  $p\text{CO}_2$  levels (such as found in shallow estuarine waters with extreme tidal or diel-cycling conditions) inhibited the ventilatory response used by fish to acquire sufficient oxygen under low-oxygen conditions and reduced survival at higher oxygen concentrations. Under experimental low oxygen conditions, Atlantic silversides tired sooner and reached the point in which they were unable to swim against a current when  $p\text{CO}_2$  was simultaneously increased (T. Targett, et al., unpublished data). Another recent study found additive negative effects on early larval survival and growth in inland silversides, but synergistically negative survival effects of low oxygen and low pH in larval Atlantic silversides (Depasquale et al., 2015).

Together, the limited empirical evidence and the likely species- and stage-specific responses to combined low oxygen and acidification preclude generalizations and do not yet afford predictions as to the occurrence of dissolved oxygen – pH interactions or their importance to marine systems. Existing bioenergetic frameworks (Pörtner, 2012; Sokolova, 2013) provide useful starting

points, because they focus on aerobic scope as the vulnerable fundamental trait (i.e. a proxy for the *surplus* energy available for growth, reproduction, predator avoidance etc.; Figure 6.11).

### 6.3.3 Deoxygenation and disease

Exposure to low oxygen can increase susceptibility of marine animals to disease by reducing immune responses of hosts, by increasing transmission, and by increasing the virulence of pathogens. The potential for low oxygen exposure to increase the prevalence and consequences of infections has been found for a wide range of pathogens and parasites, including viruses,

bacteria, protists, and helminths, and for host taxa ranging from molluscs to crustaceans to fish, including species that support important fisheries (Table 6.1). Correlations between disease prevalence and intensity and low oxygen conditions in the field suggest the potential for hypoxia to exacerbate disease in marine systems (Breitbart et al., 2015b). Because dissolved oxygen varies spatially, it can also influence the landscape-level pattern of the prevalence and intensity of infections in host species (Breitbart et al., 2015b) both because of increased susceptibilities to disease, and because low-oxygen areas can serve as a source of infections for better oxygenated areas (Keppel et al., 2016).

Table 6.1. Examples of effects of low oxygen exposure on diseases of marine organisms.

Host taxa	Host species	Pathogen taxa	Pathogen/disease	Additional stressor	Effect	Proposed or tested mechanism	Citation
Bivalve	eastern oyster ( <i>Crassostrea virginica</i> ) 	Dinoflagellate bacteria	<i>Perkinsus marinus</i> (dermo)  <i>Vibrio campbelli</i>	None  Elevated CO <sub>2</sub>	Increased acquisition and progression of infections Increased culturable bacteria in oyster tissues	Reduced ROS production; increase in granular haemocytes may provide entry point for infections Decrease in bacteriosis	Keppel et al., 2016 Breitbart et al., 2015b Macey et al., 2008
Decapod	Pacific white shrimp ( <i>Litopenaeus vannamei</i> ) 	virus	White spot syndrome virus	none	Increased mortality	Reduced ROS production	Lehmann et al., 2016
Fish	Atlantic salmon ( <i>Salmo salar</i> ) 	protist	Amoebic gill disease	none	Increased mortality	No firm conclusion	Fisk et al., 2002
Fish	European eel ( <i>Anguilla anguilla</i> ) 	helminth	<i>Anguilla crassus</i>	none	Increased stress (higher plasma cortisol)	Increased corticosteroid stress response and higher metabolic cost	Gollock et al., 2005
Decapod	Norway lobster ( <i>Nephrops norvegicus</i> ) 	bacteria	<i>Vibrio parahaemolyticus</i>	Elevated CO <sub>2</sub>	Increased culturable bacteria in hepato-pancreas	Reduced bacteriostatic response and total haemocyte count	Hernroth et al., 2015
Fish	mummichog ( <i>Fundulus heteroclitus</i> ) 	bacteria	<i>Vibrio parahaemolyticus</i>	Elevated CO <sub>2</sub>	(see mechanism)	Reduced ROS production and bactericidal activity	Boleza et al., 2001

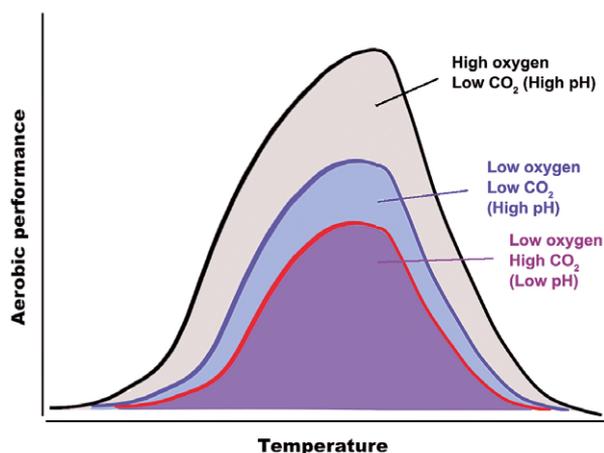


Figure 6.11 Hypothesized aerobic thermal performance curves under different  $O_2$  and  $CO_2$  conditions. For a given temperature, the performance curve narrows if the organism experiences hypoxic, hypercapnic (excessive  $CO_2$ ) or both conditions. (Redrawn after Dam & Baumann, 2017).

Experimental evidence has shown that exposure to low oxygen can increase disease by altering immune responses that rely on phagocytosis and the production of compounds that kill or disable pathogens (Mydlarz et al., 2006). For example, the bacteriostatic response of Norway lobsters (*Nephrops norvegicus*) (Figure 6.12) to *Vibrio parahaemolyticus* was reduced by 2 weeks exposure to 23% oxygen saturation, resulting in higher pathogen loads in hypoxia-exposed infected animals (Henroth et al., 2015). Hypoxia suppresses phagocytotic activity in fish (e.g. the mummichog, *Fundulus heteroclitus*), and in combination with low pH, reduces natural defence mechanisms such as the production of reactive oxygen species (ROS) (Boleza et al., 2001). Boyd and Burnett (1999) and Keppel et al., (2015) found effects of hypoxia on ROS production by eastern oyster (*Crassostrea virginica*) haemocytes, but the direction of effects differed in these two studies, perhaps due to differences in experimental methods. Nevertheless, laboratory exposures to both diel-cycling



Figure 6.12 Norway lobster *Nephrops norvegicus* © Bernard Picton.

and constant low oxygen increased the prevalence, and sometimes, the intensity of infections of the eastern oyster by *Perkinsus marinus*, the causative agent of dermo disease. *P. marinus* has led to high mortality of oyster populations and limited the success of oyster restoration efforts (Breitburg et al., 2015b; Keppel et al., 2015).

Exposure to low oxygen that is tolerated by uninfected animals can result in high mortality of infected individuals. White shrimp (*Litopenaeus stylirostris*) infected with white spot syndrome virus suffered higher mortality when exposed to 30% or 60% oxygen saturation for 96 h than did uninfected shrimp (Lehmann et al., 2016). At 30% saturation, all infected shrimp died, as compared to about a quarter of infected shrimp maintained at 100% oxygen saturation. Eastern oysters with 100% prevalence of *P. marinus* infections suffered approximately 25% greater mortality when exposed to 3 mg  $L^{-1}$  dissolved oxygen for 6 weeks than did infected animals held at high oxygen conditions (Anderson et al., 1998). Similar-length exposures to 2.2 mg  $L^{-1}$  dissolved oxygen did not increase mortality of uninfected juvenile oysters (Keppel et al., 2016).

Distribution shifts in response to unsuitable oxygen conditions can result in crowding of mobile species (Craig, 2012). Much of the evidence of increased disease transmission due to crowding comes from studies of freshwater fishes (e.g. Ficke et al., 2007); however, this process is likely important in estuaries and other water bodies as well. Crowding can be exacerbated by the combination of high temperatures in surface waters and greater hypoxia in bottom waters, which can confine fish to narrower bands of tolerable habitat (Coutant, 1985).

Hypoxia may also sometimes increase pathogen virulence (Phippen & Oliver, 2017), although we know of only one documented example. The estuarine pathogen, *Vibrio vulnificus*, is concentrated by suspension feeding bivalves. Phippen and Oliver (2017) found that exposure to hypoxia increased expression of all three virulence-related *V. vulnificus* genes tested. This one example is particularly notable because of the potential for direct effects on human health. It is probably important to consider that the gastrointestinal tract of humans is a low oxygen environment, and that human gut microbes that can survive in brackish and marine waters might thrive in hypoxic areas where they could be concentrated by edible bivalves.

## 6.4 Multi-stressor considerations in three sensitive systems:

### 6.4.1 Coastal waters

Because of close proximity to land and to large human populations, coastal systems (such as estuaries, lagoons, and semi-enclosed seas) are strongly influenced by the human activities within their watersheds, airsheds, and waters, as well as by increased global GHG emissions (Figure 6.13). Over 500 coastal systems around the world are impacted by nutrient-related hypoxia ( $<2 \text{ mg O}_2 \text{ L}^{-1}$ ) (Breitburg et al., 2018; Diaz & Rosenberg, 2008). The human footprint on these systems is not limited to nutrient discharges, and estuaries and other coastal waters are subject to intense multiple pressures (Mitchell et al., 2015). Both sewage-related low oxygen problems, pollution and overfishing have been reported in estuaries since at least the 19th century (Franz, 1982; Tinsley, 1992).



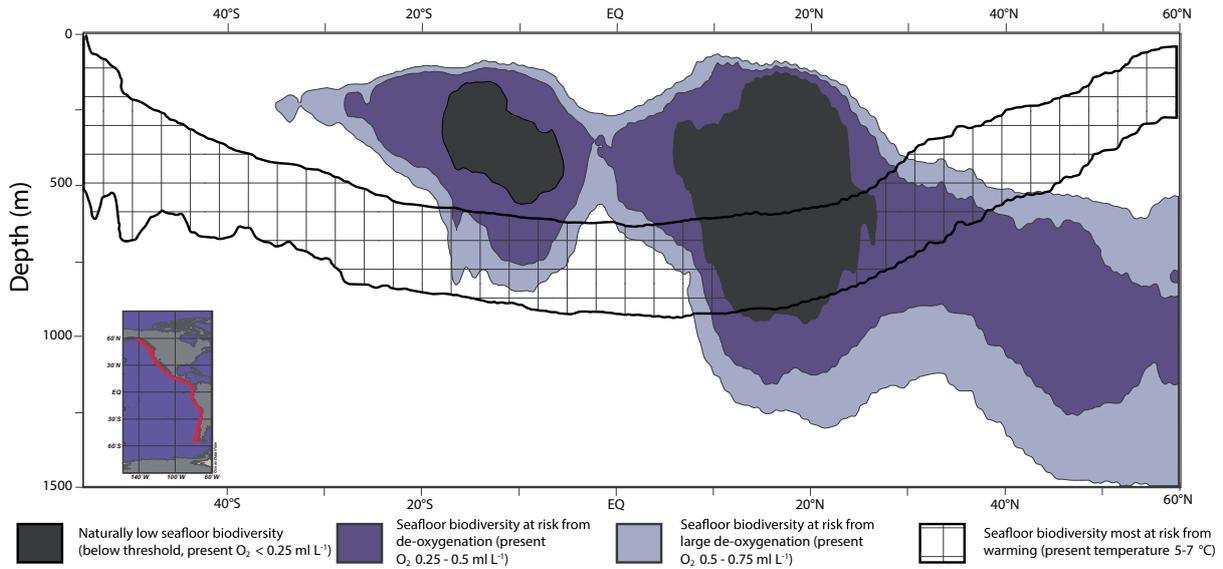
Figure 6.13 Chesapeake Bay is especially sensitive to land-based activities because of its very large watershed. © NASA.



Figure 6.14 Animals inhabiting oxygen minimum zones have evolved to reduce oxygen requirements and increase oxygen uptake – sometimes through elaborate gills as in the terebellid worm. © Greg Rouse, Scripps Institution of Oceanography.

An important characteristic of shallow coastal systems is their high temporal variability in physical and biological characteristics and processes on scales ranging from hours to years or decades (Figure 6.4). In estuaries, spatial gradients and discontinuities in salinity overlay this temporal variability. It is not surprising, therefore, that species that thrive in estuaries and similar water bodies have wide tolerances to a number of physical characteristics of the environment. That does not mean, however, that they are unaffected by multiple stressors that are common in coastal water bodies. For example, a typical estuarine species such as the eastern oyster can experience reduced growth rates, reduced reproduction and increased disease when exposed to diel-cycling hypoxia (e.g. Breitburg et al., 2015b). Nevertheless, oysters thrive in subtidal moderate-salinity waters because their tolerance to reduced salinity is sufficient for survival, and their echinoderm predators are excluded by reduced salinities in estuaries.

## A. Eastern Pacific Ocean



## B. Arabian Sea

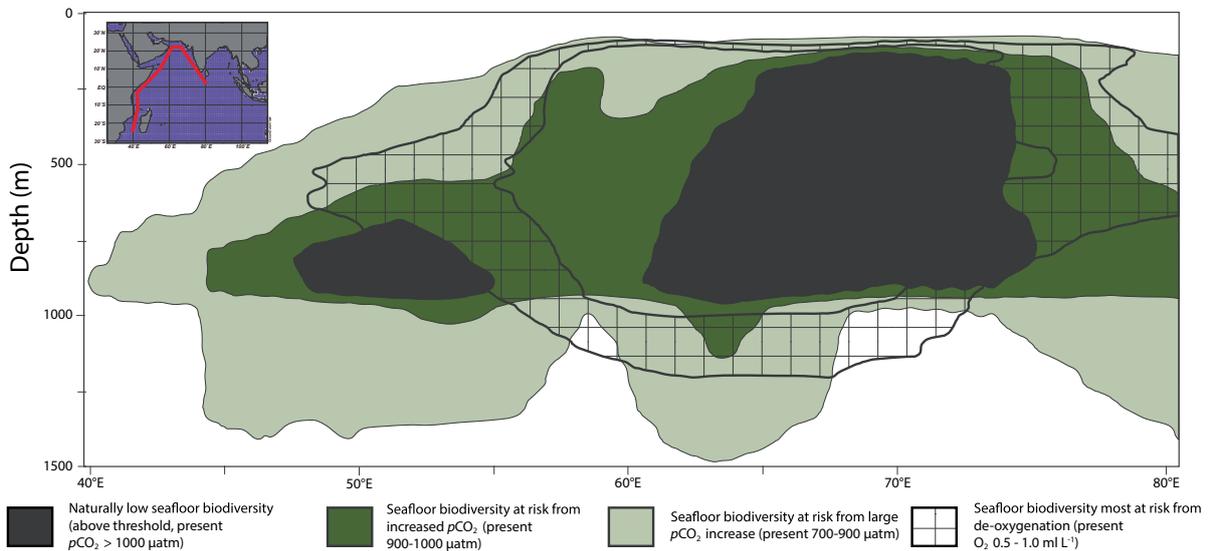


Figure 6.15 Ocean seafloor depths along (A) the eastern Pacific and (B) Arabian Sea (red transect line in inset figures) that are most likely to experience macrofaunal biodiversity loss due to further deoxygenation and increasing temperature. Locations where shading and cross-hatching overlap indicate areas of sea floor where multi-stressor effects of low oxygen and temperature could be strongest. Reproduced from Sperling et al. (2016).

### 6.4.2 Oxygen minimum zones

Oxygen minimum zones are naturally occurring low-oxygen areas that cover vast regions of the ocean at midwater depths (200 to 1,000 m). OMZs impinge on more than a million  $\text{km}^2$  of sea floor (Helly & Levin, 2004), and are most prominent below the more productive regions of the world's surface ocean, where organic matter sinks and is degraded by microbial activity. As in shallow coastal waters, microbial degradation of organic matter in the open ocean consumes oxygen while producing  $\text{CO}_2$ , so that OMZs are regions where

acidification co-occurs with low oxygen (Paulmier et al., 2011). Conditions within OMZs can be established over millions of years (Jacobs et al., 2004), but can be dynamic on glacial/interglacial (10,000 years) as well as much shorter time scales (Moffitt et al., 2015a, b).

The deep sea is not isolated from anthropogenic climate change (Mora et al., 2013). Surface waters hold less oxygen at full saturation because of increased sea-surface temperatures. As these waters travel to depth, they contain less oxygen than they otherwise would (Keeling et al., 2010). In addition, acidification at depth



Figure 6.16 Massive 'walk-out' of rock lobsters in Eland Bay, South Africa. Rock lobsters attempting to escape low oxygen and high levels of hydrogen sulphide crawl out of the ocean and become stranded on the shore. © G. Pitcher.

can be enhanced by anthropogenic  $\text{CO}_2$  (Keeling et al., 2010). The amount of anthropogenic  $\text{CO}_2$  in deep waters is dependent on the age of that water (i.e. the time elapsed since water was last at the sea surface) because anthropogenic  $\text{CO}_2$  enters the ocean at the surface. As a result, for example, waters that are decades old that upwell along the U.S. West Coast contain anthropogenic  $\text{CO}_2$  at levels reflecting atmospheric concentrations that were already elevated by the mid 20th century (Feely et al., 2008).

The upper and lower boundaries of OMZs are characterized by strong zonation in community structure, with rapid shifts in biological diversity that are responding to hydrographic changes, often in a threshold-like manner (Gooday et al., 2010; Levin, 2003). The combination of upward-expanding midwater deoxygenation with the warming and acidification of surface water reduces the vertical extent of suitable habitat for sensitive species (Gilly et al., 2013). Oxygen exerts tremendous control on marine biodiversity (Figure 6.14) through effects on evolution, physiology, reproduction, behaviour, and species interactions (Gooday et al., 2010; Stramma et al., 2010, 2012). Temperature, acidification, and food availability can act individually and in combination with low oxygen to further alter biological diversity patterns (Sperling et al., 2016; Figure 6.15).

Regional differences among OMZs reflect differences in hydrography and lead to differing combinations and intensities of multi-stressor effects. Deep-sea mining is an additional stressor proposed within some of the

ocean's low-oxygen regions. For example, phosphorites (phosphorus-containing solid particles) are targets for mining for use as an industrial fertilizer and are found along continental margins with low oxygen. Mining removes seabed sediments, including the organisms living on and in the sediment. Some nations – New Zealand and Mexico – have rejected marine phosphate mining proposals because of the associated environmental risks. Other nations, like Namibia, are still considering such projects. The combined effects of expanding low oxygen in the ocean and mining are unknown.

### 6.4.3 Upwelling margins and open coastline

Along coastal upwelling margins, cold and nutrient-rich waters are brought to the surface through the action of wind-driven currents that move surface water away from the coast to be replaced by deeper waters. Coastal upwelling supports some of the most productive fisheries in the world (Jennings et al., 2009). Upwelled water masses are, however, low in oxygen content and enriched with  $\text{CO}_2$  (that leads to low pH) due to decomposition of organic matter originating in surface waters. In some upwelling regions, such as the coasts of Peru and Namibia, extreme oxygen depletion leads to production of toxic hydrogen sulphide plumes, which can erupt and affect thousands of  $\text{km}^2$  of the ocean surface (Ohde & Dadou, 2018; Schunck et al., 2013; Weeks et al., 2004). Decomposition of harmful algal blooms in nearshore portions of upwelling regions further deplete oxygen, can fuel production of toxic hydrogen sulphides, and can result in large-scale mortality of important fishery

species (Cockcroft et al., 2001; Pitcher & Probyn, 2011) (Figure 6.16). The combined effects of GHG emissions and nutrient enrichment are projected to further reduce oxygen content, increase  $p\text{CO}_2$  and warm upwelled waters along some coasts (Doney, 2010).

Habitat diversity is a characteristic of coastal upwelling margins. Canyons, reefs, methane seeps, kelp forests, rocky subtidal, and intertidal ecosystems are thus periodically subjected to deoxygenation and co-occurring stressors (Levin & Dayton 2009). Some habitats, such as kelp forests (Figure 6.17), may mediate the effects of hypoxia and acidification through productivity. Kelps exhibit exceedingly fast growth rates that can moderate local water conditions (Frieder et al., 2012). The co-occurrence of expanding hypoxia and acidification on coastal upwelling margins might also result in less biogenic (i.e. produced by the organisms) heterogeneity (Levin, 2003). For example, cold-water corals are structure-forming species that provide shelter from predation and can act as nursery grounds for commercially important species (Koslow et al., 2000). Cold-water corals and other calcifying taxa (e.g. bivalves and echinoderms) may be susceptible to co-occurring hypoxia and acidification leading to reduced survival and growth, brittle structures and loss of habitat.

## 6.5 Conclusions

Reducing, and where possible, reversing deoxygenation, and conserving species and ecosystem services where oxygen has declined, require an understanding of the

causes and effects of deoxygenation in the real-world environmental context in which it occurs. That context includes the presence of additional stressors, many of which are caused by human activities, and some of which can have non-additive negative effects on species or ecological processes when they co-occur with low oxygen. Although the combined effects of individual stressors can sometimes be predicted by summing their individual effects, this simple approach can yield misleading results. Mitigation efforts focusing on a single stressor may not yield the desired relief, and adaptation strategies may provide less protection than desired. Because different sectors of civil society and different governmental jurisdictions can be responsible for causing or mitigating different stressors, fair assignment of responsibility is difficult without considering and evaluating the roles of multiple, potentially interacting stressors. This complexity also means that cross-disciplinary science is critical, and that management actions that cross boundaries of different agencies and jurisdictions are often required.

## Acknowledgements

We thank K. de Mustert, C. Gobler, A. Griffith and an anonymous reviewer for helpful comments on an earlier draft of this chapter. D. Breitburg acknowledges NOAA Center for Sponsored Coastal Ocean Research grant (NA10NOS4780138) and Maryland Sea Grant (NA14OAR4170090) for recent funding on the topic of multiple stressors.

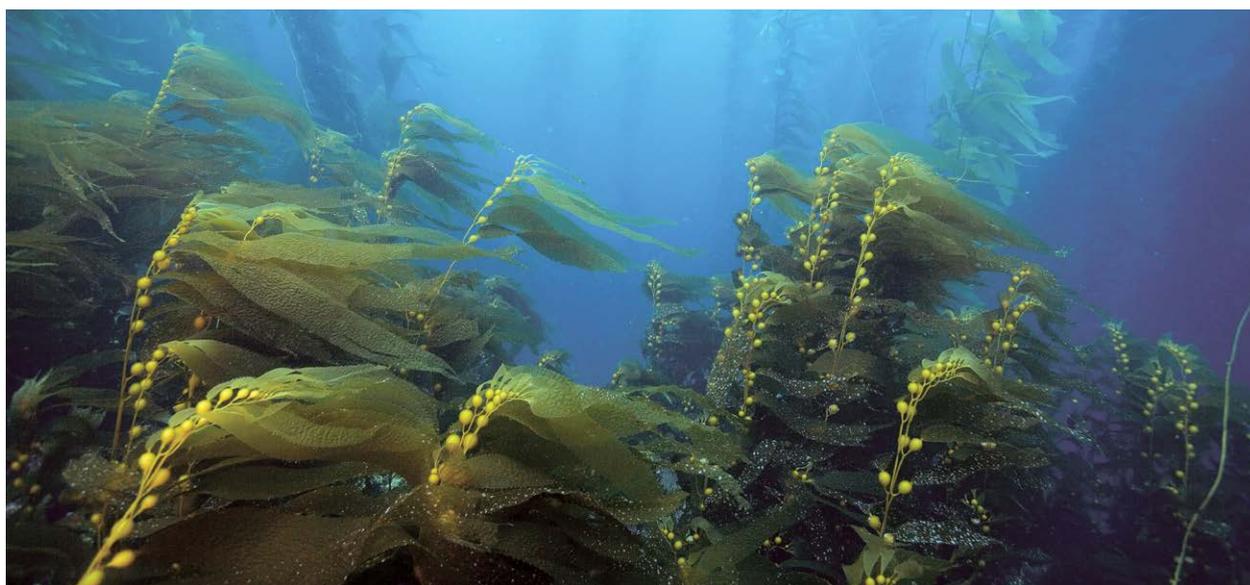


Figure 6.17 Upwelled nutrients stimulate growth of macroalgae, like this giant kelp *Macrocyctis pyrifera* along the eastern boundaries of continents. Where upwelled waters are not severely oxygen depleted, highly productive ecosystems can thrive. © Minden Pictures / Alamy stock photo.

## 6.6 References

- Anderson, R., Brubacher, L., Calvo, L.R., Unger, M., & Bureson, E. (1998). Effects of tributyltin and hypoxia on the progression of *Perkinsus marinus* infections and host defence mechanisms in oyster, *Crassostrea virginica* (Gmelin). *Journal of Fish Diseases*, 21, 371-380. <https://doi.org/10.1046/j.1365-2761.1998.00128.x>
- Anttila, K., Lewis, M., Prokkola, J.M., Kanerva, M., Seppänen, E., Kolari, I., & Nikinmaa, M. (2015). Warm acclimation and oxygen depletion induce species-specific responses in salmonids. *Journal of Experimental Biology*, 218, 1471-1477. <https://doi.org/10.1242/jeb.119115>
- Bagwe, R., Beniash, E., & Sokolova, I.M. (2015). Effects of cadmium exposure on critical temperatures of aerobic metabolism in eastern oysters *Crassostrea virginica* (Gmelin, 1791). *Aquatic Toxicology*, 167, 77-89. <https://doi.org/10.1016/j.aquatox.2015.07.012>
- Baumann, H., & Smith, E.M. (2018). Quantifying metabolically driven pH and oxygen fluctuations in US nearshore habitats at diel to interannual time scales. *Estuaries and Coasts*, 41, 1102-1117. <https://doi.org/10.1007/s12237-017-0321-3>
- Baumann, H., Wallace, R.B., Tagliaferri, T., & Gobler, C.J. (2015). Large natural pH, CO<sub>2</sub> and O<sub>2</sub> fluctuations in a temperate tidal salt marsh on diel, seasonal, and interannual time scales. *Estuaries and Coasts*, 38, 220-231. <https://doi.org/10.1007/s12237-014-9800-y>
- Baumann, H., Talmage, S.C., & Gobler, C.J. (2012). Reduced early life growth and survival in a fish in direct response to increased carbon dioxide. *Nature Climate Change*, 2, 38-41. <https://doi.org/10.1038/nclimate1291>
- Bavis, R.W., Powell, F.L., Bradford, A., Hsia, C.C.W., Peltonen, J. E., Soliz, J., ... Wilkinson, K.A. (2007). Respiratory plasticity in response to changes in oxygen supply and demand. *Integrative and Comparative Biology*, 47, 532-551. <https://doi.org/10.1093/icb/icm070>
- Boleza, K.A., Burnett, L.E., & Burnett, K.G. (2001). Hypercapnic hypoxia compromises bactericidal activity of fish anterior kidney cells against opportunistic environmental pathogens. *Fish & Shellfish Immunology*, 11, 593-610. <https://doi.org/10.1006/fsim.2001.0339>
- Bopp, L., Resplandy, L., Orr, J.C., Doney, S.C., Dunne, J.P., Gehlen, M., ... Seferian, R. (2013). Multiple stressors of ocean ecosystems in the 21st century: projections with CMIP5 models. *Biogeosciences*, 10, 6225-6245. <https://doi.org/10.5194/bg-10-6225-2013>
- Boyd, J.N., & Burnett, L.E. (1999). Reactive oxygen intermediate production by oyster hemocytes exposed to hypoxia. *Journal of Experimental Biology*, 202, 3135-3143.
- Boyd, P.W., Lennartz, S.T., Glover, D.M., & Doney, S.C. (2015). Biological ramifications of climate-change-mediated oceanic multi-stressors. *Nature Climate Change*, 5, 71-79. <https://doi.org/10.1038/nclimate2441>
- Breitburg, D.L., Loher, T., Pacey, C.A., & Gerstein, A. (1997). Varying effects of low dissolved oxygen on trophic interactions in an estuarine food web. *Ecological Monographs*, 67, 489-507. [https://doi.org/10.1890/0012-9615\(1997\)067\[0489:VEOLDO\]2.0.CO;2](https://doi.org/10.1890/0012-9615(1997)067[0489:VEOLDO]2.0.CO;2)
- Breitburg, D.L. (2002). Effects of hypoxia, and the balance between hypoxia and enrichment, on coastal fishes and fisheries. *Estuaries*, 25, 767-781. <https://doi.org/10.1007/BF02804904>
- Breitburg, D.L., & Riedel, G.F. (2005). Multiple stressors in marine systems. In E. N. Norse, & A. L. Crowder, (Eds.). *Marine Conservation Biology: The Science of Maintaining the Sea's Biodiversity*. pp. 167-182, Island Press, Washington.
- Breitburg, D.L., Hondorp, D.W., Davias, L.A., & Diaz, R.J. (2009). Hypoxia, nitrogen, and fisheries: integrating effects across local and global landscapes. *Annual Review of Marine Science*, 1, 329-349. <https://doi.org/10.1146/annurev.marine.010908.163754>
- Breitburg, D.L., Salisbury, J., Bernhard, J.M., Cai, W.-J., Dupont, S., Doney, S.C., ... Tarrant, A. M. (2015a). And on top of all that... Coping with ocean acidification in the midst of many stressors. *Oceanography*, 28, 48-61. <https://doi.org/10.5670/oceanog.2015.31>
- Breitburg, D.L., Hondorp, D., Audemard, C., Carnegie, R.B., Burrell, R.B., Trice, M., & Clark, V. (2015b). Landscape-level variation in disease susceptibility related to shallow-water hypoxia. *PLoS ONE*, 10, e0116223. <https://doi.org/10.1371/journal.pone.0116223>
- Breitburg, D., Levin, L.A., Oschlies, A., Grégoire, M., Chavez, F.P., Conley, D.J., ... Isensee, K. (2018). Declining oxygen in the global ocean and coastal waters. *Science*, 359, eaam7240. <https://doi.org/10.1126/science.aam7240>
- Brijs, J., Jutfelt, F., Clark, T.D., Gräns, A., Ekström, A., & Sandblom, E. (2015). Experimental manipulations of tissue oxygen supply do not affect warming tolerance of European perch. *Journal of Experimental Biology*, 218, 2448-2454. <https://doi.org/10.1242/jeb.121889>
- Byrne, R.H., DeGrandpre, M.D., Short, R. T., Martz, T.R., Merlivat, L., McNeil, C., ... Fietzek, P. (2010). Sensors and systems for in situ observations of marine carbon dioxide system variables. *Proceedings of OceanObs' 09: Sustained Ocean Observations and Information for Society*, Venice, Italy, 21-25 September 2009. OceanObs' 09. <https://doi.org/10.5270/OceanObs09.cwp.13>
- Cai, W.-J., Hu, X., Huang, W. -J., Murrell, M.C., Lehrter, J.C., Lohrenz, S.E., ... Wang, Y. (2011). Acidification of subsurface coastal waters enhanced by eutrophication. *Nature Geoscience*, 4, 766-770. <https://doi.org/10.1038/ngeo1297>
- Cattano, C., Claudet, J., Domenici, P., & Milazzo, M. (2018). Living in a high CO<sub>2</sub> world: a global meta-analysis shows multiple trait-mediated fish responses to ocean acidification. *Ecological Monographs*, 88, 320-335. <https://doi.org/10.1002/ecm.1297>
- Cheng, B. S., Bible, J.M., Chang, A.L., Ferner, M.C., Wasson, K., Zabin, C.J., ... Grosholz, E.D. (2015). Testing local and global stressor impacts on a coastal foundation species using an ecologically realistic framework. *Global Change Biology*, 21, 2488-2499. <https://doi.org/10.1111/gcb.12895>
- Cheung, W.W., Dunne, J., Sarmiento, J.L., & Pauly, D. (2011). Integrating ecophysiology and plankton dynamics into projected maximum fisheries catch potential under climate change in the Northeast Atlantic. *ICES Journal of Marine Science*, 68, 1008-1018. <https://doi.org/10.1093/icesjms/fsr012>
- Cheung, W.W., Sarmiento, J.L., Dunne, J., Frölicher, T.L., Lam, V.W., Palomares, M.D., ... Pauly, D. (2013). Shrinking of fishes exacerbates impacts of global ocean changes on marine

- ecosystems. *Nature Climate Change*, 3, 254-258. <https://doi.org/10.1038/nclimate1691>
- Cloern, J.E. (2001). Our evolving conceptual model of the coastal eutrophication problem. *Marine Ecology Progress Series*, 210, 223-253. <https://doi.org/10.3354/meps210223>
- Cloern, J.E., Abreu, P.C., Carstensen, J., Chauvaud, L., Elmgren, R., Grall, J., ... Sherwood, E.T. (2016). Human activities and climate variability drive fast-paced change across the world's estuarine-coastal ecosystems. *Global Change Biology*, 22, 513-529. <https://doi.org/10.1111/gcb.13059>
- Cockcroft, A.C., Schoeman, D.S., Pitcher, G. C., Bailey, G.W., & Van Zyl, D.L. (2000). A mass stranding, or 'walk out' of west coast rock lobster, *Jasus lalandii*, in Elands Bay, South Africa: Causes, results, and implications. *Crustacean Issues*, 11, 673-688.
- Costanza, R., d'Arge, R., de Groot, R., Farber, S., Grasso, M., Hannon, B., ... van den Belt, M. (1997). The value of the world's ecosystem services and natural capital. *Nature*, 387, 253-260. <https://doi.org/10.1038/387253a0>
- Coutant, C.C. (1985). Striped bass, temperature, and dissolved oxygen: A speculative hypothesis for environmental risk. *Transactions of the American Fisheries Society*, 114, 31-61. [https://doi.org/10.1577/1548-8659\(1985\)114<31:SBTADO>2.0.CO;2](https://doi.org/10.1577/1548-8659(1985)114<31:SBTADO>2.0.CO;2)
- Craig, J.K. (2012). Aggregation on the edge: effects of hypoxia avoidance on the spatial distribution of brown shrimp and demersal fishes in the Northern Gulf of Mexico. *Marine Ecology Progress Series*, 445, 75-95. <https://doi.org/10.3354/meps09437>
- Dam, H.G., & Baumann, H. (2017). Climate change, zooplankton and fisheries. In B. Phillips & M. Perez-Ramirez (Eds.). *The impacts of climate change on fisheries and aquaculture*. Wiley/Blackwell. <https://doi.org/10.1002/9781119154051.ch25>
- Delorenzo, M.E. (2015). Impacts of climate change on the ecotoxicology of chemical contaminants in estuarine organisms. *Current Zoology*, 61, 641-652. <https://doi.org/10.1093/czoolo/61.4.641>
- De Mutsert, K., Steenbeek, J., Lewis, K., Buszowski, J., Cowan, J.H. Jr., & Christensen, V. (2016). Exploring effects of hypoxia on fish and fisheries in the northern Gulf of Mexico using a dynamic spatially explicit ecosystem model. *Ecological Modelling*, 331, 142-150. <https://doi.org/10.1016/j.ecolmodel.2015.10.013>
- Depasquale, E., Baumann, H., & Gobler, C.J. (2015). Variation in early life stage vulnerability among Northwest Atlantic estuarine forage fish to ocean acidification and low oxygen. *Marine Ecology Progress Series*, 523, 145-156. <https://doi.org/10.3354/meps11142>
- Deutsch, C., Ferrel, A., Seibel, B., Pörtner, H.-O., & Huey, R.B. (2015). Climate change tightens a metabolic constraint on marine habitats. *Science*, 348, 1132-1135. <https://doi.org/10.1126/science.aaa1605>
- Diaz, R.J., & Rosenberg, R. (1995). Marine benthic hypoxia: a review of its ecological effects and the behavioural responses of benthic macrofauna. *Oceanography and Marine Biology: An Annual Review*, 33, 245-303
- Diaz, R.J., & Rosenberg, R. (2008). Spreading dead zones and consequences for marine ecosystems. *Science*, 321, 926-929. <https://doi.org/10.1126/science.1156401>
- Doney, S.C. (2010). The growing human footprint on coastal and open-ocean biogeochemistry. *Science*, 328, 1512-1516. <https://doi.org/10.1126/science.1185198>
- Dowd, W.W., King, F.A., & Denny, M.W. (2015). Thermal variation, thermal extremes and the physiological performance of individuals. *Journal of Experimental Biology*, 218, 1956-1967. <https://doi.org/10.1242/jeb.114926>
- Eby, L.A., & Crowder, L.B. (2002). Hypoxia-based habitat compression in the Neuse River Estuary: context-dependent shifts in behavioral avoidance thresholds. *Canadian Journal of Fisheries and Aquatic Sciences*, 59, 952-965. <https://doi.org/10.1139/f02-067>
- Esbaugh, A. J. (2017). Physiological implications of ocean acidification for marine fish: emerging patterns and new insights. *Journal of Comparative Physiology B*, 188, 1-13. <https://doi.org/10.1007/s00360-017-1105-6>
- Feely, R.A., Sabine, C.L., Hernandez-Ayon, J.M., Ianson, D., & Hales, B. (2008). Evidence for upwelling of corrosive "acidified" water onto the continental shelf. *Science*, 320, 1490-1492. <https://doi.org/10.1126/science.1155676>
- Ficke, A.D., Myrick, C.A., & Hansen, L.J. (2007). Potential impacts of global climate change on freshwater fisheries. *Reviews in Fish Biology and Fisheries*, 17, 581-613. <https://doi.org/10.1007/s11160-007-9059-5>
- Field, C.B., Barros, V.R., Dokken, D.J., Mach, K.J., Mastrandrea, M.D., Bilir, T.E., ... White, L.L. (2014). Climate Change 2014: Impacts, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA.
- Fisk, D., Powell, M., & Nowak, B. (2002). The effect of amoebic gill disease and hypoxia on survival and metabolic rate of Atlantic salmon (*Salmo salar*). *Bulletin – European Association of Fish Pathologists*, 22, 190-194.
- Folt, C., Chen, C., Moore, M., & Burnaford, J. (1999). Synergism and antagonism among multiple stressors. *Limnology and Oceanography*, 44, 864-877. [https://doi.org/10.4319/lo.1999.44.3\\_part\\_2.0864](https://doi.org/10.4319/lo.1999.44.3_part_2.0864)
- Franz, D.R. (1982). An historical perspective on mollusks in Lower New York Harbor, with emphasis on oysters. *Ecological Stress and the New York Bight: Science and Management*. Columbia SC: *Estuarine Research Federation*, pp. 181-197.
- Frederich, M., & Pörtner, H.-O. (2000). Oxygen limitation of thermal tolerance defined by cardiac and ventilatory performance in spider crab, *Maja squinado*. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 279, R1531-R1538. <https://doi.org/10.1152/ajpregu.2000.279.5.R1531>
- Frieder, C., Nam, S., Martz, T., & Levin, L. (2012). High temporal and spatial variability of dissolved oxygen and pH in a nearshore California kelp forest. *Biogeosciences*, 9, 3917-3930. <https://doi.org/10.5194/bg-9-3917-2012>
- Froehlich, H.E., Essington, T.E., & MacDonald, P.S. (2017). When does hypoxia affect management performance of a fishery? A management strategy evaluation of Dungeness crab (*Metacarcinus magister*) fisheries in Hood Canal, Washington, USA. *Canadian Journal of Fisheries and Aquatic Sciences*, 74, 922-932. <https://doi.org/10.1139/cjfas-2016-0269>

- Gattuso, J.-P., Magnan, A., Billé, R., Cheung, W.W., Howes, E.L., Joos, F., ... Turley, C. (2015). Contrasting futures for ocean and society from different anthropogenic CO<sub>2</sub> emissions scenarios. *Science*, 349, aac4722. <https://doi.org/10.1126/science.aac4722>
- Gedan, K.B., Altieri, A.H., Feller, I., Burrell, R., & Breitburg, D. (2017). Community composition in mangrove ponds with pulsed hypoxic and acidified conditions. *Ecosphere*, 8, e02053. <https://doi.org/10.1002/ecs2.2053>
- Gilly, W.F., Beman, J.M., Litvin, S.Y., & Robison, B.H. (2013). Oceanographic and biological effects of shoaling of the oxygen minimum zone. *Annual Review of Marine Science*, 5, 393-420. <https://doi.org/10.1146/annurev-marine-120710-100849>
- Gilmour, C.C., Podar, M., Bullock, A.L., Graham, A.M., Brown, S.D., Somenahally, A.C., ... Elias, D.A. (2013). Mercury methylation by novel microorganisms from new environments. *Environmental Science & Technology*, 47, 11810-11820. <https://doi.org/10.1021/es403075t>
- Glade, T. (2003). Landslide occurrence as a response to land use change: a review of evidence from New Zealand. *CATENA*, 51, 297-314. [https://doi.org/10.1016/S0341-8162\(02\)00170-4](https://doi.org/10.1016/S0341-8162(02)00170-4)
- Glibert, P.M., Al-Azri, A., Icarus Allen, J., Bouwman, A.F., Beusen, A.H., Burford, M.A., ... Zhou, M. (2018). Key questions and recent research advances on harmful algal blooms in relation to nutrients and eutrophication. In P.M. Gilbert, E. Berdalet, M.A. Burford, G.C. Pitcher & M. Zhou (Eds.), *Global Ecology and Oceanography of Harmful Algal Blooms*, pp.229-259, Springer. [https://doi.org/10.1007/978-3-319-70069-4\\_12](https://doi.org/10.1007/978-3-319-70069-4_12)
- Gobler, C.J., & Baumann, H. (2016). Hypoxia and acidification in marine ecosystems: Coupled dynamics and effects on ocean life. *Biology Letters*, 12, 20150976. <https://doi.org/10.1098/rsbl.2015.0976>
- Gobler, C.J., Depasquale, E., Griffith, A., & Baumann, H. (2014). Hypoxia and acidification have additive and synergistic negative effects on the growth, survival, and metamorphosis of early life stage bivalves. *PLoS ONE*, 9, e83648. <https://doi.org/10.1371/journal.pone.0083648>
- Gollock, M., Kennedy, C., & Brown, J. (2005). European eels, *Anguilla anguilla* (L.), infected with *Anguillicola crassus* exhibit a more pronounced stress response to severe hypoxia than uninfected eels. *Journal of Fish Diseases*, 28, 429-436. <https://doi.org/10.1111/j.1365-2761.2005.00649.x>
- Gooday, A.J., Bett, B.J., Escobar, E., Ingole, B., Levin, L.A., Neira, C., ... Sellanes, J. (2010). Habitat heterogeneity and its influence on benthic biodiversity in oxygen minimum zones. *Marine Ecology*, 31, 125-147. <https://doi.org/10.1111/j.1439-0485.2009.00348.x>
- Gräns, A., Jutfelt, F., Sandblom, E., Jönsson, E., Wiklander, K., Seth, H., ... Einarsdottir, I. (2014). Aerobic scope fails to explain the detrimental effects on growth resulting from warming and elevated CO<sub>2</sub> in Atlantic halibut. *Journal of Experimental Biology*, 217, 711-717. <https://doi.org/10.1242/jeb.096743>
- Gruber, N. (2011). Warming up, turning sour, losing breath: ocean biogeochemistry under global change. *Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, 369, 1980-1996. <https://doi.org/10.1098/rsta.2011.0003>
- Gruber, N., Hauri, C., Lachkar, Z., Loher, D., Frölicher, T.L., & Plattner, G. -K. (2012). Rapid progression of ocean acidification in the California Current System. *Science*, 337, 220-223. <https://doi.org/10.1126/science.1216773>
- Hansson, S., Hjerne, O., Harvey, C., Kitchell, J.F., Cox, S.P., & Essington, T.E. (2007). Managing Baltic Sea fisheries under contrasting production and predation regimes: ecosystem model analyses. *AMBIO: A Journal of the Human Environment*, 36, 265-271. [https://doi.org/10.1579/0044-7447\(2007\)36\[265:MB SFUC\]2.0.CO;2](https://doi.org/10.1579/0044-7447(2007)36[265:MB SFUC]2.0.CO;2)
- Helly, J.J., & Levin, L.A. (2004). Global distribution of naturally occurring marine hypoxia on continental margins. *Deep Sea Research Part I: Oceanographic Research Papers*, 51, 1159-1168. <https://doi.org/10.1016/j.dsr.2004.03.009>
- Herrnroth, B., Krång, A.-S., & Baden, S. (2015). Bacteriostatic suppression in Norway lobster (*Nephrops norvegicus*) exposed to manganese or hypoxia under pressure of ocean acidification. *Aquatic Toxicology*, 159, 217-224. <https://doi.org/10.1016/j.aquatox.2014.11.025>
- Hochachka, P. W., Buck, L.T., Doll, C.J., & Land, S.C. (1996). Unifying theory of hypoxia tolerance: molecular/metabolic defense and rescue mechanisms for surviving oxygen lack. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 9493-9498. <https://doi.org/10.1073/pnas.93.18.9493>
- Ishimatsu, A., Hayashi, M., & Kikkawa, T. (2008). Fishes in high-CO<sub>2</sub>, acidified oceans. *Marine Ecology Progress Series*, 373, 295-302. <https://doi.org/10.3354/meps07823>
- Ivanina, A.V., & Sokolova, I.M. (2016). Effects of intermittent hypoxia on oxidative stress and protein degradation in molluscan mitochondria. *Journal of Experimental Biology*, 219, 3794-3802. <https://doi.org/10.1242/jeb.146209>
- Jacobs, D.K., Haney, T.A., & Louie, K.D. (2004). Genes, diversity, and geologic process on the Pacific coast. *Annual Review of Earth and Planetary Science*, 32, 601-652. <https://doi.org/10.1146/annurev.earth.32.092203.122436>
- Jansson, A., Norkko, J., Dupont, S., & Norkko, A. (2015). Growth and survival in a changing environment: combined effects of moderate hypoxia and low pH on juvenile bivalve *Macoma balthica*. *Journal of Sea Research*, 102, 41-47. <https://doi.org/10.1016/j.seares.2015.04.006>
- Jennings, S., Kaiser, M., & Reynolds, J.D. (2009). *Marine fisheries ecology*. John Wiley & Sons.
- Jensen, D.L., Overgaard, J., Wang, T., Gesser, H., & Malte, H. (2017). Temperature effects on aerobic scope and cardiac performance of European perch (*Perca fluviatilis*). *Journal of Thermal Biology*, 68, 162-169. <https://doi.org/10.1016/j.jtherbio.2017.04.006>
- Jones, K.R., Klein, C.J., Halpern, B.S., Venter, O., & Grantham, H. (2018). The location and protection status of Earth's diminishing marine wilderness. *Current Biology*, 28, 2506-2512. <https://doi.org/10.1016/j.cub.2018.06.010>
- Keeling, R. F., Körtzinger, A., & Gruber, N. (2010). Ocean deoxygenation in a warming world. *Marine Science*, 2, 199-229. <https://doi.org/10.1146/annurev.marine.010908.163855>
- Kemp, W.M., Boynton, W.R., Adolf, J.E., Boesch, D.F., Boicourt, W.C., Brush, G., ... Hagy, J.D. (2005). Eutrophication of hesapeake Bay: historical trends and ecological interactions. *Marine*

- Ecology Progress Series*, 303, 1-29. <https://doi.org/10.3354/meps303001>
- Keppel, A.G., Breitburg, D.L., & Burrell, R.B. (2016). Effects of co-varying diel-cycling hypoxia and pH on growth in the juvenile eastern oyster, *Crassostrea virginica*. *PLoS ONE*, 11, e0161088. <https://doi.org/10.1371/journal.pone.0161088>
- Keppel, A.G., Breitburg, D.L., Wikfors, G.H., Burrell, R.B., & Clark, V.M. (2015). Effects of co-varying diel-cycling hypoxia and pH on disease susceptibility in the eastern oyster *Crassostrea virginica*. *Marine Ecology Progress Series*, 538, 169-183. <https://doi.org/10.3354/meps11479>
- Kim, T., Barry, J., & Micheli, F. (2013). The effects of intermittent exposure to low-pH and low-oxygen conditions on survival and growth of juvenile red abalone. *Biogeosciences*, 10, 7255. <https://doi.org/10.5194/bg-10-7255-2013>
- Kingsolver, J.G., & Buckley, L.B. (2017). Quantifying thermal extremes and biological variation to predict evolutionary responses to changing climate. *Philosophical Transactions Royal Society B: Biological Sciences*, 372, 20160147. <https://doi.org/10.1098/rstb.2016.0147>
- Kingsolver, J.G., MacLean, H.J., Goddin, S.B., & Augustine, K.E. (2016). Plasticity of upper thermal limits to acute and chronic temperature variation in *Manduca sexta* larvae. *Journal of Experimental Biology*, 219, 1290-1294. <https://doi.org/10.1242/jeb.138321>
- Koslow, J.A., Boehlert, G., Gordon, J., Haedrich, R., Lorance, P., & Parin, N. (2000). Continental slope and deep-sea fisheries: implications for a fragile ecosystem. *ICES Journal of Marine Science*, 57, 548-557. <https://doi.org/10.1006/jmsc.2000.0722>
- Lehmann, M., Schleder, D., Guertler, C., Perazzolo, L., & Vinatea, L. (2016). Hypoxia increases susceptibility of Pacific white shrimp to whitespot syndrome virus (WSSV). *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, 68, 397-403. <https://doi.org/10.1590/1678-4162-7942>
- Levin, L.A. (2003). Oxygen minimum zone benthos: adaptation and community response to hypoxia. *Oceanography and Marine Biology: An Annual Review*, 41, 1-45.
- Levin, L.A. (2018). Manifestation, drivers, and emergence of open ocean deoxygenation. *Annual Review of Marine Science*, 10, 229-260. <https://doi.org/10.1146/annurev-marine-121916-063359>
- Levin, L.A., & Dayton, P.K. (2009). Ecological theory and continental margins: where shallow meets deep. *Trends in Ecology & Evolution*, 24, 606-617. <https://doi.org/10.1016/j.tree.2009.04.012>
- Levin, L.A., & Le Bris, N. (2015). The deep ocean under climate change. *Science*, 350, 766-768. <https://doi.org/10.1126/science.aad0126>
- Macey, B.M., Achilihu, I.O., Burnett, K.G., & Burnett, L.E. (2008). Effects of hypercapnic hypoxia on inactivation and elimination of *Vibrio campbellii* in the Eastern oyster, *Crassostrea virginica*. *Applied and Environmental Microbiology*, 74, 6077-6084. <https://doi.org/10.1128/AEM.00317-08>
- Marigómez, I., Múgica, M., Izagirre, U., & Sokolova, I.M. (2017). Chronic environmental stress enhances tolerance to seasonal gradual warming in marine mussels. *PLoS ONE*, 12, e0174359. <https://doi.org/10.1371/journal.pone.0174359>
- McBryan, T.L., Healy, T.M., Haakons, K.L., & Schulte, P.M. (2016). Warm acclimation improves hypoxia tolerance in *Fundulus heteroclitus*. *Journal of Experimental Biology*, 219, 474-484. <https://doi.org/10.1242/jeb.133413>
- Miller, S.H., Breitburg, D.L., Burrell, R.B., & Keppel, A.G. (2016). Acidification increases sensitivity to hypoxia in important forage fishes. *Marine Ecology Progress Series*, 549, 1-8. <https://doi.org/10.3354/meps11695>
- Mitchell, S.B., Jennerjahn, T.C., Vizzini, S., & Zhang, W. (2015). Changes to processes in estuaries and coastal waters due to intense multiple pressures—an introduction and synthesis. *Estuarine, Coastal and Shelf Science*, 156, 1-6. <https://doi.org/10.1016/j.ecss.2014.12.027>
- Moffitt, S.E., Hill, T.M., Roopnarine, P.D., & Kennett, J.P. (2015a). Response of seafloor ecosystems to abrupt global climate change. *Proceedings of the National Academy of Sciences of the United States of America*, 112, 4684-4689. <https://doi.org/10.1073/pnas.1417130112>
- Moffitt, S.E., Moffitt, R.A., Sauthoff, W., Davis, C.V., Hewett, K., & Hill, T.M. (2015b). Paleooceanographic insights on recent oxygen minimum zone expansion: Lessons for modern oceanography. *PLoS ONE*, 10, e0115246. <https://doi.org/10.1371/journal.pone.0115246>
- Mora, C., Wei, C.-L., Rollo, A., Amaro, T., Baco, A.R., Billett, D., ... Danovaro, R. (2013). Biotic and human vulnerability to projected changes in ocean biogeochemistry over the 21st century. *PLoS Biol*, 11, e1001682. <https://doi.org/10.1371/journal.pbio.1001682>
- Mydlarz, L.D., Jones, L.E., & Harvell, C.D. (2006). Innate immunity, environmental drivers, and disease ecology of marine and freshwater invertebrates. *Annual Review of Ecology, Evolution and Systematics*, 37, 251-288. <https://doi.org/10.1146/annurev.ecolsys.37.091305.110103>
- Nilsson G.E., Östlund-Nilsson, S., & Munday, P.L. (2010). Effects of elevated temperature on coral reef fishes: loss of hypoxia tolerance and inability to acclimate. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 156, 389-393. <https://doi.org/10.1016/j.cbpa.2010.03.009>
- Nixon, S.W., & Buckley, B.A. (2002). "A strikingly rich zone" - nutrient enrichment and secondary production in coastal marine ecosystems. *Estuaries*, 25, 782-796. <https://doi.org/10.1007/BF02804905>
- Nye, J.A., Link, J.S., Hare, J.A., & Overholtz, W.J. (2009). Changing spatial distribution of fish stocks in relation to climate and population size on the Northeast United States continental shelf. *Marine Ecology Progress Series*, 393, 111-129. <https://doi.org/10.3354/meps08220>
- Ohde, T., & Dadou, I. (2018). Seasonal and annual variability of coastal sulphur plumes in the northern Benguela upwelling system. *PLoS ONE*, 13, e0192140. <https://doi.org/10.1371/journal.pone.0192140>
- O'Boyle, S., McDermott, G., Noklegaard, T., & Wilkes, R. (2013). A simple index of trophic status in estuaries and coastal bays based on measurements of pH and dissolved oxygen. *Estuaries and Coasts*, 36, 158-173. <https://doi.org/10.1007/s12237-012-9553-4>

- Odum, E.P. (1961). The role of tidal marshes in estuarine production. *The Conservationist*, 15, 12-15.
- Oschlies, A., Brandt, P., Stramma, L., & Schmidtko, S. (2018). Drivers and mechanisms of ocean deoxygenation. *Nature Geoscience*, 11, 467-473. <https://doi.org/10.1038/s41561-018-0152-2>
- Pamenter, M.E. (2014). Mitochondria: a multimodal hub of hypoxia tolerance. *Canadian Journal of Zoology*, 92, 569-589. <https://doi.org/10.1139/cjz-2013-0247>
- Paulmier, A., Ruiz-Pino, D., & Garçon, V. (2011). CO<sub>2</sub> maximum in the oxygen minimum zone (OMZ). *Biogeosciences*, 8, 239-252. <https://doi.org/10.5194/bg-8-239-2011>
- Pauly, D., & Cheung, W.W. (2017). Sound physiological knowledge and principles in modeling shrinking of fishes under climate change. *Global Change Biology*, 24, e15-e26. <https://doi.org/10.1111/gcb.13831>
- Pitcher, G.C., Figueiras, F.G., Kudela, R.M., Moita, T., Reguera, T.B., & Ruiz-Villareal, M. (2018). Key questions and recent research advances on harmful algal blooms in eastern boundary upwelling systems. In P.M. Gilbert, E. Berdalet, M.A. Burford, G.C. Pitcher, & M. Zhou (Eds.). *Global Ecology and Oceanography of Harmful Algal Blooms*, pp. 205-227. Springer. [https://doi.org/10.1007/978-3-319-70069-4\\_11](https://doi.org/10.1007/978-3-319-70069-4_11)
- Pitcher, G.C., & Probyn, T.A. (2011). Anoxia in southern Benguela during the autumn of 2009 and its linkage to a bloom of the dinoflagellate *Ceratium balechii*. *Harmful Algae*, 11, 23-32. <https://doi.org/10.1016/j.hal.2011.07.001>
- Phippen, B.L., & Oliver, J.D. (2017). Impact of hypoxia on gene expression patterns by the human pathogen, *Vibrio vulnificus*, and bacterial community composition in a North Carolina estuary. *GeoHealth*, 1, 37-50. <https://doi.org/10.1002/2016GH000024>
- Pörtner, H.-O. (2012). Integrating climate-related stressor effects on marine organisms: unifying principles linking molecule to ecosystem-level changes. *Marine Ecology Progress Series*, 470, 273-290. <https://doi.org/10.3354/meps10123>
- Pörtner, H.-O., Bock, C., & Mark, F.C. (2017). Oxygen-and capacity-limited thermal tolerance: bridging ecology and physiology. *Journal of Experimental Biology*, 220, 2685-2696. <https://doi.org/10.1242/jeb.134585>
- Prichard, E., & Granek, E.F. (2016). Effects of pharmaceuticals and personal care products on marine organisms: from single-species studies to an ecosystem-based approach. *Environmental Science and Pollution Research*, 23, 22365-22384. <https://doi.org/10.1007/s11356-016-7282-0>
- Rice, A.L., Sacco, L., Hyder, A., & Black, R.E. (2000). Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization*, 78, 1207-1221.
- Rosa, R., & Seibel, B.A. (2008). Synergistic effects of climate-related variables suggest future physiological impairment in a top oceanic predator. *Proceedings of the National Academy of Sciences of the United States of America*, 105, 20776-20780. <https://doi.org/10.1073/pnas.0806886105>
- Schunck, H., Lavik, G., Desai, D.K., Großkopf, T., Kalvelage, T., Löscher, C.R., ... Rosenstiel, P. (2013). Giant hydrogen sulfide plume in the oxygen minimum zone off Peru supports chemolithoautotrophy. *PLoS ONE*, 8, e68661. <https://doi.org/10.1371/journal.pone.0068661>
- Sokolova, I.M. (2013). Energy-limited tolerance to stress as a conceptual framework to integrate the effects of multiple stressors. *Integrative and Comparative Biology*, 53, 597-608. <https://doi.org/10.1093/icb/ict028>
- Sokolova, I.M., Sukhotin, A.A., & Lannig, G. (2011). Stress effects on metabolism and energy budgets in mollusks. In D. Abele, T. Zenteno-Savin, & J. Vazquez-Medina (Eds.). *Oxidative Stress in Aquatic Ecosystems*. Blackwell Publishing Ltd., Boston, pp. 263-280. <https://doi.org/10.1002/9781444345988.ch19>
- Sokolova, I.M., & Pörtner, H.-O. (2003). Metabolic plasticity and critical temperatures for aerobic scope in a eurythermal marine invertebrate (*Littorina saxatilis*, Gastropoda: Littorinidae) from different latitudes. *Journal of Experimental Biology*, 206, 195-207. <https://doi.org/10.1242/jeb.00054>
- Sokolova, I.M., Frederich, M., Bagwe, R., Lannig, G., & Sukhotin, A.A. (2012). Energy homeostasis as an integrative tool for assessing limits of environmental stress tolerance in aquatic invertebrates. *Marine Environmental Research*, 79, 1-15. <https://doi.org/10.1016/j.marenvres.2012.04.003>
- Solaini, G., Baracca, A., Lenaz, G., & Sgarbi, G. (2010). Hypoxia and mitochondrial oxidative metabolism. *Biochimica et Biophysica Acta (BBA) – Bioenergetics*, 1797, 1171-1177. <https://doi.org/10.1016/j.bbabi.2010.02.011>
- Sommer, A., & Pörtner, H.-O. (2004). Mitochondrial function in seasonal acclimatization versus latitudinal adaptation to cold in the lugworm *Arenicola marina* (L.). *Physiological and Biochemical Zoology*, 77, 174-186. <https://doi.org/10.1086/381468>
- Sperling, E.A., Frieder, C.A., & Levin, L.A. (2016). Biodiversity response to natural gradients of multiple stressors on continental margins. *Proceedings of the Royal Society B: Biological Sciences*, 283, 20160637. <https://doi.org/10.1098/rspb.2016.0637>
- Storey, K.B., & Storey, J.M. (2004). Metabolic rate depression in animals: transcriptional and translational controls. *Biological Reviews*, 79, 207-233. <https://doi.org/10.1017/S1464793103006195>
- Stortini, C.H., Chabot, D., & Shackell, N.L. (2017). Marine species in ambient low-oxygen regions subject to double jeopardy impacts of climate change. *Global Change Biology*, 23, 2284-2296. <https://doi.org/10.1111/gcb.13534>
- Stramma, L., Prince, E.D., Schmidtko, S., Luo, J., Hoolihan, J.P., Visbeck, M., ... Körtzinger, A. (2012). Expansion of oxygen minimum zones may reduce available habitat for tropical pelagic fishes. *Nature Climate Change*, 2, 33-37. <https://doi.org/10.1038/nclimate1304>
- Stramma, L., Schmidtko, S., Levin, L.A., & Johnson, G.C. (2010). Ocean oxygen minima expansions and their biological impacts. *Deep Sea Research Part I: Oceanographic Research Papers*, 57, 587-595. <https://doi.org/10.1016/j.dsr.2010.01.005>
- Thibodeaux, L.K., Burnett, K.G., & Burnett, L.E. (2009). Energy metabolism and metabolic depression during exercise in *Callinectes sapidus*, the Atlantic blue crab: effects of the bacterial pathogen *Vibrio campbellii*. *Journal of Experimental Biology*, 212, 3428-3439. <https://doi.org/10.1242/jeb.033431>
- Tinsley, D. (1998). The Thames estuary: a history of the impact of humans on the environment and a description of the current

- approach to environmental management. In M.A. Attrill (Ed.). *A rehabilitated estuarine ecosystem*. pp. 5-26. Springer, Boston, MA. [https://doi.org/10.1007/978-1-4419-8708-2\\_2](https://doi.org/10.1007/978-1-4419-8708-2_2)
- Vaquer-Sunyer, R., & Duarte, C.M. (2011). Temperature effects on oxygen thresholds for hypoxia in marine benthic organisms. *Global Change Biology*, 17, 1788-1797. <https://doi.org/10.1111/j.1365-2486.2010.02343.x>
- Verberk, W.C., Overgaard, J., Ern, R., Bayley, M., Wang, T., Boardman, L., & Terblanche, J.S. (2016). Does oxygen limit thermal tolerance in arthropods? A critical reevaluation of current evidence. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 192, 64-78. <https://doi.org/10.1016/j.cbpa.2015.10.020>
- Wallace, R.B., Baumann, H., Grear, J.S., Aller, R.C., & Gobler, C.J. (2014). Coastal ocean acidification: The other eutrophication problem. *Estuarine, Coastal and Shelf Science*, 148, 1-13. <https://doi.org/10.1016/j.ecss.2014.05.027>
- Wainger, L.A., Secor, D.H., Gurbisz, C., Kemp, W.M., Gilbert, P.M., Houde, E.D., ... Barber, M.C. (2017). Resilience indicators support valuation of estuarine ecosystem restoration under climate change. *Ecosystem Health and Sustainability*, 3, e01268. <https://doi.org/10.1002/ehs2.1268>
- Weber, R.E., & Jensen, F.B. (1988). Functional adaptations in hemoglobins from ectothermic vertebrates. *Annual Review of Physiology*, 50, 161-179. <https://doi.org/10.1146/annurev.ph.50.030188.001113>
- Weeks, S.J., Currie, B., Bakun, A., & Peard, K.R. (2004). Hydrogen sulphide eruptions in the Atlantic Ocean off southern Africa: implications of a new view based on SeaWiFS satellite imagery. *Deep Sea Research Part I: Oceanographic Research Papers*, 51, 153-172. <https://doi.org/10.1016/j.dsr.2003.10.004>
- Williamson, P., Turley, C.M., & Ostle, C. (2017). Ocean acidification. MCCIP Science Review 2017. <http://doi.org/10.14465/2017.arc10.001-oac>
- Wootton, J.T., Pfister, C.A., & Forester, J.D. (2008). Dynamic patterns and ecological impacts of declining ocean pH in a high-resolution multi-year dataset. *Proceedings of the National Academy of Sciences of the United States of America*, 105, 18848-18853. <https://doi.org/10.1073/pnas.0810079105>
- Yang, H., Cao, Z.-D., & Fu, S.-J. (2013). The effects of diel-cycling hypoxia acclimation on the hypoxia tolerance, swimming capacity and growth performance of southern catfish (*Silurus meridionalis*). *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 165, 131-138. <https://doi.org/10.1016/j.cbpa.2013.02.028>
- Yvon-Durocher, G., Jones, J.I., Trimmer, M., Woodward, G., & Montoya, J.M. (2010). Warming alters the metabolic balance of ecosystems. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 365, 2117-2126. <https://doi.org/10.1098/rstb.2010.0038>

---

*"Increasing carbon dioxide emissions simultaneously warm, deoxygenate, and acidify marine systems, and nutrient pollution increases the severity of deoxygenation and acidification."*

*Chapter 6 authors*

---