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REVIEW

Climate impacts on organisms, ecosystems and human societies: integrating OCLTT into a wider context

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ABSTRACT

Physiological studies contribute to a cause and effect understanding of ecological patterns under climate change and identify the scope and limits of adaptation. Across most habitats, this requires analyzing organism responses to warming, which can be modified by other drivers such as acidification and oxygen loss in aquatic environments or excess humidity or drought on land. Experimental findings support the hypothesis that the width and temperature range of thermal performance curves relate to biogeographical range. Current warming causes range shifts, hypothesized to include constraints in aerobic power budget which in turn are elicited by limitations in oxygen supply capacity in relation to demand. Different metabolic scopes involved may set the borders of both the fundamental niche (at standard metabolic rate) and the realized niche (at routine rate). Relative scopes for aerobic performance also set the capacity of species to interact with others at the ecosystem level. Niche limits and widths are shifting and probably interdependent across life stages, with young adults being least thermally vulnerable. The principles of thermal tolerance and performance may also apply to endotherms including humans, their habitat and human society. Overall, phylogenetically based comparisons would need to consider the life cycle of species as well as organism functional properties across climate zones and time scales. This Review concludes with a perspective on how mechanism-based understanding allows scrutinizing often simplified modeling approaches projecting future climate impacts and risks for aquatic and terrestrial ecosystems. It also emphasizes the usefulness of a consensus-building process among experimentalists for better recognition in the climate debate.

KEY WORDS: Ectotherms, Endotherms, Species, Habitat, Unifying principles, Experimental studies, Human habitat, Climate change, Thermal tolerance, Performance, Oxygen and capacity limited thermal tolerance, Life stages

Introduction

Research on the impacts of climate change on organisms, ecosystems and human societies should follow the urgent need to build a cause and effect understanding. Such an understanding would enhance confidence in the projections of future risks and also provide access to potential solutions. Solutions should aim to mitigate specific root causes (hazards) for impacts on vulnerable systems, reduce their exposure and, to the extent possible, reduce their vulnerabilities (IPCC, 2018, 2019a,b). For ecosystems, such efforts should become effective at two levels. Firstly, at the species level, they should consider all aspects that shape the well-being of the species. Secondly, at the

ecosystem level, efforts should consider the species composition and their interactions as well as their functioning and services. These are crucial to sustainably maintain biodiversity and, not least, form the basis for human uses. Identifying the links across these levels of biological organization is important for comprehending the interdependencies between such levels. Such needs are emphasized by the current large-scale challenges to biodiversity including the exacerbating impacts of climate change. Climate scenarios and their projected impacts and risks indicate a strong relationship between the well-being of ecosystems and species and the degree and pace of climate change (Pörtner et al., 2014; Settele et al., 2014; Dahlke et al., 2020). This Review sets out to identify some of the crucial links across levels of biological organization and to illustrate how further progress can be made in illuminating these interdependencies, with the goal to identify cause and effect relationships for ecological and societal shifts under climate change.
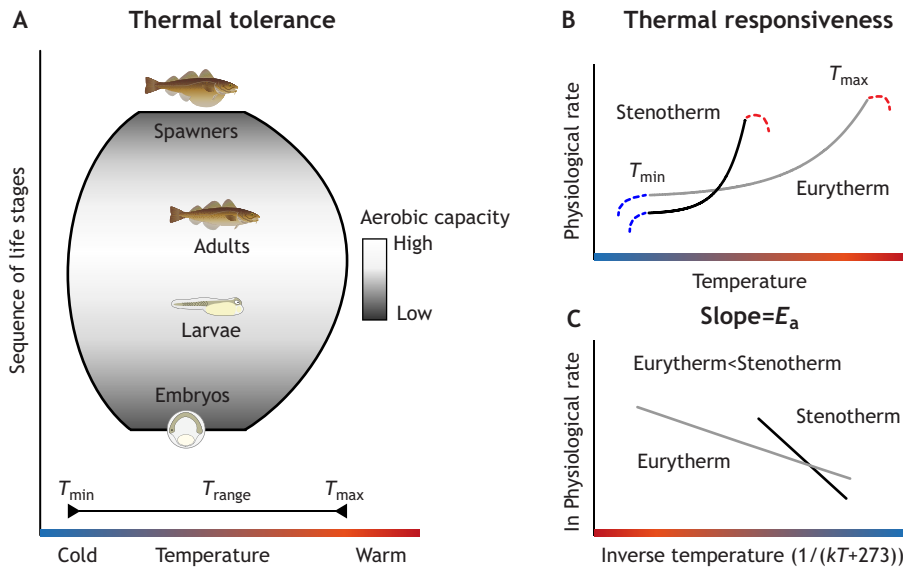
The well-being of organisms including humans and human civilization is tightly connected to the ambient temperature regime. For addressing such connections, this Review is centered on the concept of 'Oxygen and capacity limited thermal tolerance' (OCLTT; for a recent review, see Pörtner et al., 2017), which has been developed to identify the root cause of the specialization of animals on limited temperature ranges, at the organism level, considering how levels of biological organization may be integrated, from whole animal to molecular and vice versa (Pörtner, 2002a). This concept is currently debated with respect to its universal applicability. As a contribution to this debate and to widen the angle of view, OCLTT in this Review is not re-evaluated as a hypothesis valid ad hoc for any animal studied but as a principle that reflects a bottleneck during animal ontogeny and evolution. This view considers the option that the tight coupling between thermal tolerance (TT) and oxygen and capacity limitation (OCL) has been or is more relaxed for some period during ontogeny (e.g. early adulthood; see Fig. 1) but forms a principle in animal evolutionary history.

According to evolutionary biology, thermal specialization is reflected in the thermal performance curve (TPC) as a unifying principle across organism kingdoms and taxa, from bacteria to animals (e.g. Eppley, 1972; Huey and Stevenson, 1979; Angilletta, 2009). Differences, shifts and changing shapes of TPCs under climate change are hypothesized to underpin range shifts, changes in species interactions and, hence, disease dynamics and community composition (Takasuka et al., 2007, 2008; Pörtner et al., 2014; Reuman et al., 2014; Padfield et al., 2020). The width of the TPC relates to the niche width of a species. Within that niche, integrated performance reflects the capacity of individuals of that species to interact with conspecifics during reproduction or with other species in the food web, in spatial competition or disease (Figs 1 and 2). This paradigm suggests the existence of one overarching TPC of a species and its dynamic shifts. Performance here ideally integrates the rates and contributions of various processes into one overarching curve, and each of the underlying ones may have different optima (cf. Mazumder et al., 2015; Gangloff and Telemeco, 2018; Fig. 2B).
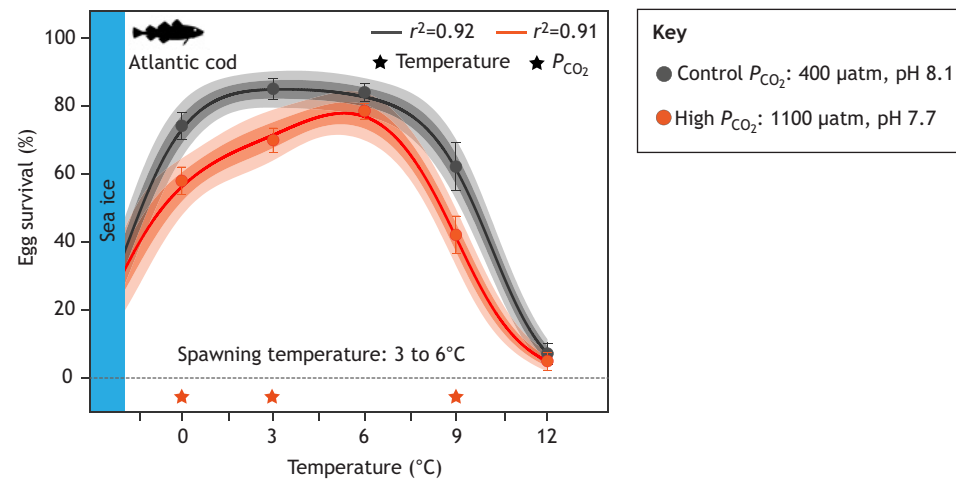
Fig. 1. Thermal relationships as a matrix for integrating effects of various drivers along spatial and temporal scales in the marine realm, building on the insight that temperature as an overarching driver shapes performance and biogeography. (A) During ontogeny, the habitat selected by a species depends on the thermal range (T_{range}) of the respective life stage (where T_{min} and T_{max} are minimum and maximum temperature, respectively). This relates to relative aerobic scope across life stages. (B) A narrow versus wide thermal range is reflected by a lower level of baseline energy turnover in the stenotherm and a steeper responsiveness of its metabolic rate to temperature, also during exercise. (C) This is mirrored in a higher activation energy (E_a) in stenotherms compared with eurytherms, indicating energy savings during stenothermal narrowing of the thermal range. (D) Because of the interaction of temperature and elevated CO_2 (ocean acidification), the window of temperature-dependent embryo survival is narrowed, thereby shrinking spawning habitat. Significant overall effects of temperature or P_{CO_2} are indicated by black stars, whereas orange stars denote significant CO_2 effects within temperature treatments (after Pörtner, 2006; Pörtner and Farrell, 2008; Pörtner et al., 2014, 2017; Dahlke et al., 2018, 2020; Reddin et al., 2020). Thermal ranges (window widths) are probably inter-dependent across life stages, e.g. wide juvenile and then adult ranges at low E_a and high functional capacity may set the stage for a sufficiently wide thermal bandwidth in the spawners. This insight should exclude a narrow focus on whether OCLTT works in one but not in another life stage.

The OCLTT concept built on findings for marine ectotherms to start with (for the evolution of the concept over time, see Frederich and Pörtner, 2000; Pörtner, 2001, 2002a, 2010, 2012; Pörtner and Farrell, 2008; Pörtner et al., 2017). According to OCLTT, performance relates to the amount of aerobic energy in excess of the energy required for maintenance and to the rate of this excess energy flowing into overall integrated performance, e.g. temperature-dependent growth, development or reproductive success, as proxies of fitness. Aerobic scope (for growth) integrates diverse performances into one overarching performance curve (see above). In that respect, OCLTT connects to the pioneering work of Shelford (1931) on tolerance windows and optima and Fry (1971) on temperature-dependent aerobic scope in fishes or to the thermal performance curve as used in evolutionary biology. The resulting overall performance curve is bell shaped and tilted to the right, i.e. the optimum is shifted from the center of its thermal range to higher temperatures (e.g. Angilletta et al., 2002). As to the overall energy source, the aerobic power budget as specified by Guderley and Pörtner (2010), with the special case of aerobic scope for exercise (Farrell, 2016), would be suitable to describe the source of energy in the sense of power or capacity for overall integrated performance.

This level of integration differentiates OCLTT from the more recent concept of 'multiple performances – multiple optima' (MPMO; Clark et al., 2013), which emphasizes the diversity of optima in different processes. This said, the step by step contribution of integrated mechanisms to the shape of the TPC remains to be elaborated (see Schulte et al., 2011). Also, the allocation of aerobic energy to various types of performance, and associated trade-offs, are not well enough understood (as emphasized by Wieser, 1991; see also Farrell, 2016).

Performance, biogeography and thermal limits

Large scale shifts in biogeographical ranges have been identified as a common phenomenon in response to climate change on land, in freshwater systems and in the ocean (e.g. Poloczanska et al., 2013; Pörtner et al., 2014; Settele et al., 2014; García Molinos et al., 2016). The genetic and functional underpinnings of such range shifts and their meaning for the composition of new ecosystems and associated biodiversity deserve in-depth investigation. Identifying the responses of organisms to multiple environmental drivers is crucial for a detailed understanding of such changes. Very clearly, the current large-scale displacements are predominantly driven by the warming trend and are, to some extent, affected by other drivers such as ocean currents. As
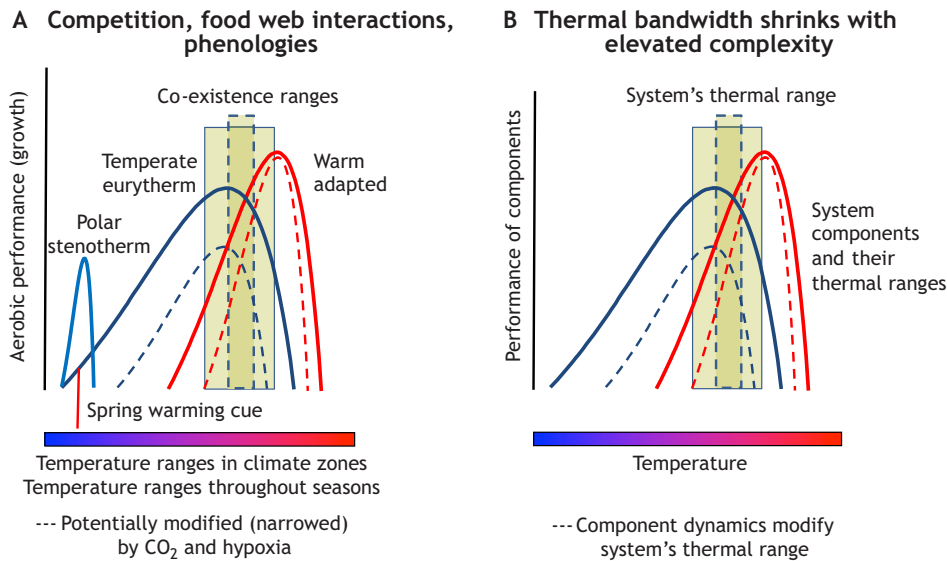
Fig. 2. Thermal performance curves and their overlap define system characteristics. (A) The outcomes of competition, food web interactions and phenologies can be understood from the seasonal development of temperature and the resulting relative performance levels of species which shape their interactions. The overlap in thermal niches defines the co-existence of species in a narrow bandwidth of temperatures in the same ecosystem. Dashed lines indicate how the performance curve and the width of the resulting co-existence ranges can be modified by additional drivers such as hypoxia and CO_2. For references, see Fig. 1. (B) In principle, the figure also illustrates how in a more complex system (ecosystem), variability in the thermal performance of system components (species) and their minimum levels of functional rates required to support the complex (eco)system represent a reason for narrowing thermal breadth with increasing levels of complexity, from molecular to ecosystem levels. For references, see Fig. 1.

these drifts concern multiple ectotherm taxa (Poloczanska et al., 2013, 2014) and biodiversity overall (García Molinos et al., 2016), they cast light on the thermal specialization of all life forms, with different characteristics depending on the taxon (Storch et al., 2014). Such specialization is the basis for temperature-dependent biogeography (e.g. Sunday et al., 2012, 2019) and ecosystem composition (Pörtner et al., 2014). For some organisms, thermal ranges may be very wide, such as seen among unicellular organisms (Storch et al., 2014). Historically, this may have blurred the overarching role of temperature in shaping species biogeography and ecosystem characteristics. In line with previous analyses, this Review emphasizes the foundational importance of temperature and integrates other drivers into thermal relationships by use of OCLTT (Pörtner, 2010).

In the context of climate warming, a key evolutionary question is what is setting the upper thermal limit of an organism group, which is so much lower among highly complex animals (41–45°C) than in unicellular organisms such as archaea in the simplest case (up to 120°C; Storch et al., 2014)? From a functional point of view, a systemic to molecular hierarchy of thermal tolerance was postulated that causes narrower thermal windows at increasing complexity level (Pörtner, 2002a; Gangloff and Telemeco, 2018; cf. Rezende and Bozinovic, 2019). A theory that explains the implications of such complexity and offers links to all functionalities involved in the survival and well-being of organisms and the sustainability of ecosystems will tend to become equally complex unless it can relate to a unifying principle and underpinning mechanisms. For animals, OCLTT has been proposed as a unifying principle (Pörtner, 2001, 2002a,b,c; Pörtner et al., 2017). By analogy with OCLTT, photosynthetic productivity bound to complex cells hosting both chloroplasts and mitochondria (Storch et al., 2014) might (co-)define heat limits to be as low as those in animals, among plants or unicellular phytoplankton (cf. Rezende and Bozinovic, 2019; see below). As a hypothesis, coordination across an increasing number of compartments may cause the observed specialization on more limited temperature ranges (Storch et al., 2014). Further experimental evidence is needed to elucidate the links between complexity, thermal range and thermal limits, in organisms other than animals.

When connecting to ecology, a general task for experimental biologists would be to explain the temperature dependence of the overarching performance curve across organism kingdoms, its width and the performance level reached, as well as its changes in response

to interacting drivers such as CO_2 or hypoxia or to interacting species (Figs 1 and 2; see below). For example, the presence of a parasite can modify the thermal performance of its host (Padfield et al., 2020). This leads to the question: which performance is sufficiently overarching and integrative to measure or trace the overarching performance curve? In animals, muscular exercise is routinely used to assess aerobic scope for exercise, e.g. in fish (Clark et al., 2013; Farrell, 2016; Kunz et al., 2018), exploiting the capacities of cardiocirculation and ventilation to their temperature-dependent maximum (Farrell, 2016). However, exercise does not or not in all cases qualify as a good integrator (Holt and Jørgensen, 2015). Clear evidence points to aerobic scope for exercise being the limiting process in spawning migrations of mature salmon under climate change (Eliason et al., 2011); however, this may only represent a bottleneck for this specific life stage and phase. Aerobic scope for exercise may indeed not fully reflect integrated performance in all species; some findings indicate potential differences between, for example, temperature constraints on exercise or on growth (Gräns et al., 2014). Comparative conclusions may then be constrained by the observation that not all species are amenable to studying exercise under steady-state conditions, which is a requirement when assessing aerobic limits (Pörtner, 2014; cf. Blasco et al., 2020). A steady-state process usefully reflecting performance capacity in bivalves is filtration, which also integrates ventilation (Eymann et al., 2020). A process representing even further integration of various processes into an overarching performance curve is temperature-dependent growth (in the field), which encompasses successful competition, foraging, behaviors, digestion, etc. (Guderley and Pörtner, 2010; Farrell, 2016), with the result of, for example, maximized growth rate at optimal temperatures in the field. Very few examples indicate that depending on the latitude and temperature cline covered, body size maxima found within species may scale along such clines depending on ambient temperature (Neuheimer et al., 2011). The thermal growth optimum shifts downward with increasing body size, as seen in several but seemingly not all fish species (Mazumder et al., 2015). The few field data existing on benthic and demersal fish reflect temperature constraints on maximum body size within a species (e.g. Pörtner and Knust, 2007; Neuheimer et al., 2011; Rogers et al., 2011). Similar findings exist for marine invertebrates (e.g. Peck et al., 2013).

Compared with growth, development of early life stages within their thermal niche may reflect integrated performance similarly

well, the scope for performance being tied to the rates of development (Dahlke et al., 2020). Reproductive success would be another process to consider; it is determined as reproductive output but is more difficult to capture as a temperature-dependent rate function.

Experimental work at the interface between ecology and physiology has, however, mostly focused on identifying (high) thermal limits beyond the onset of functional constraints. High endpoints of thermal tolerance are the temperature resulting in the death of 50% (LT_{50}) or 100% (LT_{100}) of exposed individuals, or the critical thermal maximum (CT_{max}) (Lutterschmidt and Hutchison, 1997). These have been reported for decades and have been informative in recent meta-analyses which identify the vulnerabilities of species to temperature extremes through assessing a so-called safety margin (Sunday et al., 2012; Pinsky et al., 2019; Dahlke et al., 2020). This safety margin, i.e. the difference between CT_{max} of a species and a somewhat lower value of ambient extreme temperature in a relevant habitat, has been proposed to reflect the resilience of a species to climate change. The safety margin thus approximates an empirical, albeit possibly time-limited thermal buffer zone that a species would have in its current habitat. This safety margin and probably its time dependence differ between life stages and habitats depending on whether pejus limits are surpassed (see figs 1 and 2 of Pörtner, 2010 for how the time limitation unfolds beyond pejus limits, i.e. even below CT_{max}, and involves exploitation of protective mechanisms). This makes the use of the term 'safety' questionable as fatal consequences of thermal stress can develop below CT_{max} (more slowly than captured by CT_{max} protocols).

While addressing thermal limits and range widths has its own inherent value for evaluating the suitability of any, aquatic or terrestrial, habitat for species, the thermal performance curve emphasizes that functional constraints and associated reductions in performance set in before CT_{max} is reached during warming and also become effective on the cold side of the thermal niche, before CT_{max} is reached. For understanding the dynamics of the curve, identifying the mechanisms that drive or support the continuum of temperature-dependent performance is important. A general hypothesis across organism kingdoms would be that the balance of energy production and consumption relates to overall performance. Beyond such generality, the answer to this question will be specific for and within the different organism kingdoms as they rely on different modes of energy production and use. These range from aerobic or anaerobic respiration of bacteria and archaea using diverse electron acceptors, to photosynthesis of prokaryotic and eukaryotic phytoplankton as well as of macroalgae and plants, and finally, to mitochondrial respiration used by animals (and unicellular eukaryotes as well as algae and plants during the night-time). However, for most organisms other than animals, the metabolic background of temperature-dependent performance has not been investigated. For plants and their photosynthetic production this has only recently come into focus. Considering the few existing studies that have identified optimum temperatures of photosynthetic production (T_{opt}, 24.1–27.4°C in a sub-tropical system), threshold temperatures beyond which such production becomes constrained may be exceeded in some regions under climate change (McGowan et al., 2020). This has important implications for biogeochemistry and nature-based climate mitigation, as extreme temperatures thereby constrain carbon storage.

Minimizing the cost of maintenance through the lowest possible idling of metabolism at rest would appear beneficial for maximizing the excess aerobic energy available to all types of performance contributing to growth (see above; e.g. Pörtner et al., 2005a). At the same time, having more mitochondria would support having an energy excess. However, this is complicated by the fact that having more of the same mitochondria may be costly as a result of proton leakage, which is involved as a fraction of metabolic idling costs that can increase strongly at high temperatures, eliciting OCLTT (e.g. Hardewig et al., 1999; Oellermann et al., 2020). Low energy turnover lifestyles thus have reduced mitochondrial capacity and proton leakage to save energy, even though density may be maximized as seen in the permanent (e.g. Antarctic) cold (Pörtner, 2006). Conversely, high aerobic exercise capacity comes with high oxygen demand and therefore more and higher capacity mitochondria which then also have elevated rates of proton leakage. There is thus a trade-off between energy production capacity and efficiency, growth and exercise capacities in relation to mode of life and ecological niche.

This trade-off is also relevant in shaping life in variable or constant temperature environments and, thus, the energetics of stenotherms versus eurytherms, especially in the cold (see below, Fig. 1). Accordingly, the classic view that oxygen supply capacity in animals evolved to meet maximum demand at available oxygen concentration (re-emphasized by Seibel and Deutsch, 2020) needs to take temperature and its variability into account. Indeed, the combined pressures of temperature and exercise adaptation would explain the phenomenon that active animals are more eurythermal than passive ones, nicely shown across Antarctic species (Peck et al., 2009), acclimatization not being involved. Considering acclimatization, it would also explain seasonal patterns when animals become stenotherms during winter, saving energy and avoiding expensive cold adaptation mechanisms, but become eurytherms at elevated metabolic rate and lower Q_{10} over a broad temperature range in spring, when they increase energy turnover in order to enable an active mode of life, still covering the cold temperatures (Wittmann et al., 2008; Fig. 3). This matches the observation that while acclimatization is not needed to be eurythermal (Healy and Schulte, 2012), seasonal acclimatization can widen the temperature window covered otherwise throughout the year (Wittmann et al., 2008). Also, the seasonal increase in temperature-dependent metabolic rate during spring and associated food uptake would initiate or support growth. Along similar lines, a positive correlation of metabolic scope and growth has been found in Atlantic cod (Claireaux et al., 2000).

The energy-related tradeoff also plays out in metabolic cold adaptation, where stenothermal Antarctic species have high mitochondrial density at low capacity, thereby enabling low baseline oxygen demand, which allows them to preferably shift available energy to growth (Pörtner, 2002b,c; Pörtner et al., 2005a, 2017) at low acclimation capacity (Peck et al., 2014). Stenothermy thus lowers the cost of metabolic cold adaptation (Pörtner, 2006). However, the continuum between extreme stenothermy and eurythermy as well as associated trade-offs in energy budget are not yet fully understood (cf. Fig. 3). This also holds for the link between eurythermy and exercise capacity (see below). Clearly, a wider analysis of the energetic trade-offs involved in shaping growth within and across species is warranted.

In this context, Pörtner (2006) and Pörtner et al. (2017) hypothesized that a link exists between the width of the thermal window and the thermal responsiveness of baseline energy turnover, i.e. the slope of increasing standard metabolic rate with warming. The steep slope/responsiveness in stenotherms would mirror their elevated activation energy, the kinetic hurdle to energy turnover, being visible even at a high, whole-organism level of
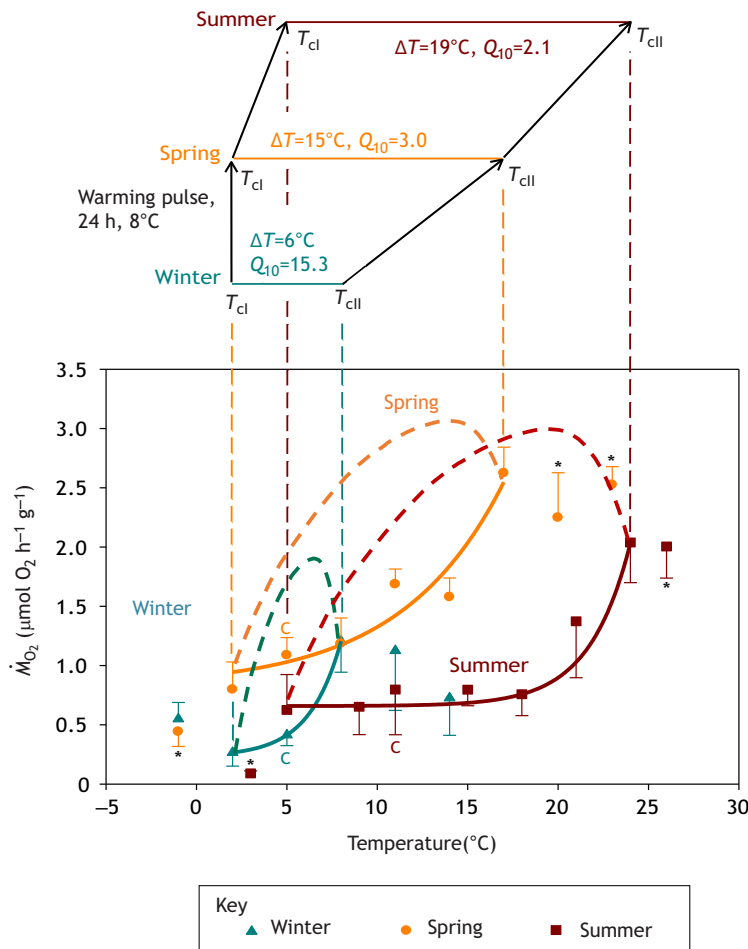
Fig. 3. Seasonal shifts of the thermal range for routinely ventilating a burrow in the lugworm *Arenicola marina*. Shrinking window width is paralleled by increasing activation energy (E_a) (Wittmann et al., 2008). Low E_a values such as during spring cause high metabolic costs of eurythermy as cold temperatures are still included, and reduced costs result during summer when cold tolerance is reduced. These findings reflect that thermal acclimation to various window widths shapes baseline energy demand and that there are tradeoffs between cost of cold acclimation and thermal window width (see Fig. 1). Dashed lines indicate putative thermal performance curves starting from baseline levels of routine metabolic rate (animals ventilating an artificial burrow). T_{cI}, lower critical temperature; T_{cII}, upper critical temperature; $\dot{M}_{O_2}$, aerobic metabolic rate. Values are means±s.e.; * indicate values significantly different from those extrapolated from the respective exponential curve fit (same colour).

biological organization. This pattern is hypothesized to enable energy savings and thus a lower metabolic rate in permanent or transient stenotherms (Figs 1–3). The relationship between range and slope was in fact confirmed as a unifying principle by a recent meta-analysis carried out by Dahlke et al. (2020). Furthermore, the analysis found a similar slope for metabolic rate and the associated rate of performance, in this case the development of embryonic fish. The findings of variable activation energy (enthalpy) confirm that postulating a universal thermal responsiveness of metabolic rate across the animal kingdom as per the metabolic theory of ecology ignores important variability against the background of thermal adaptation and acclimatization of species and individual organisms (Seebacher et al., 2015; Clarke, 2017). Among populations of the same species along latitudinal clines, such trade-offs may explain different window widths of performance and metabolic responses to temperature, considering its mean and the amplitude of temperature variation. For example, in a lugworm, *Arenicola marina*, a shift of both the thermal window and the thermal optimum of digging performance occurred towards higher temperatures with decreasing latitude. This shift was accompanied by a reduction of performance amplitude, i.e. the absolute number of digging periods, and a widening of the distance between critical temperatures, i.e. the total aerobic window of thermal tolerance (Schröer et al., 2009). This may reflect a lessening of cold-induced metabolic costs in populations at lower latitudes, supporting wider thermal ranges at reduced aerobic metabolic capacity. There is a need for further studies and meta-analyses, also concerning the slope of the temperature-induced increase in maximum steady-state oxygen

consumption during exercise until CT$_{swim}$, the critical threshold temperature for fatigue from sustained aerobic swimming, which has been proposed as an indicator of thermal stress onset below CT$_{max}$ (e.g. Blasco et al., 2020) and possibly relates to the width of the realized niche and the upper limit of routine aerobic performance (Fig. 4) and its biogeographical implications (cf. Deutsch et al., 2015).

Considering maximum body size

Another important aspect relating to temperature and energy turnover is maximum body size. Such analysis is complicated by other influences on body size such as food availability, predation and habitat structure. According to available data covering the body size spectrum of related species, e.g. among all amphipod species of a habitat, maximum body size of the largest species found rise along a falling temperature continuum towards cold, oxygen-rich waters (Chapelle and Peck, 1999, 2004). Near universally, warming causes a shrinking in body size in aquatic habitats and, with some exceptions, in terrestrial habitats (Atkinson, 1994; Kingsolver and Huey, 2008; Daufresne et al., 2009; Pauly, 2019; Forster et al., 2012; Horne et al., 2015; Ilha et al., 2018). Findings have been interpreted to be related to limited oxygen supply to tissues and indicate that oxygen limitation is a major controlling factor in water, but not so much in air (Horne et al., 2015). In parallel, aquatic animals at large body size within species become heat intolerant at lower temperatures than smaller individuals, reflecting the enhanced oxygen limitation (Pörtner and Knust, 2007; Melzner et al., 2007; Peck et al., 2007; Jakob et al., 2016; Di Santo and Lobel, 2017). Exceptions may exist, e.g. among

Fig. 4. From the fundamental niche of animals at rest to their realized niche at different levels of routine motor activity. The fundamental niche covers temperatures between upper and lower critical temperatures (T_c) and the realized niche covers temperatures between upper and lower pejus temperatures (T_p). In each case considered (for salmon building on, for example, Eliason et al., 2011; for cod on Deutsch et al., 2015; and for eelpout on Pörtner and Knust, 2007), temperature-dependent oxygen demand during activity (dashed curve) rises exponentially with warming until performance limits are reached at upper T_p. Depending on the extent of aerobic scope exploitation during lifestyle-dependent activity of the respective species, the dashed exponential curve moves up to higher performance levels, causing either a narrowing of the realized niche (shown) or adaptive widening towards enhanced eurythermy (not shown, see text). Figure updated from box 2 figure in Pörtner et al. (2017). For the sake of clarity, putative impacts of hypoxia or CO_2 on the performance curve are not included. This model was recently supported by studies of the temperature dependence of oxygen uptake during the CT_{swim} protocol, when fish are swimming aerobically and in steady state and are warmed at regular intervals until fatigue (for data, see Blasco et al., 2020). T_d, denaturation temperature; T_{opt}, optimal temperature.

Antarctic pycnogonids (Shishido et al., 2019). Various explanations have been developed for a warm-induced limitation to body size, from (a) accelerated maturity in relation to growth in the warmth (Angilletta et al., 2004) to (b) an allometric limitation of gill surface area causing an oxygen dependence of maximum body size (Pauly and Cheung, 2018), (c) a role for oxygen diffusivity and rising standard metabolic rate determining body size limitations at high temperature (Verberk et al., 2011; Verberk and Bilton, 2013), (d) variable hypoxia vulnerability according to mode of life (Spicer and Morley, 2019) and (e) low standard metabolism at high oxygen levels supporting aerobic scope in the cold as a precondition for a rise in body size (Pörtner, 2002b). Some of these relationships remain (semi-)empirical and are also lacking strong evidence at the molecular level (e.g. Callier and Nijhout, 2014). This said, there is an increasing notion of oxygen limitation causing or contributing to decreasing animal body size in warming aquatic environments. However, allometric constraints on respiratory surfaces have been questioned (Lefevre et al., 2018), which matches the finding that arterial P_{O_2} (Pa_{O_2}) shows no thermal limitation in fish (Sartoris et al., 2003). Indeed, if there is a gill O_2 diffusion limitation during warming, Pa_{O_2} should decrease. This puts an emphasis on cardiocirculatory adaptation and acclimation in response to temperature (e.g. Ekström et al., 2016). It also indicates that larger body sizes among species of a taxon indeed relate more to cost savings and thus reduced metabolic rate, which enables a larger aerobic scope for increased body size in highly oxygenated environments (Pörtner, 2002b;

Woods and Moran, 2020). While not a causal factor, this does not exclude the option to use the allometric adjustment of gill surface area as a proxy for temperature-related projections of reduced body size and biomass within species of fish (Cheung et al., 2012; Pauly and Cheung, 2018; Bindoff et al., 2019). Similar conclusions emerge from Rubalcaba et al. (2020).

Indirect evidence supports a predominant role for metabolic rate in shaping maximum body size within species and across related species. In scallops, the response to temperature along a latitudinal cline was progressively less for growth than for standard metabolism (Heilmayer et al., 2004), reflecting a maximized partitioning of less available energy into growth towards cold temperatures. This pattern is supported by cold-compensated protein synthesis capacity (Storch et al., 2003). Conversely, growth efficiency becomes constrained towards elevated temperature when metabolism rises more strongly than growth, indicating a constraint on warm acclimatization, adaptation and, finally, body size. Consequently, animals from low latitudes grow more rapidly, attain a smaller maximum size and have a shorter lifespan than do individuals from the same species or even con-familial species from higher latitudes. Here, temperature variability and its energetic consequences also play a role. An inverse relationship between growth performance and standard metabolic rate was found in Atlantic cod (*Gadus morhua*) along a northward Northern hemisphere cline; at the same temperature, growth was lower at higher temperature-specific standard metabolic rate in Arctic than in temperate populations (in contrast to the within-population correlation

of metabolic scope and growth described above). Similarly, and not only across populations of the same species along latitudinal clines, a more active mode of life among Antarctic fishes (across species) relates to higher standard metabolism and, again, lower growth performance (Pörtner et al., 2005a). Variable cell size may play a role in such body size relationships (e.g. Czarnoleski et al., 2017). Overall, however, the systematics of how these various mechanisms contribute to maximum body size or the respective cause and effect relationships remains incompletely investigated (Audzijonyte et al., 2019). This also concerns the principles and priorities of allocating energy to energy budget components, finally integrated into growth as a proxy for overall performance. It needs to be emphasized, however, that oxygen- and energetics-related body size patterns across latitudes hold for within-species comparisons or, possibly, those of con-familial species, but less widely across taxa, as clearly highlighted by large body sizes in some tropical fishes. Terrestrial examples emphasize the complexity of the aspects involved, e.g. adult body size and development time not only are shaped by temperature but also cause variation in fitness (Kingsolver and Huey, 2008). Within species, the observation of large individuals growing into a negative association between body size and thermal range (Pörtner and Knust, 2007; Rohr et al., 2018; Burton and Einum, 2020), linked to thermally induced oxygen limitations, and exacerbated at the spawning stage (e.g. Dahlke et al., 2020), highlights that, while acclimatization may counteract these constraints to some extent (Seebacher et al., 2015; Lefevre et al., 2018; Rohr et al., 2018), it cannot fully compensate for them, which contributes to shape the large-scale patterns of biogeography, biomass and, consequently, fisheries productivity seen in the oceans (Deutsch et al., 2015; Bindoff et al., 2019).

Considering life cycle

Patterns of OCLTT have repeatedly been investigated in species representing diverse animal phyla. Early investigations in different marine ectotherm phyla (all water breathers), such as annelids, sipunculids, crustaceans, mollusks and fishes, indicate broad applicability of the hypothesis. These studies used physiological indicators that identified sublethal thresholds of tolerance, starting from pejus to critical temperatures, before endpoints, i.e. CT_{max} or lethal temperatures, were reached. However, when others used classic endpoint methodology (CT_{max} determinations), warm-adapted crustaceans and some fish species did not show phenomena that were thought essential to support such evidence. Accordingly, the use of endpoints has not been overly successful when testing the applicability of OCLTT to some adult fish or crustaceans (e.g. Ern et al., 2015, 2016). As a way to capture the sensitivity of a species' thermal tolerance to oxygen, these authors suggested quantifying the water oxygen tension (Pw_{O_2}) where an organism's CT_{max} starts to decline. Contemplating why it has been difficult to demonstrate OCLTT principles in adults, a recent meta-analysis of life stage-specific heat tolerance of 694 fish species from oceans, lakes, ponds and rivers (Dahlke et al., 2020) may offer an explanation.

The meta-analysis confirmed that the fundamental niche of a species, its width and position on the temperature scale, is dynamic over time and developmental stage (Pörtner and Farrell, 2008). A narrow niche constrains embryos and large spawners of a species to a specific thermally stable spawning habitat in space and time (season) and thereby co-defines the vulnerability and reproductive success of a species. Applying CMIP6 climate scenarios (see e.g. Tokarska et al., 2020) and considering climate conditions in the spawning habitat, the fraction of vulnerable fish species increases from 10% (at RCP1.9,

temperatures not exceeding 1.5°C global warming above pre-industrial values by 2100) to 60% (at RCP8.5, at about 4°C global warming by 2100). Depending on the degree of future climate change, vulnerable species will thus be expelled from their traditional spawning areas because the water there is becoming too warm for them. An important conclusion is that the vulnerability of a species to climate change will be underestimated when considering adults only, as mostly done in the experimental literature, or when considering only one driver. For example, at RCP6.0, which may become the new 'business as usual' scenario, the full exploitation of the safety margin of vulnerable life stages indicates 40% of species at risk, whereas analysis of the same for adults only identifies 2–3% of species to be at risk. These considerations emphasize the importance of including the full life cycle and relevant habitat when assessing the climate vulnerability of any animal species. They also indicate specific life cycle bottlenecks for individual species, from spawning migration in salmon to tuna reproduction in the warming and hypoxic Gulf of Mexico.

Dahlke et al. (2020) also tested hypotheses around OCLTT. Comparison of embryos, larvae, adults and mature spawners showed a dynamic thermal window for each species, which was widest in adults and narrowest in embryos and spawning adults. This emerged as a unifying principle across about 700 species of marine and freshwater fish and matches the patterns projected according to OCLTT by Pörtner and Farrell (2008) and Pörtner and Peck (2010). A similar pattern was found across life stages of a crustacean (Schiffer et al., 2014). The question arises whether the widening of the thermal window from embryo to adult is indeed caused by the development of capacities of circulatory, ventilatory and other systems in relation to demand. If so, it seems conceivable that the most tolerant life stages might be successful in overcoming OCLTT constraints (cf. Ern et al., 2016) such that limits at lower levels of complexity (i.e. tissue, cellular, molecular) become effective. Because of the higher oxygen levels in air, such a trend would be even stronger on land. The transition to land and the higher oxygen levels in air have actually been demonstrated to widen the thermal range by increasing heat tolerance in amphibious crustaceans with bimodal respiration (Giomi et al., 2014; Levinton et al., 2020). Compared with the costs of oxygen supply in water (see Schumann and Piiper, 1966; Farrell and Steffensen, 1987; Melzner et al., 2006), reduced costs of oxygen supply in air probably contribute to this alleviation. Further, such evidence comes from work on amphibious vertebrates and their life stages (Gangloff and Telemeco, 2018). Development of sophisticated ventilatory and circulatory systems may thus facilitate thermal tolerance in adults to become (more) oxygen independent, especially with highly efficient gas exchange and upon transition to air, until finally constrained by body size. This may apply especially to the use of tracheae in insects. Examples across taxa with OCLTT demonstrated in early life but alleviated later on are salamander eggs (in air; Smith et al., 2015), bird embryos (Vimmerstedt et al., 2019), larval aquatic insects (Verberk et al., 2013a,b), as well as other larval insects which all follow OCLTT principles, whereas pupae or adults in air may or may not (no longer) show such constraints (Boardman and Terblanche, 2015; Teague et al., 2017; Gangloff and Telemeco, 2018; Zhu et al., 2018; Lombardi et al., 2020). This question deserves further investigation and again indicates that OCLTT has a time dimension, e.g. with respect to ontogeny, that has not yet been sufficiently explored in experimental research. In other words, a systematic comparison of all life stages of the same species would be required for any conclusion on whether a species is OCLTT exempt or not (e.g. Boardman and Terblanche, 2015). The finding in birds emphasizes the unexplored question of how sublethal phenomena of

heat stress in endotherms (still) relate to OCLTT as an evolutionary principle (see below).

OCLTT emerges as a bottleneck expressed during specific life stages and a principle relaxed to its maximum in immature juveniles and young adults as indicated by the recent data on fish (Dahlke et al., 2020). Staying on the cool side is important during those bottleneck periods in life in order to complete the life cycle. Indeed, for the spawning adult to then have the required thermal breadth available, the maturing adult may need to develop its oxygen supply capacity and to widen its tolerance range to the maximum possible, in order to then still have sufficient residual capacity during maturation despite constraints induced by accumulating gametes and embryos. Tolerance ranges of consecutive life stages may thus be interdependent as they develop building on the thermal breadth of the previous one. In addition to the trend of maximizing thermal tolerance during adulthood, it is unclear whether individuals are able to reduce or even abandon OCLTT constraints on other occasions, e.g. as a result of seasonal acclimatization (Figs 1 and 3).

OCLTT as an evolutionary principle: consequences for experimental biology

Viewing OCLTT as an evolutionary principle has consequences for the design of experimental studies and the interpretation of their findings. In this context, insufficient ability to demonstrate OCLTT principles may also be a methodological issue. Some approaches and their findings are supportive, others are not. In light of controversial conclusions reported in the literature, a general question is what kind of knowledge is needed before an animal species can be claimed to fall under or be exempt from OCLTT? Also, which approaches are most amenable to providing access to OCLTT evidence? What does this mean for the comparison of closely related species? Are all methods suitable to test OCLTT (Pörtner et al., 2014, 2017)? The last has been the core of previous debate, and will not be repeated here. In brief, with respect to OCLTT, CT_{max} is an insensitive endpoint essentially reflecting limiting mechanisms at a level below OCLTT. Established CT_{max} protocols (e.g. at 0.3°C min^{-1} for zebrafish; Joyce and Perry, 2020) appear too fast to witness OCLTT. OCLTT needs a minimum time period to unfold, and thus longer-term studies lasting hours to days rather than a couple of minutes are required as well as a focus on sub-lethal indicators (accordingly, studies of OCLTT do not take as long as growth studies would for determining temperature-dependent body size).

Furthermore, the question arises whether conclusions should be based exclusively on experimental evidence when testing relevant hypotheses. Relevant hypotheses are also needed for related meta-analyses (e.g., Lefevre, 2016). Assuming that building on experimental evidence may only support a relatively narrow field of view, the present Review rather calls for considering multiple lines of evidence, with the question in mind whether OCLTT and its characteristics also make sense in a wider context, e.g. when explaining palaeo-patterns (Penn et al., 2018; Reddin et al., 2020), when studying ontogeny (Dahlke et al., 2018, 2020), when connecting between physiological and ecological patterns and change (Pörtner et al., 2014, 2017) or when incorporating the impacts of other drivers associated with climate change, such as ocean acidification or hypoxia, including an identification of underpinning mechanisms (Metzger et al., 2007; Walther et al., 2009; Wittmann and Pörtner, 2013). A concept able to compete with OCLTT would need to meet the requirement of covering these aspects just like OCLTT does.

Finally, findings up to now of OCLTT phenomena in various species across aquatic, amphibious and some terrestrial animal

phyla indicate the possibility of OCLTT being a unifying principle in animal evolution. Available findings support the hypothesis that constraints in oxygen supply capacity, in relation to demand, set the limits of species' required temperature range, during some or all of their life cycle. This comes with the environmental and evolutionary challenge to overcome such limits, e.g. by selecting for lowered activation energy when widening the thermal range, at the expense of increased metabolic idling and costs (Pörtner, 2006; Dahlke et al., 2020). The associated cost increment is balanced by using highly efficient, highly coupled mitochondria and cell membranes, as well as high-capacity, efficient cardiocirculatory and ventilatory systems. Such may have been accomplished by juvenile to adult life stages that operate at full capacity in wide temperature ranges before thermal tolerance becomes constrained at reproductive stage. Reproduction is thereby constrained to a seasonal time window or environment characterized by stable environmental conditions (Figs 1 and 3). Relevant understanding may improve further by considering evolutionary time scales and steps, e.g. for transition to land. Especially in air breathers, the available evidence base needs to be widened, considering life stages and the progressive development of their thermal limits over time.

Endotherm biology, including bird and mammalian and more specifically human biology should also be considered in this context as there is an evolutionary path from ectotherms to endotherms and their physiology. According to one hypothesis, endothermy arose from eurythermal cell design and associated high dissipative energy turnover that was maximized when specializing on a narrow range of high body temperatures, higher in birds than in mammals (Pörtner, 2004; Clarke and Pörtner, 2010). Endothermy mechanisms also respond to temperature by thermal acclimatization and adaptation processes (and experience associated limits). Thermoregulation by sweating adds an energetic burden for evaporation-induced cooling. Species-specific differences exist in the capacity of thermoregulation; however, it becomes unsuccessful in maintaining body temperature during heat exposure at saturated humidity. Both cold and heat increase the risk of cardiovascular mortality in humans, especially in the elderly and those with cardiovascular disease (Moghadamnia et al., 2017), who would have a lower aerobic power budget in due course. While this mirrors OCLTT principles, OCLTT has not been sufficiently explored in endotherm physiology.

Finally, tradeoffs with other evolutionary pressures may exist that exclude the focus on just one driver as an exclusive explanation. Focusing on oxygen, a classic and still valid view would be that oxygen supply capacity in animals evolved to meet maximum demand at available oxygen concentration (Seibel and Deutsch, 2020). However, both temperature and oxygen and their variabilities would need to be considered. Indeed, these combined pressures would explain the phenomenon that active animals are more eurythermal than passive species, as nicely shown across Antarctic species (see above). It would also explain how seasonal stenotherms become eurytherms if they increase energy turnover in order to enable a maximized metabolic rate, also supporting growth (see above). However, as drivers other than temperature and oxygen can be effective, it is worth exploring whether and to what extent the interaction of all of these driver effects can be explored in a coherent way (Pörtner, 2010). This is done in the next section.

Towards ecosystems: integrating various drivers

The concept of OCLTT in animals does not just provide a basis for understanding temperature-dependent functional patterns of species and communities along large spatial and temporal scales, or the effect of temperature extremes such as those during heat waves. For

any specific point in time or space it also allows integration of the impacts of other drivers including their extremes (e.g. climate-related drivers such as CO_2, hypoxia, salinity, lack of water and drought, storms and floods) and phenomena at specific temperature values, such as food availability, energy budgets and others (Pörtner, 2010). Again, a temperature-dependent continuum may exist for each of these along spatial scales (e.g. Deutsch et al., 2015, for oxygen; Penn et al., 2018, on temperature–hypoxia interactions). Key questions are how each of these drivers interact with temperature from a mechanistic point of view.

With a focus on linking biogeography and ecosystem functioning to molecular, biochemical and physiological mechanisms shaping organism tolerance and performance, OCLTT was proposed as a matrix for integrating effects of other drivers along spatial and temporal clines (Pörtner, 2010, 2012): As of yet, few studies provide such an integrative analysis which would facilitate bridging to ecology by more precisely identifying the limits and breadth of a species' niche and thus its biogeography. The respective ranking of drivers would help the integration of individual drivers or even 'multiple drivers' (Boyd et al., 2018; Kroeker et al., 2020). As a foundation for understanding more complex ecological patterns, the consideration of metabolic demands at the ecosystem level not only allows explanation of the fundamental niche but also provides access to the realized niche of species (Deutsch et al., 2015; Pörtner et al., 2017). It can thereby more precisely explain absolute and relative shifts in species ranges and species interactions (Pörtner et al., 2014).

Such principle considerations also support generalizing beyond marine examples, as a large number of terrestrial and freshwater species also respond to increased warming with a shift in geographic distribution. Because of their thermal specialization and thus, their 'endeavor' to remain in the same or a similar temperature range, most organisms migrate or are passively drifted poleward or uphill or upstream with increasing temperatures. Ambient variability, e.g. of diurnal temperature, CO_2 or oxygen, as well as extreme events influence organism responses to change (Podrabsky and Somero, 2004; Gunderson et al., 2016; Morón Lugo et al., 2020) and probably also play a role in shaping the niche in aquatic and terrestrial environments.

Based on findings in a limited number of marine invertebrate and some vertebrate species, hypoxia and CO_2 both have the potential to constrain niche width, by reducing performance. This picture seems relatively clear for hypoxia, which is considered a more effective driver than CO_2 (Reddin et al., 2020). Very clearly, the hypoxia impact is linked to the mechanisms of OCLTT, by reducing scope in aerobic power budget with implications for body size. Elevated CO_2 may cause metabolic depression through acid–base and ion disturbances, with growth possibly affected through energy savings, either positively (McMahon et al., 2020) or negatively (e.g. Murray and Baumann, 2020). Elevated CO_2 also reduces nervous control with an impact on behavioral patterns (for review, see Wittmann and Pörtner, 2013; Clements and Hunt, 2015; Heuer et al., 2016). Overall, ocean acidification can constrain the thermal range, e.g. in crustaceans (Metzger et al., 2007; Walther et al., 2009). For fish, the hypothesis that CO_2 constrains the thermal range was confirmed in Atlantic cod embryos (Dahlke et al., 2018), indicating that bottlenecks of vulnerability to combined ocean warming and acidification again exist during the life cycle. Indeed, the diversity of findings in fishes (Esbaugh, 2018) and some debate about studying the impact of ocean acidification on adult fish behavior (Clark et al., 2020; Munday et al., 2020; Williamson et al., 2020) indicate that for a clear and comprehensive picture of species vulnerability, impacts of ocean acidification again need to be investigated across life stages

because of their inter-dependency, e.g. for maintaining reproductive output. While early life stages have been investigated (for examples, see Melzner et al., 2009; Hu et al., 2011; Parker et al., 2015; Dahlke et al., 2018), data on adult spawners are clearly missing. Investigations also need to capture the combination of all key drivers effective in an ecosystem. The combined effects of temperature, hypoxia and CO_2 as presently effective in upwelling areas have been seen to represent a 'deadly trio' as they were jointly operative during mass extinction events in Earth history (Pörtner et al., 2005b; Bijma et al., 2013). Investigations in extant fauna indicate that the three drivers combined are most detrimental, possibly through putting a particular constraint on individual plasticity, as seen in, for example, mollusks (Tripp-Valdez et al., 2017, 2019; Götze et al., 2020).

From the fundamental to the realized niche

In the discussion of why species remain within their conventional thermal niche, physiology is traditionally assigned the 'fundamental' niche and ecology the 'realized' niche. This author without hesitation would concede that ecology strives to describe its observations and findings along the realities of the habitat, and, as such, with a view to capturing ecosystem functioning at the highest complexity level. However, physiology in the end should do something similar and evaluate the complete set of fundamental reasons (building blocks) for these ecosystem-level observations. Experimental studies contributing to this exercise admittedly are reductionist by nature but connecting to the complex ecological picture should be seen as a requirement. For each of the diverse organisms involved at the ecosystem level, experiments could encompass studies of the genetic basis up to its functional expression at the protein, cellular and organismic level. The integration of these levels should then link to ecological findings and to an understanding of the specialization of organisms in limited temperature ranges and of how they respond to other environmental drivers, including species interactions. On this basis, it makes sense to study the respective performances of the organism such as muscular activity and behavioral capacity, growth and reproduction, as well as their mechanistic underpinnings, which shape the overall performance curve. Growth and reproduction and, for some life stages of species, activity capacity would be integrated measures of overall performance and fitness in the respective habitat, integrating individual performances and their potential (relative) changes within the niche. Such analyses should provide the underpinnings for any feedback between overall performance capacity and the width of the niche. In this sense, the evolutionary adjustment of aerobic scope for exercise needs consideration (cf. Pörtner, 2002b,c; Seibel and Deutsch, 2020) as it will have implications for the width of the niche, being wider in more active animal species at the expense of higher standard metabolic rate and, on average, increased levels of spontaneous exercise. At low activity, elevated aerobic scope of individuals (within species) may even benefit their growth (Claireaux et al., 2000). Conversely, if elevated aerobic scope supports higher activity levels and associated energy demand, this may in turn cause reduced growth performance, as a tradeoff (see above).

From an ecological point of view, the overall performance capacity supports the ability of the organism to interact, e.g. compete with con-specifics and also interact with other species, either as competitors for space or food, or as players in the food chain (as predators or prey) (Fig. 2). Ultimately, there is thus a need to bridge the gap between the fundamental and the realized niche, in order to approach realism with respect to the impacts found (Sommer, 2012; Boyd et al., 2018; Hodgson and Halpern, 2018). According to recent

thinking, the realized niche would result from a narrowing of the fundamental niche, as a result of a minimum necessary level of overall performance (moving upward on both the low and the high temperature shanks of the overall performance curve), yielding a minimum rate of routine performance required in the natural habitat (Deutsch et al., 2015). This minimum level is co-defined by temperature and thereby defines upper and lower limits on either the warm or cold side of the thermal niche (Pörtner et al., 2017; see Fig. 4). Routine performance would encompass all energetic costs sustaining fitness at the ecosystem level. It thus integrates individual processes supporting competitiveness, sustainable food intake and successful survival, with growth and reproductive success (or development in early life stages) under field conditions as outcomes that can serve as overall performance (and fitness) indicators. Furthermore, evolutionary adaptation along spatial clines involves thermal specialization on specific niches which has energetic and functional implications (Pörtner, 2006). These are OCLTT characteristics with consequences for species interactions and species richness (Pörtner and Gutt, 2016). They may contribute to shaping further macrophysiological patterns along latitudinal and altitudinal clines (Gaston et al., 2009; Buckley et al., 2014), which in turn will then also be affected by the interaction with other drivers. The reliance of species interactions on maintained routine performance also indicates how ecosystems are more constrained and vulnerable at lower high temperature extremes than are individual species (Fig. 2). The loss of vulnerable interactions (Simmons et al., 2020) can thus shape the future of a system under climate change. Accepting the overarching importance of temperature and thermal performance for ecology leads to one simple request to experimental biologists: the design of experiments should consider the full thermal performance curve of organisms when addressing the impact of 'other' drivers beyond temperature, rather than setting temperatures arbitrarily.

Limits to adaptation: from wild species and ecosystems to livestock, humans and society

An integrative concept such as OCLTT may thus be a suitable candidate to help detail the complex physiology underpinning the fundamental niche and also identify the upper and lower thresholds of overall routine performance, setting limits to the realized niche. These thresholds might shift during acclimatization or adaptation under climate change. In this context, successful acclimatization or adaptation would describe the mastering of changes in the environment, on time scales that fully ensure the survival of the species on site. Staying in the changing environment of the original habitat would thus be a sign of successful niche shift by acclimatization or adaptation. This can also involve a shifting niche width through a changing activation energy E_a as confirmed in the meta-analysis by Dahlke et al. (2020). Animal ectotherms and endotherms shift their (fundamental and realized) niche during acclimatization of the individual and/or during evolutionary adaptation across generations, which implies genetic shifts through mutations that are then selected for and can become heritable, securing the beneficial change in species' functional characteristics. Identifying mechanisms of (epi-genetic) acclimatization and genetic adaptation represents an area of active research not to be reviewed here.

However, these mechanisms probably have species-specific limits (mostly unexplored), which may be both time and driver dependent. In brief, the currently observed displacement of species from virtually all taxa, which follow the climate-induced shift of their temperature ranges, indicates that current climate change is too fast for acclimatization or adaptation to be fully effective in keeping organisms in their current habitat. If climate change is too fast or extremes exceed acute tolerance limits and the limits of short-term adaptability, the species can become locally extinct. Driver- or time-dependent limits to adaptation are thus indicated by the fact that current climate change causes geographic shifts through active relocation or passive drifting and successful settling of the young life stages. In some cases, a shift in tolerance limits through acclimatization or adaptation and a geographical shift may complement each other to support species survival. Niche widths may thereby also change such that upper limits (rear edges) and lower limits (leading edges) may shift by different amounts. Finally, metazoan heat limits can be reached during heat waves, which would at the same time indicate an evolutionary limit to adaptation that cannot be overcome (Storch et al., 2014). These findings underpin the strong biodiversity loss projected in the lower latitudes under unabated climate change (García Molinos et al., 2016), especially at temperatures close to the warm-water limit of species distributions (Smale et al., 2019). They are also in line with paleo-findings under severe climate-induced mass extinction, as during the end Permian–Early Triassic, when lower latitudes on land and in the oceans were depleted of higher (i.e. more heat sensitive) life forms such as animals including fish (Sun et al., 2012). Overall, mechanisms setting acclimatization and adaptation limits have not yet been identified at interdependent genetic and functional levels (considering OCLTT in the latter case), demanding further research efforts.

Climate extremes in particular make it clear how much the terms 'niche' and 'suitable living conditions' can also be applied to humans (Smith et al., 2014; Xu et al., 2020). In some regions of the world, especially in the low latitudes, increasing heat waves with high humidity in air make some traditional human habitats at least temporarily uninhabitable unless technical aids such as air conditioning are widely applied (Jones et al., 2015; Mora et al., 2017; Pal and Eltahir, 2016; Kang and Eltahir, 2018; Raymond et al., 2020). Extreme heat events are already causing human mortality, including in central Europe (Mitchell et al., 2016). The fraction of the human population exposed to extreme heat is rising with the degree of global warming. In China, such projections for the vulnerable southeast led authors to emphasize the 1.5°C temperature target (Zhan et al., 2018). Mammalian livestock will be similarly affected (Amamou et al., 2019) and, despite attempts to increase heat tolerance by breeding or genetic tools (Carabaño et al., 2019), will be tied to evolutionary mammalian heat tolerance limits, starting with performance loss (heat fatigue) as body temperature rises above 38°C and significant heat stress beyond 40°C, as also known for humans (Smith et al., 2014). Environmental thresholds eliciting such effects are captured by the temperature humidity index (THI) or wet bulb temperature (lethal threshold at 35°C and 100% humidity; Smith et al., 2014), which has recently been surpassed in several places such as the Persian Gulf region (Raymond et al., 2020). The thermal limit represented by wet bulb temperature points to a general limit to mammalian life in the heat, surpassed at about 35°C if combined with high humidity. However, the European heatwave in 2003 and the Russian heatwave in 2010 each killed tens of thousands of people with wet-bulb temperatures no higher than 28°C, indicating that critical physiological constraints set in at even lower temperature–humidity combinations in vulnerable groups such as the elderly, those with cardiovascular disease or the very young population. Furthermore, the upper temperatures limiting humans and other mammals decrease with increasing physical activity, constraining outdoor routine activities prior to heat fatigue.

These findings and considerations indicate that heat-induced loss of habitat is not restrained to ectotherms but will also affect humans and other mammals including livestock, because of evolutionary limits to adaptation set by the failure of mammalian thermal regulation at environmental extremes. Heat and drought constraints on livestock and crop production contribute to setting limits to the human (realized) niche, reflecting the climate-induced loss of food security (which includes surpassing the tolerance limits of feed organisms). Especially at lower latitudes, animals and plants probably exist close(r) to their evolutionary upper thermal tolerance limits, with the perspective of a progressive clearing of these areas from biodiversity (including agro-biodiversity) under climate warming (see above). Humans are dependent on diverse plants and animals; they all follow the very principles espoused by OCLTT. As with other species, human migratory shifts are to be expected from the need to avoid the threat of surpassing physiological limits or from unfavorable living conditions through loss of food security; in humans, this initiates the emigration of the adult population. Regions projected to become increasingly less amenable to supporting human life are, among others, the Persian Gulf region, the Amazon basin and parts of the Indian subcontinent (Mora et al., 2017). The foreseeable loss of coastal areas on all continents as a result of the ongoing rise in sea level also implies the loss of human habitat. The loss of human habitat elicited by climate change would have to be classified as an existential threat and thereby distinguished from migratory movements elicited by the search for an economically more prosperous life.

In conclusion, both the ectotherm and the human (mammalian) case indicate that displacement from the original habitat reflects avoidance of harmful climatic effects that cannot be compensated for by adaptation *in situ*. It would occur through adaptive behavior or through offspring survival in a new, more suitable habitat. These contrast successful adaptation *in situ* to changing environmental conditions. Nature conservation and human adaptation policies should take the climate-related limits to acclimatization and adaptation (to be genetically and physiologically defined) of species (including humans) and ecosystems (including managed ecosystems sustaining human life) into account when addressing climate, biodiversity and human habitat. Evolutionary adaptation limits may leave geographical shifts (migratory movements) as the only option to respond. For natural ecosystems, this can be realized by creating an extensive network of protected areas that cover a climate gradient. This makes it possible for species to escape and thrive in climatically more favorable areas provided they are under suitable protection status. The findings of high vulnerability of embryonic and spawning life stages emphasize, however, that wildlife spawning habitats and their climatic and other living conditions deserve special attention.

In a climate change policy context as under the United Nations framework convention on climate change (UNFCCC), the term 'adaptation' almost exclusively focuses on human adaptation to climate change, through technological or behavioral adjustment such as shifts in location, triggered by various environmental or economic factors. This contrasts the biological definition of acclimatization or evolutionary adaptation (*in situ*). The political perspective of adaptation is therefore different from the biological one. The two concepts overlap and apply when considering the loss of suitable habitat, due to the warming-induced general shift of the realized niche of virtually all, especially higher, life to higher latitude or altitude. It would therefore be worth establishing a formal link between these two concepts of adaptation, for the sake of effective human- and biodiversity-related policies.

Perspectives: learning from ecosystems for human society and sustainability

There are further lessons to be learned by human society from temperature-dependent performance and vulnerability, and from the drop in upper thermal limits postulated to occur with rising complexity of a system. Both ecosystems and human society rely on minimum levels of routine performance of their members to enable interactions between them and associated processes that characterize the system (see above). Assuming these principles to be applicable to highly complex human societies leads to the projection that human societal functioning and interactions become constrained at high humidity and temperatures even lower than 35°C. This may lead to constraints in economic performance (projected to occur at a level of global warming by 2°C; IPCC, 2018), or constraints in the maintenance of the food supply chain, in water supply and in other logistic operations essential for societal functioning and well-being. Such assessments would be needed to address the climate vulnerability of human societies and their prosperity in different environments and climate zones. Indeed, Fig. 2 illustrates how in a more complex system (ecosystem), variability in the thermal performance of system components (species) and their overlap at minimum levels of functional rates required to support the complex system represent a reason for narrowing thermal breadth of the whole system with increasing levels of complexity, from molecular to ecosystem.

Finally, compliance with the Paris climate targets, specifically the more ambitious 1.5°C, appears to be an essential prerequisite for the successful protection of species, biodiversity, habitat, including human habitat, ecosystems and human society. Keeping to the Paris agreement, especially warming by not more than 1.5°C, reduces not only the absolute degree of warming but also its velocity. Both increase the likelihood that geographic shifts, individual acclimatization under short-term extremes and evolutionary adaptation to progressive warming together can ensure survival and prosperity of many species, including humans. This appears as key in limiting the loss of species and constraining the magnitude of the ongoing sixth mass extinction in Earth history. Further research efforts have to show whether the current proposal to exclude 30% of the land surface and 30% of the oceans from human use (IUCN), for protecting and restoring natural ecosystems, together with ambitious emissions reduction, is sufficient to support this claim or whether a 50% target needs to be pursued. Such measures would help mitigate climate change (by rebuilding natural carbon stocks), avoid biodiversity loss (by protecting evolved species interactions and reducing ecosystem mixing) and reduce the risk of future pandemics (by separating zoonoses from humans; IPBES, 2020). Last but not least, not exceeding 1.5°C warming will also alleviate constraints on human survival as well as societal integrity and functioning. Respecting the borderlines of natural systems will be an important element of developing the planet towards sustainability, and keeping climate change on the ambitious side of the Paris agreement, below 1.5°C warming. This will facilitate reaching the Sustainable Development Goals of the United Nations (IPCC, 2018).

Despite the urgency expressed in recent IPCC and IPBES assessment reports, we currently see some policy makers failing on respecting the services provided by ecosystems (nature's contribution to people) and the ultimate borderlines to the existence of higher, complex life forms, such as animals and plants (Storch et al., 2014), but also humans on this planet. This touches the very basics of planetary functioning, with huge implications for human life and societal functions which depend on such foundations being fully operational. These basics are still relevant to high level societal

processes which can only be optimized within well-defined environmental windows, some would say within planetary boundaries. In analogy to upper thermal limits being related to biological complexity (Storch et al., 2014), it may even be that the higher the complexity level of societal organization, the more vulnerable humankind becomes and the more limited the environmental window of optimal operation, or the narrower the range of amenable temperatures. Human civilization has evolved during 6000–8000 years of relative climate stability and is now about to be pushed outside of this climate window, indicated by modern temperatures about to leave the Holocene temperature range and probably being higher than at any time during the history of human civilization on a global scale (Fig. 5; see fig. 1.2 of IPCC, 2018; Kaufman et al., 2020). Because of societal complexity and reliance on natural resources and the food supply chain, this may occur even before the surpassing of individual (human) thermal limits and loss of individual performance (see above). Heat fatigue and associated functional constraints on behavioral interactions between individuals (Hoegh-Guldberg et al., 2019) will exacerbate such societal impacts. Associated losses include economic performance and, finally, human habitat. Climate-induced collapse of human societies closely influenced by changes in natural systems has in fact repeatedly been part of human history (Xu et al., 2020).

Implementing sustainability on all fronts including successful climate change mitigation would keep societies closer to the upper margin of that window, limiting the rising risks, allowing poverty eradication to proceed, and enabling the pursuit of equity and justice, all of which would benefit from not abandoning such a window (IPCC, 2018). Without respecting such foundational issues, human societies will find it increasingly difficult to prevail and prosper. Setting up artificial human environments such as cities does not make civilization independent of natural resources and environmental conditions. For functioning, society still relies on basic biological provision systems; living in air-conditioned environments may tunnel under heat island effects but is no permanent solution for all functions. Uncovering the basic interdependencies of relevant systems, as well as using the right levers to mobilize political and societal action, will be key to mastering the climate crisis, with increasing urgency.

Perspectives: lessons for experimental biology

There are also lessons for experimental biology, which, together with other disciplines, has contributed to identifying the limits to life, and has made a start with unraveling some unifying principles and mechanisms shaping organism (and ecosystem) vulnerability and their responses to climate change. For connecting closely to ecology, experimental biology should consider the full thermal performance curve and its response to other drivers in the design of experiments (see above). Identifying cause and effect would become more comprehensive and experimental biology could thereby enhance confidence in understanding the impacts of climate change. However, experimental biology may often be too focused on its own experimental evidence. Drawing on multiple lines of evidence across disciplinary borders would enable the discussion to bridge gaps in our knowledge which may not be amenable to experimental research and otherwise appear insurmountable. And in the discursive arguments such as those developed here, it is clearly important to go beyond what can be addressed by experimental research (Hodgson and Halpern, 2018). Such insight is also relevant for modeling, which is relevant to project future climate impacts and risks for aquatic and terrestrial ecosystems as well as for human futures. From a broad viewpoint, mechanism-based understanding cannot replace such modeling efforts. However, experimental biology allows us to scrutinize and thereby improve often simplified modeling approaches. The use of these insights would improve the building of bridges between disciplines such as physiology and ecology, to develop more precise conclusions and to avoid conceptual ambiguities.
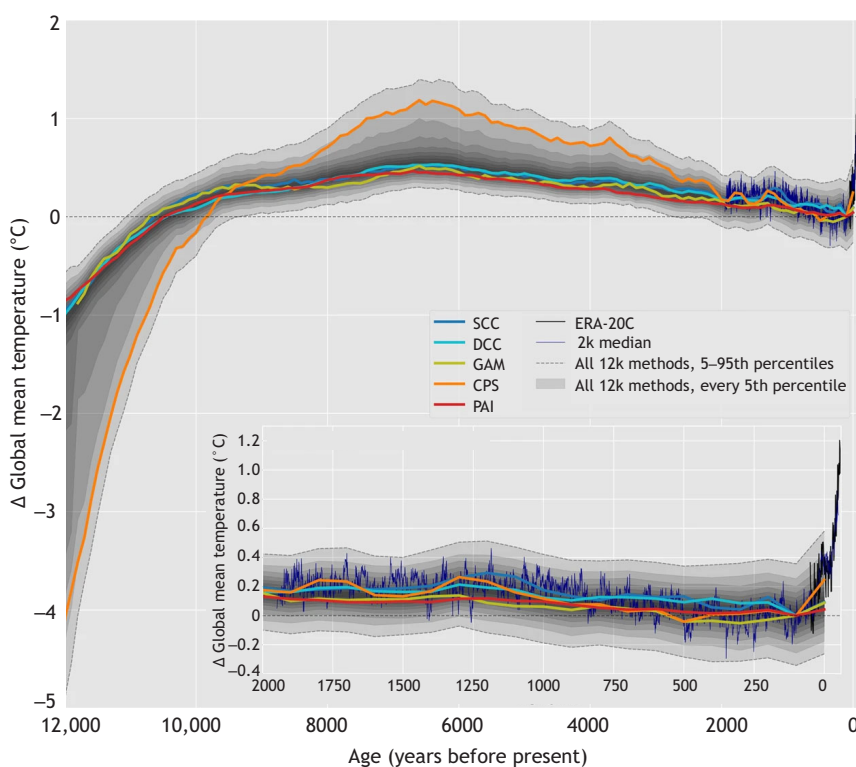

Fig. 5. Global mean temperature is moving outside the temperature range of the Holocene. The figure (adapted from Kaufman et al., 2020, Creative Commons Attribution 4.0 International License) indicates that humankind and ecosystems are beginning to be exposed to temperature regimes unprecedented for the last 6000–8000 years, during which time human civilizations have evolved in virtually all parts of the planet. This is in line with the finding that in some parts of present human habitat, temperatures may move outside of the thermal range of societal functioning and integrity, triggering a tipping point towards societal disintegration (e.g. Xu et al., 2020; see text). Global mean surface temperature was evaluated in a consensus ensemble approach from the Temperature 12k database using reconstruction methods including standard calibrated composite (SCC), dynamic calibrated composite (DCC), generalized additive model (GAM), composite plus scale (CPS) and pairwise comparison (PAI). Colored lines represent ensemble medians of each of the five reconstruction methods. The dark gray line represents instrumental data between 1900 and 2010 from the ERA-20C reanalysis (Poli et al., 2016). Gray shading represents every 5th percentile of the 2500 ensemble members from all methods. Temperature anomalies are relative to 1800–1900. The inset depicts data for the last 2000 years.

A specific risk for experimental research lies in narrowly focused interpretation around a limited set of data, collected in reductionist experiments. The reductionist approach may ignore important evidence or prematurely close options for interpretation that arise when connecting multiple lines of evidence. To do so, unraveling functional properties of high complexity systems may require leading a scientific discourse similar to that used for other high complexity systems such as societal systems, analyzed by the social sciences. The analysis may be complemented by a consensus-building process similar to that characterizing assessments carried out by the Intergovernmental Panel on Climate Change (IPCC) and the Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES). An assessment evaluates the evidence and agreement on relevant findings and assigns a level of confidence to those findings. This also means presenting key findings in light of their societal relevance and with the associated level of evidence and agreement so that high confidence findings can be identified and given priority. This forward-looking consensus-building mechanism in fact appears as a precondition for speaking with one voice to outside communities and thereby developing relevant contributions to the societal and policy debate. In turn, the experimental community may benefit from widening its perspective, thereby supporting comprehensive assessment of current knowledge, associated confidence and of gaps in knowledge concerning climate change impacts and risks. Such an approach would also strengthen the development of approaches targeted to solutions, e.g. concerning the degree and rate of adaptation and the adaptation limits of natural systems under climate change, to be considered in conservation efforts. For higher confidence in implementing the respective solutions, our current understanding of ecosystem functioning would benefit from identifying first principles as attempted along the reasoning in this Review. In light of the increasing urgency, however, the implementation of solutions through climate action cannot wait any longer for climate research, meaning that they need to proceed in parallel; we know enough to act.

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