

# Genomics for monitoring and understanding species responses to global climate change

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## Abstract

All life forms across the globe are experiencing drastic changes in environmental conditions as a result of global climate change. These environmental changes are happening rapidly, incur substantial socioeconomic costs, pose threats to biodiversity and diminish a species' potential to adapt to future environments. Understanding and monitoring how organisms respond to human-driven climate change is therefore a major priority for the conservation of biodiversity in a rapidly changing environment. Recent developments in genomic, transcriptomic and epigenomic technologies are enabling unprecedented insights into the evolutionary processes and molecular bases of adaptation. This Review summarizes methods that apply and integrate omics tools to experimentally investigate, monitor and predict how species and communities in the wild cope with global climate change, which is by genetically adapting to new environmental conditions, through range shifts or through phenotypic plasticity. We identify advantages and limitations of each method and discuss future research avenues that would improve our understanding of species' evolutionary responses to global climate change, highlighting the need for holistic, multi-omics approaches to ecosystem monitoring during global climate change.

## Sections

Introduction

Identifying adaptive genetic variation

Genomic vulnerability to GCC

Investigating temporal evolutionary change

Molecular phenotypic plasticity in GCC

eDNA community monitoring and GCC

Conclusions and perspectives

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*We wish to dedicate this review to the memory of Louis Bernatchez, who passed away shortly after its acceptance. We are all deeply grateful to Louis, not only for conceiving this piece of work, but most importantly for his outstanding contributions to the field, invaluable mentorship, and boundless generosity and compassion.*

## Introduction

The impact of global climate change (GCC) is affecting all forms of life across all biomes, with potentially detrimental consequences to the persistence of species and ecosystem functioning<sup>1–6</sup>. Shifts in environmental conditions, such as warming temperatures and ocean acidification, have direct effects on organisms by challenging physiological limits<sup>7–9</sup> or altering phenology<sup>10,11</sup>. Indirect effects of climate change can also threaten biodiversity by increasing the spread of novel pathogens and severity of disease outbreaks<sup>12</sup>, or by introducing new species that alter predation and competition dynamics in communities<sup>13</sup>.

The rapid pace of GCC may preclude adequate responses in many populations, thus increasing the rate of decline and extinction<sup>14</sup>. Extinction can be avoided by species shifting their geographical distribution to more favourable habitats, acclimatizing to stressful conditions through phenotypic plasticity – the ability of one genotype to express different phenotypes in different environments – or adapting through genetic change (Fig. 1). However, it is challenging to understand when eco-evolutionary responses will occur and to differentiate between the aforementioned responses to identify potential evolutionary ‘winners’ and ‘losers’, such as species with low adaptive capacity<sup>6,15–17</sup>. Many studies have attributed phenotypic changes in natural populations to GCC-induced phenotypic plasticity<sup>3,5,18</sup>. However, plasticity and genetic effects are difficult to disentangle as both contribute to phenotype, and plastic mechanisms are often partially genetically controlled<sup>19–21</sup>. Genomic data need to be supplemented with experiments in controlled conditions to document evolutionary change over time and by integrating other omics approaches, such as transcriptomics and epigenomics, to adequately infer the genetic versus plastic basis of responses to GCC<sup>3</sup>. Monitoring temporal genomic and phenotypic changes drastically improves our understanding of how GCC affects organisms; although this approach presents logistical issues for many species, it is becoming increasingly feasible with recent omics technologies.

Next-generation sequencing methods have transformed the field of population and functional genomics over the past decade by enabling the screening of whole-genome variation within and between species across space and time<sup>22</sup>. This makes it possible to characterize the genome-wide architecture that underlies adaptive traits and the genome-wide response to selection induced by natural or anthropogenic factors, including GCC<sup>6</sup>. New analytical methods can forecast range shifts under predicted climate change for individuals adapted to different climatic conditions and determine the potential for rescue effects to support population persistence. Moreover, genome-wide plastic responses to new environmental conditions through changes in gene expression and epigenetic modifications can be investigated using molecular approaches, in both controlled conditions and natural environments. Recent developments in metagenomics and metabarcoding also represent powerful methods to monitor community composition of all species under GCC. Together, this array of omics technologies presents a powerful toolbox to understand the effects of GCC on species and communities.

Here, we review the application of methods used in recent years to infer or predict organismal responses to GCC, in both natural and experimental conditions (Table 1). For a comprehensive review of potential

evolutionary responses to GCC<sup>23</sup> or the technical details of the methods described<sup>24–26</sup>, we refer readers to other reviews. Our aim is to summarize and highlight the broad range of applications of diverse methodologies over the past decade in the context of GCC, using key examples. We present advantages and limitations associated with the reviewed methods (Table 1), as well as future perspectives for improving predictions of the multifaceted responses to GCC across systems.

## Identifying adaptive genetic variation

Characterization of spatial patterns of adaptive genetic variation in wild populations is an important first step towards understanding the potential for adaptation to GCC. Spatially varying selection can drive local adaptation and maintain standing genetic variation, facilitating adaptive responses to environmental change. For example, one study identified physiological differences and genomic divergence despite high gene flow between *Acropora tenuis* populations occupying different habitats in an isolated coral reef system in Western Australia<sup>27</sup>. This finding supports a role for selection driven by spatially varying environmental conditions to maintain genetic variation that confers resilience to heat stress in habitats experiencing more extreme conditions.

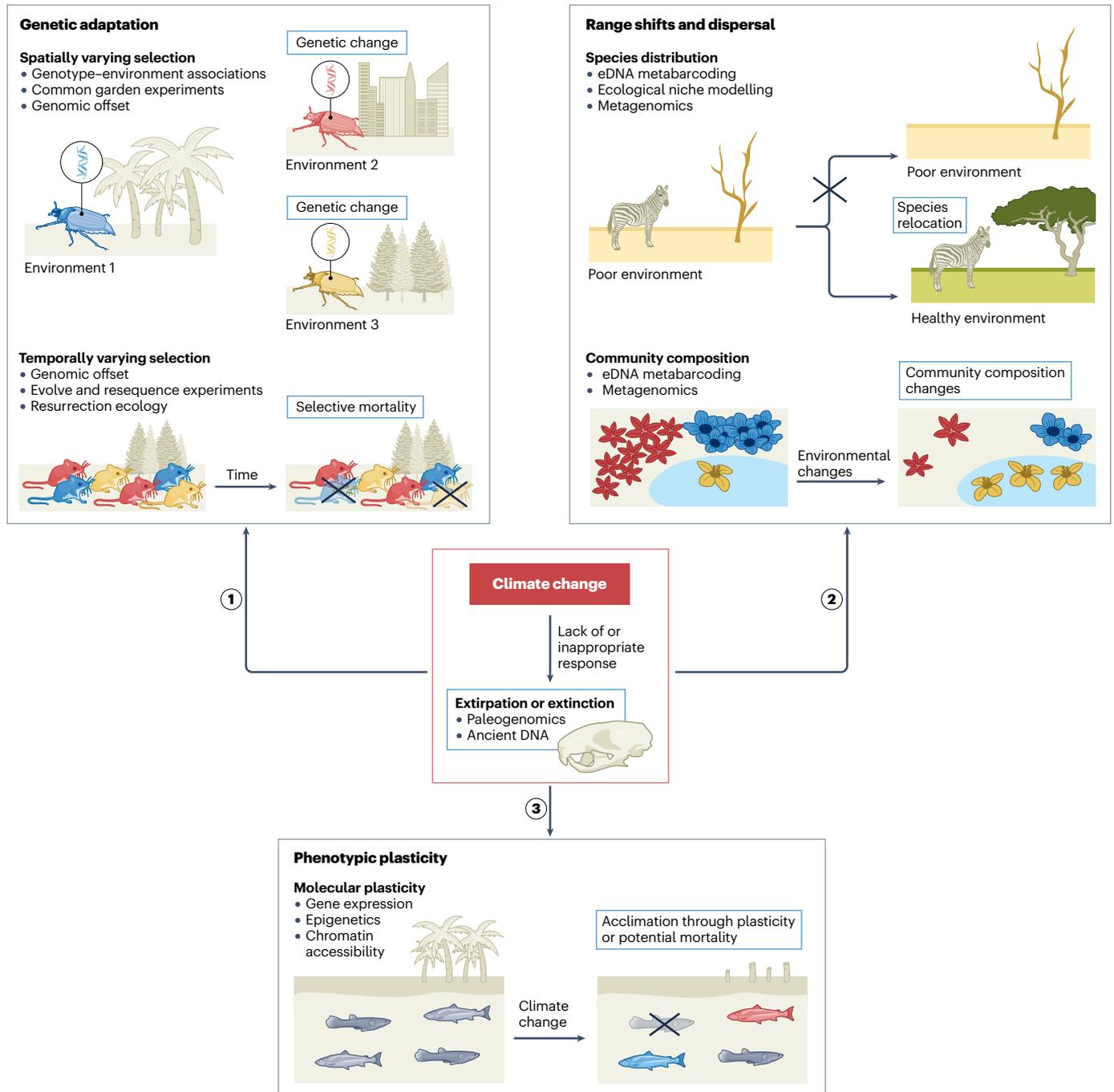
Population genomic methods, such as genome scans for signals of divergent selection, are now extensively used to identify candidate adaptive genomic variants, typically SNPs. For example, differentiation-based scans detect candidate adaptive loci on the basis of signals of locus-specific genetic differentiation between populations that deviate from expectations under a neutral model (for example,  $F_{ST}$  outliers) and are thus presumably subject to selection<sup>28</sup>. This approach has been used to identify highly differentiated SNPs across genetically distinct populations that were subsequently linked with bioclimatic variables such as temperature and salinity and functional genes potentially involved in thermal tolerance or salinity stress response mechanisms<sup>29</sup>. Other genome scan approaches that directly incorporate environmental variables, known as genotype–environment associations (GEAs)<sup>28,30,31</sup>, detect candidate adaptive loci on the basis of direct statistical associations between allele frequencies and environmental variables and can identify key climatic factors that are driving local adaptation across heterogeneous landscapes<sup>32–35</sup>. Several GEA methods exist and their performance under various scenarios has been reviewed elsewhere<sup>36–38</sup>. Most conventional GEA methods use linear models to test genetic–environment relationships<sup>30</sup>, although methods such as regression tree-based models can capture nonlinear relationships and have been used to detect genomic variants associated with climate adaptation<sup>39,40</sup>. Multivariate methods, especially redundancy analysis (RDA), are commonly used to identify GEAs given their ability to model multi-dimensional relationships and detect weak polygenic signatures of selection compared with univariate methods<sup>37,41</sup>. Window-based approaches have also been applied to characterize the genetic basis of local adaptation and have shown promising levels of performance when compared with other GEA methods<sup>42</sup>.

Understanding spatial patterns of climate-associated genetic diversity can provide insight into the adaptive potential of populations<sup>43</sup> and is a common focus of landscape genomics studies. Detection of local adaptation to environmental conditions using GEAs combined with assessments of dispersal capacity estimated with landscape resistance suggests that the potential for evolutionary responses to changing conditions may be limited in some populations, as documented in the streamside salamander *Ambystoma barbouri*<sup>44</sup>. When coupled with an ecological niche model (ENM), the spatial distribution of climate-adapted loci can be related to range-wide environmental

# Review article

suitability, thereby identifying regions that may be sources of adaptive genetic variation to unfavourable or changing conditions at niche limits<sup>45</sup> (Fig. 2). Accordingly, studies using GEAs provide essential

information for implementing strategies aimed at protecting species that may be vulnerable to effects of GCC<sup>46</sup>, spatial planning that incorporates adaptive genetic variation in delineating conservation



**Fig. 1 | A conceptual framework to assess the effects of global climate change using omics approaches.** Global climate change (GCC) poses a significant threat to species, although they can adapt genetically through spatially or temporally varying selection (response 1), cope through range shifts and dispersal when possible to avoid extirpation (response 2) or acclimate to GCC through phenotypic plasticity (response 3). Various methods

that integrate genomic and/or epigenomic tools (listed as bullet points) can be used in both natural environments and experimental laboratory conditions to assess how species are responding to GCC (Table 1). Lack of or inappropriate responses can result in extirpation or extinction (red box), which can also inform on the historical effects of GCC on species and communities. eDNA, environmental DNA.

**Table 1 | Main approaches to monitor species responses to GCC at the genomic or epigenomic level**

Approach	Context	Description	Advantages	Limitations
<b>Identifying adaptive genetic variation</b>				
Differentiation-based genome scans	Identify genomic regions subject to selection	Detect locus-specific deviations in population genetic differentiation compared with expectations under a neutral demographic model (e.g. $F_{ST}$ outliers)	Generally noninvasive sampling in natural populations Does not require genomic resources (e.g. reference genome, linkage map)	Underlying demographic models may be overly simplified Confounding effects of demographic history and neutral population structure can lead to false-positive signals of selection Do not directly infer the selective factors that act on highly differentiated loci
Genotype–environment associations	Identify genome-wide loci that are likely involved in environmental adaptation and identify key environmental drivers of local adaptation	Univariate models to test associations between individual loci and environmental predictors (e.g. latent factor mixed models) Multivariate models to test associations between many loci and multiple environmental predictors simultaneously (e.g. redundancy analysis)	Generally noninvasive sampling in natural populations Does not require genomic resources (e.g. reference genome, linkage map) Directly incorporates environmental variables to infer environment-driven selection pressures on differentiated loci	Confounding patterns of selective gradients and neutral population structure can lead to false-positive signals of selection Rely on clinal/monotonic relationships between allele frequencies and the environment Inferences are correlative; may be difficult to experimentally validate candidate loci
<b>Genomic vulnerability to GCC</b>				
Vulnerability prediction	Predict adaptive potential of populations to future environmental conditions and identifies vulnerable/donor populations	Generalization of the genome–environment relationship Measurement of the shift in genomic composition between current and future conditions Validation of the prediction	Forecast on climatic conditions available worldwide Genotype–phenotype associations can also be investigated for predictive responses to GCC Convenient and fast approach for non-model or declining species to inform decision-making	Populations are assumed to be currently adapted to their environment, and genotype–environment associations are not static through time Bias due to missing data, gene flow, genomic load, polygenic effects and correlative predictors Sampling a sufficient number of representative populations across an environment gradient or contrast
<b>Examining temporal evolutionary changes</b>				
Evolve and resequence	Study evolutionary response to selection at the genome level across many generations	Combine whole-genome sequencing (including using Pool-seq) with experimental protocols comparing different environmental conditions in replicated and temporally identical conditions	Documents the specificity and dynamics (e.g. variation in types of mutation) of genome evolution across hundreds, even thousands, of generations in totally controlled conditions	Unclear whether results from laboratory experiments can be directly translated to natural populations Limited to microbial organisms or species with very short generation times More complex organisms can only be reared for a very few generations
Resurrection ecology and genomics	Document evolutionary change between ancestral and contemporary populations	Collect samples from dormant propagule banks in aquatic sediments, soil or ice Hatch and rear in controlled conditions Measure phenotypes and obtain genomic information from whole-genome sequencing, RADseq, candidate genes or gene expression analysis	Align local population genomic and phenotypic evolution with temporal environmental changes	May require extensive experimental set-up, which comes with many technical complications Limited to species that produce dormant propagules
Evolutionary change and time series	Directly measure allele frequency change over time	Sample natural populations at multiple time points using historical samples (e.g. trees of different ages, herbarium specimens) Genotype individuals with a method suitable to the DNA quality (whole-genome sequencing when possible or selected loci)	Applicable to a broad diversity of species Does not require logistically complicated experimental settings	Link between genomic and environmental variation correlative only Confounding historical factors (e.g. bottlenecks and admixture) may cause biases

**Table 1 (continued) | Main approaches to monitor species responses to GCC at the genomic or epigenomic level**

Approach	Context	Description	Advantages	Limitations
<b>Molecular phenotypic plasticity in GCC</b>				
Transcriptomics	Assess plastic responses of organisms	Differential expression analysis Alternative splicing analysis (e.g. differential exon usage) eQTL analysis Methyl-eQTL analysis	Provides a functional genomic basis for plasticity	Requires high-quality RNA Degradation Results may differ based on tissue choice Effects on phenotype are unclear
Epigenomics	Assess mechanisms underlying plastic responses of organisms	DNA methylation sequencing Differential methylation analysis Small or non-coding RNA sequencing/expression analysis Histone modification quantification (e.g. ChIP-seq) Methyl-QTL analysis Methyl-eQTL analysis EWAS Chromatin accessibility sequencing (ATAC-seq)	Provides a heritable mechanistic basis for plasticity	Partially controlled by genetic variation Results may differ based on tissue choice Slow loss or alteration of methylation and histone modifications in stored samples Rapid degradation of small RNA Effects on phenotype unclear
<b>eDNA community monitoring and GCC</b>				
eDNA	Infer current species presence or absence and sometimes relative abundance Assess current biodiversity depending on local environmental conditions	Metabarcoding Metagenomics	Noninvasive Easy sampling Targets all taxonomic levels	Degradation Risk of contamination Marker biases Sequencing errors Limited understanding of the molecule ecology (e.g. rates of DNA production and degradation) No information on demographic or life-history parameters
aDNA	Reconstruct community responses to past environmental events	Metabarcoding Metagenomics	Greater taxonomic resolution, spatial and temporal precision than other palaeoecological methods (e.g. pollen records)	Same as eDNA Increased risks of contamination (false positives) DNA modification and strand damage
eRNA	Assess the plastic response of communities to GCC	Metabarcoding Metagenomics	Same advantages as eDNA Degrades more rapidly than eDNA, therefore represents a more accurate signal of 'real-time' biodiversity	Same as eDNA, with increased risks of degradation

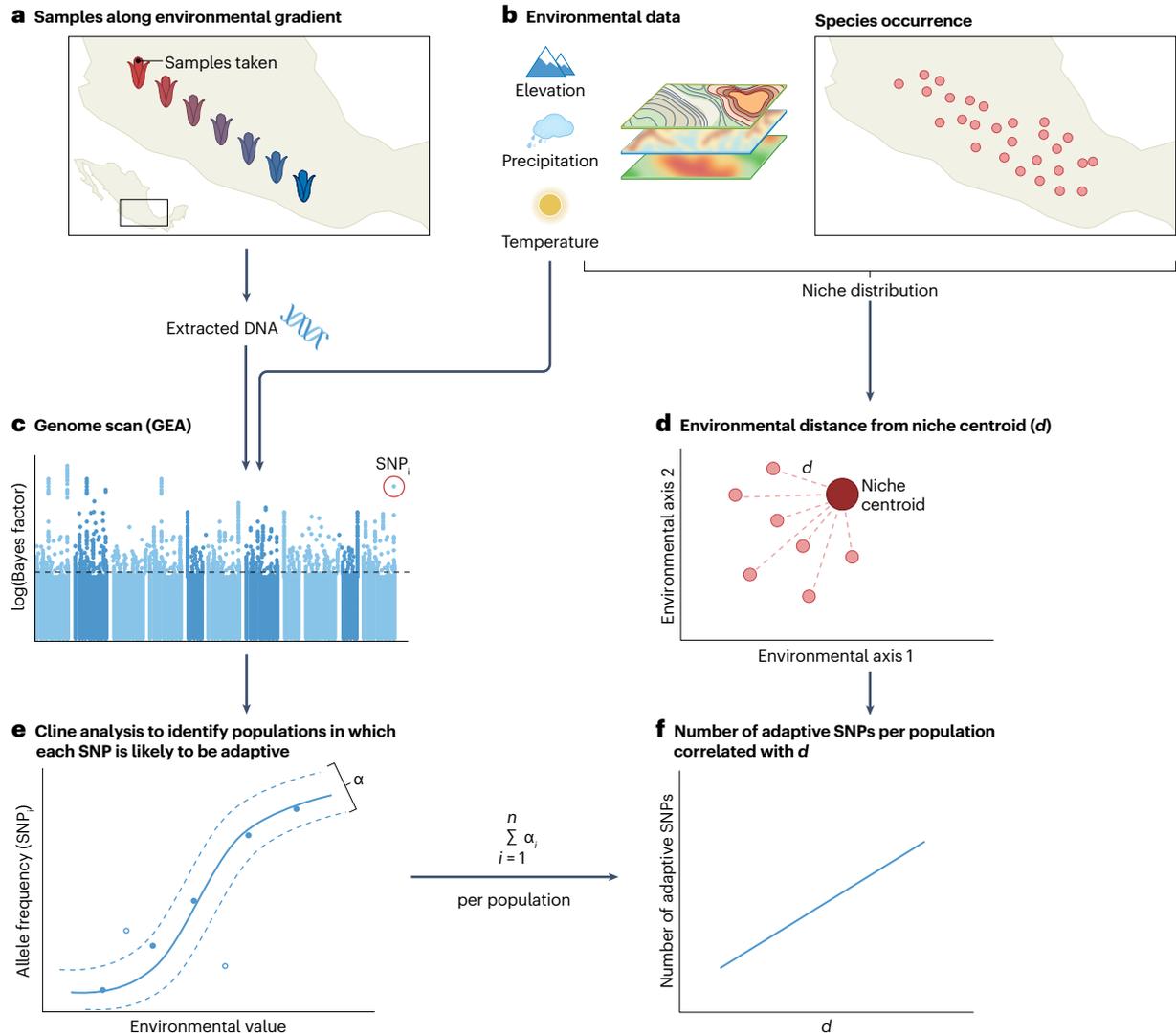
aDNA, ancient DNA; ATAC-seq, assay for transposase-accessible chromatin with high-throughput sequencing; ChIP-seq, chromatin immunoprecipitation followed by sequencing; eDNA, environmental DNA; eQTLs, expression quantitative trait loci; eRNA, environmental RNA; EWAS, epigenome-wide association studies; GCC, global climate change; RADseq, restriction site-associated DNA sequencing.

units or prioritizing areas for protection<sup>47,48</sup>, and informing actions such as assisted gene flow to enhance the adaptive potential of small populations<sup>49,50</sup>.

Signatures of selection may be confounded by neutral population structure and spatial autocorrelation with environmental factors, leading to incorrect inference of local adaptation from GEAs (and differentiation-based genome scans)<sup>28</sup>. Many GEA approaches incorporate corrections to account for the effects of demography and geography<sup>28</sup>. RDA can also be adapted to include conditioning variables using a partial RDA (pRDA), enabling variance partitioning between different sets of predictors (for example, environmental, spatial or demographic) and correcting for confounded effects<sup>41</sup>. For example, after incorporating spatial variables representing dendritic riverine network structure, 4% of genetic variation in the Australian rainbowfish (*Melanotaenia fluviatilis*) populations was attributed to the environment, and >700 loci exhibited associations with

temperature, precipitation and stream flow<sup>34</sup>. Although this approach reduces the number of false-positive detections, it can also exclude true positives when environmental gradients coincide with spatial or demographic processes<sup>37,51</sup>.

Although GEAs are powerful and convenient approaches for discovering climate-associated genetic variation, there are some recognized limitations. The development of GEA methods relies on the basic assumption that adaptive alleles will form frequency clines associated with the selective environment. However, using a range of simulations, a recent study showed that nonclinal allele frequency patterns can evolve despite phenotypic clines associated with climatic gradients, which may lead to incorrect inference of adaptive SNPs based on GEAs<sup>51</sup>. Moreover, causal variants, especially those of small effect, may not be readily detectable<sup>52</sup>, and the predictability of the genomic selection response for polygenic traits depends on an understanding of the underlying adaptive architecture (including linkage disequilibrium,



**Fig. 2 | Using genotype–environment associations to identify candidate SNPs and potential sources of adaptive variation.** **a**, Aguirre-Liguori et al. sampled populations of teosinte (*Zea mays mexicana*) along an environmental gradient in southern Mexico<sup>45</sup>. **b**, Environmental layers and species occurrence data were combined to predict the species’ niche distribution using an ecological niche model. **c**, Candidate SNPs were detected by performing genome scans of genotype–environment associations (GEAs). **d**, Using the predicted niche distribution, the authors defined the niche centroid based on the mean value of each environmental axis and calculated an environmental distance (*d*) between each population and the

niche centroid; populations with a higher *d* inhabit more unsuitable (niche edge) habitats. **e**, For each candidate SNP, the authors fitted an environmental cline and identified populations in which the SNP is likely to be adaptive (filled circles;  $\alpha$ ) versus populations in which the SNP evolves neutrally (open circles). **f**, The authors detected a significant positive correlation between the number of adaptive SNPs per population and the distance of each population from the niche centroid (*d*). This finding suggests that populations that occur at niche limits may be important sources of adaptive variation for populations experiencing environmental change. Parts **c**, **e** and **f** adapted with permission from ref. 45, Wiley.

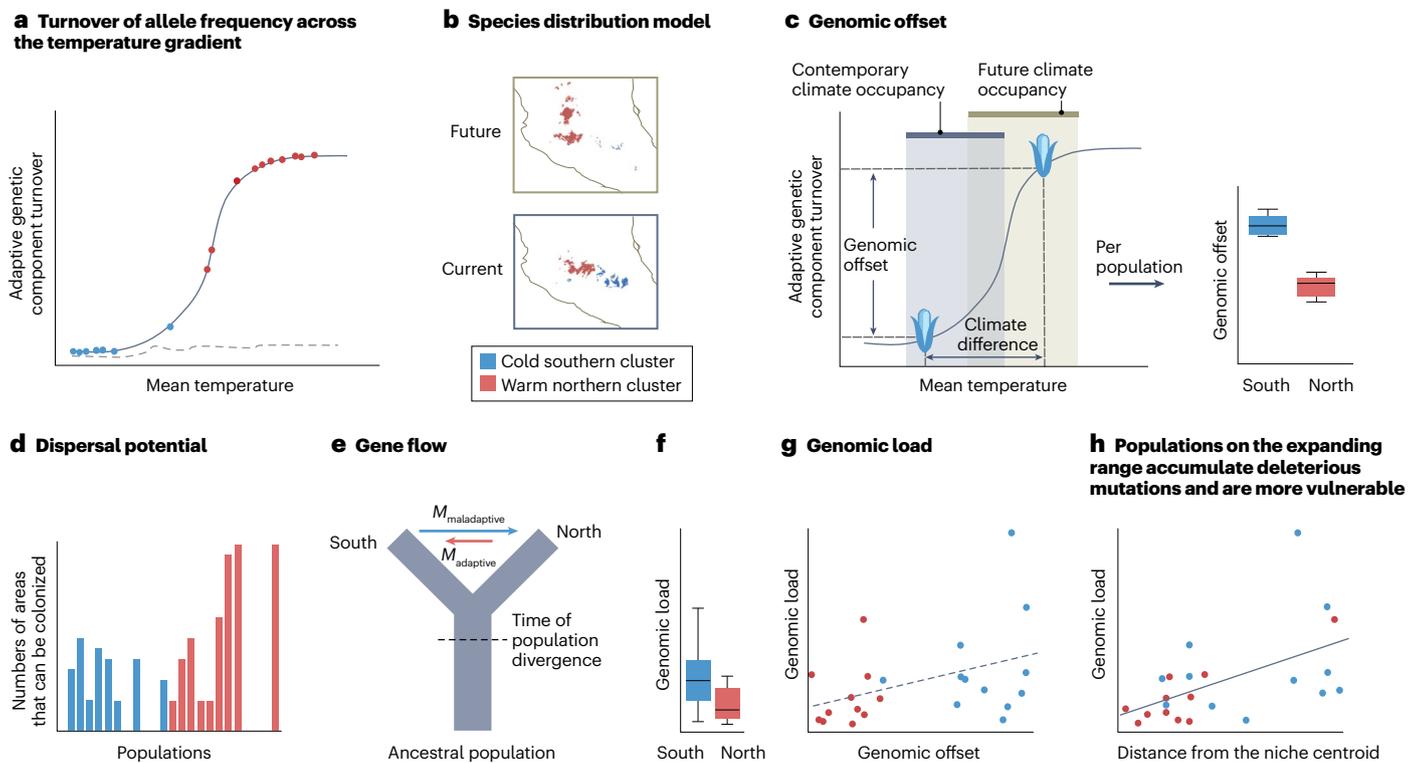
epistasis and recombination rate variation)<sup>53–55</sup>. Despite the limitations of GEA, an extension to the RDA framework has been shown to accurately predict multivariate quantitative traits from landscape genomic data across a range of demographic and selection scenarios and complex genomic architectures<sup>51</sup>. Finally, additional evidence is needed to corroborate genetic–environment associations and their involvement in climate adaptation, including experimental approaches that provide evidence of fitness differences associated with candidate variants<sup>56,57</sup>. For example, in common garden experiments, individuals from different environments are reared in a common environment to

elucidate the genetic and environmental components that underlie phenotypic differences. Alternatively, reciprocal transplants can be performed, whereby individuals originating from each of two (or more) environments are introduced into the other environment to characterize local adaptation based on fitness differences between individuals reared in home versus away environments, or between resident and immigrant individuals in a given environment. Although this type of validation is not always feasible, the outcomes of many studies support the broader application of GEAs for understanding population-level patterns of climate adaptation<sup>31,49</sup>.

## Genomic vulnerability to GCC

Genomic offset (also known as genetic offset<sup>58</sup> or genomic vulnerability<sup>59</sup>) combines genomic and environmental data from different time points and/or locations to assess the degree of possible maladaptation to new environmental conditions. It is an increasingly popular approach for predicting how populations or species will respond to GCC and was inspired by genomic selection methods that aim to predict phenotype based on genotype. This approach is classically a two-step process: first, GEA approaches identify putatively adaptive variation; and second, spatial and/or temporal extrapolation typically relates current patterns of adaptive genomic composition of populations to climate. The predicted optimal population genomic compositions are projected across a species' range (space), onto future climatic

conditions (time), or both, to estimate the magnitude of genetic shift (in allele or genotype frequencies) required by populations to maintain the current fitness status quo under different climates using a modelling approach similar to ENMs (Fig. 3). Several models have been developed to estimate genomic offset statistics (reviewed elsewhere<sup>5,60,61</sup>). Most studies that aim to predict future genomic (mal)adaptation of populations have used the Gradient Forest (GF) method<sup>58,59,62–65</sup>. GF was originally developed to model spatial variation in community composition and subsequently used on SNP data to model turnover in allele frequencies and estimate the genetic offset that climate change would induce for balsam poplar (*Populus balsamifera*) populations across North America<sup>58</sup>. Generalized dissimilarity modelling (GDM)<sup>66</sup> is the second community-level modelling method adapted



**Fig. 3 | Integrated approach to synthesize levels of risk of teosinte to GCC, based on ecological niche models, landscape resistance, local agentic adaptation, genomic offset, gene flow and genomic load.** **a**, Based on the *Zea mays mexicana* SNP data set (Fig. 2 and ref. 45), Aguirre-Liguori et al.<sup>75,76</sup> first used the current adaptive genetic turnover identified between two geographically and genetically distinct clusters and significantly associated with temperature. **b**, The authors then projected the geographical range of the two genetic clusters in the present and future (2070) conditions using Maxent<sup>228</sup> and the WorldClim database<sup>229</sup>. **c**, A Gradient Forest model was used to assess genomic offset in each sampled population. The estimated genomic offset combined across all populations within the colder southern cluster (blue) and warmer northern cluster (red) indicated that the predicted genomic offset is higher on average for southern populations. **d**, Maps of potential migration using the present and future distribution models for putative warm-adapted alleles were constructed to determine landscape resistance as a proxy of limitations to successful migration using circuit theory<sup>230</sup>. Comparison between populations suggested that some populations have few dispersal routes. **e**, Adaptive and maladaptive gene flow between populations from the two clusters were inferred

using coalescent simulations<sup>231</sup> to assess whether the population receives an influx of warmer-adapted alleles from northern populations or is swamped with maladaptive alleles from the south. **f**, The presence of genomic load, that is, genetic variants putatively reducing the fitness of a population relative to a local fitness optimum, was investigated via a measure that compared the proportion and population frequency of non-synonymous SNPs with those of synonymous SNPs. **g**, The findings indicate that southern populations have higher estimated loads than northern ones. **h**, Moreover, for both clusters there is a positive and significant trend between genomic load and distance from the niche centroid (*d* in Fig. 2). This effect is more pronounced for northern populations, suggesting that they are particularly likely to be subjected to evolutionary forces that produce genetic load. With this integrated framework, the authors highlighted the importance of taking into consideration the full 'give and take' between adaptation and potentially transgressing forces such as gene flow, dispersal and load to make accurate predictions of population vulnerability under global climate change (GCC) (particularly about the fate of small populations at the edge of a species' geographical range). Parts **a**, **c**–**h** adapted from ref. 75, Springer Nature Limited.

to extrapolate genetic–environment relationships and can be used to predict genetic differentiation ( $F_{ST}$ ) between contemporary and future populations as a function of the environmental distance between current and future climatic conditions<sup>63,67</sup>. RDA has also been used to produce spatial extrapolations of intraspecific adaptive genetic variation<sup>68</sup>, predict adaptive genotypes for reforestation sites<sup>69</sup> and spatially predict genomic offset associated with climate change<sup>41</sup>. Risk of nonadaptedness (RONA)<sup>70</sup> uses a linear regression (at a single locus level) in previously identified, putatively adaptive loci without correction for population structure to estimate the expected allele frequency required under the new environmental conditions. Pinas-Martins et al.<sup>71</sup> expanded RONA by using a weighted average  $R^2$  of the regression to investigate the adaptation potential of cork oak to survive predicted climate change. The spatial areas of genotype probability (SPAG) method uses multivariate logistic regressions to compare the adaptive landscape under current and future climatic conditions<sup>72</sup>. Recently, the ‘genetic gap’ was proposed as a geometric measure of genomic offset that unifies previously proposed genomic offset statistics in a common framework<sup>73</sup>. Considering a duality between genetic and environmental space, a theoretical framework was developed that linked genomic offset statistics to a non-Euclidean geometry of the ecological niche.

The proposed measures of genomic offset are empirically validated but also have well-identified limitations<sup>61,74,75</sup> (Table 1). Such analyses are stronger when incorporated with other approaches. Aguirre-Liguori et al.<sup>75,76</sup> combined genetic offset analysis with other approaches in a study on synthesized risk assessments of teosinte (*Zea mays parviglumis*) populations experiencing GCC (Fig. 3). In a study of yellow warbler (*Setophaga petechia*), a combination of genomic offset scores and demographic population trends across the species’ breeding range showed that populations that require the greatest shifts in allele frequencies to keep pace with future climate change have experienced the largest population declines, suggesting that failure to adapt may already be having negative effects<sup>59</sup>. Across an elevational gradient in the Australian Wet Tropics, Brauer et al.<sup>77</sup> showed that hybrid populations between a widespread generalist and several narrow-range endemic species exhibited reduced genomic vulnerability to projected climates compared with pure narrow endemic species. This study goes further than previous studies by both considering genomic vulnerability and providing empirical evidence for gene flow mitigating maladaptation. The combination of genomic offset scores and phenotypic data (flowering time) of the pearl millet (*Pennisetum glaucum*), a nutritious staple cereal cultivated in arid and low-fertility soils in sub-Saharan Africa, predicts that the most vulnerable areas will benefit from using landraces that already grow in equivalent climate conditions today<sup>78</sup>.

## Investigating temporal evolutionary change Evolve and resequence experiments

Experimental evolution allows the direct study of evolution through controlled manipulations of organisms over many generations and represents the most rigorous approach for understanding trait evolution due to different environmental conditions<sup>79–81</sup>. As many organisms have prohibitively long generation times, most studies focus on species that reproduce rapidly, such as microorganisms. Pioneering experimental evolution studies using *Escherichia coli* as a model system studied evolutionary forces and their impact on trait evolution under controlled conditions over 75,000 generations<sup>82–87</sup>. Evolve and resequence (E&R) provides a powerful means to track

molecular evolution in ‘real time’ and dissect the adaptive architecture of selected traits at the highest genomic level of resolution<sup>88–90</sup> (Fig. 4). Whole-genome sequencing is becoming more affordable and prevalent in E&R experiments, although many experiments on microbial organisms or small multicellular organisms with very short generation times still use Pool-seq to sequence pools of many individuals, which is cost-effective and yields accurate genome-wide allele frequency estimates<sup>90,91</sup>. Numerous E&R experiments, mostly using *Drosophila*, have investigated evolutionary issues pertaining to GCC, including the role of standing genetic variation versus de novo mutations in adaptation<sup>92</sup>, the synergistic effects of different stressors and population ancestry<sup>93,94</sup> and the role of genetic adaptation versus plasticity in response to high temperatures<sup>95,96</sup>. Although E&R studies are typically conducted over many generations, several studies have shown that adaptive genetic variation can be identified with a single or a few generations of selection<sup>97–100</sup>.

Despite their many benefits, it is unclear how E&R results relate to processes of adaptation in nature<sup>79</sup>. This was recently investigated by comparing patterns of gene expression divergence between populations of *Drosophila melanogaster* adapted for 80 laboratory generations to two distinct temperature regimes with those identified by contrasting natural populations across two different latitudinal clines<sup>101</sup>. The authors found that 203 genes in seven co-expression modules evolved temperature-specific expression changes in the laboratory populations. Moreover, their results revealed a positive correlation in temperature-induced expression between laboratory and natural populations from the two clines. They concluded that well-designed E&R experiments can inform how populations respond to selection in natural environments, although another recent study on the harlequin fly (*Chironomus riparius*) concluded that results from E&R experiments could not provide insights into thermal adaptation potential in natural populations<sup>102</sup>.

## Resurrection ecology and genomics

Resurrection ecology provides information on the phenotypic variation and fitness of past organisms by resurrecting dormant life stages, for example, seeds, eggs, cysts or spores that accumulate in lacustrine and marine sediments, soil or ice, allowing insight and direct study of organisms from before our lifetime<sup>79</sup>. Resurrection ecology is a powerful approach<sup>79,103</sup> that predates the ‘genomic era’<sup>104–106</sup>, yet few studies on the impact of GCC on natural populations have incorporated genomics into resurrection ecology studies<sup>107</sup> despite tremendous advantages<sup>108–113</sup>. Temporally stratified propagule banks can be accurately dated such that population genomic and phenotypic evolution can be aligned with temporal environmental changes<sup>103</sup>. Resurrection ecology combined with genomics can also assess the role of new mutations versus standing genetic variation in adaptive phenotypic responses to environmental changes<sup>114–116</sup>.

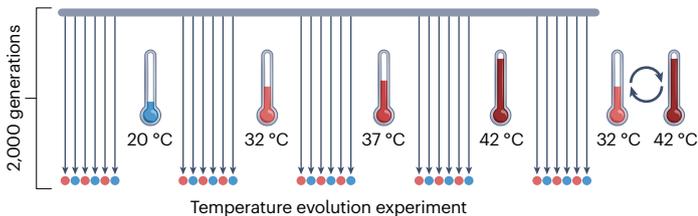
The best examples of combination of resurrection ecology with genomics come from gene expression studies, including a key study on the aquatic crustacean *Daphnia magna*<sup>117</sup> (Fig. 5). Another study in the common mustard *Brassica rapa* examined evolutionary changes in gene expression in seeds from two populations over 18 years during which precipitation fluctuated dramatically<sup>118</sup>. By comparing gene expression of ancestors and descendants of these resurrected populations grown under common conditions, they found that hundreds of genes associated with drought stress and flowering time showed transcriptional differences between ancestors and descendants of the two populations. This study, along with others<sup>119,120</sup>, indicates that

# Review article

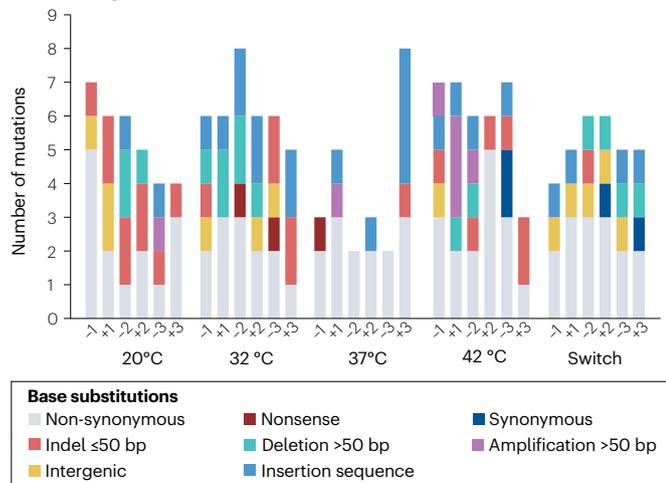
## Experimental evolution: evolve and resequence

ACGTAATTCCT → ACGTAATTCCT  
Temperature increase

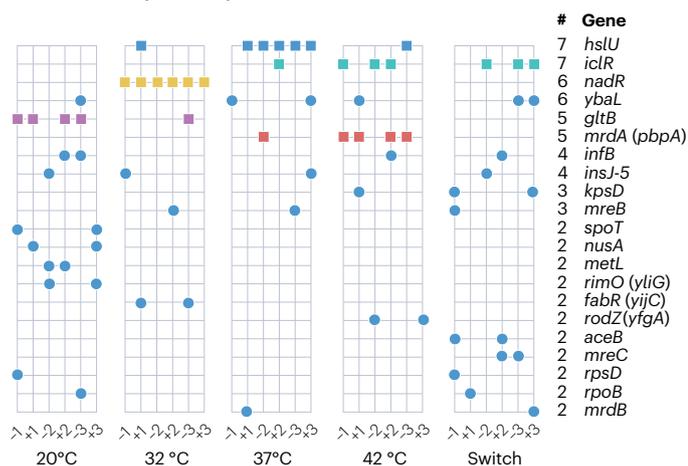
### a Evolution of 30 populations for 2,000 generations (five thermal regimes, six replicates)



### b Summary of the 159 derived mutations observed



### c Genes (rows) affected by at least two qualifying mutations in the thirty TEE clones (columns)



evolutionary changes in gene regulation may provide rapid adaptive responses to contemporary shifts in climatic conditions.

### Evolutionary change and time series

Temporal evolutionary changes can also be investigated at the genome level from time series data<sup>5,121,122</sup>. This involves sampling natural

### Fig. 4 | Experimental evolution: evolve and resequence.

Deatherage et al.<sup>232</sup> investigated the specificity of genome evolution in *Escherichia coli* at various temperatures. **a**, Thirty populations were evolved for 2,000 generations, with six replicates in each of five different thermal regimes. The genomes were sequenced at one end point from each population and compared with the ancestral population. The authors used the *breseq* program<sup>233</sup> to identify mutations in evolved genomes. **b**, Summary of the 159 derived mutations observed in the 30 sequenced genomes by the type of genetic change. Across all populations, 159 de novo mutations were found. Most mutations (57%) were single base substitutions, 87% of which were non-synonymous substitutions or nonsense substitutions, which provided a strong signal of adaptive evolution. The other 43% of the mutations in the temperature-evolution experiment (TEE) lines comprised small insertions or deletions (indels), large deletions, amplifications and rearrangements. Populations that evolved under the same thermal regime exhibited four times more overlap (17% versus 4%) in which genes were mutated compared with those evolved at different temperatures. **c**, Genes (rows) affected by at least two qualifying mutations in the 30 TEE clones (columns, organized by temperature regime and populations -1, +1, -2, +2, -3 or +3). Results revealed a clear signal of genomic specificity in how populations adapted to different temperature regimes whereby mutations converged on a distinctive set of genes with signature mutations in each treatment. The figure presents the genes containing at least two qualifying mutations. Five 'signature' mutations, shown as coloured squares, are significantly associated with one or two treatments. One of the populations that was evolved at 37 °C for another 18,000 generations accumulated mutations in signature genes that were strongly associated with adaptation to the other temperature regimes. This landmark study demonstrates that the genomic signature of adaptation is highly specific, although populations evolving under the different regimes might eventually show more genetic parallelism than divergence<sup>234</sup>. Parts a–c adapted with permission from ref. 232, PNAS.

populations, using historical samples<sup>123,124</sup> to measure allele frequency at various times, correlate genotypic and environmental variation<sup>125</sup> and thus improve inference of selection dynamics<sup>126,127</sup>. A study in Atlantic cod (*Gadus morhua*) analysed DNA from archived otoliths to search for signatures of divergent selection over a 78-year climatically variable period<sup>128</sup>. The genetic composition of some populations was temporally stable, yet complete population replacement was evident at others, and increased temporal changes at several loci suggested that adaptation to environmental change had occurred. These findings illustrate the power of spatiotemporal population genomics to inform future conservation efforts.

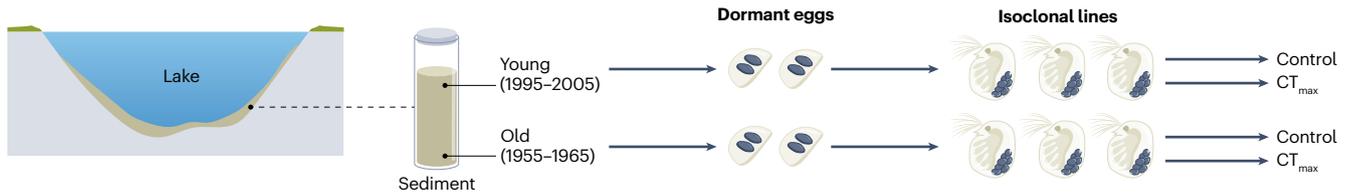
### Molecular phenotypic plasticity in GCC

Phenotypic plasticity is often the main mechanism that allows populations to cope with GCC<sup>3,129</sup>, with transcriptomics, epigenomics and proteomics being increasingly used to investigate functional plastic responses. Plasticity studies are helpful to understand the range of possible phenotypic responses to environmental change that can influence fitness within a single generation without differential mortality owing to selection. Gene expression<sup>23,130,131</sup>, epigenetic mechanisms<sup>19,132,133</sup> and the proteome<sup>134</sup> respond to temperature and environmental changes. Transcription often underlies plastic proteomic and phenotypic changes, whereas epigenetic mechanisms heritably affect transcriptional states in response to the environment<sup>135,136</sup>. Plastic responses can preclude or delay genetic adaptation if they lead to environmental acclimation<sup>137,138</sup>. They can also increase phenotypic variation and evolutionary potential<sup>129,137,139</sup>, which could prove crucial for genetically impoverished populations that experience

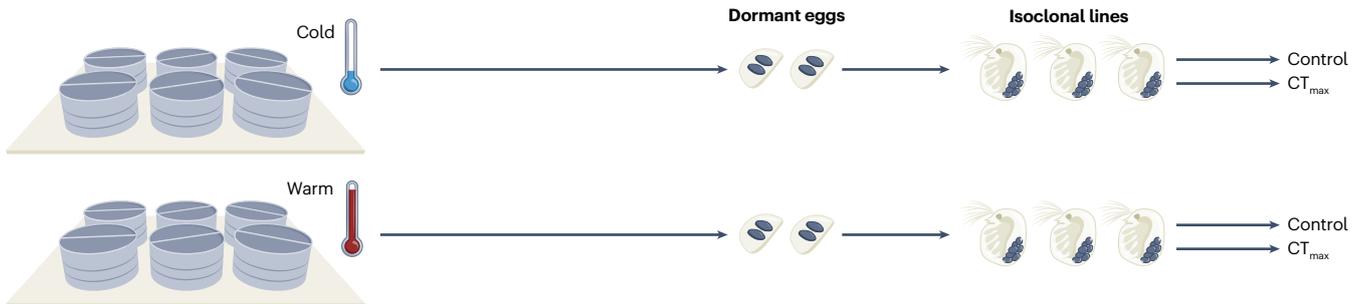
# Review article

## Combining resurrection ecology and genomics

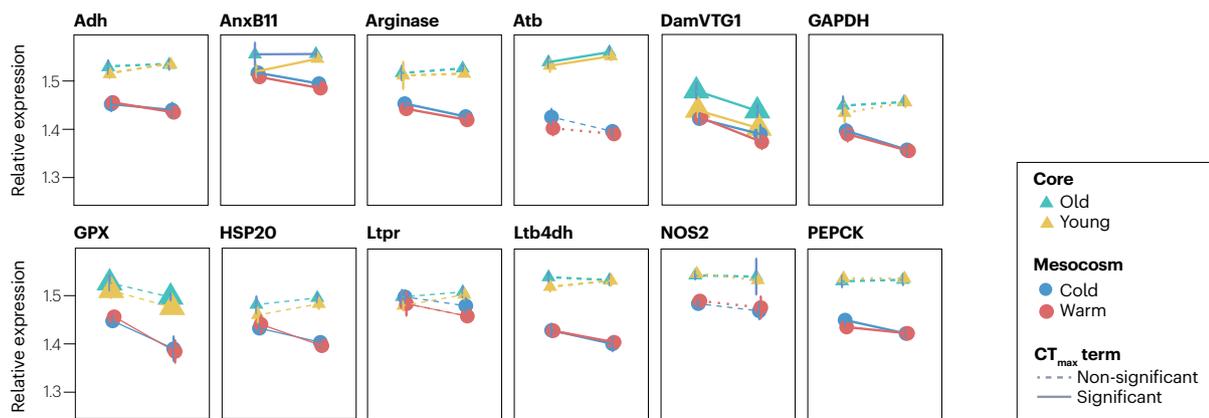
### a Core: sampling and dating of sediments from lake



### b Mesocosm: artificial selection experiment



### c Gene expression analysis at candidate genes



**Fig. 5 | Combining resurrection ecology and genomics.** Jansen et al.<sup>235</sup> used a candidate gene approach to document evolutionary response of gene expression in a resurrected population of *Daphnia magna* that experienced changes in temperature over the past 40 years and from contemporary (experimental) populations differing in thermal tolerance. **a**, Sediments from Felbrigg Hall Lake, Norfolk, UK, were sampled and dated, and dormant eggs were hatched and cultured from a colder and a warmer period. **b**, The upper 2 cm of the sediment from mesocosms exposed to either ambient or ambient + 4 °C temperature treatment was sampled for resting eggs, and hatched *D. magna* were used for candidate gene analysis. **c**, Reaction norms for differential expression were measured at the candidate genes between heat treatment and control. Authors

documented evolutionary changes in gene expression between warm and cold-adapted populations and assessed evolutionary response to temperature changes. They used model-averaged effect sizes to quantify the impact of each term and applied a false coverage ratio correction to correct for multiple testing before assessing the significance of each term. Most of the tested genes (57%, a subset of 12 genes illustrated here) in the contemporary populations showed a plastic response to heat treatment compared with only 23% in the resurrected population. These results thus indicated that most genes apparently lost plasticity of expression in the face of evolutionary (thermal) constraints in the natural (resurrected) population. Their study also identified candidate genes likely linked to thermal adaptation. Figure adapted with permission from ref. 235, Wiley.

GCC<sup>137</sup>, although lack of plasticity or maladaptive plasticity could negatively affect fitness<sup>140,141</sup>. Organisms can evolve or lose the capacity for transcriptional and epigenetic plasticity, as observed in studies of threespine stickleback (*Gasterosteus aculeatus*) colonizing freshwater environments<sup>142,143</sup> and various populations at range edges<sup>144</sup>. Plastic and genetic changes can also act synergistically in response to GCC,

with species acclimatizing through plastic changes while genetic adaptation 'catches up'<sup>138</sup>.

Molecular plasticity studies are shifting towards whole-genome, epigenome, transcriptome and proteome methods owing to decreasing costs. Many studies have assessed transcriptional responses to temperature<sup>9,145</sup>, with recent studies assessing alternative splicing in

thermal acclimation<sup>146–149</sup>, which can diversify an organism's transcriptome. Epigenetic mechanisms provide a mechanistic basis for transcriptional responses to environmental changes associated with GCC. There is a strong focus on differential DNA methylation analysis associated with thermal regime<sup>150–152</sup>, although histone modifications and non-coding RNA expression<sup>147,153–155</sup> also respond to GCC. Methods such as assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq) can directly assess chromatin accessibility, as shown through chromatin conformation and transcriptional changes due to temperature in symbiotic sea anemone (*Exaiptasia pallida*)<sup>156</sup>. Proteomics can also be used to assess functional protein responses and resilience to GCC<sup>134</sup>, which are sometimes driven by transcriptional and epigenomic variation. Although plastic mechanisms clearly respond to temperature and GCC, the integration of both genomic and transcriptomic or epigenomic data is imperative to disentangle genetic from plastic phenotypic effects.

Plasticity and genetics both affect phenotype, although the relative importance of each in the resulting phenotype is unclear. This is further complicated by SNP variation often exerting some control over transcription (for example, expression quantitative trait loci (eQTLs)) and epigenetic state (for example, methylQTLs). For example, seasonal and latitudinal allele frequency changes are associated with thermal response at previously identified eQTLs<sup>20</sup> in *Drosophila*. Both latitudinal and seasonal eQTLs were associated with chromosomal inversion breakpoints<sup>21,157</sup>, but seasonal eQTLs were not consistent between sites, suggesting that sites may differ in the selective pressures imposed by seasonal changes<sup>21</sup>. Epigenetic variation and transcription can be linked through methyl-eQTLs, site-specific methylation levels that are maximally correlated with gene expression, which have mostly been used in medical studies<sup>158,159</sup> but could be implemented in ecological studies.

The simultaneous assessment of multi-omic data is needed to disentangle the relative importance of genetics versus plasticity for phenotype and to determine the extent of genetic constraint over plasticity. First, studies should assess the extent of genetic control over transcriptional and epigenetic variation, which is present in some systems (for example, *Micrarchus* stick insects)<sup>160</sup> but not others (for example, branching staghorn coral *Acropora cervicornis*)<sup>161</sup>. Next, we need to understand how genetic control over plastic mechanisms changes depending on environmental context. For instance, combined transcriptome, methylome and phenotype data revealed genotype by environment effects on growth potential in transgenic Coho salmon (*Oncorhynchus kisutch*)<sup>162</sup>. We should further determine under what circumstances organisms evolve differential capacity for plasticity (for example, the aforementioned stickleback studies)<sup>142,143</sup> and when genetic variation becomes coupled or uncoupled from transcriptional or epigenomic variation (for example, using whole-genome DNA methylation data and predictive modelling in *Arabidopsis thaliana*)<sup>163</sup>.

Finally, multi-omic data must be related to phenotype to reinforce the importance of plasticity in GCC responses. Plasticity studies to measure fitness-related outcomes cement plasticity as an important evolutionary response to GCC<sup>9,164</sup> (Fig. 6). Epigenome-wide association studies (EWAS) could be used to link epigenetic and phenotypic changes; although EWAS is primarily used in human disease studies, it was recently used to link methylation changes with temperature fluctuations in humans<sup>165</sup> and could thus be used to identify loci involved in thermal response and tolerance. A genomic reaction norm could also be incorporated in molecular plasticity studies to understand the combined effects of environment, genotype, phenotype and demographic characteristics<sup>166</sup>. The environment is an important consideration in

these studies, as phenotype cannot be generalized across multiple environments. These issues can be addressed using common garden experiments or by assessing phenotypic plasticity across many environmental contexts.

## eDNA community monitoring and GCC

The analysis of environmental DNA (eDNA) enables the identification of organisms on the basis of their DNA released into the environment (water, soil or air), for example, through skin cells or metabolic waste. This noninvasive genetic approach can predict organism presence and/or absence and sometimes species' relative abundance<sup>167,168</sup>. High-throughput sequencing offers the possibility to assess overall biodiversity by simultaneously identifying multiple species through eDNA metabarcoding, which is being used to document community structure in both aquatic and terrestrial ecosystems<sup>169</sup>. More recently, eDNA metabarcoding protocols have been developed to detect species occurrence in airborne DNA samples<sup>170–172</sup>.

In the context of GCC, eDNA metabarcoding can be used to track shifts in community composition (animals, plants and microorganisms) across time, depending on the environmental selective pressures that occur when the DNA of organisms is trapped in substrate. Two approaches are used to study community composition changes with GCC: laboratory or mesocosm-based experiments<sup>173,174</sup> (Fig. 7a), which offer a high degree of control; and time series sampling across a spatial gradient<sup>175–177</sup> (Fig. 7b), which leverages the high variability offered by the local environment to predict which species will decline or burst relative to those present today<sup>174,176</sup>. Metagenomics and shotgun sequencing, which are generally more microorganism-focused than metabarcoding, can also inform about temporal variation in community composition (reviewed elsewhere<sup>178</sup>). A controlled laboratory experiment showed that coral-associated microbiota shifted from a community composition associated with healthy corals to one generally found on diseased corals in abiotic conditions that mimic future GCC<sup>179</sup>.

At the spatial level, eDNA metabarcoding and metagenomics allow monitoring of biogeographical community range shifts and investigate how animals and plants can cope with changing environmental conditions by migrating to sites that are more favourable to their biology<sup>178,180,181</sup>. These studies often combine eDNA results with computing projections and machine learning to build habitat occupancy models for species under different GCC scenarios. Metabarcoding data collected during five consecutive years was used to model diatom richness in response to projected GCC and predicted range shifts towards the poles<sup>180</sup>. Combining genomics with other approaches is particularly helpful for managing invasive species, whose predicted geographical expansion might affect native species ranges during GCC<sup>182,183</sup>.

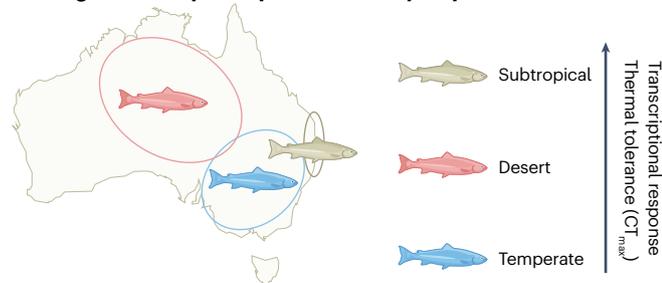
In the context of GCC, eDNA metabarcoding can be used to track temporal shifts in community composition associated with environmental change, relying on the DNA of organisms becoming trapped in substrate<sup>184</sup>. Ancient DNA (aDNA)<sup>185,186</sup> can infer previous community composition with greater taxonomic resolution, spatial and temporal precision than other palaeoecological methods<sup>184,187</sup>. However, its application is more challenging compared with eDNA because of DNA degradation, modification and strand damage that occur with time. Also, sequencing aDNA is challenging as only short reads are generally attainable<sup>184</sup>. The analysis of aDNA retrieved from permafrost and sediments can allow documentation of community composition up to 50,000 years ago<sup>185,187</sup>. The oldest aDNA discovered to date was 2-million-year-old DNA trapped in North Greenland ice sediment, which

# Review article

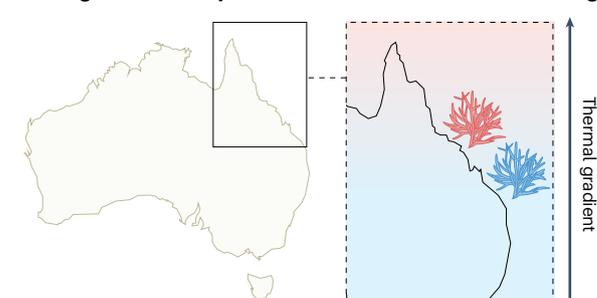
was linked to a rich assemblage of plants and animals<sup>188</sup>. aDNA analysis offers fine resolution to reconstruct temporal dynamics of community shifts<sup>184,187,189–192</sup>. aDNA extracted from fossil rodent middens, small piles of seeds, bones or leaves gathered by rodents, allowed reconstruction

of late Quaternary vegetation dynamics, showing perennial species displacement ~1,000 m downhill during pluvial events<sup>191</sup>. aDNA analysis can also track extirpations and extinctions<sup>185</sup> associated with glacial events in mammals<sup>193</sup> and plants<sup>194</sup>. Reconstruction of community

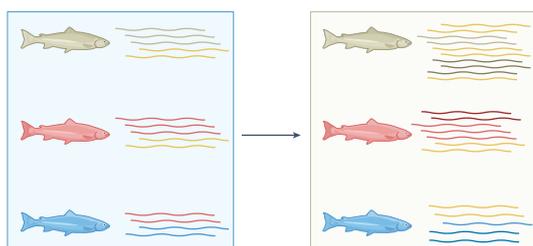
## a Divergent transcriptional profiles in locally adapted Australian rainbowfish



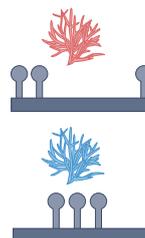
## b Divergent DNA methylation in corals from different thermal regimes



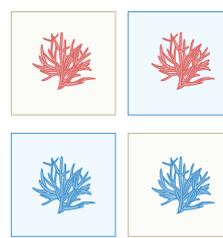
### Rearing in current versus projected thermal regimes led to non-parallel transcriptomic responses between ecotypes



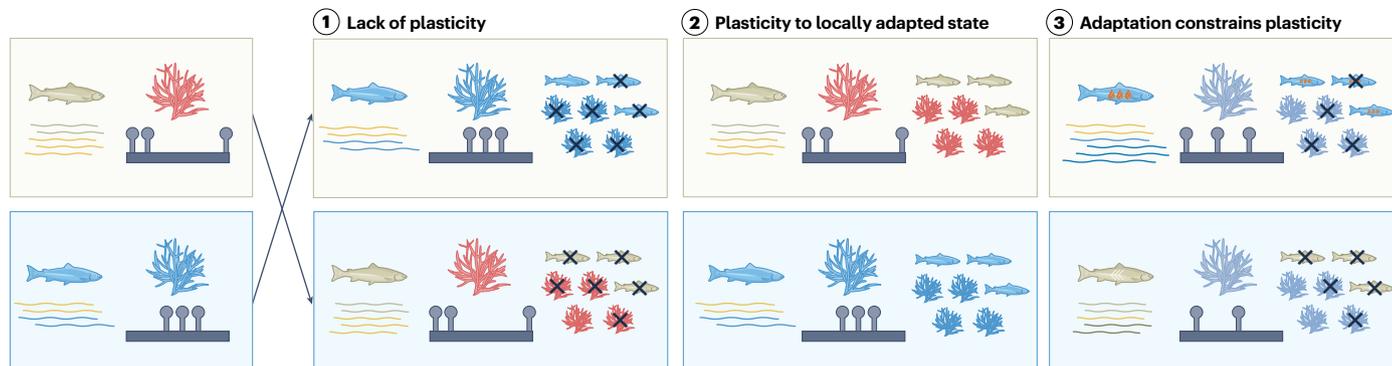
### DNA methylation differences underlie thermal tolerance



### Altered thermal regime (reciprocal transplant)



## c Hypothetical plastic responses to altered thermal environment with phenotypic and fitness outcomes



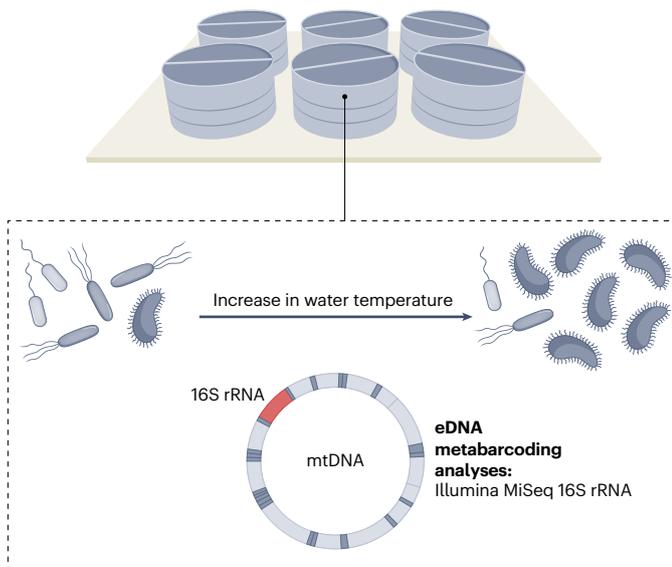
**Fig. 6 | The role of transcriptional and epigenetic plasticity in response to global climate change.** When populations exist in different thermal environments, they can develop transcriptional and epigenetic differences, potentially due to thermal acclimation or adaptation. The capacity for plasticity in response to changing thermal environments can affect the persistence of organisms enduring climate change. **a**, Sandoval-Castillo et al.<sup>9</sup> showed that divergent selection on gene expression led to non-parallel transcriptional responses to thermal stress that differed between subtropical, temperate and desert Australian rainbowfish ecotypes (*Melanotaenia* spp.). RNA sequencing detected 34,815 transcripts among the three ecotypes; 236 genes responded to temperature treatment, with only ten expression changes shared between two ecotypes and five shared between all three. The ecotypes had different thermal tolerances as measured by  $CT_{max}$ , with warm-adapted subtropical rainbowfish showing the greatest tolerance for warming and capacity for transcriptional plasticity. **b**, Dixon et al.<sup>164</sup> reciprocally transplanted stony coral (*Acropora millepora*) from two different thermal environments and used methyl-binding

domain sequencing to analyse gene body DNA methylation of 27,084 genes. Corals that were able to assume the methylation state of local corals had improved fitness-related traits relative to corals that did not resemble local corals epigenetically. Methylation differences were also correlated with transcription, as measured using TagSeq. **c**, Hypothetical effects of transcriptional and epigenetic plasticity in response to altered thermal environment: (1) if organisms are unable to respond to their environment through transcriptional or epigenetic changes, resulting in an inability to cope with changing temperatures, this could lead to increased mortality; (2) if organisms can adopt the transcriptional state or DNA methylation patterns of local conspecifics, plasticity could lead to increased fitness in altered thermal environments<sup>164</sup>; and (3) if populations differ in their capacity for plasticity (for example, owing to divergent selection from different thermal environments) or the nature of plastic responses they show (for example, different genes), they may show divergent plastic responses to altered temperature environments. This could lead to populations exhibiting differences in resistance to, and potential persistence in, novel thermal environments<sup>9</sup>.

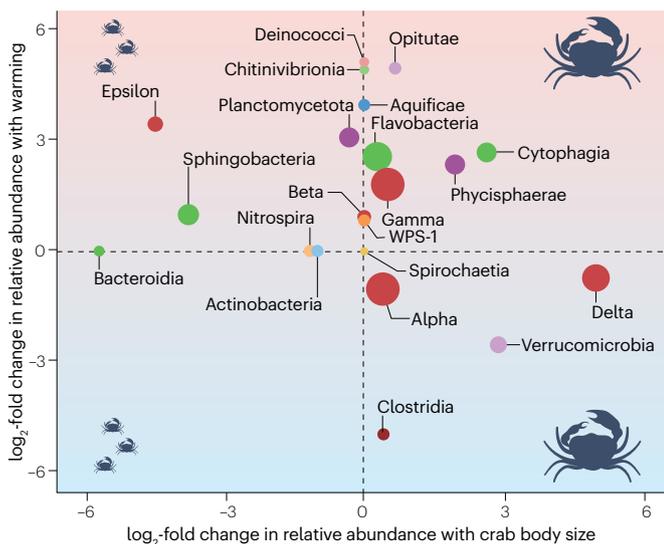
# Review article

## a Laboratory/mesocosm-based experiences

Scenarios recreating conditions of past/actual/expected climate changes



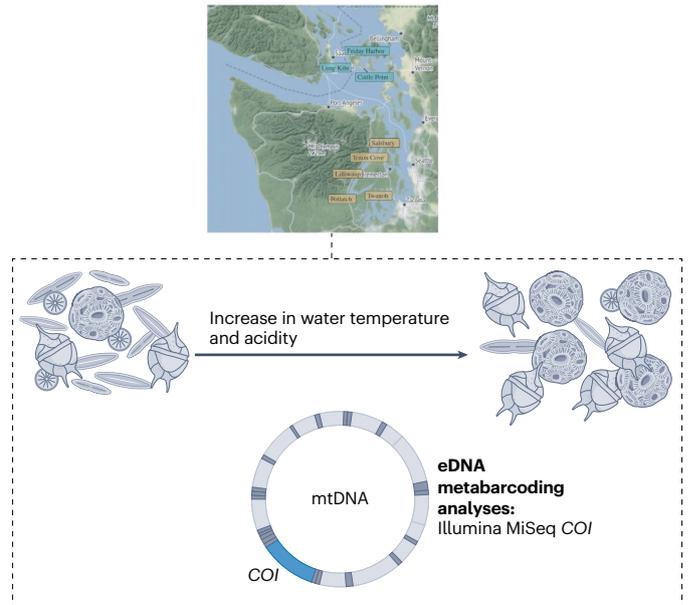
### Mean changes in relative abundance of bacterial classes with warming



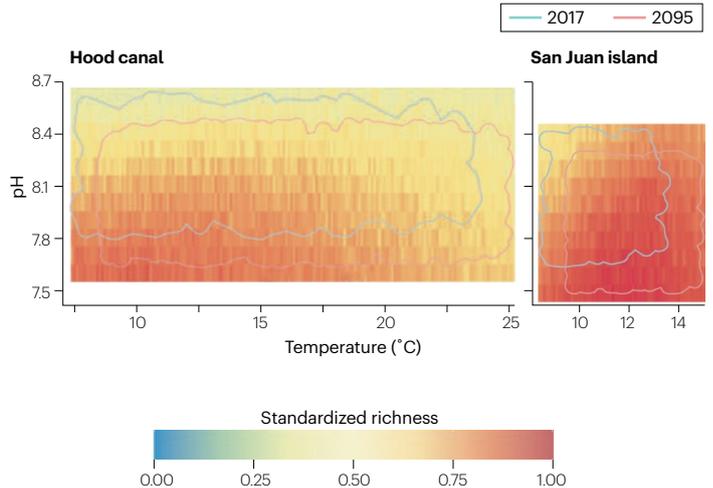
**Fig. 7 | eDNA metabarcoding approaches to monitor temporal switches in community composition with global climate change.** **a.** Ferguson et al.<sup>174</sup> used marine mesocosms to examine the impacts of warming, nutrient enrichment and altered top-predator population size structure (common shore crab *Carcinus maenas*) on coastal microbial biofilm communities in a crossed experimental design. An environmental DNA (eDNA) metabarcoding approach was used by the authors. Based on Illumina MiSeq sequencing of the 16S mitochondrial rRNA gene, they showed that warming and top-predator population size structure both affected bacterial biofilm community composition. Warming increased the abundance of bacteria capable of increased mineralization of dissolved and particulate organic matter, such as flavobacteria, Sphingobacteria and Cytophagia. **b.** Gallego et al.<sup>176</sup> took advantage of the existence of a wide variety of ecosystems within two regions (San Juan Island and the Hood Canal) of the Puget Sound in Washington (USA) to test the effect of environmental parameters on zooplankton marine communities under conditions expected worldwide in the near future. Despite their geographical

## b Time-series sampling across a spatial gradient

Environmental gradient recreating conditions of actual/expected climate changes



### Relative taxon richness for plausible ranges of pH and temperature 2095 versus 2017



proximity, these two regions experience substantial differences in environmental conditions (in terms of temperature, pH and CO<sub>2</sub>), with the Hood Canal resembling future conditions in temperate areas worldwide. The eDNA metabarcoding approach used by the authors included Illumina MiSeq sequencing of the *COI* mitochondrial gene. They identified distinct communities in warmer and more acidified conditions, with overall reduced richness in diatom assemblages and increased richness in dinoflagellates. The authors used their results to build models to forecast near-term community changes and to determine the probability of the presence of each individual taxon for 2095 compared with 2017. Their results suggest a possible change in relative dominance between diatoms and other phytoplankton species such as dinoflagellates. They also highlight an increased environmental suitability for the coccolithophore *Emiliana huxleyi* and the harmful *Alexandrium* sp. mtDNA, mitochondrial DNA. Bottom panel in part **a** is adapted from ref. 174, CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>). Map and bottom panel in part **b** adapted with permission from ref. 176, The Royal Society.

## Glossary

### Assisted gene flow

Human-mediated movement of individuals within a species range to facilitate adaptation in recipient populations.

### Conservation macrogenetics

Studies of intraspecific genetic variation across many taxonomic groups and broad spatiotemporal scales to assess evolutionary patterns and inform conservation.

### Ecological niche model

(ENM). Sometimes referred to as environmental niche model or species distribution model. A class of methods that combines environmental data layers and species' occurrence or abundance data to infer niche suitability and predict species' distributions across current and future landscapes.

### Epigenome-wide association studies

(EWAS). Statistical method that links epigenomic variation to phenotypic or physiological outcomes.

### Evolve and resequence

(E&R). Integrates high-throughput sequencing into experimental evolution studies; most commonly performed on microbial and short-generation metazoans.

### Generalized dissimilarity modelling

(GDM). A statistical approach for prediction of nonlinear patterns of beta

diversity across space; although initially developed for modelling turnover in community composition, it can also be applied to model genetic and trait differences.

### Genome scans

A genome-wide screening approach to identify candidate genomic variants (for example, SNPs) that are subject to selection.

### Genomic reaction norm

Graphical representations showing how a phenotype (generally gene expression, although other molecular phenotypes such as DNA methylation state can be used) of a single genotype changes in response to different environments.

### Individual-based modelling

(IBM). Modelling approach in which the actions of individual organisms are simulated, including interactions with other individuals and with the environment.

### Integral projection models

Models that predict the effects of individuals' traits (for example, age, reproductive success, growth rate, body size) on population size and demography.

### Landscape genomics

The study of the spatial distribution of genome-wide variation, including both neutral and adaptive variation, across heterogeneous landscapes and

the processes that shape observed distributions.

### Landscape resistance

A measure of the difficulty for organisms to move through the landscape; areas with high resistance can impede dispersal and gene flow.

### Liquid biopsy

Noninvasive test to detect noncellular DNA in bodily fluids, often used for cancer and disease detection.

### Local adaptation

Mechanism by which organisms in a population evolve phenotypes that have higher relative fitness in their home conditions compared with organisms in other populations in spatially heterogeneous environments.

### Nonsense substitutions

Point mutations in a sequence of DNA that result in a premature stop codon.

### Non-synonymous substitutions

Nucleotide mutation that alter the amino acid sequence of a protein.

### Otoliths

Calcium carbonate structures in the inner ear of vertebrates.

### Quantitative trait loci

(QTLs). Genetic variants associated with changes in expression (eQTL) or DNA methylation (methylQTL) levels.

### Rescue effects

An increase in population size or fitness, thereby reducing the risk of extinction and facilitating long-term population persistence. Three eco-evolutionary processes promote rescue effects: demographic rescue, that is, an increase in the number of individuals in a population; genetic rescue, that is, an increase in population fitness via the genetic contribution of immigrants, by either decreasing inbreeding depression or increasing genetic variation to promote adaptation; evolutionary rescue, that is, an increase in population growth rates caused by adaptation to new or changing conditions, usually from standing genetic variation but some definitions include migration.

### Standing genetic variation

Pre-existing genetic variation in a population on which selection can act readily.

### Structural variation

A region of the genome that shows inter-individual variability due to a chromosomal alteration, including variation in chromosomal location (for example, translocation), rearrangement of chromosome orientation (for example, inversion) or copy number variation (for example, duplications, insertions, deletions).

responses to past environmental events provides a unique opportunity to forecast how contemporary communities will change with GCC. Extinction models based on aDNA data that link community fluctuations with environmental variation can elucidate the role of humans in these processes<sup>195</sup>.

eDNA, aDNA metabarcoding and metagenomics provide new insights into community responses to GCC, but do not predict whether new species will colonize an environment or how species adapt to future conditions. Neither do they differentiate between living and dead organisms<sup>185</sup>. Environmental RNA (eRNA) offers a promising avenue of research that could pave the way to new disciplines, including environmental transcriptomics, which could be used to noninvasively assess at the community level the role of plasticity in coping with GCC<sup>196</sup>. However, rapid medical, forensic and environmental advances

in eDNA analysis are raising privacy and ethical concerns, requiring future legal considerations<sup>197</sup>.

The above approaches are not mutually exclusive. Holistic community reconstructions will require the integration of various methodologies such as the use of multiple markers in metabarcoding, both universal and more specific primers, and shotgun sequencing. This will ultimately allow a better understanding of how a broad array of taxa will react to GCC, which is crucial to understand, as heterogeneous taxonomic groups may show contrasting responses to GCC<sup>198</sup>.

## Conclusions and perspectives

Our capacity to monitor and understand species' responses to GCC will be enhanced by integration of multi-omics methods with other types of data<sup>5,6,60</sup>. Studies considering several evolutionary processes

to predict the fate of species are steps towards a more comprehensive integration of population genomics with GCC science<sup>199–202</sup>. Moreover, multi-omic data sets will enhance studies on the evolution of plasticity and its relationship to genomic variation, furthering our understanding of how and when plasticity can aid species experiencing GCC. Plasticity has commonly been considered separate from adaptive variation, which is often assumed to be genetic, although recent studies showing plastic contributions to fitness and adaptation or maladaptation suggest that plasticity should be considered in tandem with other sources of adaptive variation. Future incorporation of other genomic methods into plasticity studies (for example, landscape transcriptomics, epigenomics and proteomics; GEA-type analyses) would further improve our understanding of the role of plasticity in GCC response and of when plasticity and genetic adaptation occur independently or in tandem.

Relating epigenomic and genomic variation to phenotype and fitness in different environments through time could improve our understanding of species' evolutionary potential in the face of GCC<sup>203</sup>. Although this is still challenging, it is becoming feasible with methodological advances that assess multi-omics contributions to phenotypes<sup>204–207</sup> and their underlying genetic architecture<sup>204</sup>. Such an integrative approach could provide greater insight into the molecular basis of complex phenotypes that confer environmental adaptation compared with the analysis of a single type of omic data set. The rise of long-read sequencing has largely enabled the discovery of structural variation, revealing the contribution of large-effect mutations in genetic adaptation<sup>208–211</sup>. However, like single SNPs, the functional and the fitness consequences of their polymorphism remain mostly unknown. Integrating multi-omics methods with resurrection ecology or E&R experiments would be particularly powerful. Epigenomic or genomic variation between ancestors and descendants can also be compared to determine the molecular basis of phenotypic change through generations<sup>212</sup>. Once ecologically relevant genes are identified, their phenotypic effects and genetic architecture can be confirmed through methods that include controlled breeding designs and CRISPR editing<sup>113</sup>. However, some epigenetic or genetic variation may show no association with phenotype or fitness, or may show variable fitness outcomes in different environments, which may limit our ability to relate multi-omic variation to tangible GCC responses.

Advances in biomarker detection techniques could improve ecosystem monitoring and assessment of adaptive potential during GCC. Liquid biopsy could be used to noninvasively develop multi-omic biomarkers for ecosystem health, including microbial community composition<sup>213</sup>. Epigenetic biomarkers can provide information on past thermal stress<sup>214</sup> and demographic characteristics (for example, sex<sup>214</sup> or age<sup>215</sup>) and could be used to identify biomarkers of thermal resilience in natural populations, although there are still few studies that have analysed epigenetic biomarkers in the context of GCC.

Modelling techniques can predict species' responses to environmental change through time and provide an efficient means to relate temporal multi-omic variation to GCC-induced phenotypic and fitness consequences. Machine learning can aid in biomarker detection<sup>214</sup> and predict future consequences of GCC for organisms through forward modelling, whereby predictions are made about outcomes or the behaviour of a system given a particular model<sup>216</sup>. Improvements to individual-based modelling (IBM) frameworks provide a powerful way to explore impacts of GCC on species' persistence under increasingly complex eco-evolutionary scenarios<sup>217</sup>. Integral projection models are also used to model demographic changes due to genetic variation<sup>218</sup>

and could be expanded to use large-scale genomic data in the context of GCC. Integrating eDNA metabarcoding and modelling can aid in inferring the effects of environmental, geographical and socioeconomic factors on community diversity<sup>219</sup>. However, biomarkers and novel modelling approaches will require critical evaluation to assess their utility in predicting GCC responses in natural systems.

Genomics methods have provided insights into how GCC affects species, although increased availability of genomic resources and open data are needed. Reference genomes are becoming increasingly available through initiatives such as the Earth Biogenome Project<sup>220</sup>, thus improving the feasibility of studies in non-model organisms, although many remain understudied. For example, primary producers such as microbial eukaryotes are crucial for ecosystem function, although the effects of GCC on microbes, their genomes and subsequent ecosystem effects are unclear. Requirements for open data and reproducible code<sup>221</sup>, standardized data reporting and availability of georeferenced environmental data<sup>222</sup> will facilitate meta-analyses<sup>223</sup> and conservation macrogenetics<sup>224,225</sup>. Successful conservation and monitoring during GCC will require the development of science–policy–society interactions<sup>226,227</sup> and continual reassessment of evolving omics approaches to inform decision-making. Holistic applications of omics tools could mitigate the effects of GCC on biodiversity, contribute to restoring ecosystems and improve health, food security and a sustainable global bioeconomy.

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## Author contributions

The authors contributed equally to all aspects of the article.

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