14 Adaptive responses to the environment and environmental change

Orly Razgour, Jesse R. Lasky, Thibaut Capblancq and Brenna R. Forester

ABSTRACT

Identifying adaptive responses to the environment is key for understanding and predicting the ability of species to respond to human-induced global changes, such as climate change, land-use change, pollution and disease outbreaks. Adaptive responses can be studied using a variety of observational, experimental and modelling methods. The genomic revolution has led to the development of new approaches and refinement of existing approaches to identify the genomic basis of adaptive responses to the environment and environmental change. These methods often involve the application of statistical techniques that relate variation at the genomic level to environmental conditions or phenotypic variability in order to detect candidate adaptive genetic loci. The past decade has seen a proliferation of studies employing these tools in a variety of applications from informing conservation management, agricultural production and the management of invasive species, to understanding disease dynamics and modelling vulnerability to future global changes. Experimental and functional validation of these statistical inferences represents an area of increasing importance in this rapidly evolving field. Emerging approaches look beyond the organism's genome to its interactions with its associated bacterial metagenomes, at epigenetic variation and the structure of the genome itself.

INTRODUCTION

Identifying adaptive responses to the environment is key for understanding and predicting the ability of species to respond to human-induced global changes, such as climate change, land-use change, pollution and disease outbreaks. Shifts in phenotypic traits in response to local environmental conditions or environmental change can be the result of either short-term plastic responses, whereby the same genotype expresses different phenotypes within the lifetime of an individual (phenotypic plasticity), or longer-term changes in genotypes or allele frequencies in the population over generations (genetic adaptations or microevolution; Franks and Hoffmann 2012). Although phenotypic plasticity provides an important mechanism for rapid response and acclimatisation, genetic adaptations are essential for enabling populations to cope with extensive and continuing environmental changes (Gienapp *et al.* 2008).

Adaptive responses to the environment were traditionally studied by quantifying changes in phenotypes following controlled breeding, common garden, or reciprocal transplant experiments. The use of these methods has been limited, however, because they are logistically challenging and can be difficult or impossible to implement in species of conservation concern or those not amenable to experimental manipulation, like long-lived, long generation time species (Hohenlohe *et al.* 2021). The advent of high-throughput

sequencing technologies opened the door to the use of genomic approaches to identify the genetic basis of adaptations and mechanisms of adaptive responses in wild populations and notably for species of conservation concern (Allendorf *et al.* 2010). Much of the focus has been on identifying local environmental adaptations, whereby resident genotypes have, on average, higher fitness in their local habitat than genotypes originating from other habitats. Local adaptations are manifested through phenotypic and genetic differentiation across contrasting environments or environmental gradients, and therefore can be studied using genetic and genomic tools. Genomic tools, which often analyse entire genomes or exomes, are particularly suitable given that local adaptations can arise from polygenic quantitative traits (Savolainen *et al.* 2013) and that good genome marker density is needed to detect the few genes associated with oligogenic traits (Box 14.1).

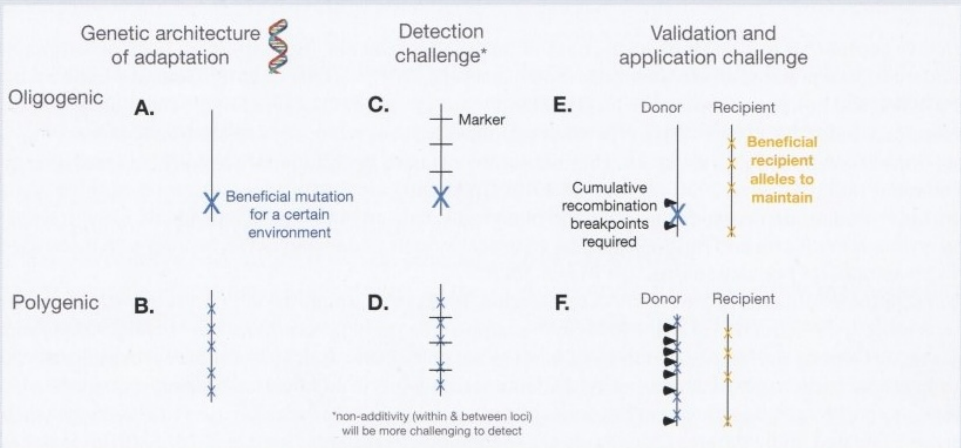
Evolutionary adaptations can be identified using different types of genomic approaches that are selected based on the research question and the species characteristics (Box 14.2). Genome scans are commonly used on large genomic datasets to relate individual genotypes or population allele frequencies to phenotypic traits associated with fitness (adaptive traits) or environmental conditions (Rellstab *et al.* 2015; Hoban *et al.* 2016). Other approaches, like **whole transcriptome sequencing**, can capture plastic gene expression responses to environmental variation within and between individuals (Todd *et al.* 2016).

Adaptive responses can be studied through comparing individuals or populations experiencing gradients of

Box 14.1: The effect of genetic architecture on the detection, validation, and application of environmental adaptations

The genetic architecture of adaptations plays a major role in facilitating or complicating the detection, validation, and application of environmental adaptations. Whether adaptation is driven by many genetic variants of small effect (polygenic), or a few variants of large effect (oligogenic) influences the nature of these challenges. In species where controlled crosses are possible, such as crops, livestock, or captive-bred species, environmentally adapted alleles can be introgressed into desired genotypic backgrounds using targeted crosses and backcrosses. Even when breeding is uncontrolled in nature, selection will favour the combination of newly introduced beneficial alleles (blue) and existing beneficial alleles (yellow). For some species, genetic engineering (e.g. transgenics, CRISPR) may be a more precise way to improve a given genetic background compared to recurrent backcrosses. If existing beneficial alleles are ignored or overlooked during introgression of environmentally adapted alleles, these existing beneficial alleles may be lost due to linkage drag and drift.

When adaptation is oligogenic (A), the detection challenge can be substantial, especially in species with large or poorly assembled genomes, where resource constraints can limit the density of genetic markers. In this case (C), a few large effect variants may be missed by a set of markers that do not cover a sufficient portion of the genome. In contrast, validating and applying the basis of oligogenic traits (E) is more straightforward. Introgression of one or a few loci into a desired genetic background requires relatively few recombination breakpoints, which are locations of crossing over between homologous chromosomes during meiosis. Alternatively, genetic engineering to alter one or a few loci is possible in some systems.



When adaptation is polygenic (B), detecting at least a subset of causal loci is much easier due to their greater abundance (D). However, polygenic adaptation faces greater constraints for validation and applications involving introgression or genetic engineering (F). When there are existing genotypes with a number of desirable alleles across the genome into which environmentally adapted alleles are to be introgressed, a large number of recombination events are required to achieve the desired end-product genotype. When species have long generation times or low outcrossing rates, the scarcity of these recombination events may limit adaptation. Similarly, engineering is more technically challenging because many loci must be targeted.

Population genetic theory provides guidance for where environmental adaptation may be oligogenic versus polygenic. For example, when existing polygenic variation results in local adaptation, local adaptation may retain a polygenic architecture for hundreds or thousands of generations (Polechová and Barton 2015). However, ongoing gene flow across environmental gradients will eventually favour more oligogenic architectures as only large effect polymorphisms can be maintained (Yeaman and Whitlock 2011). Yet, determining the true architecture of empirical environmental adaptation is challenging.

Box 14.2: Genomic methods to identify local adaptations

1. **Differentiation-based analyses**, which include the widely used Fst-outlier tests, identify candidate adaptive genetic markers that show high levels of genetic divergence between populations through differentiating locus-specific patterns (including selection) from genome-wide patterns (genetic drift, demographic processes, and gene flow; Luikart *et al.* 2003). Differentiation-based methods are especially useful for detecting strong divergent selection (Storz 2005). Most methods require population-level sampling and are based on theoretical population genetic models that are violated in many empirical systems (Lotterhos and Whitlock 2014), though individual-based model-free options are available (Luu *et al.* 2017). Recent approaches have improved on some previous problems of non-independence among populations (Lotterhos and Whitlock 2015) and of incorrectly identifying neutral markers as under selection due to failure to account for population structure (Gautier 2015).
2. **Genotype-environment associations (GEA)** methods are used to identify candidate adaptive genetic loci based on associations between allele distributions and environmental variables hypothesised to drive selection, with adaptive loci showing a pattern of selected alleles at higher frequency in certain environments (Rellstab *et al.* 2015). GEA methods are flexible (e.g. can be used with either individual- or population-based sampling), have high power to detect adaptive loci (de Villemereuil *et al.* 2014; Whitlock and Lotterhos 2015), and can detect both strong divergent selection and weaker selective signatures, such as selection on standing genetic variation (Forester *et al.* 2018). As with differentiation-based analyses, accounting for population structure can reduce false-positive rates, but can also reduce power (Forester *et al.* 2018). The design of sampling schemes, spatial population structure, and the geometry of selective gradients affect the genetic architecture of adaptation, as well as the power to detect local adaptation with GEA analysis and false-positive rates in GEA tests. These are important issues for study design and interpretation (Lotterhos and Whitlock 2015; Hoban *et al.* 2016).
3. An alternative approach is to study the genetic basis of traits under selection (Hoekstra *et al.* 2006) or components of fitness and their change across environments (Fournier-Level *et al.* 2011; Lasky *et al.* 2018). **Genome-wide association studies (GWAS)** and **linkage mapping** are used to identify the genetic basis of phenotypic variation. These approaches find markers (e.g. SNPs) that covary with a phenotype of interest, either in groups of related (linkage mapping) or unrelated (association mapping) individuals. They are commonly used in evolutionary biology to identify the genetic basis of adaptive traits (Hall *et al.* 2006; Atwell *et al.* 2010). GWAS can identify the genes responsible for trait variation with precision, but it requires dense genetic markers and phenotypic data on hundreds of individuals, ideally raised in a common environment (Korte and Farlow 2013). The statistical models underlying GWAS overlap with those used for GEAs and can also account for population structure (Hayes 2013).
4. Whole transcriptome sequencing through RNA sequencing (**RNAseq**) is a high-throughput sequencing approach for both characterising the sequence of all the RNAs in the sample (the transcriptome) and quantifying their abundance. RNAseq does not require a reference genome and is therefore particularly useful for non-model organisms (Wang *et al.* 2009). This approach is suitable for studies of local adaptation because, in addition to revealing sequence variation in the transcribed region, RNAseq directly quantifies levels of gene expression, which can be used to identify genes that are up- or down-regulated under different conditions or experimental treatments (Todd *et al.* 2016). **Differential expression**

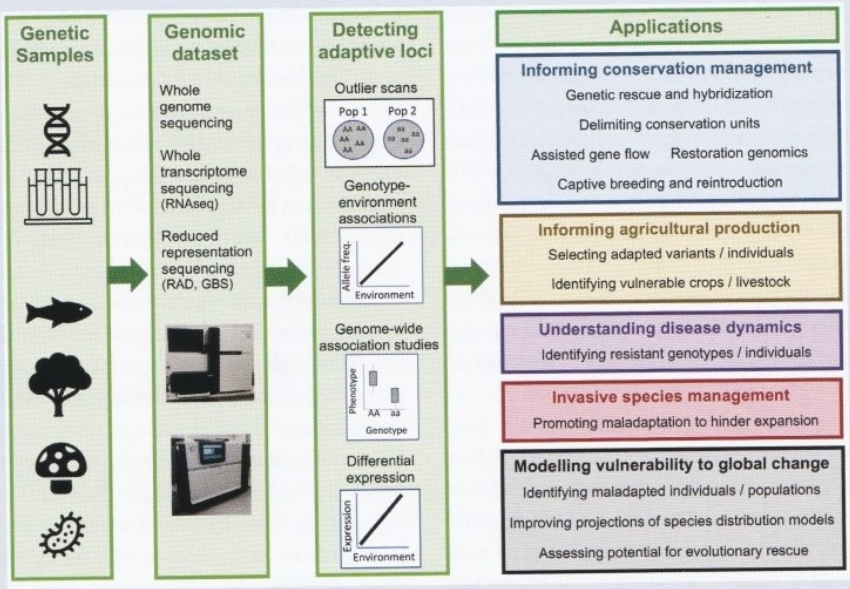


Fig. 14.1. The process of detecting adaptive genetic variation and downstream applications.

analysis is used to statistically analyse quantitative changes in the expression levels of genes between conditions based on differences in the number of reads mapped to each locus (Rapaport *et al.* 2013). Differential expression analysis can provide insight into both plastic and evolutionary responses to environmental changes (DeBiasse and Kelly 2016). However, distinguishing between the two mechanisms is not straightforward and may require controlled experiments to identify genetic differences in expression (Fig. 14.1).

environmental conditions through space or time. For example, a comparison of urban versus rural populations of white-footed mice, *Peromyscus leucopus*, identified genetic adaptations to urbanisation that suggested selection on metabolic pathways related to novel diets in urban environments (Harris and Munshi-South 2017). Alternatively, a temporal approach can be adopted using evolve and resequence experiments (Long *et al.* 2015) or longitudinal studies, whereby the same population is sampled before and after an artificial (experimental manipulation) or natural selection event, such as the outbreak of sea star wasting disease in ochre sea stars, *Pisaster ochraceus* (Schiebelhut *et al.* 2018). Other studies combine experimental approaches with genomic datasets to identify genes involved in local climatic adaptations. For example, molecular genetic studies in the model plant *Arabidopsis thaliana* first identified CBF2, a transcription factor that turns on cold acclimation pathways (Thomashow 1999). CBF2 exhibits multiple independent loss-of-function mutations in warmer Mediterranean climates (Monroe *et al.* 2016). Reciprocal transplant experiments with crosses between Italian (warmer climate) and Swedish (colder climate) individuals showed that winter cold was a main driver of differential selection between Italy and Sweden, and that CBF2 plays a key role in local adaptation to climates not experiencing freezing (Oakley *et al.* 2014).

In this chapter, we review the diversity of research on the genomics of environmental adaptation, including applications in conservation management, agriculture, disease and invasive species control, and vulnerability modelling. We conclude by highlighting outstanding questions and future directions for adaptive genomics research and applications.

APPLICATIONS

Application 1: Conservation management

The potential for adaptive genomics to inform conservation management has been recognised for over a decade (e.g. Allendorf *et al.* 2010; Sgrò *et al.* 2011). Applications have increased during this time as sequencing costs have declined, genotyping from poor-quality samples has improved, and annotated reference genomes have become

more common. Adaptive genomics has been applied to a variety of conservation applications, from guiding conservation management and prioritisation to genomic monitoring (reviewed in Forester *et al.* 2018). It is important to note that although a focus on functional (adaptive) genetic variation is important for ensuring adaptive capacity and enabling evolutionary rescue, understanding locus-specific effects on a trait and fitness is challenging and focusing on a small number of loci can lead to other beneficial genetic variation being missed (Box 14.1). Therefore, it is essential to also conserve genome-wide genetic variation to prevent inbreeding depression, reduced growth and viability and lost ability to adapt to environmental change (Kardos *et al.* 2021).

Conservation unit delineation

Conservation unit (CU) is a general term for a large set of biological and legal categories used to delineate sub-specific population units for conservation management. The reasons for defining CUs include conserving intraspecific genetic and phenotypic diversity, informing effective management strategies, and identifying a unit's listing status under legislative jurisdictions (see Chapter 23). Genomic data can inform CU delineation through both increased resolution of neutral differentiation and the characterisation of adaptive differentiation (Funk *et al.* 2012). For example, a genomic study in Baltic Sea herring (*Clupea harengus*) identified population differentiation whereas previous research using smaller genetic datasets had found little evidence for genetic structuring (Guo *et al.* 2016). This study also identified local adaptation to salinity and temperature across populations, indicating that the existing management units were poorly aligned with neutral and adaptive differentiation, with potentially negative impacts on fisheries yields and stock abundance. The inclusion of genetic divergence at adaptive markers is particularly relevant for designing genetic rescue strategies between CUs (Coates *et al.* 2018).

Genomic monitoring

Genetic monitoring has traditionally focused on using neutral markers to track individuals or distinguish species for population monitoring (e.g. abundance, vital rates, site occupancy; Chapter 10), and monitor population genetic parameters over time, such as genetic diversity or effective population size (Schwartz *et al.* 2007). The use of genomics in species of conservation concern has expanded genetic monitoring to adaptive variation, providing opportunities to monitor adaptive responses to management actions such as translocations, genetic rescue, or assisted gene flow (Flanagan *et al.* 2018; Van Rossum and Hardy 2021), as well as adaptive responses to environmental change (Hansen *et al.* 2012). Additionally, guidelines are increasingly available for effective genotyping and panel development with degraded or low-quality samples, such as those derived using non-invasive sampling methods (Carroll *et al.* 2018; von Thaden *et al.* 2020) or from museum specimens that can provide temporal genetic data to identify adaptive changes (Bi *et al.* 2013). A genetic monitoring panel that incorporates both neutral and candidate adaptive markers has been used in the management of declining Pacific lamprey (*Entosphenus tridentatus*) to assess the effectiveness of management actions including translocations and habitat restoration, as well as linking candidate adaptive markers to lamprey phenotypes, such as body size and migration timing (Hess *et al.* 2015). In another case, amplicon sequencing has been used to monitor neutral and functional loci in Tasmanian devil (*Sarcophilus harrisii*) insurance populations in response to devil facial tumor disease (Wright *et al.* 2015). In this case, adaptive loci are monitored to assess functional consequences of loss of allelic diversity due to captive breeding (Chapter 9).

Assisted gene flow (within historical range) and migration (outside historical range)

The fast pace of global warming is challenging species' natural capacity to adapt to new environments or migrate to follow suitable climates. To help them track this rapid change, some propose to artificially move, across space, individuals that are already preadapted to future local climates (Aitken and Whitlock 2013). The goal of these management actions is either to introduce new adaptive alleles into populations that will need these alleles to maintain their fitness in the future (i.e. assisted gene flow), or to move individuals beyond their current range to locations uncolonised by the species, but which will become suitable in the future (i.e. assisted migration). Potentially important to these actions is the identification of the genes involved in adaptation to local climate and the prediction of the optimal distribution of adaptive alleles across future climatic landscapes. Assisted gene flow and migration have been investigated and tested predominantly in trees (Milesi *et al.* 2019; Young *et al.* 2020), whose long generation times and strong local adaptations prevent rapid migration and make them particularly vulnerable to climate change (Aitken and Bemmels 2016). Because a poorly designed assisted gene flow strategy could induce a deleterious dilution of locally adapted alleles (outbreeding depression), and because the

conservation community is nervous to introduce species outside their natural range, both measures are still contentious and have rarely been applied in animal conservation (McLachlan *et al.* 2007). However, the increasing threats to biodiversity posed by climate change and other anthropogenic stressors are likely to increase willingness to test these emerging conservation strategies in diverse systems (Kelly *et al.* 2021).

Restoration genomics

In some cases, current local adaptations are a higher priority for conservation actions than adaptation to future conditions (Breed *et al.* 2019). For example, rehabilitation of highly degraded sites, such as mined areas and salinised soils, is focused on identifying adaptations that best match site-specific characteristics to ensure the establishment of viable populations under challenging conditions. These site-adjusted provenancing strategies will often be focused on environmental characteristics beyond climate, including terrain and soil characteristics. For example, Carvalho *et al.* (2021) used genomic, environmental, and phenotypic data to predict provenances of two common native plant species that would be best suited to restoring a highly degraded mining site. Genotype-environment associations (GEA; Box 14.2) were used to identify local adaptations to climate and at-site soil characteristics, while genome-wide associations (GWAS; Box 14.2) identified genetic variation underlying leaf macro- and micronutrient levels and specific leaf area. Adaptive genotypes were then predicted for the degraded mine site; however, none of the genotypes sampled in natural habitats matched conditions at the site, likely due to the severely degraded soil conditions. The recommendation was to combine multiple locally adapted genotypes sampled across the region in order to maximise evolutionary potential and facilitate adaptation to the novel soil conditions (Lesica and Allendorf 1999).

Captive breeding and reintroduction programs

Captive breeding is an important conservation tool used to prevent the extinction of endangered species that are unable to survive in the wild, with the aim of eventual reintroduction to their historical range. The low success rate of reintroduction programs has been attributed in part to reduced fitness when reintroduced to the wild due to genetic adaptations to the captive environment, which, by relaxing natural selection, favours rare and partially recessive deleterious alleles (Frankham 2008). Genomic approaches can contribute to detecting adaptations to captivity based on rapid changes in allele frequencies (Allendorf *et al.* 2010). Willoughby *et al.* (2017) used a **reduced-representation genome sequencing** dataset to identify SNPs under selection in experimental populations of white-footed mice, *Peromyscus leucopus,* under different captive breeding regimes. They show that the effect of adaptations to captivity can be reduced if the breeding program is designed to minimise overall levels of relatedness among individuals. Further contribution of genomic approaches is to inform the selection of suitable individuals for breeding and reintroduction based on their adaptive genetic variation (Allendorf *et al.* 2010). He *et al.* (2016) recommend that source individuals for reintroduction should be selected to maximise functional genetic variation, and consequently adaptive potential, based on their allele frequencies in SNPs associated with fitness related traits, their levels of heterozygosity in coding region SNPs and their transcription profile in genes involved in tolerance to environmental stress. However, these approaches have not been applied yet in reintroduction programs, and therefore their effectiveness is unknown.

Application 2: Agriculture

Adaptation to different environments is an essential aspect of agricultural biodiversity, allowing food production across dramatically different locations on earth. Cultivated plants and livestock have been models for understanding how organisms adapt to different conditions, given the applied importance of the systems and benefitting from existing collections of genetically diverse, local varieties. Understanding the genetic basis of environmental adaptation has long been a goal in crop and animal breeding, to adapt organisms to abiotic or biotic stressors that threaten agricultural production. Here we focus on three major goals of understanding the genomics of adaptation to environment in agricultural research: 1) identifying alleles and traits adapted to specific environments, 2) identifying optimal genotypes/individuals for specific environments, and 3) identifying genotypes vulnerable to future environmental change (Fig. 14.2).

First, for the purposes of breeding crop and livestock varieties that are resilient or adapted to specific environmental stressors, researchers often conduct genetic mapping for response to potentially stressful conditions, traits thought to be adaptive in the face of challenging conditions, or environment-associated loci. Once loci are identified, they can be introgressed into desired recipient genetic backgrounds through targeted crosses with donor genotypes, followed up with successive rounds of additional crosses to the original recipient (known as backcrosses) to reduce the introgression to the target region (Box 14.1).

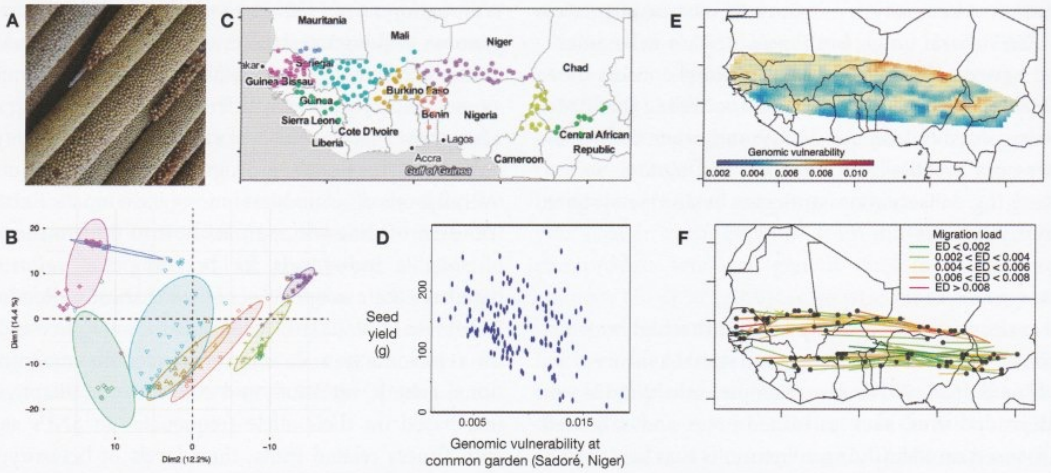


Fig. 14.2. Assessment of genomic vulnerability of local traditional varieties of pearl millet (*Pennisetum glaucum*), a staple cereal of smallholder farmers in West Africa (Rhoné *et al.* 2020). (A) Pearl millet panicles (seed heads). (B) PCA of ~140k SNPs shows genomic similarity among (C) 173 landraces from across West Africa. From these SNPs, gradient forest (GF) models were built relating climate to allele frequency to assess genomic vulnerability as the distance between the GF-predicted optimal genetic composition for a given environment and the genetic composition of a given individual or population. (D) Genomic vulnerability was validated at a single common garden in Niger where increased difference (genomic vulnerability) was associated with decreased yield. Genomic vulnerability was predicted across West Africa (E) comparing current and 2050 climates, highlighting two latitudinal bands of high vulnerability (yellow to red colours). (F) Lines connecting vulnerable regions (black circles) with the optimal current existing landrace for that region. The line colours represent the variation in the fit of the best landraces for a given location's future climate, i.e. the genomic vulnerability of the best landrace ('ED' = Euclidean distance between the genetic composition of the best available landrace versus the ideal genotype). Modified from Rhoné *et al.* 2020.

Mapping the genetic basis of adaptations to specific environments has traditionally used common garden experiments in target environments or experiments contrasting organismal performance across environments combined with association or linkage mapping (Malosetti *et al.* 2013). However, implementing such trials is logistically challenging, and so genotype-environment associations (GEA; Box 14.2) have also been implemented using traditional local crops, e.g. in sorghum (Lasky *et al.* 2015); in maize (Gates *et al.* 2019) and livestock (Lv *et al.* 2014) varieties.

The genomic basis of environmental adaptation can also be used for prediction purposes in breeding programs. In particular, when phenotypes are challenging to measure and heritability is low (which is often true of traits involved in environmental adaptation) genetic prediction can be valuable for breeding (Heffner *et al.* 2009). In these applications, the goal is to identify how a given stressor might impact a given genotype or to identify the optimal genotype for a given environment (Tiezzi *et al.* 2017). When substantial ecophysiological information exists, interactions among loci and traits can be incorporated into genetic predictions based on underlying mechanistic developmental and growth models, as in the so-called 'crop models' (Technow *et al.* 2015; Messina *et al.* 2018). Environmental associations can also be used for genetic prediction (Lasky *et al.* 2015; Gienapp *et al.* 2017) though these genotype-environment predictions have yet to be integrated into real-world breeding programs.

A final major application of the genomic basis of environment adaptation in agriculture is to identify vulnerable crop or livestock genotypes and populations in the face of future environmental changes, such as those due to greenhouse gas based warming or cooling due to volcanic eruption. One of the few examples to be implemented was in pearl millet, relying on the fact that most pearl millet farmers in west Africa grow traditional local varieties (Rhoné *et al.* 2020). The authors estimated **genomic vulnerability** of sequenced landraces under future climates, and found that adaptation could be accomplished by geographic transfer of appropriate genotypes, but that this strategy could be hindered by national boundaries and exchange regulations (Rhoné *et al.* 2020; Fig. 14.2).

Application 3: Disease dynamics

Adaptive genomics can be used to identify disease related traits and genomic regions associated with response to the selection pressures imposed by disease outbreaks (Hohenlohe *et al.* 2021). Within this context, diseases are viewed as a novel environmental condition that populations need to rapidly adapt to. Alternatively, as some diseases or pathogens are endemic to certain regions within the species' range, diseases can be viewed as part of the local

conditions to which populations are adapted to through evolving resistance and tolerance (Bellis *et al.* 2020).

Auteri and Knowles (2020) used differentiation-based genome scans (Box 14.2) on a reduced-representation genome dataset to study evolutionary changes in bats in response to white-nose syndrome, a disease that has decimated bat populations in North America and has been rapidly expanding across the continent since its introduction 15 years ago. Comparing the genomic makeup of little brown bat (*Myotis lucifugus)* survivors versus non-survivors, they identified putative adaptive shifts in allele frequencies in genes involved with regulating hibernation and arousal from hibernation, metabolism and echolocation (Auteri and Knowles 2020). Similarly, in a whole-genome sequencing study of little brown bats that survived white-nose syndrome, Gignoux-Wolfsohn *et al.* (2021) identified 63 candidate SNPs under selection located in genes associated with immunity, metabolism and hibernation, functions that are likely to contribute to hibernating bats surviving white-nose syndrome.

In another example of the rapid action of novel diseases, devil facial tumor disease (DFTD), a form of nearly universally lethal transmissible cancer, has caused rapid population declines in Tasmanian devils (*Sarcophilus harrisii*) since its identification in 1996, leading to the near extinction of this carnivorous marsupial. Adaptive genomics research has been pivotal in identifying the origins of DFTD, the genomics of susceptibility, and the adaptive evolutionary response conferring DFTD resistance (reviewed in Storfer *et al.* 2018). For example, Epstein *et al.* (2016) identified genomic regions showing extreme allele frequency changes in three populations of devils sampled before and after the identification of DFTD. They identified a rapid and parallel evolutionary response (within ~4 generations) to DFTD in these populations, with all three showing allele frequency shifts in the same two genomic regions associated with immune function and cancer risk (Fig. 14.3; Chapter 9).

In another case, Cassin-Sackett *et al.* (2019) used a suite of techniques including differentiation-based genome

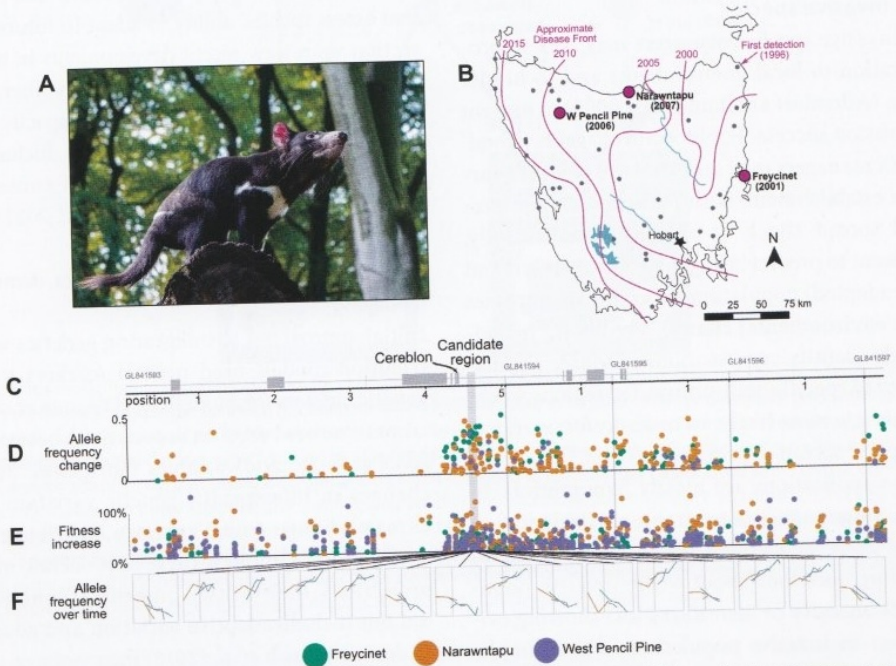


Fig. 14.3. (A) Tasmanian devil (photo by Mathias Appel). (B) The three focal populations (pink circles) sampled by Epstein *et al.* 2016, with grey points representing additional samples to assess genome-wide variation. Pink lines show devil facial tumor disease (DFTD) disease front expansion. (C) Location along a set of five scaffolds (i.e. parts of the genome sequence) on chromosome 2 of the Tasmanian devil genome: scaffolds are labeled starting with 'GL', scaffold 'Position' is shown in megabases from the start of each scaffold, and genes in the candidate region (marked by the wide vertical gray line) under strong selection in response to DFTD are shown as gray boxes. Cereblon is a myeloma therapy target in humans related to limb and brain development. (D) The location (*x*-axis) of SNPs with allele frequency changes (*y*-axis) in the top 2.5% pre- and post-disease across the three focal populations (colors). Note the peak in allele frequency change across multiple SNPs in the candidate region. (E) Estimates of the relative fitness advantage of the selected alleles in response to DFTD, which average 19%–29% across the three populations. (F) The directionality of allele frequency changes in specific SNPs (boxes) in the three populations over time (*x*-axis is time since DFTD detection, where grey vertical lines represent first detection of DFTD). Note that allele frequency changes are in the same direction in all three populations at many of the SNPs, indicating a parallel response to DFTD. All but (A) modified from Epstein *et al.* (2016).

scans to identify genetic regions conferring resistance to avian malaria in the Hawai'i 'amakihi (*Chlorodrepanis virens*). Avian malaria is a mosquito-transmitted protozoan parasite implicated in population declines and extinctions of Hawai'ian honeycreepers, including the 'amakihi, since its introduction in the 1930s. The 'amakihi is one of only a few species of honeycreeper to have exhibited adaptive responses to the parasite. Low elevation populations, where infected mosquitos are prevalent, have higher survivorship in response to infection compared to high elevation populations, where mosquitos are mostly absent. In contrast to DFTD, resistance to avian malaria in low-elevation populations was conferred by multiple changes in classes of genes related to pathogen defence and immune response, with different populations showing different adaptive pathways to resistance. In this case, selection may have been acting on differing standing variation in particular classes of genes among populations, but not on specific genes across all populations.

Application 4: Invasive species

In the case of invasive species, managers may seek to promote maladaptation to local environments and to hinder local adaptation (Allendorf and Lundquist 2003) to prevent or minimise invasion success. For biocontrol agents ('good' invasive species), managers may seek a mix of adaptive variation to enable establishment, with maladaptation to prevent unwanted spread (Bock *et al.* 2015). Additionally, managers may want to predict how genetically distinct (and possibly locally adapted) populations of an invasive species will respond to environmental change. Predicting maladaptation may help identify combinations of source populations pre-adapted to specific, still-uninvaded regions where successful invasion is most likely, in order to focus efforts on routes to stop the spread of propagules.

To date, these applications are mostly hypothetical. In invasive species, the genomics of environmental adaptation is mostly at an early descriptive phase (as opposed to applied), answering questions about where invasive populations trace their ancestry or identifying loci showing evidence of selection in invasive populations. For example, Calfee *et al.* (2020) studied the invasion history of honeybees, *Apis mellifera scutellata,* out of Brazil and showed that this invasion stalled at similar latitudes in North and South America, potentially due to selection against many loci of small effect in temperate zones. In the human commensal fruit fly *Drosophila melanogaster,* which has spread from Africa to much of the globe, diapause has apparently been selected in temperate regions. Schmidt *et al.* (2008) identified the *cpo* gene as underlying much of the variation in diapause because allele frequencies showed strong latitudinal clines, suggesting mutations at this gene underlie adaptation to the novel temperate environments.

Application 5: Modelling vulnerability

Biodiversity vulnerability to future climate change is commonly assessed using predictive **species distribution models** (Box 14.3). These approaches have been criticised for being over-simplistic, failing to take into consideration local adaptations (Hällfors *et al.* 2016), and ignoring important mechanisms affecting species vulnerability, including evolutionary mechanisms and adaptive capacity (Urban *et al.* 2016). Climate change, by rapidly modifying local environments, will impact the distribution of adaptive alleles across species' ranges. If a local population is not able to track that change by modifying its genetic composition, it may lead to a decrease in fitness and eventually decline. New genomic tools can complement species distribution models through integrating this intraspecific adaptive component into predictive models that assess species' ability to adapt to future changes. In this section we review recent developments in the field in which genomic tools are applied to model vulnerability to climate change and assess species adaptive capacity. These tools can be applied to a broad range of species, including species with long generation time and species of conservation concern (Harrisson *et al.* 2014; Hoffmann *et al.* 2021)

Integrative approaches linking genomics, demography and modelling

Initial approaches to integrating genetics with species distribution models used neutral markers to either delimit genetic clusters for modelling (D'Amen *et al.* 2013), delimit climatic zones based on associations between genetic variables and climatic variables (Sork *et al.* 2010) or forecast changes in intraspecific genetic variation in response to climate change using ancestry distribution models (Jay *et al.* 2012). Although these approaches improved model projections, they focused on **neutral genetic variation** and did not include adaptive variation and adaptive potential. In contrast, Bush *et al.* (2016) incorporated adaptive capacity into a hybrid species distribution model that took into account physiological tolerance limits (critical thermal temperature tolerance) and dispersal dynamics in Australian fruit fly species. Using a quantitative genetic model to calculate evolutionary response, this study illustrated how incorporating adaptive capacity through genetic modelling of physiological traits could affect projections of species' distributions.

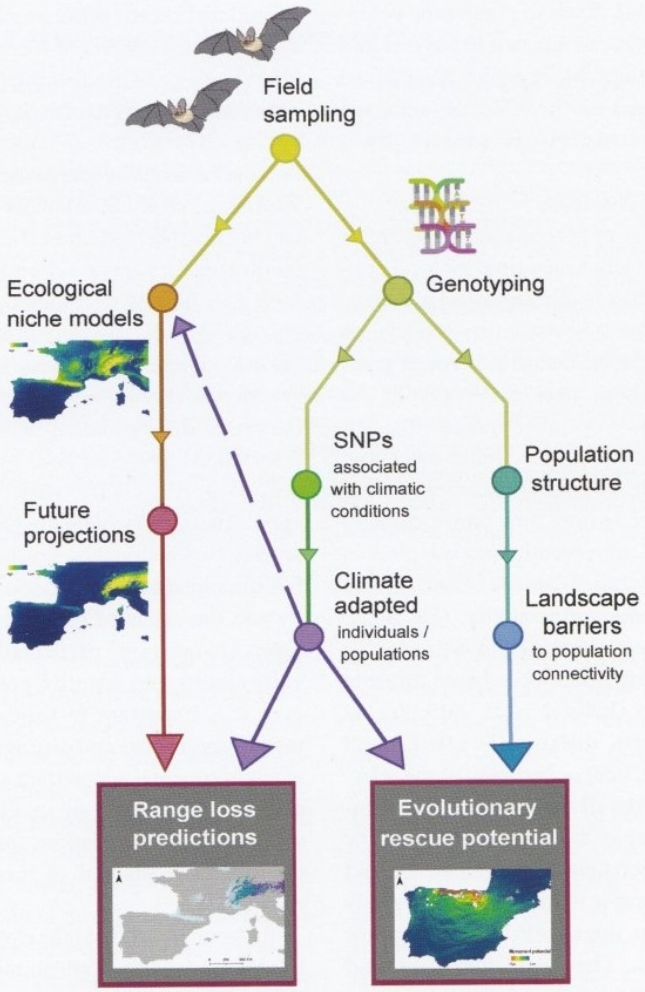


Fig. 14.4. Framework for modelling vulnerability to climate change through incorporating genomic data and climate adaptive variation into species distribution models and landscape connectivity analysis (taken from Razgour *et al.* 2019). The framework begins with field sampling to collect both samples for genomic analysis and information on the current distribution of the species. Samples are used to generate a genomic dataset that is divided into a neutral dataset, which is used to assess population structure and landscape barriers to movement using a landscape genetics approach, and an adaptive dataset, using a combination of GEA methods to identify SNPs associated with climatic conditions of interest. Based on their genomic makeup in these adaptive SNPs, individuals are divided into those potentially pre-adapted to future climatic conditions and those that are likely to be maladapted. This information is then used to assess the potential of evolutionary rescue in the form of gene flow from adapted to maladapted populations based on the identified landscape barriers to current patterns of genetic connectivity. Finally, two separate ecological niche (species distribution) model projections are generated for potentially adapted versus maladapted individuals to calculate extent of future range losses in comparison to models that do not include genomic information.

Razgour *et al.* (2019) developed an alternative framework for incorporating genomic data into species distribution models to forecast range changes under climate change and assess the potential for evolutionary rescue of maladapted populations (Fig. 14.4). This framework employs GEAs (Box 14.2) to identify putative SNPs under selection associated with climatic variables likely to affect species survival and predicted to change in the future. Then, individuals are divided into those associated with hot-dry versus cold-wet conditions based on their genomic makeup in these putative climate-adaptive SNPs. Intraspecific variation in local climatic adaptations is directly incorporated into species distribution models through generating separate predictive models for individuals adapted to different climatic conditions. Razgour *et al.* (2019) show that considering local climatic adaptations in species distribution models reduces future range loss projections for Mediterranean bat species. Moreover, they use the landscape

genetics approach (Manel *et al.* 2003) to predict the potential for gene flow from populations adapted to warmer and drier conditions to populations likely to be maladapted under future conditions based on the effect of landscape permeability on current patterns of genetic connectivity.

'Genetic offset' and 'genomic vulnerability'

Other recent studies make use of genomic data to estimate the magnitude of change that will be required for local populations to track the future shift in climate, avoid maladaptation and maintain their fitness in the future (Capblancq *et al.* 2020). By modelling the relationship between environmental and genetic variation, these studies predict the genetic composition that would optimise species fitness at any combination of site-by-environment (Fitzpatrick and Keller 2015). Measuring the difference between genetic composition predicted under current and future climates then provides an estimate of potential maladaptation, which has been subsequently called 'genetic offset', 'risk of non-adaptedness' and 'genomic vulnerability' (Fig. 14.2). Different approaches have been developed to estimate this proxy for maladaptation, using either locus-based measure of change in allele frequency (Rellstab *et al.* 2015; Rochat *et al.* 2021), multi-locus genetic distance (Fitzpatrick and Keller 2015; Capblancq *et al.* 2020) or variation of the selection coefficients averaged across all adaptive loci (Exposito-Alonso *et al.* 2019). For example, Bay *et al.* (2018) used the gradient forest approach developed by Fitzpatrick and Keller (2015) to calculate genomic vulnerability in a widely distributed North American migratory bird, the yellow warbler, *Setophaga petechia*. They first identified and visualised climate-associated genetic variation across the species' breeding range. Then they calculated the extent of mismatch between current and predicted future genomic variation based on differences in allele frequencies in SNPs identified as associated with changing climatic conditions. Finally, they compared genomic vulnerability predictions to surveyed population trends over the past ~50 years and found that areas predicted to have higher genomic vulnerability under future conditions have already experienced the greatest population declines (Bay *et al.* 2018).

It is important to note that genetic offset estimates a gap between current and future optimal genetic compositions at a specific location; it does not give any information on the population's ability to fill this gap and avoid maladaptation. The ability to avoid maladaptation will depend on many species-specific parameters, including availability of adaptive alleles, generation time and population connectivity (Hoffmann *et al.* 2021). More work is needed to validate the potential of genetic offset for management and conservation applications. However, a recent study showed that genetic offset was a good predictor of fitness after a climate translocation in poplars (Fitzpatrick *et al.* 2021).

Risk and vulnerability assessment

Hoffmann *et al.* (2015) show how evolutionary genomics can be incorporated into a decision-making framework for biodiversity conservation under climate change. Genomic tools can inform decisions on whether populations have enough genetic diversity for an evolutionary response (based on levels of inbreeding and amount of standing genetic variation), are adapted to local climatic conditions (based on differentiation-based or genotype-environment associations analyses; Box 14.2), have adequate levels of gene flow (population structure and landscape genetics approaches), and whether hybridisation with closely related species can result in a favourable evolutionary response (Hoffmann *et al.* 2015). Assessment of genomic vulnerability and the extent of genomic change needed to track climate change are particularly relevant for predicting vulnerability and adaptive potential of populations. However, it is important to validate predictions with experimental approaches and distinguish between true signatures of environmental adaptations versus low genomic variation due to genetic drift in small populations, in particular when selecting populations for genetic mixing to increase the adaptive potential of threatened species (Hoffmann *et al.* 2021).

Razgour *et al.* (2018) developed an integrated framework to identify wildlife populations under threat from climate change based on exposure, sensitivity and range shift potential. They apply the framework to a long-lived limited-dispersal bat species, *Plecotus austriacus*. Genomic data are used to inform population sensitivity to future changes based on allele frequencies in loci identified as putatively associated with climatic conditions that have a strong impact on bat survival and reproductive success and are predicted to change in the future. Genomic data are also used to assess the effect of landscape connectivity on gene flow and project how changes in landscape connectivity will affect the ability of populations to shift their ranges to track future suitable climatic conditions. The three components of the framework are combined to assign levels of risk to populations, which can be used to inform conservation priorities and select appropriate management interventions under climate change (Razgour *et al.* 2018).

Simulations provide an alternative framework for risk assessment that can integrate demographic and evolutionary

Box 14.3: Methods to model vulnerability to environmental change

Vulnerability is the extent to which biodiversity is susceptible to environmental change due to an inability to accommodate or respond to changing conditions. It is often assessed in terms of a species' *exposure* and *sensitivity* to changing conditions, and its *adaptive capacity* in response to the environmental change (Foden *et al.* 2019). Exposure describes the magnitude of the disturbance, that is, the departure from levels that the species has evolved with. It is commonly assessed using species distribution models (also known as bioclimatic-envelope or niche models). Sensitivity is characterised by aspects of a species' life history, ecophysiology, and microhabitat preferences and defines how closely tied the persistence, performance, or fitness of a species is to changing conditions (Dawson *et al.* 2011). Adaptive capacity includes attributes that allow a population or species to cope with, accommodate, or evolve in response to environmental change. It is most commonly summarised by three features: dispersal and colonisation ability, phenotypic plasticity, and evolutionary potential (the capacity to evolve genetically based changes that increase fitness under changing conditions; Dawson *et al.* 2011). These components of adaptive capacity interact with the cumulative effects of exposure and sensitivity, reducing vulnerability and mitigating extinction risk. Despite the importance of adaptive capacity, it has rarely been incorporated in climate change vulnerability assessments because it is more difficult to measure than exposure and sensitivity. Yet, even studies that have incorporated proxies of adaptive capacity, such as neutral genetic diversity, population size, number of populations and body size as a surrogate for dispersal ability, found it influenced the outcome of the vulnerability assessment (Ofori *et al.* 2017; Wade *et al.* 2017). More recent approaches (Bay *et al.* 2017; Razgour *et al.* 2018, reviewed in the 'Risk and vulnerability assessment' section) have incorporated genomic data and local environmental adaptations as measures of sensitivity and adaptive capacity.

dynamics in response to shifting environmental conditions. For example, Bay *et al.* (2017) use simulation models to assess extinction risk in a population of corals (*Acropora hyacinthus*) in Rarotonga, Cook Islands, by integrating demographic data and future climate change scenarios with genomic data related to coral thermal tolerance (identified using genotype-environment associations and differentiation-based analyses; Box 14.2). Under low-emissions climate change scenarios, corals persisted through shifts in adaptive allele frequencies, while higher-emissions scenarios resulted in population extinction due to maladaptation and negative population growth rates. Assisted gene flow through movement of warm-tolerant corals at a rate of 1% per year accelerated evolutionary responses, and prevented extinction under a high-emissions scenario (Bay *et al.* 2017). Extending this work in a spatially explicit framework to incorporate dispersal and metapopulation dynamics will be an important next step in estimating regional or even species-wide extinction risk in response to increasing temperatures.

FUTURE DIRECTIONS AND OUTSTANDING QUESTIONS

Structural variants

To date, most genomic studies have investigated genetic variation through the genotyping and analysis of SNPs. However, an increasing number of studies show that another type of genetic variation – structural variation – is associated with functional changes and phenotype variation (Wellenreuther and Bernatchez 2018). As its name suggests, a structural variant is a region of DNA that experiences a change in structure across individuals. It can be a deletion or insertion of one or several nucleotides, the duplication or inversion of a DNA segment or even the translocation or fusion of genomic regions (Wellenreuther *et al.* 2019). Structural variants include transposable elements, copy number variation and all types of chromosomal rearrangements, all of which can play a major role in species adaptation and diversification (Mérot *et al.* 2020). In particular, inversions (i.e. chromosomal rearrangement where a segment of DNA is reversed compared to the ancestral state) can limit genomic recombination (Box 14.1) among lineages and protect specific allelic combinations. When these inversions host beneficial adaptive alleles, they help maintain local adaptation, even in the face of gene flow (Wellenreuther and Bernatchez 2018). The increasing availability of good quality whole-genome references and data together with recent improvements in long-read sequencing technologies have made it easier to detect structural variation and will greatly facilitate the use of these markers to better understand the genetic architecture of adaptation in the coming years.

Epigenetics

Epigenetic modifications are heritable changes in gene function that do not involve changes in the DNA sequence. For example, environmentally induced variation in DNA methylation can cause differential gene expression that changes

phenotypes. Because epigenetic modifications are influenced by genotype-environment interactions, they can shape patterns of adaptive genomic variation across environments (Verhoeven *et al.* 2016; Whipple and Holeski 2016). Epigenetic variation can also allow for rapid adaptation to changing environmental conditions (via plasticity), potentially contributing to adaptive responses to climate change (McGuigan *et al.* 2021). Additionally, because epigenetic variation can be maintained in the face of small population sizes and low genetic diversity, it may contribute to the invasion success (Mounger *et al.* 2021) and the maintenance of evolutionary potential in species of conservation concern with otherwise low genetic diversity (Bernatchez 2016). Despite over a decade of research, our understanding of the importance of epigenetic processes in natural settings remains limited due to the need for transgenerational studies combined with the difficulty of quantifying the fitness effects of epigenetic variation and its interaction with genetic adaptations (Whipple and Holeski 2016; McGuigan *et al.* 2021). Careful study design is critical to improve our understanding of the adaptive significance of epigenetic variation in response to environmental change (McGuigan *et al.* 2021).

Hologenomics

Given the fundamental role played by symbiotic microorganisms in the form, function and fitness of their hosts, animals and plants cannot be considered as autonomous entities, but rather as biological units that include numerous microbial symbionts and their genomes – the 'holobiont' (Bordenstein and Theis 2015). Evolution can be the result of changes in the host genome and/or its associated microbial genomes (metagenome; Zilber-Rosenberg and Rosenberg 2008). Alberdi *et al.* (2016) propose that host acclimation and adaptation to rapid environmental change is likely to be facilitated by the plasticity of the gut microbiota. Therefore, the study of adaptive responses to the environment can benefit from adopting a 'hologenomic' perspective, i.e. considering the combined genetic information of the host and its microbiota (Zilber-Rosenberg and Rosenberg 2008). Hologenomics has potential far-reaching applications in agriculture, biotechnology and biomedical research, as well as ecology, evolution and conservation (Nyholm *et al.* 2020). Although applications, especially to wildlife, are still at their infancy, the Earth Hologenome Initiative (https://www.earthhologenome.org/) is currently generating paired vertebrate genomes and their gut microbial metagenomes to understand the hologenomic underpinnings of environmental adaptations, convergence evolution and ecological interactions.

Validating inference from genomics

Without experimental validation, statistical inferences about environmental adaptation must be interpreted with caution. Many of the above methods for identifying loci and genotypes adapted to specific environments are based on population genetic patterns, but not phenotypic variation. Even in the case of GWAS for adaptive phenotypes, population structure and limited characterisation of functional variants can limit the strength of inferences. Stronger evidence that a given genotype or allele is adapted to a specific environment can be obtained from several experimental approaches. For example, when adaptation is oligogenic, introgression of a putative adaptive allele can be used to create near isogenic lines, allowing one to directly test the allele's effects (Hepworth *et al.* 2020), though recombination limits how narrow the introgressed region is (Box 14.1). Alternatively, when transgenic or CRISPR mutants are made that replicate the putative causal natural allelic variation, the effect of the natural variation can be tested (Bellis *et al.* 2020). Nevertheless, in many systems adaptation is polygenic, preventing these types of locus-specific validation.

When adaptation is polygenic, the validation of genomic inferences can be done using experiments to test (out-of-sample) multi-locus predictions of adaptive traits in specific common garden environments. While this approach can validate inferences aggregated across loci, it does not allow for the identification or validation of specific causal loci. A less direct, but more relevant (for certain goals) validation approach is to test genetic predictions of environment-dependent individual performance or population growth rate in wild individuals (Gienapp *et al.* 2017; Bay *et al.* 2018; Gienapp *et al.* 2019). However, this approach is also subject to spurious associations when changes in genotypes across environments (genotype by environment interactions) are not accounted for. Hence, given the trade-off between efficiency, logistical challenges and depth of inference both experimental and population genomic inference have their place.

Reflections

As illustrated in this chapter, adaptive genomic techniques have an important role to play in the management and conservation of agricultural resources, natural ecosystems, and global biodiversity under changing environmental conditions. The genomic landscape of adaptation is often highly complex (Box 14.1), interacting with a species' environment, demographic history, life history, and evolutionary legacy. This complexity can lend uncertainty

to management and conservation efforts that incorporate adaptive genomic data. For example, predicting evolutionary responses to climate change in the annual plant *Arabidopsis thaliana* has proven difficult, despite the wealth of genomic and experimental data available for this model species (Fournier-Level *et al.* 2016). Nevertheless, simple best practices for maintaining evolutionary potential and adaptive capacity, such as maximising genetic diversity, were found to be effective (Fournier-Level *et al.* 2016). This finding confirms the importance of conserving species across phenotypic, genetic, and environmental diversity and maintaining overall genomic diversity to conserve adaptive capacity and evolutionary resilience in response to known and unknown future threats (Sgrò *et al.* 2011; Kardos *et al.* 2021).

The *Arabidopsis* case illustrates why it will be important, where possible, to move away from sole reliance on statistical inference about the genomic basis of environmental adaptation. However, because experimental and functional validation may not always be possible due to the longevity, life history or conservation status of the species in question, it remains essential to develop new methods and best practices to guide the application of this emerging field. For example, statistical inferences could be better grounded in quantitative and population genetic theory, which lags behind the complexity we see in natural systems (Balkenhol *et al.* 2015). Another approach couples statistical inference with complementary data from simulations (Epperson *et al.* 2010), such as in the case of breeding plans for transgenic blight-tolerant American chestnut trees (*Castanea dentata*; Westbrook *et al.* 2020). American chestnut was a **keystone species** of eastern North American forests before the introduction of a fungal pathogen (*Cryphonectria parasitica*) in the early 1900s. This simulation study models the efficacy of crossing transgenic, blight-tolerant trees with susceptible wild-type trees to conserve the genetic diversity and evolutionary potential of wild-type chestnuts while improving resistance to the blight pathogen. In combination with genomic prediction to introgress polygenic resistance from *Castanea mollissima* (Westbrook *et al.* 2020), these efforts could facilitate the start of large-scale restoration of this species across its former range within a few decades. As this and several studies reviewed in this chapter show, improving our understanding of the genomics of environmental adaptation can inform a range of applications, from predictions of species responses to environmental change to crop improvements that increase resilience under climate change.

DISCUSSION TOPICS

1. Compare commonly used genomic methods to identify local environmental adaptations and discuss which applications they are most suitable for and why.
2. What genomic methods and/or experimental techniques would be required to fully assess the evolutionary potential of a population or species? Is this feasible?
3. Is it important to specifically identify and conserve adaptive variation, or should we focus instead on measures that will increase neutral genetic variation?

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