

Genomic Prediction of (Mal)Adaptation Across Current and Future Climatic Landscapes

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assisted migration, conservation

Abstract

Signals of local adaptation have been found in many plants and animals, highlighting the heterogeneity in the distribution of adaptive genetic variation throughout species ranges. In the coming decades, global climate change is expected to induce shifts in the selective pressures that shape this adaptive variation. These changes in selective pressures will likely result in varying degrees of local climate maladaptation and spatial reshuffling of the underlying distributions of adaptive alleles. There is a growing interest in using population genomic data to help predict future disruptions to locally adaptive gene-environment associations. One motivation behind such work is to better understand how the effects of changing climate on populations' short-term fitness could vary spatially across species ranges. Here we review the current use of genomic data to predict the disruption of local adaptation across current and future climates. After assessing goals and motivations

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underlying the approach, we review the main steps and associated statistical methods currently in use and explore our current understanding of the limits and future potential of using genomics to predict climate change (mal)adaptation.

1. INTRODUCTION

Anthropogenic climate change is already affecting the biosphere, with uncertain consequences for biodiversity (Brondizio et al. 2019, Parry et al. 2007, Stocker et al. 2013). Given the expected widespread and detrimental effects of rapid climate change, research is increasingly focused on forecasting the nature and magnitude of these impacts across multiple scales, from long-lived individuals to populations, species, and entire communities. Studies have shown that climate change has already led to species range shifts (Chen et al. 2011, Parmesan & Yohe 2003), loss of fitness in natural populations (Brady et al. 2019a), and changes in population genetic composition (Bradshaw & Holzapfel 2006, Franks et al. 2018, Jump et al. 2006).

At the level of single species or communities, spatial predictions of climate change impacts have largely been investigated through species distribution modeling (SDM), in which the suitable climatic envelope of a species is modeled from species occurrence records and climatic data before being projected across space and/or through time (Guisan & Thuiller 2005, Thuiller et al. 2008). While SDM has several advantages, the methods typically do not consider the variation in physiological tolerance, reproductive output, and survival ability that occur within and among populations that span the climatic range of a species (Alberto et al. 2013a, Benito Garzón et al. 2019, Jay et al. 2012). Indeed, it is common for different populations of both plant and animal species to exhibit substantial genetic variation that has resulted from evolution of locally optimal phenotypes in response to spatially varying environments (i.e., local adaptation) (Davis & Shaw 2001, Hereford 2009, Jump et al. 2006, Kawecki & Ebert 2004, Leimu & Fischer 2008, Savolainen & Pyhäjärvi 2007).

Heterogeneity in the spatial distribution of adaptive standing genetic variation could mitigate or accentuate the biological impacts of climate change in the coming decades, depending on how adaptive alleles are distributed and on the nature and magnitude of climate change in a given location (Aitken et al. 2008, Chhatre et al. 2019, Jump & Peñuelas 2005, Info Flora 2020, Rehfeldt et al. 2002). In general, we expect climate change to perturb locally adapted populations off their fitness peaks on the adaptive landscape, creating varying levels of disruption between existing genotypes and optimal values of fitness under the changed environment (Aitken et al. 2008, Hoffmann & Sgró 2011). Accordingly, the magnitude of this disruption can be thought of as an adaptation debt that requires a given amount of change in local genotype frequencies in order to minimize maladaptation under the new fitness landscape.

A growing number of studies have begun employing population-level genomic data to estimate the magnitude of disruption in gene-environment relationships that may be triggered by a change in climate (Table 1). These studies typically relate current patterns of adaptive genomic composition of populations to climate; the predicted optimal population genomic compositions are then 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. Some studies have also integrated data from field experiments or historical demographic records to investigate more directly the relationship between fitness, genotype, and climate.

The ease of generating genomic data sets along with the availability of dedicated modeling procedures has greatly facilitated predictions of climate adaptation and maladaptation in nearly any

Species distribution modeling (SDM):

numerical modeling linking species occurrences or abundances and environmental variables to predict species distribution across space and/or time

Local adaptation:

higher fitness of local genotypes compared to nonlocal ones resulting from divergent selection due to environmental variation across the landscape

Standing genetic variation:

genetic variation (i.e., multiple alleles) already present in the population
















Adaptive landscape:

variation in relative fitness as a result of different combinations of allele frequencies, genotypes, or phenotypes

Maladaptation:

when local genotypes do not produce the optimal phenotypes in a local environment

Table 1 Recent studies predicting a future change in local genomic optima due to climate change

Species	Type	Spatial scale	Data	Adaptive component identification	Predictive model	Validation procedure	Reference
<i>Populus balsamifera</i>		North America	Genomic (targeted genotyping of candidate genes)	F_{ST} (Arlequin, BayeScan), GEA (Bayenv), GPA	Gradient forest and GDM	None	Fitzpatrick & Keller 2015
<i>Arabidopsis thaliana</i>		Europe	Genomic (whole genome)	GWAS (EMMAX25, BSLMM28)	Ecological niche modeling on alleles	None	Exposito-Alonso et al. 2018
<i>Populus tremula</i>		Sweden	Genomic (whole genome)	GEA (LFMM)	GDM	None	Ingvarsson & Bernhardtsson 2018
<i>Quercus rugosa</i>		Mexico	Genomic (GBS)	F_{ST}	Gradient forest	None	Martins et al. 2018
<i>Empidonax traillii</i>		North America	Genomic (RADseq)	GEA (LFMM)	Gradient forest	Correlation with population historical trends	Ruegg et al. 2018
<i>Sceloporus petechia</i>		North America	Genomic (RADseq)	GEA (LFMM)	Gradient forest	Correlation with population historical trends	Bay et al. 2018
<i>Quercus suber</i>		Western Mediterranean	Genomic (GBS)	F_{ST} (BayeScan), SelfEstim	RONA	None	Pina-Martins et al. 2019
<i>Myotis crypticus</i> and <i>Myotis esculentus</i>		Western Europe	Genomic (RADseq)	GEA (LFMM, RDA)	Ecological niche modeling separating two extreme adaptive groups	None	Razgour et al. 2019
<i>Eucalyptus melliodora</i>		Australia	Genomic (GBS)	None	GDM using the complete genomic data set	None	Supple et al. 2018
<i>Arabidopsis thaliana</i>		Europe	Genomic (whole genome) Phenotypic (common gardens)	GWAS (LM-GEMMA)	GWES	Model evaluation procedure	Exposito-Alonso et al. 2019
<i>Zea mays</i>		Mexico	Genomic (published data)	GEA (Bayenv, Bayescenv)	Gradient forest	None	Aguirre-Liguori et al. 2019
<i>Fagus sylvatica</i>		French Alps	Genomic (RADseq)	GEA (RDA)	RDA	None	Capblancq et al. 2020
<i>Capra aegagrus bircus</i>		Morocco	Genomic (whole genome)	GEA (logistic regressions, SAM)	SPAG	Model evaluation procedure	Rochat & Joost 2019
<i>Mimosa acutistipula</i> and <i>Diodaea apurensis</i>		Carajás Mineral Province (Brazil)	Genomic (GBS) Phenotypic (sample traits)	GEA (RDA, LFMM), GPA (RDA, LFMM)	RDA	None	Carvalho et al. 2019
<i>Populus balsamifera</i>		North America	Genomic (targeted genotyping of candidate genes)	GEA (LFMM, Bayenv)	GDM	None	Gougherty et al. 2020

Abbreviations: GBS, genotype-by-sequencing; GDM, generalized dissimilarity modeling; GEA, genotype-environment association; GPA, genotype-phenotype association; GWAS, genome-wide association studies; GWES, genome-wide environment selection; LFMM, latent factor mixed model; LM-GEMMA, linear model form of the genome-wide efficient mixed model; RADseq, restriction-site associated DNA sequencing; RDA, redundancy analysis; RONA, risk of nonadaptiveness; SAM, spatial analysis method; SPAG, spatial areas of genotype probability.

Organism type:  = Tree  = Plant  = Domesticated mammal  = Wild mammal  = Bird

Fitness optimum:

combination of phenotypes that maximize the survival and reproduction (i.e., fitness) of a local population

Genomic prediction:

prediction of phenotypic breeding values based on genotype-phenotype associations, extended here to include prediction of (mal)adaptation based on gene-environment associations

nonmodel species (Fitzpatrick & Keller 2015). As such, genome-informed distribution models of climate adaptation and maladaptation have immense potential to benefit biodiversity conservation efforts and management strategies, for example, by identifying populations most at risk of local extinction (Bay et al. 2018, Gougherty et al. 2020, Martins et al. 2018, Ruegg et al. 2018), focusing ex situ conservation efforts on areas containing unique climate-adaptive germplasm, or assessing the efficacy of assisted gene flow between existing populations (Aitken & Bemmels 2016, Aitken & Whitlock 2013, Steane et al. 2014). However, like SDM, projecting gene-climate relationships is inherently correlative and ultimately relies on space-for-time substitution of statistical associations between genomic and climatic variation. For these reasons, genome-informed prediction models are potentially prone to a host of errors (Fitzpatrick et al. 2018b) and must be correctly performed and validated (e.g., using robust experiments).

Here, we review the use of genome-informed prediction models to quantify and map the disruption in local adaptation due to climate change. We identify the main objectives and motivations associated with such predictions and review recent case studies, including the methods used and primary results. Finally, we outline promising future research directions for genome-informed predictions of climate maladaptation along with the main methodological challenges associated with this field of research.

2. CONCEPTS AND OBJECTIVES

2.1. Goals, Motivation, and Scope

The main goal of integrating genomic data into predictive models is to attempt to accommodate population- or individual-level variation in environmental tolerances, which is otherwise ignored in SDM. Ideally this is accomplished by identifying the relationship(s) between fitness, genotype, and environment in a diverse range-wide sample and evaluating whether the fitted relationship(s) can predict loss or gain of fitness across the landscape in the context of climate change (**Figure 1**). The first step involves identifying populations or regions of the landscape where the frequencies of adaptive alleles in local gene pools reflect an inferred fitness optimum in relation to local climate conditions. The identified spatial patterns of adaptive allele frequencies can then be used to make predictions about a population's potential loss of fitness (maladaptation) in response to climate change in the absence of an immediate evolutionary response (i.e., assuming no change in allele frequencies, recombination, migration, or mutation).

Importantly, these predictions of maladaptation do not explicitly incorporate population evolutionary dynamics or trajectories but rather are estimates of a static potential deviance from the assumed or estimated local fitness optimum given an abrupt change in the environment and assuming the genetic makeup of the population does not change accordingly. We also emphasize that the genomic prediction models we describe address a different problem from that of trying to predict a longer-term population response over multiple generations (for a discussion of limitations, see Shaw 2019), which depends on a suite of complex interactions between multiple evolutionary and ecological processes. Rather, we seek to answer the question, What would be the predicted change in the strength and direction of climate-driven selection under altered climatic conditions (Exposito-Alonso et al. 2019)? This question is particularly important for organisms with long generation times, for which the threat of climate change is likely to occur within the lifetimes of individuals.

2.2. Local Adaptation and Maladaptation as Two Sides of the Same Coin

Predicting fitness outcomes after a sudden change in climate relies on knowledge of adaptive genetic variation and the functional consequences that arise when that variation becomes

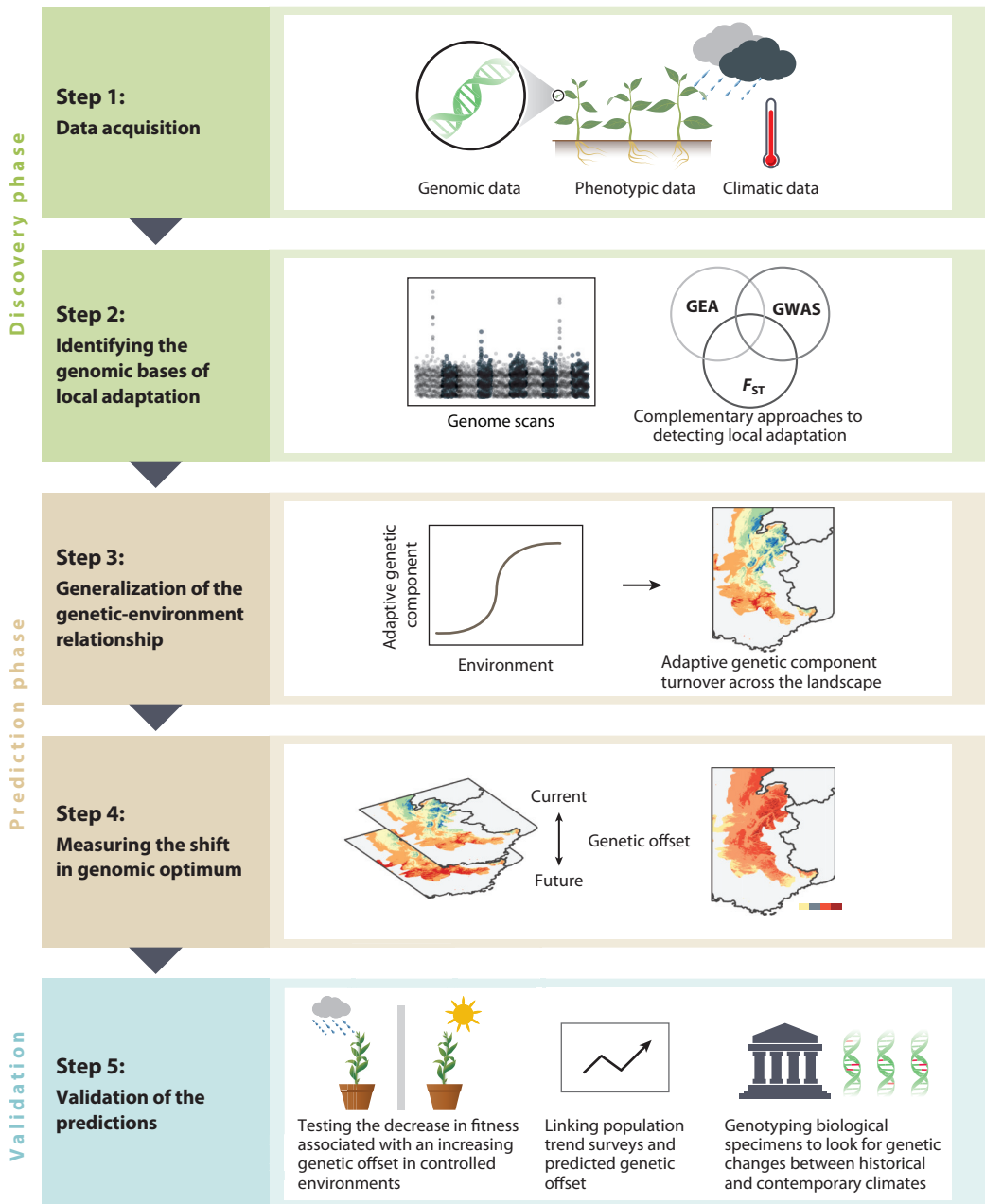


Figure 1

The different steps of a study performing genome-informed predictions of climate (mal)adaptation. Steps 1 and 2 correspond to the discovery phase mentioned in the main text; steps 3 and 4 describe the prediction phase (see Section 2.3); and step 5 gives two ideas for validating the predictions (see Section 3.3). F_{ST} is the fixation index quantifying genetic differentiation among subpopulations. Abbreviations: GEA, genotype-environment association; GWAS, genome-wide association studies.

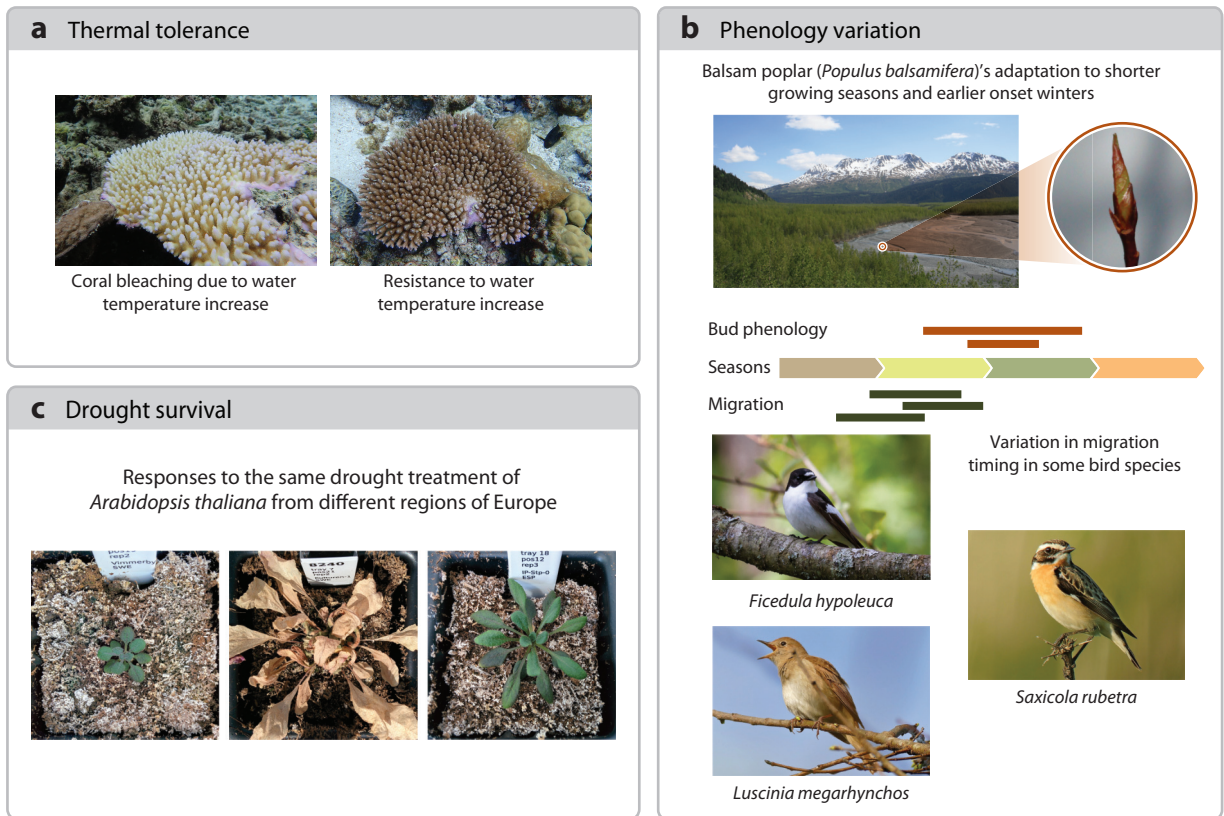


Figure 2

Examples of genetic variation in climate responses in plant and animal species. (a) Thermal tolerance. Bleaching susceptibility associated with increasing temperature varies among genotypes for *Acropora hyacinthus* in American Samoa (Palumbi et al. 2014). Photos in panel a courtesy of Rachael Bay. (b) Phenology variation. Northern populations of the forest tree balsam poplar (*Populus balsamifera*) break bud later and set bud earlier than southern populations as an adaptation to shorter growing seasons (Olson et al. 2013). In birds, circadian clock genes are known to be involved in variation in seasonal migration timing (Saino et al. 2015). Photos in panel b reproduced courtesy of Matthew Fitzpatrick and Stephen Keller (poplars); from [https://commons.wikimedia.org/wiki/File:Common_Nightingale_\(Luscinia_megarhynchos\)_25936816473.jpg](https://commons.wikimedia.org/wiki/File:Common_Nightingale_(Luscinia_megarhynchos)_25936816473.jpg) (CC BY-SA 2.0) (*Luscinia megarhynchos*); from [https://commons.wikimedia.org/wiki/File:Saxicola_rubetra_-Belgium_-male-8_\(1\).jpg](https://commons.wikimedia.org/wiki/File:Saxicola_rubetra_-Belgium_-male-8_(1).jpg) (CC BY 2.0) (*Saxicola rubetra*), and from https://commons.wikimedia.org/wiki/File:Ficedula_hypoleuca_Munkedal.jpg (CC BY-SA 2.0) (*Ficedula hypoleuca*). (c) Drought survival. Shown are results of a drought experiment performed on *Arabidopsis thaliana* from different regions of Europe (Exposito-Alonso et al. 2018). Photos in panel c courtesy of Moises Exposito-Alonso.

Common garden:

an experiment where genotypes from different populations are grown under a common environment to test the relative contributions of genetic and environmental variation on phenotypic traits using quantitative genetics

disconnected from its historic environment. Traditionally, evolutionary ecologists have focused on testing for and quantifying local adaptation using reciprocal transplant experiments, in which individuals from multiple locations are transplanted into both home and away environments, and fitness, or some proxy, is quantified (Blanquart et al. 2013, Kawecki & Ebert 2004). In a metapopulation of locally adapted demes, we should observe a home-site advantage for each deme (Kawecki & Ebert 2004). Field experiments confirm that local adaptation of climate-responsive phenotypes is common in nature (Figure 2); two separate meta-analyses of reciprocal transplant studies found evidence for local adaptation in greater than 70% of cases (Hereford 2009, Leimu & Fischer 2008). Common garden experiments comparing the fitness of individuals from different populations experiencing the same developmental environment also provide valuable insights

into the fitness-environment relationship without explicitly testing for home-site advantage (De Villemereuil et al. 2016). Because local adaptation across spatially heterogeneous environments results in a type of spatially varying balancing selection, it helps maintain standing genetic variation that can form the basis of an evolutionary response to rapid environmental change (Aitken et al. 2008, Barrett & Schluter 2008).

Although the concept of local maladaptation may have previously been seen as simply an obvious flip side of local adaptation, recent perspectives highlight the value of studying maladaptation directly, especially in the context of rapid environmental change (Brady et al. 2019a). In part, the need to study maladaptation stems from the fact that evolutionary biologists have historically focused on relative fitness to quantify adaptation. However, in conservation applications, one is often concerned with the potential for population decline, so the ability to integrate measures of absolute fitness becomes important (Derry et al. 2019). Although maladaptation can have many formulations, here we define local maladaptation in the context of an adaptive landscape in which a focal population experiences suboptimal fitness, quantified as the distance in genotypic or phenotypic space between the population's current position within the adaptive landscape and its local fitness optimum (Brady et al. 2019b, Rehfeldt et al. 2002). Under rapid climate change, we expect maladaptation to primarily occur due to a change in the environment (i.e., the moving target scenario depicted in Brady et al. 2019a, figure 2) that causes populations to become distanced from local fitness optima.

From a genomic perspective, local adaptation should occur when a population has a genome-wide complement of available alleles that maximizes fitness in the local environment (Savolainen et al. 2013). Maladaptation therefore occurs when fitness is reduced below the optimum for a particular environment, given the range of adaptive or conditionally adaptive alleles present within the species (Rehfeldt et al. 2002). The availability of dense population-level genomic data sets offers a new lens through which to view the genetic basis of local adaptation (Berg & Coop 2014, Tiffin & Ross-Ibarra 2014, Tigano & Friesen 2016) and the spatial distribution of adaptive alleles in natural landscapes (Hoban et al. 2016). Like evolutionary ecology studies, ecological genomics has primarily focused on identifying local adaptation (Savolainen et al. 2013, Vitti et al. 2013), and few studies have specifically investigated the other side of the coin (i.e., local maladaptation). The rationale behind applying genomic data to the study of maladaptation is straightforward. That is, if a genome scan for selection effectively captures a signal of local adaptation, then it should also be informative on the potential for maladaptation if the associations between adaptive allele frequencies and their environments are disrupted. To emphasize this point, we hereafter refer to the reciprocal concepts of adaptation and maladaptation using the notation (mal)adaptation.

Landscape genetics:
the study of the
processes shaping the
spatial distribution of
genetic variation
across a geographic
landscape

2.3. Why Attempt to Predict Genomic (Mal)Adaptation to Climate?

An early emphasis of the field of landscape genetics (later landscape genomics) was understanding the distribution of selectively neutral genetic variation across species ranges (Manel et al. 2003). Attention has since shifted to the study of associations between genetic, phenotypic, and climatic variation and to the identification of the functional genetic components underlying species adaptation along environmental gradients (De Kort et al. 2014, Rellstab et al. 2016, Steane et al. 2014). This led naturally to studies aimed at incorporating the effect and distribution of alleles associated with adaptive traits into predictive models (Alberto et al. 2013b, Jay et al. 2012).

More recently, a primary motivation behind predicting the genomic basis of climate adaptation has been to better evaluate the exposure of natural populations to climate change effects. First, by incorporating information on intraspecific adaptive variation, model predictions can be weighted as a function of the magnitude of genetic change and/or allele migration within the species range

(Capblancq et al. 2020, Gougherty et al. 2020, Rellstab et al. 2016). Knowing the distribution of adaptive alleles and their effect on population fitness would allow more refined predictions of species distributions, both now and under future climates. Second, spatially explicit predictions of patterns of climate (mal)adaptation can help highlight the relative vulnerability of populations to climate change (Bay et al. 2018, Fitzpatrick & Keller 2015, Gougherty et al. 2020, Martins et al. 2018, Supple et al. 2018), which may serve to guide conservation policies. Finally, predicting the overall fitness of individuals in a particular environment based on their genotypes could help inform a number of applications, from agriculture to conservation. For example, environment-based predictions of growth or productivity could predict which genotypes will provide the best crop yields under a targeted planting environment (agriculture) or which natural populations would require long-distance dispersal to reach areas of suitable climate in the future and would therefore benefit from assisted migration (conservation) (Aitken & Bemmels 2016, Aitken & Whitlock 2013, Gougherty et al. 2020, Hohenlohe et al. 2011, Keller et al. 2018, Steane et al. 2014, Supple et al. 2018).

3. IN PRACTICE: USING GENOMIC DATA TO PREDICT CLIMATE (MAL)ADAPTATION

Using genomic data to predict (mal)adaptation of populations as a result of climate change requires first identifying the population-level genetic associations underlying local adaptation to climate across landscapes and then using these associations to predict the outcome if individuals or populations were transferred to a new climate, either in space or through time. The process might reasonably be divided into an initial discovery phase, predicated on careful identification of genomic signals of climate adaptation, and a follow-up prediction phase, focused on interpolating or extrapolating the identified gene-climate associations to geographically unstudied areas or future climates to understand relative changes in (mal)adaptation (**Figure 1**).

3.1. Discovering the Genomic Variation Associated with Adaptation to Climate

The discovery phase requires sampling individuals from multiple populations distributed along the climatic gradients of interest and using dense genome-wide sequencing or genotyping to sample single nucleotide polymorphisms (SNPs) across the genome of each individual or pool of individuals. It is important to obtain a sufficient density of SNPs, relative to the extent of linkage disequilibrium in the genome, so as to have good statistical power to detect loci involved in local adaptation either directly or through indirect signals in neutral variants located near a causal one (hitchhiking selection) (Lowry et al. 2017, Tiffin & Ross-Ibarra 2014). These SNPs are then used in genome scan analyses to identify the genomic signatures left by spatially varying local selection.

Several approaches exist to identify genomic regions associated with local adaptation to climate, differing principally in whether they focus directly on association with a phenotype of interest or instead on nonrandom patterns of population divergence along spatial or environmental gradients. When researchers have prior knowledge of potential physiological, morphological, or behavioral mechanisms underlying climate adaptation (**Figure 2**), the combination of phenotypes measured under common garden environments along with genomic data on the same individuals can be used to identify SNPs associated with climate adaptive traits. Because there may not be much a priori knowledge of the specific genes or regulatory sequences underlying these phenotypes, another approach is to search for causal variants using genome-wide association studies (GWAS) to test each SNP for association with trait variation. A related approach, using

Genome-wide association studies (GWAS): studies that use a variety of statistical procedures aiming to identify associations between genetic data and phenotypic traits

genotype-environment associations (GEAs), tests for association between SNPs and climate variables measured where the sampled individuals were collected. Other approaches do not rely on a genetic association with phenotype or environment and instead assess locus-specific signals of local selection in the form of elevated allele frequency divergence (F_{ST}) across populations or skewed allele frequencies in a genomic window within populations (selective sweeps) (Jones et al. 2012, Nielsen et al. 2005, Sabeti et al. 2002). Although these genome scan approaches for local adaptation are not without issues (Hoban et al. 2016), they have helped identify promising genes and genomic regions involved in local adaptation across contemporary climate gradients (Franks & Hoffmann 2012, Hancock et al. 2011, Prunier et al. 2011, Sork et al. 2016).

Identifying the genetic basis of local adaptation is a burgeoning field within ecological and population genomics, and a rich body of theory, statistical tests, simulation testing, and empirical work has begun to emerge (Lotterhos & Whitlock 2015). It is beyond the scope of this review to discuss in detail the various association methods that can be used to discover local adaptation in genomic data (introduced in Section 2.3), and we refer interested readers to several excellent reviews on the subject (Forester et al. 2016, François et al. 2016, Hoban et al. 2016, Josephs et al. 2019, Rellstab et al. 2015, Santure & Garant 2018, Tiffin & Ross-Ibarra 2014). Rather, we focus our discussion here on when one might prefer to perform GWAS versus GEA, selective sweep, or F_{ST} studies to investigate climate adaptation and on the potential for using candidate loci identified in these studies to make predictions about the stability of gene-climate associations under environmental change.

An essential consideration when identifying adaptive genomic variation is whether to focus on finding the genetic basis of climate-adaptive phenotypes (using GWAS) or instead on identifying selection-shaping allele frequencies along climatic gradients (using GEA, selective sweep, or F_{ST} studies) (Hoban et al. 2016). GWAS are intended to identify loci associated with a particular phenotypic trait, which in the case of climate adaptation could be a physiological, morphological, phenological, or life history trait relevant to the ecology of the organism being studied. This emphasis on phenotypes is appealing since it provides a potentially more direct view of the target of selection and uses an investigator's a priori knowledge of the traits most important to climate adaptation in the study species (**Figure 2**). However, GWAS may be less insightful in the absence of this a priori knowledge, or when expression of the trait under selection occurs at developmental stages or in environments, in the case of genotype-by-environment ($G \times E$) interaction, that make measuring the phenotype difficult. The issue of developmental timing is especially challenging for long-lived organisms, for which the effects of selection on suites of fitness traits may be integrated over decades or even centuries, given that most common garden studies will be restricted to early life history traits.

An alternative is to use tests for GEAs, selective sweeps, or F_{ST} outliers, which are phenotype-free approaches that identify candidate genomic regions whose allelic variation is inferred to have a relationship to fitness that varies spatially or along an environmental gradient. Since these methods are essentially agnostic to phenotype, they do not require choices regarding which traits to measure and in which developmental stages or environments. Consequently, these tests may be more informative than GWAS for species that are long lived or have complex life histories or where the phenotypes under climate selection are not well known. With GEA studies, the emphasis is instead placed on choosing a suite of climate variables that capture the most important drivers of selection at the appropriate spatial and temporal scales. Choosing relevant climatic variables, given the life histories of the organisms, can also be a challenge. For example, while for trees the magnitude and duration of extreme climate events (e.g., heat waves, droughts) may be important drivers of selection, for an annual plant, the timing of precipitation during the growing season might be more important. Including climatic predictors that effectively capture the likely drivers

Genotype-environment association (GEA): a landscape genetics test for an association between genetic data and source environmental variables that can be used to identify adaptive loci under environmental selection

of selection is therefore key, but as more predictors are considered in univariate GEA models, the problem of multiple testing increases. Recent applications using multivariate GEAs offer promising solutions to this problem (reviewed in Forester et al. 2018) and also apply to GWAS analyses involving multiple correlated phenotypes (Zhou & Stephens 2014).

3.2. Predicting the Genomic (Mal)Adaptation of Populations

Once candidate loci or genomic regions for climate adaptation have been identified, it is statistically possible to generalize the genetic-environment relationship across the landscape using raster climate maps and thereby investigate the spatial pattern of (mal)adaptation in the prediction phase (**Figure 1**). The original use of genomic prediction (also known as genomic selection) was pioneered by molecular quantitative geneticists aiming to accelerate plant and animal breeding. Genomic prediction of quantitative traits from SNP data estimates genomic-enabled breeding values (GEBVs), either by summing the pre-estimated marginal associations of many loci on a trait (the sum is sometimes also called a polygenic risk score) or by modeling the overall random effect values of individuals whose genomes are nonindependent (i.e., a relatedness or kinship covariance matrix is inferred from genome-wide SNP similarities) (de los Campos et al. 2013). Recently, application of GEBVs has moved beyond breeding to the study of ecologically relevant adaptive traits or climate sensitivities in natural populations (Gienapp et al. 2019). In the context of genomic prediction of climate (mal)adaptation, GEBVs can be used to capture associations between genomic variation and functional responses (phenotypes and/or local fitness in a given environment) and generate predictions of individual or population performance under alternative climate scenarios (Browne et al. 2019).

Genomic (mal)adaptation to climate could also be predicted using GWAS or GEA studies in which the genome-wide association between genotypes or allele frequencies with phenotypes or climate is estimated in a training sample and then projected to a new set of genotypes or climate data. The resulting predictions can then be validated with an independent testing population. This enables the population-level adaptive genetic composition across the landscape to be predicted as a composite frequency turnover of many adaptive allele frequencies (Bay et al. 2018, Capblancq et al. 2020, Fitzpatrick & Keller 2015, Jaramillo-Correa et al. 2015, Martins et al. 2018, Steane et al. 2014) or allele counts (Exposito-Alonso et al. 2018) and eventually allows the potential for genomic (mal)adaptation of populations under environmental change to be investigated.

When focusing on current climate conditions, modeling the spatial distribution (or turnover) of adaptive alleles along climatic gradients can provide a continuous prediction of allele frequencies at climate-adaptive loci across a species range, including extrapolation to areas where climate data are available but no individuals or populations have been genotyped. These results can be used to estimate the mismatch (i.e., the residual) between the modeled and observed genetic makeup of a focal population, which could serve as an index of its maladaptation (Aitken et al. 2008, Rehfeldt et al. 2002), sometimes also called its nonadaptedness (Rellstab et al. 2016). Patterns of maladaptation could represent adaptation lags resulting from a failure of populations to migrate (Svenning & Skov 2007) or adapt fast enough to historical changes in climate (Aitken et al. 2008). Estimating the degree of (mal)adaptation of focal genotypes transferred outside their home climate could also be useful for planning restoration genetics, predicting invasive species success, or optimizing agricultural yield (Steane et al. 2014). In addition to predicting (mal)adaptation resulting from translocations in space, predictions can also be made using analogous transfer distance through time to estimate the potential impact of future climate change (**Figure 1**).

At a locus-specific scale, SDMs have been used to estimate future (mal)adaptation by predicting the distribution of alleles within the species range under future climates (Exposito-Alonso

et al. 2018, Rellstab et al. 2016). By looking at the difference in predicted allele probabilities (frequencies) between the current and future climatic conditions, Rellstab et al. (2016) showed that it is possible to estimate a risk of nonadaptedness (RONA). When performed for many adaptive alleles, an estimate of the number of alleles that must arrive into the population to adapt to climate change in the coming decades can be obtained (Exposito-Alonso et al. 2018). However, a major constraint is that, to capture polygenic effects, SDM-based approaches that model one locus at a time need to be fitted iteratively and the predictions summed, a cumbersome and computationally demanding approach. Furthermore, these combined predictions would not account for the interactive effects of loci contributing to climate adaptation.

An alternative is to create a composite frequency turnover of many genome-wide alleles along climate gradients, enabling the difference in genomic composition between current and future climates to be estimated for all loci en masse (Fitzpatrick & Keller 2015). One such method consists of fitting a statistical model using the observed spatial pattern of genomic variation across multiple outlier loci in local adaptation scans and then projecting this model over time to estimate changes in the optimal genetic composition for any given population-environment combination between current and future climatic conditions (**Figure 1; Table 1**). This predicted difference in the genetic composition of populations, which Fitzpatrick & Keller (2015) termed genetic offset, corresponds to the change in genetic composition required to maintain the existing gene-environment relationships observed under current environmental conditions (**Figure 3**). Genetic

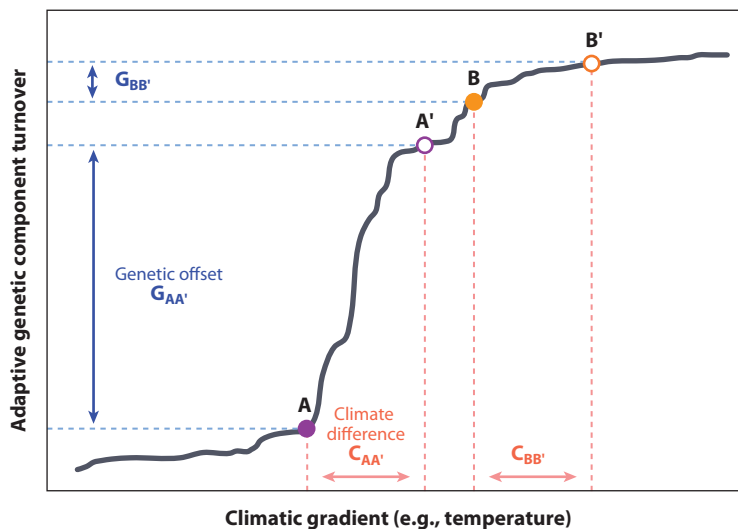


Figure 3

An illustration of the concept of genetic offset based on turnover of the estimated adaptive genetic component (e.g., the cumulative, monotonic increase in allele frequency differences or population differentiation, F_{ST}) along one or more climatic gradients. A shift along the climate gradient (for example, from low to high temperature) can be due to a spatial transfer of individuals on the climatic landscape or to a temporal (i.e., past or future) change in climatic conditions for a focal location. The climatic difference is associated with a corresponding shift in the adaptive genetic component, the magnitude of which is quantified by the genetic offset. For example, a change from A to A' on the climatic gradient occurs in a region of high turnover in the adaptive genetic component, producing a large predicted genetic offset ($G_{AA'}$), whereas the same change of climate between B and B' produces a smaller predicted genetic offset ($G_{BB'}$). This highlights intraspecific variability in the potential impact of climate change on locally adapted populations. Figure adapted from Fitzpatrick & Keller (2015).

offset is a metric of maladaptation and is similar to the RONA concept detailed above, with the primary difference being that genetic offset reflects a large number of loci simultaneously in an attempt to model the composite effects of many putatively adaptive candidate loci, whereas RONA is estimated at the level of a single locus (Pina-Martins et al. 2019).

Model fitting involves characterizing turnover functions, i.e., the turnover of the identified adaptive alleles along environmental gradient(s) (Fitzpatrick & Keller 2015), and it is these turnover functions that are used to predict the expected genetic composition for a given set of current and/or future climatic conditions. Recent studies aiming to predict future genomic (mal)adaptation of populations have mostly used a method called gradient forest (GF) (Ellis et al. 2012) that is commonly used in community ecology to model species turnover (Bay et al. 2018, Fitzpatrick & Keller 2015, Ingvarsson & Bernhardtsson 2018, Martins et al. 2018, Ruegg et al. 2018). This method, originally developed to model spatial variation in community composition, was first used on SNP data by Fitzpatrick & Keller (2015) 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 (Figure 4). GF is an extension of the random forest

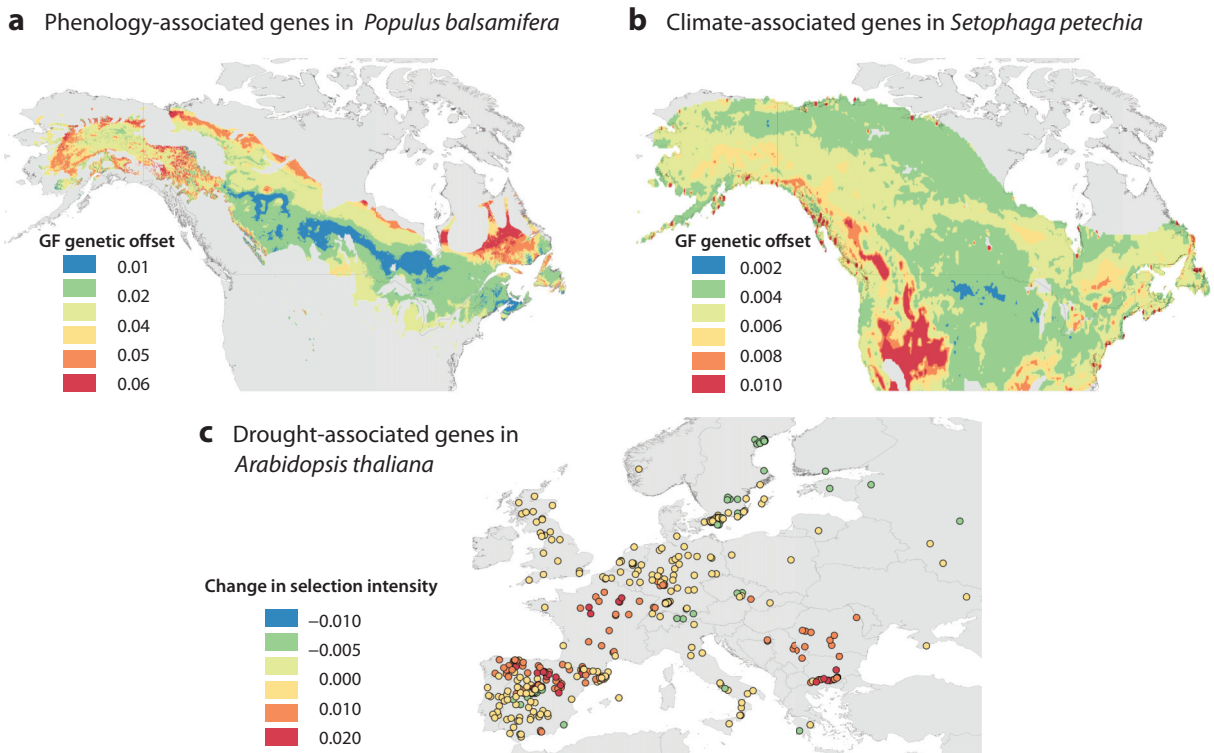


Figure 4

Predicted genetic offset for loci involved in (a) locally adaptive phenology in populations of *Populus balsamifera* in North America; (b) climate adaptation of *Setophaga petechia* populations in North America; and (c) future change in selection on drought-associated genes in *Arabidopsis thaliana* populations in Europe. For *P. balsamifera* and *S. petechia*, values represent the genetic offset quantified as the change in cumulative importance of gradient forest (GF) models between current and future climates. For *A. thaliana*, values represent the predicted changes in selection intensity under future climates based on a genome-wide environment selection model. Panel a adapted from Fitzpatrick & Keller (2015), panel b adapted from Bay et al. (2018), and panel c adapted from Exposito-Alonso et al. (2019).

machine learning approach that uses regression trees to fit a model of associations between individual response variables (e.g., individual loci) to a multivariate set of predictors (e.g., climate variables). GF uses site-wise climatic data to explain changes in population allele frequencies for the set of adaptive loci (determined in the discovery phase of a study) by fitting a model that iteratively splits populations into groups along values of the environmental gradients that best explain their allele frequency differences. The cumulative sum of the resulting split importance values is used to construct a turnover function for each locus; these functions are then combined based on their weighted importance (e.g., allele frequency variance explained) to produce a composite turnover function for the entire sample (see Ellis et al. 2012 and Fitzpatrick & Keller 2015 for additional details). Once trained, GF models can be used to create continuous predictions of allelic turnover across a species range and, when projected in time to a future set of climatic conditions, to estimate the mismatch between current and future allelic turnover as a proxy of future population maladaptation (i.e., genetic offset). The projections are often visualized as landscape maps of genetic offset to highlight regions where the climate is predicted to disrupt local adaptation most severely (Bay et al. 2018, Fitzpatrick & Keller 2015, Ingvarsson & Bernhardtsson 2018, Martins et al. 2018, Ruegg et al. 2018). Redundancy analysis (RDA) has also been used to produce spatial extrapolations of intraspecific adaptive genetic variation (Steane et al. 2014), predict adaptive genotypes for reforestation sites (Carvalho et al. 2019), and spatially predict a genetic offset associated with climate change (Capblancq et al. 2020). RDA has the advantage of decomposing the genetic-environment relationship into orthogonal axes that identify different patterns of gene-environment covariation (Capblancq et al. 2018, De Kort et al. 2014, Forester et al. 2018). Another new method called spatial areas of genotype probability (SPAG) uses multivariate logistic regressions to compare the adaptive landscape under current and future climatic conditions (e.g., Rochat & Joost 2019). We anticipate that the general approach of modeling spatial turnover in adaptive alleles and comparing turnover functions between sets of current and future (or past) environments will be an active area of research and method development.

A related approach estimates the disruption of local adaptation by predicting genetic differentiation (F_{ST}) between current and future populations as a function of the environmental distance between current and future climatic conditions (Fitzpatrick & Keller 2015, Ingvarsson & Bernhardtsson 2018, Supple et al. 2018). This is the approach used in generalized dissimilarity modeling (GDM), the second community-level modeling (Ferrier & Guisan 2006) method adapted by Fitzpatrick & Keller 2015 to extrapolate genetic-environment relationships. GDM fits a nonlinear relationship between geographical, environmental, and genetic distances; the response variable is a matrix of pairwise F_{ST} values among populations, averaged for a set of adaptive loci (ascertained in the discovery phase of study), while the explanatory variables are matrices of environmental (e.g., climatic) distances among sites and optionally other matrices that describe potential confounding effects (e.g., a matrix of geographic or cost distances). The resulting model relates pairwise genetic distances among populations to their multivariate environmental distances. Once the initial model is fit, GDM can then be used to predict pairwise F_{ST} values between any pair of locations in space or time, using the same set of environmental variables used in initial model fitting. The predicted F_{ST} provides an estimate of genetic offset, formulated as the expected divergence in allele frequencies (F_{ST}) at adaptive loci due to the difference in climatic conditions between two places or times (e.g., current versus future climates).

The above approaches all rely on the assumption that alleles found in a given environment must provide some adaptive advantage under that environment, without considering phenotypes or directly measuring individual fitness. Using an alternative approach to model fitness explicitly, Exposito-Alonso and colleagues (2019) used a multi-environment GWAS to predict the change in selection intensity and direction (i.e., relative fitness changes) in *Arabidopsis thaliana* associated

with climate change (**Figure 4c**). That is, they estimated the fitness effects of alleles in a given environment rather than predicting whether such alleles would be present or absent. To do that, they first used common garden experiments to estimate the influence of each allele on plant fitness depending on the environment (the allelic selection differential). Then they studied whether the association of an allele with the environment of origin could explain the empirically measured fitness effects at two field sites along an environmental gradient. Finally, they trained a random forest model to predict locus-specific relative fitness from a matrix of per-allele climate associations. This approach, named genome-wide environment selection (GWES) modeling by the authors, allows the direct prediction of the mean change across loci in the selection intensity or direction caused by a change in climatic environment. Spatial projection allows the visualization of where selection will be the most perturbed by climate change across the species range (**Figure 4**).

3.3. Validating Predictions of (Mal)Adaptation

The genomic predictions of (mal)adaptation to climate described above are based on a statistical simplification of genetic-environment relationships and so must be viewed cautiously as model predictions in need of experimental validation. As such, any use of these methods should consider several key assumptions that underlie the different approaches described above for predicting short-term climate (mal)adaptation: (*a*) The adaptive genetic component has been correctly identified and included in the prediction model, (*b*) the magnitude of genetic offset (or change in selection intensity) is proportional to the expected decrease in fitness, (*c*) the genetic-environment relationship identified reflects the current optima between the standing genetic variation and the available set of climatic conditions, and (*d*) the current GEAs can be used to predict the (mal)adaptation response to a change in climate across time [e.g., a space-for-time substitution (Blois et al. 2013)]. Promising approaches to validate these assumptions and the accuracy of the resulting predictions include controlled experiments on living organisms (common gardens), simulation studies (experiments in silico), and observational studies (historical records).

Confirming that the identified loci (see Section 3.1) are really involved in local adaptation (assumption *a*) is a concern of many studies using GWAS or GEA methods to find candidate genes (Ioannidis et al. 2009, Oetting et al. 2018). It can be done by adding several layers of corroborating evidence, for example, by verifying the initial genotype-phenotype association or GEA with data from independent samples (Bay et al. 2018) or testing whether the same set of climatic variables identified in GEA is important for shaping clines in fitness in common gardens or provenance tests (Aitken et al. 2008, De Kort et al. 2014, Mahony et al. 2020, Rehfeldt et al. 2002, Steane et al. 2014). More direct experimental support can be garnered by growing genotypes containing the putatively adaptive alleles under controlled conditions (Exposito-Alonso et al. 2019, Yoder et al. 2014) or by functionally validating phenotypic effects through genetic transformation of candidate loci into specific mutant backgrounds, gene editing of putatively causal sites, or knocking back expression of candidate genes (Curtin et al. 2017, Monroe et al. 2018, Rohde et al. 2018).

The assumption of equilibrium between current allele frequencies and climate conditions (assumption *b*) is implicit in all GEA tests yet rarely discussed (but see Lasky et al. 2018). This equilibrium assumption could be tested indirectly by asking whether phenotypic adaptation (i.e., fitness) is maximal when genotypes experience climates most similar to their collection site and decreases upon transfer to a climatically dissimilar environment. Such adaptational lags may be caused by insufficient dispersal in response to historical climate change (Browne et al. 2019). Using common gardens with broadly distributed *A. thaliana* ecotypes, Exposito-Alonso et al. (2019) found that alleles from environments close to those experienced at the common garden sites tended to display higher relative fitness, although the relationship was complex and often genotypes from faraway regions had the highest performance. This finding mirrors that of Fournier-Level et al. (2011).

If assumption *b* is correct, it is then critical to validate the relationship between genetic offset and the predicted decrease in fitness (assumption *c*) to evaluate whether the model is indeed informative in the face of demographic complexity (i.e., the effects of other processes on spatial variance in allele frequencies, such as expansion history and gene flow) as well as the genetic architecture of climate adaptation (polygenic trait architectures, G×E interactions, nonadditive genetic variance). Formal tests linking genetic offset with observed losses in fitness (or population declines) are needed to provide a rigorous validation of the predictions. Bay et al. (2018) took an initial step in this direction by associating genetic offset with spatial extrapolations of historic population trends for the yellow warbler (*Setophaga petechia*). They found a correlation between the mapped patterns of population decline (based on the North American Breeding Bird Survey) and predicted genetic offset under future climate conditions; this correlation could indicate that yellow warbler populations may already be declining due to a failure to adapt to climate change. Common gardens or controlled environment experiments could also be used for this purpose under the assumption that climate change is equivalent to an environmental transfer distance (Exposito-Alonso et al. 2019, Jaramillo-Correa et al. 2015, Lasky et al. 2018). The use of historical collections (Lang et al. 2019) or even resurrection studies (Etterson et al. 2016) using seed banks could also provide interesting possibilities for validating the (mal)adaptation predictions based on the genetic offset between historical and contemporary climates.

A great deal of uncertainty exists surrounding the climatic conditions populations will encounter in the future and how current adaptive genetic variation may recombine into novel genotypic combinations (assumption *d*). One major source of uncertainty is the variation in climate forecasts among different general circulation models (GCMs). These uncertainties can and should be integrated into the genomic prediction approach, for example, through the use of ensemble modeling based on multiple GCMs (Forester et al. 2013, Gougherty et al. 2020).

General circulation model (GCM):

a numerical model of the physical processes in the atmosphere, ocean, and land surface used for simulating future climates based on estimation of greenhouse gas emissions

4. FUTURE DIRECTIONS AND CHALLENGES FOR GENOMIC PREDICTION OF (MAL)ADAPTATION UNDER CLIMATE CHANGE

4.1. Toward Integrating the Relative Importance of Different Short-Term Responses to Climate (Mal)Adaptation

Standing (i.e., pre-existing) genetic variation is not the only factor that determines population persistence, and future efforts should focus on integrating genomic prediction models with other ecological and physiological processes and data sources. For example, individuals might tolerate exposure to rapidly changing environments through physiological plasticity. In many species, exposure to sublethal environmental change can decrease the magnitude of the response to more extreme subsequent stressors (Somero 2010, Stillman 2003). Thus, plasticity could help mitigate maladaptation predicted by genetic offset, potentially allowing population persistence until an adaptive response is possible (Chevin et al. 2010, Price et al. 2003). Measuring plasticity under multiple relevant climatic environments and combining organismal data (morphology, physiology, etc.) with variation at the transcriptomic and epigenomic levels could prove a more nuanced view of vulnerability to climate (mal)adaptation that could improve predictions based on genetic offset alone.

While current methods of genome-informed prediction of climate (mal)adaptation focus primarily on the match between standing genetic variation and future environments, there are in fact multiple potential sources of new adaptive variation. Standing genetic variation is the most likely source of adaptation in the short term (Barrett & Schluter 2008), but beneficial mutations can arise, especially in organisms with very large population sizes and short generation times. In addition, gene flow among populations could act to redistribute the spatial arrangement of genetic

variation within the landscape. Gene flow could have either positive or negative consequences for population persistence under environmental change, either by redistributing climate-adaptive alleles to areas where they maintain high fitness or by swamping existing populations through the immigration of climate maladaptive alleles (Lenormand 2002). Estimates of migration distances for climate adaptive alleles could add to our understanding of the potential for standing genetic variation to mitigate genetic offset (Capblancq et al. 2020, Gougherty et al. 2020).

In addition, climate change and other anthropogenic factors might alter rates of secondary contact between species (Bleeker & Hurka 2001, Harbicht et al. 2014, Seehausen et al. 1997), increasing the potential for hybridization and introgression. Adaptive introgression has the potential to produce novel allelic combinations that may be adaptive under changing environments (Grant & Grant 2016, Grant et al. 2004). A clear example of this is brown coat color in snowshoe hares, a phenotype that is beneficial in regions with decreased snowpack. The genetic variant encoding this beneficial phenotype originated through introgression from jackrabbits (Jones et al. 2018). In this case, introgression of the brown allele into snowshoe hares was adaptive under climate change conditions that otherwise led to decreased crypsis.

4.2. The Role of Future Novelty in Climate, Genotypes, and Biotic Interactions in Genomic Prediction of (Mal)Adaptation

Among quantitative geneticists using genomic prediction of phenotypes, there is common agreement that accurate predictions are dependent on using samples with similar relatedness or ancestry structure and growing in conditions similar to those used when developing the model (e.g., Resende et al. 2012). This expected dependence of prediction accuracy on relatedness and environmental similarity between training and testing populations is also likely to affect studies predicting genomic (mal)adaptation of natural populations under novel climates.

Novel environments are expected to be widespread in some regions under future climate conditions (Williams et al. 2007). Climate-analog mapping studies suggest the future formation of seasonal patterns of temperature and precipitation that do not currently exist, known as no-analog climates (Fitzpatrick et al. 2018a, Williams & Jackson 2007). No-analog climates are known to have also existed in the recent geologic past (Veloz et al. 2012), but how these environments will interact with standing genetic variation is unknown. Even if analogous climates exist between current and future conditions, the range that populations of a species occupy along a current climatic gradient may become extended to more extreme portions of the gradient in the future. This could potentially result in dramatic changes in the shape and direction of the functional form of the fitness response to the environment (**Figure 5**) and bias any extrapolation based on current genetic-environment relationships. Prediction of climate (mal)adaptation into regions where genetic ancestry or climatic environments are beyond the range used to train the model could therefore lead to poor prediction accuracy.

In addition, future changes in the abiotic climatic environment will surely induce changes in biotic interactions such as competition, predation, herbivory, disease, and symbiosis (Blois et al. 2013). The effect of changed biotic interactions under future environments may be an especially important influence contributing to maladaptation of populations by altering the relative fitness of climate-selected alleles in the presence of interacting species (Benning & Moeller 2019). For example, a recent modeling paper demonstrated that under the warmer temperatures expected in future climates, insect crop pests will experience accelerated metabolism and increased population growth, leading to greater loss of crop yields than predicted under climate losses alone (Deutsch et al. 2018). Biotic interactions may also weaken the accuracy of genomic predictions if the genetic architecture of climate adaptation contains genes exhibiting pleiotropic responses to both

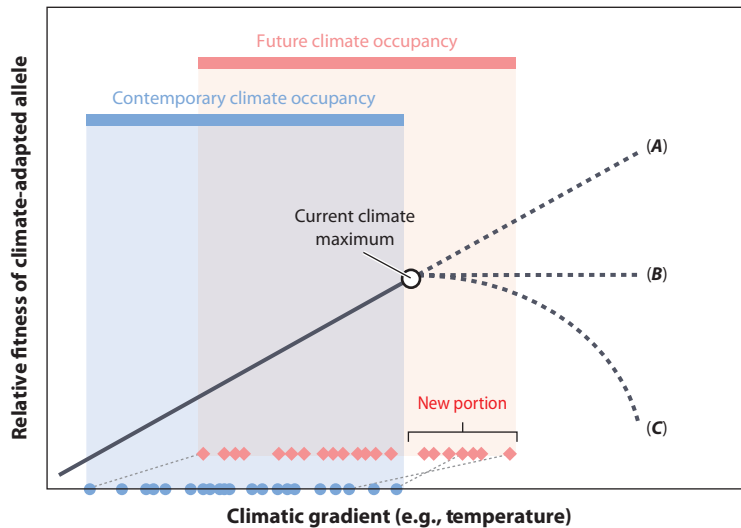


Figure 5

Unsampled gene-environment associations under novel climates may hamper genomic prediction. Genomic prediction into new environments may involve climate values beyond the occupancy of contemporary populations used to train the model (*blue circles*). Some populations are predicted to occupy new portions of the climate gradient beyond the contemporary range (*red diamonds* on the right of the current climate maximum). This may generate biased or misleading predictions if the fitness function underlying the gene-climate association differs between contemporary (*solid line*) and future portions of the climate gradient (*dashed lines*). Different modeling approaches may vary in the assumptions made when predicting climate (mal)adaptation under novel climates, including (A) linear extrapolation or (B) no change in relative fitness, leading to biased and inaccurate predictions of climate adaptation when the true fitness function (C) departs from the model extrapolation.

abiotic and biotic stress. One such example involves the plant circadian clock, which controls multiple aspects of the timing of growth and reproduction through diurnal and seasonal regulation of gene expression. While clock genes regulate responses to photoperiod, temperature, and osmotic stress, they also respond to biotic stress through temporal regulation of inducible defense genes (Greenham & McClung 2015). Genomic prediction of (mal)adaptation under future climates is therefore likely to be impacted by both novel abiotic conditions and novel biotic interactions that those new environments might induce.

Quantifying these uncertainties and integrating them into our confidence in the predictions of climate (mal)adaptation should be a priority for future work. We see several opportunities to help address these challenges, such as (a) simulation testing, (b) mapping regions of predicted gene-climate novelty, and (c) experimental quantification of climate (mal)adaptation under extreme or novel environments.

First, a potentially powerful way to assess the sensitivity of genomic predictions to different genetic architectures or extrapolation into novel climate space is through the use of spatially explicit genetic simulations. Testing the response of simulated populations to (mal)adaptation under novel and shifting climates, including simulation of conditions beyond the historic range of values, can be a useful approach to probe the limitations of genomic methods to predict climate (mal)adaptation and their associated uncertainties. While simulations have been useful for highlighting issues that arise when trying to identify the genetic basis of local adaptation (e.g., Lotterhos & Whitlock 2014), there is a need for simulations testing the methods for genetic offset

prediction discussed here under a range of demographic, genetic, and climate change scenarios. It could be especially informative to test how different methods for offset prediction (GF, GDM, RDA, etc.) behave given different possible shapes of the fitness functions under future climatic conditions (**Figure 5**). Ultimately, simulating scenarios where gene flow is possible among populations could also provide an idea of the magnitude of genetic migration required to avoid the predicted genetic offset.

Second, identifying regions of the landscape most likely to experience novel gene-environment associations due to no-analog climates is a first step toward assessing the importance of this issue. For example, Gougherty et al. (2020) used GDM to define and quantify a reverse genetic offset. The reverse genetic offset is the minimum genetic offset between a focal population under future climatic conditions and all possible locations within the range under current climate conditions. In other words, this approach asks the question, “Is there a location (population) within the current range of the species that harbors gene-environment associations similar to those expected at a focal location under future climate?” Regions that show the greatest reverse offset could help guide predictions of where we might expect changes along existing gradients of genotype-climate associations rather than the emergence of novel associations outside of those observed among contemporary populations.

Finally, in line with the importance of validating genomic predictions, common garden experiments or controlled environment tests of genotyped individuals measured for fitness (or its proxies) could be extended to measure the response of individuals to extreme or novel climate conditions. Such experimental manipulations are already part of many common garden experiments in which additional climate manipulations are added to simulate future conditions. Recent examples include treatments that increased temperatures via infrared heaters (Reich et al. 2018), lowered soil moisture and increased drought through rainfall exclusion (Exposito-Alonso et al. 2019), or decreased snowpack through snow removal (Anderson & Wadgymar 2020). Similarly, the effect of novel biotic interactions on genomic predictions of climate (mal)adaptation could be assessed by subjecting genotyped test populations to common gardens with either spatial or temporal manipulations of the interacting species (e.g., Morton & Rafferty 2017).

5. CONCLUSION

Using genomic data to predict the future climate (mal)adaptation of populations is a rapidly evolving field of research that has provided a different perspective for ecologists and evolutionary biologists working to understand the role of intraspecific genetic variation on species responses to climate change. However, efforts at genomic prediction of climate (mal)adaptation are still in their infancy and face numerous challenges and uncertainties that have not yet been fully investigated. Future studies will need to move toward not only estimating but also validating predictions in complex and natural landscapes. Testing the modeling procedures and their assumptions will hopefully help improve the accuracy of predictions while also taking into account the uncertainty in climate forecasts, the presence of no-analog climates, the importance of plastic responses, and even the potential impact of admixture or hybridization among species. The recent increase in the number of studies exploring such concepts will undoubtedly broaden and help refine the statistical approaches employed and provide more empirical examples from increasingly diverse taxa.

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LITERATURE CITED

- Aguirre-Liguori JA, Ramírez-Barahona S, Tiffin P, Eguiarte LE. 2019. Climate change is predicted to disrupt patterns of local adaptation in wild and cultivated maize. *Proc. R. Soc. B* 286:20190486. <http://doi.org/10.1098/rspb.2019.0486>
- Aitken SN, Bemmels JB. 2016. Time to get moving: assisted gene flow of forest trees. *Evol. Appl.* 9(1):271–90. <https://doi.org/10.1111/eva.12293>
- Aitken SN, Whitlock MC. 2013. Assisted gene flow to facilitate local adaptation to climate change. *Annu. Rev. Ecol. Evol. Syst.* 44:367–88. <https://doi.org/10.1146/annurev-ecolsys-110512-135747>
- Aitken SN, Yeaman S, Holliday JA, Wang T, Curtis-McLane S. 2008. Adaptation, migration or extirpation: climate change outcomes for tree populations. *Evol. Appl.* 1(1):95–111. <https://doi.org/10.1111/j.1752-4571.2007.00013.x>
- Alberto FJ, Aitken SN, Alía R, González-Martínez SC, et al. 2013a. Potential for evolutionary responses to climate change—evidence from tree populations. *Glob. Change Biol.* 19(6):1645–61. <https://doi.org/10.1111/gcb.12181>
- Alberto FJ, Derory J, Boury C, Frigerio JM, Zimmermann NE, Kremer A. 2013b. Imprints of natural selection along environmental gradients in phenology-related genes of *Quercus petraea*. *Genetics* 195(2):495–512. <https://doi.org/10.1534/genetics.113.153783>
- Anderson JT, Wadgymar SM. 2020. Climate change disrupts local adaptation and favours upslope migration. *Ecol. Lett.* 23(1):181–92. <https://doi.org/10.1111/ele.13427>
- Barrett RDH, Schluter D. 2008. Adaptation from standing genetic variation. *Trends Ecol. Evol.* 23(1):38–44. <https://doi.org/10.1016/j.tree.2007.09.008>
- Bay RA, Harrigan RJ, Underwood VL, Gibbs HL, Smith TB, Ruegg K. 2018. Genomic signals of selection predict climate-driven population declines in a migratory bird. *Science* 359(6371):83–86. <https://doi.org/10.1126/science.aan4380>
- Benito Garzón M, Robson TM, Hampe A. 2019. Δ TraitSDMs: species distribution models that account for local adaptation and phenotypic plasticity. *New Phytol.* 222(4):1757–65. <https://doi.org/10.1111/nph.15716>
- Benning JW, Moeller DA. 2019. Maladaptation beyond a geographic range limit driven by antagonistic and mutualistic biotic interactions across an abiotic gradient. *Evolution* 73(10):2044–59. <https://doi.org/10.1111/evo.13836>
- Berg JJ, Coop G. 2014. A population genetic signal of polygenic adaptation. *PLOS Genet.* 10(8):e1004412. <https://doi.org/10.1371/journal.pgen.1004412>
- Blanquart F, Kaltz O, Nuismer SL, Gandon S. 2013. A practical guide to measuring local adaptation. *Ecol. Lett.* 16(9):1195–205. <https://doi.org/10.1111/ele.12150>
- Bleeker W, Hurka H. 2001. Introgressive hybridization in *Rorippa* (Brassicaceae): gene flow and its consequences in natural and anthropogenic habitats. *Mol. Ecol.* 10(8):2013–22. <https://doi.org/10.1046/j.1365-294X.2001.01341.x>
- Blois JL, Zarnetske PL, Fitzpatrick MC, Finnegan S. 2013. Climate change and the past, present, and future of biotic interactions. *Science* 341(6145):499–504. <https://doi.org/10.1126/science.1237184>
- Bradshaw WE, Holzapfel CM. 2006. Evolutionary response to rapid climate change. *Science* 312(5779):1477–78. <https://doi.org/10.1126/science.1127000>
- Brady SP, Bolnick DI, Angert AL, Gonzalez A, et al. 2019a. Causes of maladaptation. *Evol. Appl.* 12(7):1229–42. <https://doi.org/10.1111/eva.12844>
- Brady SP, Bolnick DI, Barrett RDH, Chapman L, et al. 2019b. Understanding maladaptation by uniting ecological and evolutionary perspectives. *Am. Nat.* 194(4):495–515. <https://doi.org/10.1086/705020>

- Brondizio ES, Settele J, Díaz S, Ngo HT, eds. 2019. *Global assessment report on biodiversity and ecosystem services of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services*. Rep., IPBES Secr., Bonn, Ger. <https://ipbes.net/global-assessment>
- Browne L, Wright JW, Fitz-Gibbon S, Gugger PF, Sork VL. 2019. Adaptational lag to temperature in valley oak (*Quercus lobata*) can be mitigated by genome-informed assisted gene flow. *PNAS* 116(50):25179–85. <https://doi.org/10.1073/pnas.1908771116>
- Capblancq T, Luu K, Blum MGB, Bazin E. 2018. Evaluation of redundancy analysis to identify signatures of local adaptation. *Mol. Ecol. Resour.* 18(6):1223–33. <https://doi.org/10.1111/1755-0998.12906>
- Capblancq T, Morin X, Gueguen M, Renaud J, Lobreaux S, Bazin E. 2020. Climate-associated genetic variation in *Fagus sylvatica* and potential responses to climate change in the French Alps. *J. Evol. Biol.* <https://doi.org/10.1111/jeb.13610>
- Carvalho CS, Forester BR, Mitre SK, Alves R, Imperatriz-Fonseca VL, et al. 2019. Combining genotype, phenotype, and environmental data to delineate site-adjusted provenance strategies for ecological restoration. *BioRxiv* 2019.12.11.872747. <https://doi.org/10.1101/2019.12.11.872747>
- Chen I-C, Hill JK, Ohlemüller R, Roy DB, Thomas CD. 2011. Rapid range shifts of species associated with high levels of climate warming. *Science* 333(6045):1024–26. <https://doi.org/10.1126/science.1206432>
- Chevin LM, Lande R, Mace GM. 2010. Adaptation, plasticity, and extinction in a changing environment: towards a predictive theory. *PLOS Biol.* 8(4):e1000357. <https://doi.org/10.1371/journal.pbio.1000357>
- Chhatre VE, Fetter KC, Gougherty AV, Fitzpatrick MC, Soolanayakanahally RY, et al. 2019. Climatic niche predicts the landscape structure of locally adaptive standing genetic variation. *BioRxiv* 817411. <https://doi.org/10.1101/817411>
- Curtin SJ, Tiffin P, Guhlin J, Trujillo D, Burghart L, et al. 2017. Validating genome-wide association candidates controlling quantitative variation in nodulation. *Plant Physiol.* 173(2):921–31. <https://doi.org/10.1104/pp.16.01923>
- Davis MB, Shaw RG. 2001. Range shifts and adaptive responses to quaternary climate change. *Science* 292(5517):673–79. <https://doi.org/10.1126/science.292.5517.673>
- De Kort H, Vandepitte K, Bruun HH, Closset-Kopp D, Honnay O, Mergeay J. 2014. Landscape genomics and a common garden trial reveal adaptive differentiation to temperature across Europe in the tree species *Alnus glutinosa*. *Mol. Ecol.* 23(19):4709–21. <https://doi.org/10.1111/mec.12813>
- de los Campos G, Hickey JM, Pong-Wong R, Daetwyler HD, Calus MPL. 2013. Whole-genome regression and prediction methods applied to plant and animal breeding. *Genetics* 193(2):327–45. <https://doi.org/10.1534/genetics.112.143313>
- De Villemereuil P, Gaggiotti OE, Mouterde M, Till-Bottraud I. 2016. Common garden experiments in the genomic era: new perspectives and opportunities. *Heredity* 116(3):249–54. <https://doi.org/10.1038/hdy.2015.93>
- Derry AM, Fraser DJ, Brady SP, Astorg L, Lawrence ER, et al. 2019. Conservation through the lens of (mal)adaptation: concepts and meta-analysis. *Evol. Appl.* 12(7):1287–304. <https://doi.org/10.1111/eva.12791>
- Deutsch CA, Tewksbury JJ, Tigchelaar M, Battisti DS, Merrill SC, et al. 2018. Increase in crop losses to insect pests in a warming climate. *Science* 361(6405):916–19. <https://doi.org/10.1126/science.aat3466>
- Ellis N, Smith SJ, Pitcher CR. 2012. Gradient forests: calculating importance gradients on physical predictors. *Ecology* 93(1):156–68. <https://doi.org/10.1890/11-0252.1>
- Etterson JR, Franks SJ, Mazer SJ, Shaw RG, Soper Gorden NL, et al. 2016. Project baseline: an unprecedented resource to study plant evolution across space and time. *Am. J. Bot.* 103(1):164–73. <https://doi.org/10.3732/ajb.1500313>
- Exposito-Alonso M, Burbano HA, Bossdorf O, Nielsen R, Weigel D. 2019. Natural selection on the *Arabidopsis thaliana* genome in present and future climates. *Nature* 573(7772):126–29. <https://doi.org/10.1038/s41586-019-1520-9>
- Exposito-Alonso M, Vasseur F, Ding W, Wang G, Burbano HA, Weigel D. 2018. Genomic basis and evolutionary potential for extreme drought adaptation in *Arabidopsis thaliana*. *Nat. Ecol. Evol.* 2(2):352–58. <https://doi.org/10.1038/s41559-017-0423-0>
- Ferrier S, Guisan A. 2006. Spatial modelling of biodiversity at the community level. *J. Appl. Ecol.* 43(3):393–404. <https://doi.org/10.1111/j.1365-2664.2006.01149.x>

- Fitzpatrick MC, Blois JL, Williams JW, Nieto-Lugilde D, Maguire KC, Lorenz DJ. 2018a. How will climate novelty influence ecological forecasts? Using the quaternary to assess future reliability. *Glob. Change Biol.* 24(8):3575–86. <https://doi.org/10.1111/gcb.14138>
- Fitzpatrick MC, Keller SR. 2015. Ecological genomics meets community-level modelling of biodiversity: mapping the genomic landscape of current and future environmental adaptation. *Ecol. Lett.* 18(1):1–16. <https://doi.org/10.1111/ele.12376>
- Fitzpatrick MC, Keller SR, Lotterhos KE. 2018b. Comment on ‘Genomic signals of selection predict climate-driven population declines in a migratory bird.’ *Science* 361(6401):2–4
- Forester BR, Dechaine EG, Bunn AG. 2013. Integrating ensemble species distribution modelling and statistical phylogeography to inform projections of climate change impacts on species distributions. *Divers. Distrib.* 19(12):1480–95. <https://doi.org/10.1111/ddi.12098>
- Forester BR, Jones MR, Joost S, Landguth EL, Lasky JR. 2016. Detecting spatial genetic signatures of local adaptation in heterogeneous landscapes. *Mol. Ecol.* 25(1):104–20. <https://doi.org/10.1111/mec.13476>
- Forester BR, Lasky JR, Wagner HH, Urban DL. 2018. Comparing methods for detecting multilocus adaptation with multivariate genotype–environment associations. *Mol. Ecol.* 27(9):2215–33. <https://doi.org/10.1111/mec.14584>
- Fournier-Level A, Korte A, Cooper MD, Nordborg M, Schmitt J, Wilczek AM. 2011. A map of local adaptation in *Arabidopsis thaliana*. *Science* 334(6052):86–89. <https://doi.org/10.1126/science.1209271>
- François O, Martins H, Caye K, Schoville S. 2016. Controlling false discoveries in genome scans for selection. *Mol. Ecol.* 25:454–69. <https://doi.org/10.1111/mec.13513>
- Franks SJ, Hamann E, Weis AE. 2018. Using the resurrection approach to understand contemporary evolution in changing environments. *Evol. Appl.* 11(1):17–28. <https://doi.org/10.1111/eva.12528>
- Franks SJ, Hoffmann AA. 2012. Genetics of climate change adaptation. *Annu. Rev. Genet.* 46:185–208. <https://doi.org/10.1146/annurev-genet-110711-155511>
- Gienapp P, Calus MPL, Laine V, Visser ME. 2019. Genomic selection on breeding time in a wild bird population. *Evol. Lett.* 3(2):142–51. <https://doi.org/10.1002/evl3.103>
- Gougherty AV, Keller SR, Chhatre VE, Fitzpatrick MC. 2020. Future climate change promotes novel gene–climate associations in balsam poplar 2 (*Populus balsamifera* L.), a forest tree species. *BioRxiv* 2020.02.28.961060. <https://doi.org/10.1101/2020.02.28.961060>
- Grant PR, Grant BR. 2016. Introgressive hybridization and natural selection in Darwin’s finches. *Biol. J. Linn. Soc.* 117(4):812–22. <https://doi.org/10.1111/bij.12702>
- Grant PR, Grant BR, Markert JA, Keller LF, Petren K. 2004. Convergent evolution of Darwin’s finches caused by introgressive hybridization and selection. *Evolution* 58(7):1588–99. <https://doi.org/10.1554/04-016>
- Greenham K, McClung CR. 2015. Integrating circadian dynamics with physiological processes in plants. *Nat. Rev. Genet.* 16(10):598–610. <https://doi.org/10.1038/nrg3976>
- Guisan A, Thuiller W. 2005. Predicting species distribution: offering more than simple habitat models. *Ecol. Lett.* 8(9):993–1009. <https://doi.org/10.1111/j.1461-0248.2005.00792.x>
- Hancock AM, Brachi B, Faure N, Horton MW, Jarmowycz LB, et al. 2011. *Arabidopsis thaliana* genome. *Science* 334(6052):83–86. <https://doi.org/10.1126/science.1209244>
- Harbicht A, Wilson CC, Fraser DJ. 2014. Does human-induced hybridization have long-term genetic effects? Empirical testing with domesticated, wild and hybridized fish populations. *Evol. Appl.* 7(10):1180–91. <https://doi.org/10.1111/eva.12199>
- Hereford J. 2009. A quantitative survey of local adaptation and fitness trade-offs. *Am. Nat.* 173(5):579–88. <https://doi.org/10.1086/597611>
- Hoban S, Kelley JL, Lotterhos KE, Antolin MF, Bradburd G, et al. 2016. Finding the genomic basis of local adaptation: pitfalls, practical solutions, and future directions. *Am. Nat.* 188(4):379–97. <https://doi.org/10.1086/688018>
- Hoffmann AA, Sgró CM. 2011. Climate change and evolutionary adaptation. *Nature* 470(7335):479–85. <https://doi.org/10.1038/nature09670>
- Hohenlohe PA, Amish SJ, Catchen JM, Allendorf FW, Luikart G. 2011. Next-generation RAD sequencing identifies thousands of SNPs for assessing hybridization between rainbow and westslope cutthroat trout. *Mol. Ecol. Resour.* 11(Suppl. 1):117–22. <https://doi.org/10.1111/j.1755-0998.2010.02967.x>

- Info Flora. 2020. *Arabis Alpina* L. subsp. Alpine. Subspecies 39400, Info Flora, Geneva. <https://www.infoflora.ch/en/flora/arabis-alpina-subsp-alpina.html>
- Ingvarsson PK, Bernhardsson C. 2018. Genome-wide signatures of environmental adaptation in European aspen (*Populus tremula*) under current and future climate conditions. *Evol. Appl.* 13(1):132–42. <https://doi.org/10.1111/eva.12792>
- Ioannidis JPA, Thomas G, Daly MJ. 2009. Validating, augmenting and refining genome-wide association signals. *Nat. Rev. Genet.* 10(5):318–29. <https://doi.org/10.1038/nrg2544>
- Jaramillo-Correa JP, Rodríguez-Quilón I, Grivet D, Lepoittevin C, Sebastiani F, et al. 2015. Molecular proxies for climate maladaptation in a long-lived tree (*Pinus pinaster* Aiton, Pinaceae). *Genetics* 199(3):793–807. <https://doi.org/10.1534/genetics.114.173252>
- Jay F, Manel S, Alvarez N, Durand EY, Thuiller W, et al. 2012. Forecasting changes in population genetic structure of alpine plants in response to global warming. *Mol. Ecol.* 21(10):2354–68. <https://doi.org/10.1111/j.1365-294X.2012.05541.x>
- Jones FC, Grabherr MG, Chan YF, Russell P, Mauceli E, et al. 2012. The genomic basis of adaptive evolution in threespine sticklebacks. *Nature* 484(7392):55–61. <https://doi.org/10.1038/nature10944>
- Jones MR, Mills LS, Alves PC, Callahan CM, Alves JM, et al. 2018. Adaptive introgression underlies polymorphic seasonal camouflage in snowshoe hares. *Science* 358(6395):1355–58
- Josephs EB, Berg JJ, Ross-Ibarra J, Coop G. 2019. Detecting adaptive differentiation in structured populations with genomic data and common gardens. *Genetics* 211(3):989–1004. <https://doi.org/10.1534/genetics.118.301786>
- Jump AS, Hunt JM, Martínez-Izquierdo JA, Peñuelas J. 2006. Natural selection and climate change: temperature-linked spatial and temporal trends in gene frequency in *Fagus sylvatica*. *Mol. Ecol.* 15(11):3469–80. <https://doi.org/10.1111/j.1365-294X.2006.03027.x>
- Jump AS, Peñuelas J. 2005. Running to stand still: adaptation and the response of plants to rapid climate change. *Ecol. Lett.* 8(9):1010–20. <https://doi.org/10.1111/j.1461-0248.2005.00796.x>
- Kawecki TJ, Ebert D. 2004. Conceptual issues in local adaptation. *Ecol. Lett.* 7(12):1225–41. <https://doi.org/10.1111/j.1461-0248.2004.00684.x>
- Keller SR, Chhatre VE, Fitzpatrick MC. 2018. Influence of range position on locally adaptive gene-environment associations in *Populus* flowering time genes. *J. Hered.* 109(1):47–58. <https://doi.org/10.1093/jhered/esx098>
- Lang PLM, Willems FM, Scheepens JF, Burbano HA, Bosdorf O. 2019. Using herbaria to study global environmental change. *New Phytol.* 221(1):110–22. <https://doi.org/10.1111/nph.15401>
- Lasky JR, Forester BR, Reimherr M. 2018. Coherent synthesis of genomic associations with phenotypes and home environments. *Mol. Ecol. Resour.* 18(1):91–106. <https://doi.org/10.1111/1755-0998.12714>
- Leimu R, Fischer M. 2008. A meta-analysis of local adaptation in plants. *PLOS ONE* 3(12):e4010. <https://doi.org/10.1371/journal.pone.0004010>
- Lenormand T. 2002. Gene flow and the limits to natural selection. *Trends Ecol. Evol.* 17(4):183–89. [https://doi.org/10.1016/S0169-5347\(02\)02497-7](https://doi.org/10.1016/S0169-5347(02)02497-7)
- Lotterhos KE, Whitlock MC. 2014. Evaluation of demographic history and neutral parameterization on the performance of F_{ST} outlier tests. *Mol. Ecol.* 23(9):2178–92. <https://doi.org/10.1111/mec.12725>
- Lotterhos KE, Whitlock MC. 2015. The relative power of genome scans to detect local adaptation depends on sampling design and statistical method. *Mol. Ecol.* 24:1031–46. <https://doi.org/10.1111/mec.13100>
- Lowry DB, Hoban S, Kelley JL, Lotterhos KE, Reed LK, et al. 2017. Breaking RAD: an evaluation of the utility of restriction site-associated DNA sequencing for genome scans of adaptation. *Mol. Ecol. Resour.* 17(2):142–52. <https://doi.org/10.1111/1755-0998.12635>
- Mahony CR, MacLachlan IR, Lind BM, Yoder JB, Wang T, Aitken SN. 2020. Evaluating genomic data for management of local adaptation in a changing climate: a lodgepole pine case study. *Evol. Appl.* 13(1):116–31. <https://doi.org/10.1111/eva.12871>
- Manel S, Schwartz MK, Luikart G, Taberlet P. 2003. Landscape genetics: combining landscape ecology and population genetics. *Trends Ecol. Evol.* 18(4):189–97. [https://doi.org/10.1016/S0169-5347\(03\)00008-9](https://doi.org/10.1016/S0169-5347(03)00008-9)

- Martins K, Gugger PF, Llanderal-Mendoza J, González-Rodríguez A, Fitz-Gibbon ST, et al. 2018. Landscape genomics provides evidence of climate-associated genetic variation in Mexican populations of *Quercus rugosa*. *Evol. Appl.* 11(10):1842–58. <https://doi.org/10.1111/eva.12684>
- Monroe JG, Powell T, Price N, Mullen JL, Howard A, et al. 2018. Drought adaptation in *Arabidopsis thaliana* by extensive genetic loss-of-function. *eLife* 7:e41038. <https://doi.org/10.7554/eLife.41038>
- Morton EM, Rafferty NE. 2017. Plant-pollinator interactions under climate change: the use of spatial and temporal transplants. *Appl. Plant Sci.* 5(6):1600133. <https://doi.org/10.3732/apps.1600133>
- Nielsen R, Williamson S, Kim Y, Hubisz MJ, Clark AG, Bustamante C. 2005. Genomic scans for selective sweeps using SNP data. *Genome Res.* 15(11):1566–75. <https://doi.org/10.1101/gr.4252305>
- Oetting WS, Jacobson PA, Israni AK. 2018. Validation is critical for genome-wide association study-based associations. *Am. J. Transplant.* 17(2):318–19. <https://doi.org/10.1111/ajt.14051>
- Olson MS, Levens N, Soolanayakanahally RY, Guy RD, Schroeder WR, et al. 2013. The adaptive potential of *Populus balsamifera* L. to phenology requirements in a warmer global climate. *Mol. Ecol.* 22(5):1214–30. <https://doi.org/10.1111/mec.12067>
- Palumbi SR, Barshis DJ, Traylor-Knowles N, Bay RA. 2014. Mechanisms of reef coral resistance to future climate change. *Science* 344(6186):895–97. <https://science.sciencemag.org/content/344/6186/895>. long
- Parmesan C, Yohe G. 2003. A globally coherent fingerprint of climate change. *Nature* 421:37–42. <https://doi.org/10.1038/nature01286>
- Parry ML, Canziani OF, Palutikof JP, van der Linden PJ, Hanson CE, eds. 2007. *Climate Change 2007: Impacts, Adaptation and Vulnerability: Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge, UK: Cambridge Univ. Press
- Pina-Martins F, Baptista J, Pappas G, Paulo OS. 2019. New insights into adaptation and population structure of cork oak using genotyping by sequencing. *Glob. Change Biol.* 25(1):337–50. <https://doi.org/10.1111/gcb.14497>
- Price TD, Qvarnström A, Irwin DE. 2003. The role of phenotypic plasticity in driving genetic evolution. *Proc. R. Soc. B* 270(1523):1433–40. <https://doi.org/10.1098/rspb.2003.2372>
- Prunier J, Laroche J, Beaulieu J, Bousquet J. 2011. Scanning the genome for gene SNPs related to climate adaptation and estimating selection at the molecular level in boreal black spruce. *Mol. Ecol.* 20(8):1702–16. <https://doi.org/10.1111/j.1365-294X.2011.05045.x>
- Razgour O, Forester B, Taggart JB, Bekaert M, Juste J, et al. 2019. Considering adaptive genetic variation in climate change vulnerability assessment reduces species range loss projections. *PNAS* 116(21):10418–23. <https://doi.org/10.1073/pnas.1820663116>
- Rehfeldt GE, Tchebakova NM, Parfenova YI, Wykoff WR, Kuzmina NA, Milyutin LI. 2002. Intraspecific responses to climate in *Pinus sylvestris*. *Glob. Change Biol.* 8(9):912–29. <https://doi.org/10.1046/j.1365-2486.2002.00516.x>
- Reich PB, Sendall KM, Stefanski A, Rich RL, Hobbie SE, Montgomery RA. 2018. Effects of climate warming on photosynthesis in boreal tree species depend on soil moisture. *Nature* 562(7726):263–67. <https://doi.org/10.1038/s41586-018-0582-4>
- Rellstab C, Gugerli F, Eckert AJ, Hancock AM, Holderegger R. 2015. A practical guide to environmental association analysis in landscape genomics. *Mol. Ecol.* 24(17):4348–70. <https://doi.org/10.1111/mec.13322>
- Rellstab C, Zoller S, Walther L, Lesur I, Pluess AR, et al. 2016. Signatures of local adaptation in candidate genes of oaks (*Quercus* spp.) with respect to present and future climatic conditions. *Mol. Ecol.* 25(23):5907–24. <https://doi.org/10.1111/mec.13889>
- Resende FR Jr., Muñoz P, Resende MDV, Garrick DJ, Fernando RL, et al. 2012. Accuracy of genomic selection methods in a standard data set of loblolly pine (*Pinus taeda* L.). *Genetics* 190(4):1503–10. <https://doi.org/10.1534/genetics.111.137026>
- Rochat E, Joost S. 2019. Spatial areas of genotype probability (SPAG): predicting the spatial distribution of adaptive genetic variants under future climatic conditions. *BioRxiv* 2019.12.20.884114. <https://doi.org/10.1101/2019.12.20.884114>

- Rohde PD, Østergaard S, Kristensen TN, Sørensen P, Loeschcke V, et al. 2018. Functional validation of candidate genes detected by genomic feature models. *G3* 8(5):1659–68. <https://doi.org/10.1534/g3.118.200082>
- Ruegg K, Bay RA, Anderson EC, Saracco JF, Harrigan RJ, et al. 2018. Ecological genomics predicts climate vulnerability in an endangered southwestern songbird. *Ecol. Lett.* 21(7):1085–96. <https://doi.org/10.1111/ele.12977>
- Sabeti PC, Reich DE, Higgins JM, Levine HZP, Richter DJ, et al. 2002. Detecting recent positive selection in the human genome from haplotype structure. *Nature* 419(6909):832–37. <https://doi.org/10.1038/nature01140>
- Saino N, Bazzi G, Gatti E, Caprioli M, Cecere JG, et al. 2015. Polymorphism at the clock gene predicts phenology of long-distance migration in birds. *Mol. Ecol.* 24(8):1758–73. <https://doi.org/10.1111/mec.13159>
- Santure AW, Garant D. 2018. Wild GWAS—association mapping in natural populations. *Mol. Ecol. Resour.* 18(4):729–38. <https://doi.org/10.1111/1755-0998.12901>
- Savolainen O, Lascoux M, Merilä J. 2013. Ecological genomics of local adaptation. *Nat. Rev. Genet.* 14(11):807–20. <https://doi.org/10.1038/nrg3522>
- Savolainen O, Pyhäjärvi T. 2007. Genomic diversity in forest trees. *Curr. Opin. Plant Biol.* 10(2):162–67. <https://doi.org/10.1016/j.pbi.2007.01.011>
- Seehausen O, van Alphen JJM, Witte F. 1997. Cichlid fish diversity threatened by eutrophication that curbs sexual selection. *Science* 277(5333):1808–11. <https://doi.org/10.1126/science.277.5333.1808>
- Shaw RG. 2019. From the past to the future: considering the value and limits of evolutionary prediction. *Am. Nat.* 193(1):1–10. <https://doi.org/10.1086/700565>
- Somero GN. 2010. The physiology of climate change: how potentials for acclimatization and genetic adaptation will determine ‘winners’ and ‘losers.’ *J. Exp. Biol.* 213(6):912–20. <https://doi.org/10.1242/jeb.037473>
- Sork VL, Squire K, Gugger PF, Steele SE, Levy ED, Eckert AJ. 2016. Landscape genomic analysis of candidate genes for climate adaptation in a California endemic oak, *Quercus lobata*. *Am. J. Bot.* 103(1):33–46. <https://doi.org/10.3732/ajb.1500162>
- Steane DA, Potts BM, McLean E, Prober SM, Stock WD, et al. 2014. Genome-wide scans detect adaptation to aridity in a widespread forest tree species. *Mol. Ecol.* 23(10):2500–13. <https://doi.org/10.1111/mec.12751>
- Stillman JH. 2003. Acclimation capacity underlies susceptibility to climate change. *Science* 301(5629):65. <https://doi.org/10.1126/science.1083073>
- Stocker TF, Qin D, Plattner GK, Tignor M, Allen SK, et al., eds. 2013. *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge, UK: Cambridge Univ. Press
- Supple MA, Bragg JG, Broadhurst LM, Nicotra AB, Byrne M, et al. 2018. Landscape genomic prediction for restoration of a eucalyptus foundation species under climate change. *eLife* 7:31835. <https://doi.org/10.7554/eLife.31835>
- Svenning JC, Skov F. 2007. Could the tree diversity pattern in Europe be generated by postglacial dispersal limitation? *Ecol. Lett.* 10(6):453–60. <https://doi.org/10.1111/j.1461-0248.2007.01038.x>
- Thuiller W, Albert C, Araújo MB, Berry PM, Cabeza M, et al. 2008. Predicting global change impacts on plant species’ distributions: future challenges. *Perspect. Plant Ecol. Evol. Syst.* 9(3–4):137–52. <https://doi.org/10.1016/j.ppees.2007.09.004>
- Tiffin P, Ross-Ibarra J. 2014. Advances and limits of using population genetics to understand local adaptation. *Trends Ecol. Evol.* 29(12):673–80. <https://doi.org/10.1016/j.tree.2014.10.004>
- Tigano A, Friesen VL. 2016. Genomics of local adaptation with gene flow. *Mol. Ecol.* 25(10):2144–64. <https://doi.org/10.1111/mec.13606>
- Veloz SD, Williams JW, Blois JL, He F, Otto-Bliesner B, Liu Z. 2012. No-analog climates and shifting realized niches during the late quaternary: implications for 21st-century predictions by species distribution models. *Glob. Change Biol.* 18(5):1698–713. <https://doi.org/10.1111/j.1365-2486.2011.02635.x>
- Vitti JJ, Grossman SR, Sabeti PC. 2013. Detecting natural selection in genomic data. *Annu. Rev. Genet.* 47:97–120. <https://doi.org/10.1146/annurev-genet-111212-133526>

- Williams JW, Jackson ST. 2007. Novel climates, no-analog communities, and ecological surprises. *Front. Ecol. Environ.* 5(9):475–82. <https://doi.org/10.1890/070037>
- Williams JW, Jackson ST, Kutzbach JE. 2007. Projected distributions of novel and disappearing climates by 2100 AD. *PNAS* 104(14):5738–42. <https://doi.org/10.1073/pnas.0606292104>
- Yoder JB, Stanton-Geddes J, Zhou P, Briskine R, Young ND, Tiffin P. 2014. Genomic signature of adaptation to climate in *Medicago truncatula*. *Genetics* 196(4):1263–75. <https://doi.org/10.1534/genetics.113.159319>
- Zhou X, Stephens M. 2014. Efficient multivariate linear mixed model algorithms for genome-wide association studies. *Nat. Methods* 11(4):407–9. <https://doi.org/10.1038/nmeth.2848>