

Genetic offset and vulnerability modelling: misinterpretations of results and violations of evolutionary principles

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June 20, 2023

Abstract

Genetic offset models have become a popular component of the landscape genetics toolbox, with over 150 peer-reviewed publications applying these models to plant and animal systems. Genetic offset models are most frequently performed following the identification of putatively adaptive alleles from genotype-environment association analyses in natural populations of non-model organisms. These models allow the researcher to make predictions about the likely vulnerability of species populations to climate change, by estimating the extent of genetic change needed (i.e., genetic offset) to maintain ‘optimal’ allele frequencies and population fitness under future climate change scenarios. However, a number of critical assumptions and knowledge gaps are often overlooked when undertaking these analyses, undermining their reliability and usefulness for making genetically informed management decisions. In this commentary, we describe seven assumptions in detail and discuss a range of common violations that can lead to misleading outcomes. While genetic offset models may have a place for predicting the vulnerability of natural populations of non-model organisms in the future, we argue that current applications are likely to be problematic and risk both wasting resources and misleading conservation management.

Genetic offset and vulnerability modelling: misinterpretations of results and violations of evolutionary principles

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Abstract

Genetic offset models have become a popular component of the landscape genetics toolbox, with over 150 peer-reviewed publications applying these models to plant and animal systems. Genetic offset models are most frequently performed following the identification of putatively adaptive alleles from genotype-environment association analyses in natural populations of non-model organisms. These models allow the researcher to make predictions about the likely vulnerability of species populations to climate change, by estimating the extent of genetic change needed (i.e., genetic offset) to maintain 'optimal' allele frequencies and population fitness under future climate change scenarios. However, a number of critical assumptions and knowledge gaps are often overlooked when undertaking these analyses, undermining their reliability and usefulness for making genetically informed management decisions. In this commentary, we describe seven assumptions in detail and discuss a range of common violations that can lead to misleading outcomes. While genetic offset models may have a place for predicting the vulnerability of natural populations of non-model organisms in the future, we

argue that current applications are likely to be problematic and risk both wasting resources and misleading conservation management.

Introduction

One of the most significant challenges in biodiversity conservation is predicting the ability of species to adapt to climate change, and determining when interventions are needed to help vulnerable species overcome risks of maladaptation and local extinction (Gaitán-Espitia & Hobday, 2021). This is particularly pertinent given the increasing pressure of rapid climate change on global ecosystems, and the compounding effects of added stressors including habitat destruction, altered pathogen dynamics, and the spread of invasive species (Hoffmann et al., 2019; Weiskopf et al., 2020). Over the last decade there has been an explosion of genomic research making use of next generation sequencing technologies for characterising genome wide patterns of genetic variation among natural populations in non-model organisms (Ahrens et al., 2018; Dauphin et al., 2023). Specifically, there has been a sharp rise in studies using these technologies to assess patterns of genetic variation among species populations persisting under different environmental conditions (i.e., genotype-environment associations; GEAs), provide a glimpse into past evolutionary responses to climatic fluctuations, and the availability of standing genetic variation for adaptation to future climate challenges (Razgour et al., 2019; Forester et al., 2022). These approaches often provide opportunities for identifying specific alleles associated with local adaptation and potentially influencing the fitness of populations under local environmental conditions (Lasky et al., 2022). In theory, this information can assist managers to incorporate evolutionary processes into the management of biodiversity values (Isabel et al., 2020), and to be more targeted with interventions aimed at enhancing the resilience of species populations considered most vulnerable to climate change effects (Hoffmann et al., 2021a).

More recently, there has been growing interest in the integration of population genomic data and landscape ecology to inform management by modelling the likely vulnerability of species populations to climate change. One method gaining traction is the “genetic offset” (GO) method, which makes use of well-established community ecology modelling techniques (Rellstab et al., 2021) to determine the extent of genetic change needed for a population to persist under future climate conditions (Fitzpatrick & Keller, 2015; Gaitán-Espitia & Hobday, 2021). Specifically, genetic offset models use contemporary frequencies of adaptive alleles to predict the extent of genetic change needed to track with climate change and maintain population fitness into the

future (Rellstab et al., 2021). The interpretation is intuitive, where populations requiring the greatest genetic changes have the greatest GO and are considered most vulnerable to climate change (Gougherty et al., 2021). These models are now being widely used within genotype-environment association (GEA) workflows (Rellstab et al., 2015; Hoban et al., 2016; Ahrens et al., 2018; Lasky et al., 2022), with 151 peer-reviewed publications applying GO models to natural populations of non-model plant and animal systems (according to Google Scholar May 2023 using “genetic offset” as the search term).

Despite the rising interest in GO models, recent review articles have highlighted several limitations, pointing to lack of connection between alleles and biological function (Hoffmann et al., 2021b) and over reliance on GO models in the absence of quantitative data (Rellstab et al., 2021). In this commentary we discuss further limitations of GO models extending to basic evolutionary principles. We argue that careful consideration needs to be given to understanding what a GO is in a selection and fitness landscape, and discuss critical assumptions and common violations of evolutionary principles that introduce risks of model misinterpretation. We also make the point that GO models tend to over-simplify the process of selection and at the same time over-complicate the process of gauging risks of maladaptation. It is hoped that this discussion will lead to greater caution and contextualisation in the application of GO models for informing management aimed at preserving and enhancing biodiversity values under climate change.

Evolutionary background and premise

The relationship between genetic clines and fitness needs to be carefully considered when undertaking GO analyses as these relationships are the driving force behind local adaptation and GOs. In figure 1 we define fitness as the quantitative representation of the ability to successfully reproduce and persist under local environmental conditions. The relationship between fitness and the environment is expressed in simple terms, as a gaussian distribution with environment on the x-axis and fitness on the y-axis (Figure 1a; (Laughlin & Messier, 2015)). This simple relationship underpins GO models that assume genetic variation contributing to differences in fitness allows selection to predictably occur. This relationship becomes slightly more complex when we consider the influence of individual genotypes on fitness under local environmental conditions, where genotypes have different effects and gaussian distributions that vary along the environmental axis (Figure 1b). In essence, the varying relationships

between individual genotypes, trait expression, and fitness under local environmental conditions facilitate the process of natural selection and local adaptation. GO models require these relationships being both well understood and predictable under changing environmental conditions. Yet most landscape genetic studies focus only on allele frequency clines, while lacking information on fitness and other evolutionary principles, rendering the interpretation of most GO models unreliable.

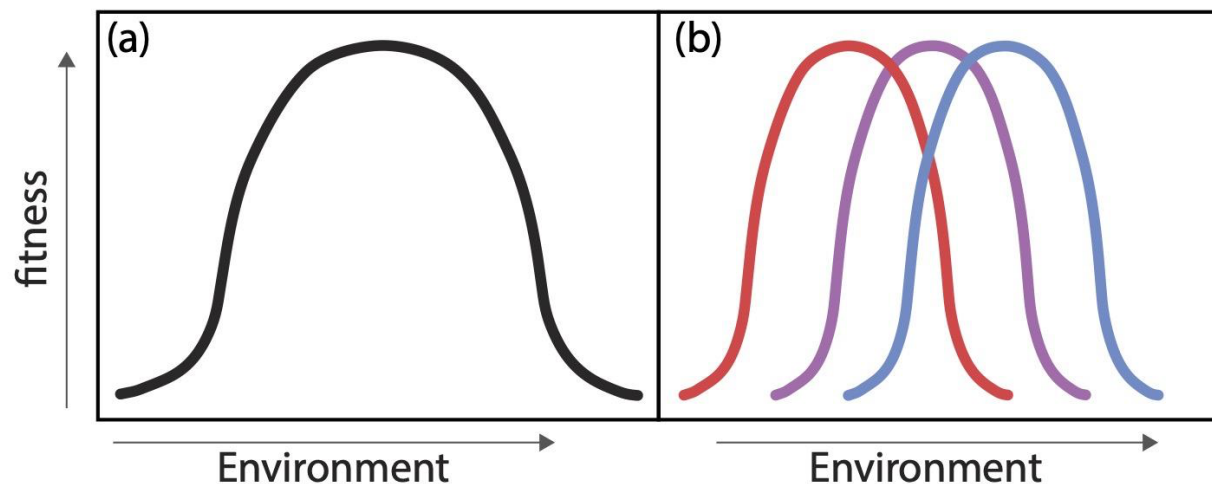


Figure 1. Fitness reaction norms across a (a) species and (b) genotypes within species (two allele model: red is aa; purple is aA; blue is AA).

GEAs provide a powerful approach for characterising correlations between allele frequencies and specific environments or habitats, and identifying loci that contribute to adaptive genetic differences among species populations (Rellstab et al., 2015; Manel et al., 2016; Ahrens et al., 2018; Lasky et al., 2022; Dauphin et al., 2023). An underlying assumption of GEAs and downstream GO models is that these candidate loci are having a measurable effect on trait expression and population fitness (Hoffmann et al., 2021), and that these loci will have a predictable effect on fitness under changing environmental conditions. We know from empirical studies that genotypic responses to novel environmental conditions can be unpredictable (Evangelou et al., 2019), and that a population's fitness is often determined by many quantitative traits that are commonly controlled by multiple gene loci (Laughlin & Messier, 2015; Laughlin et al., 2020). Consequently, the task of predicting adaptive responses to novel environments is complicated by numerous factors associated with trait complexity, including

epistatic interactions, pleiotropic effects, genetic redundancy, non-clinal patterns and fitness trade-offs among functional traits (Yeaman, 2015; Lotterhos et al., 2018; Todesco et al., 2020; Ahrens et al., 2021b; Lotterhos, 2023). Another common issue with correlative GEAs is that the true driver of adaptive genetic variation among species populations is often uncertain, particularly when quantitative experimental data (i.e., from common gardens) is unavailable. GEAs involve direct tests for correlations between specific genotypes and explanatory variables (i.e. temperature, precipitation, altitude); however, other factors correlated with these variables (abiotic and/or biotic) may be the actual driving force of selection (Rellstab et al., 2015). This is pertinent in complex landscapes where selection processes can be multidimensional (White & Butlin, 2021; Filipe et al., 2022; Lotterhos, 2023). Consequently, estimating GOs and predicting risks of maladaptation are problematic when the true driver(s) of selection are concealed.

Aside from the inherent issues associated with correlative GEAs, little attention has been paid to the basic theory behind GO models and how GO estimates relate to population vulnerability under changing environmental conditions. Even under a perfect scenario, where the genetic variants identified are truly adaptive and contribute to phenotypic variation for an important trait, which in turn is associated with a well-established environmental variable, what is a GO? We argue that in many cases GOs are likely to be misleading, using reaction norms to demonstrate how GOs can be greatest in populations that are least vulnerable to climate change. Below we expand on this and other common issues with GO models, highlighting the basic assumptions that must be met in order to reliably predict risks of future maladaptation and provide meaningful contributions to biodiversity management in light of climate change.

Basic assumptions

Here we articulate seven key assumptions that underpin GO analyses, but acknowledge that these do not consider other important biological processes such as heritability and biotic interactions. Even so, these seven assumptions are based on a perfect scenario where the candidate allele(s) being analysed are truly locally adaptive, associated with a gene whose function is known, and provide tangible fitness benefits under local environmental conditions where the driver of selection is known (Hoffmann et al., 2021).

Assumption 1: The magnitude of genetic offset is predicted to result in a corresponding fitness decline

Let's consider the relationship between genetic offset and fitness, and a basic model where populations exhibit clinal variation in adaptive allele frequencies relating to temperature. Populations occurring at the thermal extremes of the environmental distribution might be expected to be fixed or close to fixed (> 0.95) for alternate alleles (e.g., hot environment genotype = AA , cold environment genotype = aa). At some central point between the two environmental extremes, populations are expected to consist of heterozygous genotypes (Aa), where allele frequencies are close to 0.5. Below we provide theoretical depictions of the relationships between allele frequency and environment for three different adaptive loci at two sites from the centre (site 1) and extreme edge (site 2) of the environmental distribution, and demonstrate predicted shifts in allele frequencies for each site under a future climate change scenario (Figure 2a-c). We also show how allele frequency shifts might be accompanied by shifts in associated quantitative traits (Figure 2d-f) and shifts in fitness (Figure 2g-i). These figures demonstrate that the magnitude of GO depends entirely on the steepness of allele frequency change. Contrary to current interpretations of GO models, there is a small change in fitness at the steepest allele frequency shift located at the centre of the environmental distribution (site 1), while large fitness declines are expected to occur in the tails of the environmental distribution where the allele frequency is near its asymptote (site 2). Here, any environmental shift causing a change in the frequency of the adaptive genotype (AA) could lead to a major decline in fitness, yet GO is small because the allele frequency is already close to fixation and has nowhere to go. Another scenario is shown in (c) where both sites may have a similar GO but be accompanied by different traits (f) and fitness changes (i). Contrary to current interpretations, in these scenarios, populations least vulnerable to fitness declines are expected to have a high GO, while populations most vulnerable to fitness declines have low GO.

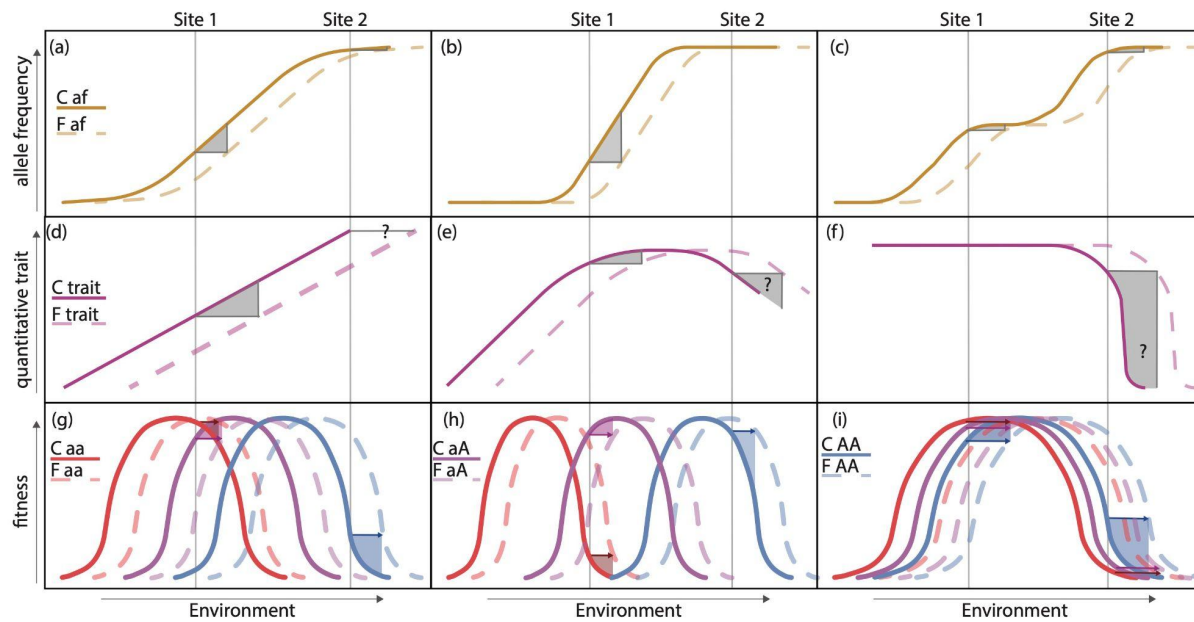


Figure 2. The theoretical relationship between change in allele frequency, various quantitative traits, and fitness across an environmental landscape. (a-c) Three different allele frequency changes across the environment. (d-f) Three different types of quantitative traits, which might represent (d) growth/height, (e) reproduction, and (f) seed germination. (g-i) We also show how fitness may change across an environment depending on genotype. Vertical lines denote two different sites, site 1 represents a site within the middle of the environmental distribution while site 2 is near its upper environmental limit. C - contemporary; F - future; af - allele frequency; (?) refers to the change in trait value to an environment that it previously did not experience, so predictions may not fit. It is important to note that these reaction norms in Figure 2 are not indicative of all allele frequency possibilities, trait responses, or fitness landscapes, but they do demonstrate how genetic offset and fitness declines can easily result in anticorrelation and misinterpretation.

Assumption 2: Allele frequencies result in optimal fitness under local environmental conditions

A common issue with GO models is that they assume allele frequencies to be at equilibrium, meaning they are in perfect balance with the local environment and that any change will have a detrimental effect on population fitness. However, we know that this is not always true as evidence suggests natural populations in both animal and plant systems can actually be maladapted to local environmental conditions (Holt et al., 2003; Brady et al., 2019). This

commonly applies to small, fragmented populations where adaptive allele frequencies have deviated from their optimum due to genetic drift, and in long lived species where allele frequencies may be a relict of adaptations to past climates. In other words, maladaptation could occur if the environment is moving, retreating or degrading, there is a genetic load, if there are mutations accumulating, or if genetic drift is occurring to name a few causes (Brady et al., 2019). Consequently, assuming that allele frequencies are optimised to provide peak fitness under local environmental conditions can be problematic, and can negatively impact the interpretation and the reliability of GO models.

Assumption 3: Selection pressure is uniform across all populations

Another problematic assumption associated with GO models is that selection is acting upon all populations with the same force (measured as selection coefficient; s). We know this to be false (Mathieson & McVean, 2013), as s changes through space and time (Exposito-Alonso et al., 2019). Instead, in locally adapted scenarios, s is typically expected to be greatest in the tails of the environmental distribution and lowest in the centre of the distribution, where demographic effects (i.e., genetic drift and gene flow) are likely to swamp the accumulation and maintenance of adaptive alleles (Figure 3; Polechová & Barton, 2015). Additionally, small and fragmented populations are particularly vulnerable to demographic effects such as genetic drift and inbreeding (Kimura et al., 1963; Whitlock, 2000; Frankham, 2005). In such cases, these demographic effects are likely to be stronger than s and have a greater influence on allele frequencies regardless of position within the environmental distribution. For better or worse, we use a term from baseball, “Mendoza Line”, to denote the threshold where selection pressure has a greater effect than other demographic processes, analogous to a threshold defining high and low batting performance (Figure 3). Consequently, the assumption that s is uniform across all populations is problematic and further complicates the interpretation of many GO models.

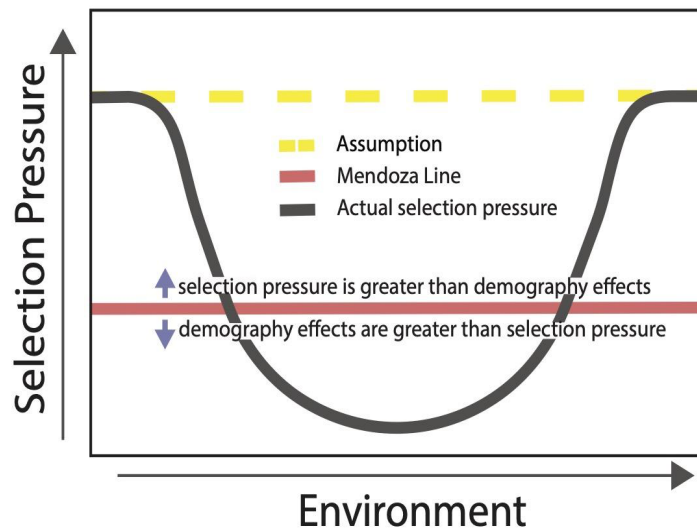


Figure 3. A simple relationship between selection pressure (s) across an environment and demographic processes in a local adaptation paradigm. Genetic offsets assume that the selection pressure is the same across the environment (dashed yellow line). However, it is more accurate to visualise how selection pressure may change across an environment gradient during the process of local adaptation (solid black line). At some point, neutral genetic effects will have a stronger effect compared to selection pressure (visualised here as the solid red line).

Assumption 4: **Adaptation is determined by alleles of medium to large effect**

Many traits are polygenic in nature where trait expression is influenced by a multitude of genes of various effect sizes (Barghi et al., 2020). GEA studies are designed to identify candidate loci with the greatest effect sizes in an additive genetic variation paradigm. However, evidence suggests that transient alleles of small effect can still have a significant influence on trait expression and the adaptation process (Yeaman, 2015). These types of small effect loci are nearly impossible to detect using correlative GEA approaches (Ahrens et al., 2021a) and are consequently overlooked in GO models. For groups of traits conferring adaptation that are polygenic and consist of many small-effect loci, genetic redundancy (alternative genotypic combinations resulting in similar phenotypes) may be a biological safeguard against new environmental challenges. Essentially, increasing trait complexity decreases the predictability of evolutionary responses to climate change (Gagnaire & Gaggiotti, 2016). However, GO models typically do not account for trait complexity and the potential influence of unidentifiable small

effect loci, which can have a significant influence on adaptive processes and the overall reliability of GO models.

Assumption 5: All genetic offsets result in fitness decline

Currently, our interpretation of GO models is that any predicted genetic change would result in a decline in population fitness. However, there are many theoretical instances, particularly at the trailing edge of the environmental shift (Figure 4), that could result in increased fitness. The change in fitness is dependent on the fact that climate change may not have a uniform effect across a species' distribution (Figure 4). In reality, GO interpretation is dependent on the direction and type of climate change. Here we show three simple scenarios (Figure 4; uniform, skewed, and reciprocal), but can imagine many scenarios that are different or more complex (such as polynomial curves or fragmented scenarios). A uniform scenario (Figure 4a&b) would result in all populations being equally affected, for this scenario we see that the 'blue' population would have an increased fitness and the 'red' population would have a decreased fitness. In a skewed scenario (Figure 4c&d), populations are differentially affected with one end having no change and the other end having a large change in climate. Here, the blue population has very little change in fitness while the 'red' population has a large change in fitness. Critically for the uniform and skewed scenarios the 'yellow' population has the largest GO but negligible change in fitness. Lastly, the reciprocal scenario (Figure 4e&f), where the climate has decreased for half of the populations and increased for the other half. It is only under this scenario where fitness is predicted to decline for both the 'blue' and 'red' populations, and there is no change for the 'yellow' population. Estimating this relationship between allele frequency, fitness, and climate change would lead to better interpretations. This subtlety is critical because we assume that any genetic offset would result in fitness decline.

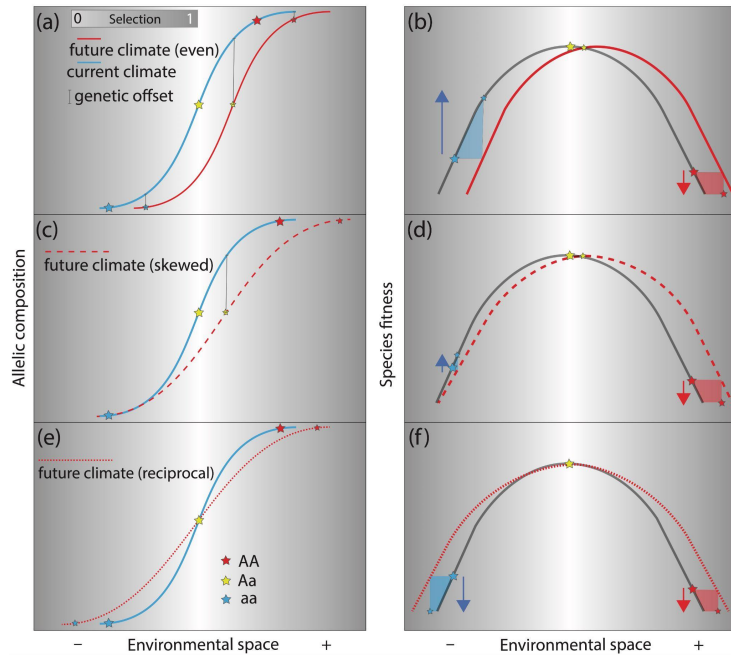


Figure 4. Climate change may affect populations differently, which affects interpretation of the genetic offset model.

Assumption 6: Loci are adapted to one environment

GO models are typically performed based on the simple assumption that candidate loci are associated with single traits that in turn are adapted to single environments. Yet we know that this is not always the case, and alleles affecting many traits are common in adaptive divergences among species populations (Thompson, 2020). We also know that populations are often exposed to multi-dimensional selection pressures, involving a multitude of environmental factors (i.e. temperature, precipitation, soil type; Dauphin et al., 2023), that in some cases produce only transient patterns of local adaptation (White 2022). Therefore, the idea that an allele may confer adaptive benefits to more than one environment, and the potential for pleiotropic effects, should be carefully considered when undertaking GO analyses (Mérot, 2022). If an allele can modulate responses to different environments, and is linked to multiple functional traits, then trade-offs may be expected as environments change asymmetrically (Mauro & Ghalambor, 2020). The obvious implication is that selection on one allele benefiting one trait may occur at the expense of another trait, and new genetic combinations must occur to avoid risks of maladaptation and fitness decline (Bono et al., 2017; Lotterhos et al., 2018; Chen & Zhang, 2020). Theoretically, pleiotropic effects could result in either impeding or facilitating adaptive response to climate change (Stitzer & Ross-Ibarra, 2018; Hämälä et al., 2020;

Rennison & Peichel, 2022). Indeed, trade-offs among pleiotropically controlled functional traits are dependent on habitat heterogeneity (Bono et al., 2017) and can compromise the ability to evolve new adaptive phenotypes when these occur at the expense of other traits critical to the fitness of the local population (Shoval et al., 2012; Ahrens et al., 2020). However, these outcomes are difficult to predict, especially in the absence of quantitative data, and simply cannot be accounted for in GO models. The idea of pleiotropy being a limitation to determining genetic vulnerability is also highlighted in Hoffmann et al., (2021).

Assumption 7: Gene flow can not account for a proportion of the genetic offset

Rellstab et al. (2021) recently argued that GO models are limited by their inability to incorporate key demographic processes, such as gene flow. Indeed, GO models typically do not account for gene flow which is known to play a key role in the adaptation process (Sgro and Hoffmann 2011; Bontrager & Angert, 2019). Efforts to estimate GO in panmictic species with wide distributions are likely to be futile, because risks of maladaptation are expected to be offset by the natural migration of alleles across environmental gradients (Pujolar et al., 2014). Therefore, one might assume that GO models are best suited to species with highly structured populations. However, this too can be problematic. In many systems, climatic and environmental factors act as barriers to gene flow and contribute to contemporary patterns of genetic structure (Bergek et al., 2010). Yet, in some cases these barriers are expected to break down due to climate change and provide new opportunities for gene flow among previously disconnected populations (Franks & Weis, 2009; Crispo et al., 2011). It is also important to acknowledge that low levels of gene flow can be occurring even in the presence of significant genetic structure (Sebbenn et al., 2011), and still be capable of enhancing the evolutionary potential of populations facing new environmental challenges (Guillaume & Whitlock, 2007; Arnold et al., 2008; Tusso et al., 2021). The interaction between gene flow, generational turnover, and the pace of climate change also needs to be carefully considered when gauging risks of vulnerability. In general, rapid evolutionary responses to climate change might be expected in species with short generation times regardless of gene flow influences (Tusso et al., 2021), while selection processes may fail to keep pace with projected shifts in climate in many long-lived species (Aitken et al., 2008). Although, evidence suggests that some long lived species, such as trees, are capable of long-distance gene flow that is expected to facilitate the evolutionary change needed for populations to adapt to new climate conditions (Kremer et al., 2012). Consequently, information on the strength and directionality of gene flow, species generation times, the timing of projected shifts

in climate, and the drivers of population genetic structure, need to be carefully considered when assessing risks of maladaptation. At this point GO models do not adequately account for these influential factors, meaning the outputs from many GO analyses are likely overstating vulnerability.

Context and implications

Despite the issues associated with these assumptions, recent studies have demonstrated the reliability of GO models in predicting risks of maladaptation in some experimental systems. Specifically, these studies have used a combination of population genomic data, common garden experiments, and/or simulations associated with quantitative traits and fitness, to quantify the GO between spatially distinct populations using contemporary allele frequencies (Fitzpatrick et al., 2021; Laruson et al., 2022); they find that the populations at the range edges have the greatest offset and the greatest decline in performance. For these studies, the GO is the contemporary allelic difference between the population's 'home' site and the common garden site. While these studies have validated the reliability of GO models in predicting performance of populations in new environments, it is important to acknowledge the limitations in using spatial approaches to predict temporal changes. These limitations have been discussed elsewhere (Damgaard, 2019; Rellstab et al., 2021), but in summary it is argued that observations across space are unlikely to hold true over time. However, most studies in the literature attempt to predict vulnerability of natural populations over time, which has not yet been supported by empirical research.

The failure to account for, accommodate, or even acknowledge these assumptions is expected to lead to significant problems during the interpretation phase of studies employing GO models. The fundamental problem is that the greatest GO is most likely to occur where the allele frequency curve is steepest while the most vulnerable populations are likely those that have the steepest fitness drop-off, but we demonstrate that these seldom overlap using theoretical reaction-norm curves (Figure 2). Yet, these two scenarios (fitness drop-off & genetic offset) are often conflated in published articles without a direct connection. The conflation of these two ideas would likely lead to harmful management practices, possibly leading to augmentation of resilient populations while those most at risk are overlooked. Ultimately, if a GO cannot be directly related to fitness, then what does a GO biologically represent?

Future considerations

Given the multitude of issues associated with GO models articulated in this and other commentaries (Hoffmann et al., 2021b; Rellstab et al., 2021), we argue that the scientific community needs to consider the fundamental value of these approaches. As discussed, selection processes are often highly complex and inherently difficult to predict. By not accounting for these complexities, GO models are effectively over-simplifying the process of selection, and in many cases are expected to produce misleading estimates of population vulnerability. With or without GO models, there will be uncertainty about how populations are likely to respond to new environmental challenges.

Despite the current limitations of GO models there may be potential for improvements in the future. Models must adequately account for fitness (Assumptions 1, 2, and 5), selection coefficients (Assumption 3), genetic redundancy from many small-effect loci (Assumption 4), pleiotropic effects (Assumption 6), and demography processes (Assumption 7). Demographic processes, such as gene flow can be easily estimated with in-hand genetic data, and should be relatively simple to incorporate within models. In contrast, other measures are inherently difficult to quantify, such as selection coefficients (s) which can vary spatially and temporally (Siepielski et al., 2009), and pleiotropic effects/trade-offs which are dependent on complicated trait-gene networks (Sikkink et al., 2015). Although, these effects can be approximated by comparing genomic and phenotypic datasets using existing computation techniques (Tyler et al., 2013; Mural et al., 2021). Either way, the only way to improve the reliability of GO models is to start integrating data that represents these evolutionary principles to existing models. Then we can overcome the current disconnect between the fitness landscape in local adaptation, selection pressure, and the biological importance of clinal allele frequency shifts, and create trustable predictions that could positively impact the conservation management of biodiversity at risk of decline or local extinction due to climate change.

Conclusions

This commentary highlights the complex nature of biological adaptations, which involve a range of mechanisms outside of the genotype-environment interaction paradigm. Our concern is that many applications of GO models are likely producing misleading estimates of population vulnerability due to violations of basic evolutionary principles. We have also demonstrated that the most vulnerable populations are at risk of being overlooked, and the vulnerability of others is

at risk of being overstated. Consequently, we argue that the adoption of GO models in their current form may compromise adaptive management of biodiversity values in a changing climate. Before we can rely on GO models as effective predictors of population vulnerability and incorporate them into conservation management frameworks, they need to be able to account for issues related to these fundamental assumptions. Yet in many cases, this information is inherently difficult to obtain for non-model organisms, meaning the task of estimating GOs is likely to be a futile exercise. As a scientific community we should not only question the reliability of current GO models, but also consider that perhaps they are doing more harm than good. Our recommendation is to resist using GO models to predict future patterns of allele frequency or vulnerability until further work is done to establish the theory behind GO models. Effectively accounting for complex evolutionary principles that influence the adaptation process is essential for robust and reliable predictions of species response to climate change.

References

- Ahrens, C.W., Andrew, M.E., Mazanec, R.A., Ruthrof, K.X., Challis, A., Hardy, G., et al. (2020) Plant functional traits differ in adaptability and are predicted to be differentially affected by climate change. *Ecology and Evolution*, 10, 232–248.
- Ahrens, C.W., Jordan, R., Bragg, J., Harrison, P.A., Hopley, T., Bothwell, H., et al. (2021a) Regarding the F-word: The effects of data filtering on inferred genotype-environment associations. *Molecular Ecology Resources*, 21, 1460–1474.
- Ahrens, C.W., Murray, K., Mazanec, R.A., Ferguson, S., Bragg, J., Jones, A., et al. (2021b) Genomic constraints to drought adaptation. *bioRxiv*, 2021.08.07.455511.
- Ahrens, C.W., Rymer, P.D., Stow, A., Bragg, J., Dillon, S., Umbers, K.D.L., et al. (2018) The search for loci under selection: trends, biases and progress. *Molecular Ecology*, 27, 1342–1356.
- Aitken, S.N., Yeaman, S., Holliday, J.A., Wang, T. & Curtis-McLane, S. (2008) Adaptation, migration or extirpation: climate change outcomes for tree populations. *Evolutionary Applications*, 1, 95–111.
- Arnold, S.J., Bürger, R., Hohenlohe, P.A., Ajie, B.C. & Jones, A.G. (2008) Understanding the evolution and stability of the G-matrix. *Evolution*, 62, 2451–2461.
- Barghi, N., Hermisson, J. & Schlötterer, C. (2020) Polygenic adaptation: a unifying framework to understand positive selection. *Nature Reviews Genetics*, 1–13.
- Bergek, S., Sundblad, G. & Björklund, M. (2010) Population differentiation in perch *Perca fluviatilis*: environmental effects on gene flow? *Journal of Fish Biology*, 76, 1159–1172.
- Bono, L.M., Smith, L.B., Pfennig, D.W. & Burch, C.L. (2017) The emergence of performance trade-offs during local adaptation: insights from experimental evolution. *Molecular Ecology*, 26, 1720–1733.
- Bontrager, M. & Angert, A.L. (2019) Gene flow improves fitness at a range edge under climate change. *Evolution Letters*, 3, 55–68.

- Brady, S.P., Bolnick, D.I., Angert, A.L., Gonzalez, A., Barrett, R.D.H., Crispo, E., et al. (2019) Causes of maladaptation. *Evolutionary Applications*, 12, 1229–1242.
- Chen, P. & Zhang, J. (2020) Antagonistic pleiotropy conceals molecular adaptations in changing environments. *Nature ecology & evolution*, 4, 461–469.
- Crispo, E., Moore, J., Lee-Yaw, J.A., Gray, S.M. & Haller, B.C. (2011) Broken barriers: Human-induced changes to gene flow and introgression in animals. *BioEssays*, 33, 508–518.
- Damgaard, C. (2019) A critique of the space-for-time substitution practice in community ecology. *Trends in Ecology & Evolution*, 34, 416–421.
- Dauphin, B., Rellstab, C., Wüest, R.O., Karger, D.N., Holderegger, R., Gugerli, F., et al. (2023) Re-thinking the environment in landscape genomics. *Trends in Ecology & Evolution*, 38, 261–274.
- Evangelou, A., Ignatiou, A., Antoniou, C., Kalanidou, S., Chatzimatthaiou, S., Shianiou, G., et al. (2019) Unpredictable Effects of the Genetic Background of Transgenic Lines in Physiological Quantitative Traits. *G3: Genes|Genomes|Genetics*, 9, 3877–3890.
- Exposito-Alonso, M., Exposito-Alonso, M., Rodríguez, R.G., Barragán, C., Capovilla, G., Chae, E., et al. (2019) Natural selection on the *Arabidopsis thaliana* genome in present and future climates. *Nature*, 573, 126–129.
- Filipe, J., Rymer, P., Byrne, M., Hardy, G., Mazanec, R. & Ahrens, C. (2022) Signatures of natural selection in a foundation tree along Mediterranean climatic gradients. *Molecular Ecology*.
- Fitzpatrick, M.C. & Keller, S.R. (2015) Ecological genomics meets community-level modelling of biodiversity: mapping the genomic landscape of current and future environmental adaptation. *Ecology Letters*, 18, 1–16.
- Forester, B.R., Beever, E.A., Darst, C., Szymanski, J. & Funk, W.C. (2022) Linking evolutionary potential to extinction risk: applications and future directions. *Frontiers in Ecology and the Environment*, 20, 507–515.

- Frankham, R. (2005) Genetics and extinction. *Biological Conservation*, 126, 131–140.
- Franks, S.J. & Weis, A.E. (2009) Climate change alters reproductive isolation and potential gene flow in an annual plant. *Evolutionary Applications*, 2, 481–488.
- Gagnaire, P.-A. & Gaggiotti, O.E. (2016) Detecting polygenic selection in marine populations by combining population genomics and quantitative genetics approaches. *Current Zoology*, 62, 603–616.
- Gaitán-Espitia, J.D. & Hobday, A.J. (2021) Evolutionary principles and genetic considerations for guiding conservation interventions under climate change. *Global Change Biology*, 27, 475–488.
- Gougherty, A.V., Keller, S.R. & Fitzpatrick, M.C. (2021) Maladaptation, migration and extirpation fuel climate change risk in a forest tree species. *Nature Climate Change*, 1–6.
- Guillaume, F. & Whitlock, M.C. (2007) Effects of migration on the genetic covariance matrix. *Evolution*, 61, 2398–2409.
- Hämälä, T., Gorton, A.J., Moeller, D.A. & Tiffin, P. (2020) Pleiotropy facilitates local adaptation to distant optima in common ragweed (*Ambrosia artemisiifolia*). *PLOS Genetics*, 16, e1008707.
- Hoban, S., Kelley, J.L., Lotterhos, K.E., Antolin, M.F., Bradburd, G., Lowry, D.B., et al. (2016) Finding the genomic basis of local adaptation: Pitfalls, practical solutions, and future directions. *The American Naturalist*, 188, 379–397.
- Hoffmann, A.A., Miller, A.D. & Weeks, A.R. (2021a) Genetic mixing for population management: From genetic rescue to provenancing. *Evolutionary Applications*, 14, 634–652.
- Hoffmann, A.A., Rymer, P.D., Byrne, M., Ruthrof, K.X., Whinam, J., McGeoch, M., et al. (2019) Impacts of recent climate change on terrestrial flora and fauna: Some emerging Australian examples. *Austral Ecology*, 44, 3–27.
- Hoffmann, A.A., Weeks, A.R. & Sgrò, C.M. (2021b) Opportunities and challenges in assessing climate change vulnerability through genomics. *Cell*, 184, 1420–1425.

Holt, R.D., Gomulkiewicz, R. & Barfield, M. (2003) The phenomenology of niche evolution via quantitative traits in a black-hole sink. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, 270, 215–224.

Isabel, N., Holliday, J.A. & Aitken, S.N. (2020) Forest genomics: Advancing climate adaptation, forest health, productivity, and conservation. *Evolutionary Applications*, 13, 3–10.

Kimura, M., Maruyama, T. & Crow, J.F. (1963) The mutation load in small populations. *Genetics*, 48, 1303–1312.

Kremer, A., Ronce, O., Robledo-Arnuncio, J.J., Guillaume, F., Bohrer, G., Nathan, R., et al. (2012) Long-distance gene flow and adaptation of forest trees to rapid climate change. *Ecology Letters*, 15, 378–392.

Lasky, J.R., Josephs, E.B. & Morris, G.P. (2022) Genotype–environment associations to reveal the molecular basis of environmental adaptation. *The Plant Cell*, 35, 125–138.

Laughlin, D.C., Gremer, J.R., Adler, P.B., Mitchell, R.M. & Moore, M.M. (2020) The net effect of functional traits on fitness. *Trends in Ecology & Evolution*, 35, 1037–1047.

Laughlin, D.C. & Messier, J. (2015) Fitness of multidimensional phenotypes in dynamic adaptive landscapes. *Trends in Ecology & Evolution*, 30, 487–496.

Lotterhos, K.E. (2023) The paradox of adaptive trait clines with nonclinal patterns in the underlying genes. *Proceedings of the National Academy of Sciences*, 120, e2220313120.

Lotterhos, K.E., Yeaman, S., Degner, J., Aitken, S. & Hodgins, K.A. (2018) Modularity of genes involved in local adaptation to climate despite physical linkage. *Genome Biology*, 19, 157.

Manel, S., Perrier, C., Pratlong, M., Abi-Rached, L., Paganini, J., Pontarotti, P., et al. (2016) Genomic resources and their influence on the detection of the signal of positive selection in genome scans. *Molecular Ecology*, 25, 170–184.

Mathieson, I. & McVean, G. (2013) Estimating Selection Coefficients in Spatially Structured Populations from Time Series Data of Allele Frequencies. *Genetics*, 193, 973–984.

Mauro, A.A. & Ghalambor, C.K. (2020) Trade-offs, pleiotropy, and shared molecular pathways: A unified view of constraints on adaptation. *Integrative and Comparative Biology*, 60, 332–347.

Mérot, C. (2022) Evolution: How important is the dimensionality of natural selection in local adaptation? *Current Biology*, 32, R274–R276.

Mural, R.V., Grzybowski, M., Miao, C., Damke, A., Sapkota, S., Boyles, R.E., et al. (2021) Meta-analysis identifies pleiotropic loci controlling phenotypic trade-offs in sorghum. *Genetics*, 218, iyab087.

Polechová, J. & Barton, N.H. (2015) Limits to adaptation along environmental gradients. *Proceedings of the National Academy of Sciences*, 112, 6401–6406.

Pujolar, J.M., Jacobsen, M.W., Als, T.D., Frydenberg, J., Munch, K., Jónsson, B., et al. (2014) Genome-wide single-generation signatures of local selection in the panmictic European eel. *Molecular Ecology*, 23, 2514–2528.

Razgour, O., Forester, B., Taggart, J.B., Bekaert, M., Juste, J., Ibáñez, C., et al. (2019) Considering adaptive genetic variation in climate change vulnerability assessment reduces species range loss projections. *Proceedings of the National Academy of Sciences*, 116, 201820663.

Rellstab, C., Dauphin, B. & Exposito-Alonso, M. (2021) Prospects and limitations of genomic offset in conservation management. *Evolutionary Applications*, 14, 1202–1212.

Rellstab, C., Gugerli, F., Eckert, A.J., Hancock, A.M. & Holderegger, R. (2015) A practical guide to environmental association analysis in landscape genomics. *Molecular Ecology*, 24, 4348–4370.

Rennison, D.J. & Peichel, C.L. (2022) Pleiotropy facilitates parallel adaptation in sticklebacks. *Molecular Ecology*.

Sebbenn, A.M., Carvalho, A.C.M., Freitas, M.L.M., Moraes, S.M.B., Gaino, A.P.S.C., Silva, J.M. da, et al. (2011) Low levels of realized seed and pollen gene flow and strong spatial genetic structure in a small, isolated and fragmented population of the tropical tree *Copaifera langsdorffii* Desf. *Heredity*, 106, 134–145.

Shoval, O., Sheftel, H., Shinar, G., Hart, Y., Ramote, O., Mayo, A., et al. (2012) Evolutionary trade-offs, Pareto optimality, and the geometry of phenotype space. *Science*, 336, 1157–1160.

Sikkink, K.L., Reynolds, R.M., Cresko, W.A. & Phillips, P.C. (2015) Environmentally induced changes in correlated responses to selection reveal variable pleiotropy across a complex genetic network. *Evolution*, 69, 1128–1142.

Stitzer, M.C. & Ross-Ibarra, J. (2018) Maize domestication and gene interaction. *New Phytologist*, 220, 395–408.

Thompson, K.A. (2020) Experimental hybridization studies suggest that pleiotropic alleles commonly underlie adaptive divergence between natural populations. *The American Naturalist*, 196, E16–E22.

Todesco, M., Owens, G.L., Bercovich, N., Légaré, J.-S., Soudi, S., Burge, D.O., et al. (2020) Massive haplotypes underlie ecotypic differentiation in sunflowers. *Nature*, 584, 602–607.

Tusso, S., Nieuwenhuis, B.P.S., Weissensteiner, B., Immler, S. & Wolf, J.B.W. (2021) Experimental evolution of adaptive divergence under varying degrees of gene flow. *Nature Ecology & Evolution*, 5, 338–349.

Tyler, A.L., Lu, W., Hendrick, J.J., Philip, V.M. & Carter, G.W. (2013) CAPE: An R package for combined analysis of pleiotropy and epistasis. *PLoS Computational Biology*, 9, e1003270.

Weiskopf, S.R., Rubenstein, M.A., Crozier, L.G., Gaichas, S., Griffis, R., Halofsky, J.E., et al. (2020) Climate change effects on biodiversity, ecosystems, ecosystem services, and natural resource management in the United States. *Science of The Total Environment*, 733, 137782.

White, N.J. & Butlin, R.K. (2021) Multidimensional divergent selection, local adaptation and speciation. *Evolution*.

Whitlock, M.C. (2000) Fixation of new alleles and the extinction of small populations: Drift load, beneficial alleles, and sexual selection. *Evolution*, 54, 1855–1861.

Yeaman, S. (2015) Local adaptation by alleles of small effect. *The American Naturalist*, 186, S74–S89.