

# Landscape Genomics: Understanding Relationships Between Environmental Heterogeneity and Genomic Characteristics of Populations

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**Abstract** Landscape genomics is a rapidly advancing research field that combines population genomics, landscape ecology, and spatial analytical techniques to explicitly quantify the effects of environmental heterogeneity on neutral and adaptive genetic variation and underlying processes. Landscape genomics has tremendous potential for addressing fundamental and applied research questions in various

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research fields, including ecology, evolution, and conservation biology. However, the unique combination of different scientific disciplines and analytical approaches also constitute a challenge to most researchers wishing to apply landscape genomics. Here, we present an introductory overview of important concepts and methods used in current landscape genomics. For this, we first define the field and explain basic concepts and methods to capture different hypotheses of landscape influences on neutral genetic variation. Next, we highlight established and emerging genomic tools for quantifying adaptive genetic variation in landscape genomic studies. To illustrate the covered topics and to demonstrate the potential of landscape genomics, we provide empirical examples addressing a variety of research question, i.e., the investigation of evolutionary processes driving population differentiation, the landscape genomics of range expanding species, and landscape genomic patterns in organisms of special interest, including species inhabiting aquatic and terrestrial environments. We conclude by outlining remaining challenges and future research avenues in landscape genomics.

**Keywords** Adaptive landscape genetics • Environmental association analysis (EAA) • Functional connectivity • Genome-wide association studies (GWAS) • Genotype-environment association (GEA) • Landscape resistance • Local adaptation • Outlier loci • Seascape genomics

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# 1 Introduction

Any geneticist will agree that environmental conditions can substantially affect the genetic variation of natural populations, with important consequences for ecological and evolutionary processes and phenomena. For instance, selection pressures induced by the heterogeneous environment can promote local adaptation by favoring different alleles in different spatial localities (e.g., Hedrick et al. 1976; Richardson et al. 2014), just as historical or contemporary environmental barriers to gene flow (e.g., ice-covered areas during glacial periods, landscape features such as roads) can increase genetic differentiation among formerly connected populations (e.g., Hitchings et al. 1997) due to genetic drift. In some cases, local adaptation due to natural selection and reduced gene flow can ultimately lead to speciation, making genetic variation a fundamental level of the biodiversity hierarchy (Via 2002; Primack 2014). Nevertheless, explicitly accounting for spatial environmental heterogeneity in genetic studies – especially those dealing with recent and contemporary population genetics at fine spatial scales – has seen an unprecedented growth only in the last ca. 15 years (Storfer et al. 2010; Dyer 2015a). In part, this is due to the emergence of the field of landscape genetics, which was formally introduced in a seminal paper by Manel et al. (2003), and later extended towards landscape genomics (Luikart et al. 2003; Joost et al. 2007). In essence, landscape genetics can be defined as *... research that combines population genetics, landscape ecology, and spatial analytical techniques to explicitly quantify the effects of landscape composition, configuration, and matrix quality on micro-evolutionary processes, such as gene flow, drift, and selection, using neutral and adaptive genetic data.* (Balkenhol et al. 2016a, p. 3). Basically, one can simply replace “population genetics” with “population genomics” to define landscape genomics (see Sect. 2.1 for details). While several earlier landscape genetic studies exist (e.g., Pamilo 1988; Merriam et al. 1989; Barbujani and Sokal 1990; Manicacci et al. 1992; Gaines et al. 1997; see also Manel et al. 2003), the recent growth of landscape genomic studies can be attributed to two main factors. First, landscape genomic studies are nowadays facilitated by novel technologies that make it possible to gather and analyze genetic and environmental data at large quantities and at high qualities. For instance, next-generation sequencing (NGS) allows us to quantify genetic variation in many individuals at dense genomic coverage at decreasing costs (e.g., Luikart et al. 2003; Andrews et al. 2016). Similarly, environmental data can be obtained at high spatial and temporal resolutions for large study areas from remote sensing devices, such as satellites or drones (e.g., Pettorelli et al. 2005; Anderson and Gaston 2013). Increased computational power also enables us to actually handle and analyze these large, spatially explicit data sets in a reasonable amount of time (e.g., Kidd and Ritchie 2006; Paul and Song 2012).

Second, the swift rise of landscape genomics can also be attributed to the increased interest in the ecological and evolutionary consequences of contemporary environmental change, such as habitat loss and fragmentation or human-expedited climate change. Specifically, understanding and predicting the consequences of ongoing environmental changes can be regarded as a major research need in the current Anthropocene, where humans are causing substantial environmental

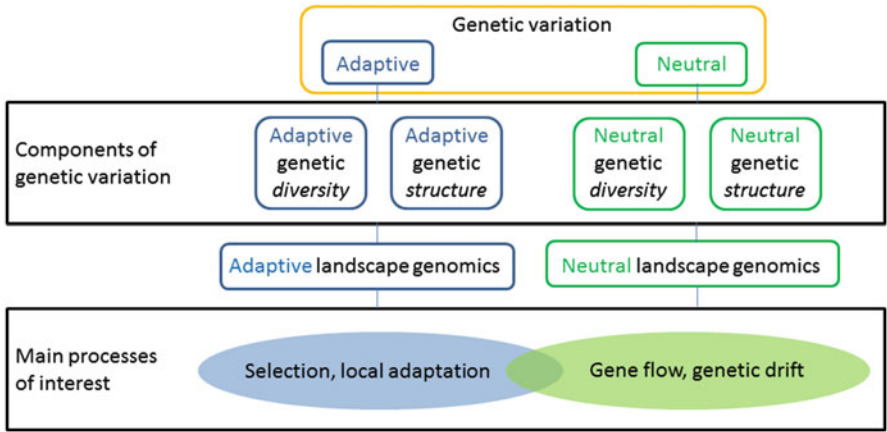
changes and associated biodiversity losses (e.g., Haddad et al. 2015). Due to the technological advances mentioned above, landscape genomics has tremendous potential for contributing to such research, so it is not surprising that the number of landscape genomic studies has been rising exponentially since 2003 (Storfer et al. 2010; Dyer 2015a). However, getting started in landscape genomics can still be a daunting task, because the field amalgamates concepts, data, and methods from seemingly disparate disciplines that relatively few scientists are familiar with. Furthermore, many of the analytical approaches employed in landscape genomics develop very rapidly, making it challenging to keep up-to-date with all methods and concepts that are relevant for a landscape genomic study.

Here, our goal is to provide a general introduction to the field of landscape genomics. The chapter complements other recent work that provided a more general overview of landscape genetics (Balkenhol et al. 2016b), because we here focus more strongly on genomic approaches for landscape genetics and specifically address geneticists interested in applying landscape genomic approaches. Because of this, we assume that readers are familiar with basic population genetic concepts, which are discussed elsewhere (e.g., Waits and Storfer 2016) and in two other chapters of this book.

The chapter starts with a description of basic concepts and definitions that are a prerequisite for understanding the remaining sections. Next, we briefly summarize concepts and approaches for neutral landscape genomics, before focusing on more novel approaches that are particularly suitable for adaptive landscape genomics (see Sect. 2.1 for definition of the different terms). To illustrate the covered concepts and methods, we provide several empirical examples of landscape genomic applications, and finally outline several remaining challenges and future opportunities in landscape genomics.

## 2 Basic Concepts and Definitions

We can distinguish two components of genetic variation, namely the amount of genetic variation (genetic diversity, sometimes also called genetic variability) and the spatial distribution of genetic variation (genetic structure, e.g., via measures of genetic differentiation or genetic distances). Both components of genetic variation can be quantified using loci or genomic regions that are affected by selection (adaptive genetic variation) and those loci or regions that are not affected by it (neutral genetic variation). However, it is important to note that genetic data showing signs of selection may not actually be under selection, because selection may actually be acting on other loci or regions that the analyzed genetic data are linked to. Similarly, genetic data that appear to be selectively neutral could still be under selection, for example when selection acts upon highly polygenic traits so that the influence of selection on individual loci or small genomic regions is too small to be detected. In general, it is hard to truly discriminate selectively neutral from selectively adaptive genetic variation, except in a few cases, such as microsatellite or SNP variation controlled by loci in the noncoding regions. Nevertheless, we here follow the vast majority of publications



**Fig. 1** Conceptual chart illustrating adaptive and neutral landscape genomics. Note that the processes of interest overlap between the two types of landscape genomics, and the greatest insights can be accomplished by combining neutral and adaptive data

that use the term adaptive genetic data to refer to those loci or regions that show signs of selection, and neutral genetic data for those loci or regions that do not show any evidence of selection. Depending on whether we use neutral or adaptive genetic data, we can focus on different underlying processes and research questions (Fig. 1).

Furthermore, landscape genomic studies can focus on analyzing environmental effects on neutral or adaptive genetic variation per se, which is particularly interesting for geneticists investigating the emergence and maintenance of genetic variation in nature. Alternatively, studies can use landscape genomic approaches to investigate how the environment impacts the processes that underlie observed patterns of genetic variation, which is often most interesting for ecologists who study effective dispersal (i.e., migration) and gene flow, and evolutionary biologists studying natural selection, adaptation, etc.

## 2.1 Landscape Genetics vs. Genomics

Given the different types of genetic variation, processes, and questions that landscape genetic studies can focus on, we can distinguish between “neutral” and “adaptive” landscape genetics (Holderegger et al. 2006). While the former focuses on putatively neutral processes, such as gene flow and genetic drift, the latter focuses on adaptive processes, such as selection and local adaptation. Since genomic approaches greatly facilitate the detection of loci or genomic regions under selection (e.g., Andrews et al. 2016), the term landscape genomics is now often used for studies seeking to identify environmental influences on adaptive genetic variation (Schwartz et al. 2009; Hand et al. 2015). In contrast, the term landscape genetics usually applies to studies dealing with selectively neutral genetic markers

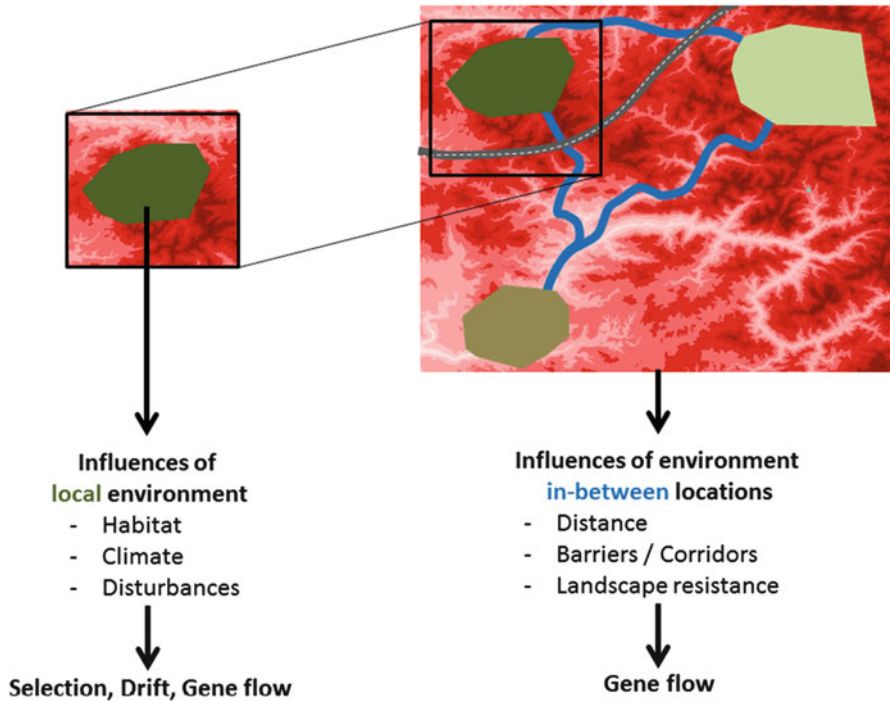
and underlying processes (Manel and Holderegger 2013). However, it is possible to conduct an adaptive landscape genetic study without applying population genomics, for example through the use of established quantitative trait loci (QTLs) that are known to be under selection (Holderegger et al. 2006; Manel et al. 2010). Similarly, it is possible to conduct a neutral landscape genomic study, for example when an NGS approach is used to develop thousands of single-nucleotide polymorphisms (SNPs) and then choosing only those that are likely not under selection (i.e., by excluding outlier loci, e.g., Whitlock and Lotterhos 2015). This subset of tentative selectively neutral SNPs can then be used to evaluate landscape influences on neutral gene flow (e.g., Rasic et al. 2014).

While we acknowledge that not all of the examples we discuss in this chapter have been derived from genome-wide sequencing approaches, genomic data will undoubtedly become the standard for all landscape genetic studies in the near future, and the difference in nomenclature between landscape genetics and genomics will further diminish and eventually disappear. Hence, we here use the term landscape genomics to encompass all studies that explicitly test for environmental impacts on genome-wide genetic variation, even if they do not (yet) rely fully on the whole genome sequencing approaches. However, we distinguish between neutral landscape genomics and adaptive landscape genomics, depending on the type of genetic data and the processes of interest (Fig. 1). Ideally, neutral and adaptive landscape genomics should be combined to fully elucidate the ecological and evolutionary processes affecting different components of genetic variation (Hand et al. 2015; Balkenhol et al. 2016c). However, since underlying assumptions, data types, and methods differ for these two types of landscape genomics, we discuss them separately in Sects. 3 and 4, respectively.

## 2.2 *Influences of Spatial Environmental Heterogeneity on Genetic Variation*

From conceptual and analytical standpoints, genetic variation can be influenced by *local* environmental conditions, as well as the environment occurring *in-between* sampling locations (Fig. 2).

Local environmental conditions can include, for example, factors such as local climate, or habitat characteristics such as vegetation type and quality. Local environmental conditions can be measured *at* sampling locations, *within* areas, or *around* sampling locations or areas, for example within a certain radius around sampling points or habitat patches (Wagner and Fortin 2013; Pflüger and Balkenhol 2014). Local environmental conditions can induce spatially varying selective pressures, which directly affect adaptive genetic variation (Schoville et al. 2012). The local environment can favor certain alleles over others, or select against migrant individuals or their offspring via natural or sexual selection (e.g., Nosil et al. 2005). Local environmental conditions can also bias dispersal, for example



**Fig. 2** Potential environmental influences on genetic variation. The green areas show sampling locations or patches, with local environmental conditions indicated by different green color shades. The red gradient represents the heterogeneous quality of the landscape matrix. Left: Local environmental conditions, such as habitat type and quality, can directly impact genetic variation via natural selection, but can also impact drift and effective dispersal, for example when the local carrying capacity affects population size or density-dependent emi- and immigration. Right: Environmental conditions in-between locations can impact effective dispersal and resulting gene flow. In nature, both local and in-between influences will be important for shaping both neutral and adaptive genetic variation

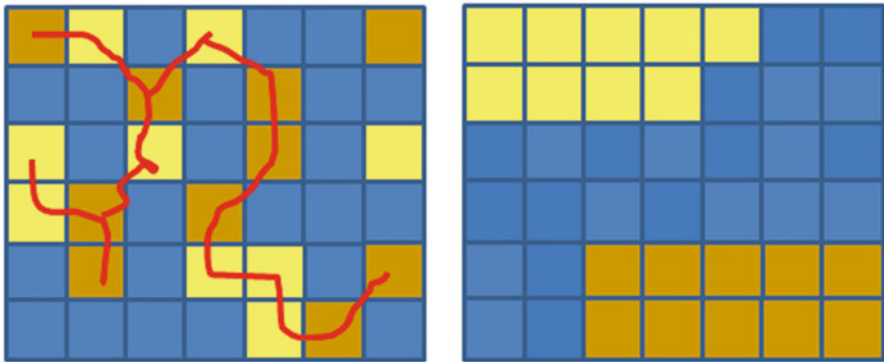
when dispersing individuals prefer to settle into specific environments, or into environments that are similar to their natal environment (Wang and Bradburd 2014). Additionally, local environmental conditions can impact local population sizes and carrying capacities, which impact drift and also density-dependent dispersal and resulting patterns of gene flow (Pflüger and Balkenhol 2014).

The environment in-between locations can include barriers that impede gene flow or corridors that facilitate it. More generally, the environment in-between locations can be characterized in terms of landscape resistance, which essentially reflects the probability that organisms will successfully cross a particular environment (Zeller et al. 2012). The resistance of a landscape is largely determined by the intervening “matrix,” which is the term used to describe the landscape found in-between sampling locations that is not primary habitat of the study species. The matrix can alter levels of gene flow among locations, because matrix quality



impacts effective dispersal (i.e., dispersal leading to successful reproduction), either because individuals respond to environmental heterogeneity during dispersal movements, or because the environment experienced during dispersal alters their survival (Zeller et al. 2012). Many studies have shown that the quality and heterogeneity of the matrix (i.e., its resistance) can have profound influences on effective dispersal, gene flow, and resulting patterns of genetic variation (e.g., reviewed in Waits et al. 2016). Analyzing such in-between environmental characteristics is probably the most novel contribution that landscape genomics has made to population genetic studies (Holderegger and Wagner 2008; Manel and Holderegger 2013). While local environmental characteristics, such as patch size or climate, have been considered in many genetic studies even before the terms landscape genetics and landscape genomics were coined (see, e.g., Keyghobadi 2007), explicitly including the effects of landscape structure is relatively new. Landscape structure basically consists of two components, called *composition* and *configuration*. While composition refers to the amount of certain elements within a landscape (e.g., percentage of area covered by different vegetation types), landscape composition refers to the spatial arrangement of these elements (Fig. 3).

The spatial arrangement of the landscape is particularly important for analyzing the effects of the landscape matrix on functional connectivity, or the degree to which a landscape facilitates the dispersal of individual organisms (or their propagules) and resulting gene flow (Taylor et al. 2006).



**Fig. 3** Landscape composition and configuration. Two hypothetical landscapes with the same composition (i.e., number of blue, yellow, and brown cells), but different configuration (i.e., spatial arrangement of differently colored cells). Assuming that a study species cannot move through the blue cells, the left landscape can actually still be crossed (i.e., the cells in the landscape are still functionally connected, as demonstrated by the red path), even though the left landscape looks more fragmented than the right one



### 2.3 Analytical Steps

To reflect the different potential genetic influences of the local environment and the matrix, Wagner and Fortin (2013) presented a conceptual framework for the spatial analysis of landscape genetic data. They distinguish among analytical approaches that are based on nodes, neighborhoods, links, or boundaries. While the first two types of methods are most appropriate for analyzing effects of the local environment on genetic variation, the latter two methods are most suitable for analyzing effects of the environment in-between the sampled locations. Importantly, the different environmental influences are not mutually exclusive and probably often interact in nature. Thus, to fully understand the effects of environmental heterogeneity on genetic variation, landscape genomic studies should ideally test and contrast multiple hypotheses relating to different influences.

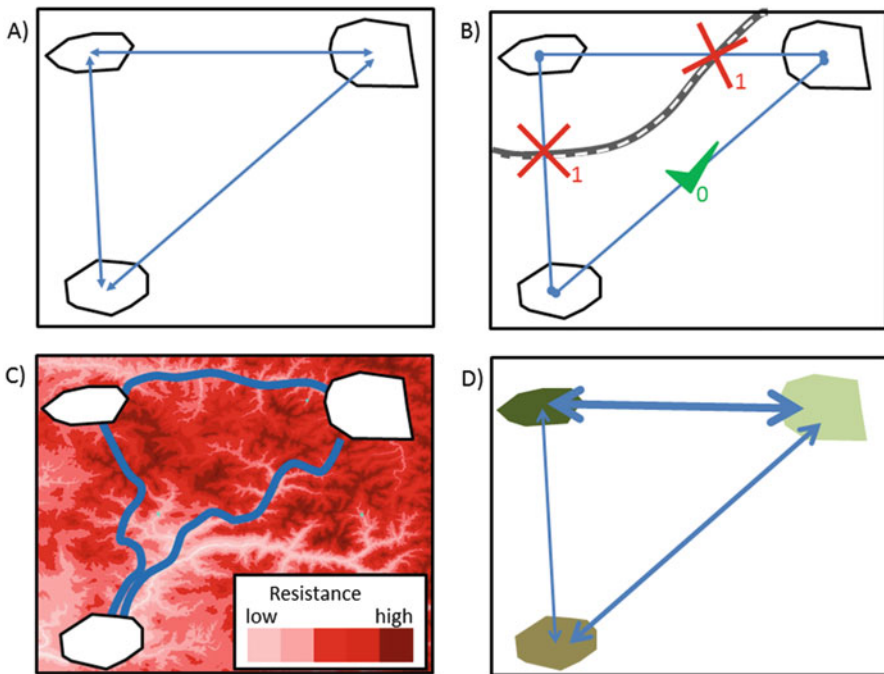
To assess these various effects, landscape genomic studies essentially have to conduct three analytical steps (Balkenhol et al. 2016a). First, they have to quantify genetic variation so that the genetic data captures the patterns and micro-evolutionary processes of interest. Second, they have to quantify environmental heterogeneity so that the landscape data reflects different hypotheses to be tested. Finally, they have to statistically link genetic and environmental data so that landscape-genetic hypotheses can be tested explicitly. In reality, these different steps are not always separated, for example because some methods simultaneously accomplish steps 2 and 3. However, to get started with landscape genomics, it often helps to envisage the analysis along these three steps. Hence, we encourage readers to keep the three analytical steps in mind when reading the next sections, where we describe different analytical approaches for neutral and adaptive landscape genomics.

## 3 Neutral Landscape Genomics

Landscape genomic studies based on selectively neutral genetic data often focus on environmental effects on genetic *structure*. Specifically, most neutral landscape genomic studies analyze environmental effects on functional connectivity, as defined above. To test for environmental effects on functional connectivity, most studies statistically compare measures of genetic similarity with measures of landscape connectivity among sampling units, which may be either individuals or populations (i.e., groups of individual). Individual-based analyses have been shown to have higher power for detecting landscape-genetic relationships (Landguth et al. 2012; Prunier et al. 2013), and are especially suitable for continuously distributed species. However, population-based analyses remain meaningful whenever genetic populations can be defined and delineated with no or little uncertainty, or when analyses are conducted between distinct spatial areas, such as management units.

### 3.1 Distance-Based Analysis Framework

Regardless of how sampling units are defined, most studies use a distance-based analysis for their inferences (Storfer et al. 2010; DiLeo and Wagner 2016). For this, genetic dissimilarity is usually estimated in the form of genetic distances or indices of genetic differentiation, such as  $F_{ST}$  values. Higher values of these pairwise estimates are interpreted as indicating lower levels of gene flow and underlying functional connectivity. These values are then compared to estimates of functional landscape connectivity, which are often calculated in the form of effective distances. These effective distances account for the hypothesized heterogeneity of the landscape and can reflect different landscape-genetic hypotheses (Fig. 4).



**Fig. 4** Hypotheses typically tested in neutral landscape genomics, with blue arrows depicting the effective distances estimated to reflect each hypothesis. (a) Isolation-by-distance (IBD) is tested by correlating genetic with geographic distances among locations (straight-line). (b) To test isolation-by-barrier (IBB), the occurrence or number of linear barriers found in-between locations is calculated. (c) Testing isolation-by-resistance (IBR) requires the estimation of effective distances that account for the heterogeneous resistance of the landscape. (d) For isolation-by-environment (IBE), environmental (dis-)similarities are estimated that quantify the differences in local environmental conditions among sampling locations

### 3.1.1 Isolation-by-Distance (IBD)

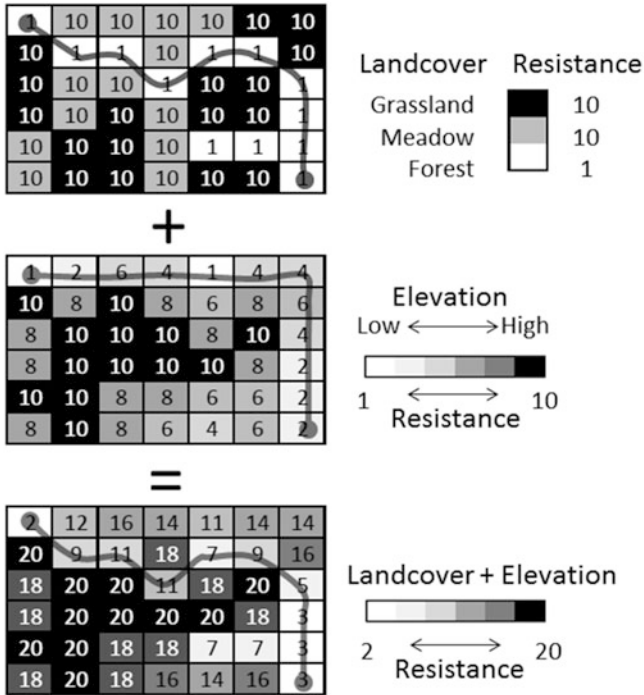
An often-tested hypothesis is based on the classical IBD model originally developed by Wright (1943). In this model, gene flow among locations is affected by the geographic (i.e., straight-line) distance separating them (Fig. 4a). The strength of IBD depends on the scale of the study area in relation to the dispersal distance of the species, and the model assumes a homogeneous environment. IBD has been confirmed in many study systems, and it often serves as a null model in both neutral and adaptive landscape genomics.

### 3.1.2 Isolation-by-Barrier (IBB)

The first alternative to IBD is the hypothesis of IBB (Fig. 4b). Here, effective dispersal and resulting gene flow are assumed to be influenced by linear barriers that cross the study area either partially or completely. Barriers can include mountain ranges, rivers, roads, habitat edges, etc. and can impede gene flow either completely or partially. Analyzing IBB within the distance-based framework can, for example, be accomplished via a dummy matrix, where those sampling location pairs that are separated by a barrier receive a value of 1, whereas locations not separated by a barrier receive a pairwise value of 0. Alternatively, the number of times that a straight line between two sampling locations crosses potential barriers can be used to estimate a pairwise effective distance reflecting IBB.

### 3.1.3 Isolation-by-Resistance (IBR)

The third and perhaps most prominent landscape-genetic hypothesis is termed IBR (Fig. 4c). This hypothesis considers the heterogeneous resistance of the landscape matrix to movement and gene flow (McRae 2006). To test IBR, various types of effective distances can be estimated that account for the resistance of the environment by calculating the least-costly route among pairs of sampling locations. The two most commonly used effective distances accounting for landscape resistance are based on (a) least-cost and (b) circuit-theoretic algorithms. Least-cost algorithms attempt to find the single, least-costly path, and essentially assume that a dispersing individual has perfect knowledge of the entire landscape and moves through it in an optimal fashion (Adriaensen et al. 2003). In contrast, circuit-theory considers all possible pathways among locations, assumes that individuals move across the landscape randomly, and that their probability of crossing a certain area of the landscape depends on the resistance of that area (McRae et al. 2008). Another option for capturing the landscape resistance among sampling locations is to use transects or corridors of a certain width connecting sampling locations, and to quantify the resistance within these transects (e.g., van Strien et al. 2012).



**Fig. 5** Illustration of landscape resistance surfaces. For both variables “landcover” and “elevation” resistance values range from 1 (lowest resistance) to 10 (highest resistance). Based on each surface, effective distances can be calculated, for example using least-cost paths (gray lines). Note that in this example, the route of the least-cost path is the same for the “landcover” and the combined surface, but the cumulative costs distance is different between all three surfaces

*Landscape Resistance Surfaces* All of these approaches are based on resistance surfaces, which are spatial data layers where each raster cell of the study landscape receives a value that represents the hypothesized resistance of the landscape in that cell. For example, in Fig. 5, two variables are hypothesized to influence landscape resistance in a hypothetical species that preferentially moves through forest, but tends to avoid high-elevation areas. For the variable “landcover,” the resistance value is set to 1 (no resistance), if a cell is covered by forest, and 10 otherwise. Similarly, for the variable “elevation,” resistance values range from 1 (lowest elevation) to 10 (highest elevation). The combined resistance surface reflecting both variables ranges from 2 to 20. Based on each surface, effective distances based on least-cost or circuit-theoretic algorithms can be calculated. Many other approaches for parameterizing and optimizing resistance surfaces exist, and they can reflect various hypotheses of linear or nonlinear relationships between the landscape data and resistance to gene flow (e.g., Dudaniec et al. 2013, 2016; Mateo-Sánchez et al. 2015). The resistance surface leading to effective distances that show the strongest statistical association with the genetic distances is chosen as

the surface that best captures the impacts of landscape resistance on gene flow and spatial genetic structure.

Since resistance values are only hypothesized (i.e., the true impact of the environment on effective dispersal in the study species is not known with certainty), many different combinations of variables and different resistance values of each variable have to be evaluated in empirical studies (Cushman et al. 2006). Due to the complexity of this task, many options exist for parameterizing and evaluating resistance surfaces, and we refer readers to the comprehensive reviews of Spear et al. (2010, 2016) for further details. In landscape genomics, the main result of resistance surface modeling is one or several pairwise matrices of distances (in cost units or electric current values) that measure the effective separation distance between any two sampling locations. Each matrix reflects a different hypothesis of how the study species might be influenced by landscape resistance. The best representation of landscape resistance can then be identified by statistically comparing these different distances to the measures of genetic distances among sampling units, essentially identifying which resistance hypothesis best explains the observed genetic distance.

### 3.1.4 Isolation-by-Environment (IBE)

The fourth major hypothesis in neutral landscape genomics is IBE (Fig. 4d). Under this hypothesis, the degree of genetic differentiation among sampling units should increase with increasing environmental dissimilarity (Wang and Bradburd 2014). Put differently, higher levels of gene flow should occur among locations that are more similar with respect to local environmental conditions, such as habitat type, temperature, or precipitation. IBE can arise from many different processes, both adaptive and neutral, as discussed in Sect. 5.1.

To test for IBE, effective distances among sampling locations are usually calculated in the form of environmental distances (also called environmental resemblances, similarities, or dissimilarities). These distances essentially estimate a pairwise measure of how close sampling units are in the single or multivariate variable space, so that location pairs with more similar environmental conditions will have lower pairwise environmental distance (i.e., low dissimilarity, high similarity or resemblance). A variety of such environmental distance metrics exist and their advantages and limitations are, for example, discussed in Legendre and Legendre (2012).

Importantly, within the distance-based analytical framework commonly applied in neutral landscape genomics, IBE is the only hypothesis that considers local environmental conditions, rather than influences of the environment in-between sampling locations (i.e., distance, barriers, or resistance).

As stated before, the different hypotheses are not mutually exclusive, and all of them can and should be considered in landscape genomic studies. Also, it should be noted that there are many other approaches for quantifying neutral genetic variation and environmental heterogeneity that we have not discussed here. For example,

there is a suite of methods for detecting (local) linear barriers to gene flow, such as Monmonier's algorithm (Monmonier 1973) or the Wombling method (Womble 1951; Crida and Manel 2007). Results of these methods can be compared to the spatial occurrence of environmental boundaries, such as habitat edges or roads (Blair et al. 2012). Similarly, genetic structure is now often quantified using a variety of genetic clustering methods, for example via the well-known software STRUCTURE (Pritchard et al. 2000; see also François and Waits 2016 for a review of genetic clustering methods). The outcome of such clustering methods can either be used directly for landscape genetic inferences, or they can be used to estimate genetic distances among individuals, which then can be compared to effective distances for enhanced ecological insight (e.g., Balkenhol et al. 2014).

### ***3.2 Statistically Linking Neutral Genetic and Environmental Data***

A large variety of statistical approaches exists for the final analytical step, where genetic variation and environmental variables have to be linked statistically (Wagner and Fortin 2013, 2016). Analytical methods commonly used in other fields (e.g., standard regression) can generally not be used in neutral landscape genomics, because we are dealing with pairwise data (genetic and effective distances among all pairs of sampling locations), and because data often show significant positive spatial autocorrelation, basically meaning that data from locations that are close in space tend to be more similar than data from locations far apart. In essence, both of these challenges lead to non-independent data values that violate fundamental assumptions of most standard statistical methods. Hence, the final step often requires the use of special analytical techniques that can deal with the data structure typically encountered in neutral landscape genomics. A detailed review of existing methods for this is beyond the scope of this chapter, and readers are referred to Wagner and Fortin (2016) for a thorough overview of the various available approaches.

Within the distance-based framework outlined above, assessing the relative support for the different landscape genetic hypotheses is often particularly challenging because the various effective distances can be strongly correlated with each other. This challenge is especially severe when effective distances are compared that have been calculated from different parameterizations of the same resistance surface (Zeller et al. 2016). The most commonly used methods are still the Mantel test and the partial Mantel test (Storfer et al. 2010; DiLeo and Wagner 2016), which are basically correlation approaches with significance values estimated via a specific permutation approach. Mantel tests have been severely criticized for various reasons, and alternative approaches should be used whenever possible (Balkenhol et al. 2009; Legendre and Fortin 2010; Guillot and Rousset 2013; Legendre et al. 2015). However, there is currently no consensus on the most appropriate method for

statistically testing associations between environmental and neutral genetic data. More studies are required to assess the relative utility of different methods for specific research questions and data sets.

In sum, a large variety of methods are available for neutral landscape genomics, and their application to different terrestrial and aquatic systems has already led to important findings in ecology, evolution, and conservation biology (see, e.g., Wang et al. 2013; Selkoe et al. 2016a; Waits et al. 2016). This large analytical variety is also one of the main challenges for current studies, because it hinders the comparability of results, and choosing among methods is not trivial (see Sect. 6). However, we highlight that in addition to methodological considerations, another, perhaps even more important aspect for neutral landscape genomics is the precise, a priori definition of multiple, testable hypothesis. This is also important for guiding general study design and sampling in landscape genomics (Balkenhol and Fortin 2016). Thus, rather than getting lost in analytical details, we encourage researchers to first and foremost focus on defining good research questions and design landscape genomic studies that lead to strong scientific inferences.

## 4 Adaptive Landscape Genomics

Most studies cited above have actually not used genome-wide approaches to quantify genetic variation, but instead have largely relied on microsatellites or relatively short sequences of mitochondrial DNA. Such data are appropriate for addressing questions related to neutral genetic data and underlying processes, but are not quite suitable for addressing landscape genomic research questions dealing with selection and adaptation. For these kinds of questions, we usually have to identify loci or regions under selection, and then statistically relate this adaptive genetic data to environmental heterogeneity. Storfer et al. (2016) distinguish four general frameworks for accomplishing this: (a) a *correlative* framework that is based on outlier detection and/or environmental association analysis, (b) a *phenotypic* framework which relies on quantitative trait loci (QTL) or genome-wide association studies (GWAS), (c) a framework based on *candidate genes*, and (d) a framework based on *exomes and transcriptomes*. We discuss all of these frameworks below, but largely focus on correlative approaches, and especially environmental association analysis (EAA). This is arguably the most widely used framework in landscape genomics right now, it seems to outperform other approaches for identifying adaptive genetic variation in heterogeneous environments (Jones et al. 2013), and it is the only of the four frameworks that directly incorporates environmental data into the detection of selection.



## 4.1 Correlative Approaches

Correlative landscape genomic approaches often rely on identifying loci or regions under selection via different types of “outlier detection” methods. As pointed out by Luikart et al. (2003), this population genomics approach aims at finding the genes whose diversity patterns do not follow the ones of the rest of the genome. This is greatly facilitated by high-throughput sequencing techniques, which enable genome-wide genotyping and sampling of genetic markers that may be situated in, or linked to, functional genes that are under selection. Popular “reduced representation” sequencing approaches to obtain genome-wide markers such as Single Nucleotide Polymorphisms (SNPs) include Restriction-site Associated DNA Sequencing (RADseq, Miller et al. 2007) or Genotype by Sequencing (GBS, Elshire et al. 2011; Narum et al. 2013) and target enrichment (Dasgupta et al. 2015; Lu et al. 2016, 2017; Suren et al. 2016). Details on these approaches can be found in another chapter of this book specifically focusing on genotyping and sequencing technologies in population genetics and genomics.

These techniques can recover numerous (100s to 1,000s) genetic markers that can then be partitioned into neutral and selective loci using a wide variety of statistical approaches (e.g., Günther and Coop 2013; Whitlock and Lotterhos 2015). The idea beneath is that a gene under selection will not obey to the neutral forces rather than by selection that shape genetic variation and hence show genotype frequencies that cannot be explained by the neutral theory of molecular evolution. The fixation index ( $F_{ST}$ ) and the deviation from Hardy-Weinberg proportions ( $F_{IS}$ ) are popular measures of the genetic differentiation among populations for a specific gene. For example, SNPs under putative selection may be identified using  $F_{ST}$  outlier tests, which identify loci with higher or lower  $F_{ST}$  than expected from the  $F_{ST}$  distribution expected under neutrality. Numerous statistical tests have been designed to detect genes significantly differing in these proxy variables in comparison to the rest of the genome. The earliest types of significance tests developed for outlier loci detection are listed by Luikart et al. (2003). More recently, elaborated statistical analysis of  $F_{ST}$  has been developed following Bayesian approaches (e.g., BAYESCAN, Foll and Gaggiotti 2008) or analyses based on principal components (e.g., PCadapt, Duforet-Frebourg et al. 2016). Hoban et al. (2016) provide an in-depth review of the advantages and limitations of such “genome-scan” approaches for finding signals of local adaptation. Once adaptive genetic data have been identified, it can be statistically compared among different landscapes or among different environmental categories (e.g., Turner et al. 2010).

### 4.1.1 Environmental Association Analysis (EAA)

Alternatively or in addition to outlier detection, EAA can be used to detect signatures of local adaptation to environmental heterogeneity. EAA is at the

interface of bioinformatics, genomics, spatial statistics, and landscape ecology and uses correlation studies between the genomic data and the environment to identify genes either potentially linked to candidate genes or the genes themselves under selection. Note that various other terms are used to describe EAA, including that the terms “genetic-environment correlation” or “genotype-environment association” (GEA, e.g., Whitlock and Lotterhos 2015).

Luikart et al. (2003) were the first to realize the potential of combining landscape genetic analyses with population genomic data. The first implementation of such an approach was published by Joost et al. (2007) in a study dedicated to the detection of candidate loci for selection in insect and livestock species.

Environmental association studies relate environmental variation to genetic polymorphisms, searching for correlative indication of evolutionary responses to spatial heterogeneity (Holderegger et al. 2010). Such associations depend on precisely describing environmental conditions, which require elaborated engineering tools for high-resolution, area-wide coverage of microsite characteristics. In parallel, a whole-genome perspective should enable one to identify potentially adaptive loci or genomic elements, which can then be tested for how they correlate with variation in site conditions (Parisod and Holderegger 2012).

Numerous tools have been developed to perform EAA analysis, each differing mainly by the type of model employed, the statistical procedure used to test for the association, and the way population structure is dealt with (see below; Rellstab et al. 2015). EAA can be performed with various statistical approaches, including logistic regressions (Stucki et al. 2016; Joost et al. 2007; Carl and Kühn 2007), matrix correlations (Hancock et al. 2011; Fischer et al. 2013), general linear models (Zulliger et al. 2013; Manel et al. 2012; Bradbury et al. 2013a; Legendre et al. 2012), and mixed effect models (Frichot et al. 2013; Coop et al. 2010). Excellent reviews and comparisons of the different analytical approaches for EAA can be found in Rellstab et al. (2015) and Forester et al. (2016).

#### 4.1.2 Accounting for Population Structure

Regardless of the statistical approach chosen to conduct EAA, a specific issue is the incorporation of population structure as a confounding factor. Individuals close in space tend to be genetically similar, producing a gradient of neutral genetic differentiation that might overlap with environmental gradients and result in false signals of adaptation (Rellstab et al. 2015; Joost et al. 2013).

The earliest EAA methods did not incorporate the neutral genetic structure and simply aimed at testing the association between genotype frequencies and environmental gradients (Joost et al. 2007; Carl and Kühn 2007). These approaches tend to increase the false discovery rate but are less demanding in terms of calculation (Rellstab et al. 2015). More recently, several methods have been developed to take into account population structure (Rellstab et al. 2015). Among them some are employing mixed effects models (Rellstab et al. 2015), such as BayEnv (Coop et al. 2010; Günther and Coop 2013), LFMM (Frichot et al. 2013), or BayPass (Gautier

2015), while BayEscEnv is based on an alternative model (de Villemereuil and Gaggiotti 2015). The inclusion of population structure in the models allows these methods to get a relatively low false positive rate (De Mita et al. 2013; Frichot et al. 2013; Forester et al. 2016). These approaches interpret the overall variance within the genotype matrix as neutral genetic structure (Rellstab et al. 2015). This can be a major drawback, if the considered population is not genetically structured and can, therefore, result in a loss of statistical power. Moreover, these methods use Markov Chain Monte Carlo (MCMC) as stochastic algorithm, which requires multiple runs in order to obtain representative results (Rellstab et al. 2015; Coop et al. 2010; Frichot et al. 2013). The computation time requested is therefore substantial (Rellstab et al. 2015; Stucki et al. 2016). For this reason, high performance computation methods like Samβada (Stucki et al. 2016) can be a valuable alternative. The population structure can be previously investigated using specific tools like ADMIXTURE (Alexander et al. 2009), STRUCTURE (Pritchard et al. 2000), Localdiff (Duforet-Frebourg and Blum 2014), or a principal component analysis (PCA, Patterson et al. 2006). If the population structure is meaningful, the coefficients of membership to the subpopulations can be included in a bivariate model; otherwise a univariate model is employed considering the environmental variables by themselves (Stucki et al. 2016).

#### 4.1.3 Global and Local Spatial Autocorrelation

Beyond detection of selection signatures, it is possible to quantify the level of spatial dependence in the distribution of genotypes analyzed. This measure of spatial autocorrelation refers to similarities or differences among neighboring individuals that cannot be explained by chance. Assessing whether the geographic location has an effect on allele frequency is especially important in landscape genomics since statistical models assume independence between events. Thus, if individuals with similar genotypes tend to concentrate in space, spurious correlations may co-occur with specific values of environmental variables. On the other hand, spatial independence of data strengthens the confidence in the detections.

Samβada software (Stucki et al. 2016) measures the global spatial autocorrelation in the whole dataset with Moran's  $I$ , as well as the spatial dependency of each point with Local Indicators of Spatial Association (LISA, Moran 1950; Anselin 1995). In practice, LISAs are computed by comparing the value of each point with the mean value of its neighbors as defined by a specific weighting scheme based on a kernel function. Both a spatially fixed kernel type relying on distance only and a varying kernel type considering point density can be used. There are three fixed kernels (moving window, Gaussian, and bi-square) and a varying one (nearest neighbors). The sum of LISAs on the whole dataset is proportional to the Moran's  $I$  (Anselin 1995). Significance assessment relies on an empirical distribution of the indices. For Moran's  $I$ , genotype occurrences are permuted among the locations of individuals of the whole dataset and a pseudo  $p$ -value is computed as the proportion of permutations, for which  $I$  is equal to – or more extreme (higher for

a positive Moran's  $I$  or lower for a negative Moran's  $I$ ) – than the observed  $I$ . For LISA, the pseudo  $p$ -value is separately computed for each point (individual), by keeping the value of the individuals of interest fixed and permuting its neighboring points with the rest of the dataset.

Once a diagnostic of spatial dependence in loci of interest has been carried out, a clever approach is to develop spatially explicit models that directly include autocorrelation. SGLMM (Guillot et al. 2014) provides such a model; however, the current  $R$ -based implementation does not fit the computational requirements of whole-genome analysis. Alternatively, Geographically Weighted Regressions (GWR) measure the spatial stationarity of regression coefficients by fitting a distinct model for each sampling location. The number of neighboring points considered for each sampling location is given by the weighting scheme. These models allow some local coefficients to differ between sampling points while some “global” coefficients are common to all points (Fotheringham et al. 2002; Joost et al. 2013). Thus GWR enable building a null model where the constant term may vary in space and then refining it by adding a global environmental effect for all locations. Comparing these two models would enable assessing whether the global environmental effect is needed to describe the distribution of the genotype. The key advantage of allowing the constant term to vary in space is to take spatial autocorrelation into account in the models. This way, GWR allow investigating the spatial behavior of loci showing selection signatures with standard logistic regressions and may help to distinguish between local adaptation and population structure in landscape genomics. However, GWR models require a fine-tuning of the weighting scheme from the user, which restrains their application to very large datasets. Another method borrows from techniques that examine changes in species community composition through space, but instead assesses the effect of environmental gradients on changing allele frequencies using Generalized Dissimilarity Modeling (GDM) or Gradient Forest (GF) analysis (Fitzpatrick and Keller 2015). The GDM/GF approach may be applied to any system but is particularly useful for range expanding species (see Sect. 5.2), as it allows the effects of geography to be filtered out (e.g., by integrating latitude and longitude into the model) as well as neutral genetic processes (Fitzpatrick and Keller 2015).

#### 4.1.4 Combining EAA Approaches

In the sections above, we listed strengths and drawbacks of several EAA approaches. It is important to point out that all of these approaches have implicit common assumptions concerning the functional relationship between allele distribution and environmental variables (Joost et al. 2013). In particular, such a relationship needs to be constant and requires time to be established after environmental change arises (Joost et al. 2013). A good way to deal with the uncertainty in the results produced by EAA analysis is the combination with other adaptive landscape genomics approaches (see below), and also the combination of multiple EAA approaches. Loci that are detected to be under selection by different methods can alleviate the weaknesses of

each approach, thus leading to greater reliability of inferences (Rellstab et al. 2015). Similarly, combining population genomics approaches (i.e., outlier detection) with EAA can cope with the intrinsic limitations of each paradigm (Rellstab et al. 2015; Joost et al. 2013).

## 4.2 *Phenotypic Approaches*

Another approach for identifying loci under selection involves finding associations between genetic variation and fitness-relevant phenotypes. Quantitative Trait Loci (QTL) mapping has been employed way before the advent of genome-wide scanning technologies and represents nonetheless a powerful tool to detect genes responsible for adaptation (Ehrenreich and Purugganan 2006; Stinchcombe and Hoekstra 2008). In QTL mapping, the genetic contribution to a measurable phenotype is investigated by crossing two parental individual differing in this phenotype and by analyzing how the genetic markers segregate with the phenotype in the successive generations (Stinchcombe and Hoekstra 2008). When studying adaptation, it is therefore necessary to focus on a phenotype on which the selection force acts (Ehrenreich and Purugganan 2006). The onset of genomics allowed to increase the accuracy of mapping the QTLs, but didn't help overcoming the major limitations of this approach: the need for an experimental breeding and the certainty about the adaptive phenotype (Borevitz and Chory 2004; Stinchcombe and Hoekstra 2008).

GWAS solve many of the abovementioned shortcomings of the QTL mapping. GWAS accompanied the appearance of high-throughput technologies for genetic marker identification and investigates the association between quantifiable phenotypes and genome-wide genetic markers (McCarthy et al. 2008). This method requires a large sample size, but overcomes the need for experimental breeding (McCarthy et al. 2008). It also has a higher resolution for marker-trait associations, and some of these associations could be rather causative and not only due to the close linkage between markers and causative genes. By using adaptive, trait-related phenotypes, GWAS can facilitate the search for the genetic variants responsible for the adaptation (Morris et al. 2013). After identifying adaptive genetic variation through QTLs or GWAS, this variation can be statistically linked to environmental data. Some EAA studies have even directly employed GWAS-inspired methods considering environmental variables as phenotypes (Bradbury et al. 2013a; Eckert et al. 2009; Porth et al. 2015), stressing therefore the symmetry between these two paradigms (Rellstab et al. 2015).

### 4.3 *Candidate Genes*

Rather than scanning the whole genome for loci potentially under selection (as in GWAS), the candidate gene approach makes use of information available from model species (i.e., those with an annotated reference genome), where adaptive genes or gene regions have already been identified. Focusing on these regions in phylogenetically related non-model species can increase the chances of finding signals of selection. The candidate gene approach applied to adaptive traits can lead to the detection of gene variants implied in an adaptive response (Pel et al. 2009). The candidate loci can be chosen because of the homology with genes of known function in other species, proximity to the genomic region associated with a phenotype, because of the function predicted from its sequence, or from studies of mutants (Pflieger et al. 2001; Rellstab et al. 2015). The candidate gene approach represents an appealing source of genetic information in EAA analysis when costs or other technical reasons do not allow for a complete coverage of the genome (Rellstab et al. 2015). In a landscape genomics context, candidate genes have been statistically linked to habitat types (Hoekstra et al. 2006) and climate (Sork et al. 2016), and the framework will likely be used more often in future studies (see also Bragg et al. 2015).

### 4.4 *Exomes and Transcriptomes*

The fourth and final framework for adaptive landscape genomics identified by Storfer et al. (2016) also relies heavily on high-throughput sequencing data. The large amounts of high-quality data make it possible to analyze exome and transcriptome variation, i.e., the types and amounts of RNAs that could be associated with differences in gene regulation among different environments. Approaches for exome and transcriptome analysis are discussed by Storfer et al. (2016), who highlight the potential of these approaches for creating novel data, and hence new insights on how environmental change alters gene expression. However, while exome and transcriptome analyses indeed have tremendous potential for elucidating adaptive landscape genomic processes, they have not yet been applied in an actual landscape genomic study.

## 5 Examples of Landscape Genomics Applications

Both neutral and adaptive landscape genomic approaches have been applied to a large variety of organisms and to address a substantial diversity of research questions. Indeed, the scope of landscape genomic applications is ever-increasing, and is now stretching well beyond the focus on plants and animals inhabiting terrestrial

ecosystems (e.g., Manel et al. 2003). For example, metagenomic sequencing of microorganisms enables understanding of microbial community structure and the landscape or climatic characteristics that determine their diversity and persistence, and landscape genomic analyses are beginning to be explored in this area (reviewed in Dudaniec and Tesson 2016). In addition to community structure, metagenomics may also allow for identification of functional, adaptive genes among microorganisms, which may be used in a landscape genomics framework as done for macroorganisms (Dudaniec and Tesson 2016). Similarly, landscape genomic approaches are now used to understand the spread and dynamics of pathogens in heterogeneous environments (Biek and Real 2010; Alamouti et al. 2014; Schwabl et al. 2017).

Here, we provide several examples of landscape genomic applications that have either not been covered elsewhere, or because they nicely illustrate the high flexibility of landscape genomics approaches in nontypical “landscapes” (e.g., seascapes, see Sect. 5.4). We refer readers to other recent publications that provide more detailed reviews on specific systems or taxa, e.g., Montgelard et al. (2014) for terrestrial mammals, Selkoe et al. (2016a, b) for aquatic systems, and Dyer (2016) for plants in general.

## 5.1 *Landscape Genomics of Terrestrial Organisms*

In this section, we provide a critical review of how landscape genomics has been used to assess both neutral and adaptive genomic variation in terrestrial plant and animal organisms. Though our review of the literature is not exhaustive, the articles chosen should serve as a barometer for the state of research in this niche area of the field. We feel that the papers reviewed here provide a sufficient overview of where the field has been, and where it is heading.

### 5.1.1 *Landscape Genomics of Forest Trees*

Forest trees are ideal model organisms illustrating the use of landscape genomics within terrestrial systems. Forests are charismatic components of many landscapes and keystone species in many ecosystems. They provide habitat for a wide range of species and are a central component of the landscape matrix. Yet beyond their ecological function, forest trees are economically important and provide a wide range of ecosystem services to society (Costanza et al. 1997). Because of their economic importance many tree species are exploited, and the remaining landscapes can become disconnected and fragmented, leading to concerns about the preservation of genetic diversity and adaptive capacity (Krutovsky et al. 2012; Ratnam et al. 2014). In conjunction with man-made landscape fragmentation, climate change (Allen et al. 2010) and forest disturbance (Dale et al. 2001) threaten large tracts of these long-lived species. As patches of forest become less functionally connected cascading effects may disrupt the flow of energy and nutrients



destabilizing the entire system. In order to better understand how changes in climate and landscape structure will affect the long-term stability and resilience of terrestrial systems, like forests, researchers must find ways of linking the processes of gene flow, dispersal, and adaptation to landscape change.

Because of their unique life history characteristics and high levels of genomic and phenotypic variation, forest trees are good models for understanding evolution and population processes (González-Martínez et al. 2006; Sork et al. 2013). Like other terrestrial plants, trees are fixed in space and cannot directly move away from changing environments. Thus, their ability to respond to change is limited to dispersal, local adaptation, and phenotypic plasticity (Aitken et al. 2008). While assessing genetic versus plastic response in forest trees remains a challenge (but see Benomar et al. 2016), landscape genomics allows us to investigate both migration and adaptation across many spatial scales and across a wide range of environmental heterogeneity (Johnson et al. 2016, 2017a, b).

### The Beginnings of Forest Tree Landscape Genomics

Forest ecologists and geneticists have long realized that seed and pollen dispersal must be understood within a spatial and temporal framework (Loiselle et al. 1995; Schupp and Fuentes 1995; Sork et al. 1999). Understanding landscape connectivity and gene flow, with an emphasis on barrier detection and the effects of forest fragmentation, and its impacts on the distribution of genetic variation and diversity has been a common focus in terrestrial systems. Until recently, neutral genetic variation assessed using microsatellite markers (SSRs) was the primary genetic approach. Most of the work assessed functional connectivity. While the use of selectively neutral genetic markers such as SSRs was very important for understanding demographic and neutral processes in forest systems, they did not allow for the direct assessment of adaptation and selection in the face of change. Fortunately, recent progress in genomics and nucleotide sequencing provides researchers with practically unlimited numbers of markers including both selectively neutral (such as SSRs and SNPs in noncoding regions) and potentially affected by selection (for instance, non-synonymous SNPs). Arguments were made for understanding forest fragmentation on seed and pollen gene flow (Smouse and Sork 2004; Sork and Smouse 2006), evolutionary adaptation in forest trees (González-Martínez et al. 2006; Holderegger et al. 2008; Kremer et al. 2012; Sork et al. 2013; Lepais and Bacles 2014), and a broad incorporation of landscape genomics into plant and tree research (Holderegger et al. 2010). Many of these papers highlighted the benefits of landscape genomics in investigating how forests will respond to global ecological change, yet the generality and transferability of single species studies have recently been questioned (Calic et al. 2016), and a shift from descriptive to predictive studies still has not been fully achieved (Manel and Holderegger 2013).

## Neutral Landscape Genomics of Forest Trees

An important avenue of landscape genomics using neutral genetic variation has been to identify barriers impacting gene movement. For example, estuarine barriers and ocean currents were found to restrict gene flow in the mangrove species *Avicennia germinans*, *Rhizophora mangle*, and *Rhizophora mucronata* (Ceron-Souza et al. 2012; Wee et al. 2014), and ocean barriers limited gene flow in sandalwood (*Santalum insular*) (Lhuillier et al. 2006). Likewise, barriers have been detected in terrestrial landscapes. Mountain ranges have been found to restrict gene flow in ash (*Fraxinus mandshurica*) (Hu et al. 2010), birch (*Betula maximowicziana*) (Tsuda et al. 2010), and oak (*Quercus lobata*) (Ashley et al. 2015), and decreasing river size was found to restrict gene flow in cottonwood (*Populus fremonti*) (Cushman et al. 2014). In their study of valley oak (*Q. lobata*), Ashley et al. (2015) found that not only did mountain ranges restrict gene flow, but wide open expanses also limited the movement of pollen. Though mountain ranges and landscape features can limit gene flow, the finding is not universal. A range wide study of sweet chestnut (*Castanea sativa*) identified population genetic structure, but did not identify barriers to dispersal using Monmonier's algorithm, concluding that the large population differentiation was due to divergent selection and not barriers to gene movement (Martin et al. 2012).

Another major focus of forest landscape genomics using neutral genetic variation is the assessment of the effects of forest fragmentation on the distribution of genetic diversity. From conservation and management perspectives, understanding how the spatial configuration of harvest tracts or the pattern of disturbance impacts landscape connectivity and gene flow is of critical importance to preserving genetic diversity (Krutovsky et al. 2012; Ratnam et al. 2014). In the case of forest fragmentation, many studies have shown trees to be resilient to fragmentation due to long distance dispersal and high levels of pollen gene flow among forest fragments (Savolainen et al. 2007; O'Connell et al. 2006, 2007). Fragmented landscapes were found to be functionally connected in oak species, *Quercus macrocarpa* and *Q. sclerophylla* (Craft and Ashley 2007; Wang et al. 2011, 2012), mountain hemlock, *Tsuga mertensiana* (Ally and Ritland 2007; Johnson et al. 2017a, b), service tree, *Sorbus domestica* (Kamm et al. 2009, 2010), mountain birch, *Betula pubescens* (Truong et al. 2007), white spruce, *Picea glauca* (Fageria and Rajora 2013; O'Connell et al. 2006, 2007), and papaya, *Carica papaya* (Chavez-Pesqueira et al. 2014). In contrast, an analysis of cottonwood, *P. fremonti* found increased fragmentation resulted in decreased genetic diversity with important conservation implications for other terrestrial species (Cushman et al. 2014).

Abiotic factors can also impact gene flow. Temporal patterns of wind speed and direction can shape spatial genetic structure in forest species. The seasonal differences in wind direction explained the spatial genetic structure of *Engelhardia roxburghiana* due to timing of pollen and seed release (Wang et al. 2016). Few studies have incorporated wind timing, or other temporally variable factors into landscape genetic analysis in terrestrial systems.

Within a range wide context, genetic diversity is often structured according to the center-periphery (central-peripheral or central-marginal) model. In this model

higher gene flow from large central populations into small peripheral ones maintains genetic diversity (Kremer et al. 2012). It is often associated with a reduction in the adaptive potential of individuals at the edge, because the influx of individuals adapted to the center of the range counters the impact of selection for traits suitable to the surrounding environment (e.g., gene swamping) (Kirkpatrick and Barton 1997; Lenormand 2002; Gaston 2009; Kubisch et al. 2014). On balance, there are cases where curtailment of gene flow to marginal populations at range edges can reduce genetic diversity within the marginal populations. Populations of eastern white pine (*Pinus strobus*) in northern Ontario had significantly lower allelic diversity and effective population size at the margins than did central populations (Chhatre and Rajora 2014).

Studies assessing postglacial colonization of northern landscapes have shown forest trees to be capable of long distance dispersal and gene flow, despite the negative effects of diversity loss due to bottleneck effects (Roberts and Hamann 2015). This phenomenon has been demonstrated in pequi, *Caryocar brasiliense* (Diniz-Filho et al. 2009), Sitka spruce, *Picea sitchensis* (Holliday et al. 2012), eastern white pine (Zinck and Rajora 2016), and mountain hemlock, *Tsuga mertensiana* (Ally et al. 2000; Johnson et al. 2017a, b).

### Adaptive Landscape Genomics of Trees

A handful of papers helped initialize the landscape genomic approach in forest trees using genome-wide SNP and AFLP markers to identify putative loci under selection for different climatic variable using EAA (Table 1). The bioclimatic factors of temperature and precipitation were associated with outlier loci in white spruce, *Picea glauca* (Namroud et al. 2008), black spruce, *Picea mariana* (Prunier et al. 2011), black alder, *Alnus glutinosa* (Cox et al. 2011), and European beech, *Fagus sylvatica* L. (Cuervo-Alarcon 2017). An EAA identified SNP loci associated with aridity, precipitation, and temperature in loblolly pine, *Pinus taeda* (Eckert et al. 2010a, b; Chhatre et al. 2013). A nice example of the EAA approach in forest trees is the association of outlier loci with serotiny in lodgepole pine, *Pinus contorta* (Parchman et al. 2012). It was found that 50% of phenotypic variation was associated with just 11 loci across three different populations.

Recently, landscape genomics has been combined with common garden approaches to associate genomic variation with phenotypic variation across environmental gradients (Table 1). Sork et al. (2010) used SSRs to correlated geographic patterns of genetic variation to climate using ecological niche modeling in California valley oak (*Q. lobata*), illustrating that, historically, the species was connected across its range through dispersal, and that observed genetic structure was thus related to climatic adaptation and not dispersal limitation. By combining common gardens with landscape genomic analysis we have the potential to separate out genotype by phenotype by environment interactions (Lepais and Bacles 2014). The approach has been used in a variety of system to link specific phenotypic traits to geographic gradients of environmental and climate variables. Leaf size was

**Table 1** Selected landscape genomic studies of forest trees using adaptive genetic markers

Species	Markers	Analysis and approach	Inference	Reference
<i>Picea glauca</i>	534 SNPs	$F_{ST}$ outlier	Candidate genes were identified and associated with temperature and precipitation	Namroud et al. (2008)
<i>Pinus taeda</i>	3,059 SNPs	Association	8 outlier SNPs associated with aridity and genome-wide population structure	Eckert et al. (2010b)
<i>Pinus taeda</i>	1,730 SNPs	Association/generalized linear mixed model (GLMM)	48 SNPs were correlated to PCs describing temperature, precipitation, and winter aridity	Eckert et al. (2010a)
<i>Alnus glutinosa</i>	163/154 AFLPs	Association	Identified 4 outlier loci associated with climate, mainly temperature	Cox et al. (2011)
<i>Picea sitchensis</i>	339 SNPs	Outlier	14 SNP outliers, asymmetrical gene flow from center to edge effects adaptive capacity	Holliday et al. (2012)
<i>Picea mariana</i>	583 SNPs	Outlier	26 SNPs identified as outliers associated with temperature and precipitation	Prunier et al. (2011)
<i>Populus balsamifera</i>	335 cand. SNPs 412 ref. SNPs	$F_{ST}$ outlier	46 outlier SNPs identified and associated with <i>Arabidopsis</i> flower-time network	Keller et al. (2012)
<i>Abies alba</i> <i>Larix decidua</i> <i>Pinus cembra</i> <i>Pinus mugo</i>	249 SNPs 267 SNPs 459 SNPs 693 SNPs	Association	Seasonal minimum temperature was the most important climate variable for all species; genetic data were correlated with geography	Mosca et al. (2012)

(continued)

**Table 1** (continued)

Species	Markers	Analysis and approach	Inference	Reference
<i>Pinus contorta</i>	97,616 SNPs	Association	11 loci were associated with serotiny, explaining 50% of genetic variation	Parchman et al. (2012)
<i>Eucalyptus gomphocephala</i>	7 SSRs 11 EST-SSRs	$F_{ST}$ outlier/association	2 EST-SSRs were identified as undergoing diversifying selection; these loci were associated with climate and gradient variables; the study identified adaptive genetic markers	Bradbury et al. (2013a)
<i>Picea rubens</i>	61 SNPs in 36 candidate genes	Outlier/association	This study assessed how climate and pollution led to local adaptation; 7 SNP loci were associated with climate in older trees (cohort), while 3 SNP loci were associated with pollution in younger trees (cohort)	Bashalkhanov et al. (2013)
<i>Pinus taeda</i>	2,665 unigene based SNPs	Outlier/association/principal component analysis/logistic regression/Bayesian mixed linear model implemented in BAYENV	Multiple associations with latitudinal, elevational, and climatic variables were identified	Chhatre (2013); K. V. Krutovsky and V. E. Chhatre, (unpublished)
<i>Alnus glutinosa</i>	1,990 SNPs	Common garden + outlier and association	Phenotypic variation in leaf size is linked with outlier analysis and associated with variation in temperature	De Kort et al. (2014)

(continued)

**Table 1** (continued)

Species	Markers	Analysis and approach	Inference	Reference
<i>Populus trichocarpa</i>	29,354 SNPs	Common garden + outlier and association	Heritability was strong for phenology traits compared to biomass/growth traits; variability was associated with latitude, max day length, and temperature of tree origin	McKown et al. (2014)
<i>Abies alba</i> <i>Larix decidua</i>	231 SNPs 233 SNPs	IBD vs. IBA/outlier	Both isolation and adaptation occur at landscape scales; 2–7 outlier SNPs were associated with temperature and soil	Mosca et al. (2014)
<i>Pinus massoniana</i> <i>Pinus hwangshanensis</i>	25 candidate genes	Isolation with migration and adaptation	Ecological divergence of two species associated with climate	Zhou et al. (2014)
<i>Pinus lambertiana</i>	475 SNPs	Common garden + outlier and association	SNPs were associated with 5 phenotypic traits and 11 environmental variables; 6 SNPs were associated with phenotype and 31 with environmental variables; 2 SNPs associated with both phenotype and environment and 1 of those was associated with carbon isotope and soil/climate factors	Eckert et al. (2015)
<i>Pinus lambertiana</i>	186 SNP candidates	Neutral population genetic structure/outlier	The candidate approach identified 2 population clusters and 9 candidate SNPs associated with drought	Vangestel et al. (2016)

(continued)

**Table 1** (continued)

Species	Markers	Analysis and approach	Inference	Reference
<i>Quercus lobata</i>	195 SNPs 40 candidate genes	Candidate gene/ association	3 SNPs were associated with bud burst and flowering; 2 SNPs were associated with temperature and precipitation; these associations varied with climate and provide support for spatially divergent selection	Sork et al. (2016)
<i>Abies alba</i>	267 SNPs in 175 candidate genes	Candidate gene/ association	16 SNPs showed divergent selection; all outlier SNPs were associated with winter drought and one of them showed selection in relation to elevation; 2 $F_{ST}$ outliers suggested adaptive divergence for date of bud flush and growth rate	Roschanski et al. (2016)
<i>Pinus cembra</i> <i>Pinus mugo</i>	768 SNPs 1,152 SNPs	Outlier/ association	Outlier and association analysis tested to what degree elevation effected genomic diversity; low genomic differentiation was found; outliers were associated with temperature and precipitation; 5 SNPs were in common between the species and associated with abiotic stress response; temperature was shown to be an important component of adaptive potential	Mosca et al. (2016)

(continued)



**Table 1** (continued)

Species	Markers	Analysis and approach	Inference	Reference
<i>Pinus strobus</i>	44 SNPs	$F_{ST}$ outlier	SNPs in 25 candidate genes were identified and associated with 19 bioclimatic variables	Rajora et al. (2016)
<i>Fagus sylvatica</i> L.	13 microsatellite markers and 70 SNPs in 24 climate adaptation related candidate genes	Outlier/association/principal component analysis/logistic regression/Bayesian mixed linear model implemented in BAYENV	Association with environmental variables was detected for 24 (34.3%) SNPs, and 5 (7.14%) of them were identified also as $F_{ST}$ outliers	Cuervo-Alarcon (2017)

linked with range wide temperature variation in *A. glutinosa* (De Kort et al. 2014). Variability in phenology was associated with latitude, maximum day length, and temperature of tree origin in black cottonwood, *Populus trichocarpa* (McKown et al. 2014). In a broad analysis of sugar pine (*Pinus lambertiana*) Eckert et al. (2015) associated five different phenotypic traits, including height, bud flush, carbon isotope, and nitrogen concentration, and 11 environmental variables with hundreds of genome-wide SNPs. Their analysis revealed an association with both phenotype (carbon isotope) and environment (soil/climate factors associated with water availability) at a single SNP locus.

The candidate gene framework discussed in Sect. 4.3 has also been increasingly used in forest systems (Table 1). Phenotype (bud burst/flowering) and environment (temperature and precipitation) were found to vary with climate in *Q. lobata* (Sork et al. 2016), and *P. lambertiana* candidate loci were associated with drought (Vangestel et al. 2016). A novel assessment of tree age structure in red spruce (*Picea rubens*) found that candidate loci in older trees were associated with climate while candidate loci in young trees were associated with air pollution (Bashalkhanov et al. 2013). Candidate loci associated with photoperiod were found to vary with latitude, temperature, and precipitation in balsam poplar, *Populus balsamifera* (Keller et al. 2012). Additionally, the approach has been used to assess ecological divergence between two closely related species *Pinus massoniana* and *Pinus hwangshanensis* (Zhou et al. 2014). Though many association studies have focused on single gene effects, multilocus effects may provide a better correlation with environmental predictors. Single gene outlier analysis approaches were compared to single and multilocus environmental association analyses in eastern white pine where among-population multilocus genetic covariance had a much higher correlation with climate

factors than did single gene effects (Rajora et al. 2016). The aforementioned study used a population graph approach (Dyer and Nason 2004; Dyer 2015b) to construct among-population multilocus covariance genetic distances (cGD) separately for the SSR and SNP loci based on the topology of the constructed population graphs. This approach is an emerging method in landscape genomics that can account for patterns of population genetic structure where  $F_{ST}$  outlier approaches that rely on unreasonable assumptions fail (Dyer 2015b; Murphy et al. 2016).

## Comparative Landscape Genomics in Forest Trees

To date, most landscape genomic studies in forest trees, and terrestrial systems more broadly, have focused on single species. Comparative studies are now being conducted to identify if similar landscape and climate processes affect different species within a landscape in the same way. Assessing neutral genomic variation, a multispecies study found that different landscape processes best explained population genomic structure in *Bursera simarubra*, *Ficus insipida*, and *Brosimum alicastrum* (Poelchau and Hamrick 2012). Differences in pairwise  $F_{ST}$  between populations of the three species were each associated with different environmental variables using partial Mantel's tests: environmental niche distance in *B. simarubra*, geographic distance in *F. insipida*, and historic barriers in *B. alicastrum*. A multispecies study in *Abies alba*, *Larix decidua*, *Pinus cembra*, and *Pinus mugo* used SNPs developed from a common gene pool to identify common associations with climate, environment, and population genomic structure ( $F_{ST}$ ). A multivariate approach found that SNPs in all four species were strongly correlated with principle components corresponding to seasonal minimum temperature. However, individually each species was also correlated with a wide range of environmental variables (Mosca et al. 2012). This study was further expanded upon to test if either isolation by distance (IBD) or isolation by adaptation (IBA) was responsible for the differences among the populations of each of the two species: *Abies alba* and *Larix decidua* (Mosca et al. 2014). As it turns out, both IBD and IBA were present, and even though IBD was stronger than IBA, after accounting for geographic distance, 2–7 outlier loci were associated with temperature and soil (Mosca et al. 2014) (Table 1).

### 5.1.2 Landscape Genomics of Wildlife

The vast majority of landscape genomic studies in terrestrial wildlife have focused on neutral processes, particularly concerning dispersal movements and resulting patterns of gene flow (Storfer et al. 2010). These landscape genomic studies focusing on wildlife connectivity have recently been reviewed by Waits et al. (2016) and will therefore not be discussed here. Instead, we highlight three recent studies on adaptive landscape genomics in non-model terrestrial vertebrates that nicely illustrate the diversity of landscape genomic approaches for wildlife research.

## Relating Candidate Genes to Parasite Load in Red Grouse

Wenzel and Piertney (2015) selected 12 candidate genes previously developed for red grouse (*Trichostrongylus tenuis*) using genomic and transcriptomic data. These genes were chosen based on their association with various physiological functions, including regulation of immune responses. Wenzel and Piertney (2015) then used both population- and individual-based statistical approaches to relate variation in these genes to gastrointestinal nematode burden of the sampled birds. The various population genomic approaches identified only few associations of genetic variation with nematode burden, and these associations varied strongly among different statistical methods. In contrast, the individual-based analysis clearly identified signatures of natural selection, with nine of the 12 tested loci showing significant associations with parasite load. While this study focused on a phenotypic trait (i.e., nematode burden) and did not relate variation in candidate genes to environmental heterogeneity, it accounted for landscape-level management actions and spatial sampling design in the statistical analysis. Importantly, the study demonstrates that landscape genomic approaches where allelic variation of individuals is statistically linked to environmental data have higher power to detect loci under selection compared to classical population genomic approaches.

## Detecting Selection-Driven Loci and Environmental Associations in Dall's Sheep

The study by Wenzel and Piertney (2015) took advantage of previously developed candidate genes in a species that is relatively well researched under both natural and experimental settings. When such candidate genes are not available for the study species, information from other closely related species can be helpful. For example, Roffler et al. (2016a) used targeted exon capture to discover SNPs in Dall's sheep (*Ovis dalli dalli*) using available sequences from candidate genes in a closely related wild species (bighorn sheep, *Ovis canadensis*) and the domestic sheep (*Ovis aries*) genome. They used the discovered SNPs to genotype 476 Dall's sheep from across their range and applied two outlier tests and one EAA approach to detect signatures of selection. Across the three statistical methods, nine genes were identified as selection-driven, and they all were significantly correlated with precipitation, temperature, latitude, longitude, and elevation. These results indicate adaptation to local environmental conditions, especially because five of the selection-driven candidate genes are associated with immune responses and respiratory health, respectively, in the species in which they were originally discovered. The study by Roffler et al. (2016a) is an excellent example of how to maximize the interpretability and eco-evolutionary meaningfulness of adaptive landscape genomic studies in non-model wildlife species, for which whole genome data is not yet available.

## Disentangling Processes Causing Genomic Differentiation in Islands Foxes

When genomic information for closely related (model) species is not available, high-throughput sequencing technology can be used to sample genomic variation across a large portion of the genome. For example, Funk et al. (2016) used RADseq to develop 5,293 SNP loci for the island fox (*Urocyon littoralis*). They then used this genomic data to test whether differentiation among six island fox populations off the coast of southern California was mainly explained by drift or local adaptation. Using a combination of statistical methods, Funk et al. (2016) concluded that overall genomic differentiation among the six islands was largely explained by strong drift. However, different outlier tests suggested between 3.3 and 6.6% of the loci to be under selection. While none of the utilized EAA approaches could detect any significant associations with these loci and environmental data, genomic differentiation estimated from the outlier loci matched patterns of morphological similarity among the sampled populations. These results suggest that despite strong drift, divergence due to local adaptation explains at least some of the selection-driven genomic variation, and that the tested environmental data do not reflect heterogeneity in underlying selection pressures.

These examples show that adaptive landscape genomics can help to advance our understanding of selection and local adaptation in non-model terrestrial wildlife species. Two particularly interesting research topics that can be addressed using landscape genomics relate to the evolutionary processes underlying IBE, and to range-expanding species in changing environments. We discuss these two topics in the next sections.

## 5.2 Using Landscape Genomics to Study IBE and Underlying Evolutionary Processes

Patterns of IBE can result from many different processes, both selective and neutral (Wang and Bradburd 2014). Divergent selection is frequently invoked and may be the primary mechanism driving IBE (Kawecki and Ebert 2004; Nosil et al. 2005). When populations inhabiting different environments are locally adapted, natural or sexual selection can act against dispersers with phenotypes adapted to a different environment, limiting the reproductive success of dispersers moving between habitats (Servedio 2004; Nosil 2004; Nosil et al. 2005; Safran et al. 2013). We can expect the strength of selection to be proportional to the difference between the environment to which an individual is adapted and the environment to which it has dispersed. Thus, nonnative individuals will experience an increasing reduction in fitness, relative to native individuals, when dispersing into increasingly different environments. This, naturally, reduces gene flow between divergent environments and leads to a pattern in which genetic differentiation increases with the environmental differences between populations (Sexton et al. 2014; Wang and Bradburd

2014). Moreover, when selection is generally weak or incomplete, dispersers that are reproductively successful in a new environment may produce offspring with traits, or combinations of traits, that are not ideally suited to the local environment. This can result in these offspring having reduced fitness compared to offspring from native parents and will lead to a further reduction in long-term gene flow between divergent environments (Servedio 2004; Nosil et al. 2005). The agents of selection that act upon adult dispersers and offspring of native and nonnative parents may be the same, but could also be very different – for instance, if different agents of selection act at different times of year or on different life history stages (Wang and Bradburd 2014). Finally, even when selection is absent, biased dispersal, in which different individuals or populations have a preference for dispersal to different habitats, can also produce a pattern of IBE (Edelaar et al. 2008; Bolnick et al. 2009; Edelaar and Bolnick 2012). Though biased dispersal can be linked to divergent selection – for instance, if a trait associated with biased dispersal provides a fitness advantage in a particular environment – but it need not – for instance, when dispersers avoid novel habitat or have a preference for their natal habitat (Davis and Stamps 2004; Feder and Forbes 2007; Rosenblum and Harmon 2011; Bolnick and Otto 2013).

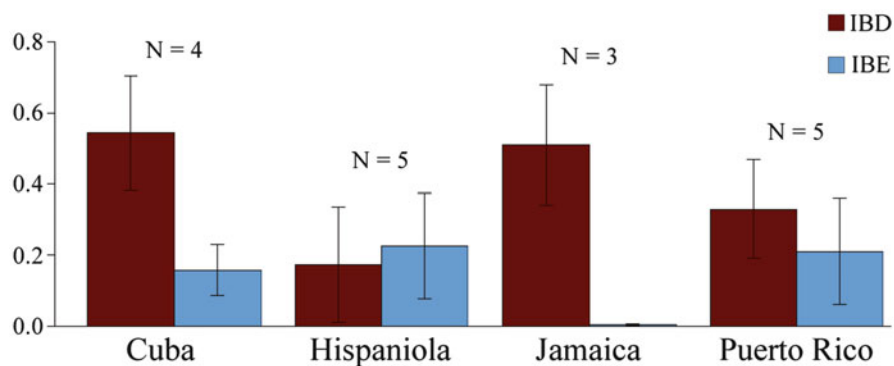
Under any of these scenarios, studying IBE can be a gateway to investigating how evolutionary processes play out over a landscape. The various selective processes that can generate IBE form natural links to examining divergent natural and sexual selection, and how they drive microevolutionary responses (Lee and Mitchell-Olds 2011; Sexton et al. 2014). What the agents of selection acting on spatial genetic variation are and how selective agents and the strength of selection vary across space are sure to feature prominently in future landscape genomics work (Wang and Bradburd 2014). Even when the mechanisms underlying IBE are not selective in nature, interesting questions about what processes lead to the evolution of biased dispersal or that lead to divergent habitat preferences in different populations can still be asked (Davis and Stamps 2004; Bolnick et al. 2009). There are now a number of rigorous empirical studies that have investigated IBD and IBE to examine how evolutionary processes play out over a landscape and influence the evolution of genetic and phenotypic diversity (Sexton et al. 2014). These studies have been performed in diverse taxa, and there are no particular study organisms in which these studies are more valuable than others. However, several of the earliest studies that explicitly considered IBE were performed in lizards (*Anolis* spp.), and a nice set of empirical studies that were conducted on lizard species in different parts of the world exists and presents excellent examples of how landscape genomics can be used to investigate evolutionary processes.

To examine whether the ecological and evolutionary processes across landscapes will generate similar genetic patterns in closely related species, Wang et al. (2013) performed a comparative landscape genetic analysis of 17 species of *Anolis* lizards from the Greater Antilles using structural equation modeling (SEM). As a form of latent variable modeling, SEM allowed them to infer the contributions of individual environmental variables to IBE without any a priori knowledge or expectation for how they should be weighted. *Anolis* lizards on the Greater Antilles

evolved through repeated adaptive radiations, in which species diversified to fill available environmental niche space. There are now species on each island with traits adapted to particular parts of the vertical habitat structure, and together these species, with convergent traits that have evolved for the microhabitat in which they are found, compose what are called ecomorph classes. The adaptive radiations and ecomorph evolution mean that multiple congeneric species are now found in sympatry, presenting an excellent opportunity to examine how the same landscape affects genetic diversity in different species. Landscape heterogeneity on each island is quite diverse, encompassing a range of ecosystems and environmental clines in temperature and precipitation that often form xeric to mesic habitat gradients. Wang et al. (2013) sampled an average of 21 populations per species, spanning a wide variety of the environmental conditions on each of the four Greater Antillean islands.

The results of their SEM analysis revealed a pattern that was fairly consistent across most species in the study, in which IBD explained 36.3%, and IBE explained 17.9% of the variance in genetic distances between populations (Wang et al. 2013). So, overall, the geographic distance between populations had about twice as much of an effect on genetic divergence as the differences in their environments did. This result was quite consistent between the species within islands, suggesting that congeneric species experience the landscape in similar ways, but there were some distinct differences between islands. For instance, the species on Hispaniola showed a stronger pattern of IBE than IBD, while the species on Jamaica showed only minimal signals of IBE (Fig. 6).

The SEM analysis also found that temperature gradients were the primary drivers of IBE, while precipitation gradients also contributed strongly in some species (Wang et al. 2013). Altogether, these results suggest that, in addition to geographic isolation, local adaptation or biased dispersal also played an important



**Fig. 6** The proportion of variance in genetic distances explained by isolation-by-distance (IBD) and isolation-by-environment (IBE) among populations of *Anolis* lizards from the four Greater Antillean islands. For each island, the mean estimates of IBD (red) and IBE (blue) for each study species inhabiting the island are presented, error bars represent one standard deviation from the mean (modified from Wang et al. 2013)

role in population genetic divergence in the Greater Antillean *Anolis* lizards, and that ecological and evolutionary processes on landscape (and species responses to landscape composition and configuration) can affect related species in similar ways, resulting in similar evolutionary outcomes.

To test evolutionary hypotheses about the factors that generate population divergence and biodiversity in the tropics, Freedman et al. (2010) investigated divergence and selection along ecological gradients in a species of rainforest skink (*Trachylepis affinis*) in Cameroon using a set of genome-wide amplified fragment length polymorphisms (AFLPs) and generalized dissimilarity modeling, a form of nonlinear regression modeling. Their study landscape included multiple environmental gradients, including habitat clines from lowland to montane forest and a forest-savanna ecotone, and it also encompassed several regions that formed refuges for skink populations during the last glacial maximum. The goal of the study was to test whether diversification occurred across ecological gradients (the ecological speciation/diversification hypothesis, Smith et al. 1997) or out of glacial refugia (the Pleistocene forest refuge hypothesis, Mayr and O'Hara 1986; Moritz et al. 2000).

The results of their GDM analysis identified that neutral genetic differentiation occurred primarily along the forest-savanna ecotone and found evidence of both IBD and IBE, which was primarily associated with variation in precipitation (Freedman et al. 2010). They also found evidence for a set of loci under divergent selection along the forest-savanna ecotone, which matched a pattern of morphological divergence in fitness-related traits along the same ecotone. Two other sets of loci, also bearing signatures of divergent selection, were significantly differentiated across the lowland-montane forest gradient and between glacial refugia. Thus, although divergent selection was detected between lowland and montane forests and between glacial refugia, it does not appear to inhibit gene flow between these different environments. Whether selection and a reduction in gene flow are sufficient to initiate reproductive isolation remains unclear, but the strong evidence for divergent selection on adaptive loci across the forest-savanna ecotone associated with greater genome-wide neutral genetic divergence provides stronger support for the ecological diversification hypothesis than for the Pleistocene forest refuge hypothesis (Freedman et al. 2010).

To investigate the microevolutionary processes that govern population genetic and morphological divergence, Barley et al. (2015) studied IBD and IBE in sun skinks (*Eutropis multifasciata*) in Southeastern Asia using a panel of genome-wide SNPs and Bayesian geostatistical modeling (Bradburd et al. 2013). Skinks, as a clade, express a great deal of morphological conservatism across different species, with considerable cryptic diversity and many species showing only a few distinguishable differences. So, Barley et al. (2015) also measured a suite of morphological traits for all of the individuals they sampled to see if this general pattern was found within species as well. They collected specimens from 20 populations spread out on a landscape encompassing highly heterogeneous habitat on mainland Southeast Asia and the nearby Philippine Islands Archipelago. Thus, some regions of the study area contained relatively contiguous stretches of suitable habitat, while others



were highly fragmented. In addition, both the islands and the mainland housed several broad climate gradients often associated with local topography.

The results of the above skink study showed that, as expected, the more isolated populations in fragmented areas showed higher levels of genetic differentiation overall. The skink populations showed a clear pattern of IBD but no discernible signal of IBE, and thus it appears that divergent selection or biased dispersal plays little, if any, role in generating overall genomic divergence in this species (Barley et al. 2015). Comparing the phenotypic divergence between populations ( $P_{ST}$ ) to their genetic divergence ( $F_{ST}$ ) revealed that populations were less morphologically differentiated than expected based on their overall levels of genetic isolation ( $P_{ST} < F_{ST}$ ). Thus, some selective mechanism is needed to explain why the populations have not diverged morphologically to the extent expected purely from neutral population divergence. One such mechanism, as presented by the authors, is stabilizing selection on the measured morphological traits, which effectively constrains phenotypic divergence in this system (Barley et al. 2015). Hence, this study illustrates that even when no pattern of IBE is detected, landscape genomic studies that explicitly account for environmental heterogeneity can still reveal the evolutionary processes driving the distribution of genetic and phenotypic variation on a landscape. In this case, it's actually stabilizing selection, rather than divergent selection, that governs morphological evolution in sun skinks, which appears broadly consistent with the evolutionary processes that control morphological evolution between species of skinks as well (Barley et al. 2015).

Future work investigating IBE is poised to take advantage of new genomic resources and the declining cost of genome sequencing technologies. An exciting area of development will be characterizing how spatial patterns, including IBD and IBE, vary among different sites across the genome. We already know that genomic divergence can be highly heterogeneous (Nosil et al. 2008, 2009), because some evolutionary forces act on the entire genome, while others are highly localized (Nosil et al. 2009; Turner and Hahn 2010; Flaxman et al. 2013). New studies can investigate why some regions of the genome show greater IBE than others, and which environmental factors contribute to these patterns in different loci (Wang and Bradburd 2014). We generally expect that loci associated with adaptive traits will show elevated IBE when populations are locally adapted, but adaptive loci could also show less IBE than the genomic background when they are advantageous across different environments. For instance, Fountain et al. (2016) found evidence for positive selection on loci underlying traits associated with dispersal ability in populations of Glanville fritillary butterflies inhabiting fragmented landscapes, and, intuitively, loci linked to traits like dispersal ability are among those expected to show different patterns of IBE. Hence, many opportunities now exist for increasing our understanding of the diverse evolutionary processes, often linked to spatial environmental variation, that act heterogeneously across the genome and for better understanding the processes driving genome evolution in general.

### 5.3 *Landscape Genomics of Range-Expanding Species Under Changing Climate Conditions*

As climate change proceeds, the evolutionary processes that govern species range shifts and expansions are becoming increasingly under focus. Landscape genomics approaches, in combination with modeling, offer unmatched tools for examining these processes in changing environments. However, the challenges of detecting patterns of adaptive variation along environmental gradients occupied by range shifting or invasive species are not trivial. During a range expansion, allelic richness and heterozygosity may decline along the axis of the expansion due to a series of founder events and stochastic allele loss (White et al. 2013). Since this can generate genetic drift in the same direction of species' colonization, allele frequencies can be driven to fixation, making it problematic to distinguish neutral from adaptive genetic signatures (Klopfstein et al. 2006; Frichot et al. 2015). This phenomenon of "allele surfing," whereby rare alleles become more frequent at range expansion fronts according to the strength of genetic drift rather than selection, can increase population genetic differentiation and confound signatures of local adaptation (Klopfstein et al. 2006). Notably allele surfing may also promote adaptation as well when beneficial alleles are "surfing" on the wave of expansion (Gralka et al. 2016), but deleterious alleles may also be "surfing" at the range expansion front (Travis et al. 2007).

Considering the effects of genetic drift in EAA analysis is particularly important given that environmental variation typically corresponds with latitudinal or altitudinal gradients from which genetic samples are obtained. Therefore, both environmental gradients and expansion axes are often aligned when species are tracking their environmental niches during expansion (Frichot et al. 2015; Lancaster 2016). Not accounting for genetic drift may increase the likelihood of erroneous EAAs because neutral allele frequencies can behave similarly to those under environmental selection. As mentioned above, spatial analysis of allele frequencies across environmental gradients can be used to tease apart genetic drift from selection processes. Local Indicators of Spatial Association (LISA) analysis is mentioned above and addresses the effect of spatial autocorrelation on allele frequencies (e.g., Stucki et al. 2016). Another approach for applying landscape genomics to range expanding species is the use of GDM/GF analysis mentioned earlier. The GDM/GF approach may be applied to any system but it is particularly useful for range expanding species as it allows the effects of geography and neutral processes to be filtered out (Fitzpatrick and Keller 2015). The latter can be accounted for by integrating a pre-identified set of neutral genes into the model and evaluating their contribution relative to putative candidate genes under selection via their allele frequency response curve (termed "allelic turnover") across environmental gradients (Fitzpatrick and Keller 2015). For example, a putatively adaptive gene in a temperature-sensitive species (e.g., a butterfly) may show a twofold allelic turnover at 18°C along a temperature gradient, but if allelic turnover of the neutral "reference" genes shows an identically shaped fourfold response at 18°C, our confidence

in this gene being adaptive becomes diminished. Alternatively, if the neutral allelic turnover shows a 0.5-fold change with a response curve that differed in shape to the adaptive candidate genes, this would offer greater support that the relationship we see in the candidate gene is adaptive to the environmental gradient. This method offers a useful approach for identifying thresholds of adaptation in species affected by climate change and diverse environments, such as those undergoing range shifts and expansions. The ability to identify thresholds of adaptation can aid in making predictions about species distributions, climate sensitivity, and persistence.

In addition to environmental adaptation, range expanding and invasive species often exhibit differential morphological or developmental traits along their range (e.g., Ducatez et al. 2016), but the evolutionary bases of these traits are rarely teased apart from environmental effects (but see Buckley et al. 2012; Swaegers et al. 2015). Many traits under selection may be highly polygenic (i.e., many small-effect loci under weak selection) and detecting loci under selection may be difficult in these cases. Notably, EAA analyses are likely to be more sensitive at detecting multiple loci under weak selection compared with  $F_{ST}$  outlier tests (Frichot et al. 2013, 2015), which are best used for detecting large-effect loci under strong selection (Whitlock and Lotterhos 2015). Given the multiple selection pressures exerted upon species from both abiotic and biotic sources during range expansion, teasing apart which loci are associated with environmental or phenotypic variables is likely to result in many overlapping and correlated loci of both small and large effects.

In the absence of a reference genome or candidate genes, EAA enables identification of loci that may be involved in local adaptation along environmental gradients occupied by range expanding species. There are a few examples to date that document increased signatures of selection for adaptive loci at range expanding edges. For example, a study on European damselflies (*Coenagrion scitulum*, Swaegers et al. 2015) documents parallel, non-neutral evolutionary changes in allele frequencies within independent expanding edge populations with respect to flight performance and thermal regime. In addition, evidence for genetically determined phenotypic differences was obtained along the range expansion (Swaegers et al. 2015), which is an important step for teasing apart changes resulting from heritable genetic variation versus trait plasticity (Merilä and Hendry 2014). An earlier study investigated a butterfly range expansion with AFLP (Amplified Fragment Length Polymorphisms) genetic markers using an “Isolation by Adaptation” (IBA) approach based on partial Mantel tests (Nosil et al. 2008), and found significant associations among allele frequencies with habitat type, independent of colonization history (Buckley et al. 2012). Furthermore, a study examining adaptive evolution in range expanding bank voles (*Myodes glareolus*) found a loss of genetic diversity (with SNPs) towards the range margin due to genetic drift, no increase in deleterious alleles, but an increase in outlier loci that coded for functional genes, suggesting enhanced selection (White et al. 2013). Lower genetic diversity and signatures of natural selection were also detected in marginal populations of eastern white pine (Chhatre and Rajora 2014).

Although more complex models can now be used to examine range expansion effects on local adaptation (e.g., Schumaker 2013; Landguth et al. 2016) empirical studies using EAA methods are still relatively few, but offer a promising approach for validating simulation findings and ultimately understanding how species are spatially responding to climate change. By identifying the spatial distribution of adaptive variation in species that are shifting their ranges, we may be better able to manage for species' current and potential habitat, novel species' interactions, the spread of invasive species, or the diseases that expanding species carry into new areas.

#### ***5.4 Seascape Genomics: Applying Landscape Genomics in Aquatic Environments***

Seascape genomics is a natural extension of landscape genetic approaches, with great relevance to conservation and management of marine species (Gagnaire et al. 2015; Selkoe et al. 2016a, b; Kelly and Phillips 2016; Riginos et al. 2016). However, there are distinct differences between marine and terrestrial settings that affect the spatiotemporal distribution of species and genes. Solid barriers to movement are rare in the sea. While the fluid environment might seem like a vast shapeless surface promoting homogeneous, diffusive spread of migrants, in fact, strong currents create asymmetrical and circuitous pathways that channel drifting particles and counteract diffusion. Mapping dispersal corridors and quantifying dispersal resistance differ dramatically between landscapes and seascapes. Application of resistance modeling (e.g., McRae et al. 2008; Spear et al. 2016) has been stymied by the unidirectional nature of marine dispersal by ocean currents. Most marine species disperse during a tiny larval stage that can last from minutes to months, potentially taking them hundreds of kilometers in the currents before metamorphosis into a sedentary or mobile adult. Successfully reaching suitable adult habitat may require careful timing of reproduction for spawned larvae to exploit countercurrents, upwelling cycles, and gyres that may return offspring to natal habitat after forays into open ocean currents, and also active behaviors to counteract passive drifting (Paris et al. 2007; Morgan 2014). Thus, understanding functional connectivity and not just structural connectivity associated with currents is critical for seascape genetics (Selkoe et al. 2016a). There is strong interest in testing the link between ocean currents and gene flow by comparing outputs of ocean circulation models and genetic data, and in fact, disagreement of outputs is not uncommon (e.g., White et al. 2010; Selkoe and Toonen 2011).

Aside from current flows, sharp gradients in the ocean's temperature, salinity, and oxygen also act as obstacles to successful dispersal and gene flow, even in larger bodied species such as fishes (Caldwell and Gergel 2013). For the American lobster, *Homarus americanus*, two disparate current systems contribute to the neutral genetic divergence of lobster populations, which is further cemented by

local adaptation to temperature (Benestan et al. 2016). Temperature is especially critical to marine ecosystems (Bowen et al. 2016), acting at macro scales to define distributions of marine biodiversity (Belanger et al. 2012), as well as micro scales to, e.g., set timing of spawning (Afán et al. 2015). Due to the combination of large species ranges and exothermic physiology, spatial temperature differences – a.k.a., the “therma-scape,” – appear to very commonly shape marine population genetic structure at both neutral and adaptive markers (Conover et al. 2006; Selkoe et al. 2016a).

Marine study systems have an important role to play in uncovering the dynamics of local adaptation in the face of high dispersal (Hauser and Carvalho 2008). Local adaptation may be especially apparent in marine species due to their large effective population sizes which lead to low rates of drift and higher rates of weak selection, selective sweeps, and diversifying selection (Nielsen et al. 2009). Large effective population size also leads to long-lasting genome-wide impacts of founder effects following colonization (Orsini et al. 2013). Seascape genomics studies hold promise to uncover drivers of fine-scale genetic divergence, and are rapidly overturning long-standing beliefs that marine populations are genetically homogeneous over large scales, even in cases of highly mobile species (Gaither et al. 2016). These advances collectively provide powerful insights for conservation and management strategies (Bradbury et al. 2013b; von der Heyden et al. 2014; Gagnaire et al. 2015; Riginos et al. 2016).

Most marine genomic studies utilize SNP discovery in conjunction with outlier tests to detect islands of genomic differentiation and the environmental drivers leading to ecological differentiation rather than allopatric speciation. The low genetic differentiation common to marine populations increases power to detect “true” outliers if the population is at drift-migration equilibrium. However, it can lead to high false positive rates if the population is not at equilibrium. These nonequilibrium situations may be common in nearshore environments due to widespread impacts of past sea level fluctuation, glaciation, or recolonization following stochastic events such as storm surges (Marko and Hart 2011). Increasing the “q-value threshold” in outlier detection with BayScan or similar methods can reduce false positives. For example, BayScEnv incorporates a locus-specific term to account for nonequilibrium effects (de Villemereuil and Gaggiotti 2015), which is needed to minimize false inference of selection, which can ultimately impact management applications such as delineation of fishery stocks. Gagnaire et al. (2015) detail methods well suited to detecting low rates of spatial genetic differentiation and revealing the role of clines in marine connectivity, such as metrics of haplotype sharing and focusing on rare alleles, or “migrant tracts” of DNA segments that resist recombination after admixture.

The handful of seascape genomics studies published to date focused primarily on species with high-value fisheries, and overall there is a strong bias toward temperate systems compared to polar and tropical zones (Selkoe et al. 2016a). Nevertheless, the first crop of seascape genomic studies provides fascinating insights into the interaction between the genome and environment (Riginos et al. 2016). Here, we

highlight a few empirical examples that speak to the complexity of how environment shapes population genetics in a dynamic ocean setting.

The three-dimensionality of the seascape requires careful measurement of an organism's environmental influences. For example, a study on Atlantic cod, *Gadus morhua*, revealed that salinity and oxygen at spawning depth, rather than at the sea surface, best explained outlier loci (Berg et al. 2015). The complex life histories of marine species often factor into which seascape factors drive population structure. In the cod example, some outlier loci were associated with genes involved in egg buoyancy (which impacts a developing egg's exposure to high salinity surface waters), highlighting the critical role of early life stages in shaping local adaptation. Focusing on single life history stages will miss some of the more subtle processes affecting overall structure. Von der Heyden et al. (2007) show differentially structured populations of adult and juvenile Cape hakes (*Merluccius paradoxus*), suggesting different environmental factors influence the spatial genetics of each stage. Marine populations show not only temporal genetic shifts across age classes, but also responses to dramatic inter-annual and decadal-scale changes in the ocean environment. Sampling at single time points can miss these ephemeral dynamics that can produce lasting signatures of selection or isolation. For example, Henriques et al. (2016) used three successive years of sampling of the shelf-associated hake, *Merluccius capensis*, that in years with increased upwelling and associated low oxygen water events show a distinct movement of fish from the northern range southwards associated with physiological tolerance to hypoxia. The ephemeral pattern in these anomalous years disrupts an otherwise stable barrier limiting gene flow between regions.

The future success of seascape genetics will be shaped, in part, by overcoming obstacles to de novo genome assembly. For example, high levels of heterozygosity must often be bred out of organisms in captivity, which is often not possible for marine species. As of 2015, only 18 genomes of marine species had been assembled, compared to ~70 for terrestrial species (Kelley et al. 2016). The power of whole genome assembly and annotation promises to provide deeper insights into the function and interactions of gene regions in local adaptation (Hemmer-Hansen et al. 2014). The stickleback fish was an early target of whole genome assembly due to interest in understanding recurrent marine–freshwater evolution by the lineage (Jones et al. 2012). Strong signatures of directional selection were found on every chromosome for the three-spined stickleback (*Gasterosteus aculeatus*), with many loci linked to strong salinity and temperature gradients over the sampling domain (Guo et al. 2015). In contrast, the Atlantic cod genome shows SNP outliers to be highly clustered within three chromosomes, where chromosomal inversions led to “islands of divergence” within the genome (Bradbury et al. 2013b). Despite very high neutral gene flow, the repression of recombination in the inverted regions has enabled oceanic and coastal cod population to adapt to local oxygen, temperature, and salinity regimes throughout its species range (Sodeland et al. 2016).

Seascape genomics have thus far highlighted an array of factors influencing the spatial distribution of species and genes in marine systems. However, the majority of factors tested are abiotic, thereby limiting our understanding of the ecological

context of species distributions. A major aim of future studies should be the incorporation of ecological factors, such as species and community-level interactions, to begin to elucidate this poorly characterized component shaping marine biodiversity and future responses to climate change.

## 6 Remaining Challenges and Future Research Avenues in Landscape Genomics

As shown throughout this chapter, the potential of landscape genomics for fundamental and applied research is substantial. The increasing interest in the field has led to the rapid development of a large variety of analytical approaches for assessing landscape-genomics influences. This variety is a challenge in several ways. First, it makes it difficult to obtain an overview of landscape genomics as a beginner, to choose among the available methods for analyzing empirical data sets, and to keep up-to-date as a more experienced landscape geneticist. There will never be a single analytical approach that is optimal for addressing all types of landscape genomics research questions, and interdisciplinary collaboration in research and teaching will continue to be a cornerstone for progress in landscape genomics. Nevertheless, more studies are needed that identify those methods that work particularly well or particularly poorly for different systems and questions, and provide practical advice on how to conduct both neutral and adaptive landscape genomics studies for specific research questions. Simulation studies are an important way of testing methods (Hoban et al. 2012), and they have already provided valuable assessments of different methods and sampling designs in landscape genomics (see Landguth et al. 2016).

Second, the variety of approaches, with their different assumptions, advantages, and limitations, also makes it challenging to synthesize results obtained from landscape genomics studies. The choice of analytical methods, and the choice of landscape-genomic hypotheses tested with them, can strongly influence conclusions of a study (Balkenhol et al. 2009; Jaquiere et al. 2011). Again, simulation studies are an excellent way for testing the reliability of drawn conclusions (e.g., Gauffre et al. 2008), and to assess in how far results of a specific study can be extrapolated to other study systems (e.g., other landscapes or species). In addition to simulations, several studies have suggested that using more than one method for final inferences can increase reliability and certainty in landscape genomics (e.g., Balkenhol et al. 2009; Rellstab et al. 2015; Rajora et al. 2016).

Third, due to the remaining methodological issues in landscape genomics, too little progress has been made on the theoretical and conceptual development of landscape genomics. Currently, landscape genomics is often viewed merely as a set of tools for statistically linking environmental and genomic data, and one can rightfully question whether this justifies the definition of a distinct scientific field. For instance, Dyer (2015a) showed that most studies using the term “landscape genetics” can actually be defined as a highly nonuniform set of population genetic



studies, and that the scope of the so-called landscape genetic studies is still very limited. Dyer (2015a) argued that to develop landscape genomics into a distinct field, much more emphasis should be placed on theory development that links individual- and population-based patterns and processes, and that amalgamates ecology and evolution in a truly interdisciplinary way. This view is supported by Balkenhol et al. (2016b, c), who called for a shift in landscape genomics from the current, statistical, and pattern-oriented framework towards an eco-evolutionary and process-oriented framework. Developing the theory underlying such a framework is a major research task, but will be vital for understanding how and why genetic variation is influenced by environmental heterogeneity across spatial and temporal scales.

Another challenge of current landscape genomic studies is adequate study design and sampling. Too often, genetic and genomic data are gathered for other research purposes, and landscape genomic questions are only considered after sampling is finished. This can impede our ability to draw strong scientific inferences about landscape-genomic relationships, and targeted sampling should instead be preferred (e.g., Storfer et al. 2007; Manel et al. 2010). Specifically, deriving hypotheses or expectation about how the environment potentially influences genetic variation (Fig. 2) *before* sampling can greatly enhance our power to detect these influences, if they indeed exist (Balkenhol and Fortin 2016).

Apart from spatial considerations in sampling design, one must also consider the genomic sequencing strategy employed and the genomic resources available for the study organism. Reduced-representation sequencing methods like Genotyping by Sequencing (GBS), Restriction-Site Associated DNA sequencing (RADseq; Miller et al. 2007), and RNA sequencing are popular methods for obtaining many thousands of single nucleotide polymorphism markers (SNPs) that may be neutral or adaptive (Narum et al. 2013). However, the number of markers obtained and hence the ability to detect genes under selection from such sequencing methods may be influenced by library preparation method, density of SNPs according to genome size, the bioinformatics parameters applied to SNP filtering, and for identifying gene function, the existence of an annotated reference genome or transcriptome (discussed in Lowry et al. 2017). However, the resources available for most projects are well below those required for whole genome sequencing of every sample, making reduced-representation sequencing an appropriate and informative choice for the objectives of most landscape genomics projects.

## 6.1 *Future Research in Landscape Genomics*

What will the future of landscape genomics likely hold? First, we envisage that in the next years, the variety and complexity of analytical approaches will increase even further. After all, the increasing availability of genomic data will also lead to new approaches and statistical methods for analyzing them. As stated above, comparing and evaluating existing as well as novel methods are in high demand



for the applicability of landscape genomics. We are hopeful that after a phase of rapid development, landscape genomics will eventually identify a set of methods that work particularly well for specific questions, while other, problematic methods will disappear from the field. For example, several very helpful studies already exist that compare different approaches for identifying adaptive genetic variation in landscape genomics (e.g., Rellstab et al. 2015; Forester et al. 2016; Hoban et al. 2016; Rajora et al. 2016) and that highlight issues with some of the more prominent laboratory techniques used in these approaches (e.g., RADseq, Lowry et al. 2017).

In addition to reducing methodological issues, the future of landscape genomics will likely be characterized by an expanded research scope that will include additional concepts, data types, and processes. Specifically, we see great potential for future research avenues in landscape genomics along the following topics.

## ***6.2 Landscape Genomics and Nongenetic Data***

In the future, increasing effort will likely be given to amalgamating landscape genomics with other research approaches producing nongenetic data. For instance, habitat models derived from presence-absence or occurrence data are often used to parameterize resistance surfaces in landscape genomics (e.g., Wang et al. 2008; Engler et al. 2014). However, recent landscape genomic studies have shown that habitat models do not always adequately capture landscape influences on effective dispersal and resulting genetic structures (Mateo-Sánchez et al. 2015; Roffler et al. 2016b), because habitats are used differently during dispersal compared to other behaviors, such as foraging (e.g., Benz et al. 2016; Ziólkowska et al. 2016; Abrahms et al. 2017). A better option for parameterizing resistance surfaces in animals might hence be actual movement data, which can be gathered at increasingly fine spatial and temporal resolutions using satellite-telemetry. A variety of methods exist for distinguishing different behaviors within individual movement paths (reviewed in Edelhoff et al. 2016) and for quantifying how dispersal behavior is influenced by environmental heterogeneity (e.g., Cushman and Lewis 2010). Similarly, landscape genomic data can be combined with demographic estimates of population size, survival, or fecundity to understand the interplay between local demography and population genomics in heterogeneous environments. Addressing the complex questions involving demography and genomics can already be accomplished via simulations, for example in software CDMetaPOP (Landguth et al. 2017).

## ***6.3 Landscape Genomics and Eco-Evolutionary Dynamics***

Collecting demographic data in combination with genomic data is also important for investigating eco-evolutionary dynamics, which refers to tight feedback mechanisms between ecological and evolutionary processes (Pelletier et al. 2009;

Legrand et al. 2016). An increasing number of studies shows that these feedbacks can occur across ecological timescales, meaning that evolution acts fast enough to influence the ecology of organisms within a few generations (e.g., Fronhofer and Altermatt 2015; DeLong et al. 2016). Since a major goal of landscape genomics is to understand and eventually predict the consequences of ongoing contemporary environmental change for genetic variation, future studies should consider eco-evolutionary dynamics and assess how the potential for adaptive evolution impacts the genetic response of populations of species in changing environments. For this, it will be particularly vital to consider the polygenic architecture of many traits that influence the survival and reproductive success of individuals. Understanding environmental selection pressures on these traits and their underlying genes will require landscape genomic approaches that statistically link multi-locus variation to environmental heterogeneity (e.g., Rajora et al. 2016). Most EAA approaches in landscape genomics use only a single locus at a time, but several of the methods discussed in Sect. 4.1.1 can also test for multi-locus signatures of selection. Forester et al. (2017) compared the reliability of several EAA approaches for detecting selection acting on multiple loci and demonstrated substantial differences among methods. These differences likely also depend on underlying demographic history and sampling design, and future studies are needed to clarify how environmental effects on polygenic selection can best be detected.

## 6.4 *Landscape Community Genomics*

Recently, Hand et al. (2015) suggested “landscape community genomics (LCG)” as a framework for assessing the eco-evolutionary responses of multiple species in complex and dynamic environments. The sampling design for LCG requires landscape genomic studies to be conducted for at least two interacting species (i.e., a community) in multiple, diverse study landscapes. LCG also requires the combination of adaptive and neutral landscape genomics that we have advocated throughout the chapter, but with several additional benefits. First, analyzing multiple species within the same landscapes makes it possible to assess the generality of findings and hence can help to synthesize results across species and landscapes (e.g., Dudaniec et al. 2016). Second, LCG can account for biotic interactions among species, such as competition or coevolution. These biotic interactions can influence spatial genetic variation, but are seldom considered in current landscape genomic studies. Third, LCG explicitly considers the interaction between biotic and abiotic (i.e., environmental) factors shaping genetic variation, thus potentially resulting in the most thorough picture of how genetic variation is shaped in nature. Finally, LCG can ultimately also help to evaluate how environmental impacts on community genetics will alter ecosystem properties, because important factors shaping ecosystems are indirectly impacted by genetic variation (e.g., the distribution, abundance, structure, demography, and interaction of coexisting populations;

Whitham et al. 2006). In sum, LCG can be seen as the most advanced type of landscape genomic study, and the framework will likely lead to important insights on eco-evolutionary dynamics in heterogeneous and changing environments.

## **6.5 *Application of Landscape Genomics in Conservation Management***

Clearly, landscape genomics has great potential for conservation management. However, while the gap between conservation practitioners and population geneticists is already an issue for any genetic study, the uptake by conservation managers from even more complex genomic studies is even more challenging (Hoffmann et al. 2015; Shafer et al. 2015). There is indeed still a large gap between scientists working within the field of genetics and those dealing with conservation problems on the ground. Several studies identified this science policy gap (e.g., Hoban et al. 2013; Taylor and Soanes 2016) which is getting even more prominent when it comes to the field of genomics (Shafer et al. 2015). However, for many of the pressing conservation topics, genomic tools may be able to get us further than using classic neutral genetic approaches. For the field of landscape genomics, this is specifically true when adaptive genetic variation could be used for inferring the potential of local populations to changing environments. However, until now in conservation contexts this has been rarely used so far and then mostly focusing on population correlations or single candidate gene approaches (Shafer et al. 2015). While there is a strong need from the conservation community to better evaluate if species or populations may be able to adapt to certain environmental conditions there is still quite some uncertainty involved in how the results of landscape genomic analyses should actually be interpreted. While more and more adaptive loci can be identified, methods are still developing fast in screening such loci and in analyzing large amounts of data. This calls for validation studies, multispecies approaches, and also common garden experiments to actually demonstrate that our results are of practical relevance.

## **7 Conclusion**

To conclude, landscape genomics provides a complex but powerful framework for addressing fundamental and applied research questions in many different fields. As discussed throughout this chapter, concepts and methods in the field advance rapidly. On the one hand, this makes it challenging to establish and maintain a thorough overview of newest developments and to discern subtle analytical nuances from crucial improvements. On the other hand, the large diversity of neutral and

adaptive landscape genomic approaches associated with the swift progress in the field makes it particularly vibrant and exciting.

Soon we will begin to see whole genome comparisons across heterogeneous landscapes allowing researchers to identify a broad array of ecological and climatic factors influencing neutral and adaptive processes. In the future it will be important to move beyond an assessment of population genetic structure in single species to infer potential future responses to climate and landscape change and to begin to predict how communities of species will respond based on our knowledge of adaptive capacity (Holderegger et al. 2010; Storfer et al. 2010; Neale and Kremer 2011; Manel and Holderegger 2013; Sork et al. 2013). Finding general responses across multiple species and further assessing multilocus effects will continue to be important goals for future landscape genomic studies (Calic et al. 2016; Rajora et al. 2016).

We are convinced that we have only just begun to realize the potential of landscape genomics, but as highlighted above, there is much room – and need – not only for methodological, but also for conceptual and theoretical improvement in landscape genomics (see also Dyer 2015a; Balkenhol et al. 2016c). Hence, we are curious to see how the field will develop from here, and hope that this chapter will help to further motivate population geneticists to apply and enhance landscape genomics.

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