

GENETIC ISOLATION BY ENVIRONMENT OR DISTANCE: WHICH PATTERN OF GENE FLOW IS MOST COMMON?

Jason P. Sexton,^{1,2} Sandra B. Hangartner,¹ and Ary A. Hoffmann¹

¹Bio21 Molecular Science Institute, The University of Melbourne, Parkville, Victoria 3010, Australia

²E-mail: sexton.jp@gmail.com

Received November 20, 2012

Accepted August 19, 2013

Gene flow among populations can enhance local adaptation if it introduces new genetic variants available for selection, but strong gene flow can also stall adaptation by swamping locally beneficial genes. These outcomes can depend on population size, genetic variation, and the environmental context. Gene flow patterns may align with geographic distance (IBD—*isolation by distance*), whereby immigration rates are inversely proportional to the distance between populations. Alternatively gene flow may follow patterns of *isolation by environment* (IBE), whereby gene flow rates are higher among similar environments. Finally, gene flow may be highest among dissimilar environments (*counter-gradient gene flow*), the classic “*gene-swamping*” scenario. Here we survey relevant studies to determine the prevalence of each pattern across environmental gradients. Of 70 studies, we found evidence of IBD in 20.0%, IBE in 37.1%, and both patterns in 37.1%. In addition, 10.0% of studies exhibited counter-gradient gene flow. In total, 74.3% showed significant IBE patterns. This predominant IBE pattern of gene flow may have arisen directly through natural selection or reflect other adaptive and nonadaptive processes leading to nonrandom gene flow. It also precludes gene swamping as a widespread phenomenon. Implications for evolutionary processes and management under rapidly changing environments (e.g., climate change) are discussed.

KEY WORDS: Climate change, environmental management, isolation by distance, isolation by ecology, isolation by environment, swamping gene flow.

The role of gene flow on adaptation by natural selection is a key topic in evolution because it can have starkly contrasting effects: from increasing genetic variation and population size, to diluting specialized adaptive genetic combinations and thereby reducing population size (Slatkin 1987; Lenormand 2002). It has become a critically important topic for understanding and predicting vulnerability and responses of organisms under rapid environmental change, yet we know very little about the background pattern of gene flow with respect to environmental and spatial variation in nature. The role of gene flow has encompassed many contexts, including migration-selection balance (Haldane 1948; Fisher 1950; Bolnick and Nosil 2007), niche evolution (Holt and Gomulkiewicz 1997), limits to adaptation in marginal populations (Kirkpatrick and Barton 1997), and genetic rescue (Tallmon

et al. 2004). One issue that is particularly important is the effect of gene flow on populations under rapidly changing or *stressful* conditions—conditions that lead to a sharp reduction in the fitness of individuals and may lead to long-term damage to populations (e.g., a rapid decrease in population size resulting from mortality and reproductive failure; Hoffmann and Parsons 1991).

When populations are small and individuals experience strong selection, gene flow may increase population size, even if the resulting phenotypes are generally maladapted, leading to increases in genetic variation that might allow new adaptations to take hold and even expand a niche (Holt and Gomulkiewicz 1997). In this vein, gene flow may have beneficial ecological and evolutionary effects under stressful conditions, such as “*sink*” habitats (Holt and Gomulkiewicz 1997; Gomulkiewicz et al. 1999).

Beneficial effects resulting from gene flow into small populations in stressful environments (i.e., increased fitness or survival of offspring relative to parental genotypes resulting from breeding with outside populations) have been demonstrated across a wide range of taxa, including vertebrates (e.g., Westemeier et al. 1998; Madsen et al. 1999), invertebrates (e.g., Lenormand and Raymond 2000; Ebert et al. 2002), plants (e.g., Willi et al. 2007; Sexton et al. 2011), and microbes (e.g., Ching et al. 2013).

Gene flow may alternatively have negative consequences in populations inhabiting stressful conditions through further decreasing fitness as a result of outbreeding depression (Edmands 1999; Tallmon et al. 2004) or the suppression of locally adapted individuals through density-dependent effects (Gomulkiewicz et al. 1999). The negative effects of outbreeding depression via disruption of local adaptation (interactions between genes and environments) and/or genetic incompatibilities (interactions between genes) have been explored theoretically (e.g., Antonovics 1968; Edmands and Timmerman 2003) and demonstrated empirically (e.g., De Meester 1993; Edmands 1999; Fenster and Galloway 2000; Marr et al. 2002; Tallmon et al. 2004; Costa e Silva et al. 2012). The introduction of locally maladapted genes and phenotypes into populations because of strong and asymmetrical gene flow may prevent adaptation. Theoretical models have explored this possibility in sink and marginal populations at the extremes of gradients where gene flow from larger populations adapted to central conditions might overwhelm (swamp) edge-adapted genotypes (Holt and Gomulkiewicz 1997; Kirkpatrick and Barton 1997; Gomulkiewicz et al. 1999; Bridle et al. 2010), although empirical examples supporting this phenomenon remain rare (but see Magiafoglou et al. 2002; Fedorka et al. 2012). There is a need for empirical research to understand factors that may lead to outbreeding depression, but theoretical studies suggest that the likelihood of outbreeding depression from gene flow may increase when there are genomic incompatibilities (e.g., ploidy differences) or when gene flow results in breeding between populations that have long been isolated (diverged) and adapted to very different environments (Frankham et al. 2011; Pekkala et al. 2012). Empirical studies have shown that local adaptation to different environments can result in strong selection against immigrants (e.g., Via et al. 2000; Hendry 2004; Nosil et al. 2005) and against hybrids (Schluter 2000; Rundle and Whitlock 2001). In addition, immigration can initially increase the fitness of a population, but later generations may suffer outbreeding depression (Marr et al. 2002). Adaptive divergence may therefore constrain gene flow between different environments either through selection against immigrants or hybrids (e.g., Schluter 2000; Räsänen and Hendry 2008).

The extent to which gene flow has negative or positive effects on adaptation will depend to a large extent on how patterns of gene flow relate to environmental variation (Lenormand 2002). If

gene flow is high among populations from different environments (e.g., along a cline), adaptation to local environments may be stalled. This theory has been extensively developed and discussed in the context of migration-selection balance, where migration between populations can essentially cancel the diverging effects of selection (Haldane 1930; Fisher 1950; Mayr 1963; Endler 1973; May et al. 1975; Slatkin 1985, 1987; Barton 2001; Lenormand 2002; Bridle et al. 2010). Theory on the effects of gene flow on adaptation has mainly been developed in the context of different environments, often along a one-dimensional range, among which populations experience different selection pressures and gene flow may serve to dampen local adaptation through genetic homogenization. However, gene flow among similar environments (i.e., within a two-dimensional range) might facilitate local adaptation to stressful conditions by both increasing population size and introducing new alleles that are locally beneficial (Sexton et al. 2011). With the threats of habitat fragmentation and rapid environmental shifts under human-induced global change, predicting the effects of gene flow from varying environmental and spatial scales is critical because there is potential for gene flow to buffer populations during contemporary change (e.g., Edmands 2007; Frankham et al. 2011; Sexton et al. 2011; Sgrò et al. 2011; Kremer et al. 2012). Despite the large body of literature to understand the potential effects of gene flow on adaptation, we know surprisingly little about the actual patterns of gene flow across species ranges, and whether there are prevailing patterns with respect to spatial and environmental gradients. Understanding how gene flow corresponds with environmental gradients can inform evolutionary theory on adaptation and inform management of populations under environmental stress particularly during periods of rapid environmental change.

Gene Flow Scenarios

There are several scenarios regarding patterns of gene flow with respect to environmental variation, and here we discuss the predictions, potential causes, and consequences of each scenario under rapid environmental shifts (Table 1). The first scenario (S1) is that gene flow patterns with respect to environmental variation represent those expected under a model of isolation by distance (IBD). Wright (1943) proposed that, given limits on dispersal and in the absence of selection, drift would cause populations to become more differentiated at greater distances and that this process should be more pronounced as average population size decreases. Thus, under strict IBD, distance predicts differentiation as a result of dispersal limitation and drift, irrespective of environmental differences, and gene exchange may happen equally along (similar environments) and across (different environments) gradients within dispersal limits. In rapidly changing environments,

Table 1. Summary of scenarios, predictions, potential causes, and consequences of rapid environmental change with regards to patterns of gene flow with respect to environmental gradients.

Scenarios	Prediction/pattern	Potential causes	Potential consequences under rapid environmental change
S1: Genetic isolation by distance (IBD)	Gene exchange (genetic similarity) is greater at shorter distances	Dispersal limitation and drift, irrespective of environmental differences among sites	Adaptive responses may be more rapid under strict IBD than under S2, but will be constrained by the natural dispersal mechanisms of an organism
S2: Environment-driven gene flow: in the direction of adaptation (IBE—isolation by environment)	Gene exchange strongest among similar environments; gene exchange among similar environments is greater than predicted under IBD	Nonrandom mating due to environmental differences (e.g., phenological timing); local adaptation due to strong selection	Adaptation may be faster under stable conditions, but not necessarily under rapid environmental change
S3: Environment-driven gene flow: against the direction of adaptation (counter-gradient gene flow)	Gene exchange strongest among dissimilar environments: gene exchange among dissimilar environments is greater than predicted by IBD	Dispersal patterns against gradient (e.g., direction of prevailing wind); gene swamping	Adaptation may be more difficult, or prevented, under stable conditions, but might be faster under rapid environmental change
S4: Unrestricted gene flow	No structure and low differentiation	Few dispersal limits; random mating; weak or no selection across gradients	Could lead to more rapid adaptation because of gene shuffling across environments, but local adaptation may be constrained by migration load
S5: Historical limits/limited gene flow	Gene exchange patterns correspond with historical population patterns	Very low gene flow due to strong historical influences such as colonization, extinction, or refugia; or cases of severe dispersal limitation due to geographic factors (e.g., islands) and/or biological constraints (e.g., species having few, small populations, or having extremely limited dispersal capabilities)	High extinction possible when adaptive genetic variation is limited

adaptive responses to environmental stress (i.e., genetic variation to respond to novel selection pressures) under strict IBD will therefore be constrained by the natural dispersal limitations of the organism and the size of its populations, but not by the nature or structure of environmental variation.

A second scenario (S2) may find gene flow to be strongest among similar environments (i.e., among sites with similar environmental values), to a greater extent than predicted under IBD. This environment-driven pattern of gene flow, termed “isolation by environment” or “isolation by ecology” (IBE; Cooke et al. 2012; Zellmer et al. 2012; Bradburd et al. 2013; Shafer and Wolf 2013; Wang et al. 2013) may arise by several mechanisms (Crispo et al. 2006; Räsänen and Hendry 2008; Schluter 2009; Sobel et al. 2010; Lee and Mitchell-Olds 2011). First, selection and local

adaptation will disrupt patterns of IBD (Wright 1943), and IBE might arise as a consequence, whereby maladapted immigrants (and/or hybrids derived from them) from different environments are selected against, representing strong barriers to gene flow. Second, IBE may arise through nonrandom mating that is the result of adaptation to different environments (e.g., mismatches in flowering windows between locals and immigrants). A classic example of this scenario comes from plants growing on and near mine tailings, where adaptation to different soil types has occurred (Antonovics 1968). McNeilly and Antonovics (1968) showed that reproductive barriers arose between soil types through evolved differences in flower bud development as a result of local adaptation. Third, nonrandom mating due to environmentally mediated phenotypic plasticity, as opposed to genetically based adaptive

mechanisms above, may cause IBE (see Edelaar and Bolnick 2012). For example, plants growing along an elevation cline or among different soil types might flower at different times in response to the availability of heat and water. In addition, behavioral plasticity in animals could result in IBE; animals might choose particular environments to seek food items based on learned experiences (e.g., predators hunting within territories). Local adaptation may be enhanced with IBE, including through nonrandom migration that is not the outcome of selection. Under IBE, adaptation may be faster under stable conditions if populations from similar environments are exchanging beneficial alleles and increasing population size through immigration; however, with rapid environmental change, IBE could result in maladaptation if alleles from dissimilar environments are required for rapid adaptation.

In a third scenario (S3), “counter-gradient gene flow,” gene flow may run counter to patterns of environmental variation or local adaptation, being higher across dissimilar environments (the classic gene-swamping scenario). This might occur if there is strong directional gene flow from central to marginal populations along gradients due to differences in the production of propagules (e.g., Kirkpatrick and Barton 1997; Barton 2001) or where there is dispersal in one direction (such as through prevailing winds pushing propagules up or down a slope (Endler 1973; May et al. 1975). Under this scenario, adaptation may be difficult, or prevented, under stable conditions, but might be faster under rapid environmental change if strong gene flow across different environments maintains high genetic variation. Note that scenarios 2 and 3 are inherently mutually exclusive.

The final two scenarios in Table 1 concern unrestricted (S4) versus highly restricted (S5) gene flow patterns and are an extension of the first two scenarios. First, gene flow may follow no pattern with respect to space or environmental gradients (i.e., no IBD or IBE). Species may have nearly unlimited dispersal capability (e.g., spore-borne organisms) and may exhibit random (or nearly random) mating across their distribution. Local adaptation might then be limited as a consequence of unrestricted high gene flow unless selection was particularly strong; that is to say, populations may be subject to a “migration load” (Lenormand 2002). Nevertheless, unrestricted gene flow could have benefits for populations facing rapid environmental shifts across their entire range due to maximizing the benefits of gene shuffling across distributions. Second, there are scenarios in which historical or biogeographic processes dominate current patterns of gene flow (and IBD or IBE has not yet established). Potential causes of such scenarios include recent colonization or extinction events and/or historical migration events limited by mountain ranges or other topographic factors. In addition, cases of geographic and/or biological migration constraints, such as insular systems or species with extremely limited dispersal capacities and few populations (e.g., insular tortoise species), will exhibit highly restricted gene flow (Manel et al.

2003). In addition to historical processes, habitat fragmentation can restrict gene flow in many contemporary populations (Fahrig 2003). Although this scenario can result in populations becoming locally adapted, populations might be unable to accrue benefits from further immigration and may be at high risk of extinction under rapid climate shifts if within-population adaptive genetic variation and population size is low. A continuum of possibilities among the above five scenarios may exist depending on particular combinations of factors (e.g., dispersal limitation and the strength of selection). However, they do each offer distinct predictions for evaluation in natural systems.

Here we investigate general patterns of gene flow across environments versus geographic distance through a literature review of empirical studies that have examined patterns in putatively neutral genetic markers across environments. We then discuss what these patterns of gene flow indicate about evolutionary processes in nature and how they might influence the ability of populations to counter rapid environmental change through evolutionary adaptation. Answers to these questions have important implications for the management of threatened populations and species as well as for understanding the organization of genetic diversity across landscapes.

Empirical Patterns of Gene Flow

To assess studies that investigated gene flow with respect to environmental gradients, we queried Google Scholar and the ISI Web of Science databases during October 2012 using the following search terms: cline, climate, environmental gradient, gene flow, IBD, IBE, isolation by adaptation, isolation by elevation, isolation by altitude, isolation by depth, latitude, maladaptive gene flow, population structure, partial Mantel test, replicated transects, and hierarchical Bayesian analysis. We restricted papers to natural field studies (i.e., nonlab studies, nonhuman studies), non-hybrid-zone studies, nontheoretical studies, studies that estimated gene flow through putatively neutral genetic markers (not just adaptation to a cline), and studies examining a clear environmental gradient or source of environmental variability, and those that tested for a significant relationship of gene flow or genetic differentiation in neutral genetic markers with respect to the gradient or other source of variability. We supplemented the database with papers from personal databases. In total, 315 relevant studies were examined and 110 could be used to evaluate Scenarios 1–5 using the restrictions we defined earlier.

Methods used in studies to detect, describe, and understand patterns of gene flow fell into four broad categories: Mantel tests, nested analyses of molecular variance (AMOVAs), analyses of directional gene flow or genetic differentiation, and multivariate model-based approaches. Table 2 describes each method category

Table 2. Summary of analytical methods used to contrast patterns of gene flow across landscapes with geographic and environmental distance.

Method	Description	Evidence for IBD/IBE	Advantages	Issues	Example studies
Mantel and Partial Mantel test	Examines the relationship between data matrices of any type. Partial Mantel tests allow the comparison of matrices while holding other matrix effects constant	IBD only: Mantel test detects significant IBD, but no significant IBE; IBE only: Mantel test detects a significant IBE, but no significant IBD; IBD and IBE: Partial mantel tests detect a significant IBD (after accounting for environmental differences) and IBE (after accounting for distance)	Can easily compare the relative strength and direction of effects of different gradients (e.g., spatial, environmental) on genetic variation. Flexible and few assumptions required in its application	Partial Mantel tests have been criticized for having high Type I error rates. Identifies signal and further work is needed to determine significance	McCairns and Bernatchez (2008), Wassermann et al. (2010)
Nested analysis of molecular variance (AMOVA)	Estimates genetic variance within and among nested sampling sets or regions (e.g., replicate transects along gradients)	IBD only: Significant F_{ST} /genetic variation among regions, but not among environments within the same region; IBE only: Significant F_{ST} /genetic variation among environments within the same region, but not among regions; IBD and IBE: Significant F_{ST} /genetic variation among regions and among environments within the same region	Provides a straightforward test to compare the contributions of spatial versus gradient effects	Utility to parsing IBD vs. other gradients is sensitive to sampling scale rather than using quantitative measures. For example, may be unable to distinguish IBE from IBD when transect distances are equal to inter-transect distances	Hirao and Kudo (2004), Hadado et al. (2010)
Analyses of directional gene flow or genetic differentiation	Various methods to estimate gene flow strength and directionality (e.g., N_m , BayesAss, Migrate) and to compare levels of differentiation among populations (especially F_{ST} s)	Counter-gradient gene flow: N_m or m is higher in one direction of the geographic/environmental gradient	Can identify asymmetric gene flow such as source-sink dynamics, local and complex patterns, and strength of differentiation based on distance vs. environment	Sensitive to incomplete population sampling and can be sensitive to HWE violations; does not implicitly compare strength of IBD and IBE	Byars et al. (2009), Holliday et al. (2012)

(Continued)

Table 2. Continued.

Method	Description	Evidence for IBD/IBE	Advantages	Issues	Example studies
Multivariate, model-based analyses	Different multivariate, model-based approaches such as GESTE, BIOENV, BIMR and similar programs; multiple regression; structural equation modeling (SEM)	IBD only: the model with the highest probability includes only distance. IBE only: the model with the highest probability includes only the environmental factor; IBD and IBE: the model with the highest probability includes distance and the environmental factor	Can identify the relative impacts of multiple environmental and spatial distances on genetic patterns within the landscape; can also test for different scenarios such as range expansion and marginality	Can have high false discovery rate due to large number of models being compared; inference may suffer from low sample sizes when high numbers of variables and/or models are being compared	Clark and Ainsworth (1993); Foll and Gaggiotti (2006); Faubet and Gaggiotti (2008); Bradburd et al. (2013); Wang et al. (2013)

as well as some advantages, issues, and examples and lists the criteria within each method category by which studies were evaluated for supporting the various scenarios. Mantel tests provide a straightforward way to test for IBD and IBE. If both IBD and IBE were significant, studies were only included if Partial Mantel tests were used to test for the relative contribution of distance and environment (see Table 2). Table S1 reports the Mantel tests results for IBD and IBE, as well as the Partial Mantel test results for IBD correcting for environmental variation and for IBE correcting for spatial variation. Studies using an AMOVA approach were included when genetic variation/differentiation was estimated within and among environmental and spatial transects (see Table 2). In addition, Table S1 reports if phenotypic traits were included, if the study found evidence for adaptive divergence, and the marker type, average F_{ST} and the scale of the studies.

Our initial evaluation of the studies led to cases where there was very limited structure (supporting S4—unlimited gene flow), or cases where patterns of genetic structure were mostly related to historical or phylogeographic patterns supporting S5 (geographically limited gene flow). The remaining studies ($N = 70$) finding structure in relation to gradients were evaluated for their support of Scenarios 1–3. Studies tested genetic structure against a variety of potential explanatory environmental variables, and often used proxies for climate variation such as elevation and latitude. Some studies considered only a single environmental variable (e.g., elevation), but others considered a number (e.g., air temperature, rainfall, etc.).

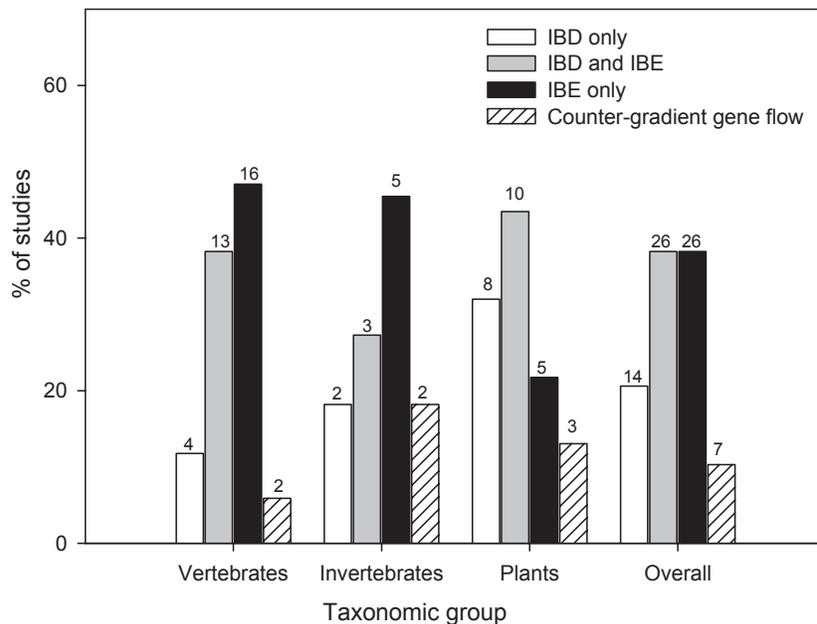
The 110 studies examined represented a broad spectrum of variation in taxonomic groups, environmental factors, analytical methods, and genetic markers (Table 3). Data recorded from all studies can be found in Table S1. Ten studies that could not differentiate between Scenarios 1–3 due to strong correlations between geography and the environmental gradient were excluded and 100 studies could therefore be used for the analysis. Twenty-one studies (21%) found support for S4 and 9 studies (9%) supported S5. For vertebrates, six studies (13.0%) supported S4 and six studies (13.0%) supported S5. For invertebrates, 10 studies (41.7%) supported S4 and three studies (12.5%) supported S5. For plants, five studies (16.7%) supported S4 and none supported S5. For the remaining 70 studies (70%) supporting Scenarios 1–3, results are described later by broad taxonomic category and overall, and they are also summarized in Figure 1. Three studies supporting S3 also supported other scenarios (S2 and S1, 2) and are represented multiple times in Figure 1.

VERTEBRATES

IBE (S2) was the strongest pattern observed among vertebrate studies, with moderate evidence of strict IBD (S1) and only two examples of counter-gradient gene flow (S3). Thirty-four vertebrate studies showed genetic structure and could differentiate

Table 3. Summary of taxonomic, environmental, analytical, and genetic marker variation among 100 studies examined for gene flow patterns. Some studies included more than one subcategory.

Category	Vertebrates	Invertebrates	Plants	Overall
Gradient				
Elevation	15	7	11	33
Latitude/longitude	3	11	2	16
Climate factors (e.g., rainfall)	13	3	9	25
Habitat type (e.g., vegetation)	20	3	9	32
Analyses				
Mantel tests	40	16	26	82
AMOVA	9	14	11	34
<i>F</i> -statistic	1	2		3
Directional gene flow	1	3	3	7
Multivariate, model based	16	2	3	21
Phylogeographic analyses	5	4		9
Markers				
Microsatellites (SSRs)	34	13	16	63
Allozymes	3	4	7	14
AFLP	2	3	3	8
RAPD	2	1	2	5
DNA sequence	6	8	3	17

**Figure 1.** Summary of findings among 70 studies having data to support Scenarios 1–3 (1: IBD— isolation by distance; 2: IBE— isolation by environment; 3: counter-gradient gene flow) regarding patterns of gene flow with respect to environmental gradients. Studies are shown by broad taxonomic category and overall. The number of studies within each category is given above each bar.

between IBD and IBE patterns. Sixteen studies (47.1%) showed evidence for IBE, but no significant IBD. Thirteen studies (38.2%) showed both evidence for IBD and IBE after accounting for distance, resulting in a total of 29 studies (85.3%) that showed significant IBE patterns after accounting for distance. Only four studies (11.8%) showed significant IBD relationship, but no IBE, and two studies (5.9%) showed evidence for counter-gradient gene

flow. One study, Wang et al. (2013), evaluated IBD versus IBE in 17 species of *Anolis* lizards from the Greater Antillean islands. They found significant patterns of both IBD and IBE, with IBD explaining a greater level of variance than IBE. Due to the phylogenetic and geographic non-independence of this system, we counted this study as one study supporting both evidence for IBD and IBE in our tally.

The average F_{ST} was similar between studies that found IBE only (mean \pm SE, $F_{ST} = 0.079 \pm 0.025$), IBD and IBE ($F_{ST} = 0.111 \pm 0.036$), IBD only ($F_{ST} = 0.077 \pm 0.043$), or counter-gradient gene flow ($F_{ST} = 0.052 \pm 0.013$). Studies that did not reveal genetic structure had a low average F_{ST} (0.021 ± 0.010), whereas studies with a historical/topographic structure had a very high average F_{ST} (0.399 ± 0.145).

INVERTEBRATES

IBE (S2) was the strongest pattern observed among invertebrate studies, with some evidence for IBD (S1) and counter-gradient gene flow (S3). Eleven invertebrate studies showed genetic structure and could differentiate between IBD and IBE patterns. Five studies (45.5%) showed evidence for IBE, but no significant IBD. Three studies (27.3%) showed both evidence for IBD and IBE after accounting for distance, resulting in a total of eight studies (72.7%) that showed significant IBE patterns. In addition, two studies (18.2%) showed significant IBD relationship but no IBE, and two studies (18.2%) showed evidence for counter-gradient gene flow.

The average F_{ST} was higher in studies that found IBE only (mean \pm SE, $F_{ST} = 0.112 \pm 0.036$) than in studies that found IBD and IBE (0.023 ± 0.012), IBD only ($F_{ST} = 0.022$), or counter-gradient gene flow (0.068 ± 0.057), although these F_{ST} s are based on few studies. Studies that did not reveal genetic structure had a low average F_{ST} (0.019 ± 0.005), whereas studies with a historical/topographic structure had high average F_{ST} (0.349 ± 0.223).

PLANTS

In contrast to patterns found in animals, IBD (S1) was the strongest pattern observed among plant studies, with similarly strong evidence for IBE (S2) and some evidence of counter-gradient gene flow (S3). Twenty-five plant studies showed genetic structure and could differentiate between IBD and IBE patterns. Five studies (21.7%) showed evidence for IBE, but no significant IBD. Ten studies (40.0%) showed both evidence for IBD and IBE after accounting for distance, resulting in a total of 15 studies (60.0%) that showed significant IBE. Eight studies (32.0%) showed significant IBD relationship, but no IBE and three studies (12.0%) showed evidence for counter-gradient gene flow.

The average F_{ST} was similar between studies that showed IBD only (mean \pm SE, $F_{ST} = 0.111 \pm 0.067$) and in studies that showed both IBD and IBE (0.102 ± 0.068). It was lower in studies that found IBE (0.025 ± 0.007) and counter-gradient gene flow (0.060), although these F_{ST} s are based on few studies. Studies that did not reveal genetic structure had a low average F_{ST} (0.039 ± 0.008), whereas none of the plant studies showed a historical/topographic structure.

OVERALL

IBE (S2) was the strongest pattern observed across all studies, with moderate evidence of strict IBD (S1) and rare evidence of counter-gradient gene flow (S3). Seventy studies showed genetic structure and could differentiate between IBD and IBE patterns. Twenty-six studies (37.1%) showed evidence for IBE, but no significant IBD. Twenty-six studies (37.1%) showed both evidence for IBD and IBE (after accounting for distance), resulting in a total of 52 studies (74.3%) that showed significant IBE patterns. Fourteen studies (20.0%) showed significant IBD relationship, but no IBE. Seven studies (10.0%) showed evidence for counter-gradient gene flow.

The average F_{ST} was similar between studies that found IBE only (mean \pm SE, $F_{ST} = 0.077 \pm 0.017$), IBD and IBE (0.098 ± 0.026), IBD only (0.090 ± 0.039), or counter-gradient gene flow (0.056 ± 0.016). Studies that did not reveal genetic structure had a low average F_{ST} (0.024 ± 0.004), whereas studies with a historical/topographic structure had very high average F_{ST} (0.382 ± 0.114).

EFFECTS OF DIVERGENCE, MARKERS, AND SCALE

To test for consistency among studies that varied in divergence, scale, and molecular marker variables, we compared results among categories within each variable. When excluding F_{ST} values > 0.1 (16 studies), patterns remained qualitatively similar to overall patterns. Twenty of 54 studies (37.0%) found IBE, 20 studies (37.0%) found IBE and IBD, 11 studies (20.4%) found IBD, and six studies (11.1%) found counter-gradient gene flow. Similarly, results remained similar when only including studies that used microsatellites (45 studies). Seventeen studies (37.8%) found IBE, 21 studies (46.7%) found IBE and IBD, six studies (13.3%) found IBD, and two studies (4.4%) found counter-gradient gene flow.

To test for scale effects, studies were divided in three categories: 0–3500 km² (category 1), 3501–320,000 km² (category 2), and 320,001–450,000,000 km² (category 3). In category 1 (22 studies), 10 studies (45.5%) found IBE, five studies (22.7%) found IBE and IBD, six studies (27.3%) found IBD, and two studies (9.1%) found counter-gradient gene flow. In category 2 (22 studies), eight studies (36.4%) found IBE, eight studies (36.4%) found IBE and IBD, five studies (22.7%) found IBD, and two studies (9.1%) found counter-gradient gene flow. In category 3 (21 studies), seven studies (33.3%) found IBE, nine studies (42.9%) found IBE and IBD, four studies (19.0%) found IBD, and one study (4.8%) found counter-gradient gene flow. In addition, the average F_{ST} was lowest at the largest scale (mean \pm SE F_{ST} , category 1: 0.088 ± 0.021 , category 2: 0.106 ± 0.026 , category 3: 0.062 ± 0.021).

GENERAL CONSIDERATIONS

Nearly a third of cases (30%) did not exhibit spatial or environmental gradient structure including systems that fall under unlimited gene flow (S4) and highly restricted gene flow (S5) categories. A notably high proportion of invertebrate studies (54.2%, compared to 26.1% and 16.% for vertebrates and plants, respectively) fell into these categories. Of the cases that did show patterns with respect to gradients, patterns were qualitatively similar across organisms, spatial scales, divergence levels, and marker types, with the exception of plants, which had a higher prevalence of IBD rather than IBE (Fig. 1). It is unclear what causes this disparity between plants and animals. Animal studies occurred over smaller geographic scales than plant studies on average: animals (5,390,130 km²), plants (13,252,117 km²), vertebrates (7,282,901 km²), invertebrates (1,680,301 km²). This difference in average scale might have affected the relative importance of IBD versus IBE. Nevertheless, the prevalence of different scenarios generally did not change across scales or differentiation levels. In addition, plants exhibited a lower average F_{ST} than animals (mean \pm SE F_{ST} , plants: 0.077 ± 0.022 , animals: 0.112 ± 0.022 , vertebrates: 0.127 ± 0.030 , invertebrates: 0.086 ± 0.033), which suggests that limited dispersal in plants did not contribute (although F_{ST} estimates can vary with the markers used).

Of the studies examined ($N = 110$), only 32 (29.1%) were designed in such a way as to be able to simultaneously account for both environmental and spatial variation. However, there appears to be a continuum of scenarios, from pure IBE through contributions of both IBE and IBD, and then to pure IBD, with at least a few cases of counter-gradient gene flow. For studies that identified IBE as the main pattern, divergent selection was most often invoked in invertebrates and vertebrate studies. Conversely, phenological separation was most often invoked to explain IBE in plants (Table S1).

The type of genetic markers, size, shape, and dimensionality of geographic ranges and the methods used to detect gene flow with regards to environmental gradients may influence patterns and the likelihood of supporting different gene flow scenarios. Different genetic markers were used, with microsatellites being the most common (63% of studies; Table 3). Microsatellites are expected to be neutral and therefore to represent neutral genetic structure. Other markers such as allozymes are more likely to be under selection and could therefore be expected to reflect IBE patterns more often (e.g., Zhang and Hewitt 2003). We did however find a similar IBD/IBE ratio when comparing microsatellites with other markers, suggesting that the patterns found here were not affected by marker type. Although neutral markers should not be under selection, barriers to gene flow imposed by strong selection and local adaptation between populations will be detectable in neutral markers, as in the case where maladapted immigrants do not successfully breed with individuals from local populations. In

this sense, IBE arising from selection leads to decreased effective dispersal rates (Crispo et al. 2006; Räsänen and Hendry 2008; Schluter 2009; Sobel et al. 2010; Lee and Mitchell-Olds 2011). IBE arising from causes other than selection (e.g., nonrandom mating driven by phenotypic plasticity) will also be detectable through neutral markers.

The scale of the study area varied extremely among studies (5–450,000,000 km²) and genetic structure, as well as the importance of IBD versus IBE, might depend on the scale. Our results however suggest that IBD/IBE ratios are similar among scale classes and that IBE is more important than IBD at all scales. We also found the lowest F_{ST} value in the largest scale class; most of the study organisms in this class have the potential for long-distance dispersal (e.g., wolves, dolphins) and show very low genetic structure, leading to the pattern that genetic differentiation does not increase with increasing study area. The shape and dimensionality of a geographic range may influence the scenario supported. For instance, geographic ranges that are essentially linear or sampling designs that sample along one linear transect will be unable to disentangle IBD from IBE, but can at least test for the presence of counter-gradient gene flow using directional gene flow analyses. For geographic ranges that include more dimensions (i.e., latitude, longitude, elevation), broad and replicated sampling of gradients allows for the inclusion of more analyses (Table 2) and the testing of more scenarios.

Most of the methods used in the evaluated studies were recently reviewed or discussed by Balkenhol et al. (2009), Legendre and Legendre (2012), or Sork et al. (2013). The most commonly used Mantel tests can test for the relative strength and direction of effects of different gradients (Table 2). However, Mantel tests have been criticized for having high Type 1 error rates, caused by the inability to distinguish between different correlated factors (Balkenhol et al. 2009; Guillot and Rousset 2013). If multicollinearity is a problem, we would however expect that this error rate is similar when testing for IBD and IBE, and therefore not biasing the likelihood of data fitting either of these patterns. Analyses of molecular variances can compare the contributions of spatial versus gradient effects, yet they are more sensitive to sampling scales in distinguishing between IBD and IBE (Table 2).

Many of the evaluated studies only compared genetic distance with one environmental factor, whereas distance is likely correlated with several environmental factors that might or might not affect gene flow. Our estimates of IBE should therefore be rather conservative, as some of the IBD patterns found might be driven by an unmeasured environmental factor. Ideally, many factors should be tested simultaneously. Multivariate model-based approaches can be very effective in testing how distance, landscape, and other environmental factors interact and may influence gene flow (Balkenhol et al. 2009; Legendre and Legendre 2012; Sork et al. 2013). These models are therefore better suited for

studies that include multiple environmental and/or landscape factors. They can however produce false discoveries if a large number of models are being compared (Balkenhol et al. 2009) and will require larger sample sizes to simultaneously evaluate many environmental variables and competing models. Most studies that used model-based approaches did compare the results with other methods, suggesting that model-based approaches were unlikely to increase the discovery rate of false IBD and/or IBE. However, landscape genetics approaches continue to be developed to minimize detection error rates and to maximize not only the power to detect accurate signals, but to determine the relative strengths of multiple factors influencing gene flow (e.g., Bradburd et al. 2013). Whatever the analytical method employed, future studies should focus on understanding the relative importance of spatial and environmental (i.e., ecological) variation on genetic differentiation, both within and among geographic systems and across functional and phylogenetic groups.

Evolutionary Implications

The common occurrence of IBE found in this review and another recent compilation (Shafer and Wolf 2013) has implications for rates of local adaptation. Where IBE occurs rather than IBD, local adaptation in populations may be more likely because there is little or no counter-gradient gene flow potentially introducing poorly adapted genotypes into populations. Adaptive phenotypic divergence can be found to some degree in studies across all five scenario categories, documented either in terms of divergence in adaptive loci or quantitative traits (Table S1). Nevertheless, most studies have not tested whether phenotypic patterns are plastic or genetically based, so it is difficult to assess the extent to which patterns might affect genetic adaptation. In addition, a direct comparison of the likelihood of adaptation and the presence of IBE is not possible here; this would require (for instance) information on gene flow across multiple species from the same gradient, an important future direction for comparative studies and systems of high conservation priority. If IBE promotes local adaptation as we predict, we anticipate that the likelihood and strength of local adaptation would depend on the pattern of gene flow within species.

The common occurrence of IBE raises questions about the types of mechanisms that might promote this pattern. These mechanisms include strong natural selection where individuals that migrate into an area, but are poorly adapted to it fail to survive and reproduce, reducing rates of gene flow between different environments. They also include assortative migration and mating that might have developed over time in response to ongoing selection. However, IBE might also arise because organisms are often affected by environmental influences (in the plasticity of their

reproduction and dispersal) and this can contribute to IBE in the absence of direct selection for traits contributing to IBE. These different mechanisms could be disentangled with manipulative studies such as transplant experiments.

Although we have focused on neutral variation, neutral and adaptive alleles may show very different patterns of genetic differentiation. Local and immigrant beneficial alleles can be maintained, favored, and established under strong selection, even when there is high gene flow for neutral alleles. With genomic tools, it is possible to identify candidate neutral and adaptive alleles and loci to understand whether gene flow limits local adaptation. Although immigrant propagules might not become established in populations if they are locally maladapted, there will still be an ongoing exchange of neutral and selected alleles among populations in the absence of reproductive isolation, potentially resulting in ongoing evolutionary divergence among populations exposed to different selection pressures.

In addressing the effects of gene flow on adaptation, it is important to determine whether adaptive gene flow effects also depend on the genetic architecture or basis of local adaptation—that is to say, whether adaptation occurs without trade-offs (i.e., conditional neutrality; Anderson et al. 2013) or with trade-offs under conditions of antagonistic pleiotropy or mutation accumulation (Gray and Goddard 2012). Under antagonistic pleiotropy, gene flow is expected to retard adaptation, because when populations are locally adapted to two environments gene flow coupled with sexual reproduction will result in the ongoing production and spread of poorly adapted genotypes into those environments (Nosil and Crespi 2004). Nevertheless it is in this situation where IBE is likely to be a powerful mechanism enhancing local adaptation by reducing the spread of poorly adapted genotypes. Under conditional neutrality or mutation accumulation, gene flow is more likely to be adaptive because local adaptation is not expected to result in poorer performance in other environments, and in this case the benefits of IBE in promoting adaptation should be reduced. Populations isolated for a long time may have accrued genetic incompatibilities, even if occurring in similar environments, and this might negate the potential adaptive benefits of IBE.

Several studies have found differences in local adaptation across species from the same gradient; for instance, Byars et al. (2007) found local adaptation across an elevation gradient in a grass, but a forb failed to show a similar pattern of local adaptation (Byars and Hoffmann 2009). Similarly, Clausen et al. (1940) considered local adaptation in multiple species of plants across central California and found evidence of strong differentiation in many species but not all, whereas Haider et al. (2012) found adaptive genetic differences in many species, but not others, in response to elevation in invasive species in Tenerife. In addition, adaptive structure has been found across latitude in multiple conifer

species of the Pacific Northwest of North America (e.g., Rehfeldt et al. 1999; Mimura and Aitken 2007). However, although these types of studies show differences among species in adaptive patterns, they do not establish whether these differences reflect variation in patterns of gene flow and/or pleiotropy/mutation. The *Poa* grass studied by Byars et al. (2009) showed evidence of IBE, but gene flow was not considered in the forb they investigated (Byars and Hoffmann 2009). To allow for comparisons, patterns of gene flow across multiple phylogenetically independent species groups should ideally be established.

Given the prominence of IBE in nature, swamping gene flow, a scenario that is not compatible with IBE, is less likely than one might expect. This finding is particularly interesting within the context of limits to adaptation given the prominent role often assigned to gene swamping in the scientific literature in stalling adaptation (e.g., Slatkin 1987) and species range expansion (e.g., Kirkpatrick and Barton 1997). Although most studies support S2, our overview did point to a few studies that suggested cases where gene flow could inhibit local adaptation (S3). One of these involved *Drosophila serrata*; in this species, populations at the southern (high latitude) border develop increased (genetically-based) levels of cold resistance after winter, which are lost by autumn, most likely reflecting high levels of gene flow bringing poorly adapted genotypes into the population (Magiafoglou et al. 2002). Similarly in crickets unidirectional gene flow toward northern border populations probably leads to the presence of genotypes with inappropriate diapause patterns in northern populations (Fedorka et al. 2012). These studies and others suggesting reduced local adaptation under high gene flow (Nosil and Crespi 2004; Paul et al. 2011; Holliday et al. 2012) indicate that gene flow can have negative effects across environmental gradients.

Under strong selection, adaptive differences can be maintained among populations despite high levels of gene flow. There are numerous examples in the literature of genetic divergence in quantitative traits despite a lack of population structure, including early studies on responses to toxins and other stresses in plants (Linhart and Grant 1996) as well as more recent work on adaptation to elevation and other gradients (Ribeiro et al. 2011). These studies highlight the discordant patterns exhibited by neutral and nonneutral genetic markers (Mckay and Latta 2002). Nevertheless, patterns of differentiation might be predictable based on gene flow and the genetic architecture of local adaptation (e.g., antagonistic pleiotropy, etc.) as discussed earlier. The ideal level of gene flow to promote adaptive divergence may be an intermediate level as has been demonstrated theoretically (e.g., Gomulkiewicz et al. 1999) and in the laboratory (e.g., Venail et al. 2008). To our knowledge ideal levels and environmental sources of gene flow for adaptation have not been directly tested in natural environments. Experimental gene flow studies testing various spatial and

environmental separation are needed to develop a predictive, contextual framework for the effects of gene flow (Frankham et al. 2011), including the effects of gradient steepness (Bridle et al. 2010).

Management Implications Under Rapid Environmental Shifts

Patterns of gene flow have implications for the adaptive management of populations faced with stressful conditions or rapid climate change. Environments change and therefore optimal levels of gene flow under one set of conditions might be suboptimal under a different set of conditions. This may not be an issue under IBE if the environmental changes are the same as those affecting gene flow. For instance, along elevation or latitudinal gradients, which include several of the studies in Table S1, climate warming may change flowering time, but this would lead to continued IBE. In contrast, IBD or IBE associated with different variables might result in patterns of gene flow that are maladaptive. Gene flow has to extend far enough to cover predicted habitat changes within generations, and this may hold even in the case of trees with slow generation times (Kremer et al. 2012).

From a practical perspective, these types of considerations can be important when thinking about how gene flow might deliberately be modified to increase evolutionary resilience of species faced with environmental change. Particularly where landscapes are disconnected and revegetation efforts are being implemented, there are likely to be opportunities to promote gene flow in species to increase their adaptability (Broadhurst et al. 2008; Sexton et al. 2011; Sgrò et al. 2011). Strategies include revegetating with a wider genotypic base that includes source areas locally adapted to different climates and also potentially deliberately moving propagules across fragmented landscapes (Sgrò et al. 2011), including “prescriptive” gene flow in cases where populations inhabiting similar environments might bolster each other (Sexton et al. 2011). In addition, maintaining gene flow may be vital for maintaining coevolutionary potential, and in particular for permitting hosts to tolerate rapidly evolving pathogens (Gandon and Nuismer 2009). These approaches can provide an insurance policy in species where generation times are long and where the velocity of climate change (Burrows et al. 2011) is expected to be high, making it challenging for natural gene flow to move adapted genotypes across the landscape. Such approaches are related, but different than, “managed relocation,” the idea of proactively moving individuals outside their current geographic ranges to colonize areas of predicted future suitability (Richardson et al. 2009).

Where IBE occurs, and species have relatively short generation times, there is likely to be ongoing adaptive gene flow

to enhance rates of local adaptation unless levels of landscape fragmentation are too high to allow exchange between similar environments. However, strong IBD and high genetic differentiation among species may preclude much local adaptation and in these cases any manipulated genetic exchange may be mostly beneficial. The issue of adaptive gene flow and phenotypic plasticity is also worth exploring further; where there is a history of ongoing maladaptive gene flow preventing local adaptation, selection for high plasticity (and dispersal rate—explored in Scheiner et al. 2012) may be strong and these species could be relatively robust.

Concluding Remarks

Although this review suggests that gene flow in natural populations may often be environmentally structured, several issues remain to be addressed. First, the connection between mechanism and patterns of gene flow remains poorly understood in most cases. IBE is likely where environmental conditions affect synchronization of mating (e.g., flowering time, pollinator availability, gamete release, timing of lekking, etc.) and patterns of dispersal. In addition, IBE may be a result of strong natural selection. If strong selection is maintaining IBE, rapid environmental shifts will change the phenotypic targets of selection, allowing for successful immigration from different environments (e.g., allowing successful immigration of genotypes from warmer climates under climate warming). Field studies are needed that can disentangle the contributions of selection and environmental structuring to patterns of gene flow (e.g., Stanton and Galen 1997). With enough information about the biological attributes of plants and animals, it may be possible to predict when adaptive IBE as opposed to IBD or counter-gradient gene flow is likely, even in the absence of genetic data. Once these attributes are clearly defined, it may even be possible to link phenological patterns to the rates of adaptation and extinction risks. For instance, population responses and local extinction risk in recent times have been linked to changes in phenology, either in relation to the environment or to interacting species (Willis et al. 2008; Morin and Thuiller 2009; Bradshaw and Holzapfel 2010; Cahill et al. 2013). Perhaps organisms that shift their reproductive time more readily in response to climate rather than (for instance) photoperiod (Bradshaw and Holzapfel 2008) are more likely to become locally adapted.

Second, the association between gene flow patterns and local adaptation needs to be examined. For instance, how do fitness, abundance, and population growth rates vary among populations with different patterns of gene flow? Although quite a few studies looking at gene flow have also considered trait variation, this is often not separated into environmental and genetic components to test for local adaptation, whereas the strength of selection is rarely assessed. Therefore, although IBE and strong selection should

promote local genetic adaptation, it is unclear how often this is the case, particularly for animal studies. Where transplants and other approaches cannot be used to establish patterns of local adaptation, it might nevertheless be possible to test for the presence of adaptive differentiation based on comparisons of genomes from different populations. These can reveal chromosomal regions of adaptive divergence and the strength of selection associated with these regions as well as uncovering relationships to functional genes under selection (e.g., Coop et al. 2010; Eckert et al. 2010; Fournier-Level et al. 2011; Keller et al. 2011). Under IBE, divergence among these regions may be enhanced when compared to populations showing IBD or counter-gradient gene flow patterns.

Third, the long-term impacts of different patterns of gene flow on the evolution of plasticity remain to be evaluated. Under counter-gradient or high levels of gene flow, selection for plasticity and epigenetic effects are expected to be particularly strong, because counter-gradient or high gene flow should limit the potential for local, genetically based adaptation (Sultan and Spencer 2002; Scheiner et al. 2012). Therefore, different patterns of plasticity might be expected under different gene flow scenarios, and patterns of gene flow might shape the evolution of specific characteristics.

Finally, climate change should affect all of the above patterns and processes by changing the degree to which systems are at equilibrium. For example, the balance between migration and climate-driven selection among populations will surely shift for some organisms with rapid climate change. In addition, gene flow might increase or decrease with climate change, depending on how climate change affects suitable habitat (Wasserman et al. 2010; Olsen et al. 2011). Understanding current gene flow effects across environmental gradients will improve predictions on the adaptive capacity of species under climate change scenarios.

ACKNOWLEDGMENTS

The authors thank C. Lee, G. Bradburd, and three anonymous reviewers for comments that improved the manuscript. JPS was supported by the United States National Science Foundation under Award No. 1003009, SBH was supported by the Swiss National Science Foundation, and AAH was supported by the Australian Research Council and the CSIRO Science Industry Endowment Fund during the preparation of this manuscript.

LITERATURE CITED

- Anderson, J. T., C.-R. Lee, C. A. Rushworth, R. I. Colautti, and T. Mitchell-Olds. 2013. Genetic trade-offs and conditional neutrality contribute to local adaptation. *Mol. Ecol.* 22:699–708.
- Antonovics, J. 1968. Evolution in closely adjacent plant populations. VI. Manifold effects of gene flow. *Heredity* 23:507–524.
- Balkenhol, N., L. P. Waits, and R. J. Dezzani. 2009. Statistical approaches in landscape genetics: an evaluation of methods for linking landscape and genetic data. *Ecography* 32:818–830.
- Barton, N. 2001. Adaptation at the edge of a species' range. Pp. 365–392 *in* J. Silvertown and J. Antonovics, eds. *Integrating ecology and evolution in a spatial context*. Blackwell, Lond.

- Bolnick, D. I., and P. Nosil. 2007. Natural selection in populations subject to a migration load. *Evolution* 61:2229–2243.
- Bradburd, G. S., P. L. Ralph, and G. M. Coop. 2013. Disentangling the effects of geographic and ecological isolation on genetic differentiation. *Evolution*. doi:10.1111/evo.12193.
- Bradshaw, W. E., and C. M. Holzapfel. 2008. Genetic response to rapid climate change: it's seasonal timing that matters. *Mol. Ecol.* 17:157–166.
- . 2010. Light, time, and the physiology of biotic response to rapid climate change in animals. *Annu. Rev. Physiol.* 72:147–166.
- Bridle, J. R., J. Polechová, M. Kawata, and R. K. Butlin. 2010. Why is adaptation prevented at ecological margins? New insights from individual-based simulations. *Ecol. Lett.* 13:485–494.
- Broadhurst, L. M., A. Lowe, D. J. Coates, S. A. Cunningham, M. McDonald, P. A. Vesik, and C. Yates. 2008. Seed supply for broadscale restoration: maximizing evolutionary potential. *Evol. Appl.* 1:587–597.
- Burrows, M. T., D. S. Schoeman, L. B. Buckley, P. Moore, E. S. Poloczanska, K. M. Brander, C. Brown, J. F. Bruno, C. M. Duarte, B. S. Halpern, et al. 2011. The pace of shifting climate in marine and terrestrial ecosystems. *Science* 334:652–655.
- Byars, S. G., and A. A. Hoffmann. 2009. Lack of strong local adaptation in the alpine forb *Craspedia lamicola* in southeastern Australia. *Int. J. Plant Sci.* 170:906–917.
- Byars, S. G., W. Papst, and A. A. Hoffmann. 2007. Local adaptation and cogradient selection in the alpine plant, *Poa hiemata*, along a narrow altitudinal gradient. *Evolution* 61:2925–2941.
- Byars, S. G., Y. Parsons, and A. A. Hoffmann. 2009. Effect of altitude on the genetic structure of an Alpine grass, *Poa hiemata*. *Ann. Bot.* 103:885–899.
- Cahill, A. E., M. E. Aiello-Lammens, M. C. Fisher-Reid, X. Hua, C. J. Karanewsky, H. Y. Ryu, G. C. Sbeglia, F. Spagnolo, J. B. Waldron, O. Warsi et al. 2013. How does climate change cause extinction? *Proc. R. Soc. B.* 280. doi:10.1098/rspb.2012.1890.
- Ching, J., S. A. Musheyev, D. Chowdhury, J. A. Kim, Y. Choi, and J. J. Denny. 2013. Migration enhances adaptation in bacteriophage populations evolving in ecological sinks. *Evolution* 67:10–17.
- Clarke, K., and M. Ainsworth. 1993. A method of linking multivariate community structure to environmental variables. *Mar. Ecol.-Prog. Ser.* 92:205–205.
- Clausen, J., D. D. Keck, and W. M. Hiesey. 1940. Experimental studies on the nature of species. I. Effect of varied environments on western North American plants. Carnegie Institution of Washington, Publication 520. Washington, DC.
- Cooke, G. M., N. L. Chao, and L. B. Beheregaray. 2012. Divergent natural selection with gene flow along major environmental gradients in Amazonia: insights from genome scans, population genetics and phylogeography of the characin fish *Tripottheus albus*. *Mol. Ecol.* 21:2410–2427.
- Coop, G., D. Witonsky, A. D. Rienzo, and J. K. Pritchard. 2010. Using environmental correlations to identify loci underlying local adaptation. *Genetics* 185:1411–1423.
- Costa e Silva, J., B. M. Potts, and P. Tilyard. 2012. Epistasis causes outbreeding depression in eucalypt hybrids. *Tree Genet. Genomes* 8:249–265.
- Crispo, E., P. Bentzen, D. N. Reznick, M. T. Kinnison, and A. P. Hendry. 2006. The relative influence of natural selection and geography on gene flow in guppies. *Mol. Ecol.* 15:49–62.
- De Meester, L. 1993. Inbreeding and outbreeding depression in *Daphnia*. *Oecologia* 96:80–84.
- Ebert, D., C. Haag, M. Kirkpatrick, M. Riek, J. Hottinger, and V. Pajunen. 2002. A selective advantage to immigrant genes in a *Daphnia* metapopulation. *Science* 295:485–488.
- Eckert, A. J., A. D. Bower, S. C. González-Martínez, J. L. Wegrzyn, G. Coop, and D. B. Neale. 2010. Back to nature: ecological genomics of loblolly pine (*Pinus taeda*, Pinaceae). *Mol. Ecol.* 19:3789–3805.
- Edelaar, P., and D. I. Bolnick. 2012. Non-random gene flow: an underappreciated force in evolution and ecology. *Trends Ecol. Evol.* 27:659–665.
- Edmands, S. 1999. Heterosis and outbreeding depression in interpopulation crosses spanning a wide range of divergence. *Evolution* 53:1757–1768.
- . 2007. Between a rock and a hard place: evaluating the relative risks of inbreeding and outbreeding for conservation and management. *Mol. Ecol.* 16:463–475.
- Edmands, S., and C. C. Timmerman. 2003. Modeling factors affecting the severity of outbreeding depression. *Conserv. Biol.* 17:883–892.
- Endler, J. A. 1973. Gene flow and population differentiation: studies of clines suggest that differentiation along environmental gradients may be independent of gene flow. *Science* 179:243–250.
- Fahrig, L. 2003. Effects of habitat fragmentation on biodiversity. *Ann. Rev. Ecol. Syst.* 34:487–515.
- Faubet, P., and O. E. Gaggiotti. 2008. A new Bayesian method to identify the environmental factors that influence recent migration. *Genetics* 178:1491–1504.
- Fedoraka, K. M., W. E. Winterhalter, K. L. Shaw, W. R. Brogan, and T. A. Mousseau. 2012. The role of gene flow asymmetry along an environmental gradient in constraining local adaptation and range expansion. *J. Evol. Biol.* 25:1676–1685.
- Fenster, C. B., and L. F. Galloway. 2000. Inbreeding and outbreeding depression in natural populations of *Chamaecrista fasciculata* (Fabaceae). *Cons. Biol.* 14:1406–1412.
- Fisher, R. A. 1950. Gene frequencies in a cline determined by selection and diffusion. *Biometrics* 6:353–361.
- Foll, M., and O. Gaggiotti. 2006. Identifying the environmental factors that determine the genetic structure of populations. *Genetics* 174:875–891.
- Fournier-Level, A., A. Korte, M. D. Cooper, M. Nordborg, J. Schmitt, and A. M. Wilczek. 2011. A map of local adaptation in *Arabidopsis thaliana*. *Science* 334:86–89.
- Frankham, R., J. D. Ballou, M. D. B. Eldridge, R. C. Lacy, K. Ralls, M. R. Durdash, and C. B. Fenster. 2011. Predicting the probability of outbreeding depression. *Cons. Biol.* 25:465–475.
- Gandon, S., and S. L. Nuismer. 2009. Interactions between genetic drift, gene flow, and selection mosaics drive parasite local adaptation. *Am. Nat.* 173:212–224.
- Gomulkiewicz, R., R. D. Holt, and M. Barfield. 1999. The effects of density dependence and immigration on local adaptation and niche evolution in a black-hole sink environment. *Theor. Popul. Biol.* 55:283–296.
- Gray, J. C., and M. R. Goddard. 2012. Gene-flow between niches facilitates local adaptation in sexual populations. *Ecol. Lett.* 15:955–962.
- Guillot, G., and F. Rousset. 2013. Dismantling the Mantel tests. *Methods Ecol. Evol.* 4:336–344.
- Haider, S., C. Kueffer, P. J. Edwards, and J. M. Alexander. 2012. Genetically based differentiation in growth of multiple non-native plant species along a steep environmental gradient. *Oecologia* 170:89–99.
- Hadado, T. T., D. Rau, E. Bitocchi, and R. Papa. 2010. Adaptation and diversity along an altitudinal gradient in Ethiopian barley (*Hordeum vulgare* L.) landraces revealed by molecular analysis. *BMC Plant Biol.* 10:121.
- Haldane, J. B. S. 1930. A mathematical theory of natural and artificial selection. (Part VI. Isolation.) *Math. Proc. Cambridge* 26:220–230.
- . 1948. The theory of a cline. *J. Genet.* 48:277–284.
- Hendry, A. P. 2004. Selection against migrants contributes to the rapid evolution of ecologically dependent reproductive isolation. *Evol. Ecol. Res.* 6:1219–1236.

- Hirao, A. S., and G. Kudo. 2004. Landscape genetics of alpine-snowbed plants: comparisons along geographic and snowmelt gradients. *Heredity* 93:290–298.
- Hoffmann, A. A., and P. A. Parsons. 1991. Evolutionary genetics and environmental stress. Oxford Univ. Press, Oxford, U.K.
- Holliday, J. A., H. Suren, and S. N. Aitken. 2012. Divergent selection and heterogeneous migration rates across the range of Sitka spruce (*Picea sitchensis*). *Proc. R. Soc. B* 279:1675–1683.
- Holt, R. D., and R. Gomulkiewicz. 1997. How does immigration influence local adaptation? A reexamination of a familiar paradigm. *Am. Nat.* 149:563–572.
- Keller, S. R., N. Levens, P. K. Ingvarsson, M. S. Olson, and P. Tiffin. 2011. Local selection across a latitudinal gradient shapes nucleotide diversity in Balsam Poplar, *Populus balsamifera* L. *Genetics* 188: 941–952.
- Kirkpatrick, M., and N. H. Barton. 1997. Evolution of a species' range. *Am. Nat.* 150:1–23.
- Kremer, A., O. Ronce, J. J. Robledo Arancio, F. Guillaume, G. Bohrer, R. Nathan, J. R. Bridle, R. Gomulkiewicz, E. K. Klein, K. Ritland, et al. 2012. Long distance gene flow and adaptation of forest trees to rapid climate change. *Ecol. Lett.* 15:378–392.
- Lee, C.-R., and T. Mitchell-Olds. 2011. Quantifying effects of environmental and geographical factors on patterns of genetic differentiation. *Mol. Ecol.* 20:4631–4642.
- Legendre, P., and L. Legendre. 2012. Numerical ecology. 3rd ed. Elsevier, Amsterdam.
- Lenormand, T. 2002. Gene flow and the limits to natural selection. *Trends Ecol. Evol.* 17:183–189.
- Lenormand, T., and M. Raymond. 2000. Analysis of clines with variable selection and variable migration. *Am. Nat.* 155:70–82.
- Linhart, Y. B., and M. C. Grant. 1996. Evolutionary significance of local genetic differentiation in plants. *Annu. Rev. Ecol. Syst.* 27:237–291.
- Madsen, T., R. Shine, M. Olsson, and H. Wittzell. 1999. Conservation biology: restoration of an inbred adder population. *Nature* 402:34–35.
- Magiafoglou, A., M. E. Carew, and A. A. Hoffmann. 2002. Shifting clinal patterns and microsatellite variation in *Drosophila serrata* populations: a comparison of populations near the southern border of the species range. *J. Evol. Biol.* 15:763–774.
- Manel, S., M. K. Schwartz, G. Luikart, and P. Taberlet. 2003. Landscape genetics: combining landscape ecology and population genetics. *Trends Ecol. Evol.* 18:189–197.
- Marr, A. B., L. F. Keller, and P. Arcese. 2002. Heterosis and outbreeding depression in descendants of natural immigrants to an inbred population of song sparrows (*Melospiza melodia*). *Evolution* 56:131–142.
- May, R. M., J. A. Endler, and R. E. McMurtrie. 1975. Gene frequency clines in the presence of selection opposed by gene flow. *Am. Nat.* 109:659–676.
- Mayr, E. 1963. Animal species and evolution. Oxford Univ. Press, Lond.
- McCairns, R. J. S., and L. Bernatchez. 2008. Landscape genetic analyses reveal cryptic population structure and putative selection gradients in a large-scale estuarine environment. *Mol. Ecol.* 17:3901–3916.
- McKay, J. K., and R. G. Latta. 2002. Adaptive population divergence: markers, QTL and traits. *Trends Ecol. Evol.* 17:285–291.
- McNeilly, T., and J. Antonovics. 1968. Evolution in closely adjacent plant populations. IV. Barriers to gene flow. *Heredity* 23:205–218.
- Mimura, M., and S. N. Aitken. 2007. Adaptive gradients and isolation-by-distance with postglacial migration in *Picea sitchensis*. *Heredity* 99:224–232.
- Morin, X., and W. Thuiller. 2009. Comparing niche- and process-based models to reduce prediction uncertainty in species range shifts under climate change. *Ecology* 90:1301–1313.
- Nosil, P., and B. J. Crespi. 2004. Does gene flow constrain adaptive divergence or vice versa? A test using ecomorphology and sexual isolation in *Timema cristinae* walking-sticks. *Evolution* 58:102–112.
- Nosil, P., T. H. Vines, and D. J. Funk. 2005. Perspective: reproductive isolation caused by natural selection against immigrants from divergent habitats. *Evolution* 59:705–719.
- Olsen, J. B., P. A. Crane, B. G. Flannery, K. Dunmall, W. D. Templin, and J. K. Wenburg. 2011. Comparative landscape genetic analysis of three Pacific salmon species from subarctic North America. *Conserv. Genet.* 12:223–241.
- Paul, J. R., S. N. Sheth, and A. L. Angert. 2011. Quantifying the impact of gene flow on phenotype-environment mismatch: a demonstration with the scarlet monkeyflower *Mimulus cardinalis*. *Am. Nat.* 178:S62–S79.
- Pekkala, N., K. E. Knott, J. S. Kotiaho, K. Nissinen, and M. Puurtinen. 2012. The benefits of interpopulation hybridization diminish with increasing divergence of small populations. *J. Evolution. Biol.* 25:2181–2193.
- Räsänen, K., and A. P. Hendry. 2008. Disentangling interactions between adaptive divergence and gene flow when ecology drives diversification. *Ecol. Lett.* 11:624–636.
- Rehfeldt, G. E., C. C. Ying, D. L. Spittlehouse, and D. A. Hamilton. 1999. Genetic responses to climate in *Pinus contorta*: niche breadth, climate change, and reforestation. *Ecol. Monogr.* 69:375–407.
- Ribeiro, A. M., P. Lloyd, and R. C. K. Bowie. 2011. A tight balance between natural selection and gene flow in a Southern African arid-zone endemic bird. *Evolution* 65:3499–3514.
- Richardson, D. M., J. J. Hellmann, J. S. McLachlan, D. F. Sax, M. W. Schwartz, P. Gonzalez, E. J. Brennan, A. Camacho, T. L. Root, O. E. Sala, et al. 2009. Multidimensional evaluation of managed relocation. *Proc. Natl. Acad. Sci. USA* 106:9721–9724.
- Rundle, H. D., and M. C. Whitlock. 2001. A genetic interpretation of ecologically dependent isolation. *Evolution* 55:198–201.
- Scheiner, S. M., M. Barfield, and R. D. Holt. 2012. The genetics of phenotypic plasticity. XI. Joint evolution of plasticity and dispersal rate. *Ecol. Evol.* 2:2027–2039.
- Schluter, D. 2000. The ecology of adaptive radiations. Oxford Univ. Press, Oxford, U.K.
- . 2009. Evidence for ecological speciation and its alternative. *Science* 323:737–741.
- Sexton, J. P., S. Y. Strauss, and K. J. Rice. 2011. Gene flow increases fitness at the warm edge of a species' range. *Proc. Natl. Acad. Sci. USA* 108:11704–11709.
- Sgrò, C. M., A. J. Lowe, and A. A. Hoffmann. 2011. Building evolutionary resilience for conserving biodiversity under climate change. *Evol. Appl.* 4:326–337.
- Shafer, A. B. A., and J. B. W. Wolf. 2013. Widespread evidence for incipient ecological speciation: a meta-analysis of isolation-by-ecology. *Ecol. Lett.* 16:940–950.
- Slatkin, M. 1985. Gene flow in natural populations. *Ann. Rev. Ecol. Syst.* 16:393–430.
- . 1987. Gene flow and the geographic structure of natural populations. *Science* 236:787.
- Sobel, J. M., G. F. Chen, L. R. Watt, and D. W. Schemske. 2010. The biology of speciation. *Evolution* 64:295–315.
- Sork, V. L., S. N. Aitken, R. J. Dyer, A. J. Eckert, P. Legendre, and D. B. Neale. 2013. Putting the landscape into the genomics of trees: approaches for understanding local adaptation and population responses to changing climate. *Tree Genet. Genomes*. doi: 10.1007/s11295-013-0596-x.
- Stanton, M. L., and C. Galen. 1997. Life on the edge: adaptation versus environmentally mediated gene flow in the snow buttercup, *Ranunculus adoneus*. *Am. Nat.* 150:143–178.

- Sultan, S., and H. Spencer. 2002. Metapopulation structure favors plasticity over local adaptation. *Am. Nat.* 160:271–283.
- Tallmon, D. A., G. Luikart, and R. S. Waples. 2004. The alluring simplicity and complex reality of genetic rescue. *Trends Ecol. Evol.* 19:489–496.
- Venail, P. A., R. C. MacLean, T. Bouvier, M. A. Brockhurst, M. E. Hochberg, and N. Mouquet. 2008. Diversity and productivity peak at intermediate dispersal rate in evolving metacommunities. *Nature* 452:210–214.
- Via, S., A. C. Bouck, and S. Skillman. 2000. Reproductive isolation between divergent races of pea aphids on two hosts. II. Selection against migrants and hybrids in the parental environments. *Evolution* 54:1626–1637.
- Wang, I. J., R. E. Glor, and J. B. Losos. 2013. Quantifying the roles of ecology and geography in spatial genetic divergence. *Ecol. Lett.* 16:175–182.
- Wasserman, T. N., S. A. Cushman, M. K. Schwartz, and D. O. Wallin. 2010. Spatial scaling and multi-model inference in landscape genetics: *Martes americana* in northern Idaho. *Landscape Ecol.* 25:1601–1612.
- Westemeier, R. L., J. D. Brawn, S. A. Simpson, T. L. Esker, R. W. Jansen, J. W. Walk, E. L. Kershner, J. L. Bouzat, and K. N. Paige. 1998. Tracking the long-term decline and recovery of an isolated population. *Science* 282:1695–1698.
- Willi, Y., M. Kleunen, and S. Dietrich. 2007. Genetic rescue persists beyond first-generation outbreeding in small populations of a rare plant. *Proc. Roy. Soc. B* 274:2357–2364.
- Willis, C. G., B. Ruhfel, R. B. Primack, A. J. Miller-Rushing, and C. C. Davis. 2008. Phylogenetic patterns of species loss in Thoreau's woods are driven by climate change. *Proc. Natl. Acad. Sci. USA* 105:17029–17033.
- Wright, S. 1943. Isolation by distance. *Genetics* 28:114–138.
- Zellmer, A. J., M. M. Hanes, S. M. Hird, and B. C. Carstens. 2012. Deep phylogeographic structure and environmental differentiation in the carnivorous plant *Sarracenia alata*. *Syst. Biol.* 61:763–777.
- Zhang, D.-X., and G. M. Hewitt. 2003. Nuclear DNA analyses in genetic studies of populations: practice, problems and prospects. *Mol. Ecol.* 12:563–584.

Associate Editor: C. Lee

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1. Details from all studies included in the review and evidence for gene flow scenario designations, including study methods and IBD and IBE tests, marker type, average F_{ST} , scale, gradient type, and notes on phenotypic and adaptive divergence. See text for gene flow scenario descriptions.