CellPress REVIEWS

Opinion

The Exciting Potential and Remaining Uncertainties of Genetic Rescue

Donovan A. Bell,[1,7,*] Zachary L. Robinson,[1,7] W. Chris Funk,[2] Sarah W. Fitzpatrick,[3,4] Fred W. Allendorf,[5] David A. Tallmon,[6] and Andrew R. Whiteley[1]

Restoring gene flow into small, isolated populations can alleviate genetic load and decrease extinction risk (i.e., genetic rescue), yet gene flow is rarely augmented as a conservation strategy. Due to this discrepancy between opportunity and action, a recent call was made for widespread genetic rescue attempts. However, several aspects of augmenting gene flow are poorly understood, including the magnitude and duration of beneficial effects and when deleterious effects are likely to occur. We discuss the remaining uncertainties of genetic rescue in order to promote and direct future research and to hasten progress toward implementing this potentially powerful conservation strategy on a broader scale.

Highlights

Genetic rescue has helped prevent the extinction of several populations, yet augmented gene flow is rarely used as a conservation strategy.

Recent calls have been made for a paradigm shift in the conservation of small, isolated populations away from managing populations in isolation and toward widespread restoration of gene flow.

Several aspects of genetic rescue remain poorly understood.

Genetic rescue is inherently an eco-evolutionary process, and successful genetic rescue attempts have been part of comprehensive conservation plans that consider habitat, life history, and genetics.

Genomics is being increasingly used in the implementation and monitoring of genetic rescue attempts.

The Promise of Genetic Rescue and Calls for a Paradigm Shift

Restoring gene flow is a promising strategy to combat the global threat of human-driven population declines and extinctions. Habitat destruction and fragmentation have isolated many small populations [1], and interactions between demographic and genetic factors can drive these populations toward extinction [2]. Over the last two decades, researchers have provided strong evidence that restoring gene flow into these small, isolated populations can alleviate **genetic load** (see Glossary) and increase persistence probability [3–5], termed **genetic rescue** [4]. Evidence for genetic rescue has now been documented across a wide range of taxa, including plants [6], invertebrates [7], fish [8,9], birds [10,11], reptiles [12], and mammals [13–15].

Despite the promise of genetic rescue, augmented gene flow is rarely used as a conservation strategy [16]. Recommendations have been made for cautious and limited application of augmented gene flow due to concerns about **outbreeding depression** [17] and **genetic homogenization** [18]. The standard conservation practice is to manage populations in isolation to preserve genetic distinctiveness [19,20]. However, genetic distinctiveness can be caused by genetic drift in small, isolated populations, and managing these populations in isolation may increase their extinction risk [19]. Recent calls have been made for a paradigm shift in the genetic management of small, isolated populations away from inaction and toward widespread consideration of augmenting gene flow [16,19–21].

We agree that genetic rescue should be attempted more frequently. Nevertheless, several aspects of genetic rescue are poorly understood. Importantly, the benefits and risks of restoring gene flow need to be better characterized to provide realistic expectations and to enable accurate cost-benefit analyses with competing conservation strategies. Conservation practitioners also need a clearer understanding of how to best implement genetic rescue attempts across a broad range of scenarios in order to maximize the utility of restoring gene flow. Here, we highlight aspects of genetic rescue that remain uncertain. Our goal is to promote and direct additional research that will help transition the conservation community toward widespread genetic rescue attempts.

The Definition of Genetic Rescue

The 'rescue effect' was coined nearly 50 years ago to refer to decreased extinction risk of populations following immigration [22]. The rescue effect was primarily attributed to the simple addition of immigrants to the population, which decreases **Allee effects** and **demographic stochasticity** [23] (i.e., **demographic rescue**). Genetic rescue was distinguished from demographic rescue after studies provided empirical evidence that the genetic contribution of immigrants can cause a further increase in abundance [11,12,23].

[1]Wildlife Biology Program, W.A. Franke College of Forestry and Conservation, University of Montana, Missoula, MT, USA
[2]Department of Biology and Graduate Degree Program in Ecology, Colorado State University, Fort Collins, CO, USA
[3]W.K. Kellogg Biological Station, Department of Integrative Biology, Michigan State University, Hickory Corners, MI, USA
[4]Ecology, Evolutionary Biology, and Behavior Program, Michigan State University, East Lansing, MI, USA
[5]Division of Biological Sciences, University of Montana, Missoula, MT, USA
[6]Biology and Marine Biology Program, University of Alaska Southeast, Juneau, AK, USA
[7]These authors contributed equally to this work
*Correspondence: donovan.bell@umontana.edu

Genetic rescue was originally defined as 'the increase in the probability of a population's survival due to the immigration of genes from another population' [24]. Several competing definitions of genetic rescue have since been used. Definitions that reduce the emphasis on extinction risk can cause confusion in how genetic rescue is best evaluated, which in turn may be inhibiting much needed progress. We contend that genetic rescue is best defined as 'a decrease in population extinction probability owing to gene flow, best measured as an increase in **population growth rate**'. This is consistent with the original more theoretical definition [22,24] but also emphasizes that, in practice, genetic rescue is best measured as an increase in population growth rate (Box 1).

Box 1. Expanding the Definition of Genetic Rescue and Providing a Framework for Its Evaluation

The ultimate goal of attempting genetic rescue is to decrease a population's risk of extinction. Whether a population persists or goes extinct is determined primarily by the population growth rate [68], making population growth rate the critical parameter for conservation. For this reason, we emphasized population growth rate in our previous definition of genetic rescue: 'an increase in population growth rate owing to gene flow' [3,4]. This definition has received criticism for being overly narrow [69]. Populations cannot expand when habitat is limiting, even when gene flow alleviates genetic load. Additionally, an increase in population growth rate is difficult to measure in wild populations. In order to capture a wider range of beneficial outcomes, we expand our definition of genetic rescue to 'a decrease in population extinction probability owing to gene flow, best measured as an increase in population growth rate'.

A concern arising from this broader definition is that studies may report genetic rescue based on parameters that are weakly associated with persistence probability. Importantly, an increase in heterozygosity (i.e., decrease in inbreeding) by itself provides very limited evidence for genetic rescue. Increased heterozygosity is associated with future adaptive potential, but resulting demographic responses will typically occur outside of the timeframe of monitoring and conservation objectives. Increased genetic variation is a weak indicator of contemporary extinction risk because gene flow initially increases heterozygosity irrespective of whether genetic rescue or outbreeding depression occurs.

A positive demographic response is needed to infer increased persistence probability in the short-term (Figure I). An increase in migrant ancestry, beyond expectations under genetic drift alone, provides evidence for elevated fitness of hybrids compared with residents [69], but determining neutral gene flow expectations is difficult in practice. Better evidence for increased persistence probability is an increase in vital rates to which population growth rate has a high sensitivity [70]. The best evidence is an increase in population growth rate due to gene flow. Monitoring should cover multiple generations and focus on the metrics that provide the strongest evidence for evaluating whether genetic rescue occurred given the available resources. Conservation practitioners can follow similar criteria for evaluating genetic rescue attempts, but will often be less concerned with separating the genetic versus demographic contribution of immigrants.

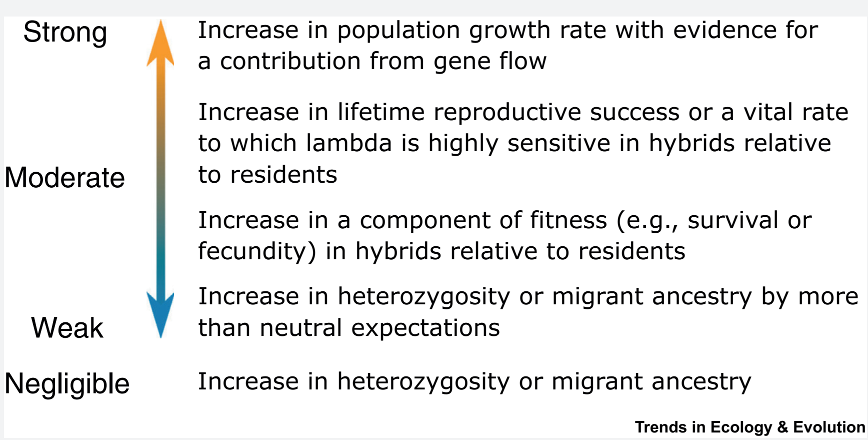

Figure I. The Relative Strength of Different Types of Evidence for Genetic Rescue.

Glossary

Allee effects: a positive relationship between population growth rate and density. Allee effects can increase extinction probability in small populations.

Carrying capacity: the maximum number of individuals that a habitat can sustain given no genetic load.

Demographic rescue: a decrease in population extinction probability owing to the simple addition of immigrants.

Demographic stochasticity: fluctuations in population size due to random variation in survival and birth rates. Demographic stochasticity can increase extinction probability in small populations.

Evolutionary rescue: a decrease in population extinction probability owing to adaptation to environmental stress from standing genetic variation, *de novo* mutation, or gene flow.

Genetic homogenization: an increase in genetic similarity of populations due to gene flow. Genetic homogenization can lead to loss of species-level genetic diversity (see [18]).

Genetic incompatibilities: reduced fitness due to deleterious interactions among loci.

Genetic load: the proportional decrease in fitness between the average genotype in a population and the theoretically fittest genotype (see [54,74]). Genetic rescue can alleviate genetic load that is due to inbreeding depression, deleterious alleles that have reached high frequency or fixation by genetic drift, and maladaptation to changing environmental conditions.

Genetic rescue: a decrease in population extinction probability owing to gene flow, best measured as an increase in population growth rate.

Genetic swamping: loss of locally adaptive alleles due to gene flow.

Heterosis: elevated fitness of F1 hybrids relative to their parents (see [30]). Heterosis is due to increased genome-wide heterozygosity following mating between individuals from divergent lineages.

Hybrid: an individual with both migrant and resident ancestry. Here, we are referring to both intraspecific and interspecific

Genetic rescue is typically attributed to the masking of deleterious alleles. However, gene flow can also promote adaptation to changing environmental conditions by increasing the variation upon which selection acts. These mechanisms are not mutually exclusive and will often co-occur in small populations that suffer from both **inbreeding depression** and maladaptation. Genetic rescue overlaps with **evolutionary rescue** when gene flow provides the variation needed for evolution to reverse population declines, which is often the case for small populations [25].

hybrids and include first and later generation hybrids.
Inbreeding depression: reduced fitness of offspring with related parents.
Outbreeding depression: reduced fitness of hybrids. Outbreeding depression is typically attributed to maladaptation to local environmental conditions or genetic incompatibilities.
Population divergence: the time since isolation between populations (see [17]).
Population growth rate: change in abundance over time.

The Complex Reality of Genetic Rescue

Although genetic rescue is conceptually simple, gene flow has complex influences on individual fitness and population dynamics. These influences depend on the genetic composition and environmental conditions of the recipient and source populations. The maximum potential increase in fitness is determined by the severity of the genetic load in the recipient population, but realized fitness effects also depend on the introduced genetic material. Migrants introduce both beneficial and deleterious genetic variation. Beneficial effects of gene flow include masking deleterious, recessive alleles and increasing additive genetic variation [3]. Deleterious effects of gene flow can be caused by a reduction in local adaptation or **genetic incompatibilities** between the source and recipient populations. The net effect of introduced beneficial and deleterious genetic variation determines whether genetic rescue, outbreeding depression, or neither occurs.

The fitness effects of gene flow change over time because beneficial and deleterious genetic variation manifest at different time scales. In the first (F1) generation, the maximum number of deleterious, recessive alleles are expected to be masked, often causing **heterosis**. In the second (F2) generation, **hybrid** fitness declines as the population approaches Hardy-Weinberg equilibrium [4], but maternal effects can transfer the fitness benefits of heterosis to F2 progeny [5]. As a result, fitness benefits are predicted to be maximal in the F1 and F2 generations and can decline in later generations as genetic load reaccumulates due to inbreeding and genetic drift. In the F2 and later generations, recombination can expose genetic incompatibilities [26,27] or form novel beneficial genotypes [28]. The fitness effects of gene flow are also influenced by the effective population size and the strength of natural selection, which determine whether novel beneficial alleles and genotypes increase in frequency.

These evolutionary dynamics, of course, play out in an ecological theater. Gene flow can only increase population growth rate when abundance is suppressed below **carrying capacity** due, in part, to a high genetic load. Additionally, population growth rate is influenced by environmental conditions. For example, in a deteriorating habitat, abundance may continue to decline despite beneficial effects of gene flow. These complex eco-evolutionary interactions make it difficult to accurately predict how restoring gene flow will influence a population.

Uncertainties Surrounding Genetic Rescue

What Is the Magnitude of Genetic Rescue?

Understanding how often gene flow appreciably decreases population extinction risk is critical for informing conservation decisions. As genetic rescue is due to alleviating genetic load, uncertainty about the magnitude of genetic rescue is related to the long-standing debate over how often genetic load is a key contributor to extinction. Substantial evidence now suggests that inbreeding and genetic drift can depress individual fitness [29,30], with strong evidence coming from genetic rescue studies [5]. Less is known about how often elevated hybrid fitness will translate into increased population growth rate. Evidence for increased population growth rate following gene flow has been found in laboratory and wild populations [3,4]. In wild populations, concurrent habitat improvements and lack of control and replicate populations make it difficult to characterize the contribution of genetic factors to increased population growth rate [31]. Additionally, current genetic rescue attempts have involved severely inbred populations, but many populations with less severe genetic loads could still benefit from gene flow. In these cases, the magnitude of genetic rescue is not expected to be as large. Better characterization of the magnitude of genetic rescue will increase confidence and interest in conservation applications of restoring gene flow.

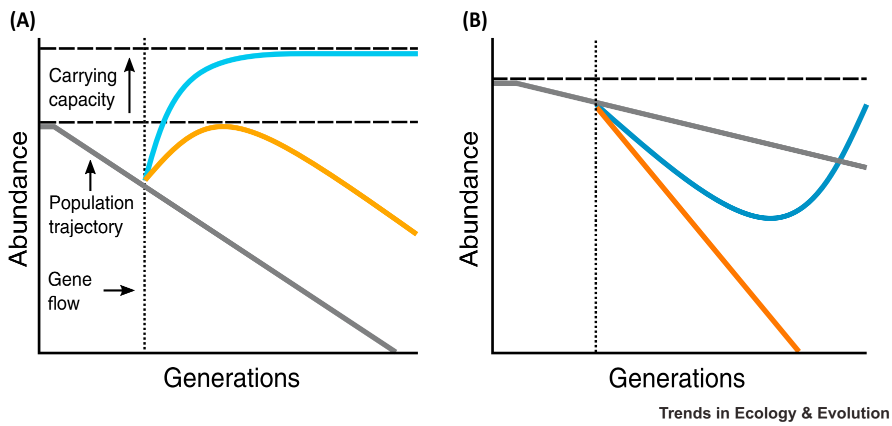

Figure 1. Potential Trends in Abundance Following Gene Flow into a Declining Population.
(A) Genetic rescue will likely be ephemeral (orange line) unless the habitat constraints that caused the initial population decline are removed (light blue line). (B) Severe outbreeding depression may drive populations toward extinction (red line) unless the efficacy of natural selection is sufficient to allow for recovery (dark blue line). The initial population trajectory is represented by the unbroken grey line, gene flow is represented by the dotted line, and carrying capacity is represented by the dashed line.

What Is the Duration of Genetic Rescue?

The duration of genetic rescue is a major outstanding question [32]. Most studies have been limited to the period when beneficial effects are expected to be maximal (i.e., F1 and F2 generations). A recent meta-analysis provided evidence that increased fitness due to gene flow can persist through, and may even be higher in, the F3 generation [33]. However, this meta-analysis was based on a small number of mostly laboratory invertebrate populations (16 of 17 comparisons). These data limitations highlight the lack of long-term studies on genetic rescue. Even if elevated hybrid fitness is primarily limited to the F1 and F2 generations, abundance may still increase if sufficient habitat is available, which in turn would decrease Allee effects and demographic stochasticity. Importantly, genetic rescue is still beneficial in this scenario because it can buy time while further conservation strategies are planned and implemented.

Genetic rescue is expected to be temporary when the same habitat constraints that caused the initial population decline remain present or when habitat is deteriorating (Figure 1A; Box 2). Unfortunately, habitat constraints are a recurring theme in the limited number of conservation-motivated genetic rescue attempts. For example, the abundance of greater prairie chickens (*Tympanuchus cupido*) initially increased following gene flow [11], but habitat constraints likely contributed to the subsequent population decline [34]. In another recent example, gene flow was augmented as part of a broader conservation strategy to protect mountain pygmy possums (*Burramys parvus*) [14]. Genetic rescue likely contributed to the rapid increase in abundance, and concurrent habitat improvements may allow for abundance to remain elevated. However, climate change is beginning to cause large declines in a key food resource for mountain pygmy possums [35], and continued conservation efforts will be essential for the possums' persistence. Both examples were last-ditch efforts to prevent extinctions in populations that face extreme habitat constraints. Future genetic rescue attempts are likely to include populations where habitat constraints are more easily alleviated and the benefits of gene flow are longer lasting (Figure 1A).

When Will Outbreeding Depression Occur?

The limited number of genetic rescue attempts is partly due to concerns over outbreeding depression. Risks of outbreeding depression can be minimized by following current genetic rescue guidelines [27,36]. These guidelines call for selecting populations that occur in similar habitats and have low **population divergence** to avoid reducing local adaptation and genetic incompatibilities,

Box 2. The Mystery on Isle Royale

Isle Royale wolves present perhaps the most detailed example of inbreeding depression contributing to a functional extinction of a habitat-limited population [61,71], but the influence of gene flow on this extinction is unclear. Isle Royale (on Lake Superior, Michigan, USA) contains a small population of highly inbred wolves (mean census size of 24 [50]). In 1997, a single male immigrated to Isle Royale. Due to extremely high fitness, his ancestry constituted 56% of the genomic composition of the population within two generations [50]. Inbreeding coefficients rapidly increased within the population, which likely contributed to a precipitous decline in abundance. By 2018, only two highly related wolves remained on the island, with the male being both the father and half-sibling of the female. They produced one inviable offspring [61] and have shown no further signs of courtship [72].

It is uncertain whether the migrant's arrival forestalled or contributed to the demise of the Isle Royale wolves. If the migrant increased the rate of extinction, it would be the first documentation of a distinct negative effect of gene flow in which a genomic sweep leads to a rapid increase in inbreeding depression (Figure I). Current genetic rescue guidelines would not be relevant for this deleterious effect because individuals with a low risk of outbreeding depression could still cause a genomic sweep. Interestingly, if more than one wolf had immigrated to Isle Royale, inbreeding depression may have been less severe because inbreeding coefficients would have increased less rapidly. Alternatively, additional immigrants may have introduced more deleterious alleles into the population and increased the extent of inbreeding depression for a given inbreeding coefficient. Further research is needed to understand how gene flow into populations with severe habitat constraints can influence the duration of genetic rescue or potentially increase extinction risk. A wolf reintroduction program was recently announced [72] and translocations began in 2018, which will allow researchers to observe the process unfold again.

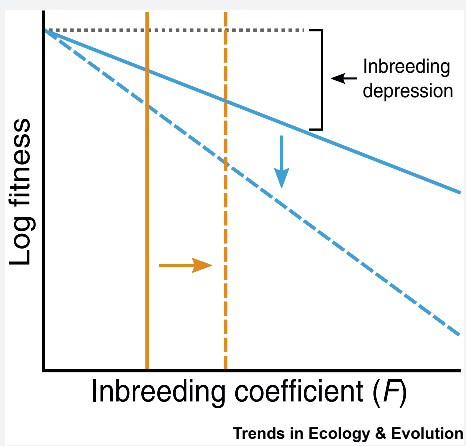

Figure I. Can Gene Flow Increase Inbreeding Depression?

Blue lines represent the relationship between inbreeding coefficients and fitness, and orange lines represent the mean inbreeding coefficient of a population. Gene flow may be able to increase inbreeding depression by causing a genomic sweep that increases the mean inbreeding coefficient in a population (orange dashed line), that introduces novel deleterious alleles that increase the severity of inbreeding depression for a given inbreeding coefficient (blue dashed line), or both. Unbroken lines represent the pre-gene flow and dashed lines represent the post-gene flow conditions. Inbreeding depression is the reduction in fitness of an inbred individual relative to a non-inbred individual (dotted grey line). The intersection of blue and orange lines represents the mean inbreeding depression of individuals in a population.

respectively. A meta-analysis of studies adhering to these guidelines found very limited evidence for outbreeding depression [27]. This has led several researchers to assert that outbreeding depression is avoidable and concerns are overstated [20,21].

However, current guidelines are mostly based on studies that are limited to the F1 and F2 generations. Delayed onset of outbreeding depression until F3 and later generations has not been well examined and may be a concern in some circumstances. Outbreeding depression may not manifest until later generations because heterosis is temporary and recombination can expose additional genetic incompatibilities over time [37]. Although concerning, severe genetic incompatibilities are unlikely to occur in closely related populations because they tend to form over long time periods. The onset of outbreeding depression may be further delayed if local adaptations are to extreme, periodic events (e.g., floods or fires). This would delay the manifestation of outbreeding depression until the next extreme event, though this has not been demonstrated to our knowledge. The potential for late onset of outbreeding depression further emphasizes the need for long-term studies on genetic rescue, but should not dissuade genetic rescue attempts that fall within existing guidelines.

Outbreeding depression is less predictable and presents a greater concern when source populations that meet the criteria in the current guidelines are unavailable [38]. This may be common for endangered species with few remaining populations. Evolutionary theory predicts that natural selection tailors populations to their local environment and gene flow predominantly reduces these local adaptations [39]. For example, migrants had substantially reduced fitness compared with residents in large Atlantic salmon (*Salmo salar*) populations [40]. However, small populations that are governed by strong genetic drift are less likely to have fine-scale local adaptations [41], especially in changing or stressful environments, and alleviation of genetic load may overpower the deleterious effects of reduced local adaptation [42]. A recent study documented genetic rescue in Trinidadian guppies (*Poecilia reticulata*) despite many generations of divergent selection pressure to high versus low predation [43]. Trinidadian guppies offer a classic example of adaptive differentiation [44], but local adaptation is generally difficult to identify in wild populations [45]. More studies will be required to understand when differences in local adaptation will cause outbreeding depression in small, inbred populations.

Population divergence is less likely to cause outbreeding depression than differences in environmental conditions [27]. The extent of population divergence before strong genetic incompatibilities form is highly variable among taxa (Box 3), but complete reproductive isolation often takes millions of years [17]. The genetic rescue guideline of 500 years of divergence is purposely conservative to minimize risk [27]. However, genetic rescue attempts with greater divergence times are being increasingly considered (e.g., [38]) and may become common in the future. Researchers need to carefully evaluate what is known about outbreeding depression in their focal species because the extent of local adaptation and the potential for genetic incompatibilities varies widely among taxa.

When Will Outbreeding Depression Increase the Probability of Population Extinction?

Compared with inbreeding depression, even less is known about when outbreeding depression will substantially decrease persistence probability, but outbreeding depression does not appear to be a common contributor to extinction. In the commonly cited example, outbreeding depression resulting from maladaptive birth timing contributed to the extinction of Tatra Mountain ibex (*Capra ibex*) [46]. However, immigrants were moved from arid to alpine environments and are now considered to be different species (*Capra nubiana* and *Capra aegagrus*). This example should not deter genetic rescue attempts because most conservation practitioners would not consider such a high-risk translocation today. Generally, outbreeding depression is most likely to appreciably depress population growth rate when increases in migrant ancestry are large, either due to high migration rates or substantial reproductive success of migrants and their offspring.

In some cases, populations have recovered from outbreeding depression [28,47,48] (Figure 1B). Crosses between marine copepod (*Tigriopus californicus*) populations with known genetic incompatibilities had reduced fitness in the F2 generation but elevated fitness in the F3 generation [28]. These examples have led several researchers to suggest that outbreeding depression is often temporary [20,49]. However, in small populations, a rebound in abundance following outbreeding depression may be prevented by low efficacy of natural selection. In some cases, even subtle outbreeding depression could tip the scale toward extinction.

Box 3. Intermediate Optima in Population Divergence and Number of Migrants

Intermediate amounts of population divergence and immigration rates should result in the strongest genetic rescue effects. Populations with low divergence may minimize rescue effects because they will often share the majority of the loci underlying their genetic load. However, high divergence may lead to outbreeding depression [65,73]. Making matters more complicated, the relationship between population divergence and rescue effects is taxon-specific and is also influenced by demographic history and the extent of local adaptation within the species (Figure IA). These complexities make it difficult to predict the amount of population divergence that will have high risks of outbreeding depression. Attempts to identify optimally divergent source populations can be difficult, risky, and often unnecessary. However, more detailed considerations are necessary for cases where few, divergent source populations remain, especially for species with fine-scale local adaptations.

Likewise, intermediate immigration rates will typically result in the greatest rescue effects [36]. Moving too few individuals may limit rescue effects and potentially accelerate the reaccumulation of genetic load (Box 2). However, moving too many individuals may result in genetic swamping and can potentially make outbreeding depression more likely to have large demographic effects. The relationship between migration rate and rescue effects is influenced by life history, the magnitude of the genetic load, habitat constraints, and the extent of local adaptation in the recipient population (Figure IB). Experimental tests of genetic rescue across various scenarios will help to identify these intermediate optima for diverse taxa and maximize genetic rescue effects.

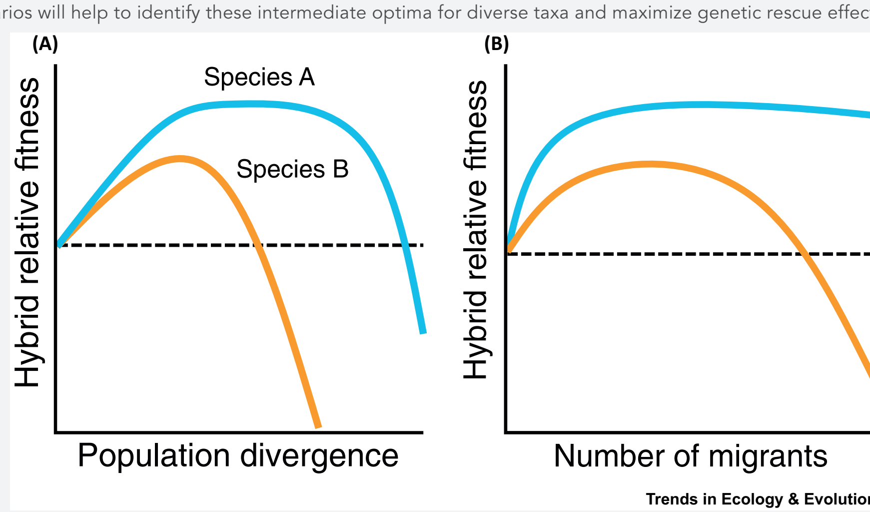

Figure I. The Influence of Population Divergence and Migration Rates on Hybrid Relative Fitness.

Intermediate amounts of population divergence (A) and migration rates (B) typically maximize genetic rescue effects (e.g., the fitness of hybrids relative to residents). However, relationships between these factors vary considerably due to taxonomic, evolutionary, and environmental differences. For example, divergent crosses or high immigration rates may be less risky for a generalist species (Species A; blue line) than a species with fine-scale local adaptation (Species B; orange line). Equal fitness between resident and hybrid individuals is represented by the dashed line.

Can Native Ancestry Be Preserved Following Genetic Rescue?

The potential for loss of evolutionary lineages and genetic homogenization are prominent concerns for restoring gene flow. **Genetic swamping** may eliminate the unique adaptations that made the population of such high conservation value in the first place. Large increases in migrant ancestry appear common and difficult to prevent. High profile genetic rescue studies consistently document large increases in migrant ancestry [8,9,13,50]. For example, migrant ancestry reached approximately 70% following translocations into an inbred bighorn sheep population (*Ovis canadensis*) [51]. Further, recent simulation work shows that the magnitude of genetic rescue can be strongly associated with loss of native ancestry [52]. Although the increase in migrant ancestry is a stochastic process and will be hard to anticipate, conservation practitioners can influence migrant ancestry by introducing an appropriate number of migrants (see [53]; Box 3), or potentially using controlled crosses in a captive environment [36,54]. The challenge facing conservation practitioners is to determine if the consequences of inbreeding depression outweigh the risk of genetic homogenization [18] and if genetic distinctiveness is the product of unique local adaptations.

Genomics and Genetic Rescue

The genomic revolution provides new and exciting opportunities to address many of the uncertainties described above [55]. Understanding the genomic architecture of the genetic load will be valuable for informing expectations about the magnitude and duration of genetic rescue. However, the genomic architecture remains poorly understood [56]. The genetic load in small, inbred populations is likely caused by many loci of varying effect [30,57]. If the loci underlying the genetic load are also highly variable among populations, the notion that inbred source populations can produce genetic rescue will be reinforced [10]. This would also imply that specifically tailoring source populations and immigrants to maximize genetic rescue effects would be difficult. Another related uncertainty is whether loci contributing to genetic load contain deleterious alleles that are segregating within a population or have become fixed due to strong genetic drift. If most deleterious alleles are segregating, we expect genetic rescue effects to be ephemeral unless the effective population size increases, subsequently allowing selection to overwhelm genetic drift [52]. Alternatively, if fixed deleterious alleles are primarily responsible for reduced fitness, gene flow will expose novel genetic variation to selection and the duration of genetic rescue may be greater, particularly if fixation occurred during a period of low effective population size.

Genomic techniques can help identify recipient populations in need of genetic rescue and source populations that will maximize benefits and minimize risks. Genomic approaches allow for precise estimates of inbreeding [56], which is a useful indicator of genetic load in the recipient population (see [55]). Genomic techniques can also help researchers to identify loci that have a large contribution to the genetic load. When large effect loci are identified, specifically selecting immigrants or source populations that possess beneficial alleles will be more practical. Similarly, facilitating adaptation to climate change may be improved by targeting specific loci (but see [58]). Researchers can also use genomic approaches to identify inversions and other structural differences that may cause outbreeding depression. In addition, researchers can increasingly identify adaptive differentiation among populations [59], which will help to minimize the risk of outbreeding depression and also to distinguish between neutral versus adaptive genetic distinctiveness.

Concluding Remarks: The Path Forward for Genetic Rescue

Evidence for genetic rescue is rapidly accumulating and a transition toward widespread restoration of gene flow is likely warranted. However, further research is needed to address remaining uncertainties and to increase confidence in this promising strategy (see Outstanding Questions). Researchers should take advantage of naturally occurring genetic rescue and outbreeding depression to help reduce this uncertainty (e.g., natural immigration [60,61], hybrid zones [62], and invasive species [63]). In addition, academics should continue to collaborate with managers to assist with detailed evaluation of genetic rescue attempts and publish findings (for an excellent example, see [13]). When possible, multigenerational genetic rescue experiments should be implemented [31].

Additionally, deliberate efforts to experimentally examine genetic rescue and outbreeding depression across a wide range of conditions would enhance our ability to refine current guidelines. Although diverse outcrossing scenarios have been explored in the plant literature (e.g., [37,64,65]), examining these relationships across diverse taxa would be informative. A more detailed understanding of genetic rescue will help conservation practitioners weigh restoring gene flow as a stop-gap measure against alternative conservation strategies, or better still, to incorporate genetic rescue into broader conservation plans that include restoring, expanding, and reconnecting habitat.

Although uncertainties remain, the extinction crisis is happening now [66]. Genetic rescue should be attempted more aggressively when proposed translocations conform to current guidelines. When

Outstanding Questions

How will the magnitude of genetic rescue vary across diverse scenarios and can it be predicted?

For how many generations will genetic rescue persist?

Under what conditions will severe outbreeding depression occur?

When and how often will gene flow increase, decrease, or have no influence on population growth rate?

How often will small, inbred populations have unique local adaptations, and how can the risks of genetic swamping be minimized?

How should populations and individuals be selected for translocations?

Can gene flow increase inbreeding depression and, if so, how can this be avoided?

What is the genomic architecture of inbreeding depression, outbreeding depression, and genetic rescue?

translocations do not meet guidelines, potential risks of outbreeding depression and genetic homogenization need to be compared against inaction [20]. In these instances, genetic rescue should be attempted with caution because even if severe outbreeding depression is rare, one high profile case may inhibit progress by altering perceptions [67]. Researchers should strive to improve our understanding of genetic rescue to the point where we can confidently and effectively restore gene flow with minimal monitoring. Once this is achieved, restoring gene flow may become one of the most practical, powerful, and inexpensive tools in conservation biology, potentially decreasing the extinction risk for a vast number of populations.

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