How bottlenecks shape adaptive potential: from theory and microbiology to conservation biology

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Abstract

Wild populations frequently undergo demographic changes that can challenge their persistence and, thus, the equilibrium of ecosystems. For instance, habitat fragmentation due to human activity leads to a drastic population size reduction, a process called a bottleneck. By reducing genetic diversity, a bottleneck may prevent a population from adapting to subsequent environmental changes. In the context of climate change, it is crucial to accurately predict how a wild population evolves after a bottleneck and how it affects its persistence. Mathematical models have provided valuable insights into the impact of bottlenecks on the adaptive potential of populations. However, their application to wild populations requires further improvement as these theoretical predictions have been mostly experimentally tested with microbial populations. Thus, it remains unclear what the implications of the theoretical predictions are at the macroscopic scale, although these predictions are crucial for conservation biology. This review aims to determine how the knowledge acquired through evolutionary theory and experimental microbiology applies to wild populations. To achieve this aim, we address the following questions: (i) What do theory and microbiology experiments tell us about the impact of bottlenecks on the ability of populations to adapt to future environmental changes? (ii) Do these theoretical predictions apply to wild populations? and (iii) What is missing to better predict the evolution of wild populations after a bottleneck? We analyze how the four main evolutionary processes (i.e., mutation, genetic drift, natural selection, and gene flow) impact the fate of populations facing bottlenecks. By linking theory, microbial experiments, and empirical studies on natural populations, we identify research directions that could help manage populations undergoing bottlenecks and plead for increased communication between these fields.

Keywords: Bottleneck, Adaptive potential, Demography, Evolutionary rescue, Population size, Stress, Fragmentation, Mathematical models, Microbiology, Conservation biology

1 Introduction

Most natural populations experience bottlenecks that can be caused, for example, by severe climate events, habitat loss, and overhunting (Lande, 1988; Frankham et al., 2002). The bottleneck-induced population size reduction increases the extinction risk of populations and, thus, may destabilize ecosystems (Frankham et al., 1999). As the current intensive anthropogenic perturbations of Earth's systems are increasing the occurrence of bottlenecks (Barnosky et al., 2011; Ceballos et al., 2015), there is an urgent need to understand how bottlenecks impact the evolutionary fate of at-risk populations. This review examines the evolutionary fate of populations undergoing sudden random decreases in size that are selectively neutral, as opposed to those caused by directional selection. Specifically, this review focuses on bottlenecks involving random reductions in population size rather than selective bottlenecks involving non-random reductions in population size (but see section 4.2).

Forecasting the effects of population bottlenecks is crucial in conservation biology (Frankham et al., 2002). However, our ability to predict the long-term consequences of bottlenecks under natural conditions remains weak. First, predictions in the wild are generally made retrospectively, i.e., after a bottleneck has occurred and the population has gone extinct or survived (Bouzat, 2010). Second, predictions are often made case-by-case, preventing their applicability to other systems. To fill this knowledge gap and improve our understanding of bottlenecks, we need to develop a comprehensive overview combining theoretical predictions and empirical evidence. Although connections between fundamental evolutionary biology and wildlife conservation have slowly developed, they are increasingly strengthening, highlighting their importance (Hohenlohe et al., 2020).

Microbiology is a field that allows for experimentally assessing the impact of bottlenecks on the adaptive potential of microbial populations (LeClair and Wahl, 2017). A common experimental evolution technique is subjecting micro-organisms to serial passaging, which involves repeated bottlenecks. In such experiments, a microbial population is inoculated into a medium and grows. Then, the experimenter takes a fraction of this population, inoculates a new medium, and repeats the process several times. This common technique explains why the literature in experimental microbiology has so well documented the impact of bottlenecks on the adaptation of microbial populations (LeClair and Wahl, 2017). Micro-organisms, such as bacteria and fungi, can reproduce rapidly and reach large numbers in small spaces, allowing for highly replicated experiments and, therefore, highly accurate predictions (Elena and Lenski, 2003). In summary, the simplicity of these experiments makes microbiology an excellent field for testing theoretical predictions.

To the best of our knowledge, no study has yet bridged the gap between what microbiology tells us about the impact of bottlenecks on the adaptive potential of populations and

conservation biology. The lack of direct links between both fields likely results from the many differences between microbial populations in controlled laboratory experiments and wild populations in natural ecosystems [see Box 4 in Kawecki et al. (2012)]:

1. Microbes used in experiments substantially differ from endangered natural species targeted by conservation efforts, mostly diploid and sexual.

2. The demography of microbial populations studied in laboratory conditions also differ from that of wild populations. For example, the size of microbial populations is likely larger than that of wild populations. As a result, the genetic load is likely higher in wild populations than in laboratory populations.

3. Bottlenecks in the wild likely vary in intensity and frequency, whereas they are typically periodic in microbiology experiments.

4. The number of generations before adapting to a new environment differs for microbial and wild populations.

Many other differences exist, such as variations in environmental constraints, and anthropogenic pressures, which affect wild population dynamics but are absent from laboratory conditions. Despite these differences, our review describes how microbiology findings apply to wild populations.

The evolution of wild populations involves multiple evolutionary and ecological processes that act simultaneously. Understanding the influence of each process independently is crucial for a better understanding of the overall effect of a bottleneck during demographic history on future response to selection to a new environment. Yet, empirical studies under laboratory conditions involving models other than micro-organisms have never examined the effects of bottlenecks in anything other than a holistic way [e.g., fish populations of *Heterandria formosa* in Klerks et al. (2019), insect populations of *Tribolium castaneum* in Olazcuaga et al. (2023), *Drosophila melanogaster* in Ørsted et al. (2019)]. Therefore, it is impossible to quantify the contribution of each process. Conversely, theory and microbiology have studied each ecological and evolutionary process independently [e.g., the fraction of beneficial mutations lost due to bottlenecks in Wahl et al. (2002)]. Therefore, we discuss in this review the impact on adaptive potential of each of the following evolutionary processes occurring during a bottleneck: mutation, genetic drift, natural selection, and gene flow.

This review aims to enhance our comprehension of how bottlenecks impact adaptive potential to a new environment of a population. This aim is achieved by synthesizing theoretical and microbiological knowledge and applying it to wild populations. For each of the evolutionary processes of interest, we inquire: (i) What do theory and microbiology experiments tell us about the impact of bottlenecks during demographic history on the ability of populations to adapt to a future environmental change? (ii) Do these theoretical predictions apply to wild populations? and (iii) What is needed to better predict the wild population evolution after a bottleneck? Our review aims to increase the effectiveness of conservation efforts by anticipating the evolutionary consequences of demographic changes in wild ecosystems.

2 Disentangling the influence of each evolutionary process during a bottleneck on the future adaptive potential of populations

2.1 Mutation

Population bottlenecks can impact mutations' appearance, fixation, and frequency, potentially disturbing future adaptation. Indeed, mutations introduce genetic variation on which selection can act, allowing populations to adapt to their environment. A population will adapt to future environmental changes by increasing the frequency of mutations that are beneficial in the new environment. The population can adapt via (i) the appearance of new beneficial mutations, known as an adaptation from *de novo* mutations, and (ii) the pre-existence of beneficial mutations in the population, known as an adaptation from standing genetic variation. The relative importance of these two mechanisms varies depending on the population properties, such as the population size, and some timescales, such as the number of generations between the bottleneck and the environmental change. In the following section, we discuss how these two mechanisms, i.e., the appearance of *de novo* mutations and mutations from standing genetic variation (or pre-existing mutations), can be impacted during a bottleneck.

2.1.1 Impact of bottleneck on *de novo* mutations

Theoretical work has shown that bottlenecks can reduce the mutation supply and the fixation probability of beneficial mutations in populations experiencing them (Wahl et al., 2002). More precisely, populations adapting mainly from *de novo* mutations have an adaptation rate limited by the mutation supply, which depends on population size and the appearance rate of adaptive beneficial mutations. These theoretical predictions were experimentally confirmed with asexual populations where adaptation depends mainly on *de novo* mutations [see, e.g., de Visser and Rozen (2005)]. Campos and Wahl (2010) even derived a more complex expression of the adaptation rate of asexuals, taking into account clonal interference. Mechanically, a bottleneck reduces the population size and, thus, limits adaptation.

Additionally, the adaptation rate of populations adapting through *de novo* mutations also depends on the distribution of fitness effects of beneficial mutations, which may also be affected by bottlenecks. Indeed, the fixation probability of all beneficial mutations is predicted to be reduced in a population undergoing bottlenecks (Wahl et al., 2002). However, mutations are affected differently depending on their rate and the fitness benefit they confer, which are usually negatively correlated. Gamblin et al. (2023) used a stochastic model to show that severe bottlenecks following a long growth phase favor rare beneficial mutations [as shown by Wahl et al. (2002)]. In contrast, relaxed bottlenecks following short growth phases favor frequent weakly beneficial ones. A similar effect has been observed in microbial experiments studying antimicrobial resistance. Garoff et al. (2020) and Schenk et al. (2022) found that antimicrobial resistance evolved through weakly beneficial mutations with large mutational targets when

the population size prior to the bottleneck was small. When the population size prior to the bottleneck was larger, antimicrobial resistance evolved through rarer and more beneficial mutations.

The theoretical and experimental studies mentioned above mostly deal with asexual populations, which rely more on *de novo* mutations to adapt to environmental changes than sexual populations, the latter being more frequently genetically diverse. Even if most endangered species, which are the focus of conservation efforts, are sexual, these predictions could apply to them. Indeed, recent evidence suggests that some animal species are also limited by mutation supply on recent evolutionary scales (Rousselle et al., 2020).

2.1.2 Impact of bottleneck on pre-existing genetic variation

Populations experiencing a bottleneck are theoretically expected to have reduced genetic diversity (Chakraborty and Nei, 1982; Lynch and Hill, 1986; Nei et al., 1975; Tajima, 1989, 1996). This reduction can limit their ability to adapt to future changing environments (Frankham et al., 2002; Willi et al., 2006). This effect is especially important for sexual populations, as their adaptation in a short timescale is mostly driven by standing genetic variation. Indeed, sexual populations have constrained access to beneficial mutations due to Haldane's sieve, which results from selection mainly acting on heterozygotes, thus decreasing the fixation probability of beneficial recessive mutations compared to asexual populations [see Marad et al. (2018) for a comparison in yeast]. Also, sexual reproduction allows selection to act on individual loci rather than haplotypes, thus making it possible to exploit the standing diversity [see Burke et al. (2014) for this observation in yeast]. Finally, higher organisms typically have smaller population sizes and lower mutation rates than micro-organisms, resulting in a limited supply of new mutations to rely on for adaptation.

Studies on asexual yeasts have shown that standing genetic variation drives adaptation along with *de novo* mutations (Vázquez-García et al., 2017; Ament-Velásquez et al., 2022). However, this aspect of microbial adaptation has not been extensively studied because experiments involving asexual individuals often start with a clonal population. Thus, there are no results yet from microbial experiments based on standing genetic variation that could apply to wild endangered populations.

Nonetheless, some observations from *Drosophila* experiments show how bottlenecks impact adaptation from standing genetic variation by disrupting allele frequencies. Rare alleles are likely to be lost during the bottleneck, resulting in a reduced allelic diversity (Allendorf, 1986; Fuerst and Maruyama, 1986). Swindell and Bouzat (2005) performed an empirical test of the drift-mutation model using *Drosophila*. This drift-mutation model aimed to predict the adaptive potential of a population through genetic variation, which is modeled as an equilibrium between mutations and fixation due to inbreeding (Lynch and Hill, 1986; Clayton and Robertson, 1955). In particular, this model assumes that the adaptive potential only depends on heterozygosity and not on allelic diversity (Falconer, 1960), which are two different aspects of the genetic diversity of a population. During their experiment, Swindell and Bouzat (2005)

observed a good agreement between model predictions and empirical observations, except after a severe bottleneck. The authors hypothesized that not considering the loss of allelic diversity during the bottleneck leads to overestimating the adaptive capacity following this event. This result suggests that the loss of heterozygosity and rare alleles are to be accounted for when predicting the effect of a bottleneck on a wild endangered population.

2.1.3 Additive genetic variance from a quantitative genetics perspective

For quantitative traits, the additive component of the genetic variance, which is denoted V_A, is often taken as a proxy for the adaptive potential. The effect of a bottleneck on quantitative genetic variation is more complex to predict (Hoffmann et al., 2017). In theory, the genetic variance should decrease after a bottleneck as it is proportional to the effective population size (Lynch and Hill, 1986). This effect is usually observed in morphological traits (Willi et al., 2007), whereas fitness-associated life-history traits often show an increased genetic variance following a bottleneck (van Heerwaarden et al., 2008). A possible explanation is that, after a bottleneck, the disruption of allele frequencies could result in a transfer of epistatic and dominance variance to additive variance, especially for life-history traits, which are more influenced by these non-additive effects (Crnokrak and Roff, 1995; Roff and Emerson, 2006). However, these life-history traits also typically experience high inbreeding depression (DeRose and Roff, 1999). As a result, an increase in additive variance for the genes associated with these traits may mitigate the fitness decrease. Still, it will not allow an increase in fitness compared to the pre-bottleneck level.

Overall, Willi et al. (2006) and Lopez-Fanjul and Villaverde (1989) concluded that genetic variance, and thus the future adaptive response, may increase in a population facing a bottleneck ("bottlenecked population" hereafter). However, this phenomenon is unlikely to result in a full fitness recovery, let alone a fitness increase.

The implication for endangered species management is that computing the additive genetic variance just after a bottleneck event may not reflect long-term adaptive potential but merely short-term adaptation in reaction to this event.

2.1.4 Prospects for filling knowledge gaps

Understanding the effect of bottlenecks simultaneously on pre-existing mutations and *de novo* mutations appearing during a bottleneck is important to predict the impact of bottlenecks on adaptability better. Performing microbial experiments that include initial genetic variation, allowing for better differentiating the effect of *de novo* mutations from standing genetic variation after a bottleneck, could improve this understanding. A recent review (Burke, 2023) suggested using yeast evolution experiments with standing genetic variation to study eukaryote adaptation. Indeed, yeast can combine short generation time and easy handling in the lab with sexual reproduction. Performing such experiments, particularly with small populations undergoing different types of bottlenecks, would help quantify the importance of standing genetic variation versus *de novo* mutations for eukaryote adaptation.

To improve our knowledge of which quantitative traits have their variance decreased after a bottleneck, we would need experiments to estimate the genetic variance in a wide range of traits (Willi et al., 2006). Estimating the genetic variance seems essential to predict the overall effect of a bottleneck on the population's adaptive potential. Moreover, in natural populations, the link between genetic diversity and response to selection is not always clear (Pujol et al., 2018). For example, Albatross persists despite losing genetic diversity (Milot et al., 2007). Clarifying the link between genetic variation and response to selection would help understand if genetic diversity can be used to accurately predict the natural populations' potential to adapt after one or more bottlenecks.

2.2 Genetic drift

Populations suffering from bottlenecks are particularly affected by genetic drift, which is the change in allele frequencies caused by population size fluctuations rather than by selection, mutation, or migration. Indeed, the strength of this process is inversely proportional to the effective size of the population (Kimura, 1955). These population size fluctuations caused by chance likely lead to negative impacts on a population, such as (i) the fixation of deleterious mutations, which decreases the population's fitness; (ii) the reduction in the fixation probability of beneficial mutations, which limits adaptation, and (iii) the increase of alleles at extreme frequencies (i.e., 0 or 1), which reduces genetic variation (Falconer, 1960). The latter point has already been covered in section 2.1 about mutation. Taken together, these effects may limit the adaptation of bottlenecked populations to future environmental changes.

2.2.1 Fixation of deleterious mutations

The accumulation of deleterious mutations caused by genetic drift in a population undergoing repeated bottlenecks predicted by theoretical work was highlighted numerous times in microbial experiments (Muller, 1964). In particular, many experiments used clone-to-clone transfers to maximize the rate and the speed of accumulation (Clarke et al., 1993) [see the review Elena and Lenski (2003) for references on viruses, bacteria, and yeast]. For instance, a linear decay of the average fitness of a hypermutator *Escherichia coli* strain subject to repeated single-cell bottlenecks was observed in (Heilbron et al., 2014).

Sexual populations are also theoretically expected to suffer from deleterious mutation accumulation (Lynch et al., 1995). This accumulation was observed in domesticated species due to bottlenecks and selective sweeps (Marsden et al., 2016; Xie et al., 2018), but also in some wild bottlenecked populations such as the Florida panther (Roelke et al., 1993). However, the deleterious mutation is potentially less common than in asexual microorganisms, where, due to the absence of recombination, the offsprings are expected to bear at least as much mutational load as their ancestors, a process called Muller's ratchet (Muller, 1964, 1932). In wild populations that reproduce sexually, recombination can break this process (McDonald et al., 2016). Therefore, the populations being the focus of conservation efforts are probably less affected by this particular bottleneck effect.

2.2.2 Reduced fixation probability of beneficial mutations

Some theoretical studies reproducing microbiology experiments showed that bottlenecks can reduce the fixation probability of a beneficial mutation. For example, Wahl et al. (2002) found that the fixation probability of a beneficial mutation in a periodically bottlenecked population was reduced by a factor accounting for the probability of losing the mutation during the dilution. As a reminder, the fixation probability of a beneficial mutation in a fixed-size population is approximately twice the selective advantage (Haldane, 1927). Heffernan and Wahl (2002) also considered that genetic drift is increased in bottlenecked populations due to a lower size resulting from the bottleneck. This effect reduces the fixation probability by about 25% compared to previous estimates. These theoretical predictions were confirmed by experiments using microorganisms where bottlenecks and genetic drift hindered adaptation. In the case of experimental evolution of antibiotic resistance, Huseby et al. (2017) found a positive correlation between bottleneck size and ciprofloxacin tolerance. In addition, Garoff et al. (2020) highlighted that a low-intensity bottleneck (i.e., a small reduction in population size) leads to higher fluoroquinolone tolerance than a high-intensity bottleneck. This effect is also likely to impact wild populations of endangered species, though the extent of this impact is not clear as their adaptation relies mostly on standing genetic variation.

2.2.3 Prospects for filling knowledge gaps

As bottleneck-induced drift affects both new and existing mutations, estimating its impact on the adaptive potential of bottlenecked populations would require quantifying the respective importance of *de novo* mutations versus standing genetic variation for the adaptation of a given population on a given timescale. This problem was previously mentioned in section 2.1 about mutation. The review (Barrett and Schluter, 2008) presents the relative contribution of these two sources of genetic variation in wild populations. This review suggested ways to detect molecular signatures of adaptation from standing genetic variation (Barrett and Schluter, 2008; Przeworski et al., 2005).

Another open question deals with the potential beneficial effect of genetic drift on the adaptive potential of populations. In a modeling study, Handel and Rozen (2009) found that small asexual populations could reach higher fitness peaks than large ones on rugged landscapes because drift prevents them from being stuck on a local maximum. The authors concluded that there is an optimal population size to maximize adaptation, depending on the fitness landscape's characteristics and the relative importance of adapting rapidly versus reaching high fitness peaks (Handel and Rozen, 2009). Assessing whether these effects are also observed in wild populations would be interesting.

2.3 Natural selection

Natural selection will act more or less effectively on the bottlenecked population depending on several factors, such as the severity of the bottleneck, its duration, and the population's

genetic diversity before and after the bottleneck. Some general predictions can be drawn from microbiology about the impact of natural selection after a bottleneck, regardless of the characteristics of the bottleneck: (i) Several mechanisms tend to reduce the population fitness, such as genetic load and inbreeding depression, but (ii) natural selection can also purge deleterious alleles in sexual populations. These mechanisms will modify the population's fitness, impacting its ability to adapt to future environmental changes.

2.3.1 Fitness decrease due to bottlenecks

Several factors may explain why a bottlenecked population experiences a fitness decline, even without any environmental change.

As detailed in section 2.2 about genetic drift, bottlenecks are expected to cause an accumulation of deleterious mutations in the population due to genetic drift, leading to a decrease in fitness if the bottlenecks are severe.

It is important to note a major difference between microbial populations and the endangered wild populations of diploid eukaryotes that we are considering in this review: the latter can suffer from inbreeding depression because bottlenecks reduce population sizes (Charlesworth and Charlesworth, 1987; Keller, 2002), leading to more reproductive events between related individuals. This inbreeding depression results in a loss of heterozygosity that can unmask recessive deleterious alleles, ultimately decreasing this population's fitness and adaptive potential (Barrett and Kohn, 1991; Ellstrand and Elam, 2003). More generally, genetic load (i.e., the actual or potential reduction in population mean fitness due to drift load, inbreeding load, and mutation load) is responsible for a direct decline in population fitness following a bottleneck (Hedrick and Garcia-Dorado, 2016; Kirkpatrick and Jarne, 2000).

In less well-understood ways, bottlenecks can affect other characteristics of the populations than genetics but still influence their fitness and future ability to adapt. Specifically, a bottleneck can impact the balanced relationship between host and microbiome in eukaryotes. For instance, Ørsted et al. (2022) showed that *Drosophila* populations that had undergone bottleneck treatment also lost the diversity and richness of their microbiome. The direct consequence of this loss is a reduction in the fitness of individuals belonging to bottlenecked populations (Ørsted et al., 2022).

2.3.2 Purge of deleterious alleles by natural selection increases population fitness

Whereas a bottleneck can increase the frequency of deleterious alleles (see section 2.2 about genetic drift), natural selection can purge these deleterious alleles (Kirkpatrick and Jarne, 2000; Hedrick and Garcia-Dorado, 2016). If a purging process is more efficient during a bottleneck, then going through a bottleneck could be beneficial for the adaptive potential of the population (Bouzat, 2010; Bertorelle et al., 2022; Dussex et al., 2023).

Purifying selection can play out in microorganism experiments and yet population evolution, but inbreeding facilitates the purge in diploid eukaryotes (Hedrick and Garcia-Dorado, 2016). As mentioned above, inbreeding increases homozygosity and, thus, the unmasking of recessive

deleterious alleles. Whereas inbreeding depression decreases population fitness, it is also an opportunity for selection to act on these deleterious alleles and purge them.

The empirical evidence for a purge of deleterious alleles following a bottleneck appears to be mixed (Bouzat, 2010). There is some evidence that purge can strongly affect experimental populations (Crnokrak and Barrett, 2002) and captive populations (López-Cortegano et al., 2021; Boakes et al., 2006). In experimental yeast populations, Agrawal and Whitlock (2011) used data from the Saccharomyces Genome Deletion Project to estimate fitness and dominance coefficient at about 1000 loci. From this, the authors estimated that the effect of one generation of purging (i.e., deliberate inbreeding) in an already partially inbred population would substantially decrease inbreeding depression.

Evidence of a purge process in wild endangered populations is mostly indirect (Bouzat, 2010). However, some direct evidence exists. For example, the deleterious load was significantly lower for the endangered species Iberian lynx (*Lynx pardinus*) than for the widespread Eurasian lynx (*Lynx lynx*) due to a genetic purging process (Kleinman-Ruiz et al., 2022). Other examples of purging in natural environments after a bottleneck exist [e.g., the Alpine ibex Grossen et al. (2020)]. As discussed in (Bouzat, 2010), the role of purging during a bottleneck and the factors influencing its role in natural populations still need to be discovered.

2.3.3 Prospects for filling knowledge gaps

While allele purging appears to be a key process for understanding the adaptive potential of bottlenecked populations, empirical evidence is still mixed, proving that we do not yet fully understand this mechanism. Therefore, it would be useful to use diploid eukaryotic microorganisms to test the factors and conditions under which allele purging occurs.

In addition, a study suggested carefully handling the results of selection detection methods when working with bottlenecked populations (Leigh et al., 2021). Indeed, Leigh et al. (2021) found that, due to the high level of genetic drift, methods commonly used to detect selection (e.g., F_{ST} outlier scans and Genome-Environment Association analyses) presented high false positive rates when applied to bottlenecked Alpine Ibex populations. Detecting adaptation is essential for managing endangered populations, so testing other methods' false positive and negative rates and developing new methods to distinguish between drift and selection is necessary.

2.4 Gene flow

Human activity causes fragmentation of populations in the wild, leading to spatially structured populations divided into sub-populations (also called demes or islands) of reduced sizes between which individuals may migrate. Thus, population fragmentation results in a bottleneck that risks reducing genetic diversity within sub-populations (i.e., genetic depression), losing adaptive potential, and accumulating deleterious mutations (Keyghobadi, 2007; Frankham et al., 2017). However, the migration of individuals between sub-populations can induce gene flow, which represents an opportunity to diversify the gene pool of the sub-populations despite the

fragmentation-induced bottleneck. Quantifying the genetic diversity of sub-populations is crucial to assessing the adaptive potential of fragmented populations, particularly in the case of changing environments threatening their persistence. This section reviews how and in what conditions gene flow can restore the adaptive potential of a bottlenecked population. Gene flow can (i) restore lost genetic variation, (ii) mitigate inbreeding depression, (iii) resulting in a decreased probability of extinction and restoration of adaptive potential, and (iv) amplify natural selection depending on the meta-population structure.

2.4.1 Restoration of lost genetic variation

One of the main effects of gene flow in a bottleneck population is the restoration of lost genetic variation (Soulé, 1987; Franklin and Frankham, 1998). This theoretical expectation is observed experimentally (Swindell and Bouzat, 2006) and in natural populations (Jangjoo et al., 2016; Goodman et al., 2001; Chiucchi and Gibbs, 2010).

Habitat fragmentation can cause the extinction of bottlenecked populations. Gene flow between sub-populations can mitigate the negative effects of bottlenecks by restoring lost genetic diversity (Ingvarsson, 2001). For example, Jangjoo et al. (2016) discovered that connectivity in a meta-population of the alpine butterfly *Parnassius smintheus* preserves genetic diversity before, during, and after a two-generation bottleneck. The Roseate Tern (*Sterna dougallii dougallii*) is an endangered Atlantic seabird population that provides another example of how connectivity and gene flow across populations can help retain genetic diversity despite a severe bottleneck (Dayton and Szczys, 2021). Seed dispersal with water facilitates gene flow between bottlenecked populations, mitigating the decrease in allelic diversity caused by a bottleneck (Yu et al., 2020). These examples are not isolated cases and are found in many endangered species. To further elaborate, gene flow between sub-populations undergoing a bottleneck can even erase the genetic variation effects of a bottleneck to the point where no negative genetic effects can be detected [e.g., *Actinidia chinensis* populations (Yu et al., 2020)].

2.4.2 Change in genetic load composition

One less studied effect of gene flow on bottleneck populations, which could be predominant in the populations' fate, is its impact on genetic load. Gene flow is theoretically expected to reduce the deleterious effects of inbreeding in bottleneck populations. Gene flow in metapopulations can mitigate inbreeding load by preventing the fixation of deleterious alleles in bottleneck populations (Whitlock, 2003). However, gene flow can also reduce the effectiveness of the purge of these deleterious alleles by increasing heterozygosity. With individual-based simulations, a study found that an intermediate rate of gene flow can minimize the mutation load and prevent the extinction of local populations while still allowing some purging of deleterious alleles (Sachdeva et al., 2022).

2.4.3 Gene flow mitigate extinction risk

Bottlenecked populations are highly vulnerable to extinction via (i) demographic stochasticity (e.g., random births and deaths), demographic heterogeneity and sampling variation in sex ratios (Melbourne and Hastings, 2008), and (ii) environmental stochasticity [e.g., catastrophic events Lande (1988)]. Specifically, bottlenecked populations can fall into an "extinction vortex", often characterized by a complex interplay between genetic drift, demographic stochasticity, and environmental fluctuations (Soulé, 1986). A population bottleneck reduces fitness directly through increased genetic load and indirectly through erosion of genetic variation, leading to population decline, exacerbating the effects of genetic drift, demographic stochasticity, and environmental fluctuations until extinction (Nordstrom et al., 2023). Theoretical models have highlighted a critical level of gene flow that allows a metapopulation to survive over long timescales, even if it is often ultimately driven to extinction (Hanski and Ovaskainen, 2003; Gyllenberg and Hanski, 1992; Lande et al., 1998).

The process of restoring gene flow in these bottlenecked populations to alleviate genetic load, increase genetic variation, and increase persistence probability is termed genetic rescue (Bell et al., 2019; Tallmon et al., 2004; Whiteley et al., 2015). Much empirical evidence suggests that recently fragmented populations will likely receive a demographic benefit from gene flow, beyond the addition of immigrant individuals, through genetic rescue (Whiteley et al., 2015; Frankham, 2015; Hufbauer et al., 2015; Fitzpatrick and Reid, 2019). A recent meta-analysis revealed the significant and consistent benefits of gene flow for the adaptive potential of endangered species experiencing a fragmentation-induced population bottleneck (Frankham, 2015).

When a population faces deteriorating environmental conditions and is doomed to extinction, gene flow may allow its evolutionary rescue. For example, Bell and Gonzalez (2011) set up an experiment in which a yeast metapopulation was subjected to salt-induced environmental stress. This experiment showed that local yeast dispersal and gradual deterioration favored the evolutionary rescue of the metapopulation, which would otherwise die out due to environmental stress. This experimental result later led to the development of theoretical models investigating the probability of evolutionary rescue by including a hitherto overlooked ecological factor: population structure, which may result from fragmentation. Interestingly, these models showed that the probability of evolutionary rescue in an island model, in which demes deteriorate one by one, does not vary monotonically with gene flow rate (Uecker et al., 2014). In other words, there is a gene flow rate that optimizes the evolutionary rescue of a population. Gene flow allows genetic variation and the introduction of beneficial mutants necessary for adaptation. However, a too-strong gene flow risks preventing local beneficial mutants from becoming permanently established, hence the need for intermediate gene flow to optimize adaptation (Tomasini and Peischl, 2022). Further studies showed that directed gene flow based on habitat choice could favor evolutionary rescue (Czuppon et al., 2021). Habitat choice occurs, for example, when individuals, whether mutant or wild-type, preferentially immigrate to demes whose environment has already changed. Other details of population fragmentation, such as between which sub-populations gene flow is allowed (e.g., island model, stepping-stone model)

or its asymmetry, impact the probability of evolutionary rescue (Tomasini and Peischl, 2020, 2022). To our knowledge, the above-mentioned theoretical predictions have not been tested experimentally.

2.4.4 Meta-population structure can amplify or suppress natural selection

The fragmentation of a population induces a bottleneck that divides the population into smaller sub-populations. This bottleneck accentuates genetic drift within sub-populations, but its effect on natural selection is more subtle. Its effect may depend on the meta-population structure resulting from fragmentation and the gene flow pattern.

Many scientific publications address whether population fragmentation and gene flow change the fixation probability of a mutation compared to a non-fragmented population of the same size. In (Pollak, 1966), the author focused on a population fragmented into a finite number of demes between which individuals can migrate and showed that symmetric migrations lead to the same fixation probability as in a non-subivided population.

Whitlock (2003) and Whigham et al. (2008) challenged this independence of the fixation probability from the meta-population structure resulting from fragmentation. Further works showed that the meta-population structure resulting from fragmentation could either amplify or suppress natural selection (Lieberman et al., 2005; Houchmandzadeh and Vallade, 2011) (i.e., increase or decrease the efficacy of natural selection, respectively). Amplifying natural selection means reducing the fixation probability of deleterious mutations and increasing that of beneficial ones, whereas suppressing natural selection does the opposite. Importantly, the meta-population structure alone is insufficient to assess the impact of a fragmentation-induced bottleneck on natural selection (i.e., amplifier, suppressor, or without effect) as the gene flow pattern needs to be taken into account (Marrec et al., 2021). Many theoretical studies assessing the impact of fragmentation on evolutionary dynamics focused on the fixation probability, but other important quantities are impacted, such as the adaptation rates (Hindersin and Traulsen, 2014). An experiment in which ciprofloxacin-resistant mutants were tracked in a *Pseudomonas aeruginosa* meta-population showed that for low migration rates, natural selection is amplified in a star topology compared to a well-mixed population (Chakraborty et al., 2023), thus confirming a theoretical prediction made by (Marrec et al., 2021).

2.4.5 Prospects for filling knowledge gaps

Human activity fragments populations into several sub-populations (also called demes or islands), which can become isolated if gene flow between them is limited. As biodiversity declines, it is crucial to understand the impact of fragmentation and gene flow on the evolutionary dynamics of bottlenecked populations and, in particular, their adaptive potential. In this review, we have shown that there are many theoretical studies investigating this impact. However, theoretical predictions are rarely directly tested or mostly with microbiology experiments whose design does not allow comparison with mathematical models. A stronger collaboration between theory and experiment [e.g., Marrec et al. (2021) combined with Chakraborty et al.

(2023)] would lead to a better understanding of fragmentation and gene flow on the evolutionary dynamics of meta-populations. Also, more experiments with diploid organisms would enable better comparison with wild populations [e.g., Bakker et al. (2010)].

3 Relative importance of these processes

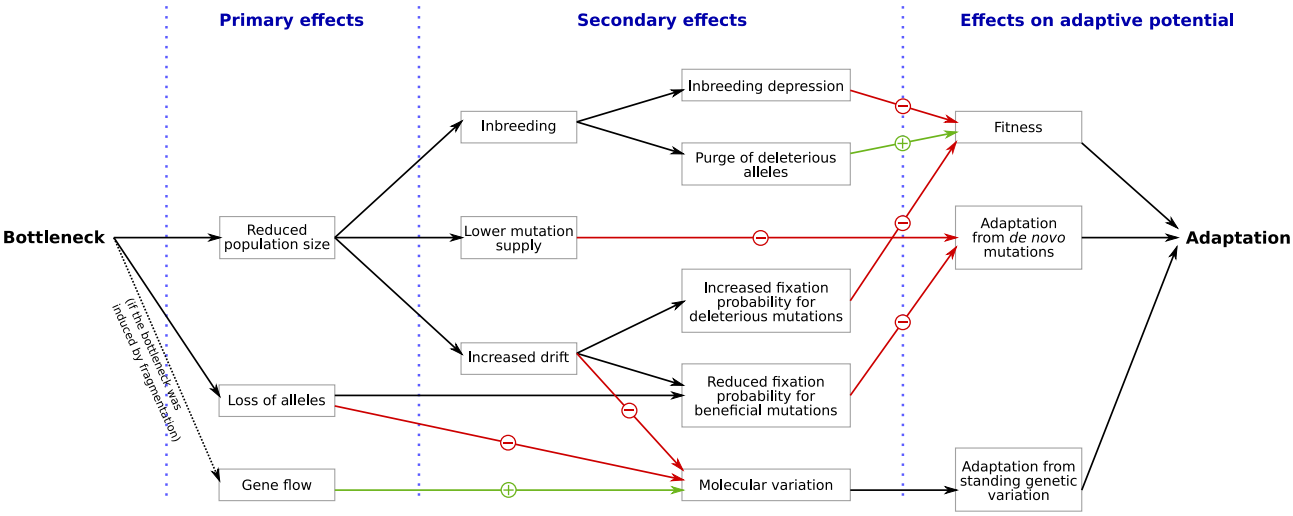

Figure 1: **Potential effects of a bottleneck on adaptive potential.** Summary of the main effects of bottlenecks on the adaptive potential of a population, as described in this review. The existence and relative importance of these different effects vary across populations, bottleneck characteristics, and environments. Black arrows represent a causal effect, green arrows represent a positive effect, and red arrows represent a negative effect.

3.1 Summary of the previous parts

We have reviewed in the previous parts how the different evolutionary processes can be disrupted during a bottleneck and how these processes shape the adaptive potential of bottlenecked populations (see Figure 1).

As expected, most of these mechanisms are predicted to decrease the adaptive potential following a bottleneck. Bottlenecks limit adaptation from *de novo* mutations by reducing the mutation supply and the fixation probability of beneficial mutations. More importantly for sexual populations, they also limit adaptation from standing genetic variation. Indeed, molecular variation is decreased due to smaller population sizes, increased drift, and the loss of rare alleles during bottlenecks. In addition, the fitness of a bottlenecked population may decrease due to the accumulation of deleterious mutations and genetic load in general, which for sexual diploids includes inbreeding depression. A population with lower fitness will struggle to survive future environmental changes that may increase its probability of extinction.

Conversely, only two mechanisms can mitigate the negative impacts of bottlenecks. When the population is part of a meta-population, gene flow can restore some of the lost genetic variation by introducing new variation. In addition, in the case of sexual diploid populations,

inbreeding could, under some conditions, facilitate the purge of deleterious alleles and, thus, reduce the masked genetic load.

These findings show that knowledge transfer from microbial to endangered wild populations is possible. A collaboration between microbiology and conservation biology would be fruitful if microbial experiments were adapted to include more characteristics of these endangered populations. For example, one could use (facultative) sexual micro-organisms, such as yeast, or include standing genetic variation in evolution experiments.

3.2 Relative importance of each of these processes

Several evolutionary processes come into play when trying to predict the impact of a bottleneck. As some of these processes have opposite effects, a major concern is to estimate the relative importance of these processes to predict the fate of a population. Even when two processes negatively affect the adaptive potential of populations, it may be useful to know which one is predominant to determine the conditions threatening the persistence of wild populations precisely. Determining these conditions would help identify the key priorities in population management. In the following of this review, we discuss the relative contribution of the evolutionary processes seen above.

3.2.1 Selection vs. genetic drift

One of the major concerns during a bottleneck is the increase of genetic drift. The positive or negative aspect of genetic drift depends on whether the alleles are deleterious or beneficial.

In section 2.2 about genetic drift, we have seen that a bottleneck reduces the fixation probability of beneficial alleles and increases the chance that they are lost compared to a fixed-size population.

The impact of a bottleneck on deleterious alleles is more complex, as inbreeding can facilitate their purge by natural selection. As previously said, little is known about the conditions required for selection to overcome drift. Even if these conditions were known, we would still have to choose if the management priority is to purge deleterious alleles, which requires inbreeding, or to restore genetic diversity, which requires outcrossing. Conservation biology often deals with small endangered wild populations that have already experienced severe bottlenecks. For such populations, the loss of genetic diversity may be a major concern, and the impact of the purge is minor, which has been confirmed in wild populations (Bouzat, 2010) [but see van Heerwaarden et al. (2008)]. For example, wild populations of elephants in South Africa underwent a severe bottleneck due to widespread hunting. Microsatellite comparisons of current wild populations with museum specimens of this elephant population before the bottleneck confirmed the loss of genetic diversity (Whitehouse and Harley, 2001). In such wild populations, the response to selection can be expected to be less effective, as the probability of having beneficial mutations is low (Frankham, 2009). A reduced response to selection after a bottleneck has already been highlighted in experimental fish populations. For example, populations of *Heterandria formosa* having undergone a bottleneck during their demographic history showed a 50% slower response

to selection for heat tolerance than populations having not undergone a bottleneck (Klerks et al., 2019). An experiment showed that housefly populations that faced a short bottleneck followed by a period of expansion had better fitness and lower genetic load than populations kept at a constant size with a similar expected inbreeding score (Reed and Bryant, 2001). Reed and Bryant (2001) concluded that, when managing endangered wild populations, the priority is to act on the cause of decline to promote rapid expansion and avoid inbreeding.

For adaptive polymorphisms such as the Major Histocompatibility Complex (MHC), the predominance of selection over drift probably depends on the duration of the bottleneck. The MHC is a set of polymorphic genes essential to the adaptive immune system of vertebrates and can be particularly affected by bottlenecks. The potential loss of diversity at this locus is of great concern as it is associated with increased disease susceptibility (Sommer, 2005). In the meta-analysis (Sutton et al., 2011), the adaptive polymorphism of the MHC was shown to be significantly reduced after a bottleneck, and even more so than neutral polymorphisms (by 15%). One possible explanation found by Sutton et al. (2011) is that negative frequency-dependent selection is an important force shaping pre-bottleneck Major Histocompatibility Complex diversity, resulting in a high frequency of very rare alleles. As these rare alleles are more at risk of being lost during a bottleneck, this would explain the greater reduction in Major Histocompatibility Complex diversity. The authors concluded that diversifying selection cannot counter genetic drift in recently bottlenecked populations. However, this conclusion can be mitigated as the authors did not find a significant effect on Major Histocompatibility Complex diversity for short-scale bottlenecks. For instance, in a water vole population undergoing a 4-month bottleneck, the Major Histocompatibility Complex diversity was greatly reduced during this period but recovered in a few generations to reach the pre-bottleneck level (Oliver and Piertney, 2012).

3.2.2 Loss of heterozygosity vs. loss of genetic variation

Another open question is to identify the mechanism causing the more significant reduction in the adaptive potential of bottlenecked populations between the loss of heterozygosity and the loss of genetic variation. In population genetics theory, heterozygosity determines the evolutionary potential, particularly the short-term response to selection (Falconer, 1960). Accordingly, *Drosophila* populations that faced intense or diffuse bottlenecks leading to the same level of heterozygosity showed no difference in their response to selection (England et al., 2003). Whereas both bottleneck regimes were expected to yield different allelic diversities, the measured allelic diversities were not significantly different (England et al., 2003).

On the other hand, Ørsted et al. (2019), focusing on *Drosophila* populations having experienced different levels of inbreeding, showed that molecular diversity was more strongly correlated to adaptation than was the expected inbreeding coefficient. This result highlights the importance of molecular diversity for adaptation. It provides a way to summarize the history of a population, which seems more relevant than keeping track of population sizes.

However, to our knowledge, the methods used to restore heterozygosity are the same as

those used to restore diversity and consist of outcrossing (i.e., crossing the population with individuals from other populations and/or expanding the population size).

4 Thoughts for future research directions

In the future, conservation biology could benefit even more from microbiology by maintaining a close link between the two fields. With a reverse approach, evolution experiments using microorganisms could directly address the conservation biology needs. We make the following suggestions:

1. Include ecological factors within experimental evolution studies.
2. Include selective history when considering the demographic history of populations.
3. Include bottleneck characteristics and demographic history.

4.1 Testing the influence of ecological factors on population response

As discussed in this review, most microbiology studies investigating the adaptive potential of bottlenecked populations have taken an evolutionary perspective without considering ecological factors. However, natural populations evolve in interaction with their biotic and abiotic environment. Theoretical predictions could be biased without considering these ecological factors. For instance, Nordstrom et al. (2023) showed through stochastic individual-based simulations that considering population growth with negative density dependence (i.e., intraspecific competition) or density independence leads to different outcomes of evolutionary rescue. This prediction regarding the impact of density dependence vs. independence was empirically tested and confirmed with flour beetles (Olazcuaga et al. in prep.). More precisely, Olazcuaga et al. showed that the effect of negative density dependence varies depending on whether the populations have experienced a bottleneck in their demographic history. Osmond and de Mazancourt (2013) proved with an adaptive dynamic model that interspecific competition can favor evolutionary rescue by increasing the strength of selection and speeding up adaptation. Following Olazcuaga et al.'s example, examining how interspecific competition affects the probability of rescue in bottlenecked populations would be valuable.

4.2 Testing the influence of selective and demographic history on population response

In this review, we focused on the effects of bottlenecks, which entail random reductions in population size ("random bottleneck" hereafter), rather than selective bottlenecks, which involve non-random decreases in population size. Wild populations can experience both random

and selective bottlenecks. Random bottlenecks can occur due to fragmentation, whereas selective bottlenecks are more likely to occur when adapting to a drastic environmental change, such as pollutants or antibiotic resistance. These selective bottlenecks can result in U-shaped population size curves during evolutionary rescue processes (Gomulkiewicz and Holt, 1995). Selective bottlenecks, as random bottlenecks, can impact how populations respond to future stress. A few studies tested how adaptation to a first environmental change, which was associated with a decrease in population size, impacted the response to future adaptation to a new environment (Lachapelle et al., 2017; O'Connor et al., 2020; Samani and Bell, 2016; Gonzalez and Bell, 2013) using microorganisms: *Chlamydomonas reinhardtii*, *Pseudomonas fluorescens*, *Saccharomyces paradoxus*, and *Saccharomyces spp*, respectively). Adaptation to a new environmental change would be favored for populations that have already undergone similar stress in their demographic history (Lachapelle et al., 2017) [see O'Connor et al. (2020) for a change in the speed of future adaptation]. Conversely, if the stress is different, adaptation would be less likely (Lachapelle et al., 2017). This impact of the first dissimilar stress makes sense since the response to the selection of the first stress would reduce genetic variability (Carlson et al., 2014). Additionally, populations that have evolved under first stress during their demographic history seem to have a higher probability of extinction when they experience new and different stress (Lachapelle et al., 2017; Samani and Bell, 2016; Gonzalez and Bell, 2013). An increase in genetic load is expected during selective bottleneck (Stewart et al., 2017), which could explain this result. However, whether these deleterious mutations can be purged as efficiently as in a random bottleneck is unclear. Furthermore, the mean frequency of mutations and the genetic load can change in a complex way during a selective bottleneck, in contrast to a random bottleneck (Dussex et al., 2023). Overall, the evidence that adaptive bottlenecks increase the probability of extinction and impact the probability of adaptation suggests that the processes involved differ from those occurring in a random bottleneck or are not as straightforward as expected. The impacts of random bottlenecks *versus* selective bottlenecks have been studied theoretically in infection models and host-pathogen infection processes [as reviewed in Abel et al. (2015), e.g., Moxon and Kussell (2017) and De Ste Croix et al. (2020)]. However, how a selective bottleneck, compared to a random bottleneck, impacts the response to future stress has never been empirically studied. Integrating demographic and selective history can improve predictions of population response to different stresses.

Finally, it is essential to note that bottlenecks exist on a gradient and cannot be categorized into two binary categories. Selective and random bottlenecks represent the extreme points of this gradient, where the relative contribution of drift and selection varies. Moreover, we have discussed that natural selection can play a role in a random bottleneck process, challenging the assumption that a random bottleneck is entirely random. As a first step, it would be useful to compare the effects of selective and random bottlenecks on the probability of adaptation to future environmental conditions. Then, it would be important to study how the contribution of genetic drift and selection during demographic history influences the response of bottlenecked populations.

4.3 Testing the influence of bottleneck characteristics on future population response

In this review, we have focused on the impact of a single bottleneck on population response, except when considering microbial experiments that usually involve multiple bottlenecks. However, the demographic history of natural populations is never restricted to a single bottleneck (Hohenlohe et al., 2020; Gladstone et al., 2022). Therefore, it is essential to consider the entire demographic history of natural populations, including the intensity and frequency of these bottlenecks.

Microbiology informs us about the impact of the intensity and frequency of bottlenecks, which can be useful to conservation biology. Microbiologists can control the characteristics of the bottleneck, such as its frequency, intensity, and duration (LeClair and Wahl, 2017). The impact of bottleneck intensity has been tested in microbial experimental evolution. The adaptive pathways differ depending on whether the bottleneck is weak or intense (Garoff et al., 2020; Vogwill et al., 2016; Mahrt et al., 2021). Overall, empirical studies on the evolution of antibiotic resistance have observed a negative correlation between bottleneck severity and adaptive response (Garoff et al., 2020; Huseby et al., 2017; Mahrt et al., 2021). In addition, Mahrt et al. (2021) showed a decrease in parallel evolution with increasing bottleneck intensity. This result suggests that after experiencing strong bottlenecks, resistance evolves through a wider range of genetic mechanisms, likely due to increased genetic drift. Theoretical studies of bottleneck characteristics suggest that smaller population sizes before or after the bottleneck constrain evolutionary paths, thus limiting the supply of beneficial mutations and adaptation (Gamblin et al., 2023). In addition, Wein and Dagan (2019) pointed out that while bottleneck intensity is a factor in determining population evolvability, selective conditions during evolution can play a more significant role. Mahrt et al. (2021) notably examined the interaction between bottleneck intensity and intensity of selective pressure. The application of the effect of bottleneck intensity to natural populations remains unclear. Olazcuaga et al. (2023) conducted an experiment demonstrating that *Tribolium castaneum* populations responds similarly to environmental change, regardless of the intensity of the bottleneck they experienced in their demographic history. England et al. (2003) also found no difference in adaptive potential between *Drosophila melanogaster* populations that underwent an intense or diffuse bottleneck designed to produce similar inbreeding levels.

The duration for which populations can recover, which is the time between two bottlenecks, also affects the adaptive potential of populations. For instance, Moxon and Kussell (2017) showed that increasing the severity of bottlenecks or reducing the growth period leads to faster adaptation during pathogen microbial infection. Natural microbial populations that experience frequent bottlenecks, such as pathogens, can adapt to changing environmental conditions. A theoretical study predicted a high probability that some mutations acquired during growth in a given host will be passed to the next one in viruses (Sigal et al., 2018). These results could apply to conservation biology since frequent bottlenecks are commonly observed in wild populations (Hohenlohe et al., 2020). Recent genomic approaches have been used to determine the timing

and nature of past population bottlenecks by detecting changes in the shape of the deleterious variation landscape [see Bortoluzzi et al. (2019) for an application with chicken populations as well as Cornuet and Luikart (1996) and Peery et al. (2012) for classical approaches].

An important area for future research is to investigate whether the cumulative effects of multiple bottlenecks are additive or synergistic. This effect could be studied experimentally in microbiology and then applied to natural populations. In theory, multiple bottlenecks will not have the same impact on the population's ability to adapt from *de novo* mutations and from standing genetic variation. What matters for adaptation from *de novo* mutation is the current population census size, which is the result of the last bottleneck only. What matters for adaptation from standing genetic variation is the genetic diversity of the population, which results from past variations in population size (i.e., from the last common ancestor of the population to the present). Genetic diversity is proportional to the effective population size, which is usually computed as the harmonic mean of past population sizes for populations of varying sizes (Crow and Kimura, 2009; Otto and Whitlock, 1997; Charlesworth, 2009). However, other parameters, such as population structure and selection, can also impact the effective population size. As these parameters can vary between different environments, comparisons between experimental and wild populations must be made with caution. Advances in population genomics applied to conservation biology are very useful in this case and are a fruitful avenue of research (Hohenlohe et al., 2020). Moreover, even if genetic diversity should theoretically correlate with the response to selection, this effect is rarely observed in the wild due to interference from other biological mechanisms [e.g., plasticity or coevolution, see Pujol et al. (2018)]. We would need experiments with populations undergoing bottlenecks of different severity and duration to assess the differential impacts of such bottlenecks on genetic variation. Indeed, some studies have observed that genetic variation quickly recovers after a short bottleneck, with examples of both short-generation (water vole) and long-generation (white-tailed eagle) species (Oliver and Piertney, 2012; Keller et al., 2001; Hailer et al., 2006). Moreover, low initial genetic variation does not seem to be limiting for the adaptation of invaders [see the review Bock et al. (2015)]. Thus, there is likely to be a threshold of severity and duration above which a population struggles to recover.

To conclude, in this section and throughout the review, we have proposed several research directions and suggested new experiments that could help to understand the adaptation of bottlenecked populations. The new knowledge gained from these experiments could ultimately be integrated into existing methods for detecting species most at risk of extinction due to climate change [reviewed in Hoffmann and Sgrò (2011)].

5 Perspectives

Our review has shown that the impact of bottlenecks on the evolutionary dynamics of populations is a topic that spans several fields, such as microbiology and conservation biology, and has inspired theoretical, and empirical works. Our review emphasizes that these fields share

a common goal and are not as distinct as previously thought. We believe that an improved collaboration between these fields will lead to a better understanding of how bottlenecks affect the evolutionary dynamics of populations.

Similar to our review, Alexander et al. (2014) showed how seemingly unrelated fields address the evolution of declining populations. Specifically, Alexander et al. (2014) emphasized that evolutionary rescue is a research topic in medicine (e.g., drug resistance evolution in patients undergoing chemotherapy) and conservation biology (e.g., survival of species undergoing habitat deterioration). Similar to our review, Alexander et al. (2014) pointed out that integrating different fields could accelerate our scientific knowledge.

We hope that these synthesis reviews will pave the way for empirical studies that combine different fields. Given the challenges of the 21st century, such as the loss of biodiversity, it would be highly valuable to employ approaches that enhance our comprehension of biological processes and our ability to forecast the reaction of natural populations to environmental change.

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Conflict of interest declaration

The authors declare they have no competing interests.

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