

Conservation genetics of population bottlenecks: the role of chance, selection, and history

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Abstract Conservation genetics studies of populations bottlenecks are commonly framed under the detrimental paradigm of inbreeding depression. This conceptual paradigm presupposes a direct and unambiguous relationship between population size, genetic diversity, fitness, and extinction. Here, I review a series of studies that emphasize the role of chance, selection, and history in determining the genetic consequences of population bottlenecks. The variable responses of bottlenecks to fitness, phenotypic variation, and heritable variation emphasize the necessity to explore the relationship between molecular genetic diversity, fitness, adaptive genetic diversity, and extinction beyond the detrimental paradigm of inbreeding depression. Implications for conservation and management are presented as guidelines and testable predictions regarding the potential effects of bottlenecks on population viability and extinction.

Keywords Extinction · Fitness · Genetic diversity · Inbreeding depression · Population bottlenecks

Introduction

Since the early development of conservation biology as an independent field of study, scientists have focused on the genetic consequences of small population size (Soulé and Wilcox 1980; Schonewald-Cox et al. 1983). Although massive declines in the abundances of most species have been mainly driven by anthropogenic and ecological

factors, including habitat destruction, introduction of exotics, demographic stochasticity and environmental fluctuations, the long-term persistence of natural populations will ultimately depend on the retention of genetic diversity.

Two major aspects of genetic diversity have been emphasized in relation to the viability of natural populations. First, numerous studies have shown that a loss in genetic diversity is commonly associated with decreases in fitness, both at the individual and population levels (Charlesworth and Charlesworth 1987; Charpentier et al. 2005; Da Silva et al. 2006; Hanski and Saccheri 2006; Grueber et al. 2008). This can occur through inbreeding depression or increases in the genetic load of populations (Ralls et al. 1979; Kirkpatrick and Jarne 2000; Fox et al. 2008; Charlesworth and Willis 2009; Hedrick and Fredrickson 2010). Second, as predicted by Fisher's fundamental theorem of natural selection, populations with low genetic variation also have reduced evolutionary potential (Fisher 1958). That is, populations with decreased genetic diversity will be less likely to adapt to future environmental changes. On the bases of these two premises, a considerable number of conservation studies have focused on the survey and characterization of genetic diversity of natural populations, particularly of those populations that are currently at the verge of extinction.

In this study, I review the state of conservation genetics in relation to the study of population bottlenecks. In particular, I reassess the detrimental paradigm of inbreeding depression, which assumes a direct and simple relationship between population size and fitness as a consequence of increased homozygosity for alleles common by descent due to inbreeding. I review a series of studies that emphasize the role of chance, selection, and history on small populations, which I believe help expanding our understanding of the genetic consequences of population bottlenecks

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beyond the traditional detrimental paradigm of inbreeding depression. Finally, I discuss potential implications for the conservation and management of natural populations under the current extinction crisis.

The detrimental paradigm of inbreeding depression

Predicting the genetics consequences of small population size has been one of the major tasks of conservation biology. The effects of population bottlenecks are directly related to the increase of stochastic events associated with small population size, which lead in most cases to losses in genetic diversity (Hedrick 2005). As indicated above, there are two fundamentally different consequences of small population size with regards to genetic variation, namely inbreeding depression caused by increased homozygosity for alleles common by descent and loss of genetic variation caused by genetic drift (Fig. 1). Under the inbreeding depression conceptual framework, small population size is believed to consistently lead to increased inbreeding, which in turn reduces fitness and population growth rates, having a negative feedback on population size and thus, increasing extinction probabilities. This process has led to the characterization of the so-called extinction vortex (Gilpin and Soulé 1986), in which populations below a critical size seem destined to extinction due to the increased effects of genetic, demographic and environmental stochasticities.

The study of small populations represented one of the foundations of conservation biology. As a consequence, genetic considerations for the persistence of natural populations have focused largely on the genetic effects of small-population processes. As expected, seminal books that initially defined the field of conservation biology devoted significant sections to the genetic effects of inbreeding, founding events, population bottlenecks, genetic diversity, and the viability of genetically depauperate populations (e.g., Soulé and Wilcox 1980; Schonewald-Cox et al. 1983; Soulé 1987). One of the major goals in conservation genetics became, therefore, reducing extinction risks by minimizing inbreeding and the loss of genetic diversity (Hedrick and Kalinowski 2000; Frankham et al. 2002).

It is obvious that the inbreeding depression paradigm has been crucial for understanding the biology of small

populations and its implication for conservation. Today, a few studies have become textbook examples on the role of population size on genetic diversity, fitness, and extinction in natural populations (e.g., Packer et al. 1991; Westemeier et al. 1998; Saccheri et al. 1998). As a consequence, some of the focal species studied became flag-species for promoting public awareness on the current extinction crisis (e.g., the Florida panther and the Atwater prairie-chicken). I believe, however, that some classic studies as well as new advances on the nature of quantitative traits, fitness characters, and the potential role of selection in purging the genetic load of small populations warrants a reassessment of the detrimental paradigm of inbreeding depression. Numerous studies have accumulated both experimental and field evidence that require novel interpretations on the role that population bottlenecks may have on molecular and quantitative genetic diversity, fitness, and ultimately, extinction.

Here, I suggest that the detrimental paradigm of inbreeding depression presupposes a direct and unambiguous relationship between genetic diversity, fitness, and extinction (Fig. 1), with small population size consistently decreasing levels of molecular and quantitative genetic diversity, decreasing fitness (i.e., inbreeding depression), and increasing extinction risk. During the last decade, however, the empirical evidence for these relationships seems somewhat conflictive. That is, there is good evidence that small population size decreases genetic variation, and temporal studies on genetic diversity have demonstrated this, particularly at the molecular level (e.g., Bouzat et al. 1998; Hadly et al. 1998; Nielsen et al. 1999). However, results on population bottlenecks, quantitative genetic variation and inbreeding depression do not necessarily show consistent trends. For example, since the earlier studies by Bryant et al. (1986), multiple researchers have shown variable effects of bottlenecks on both phenotypic (e.g., Bryant and Meffert 1993, 1995; Fernández et al. 1995; Wade et al. 1996) and genetic variance (e.g., Carson and Wisotzky 1989; López-Fanjul and Villaverde 1989; Willis and Orr 1993; García et al. 1994). Furthermore, although inbreeding depression has been well documented in both experimental and natural populations, several studies have shown variable effects of inbreeding on

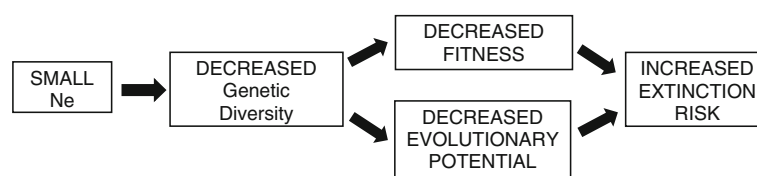


Fig. 1 The relationship between small population size (N_e) genetic diversity and extinction risk. Under the detrimental paradigm of inbreeding depression (upper pathway), arrows presuppose a

consistent an unambiguous relationship between population size, genetic diversity, fitness and extinction risks

fitness. Classic studies by Pray and Goodnight (1995) and Wade et al. (1996) on *Tribolium castaneum*, Lacy et al. (1996) on *Peromyscus polionotus*, and Holtsford (1996) on *Clarkia* have shown population-specific effects of bottlenecks on inbreeding depression. That is, while some populations showed signs of decreased genetic diversity and inbreeding depression, others revealed no declines or even increases in genetic variation and fitness following bottlenecks. Studies on inbreeding depression also documented non-significant declines in fitness in a wide variety of species, including wild populations (Kalinowski et al. 1999; Duarte et al. 2003), domestic species (Visscher et al. 2001), and laboratory model organisms (Fernández et al. 2003). The relationship between inbreeding and extinction has been even more complex, with only a few studies demonstrating a direct association between levels of genetic diversity, fitness, and extinction (e.g., Frankham 1995a; Newman and Pilson 1997; Saccheri et al. 1998; Bijlsma et al. 2000; Spielman et al. 2004; Hanski and Saccheri 2006; O’Grady et al. 2006; Vilas et al. 2006).

A survey of the papers published in the journal *Conservation Genetics* in 2008–2009 (vol. 9 and vol. 10, issues 1–2) show the significant impact of the detrimental paradigm of inbreeding depression, with specific reference to estimates of molecular genetic diversity, fitness and extinction risks. From a total of 345 studies surveyed (without considering any technical papers on markers development), the majority (91; 26.4%) represented surveys of genetic diversity based on molecular markers (mostly microsatellites), usually quantifying genetic structure or lack of genetic diversity associated with isolation, small population size, and/or fragmentation. Only nine papers (2.6%) showed concurrent estimates of fitness, which may be indicative of inbreeding depression; and only one (Wright et al. 2008) linked levels of genetic diversity and extinction. One could argue that this trend is driven by the fact that it is more difficult to measure fitness and extinction probabilities than survey levels of genetic diversity using molecular genetic markers. It is obvious that the technical difficulties in obtaining accurate estimates of fitness and extinction probabilities may limit our ability to obtain direct evidence for a relationship between molecular genetic diversity, fitness, and extinction. However, we cannot disregard the variable nature of the potential outcomes of population bottlenecks, which makes their consequences on mean values and variances hard to predict.

Below, I summarize some of the major issues related to the genetic consequences of demographic bottlenecks. In particular, I focus on the overall effects of small population size on inbreeding and the mean values of phenotypic and fitness traits as well as on the role of genetic drift on the potential loss of genetic variation and fitness. The review

has been divided in terms of the role that chance, selection, and history may play in determining the genetic effects of population bottlenecks.

The role of chance

The role of chance in determining the genetic consequences of population bottlenecks is directly related to the stochastic processes associated with small population size (Frankham et al. 2002; Hedrick 2005). In particular, genetic stochasticity has been shown to have a significant effect on both fitness and extinction, particularly after populations have reached a threshold level of inbreeding (Frankham 1995a). Further comparisons of threatened and non-threatened taxa suggest that most taxa are driven to extinction only after genetic factors affect populations adversely (Spielman et al. 2004).

The potential genetic outcomes of demographic bottlenecks can only be assessed when considering replicated bottlenecked populations. Overall, bottlenecked populations show reduced genetic diversity at the molecular level (i.e., reduced allelic diversity and heterozygosity). However, the genetic composition of each replicate population may differ significantly after the bottlenecks. Specifically, replicate populations most likely will end up having different alleles at each locus as well as different allele combinations from multiple loci.

As indicated above, the detrimental paradigm of inbreeding depression generally assumes that fitness levels consistently decrease following population bottlenecks as a result of inbreeding depression (see Fig. 1). However, the genetic consequences of individual bottlenecks will depend on the specific relationship between the genetic composition of populations following bottlenecks (which is determined by the allele combinations both within and among loci), the genetic basis of quantitative traits determined by those loci, and their effects on the adaptive potential of populations (determined by the amount of additive genetic diversity and the heritability of the traits in question). The main point is that differences in the genetic outcome of independent bottlenecks have direct consequences not only on the genetic diversity at the molecular level but drastic effects on the diversity of quantitative traits and, as a consequence, on levels of additive genetic diversity and selection potential (Charlesworth and Charlesworth 1987; Fowler and Whitlock 1999a, b).

Drift effects on quantitative traits and adaptive potential

One of the major consequences of population bottlenecks relates to their genetic and phenotypic effects on quantitative traits (Lynch 1991; Whitlock and Fowler 1996;

Lynch and Walsh 1998; Moorad and Wade 2005; Van Buskirk and Willi 2006; Charlesworth 2009). The multi-locus nature of these traits makes them particularly vulnerable to stochastic changes associated with small population size, and thus, unpredictable regarding the potential consequences of individual bottleneck events. One of the problems in conservation genetics is that studied populations often represent unique historical events. That is, in most cases, particularly when we study populations in the wild, we are dealing with populations at the verge of extinction; i.e., we are often studying the last remaining population of a species in a particular geographic region. As a consequence, we are observing just one of multiple potential outcomes that may result from the stochasticity associated with population bottlenecks. Individual bottlenecks may have important consequences by changing dominance and epistatic interactions as a result of random changes in allele combinations both within and among loci, which in turns can have significant effects on the phenotypic and genetic variance of quantitative traits (Goodnight 1988; Lynch 1991; Charlesworth and Charlesworth 1999; Turelli and Barton 2006; Charlesworth et al. 2007).

As previously mentioned, several studies have shown variable outcomes regarding changes in phenotypic and genetic variance in experimentally bottlenecked populations. Although many studies showed that bottlenecks tended to reduce overall levels of genetic and phenotypic variance, several studies revealed no changes, or even increases, in quantitative genetic diversity following bottlenecks. For example, Brewer et al. (1990) found no correlation between the severity of inbreeding depression and the initial genetic diversity of mice population stocks. Increases in variance following bottlenecks have also been reported in *Musca domestica* (Bryant et al. 1986; Bryant and Meffert 1993), *Drosophila melanogaster* (López-Fanjul and Villaverde 1989; García et al. 1994; Van Heerwaarden et al. 2008) and *Tribolium castaneum* (Fernández et al. 1995; Wade et al. 1996).

Recent studies have also shown that bottlenecks and inbreeding can have considerable impact on the significance of heterozygosity-fitness correlations (e.g., Lesbarreres et al. 2005; Lieutenant-Gosselin and Bernatchez 2006; Brouwer et al. 2007; Hansson and Westerberg 2008). These studies showed that an individual's fitness is not necessarily correlated to the levels of genome-wide multi-locus heterozygosity. Genetic-fitness correlations have shown to vary depending on the population history, levels of inbreeding, and environmental conditions. As a consequence, Hansson and Westerberg (2008) have recently cautioned against a direct interpretation of significant heterozygosity-fitness correlations as evidence of inbreeding depression, and vice versa.

The variable outcomes of population bottlenecks are not unexpected since the combined effects of genetic drift and inbreeding will alter the distribution of alleles following demographic bottlenecks, potentially changing dominance relationships within loci and epistatic interactions among loci (Lynch and Walsh 1998; Fowler and Whitlock 1999b). As a consequence, it would be expected that population bottlenecks have variable responses with regards to fitness, the amount of additive genetic diversity remaining, and therefore, the adaptive potential of populations.

Although multiple studies have assessed the effects of bottlenecks on both genetic and phenotypic variation of quantitative traits, only a few studies have documented the consequent role of population bottlenecks in determining changes in adaptive potential (e.g., Day et al. 2003; Turelli and Barton 2006). Swindell and Bouzat (2005) provided an example of the differential effects of replicated bottlenecks on the adaptive potential of *Drosophila melanogaster*, as measured by the response of experimental populations to artificial selection. Experimentally replicated population bottlenecks of size 4 and 20 were maintained at constant size for many generations, and their selection response was measured at generations 1, 10, 20 and 30. Figure 2 reproduces the results from this experiment, showing the response of individual replicates following a selection regime for increased abdominal bristle number.

As expected, as time passed smaller bottlenecks had a more rapid reduction in the selection responses, given here by the slopes of the selection lines, which represent changes in bristle number following a selection scheme over six generations. The reduced selection response is directly related to the amount of additive genetic variation remaining in the population after a bottleneck over t generations. Interestingly, some of the individual replicates had very different responses; even after 10 or 20 generation bottlenecks. In fact, Fig. 2 shows that some replicates retained considerable levels of additive genetic variation, even after populations were maintained at 20 pairs for 20 generations (which can reflect similar conditions to those observed in wild populations of *Drosophila*). Interestingly, these lines showed reduced levels of molecular diversity, as measured by microsatellite analysis (Bouzat, unpublished data). The retention of significant additive genetic variation in spite of high levels of inbreeding and low levels of molecular genetic diversity has been previously reported in captive populations such as that of the Cotton-top Tamarin (*Saguinus oedipus*) (Cheverud et al. 1994). In our experiment, the differential effects of bottlenecks on the adaptive potential of individual populations represent, at least in part, the stochastic effects of genetic drift as a consequence of sampling during the generation of experimental bottlenecks. This example shows that stochastic processes such as genetic drift can have different outcomes in terms of the

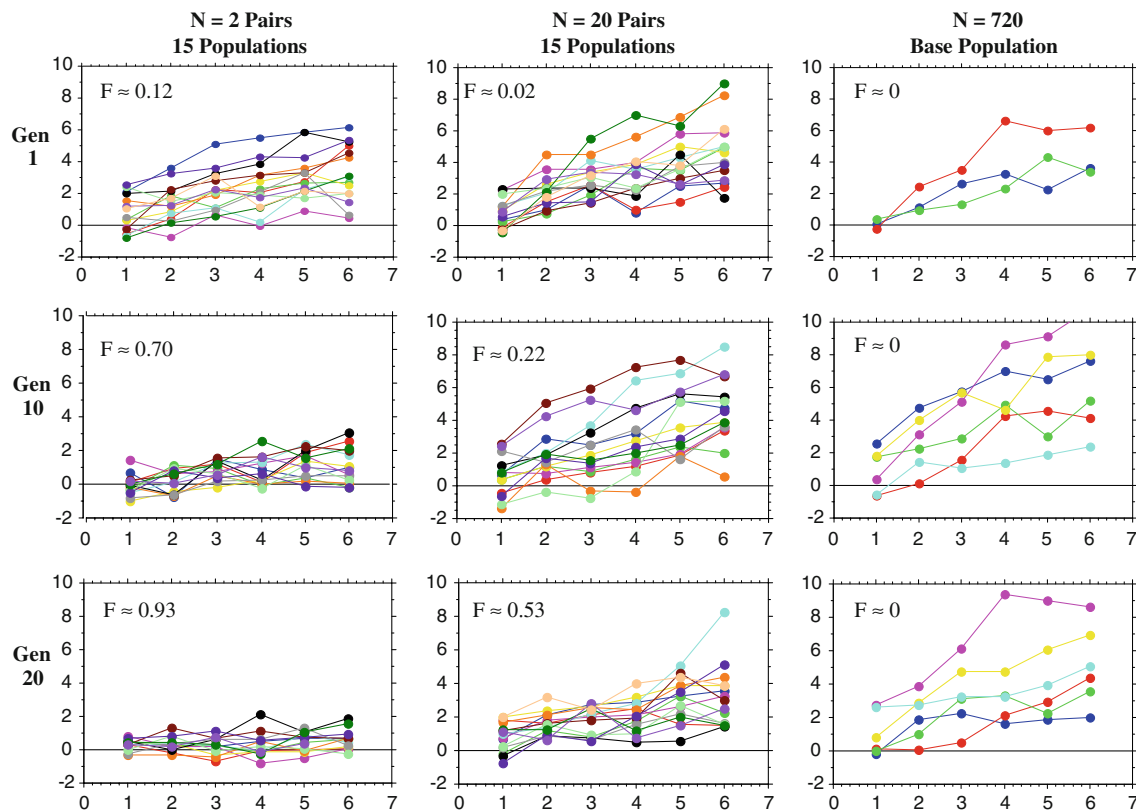


Fig. 2 Selection responses for increased bristle number in experimental populations of *D. melanogaster* maintained at constant $N = 4$ and $N = 40$ (compared to a Base population $N = 720$) over 20 generations. Selections responses were measured at generations 1, 10 and 20 (Gen 1, Gen 10, and Gen 20, respectively). F measures the

inbreeding coefficient estimated for each population at a given generation. The selection response of independent replicates is given by the slopes of the selection lines, which represent changes in bristle number (y axis) following a selection scheme over six generations (x axis). Adapted from Swindell and Bouzat (2005)

retention of phenotypic and genetic diversity, and as a consequence on the adaptive potential of populations following bottlenecks. This also emphasizes that the outcome of an individual bottleneck tends to be population-specific, and depends on the specific lineage and genetic background of the population under consideration.

Stochasticity under different environmental conditions

Since the early studies on inbreeding depression, it was apparent that the effects of inbreeding on fitness were also dependent on the environmental conditions under which inbreeding occurred (see e.g., Bijlsma et al. 1999; Dahlggaard and Hoffmann 2000; Fowler and Whitlock 2002; Kristensen et al. 2003; Waller et al. 2008). If the effects of inbreeding have shown to vary among populations (Pray and Goodnight 1995), then one would expect that these would become more variable under different environments, particularly if the environment is a stressful one in terms of its fitness impacts.

In a recent paper Armbruster and Reed (2005) reviewed 34 studies in which inbreeding depression was estimated as

the number of lethal equivalents expressed at different levels of inbreeding and under different environmental conditions. Their meta-analysis demonstrated that inbreeding depression was significantly greater under stressful conditions compared to benign environments. The expression of inbreeding depression was lineage-specific but the magnitude was uncorrelated across environments, suggesting a lineage by environment interaction. These results are consistent with Haag et al.’s (2003) statement emphasizing that “environmental factors could play a major role in determining the level of inbreeding depression, because selection coefficients against deleterious mutations might depend on the environment...” Bijlsma et al. (1999) had previously shown this when they observed that experimental lines exposed to environmental stressors, like DDT and high temperature, had significantly higher selection coefficients compared to controls.

The environmental dependence of inbreeding depression and its effects on selection coefficients may have significant impacts on the potential purging of deleterious alleles from populations (see section on “The role of selection”), and ultimately on their probability of extinction. For

example, Bijlsma et al. (2000) evaluated the effect of inbreeding and environmental stress on the probability of extinction of laboratory populations. As expected, they found that extinction probabilities increased with increased inbreeding and became greatly enhanced under stressful environmental conditions (see also Reed et al. 2002). However, most interestingly was the fact that inbreeding and environmental stress were not independent but acted synergistically.

Evidence for the environmental dependence of inbreeding depression has also been reported in populations from the wild. For example, Keller et al. (2002) showed that environmental conditions affected the magnitude of inbreeding depression in Darwin's finches, and Richardson et al. (2004) showed that the magnitude of inbreeding depression in Seychelles warblers revealed environment-dependent maternal effects (demonstrated through experimental cross-fostering of nestlings). In addition, long-term studies on the song sparrows of the Mandarte Island revealed that inbreeding depression for hatching success varied with environmental stress (Marr et al. 2006). Lesbarreres et al. (2005) further investigated not only the effects of environmental variation on fitness but on its correlation with genetic variability in the common frog. Their study demonstrated that genetic variability-fitness correlations can also be environment-dependent. These results question the idea of a direct and consistent relationship between genetic variation and fitness, and the potential use of molecular genetic markers to relate heterozygosity and fitness. Furthermore, these studies provide clear evidence that both the genetic background of populations and the environmental conditions in which these are reared affect the fitness outcome of the specific lineage under consideration and their extinction probabilities.

Drift effects on multiple trait components

The effects of inbreeding have also shown to vary considerably among different types of traits (e.g., morphological versus fitness-related traits), and even among different components of complex traits such as fitness (Ouborg and Van Treuren 1995; Fry et al. 1998; Margulis 1998; Roff 1998; DeRose and Roff 1999; Ellmer and Andersson 2004). There has been considerable debate regarding the genetic basis of inbreeding depression. It seems, however, clear that the major processes leading to a decrease in fitness in highly inbred populations include an increase in the frequency of homozygotes, which may lead to the expression of deleterious recessive alleles (i.e., the partial dominance hypothesis), a reduction of heterozygotes at overdominant loci (i.e., the overdominance hypothesis), and changes in gene interactions (e.g., epistatic effects) (Charlesworth and Charlesworth 1987, 1999;

Lynch 1991; Roff 2002; Carr and Dudash 2003). The expression of inbreeding depression depends therefore on the multi-locus nature of quantitative traits, and as such may be highly affected by drift effects on the distribution of alleles (both within and among loci) following bottlenecks.

There is a general agreement that traits associated with fitness will tend to have greater inbreeding depression than morphological traits, due to their larger dominance variance components (Crnokrak and Roff 1995). Results by Roff (1998) on the sand cricket (*Gryllus firmus*) were consistent with this prediction, since life history and fitness-related traits such as growth rate and fecundity showed higher levels of inbreeding depression than other morphological traits. This trend was also reported in a meta-analysis of inbreeding depression studies on different trait types (DeRose and Roff 1999).

Finally, the magnitude of inbreeding depression may also vary with regards to the particular component of fitness measured or life-history stage (Keller et al. 2008). This is apparent when estimating the effects of inbreeding on male and female fitness (e.g., female fecundity and male fertility; Fry et al. 1998). However, it is not uncommon to find that inbreeding may have drastic effects on particular fitness measures while no significant effects on others (Lacy et al. 1996). As a general rule, there seems to be little correlation on the effects of inbreeding among different fitness trait components (Kuke Bijlsma, personal communication).

The environmental dependency of inbreeding depression will also vary upon the particular component of fitness studied. For example, Marr et al. (2006) found that inbreeding depression interacted with environmental stress to reduce hatching success in a wild population of song sparrows. They found no evidence, however, that inbreeding depression varied with environmental stress in other fitness components, including laying date, male mating success and fledging survival. All these studies emphasize that the genetic consequences of inbreeding may vary depending on the trait under consideration. Furthermore, potential interactions between inbreeding and environmental stress (reviewed in the previous point) may not occur in all traits affected by inbreeding depression, and if they do occur, may not always act synergistically in determining overall levels of inbreeding depression (see Marr et al. 2006 and Waller et al. 2008).

Chance effects on extinction: moving from individuals to populations

Arguably, a relatively overlooked aspect regarding the potential effects of bottlenecks on fitness and extinction relates to the statistical nature of parameter estimates at the

population level. Since estimates of population-level parameters such as population growth, average fitness, or extinction probabilities are commonly individual-based estimates (i.e., based on fitness or productivity estimates from single individuals) these parameters are highly subjected to stochastic variance.

In addition, given that populations are collections of individuals, extinction becomes a probabilistic phenomenon subjected to chance events. It is therefore likely that average estimates of population fitness, which may be indicative of inbreeding depression, may change drastically, for example, as a result of chance events associated with the survival (or sampling) of particularly “well-fit” or “weak” individuals. The long-term persistence or extinction of populations (or their actual estimate of extinction risk) may, therefore, be affected by the stochasticity associated with the fate of single individuals within a population or their representation in a population sample. Although this particular aspect may not play a major role in relatively large populations, in which the fate of single individuals do not affect significantly parameter estimates of the population as a whole, it may have a significant impact in bottlenecked populations with small effective sizes.

The role of selection

A second aspect of the detrimental paradigm of inbreeding depression relates to the potential role of selection in populations that have experienced bottlenecks. As mentioned above, most studies tend to assume that a decrease in fitness will follow a population bottleneck as a result of inbreeding depression, and many studies have documented this in both experimental and natural populations (Ralls et al. 1979; Crnokrak and Roff 1999; Keller and Waller 2002). For examples on the detrimental effects of inbreeding in small populations, see the classical reviews by Thornhill (1993), Hedrick and Kalinowski (2000), and Frankham (1995b, 2005a). Here, I will focus on two aspects of selection in relation to its potential effects in reducing inbreeding depression and, ultimately, affecting extinction.

The effects of purging

In general, two different hypotheses have been proposed to explain the possible effects of genetic diversity on population fitness. When lack of genetic diversity is associated with a decrease in fitness, inbreeding depression is assumed to be the result of deleterious recessive alleles expressed through an increased in homozygosity. On the other hand, when fitness reductions are not observed, then the purging

of deleterious alleles through natural selection is commonly proposed to lead to either an increase or no change in population viability. As previously mentioned, several examples from natural populations support the inbreeding depression hypothesis. These include, e.g., the long-term decline in fitness associated with temporal decreases in genetic diversity reported in the Greater prairie-chicken (Westemeier et al. 1998), a Scandinavian adder population (Madsen et al. 1999), Black-footed ferrets (Wisely et al. 2002), and butterflies (Saccheri et al. 1998, 1999; Nieminen et al. 2001) among many others (e.g., Kalinowski et al. 2000; Kalinowski and Hedrick 2001; Reid et al. 2003, 2007). In contrast, examples on purging have been less common and mostly inferred from documented cases of decreased genetic variation at the molecular level with no apparent effects on fitness.

Two classic examples from natural populations that could potentially be attributed to selective purging include the Northern elephant seal (*Mirounga angustirostris*) (Bonnell and Selander 1974) and the Mauritius kestrel (Groombridge et al. 2000). Both species have been reduced to very small numbers as a result of human activities (less than 100 estimated for the elephant seal as a result of hunting, and believed to be only two for the Mauritius kestrel as a result of habitat destruction). Both species have also been shown to have reduced genetic diversity compared to sister species. Yet, each species recovered relatively well and, in the case of the elephant seal, to very large numbers throughout most of its range. These studies, however, represent only indirect and inferential evidence on the potential role of purging. Non-significant declines in fitness in highly inbred populations have also been reported in Mexican and Red wolves (Kalinowski et al. 1999), domestic cattle (Visscher et al. 2001), White-toothed shrews (Duarte et al. 2003), and experimental populations of *Drosophila melanogaster* (Fernández et al. 2003). A review of the experimental evidence by Crnokrak and Barrett (2002) and of studies from captive populations by Boakes et al. (2007) suggest, however, that purging may not be a strong force in small populations. As a consequence, many researchers detecting no apparent effects on fitness tend to subscribe to the detrimental paradigm of inbreeding depression, with the lack of fitness effects being generally interpreted as a negative result or as a technical limitation for detecting a change in fitness.

Two factors have probably influenced the dismissal of selective purging as having a major role in populations subjected to demographic bottlenecks. First, it has been commonly accepted that purging is a very unlikely process in small populations. For example, Frankham et al. (2001) indicated that “purging using rapid inbreeding in very small populations cannot be relied upon to eliminate the deleterious effects of inbreeding;” and Radwan (2003)

reported that “most of the evidence collected so far suggests that the purging process does not play a substantial role in the majority of populations. Second, until recently there have been no studies providing direct evidence on the role of selective purging in small populations, particularly from animal species (but see Lacy and Ballou 1998; Miller and Hedrick 2001; Reed and Bryant 2001).

Swindell and Bouzat (2006a, b) provided experimental evidence that natural selection may play a significant role in reducing or eliminating inbreeding depression in populations of *Drosophila melanogaster*. Our studies showed that: (1) compared to outbred populations, experimental populations that have been previously subjected to inbreeding were less susceptible to suffer inbreeding depression; and (2) populations with higher levels of ancestral inbreeding had comparatively reduced inbreeding depression.

Results from the first study indicated that, overall, full-sib crosses from purged populations produced significantly more offspring than inbred crosses from a control base population, which led to significant lower levels of inbreeding depression in the purged versus base population (as measured by $d = 1 - W_i/W_o$, where W_i and W_o represent the fitness of inbred and outbred crosses, respectively). In fact, the purged population revealed about 1/3 ($d = 0.049$) of the inbreeding depression experienced by the base population ($d = 0.145$).

In the second study we designed two breeding schemes to assess inbreeding depression in experimental lines with different levels of ancestral inbreeding (Swindell and Bouzat 2006b). The ancestral inbreeding (f_a) measures the cumulative proportion of the genome that has been previously exposed to inbreeding in its ancestors (Ballou 1997; Lacy and Ballou 1998). Thus, f_a not only measures current levels of inbreeding (as estimated by the standard inbreeding coefficient F), but also how much inbreeding a particular lineage has been exposed to in the past. Results from this study showed that, overall, lineages with high levels of ancestral inbreeding had significantly higher fitness than those with low ancestral inbreeding (Table 1;

$W_i = 28.6$ versus 19.4). The median level of inbreeding depression (d) in the high ancestral inbreeding treatment was also significantly lower than the low ancestral inbreeding treatment. In fact, the inbreeding depression in the high ancestral inbreeding treatment was about 40% that of the low ancestral inbreeding treatment (see Table 1).

These two studies provide direct evidence that purging may be an effective force in reducing the magnitude of inbreeding depression that a population may experience following a bottleneck. Significant reductions in inbreeding depression can be explained, therefore, as a result of natural selection eliminating deleterious recessive alleles by purging the genetic load of populations subjected to high levels of inbreeding. Recent studies using SNP markers on genes that are differentially expressed in inbred and outbred individuals further suggest that strong selection on a small number of loci, some of which are subject to purging and some to balancing selection, may also help maintaining genetic diversity and fitness in inbred populations (Kristensen et al. 2005, Demontis et al. 2009). In summary, it seems clear that the fitness consequences of population bottlenecks should not always be interpreted under the detrimental paradigm of inbreeding depression, but rather be open to the potential effects of natural selection for eliminating deleterious recessive alleles exposed through inbreeding.

Purging and extinction

As expected, the hypothesis that purging may decrease extinction probabilities is much more difficult to test, and to date there has been few studies on this particular question (Bijlsma et al. 2000; Frankham et al. 2001; Miller and Hedrick 2001; Reed et al. 2003b; Kristensen et al. 2008a). A few case studies from the wild suggest however that, in some occasions, populations that have undergone drastic reductions in population size retained relatively high reproductive rates and recovered rapidly with minimal management intervention (e.g., Saccheri et al. 1996; Groombridge et al. 2000, 2009).

The cases of the Northern elephant seal and the Mauritius kestrel reported above and a recent study on the Seychelles kestrel (Groombridge et al. 2009) suggest that, in spite of their significant loss in genetic diversity following drastic demographic bottlenecks, their populations recovered without major management intervention. In the case of the Mauritius kestrel, the recovery of the population occurred following an initial period of lowered fitness in the early post-bottleneck population (Groombridge et al. 2000).

These examples are in clear contrast to most studies on demographic bottlenecks that commonly report wild populations that are at the verge of extinction. In most cases

Table 1 Fitness estimates of inbred (W_i) and outbred (W_o) individuals (based on offspring productivity) and mean a median inbreeding depression estimates ($\delta = 1 - W_i/W_o$) of n experimental populations of *D. melanogaster* maintained at 0.250 and 0.531 ancestral inbreeding coefficients (f_a)

Treatment (f_a)	0.250 ($n = 30$)	0.531 ($n = 31$)
Inbred Fitness (W_i)	19.38 (1.83)	28.63 (1.81)
Outbred Fitness (W_o)	28.61 (2.42)	33.35 (1.86)
Mean δ	0.270 (0.062)	0.099 (0.057)
Median δ	0.261	0.155

Standard errors are indicated in parentheses. Adapted from Swindell and Bouzat (2006b)

these populations have limited reproductive potential, requiring intensive management, e.g., through captive breeding programs and translocations, to ensure their persistence and long-term viability. Translocation programs in the Florida panther and the Mexican wolf (Hedrick and Fredrickson 2010), Greater prairie-chickens (Bouzat et al. 2009), bighorn sheep (Hogg et al. 2006), and the Peregrine falcon in southern Scandinavia (Jacobsen et al. 2008), emphasize the potential benefits and pitfalls of genetic rescue (see also Tallmon et al. 2004; Edmands 2007).

In spite of recent studies highlighting the potential role of selection on inbreeding depression and extinction, caution should be taken when making generalizations that may have direct implications on defining conservation and management strategies. Although experimental evidence showed that purging may ameliorate the detrimental effects of inbreeding depression, it is unlikely that it would eliminate it completely (see Boakes et al. 2007). The efficiency of purging may be affected by multiple factors, including (but not limited to) the relative role of selection in small populations, the rate of inbreeding, the relative role of purging versus balancing selection, and the trait- and population-specific nature of inbreeding depression (Ayroles et al. 2009; Demontis et al. 2009). As in the case of inbreeding depression selective purging is a complex phenomenon, and the potential efficiency of purging may be as variable as other consequences of small population size.

The role of history

Two different but equally important issues emphasize the potential role of history in determining the outcome of population bottlenecks. One relates to the fact that individual bottlenecks represent unique historical events. The second feature relates to the past history of populations prior to the bottleneck event. Both aspects can have significant impacts on the genetic outcomes of demographic bottlenecks.

Bottlenecks as unique historical events

As indicated above in relation to the effects of chance on genetic diversity, population bottlenecks represent unique historical events. As a consequence, the stochasticity associated with the effects of small population size makes the outcome of individual bottlenecks unpredictable. That is, although one could predict changes in the variance of genetic diversity within and among replicated bottlenecks, one can never predict changes in the mean value of any particular trait (e.g., heterozygosity, a quantitative trait, or any fitness trait) (Hedrick 2005).

One of the main consequences of the unique nature of historical events is that we can only make inferential statements. That is, we can only infer conclusions *a posteriori*, particularly regarding the potential effects of stochastic processes on traits such as fitness and, ultimately, extinction. The implicit assumptions of the detrimental paradigm of inbreeding depression predict, however, that demographic bottlenecks will consistently lead to a decline in genetic diversity at the molecular and quantitative levels, a decrease in fitness as a result of inbreeding depression, and ultimately, an increase in extinction probabilities (Fig. 1). However, from a genetic perspective, the relationship between genetic variation, phenotypic diversity, fitness, and extinction will depend on the specific genetic composition of populations after the bottleneck, which will ultimately define the specific alleles and allele combinations determining quantitative traits. As reviewed in this article, stochastic and deterministic processes such as genetic drift, inbreeding, and selection, operating in populations that undergo demographic bottlenecks can have unique historical outcomes regarding the genetic effects on fitness and extinction, which will ultimately determine the fate of the population. This aspect of history on the consequences of population bottlenecks can be visualized as lineage effects in studies with replicated populations (e.g., Pray and Goodnight 1995; Wade et al. 1996; Whitlock and Fowler 1996; Groom and Preuninger 2000; Reed et al. 2002, 2003a; Lesbarreres et al. 2005). For example, the early studies by Pray and Goodnight (1995) and Wade et al. (1996) showed significant variation in inbreeding depression among replicated bottlenecks. Furthermore, Reed et al. (2003a) found strong lineage effects when inbred and outbred *Drosophila* populations were maintained in benign and stressful environments, and then exposed to a novel stressor. These studies are consistent with the review by Armbruster and Reed (2005), who found that strong lineage effects are ubiquitous among studies on inbreeding depression, and that the detrimental effects of inbreeding within lineage are uncorrelated across environments (based on a review of 34 studies).

It is important to mention that the historical nature of bottlenecks as unique events does not minimize the detrimental effects of small population size on fitness and extinction. As a probabilistic process, extinction is highly affected by genetic, demographic and environmental stochasticities operating in small populations (Shaffer 1981). As a result, there is a clear association between population size and extinction probabilities. The specific role of genetics following bottlenecks will, however, depend on the effects of chance, selection, and history, and on the nature of quantitative traits associated with fitness (see “Conclusions”).

The role of history prior to bottlenecks

History may also play an important role with respect to the potential effects of population bottlenecks on inbreeding depression. Specifically, the prior inbreeding history and the inbreeding environment can have important consequences on the outcome of demographic bottlenecks, particularly in relation to their influence on the effectiveness of purging (Latta and Ritland 1994; Fowler and Whitlock 2002; Reed et al. 2003a, b; Pedersen et al. 2005; Swindell and Bouzat 2006c). For example, one can expect that different rates of inbreeding, i.e., how fast or slow inbreeding occurs, will enhance or decrease the purging of the populations' genetic load (Kristensen et al. 2005; Day et al. 2003; Swindell and Bouzat 2006c). We can assume that slower rates of inbreeding would enhance the effectiveness of selective purging. This is firstly because more generations are required to reach a given inbreeding coefficient F , and thus more opportunities for selection are present every generation. And secondly, because slower inbreeding rates occur at higher effective population sizes (N_e), which reduces the relative influence of genetic drift over selection by increasing the selection coefficient (s) beyond the critical value ($s = 1/2N_e$) under which alleles tend to behave neutrally (Hedrick 2005).

Regarding the inbreeding environment, one would expect that recessive alleles may become more deleterious under stressful conditions (Dahlggaard and Hoffmann 2000; Frankham 2005b; Kristensen et al. 2008b) (see section on "Stochasticity under different environmental conditions"), increasing the strength of selection. Recessive deleterious alleles may, therefore, be more readily eliminated through natural selection decreasing the genetic load of populations and reducing inbreeding depression. The predicted effects of inbreeding rate and inbreeding environment are presented in Fig. 3, which represents a schematic of the reaction norms of populations under different inbreeding rates and inbreeding environments. Mean comparisons show that slower rates and more stressful environments would tend to decrease inbreeding depression. A significant interaction between inbreeding rate and inbreeding environment would be determined by a significant difference in the slopes of the reaction norms (Fig. 3).

The history of populations may, therefore, significantly influence the outcome of a bottleneck event. For example, one can expect that populations that have been exposed to stressful environments or that were commonly subjected to serial bottlenecks or drastic changes in population size may be less prone to suffer inbreeding depression and, consequently, have lower probabilities of extinction. Prior experimental studies of *Drosophila* populations (e.g., Kristensen et al. 2003, 2005, 2006; Pedersen et al. 2005; Swindell and Bouzat 2006c; Demontis et al. 2009)

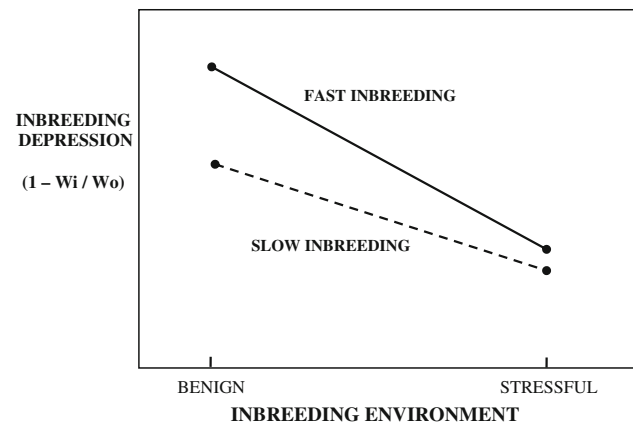


Fig. 3 Potential effects of inbreeding rate and inbreeding environment on the magnitude of inbreeding depression. A history of slow inbreeding rate (*dashed line*) and stressful environment may decrease inbreeding depression as a result of purging. Differences in the slopes of the reaction norms would suggest a significant inbreeding rate by environment interaction

suggested that in some instances the inbreeding rate and the specific environment in which inbreeding occurs (e.g., more stressful environments) may play an important role in the effectiveness of purging effects against deleterious recessive alleles. Thus, it seems clear that population history, particularly in terms of inbreeding rate and inbreeding environment (which may increase the strength of selection against deleterious recessive alleles) may decrease the threat that inbreeding depression poses to population viability.

Conclusions

In this study we have explored the roles that chance, selection, and history may play in determining the genetic consequences of population bottlenecks. In particular, we have emphasized the importance of these processes in changing our interpretation of the detrimental paradigm of inbreeding depression. Past and current studies on the genetic consequences of population bottlenecks warrant a reevaluation of the commonly assumed relationships between population bottlenecks, genetic diversity, fitness, and extinction risks, including the potential effects on fitness and adaptive potential (Fig. 1). The acceptance of the detrimental paradigm of inbreeding depression has led many conservation genetic studies to focus mainly on the detection of low levels of genetic diversity at the molecular level, to immediately suggest a consequent detrimental effect on fitness and increase in extinction probabilities, too often without having any direct evidence for such potential relationships. This critique does not minimize the role of genetics (and in particular of genetic diversity) in

conservation and extinction, but rather suggests that a complete ascription to this paradigm may limit our understanding of relevant processes on the population genetics of bottlenecks and extinction.

The limitation of the detrimental paradigm of inbreeding depression is based on a very old question about the nature of heritable variation. That is, how genotypes translate into phenotypes? Or, in other words, how molecular genetic diversity translates into adaptive genetic diversity? An oversimplification of this relationship, probably based on a single-locus conceptual framework, is what may have caused conservation geneticists to focus on molecular genetic diversity as a direct surrogate of adaptive genetic variation. Several studies, however, have emphasized the limitations of this approach for conservation (see e.g., Crandall et al. 2000).

The schematic in Fig. 4 summarizes the potential outcomes of replicated bottlenecks with regards to fitness, phenotypic variance, additive genetic variance, and adaptive

potential. We have seen that although demographic bottlenecks may result in severe inbreeding depression, represented by the negative slope of the regression line between fitness and the inbreeding coefficient, in many cases inbred populations may experience no effects or even increase in fitness. Similarly, while some bottlenecked populations experience a reduction in phenotypic variance others may show increased variance following bottlenecks (Fig. 4). As a consequence, one can expect that different populations will vary in their additive genetic variance and, thus, their adaptive potential, represented in Fig. 4 by the regression line between the selection coefficient (S) and the response to selection (R).

The variable responses of bottlenecks on fitness, phenotypic variation, and heritable variation emphasize the necessity to explore the relationship between molecular genetic diversity, adaptive genetic diversity, and extinction beyond the predominant detrimental paradigm that leads many studies in conservation genetics.

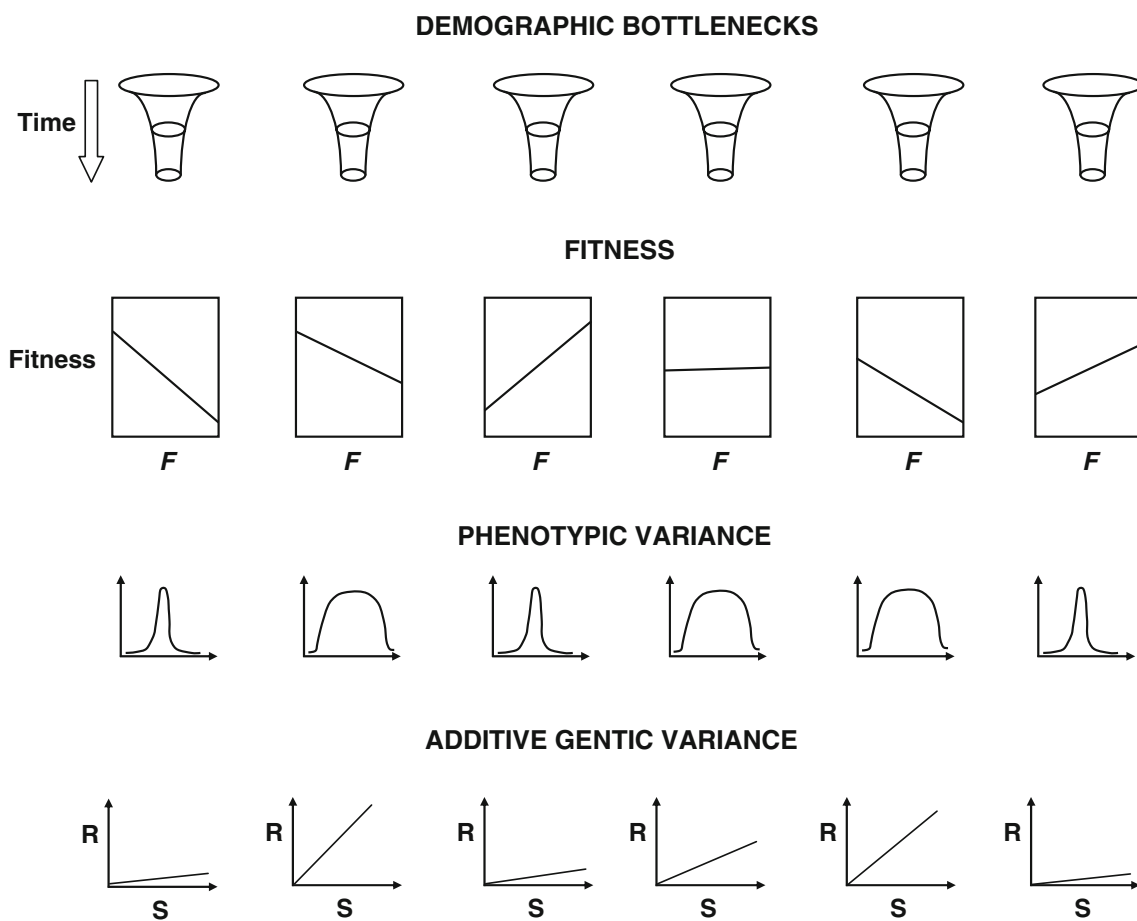


Fig. 4 Schematic representation of the variable responses of demographic bottlenecks to fitness, phenotypic variance, and additive genetic variance. Fitness is plotted against the inbreeding coefficient F ; phenotypic variance is represented as the frequency distribution of

a trait; and the amount of additive genetic variation is represented by the regression line between the selection response (R) and the selection coefficient (S). Chance, selection, and history all contribute to the differential genetic consequences of population bottlenecks

The relatively recent development of “omic” technologies (i.e., genomic, transcriptomic, proteomic and metabolomic techniques) promises an increase in our understanding of the molecular and physiological causes and consequences of inbreeding (Charlesworth 2009; Kristensen et al. 2009). For example, the utilization of non-neutral molecular markers (such as SNPs) located in coding regions throughout the genome (see e.g., Demontis et al. 2009) suggest that genetic diversity can be maintained in inbred populations by associative overdominance, with some loci being subject to purging and others to balancing selection. Furthermore, studies using transcription arrays demonstrate that inbreeding not only changes the expression profile of genes associated with fundamental metabolic processes (Ayroles et al. 2009), but that in several cases these changes tend to counteract the deleterious effects resulting from the expression of the genetic load (e.g., by increasing protein turnover rate, expression of chaperones, etc.) (Kristensen et al. 2009). The application of these technologies to both experimental and field studies on small populations under different environmental conditions will surely open new avenues to increase our understanding of the nature of inbreeding and its effects on evolutionary potential.

Implications for conservation and management

The reevaluation of the detrimental paradigm of inbreeding depression with regards to the effects of chance, selection, and history on population bottlenecks has direct implications for conservation and management. In light of the ideas reviewed in this study we can list some guidelines and a set of testable predictions regarding the potential effects of bottlenecks on population viability and extinction.

The first caveat is that population bottlenecks may have variable outcomes regarding their effects on genetic diversity, fitness, and extinction. The specific outcome of a single bottleneck event will depend on the particular trait under consideration (e.g., molecular versus quantitative, morphological versus fitness), the specific component of fitness assessed (e.g., fertility versus fecundity versus longevity), and the specific environmental conditions under which a bottleneck event occurs (e.g., benign versus stressful environments).

Second, it is apparent that molecular genetic markers do not always represent proper surrogates of quantitative variation, fitness and extinction. That is, although lack of genetic diversity at the molecular level may be indicative of past population bottlenecks and inbreeding, it does not follow that bottlenecked populations would have

inbreeding depression, and consequently decreased viability as a consequence of genetic factors. Quoting Brodie (2007), it seems clear that “Populations size is not genetic quality.”

Third, we cannot disregard the potential role of selective purging in alleviating the threat of inbreeding following population bottlenecks. However, the efficiency of purging in decreasing inbreeding depression may also be highly variable. Results from experimental studies and a few examples of natural populations recovering from drastic demographic bottlenecks without major management actions suggest that selection may, in some instances, help alleviating the detrimental effects of inbreeding in bottlenecked populations.

Finally, it seems clear that population history, particularly in terms of the inbreeding rate and the inbreeding environment under which populations may have been exposed prior to or during bottleneck events can have direct impacts on the levels of inbreeding depression expressed, and therefore, on the long-term viability of populations.

At least, we can think of three major predictions that could be testable in the near future with regards to the role of bottlenecks on inbreeding depression and population viability:

First, one could predict that species or populations that have undergone serial population bottlenecks throughout their evolutionary history may have reduced genetic load, and therefore, may be less prone to have inbreeding depression. As a consequence, these populations may have increased viability and be more likely to recover from near-extinction than populations lacking such a history. This could be the case, e.g., for populations that regularly undergo natural demographic cycles, serial bottlenecks, or population crashes.

Second, we could also argue that populations that remain small in size over long periods of time may have more opportunity for purging their genetic load and therefore be less prone to have fitness decreases during population bottlenecks. For example, demographic bottlenecks may be less detrimental in island endemics, which throughout their evolutionary history tend to have smaller effective sizes than their continental counterpart species (Jamieson 2007; Reed 2007).

Finally, one could expect that species that have evolved or are commonly exposed to stressful environmental conditions may have decreased genetic loads and, therefore, have reduced inbreeding depression following bottlenecks.

The testing of these predictions will surely provide valuable information to design proper management strategies aimed at the conservation of endangered species, most of which are currently undergone human-induced population bottlenecks.

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