

Quantitative genetics in conservation biology

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Summary

Most of the major genetic concerns in conservation biology, including inbreeding depression, loss of evolutionary potential, genetic adaptation to captivity and outbreeding depression, involve quantitative genetics. Small population size leads to inbreeding and loss of genetic diversity and so increases extinction risk. Captive populations of endangered species are managed to maximize the retention of genetic diversity by minimizing kinship, with subsidiary efforts to minimize inbreeding. There is growing evidence that genetic adaptation to captivity is a major issue in the genetic management of captive populations of endangered species as it reduces reproductive fitness when captive populations are reintroduced into the wild. This problem is not currently addressed, but it can be alleviated by deliberately fragmenting captive populations, with occasional exchange of immigrants to avoid excessive inbreeding. The extent and importance of outbreeding depression is a matter of controversy. Currently, an extremely cautious approach is taken to mixing populations. However, this cannot continue if fragmented populations are to be adequately managed to minimize extinctions. Most genetic management recommendations for endangered species arise directly, or indirectly, from quantitative genetic considerations.

1. Loss of biodiversity

The biological diversity of the planet is rapidly being depleted due to loss of habitat, overexploitation, introduced species and pollution. A large but unknown number of species have gone to extinction, and many others have been reduced to the point where they require benign human intervention to save them from extinction (World Conservation Monitoring Centre, 1992; Lawton & May, 1995).

There have been almost 900 recorded extinctions since 1600, the majority being of island forms (see Primack, 1998). The rate of extinctions has generally increased over time (Smith *et al.*, 1993). Many other species have gone extinct due to habitat loss before they were described.

The scale of current threat is immense. Of all species, 25% of mammals, 11% of birds, 20% of reptiles, 25% of amphibians, 34% of fish, 32% of gymnosperms and 9% of angiosperms are listed as

threatened (critically endangered, endangered or vulnerable) (IUCN, 1996; Primack, 1998). Projected extinction rates per decade, based on a range of different methods, range from 1–5% to 8–11% (World Conservation Monitoring Centre, 1992). All reputable conservation authorities project major future extinctions.

Loss of habitat is currently the most important factor causing loss of biodiversity, but global climate change due to pollution may overtake it in the future. At small population size, additional stochastic factors (demographic, environmental, catastrophic and genetic) come into play and accelerate the decline to extinction. These stochastic factors operate in a negative feedback leading species to spiral downwards towards extinction ('the extinction vortex').

2. What is an endangered species?

Mace & Lande (1991) defined objective criteria for classifying species as in danger of extinction, based on population biology principles. They defined endanger-

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ment as a high probability of extinction in a short time. For example, critically endangered was defined as having at least a 50% probability of extinction within 10 years, or three generations, whichever is the longer.

Surrogate measures were devised to classify species into these categories; these were based on population decline, area of occupancy, population size and decline, or population size alone. One of the criteria was clearly influenced by genetic considerations. Effective population sizes of less than 50, 500 or 2000 were involved in critically endangered, endangered and vulnerable classifications, respectively. When translating these to actual census sizes, a N_e/N ratio of 0.2 was assumed. With revision, these principles formed the basis of revised IUCN (the World Conservation Union) categories of risk (IUCN, 1994, 1996).

3. Genetic concerns in conservation biology

Sir Otto Frankel was largely responsible for the recognition of genetic factors in conservation biology (Frankel, 1970, 1974; Frankel & Soulé, 1981). Frankel was also a major figure in efforts to conserve genetic diversity for crop plants (see Frankel *et al.*, 1995).

The concerns of Frankel and others have led to the identification of nine major genetic issues in conservation biology (Frankham, 1995a):

- (1) Inbreeding depression affecting reproductive fitness.
- (2) Loss of genetic diversity reducing the ability of species to adapt in response to environmental change.
- (3) Fragmentation of populations and reduction in migration.
- (4) Accumulation and loss of deleterious mutations.
- (5) Genetic adaptation to captivity and its adverse effects on reintroduction success.
- (6) Outbreeding depression.
- (7) Taxonomic uncertainties.
- (8) Use of genetics to understand aspects of species biology important to conservation.
- (9) Use of genetic markers in forensics.

The first six of these involve primarily, or solely, quantitative genetics. Even the resolution of taxonomic uncertainties involves inferences about the probable fitness of crosses between populations.

IUCN, the premier international conservation body, has recognized the importance of genetic issues in conservation. They have designated genetic diversity, along with species diversity and ecosystem diversity, as requiring conservation (McNeely *et al.*, 1990). Genetics contributes not only to the conservation of genetic diversity, but also to the conservation of species.

4. Relationship between genetics and extinctions

The assumption underlying genetic concerns in conservation biology is that inbreeding and loss of genetic diversity increase the risk of extinction (Frankel & Soulé, 1981). While this is a logical extension from observed effects of inbreeding on reproductive fitness and impacts of reduced genetic diversity on ability to evolve, direct evidence has been limited and the issue is controversial. In a highly influential paper, Lande (1988) argued that random demographic and environmental events would drive small wild populations to extinction before genetic factors came into play (see also Caro & Laurenson, 1994; Caughley, 1994).

Do genetic problems contribute to the endangerment and extinction of wild populations? Inbreeding has been shown to increase extinction rates in laboratory populations of *Drosophila* and mice under conditions where non-genetic factors could be excluded (Frankham, 1995b). Further, simulation studies by Mills & Smouse (1994) have shown that genetic factors are likely to contribute to extinctions even when demographic and environmental stochasticity and catastrophes are operating. Saccheri *et al.* (1998) provided direct evidence for the involvement of inbreeding and genetic diversity in extinctions of wild butterfly populations in Finland.

Several indirect lines of evidence indicate that the butterfly results are likely to apply to other species (Frankham & Ralls, 1998). Genetics may contribute to the extinction proneness of island populations. Island populations have lower genetic diversity than mainland populations (Frankham, 1997) and many are inbred to levels where captive populations show elevated extinction risk from inbreeding (Frankham, 1998). Notably, endemic island populations that are more prone to extinction than non-endemic populations have lower genetic diversity and higher inbreeding levels than non-endemic populations. Since there are no demographic or environmental reasons to predict higher extinction rates in endemic than non-endemic island populations, genetic factors, or their interaction with environmental and demographic stochasticity are probably involved in the differences in extinction rates.

Ratios of effective to census population sizes average only 0.11, much lower than previously suspected (Frankham, 1995c). Consequently, genetic concerns become important at larger population sizes than previously believed. A majority of endangered species have lower genetic diversity than non-endangered species (Frankham, 1995a; Haig & Avise, 1996), which would not be expected if ecological factors drove populations to extinction before genetic factors became important. Experimental populations of a wild plant with reduced genetic variation showed higher extinction rates than populations with normal

levels when both were planted in the field (Newman & Pilson, 1997). Finally, genetic factors appear to be implicated in declines or extinctions of wild populations of Florida panthers, Puerto Rican parrots, Isle Royale grey wolves, inbreeding colonial spiders, heath hens, bighorn sheep, middle spotted woodpeckers, Asiatic lions and Ngorongoro crater lions (see O'Brien, 1994; Frankham, 1995a). Consequently, it is probable that genetic factors play a significant role in extinctions of wild populations.

5. Inbreeding depression in small populations

Reduced reproductive fitness due to inbreeding has been known since Darwin's time. Subsequent work in laboratory and domestic species demonstrated inbreeding depression in essentially all naturally outbreeding species (see Falconer & Mackay, 1996; Lynch & Walsh, 1998). However, there was still scepticism that inbreeding was deleterious in wildlife. This scepticism was stilled for captive wildlife when Ralls & Ballou (1983) showed that 41 of 44 captive mammalian populations had higher juvenile mortality for inbred than outbred offspring.

Scepticism subsequently focussed on the existence of inbreeding depression in populations of animals and plants in their natural habitats (Caro & Laurenson, 1994; Caughley, 1994). This has been largely resolved by reports of inbreeding depression in natural habitats in several species of fish, shrews, *Peromyscus* mice, golden lion tamarins, lions, snakes, snails, birds, insects and several species of outbreeding plants (see Frankham, 1995a; Brown & Brown, 1998; Saccheri *et al.*, 1998). Generally, inbreeding depression is greater in more stressful wild environments than in captivity, though data are limited (Frankham, 1995a).

How large must populations be to avoid inbreeding depression? Early influential papers by Franklin (1980) and Soulé (1980) suggested that populations with effective sizes of 50 or greater would not experience inbreeding depression in the short term. Inbreeding depression due to finite population size has been reported in *Drosophila*, house flies, plants, snakes, and marsupials (see Frankham 1995a; Madsen *et al.*, 1996; Woodworth, 1996; Bryant *et al.*, 1999; Eldridge *et al.*, 1999). Inbreeding depression over the long term has been reported in populations with effective sizes of 50, or even greater (Latter & Mulley, 1995; Woodworth, 1996; Bryant *et al.*, 1999), so there is no finite-sized population that is known to be immune from inbreeding depression.

Natural selection may reduce the frequency of deleterious recessive alleles in populations previously subjected to inbreeding. The importance of such purging has been a highly contentious issue in conservation genetics (see Frankham, 1995a). A

regime designed to adapt endangered species to tolerate inbreeding was devised by Templeton & Read (1984) and applied to the endangered Speke's gazelle.

Subsequent research has clarified the impact of purging and led to it being dropped as a serious management option for endangered species. Ballou (1997) found lower inbreeding depression in the progeny of inbred than non-inbred parents in 15 of 17 cases in captive wildlife. However, in only one case was the effect of purging significant and the overall magnitude of the purging effect was modest. Further, Lacy & Ballou (1998) reported purging effects on different characters in *Peromyscus* ranging from positive, through zero to negative. In a meta-analysis of plant data, Husband & Schemske (1996) reported significantly lower inbreeding depression in selfing than outcrossing species and a negative correlation between inbreeding depression and selfing rate, as expected with purging. Clearly, purging exists but its impact is often modest and variable.

6. Effective population size

The genetic impacts of small population size on inbreeding and genetic diversity are predicted to depend on the effective size rather than the census size (see Falconer & Mackay, 1996). In spite of its origins in 1931 (Wright, 1931), most of this theory had not been subject to experimental evaluation. Borlase *et al.* (1993) verified that equal family sizes (EFS) led to less inbreeding and loss of genetic diversity and maintained more reproductive fitness than equivalent-sized populations maintained with variable family sizes (VFS). Surprisingly, quantitative genetic variation showed no difference between the two treatments after 11 generations. However, this was apparently due to linkage disequilibrium as there was significantly higher quantitative genetic variation in the EFS treatment than in VFS after a period of random mating at larger population sizes where linkage disequilibrium could decay (Frankham, 1999). These experiments confirmed that equalization of family sizes could be used to effectively double the size of the scarce captive breeding space.

Experiments on unequal sex ratios and fluctuating population sizes verified the predicted effects of these on effective population sizes, inbreeding, genetic diversity and reproductive fitness (Briton *et al.*, 1994; Woodworth *et al.*, 1994).

Very low effective to census size ratios (N_e/N) were found in large populations of *Drosophila melanogaster* and *D. pseudoobscura* (Briscoe *et al.*, 1992). Ratios were 0.05 and lower. These estimates were much lower than previous reports, where N_e/N was reported to be 0.5–0.8 (Falconer, 1981) or 0.2–0.5 (Mace & Lande, 1991). The generality of our *Drosophila* results was

queried by several authors (see Nunney & Campbell, 1993). A meta-analysis revealed that the *Drosophila* results were not atypical of those for a wide range of taxa (Frankham, 1995c). Comprehensive estimates that included all relevant variables averaged 0.11. Unfortunately, this implies that unmanaged populations of wildlife are about an order of magnitude smaller genetically than their census sizes indicate.

7. Loss of evolutionary potential in small populations

Threatened species are, by definition, small (IUCN, 1994). Consequently, they are expected to lose genetic diversity over time (Falconer & Mackay, 1996). However, there was much scepticism about the reality of the relationship between population size and genetic diversity in wild populations (see Frankham, 1996). Since many of the studies reporting non-significant associations were based on few populations, statistical power may have been a major issue. A meta-analysis of the published data revealed significant positive relationships between population size, or its surrogates, and genetic diversity in nine of 10 tests and a trend in the other (Frankham, 1996).

A major unresolved issue is the relationship between molecular measures of genetic diversity and quantitative genetic variation. Most of what we know about levels of genetic diversity is based on allozymes, yet we are interested in ability to evolve and this is determined by quantitative genetic variation for reproductive fitness. Neutral theory predicts that there will be a correlation between heterozygosity for molecular markers and additive genetic variation due to genetic drift (see Falconer & Mackay, 1996). However, following population bottlenecks, the rates of recovery for quantitative variation may be higher than that for allozymes due to their different mutation rates (see Lynch, 1996). Correlations may also be low if the quantitative character is subject to stabilizing selection (Foley, 1992) or directional selection. Briscoe *et al.* (1992) found a correlation of 0.89 between allozyme heterozygosity and heritability for sternopleural bristle number in *Drosophila* cage populations with varying times in captivity. Further, the lower level of allozyme heterozygosity found in selfing versus outbreeding species (Hamrick & Godt, 1989) is paralleled by differences in the same direction for quantitative genetic variation (Charlesworth & Charlesworth, 1995). However, others have found a diversity of relationships from positive to negative (see Cheverud *et al.*, 1994; Lynch, 1996). There is a need for both more data on this issue and a meta-analysis of available data to resolve the issue.

There has been controversy over the effect of population size bottlenecks on the ability of populations to evolve. Theory for additive gene action predicts that a single-generation bottleneck of size n

will reduce additive genetic variation by $1/2n$ (James, 1971). Studies with characters showing predominantly additive genetic variation have confirmed this prediction (see Frankham, 1995a). However, Bryant *et al.* (1986) and Lopez-Fanjul & Villaverde (1989) both reported increased additive genetic variation for characters showing non-additive genetic variation. The relevance of the latter results to the ability of populations to evolve is doubtful as fitness was reduced in these studies. A direct evaluation of the effects of population bottlenecks on the ability of *Drosophila* populations to cope with increasing concentration of NaCl showed lower extinction concentrations in bottlenecked populations than in the outbred base population (Frankham *et al.*, 1999). Further, extinction concentrations were positively related to population size in populations maintained at effective sizes of 25, 50, 100, 250 and 500 for 50 generations (Frankham, Montgomery, Woodworth, Lowe and Briscoe, unpublished data). There can be no doubt that evolutionary potential is reduced by genetic drift and inbreeding in small populations.

How large do populations have to be to retain their evolutionary potential? In his seminal paper, Franklin (1980) argued that an effective size of 500 was sufficient to maintain long-term evolutionary potential due to a balance between mutation and drift for quantitative characters. Lande & Barrowclough (1987) reached a similar conclusion based on a model of mutation, drift and stabilizing selection. Subsequently, Lande (1995) argued that an effective size of 5000 was required, as about 90% of new mutational variance was deleterious. Franklin & Frankham (1998) queried this figure on the grounds that many estimates of the required mutational variance already account, at least in part, for deleterious mutations. Further, heritabilities are often lower than the 50% value used by Lande (1995) and others. Both of these points move the required N_e back towards the original 500.

Considerations of adaptive evolutionary potential have concentrated on standing genetic variation for quantitative characters. However, evolution in the medium to long term depends on the effective population size (Robertson, 1960; Hill, 1982). Consequently, endangered species with their small population sizes are likely to have greatly compromised ability to evolve.

Three other arguments lead to further reductions in evolutionary potential for endangered species. First, they often have low reproductive rates, so that the potential selection differentials are lower than typical for non-endangered species. Reproductive rates will decline further as a consequence of inbreeding in small populations, further lowering selection differentials. Secondly, endangered species, on average, have lower levels of genetic diversity than non-endangered species (Frankham, 1995a; Haig & Avise, 1996). Thirdly,

endangered species are predominantly long-lived species with long generation times. Consequently, evolutionary rates per unit time will generally be slower than in species with short generation times. Overall, endangered species are likely to have greatly reduced long-term evolutionary potential compared with non-endangered species.

8. Genotype \times environment interactions revisited

Genotype \times environment interactions are of major concern in conservation biology in the contexts of reintroducing captive populations into the wild, and in moving individuals among populations to alleviate inbreeding depression.

Captive populations adapt to the captive environments and this typically reduces reintroduction success (see Frankham, 1995*d*). Several lines of evidence indicate that genetic adaptation to captivity is a serious issue in conservation. King (1939) reported substantial improvement in reproduction for wild rats maintained for 14 years in captivity (25 generations). The length of reproductive life doubled (204 days to 440 days), age at first litter dropped by 147 days and number of litters per female increased almost threefold (3.7 to 10). There is ample evidence for the occurrence of genetic adaptation to captivity in fish, several species of *Drosophila*, plants and bacteria (see Frankham, 1995*d*).

Genetic adaptation to captivity may substantially reduce the fitness of reintroduced populations (Woodworth, 1996). Captive populations of *Drosophila* maintained at effective sizes of 25, 50, 100, 250 and 500 for 50 generations using equalization of family sizes (designed to minimize genetic adaptation to captivity) declined in fitness by at least 67%, compared with a wild control, when transferred to crowded, competitive 'wild' conditions. The largest populations with a N_e of 500 lost 'wild' fitness at 1.7% per generation, while Shabalina *et al.* (1997) reported a 2% decline per generation in 'wild' fitness over 30 generations in a similar experiment. Our analyses implicated genetic adaptation as the cause of the fitness declines in the large populations (Woodworth, 1996). Consequently, there may be substantial genotype \times environment interactions between captive and wild conditions.

Fragmentation with occasional migration to avoid extinctions from inbreeding depression has been suggested as an improved strategy for maintaining endangered species in captivity, while preserving the reintroduction option (Margan *et al.*, 1998). Such a strategy is also expected to lead to preservation of higher levels of genetic diversity. A critical assumption of the use of fragmentation is that there is no extinction of sub-populations. The predicted benefits

of fragmentation on 'wild' fitness and genetic diversity have been verified in experiments with *Drosophila* (Margan *et al.*, 1998).

This structure fits other requirements in captive breeding. Currently, individuals are being moved among zoos to create, effectively, a single large population. The recommended structure reduces the costs involved in moving animals, and reduces the risk of transferring disease. This strategy has only recently been advocated, so it does not represent recommended genetic management for captive populations of endangered species. However, it has many advantages over current management.

The second context where genotype \times environment interactions are important is that of crossing populations from different locations. Fear of outbreeding depression has led to an extremely cautious approach being taken to mixing populations. The extent and importance of outbreeding depression is a matter of controversy, but there is little evidence that it is important in mobile animals (Frankham, 1995*a*). Conversely, inbreeding depression is a well-established threat to fragmented populations with limited dispersal. Consequently, the current overly cautious approach to mixing populations cannot continue if fragmented populations are to be adequately managed to minimize extinctions.

9. Mutational accumulation

Mildly deleterious mutations may be fixed by chance in small populations, and so result in reduced reproductive fitness (Lande, 1995; Lynch *et al.*, 1995*a, b*). This causes declines in asexual populations (see Gilligan *et al.*, 1997). However, its importance in sexually reproducing populations is controversial. Lande (1995) suggested that populations below 1000 will suffer serious declines from the chance fixation of new mildly deleterious mutations, while Lynch *et al.* (1995*b*) suggest it would cause problems in populations with sizes up to an N_e of 100. Conversely, Charlesworth *et al.* (1993) did not consider this factor to be a serious threat unless population sizes were less than 12. Direct tests for mutational accumulation in populations maintained for 45–50 generations at effective sizes of 25, 50, 100, 250 and 500 failed to find evidence of mutational accumulation in three experiments (Gilligan *et al.*, 1997). Shabalina *et al.* (1997) reported rapid declines in reproductive fitness over time in large populations ($N_e = 400$) of *Drosophila* maintained under benign uncrowded conditions, but assessed under crowded, competitive conditions. They attributed the changes in fitness to mutational accumulation. However, similar fitness declines in the populations studied by Gilligan *et al.* (1997) were due to genotype \times environment interactions, i.e. genetic

adaptations to the benign, uncrowded conditions were deleterious under crowded, competitive conditions (Woodworth, 1996). Consequently, mutational accumulation does not appear to be of importance in the time frame of most conservation concerns in naturally outbreeding species (100–200 years).

10. Genetic management of endangered species

Management to alleviate inbreeding and loss of genetic diversity is common in captivity and has begun in wild populations (Ballou *et al.*, 1995). The explicit objective of most captive genetic management programmes for endangered species is to retain 90% of initial genetic diversity for 200 or 100 years (Ballou & Foose, 1996). This objective is predicated on the assumption that human population sizes may decline within this time frame, releasing habitat suitable for reintroduction of endangered species to natural habitats. A secondary goal is typically to retain the option to reintroduce populations into the wild. A number of zoos and zoo organizations employ staff with population and quantitative genetics expertise to genetically manage endangered species. Studbooks are maintained for many endangered species, so that pedigrees are typically available for use in genetic management.

Simulations by Ballou & Lacy (1995) suggested that minimization of kinship was the optimum management procedure for retaining genetic diversity. Experiments in *Drosophila* by Montgomery *et al.* (1997) verified this prediction. Surprisingly, there were no significant reproductive fitness benefits of minimizing kinship over random choice of parents in spite of substantially lower inbreeding in the former than the latter. In practice, endangered golden lion tamarins are managed to maintain maximum genetic diversity by minimizing kinship (Ballou & Foose, 1996). This also results in low inbreeding levels, so it should minimize extinction risk from genetic causes. Related programmes are being carried out for many other threatened species.

Genetic management of endangered species in the wild is in its infancy, apart from the use of genetics to resolve taxonomic uncertainties. I am aware of only three cases where genetic management is being used to address inbreeding and loss of genetic diversity in wild populations. The endangered Florida panther has very low genetic diversity and is suffering from inbreeding depression (Roelke *et al.*, 1993). To alleviate these genetic problems, individuals have been introduced into this population from its most closely related sub-species in Texas. Individuals are being introduced into small wild populations of the red-cockaded woodpecker in the south-east of the USA to alleviate inbreeding and loss of genetic diversity (Kulhavy *et al.*, 1995). In the endangered Mauna Kea

silversword plant in Hawaii, artificial pollination is being used to redress problems of reduced genetic diversity caused by outplanting 450 individuals derived from only two female plants (Robichaux *et al.*, 1997).

11. Conclusions

The relationship between conservation genetics and quantitative genetics is akin to that between animal breeding and quantitative genetics. One is an applied discipline and the other is a more academic discipline, with the two having intimate connections. There has been considerable two-way flow of information between conservation genetics and quantitative genetics. Many studies done in conservation genetics have been of general interest in quantitative genetics. In the early phase of conservation genetics, various editions of Falconer's classic *Introduction to Quantitative Genetics* (see Falconer & Mackay, 1996) have provided an accessible entry to the required population and quantitative genetic principles for those entering the field.

Methodologies from conservation genetics have considerable potential in quantitative genetics generally. Of necessity, meta-analyses are commonly used in conservation biology as most data sets for endangered species are small. Meta-analyses have the potential to be a much more useful tool in quantitative genetics than their current use indicates.

In conclusion, most of the major genetic concerns in conservation biology are quantitative genetic issues. The application of quantitative genetics has led to important insights and management regimes in conservation biology.

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