IMPORTANCE OF GENETIC VARIATION TO THE VIABILITY OF MAMMALIAN POPULATIONS

ROBERT C. LACY

Department of Conservation Biology, Daniel F. and Ada L. Rice Center, Brookfield Zoo, Brookfield, IL 60513

Small populations lose genetic variability because of genetic drift, and inbreeding within populations can further decrease individual variability. Lower variation depresses individual fitness, resistance to disease and parasites, and flexibility in coping with environmental challenges. Lower variation decreases mean fitness of populations (population growth rates), resilience, and long-term adaptability. Genetic drift can threaten viability of populations not just by depleting variation, but also by replacing natural selection as the predominant force driving evolutionary change. Although most genetic studies use laboratory or domesticated populations, evidence is accumulating that the effects of inbreeding are at least as severe on wild animals in natural habitats. Natural selection is expected to reduce the frequency of deleterious alleles in populations that persist through bottlenecks, but as yet there is little evidence for such purging of the genetic load in mammalian populations. No species of mammal has been shown to be unaffected by inbreeding. Genetic problems are contributing to the decline and vulnerability of at least several mammalian taxa. Genetic threats to population viability will be expressed through their effects on and interactions with demographic and ecological processes. Theoretical analyses, experimental tests, field studies, and conservation actions should recognize the fundamental interdependency of genetic and non-genetic processes affecting viability of populations.

Key words: conservation, extinction, genetic drift, genetic variation, inbreeding depression, population viability

Biodiversity, both in terms of the numbers of varieties of living organisms and the variety of processes that support and interlink forms of life, is being depleted at an unparalleled rate. The loss of biodiversity is occurring at all levels; damaged ecosystems, destroyed ecological communities, extinction of species, loss of genetically and ecologically distinctive populations, and loss of genetic variation among and within individuals in local populations. While most biologists bemoan losses of biodiversity at all of its levels, and all levels are clearly dependent upon the health of the others, there has been considerable debate regarding which levels are fundamental to sustaining biodiversity. In this essay, I address the importance of genetic variation within and among individuals to the viability of populations, and, therefore, also to the higher levels of biodiversity of which those populations are functional components. Although I will argue that individual variation is critical to population viability and deserves more attention in conservation efforts, I do not presume to make a case for the urgency or importance of such attention compared to actions focussed on other levels of biodiversity.

ROLES OF GENETIC VARIATION IN POPULATION VIABILITY: THEORETICAL FOUNDATIONS

Genetic variation is both a trait of individuals and a trait of populations. Variation within individuals of diploid species is most commonly characterized by the percentage of loci at which an individual is heterozy-

gous. Variation within populations includes also inter-individual variation, and often is quantified by the gene diversity (the heterozygosity expected under Hardy-Weinberg equilibrium), by the number of distinct alleles per locus, or by the percentage of loci that are polymorphic (Nei, 1973). Mean within-individual variation usually is highly correlated with populational (between-individual) variation, and all measures of populational variation encompass also the within-individual variation in the population. Thus, the distinction between within- and between-individual variation and the distinct roles of variation at these different levels are easily confused.

Effects on individual fitness.—Heterozygosity is depleted by inbreeding (mating between relatives), which leads to a greater probability of the two alleles at a locus being identical by descent from an ancestor common to both sides of the pedigree, and by genetic drift (random fluctuations in allele frequencies). Inbreeding has been observed to cause higher mortality, lower fecundity, reduced mating ability, slower growth, developmental instability, more frequent developmental defects, greater susceptibility to disease, lowered ability to withstand stress, and reduced intra- and inter-specific competitive ability (Allendorf and Leary, 1986; Darwin, 1868, 1876; Falconer, 1989; Ledig, 1986; Lerner, 1954; Ralls et al., 1988; Wright, 1977). The variety of impacts on fitness is collectively termed inbreeding depression. Inbreeding depression could result from the increased exposure in homozygotes of deleterious recessive alleles, or from an advantage of heterozygotes over each homozygous type (heterozygote advantage), or both (Crow, 1948).

Effects on population fitness.—Loss of genetic variation can impact population persistence in several ways. First, the lower fecundity and survival of inbred individuals within a population will depress population growth rate, which in turn can increase the probability of extinction from stochastic fluctuations (Goodman, 1987). Lower capacity for population growth also will reduce ability to rebound from population declines, especially as the impacts of inbreeding on individuals are accentuated in stressful environments (Keller et al., 1994; Lerner, 1954; Miller, 1994; Schmitt and Ehrhardt, 1990). Prolonged population bottlenecks will lead to yet greater loss of variation through genetic drift.

Even if lowered variation has little impact on a population's fitness in its present environment, or if the reduction in population growth and resilience is not sufficient to threaten short-term persistence, a decrease in variation will reduce the ability of the population to adapt to changing environments. First, the rate of evolutionary response to selection on a trait is proportional to the additive genetic variation (heritability) of that trait (Fisher, 1958), which is in turn proportional to expected heterozygosity or gene diversity of loci influencing the trait (Falconer, 1989). Second, the scope for evolutionary adaptation is delimited by the existence of alternate alleles within the population (James, 1971; Robertson, 1960). Thus, a population with low heritability, low heterozygosity, and few polymorphic loci will adapt more slowly and attain lesser adaptation before reaching the limits of response to selection than will a more diverse population. Selfing and parthenogenetic species, with little variation within individuals and between individuals, respectively, tend to have short evolutionary histories (Selander, 1983; Vrijenhoek, 1989). Bürger and Lynch (1995) found that fluctuations in genetic variance in small populations can reduce the rate of adaptation sufficiently to cause small populations to go extinct in the face of environmental change to which large populations would be able to adapt. We cannot know what adaptations will be required for persistence in future environments, but we do know that the rate of environmental change is much more rapid presently than perhaps at any time in past evolutionary history.

Franklin (1980) first suggested that populations would need effective sizes of ca. 500 for mutation to offset the loss of variation through genetic drift, thereby preserving long-term adaptive potential. Further analyses led to similar conclusions, even when the effects of stabilizing selection on quantitative traits were considered (Lande and Barrowclough, 1987). As a result of more recent work, however, Lande (1995*a*) has become even less optimistic about the potential for small populations to retain adaptive potential. Because most mutations with large effects are highly detrimental, the rate of incorporation of new genetic variation into populations is much slower than the overall mutation rate. Considering the rate of mutations that are not strongly detrimental, Lande (1995*a*) concluded that "effective population size" will need to be on the order of 5,000, rather than 500, to ensure long-term viability. Given that total population sizes of mammals are usually several-fold larger than effective population sizes (Frankham, 1995*a*), the long-term genetic risks to small, isolated populations probably have been substantially underestimated in most conservation programs.

Recent theoretical models (Lande, 1994; Lynch and Gabriel, 1990) demonstrate yet another process by which the long-term viability of small populations might be threatened by genetic drift. In small populations (on the order of hundreds of breeding individuals), changes in allele frequencies are more strongly determined by random genetic drift than by natural selection, except when selection is strong (Kimura, 1983; Lacy, 1987). Therefore, deleterious mutations occasionally become fixed in a small population, due to chance drift, replacing more adaptive alleles. As deleterious mutations accumulate, population size may decrease, causing genetic drift to become even more rapid. This feedback has been termed mutational meltdown. The time course of mutational meltdown is on the order of hundreds of generations, however, so it would not be a significant contributor to recent and rapid declines of populations.

Evidence for Effects of Genetic Variation on the Viability of Populations of Mammals

The possibility that decreased genetic variation can impact individual and population fitness does not necessarily mean that lack of genetic variation is a causal factor in population declines and extirpation. First, the inbreeding depression observed in laboratory animals and domesticated livestock might not be generalizable to natural populations. Second, populations that remain small may become adapted to low levels of genetic variation. Third, because of habitat destruction, direct killing by humans, replacement by exotic competitors, and the demographic instability inherent in small numbers, natural populations may rarely persist at small numbers long enough to be threatened by genetic processes (Caughley, 1994; Lande, 1988). Finally, mechanisms maintaining and restoring adaptive variation may be sufficient to preserve adequate variation for adaptive evolution even in rather small populations (Lande, 1975, 1995*b*). Each of these points will be addressed below.

Does inbreeding depression affect mammals in natural habitats?—Inbreeding depression has been assessed mostly in domesticated livestock and laboratory organisms, with relatively few studies on inbreeding in wildlife populations or recently established captive populations of wild species (Lacy, 1993*a*; Lacy et al., 1993). Domesticated and laboratory populations have had their genomes considerably modified by centuries of artificial selection, most have been specifically selected for viability under inbreeding, and they are studied in highly modified and benign habitats. Therefore, it is possible that effects of inbreeding on such populations might be different from effects on wild populations in natural habitats. House mice (*Mus domesticus*) are believed to inbreed frequently in the wild

(Selander, 1970; Smith, 1993), and extensive inbred lines have been developed for biomedical research, so it might be expected that they would be less affected by inbreeding than are most mammals. Yet, much of what is known about the deleterious effects of inbreeding in mammals comes from studies on house mice (Falconer, 1989). Production of inbred mice entails losses of many of the lines (Bowman and Falconer, 1960; Lynch, 1977), established inbred lines still show strong increases in fitness when outcrossed (Falconer, 1989; Wright, 1977), and renewed inbreeding of heterogeneous stocks created by crossing previously inbred lines results again in depression of a wide variety of fitness traits (Deckard et al., 1989).

Experiments on plants (Dudash, 1990) and animals (Jiménez et al., 1994) indicate that the deleterious impacts of inbreeding are more severe in more natural environments than in controlled laboratory or agricultural settings. However, Shields (1982, 1993) argues that natural populations might be much less impacted by inbreeding than would be suggested by laboratory studies. With respect to wild populations of vertebrates, Shields (1993:169) states "in every case with sufficient evidence there is either no inbreeding depression or in a few cases even significant inbreeding enhancement." Indeed, a few studies have purported to show (or have been claimed by others to show) that a natural population of mammals was unaffected by inbreeding (Bulger and Hamilton, 1988; Hoogland, 1992; Rood, 1987). However, in each case, the sample size examined was inadequate to allow detection of inbreeding depression, even if it were more severe than is typically reported in experimental populations.

It is important to recognize, especially when samples are small and confounding factors are difficult to control, that the lack of statistical evidence for inbreeding depression is not equivalent to evidence for the lack of inbreeding depression. For example, Bulger and Hamilton (1988) reported that the mortality among infants born in baboon troops in which the dominant male had remained in his natal troop was similar to the mortality of infants born in troops into which the dominant male had immigrated (5 of 20 inbred versus 4 of 27 non-inbred deaths). Yet, guessing that nondispersing males were on average breeding with half-siblings, the 12% lower survival of their progeny reported in the study, while not approaching statistical significance, would be comparable to the typical depression in survival of progeny from half-sibling matings in domesticated and experimental populations of mammals (Falconer, 1989). Another study on a natural population of baboons indicated significant damaging effects of inbreeding, albeit also with small samples (Alberts and Altmann, 1995). Hoogland (1992) analyzed a much larger dataset, but because prairie dogs avoid close inbreeding most of his inbred matings were between relatives more distant than first-cousins (inbreeding coefficient $F < 0.0625$). There were too few matings between closer relatives to allow statistical detection of any impacts of inbreeding. To achieve a 50% probability of detecting a difference in survival (D) between inbred and non-inbred animals at a significance level of $P < 0.05$ requires samples as large as $2/D^2$ for each of the two groups. Thus, detecting a 1% decline of survival for each 1% increase in inbreeding requires samples of >128 half-sib matings, 500 first-cousin matings, or 8,000 second-cousin matings, as well as comparable numbers of non-inbred matings. These numbers make clear that the demonstration of effects of inbreeding on wild populations will continue to be difficult. With samples attainable in wild populations, we usually will not be able to detect fitness differentials of a few percent. Yet a few percent decline in demographic rates is sufficient to turn many healthy populations of wildlife into declining ones.

Contrary to suggestions that the existence of some inbreeding in natural populations indicates that inbreeding depression may

not be a real phenomenon in the wild (Shields, 1993), measuring the degree of inbreeding in a natural population is not the same as testing for inbreeding depression. There are costs to dispersal that might make absolute avoidance of inbreeding counterproductive, and harmful inbreeding could result from the inability of individuals to distinguish kin or the inability to disperse randomly (Smith, 1993). Because many habitats have been severely reduced and fragmented, some species may have dispersal behaviors that are no longer optimal for the landscapes in which they find themselves, or they may simply be unable to avoid inbreeding. The naked mole rat (*Heterocephalus glaber*) is a particularly interesting mammalian species with regard to inbreeding. DNA-fingerprinting data indicate that colonies of mole rats are highly inbred (Reeve et al., 1990), presumably as a result of the difficulty in dispersing and entering or establishing new colonies. Clearly, this high level of inbreeding has not been frequently fatal to colonies, and the species may have evolved a genome that is relatively unaffected by inbreeding. It would be of considerable interest to know whether more heterozygous colonies (e.g., those more recently established) have greater fecundity and survival than those colonies that have accumulated higher levels of inbreeding.

In spite of the difficulty of demonstrating inbreeding depression in the wild, several recent studies have demonstrated effects of inbreeding on mammals in natural habitats. Stockley et al. (1993) studied a population of common shrews (*Sorex araneus*) in England, using multilocus DNA fingerprinting to identify pairs that were closely related. They found that more inbred shrews tended to be smaller at weaning and less likely to survive to maturity than more outbred individuals. Jiménez et al. (1994) released into a woodland habitat 367 *Peromyscus leucopus* produced by brother-sister matings ($F = 0.25$), and 419 mice produced by matings between non-relatives. Retrapping showed a more rapid loss of inbred than non-inbred mice.

Although the correlation between heterozygosity at a few sampled allozyme loci and overall heterozygosity across the genome is expected to be weak, a few studies of mammals have found significant associations between allozyme variation and fitness components. Cothran et al. (1983) reported a greater rate of twinning, higher maternal weight, and faster fetal growth in white-tailed deer (*Odocoileus virginianus*) that were heterozygous at more allozyme loci. Growth of horns is faster in more heterozygous bighorn sheep (*Ovis canadensis*), presumably giving them an advantage in competition for mates (Fitzsimmons et al., 1995). It is possible that the allozyme loci themselves were responsible for these fitness differences, but it is more likely that allozyme heterozygosity was serving as a marker for important variation at linked loci, or that allozyme variation was correlated with inbreeding and that the effects of inbreeding were manifest through actions of genes elsewhere in the genome. Many non-mammalian examples of effects of allozyme heterozygosity on fitness components are known, including some in which heterozygosity of the enzyme variants themselves has been shown to be responsible for the fitness benefits (Mitton, 1993).

Do natural populations of mammals become adapted to inbreeding?—If the impacts of inbreeding are primarily due to the expression of a genetic load of deleterious recessive alleles in the more homozygous inbred individuals, then a population that weathers several generations of inbreeding may become purged of this genetic load (Charlesworth and Charlesworth, 1987; Hedrick and Miller, 1992). Thus, some inbreeding may actually be beneficial to future viability of populations by improving the efficiency with which natural selection removes deleterious recessive mutations from the gene pool.

There are data suggesting that selfing plants become partly purged of their genetic

loads (Barrett and Charlesworth, 1991; Barrett and Kohn, 1991), and some data on human populations is suggestive that purging takes place (Bittles et al., 1991), but Lande and Schemske (1985) and Rao and Inbaraj (1980) present counter evidence to these two claims. Overall, however, there is as yet little evidence for purging of the genetic load through bouts of inbreeding in mammalian populations. For example, mammalian taxa that are endangered or known to have gone through bottlenecks (e.g., parma wallaby, *Macropus parma*; golden lion tamarins, *Leontopithecus rosalia*; Pere David's deer, *Elaphurus davidianus*; Eld's deer, *Cervus eldi thamin*; scimitar-horned oryx, *Oryx dammah*; Speke's gazelle, *Gazella spekei*) have genetic loads as great as the common species listed in a survey of 40 populations of mammals by Ralls et al. (1988). Templeton and Read (1983, 1984) reported a reduction in genetic load in a captive population of Speke's gazelle when measured in the progeny of inbred parents, but their statistical approach was flawed. The small sample correction they applied to survival at each level of inbreeding causes a bias toward lower estimates of genetic load. Because the samples for animals with inbred parents were smaller than the samples for animals with non-inbred parents, this bias could have created the appearance of reduced inbreeding depression. In addition, they forced the regression lines of viability against inbreeding to have a y-intercept equal to the weighted average of the intercepts estimated for inbred and non-inbred parents. This exaggerated the difference in slopes and greatly reduced the estimated error variances of the slopes. Their analysis would be appropriate only if it could be assumed that the survival of non-inbred progeny did not change over time and was unaffected by the inbreeding level of the dam, and if the intercept were known without error. These assumptions are not warranted. When the lines are not forced to have a common fixed intercept, the difference between the genetic loads measured in progeny of inbred versus non-inbred parents becomes small and non-significant, even with the bias of the small-sample correction. More appropriate analyses of the now larger pedigree of Speke's gazelle do not support the claim for purging (Ballou, 1995; Willis and Wiese, in press). Ballou (1995) found evidence for only slight amelioration of the effects of inbreeding through generations of captive breeding in zoo populations. While most species showed a shift in the expected direction of lower genetic loads, significant ($P < 0.05$) purging was seen in just one of 25 species.

The recovery of European bison (*Bison bonasus*) from a bottleneck of 17 animals earlier this century often is cited as evidence for the ability of natural selection to purge populations of their genetic load and allow recovery in spite of low genetic variation (Simberloff, 1988; Templeton and Read, 1983). Although Slatis (1960) reported low inbreeding depression in the post-bottleneck herd of bison, more recent analyses show that significant inbreeding depression still occurs (Lacy et al., 1993), and that there has been no significant purging of the genetic load in the pedigree of the captive population (Ballou, 1995).

In a controlled breeding experiment designed to test the hypothesis that small natural populations have become partly adapted to inbreeding, Brewer et al. (1990) found that insular populations of *Peromyscus* had genetic loads at least as great as the larger central populations. Ribble and Millar (1992) compared the effect of full-sib matings in a stock of *Peromyscus maniculatus* that had become moderately inbred over 20 generations of laboratory breeding to the effect of inbreeding in a recently established stock. The recently established stock showed significant inbreeding depression; the previously inbred stock did not. Their data are suggestive of prior purging in the long-established laboratory stock. However, small samples precluded statistical significance of even sizable inbreeding depression, as the full-sib matings in the older

stock produced 21% fewer progeny than the control matings in this stock. Moreover, the recently established stock cannot be considered to be a control group against which to compare inbreeding depression in the older stock, because they were derived from different source populations. Inbreeding depression in the base population from which the older stock had been derived may have been no different than the inbreeding depression observed after 20 generations of selection for productivity.

Unless the genetic load consists of a few highly deleterious recessive alleles, selection is inefficient at purging the genetic load, and inbreeding is more likely to result in extinction than in removal of the genetic load (Hedrick, 1994). If the impacts of inbreeding are due to numerous weakly deleterious alleles, alleles that are damaging only in some environments, or alleles maintained by heterozygote advantage, then genetic drift often will lead to fixation of deleterious alleles during population bottlenecks. Technically, if deleterious alleles are fixed in a population, reducing its average fitness but perhaps not causing extinction, then the genetic load has been removed because no genetic variance in fitness remains. Further inbreeding may not cause further harm, because there is no scope for getting worse.

Does variation affect the viability of natural populations?—Northern elephant seals (*Mirounga angustirostrus*) recovered to large populations even after they apparently lost much of their genetic variation during a population bottleneck (Bonnell and Selander, 1974), and populations of cheetahs (*Acinonyx jubatus*) persisted with low levels of variation (O'Brien, 1994*a*; O'Brien et al., 1983, 1985). These examples sometimes are cited as evidence that losses of genetic variation might be unimportant to population viability (Caro and Laurenson, 1994; Simberloff, 1988). However, it is not known how many comparable populations went extinct following such bottlenecks.

In questioning the importance of genetics to conservation, Caughley (1994:239) stated "no instance of extinction by genetic malfunction has been reported." Similar claims have been made by others (e.g., Caro and Laurenson, 1994; Harcourt, 1995; Lande, 1988). Unfortunately, evidence is accumulating that some small and isolated populations of mammals have been depleted of genetic variation and as a result are suffering decreased fitness. The population of lions isolated in the Ngorongoro Crater in Tanzania was reduced to just 10 animals in 1962, with seven subsequent immigrants. The descendant population has less genetic variation, a higher rate of sperm abnormalities, and lower sperm motility than the nearby population in the Serengeti (Packer et al., 1991). Similarly, the remnant population of Asian lions in the Gir Forest has relatively little genetic variation, low sperm counts, and a high rate of deformed spermatozoa (O'Brien et al., 1987*a*; Wildt et al., 1987*b*). Florida panthers (*Puma concolor coryi*) have been reduced to about 30 individuals in the remnant population in southern Florida, and parent-offspring breeding has been documented. Compared to the larger populations of the species in the western United States, Florida panthers have low genetic variation, poor sperm quality, frequent cryptorchidism, and high susceptibility to microbial parasites (O'Brien, 1994*a*; Roelke et al., 1993). Cheetahs may have recovered from one or more ancient bottlenecks (O'Brien et al., 1987*b*) and may suffer presently from numerous non-genetic threats (Caro and Laurenson, 1994; Merola, 1994), but they also have a high rate of defective sperm (Wildt et al., 1987*a*), appear unusually susceptible to diseases (O'Brien, 1994*a*; O'Brien et al., 1985), have high fluctuating asymmetry (Wayne et al., 1986), but see Willig and Owen (1987) and the rebuttal by Modi et al. (1987), and suffer increased mortality of juveniles when inbred further in captivity (Caughley, 1994). Further discussion of the continuing debate on the cheetah controversy are provided by Hedrick et al. (1996), Merola (1994), and O'Brien (1994*b*).

The concentration of examples of damaging effects of loss of genetic variation among the large cats might be because large solitary carnivores are likely to be more quickly impacted by fragmentation and loss of habitat than are species with greater population densities, or it might simply be a consequence of the focus on the conservation genetics of felids by O'Brien and his collaborators versus the lack of such attention to other taxa. Similarly, the frequency of reports of impacts on fertility of males might indicate a particular vulnerability to inbreeding, or it might simply reflect that quality of semen is more easily monitored in natural populations than fecundity of females, resistance to disease, feeding efficiency, social dominance, or other components of fitness.

Caughley (1994) questioned the relevance of measures of genetic variation in natural populations, pointing out that there are not data to show a correlation between equilibrium heterozygosity and individual or population fitness. Equilibrium levels of genetic variation result from the balance between the forces of mutation, genetic drift, migration, and various types of selection (Wright, 1969); low-equilibrium heterozygosity can occur for any of a number of reasons, and the amount of genetic variation observed in apparently healthy natural populations varies widely (Nevo, 1978). Thus, it would not be justified to assume that populations with lower equilibrium levels of genetic variation are less viable.

Caughley (1994) apparently overlooked, however, that low genetic variation resulting from a bottleneck is not in evolutionary equilibrium. Concern about genetic variation is appropriate when there is evidence that variation has been reduced below historic equilibrium levels. The evidence that variation is depressed is admittedly indirect, but comes from comparisons to similar taxa (cheetahs and lions—O'Brien, 1994*a*, Florida panthers—Roelke et al., 1993, elephant seals—Hedrick, 1995; Hoelzel et al., 1993), from analytical calculations (elephant seals—Hedrick, 1995, black-footed ferrets *Mustela nigripes*—Lacy and Clark, 1989), from simulation models (Florida panthers—U. S. Seal and R. C. Lacy, in litt., elephant seals—Hoelzel et al., 1993), or from documentation of matings between close relatives (Florida panthers—Roelke et al., 1993). Unfortunately, in none of these cases do we have a direct measure of the genetic variation that was present before the observed or hypothesized bottleneck. Similarly, although we have some cross-populational comparative data for the big cats, we do not have measures of fitness in these populations prior to the bottlenecks.

While none of the above taxa has yet gone extinct, and all suffer more from nongenetic threats than genetic ones, Berger (1990) found that populations smaller than 50 bighorn sheep went extinct within 50 years, whereas populations of >100 persisted for >70 years. He speculated that loss of genetic variation in smaller populations contributed to the more rapid population extinctions. Outside of the Mammalia, there is evidence that inbreeding depression was a contributing proximate cause of the extinction of the Swedish population of middle spotted woodpeckers (*Dendrocopos medius*; Pettersson, 1985) and the heath hen (*Tympanuchus cupido*; Simberloff, 1988). While the evidence of genetic problems in these cases is circumstantial, it is not true that "no instance of extinction by genetic malfunction has been reported" (Caughley, 1994:239).

Assessing the impacts of inbreeding on population viability can be difficult because usually only one or a few components of fitness are monitored (Hedrick and Miller, 1992; Shields, 1993). English great tits (*Parus major*) showed reduced nesting success when inbred (Greenwood et al., 1978). An island population of the same species in The Netherlands had a reduced hatching rate when inbred, but also greater nestling survival and consequently no difference in recruitment into the breeding population (van Noordwijk and Scharloo, 1981). A series of

studies of natural populations of desert topminnows (*Poeciliopsis*) demonstrated multiple impacts of genetic variation on population viability. Loss of genetic variation during population bottlenecks caused slower growth, lower fecundity, greater fluctuating asymmetry, high frequency of developmental abnormalities, poorer survival under stressful conditions (hypoxia), higher parasite loads, and lower interspecific competitive ability. These multiple impacts were reversed when genetic variation was restored via outcrossing (Quattro and Vrijenhoek, 1989; Vrijenhoek, 1994). Contrary to claims that "it has yet to be shown that inbreeding depression has caused any wild population to decline" (Caro and Laurenson, 1994:485), population levels of the topminnows responded as expected when genetic variation was lost and then restored.

It will be difficult to obtain data on sufficient numbers of populations of any species in the wild to allow determination of the functional relationship between inbreeding and population extinction. To examine this relationship, Frankham (1995*b*) analyzed the effect of inbreeding on population survival in four studies using 60–120 experimental populations of *Mus* and *Drosophila*. In each case, he found that rates of population extinction were strongly elevated by progressive inbreeding within the populations. Moreover, he found that the relationship was a threshold effect. Rates of extinction remained low through early generations of inbreeding, but increased sharply after several generations of inbreeding. This was especially true of the populations of *Mus* in which only three of 60 populations survived. Frankham (1995*b*:797) appropriately cautions: "There may be little warning of impending extinction due to inbreeding in wildlife, especially with species that are not intensively monitored."

Is evolutionary potential constrained by extant genetic variation?—The limitation of adaptive potential by reduced levels of genetic variation has been demonstrated with respect to the response by experimental populations to selection for specific traits (Wright, 1977), and is a fundamental principle of modern agricultural genetics. Response to selection is one means of measuring the heritable variation in a population (Falconer, 1989). One of the arguments made for the preservation of natural biodiversity is that the genetic variability contained in wild populations of domesticated species is an essential resource needed to bolster the resilience of domesticated strains to disease and other stresses, and to allow rapid development of new, advantageous traits.

While the dependency of response to selection on genetic variation has been demonstrated theoretically and experimentally, it is much more difficult to document that natural populations have gone extinct or been locally extirpated because of a lack of adaptive potential. Yet, every extinction is an example of a population not adapting rapidly enough to a changing environment, whether that change is the presence of new predators or disease, the disappearance of preferred food resources, or any other ecological threat. Thus, debates about whether genetic variation is relevant to population viability are moot. From a conservation perspective, however, the more pressing question is whether recent reductions in levels of genetic variability in natural populations, due to human-caused destruction and fragmentation of habitats, has contributed to accelerated rates of extinction.

Although mutational meltdown is unlikely to be an imminent threat to any population, it also is unlikely that we would be able to detect the process until it had considerably and irreversibly degraded population fitness. Gilligan et al. (in press) found no evidence of accumulation of mutations in small populations of *Drosophilia* that had been maintained in the laboratory for 45 generations. It is not clear to me how we could demonstrate that a population decline in nature was due to the accumulation of deleterious alleles and loss of previous ad-

aptations, rather than to degradation of habitat or introduction of threats to which the population had never been adapted.

Population-Viability Analysis and the Interaction Between Genetic and Non-Genetic Threats

Recently, analytical and simulation models have been used to estimate the probability of extinction and the likely time to extinction. Such population-viability analyses commonly examine both deterministic impacts, which depress mean population growth (the driven declines of Caughley, 1994), and stochastic or probabilistic processes that increase variation in size of populations (Boyce, 1992; Hedrick et al., 1996; Lacy, 1993/1994; Shaffer, 1981). The deterministic factors include those that are the familiar and all-too-common threats to biodiversity, such as over-harvest, habitat destruction, and ecological replacement by introduced competitors. The contribution of stochastic processes to destabilization of populations only recently has been recognized (Simberloff, 1988). These stochastic processes include genetic drift, random demographic fluctuations due to the uncertainty of mating and surviving in small populations, spatial and temporal variation in environmental conditions, and local catastrophes such as disease epidemics and severe weather.

The loss of genetic variation should not be viewed in as an independent threat to population viability, but in the context of interactions with non-genetic threats (Gilpin and Soulé, 1986). Genetic instability and decline can cause demographic instability and decline, and greater susceptibility to environmental fluctuations and catastrophes. Demographic fluctuations and catastrophe-caused bottlenecks can in turn cause more genetic instability and depletion of genetic variation. Using Leslie-matrix-projection models that incorporated inbreeding depression, Mills and Smouse (1994) demonstrated the importance of considering the joint and interacting impacts of genetic and other factors on population viability. Thus, a distinction between genetically minimum viable populations and demographically minimum viable populations (Reed et al., 1993; Shaffer, 1981) is inappropriate.

The interactions among destabilizing processes is easier to model than to study in the field. The cumulative effects of feedbacks between genetic variation, demographic rates, and environmental effects can be simulated by computer (Lacy, 1993*b*). It is much more difficult to determine, for example, whether high mortality due to disease is attributable to increased environmental stresses, lowered variability of genes of the immune system, or both. The greater losses of inbred *Peromyscus leucopus* in the release-recapture study by Jiménez et al. (1994) were not directly genetic deaths. The inbred mice had good viability in the lab, but suffered losses in the woodland habitat due to perhaps greater predation, disease, energy stress, or lower social dominance in competition for territories; all non-genetic processes. The practice of excluding deaths due to accident, disease (Slatis, 1960), predation, infanticide (Bulger and Hamilton, 1988), or abandonment by parents (Caro and Laurenson, 1994) from determinations of the effects of inbreeding mistakenly assumes that inbreeding depression is manifested only in obvious congenital defects of development. The effects of genetic variation on the viability of individuals and populations is through demographic and ecological processes. Accordingly, demographic rates assessed by field biologists and the response of populations to environmental change are each modified by genetic variation both within individuals and within populations, as was illustrated by the lower survival of inbred song sparrows during a severe winter (Keller et al., 1994).

Directions for Future Research

In spite of the abundance of data on the importance of genetic variation to the viability of domesticated and laboratory populations of mammals, or perhaps be-

cause the experimental data are so compelling, relatively few data have been collected on the effects of inbreeding on wild populations in natural habitats. To confirm that lab models are appropriate models for populations of wildlife, and to determine how the effects of changes in genetic variation interact with the multiple stresses faced by animals in the wild, there is a need for more experimental studies examining the role of genetic variation on multiple aspects of fitness of individuals in natural habitats. Although the experiments would be even more difficult, there is a need also for direct tests of the effects of genetic variation on demographic performance and stability, and on rates of extinction, of populations in their natural environments. Anecdotes about populations that survived or did not survive depletion of genetic variation are not adequate; we need controlled experimental tests that can be analyzed statistically.

We need to broaden and deepen our examinations of the effects of inbreeding. Higher infant mortality has been demonstrated in many taxa of mammals, but we have few data on acquisition of mates, fecundity, resistance to disease, physiological response to stress, social dominance, longevity, or other components of fitness. Data on *Drosophila* and lab mice suggest that some of these components might be more influenced by genetic variability than is survival (Falconer, 1989; Hedrick and Miller, 1992; Miller and Hedrick, 1993; Wright, 1977). The mechanisms of inbreeding depression need to be explored at a more proximate level. Is poor reproduction of inbred animals due to inability to acquire mates, infertility, embryonic or fetal death, poor development of neonates, or lack of adequate parental care? Is higher mortality due to metabolic disorders, developmental defects, susceptibility to diseases and parasites, inability to obtain prey or to avoid becoming prey, or social conflicts?

The underlying genetic mechanisms of inbreeding depression require elucidation. Experimental genetics has shown that inbreeding depression can have multiple bases, including expression of deleterious recessive alleles, loss of heterozygote advantage or flexibility, and disruption of the coevolved genetic system. Theoretical work has shown that these different mechanisms have different evolutionary consequences, but how much each of these contributes to the genetic loads of mammalian populations has not been determined. Why do different populations of mammals have different equilibrium levels of variation? What causes populations to respond differently to inbreeding? Is the genetic load of small, isolated populations purged in a self-correcting evolutionary process, or does further inbreeding beget further inbreeding depression?

Recognizing that genetic variation can impact individual fitness and population viability, there is a need for closer monitoring of genetic variation and its effects in a number of populations of wildlife. Such data will allow us to build an understanding of the frequency and ways in which changes in genetic variation are contributing to losses of biodiversity at the higher levels of populations, species, interdependent communities, and ecosystem functions. Only through genetic monitoring of threatened populations can we determine when genetic intervention would be an important component of a conservation strategy, and when it is not. Although acute genetic changes that imminently threaten populations require immediate corrective actions, we also need to understand better and manage the long-term, cumulative changes to and impacts of genetic variation. Often the consequences of losses of variation will be delayed considerably from when the genetic changes occurred.

In theoretical work, experimental studies, and field monitoring, there needs to be greater consideration and examination of the many interactions between genetic, demographic, and environmental processes. For example, population-viability-analysis models presently in use never consider

more than a few of the many possible effects of genetic variation on population viability, and often do not consider genetic effects at all (Frankham, 1995*c*).

Conclusions

An initial flurry of books and papers in conservation biology highlighting the potential importance of genetic variation to population viability was followed by a backlash of papers doubting the role of genetic variation in the persistence of natural populations. Recent theoretical analyses, experimental verifications of theory, and field studies on natural populations (Frankham, 1995*c*) are now providing evidence to support even the more pessimistic conclusions of earlier authors.

I have been unable to find statistically defensible evidence showing that any mammalian species is unaffected by inbreeding. Moreover, endangered species seem no less impacted by inbreeding, on average, than are common taxa. More research is needed to determine if, and under what circumstances, populations could be purged of their genetic loads, but data do not yet allow us to presume that any mammalian population will emerge from a bottleneck with constant or recovered fitness and a greater ability to withstand future inbreeding.

Other processes that involve genetic-demographic-environmental interactions have been hypothesized to threaten population viability. The depletion of genetic variability will slow adaptive evolution, and genetic drift in small populations can lead to accumulation of maladaptive traits. Both of these processes occur so slowly that their effects on population viability would be hard to recognize. Their impacts would be seen in a reduced ability to survive in present environments and to adapt to new environments, and thus would be intertwined with non-genetic threats. While the impacts of losses of genetic variation might be slow, they also would be insidious. Once the impacts are sufficiently large as to be easily recognized, they also would be difficult to reverse. Exchange with other populations can restore variation, but only with the risk of losing genetic variants that had been unique to the local population. When a population is the only representative of its taxon, or exchange with other populations is not possible, then reversal of genetic depletion would come about only if the population can recover to large numbers and survive the 100s–1000s of generations needed for new mutations to restore variation.

The effects of genetic variation on population viability have received extensive theoretical treatment and experimental verification. Yet, few conservation efforts for endangered mammalian taxa recognize that ecological and anthropological threats to persistence could be magnified by interactions with the effects of depleted genetic variation. One notable exception is the recovery program of the Florida panther. The evidence for inbreeding, depletion of genetic variation, and their consequences on fitness was too great to ignore, and led to actions to restore genetic variability through reestablishing gene flow with western populations of puma by selective translocations (U. S. Seal, in litt.).

Because the contribution of genetic variation to population viability is fundamentally an interaction with physiological, behavioral, and ecological processes, conservation efforts need not necessarily target directly the components of the system that have been disrupted. A population low in variation is likely to be less resilient to other threats and less adaptable. Thus, the most productive management options might involve better preservation of natural habitats, more aggressive control of introduced exotics, and lower limits on harvest, in addition to or instead of genetic management. For example, even if there is a genetic basis to species vulnerability in the cheetah (O'Brien et al., 1985), reducing predation, eliminating disturbance by humans, and controlling disease might be effective at re-

versing population decline. The decimation of biodiversity has a singular predominant cause, the over-abundance of humans, but it is a multi-faceted problem simultaneously impinging on many levels of biotic organization. Stemming losses of biodiversity will require a diversity of conservation actions applied at many levels.

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