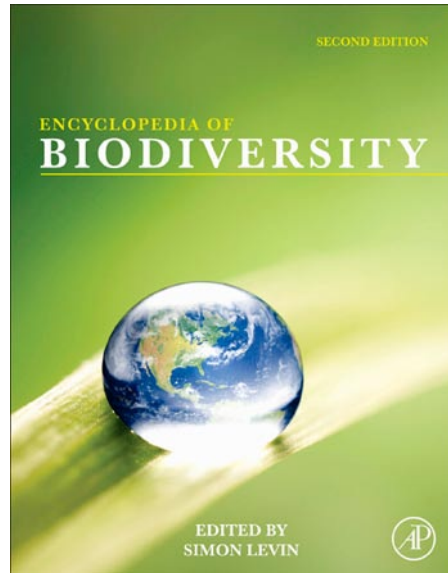


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Ralls Katherine, Frankham Richard, and Ballou Jonathan D. (2013) Inbreeding and Outbreeding. In: Levin S.A. (ed.) Encyclopedia of Biodiversity, second edition, Volume 4, pp. 245-252. Waltham, MA: Academic Press.

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Inbreeding and Outbreeding

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Published by Elsevier Inc.

Glossary

Allele One of two or more different forms of a gene.

Coadapted gene complexes Chromosomes, loci, or genes that are adapted to function well together.

Effective population size (N_e) Size of the ideal population used in population genetics theory that would have the same rate of increase in inbreeding or decrease in genetic diversity as the actual population under study.

Genetic drift Changes in the frequency of alleles within a population over time due to the random process of passing alleles from parents to offspring.

Lethal equivalent Group of mutant alleles that would cause an average of one death if homozygous; for example, one lethal equivalent might represent two mutant alleles, each with a 50% probability of causing death, or any other combination of mutant alleles that would produce an average of one death.

Outcrossing A mating system in which individuals breed with other individuals that are not related to them.

Selection differential(s) A measure of the intensity of selection on a phenotypic character.

Inbreeding

Inbreeding is the production of offspring from the mating of individuals related by ancestry. This includes self-fertilization, brother–sister, parent–offspring, and cousin matings, as well as matings between more distant relatives. Inbred offspring are more likely to inherit recent copies of the same allele from both parents, that is, alleles that are identical by descent (derived from a common ancestor of both the parents). Two alleles that are identical by descent are homozygous, but not all homozygous alleles are identical by descent. A homozygous individual has two alleles at a locus that are functionally similar. However, these two alleles may or may not be identical by descent.

The inbreeding coefficient (usually symbolized by F) of an individual is the probability that the individual has two alleles at a locus that are identical by descent. Because F is a probability, it ranges from 0 for noninbred individuals to 1 for completely inbred individuals. For example, the inbreeding coefficient of an individual resulting from self-fertilization is $1/2$ and that for an individual resulting from a parent–offspring or brother–sister mating is $1/4$.

Because the process of inbreeding increases the likelihood that two alleles in a genotype are identical by descent, inbreeding increases the frequency of homozygotes, and reduces the frequency of heterozygotes in direct proportion to the inbreeding coefficient. A population with an average inbreeding coefficient of 10% will have 10% less heterozygosity than a similar noninbred population.

Inbreeding Depression

Natural populations contain low frequencies of deleterious recessive mutations (due to the balance between their occurrence by mutation and removal by selection) that are normally found as heterozygotes and are thus not expressed. Inbreeding

increases the probability of individuals inheriting these recessive alleles as homozygotes, thus enabling the expression of their deleterious effects. Consequently, in most populations of animals and plants, inbreeding results in a decline in reproduction and survival (reproductive fitness), which is called inbreeding depression.

Another cause of inbreeding depression is overdominance. Different genotypes have different effects on fitness. In some traits or loci, even though alleles are not recessive, the homozygous genotypes (e.g., AA and aa) are, on average, less fit than the heterozygous genotype (Aa). These traits or loci are referred to as overdominant or showing heterozygote advantage. As inbreeding decreases the proportion of the fitter heterozygotes in a population, the average fitness (e.g., reproduction and survival) of the population declines, resulting in inbreeding depression.

Studies show that most inbreeding depression is due to the accumulation of deleterious recessive mutations, rather than overdominance.

Evidence for Inbreeding Depression

The deleterious effects of inbreeding were known long before the discovery of the underlying Mendelian mechanisms that cause it. In the nineteenth century, Charles Darwin clearly documented inbreeding depression based on studies in 57 species of plants, as well as the experience of livestock breeders. These early observations were amply confirmed by subsequent studies. There is now extensive evidence for inbreeding depression in laboratory and domestic animals and plants, as well as considerable evidence for inbreeding depression in wild animals and plants. Many studies on inbreeding were massive, involving large numbers of animals over many years, and the literature is extensive. For example, Sewall Wright's classic experiments on inbreeding in guinea pigs resulted in the production of 29,310 inbred and 5105 control young from 1906 to 1924. Only the five most vigorous inbred lines survived to the

end of the experiments; 30 other inbred lines went extinct or declined so severely that Wright discontinued breeding them before the end of the experiment. Nevertheless, the surviving inbred guinea pigs were consistently inferior to the controls in number of young born, percentage of young born alive and raised to 33 days, and weight at 33 days.

Inbreeding and selection have been used to fix desirable traits in modern breeds of livestock. However, reduced fertility was a major problem during the early periods of inbreeding and the inbred lines were repeatedly outcrossed to restore vigor and fertility. The North Central regional dairy cattle-breeding project (involving Iowa, Michigan, Minnesota, Missouri, Ohio, South Dakota, and Wisconsin), begun in 1947, is an example of the many extensive studies on inbreeding in livestock. This study found that inbreeding usually increased juvenile mortality and decreased milk yield, fat yield, growth, and reproductive performance.

Inbreeding depression is also well known in zoo animals. For example, in the early 1980s, scientists at the National Zoo found that juvenile mortality was higher in inbred than in noninbred offspring in 41 of 44 populations of mammals in zoos, including many primates, antelopes, and deer, as well as a variety of smaller mammal species (Figure 1). On average, the progeny of father–daughter and brother–sister matings suffered a 33% reduction in juvenile survival compared with outbred offspring. However, the severity of inbreeding depression varied widely across species. Although inbreeding in zoo animals usually results in less vigorous and fertile

individuals that appear phenotypically normal, it is also responsible for some genetic diseases in captive populations, including blindness in wolves and dwarfism in California condors. Zoo populations are now routinely managed to avoid inbreeding.

Evidence for inbreeding depression in natural environments has been reported in many species (Keller and Waller, 2002). A review of the literature on inbreeding effects in wild vertebrates and plants found that 90% of 157 data sets showed inbreeding depression, indicating that species frequently exhibit moderate to high levels of inbreeding depression under natural conditions (Crnokrak and Roff, 1999). Species showing inbreeding depression include mammals (golden lion tamarins, lions, native mice, shrews, and Soay sheep), birds (greater prairie chicken, Mexican jay, song sparrow, American kestrel, and reed warbler), fish (Atlantic salmon, desert topminnow, and rainbow trout), a reptile, a snail, an insect (butterfly), and many species of plants. Some studies have failed to find inbreeding depression, but these have typically been small studies or ones where paternity has not been verified. For example, no inbreeding depression was found in superb fairy wrens in Western Australia, but subsequent paternity studies using molecular genetic methods revealed that 64% of progeny were not fathered by the males to whom paternity had previously been attributed. Because inbreeding depression is so common, management of an unstudied outbreeding species should be based on the assumption that it will suffer reductions in reproductive fitness if it is inbred.

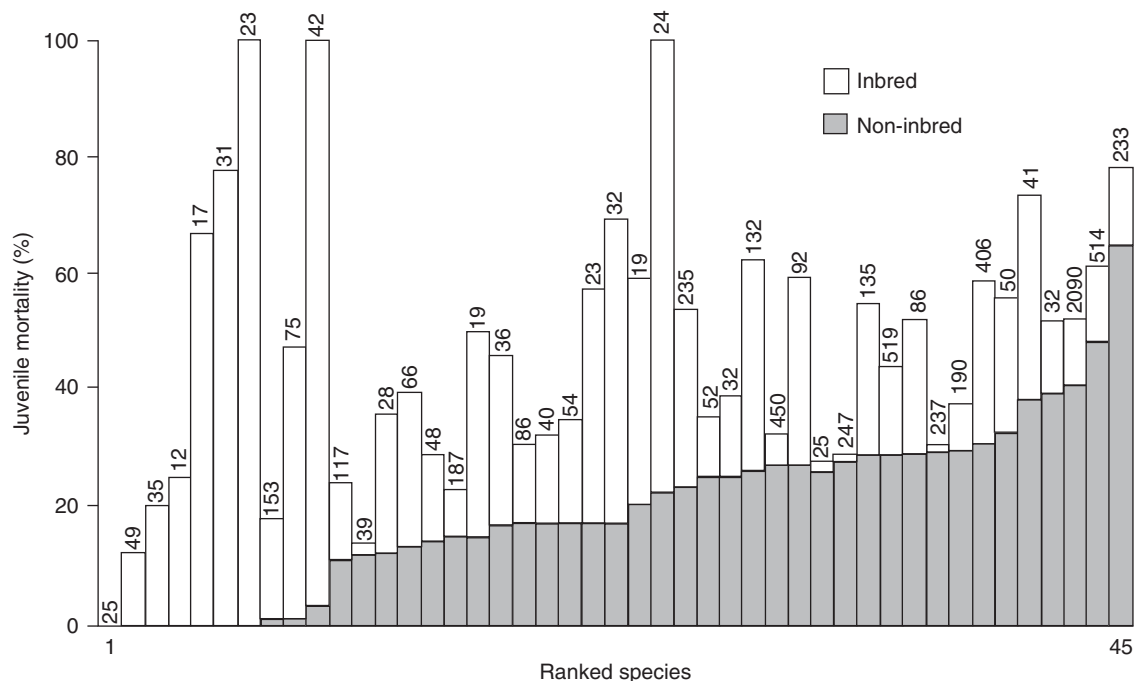


Figure 1 Juvenile mortality in inbred and noninbred young in 45 populations of mammals in captivity. Inbreeding levels were calculated with respect to the founders of the population for which the pedigree data were available. Most populations were founded with wild-caught animals but some were founded with animals from other zoos or of unknown origin. The noninbred category includes all animals with an inbreeding coefficient of 0 and the inbred category included all of those with an inbreeding coefficient greater than 0. For the larger species, all young surviving up to 6 months or more were considered to have survived. For the small species, one-half of the age at sexual maturity was used as the criterion age. Numbers above the bars indicate sample sizes for each species. Reproduced from Ralls K and Ballou J (1986) Captive breeding programs for populations with a small number of founders. *Trends in Ecology and Evolution* 1: 19–22.

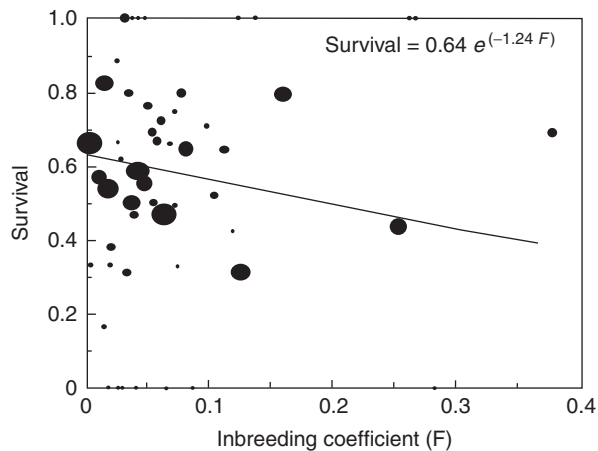


Figure 2 Decreasing juvenile survival with increasing inbreeding in golden lion tamarins (*Leontopithecus rosalia*). The proportion of offspring with a given inbreeding coefficient surviving to 7 days of age is plotted against the inbreeding coefficient. The sizes of the ovals represent the number of offspring available to estimate survival for each level of inbreeding. Large ovals represent samples of more than 50 offspring, medium ovals from 30 to 50, small ovals from 10 to 30, and tiny ovals from 1 to 10.

Factors Affecting the Severity of Inbreeding Depression

The degree of inbreeding depression in a population depends on the extent of inbreeding, the original frequency of deleterious recessives, the environment, and chance. Continued inbreeding results in greater inbreeding depression. For example, average levels of various components of reproductive fitness, such as juvenile survival in mammals (Figure 2) or grain yield in maize, theoretically decrease in a linear fashion as the inbreeding coefficient increases. The more deleterious alleles that were formerly masked by heterozygosity, the more severe the effects of inbreeding will be.

Severity of inbreeding depression also depends on the environmental conditions. Under benign conditions, many inbred plants and animals may survive. However, inbreeding depression is greater under more stressful conditions. Selfed progeny of one species of plant showed 75% inbreeding depression in the field but only 59% in garden plots and 53% in a greenhouse (Dudash and Fenster, 2000). A meta-analysis of 34 studies concluded that inbreeding depression was, on average, 69% more severe in stressful than in benign environments (Crnokrak and Roff, 1999).

Measuring Inbreeding Depression as Lethal Equivalents

The extent of inbreeding depression in survival of animals can be measured in terms of lethal equivalents. The number of lethal equivalents per gamete or individual can be calculated from the rate that survival decreases with increasing inbreeding. A study of 40 captive populations of mammals found an average of 4.6 lethal equivalents per individual for juvenile survival (Ralls *et al.*, 1988). Thus, each individual contained enough deleterious mutations to have an effect equivalent to slightly <5 single lethal mutations if they were homozygous. This figure is similar to estimates done in humans and birds.

However, the number of lethal equivalents varied widely across captive populations. Estimates of lethal equivalents based on survival to progressively older ages tend to increase. For example, wild song sparrows had 2.9 lethal equivalents based on survival from egg to independence but 5.4 lethal equivalents based on survival from egg to age at first breeding (Keller, 1998).

Inbreeding Depression in Total Reproductive Fitness

Most studies of inbreeding depression measure only one or a few components of reproductive fitness. However, since all traits have the potential to accumulate deleterious recessive alleles as a result of mutations, it is expected that all components of reproductive fitness will be subject to inbreeding depression. In animals, this includes offspring survival, number of offspring per female, male mating ability, sperm quality, disease resistance, and the quality and quantity of maternal care. Greater inbreeding depression for overall fitness than for its components has been found for old field mice, house mice, chickens, turkeys, Japanese quail, chukar partridges, and song sparrows. A meta-analysis estimated that wild populations have an average of about 12 lethal equivalents across the lifecycle (O'Grady *et al.*, 2006). In song sparrows, eggs with an average inbreeding coefficient of 0.25 have a 79% loss of fitness distributed over various life history stages: egg survival to breeding age was reduced by 49%, adult survival by 24%, and lifetime reproductive success of females by 48%. In the Takahē, an endangered New Zealand rail, inbreeding led to only small reductions in fitness at individual life history stages, the deleterious effects were cumulative across multiple life history stages and significantly reduced long-term fitness. Successful recruitment of second-generation offspring was reduced by 88% in full sib pairs compared to unrelated pairs.

Susceptibility to Inbreeding Depression

Inbreeding depression has a large chance (stochastic) element because of the random sampling of alleles during reproduction. Individuals with the same inbreeding coefficient, that is, the same probability of carrying alleles identical by descent, will differ in actual levels of homozygosity for any given trait, and, thus, will vary in the degree to which they experience inbreeding depression. Families and populations within a species carry different types and numbers of deleterious mutations and differ in their susceptibility to inbreeding depression. Differences in the extent of inbreeding depression among lineages within species are common, including mice, dairy cattle, fruit flies, and flour beetles and are to be expected in all outbreeding species. These differences contribute to the occasional success in establishing inbred lines or wild populations from the progeny of a small number of founding individuals even in species that typically show high levels of inbreeding depression. Differences among populations within species have also been reported. No differences in susceptibility to inbreeding depression among major taxonomic groups are known, but the relevant data are limited.

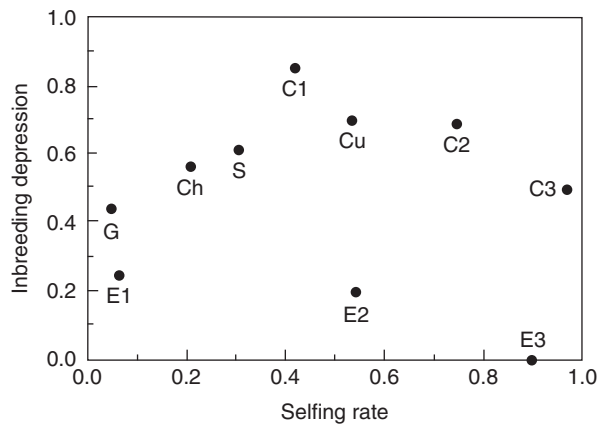


Figure 3 Relationship between inbreeding depression and the selfing rate in several species of herbaceous angiosperms. Species are G, *Gila achilleifolia*; Ch, *Chamaecrista fasciculata*; S, *Sabatia angularis*; Cu, *Cucurbita foetidissima*; C, *Clarkia tembloriensis*; and E, *Eichhornia paniculata*. For *Clarkia* and *Eichhornia*, data from three populations are plotted. Inbreeding depression for these species was measured in the lath house and glasshouse, respectively; all others were measured in the field. Reproduced with permission from original Figure 1.7 in Falk DA and Holsinger KE (1991) *Genetics and Conservation of Rare Plants*, 23 pp. New York: Oxford University Press, Inc.

Species that naturally inbreed (e.g., selfing plants and mole rats) occasionally show lower levels of inbreeding depression than naturally outbreeding species (Figure 3). Slow rates of inbreeding over long periods of time have the potential to select against and remove deleterious alleles (i.e., purge, see below) in these inbreeding populations, reducing their inbreeding depression. While these types of species often show less inbreeding depression, they still do exhibit detectable levels of inbreeding depression when inbred further.

Efforts to predict the susceptibility of specific populations or species to inbreeding depression have not been successful owing to the extremely stochastic nature of inbreeding depression.

Inbreeding and Outbreeding in the Wild

Only about 20% of species regularly self-fertilize and these tend to have life histories that strongly favor mating with relatives. For example, many are colonizing species in which the chances of successfully dispersing are much higher if only a single individual has to reach a new habitat. The restricted taxonomic distribution of selfing to some plants, terrestrial slugs, and marine invertebrates suggests that it is an evolutionary dead end.

The majority of species appear to be naturally outbreeding. Many plants that are pollinated by insects have elaborate morphological mechanisms that favor cross-pollination. In other plants, cross-pollination is ensured because the male and female gametes do not mature at the same time. Another mechanism that prevents self-fertilization is self-sterility, in which the pollen either fails to germinate on a stigma of its own flower or germinates, but does not develop sufficiently to fertilize the egg.

Many animals are also thought to avoid close inbreeding. Although a few mammals, notably the naked mole rat, normally mate with close relatives and are highly inbred, most mammals and birds rarely mate with close relatives. Sex differences in dispersal patterns often limit opportunities for inbreeding. In most mammals, males tend to disperse more frequently or farther than females, whereas the reverse is true in birds. Furthermore, many species can recognize close kin, and a variety of species such as jays, woodpeckers, mice, voles, ground squirrels, black-tailed prairie dogs, and chimpanzees are known to actively avoid mating with them.

Inbreeding Depression in Small Populations

Inbreeding is unavoidable in small, closed populations because all individuals eventually become related to each other. Inbreeding in a population of size N_e increases at a rate of $1/(2N_e)$, per generation with random mating. For example, in an effective population of size 10, there is a 5% increase in inbreeding per generation. Consequently, small, isolated populations that have existed for many generations are expected to show inbreeding depression. Small populations of plants, fruit flies, a rock wallaby, Florida panthers, and a snake have been found to suffer from inbreeding depression. However, inbreeding depression may not cause declines in population size. Reduced fecundity and survival will only cause a population to decline to extinction if the reproductive rate drops below the replacement level. Small (and large) populations can also suffer from reduced reproductive fitness because of declines in environmental quality.

Reduction of Inbreeding Depression

Inbreeding depression may be reduced by selection against deleterious alleles, which eliminates, or purges, them from the population. Purging has been documented in plants, mice, birds, and fruit flies, and during the development of inbred lines in a variety of species. Species that naturally inbreed should theoretically show less inbreeding depression than naturally outbreeding species because of the greater opportunity for selection against deleterious recessives.

Purging can reduce inbreeding depression, but it is unlikely to eliminate it. In captive mammals, selection led to a small reduction of inbreeding depression in neonatal survival in 15 of 17 populations. No trends in purging effects were observed in survival to weaning or litter size. The purging effects were not strong enough to be of practical use in captive breeding programs. Lacy and colleagues found that the effectiveness of natural selection in reducing inbreeding depression varied substantially in experiments with three subspecies of captive deer mice, probably due to different histories of inbreeding and selection in the wild prior to capture. Reviews on the effects of purging have pointed to a variety of effects from nil to moderate. In sum, it remains impossible to make strong predictions about the situations under which purging will occur and the probable magnitude of purging effects in individual populations. Therefore, genetic management programs for captive populations currently aim to minimize inbreeding

rather than undertake deliberate inbreeding in an attempt to purge deleterious alleles from populations.

Inbreeding depression can be completely reversed by outcrossing an inbred population to another unrelated population, either an outbred population or an independently inbred population. Crossing two highly inbred, but unrelated, populations results in an outbred population with a high level of heterozygosity and little inbreeding depression, since the high heterozygosity effectively masks the deleterious alleles that were being expressed in the inbred populations. This effect is termed "hybrid vigor." Partial recovery can be achieved by introducing unrelated individuals into an inbred population. Several wild populations showing signs of severe inbreeding depression have benefited dramatically from the introduction of unrelated individuals. Examples of such genetically stimulated recovery are known from a broad range of taxa including mammals (deer mice, gray wolves, Florida panthers), birds (prairie chickens), reptiles (adders), fish, and plants.

Inbreeding, Loss of Genetic Diversity, and Extinction

Many conservation biologists have been concerned that inbreeding and loss of genetic diversity in small populations will increase the risk of extinction. However, some researchers have questioned this view because of the difficulty of obtaining direct evidence that inbreeding contributes to the extinction of wild populations.

Inbreeding and Extinction in Captivity

There is overwhelming evidence that deliberately inbred populations of laboratory and domestic animals and plants suffer elevated extinction rates, as illustrated in Figure 4. Extinctions were rare at low levels of inbreeding but sharply increased when inbreeding reached intermediate levels as it generally takes several generations and considerable inbreeding until the growth rate of the population becomes negative.

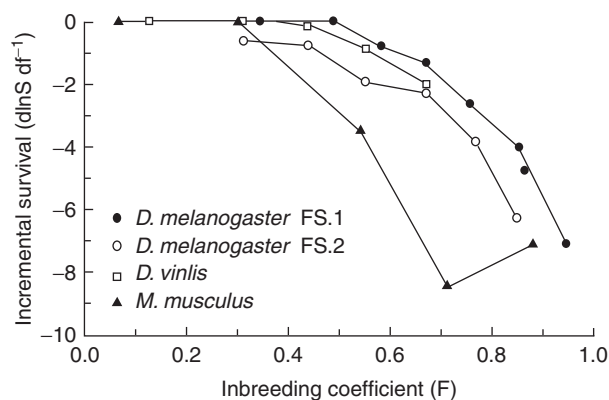


Figure 4 Relationships between survival of populations and inbreeding (F) for *Drosophila melanogaster*, *Drosophila virilis*, and house mice. All populations were inbred using full-sibling mating, except for the use of cousin mating in the first generation in *Mus musculus*. Reproduced from Frankham R (1995) Inbreeding extinction: A threshold effect. *Conservation Biology* 9: 792–799, with permission from Wiley.

Most attempts to develop inbred lines by intense inbreeding are unsuccessful. Of the 20 colonies of laboratory mice maintained by sibling mating in Figure 4, 19 became extinct by generation 12, but the remaining colony showed no decline in litter size and became a successful inbred line. Results with fruit flies, guinea pigs, poultry, and Japanese quail are similar.

Slower rates of inbreeding also lead to extinctions. Small populations of fruit flies maintained at effective sizes of 10 and 20 had greatly elevated extinction risks, even though these were slightly lower than those of populations subjected to intense inbreeding (full-sibling mating) when all were compared at the same inbreeding levels. Further, all the larger populations that survived to high levels of inbreeding had fitness levels lower than those of outbred controls, leading these authors to conclude that although slower rates of inbreeding may slightly slow extinction rates, they do not offer a solution to the increased extinction risk associated with inbreeding in small populations. The effects of inbreeding on population viability are complex and will interact with other factors affecting population growth, population fluctuations, or N_e , but they will be deleterious in the long term (Figure 4).

Inbreeding and Extinction Risk in Wild Populations

Conservation biologists initially thought that genetic problems played a role in the endangerment and extinction of wild populations. It was clear that inbreeding increased extinction risk in laboratory populations and theoretical work in the 1980s suggested that small populations in the wild should also suffer from increased extinction due to the unavoidable increase in mating between close relatives. However, in an influential paper, Lande argued that random demographic and environmental events drive small wild populations to extinction before genetic factors cause problems. Environmental events, ranging from annual variation in climatic variables (such as rainfall) to catastrophes (such as fires and disease epidemics), do increase the probability of extinction and it is extremely difficult to isolate genetic effects from these other effects because inbreeding typically interacts with demography by reducing fecundity, juvenile survival, and life span. Consequently, other researchers continued to question the significance of genetic factors because of the lack of direct evidence that inbreeding can contribute to the extinction of wild populations. However, more recent work has supported the original view that genetic factors can contribute to the extinction of wild populations.

The hypothesis that nongenetic factors would usually drive species to extinction before genetic factors could impact them was evaluated by comparing heterozygosity levels in threatened taxa with those of taxonomically related nonthreatened taxa (Spielman *et al.*, 2004). In 77% of 170 comparisons, heterozygosity levels were lower in the threatened taxa, which would not be expected under the hypothesis that extinction generally occurs prior to genetic impacts. Thus, the view that extinction would occur prior to genetic impacts was rejected. Direct evidence for an impact of inbreeding on extinction risk was provided by studies on the Glanville fritillary butterfly in Finland (Saccheri *et al.*, 1998). They studied a metapopulation (a population of populations) of this butterfly that consists of

numerous small populations that breed in about 1600 dry meadows of different sizes at varying distances from each other. Caterpillars feed in conspicuous family groups of 50–250 individuals and the smallest populations consist of the offspring of a single pair. Populations in individual meadows often go extinct, but many meadows are eventually recolonized, with an average of 200 extinctions and 114 colonizations per year.

Because small population size results in both inbreeding and loss of genetic variation, the researchers were able to use the degree of genetic variation in each population as a measure of the extent to which it was inbred. They sampled 42 populations and found that populations with less genetic variation were more likely to go extinct. Furthermore, genetic diversity predicted extinction risk after they had accounted for all other known causes of extinction in this well-studied butterfly metapopulation. Inbreeding reduced egg-hatching rate and larval survival, lengthened the duration of the pupal period (so that inbred pupae were more likely to be parasitized), and shortened female life span (so that inbred females tended to lay fewer eggs).

Extensive replicated experiments with the annual plant, *Clarkia pulchella*, also found that decreased genetic effective population size (resulting in both inbreeding and loss of alleles through genetic drift) increased the probability of population extinction substantially above that expected from demographic and environmental stochasticity alone. A Spanish study of the shore campion plant reached similar conclusion.

More indirect evidence that inbreeding depression increases the extinction risk of threatened taxa has been provided by stochastic computer simulation models that include inbreeding effects. For example, O'Grady *et al.* (2006) found that incorporating realistic levels of inbreeding depression in population viability models decreased median times to extinction for 30 species by an average of 37%.

Outbreeding and Outbreeding Depression

Mating between distantly related individuals, such as individuals from different populations or subspecies, is called outbreeding. Crossing populations may increase reproductive fitness by increasing heterozygosity and thus preventing the expression of deleterious recessive alleles ("hybrid vigor") or may decrease fitness because of various kinds of genetic incompatibilities between the genes from the different populations (outbreeding depression). Outbreeding depression is a reduction in reproductive fitness, reduced ability to mate or pollinate, fertilize, produce offspring, survive, or reproduce, in the first or later generations following the crossing of populations.

Causes of Outbreeding Depression

Three main mechanisms have been proposed as causes of outbreeding depression: chromosomal incompatibilities, adaptive differentiation among populations, and genetic drift. It is well known that fixed chromosomal differences between two populations increase the probability of outbreeding

depression if the populations are crossed and many cases have been documented in both animals and plants. Although the risk of outbreeding depression differs according to the type of chromosomal differences between populations, it generally increases as the number of fixed differences increases. The risk is greatest with polyploidy, followed by translocations, centric fusions, and inversions.

There is also theoretical and empirical evidence for outbreeding depression between populations that have adapted to different environments. Natural selection can promote rapid development of reproductive isolation, which results in outbreeding depression, between populations in differing environments. A positive association between ecological divergence in reproductive isolation was found in over 500 species pairs of vertebrates, invertebrates, and plants. Most genes involved in prezygotic reproductive isolation that have been investigated show molecular signals of positive selection. Whether or not all cases of reproductive isolation not due to chromosomal incompatibilities are due to adaptation to differing environments remains controversial but adaptation is clearly involved in many cases.

The ecological mechanism of outbreeding depression requires that populations develop different adaptations in response to different local environments. Crossing individuals from the populations may then produce progeny that are less well suited to either local environment. This kind of outbreeding depression is usually observed in the F1 generation. Populations isolated in different environments may also develop coadapted gene complexes, which are sets of genes that have evolved together to produce a fitter phenotype. Crossing individuals from populations with different coadapted gene complexes could then disrupt these complexes and reduce reproductive fitness in the F2 and subsequent generations, when recombination during meiosis disrupts gene complexes.

Genetic drift in small populations has been proposed as a mechanism leading to reproductive isolation (and hence outbreeding depression). Genetic drift can result in chromosomal differences between populations and this often results in outbreeding depression. However, when the chromosomes in two populations are the same, selection is much more likely to result in reproductive isolation than genetic drift. Both theory and extensive empirical evidence indicate that reproductive isolation results predominantly from selection, rather than drift. For example, phenotypic differences due to natural selection were a better predictor of reproductive isolation than genetic distance due to drift in several groups of organisms, including poison-dart frogs, anole lizards, and cichlid fish.

Evidence for Outbreeding Depression

Evidence for outbreeding depression comes primarily from organisms with extremely limited dispersal, such as some plants, copepods, and scale insects, or from crosses between individuals from vastly different geographic sources, or with significant chromosomal differences. Outbreeding depression appears to be more common in plants than in animals. A recent review listed 35 cases of outbreeding depression in vertebrates, invertebrates, and plants. There is not much evidence for outbreeding depression in larger animals, although

it has been observed in crosses where there are chromosomal differences between populations such as in dik-diks and spider monkeys. Such cases usually indicate the existence of unrecognized species or subspecies. The Arabian oryx suffers simultaneously from inbreeding and outbreeding depression. Outbreeding depression appears to be the larger effect but there are chromosomal differences segregating in the population. The most widely quoted mammalian case concerns two ibex populations in Slovakia that lived in very different environments. Several studies have failed to find outbreeding depression in mammals, including in rhesus macaques and saddle-back tamarins. Studies also found no outbreeding depression in survival in several captive populations, including crosses between Borneo and Sumatran orangutans. Lacy and colleagues conducted numerous crosses among five subspecies of deer mice. These subspecies included closely related populations from similar, contiguous habitats, as well as very divergent subspecies that had long been isolated in dissimilar habitats. In general, the benefits of increased heterozygosity outweighed the costs of disrupted gene complexes.

Predicting the Risk of Outbreeding Depression

The question of whether crossing geographically distinct populations of a species is likely to have beneficial or detrimental effects is an important conservation issue because many species now exist as a series of isolated or semi-isolated populations due to human activities. Inbreeding depression and loss of genetic diversity will ultimately contribute to the extirpation of many isolated populations unless gene flow

with other populations is reestablished. The introduction of individuals from other populations to improve reproductive fitness and restore genetic diversity can be an effective management strategy to aid the recovery of small inbred populations with low genetic diversity and has been successful in several natural populations including deer mice, wolves, mountain lions, greater prairie chickens, Swedish adders, desert topminnows, and several species of plants. However, before establishing gene flow between isolated populations, the risk of outbreeding depression should be evaluated.

Inadvertent crossing of populations that belong to separate species can result in outbreeding depression. This problem occurred with small antelopes called dik-diks, as zoos did not originally appreciate that the individuals in captivity belonged to more than one species. Thus, managers should make sure that two populations to be crossed belong to the same species. Fixed chromosomal differences between populations increase the probability of outbreeding depression so karyotyping of populations prior to crossing them is advisable. Predicting the likelihood of outbreeding depression resulting from adaptations to differing environmental conditions is more challenging. Because reproductive fitness is a quantitative character, Frankham and colleagues (Frankham *et al.*, 2011) recently provided theoretical and practical guidance in this area based on an extension of the breeder's equation:

$$\sum AD_t \sim h^2 \sum_{i=1}^t S_i (1 - 1/[2N_e])^{t-1}$$

where *AD* is the adaptive difference between two populations, *h*² the heritability of reproductive fitness, *S*_{*i*} the selection

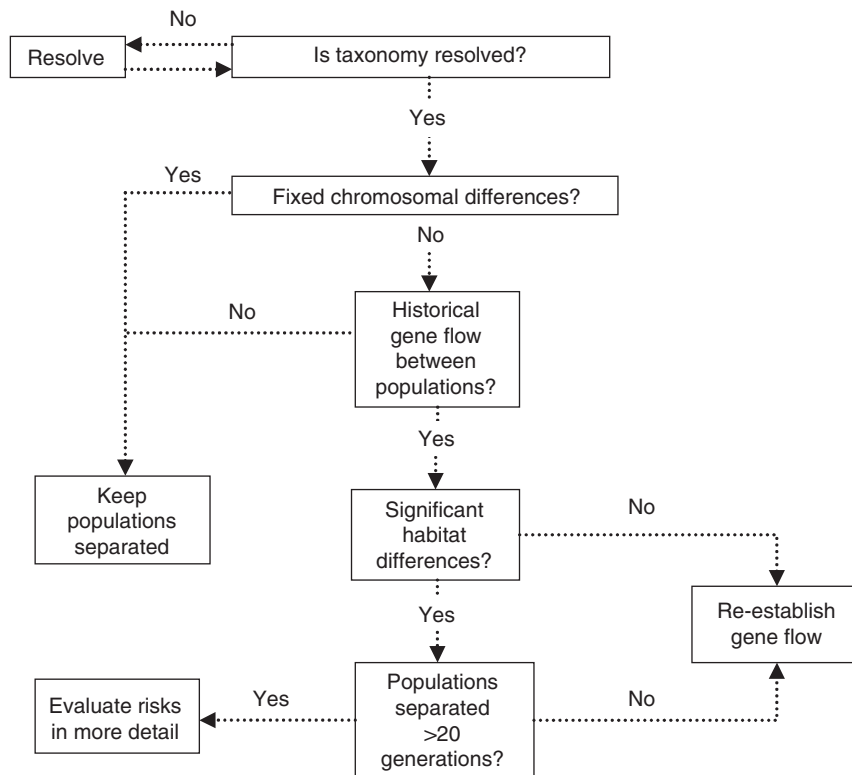


Figure 5 Decision tree for predicting the risk of outbreeding depression when two populations are crossed.

differential in the i th generation, and N_e the effective population size. This work indicated that the degree of adaptive differentiation between two populations, and thus the probability of outbreeding depression if they are crossed, is an increasing function of four factors: (1) the selection differential, which increases with the difference between the environment to which the population was previously adapted and the current environment or environments of the populations to be crossed; (2) the heritability of the traits involved (which depends on the genetic diversity in the populations); (3) the effective population size (which is almost always smaller than the actual population size); and (4) the number of generations the populations have been separated. Calibration of the equation with data from the literature indicated that thousands of generations are required before populations isolated in the same environment begin to develop reproductive isolation but only dozens of generations are required if the populations are adapting to differing environments.

Based on these ideas, Frankham and colleagues developed a decision tree to assess the risk of outbreeding depression if two populations are crossed (Figure 5). Applying the tree to known cases successfully predicted the occurrence of outbreeding depression. The questions are based on the findings that small populations whose taxonomy is well-studied and generally accepted, that exhibit no fixed chromosomal differences, have experienced gene flow between the populations within the past 500 years, and inhabit similar environments, or have been in different environments for less than 20 generations have little risk of exhibiting outbreeding depression if crossed. In such circumstances, establishing gene flow between the populations is likely to have beneficial genetic and demographic consequences. Conversely, if the two populations belong to separate species, or exhibit fixed chromosomal differences, or have been isolated for 500 years or longer, or have been living in significantly differing environments for more than 20 generations, there is a modest to high risk of outbreeding depression if the populations are crossed. However, even when crosses of populations result in outbreeding depression, it will not be a long-term phenomenon

unless F1 individuals are sterile or have very low fitness, as natural selection will act on the extensive genetic variation in the hybrid population, resulting in better adaptation to its environment.

See also: Ecological Genetics. Genetic Diversity. Population Genetics

References

- Crnokrak P and Roff DA (1999) Inbreeding depression in the wild. *Heredity* 83: 260–270.
- Dudash MR and Fenster CB (2000) Inbreeding and outbreeding in fragmented populations. In: Young AG and Clarke J (eds.) *Genetics, Demography and Viability of Fragmented Populations*, pp. 35–53. Cambridge: Cambridge University Press.
- Frankham R, Ballou JD, and Briscoe DA (2002) *Introduction to Conservation Genetics*. Cambridge: Cambridge University Press.
- Frankham R, Ballou JD, and Briscoe DA (2010) *Introduction to Conservation Genetics*, 2nd edn. Cambridge, UK: Cambridge University Press.
- Frankham R, Ballou JD, Eldridge MDB, Lacy RC, Ralls K, Dudash MR, and Fenster CR (2011) Predicting the risk of outbreeding depression. *Conservation Biology* 25: 465–475.
- Keller LF (1998) Inbreeding and its fitness effects in an insular population of song sparrows (*Melospiza melodia*). *Evolution* 52: 240–250.
- Keller LF and Waller DM (2002) Inbreeding effects in wild populations. *Trends in Ecology and Evolution* 17: 230–241.
- Lande R (1988) Genetics and demography in biological conservation. *Science* 241: 1455–1460.
- O'Grady JJ, Brook BW, Reed DH, Ballou JD, Tonkyn DW, and Frankham R (2006) Realistic levels of inbreeding depression strongly affect extinction risk in wild populations. *Conservation Biology* 133: 42–51.
- Ralls K and Ballou J (1986) Captive breeding programs for populations with a small number of founders. *Trends in Ecology and Evolution* 1: 19–22.
- Ralls K, Ballou JD, and Templeton A (1988) Estimates of lethal equivalents and the cost of inbreeding in mammals. *Conservation Biology* 2: 185–193.
- Saccheri I, Kuussaari M, Kankare M, Vikram P, Fortelius W, and Hanski I (1998) Inbreeding and extinction in a butterfly metapopulation. *Nature* 392: 491–494.
- Spielman D, Brook BW, and Frankham R (2004) Most species are not driven to extinction before genetic factors impact them. *Proceeding of the National Academy of Sciences, USA* 101: 15261–15264.