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Loss of Genetic Diversity from Managed Populations: Interacting Effects of Drift, Mutation, Immigration, Selection, and Population Subdivision

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Abstract: A computer simulation program was used to examine interacting effects of genetic drift, mutation, immigration from outside populations, directional and balancing selection, and population subdivision on the loss of genetic variability from small, managed populations. Stochastic events were simulated with a pseudo-random number generator, and the genetic variation (expected heterozygosity) within and between populations was monitored in 25 populations for 100 generations.

Genetic drift was the overriding factor controlling the loss of genetic variation. Mutation has no noticeable effect on populations of the size typically managed in zoos and nature preserves. Immigration from a large source population can strikingly slow, halt, or even reverse the loss of genetic variation, even with only one or a few migrants per generation. Unless selection is stronger than commonly observed in natural populations, it is inefficient in countering drift when population sizes are on the order of 100 or fewer. Subdivided populations rapidly lose variability from within each subpopulation but retain variation across the subpopulations better than does a panmictic population.

These results suggest that population managers should be concerned with the variation-depleting effects of genetic drift, perhaps almost to the exclusion of consideration of selection and mutation. Drift can be countered by the introduction of very occasional immigrants or, less effectively, by division of the managed population into smaller breeding groups that interchange enough migrants to prevent unacceptably deleterious inbreeding within each subpopulation.

Resumen: A través de un programa de simulación por computadora se examinaron los efectos interactivos de la deriva génica, las mutaciones, la inmigración de poblaciones externas, la selección balanceada y direccional, y la subdivisión de poblaciones pequeñas sujetas a manejo, debido a la pérdida de variabilidad genética. Se simularon eventos estocásticos con un generador de números pseudo-azarosos y se estudió la variación genética intra e interpoblacional (heterocigosis esperada) en 25 poblaciones durante 100 generaciones.

La deriva génica fue el factor predominante que controló la pérdida de variación genética. Las mutaciones no tuvieron un efecto notable en poblaciones del tamaño típico manejado en zoológicos y áreas protegidas. La inmigración proveniente de otras poblaciones más grandes puede asombrosamente disminuir, detener ó invertir la pérdida de variación genética, aún con la influencia de sólo uno o pocos migrantes por generación. Cuando el tamaño de las poblaciones es del orden de 100 individuos ó menos, no es necesario evaluar la deriva génica, a menos que la selección sea más fuerte que la comunmente observada en poblaciones naturales. Las poblaciones divididas pierden rápidamente su variabilidad intra-subpoblacional, pero retienen una mayor variación intersubpoblacional que las poblaciones panmíticas.

Los resultados sugieren que los manejadores de poblaciones deben estar más atentos a la disminución de la variación genética producida por la deriva génica, que a las mutaciones ó a la selección natural. La deriva génica puede invertirse con la introducción de migrantes ocasionales, ó (aunque menos efectivamente) a través de la división de las poblaciones manejadas en pequeños grupos de crianza que puedan intercambiar migrantes para prevenir cruzamientos deletéreos dentro de cada subpoblación.

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Introduction

As natural habitats disappear and populations of organisms within remaining natural areas are increasingly exploited, many species are reduced to small, remnant populations occupying what is left of the habitat. Populations being propagated in zoos and intensively managed wildlife parks represent an extreme in these respects, at times being the last hope for survival of a species. By virtue of careful management, captive populations can be largely freed from the hazards of predation, inadequate nutrition, severe weather, disease, and difficulty in finding mates. Thus, smaller and more stable populations can be maintained in zoos or closely managed nature preserves than would persist in more natural environments.

Yet small populations of organisms lose genetic diversity over time. In the absence of any deterministic or directional forces on gene frequencies (selection, migration, mutation), frequencies of alleles follow a random walk process ("genetic drift") due to the random sampling of genes during transmission from one generation to the next. The random sampling of a small number of genes at each new generation results in greater fluctuations in gene frequencies than does the sampling of a larger number of genes. Therefore, small populations will tend to lose genetic variation by genetic drift more rapidly than will larger populations. The ultimate fate of any sexual population lacking mechanisms to restore genetic variation would be fixation of one allele at each genetic locus throughout the genome.

An immediate effect of the depletion of genetic variability is increasing homozygosity of the individuals in the population. Although the causes are still debated (Crow 1948, Lerner 1954, Clarke 1979, Frankel 1983), it has been widely recognized that increases in homozygosity often lead to lower viability and fecundity ("inbreeding depression") (Falconer 1981, Ralls & Ballou 1983).

Over a longer time scale, although the harmful effects of inbreeding on individuals may diminish as deleterious recessive genes are removed from the population by selection (Lynch 1977, Templeton & Read 1983), the population as a whole loses the evolutionary flexibility conferred by genetic diversity (Selander 1983). Without genetic variation between individuals on which natural selection can act, a population cannot adapt to changing environments and is vulnerable to new predators, diseases, parasites, climatic conditions, and competitors, and to changing food supplies.

For captive populations the loss of evolutionary flexibility may be especially rapid and particularly hazardous to long-term survival. The combined effect of rapid genetic drift in small captive populations and strong directional selection for survival in a novel captive environment might quickly deplete genetic variation.

The relative lack of predators and abundance of food and shelter might lead to a relaxation of many selective pressures to which wild populations would be exposed. Yet the restoration of genetic variation by mutation following this relaxation of selection for traits formerly under stringent selection is a very slow process—probably too slow to be of consequence in current efforts toward the preservation of species. For a given genetic locus, only one new mutation per thousand generations would be expected in a typical captive population of 100 to 1000 individuals. The rapid rate of habitat alteration is not likely to slow, so the species harbored by zoos will need considerable adaptive flexibility (evolutionary, physiological, and behavioral) if they are ever again to thrive in a noncaptive setting.

If zoos (or wildlife preserves and parks) are to propagate long-term viable populations, and especially if they are to contribute to the preservation of species diversity, they will have to manage their populations in such a way as to minimize, halt, or even reverse the decline in genetic variability that occurs in captive populations. Large breeding populations, exposed to varied environments, will maintain genetic variation and evolutionary flexibility better than will smaller populations in less varied habitats (Levins 1968, Hedrick et al. 1976, Lacy 1982). With finite resources, however, allocation of space and facilities for one species necessarily limits space allocated to others. Efforts are needed to determine how best to manage captive breeding populations so as to make optimal use of those resources set aside for each species.

One approach to understanding how varied evolutionary forces effect genetic variation in small populations, and how populations can be managed to make those forces work toward the goals of captive management instead of against them, is to use computers to simulate the complex interactions of factors impinging on hypothetical populations. Computer models share with analytical theoretical approaches the property that results are dependent upon necessarily incomplete representations of natural processes. Models may be sensitive to incorrect assumptions, and important factors may have been omitted. Yet, for studying the effects of variables that can be well-defined, and for examining interactions among those variables, computer simulations can provide answers that may not be intuitive and that may not be readily obtainable by mathematical analysis. Moreover, many of the analytical models in the literature and many of the intuitive concepts about genetic diversity in small populations have been inadequately if at all examined by simulations. Unlike many analytical models, computer simulations do not make approximations that depend on the range of parameters for accuracy. The order-of-magnitude approximations of many analytical treatments are often not sufficiently informative for population managers.

In this paper I describe a general computer simulation model used to examine the effects of population size, mutation, immigration, selection, and population subdivision, and their interactions, on the maintenance of genetic variability in small, managed populations. Many of these factors have been examined before, either analytically or by simulation models, but the disparity among the models used to examine these factors makes comparisons of the effects, and of the resulting recommendations, difficult. Finally, because models are built on simplifying assumptions, the robustness of the conclusions derived from any model (including those presented here) should be verified by alternative approaches before they are put into practice.

Methods

A computer simulation program was written in the C programming language for use on microcomputers using the MS-DOS (Microsoft, Inc.) operating system. Results were output numerically via a printer and graphically via a Hewlett-Packard 7475A plotter.

To simulate the fate of two alleles at a genetic locus, the program

1. Prompts the user to input the number of populations to be simulated, number of generations, population size, genotype fitnesses, forward and backward mutation rates, frequency of immigration into the population from an outside population, number of subpopulations into which the total population is fragmented, and migration rate between subdivisions.
2. Creates a population (composed of several subpopulations, if specified in step 1) of diploid individuals, assigning two alleles to each individual with probability 0.5 that each allele is of one type (say, "A") rather than the other ("a"). (Probabilistic events in the simulation are determined to occur when a real number drawn at random from a uniform distribution from 0 to 1 is less than the specified probability.)
3. Selects two parents at random from each (sub)population. Each parent is used for that mating with a probability equal to the fitness assigned to its genotype relative to the fitness of the most fit genotype. If a parent is not used, a replacement is drawn at random from the (sub)population, and then that newly chosen parent is in turn kept or discarded with probability determined by its relative fitness.
4. Randomly selects one allele from each of the two parents and assigns that allele pair to an offspring.
5. Replaces the offspring with a migrant from another subpopulation, with probability equal to the migration rate between subpopulations. The migrant has a genotype that is drawn at random from the pool of genotypes present in the other subpopulations.
6. Replaces the individual with an immigrant from an outside population, with probability equal to the specified outside immigration rate. The immigrant has a genotype randomly drawn from a gene pool in which the two allelic variants are equally frequent (as in the starting population).
7. Allows each of the two alleles of the individual to mutate to their respective alternate form, with probabilities equal to the specified mutation rate.
8. Repeats steps 3 through 7 (for each subpopulation) as often as is necessary to create a new generation of the specified size.
9. Calculates allele frequencies and percent "expected" heterozygosity within each subpopulation, that is, the heterozygosity that would be observed if the subpopulation were in perfect Hardy-Weinberg equilibrium. The expected heterozygosity (calculated as $2pq$, in which p and q are the frequencies of the two alleles) is twice the binomial variance in allelic frequencies in the population (Crow & Kimura 1970). The program also calculates allele frequencies averaged over subpopulations and from these overall allele frequencies calculates the "total heterozygosity" or "gene diversity" that would be present in the population if it were in Hardy-Weinberg equilibrium (mating at random with no subdivision) (Nei 1973, 1977). The total heterozygosity reflects both within-subpopulation heterozygosity and any between-subpopulation genetic differentiation. If all subpopulations are genetically alike, then the total heterozygosity will be equal to the (also equal) heterozygosities of the subpopulations. If subpopulations are genetically quite distinct, then the total heterozygosity will be much larger than is the average within-subpopulation heterozygosity, and it is the heterozygosity that would be present in a single randomly breeding population with the same amount of genetic diversity (strictly, the same total variance in alleles) as is present across the subpopulations.
10. Repeats steps 3 through 9 for the specified number of generations, beginning each generation with the offspring from the previous generation.

Thus, the program simulates genetic processes in a constant size, randomly breeding population of sexually reproducing hermaphrodites with discrete generations. An individual can mate with itself, but is no more likely to do so than to mate with any other given individual. One important way in which the modeled population deviates from reality is the randomness of breeding within

the (sub)populations. In almost any real population, mate selection, polygamy, and sex-biased dispersal and mortality lead to deviations from panmixia. If these factors can be estimated for a population under study, then the "effective population size" can be calculated and a conversion made between the real population and the ideal populations presented in generalized models such as this. The effective size of a population is the size of an idealized monoecious population with random union of gametes, that would lose heterozygosity at the same rate as the observed population (Wright 1969). Thus, in the simulated (sub)populations, the actual population size is also the effective population size.

The lack of separate sexes and the self-compatibility are atypical of most captive populations, but the genetic behavior of such a population is almost indistinguishable from that of a population with separate sexes. A few simulations were run with the constraint that an individual could not mate with itself, and the results did not differ from simulations without such a constraint. Excluding self-fertilization has the same effect as consideration of separate sexes; either increases the genetically effective population size by 0.5 individuals (Wright 1969). The exclusion of sib-mating, as is commonly observed in wild populations (Ralls et al. 1986) and is often an intent of captive breeding programs, results in an effective population of just two greater than the idealized population modeled here (Wright 1969). An unequal sex ratio or nonrandom mating (producing a variance in family sizes that is greater than Poisson) can reduce the effective size to a fraction of the total population size (Crow & Kimura 1970, Ryman et al. 1981). In captive populations, these causes of low effective population size can be minimized (Flesness 1977, Denniston 1978). In fact, if family sizes are equalized, effective population approaches twice the real population size (Crow & Kimura 1970).

I monitored genetic diversity in the simulations using expected heterozygosities, both average within-subpopulation heterozygosity and the total (within- and between-subpopulation) heterozygosity that would be observed if all subpopulations were mixed at random and the genotypes were in Hardy-Weinberg proportions. Genetic diversity could have been expressed as the number of alleles present ("allelic diversity"), as in the simulations of Allendorf (1986) and the analytical models of Fuerst and Maruyama (1986). For several reasons heterozygosity is the more common measure of genetic diversity, but both measures yield important insights. Being proportional to genetic variance, the expected heterozygosity is also proportional to the short-term response to selection on that genetic locus (Fisher's Fundamental Theorem of Natural Selection: Fisher 1958). Long-term response to selection, however, is more dependent upon the alleles present in the population than on initial frequencies or heterozygosity (Allendorf 1986).

Unlike allelic diversity, the estimation of expected heterozygosity from a sample of a population is not highly dependent upon the sample size observed. Also, the fate of allelic diversity in a population is quite dependent upon the starting conditions (numbers and frequencies of alleles: Allendorf 1986), whereas heterozygosity decays at a steady average rate regardless of the initial allele frequencies in the population (Crow & Kimura 1970).

Results

Figure 1 shows the fate of heterozygosity in 25 simulated populations of 120 individuals across 100 generations. (A population size of 120 will be used frequently in this paper as a standard of comparison.) The only force leading to changes in gene frequencies and heterozygosities in Figure 1 is random genetic drift. All genotypes were assigned the same fitness, there was no mutation or immigration, and mating was random.

The stochastic nature of genetic transmission is apparent in the simulated populations, even though the populations are not unrealistically small for captive or even wild populations of large vertebrates. Three of the 25 populations lost all heterozygosity at the genetic locus within 100 generations (i.e., one of the two allelic variants was lost, the other was fixed), and yet six populations had virtually the same allele frequencies and heterozygosities after 100 generations as they had at the outset. The average heterozygosity in these 25 simulated populations after 100 generations was 58.25 percent of the initial value (SE = 7.19%), not significantly different from the 66 percent predicted from the commonly used equation for the loss of heterozygosity by random drift

$$H_t = (1 - 1/[2N_e])^t H_0$$

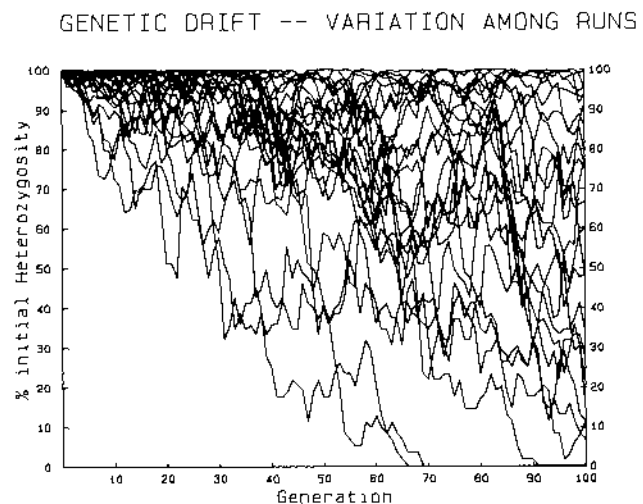


Figure 1. Percent heterozygosity retained across 100 generations in 25 simulated populations of 120 randomly mating individuals each.

in which N_e is the effective population size, and H_0 and H_t are heterozygosities at generations 0 and t , respectively.

Throughout the remainder of this paper, heterozygosities averaged across 25 simulated populations will be shown for each set of conditions discussed. The average behavior of the 25 simulations can represent the fate of a given genetic locus across 25 populations, or the fate of 25 genetic loci within one population. The relative smoothness of average heterozygosities shown in all subsequent figures should not obscure the fact that underlying the average heterozygosities are fates of individual populations that are as diverse as those shown in Figure 1. Results revealed by simulations are thus the "expected" behavior of a population only in a statistical sense: They should not be used to predict the behavior of a particular gene of interest. For example, only a few populations in Figure 1 were left with fractions of the initial heterozygosity close to the theoretical prediction of 66 percent.

Effect of Population Size

Figure 2 compares average heterozygosities of 25 simulated populations of various sizes and shows the effect of population size on the rate at which genetic drift depletes variation. Mean heterozygosities after 100 generations did not vary significantly from the theoretical values of 90.5 percent, 81.2 percent, 65.9 percent, 43.3 percent, 28.4 percent, and 8.0 percent that are expected

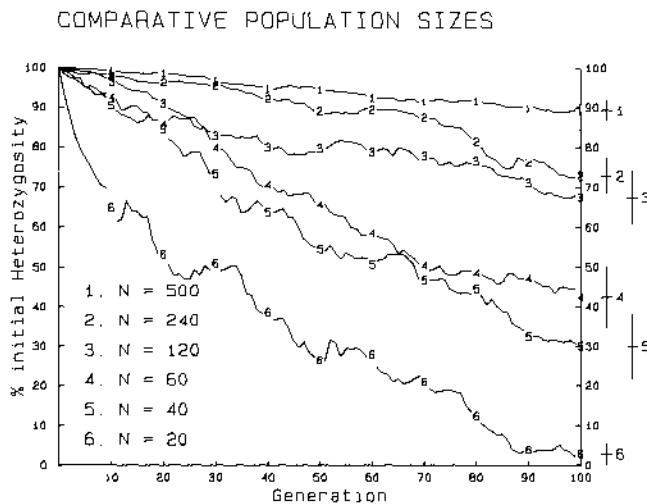


Figure 2. Percent heterozygosity retained in populations of 20, 40, 60, 120, 240, or 500 randomly mating individuals. Each line in this and all subsequent figures represents the average of 25 simulated populations. Means and standard errors of the final heterozygosities are indicated at the right. Except when otherwise specified, all subsequent figures are based on simulated populations of 120 animals.

for populations of size 500, 240, 120, 60, 40, and 20, respectively. Standard errors of the mean heterozygosities across these 25 simulated populations of each size (SE = 2.73%, 4.58%, 6.86%, 7.75%, 8.48%, and 2.79%, respectively) approximate the theoretical standard errors for heterozygosities remaining after 100 generations of drift (2.43%, 4.35%, 6.60%, 8.00%, 7.66%, and 4.79%; equation from Bulmer 1985).

Putting the loss of genetic variability into a perspective that is meaningful for a species or population of interest can be difficult. The history of inbreeding in a population (Lynch 1977) and the need to adapt to changing environments will affect the loss of heterozygosity that a population can withstand (Selander 1983). To provide some benchmarks, note that inbreeding of 1 percent per generation is considered by animal breeders to have negligible effect (Franklin 1980) and that many human societies prohibit marriages between relatives that would produce offspring with inbreeding coefficients of 6.25 percent or more. (Inbreeding reduces heterozygosity by 1% per 1% increase in the inbreeding coefficient, and losses of heterozygosity due to any kind of population structure are often measured by inbreeding coefficients or F -statistics [Wright 1965, Jacquard 1975]). Experimental populations have responded to artificial selection for more than 75 generations (Falconer 1981), suggesting that sufficient variability exists to allow "adaptation" even after genetic variation has been considerably depleted. Such experimental populations do not cope simultaneously with the diversity of selective constraints that are faced by natural populations, however, and clearly the many species that have gone extinct did not adapt sufficiently and rapidly to changing environments.

Mutation

The ultimate source of new genetic variability is mutation, although recombination, migration, and selection can increase variability within a population by reshuffling existing alleles within and between populations and by changing allele frequencies. Figure 3 shows the effects of mutation on heterozygosity within populations of 120 individuals. Mutation can counter the effects of drift, but not at rates of mutation that are observed in any real population. Mutation rates typically range from 10^{-8} to 10^{-4} per gene per generation in eukaryotes and from 10^{-6} to 10^{-4} in mammals (Hedrick 1983, Strickberger 1985). Only at mutation rates greater than 10^{-3} did new mutation noticeably counter drift in the simulations. (The increased heterozygosity with $m = 10^{-4}$ in Figure 3 was due to chance, not the effects of mutation; note that the higher mutation rate of 10^{-3} had no effect on heterozygosity.)

In part, the minimal effect of mutation in the simulations results from the very high heterozygosity (50%)

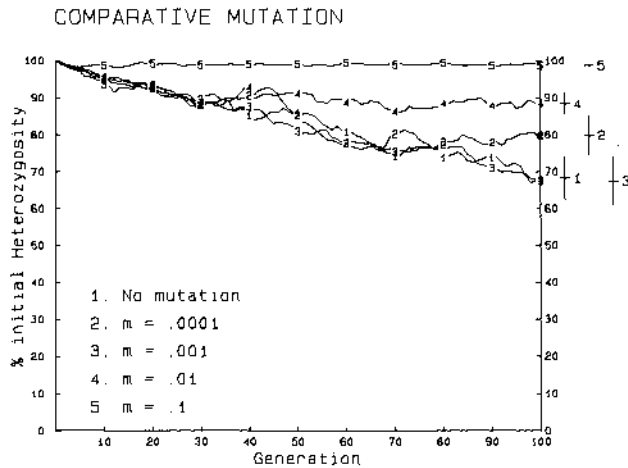


Figure 3. Percent heterozygosity retained in populations with equal forward and backward mutation rates of 0, 10^{-4} , 10^{-3} , 10^{-2} , or 10^{-1} per generation.

at generation 0. New variation introduced by mutation increases additively, independent of current heterozygosity, while drift leads to a geometric decrease in heterozygosity, the loss being proportional to extant heterozygosity. After heterozygosity reaches a low value, further loss due to drift will have diminished to the rate of gain by mutation: The population will be in mutation-drift equilibrium. For a population of 120 animals with a mutation rate of 10^{-5} , mutation-drift balance is reached when heterozygosity drops to 0.0048, about 1 percent of the initial value in the simulations and about an order of magnitude lower than is commonly observed in natural populations of vertebrates. (In an ideal population such as the one modeled, mutation-drift equilibrium is reached when $H = 4N_e m / (1 + 4N_e m)$ [Crow & Kimura 1970].)

Immigration

For a captive or otherwise isolated population of a species that retains relatively large populations elsewhere, immigration of individuals from the large source population constitutes a mechanism, similar to mutation, for reintroduction of genetic variability. Immigration differs in several important respects from mutation, however. Immigration rates can be much greater than are mutation rates. Moreover, immigration is often under control of a population manager. Most importantly, genetic variants introduced into a population by immigration act to restore alleles that formerly existed in the captive population or the ancestral stock from which it was derived.

Effects on heterozygosity of immigration from a hypothetical, genetically unchanging, source population into a population of 120 individuals are shown in Figure 4. Given the standard errors observed around final heterozygosities, there is no evidence that an immigration

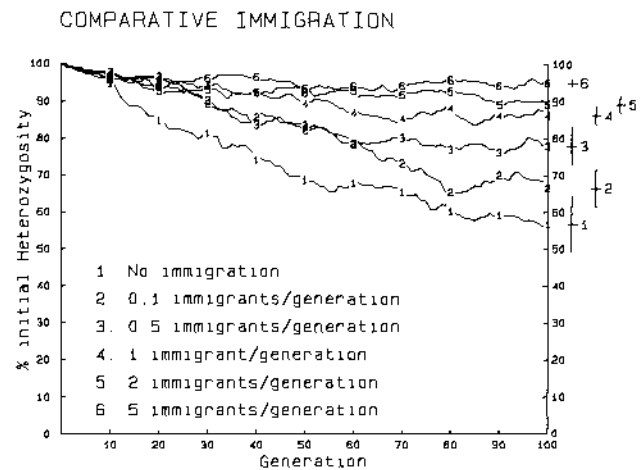


Figure 4. Percent heterozygosity retained in populations receiving an average of 0, 0.1, 0.5, 1, 2, or 5 immigrants per generation from an infinitely large source population with allele frequencies equal to those of the initial populations.

rate of 0.1 immigrants or less per generation causes a biologically significant effect.

Immigration rates as low as 0.5 immigrants per generation, obtainable for many captive propagation efforts, strikingly reduce the loss of variability from small populations. Although it is not obvious in Figure 4, the immigration causes genetic variation to approach an asymptote: The farther from the initial state a population becomes, the greater the restorative effect of immigration. Therefore, immigration can bring a formerly isolated and considerably divergent population back toward the genetic condition of the source population.

Because the degree to which immigration restores heterozygosity is dependent upon the extent to which the population has diverged from the source population, the effect of immigration is much greater on smaller populations than on larger populations. With moderate rates of immigration, the long-term (asymptotic) genetic fate of a population is almost independent of population size (Fig. 5).

Selection

Three types of selection were modeled: directional selection in which one homozygote has superior fitness to the other and the heterozygote has intermediate fitness, balancing selection in which the heterozygote has superior fitness and the two homozygotes have equal fitness, and disruptive selection in which the heterozygote has inferior fitness and the two homozygotes have equal fitness. As expected, under strong selection (Fig. 6A: relative fitnesses of 1.0:0.8:0.6 for directional selection; 0.8:1.0:0.8 for balancing selection; and 1.0:0.8:1.0 for disruptive selection), balancing selection maintains allele frequencies and heterozygosity,

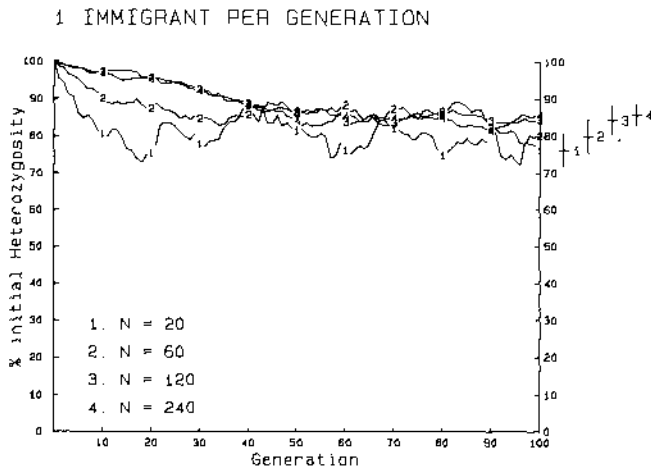


Figure 5. Percent heterozygosity retained in populations of size 20, 60, 120, or 240 receiving 1 immigrant per generation from a source population.

while directional and disruptive selection rapidly fix one allele in each population and thereby deplete genetic variation. Under symmetrical disruptive selection, about half the populations are fixed for one allele and half are fixed for the other. All populations were fixed for the selectively favored allele under directional selection.

Fitness differentials of 20 percent are probably rare, although such strong natural selection has been reported for some polymorphic traits (Endler 1986). Under more moderate selection (relative fitness of 1.0:0.95:0.90 for directional selection; 0.95:1.0:0.95 for balancing selection; and 1.0:0.95:1.0 for disruptive selection), the trends in heterozygosity are the same, but diminished (Fig. 6B). Over five to 10 generations, a 5 percent fitness differential has little effect on levels of genetic variation. Weak selection pressures (Fig. 6C, relative fitnesses of 1.0:0.99:0.98 for directional selection; 0.99:1.0:0.99 for balancing selection; and 1.0:0.99:1.0 for disruptive selection) affect heterozygosities, but the effects are hardly discernible over the background noise of random drift. This is in accord with analytical results of Kimura (1955), Robertson (1962), and others (Crow & Kimura 1970, Wright 1969) that show that selection is effective over random genetic drift when the product of the effective population size and the selection coefficient is much greater than one.

Population Subdivision

Captive populations are often fragmented into partially or wholly isolated subpopulations, each consisting of a breeding population held by a zoo or a group of zoos in close geographical proximity or in close cooperation. One effect of this subdivision is to allow genetic differentiation to develop between subpopulations, as a result of genetic drift or differential selection on the subpopulations inhabiting different environments (Chesser et

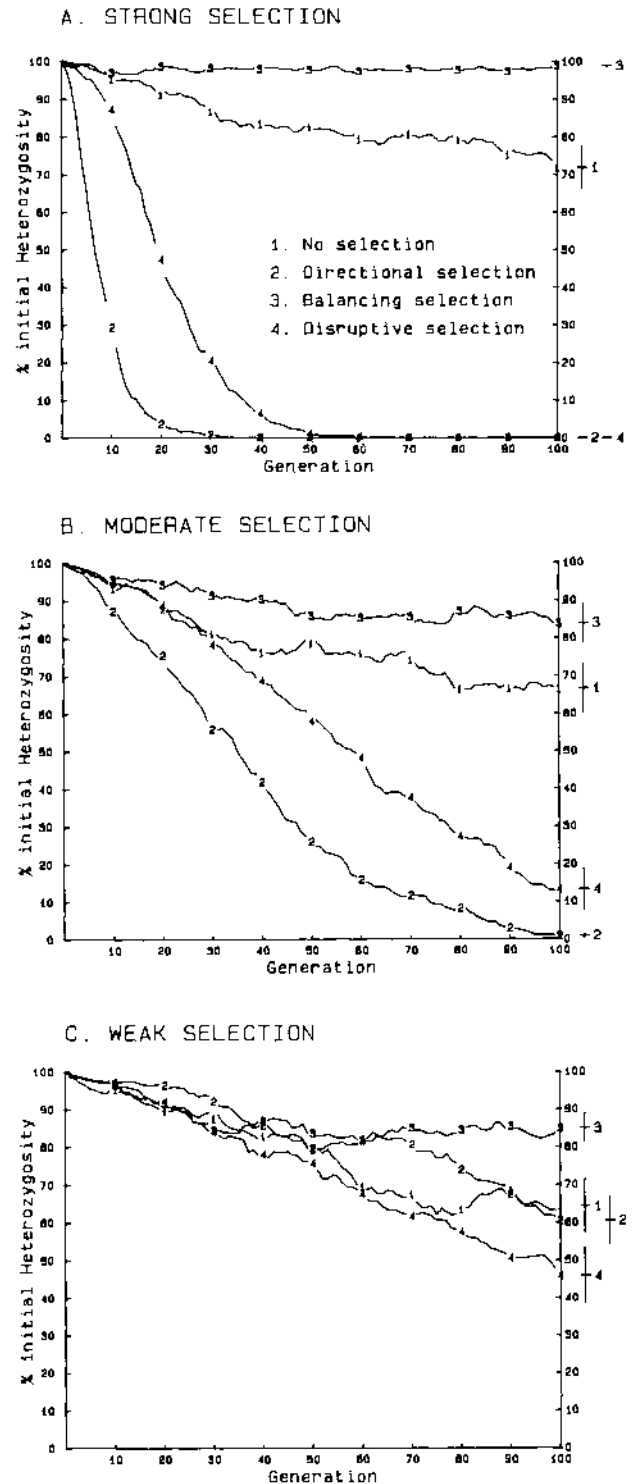


Figure 6. Percent heterozygosity retained in populations subjected to no selection, balancing selection, disruptive selection, or directional selection. (A) strong selection (relative fitnesses of 0.8:1.0:0.8, 1.0:0.8:1.0, and 1.0:0.8:0.6); (B) moderate selection (relative fitnesses of 0.95:1.0:0.95, 1.0:0.95:1.0, and 1.0:0.95:0.90); (C) weak selection (relative fitnesses of 0.99:1.0:0.99, 1.0:0.99:1.0, and 1.0:0.99:0.98).

al. 1980). Furthermore, because the subpopulations are necessarily smaller than is the total population and because each subpopulation would occupy a narrower range of habitats than does the total population, two processes that deplete genetic variation will be enhanced in isolated subpopulations relative to a panmictic population. Genetic drift will inevitably be greater in fragmented subpopulations; and while heterogeneous selection on large populations utilizing diverse habitats can maintain genetic variation (Levene 1953, Levins 1968, Hedrick et al. 1976, Taylor 1976, Lacy 1982), directional selection on isolated subpopulations for traits advantageous in narrow habitats would deplete variation (Karlin 1982).

Figure 7 illustrates the effect of dividing a population of 120 individuals into one, three, five, or 10 fully isolated breeding units. Average within-subpopulation het-

erozygosities (shown by points unconnected by lines) are strikingly diminished when the population is fragmented, while total gene diversity within and between subpopulations (points connected by lines) is better maintained by population subdivision.

Total gene diversity in a highly fragmented population asymptotes at a high level. In each generation some of the variation formerly present within each subpopulation is converted to variance between populations as the subpopulations randomly diverge. This between-subpopulation variation is then protected from further decay due to genetic drift. When subpopulations become totally inbred (no heterozygosity within subpopulations), total variation is fixed at a level equal to the between-subpopulation genetic variation. Maintenance of total variation in simulated populations depends on the persistence of each subpopulation at a constant size,

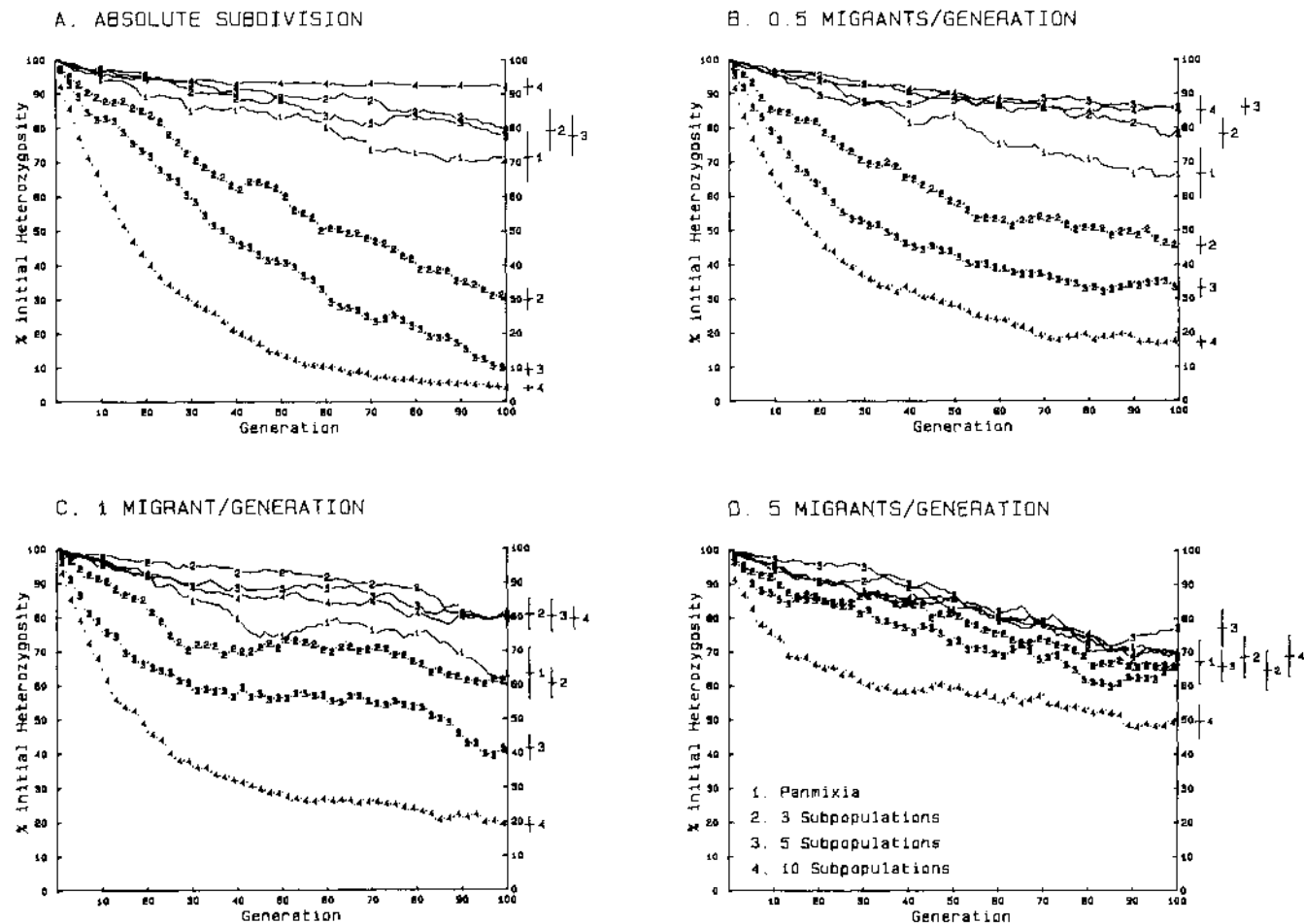


Figure 7. Percent heterozygosity retained within subpopulations (points and numbers not connected by lines) and total heterozygosity retained within and between subpopulations (points connected by lines) in populations of total size 120 divided into 1, 3, 5, or 10 subpopulations. (A) no migration between subpopulations; (B) 0.5 inter-subpopulation migrants per generation; (C) 1 migrant per generation; (D) 5 migrants per generation.

however. If some subpopulations were to go extinct, some between-population diversity would be lost with them.

Subpopulations need not be totally isolated. As few as 0.5 inter-subpopulation migrants per generation (over all subpopulations, not per subpopulation) will reduce inbreeding within subpopulations (compare within-subpopulation heterozygosities in Fig. 7B to those in 7A). Higher rates of migration between subpopulations (Fig. 7C and 7D) bring both the within-subpopulation heterozygosities and the total gene diversities closer to the heterozygosity expected under panmixia. Theoretical analyses (Wright 1969) and simulations (not shown) demonstrate that the effect of migration between populations on preventing divergence among subpopulations is dependent upon the number of migrants per generation, and independent of total population size.

Migration reintroduces genetic variation to subpopulations, causing within-subpopulation heterozygosities to level out after an initial rapid decline. (As was the case for immigration from an external population, migration between subpopulations only becomes effective after populations have diverged and lost variability.) By preventing subpopulations from becoming fixed with different genetic compositions, migration also prevents the subdivided population structure from retaining large total gene diversity. Under high rates of migration (Fig. 7D) subdivided populations do not retain within-subpopulation variation as well as do panmictic populations, nor do they retain measurably more total variation.

Figure 8 compares the effects of different rates of migration between subpopulations of a population divided into five breeding units of 24 individuals. Increasing migration lessens inbreeding within subpopulations, though not until generation 10 or beyond. Very low levels of migration perhaps actually increase total genetic variation maintained relative to the no migration case, while higher rates of migration bring total heterozygosity down.

Interaction Between Selection and Population Subdivision

By augmenting genetic drift within subpopulations, subdivision alters the effectiveness of selection on small populations. Strong directional selection usually overwhelms genetic drift (Fig. 9A), even in highly subdivided populations. (About 1 percent of subpopulations of 12 individuals will be fixed for an allele strongly opposed by selection.) With more moderate selection, genetic drift within subpopulations prevents selection from being wholly effective (Fig. 9B). Among subpopulations of 12 individuals each, an average of 22 percent became fixed for the allele whose homozygote had 10 percent lower fitness than did the other homozygote. The selectively disadvantageous allele also remained longer within subpopulations of 24 and 40 individuals (five and three

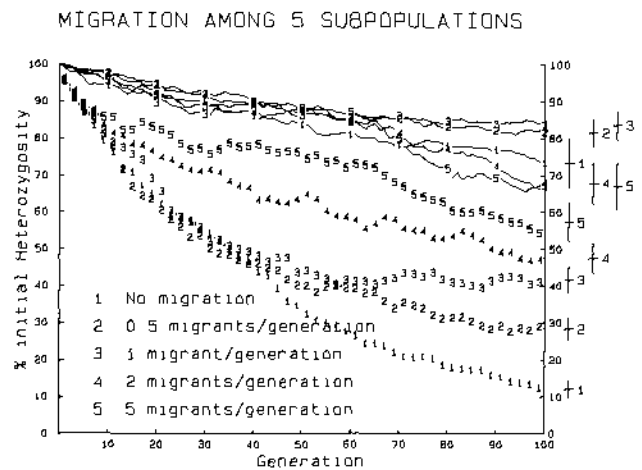


Figure 8. Percent heterozygosity retained within subpopulations (points not connected by lines) and total heterozygosity retained within and between subpopulations (points connected by lines) in populations divided into 5 subpopulations with an average of 0, 0.5, 1, 2, or 5 inter-subpopulation migrants per generation.

subpopulations, respectively) than it did within a panmictic population of 120. Weak directional selection (not shown), with only minor effects on a panmictic population, had no effect on the fate of alleles in subdivided populations.

The heterozygosity-preserving effects of balancing selection are also diminished by drift within small subpopulations (Figs. 9C and 9D). Balancing selection slows, but does not stop, fixation of alleles in small subpopulations, therefore also countering potential advantages of population subdivision. Rather than maintaining total heterogeneity by furthering between-subpopulation genetic differentiation, subdivision of a population under balancing selection causes a greater loss of total heterozygosity than would occur if the population were panmictic.

Discussion

Flesness (1977), Denniston (1978), Chesser et al. (1980), Allendorf (1983), Chesser (1983), Fuerst and Maruyama (1986), and Foose et al. (1986) have made recommendations about the optimal genetic management of captive populations. The simulations presented here provide further basis for making decisions about the genetic management of small populations. The goal of presenting simulations is not to prescribe a population size and structure to be used in the management of all populations: The opportunities, constraints, and goals of captive propagation programs are too diverse to permit such broad recommendations. Simulations, however, can help

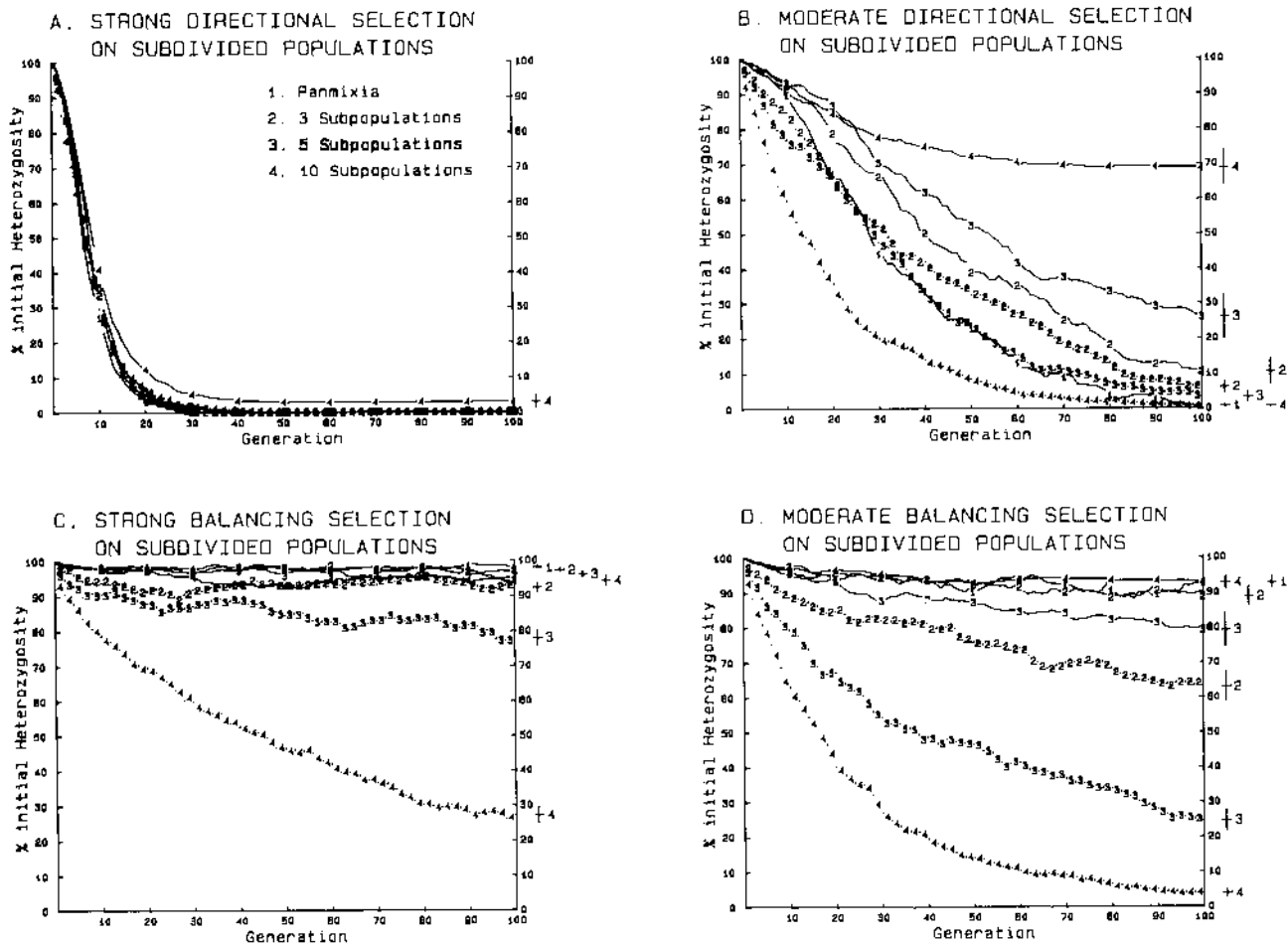


Figure 9. Percent heterozygosity retained within fully isolated subpopulations (points not connected by lines) and total heterozygosity retained within and between subpopulations (points connected by lines) in populations divided into 1, 3, 5, or 10 subpopulations subjected to selection. (A) strong directional selection (relative fitnesses of 1.0 : 0.8 : 0.6, except for total heterozygosity in 10 subpopulations, all heterozygosities have mean and standard error zero by generation 50); (B) moderate directional selection (relative fitnesses of 1.0 : 0.95 : 0.90); (C) strong balancing selection (relative fitnesses of 0.8 : 1.0 : 0.8); (D) moderate balancing selection (relative fitnesses of 0.95 : 1.0 : 0.95).

to define the effects that different management strategies will have on the genetic constitution of a population. With such knowledge, management plans can become tailored, informed attempts to achieve the long-term genetic goals of captive propagation.

Genetic drift is commonly the most powerful evolutionary force acting on small populations, so, to a first approximation, management concerns can be focused solely on effects of drift. Under stringent conditions of selection and/or population structure, imposed artificially or naturally, other evolutionary forces can overcome the stochastic effects of drift. Genetic drift is a sampling phenomenon, and thus can be most effectively controlled by keeping large (effective) breeding populations. In unmanaged populations, many individuals contribute little or nothing to future generations, and careful management of a population is usually necessary

to assure that the genetically effective population size is not greatly smaller than the censused population (Foose 1977, Flesness 1977, Foose et al. 1986). Chesser (1983) points out that increases in the effective population size by demographic management may not be sufficient to slow drift adequately, and even suggests that "exclusive focus on population size can have disastrous results for the management of genetic resources." He then paradoxically discusses various means of managing the demography of a population to increase the effective population size (by managing migration between subpopulations) and thereby decrease inbreeding.

Mutation can reasonably be ignored as an evolutionary force in small captive populations. For example, a captive population of 100 individuals is unlikely to experience a mutation in any individual at more than 10 percent of its genetic loci over 100 generations. More-

over, the minor additional variation inserted into a captive population by mutation over any timespan of human interest is likely to be counterproductive for the goal of preserving the genetic uniqueness of a population.

One approach to the question of what size captive population is needed to preserve sufficient variability for long-term viability is to determine the number that would maintain adequate heterozygosity when at mutation-drift equilibrium. For example, Franklin (1980) suggested that a population of 500 would be sufficiently large to be in mutation-drift balance for adequate variability of quantitative (polygenic) traits. (Franklin's estimate was based on papers by Lande [1976] and others that suggested mutation could maintain considerable variation for quantitative traits under moderate stabilizing selection. Turelli [1984] questioned Lande's conclusions, showing that with somewhat different [and perhaps more realistic] assumptions about mutation rates, phenotypic effects of mutation, and the intensity of selection, mutation is much less capable of maintaining variation in a selected trait.) Franklin's estimate has often been proposed as a guideline for management of endangered species (e.g., Soulé & Wilcox 1980, Frankel & Soulé 1981, Schonewald-Cox et al. 1983) and has been applied to management plans for the Siberian tiger (Foose & Seal 1981, Foose 1983).

The use of a mutation-drift equilibrium model, or perhaps any equilibrium model, for the management of small captive populations may be misguided, however. At equilibrium, heterozygosity remains constant, but the genome does not. Allelic losses still occur due to drift, but those alleles are replaced by new, generally different mutations. In a natural population, most new mutations are lost by drift, a few increase to sufficient frequencies to be subject to the positive or negative force of selection, and the population slowly evolves. In a captive environment, such changes also occur, but selection is likely to be very different from that experienced by a population living in a more natural habitat. While in mutation-drift equilibrium, a captive population may be rapidly evolving into something quite different genetically from what it was initially. Unless captive propagation seeks to create domesticated stocks or to make specific changes in the genetic make-up of a population, genetic captive-management plans should aim for a cessation of evolutionary processes to the extent possible. (Planned genetic alteration of a population might occasionally be necessary to assure survival in captivity or other highly modified environments, and this consideration may override concerns about preservation of an unaltered population [Templeton & Read 1983, Foose et al. 1986].)

For assessing success in preserving the genetic characteristics of a population, captive management plans should be concerned with the loss of the variation present in the founding population. The consensus that arose from the 1984 Front Royal conference to strive for a

retention of 90 percent of heterozygosity for 200 years (Soulé et al. 1986) reflects a recognition of the non-equilibrium nature of genetic management of captive populations.

Fuerst and Maruyama (1986) also stressed the lack of equilibria in early generations of captive breeding, pointing out that most rare alleles present in natural populations would not be sampled when a small number of founders is obtained to begin captive breeding, or would be lost within the first few generations of captivity. Because rare alleles are lost during bottlenecks much more rapidly than is heterozygosity, Fuerst and Maruyama (1986) recommend that emphasis be placed on the preservation of allelic diversity and, therefore, that larger founding populations than those suggested by studies of heterozygosity will be needed. Unfortunately, except for short-term captive propagation plans, it is unlikely that sufficient wild stock can be obtained and sufficient captive stock maintained to give much hope for the preservation of rare alleles. Managers of very small populations may be forced to focus efforts on minimizing the deleterious consequences of severe loss of heterozygosity.

If a large wild population exists and can be used to supplement the captive population, periodic immigration (capture of new founder stock) can drastically reduce drift of the captive population away from the genetic characteristics of the wild population. As few as one immigrant per two generations would be beneficial, and five or more immigrants per generation would virtually halt genetic drift within the captive population. Immigration into very small populations is especially effective (and important), as loss of genetic variability is almost independent of population size when immigrants are introduced at a rate of one or more per generation. A population of only 20 individuals that receives an immigrant per generation retains almost as much genetic variability as does a population an order of magnitude larger. Because immigration reverses extant genetic differentiation between captive and source populations, sporadic immigration at the same long-term average rate can be just as effective as is a regular schedule of immigration in maintaining a population close to its initial state.

For an endangered species, there may be no large source population available. If the captive population is much larger than is the wild population (as with Siberian tigers), migration into the wild population from the captive population can help to maintain genetic variability in an endangered wild population that otherwise might experience excessive inbreeding. If both the wild and captive populations are small, migration between them could give to both some of the advantages of a population size equal to their combined numbers (*see results and discussion concerning population subdivision*).

Selection can deplete, maintain, or even augment genetic variation, yet magnitudes of selection likely to act on populations not under artificial selection are not ef-

fective when populations are of a size typical of captive populations. The inefficiency of selection in the face of rapid genetic drift suggests that some concerns and some hopes of captive propagation are unlikely to be realized. The altered environment of captivity creates new selective pressures not experienced by a natural population, and releases the captive population from selective constraints experienced by the wild counterpart. Unless some traits are strongly deleterious or advantageous in a captive environment (causing perhaps a 10% differential in mortality between those individuals with the traits and those without), response to selection for "captive" traits is unlikely to be apparent amid random fluctuations in allele frequencies. Inadvertent and unavoidable selection for domestication has probably not produced "zoo species" in which genetic characteristics important to survival in the wild have been selected away. (Behavioral changes in captive populations are much more likely to cause problems for reintroduction programs.)

Unfortunately, the inefficiency of selection also means that drift will often fix deleterious alleles by chance in small captive populations. Genetic variants poorly adapted to either a captive or wild habitat may become prevalent in long-term captive populations. If continued survival and propagation of a species seems threatened by genetic changes occurring in the captive population, it may be necessary to impose strong artificial selection for a zoo-adapted, domesticated animal.

By dividing a captive population into several subpopulations (management units for breeding loans, trades, and sales), more of the genetic variability originally present in the founding stock can be maintained overall. The genetic cost of population subdivision is increased inbreeding within each subpopulation, and greater divergence of individual subpopulations from the genetic characteristics of the founders (Chesser et al. 1980, Chesser 1983).

The frequency of movement of animals between captive populations determines whether a species is managed as one interbreeding population or a number of more or less isolated subpopulations. An often-cited (e.g., Spieth 1974, Frankel & Soulé 1981, Hedrick 1983, Foose et al. 1986) theoretical result is that when the number of migrants per generation much exceeds one, the subdivided population behaves as though it were panmictic (Moran 1962). As shown in Figure 7D and Figure 8, however, five migrants per generation are not sufficient to bring the population to effective panmixia. Even 20 migrants per generation were not sufficient to prevent fully loss of genetic diversity within, and divergence among, subpopulations (simulations not shown). Allendorf and Phelps (1981) found that 10 migrants per generation were insufficient to prevent significant divergence among subpopulations in their very similar computer model of genetic drift in subdivided populations. The

difference between 20 and "greater than one" may not be important to the theoretical results, but it certainly has meaning to the population manager.

Fuerst and Maruyama (1986) considered the fate of allelic diversity in subdivided populations. Pointing out that rare alleles are likely to be lost in small populations (even if substantial heterozygosity remains), and that most subpopulations would retain only the common alleles of the source population, they suggested that population subdivision is not beneficial to the preservation of allelic diversity. To the contrary, a subdivided population structure may be the only way to preserve allelic diversity in small populations. In the absence of balancing selection, eventually all alleles but one would be lost at each genetic locus of an isolated population. The probability that a neutral allele will be retained is equal to its initial frequency. Thus, a neutral allele with initial frequency in the source population of 0.01 has a 1 percent chance of being sampled and retained in any population. If 10 subpopulations are maintained, the probability that at least one will retain a rare allele is about 10 times the probability that a single panmictic population would retain the allele. (In the extreme, a clonally reproducing organism, with as many subpopulations as individuals, would never lose allelic diversity so long as all lines were maintained.)

Even in the first few, nonequilibrium, generations, a subdivided population will retain allelic diversity better than would a panmictic population. The probability that a rare allele is initially sampled from the wild population is not dependent upon how founders are partitioned into breeding groups for production of future generations. After the initial sampling, rare alleles will be present at much higher frequencies in those subpopulations where they exist than they would have been in a panmictic population, and this helps protect them from random loss. Mathematically, the probability of loss from a randomly mating population in any one generation is $(1 - p)^{2N}$, in which p is the allele frequency and $2N$ is the number of alleles in the population. The probability of loss in any one generation from all k equal-size subpopulation is

$$\begin{aligned} & (1 - p_1)^{2N/k} \cdot (1 - p_2)^{2N/k} \cdot \dots \cdot (1 - p_k)^{2N/k} \\ &= [(1 - p_1) \cdot (1 - p_2) \cdot \dots \cdot (1 - p_k)]^{2N/k} \\ &= [\text{geometrical mean of } (1 - p_i)]^{2N}, \end{aligned}$$

in which p_i is the frequency of the allele in subpopulation i . The frequency of any allele in the panmictic population will be equal to the arithmetic mean frequency across the subpopulations, $((1 - p_1) + (1 - p_2) + \dots + (1 - p_k))/k = (1 - p)$, and thus the probability of loss from the panmictic population is $[\text{arithmetic mean of } (1 - p_i)]^{2N}$. The geometric mean of a series of numbers is smaller than or equal to the arithmetic mean. Thus the probability of loss from all subpopulations is always less than the probability of loss from the one panmictic

population. Contrary to Fuerst and Maruyama (1986), perhaps the most beneficial result of population subdivision is the greater conservation of allelic diversity.

Population subdivision also slows the genetic response of a population to selection because it increases genetic drift within subpopulations where selection would act. By inhibiting directional selection, subdivision will help maintain variability and will slow inadvertent domestication of captive stocks. (If whole subpopulations were selectively eliminated after subpopulations have diverged [between-population selection]; perhaps with the intent of eliminating less successful stocks, there would be considerable loss of genetic diversity.) Although not modeled here, different selection pressures among subpopulations can also maintain genetic variability (reviewed by Hedrick et al. 1976, Karlin 1982).

To the extent that balancing selection (favoring heterozygotes within each population) maintains genetic variability (an issue under much debate among evolutionary biologists), the increased drift that occurs with subdivision will push populations away from equilibria maintained by balancing selection and thereby cause loss of adaptive genetic variability. The disruption of balanced equilibria by drift is simply a restatement, in causal terms, of the deleterious effects of inbreeding ("inbreeding depression") in subdivided populations. Concern about the reduced efficacy of balancing selection should be tempered, however, by the realization that natural selection on captive populations is probably quite different from natural selection on wild populations. Polymorphisms maintained by balancing selection in the wild may not be protected by balancing selection in captive populations.

Chesser et al. (1980) suggested a management scheme for using subdivision to maximize balancing selection in order to preserve polymorphism in small populations. In examining equilibrium models of polymorphism, they point out that polymorphism can be maintained indefinitely in a small population only if there is strong balancing selection. They proposed to let subpopulations become partially inbred, so that the general heterosis (hybrid vigor) produced with subsequent migration would result in temporary strong balancing selection on the genome. If there is much variation that is not strongly adaptive in a captive environment, however, or if the time scales of conservation goals are finite (on the order of tens to perhaps hundreds of generations), then practices aimed at slowing evolutionary processes are probably more desirable.

Slatkin (1981) presented both analytical and simulation analyses of the efficacy of selection in a subdivided population with migration between subpopulations. He found that when migration is low (less than about 0.5 per generation), the ultimate result of selection (prob-

ability of fixation of a favored allele) is quite similar to the case of minimal migration; when migration is much above one per generation, the ultimate response was usually similar to the case of a panmictic population. The times to fixation (i.e., the rate of response rather than the ultimate result of selection) always increased with decreasing migration between subpopulations. Thus, as would be expected from the simulation results presented here, increasing isolation of the subpopulations slowed the rate of evolutionary change.

Allendorf (1983) recommended a management strategy of 1 migrant per generation among isolated nature reserves, pointing out that low levels of migration prevent the total loss of alleles from local populations, while not preventing adaptive genetic divergence. My simulations suggest that that level of migration might be advantageous among small captive populations also, although the costs and benefits of subdivision of captive populations are perhaps somewhat different from those for populations managed in nature reserves. Random genetic divergence between subpopulations allows for better maintenance of alleles and total gene diversity, but local adaptation of subpopulations resulting from differential selection might be an unfortunate consequence of captive propagation programs aimed at eventual restoration of diverse gene pools in more natural habitats. (As pointed out above, however, I see selection as relatively inefficient in small subdivided populations.) Also, while Allendorf emphasizes preventing the total loss of allelic variants from populations, I worry more about potentially severe losses of heterozygosity and any consequent loss of fitness. Reintroduced populations and augmented remnant wild populations will need both allelic diversity and moderate levels of heterozygosity to become securely reestablished.

The value of population subdivision to captive propagation depends considerably on the time scale for which captive management goals are set. The genetic cost of subdivision occurs primarily in early generations, as inbreeding is especially rapid over the first 10 to 20 generations. The benefit of improved maintenance of total variability and the ability of between-subpopulation migration to reduce inbreeding both become apparent only after 10 to 20 generations, because both are dependent upon genetic divergence of subpopulations. For short-term management plans, there would be no genetic advantage to subdivision of the population, although isolation of smaller breeding groups may be important in the prevention of catastrophic disease outbreaks. For very long-term management (30 or more generations), the optimal management plan might be to subdivide the captive population into units of perhaps 20 breeding individuals each and then carefully to regulate inter-unit migration at the lowest level that does not lead to unacceptably deleterious effects of inbreeding. Apparently

more concerned about the effects of inbreeding, Foose et al. (1986) recommended keeping subpopulations sizes greater than 25, and preferably between 50 and 100. Unfortunately, the maximum acceptable level of inbreeding almost certainly differs among species. Currently, information does not exist for any species that would allow accurate determination of the degree of inbreeding that would jeopardize long-term survival.

Population subdivision is reversible, however, up to the point that one or more subpopulations go extinct. If a preliminary plan for subdivision seemed not to be producing desired results, subpopulations could be merged to produce a panmictic population that almost always would be more diverse genetically than it would have been had it never been subdivided. Unfortunately, such a reconstituted panmictic population, while high in genetic diversity and with allele frequencies approximating those in the founders, may be rather different from the ancestral stock with respect to genetic linkage relationships. On the other hand, if a captive population is kept panmictic there is no way to recover genetic variants that are lost by drift without introducing new founder stock from the wild.

Perhaps the biggest difficulty in a management plan centered around a divided breeding population lies in administration. Moderate levels of migration cancel the genetic benefits of subdivision, and more quickly so than the genetic costs of inbreeding are removed. For population subdivision to be a useful management tool, movement of animals between breeding units must be strictly controlled. Two or three unplanned movements per generation could turn genetic benefits into costs. For example, a highly subdivided population (10 subpopulations of 12 individuals each) with high migration rates (5 to 10 migrants per generation over the total population) will suffer effects of moderate inbreeding within subpopulations and yet likely retain no more total gene diversity than would a panmictic population. Unfortunately, many captive breeding programs currently result in just such a population structure. Given the primitive state of knowledge about the effects of population subdivision, management plans need to be carefully monitored and revised when necessary.

A preliminary attempt has been made to use computer simulations to explore some genetic consequences of evolutionary forces acting on managed populations. Much more detailed examination of the genetics of small populations is possible by computer simulation. There is perhaps a greater need at this point, however, to obtain empirical data on genetic responses by particular species of interest. If possible, work should focus on developing generalizations that allow prediction of the genetic behavior of a population based on knowledge of its biology and the biology of taxonomically and ecologically similar organisms. As empirical data on the effects of in-

breeding, the importance of genetic variation to captive and wild populations, and the factors maintaining or depleting variation are gathered, computer modeling can focus on factors of most importance, using appropriate parameters. Computer models such as the one presented here can be useful almost immediately in the comparison of possible alternative management plans being considered for species propagated in captivity.

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