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Selection versus random drift: long-term polymorphism persistence in small populations (evidence and modelling)

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SUMMARY

Our data on a subterranean mammal, *Spalax ehrenbergi*, and other evidence, indicate that appreciable polymorphism can be preserved in small isolated populations consisting of several dozens of, or a hundred, individuals. Current theoretical models predict fast gene fixation in small panmictic populations without selection, mutation, or gene inflow. Using simple multilocus models, we demonstrate here that moderate stabilizing selection (with stable or fluctuating optimum) for traits controlled by additive genes could oppose random fixation in such isolates during thousands of generations. We also show that in selection-free models polymorphism persists only for a few hundred generations even under high mutation rates. Our multi-chromosome models challenge the hitchhiking hypothesis of polymorphism maintenance for many neutral loci due to close linkage with few selected loci.

1. INTRODUCTION

The problem of polymorphism maintenance in small populations has been a constant challenge to evolutionary biologists (Wright 1931; Mayr 1954; Wright 1965; Dobzhansky *et al.* 1977; Carson 1990; Grant 1991). This problem is critical for conservation biology, which focuses on saving endangered species and on acclimatization projects that are designed to introduce new species into impoverished biotic communities (Frankel & Soulé 1981; Lande 1988; Fiedler & Jain 1992; Nunney & Campbell 1993). But how can genetic diversity be maintained in small isolated populations, in spite of genetic drift, potential inbreeding, or sporadic bottleneck events? Our data on the subterranean mole rat *Spalax ehrenbergi* (Nevo 1989, 1991; Nevo *et al.* 1994*a*) and pocket gopher *Thomomys talpoides* (Nevo *et al.* 1974) and other evidence (Carson 1990; Coates 1992; Hartl & Hell 1994) indicate that polymorphism could be preserved in rather small populations (less than 50–100 individuals), or even in those subjected to or recovered from narrow bottlenecks (Bryant & Meffert 1986; Carson 1990; Coates 1992; Hartl & Hell 1994).

2. GENETIC POLYMORPHISM IN SMALL POPULATIONS OF *SPALAX*

Our long-term local, regional, and global studies of natural populations of *Spalax*, and of more than a thousand plant and animal species tested for multilocus allozyme variation, indicate that the level of genetic diversity varies non-randomly among populations, species, and higher taxa (Nevo 1978, 1988; Nevo *et al.* 1984). Genetic diversity across coding and non-coding regions of nuclear and extranuclear genomes was shown to be correlated with and predictable by ecological factors (Nevo *et al.* 1996). These results corroborate the adaptive environmental theory of genetic diversity, and they were confirmed in controlled laboratory experiments on pollution biology (Nevo 1988). Natural selection appears to be a major differentiating, maintaining and orienting force of evolutionary changes at the DNA and protein levels (Nevo 1988; Nevo *et al.* 1984, 1996).

Special analyses were devoted to protein, DNA and phenotypic variation in subterranean mammals (Nevo 1979, 1989, 1991, 1995; Nevo *et al.* 1990, 1994*a*, *b*), including the *Spalax ehrenbergi* super-species (Nevo 1989, 1991; Nevo *et al.* 1994*a*). Generally, protein polymorphism is significantly lower in subterranean mammals than in aboveground mammals of similar size (Nevo *et al.* 1990). However, the level of polymorphism increases with aridity stress (Nevo 1989, 1991; Nevo *et al.* 1994*a*, *b*, 1996). Remarkably, we found high levels of allozyme, nuclear DNA, and mitochondrial DNA diversity in small peripheral isolated populations of the chromosomal species *S. ehrenbergi* $2n = 60$ in the northern Negev (Nevo 1989; Nevo *et al.* 1994*a*). These populations are separated by 40 km from the main range by an inhospitable desert environment. The separation may have occurred more than 10000 years ago in the post-Würm period. However, intermittent rainier periods may have occurred during the late Pleistocene in Israel (Horowitz & Weinstein-Evron 1986). What are the mechanisms that might explain the high (up to 40–50%) level of polymorphism in these very small isolates, each of which involves 50–100 individuals?

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3. LONG-TERM POLYMORPHISM PERSISTENCE IN SMALL POPULATIONS: PATTERNS AND MODELS

Several mechanisms have been proposed to explain multilocus genetic polymorphism maintenance in large (infinite) populations. These include heterozygote advantage, stabilizing selection in constant environments, variable selection (in space and/or in time), genotype–environment interaction, frequency-dependent selection, selection–mutation balance, and others (Crow & Kimura 1970; Lande 1976; Karlin 1977; Hedrick 1986; Via & Lande 1987; Burger 1989; Turelli & Barton 1990; Nagylaki 1992; Zhivotovsky & Feldman 1992; Gavrilets & Hastings 1994; Korol *et al.* 1996). An important evolutionary question is whether these forms of selection may contribute to polymorphism maintenance in small populations. Many efforts attempted to analyse the consequences of selection in finite multilocus populations (Sved 1968; Franklin & Lewontin 1970; Wills *et al.* 1970; Robertson & Hill 1983; Keightley & Hill 1988; Gavrilets & Hastings 1995). However, the question of how to explain the long-term maintenance of polymorphism in small isolates (especially of multi-chromosomal species) remains open. The closest discussion to this problem and to the subject of this paper is the simulation studies of multilocus heterotic selection for either linked or randomly segregating loci (e.g. Franklin & Lewontin 1970; Gavrilets & Hastings 1995).

The objective of our modelling was to analyse more natural modes of selection capable of long-term polymorphism maintenance in small populations. Here we consider two such mechanisms: (i) stabilizing selection, and (ii) stabilizing selection with a cyclically moving optimum. The selected trait is assumed to depend on semi-dominant genes with additive effects across loci or additive genes with unequal effects; the first mode is analysed here to a larger extent.

Previous studies on *infinite* population models have shown that intense stabilizing selection for closely linked loci results in the formation of strong linkage disequilibria. Very few prevailing haplotypes represent the entire multilocus variation in the population at any moment (Lewontin 1964). Likewise, in infinite populations, selection for an intermediate optimum of a trait controlled by semi-dominant loci can also contribute to polymorphism with no linkage disequilibrium, and with stable points deviating from a central polymorphism being proportional to the number of participating loci (Kojima 1959; Lewontin 1964). Moreover, a combination of these two models maintains polymorphism in an *infinite* population in a ‘hybrid’ form of a central polymorphism, with linkage disequilibria between linked loci and linkage equilibria between unlinked gene blocks (our unpublished results).

Franklin & Lewontin (1970) also found that formation and maintenance of strong linkage disequilibria due to heterotic selection for closely linked loci is an effect which can be preserved under a *finite* population size. Clearly, it is expected that the effects produced by selection in infinite populations may be reproducible also, to a large extent, in small populations, provided selection is strong enough. Here, we address this problem by employing computer modelling. We show that *moderate* selection compatible with the reproductive capacity of even K-selected mammals, is capable of overriding Wrightian random fixation, resulting in polymorphism maintenance during thousands of generations in small and isolated groups of only 100 individuals.

4. DESCRIPTION OF THE MODEL

Monte-Carlo simulations were conducted of small panmictic populations with non-overlapping generations. The genotypes of $n_1 = 50$ males and $n_2 = 50$ females were presented by a set of L autosomal di-allelic loci, controlling the selected trait, μ. The participating loci are distributed over several chromosomes (from one to six). No more than one (evenly distributed) crossing-over was assumed per chromosome. In the model, each male can participate in more than one pairing. Each female is fertilized once by a randomly chosen male, producing four newborns with equal probabilities of sons and daughters. To establish the new generation, the resulting progeny is subjected to selection for the fitness trait as follows. The genotypic value of the selected trait is defined as

$$\mu = \sum_i d_i\{\max(a_i, a_i') - |a_i - a_i'|(1-h_i/d_i)\},$$

where $a_i = \{0 \text{ or } 1\}$ and $a_i' = \{0 \text{ or } 1\}$ are symbols for alleles at the ith locus, d_i is the additive effect, and h_i is the heterozygous effect at the ith locus. Thus, the input of the ith locus to the genotypic trait value is 0 and d_i for the homozygotes $a_i a_i$ and $a_i' a_i'$, respectively, and h_i for the heterozygote. Two versions of the dominance effect will be considered: (i) h_i is independent of the environmental state; and (ii) h_i deviates from the mid-parental value towards the fittest of the two homozygotes, $a_i a_i$ and $a_i' a_i'$. The last model (variable h_i) was considered by Gillespie (1978) in the context of a spatially heterogeneous environment for infinite populations, and proved to be quite robust with respect to polymorphism maintenance (Maynard Smith & Hoekstra 1980).

In general, it is well known that stabilizing selection for a trait controlled by additive loci produces epistatic interaction of these loci with respect to their fitness effects. The fitness of a genotype with a trait value, μ, is $w(\mu) = \exp[-(|\mu - z|/s)^2]$, where z stands for the selected optimum. Two types of selection regimes were considered: stabilizing selection (z is constant over generations) and cyclical selection (over the period $T = t_1 + t_2$, z takes sequentially the values z_1 and z_2). Selection of a newborn with a genotypic trait value, μ, is conducted by considering its relative fitness $\tilde{w}(\mu)$ as the probability of survival. To calculate $\tilde{w}(\mu)$ of a genotype, $\tilde{w}(\mu)$ was scaled on $w_{\max}$, corresponding to the fittest genotype in the current generation of the newborns.

Initial populations were randomly sampled from a set of genotypes with all of the loci affecting the selected trait being heterozygous and in linkage equilibria. The foregoing cited evidence on *Spalax* indicated that up to 30–50% of the analysed allozymic loci can be polymorphic in the populations approaching stressful xeric conditions (Nevo 1989; Nevo *et al*. 1994*a*). Thus, in our simulations, the moment when 50% of initially heterozygous loci reach fixation was used to stop the trajectory. Namely, a run was stopped when 50% or more loci enter the region of 1% or less polymorphism and remain within it continuously during ten generations. Otherwise, the trajectory was continued for up to 5000 generations, a realistic estimate for small polymorphic isolates of *Spalax* (Nevo 1991). For each combination of the parameters 200 runs were conducted, employing DEC-station (alpha 600/5–266).

Three types of the genetic architecture of the selected trait were studied: (1) a block of six linked loci; (2) a set of six unlinked loci; and (3) three non-linked blocks each consisting of two linked loci. These configurations were tested with respect to polymorphism maintenance under a stable selection regime (stabilizing selection), and fluctuating selection (stabilizing selection with alternating optimum). Ideally, the best simulation strategy should screen all possible parameter combinations. We employed this approach for parameters of major interest, i.e. selection intensity and recombination rate: parameters characterizing gene effects are represented by a few sets compatible with long-term polymorphism maintenance. For each of the major three foregoing genetic architectures, we employed a selection-free regime complemented by mutations, for comparison. Likewise, we also analysed a few examples where the three genetic architectures are complemented by linked neutral loci.

5. RESULTS OF THE SIMULATION

(*a*) *Stabilizing selection*

Of the two analysed modes of gene action, i.e. semi-dominant genes with additive effects across loci, and additive genes with unequal effects, the former was better for polymorphism maintenance by stabilizing selection. For each of the three genetic architectures, we provide the simulation results for several sets of parameters characterizing the selected gene effects, coupled with sliding along the recombination rates (where possible, i.e. in cases 1 and 3) and selection intensity.

(*b*) *One group of a few linked genes*

The major conclusion one can derive from figure 1 is a strong dependence of the polymorphism persistence on selection intensity and recombination rate. The proportion of runs with no less than half of the loci retaining polymorphism during the first 5000 generations increases with tighter linkage and higher selection intensity. For the chosen sets of parameters, the mean fitness of the population at the quasi steady-state is rather high (ranging from 0.78 to 0.90), and quite compatible with the reproductive capabilities of *K*-selected mammalian species. However, mean fitness may be rather low at the initial points of some trajectories.

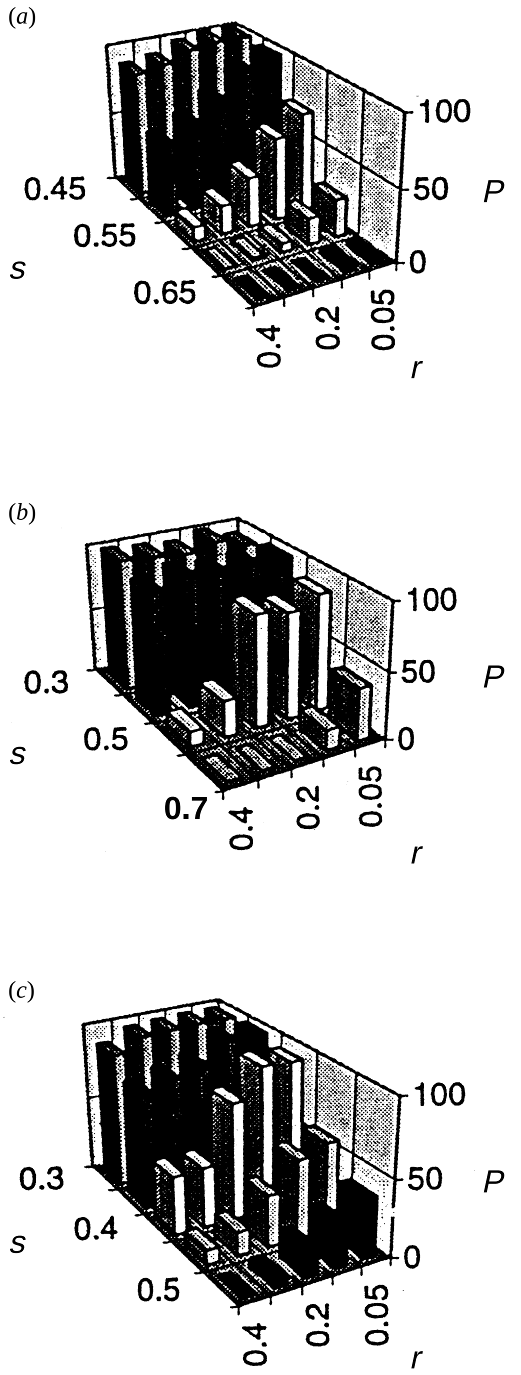


Figure. 1. Polymorphism maintenance in small populations due to stabilizing selection for a trait controlled by a block of six linked loci. Monte-Carlo simulations of panmictic populations with non-overlapping generations ($n_{♀} = 50$ and $n_{♂} = 50$) were conducted in order to estimate the effect of selection on the proportion P (%) of population trajectories which appeared to maintain polymorphism for at least half of the loci at generation 5000. The fitness of an individual with a genotypic trait value μ is $w(\mu) = \exp[-(|\mu - z|/s)^m]$, where z stands for the selected optimum. In the figure, r is the recombination frequency per the selected gene block, and s is the parameter of selection intensity in the fitness function. (Note that lower s values correspond to higher selection intensity.) The dominance coefficients and optimum trait value z were as follows: (*a*) $h_i = 0.8$ $(i = 1, \ldots, 6)$, $z = 3.43$; (*b*) $\{h_i\} = (0.92,\ 0.26,\ 0.8,\ 0.25,\ 0.91,\ 0.2)$, $z = 2.59$; (*c*) $\{h_i\} = (0.6, 0.3, 0.7, 0.61, 0.68, 0.67)$, $z = 3.49$.

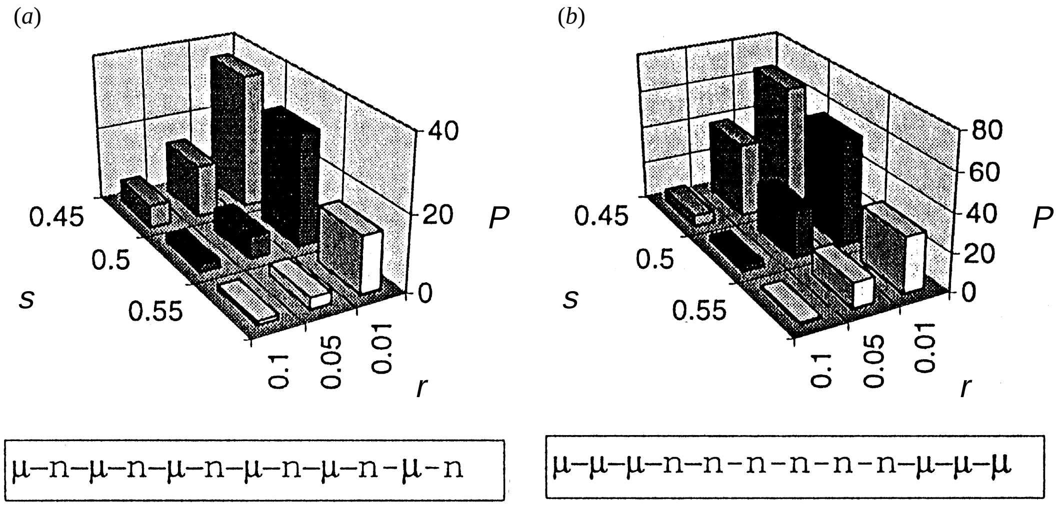


Figure 2. Polymorphism for selectively neutral loci due to hitchhiking: (*a*) alternating of selected and neutral loci; and (*b*) a block of neutral loci inserted between two blocks of selected loci. Symbols μ and n stand for loci affecting the selected trait and neutral loci, respectively. The selection regime corresponds to the case (*a*) of figure 1.

The following examples demonstrate the importance of the last effect. For several regimes that resulted in a moderate-to-low polymorphism duration, the experiments were repeated. We examined runs with initial points taken randomly from the set of states characteristic of the trajectories where polymorphism has persisted at generation 5000. Here are some pairs with the first number (P_1) representing the percentage of polymorphic trajectories when starting from a random initial point and the second one (P_2), when the start is from the foregoing 'final' set of polymorphic trajectories:

$$P_1 = 50\,\%,\ P_2 = 80\,\%\ (r = 0.4,\ s = 0.5)$$

$$P_1 = 18\,\%,\ P_2 = 32\,\%\ (r = 0.1,\ s = 0.6).$$

(In this example all h_i were equal to 0.8.)

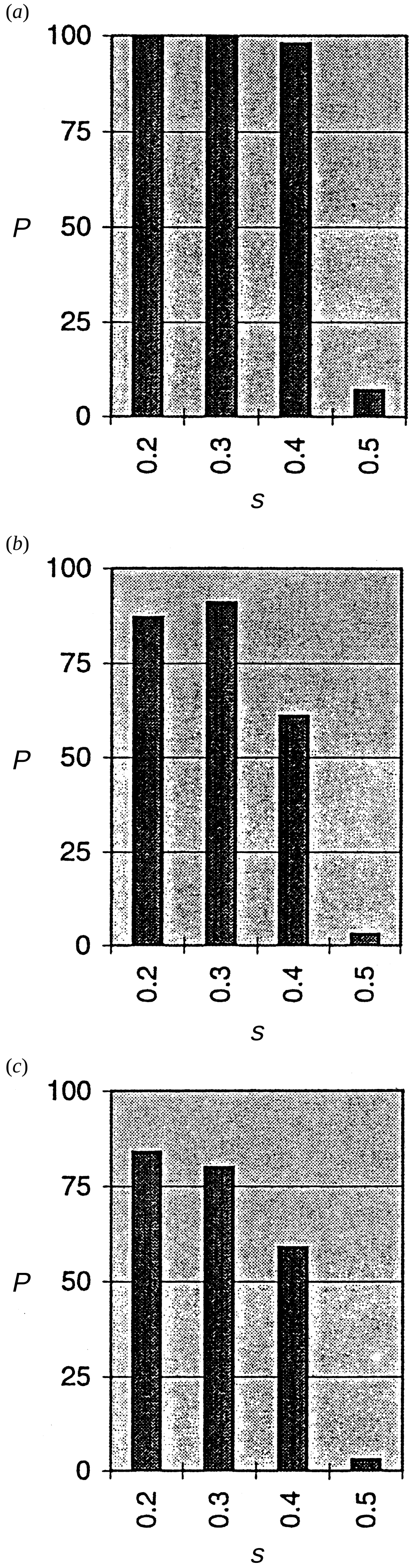
The common feature of the polymorphic population trajectories in the case of linked loci is the formation of strong linkage disequilibria, with very few prevailing haplotypes that represent the entire multilocus variation in the population at any moment. Such structures are well studied in *infinite* population models (e.g. Lewontin 1964; Franklin & Lewontin 1970). Their formation even in small isolated populations may be an efficient way to oppose random drift and gene fixation in nature. Actually, the formed structures can be approximated by a single locus model with the number of 'super alleles' equal to the number of predominating multilocus haplotypes. New haplotypes produced by recombination could be considered as mutation events. The stabilizing selection in the initial system is equivalent to (associated) overdominance at the resulting 'super locus'.

It is instructive to compare and contrast the obtained duration of polymorphism caused by stabilizing selection with that obtained for selection-free cases with the same configuration of the involved loci and the same population size. Numerical simulations show that even with an unrealistically high mutation rate (10^{-4} per locus per generation), a selection-free population loses allelic variation in a few hundred generations (not more than 300–400, for the considered range of recombination frequencies).

Another, much more interesting aspect of the selection–neutrality dichotomy is related to the hitchhiking concept (Hedrick 1982). Namely, one could ask (i) whether long-term polymorphism maintenance is possible in such a model for purely neutral loci, only due to their linkage with selective ones, and (ii) if so, how many neutral loci per one selected locus could, on average, hitchhike. Here we provide some examples showing that if the target trait is controlled by one block of linked loci, then linkage to the selected loci may significantly slow down fixation at neutral loci. However, this may not be the case when the selected loci are spread over several linkage groups (see below).

Let us consider two configurations of neutral and selected loci (figure 2): (*a*) *alternating configuration*: six selected loci are sequentially alternated with six neutral ones; (*b*) *block configuration*: a block of six neutral loci is bordered by two selected blocks, each of three loci.

In both cases, the proportion of the neutral loci that remain polymorphic at generation 5000 decreases abruptly when recombination rate increases and selection intensity decreases (see figure 2). To exclude the effect of the initial linkage disequilibria between the selected and the neutral loci, these experiments were repeated employing the following approach. Trajectories, with at least 50 % of the selected loci remaining polymorphic after 5000 generations, were continued for the next 5000 generations. However, at generation 5001 the neutral loci were restarted, each at 50 % allele frequency and in linkage equilibria with all other loci, both selected and neutral. The result was that in the next 5000 generations the rate of decay in polymorphisms was the same as that in the first 5000 generations. This means that the mode of hitchhiking does not depend strongly on the initial process that structures the selected system. Presumably, random fluctuations in disequilibria between neutral loci and selected haplotypes became partly frozen, allowing for a long-term hitchhiking in a part of the neutral loci.



(*c*) *A set of unlinked loci*

For this configuration of the selected system, the major parameter affecting the duration of polymorphism at any population size is the intensity of selection (figure 3). It is not surprising that a stronger selection is needed, compared to the previous configuration with one block of linked genes, to get approximately the same proportion of retained polymorphism (after the chosen period of 5000 generations) dynamics (see also Wills *et al.* 1970). Much less expected is the result that moderate stabilizing selection for a trait controlled by unlinked semi-dominant loci (with additivity across loci) is capable of overriding random fixation during extended periods. Note that although the mean fitness at quasi steady-state is lower here than that for the linked block configuration, it is still high enough ($W \sim 0.65$–0.75, i.e. the load is 0.25–0.35 per six loci) and compatible with the reproductive capabilities of *K*-selected mammals.

It is useful to compare the present results with previous results. Wills *et al.* (1970) showed that *heterotic selection* for many unlinked loci could result in a considerable proportion of polymorphisms after hundreds of generations with a population size of $N \sim 100$. Our model is based on a much more natural assumption of additive (across loci) control of the selected trait. Kojima (1959) found that stabilizing selection for a trait controlled by unlinked semi-dominant genes with equal effects can produce polymorphism in infinite panmictic populations. Our model differs from that of Kojima with respect to the allowed between-loci variation in the dominance level, as well as in population size.

Note that as in the case of 'a linked block' configuration (see above), the duration of polymorphism in a selection-free system does not exceed 200–300 generations. The hitchhiking hypothesis was tested for a system consisting of six chromosomes, each carrying two linked loci, a selected and a neutral one (with the rate of recombination, r). We found that for $r \sim 0.01$ or more, the neutral loci were quickly fixed. Only with very tight linkage ($r \sim 0.001$), were a small proportion (less than 5%) of the polymorphic trajectories for the selected loci at generation 5000, also polymorphic for one or two neutral loci.

(*d*) *Non-linked blocks each consisting of two linked loci*

In a sense this configuration is intermediate between those considered in the previous two sections. Thus, as expected, the polymorphism duration depended on selection intensity and recombination rate. The proportion of trajectories involving more than 50% of polymorphic loci at generation 5000 was positively

Figure 3. Polymorphism maintenance in small populations due to stabilizing selection for a trait controlled by six unlinked loci. The dominance coefficients and the optimum trait value z were as follows: (*a*) $h_i = 0.8$ ($i = 1, \ldots, 6$), $z = 3.43$; (*b*) $\{h_i\} = (0.92, 0.26, 0.8, 0.25, 0.91, 0.2)$, $z = 2.59$; (*c*) $\{h_i\} = (0.6, 0.3, 0.7, 0.61, 0.68, 0.67)$, $z = 3.49$.

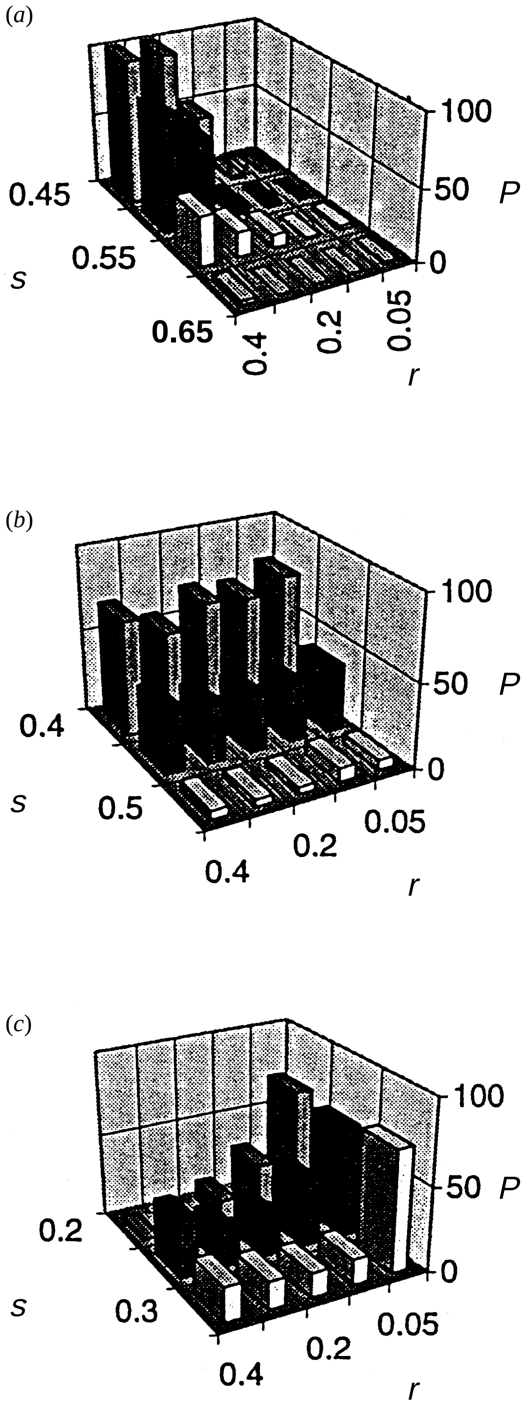


Figure 4. Polymorphism maintenance in small populations due to stabilizing selection for a trait controlled by three blocks each consisting of two linked loci. The dominance coefficients and optimum trait values, z, were as follows: (*a*) $h_i = 0.8$ ($i = 1, \dots, 6$), $z = 3.43$; (*b*) $\{h_i\} = (0.92, 0.26, 0.8, 0.25, 0.91, 0.2)$, $z = 2.59$; (*c*) $\{h_i\} = (0.6, 0.3, 0.7, 0.61, 0.68, 0.67)$, $z = 3.42$. Note the non-standard effect of recombination on polymorphism maintenance.

correlated with selection intensity (figure 4). As in the former two configurations, population mean fitness at the quasi steady-state is also rather high (ranging from 0.70–0.87) and compatible with the low reproductive ranges of many vertebrates.

The question of the expected mode of the effect of linkage on polymorphism is more complicated. The behaviour of the examined configuration may 'inherit' from the first configuration the tendency of higher polymorphism at closer linkage. However, it depends simultaneously on the mechanism of Kojima's (1959)

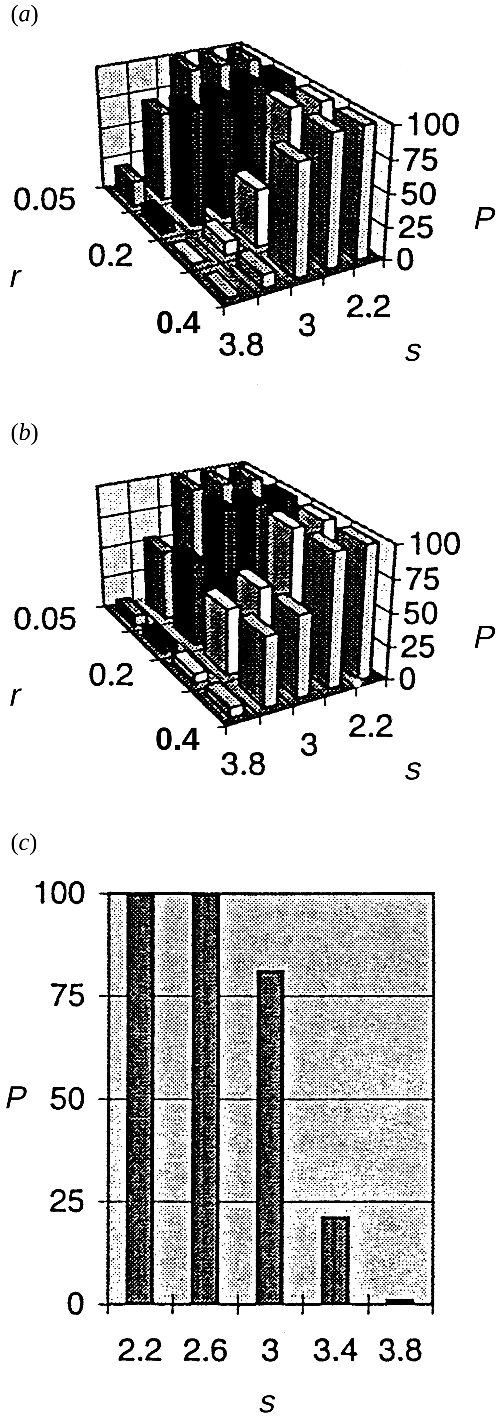


Figure 5. Polymorphism maintenance in small populations due to stabilizing selection with cyclically changing optimum. The parameters of the period $T = t_1 + t_2$ in our simulations were $t_1 = t_2 = 1$ with the selected optima $z_1 = 0$ and $z_2 = 6$. The dominance coefficients h_i deviated from the mid-parental value towards the fittest of the two homozygotes $a_i a_i$ and $a'_i a'_i$, according to Gillespie's (1978) model; thus at $z = z_1 = 0$ all h_i were 0.3 while at $z = z_2 = 6$ all h_i were 0.7 ($i = 1, \dots, 6$). The selected trait is controlled by (*a*) a block of six linked loci; (*b*) three blocks each consisting of two linked loci; and (*c*) six unlinked loci.

model based on linkage equilibrium for unlinked loci. Thus, in the third configuration, polymorphism may represent a combination of these two mechanisms. Indeed, as can be seen from figure 4, the dependence of polymorphism on recombination is quite different from the heuristic expectation: an absence of a ubiquitous tendency for increased levels of polymorphism at lower recombination rates. For example, with the set h_i in figure 4*a*, the proportion of endured polymorphisms increases at higher recombination rates. It is noteworthy that related infinite population models (with respect to the configuration of the selected system) manifest the same mode for the effect of recombination on the volume of polymorphism attracting domain (our unpublished results).

The duration of polymorphism in the corresponding selection-free system does not exceed 200–300 generations; mutations add a little to polymorphism persistence. The effect of hitchhiking of neutral loci in this configuration is much lower than that in the case of multiple linked loci. The reason for this difference stems from the foregoing unanticipated effect of recombination on polymorphism. Indeed, the demand for increased recombination between selected loci (see figure 4*a*) reduces the efficiency of hitchhiking to a negligible level.

(*e*) *Stabilizing selection with a cyclically moving optimum*

For a changing environment we employed the dominance model of gene effects on the selected trait. It appeared that the constant dominance (h_i independent of the environmental state) version is relatively poor with respect to the ability of producing regimes with long-term polymorphisms. By contrast, in the model of variable dominance proposed by Gillespie (1978) in the context of a spatially variable environment, plenty of parameter combinations allow for long-term polymorphism maintenance. The foregoing three configurations of selected loci positioning were examined for the cyclical selection regime. The results, presented in figure 5, indicate that cyclical selection is an effective mechanism overriding random fixation in all configurations. Clearly, polymorphism maintenance here is a phenomenon which is causally related to environmental change. Stabilizing selection for the trait values, corresponding to either of the two environmental states, immediately leads to fixation for all loci.

6. DISCUSSION

The major conclusion resulting from this modelling is that both mechanisms (stabilizing selection or cyclical selection) can maintain polymorphism for many semi-dominant loci during thousands of generations, in spite of a small population size. This conclusion is quite robust with respect to concrete configurations of the selected loci within and between chromosomes. It is noteworthy that some of the results presented here follow the previous studies of infinite population models (Kojima 1959; Lewontin 1964; Gavrilets & Hastings 1994; Korol *et al*. 1996). This is true for the results obtained with configurations 1 (a block of linked genes) and 3 (several unlinked loci). However, the behaviour of the system of multiple unlinked blocks (configuration 2) upon stabilizing selection may be less expected: here polymorphism results from a combination of two different mechanisms, based on (a) high linkage disequilibria (Lewontin 1964; Franklin & Lewontin 1970), and (b) no linkage disequilibria at the stable state (Kojima 1959).

An important point concerning this model, which is relevant to situations of very small isolated mammalian populations like *Spalax*, is the consideration of multiple linkage groups. As applied to the case of stabilizing selection, this challenged the hitchhiking mechanism as a major causal factor of the observed polymorphisms. Indeed, as shown above, if all selected loci are linked within a block, polymorphism maintenance for these loci is directly dependent on linkage within the block. Consequently, this provides the possibility for polymorphism at neutral loci residing within the same block, and the last phenomenon does not even depend on the initial linkage disequilibria between the selected and the neutral loci. However, the effect of linkage may be opposite for the configuration with multiple unlinked blocks of selected loci (figure 4*a*). Here the chances of polymorphism maintenance increase at looser linkage within the blocks, so that hitchhiking becomes ineffective.

There is evidence for polymorphism maintenance in small populations in nature after severe bottlenecks (Coates 1992; Hartl & Hell 1994; Keller *et al*. 1994). In selection experiments with *Tribolium*, Rich *et al*. (1984) found no considerable differences among small lines established from a large population. Based on these results, they concluded that stabilizing selection effectively counters the drift processes that otherwise should lead to strong differentiation of the resulting lines, as predicted by the idea of drift as a major evolutionary force in small populations (Wright 1931).

Some additional aspects of our modelling results are worth mentioning.

(i) The strength of selection needed to protect polymorphism is not too demanding and is quite compatible with the reproductive potential of many mammalian species, including *K*-selected taxa such as *Spalax*. Indeed, for the majority of regimes conditioned by our parameter sets, the mean fitness in the quasi-stationary state was in the range 0.7–0.9. Significantly, the available measurements indicate the possibility of moderate to strong selection operating in natural populations (Ford 1971; Endler 1986).

(ii) For the examined model situations, the mean time needed for a selection-free system to lose polymorphism in half of its initially polymorphic loci, even with a high mutation rate (10^{-4} per locus per generation), is by one-to-two orders of magnitude lower than in the presence of selection.

(iii) Fluctuating (cyclical) selection appeared to be a promising mechanism in polymorphism maintenance, provided the dominance effects of the selected loci are formalized according to Gillespie's (1978) model.

(iv) In situations where selection for many loci was modelled, a qualitative correspondence of the resulting estimates of the mean proportion of heterozygote loci per individual was obtained when compared with the data on small populations of *Spalax* (Nevo 1989, 1991; Nevo *et al*. 1990, 1994*a*, *b*). Thus, the average level of individual heterozygosity of 36 assessed allozymic loci was about 7–10%, and 17–25% for the polymorphic loci. In our simulations the corresponding range was a 20–25% polymorphism.

(v) Most importantly, the polymorphisms prevalent in the very small, long-isolated populations of *Spalax* in the northern Negev Desert are precisely those ranging in the main range of the xeric species, $2n = 60$ (Nevo 1989, 1991; Nevo *et al*. 1994*a*). This clearly highlights their adaptive nature. Rather than being neutral (Kimura 1983), or even nearly neutral (Ohta & Gillespie 1996), they are selected and contribute to fitness and survivorship in the harsh desert ecology.

7. CONCLUSION

Strong selection (more than 10% per trait) may be quite a common phenomenon in nature, as first emphasized by Ford (1971) (see also Endler 1986). This could have important evolutionary consequences in the case of small peripheral populations (Mayr 1954). Our modelling clearly demonstrates that moderate or strong selection in a small population can oppose random drift and maintain polymorphism during thousands of generations. These results are significant for the theories of adaptation and speciation, particularly for peripatric speciation (Mayr 1954).

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