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Genetic variation in heterogeneous environments

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The theories on the maintenance of genetic variation in a heterogeneous environment are reviewed. The genetic response of a population to the pattern of the environment can be divided into direct and indirect effects. The direct effects refer to adaptive responses due to selective differences between the genotypes. The indirect effects result from the fact that environmental variation affects the population demography (size, subdivision etc.) and this affects the stochastic processes which shape genetic variation. Although the deterministic models show that environmental heterogeneity can help to maintain genetic polymorphism of specific characters, the parameter space leading to a stable polymorphism is heavily constrained, for example due to stochastic changes. Genotype-specific habitat selection and the reversal of genetic dominance in different environmental patches help the maintenance of polymorphism considerably. The theories concerning single characters have been extended to explain the overall gene diversity detected by studies of proteins and DNA. The theoretical basis for this extension is unclear and the experimental evidence for it is equivocal. It seems likely that the indirect effects of the environment are more important in determining the levels of multilocus genic variation and differentiation. Selection in a heterogeneous environment can, in some circumstances, even act as a factor reducing genetic variation below the level expected under a completely neutral model. Genetic variation in quantitative characters depends both on the pattern of environmental variation and on the genetic correlation of the character states expressed in different habitats.

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1. Introduction

One of the basic questions in population genetics is to what extent genetic change and genetic variation of populations can be attributed to adaptation. This problem can be studied by focusing on specific characters and the putative mechanisms of adaptation. Alternatively, we can examine the forces affecting the whole genome, namely, its change and variation at the nucleotide level. Here I will concentrate on the maintenance of genetic variation within populations, but it is necessary to emphasize that the genetic variation in a population at any given moment and the genetic change in a long-term evolution are two aspects of a single process (Nei 1987). Although Endler (1986: 229) considers these to be two very different questions in the context of specific polymorphisms, they cannot be separated when searching for a general theory of molecular population genetics and evolution. A genetic theory explaining the maintenance of genetic variation should simultaneously explain the long-term change; or to phrase it differently, the explanations for these two phenomena cannot contradict each other.

The possible association between the environment and phenotypic variation is theoretically best understood, and experimentally best studied, in the case of specific polymorphisms occurring due to variation at single loci. But speculations have widely exceeded this simple case and the overall multilocus heterozygosity is considered as an adaptive strategy associated with the pattern of environmental hetero-

geneity (Nevo et al. 1984). The latter problem is the core of what has been known as the selectionism-neutralism controversy in population genetics.

Two different mechanisms connecting environmental heterogeneity and the maintenance of genetic variation have been recognized: 1) The classic overdominance could lead to balanced polymorphism if the heterozygous genotypes give individuals the highest fitness in varying environments — the heterozygous generalist hypothesis. 2) Balanced genetic polymorphism can also result from the homozygous genotypes either specializing to utilize the available resources selectively or being otherwise differently favoured in various environmental conditions — the homozygous specialists hypothesis.

In this paper, I will present the theoretical models concerning selection in an heterogeneous environment and then critically overview the explanations of multilocus genetic variation (see Hedrick 1986 for a general review). A statistical association between environmental heterogeneity and genetic polymorphism does not necessarily mean that the polymorphism is adaptive. Such an association can be due to direct or indirect effects. The direct effects refer to cases where the genotypes respond differently to environmental heterogeneity and the resulting genetic variation has a selective basis. An indirect association between the environment and genetic variation arises from the fact that the environmental pattern affects the population demography and this has genetic consequences without any selective differences between the genotypes.

2. Maintenance of specific polymorphisms

2.1. Deterministic models

The pattern and scale of environmental variation can take many forms, but we can simplify our assumptions in order to make workable models. We can distinguish between temporal and spatial heterogeneity. Spatial heterogeneity can be further divided into two categories taking into account the scale of variation or environmental grain. The grain can be defined in terms of environmental variances (Lynch & Gabriel 1987). In a fine-grained environment the spatial variance among the individuals is small and the within-generation temporal variance is large. When the spatial component is large and the temporal variance during an individual's lifetime is small, the environment is said to be coarse-grained.

The topic "selection in an heterogeneous environment" generally refers to a situation where each homozygous genotype is selected for in one and against in another environmental condition. In a fine-grained environment, where the individuals face the whole range of environmental variation during their lifetime, the necessary condition for stable polymorphism is that the arithmetic mean fitness of the heterozygote is greater than those of the homozygotes (Strobeck 1975). The mean is calculated by weighting the various environmental conditions with their proportions. This requirement is in fact close to, if not identical with, the classic overdominance model — the heterozygote being a flexible genotype with the highest overall fitness.

When the environment varies temporally, the requirement for stable polymorphism is that the heterozygote has the highest geometric mean fitness (Haldane & Jayakar 1963). The means are again calculated by weighting the different time periods with their durations. In the case of complete genetic dominance, polymorphism is maintained if the geometric mean fitness of the recessive homozygote is smaller, but the arithmetic mean fitness larger than the fitness of the dominant type (Haldane & Jayakar 1963).

Before examining the conditions for stable polymorphism in a coarse-grained environment, we have to specify the nature of selection. In this model, the population is subdivided, each subdivision living in one environmental patch. At the time of mating, the subpopulations fuse and form one panmictic unit, whereafter the population again subdivides. From the polymorphism point of view there is an essential difference in whether the productivity of each patch is constant, depending only on the size of the patch and not on the genotypes inhabiting it (soft selection), or whether the productivity is a function of the genetic constitution of the subpopulation (hard selection).

The model of hard selection was introduced by Dempster (1955) who called it a "constant-zygote-number" model. If the distribution of individuals in different subpopulations is random, the essence of the model is that the net selective value of each genotype is determined by the actual proportions of different environmental types. Statistically, this means that the model is comparable with that of selection in a fine-grained environment, and that the principle of arithmetic mean fitness superiority of heterozygotes applies here.

In the model of soft selection there is selection within the patches, but the total output from a given patch remains constant, hence the term "constant-fer-

tile-adult-number" selection (Dempster 1955). It was first shown by Levene (1953) that the necessary condition for stable polymorphism under this model is that the harmonic mean fitness of the heterozygote is greater than those of the homozygotes, when the fitnesses are scaled by making that of the heterozygote equal one in each patch.

Because the harmonic mean is always the smallest and the arithmetic mean the largest of the three means, the situation most favourable to stable genetic polymorphism is soft selection in a coarse-grained environment.

The work of Levene (1953) is sometimes regarded as a starting point of theoretical ecological genetics (e.g. Arnold & Anderson 1983). Another attempt to combine ecology and genetics has been to consider genetic variation in parameters defining population growth. This has led to models of density-dependent selection. Arnold & Anderson (1983) combined the two traditions of ecological genetics in a model of density-dependent selection in an heterogeneous environment. Assuming logistic population growth, they showed that genetic polymorphism can be maintained in a hard-selection model under conditions very much like those ordinarily obtained under soft selection. Namely, the necessary condition for protected polymorphism is that the harmonic mean of an adjusted carrying capacity in each homozygote is smaller than that of the heterozygote.

2.2. Constraints

The above shows that selection in a heterogeneous environment can maintain stable polymorphism. The importance of this phenomenon in natural populations is, however, severely limited by several constraints. The mean fitness of the heterozygote — be it arithmetic, geometric or harmonic — is likely to be largest only if the environmental types exist in approximately equal proportions, and if the dominance relationship between the alleles is reversed when moving from one environment to another.

If one environmental type is very common, the homozygote favoured in that environment has the best overall fitness and selection will lead to genetic monomorphism (Maynard Smith & Hoekstra 1980, Hoekstra et al. 1985). When selection is weak, this constraint can be very stringent.

The models discussed above assume that one homozygote is the fittest genotype in one environmental patch and the order of the fitnesses is reversed in the other patch. If the heterozygote is always intermediate in fitness, the two environmental types should be close to equal in frequency for polymorphism to be maintained. Gillespie (1978) proposed a fitness scheme that maintains polymorphism more easily. Namely, if the heterozygote is intermediate but always has a fitness closer to the better homozygote, selection is more likely to result in stable polymorphism. This conclusion was also shown as being true by Hoekstra et al. (1985). The question then is whether dominance is reversed in the way suggested in this SAS-CFF model (stochastic additive scale — concave fitness function).

Some recent ideas on the evolution of dominance in biochemical characters associated with metabolic flux, support the view of physiological dominance in spite of biochemical intermediacy in activity (Kacser & Burns 1981, Hartl et al. 1985). Dominance at the phenotypic level is also possible if the heterozygote covers the activity ranges of the specialized homozygotes; substrate specificity of allozymes is a case in point (Hoekstra et al. 1985).

2.3. Stochasticity

The above conclusions are all based on deterministic models. The situation in nature may be different, even if all the necessary conditions of polymorphism exist. In finite populations, gene frequencies drift. Chance variation may temporarily increase heterozygosity, but the overall effect of drift is the loss of genetic variation. In the long run this will counter the force of balancing selection. In fact, a mechanism of selection, which in a deterministic model leads to a stable equilibrium, can in a finite population accelerate the loss of variation.

This was first noticed in overdominance (Robertson 1962) and can be examined with the help of a retardation factor. It is known that heterozygosity due to neutral alleles decreases at an average rate of $1/(2N_e)$ per generation, where N_e is the effective population size. More generally we can write this in the form $1/(2rN_e)$, where r is the retardation factor. For neutral variation, $r=1$. Selection can either slow down the rate of loss of variation ($r>1$), or accelerate it ($r<1$). In other words, the retardation factor compares the selected locus in question with a neutral one and shows how large a population can lose neutral variation at the same rate.

The exact behaviour of the retardation factor depends on the population size and the strength of se-

lection. The main result under overdominance is that the retardation factor exceeds one when the equilibrium allele frequencies of the deterministic model are between 0.2 and 0.8, but outside this range the retardation factor drops below one (Robertson 1962). This means that with extreme equilibrium frequencies, overdominance does not form a mechanism maintaining polymorphism in finite populations but accelerates the loss of genetic variation. The reason for this is obvious. Because of selection, the allele frequencies drift around the equilibrium value and are always close to the fixation point.

The effect of stochastic changes is not restricted to overdominance but is more general. Hedrick (1978) has shown that the same applies to multiple-niche polymorphism. As mentioned above, the parameter space giving a stable polymorphism is constrained in deterministic models, and in stochastic models it becomes still more constrained.

In summary, although the different genotypes were specialized in the way they utilize the heterogeneous environment, selection will not necessarily result in stable polymorphism. The parameter space allowing polymorphism can be very limited, particularly in the case of weak selection, unless the individuals can select the favourable habitat.

2.4. Habitat selection

The above conclusions are based on the assumption that the individuals are randomly distributed in the environment. If this is the case, the parameter space (defined by selection intensity and environmental heterogeneity) leading to stable polymorphism is very limited (Hoekstra et al. 1985). However, it is likely that the individuals do not always disperse randomly, but actively select the habitat where they live or breed.

Habitat preference is a well-known phenomenon in nature, for instance in host selection of parasites and herbivorous insects. Such habitat preference, based on conditioning, can evolve without any viability differences in the microhabitats. The situation, as noted by Rausher (1984), is analogous to the sex allocation problem: the average unit of investment in each microhabitat should give the same genetic payoff to the ovipositioning females. This kind of evolution can lead to habitat preference and it only concerns the locus affecting this preference. After the preference has developed, the populations can evolve other characters affecting the viability in a given habitat. This process benefits from the initial linkage disequilibrium between the viability genes and the habitat preference genes. According to Garcia-Dorado (1987), it may be unlikely to find protected polymorphisms for habitat preferences without an association to selection within the niches.

Hoekstra et al. (1985) examined a model of habitat selection based on conditioning. It is assumed that there is random mating in the population, whereafter the females return to lay eggs in the same microhabitat where they, themselves, grew up. If there is selection within the habitats, this kind of habitat preference relaxes the constraints of stable polymorphism but does not increase the parameter space leading to polymorphism much. Limited dispersal of individuals has a similar effect.

The robustness of the model increases considerably if the niche preference is positively associated with selection within the niches (Garcia-Dorado 1986, 1987). Such an association can result from pleiotropy or close linkage. Although genotype-dependent habitat selection seems to be very important in maintaining polymorphism, it has only rarely been documented in nature (see Endler 1986: 106–7). One of the rare examples is provided by the *Cepaea* snails; their colour variation has been much studied. The experiments of Jones (1982) suggest that different colour morphs stay in differently exposed microhabitats. If this genotype-dependent habitat selection is associated with differences in survival in these microhabitats, it makes the maintenance of colour polymorphism more understandable. This kind of habitat selection would maintain genetic polymorphism effectively, but it is hard to believe that many characters could be maintained polymorphic simultaneously by this mechanism. Many more studies on genotype-specific habitat selection are needed.

3. Quantitative characters

The above discussion concerned single-locus polymorphisms. Similar arguments can be extended to quantitative characters under polygenic control, when there is a specific association between the character value and the pattern the individuals utilize in the environment (Van Valen 1965, Smith 1987). However, a straightforward extension of the theory is not possible when there are genotype-environment interactions, namely, when the same genotype is differently expressed in different environments (Via &

Lande 1985). Host specialization provides a case in point (Via 1984).

The quantitative genetic theory of evolution in a heterogeneous environment has been developed by noting that a character expressed in two environments can be considered as a set of two genetically correlated characters (Via & Lande 1985). If the correlation is not perfect (±1), a joint optimum for both environments is obtained, but the rate and course of the phenotypic change are affected by the correlation. Correlated responses to selection can lead to temporary maladaptation in rare habitats. A difference in the phenotypic optima is an expression of phenotypic plasticity (Via & Lande 1985). At equilibrium, the character is under stabilizing selection, and such selection depletes genetic variation (e.g. Kimura 1983). Any genetic variation in the characters in question is thus neutral or due to new mutations (Lande 1976, Turelli 1984), or the population may not be at equilibrium. Genetic variance at the mutation-selection equilibrium is determined by stabilizing selection within the habitats. Disruptive selection between the habitats increases the genetic variance temporarily when the population is perturbed, but not at equilibrium (Via & Lande 1987). Only if the perturbations are large or the environmental optima change frequently, will the effects of disruptive selection accumulate and the genetic variance increase in the population.

If the environmental variation is not discrete, as was assumed above, the picture is different. For example, if there is a non-random association between the phenotype and the individual fitness in an environmental gradient, the distribution of the character values will be affected by this gradient (Roughgarden 1972). The evolution of the niche width and the level of genetic variation in the population depend on both the between-individual differences in the environmental optima and the within-individual breadth of adaptation. Lynch & Gabriel (1987) developed a model where both the genetically determined environmental optimum and the genetic component of environmental tolerance have some developmental noise, and the realized breadth of individual adaptation is subject to selection. The model is for density-independent environmental factors. According to their results, spatial heterogeneity can promote the specialization of different phenotypes. This leads to increasing genetic variation. Temporal heterogeneity favours generalist phenotypes and selects for broader tolerance curves of individual genotypes. The within-generation temporal heterogeneity plays a more important role than the heterogeneity between generations. There is also an important interaction between the spatial and temporal components of heterogeneity.

The evolution of niche width, based on characters related to the exploitation of environmental resources, leads to density-dependent models. In addition to the relevance of intraspecific specialization, such models connect the intraspecific genetic change with the coevolution of competing species and the species packing in the community (Loeschke 1984). The interplay between genetics and ecology should lead to an alternation of directional, stabilizing and disruptive selection, depending on the invasion (extinction) of the species in the community, and on the consequent shifts in the optimal resource utilization curves. The expected level of genetic variation depends on the phase of such a community-wide evolutionary process (Loeschke 1984).

4. Multilocus heterozygosity

4.1. Hypotheses

The multilocus heterozygosity detected by studies of proteins and DNA has also been considered by some as an adative response to the environmental pattern (e.g. Nevo et al. 1984). The theoretical basis of extending the single-character models to deal with the whole genome is not unequivocal. The problem is that such adaptive hypotheses of genetic variation do not specify the exact relationships between the polymorphisms and specific environmental variables. Therefore, a number of different hypotheses have been formulated. All hypotheses share the assumption that genetic variation is adaptive and that the same (or correlated) environmental factors simultaneously maintain polymorphisms at many loci.

The niche-width variation hypothesis was first presented for morphological characters and later suggested for enzyme gene variation (see Soule 1976). The basic assumption is that the niche width of a population represents the environmental heterogeneity experienced by its members and that a wide niche results in higher heterozygosity. The environmental variables used as a niche axis include, for example, temperature and food resources, but often the niche width is postulated by rather subjective opinions (Noy et al. 1987). Several studies have shown a positive association between the mean heterozygosity and the postulated niche width, but counter examples

do exist (Somero & Soule 1974). A similar hypothesis, based on temporal variation, is the environmental-amplitude hypothesis (Soule 1976), according to which heterozygosity should be higher in organisms living in temporally varying environment.

Based on the niche-width variation hypothesis, it was expected that the deep-sea organisms, living in a very stable environment, should have a low level of heterozygosity. The contrary turned out to be true (Ayala et al. 1975), and this gave support to the resource-stability hypothesis. According to this hypothesis, the organisms living in a very stable and predictable environment can specialize in resource utilization, and this specialization increases genetic variation. The effect of such a specialization should be similar to that of habitat choice.

4.2. Experimental evidence

The experimental studies concerning the abovementioned hypotheses can be classified into three categories: 1) biochemical and physiological studies on the functional differences between the allozymes, 2) statistical associations between genetic variation and environmental variables in nature, and 3) experimental laboratory studies on the effects of environmental heterogeneity.

Functional differences between the allozymes have been detected in several studies, and in some cases these differences seem to be associated with environmental variables, for example, temperature (Zera et al. 1985). Whether these differences give rise to fitness variation, or not, is much more difficult to conclude. We should also note that fitness variation among the genotypes may often lead to monomorphism within a population. If different homozygotes are favoured in separate geographical areas, the respective populations tend to become fixed for alternative alleles but gene flow leads to a cline. It should be noted, however, that a reverse is not generally true: a cline does not necessarily indicate differential selection optima at the terminal populations.

Indirect support for the environmental hypotheses have been sought from statistical associations between the enzyme gene heterozygosity and environmental variables. The associations can refer to specific loci and alleles or to total heterozygosity on one hand, and to specific variables or to environmental pattern on the other (see e.g. Manly 1985). Some significant associations have been found, but this kind of evidence of adaptation is circumstantial and alternative explanations should be carefully examined.

The experimental population studies have been done mainly with *Drosophila* in laboratory cultures with different numbers of environmental variables (such as temperature, food sources). The hypothesis is that the populations in the most variable environments should have the highest heterozygosities. The results from such experiments are not convincing, and they appear to be somewhat contradictory (Hedrick 1986). A major problem is how to homogenize the genetic background of the marker loci at the beginning of the experiments. Therefore, we do not know the extent to wich the results reflect "hitchhiking". The experiment of Mackay (1981) is exceptional in that genetic variation was measured with the additive variances of three quantitative characters and not by direct estimates of heterozygosity. The conclusion from that experiment was that a population may adapt to a heterogeneous environment by selection of heterozygosity.

One problem in evaluating the environmental hypotheses, particularly the niche-variation hypothesis, concerns the relevant niche axes. It is well conceivable that population 1 faces a wider range of temperatures while population 2 has more diverse food resources. A connection between the niche axes and genetic variation has been sought by dividing the enzymes into different groups based on their function. So-called group I enzymes include those with a specific intracellular substrate and group II is formed by enzymes using several, normally extracellular substrates (Gillespie & Langley 1974). If the food resources have anything to do with enzyme gene variability, we might expect that the resource diversity affects the group II enzymes the most (Nelson & Hedgecock 1980). We should have a similar expectation in the resource-stability hypothesis. The advocates of this hypothesis have used the krills as an example (Ayala & Valentine 1979). The heterozygosity in a tropical krill *Euphausia distinguenda* is much higher (H=0.216) than in the arctic species *E. superba* (H=0.084; only enzymes examined in both species are included here). Reanalysis of these data shows that the difference in heterozygosity between these two species is approximately of the same magnitude, both in group I (heterozygosities 0.253 and 0.101) and group II enzymes (0.158 and 0.057). Therefore, the trophic specialization hypothesis seems unsatisfactory and we should seek alternative explanations for the observed difference.

4.3. Alternative hypotheses

There are so many experimental observations of an association between heterozygosity and environmental heterogeneity that at least some of the cases are likely to involve a causal relationship (Zera et al. 1985). But causality does not necessarily mean that the genetic variation is adaptive and maintained by balancing selection. I want to recognize direct and indirect causality.

Direct causality refers to "selection in an heterogeneous environment" in the sense discussed above. This implies an adaptive mechanism depending on a specific association between the enzyme function and environmental variation. This is certainly true in a few cases but its generality can be doubted. A good research strategy for studying the nature of total heterozygosity is to make a null hypothesis, based on the factors known to affect it (Manly 1985, Endler 1986). Such a null hypothesis in molecular population genetics and evolution is given by the neutral theory (Kimura 1979, 1983, Nei 1987).

The neutral theory forms a null hypothesis and includes those factors which are known to affect genetic variation: mutation, migration, and drift due to a finite population size. Based on such a null hypothesis, we can make certain predictions. One prediction is that the level of heterozygosity is positively correlated with the species population size. Nei & Graur (1984) claimed such a correlation in a combined data set from 77 species. Some caution is necessary because heterozygosity is affected by the long-term population size, which is not really known.

The indirect effects of environmental heterogeneity on genetic variation can be mediated through population dynamics and selective constraints. A species with a wide niche may build up larger populations than narrow-niche specialists and therefore we expect higher heterozygosity. There are only a few studies addressing this problem, but they indicate that the indirect effect of the environment is significant: the levels of heterozygosity and the genetic differentiation of populations can be explained using the information on the species population sizes and dispersal capacities (Varvio-Aho 1981, 1983; Waples 1987). Traditionally, the term 'heterogeneous environment' has, in population genetic literature, referred to a situation with specific fitness differences in different habitats. However, genetic studies of subdivided populations in a patchy environment are likely to address a more relevant aspect of environmental heterogeneity, even though genetic variation was selectively neutral.

Nei & Graur (1984) stressed the point that most natural populations are less heterozygous than predicted by the neutral theory. From this point of view we should not search for factors maintaining variation, but for factors reducing it. Most polymorphisms at the level of DNA and proteins seem likely to be selectively neutral (Kimura 1983, Nei 1987), but it has also been suggested that much of the variation can be slightly harmful (Ohta 1976). These deleterious effects may become emphasized under stressful conditions (Hartl et al. 1985). In other words, the difference between the genotypes is small in an optimal environment but becomes pronounced in a suboptimal one. If so, populations in stressful and unstable environments should be less heterozygous, not because the variation in a stable environment is adaptive and maintained by balancing selection, but because variation in an unstable environment has harmful consequences. We might expect such a result in the housekeeping enzymes with saturation kinetics (Hartl et al. 1985), but we lack sufficient information on both enzyme kinetics and measures of environmental stress to test this hypothesis.

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