

Population Structure in Relation to Cost of Selection

(genetic load/substitutional load/gene substitution/evolutionary rate)

VERNE GRANT AND ROBERT H. FLAKE

Departments of Botany and Electrical Engineering, University of Texas, Austin, Texas 78712

Contributed by Verne Grant, February 7, 1974

ABSTRACT The opposing requirements in an evolving population for a rapid rate of multiple gene substitution and for the maintenance of normal population size can be reconciled in a variety of ways. The ways out of the impasse suggested here invoke deviations from the usual assumption of a large continuous population with constant numbers. In a colonial population system there may be significant random fluctuations in the accidental mortality rate between different colonies; and those colonies with reduced numbers of accidental deaths could tolerate the larger number of selective deaths that go hand in hand with rapid evolution. In new daughter colonies founded by one or a few colonizing individuals from a large polymorphic ancestral population, some genes may reach complete fixation in one or a few generations, without the usual concomitant selective cost. Or, in the same setup, the favored alleles may change by chance from rare to moderately common, but not to complete fixation, during the founding of some daughter colonies; and this raises the allele frequencies above the low range, where the cost of selection is greatest, so that the cost of further selective changes is bearable.

The cost-of-selection dilemma posed by Haldane (1, 2) refers to the apparently incompatible relation between rapid multiple gene substitution and the maintenance of numerical strength in an evolving population. The process of gene substitution must be spread out over numerous generations if the population is to maintain a sufficient strength in numbers continuously, and this restriction places an upper limit on the rate of evolutionary change. The restriction becomes more severe with increase in the number of independent genes undergoing substitution simultaneously.

Yet rapid evolutionary changes in genetically complex characters do occur occasionally in various groups of organisms. For example, racial differentiation in quantitative characters in *Mimulus guttatus* (Scrophulariaceae) has taken place in 4000 years in certain recent habitats in Utah (3). This herbaceous plant could pass through 4000 generations in this time period. The character differences between races of another herbaceous plant, *Potentilla glandulosa* (Rosaceae) are due to allelic differences in at least 100 genes (4). If the genetic differences between races in *Mimulus* are of the same order as those in *Potentilla*, approximately 100 genes would be undergoing substitution in 4000 generations. This estimate errs on the conservative side as regards both the time element and the gene number. Complex evolutionary changes which are more rapid than this example undoubtedly occur in some situations in nature.

The paradox thus arises that some organisms have managed to evolve at rates which apparently exceed the ceiling imposed by a tolerable cost of selection.

This problem has been extensively discussed in the population genetics literature since 1960. Haldane had postulated certain conditions, such as effectively infinite population size, constant selective values of the favored genes, and independence of the genes in respect to linkage and gene action. Subsequent papers have mostly altered one or the other of these conditions. Thus some of the genes undergoing replacement are assumed to be selectively neutral (5). The selective values are not constant but "soft" or "flexible" (6-8). Special modes of gene interaction are involved (9-15). The favored genes are linked (16). Or the populations are finite and subject to random fluctuations (17, 18).

We wish to suggest a different approach to the problem. What is the bearing of population structure on the cost-of-selection restriction? We will consider two related models. Our approach is similar to that of Kimura and Maruyama (18) in that we consider the effects of finite population size; but theirs is a purely mathematical treatment, whereas we discuss the problem in terms of biologically realistic population setups.

The subdivided population

Wright (19-21) considered the evolutionary advantages of a subdivided population in relation to the joint action of selection and drift. Let us extend Wright's concept to the cost-of-selection problem, following an earlier preliminary attempt by one of us (22). The essential point in Wright's concept is a random component in the variation in gene frequencies; the essential point in our first model is a random component in the accidental mortality rate.

Let us compare a subdivided population with a continuous population of the same total size, $N = 10^6$. The subdivided population consists of 1000 endogamous colonies of $N = 1000$ each. The intensity of selection is assumed to be the same in the two populations and constant from generation to generation. The total cost of selection will also be the same in the contrasting types of populations for the substitution of some given number and type of genes. And the accidental mortality rate is assumed to be the same overall in the continuous and the subdivided populations.

At some point, determined by the interplay between the number of genes involved, the rate of replacement, and the accidental mortality rate, the combined total of selective deaths and accidental deaths will take up all of the population's reproductive excess. At that critical point the cost of selection becomes prohibitive. The population may then decline in size, in consequence of the high selective death rate, and eventually become extinct. The decline is statistically

inexorable in the large continuous population. But the subdivided population with its 1000 colonies has, in effect, 1000 trial parties to explore ways out of the course to extinction.

The accidental mortality rate, which is set at some level for the subdivided population as a whole, as it is also in the continuous population, is subject to random fluctuations in the series of 1000 colonies. Different colonies experience average, high, or low accidental mortalities during a succession of generations. Most of the 1000 colonies will succumb due to the combined total of accidental and selective deaths where the selection is intense. But those sister colonies favored by chance with lighter accidental mortalities can bear a compensatingly heavier burden of selective deaths without a serious reduction in the number of adult individuals. A few such colonies may be able to pull through a process of rapid multiple gene substitution which would prove fatal to a single large continuous population.

Founder populations

The second setup to be considered is that of a large ancestral polymorphic population in a colonizing species. The ancestral population gives rise to a series of daughter colonies founded by one or a few colonizing individuals. The daughter colonies begin with a non-random sample of the ancestral gene pool. This setup has been discussed in relation to genetic revolutions by Mayr (14). It can also be considered in relation to the cost-of-selection restriction on evolutionary rate.

It is generally agreed that previously rare alleles could be fixed rapidly, by partly random factors, in one or a few generations during the founding of some new daughter colonies, leading to rapid deviations from the ancestral condition. The aspect which we wish to emphasize here is that the cost of steady directional selection for the new alleles is evaded in the case of the rapid deviation of the successful founder populations.

A variant possibility is that the allele frequencies of some genes change from low to middle values (rather than to complete fixation), during the early generations in a newly founded colony. Now the cost of selection is greatest in the low range of gene frequencies (9, 23). Let the frequencies of favorable alleles rise above the critical lower level, and reach 10% or more, for example, by processes other than selection alone. Then the population, whether it remains small or becomes

large, may be able to bear the cost of selection for all subsequent increases in frequency up to complete substitution. Rapid multiple gene substitutions could be achieved with fewer trial colonies by this pathway than in the other models discussed here.

It should be possible to test these models experimentally or by computer simulation.

The study was supported in part by NSF Grant GB-16411 and in part by a special grant from the University Research Institute of the University of Texas, both of which are gratefully acknowledged.

1. Haldane, J. B. S. (1957) *J. Genet.* **55**, 511-524.
2. Haldane, J. B. S. (1960) *J. Genet.* **57**, 351-360.
3. Lindsay, D. W. & Vickery, R. K. (1967) *Evolution* **21**, 439-456.
4. Clausen, J. & Hiesey, W. M. (1958) *Experimental Studies on the Nature of Species. IV. Genetic Structure of Ecological Races* (Carnegie Inst. of Washington, Washington D.C.).
5. Kimura, M. (1968) *Nature* **217**, 624-626.
6. Dobzhansky, Th. (1970) *Genetics of the Evolutionary Process* (Columbia Univ. Press, New York).
7. Wallace, B. (1968) *Topics in Population Genetics* (Norton, New York).
8. Wallace, B. (1970) *Genetic Load* (Prentice-Hall, Englewood Cliffs, N.J.).
9. Crow, J. F. (1970) *Mathematical Topics in Population Genetics*, ed. Kojima, K. (Springer Verlag, New York).
10. Felsenstein, J. (1971) *Amer. Natur.* **105**, 1-11.
11. King, J. L. (1966) *Genetics* **53**, 403-413.
12. King, J. L. (1967) *Genetics* **55**, 483-492.
13. Maynard Smith, J. (1968) *Nature* **219**, 1114-1116.
14. Mayr, E. (1963) *Animal Species and Evolution* (Harvard Univ. Press, Cambridge, Mass.).
15. Mettler, L. E. & Gregg, T. G. (1969) *Population Genetics and Evolution* (Prentice-Hall, Englewood Cliffs, N.J.).
16. Kimura, M. & Crow, J. F. (1969) *Genet. Res.* **13**, 127-141.
17. Ewens, W. J. (1972) *Amer. Natur.* **106**, 273-282.
18. Kimura, M. & Maruyama, T. (1969) *Heredity* **24**, 101-114.
19. Wright, S. (1931) *Genetics* **16**, 97-159.
20. Wright, S. (1949) *Genetics, Paleontology and Evolution*, eds. Jepsen, G. L., Mayr, E. & Simpson, G. G. (Princeton Univ. Press, Princeton, N.J.).
21. Wright, S. (1960) *Evolution After Darwin*, ed. Tax, S. (Univ. of Chicago Press, Chicago).
22. Grant, V. (1963) *The Origin of Adaptations* (Columbia Univ. Press, New York).
23. Crow, J. F. & Kimura, M. (1970) *An Introduction to Population Genetics Theory* (Harper and Row, New York).