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Update to "Some Possibilities for Measuring Selection Intensities in Man"

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My 1958 article had two main objectives: (1) to introduce an index of total selection, later called the index of opportunity for selection, and (2) to extend some concepts in the theory of genetic loads. It was based on a talk given at the Wenner-Gren conference held at the University of Michigan on April 12, 1957.

Index of Opportunity for Selection

The index was developed in response to a point raised at the conference by James V. Neel. Newton Morton and I drove back to Madison, Wisconsin, after the conference and discussed this question for much of the way. The basic approach was formulated during and immediately after the trip, and I am indebted to Morton for his help.

The index is a measure of the total amount of selection possible, given the demographics of a population. It answers the question, By what fraction would the mean population fitness increase in one generation of selection if its heritability were perfect (i.e., $h^2 = 1$)? This places an upper limit on the change of fitness, or of a trait correlated with fitness, that could be brought about by natural selection. Let w stand for fitness. The index is

$$I = \frac{\Delta \overline{w}}{\overline{w}} = \frac{V_w}{\overline{w}^2}, \tag{1}$$

in which V_w is the variance of fitness. In the earlier article I described the subdivision of this index into components acting at different stages of the life cycle.

If I were writing the article today, I would derive this subdivision differently. It is easy to show that the index for the whole life cycle can be written in terms of its components during stages $1, 2, \ldots, i, \ldots, n$:

$$1 + I = \overline{w}_{t+1}/\overline{w} = \prod(1 + I_i), \tag{2}$$

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in which t is time measured in generations (Crow 1989). It might have been better to define the index as the ratio of the two fitnesses, in which case the value is the second moment around the origin (rather than the variance) divided by the square of the mean. If, for example, we are interested in three stages, prenatal mortality *ma*, postnatal prereproductive mortality *mb*, and fertility f, the index can be written

$$I = I_{ma} + \frac{I_{mb}}{p_{ma}} + \frac{I_f}{p_{ma}p_{mb}}, \tag{3}$$

where p_m is the proportion surviving the relevant stage. The index of opportunity for mortality is $(1 - p_m)/p_m$. Equation (3) can be written

$$1 + I = (1 + I_{ma})(1 + I_{mb})(1 + I_f). \tag{4}$$

Equation (4) is perhaps more natural than Eq. (3), because it brings out the geometric nature of fitness changes between generations.

The index has been applied to a number of populations. A recent example is the study by Jorde and Durbize (1986) using extensive data from the Utah Mormon population. This study shows a large male fertility index during the period when some males were polygynous and its drop to the female value with increasing monogamy. In fact, in recent years the index for both sexes has attained essentially its Poisson value (Crow 1989).

That the indexes in Eq. (3) are not simply additive has caused consternation among some users, and it has been suggested that the products be combined into a single term (e.g., $I_f^* = I_f/p_a p_b$), thus making the components additive (Neel and Schull 1972). This practice has been followed by others, most recently in *Human Biology* by Hed (1987). My personal preference is for Eq. (3) or Eq. (4), because fitnesses between generations are multiplicative rather than additive; but all formulations provide equivalent information and are easily interconvertible.

There are two clear directions for improvement of the formulas. The variances do not account for possible covariances between stages. Arnold and Wade (1984a,b) have taken this into account in analyzing data on bullfrog populations. Much of the nonadditivity that they found is caused by the multiplicative nature of fitness components and is eliminated if Eq. (4) is used, but part of the nonadditivity is correlation between the stages.

A second improvement is to take age structure into account. Obviously, no modification is required for components associated with prereproductive mortality. Differences in ages of reproduction can be taken into account with sufficient accuracy for most purposes as follows. Let g be the geometric mean of the ages of reproduction of a single multiparous individual. Then, if n is

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the total number of children of this individual, use $n^{\bar{g}/g}$ instead of n in computing the mean and mean square. In this expression $\bar{g}$ is the geometric mean reproductive age of the whole population. This gives the ratio of mean fitnesses of two successive generations, taking age of reproduction into account; a generation is measured by $\bar{g}$.

Both of these improvements could use a more detailed analysis. A theoretically better alternative would be to measure fitness in Malthusian parameters (Fisher 1930), in which case the fitness variance is the appropriate metric for the opportunity for selection. However, I doubt that appropriate data for measuring this variance can be found.

I should emphasize that the index is a property solely of the demography of a population. It gives no information on what part of the variance in mortality and fertility is genetic or assignable to any other specific cause. Such information has to come from other sources.

Genetic Load

Before the 1958 article Morton et al. (1956), in an earlier article, had defined the mutation load as the fraction by which the mean fitness is reduced by recurrent mutation. The basic idea had come from Haldane (1937). Morton et al. showed how to estimate the total load, mostly hidden by recessivity, from the fitness-reducing effects of consanguineous matings. *In the 1958 article I introduced the segregation load.* This is the load caused by homozygotes segregating at a locus at which a heterozygote is favored. I showed that the inbred segregation load is twice that in a randomly mating population and k times as great if there are k alleles segregating (and all heterozygotes are equally fit).

At the time there was a great controversy about the amount of overdominance for fitness in natural populations. Dobzhansky (1955 and later) strongly upheld the view that a large fraction of loci were of this type, with harmful alleles maintained in the population by producing superior fitness in heterozygotes. The other view, argued especially by Muller (1950 and later), was that such loci were rare; if they were common, they would generate an intolerably large genetic load. For a history of this controversy, see Crow (1987).

At the time my 1958 article was written, I had hoped that inbreeding analysis would help to resolve the controversy. Actually, results in the 1958 article and subsequent refinements did contribute some population genetics theory, but the paucity of sufficiently accurate data and uncertainty about the necessary assumptions rendered the method almost useless for this purpose.

The controversy abated because of later evidence from three different

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directions. First was the realization that epistasis, especially that induced by truncation (rank order) selection, could greatly reduce the load, thus removing much of the weight of the load argument against overdominance. Second, and most important, abundant data from *Drosophila* and maize failed to reveal any significant amount of overdominance. Third came the discovery of a large amount of molecular polymorphism in natural populations (Harris 1966; Lewontin and Hubby 1966) and emergence of the neutral theory (Kimura 1983). The overdominance controversy was replaced by the neutralist-selectionist argument.

Thus the load results of my 1958 article did not settle any major issue, although they are now a (small) part of the standard body of theory in population genetics.

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