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Genetics

Efficiency of truncation selection*

(rank-order selection/fitness potential/mutation load/viability/fitness)

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ABSTRACT **Truncation selection is known to be the most efficient form of directional selection. When this is modified so that the fitness increases linearly over a range of one or two standard deviations of the value of the selected character, the efficiency is reduced, but not greatly. When truncation selection is compared to a system in which fitness is strictly proportional to the character value, the relative efficiency of truncation selection is given by $i(c)/\sigma$, in which $i(c)$ is the ordinate of the frequency distribution at the truncation point and σ is the standard deviation of the character. It is shown, for mutations affecting viability in *Drosophila*, that truncation selection or reasonable departures therefrom can reduce the mutation load greatly. This may be one way to reconcile the very high mutation rate of such genes with a small mutation load. The truncation model with directional selection is appropriate for this situation because of the approximate additivity of these mutations. On the other hand, it is doubtful that this simple model can be applied to all genes affecting fitness, for which there are intermediate optima and antagonistic selection among components with negative correlations. Whether nature ranks and truncates, or approximates this behavior, is an empirical question, yet to be answered.**

In the preceding paper (1) we showed the relation between the average increase in a character caused by a gene substitution and the corresponding increase in fitness, for various fitness functions. It is generally known that truncation selection is the most efficient form of directional selection from the standpoint of maximum change of gene frequency for a given effect of the gene on the character, but we quantify this by comparison with specific alternatives. Then, using *Drosophila* data on mutation rates and selection intensities for viability-reducing mutants, we show that truncation selection can indeed reduce the mutation load to an acceptable value despite a high mutation rate.

A broken line approximation

We follow the example of Milkman (2) and approximate various alternatives to truncation selection by connected straight lines (Fig. 1). The fitness function increases linearly between $c - d$ and $c + d$, in which c and d are measured in units of σ. As d becomes 0 we have truncation selection. As d increases so that the slanted line covers the whole range of values of the character, fitness becomes simply proportional to the character value.

As before (1), X is the measured character, $F(X)$ is the frequency function, and $W(X)$ is the fitness function. It is convenient to measure the character as a deviation of X from its mean, m, and in units of the standard deviation, σ; $x = (X - m)/\sigma$. The frequency function on the transformed scale will be designated $f(x)$.

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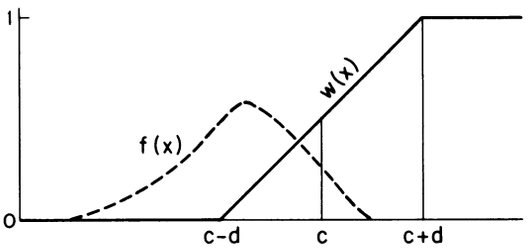

FIG. 1. Broken-line approximation to various fitness functions. As d becomes small the model approaches truncation selection. The x axis is scaled in units of the standard deviation σ. Fitness $w(x)$ is expressed as a fraction of the maximum fitness, W_{max}.

From Fig. 1 and letting $w(x) = W(x)/W_{max}$ we see that

$$w(x) = \begin{cases} 0 & x < c - d \\ (x + d - c)/2d & c - d < x < c + d \\ 1 & x > c + d. \end{cases}$$

From Eqs. 3 and **10a** in the previous paper (1) we have

$$\bar{w} = \int_{-\infty}^{\infty} w(x)f(x)\mathrm{d}x \qquad [1]$$

$$\frac{s_i}{a_i} = -\int_{-\infty}^{\infty} w(x)f'(x)\mathrm{d}x/\bar{w}. \qquad [2]$$

From Eq. **2** we can compare the efficiency of truncation selection with various broken-line alternatives. Some numerical values are given in Table 1, in which the frequency is normally distributed, $f(x) = (1/\sqrt{2\pi})\exp(-x^2/2)$. It is clear, as emphasized by Milkman (2), that truncation selection is more efficient than the alternatives, but not by an enormous amount.

The broken line approximation is very close to the more biological integrated normal fitness function discussed in the earlier paper (1). Fig. 2 shows an example for comparison. The variance of the frequency function, assumed to be normally distributed, is taken to be the same as that of the integrated normal fitness function, so $R = 1$. The value of c is assumed to be 0, which implies that $\bar{W}/W_{max} = \bar{w} = \frac{1}{2}$. From equation **27** in ref. 1 we see that $s_i/a_i = 0.564$. The broken-line model with the same value of s_i/a_i has $d = 1.56$. The two functions are shown in Fig. 2, along with the truncation fitness function, for which $s_i/a_i = 0.798$. Truncation selection is 1.77 times as efficient.

There is no obvious way to decide how large d may become. Is it meaningful for d to be greater than 3–5 standard deviations? In most cases there is not information enough to decide. However, a natural extreme alternative to truncate selection is for fitness to be simply proportional to the character value, X. This is reasonable for a trait, such as viability, for which there is a natural maximum and minimum value.

* This is the second of two related papers. Paper no. 1 is ref. 1.

Table 1. Measures of the relative efficiency of truncation selection against a broken-line alternative

d	$\bar{w} = 0.9$	$\bar{w} = 0.5$	$\bar{w} = 0.1$
0	0.195 (1.00)	0.798 (1.00)	1.755 (1.00)
0.5	0.187 (0.96)	0.765 (0.96)	1.687 (0.96)
1.0	0.170 (0.87)	0.683 (0.86)	1.535 (0.87)
1.5	0.153 (0.79)	0.578 (0.72)	1.379 (0.79)
2.0	0.139 (0.71)	0.479 (0.60)	1.252 (0.71)
3.0	0.118 (0.61)	0.332 (0.42)	1.063 (0.61)
4.0	0.103 (0.53)	0.250 (0.31)	0.925 (0.53)
5.0	0.091 (0.46)	0.200 (0.25)	0.816 (0.46)

The table gives s_i/a_i for specified values of the proportion selected, $\bar{w}$. The values in parentheses are relative to $d = 0$, truncation selection.

This is illustrated in Fig. 3. The character value X goes from 0 to 1, as does the fitness value $W(X)/W_{max} = w(X)$. If the fitness is proportional to the character, $w(X) = X$ and

$$s_i = \frac{X_i - m}{\bar{X}} = \frac{A_i}{\bar{w}} \quad [3]$$

or

$$\frac{s_i}{a_i} = \frac{\sigma}{\bar{w}}. \quad [4]$$

With truncation selection we use equation 11 from the previous paper (1):

$$s_i = \frac{A_i}{\bar{w}} F(C) = \frac{A_i}{\bar{w}} \cdot \frac{f(c)}{\sigma} \quad [5]$$

$$\frac{s_i}{a_i} = \frac{f(c)}{\bar{w}}, \quad [6]$$

in which $c = (C - m)/\sigma$. For a corresponding intensity of selection and phenotypic effect of an allele, the relative efficiency of truncation selection against the alternative of simple proportionality from Eqs. 4 and 6 is

$$RE = \frac{f(c)}{\sigma}. \quad [7]$$

Some numerical values are given in Table 2. The smaller the standard deviation, σ, relative to the range of X, the greater is the relative efficiency of truncation selection. Although s_i/a_i increases with the intensity of selection (i.e., as $\bar{w}$ decreases), as expected, the relative efficiency of truncation selection is greater as $\bar{w}$ approaches ½. Intermediate models are not shown, but from Table 1 it can be seen that when D is nearly σ (or $d = 1$) the selection is about 85% as efficient as truncation selection. Although it is unreasonable to expect nature to practice perfect truncation selection, a model in which d is 1 or 2 may often be appropriate.

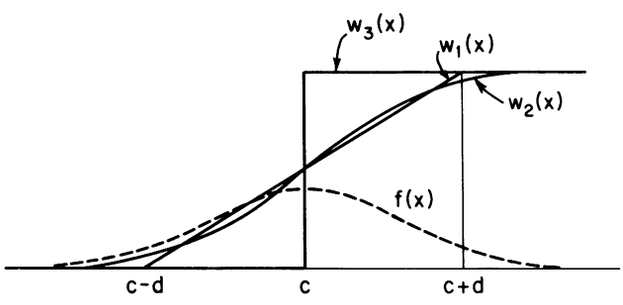

FIG. 2. Close agreement between a broken-line fitness function, $w_1(x)$, and an integrated normal distribution, $w_2(x)$, with the same efficiency of selection. Truncation selection, $w_3(x)$, is 1.77 times as efficient.

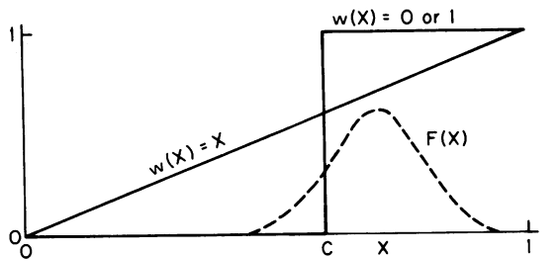

FIG. 3. Truncation selection, $w(X) = 0$ or 1, compared to fitness proportional to the character value, $w(X) = X$. The character value, X, is scaled from 0 to 1.

Application to viability mutants in *Drosophila*

Mutants causing a small decrease in homozygous viability have been studied extensively by Mukai and others (3–5). The individual effects of the mutants are small, no larger than about 0.03 on a scale for which 1.00 is maximum, and possibly considerably smaller because the procedure provides only a maximum estimate. The mutants are approximately additive over the range of interest here (6). They show considerable dominance, enough that the major impact of the mutants is through heterozyous expression (4, 7, 8). The minimum estimate of the mutation rate is about 0.4 per gamete. If fitness is proportional to viability and the genes act independently, the equilibrium fitness, relative to a maximum of 1, is exp(−0.8), or 0.45; the mutation load, by the Haldane mutation load principle (9, 6), is 0.55. If the mutation rate is twice this high, as is quite reasonable because the estimate is only a minimum, the load is 0.80. Can this large load be reduced by truncation selection?

Viability is restricted to the range 0–1 and, if not normally distributed, is at least unimodal (lethals and mutants causing large effects are not included in the data). Furthermore, the mutants are individually small and approximately additive in their homozygous effects. So this trait fits the requirements of our variable X. However, it is clear that natural selection acts not on the homozygous effects of these mutants on viability but on their pleiotropic heterozygous effects on total fitness. That the heterozygous effects of these mutants on "fitness potential" (2) are also approximately additive is suggested by the high correlation between homozygous effect on viability and heterozygous effects on fitness of chromosomes with accumulated mutants (7).

Keeping in mind that the variable X is not viability *per se* but the pleiotropic heterozygous effects of the viability mutants on total fitness, which is assumed to be proportional, we can attempt a rough quantitative interpretation. The value of s_i can be inferred from the inbred viability load in natural populations (10, 11) and the decrement in viability per generation of mutation accumulation (4). The observed ratio of these quantities is 30–40 (7, 8), but there is reason to think that this is a

Table 2. Relative efficiency, $RE = f(c)/\sigma$, of truncation selection against the alternative of fitness being proportional to the measured character

	Standard deviation, σ				
$\bar{w}$	0.01	0.02	0.05	0.10	0.167
0.97, 0.03	6.8				
0.94, 0.06	11.9	6.0			
0.85, 0.15	23.3	11.7	4.66		
0.70, 0.30	34.8	17.4	6.96	3.48	
0.50	39.9	19.9	7.98	3.99	2.39

The values in the upper right corner of the table are omitted to keep the character distribution mainly within the range of 0–1.

slight underestimate, so we use 50.[§] This means that there are about 50 times as many mutants in an equilibrium population as arise in a single generation of mutation, so the mean persistence time for a mutant is 50 generations. The average rate of elimination per generation is roughly the reciprocal of this, or 0.02, so s_i has an average value of about −0.02. This value is quite reliable, being based on direct measurements that are reproducible and on simple theory.

Note that if the individual s_i values vary, the value −0.02 is the average for mutants in the equilibrium population. It is the harmonic mean of the value for newly arisen mutants, whose arithmetic mean would be somewhat larger. The value that we use, and quantities derived from it, apply to those mutants in an equilibrium population, among which those with longer persistence times are disproportionately represented. However, it is the mutation load of a population at equilibrium in which we are interested, so the −0.02 value is appropriate.

If fitness is proportional to viability and $s = -0.02$, then this is the value of $A_i/\overline{w}$. If fitness is subject to truncation selection, then from Eq. 7 this is multiplied by $\sigma/f(c)$.

We can get some idea of the value of σ from mutation experiments. The genetic variance of viability from accumulated viability mutations increases at a rate of about 0.0005 per generation per zygote (4). Because of the 50 generations of mean persistence of a mutant in the population, the equilibrium value is 50 times as large, or 0.0250. This is for homozygous effects. Dominant effects have been estimated at about 1/4th of the homozygous effects (4), so the heterozygous variance, σ^2, is 0.0250/16, or 0.0016. So $\sigma = 0.04$ by this crude procedure.

It is reasonable that the standard deviation be less than 0.1, and probably considerably less, because the whole distribution is restricted to the range 0–1 and there are other causes of viability reduction that we are not including in this mutational analysis (e.g., balancing selection). We shall assume that σ lies in the range of 0.02–0.05. For these values, we see from Table 2 that the relative efficiency of truncation selection ranges from 5 to 20. Thus the decrease in fitness per mutant need be only 1/5th to 1/20th of the 0.02 inferred from the mean persistence time of mutants in the population, or 0.001–0.004. In other words, with truncation selection, mutants with an effect on fitness of 0.1–0.4% are eliminated from the population as efficiently as if they had effects of 2.0% but were eliminated by additive selection. Truncation selection eliminates the mutants in groups so that the conventional H. J. Muller principle of "one mutant—one genetic death" is bypassed by picking off several mutants by a single extinction.

Of course nature does not practice perfect truncation selection. But, as shown earlier, there can be a considerable departure therefrom with retention of a large proportion of the benefit. We conclude that truncation selection, or something even very roughly approximating it, can be very effective in reducing the mutation load for mutants having minor deleterious effects on viability.

Discussion

We have made several assumptions that are uncertain, although not gratuitous. The major assumption is that the effects of these genes on heterozygous fitness, or fitness potential in Milkman's term (2), are additive. This is justified partially because of the high correlation between homozygous and heterozygous viability (4, 7). More to the point is the correlation between homozygous *viability* and heterozygous *fitness* effects, evidenced both by direct experiments (12–14) and by the short persistence time of the viability mutants, which implies a great deal of heterozygous selection on total fitness. Of greater uncertainty are the assumptions about the variance of viability. Although this can be estimated under *laboratory* conditions for *homozygous* chromosomes, there is a large extrapolation to the variance of *heterozygous* effects in a *natural* population. The strength of our conclusions depends on the extent to which these plausible assumptions can be verified experimentally.

We can summarize the principal numerical conclusions as follows:

$U = 0.4$	Mutation rate per gamete for polygenic viability mutants (minimum)
$s_i = -0.02$	Mean selective disadvantage per mutant, the reciprocal of the number of generations that a mutant persists in the population
$n_m = 2U/s_i = 40$	Number of mutants per diploid individual at equilibrium (minimum)
$\overline{w} = 0.9$	Proportion selected (weak truncation selection assumed for illustration)
$s_i/a_i = 0.195$	From Table 1
$a_i = -0.103$	Mean effect of a mutant on standardized fitness potential (assuming 10% truncation)
$\sigma = 0.02$–0.05	Standard deviation of fitness potential X
$A_i = a_i\sigma = -0.002$–-0.005	Average effect of a single mutant on fitness potential
$1 - n_mA_i = 0.80$–0.92	Mean fitness potential, relative to a maximum of 1, consistent with 10% truncation selection

The striking point, as already emphasized, is the large difference between s_i and A_i. With perfect truncation, a reproductive excess sufficient to permit culling only 10% of the population can sustain the observed rate of mutation and mutant elimination. If fitness effects were strictly additive the mean fitness would be decreased by $-n_ms$, or 80%. Yet with truncation selection the mean fitness potential is reduced by only 10–18%. With more intense selection, say truncation at 20%, the reduction would be less, and a larger mutation rate could easily be balanced.

Experiments of Latter and Robertson (15), Sved and Ayala (16, 17), and Simmons, Mitchell, and others (12–14) have shown that there is much stronger selection against the same chromosome for total fitness than for viability alone. In *Drosophila* the reproductive capacity is so great that there is an enormous opportunity for selection in nature either through viability or fertility differences. Truncation selection, or a close approximation to it, may not be needed, at least for elimination of recurrent mutations, even with the high overall mutation rates implied by Mukai's work (3, 4).

On the other hand, many organisms, such as most mammals, have a limited reproductive rate. There is no reason to think that the mutation rates are less; if any part of the mutation rate is time dependent rather than generation dependent or if the process of evolutionary adjustment of mutation rates to increasing generation length lags far behind such increases, we might expect the mutation rate in long-lived mammals to be higher. Yet, animals with low reproductive capacity are not overtly handicapped by a large mutation load. Furthermore, their rates of morphological and cytological evolution are in many cases higher than those in organisms, such as insects and many invertebrates, with enormously greater reproductive capacity. Clearly, a high reproductive rate is not needed for

[§] The mutation accumulation is measured against a standard chromosome with no accumulated mutations, while the equilibrium population standard is a normal heterozygote, which includes dominant effects. With 25% dominance (4) the ratio should be increased by 33%; hence we take 50 as the value.

elimination of recurrent mutations or for adaptive evolution and maintenance of polymorphisms. Truncation selection provides one mechanism whereby a small selective intensity can be magnified in its effect on gene frequency change without a great requirement for excess fertility. This conclusion is consistent with the pioneering work of King (18), Sved *et al.* (19), and Milkman (20), as well as the more recent studies of Milkman (2) and Wills (21).

Yet, in our view, it is risky to carry this argument much further. The rank-order model assumes that the genes affecting fitness contribute additively, or at least that the rank order does not change with changes of environment or residual genotype. This is reasonable for genes contributing to a single trait such as size and, as we have discussed, is experimentally shown for new mutants reducing fitness. But, for the normal variance in fitness there are often negative correlations among components. Hiraizumi (22) found that, although the fitness components were positively correlated among the less fit genotypes, these correlations were negative for highly fit genotypes. Most traits that are fitness components have an intermediate optimum, thus making the same allele positively selected in some individuals and negatively in others, as emphasized especially by Wright (ref. 23, and many earlier papers referred to in this reference). Lande (24) has discussed the lowered effectiveness of directional selection when two characters with negative correlations are selected simultaneously. With many loci acting on traits that are sometimes negatively correlated, the additivity assumption necessary for a consistent ranking of all genes seems untenable when all components of fitness are considered. Although truncation can increase the efficiency of selection, it cannot solve all the problems.

It is clear that the mutation load can be substantially reduced and the efficiency of selection substantially increased by truncation selection, and almost as much by similar but less extreme selection schemes. In addition to the broken-line model that we have discussed, it is known that, if the deleterious effect of mutant genes is proportional to the square of their number, the mutation load is half as large as with no epistasis (25). The actual amount of epistasis observed for homozygous effects on viability would produce about the same reduction (6). But the actual shape of the fitness curve in nature is not known. The question is: Does nature rank and truncate, or do something approximating this? It will have to be answered empirically.

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