Population- and Quantitative-Genetic Models of Selection Limits*

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* The author is very pleased to dedicate this paper to John Dudley for his contributions to both maize and quantitative genetics. John answered what must have seemed to be an endless number of trivial questions and I thank him for his patience. Torbert Rocheford and Irwin Goldman also provided valuable input on the Illinois selection lines, and Jean-Luc Jannink for many useful comments on a draft version of this paper.

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I. INTRODUCTION

The classic breeders' equation, first introduced by Jay Lush, predicts that the response to selection is given by $R = h^2 S$. Strictly speaking, the breeders' equation is valid only for single generation of response from an unselected base population. In subsequent generations, selection and genetic drift change the genetic variances, and hence h^2 and the response to selection. More subtlely, the breeders' equation also requires a linear parent-offspring regression, which is guaranteed if the joint distribution of parental and offspring breeding values is multivariate normal (Bulmer 1971). Selection can drive this distribution away from normality by generating skew and/or kurtosis, potentially further altering the response relative to the breeders' equation (Bulmer 1980; Zeng 1987; Turelli and Barton 1990, 1994; Bürger 2000). It is thus not surprising that while the breeders' equation typically provides a reasonable description of the first few generations of selection, it (at best) provides a very poor predictor of long-term response.

One can partition the response in a selection experiment into two components. The first is the response from the initial genetic variation present in the population at the start of selection. The second component is the continued response from mutations that have arisen during the course of the selection experiment. During the initial phase of selection, the first component dominates, while after a sufficient amount of time, all response is due to the second component. We will largely focus on the exploitation of the initial variation in this review, as Keightley (this volume) provides an excellent overview of the mutational contribution to response. If population size is sufficiently small, these two components correspond to two distinct phases of response, with an initial plateau followed by a waiting period before significant new response can occur. In larger populations, these two components blur, as new mutations start to make significant contributions before all the initial variation is exhausted. As a result, it can be extremely difficult, if not impossible, to partition a selection response into these two casual components.

Our goal here is to review the population- and quantitative-genetics theory of the prediction of long-term response. Alas, in the most general biological setting, one cannot predict long-term response simply from knowledge of the base-population variance components. However, in many settings, we can still gain significant insight into the course of response from some basic theory. We start by considering the infinitesimal model wherein each locus has only a small effect on the character, first introducing the basic model and then adding various layers of more realistic assumptions. One central theme throughout our review is that genetic drift is of fundamental importance in understanding long-term response. Finally, any review of long-term response would not be complete without at least mentioning that there have recently been a several rather technical (but important) papers on short-term selection response under very general settings (Barton and Turelli 1987, 1991; Turelli and Barton 1990, Bürger 1991, 1993). Bürger (2000) provides an excellent, although fairly technical, review of this literature.

II. LET'S GET SMALL: RESPONSE UNDER THE INFINITESIMAL MODEL

A. Basic Structure of the Infinitesimal Model

Under the classic infinitesimal model, implicitly introduced by Fisher (1918), the character is determined by a very large (approaching infinite) number of unlinked and nonepistatic loci, each with a very small effect on the trait. Under this model, the amount of selection acting on any given locus is extremely small, and hence the expected change in allele frequencies is negligible. When summed over a large number of loci, these very small allele frequency changes nonetheless allow for significant changes in the mean with essentially no changes in the variance and other moments of the genotypic distribution. Thus, under the infinitesimal model (in an infinite population) there are no changes in the genetic variance caused by changes in allele frequencies.

Changes in allele frequencies, however, are not the only route by which selection can change

the variance (and other moments) of the genotypic distribution. Selection also creates associations (covariances) between alleles at different loci through the generation of gametic-phase (or linkage) disequilibrium, and such covariances can have a significant effect on the genetic variance. Disequilibrium can also change higher-order moments of the genotypic distribution as well, driving it away from normality and hence potentially causing parent-offspring regressions to deviate from linearity.

B. Gametic Phase Disequilibrium and the Additive Genetic Variance

To predict the changes in the genetic variances under the infinitesimal model, we first need to examine the behavior of the additive genetic variance in the presence of linkage disequilibrium. In general, the additive genetic variance σ_A^2 can be written as

$$\sigma_A^2 = \sigma_a^2 + d \tag{1}$$

where σ_a^2 is the additive genetic variance in the absence of disequilibrium and d the disequilibrium contribution. To formally define σ_a^2 and d, let $a_1^{(k)}$ and $a_2^{(k)}$ be average effects of the two alleles at locus k from a random individual. Since σ_A^2 is the variance of the sum of average effects over all loci,

$$\sigma^2\left(\sum_{k=1}^{n}\left(a_1^{(k)}+a_2^{(k)}\right)\right) = 2\sum_{k=1}^{n}\sigma^2\left(a^{(k)}\right) + 4\sum_{k<j}^{n}\sigma\left(a^{(j)},a^{(k)}\right) \tag{2a}$$

$$= 2\sum_{k=1}^{n} C_{kk} + 4\sum_{k<j}^{n} C_{jk} \tag{2b}$$

where n the number of loci and $C_{jk} = \sigma(a^{(j)}, a^{(k)})$ is the covariance between allelic effects at locus j and k. Thus $\sigma_a^2 = 2\sum C_{kk}$ is the additive variance in the absence of gametic-phase disequilibrium and the disequilibrium contribution $d = 4\sum_{j<k} C_{kj}$ is the covariance between allelic effects at different loci. The component of the additive genetic variance that is unaltered by changes in gametic-phase disequilibrium, σ_a^2, is often referred to as the **additive genic variance** (or simply the **genic variance**) to distinguish it from the additive genetic variance σ_A^2.

Under the infinitesimal model, selection does not change the C_{kk} (as this requires changes in the allele frequencies), and hence does not alter σ_a^2. However, selection does generate correlations between loci ($C_{ik} \neq 0$), and this can result in significant changes in the overall additive variance σ_A^2. Changes in the covariances C_{ij} between loci i and j (for $i \neq j$) are roughly of order n^{-2} (Bulmer 1980, Turelli and Barton 1990). Since there are n^2 terms contributing to d, the total disequilibrium is of order one ($n^2 \cdot n^{-2}$) and does not necessarily approach zero as the number of loci becomes infinite. Similar reasoning holds for changes in the higher-order moments, which are caused by higher-order associations between groups of loci (Turelli and Barton 1990).

C. The Bulmer Effect: Disequilibrium-Induced Changes in the Variances

The reduction in selection response due to the generation of negative disequilibrium ($d < 0$) is often called the **Bulmer effect**, after the pioneering work of Michael Bulmer (1971). Under the infinitesimal model, gametic-phase disequilibrium changes the additive, but not the dominance, variance. Hence, the phenotypic variance in generation t of selection is

$$\sigma_z^2(t) = \sigma_E^2 + \sigma_D^2 + \sigma_A^2(t) = \sigma_z^2 + d(t) \tag{3a}$$

where $\sigma_z^2 = \sigma_z^2(0)$ is the phenotypic variance before selection in the initial (unselected) base population. The resulting heritability in generation t becomes

$$h^2(t) = \frac{\sigma_A^2(t)}{\sigma_z^2(t)} = \frac{\sigma_a^2 + d(t)}{\sigma_z^2 + d(t)} \tag{3b}$$

Assuming that the parent-offspring regression remains linear, the selection response in generation t becomes $R(t) = h^2(t)\, S(t)$. One subtle point is that changes in the variance not only change h^2, but also S as well. For example, under truncation selection with a contrast fraction p of the population saved, the selection intensity $i = S/\sigma_z$ remains constant (for example, $i = 1.4$ for $p = 0.2$). However, changes in σ_z results in a change in S even if i remains constant. Expressing the response in terms of the selection intensity gives

$$R(t) = i\, h^2(t)\, \sigma_z(t) = i\, \frac{\sigma_A^2(t)}{\sigma_z(t)} \tag{4a}$$

Thus the single-generation response in generation t becomes

$$R(t) = i\, \frac{\sigma_a^2 + d(t)}{\sqrt{\sigma_z^2 + d(t)}} \tag{4b}$$

Making the standard infinitesimal assumption that σ_a^2 remains unchanged (in an infinite population), the complete dynamics of the response to selection (assuming the parent-offspring regression remains linear) is given by the dynamics of disequilibrium $d(t)$.

Assuming unlinked loci, Bulmer (1971) showed that the change in disequilibrium is given by

$$d(t+1) = \frac{d(t)}{2} + \frac{h^4(t)}{2}\, \left(\sigma_{z^*(t)}^2 - \sigma_{z(t)}^2 \right) \tag{5}$$

where $\sigma_{z^*(t)}^2 - \sigma_{z(t)}^2$ is the within-generation change in the phenotypic variance. The first term represents the removal of disequilibrium by recombination, while the second is the generation of disequilibrium by selection. Note that a within-generation reduction in variances generates negative d, while an increase generates positive d.

D. The Dynamics of *d* Under Truncation Selection

1. Dynamical Equations for *d*. With truncation selection saving a fraction p of a normally-distributed trait, the within-generation change in the phenotypic variance is

$$\sigma_{z^*(t)}^2 - \sigma_{z(t)}^2 = -\kappa\, \sigma_{z(t)}^2, \quad \text{where} \quad \kappa = i\, \left(i - z_{[1-p]} \right) \tag{6}$$

Here $z_{[p]}$ satisfies $\Pr(U \le z_{[p]}) = p$ where U is a unit normal random variable. Truncation selection reduces the phenotypic variance, creating negative disequilibrium ($d < 0$), which in turn reduces the additive variance and hence the rate of selection response.

Noting that $\sigma_{z(t)}^2 = \sigma_A^2(t)/h^2(t)$ and substituting Equation 6 into Equation 5 recovers the result of Bulmer (1974),

$$d(t+1) = \frac{d(t)}{2} - \frac{\kappa}{2}\, h^2(t)\, \sigma_A^2(t) = \frac{d(t)}{2} - \frac{\kappa}{2}\, \frac{[\, \sigma_a^2 + d(t)\,]^2}{\sigma_z^2 + d(t)} \tag{7}$$

Starting with an unselected base population ($d(0) = 0$), iteration of Equation 7 gives the disequilibrium (and hence the heritability, phenotypic variance, and response) in any desired generation. Under truncation selection most of the disequilibrium is generated in the first three to five generations (Fig. 1), after which d is very close to its equilibrium value $\widetilde{d}$. Fig. 1 shows the effect of the infinitesimal correction on the selection response. For the values assumed ($p = 0.2$, $h^2(0) = 0.3$), the rate of response at equilibrium is reduced to about 85% of the initial response.

—> Fig. ONE HERE <—

2. Equilibrium Variances and Rates of Response. The equilibrium variances, and hence the equilibrium rate of response, are easily obtained. At equilibrium,

$$\widetilde{d} = -\kappa\, \widetilde{h}^2\, \widetilde{\sigma}_A^2 = -\kappa\, \frac{(\,\sigma_a^2 + \widetilde{d}\,)^2}{\sigma_z^2 + \widetilde{d}}$$

Solving for $\widetilde{d}$ gives the equilibrium value for the additive genetic variance under constant truncation selection as

$$\widetilde{\sigma}_A^2 = \sigma_z^2\, \theta, \quad \text{where} \quad \theta = \frac{2h^2 - 1 + \sqrt{1 + 4h^2(1-h^2)\,\kappa}}{2(1+\kappa)} \tag{8a}$$

This gives the equilibrium heritability as

$$\widetilde{h}^2 = \frac{\widetilde{\sigma}_A^2}{\widetilde{\sigma}_z^2} = \frac{\widetilde{\sigma}_A^2}{\sigma_z^2 + (\widetilde{\sigma}_A^2 - \sigma_A^2)} = \frac{\theta}{1 + \theta - h^2} \tag{8b}$$

The resulting reduction in the rate of response (relative to a population under no selection) becomes

$$\frac{\widetilde{R}}{R} = \frac{i\, \widetilde{h}^2\, \widetilde{\sigma}_z}{i\, h^2\, \sigma_z} = \frac{\widetilde{h}^2}{h^2}\, \sqrt{1 - h^2 + \theta} = \frac{\theta/h^2}{\sqrt{1 + \theta - h^2}} \tag{9}$$

This ratio is entirely a function of the initial heritability and the strength of selection (as p entirely determines κ) and is plotted in Fig. 2. The relative response is reduced by increasing either the strength of selection (i.e., decreasing p) or the heritability.

—> Fig. TWO HERE <—

3. Testing the Fit to the Infinitesimal. Ideally, one could test the fit of the infinitesimal model to an observed pattern of selection response by seeing if the decrease in heritiability is as predicted from Equation 9. This is generally difficult given the large standard errors typically associated with estimates of realized heritability. One attempt was made by Atkins and Thompson (1986), who subjected blackface sheep to selection for increased bone length. Following 18 years of selection, realized heritability was estimated to be 0.52 ± 0.02. Using the infinitesimal model, they predicted the expected base population heritability should be 0.57, in agreement with the estimated base population heritiability of 0.56 ± 0.04. Further, the infinitesimal model predicts a 10% decrease in phenotypic variance. The observed values were a 9% decrease in the upwardly-selected line and an 11% decrease in the downwardly-selected line.

E. Within and Between-Family Contributions to Additive Genetic Variance

Further insight into the behavior of the infinitesimal model can be obtained by considering the regression of offspring breeding value (A_o) on the breeding values of its parents (A_f, A_m). Under the infinitesimal model, the joint distribution of parental and offspring breeding values before selection is multivariate normal (Bulmer 1971), and the distribution of breeding values in the offspring is given by the regression

$$A_o = \frac{1}{2} A_m + \frac{1}{2} A_f + e \tag{10a}$$

The residual e is the contribution due to segregation, which is normally distributed with mean zero and variance $\sigma_a^2/2 = \sigma_A^2(0)/2$, half the additive genetic variance present in the absence of disequilibrium (Bulmer 1971, Felsenstein 1981, Tallis 1987). Since e is the residual of a regression,

it is independent of both A_f and A_m. Taking variances and assuming random mating (so that A_f and A_m are independent),

$$\begin{aligned}\sigma_A^2(t+1) = \sigma_{A_o}^2(t+1) &= \sigma^2\left(\frac{A_m(t)}{2} + \frac{A_f(t)}{2}\right) + \sigma_e^2 \\ &= \frac{1}{4}\left[\sigma_{A_m}^2(t) + \sigma_{A_f}^2(t)\right] + \frac{1}{2}\sigma_A^2(0) \\ &= \frac{1}{2}\sigma_{A^*}^2(t) + \frac{1}{2}\sigma_a^2 \end{aligned} \tag{10b}$$

where $\sigma_{A^*}^2(t)$ is the variance of the breeding values of the selected parents. Thus the offspring additive variance can be decomposed into a between-family component (half the additive *genetic* variance, $\sigma_{A^*}^2(t)/2$) that measures the differences between the mean breeding values of families and a within-family component (half the additive *genic* variance, $\sigma_A^2(0)/2 = \sigma_a^2/2$) due to segregation that measures the variation within families. Equations 10a and 10b imply that the within-family additive variance remains constant under the infinitesimal model (in an infinite population). The change in the population additive genetic variance is entirely due to changes in the expected variance between the mean values of different families. Positive disequilibrium ($d > 0$) increases the between-family component while negative disequilibrium ($d < 0$) decreases it (Wright 1921, Reeve 1953).

An important implication of the constant within-family segregation variance is that it tends to largely restore a normal distribution of breeding values following selection. Even if the distribution of breeding values in the selected parents departs significantly from normality, segregation tends to reduce this departure. Interestingly, Smith and Hammond (1987) found that the deviation from normality is largest when selection is moderate, becoming smaller as selection increases. This can be seen from Equation 10a by writing $A_o = A_{mp} + e$, where A_{mp} is the midparental breeding value and e the contribution due to segregation. Under the assumption that e is normally distributed, as selection intensity increases, the variance of A_{mp} decreases, and more and more of the variance of A_o is accounted for by e, decreasing the departure from normality.

III. MODIFICATIONS OF THE BASIC INFINITESIMAL MODEL

A. Drift and the Infinitesimal Model

Under the infinitesimal model, while selection-generated disequilibrium slows the rate of response, since there are no changes in allele frequencies, there is no selection limit (unless natural selection opposes artificial selection). Of course, natural populations are finite and the effective population size N_e in most selection experiments is small, usually under 100 and often much closer to 20. In such cases, genetic drift will rather quickly remove all the genetic variation as alleles drift towards loss or fixation. Under the infinitesimal model, there is no selective effect on any particular locus and hence the dynamics of allele frequency change is exactly that for neutral alleles in a finite population. In the real world where the number of loci is finite, any particular locus no longer has an infinitesimal effect on the character, and hence if the effective population size is sufficiently large, selection can influence allelic frequency changes at that locus (see Equation 27). However, if each locus has at most a minor effect and population size is also modest, allele frequency change is largely governed by drift and the infinitesimal model is a very reasonable approximation.

Assuming no dominance or epistasis, with drift the expected genic variation σ_a^2 declines each generation from its initial value,

$$\sigma_a^2(t) = \sigma_a^2(0)\left(1 - \frac{1}{2N_e}\right)^t \tag{11}$$

Hence, the segregation variance (Equation 10b) declines each generation. If dominance or epsitasis is present, the additive variation can actually increase (at least while the level is inbreeding is moderate) before it ultimately declines to zero.

B. Robertson's Theory of Selection Limits Under Drift

1. Robertson's Limits. Equation 11 forms the basis for Robertson's (1960) classic theory of selection limits. Robertson ignored the effect of disequilibrium, assuming that $\sigma_A^2(t) = \sigma_a^2(t)$. He further assumed that the phenotypic variance remains roughly constant. These two assumptions give the rate response to selection in generation t as

$$R(t) = i\,\frac{\sigma_A^2(t)}{\sigma_z} = \left(1 - \frac{1}{2N_e}\right)^t i\,\frac{\sigma_A^2(0)}{\sigma_z} = \left(1 - \frac{1}{2N_e}\right)^t R(1) \tag{12a}$$

where $R(1)$ is the response in the first generation. Noting that

$$\sum_{j=0}^{t}\left(1 - \frac{1}{2N_e}\right)^j \simeq 2N_e\left(1 - e^{-t/2N_e}\right)$$

the total (cumulative) response at generation T becomes

$$R^{(T)} = 2N_e\left(1 - e^{-t/2N_e}\right)\,R(1) \tag{12b}$$

Thus under Robertson's model the total response is just $2N_e$ times the initial response. This result was first suggested by Dempster (1955) and formally derived by Robertson (1960).

Under the assumption that only additive variation is present, Equation 12b is an *upper limit* for total response, which may seem somewhat counterintuitive since it was derived by assuming weak selection on any underlying QTL (i.e., the infinitesimal model). The key is that (everything else being equal) the initial response $R(1)$ is much larger when selection dominates than when drift dominates, so that $2N_e$ times the initial response overestimates the total response when selection dominates. Thus, when the number of loci is finite, if the effect of selection and/or the population size is sufficiently small on any given locus, Robertson's limit is a reasonable approximation. As the strength of selection relative to drift increases, this limit becomes an upper bound on the total response.

Another quantity of interest is the expected half-life of response, $t_{0.5}$, the time required to obtain half the selection limit. Solving $1 - e^{-t_{0.5}/2N_e} = 1/2$ gives the expected half-life as

$$t_{0.5} = N_e\,\ln 2 \simeq 1.4N_e \tag{13}$$

Again, for strictly additive gene action, this is an upper limit with the half-life decreasing as the product $N_e i$ increases (again, reflecting selection becoming increasingly important relative to drift on an underlying finite number of loci). An observed half-life considerably below that predicted by Equation 13 suggests that a large portion of the response is due to fixation of favorable alleles by selection, as selection (when it dominates) changes allele frequencies much faster than drift.

2. Optimal Selection Intensity. One of Robertson's (1960) key observations from Equation 12b is that there is a potential tradeoff between short- and long-term response. Suppose M individuals are measured and the top N chosen, so that the fraction saved is $p = N/M$. In this case, the associated effective population size is proportional to N. For a fixed number M of individuals measured, decreasing the fraction saved p increases the selection intensity i and hence the short-term response, but decreases the effective population size, potentially decreasing long-term response. Equation 12b illustrates this tradeoff since the long-term response scales with the product $N_e\,i$. Some specific examples given in Table 1. For example, while the single-generation response using $p = 0.5$ is less than half that for $p = 0.1$, it gives a selection limit over twice as large.

Robertson (1960) found that the intensity of selection giving the largest total response is $p = 0.5$, as $N_e\, i$ is maximized for fixed M when half the population is saved. The selection limit as a function of p becomes extremely flat-topped as M increases, so even fairly large deviations from $p = 0.5$ give essentially the same limit. Cockerham and Burrows (1980), relaxing the assumption of normality, found that the optimal proportion for truncation selection is still near 50%, unless the phenotypic distribution is extremely skewed. Hill and Robertson (1966), Robertson (1970), and Hospital and Chevalet (1993) found that the optimal proportion increases above $p = 0.5$ when linkage is important.

Robertson's prediction of the optimal selection intensity for long-term response is supported experimentally. For example, Madalena and Robertson (1975) selected for decreased sternopleural bristle number in *Drosophila*. When the best 5 of 25 were chosen, the limit was 17.98 bristles, less extreme than the limit of 17.08 when the best 10 of 25 were chosen. Similar results were seen for increased abdominal bristle number in *Drosophila* (Jones et al. 1968), increased egg-laying in *Tribolium castaneum* (Ruano et al. 1975), and increased post-weaning weight in mice (Hanrahan et al. 1973).

C. Joint Treatment of Drift and Disequilibrium

Robertson's (1960) classic result (Equation 12b) requires two key assumptions — no gametic-phase disequilibrium and constant phenotypic variance. Both of these assumption can be relaxed. Assume only additive variation, and write $\sigma_A^2(t) = \sigma_a^2(t) + d(t)$, so that equations for $\sigma_a(t)$ and $d(t)$ are sufficiently to describe the response to selection under the infinitesimal model (assuming regressions remain essentially linear). Change in $\sigma_a^2(t)$ is given by Equation 11, while Keightley and Hill (1987) show that, under drift, the change in the disequilibrium is given by

$$\Delta d(t) = -\frac{d(t)}{2}\left(1 + \frac{1}{N_e}\right) - \frac{1}{2}\left(1 - \frac{1}{N_e}\right)\kappa h^2(t)\sigma_A^2(t) \tag{14}$$

Hence, when the population size is finite, the variance in any particular generation can be computed by jointly iterating Equations 11 and 14. Writing the phenotypic variance in generation t as

$$\sigma_z^2(t) = \sigma_z^2(0) + [\,\sigma_a^2(t) + d(t) - \sigma_A^2(0)\,] \tag{15a}$$

gives the response as

$$R(t) = i\,\frac{\sigma_a^2(t) + d(t)}{\sigma_z(t)} = i\,\frac{\sigma_a^2(t) + d(t)}{\sqrt{\sigma_z^2(0) + \sigma_a^2(t) + d(t) - \sigma_A^2(0)}} \tag{15b}$$

Fig. 3 compares the expected response under Robertson's assumption (Equation 12a) with the full model (iteration of Equations 11 and 14). It is especially instructive to compare the heritabilities under these two models. Initially, (as expected) the heritability under the full model is less than under the Robertson model (which ignores disequilibrium). Eventually, however (around generation 20 for the parameters in Fig. 3, the heritability under the full model exceeds that under Robertson's model. The reason for this is that the full model incorporates changes in the phenotypic variance. By ignoring this change in the phenotypic variance, the Robertson model underestimates the heritabilities. The net result is that the reduction in the additive variance by disequilibrium almost balances out the Robertson's model underestimation of the heritability, resulting in very similar values for the selection limit.

—> Fig. THREE HERE <—

D. The Expected Reduction in N_e from Directional Selection

1. Selection Inflates the Between-family Variance, Decreasing N_e. Selection has an obvious effect on effective population size, in that if a fraction p of the M scored individuals are allow to reproduce,

the number of parents becomes $N = pM$. For a fixed number of scored individuals, increasing the intensity of selection (i.e., decreasing p) decreases N and hence N_e. Thus, (all else being equal) the stronger selection, the lower the effective population size. Selection also has a more subtle (and cumulative) effect in that it reduces the effective population size below that of an unselected control population with the same number of parents (so that $N_e < Mp$). This phenomenon was initially mentioned by Morley (1954), who noted in sheep flocks exposed to selection that "the genetically superior individuals will tend to be most inbred". One of the assumptions of an ideal population (where the actual size N equals the effective size N_e) is that all parents have an equal chance of contributing offspring. With a character under selection this is no longer true, as superior families contribute more offspring to the next generation than inferior families, inflating the offspring variance and reducing N_e. In particular, for a random-mating diploid population

$$N_e = \frac{N - 1/2}{\sigma_k^2/4 + 1/2}$$

where σ_k^2 is the variance in offspring number. If the number of offspring follows a Poisson distribution, then $\sigma_k^2 = 2$ and $N_e = N - 1/2 \simeq N$. However, if some parents contribute a disproportionate number of offspring, $\sigma_k^2 > 2$ and $N_e < N$. The more disproportionate the contribution from some families, the larger the variance and the smaller N_e. Thus, a single generation of selection reduces N_e by inflating σ_k^2 over that for a population not under selection. A second factor, and the major complication in computing N_e for a population under selection, is that continued selection has a *cumulative* effect in reducing the variance beyond the single-generation effect. This occurs because for a heritable character under selection, parents pass on some of their ability to have an increased contribution to their offspring which inflates σ_k^2, further reducing in N_e. This reduction becomes more pronounced as either heritability and/or selection intensity increases.

2. Predicting the Selection-Induced Decrease in N_e. While the reduction in effective population size due to artificial selection can easily be retrospectively computed from either pedigree information or from the sampling variance in marker allele frequencies, predicting this reduction *in advance* is considerably more difficult. The exact value of N_e/N depends on a variety of assumptions about both the family and population structure and on the underlying genetical model (the infinitesimal is typically assumed). Theoretical investigations of the effects of selection on reducing N_e were initiated by Robertson (1961), who gave simple approximations for both the single generation change in N_e and the asymptotic change following many generations of selection. Two different approaches have been used to examine the reduction in N_e — computing the expected variance in gene frequency for an unselected locus in a population under selection (Robertson 1961, Nei and Murata 1966, Caballero 1994, Santiago and Caballero 1995) and computing the rate of inbreeding from the number of ancestors (Burrows 1984a,b; Wolliams 1989; Verrier et al. 1990; Wray and Thompson 1990; Wray et al. 1990, 1994; Wolliams et al. 1994). The former approach computes variance effective population sizes, the latter inbreeding effective sizes. Both approaches should be essentially equivalent as the inbreeding and variance size are usually equivalent unless the population size is changing over time. While these treatments consider the effective population size on a neutral locus unlinked to loci influencing the traits(s) under selection, the results should be very similar for selected loci under the infinitesimal model, as in this case drift (rather than selection) is the dominant force for allele frequency change.

3. Santiago and Caballero's Approximation for N_e. Building on Robertson (1961), Santiago and Caballero (1995) developed an improved approximation for the effects of selection on N_e, with relative value of the effective population size in generation t versus the actual population size being approximately

$$\frac{N_{e,t}}{N} \simeq \frac{1}{1 + Q_t^2 i^2 \tau} \tag{16a}$$

where $\tau = \text{Cov}(FS)/\sigma_z^2$ is the intraclass correlation of full sibs. The value of Q_t, the cumulative effect of selection, is complex, but the limiting values approaches

$$Q \simeq \frac{2}{2 - \kappa\, h^2} \tag{16b}$$

Equation 16 shows that approximating N_e by N can be a severe overestimate, as N_e/N decreases as selection intensity increases (Equation 16a). Increasing selection intensity increases drift by both reducing N and by further reducing the ratio of N_e/N. Table 2 illustrates this effect using the same parameters as Table 1. Without incorporating this further reduction in N_e, the ratio of expected limits when $p = 0.5$ versus $p = 0.1$ is $200/90 = 2.2$. When this reduction in N_e due to selection is accounted for, this increases to $161/41 = 3.9$.

E. Test's of Robertson's Model

Tests of whether an observed pattern of selection response is compatible with the infinitesimal model have tended to focus on fit to Robertson's model to an observed pattern of response. Comparison of the predicted and expected half-life ($t_{0.5}$) and whether the selection limit is consistent with $2N_e$ times the initial response have been done in a number of studies. Observed limits and half-lives are usually considerably below the values predicted from Robertson's theory (reviewed in Roberts 1966, Kress 1975, Eisen 1980, Falconer and Mackay 1996). However, most of these reviews have not attempted to correct for the reduction in N_e from the accumulated effects of selection (Equation 16), which can be considerable (Table 2).

Another test of Robertson's theory is that the selection limit should increase, and half-life decrease, as $N_e\, i$ increases. In general, both these predictions hold. Robertson's theory further predicts that when the effective population size is sufficiently large, further increases in N_e should not change the limit (provided mutational input can be ignored), as (assuming the real-world model of a finite number of loci) all favorable alleles initially present become fixed. This has yet to be observed, which is perhaps not surprising given that most experiments have N_e below 50. By designing ingenious devices to facilitate mass selection in *Drosophila melanogaster*, Weber and colleagues (Weber 1990; Weber and Diggins 1990) have been able to examine the consequences of larger population sizes. Selection experiments on wing-tip height (Weber 1990) and ethanol tolerance (Weber and Diggins 1990) had effective population sizes on the order of $N_e \simeq$ 200–400. Both characters showed an increased response with increasing N_e. The implication is that there is additional "usable" genetic variation present in the base population that can be exploited by increasing the strength of selection ($N_e\, i$). In very small populations, only major alleles are influenced by selection (see Equation 28). That response continues to increase with N_e suggests that there is a large pool of loci of smaller effects. As $N_e\, i$ increases, favorable alleles at these loci are more likely to become fixed, increasing response. Larger populations also provide a greater chance for recombination to breakup deleterious linked combinations, which might be fixed in smaller populations, further increasing the potential for response. One complication is that as population size increases, the contribution from mutational input becomes increasingly important over the time scales it takes to remove the initial variation. A second complication is that when the character value is influenced by inbreeding depression (as would occur if directional dominance is present), over the same number of generations, the effects on inbreeding depression will be more dramatic is smaller populations. One test for whether inbreeding depression is reducing response is to cross divergently selected lines and look for significant changes in the mean in the resulting F_1 population (e.g., Eisen 1975, Kownacki 1979).

F. Gaussian Approximations Allowing for a Finite Number of Loci

Several simulation studies (Bulmer 1974, 1976; Sorensen and Hill 1983; Mueller and James 1983; Chevalet 1988) have shown that the infinitesimal model gives a reasonably good fit of the change

in variance over a few generations of selection when the number of loci is finite. However, with a finite number of loci, allele frequency changes occur and after a sufficient number of generations the cumulative effects of these changes become large enough that they cannot be ignored. Thus when either the number of loci n or the population size N is finite, we must incorporate changes in the genic variance σ_a^2 into our model.

If we are willing to assume that the distribution of allelic effects *at each locus* is normal, so that the vector of contributions for all underlying loci is multivariate-normal, then fairly simple expressions for predicting the joint change in both σ_a^2 and d assuming a finite number of loci can be obtained. This assumption is often referred to as the **continuum-of-alleles model**, and is also only an approximation, as it requires an infinite number of alleles at each locus, an assumption clearly violated in finite populations. The continuum-of-alleles model replaces the assumption of an infinite number of loci with the assumption of an infinite (or at least very large) number of alleles at each of the n loci.

The historical roots of this model trace back to the classic paper of Kimura and Crow (1964), which represents the first serious treatment of molecular evolution. The first application of this model in quantitative genetics was by Kimura (1965), who used this approach to examine the amount additive variance maintained under the balance between mutation and selection.

Modifications of the Bulmer equations allowing for a finite number of loci (n) were introduced by Lande (1975) and Felsenstein (1977). The most general result is due to Chevalet (1988, 1994), who considers the general case where both N_e and n are finite. The resulting recursion equations for the genetic variance and the disequilibrium are

$$\Delta\,\sigma_a^2(t) = -\left[\,\frac{\sigma_a^2(t)}{2N_e} + \left(1-\frac{1}{N_e}\right)\frac{\kappa\,h^2(t)\,\sigma_A^2(t)}{2n}\,\right] \tag{17a}$$

$$\Delta\,d(t) = -\frac{1}{2}\left[\left(1+\frac{1}{N_e}\right)d(t) + \left(1-\frac{1}{n}\right)\left(1-\frac{1}{N_e}\right)\kappa\,h^2(t)\,\sigma_A^2(t)\right] \tag{17b}$$

Decreases in the genic variance (which result in a selection limit) scales as the reciprocal of both the population size and the number of loci. As Fig. 4 illustrates, even when the number of loci is assumed to be rather small (10), there is only a modest reduction in the selection limit. For the parameters used in Fig. 4, the limit for 50, 20, and 10 loci is 97%, 92% and 85% (respectively) of the infinitesimal (finite population) limit.

—> Fig. FOUR HERE <—

IV. STRICTLY DETERMINISTIC MODELS OF RESPONSE

A. Single-locus Models in Large Populations

A complement to analysis under the infinitesimal is to analyze the response based on single-locus models. The infinitesimal model considers the effects of gametic-phase disequilibrium but ignores selection-induced allele-frequency change, while single locus models consider allele-frequency change and ignore disequilibrium. Single-locus models focus on how phenotypic selection influences a particular locus underlying the trait and the contribution of that locus towards the selection response. Multiple loci are modeled by simply summing the single-locus results.

The general pattern expected in long-term response to directional selection from these models is roughly as follows. In the absence of segregating major genes, additive variance (and hence response) is roughly constant over the first few generations giving a nearly linear response (Fig. 5). There is a slight reduction in the variance due to the generation of gametic-phase disequilibrium, but this is generally small unless directional selection is very strong, heritability is high, and the number of loci is very large. As generations proceed, sufficient allele frequency change accrues to

significantly alter genetic variances. At this point, additive variance can either increase or decrease, depending on the starting distribution of allelic frequencies and effects. Eventually the additive variance attributable to the initial variation in the base population declines, and with it response (assuming no source of new genetic variation such as mutation or migration/line crosses). Ultimately, a selection limit (or plateau) is reached, reflecting fixation of all favorable alleles and loss of additive genetic variance at those loci still segregating (e.g., loci overdominant for the character under selection). If both major and minor alleles influence the character, an initial rapid response due to large changes in allele frequencies at major loci is followed by a much longer period of slower response due to allele frequency changes at loci having smaller effects. Such differences in rates of response can make it difficult to determine whether a selection limit has actually been reached. As the genetic variation in the base population becomes exhausted, continued response is entirely dependent on new mutations.

—> Fig. FIVE HERE <—

One reason for the popularity of the infinitesimal model is that we can fully specify the complete response to selection (including the limit) with just two composite genetic parameters, $\sigma_A^2(0)$ and $h^2(0)$. In contrast, the dynamics of response considering the summed contributions of single-locus models is not a simple function of the base population genetic variances. Rather, the response is a complex function of the underlying genetic parameters at the individual loci (i.e., allele frequencies and effects). This is seen in Fig. 5, which illustrates differences in the long-term response for four hypothetical populations with the same initial heritability but different numbers of loci. All show essentially the same response over the first few generations. By generation five, allele frequencies have changed enough in the 10- and 25-locus populations to reduce response, while the 250-locus population shows a roughly constant response through 20–25 generations. The mixed population (5 major loci, each with initial frequency of the favored allele q_0 = 0.25, 125 minor loci with q_0 = 0.5) shows an enhanced response relative to the others in generations 3 – 7. This results from an increase in heritability as the frequencies of alleles with large effects increase from $1/4$ to $1/2$, increasing the additive variance contributed by these loci. If rare recessives are present, there can be a considerable time lag until an enhanced response appears (e.g., Fig. 8).

B. Single-locus Deterministic Limits

1. General Results. The contribution to the selection limit from a single locus, and the half-life associated with this contribution, depend on the initial allele frequencies, allelic effects and dominance relationship among alleles. Let **A** be the allele favored by directional selection, where the genotypes $\mathbf{aa}:\mathbf{Aa}:\mathbf{AA}$ have genotypic values of $0:a(1+k):2a$. Assuming genotypes are in Hardy-Weinberg proportions, the contribution to the mean character value from this locus is a function of q (the frequency of **A**) and is given by

$$m(q) = 2aq\,[\,1 + (\,1 - q\,)k\,] \tag{18a}$$

The presence or absence of gametic-phase disequilibrium has no influence on this contribution to the mean, provided there is no epistasis. The total contribution to the selection limit from this locus if **A** is fixed, given it starts at initial frequency q_0, is thus

$$m(1) - m(q_0) = 2a - 2aq_0\,[\,1 + (\,1 - q_0\,)k\,] = 2a\,(\,1 - q_0\,)(\,1 - q_0 k\,) \tag{18b}$$

Some specific values are plotted in Fig. 6.

—> Fig. SIX HERE <—

If all initially segregating favorable alleles are fixed the total response at the selection limit is just the sum of the individual locus contributions.. For n underlying loci,

$$R^{(\infty)} = \sum_{i=1}^{n} 2a_i\,(\,1 - q_{i,0}\,)(\,1 - q_{i,0}k_i\,) \tag{19a}$$

This equation is the upper limit of response, as in a finite population not all favorable alleles are fixed. If all loci are additive ($k_i = 0$), the total response can be written as

$$R_H^{(\infty)} = 2n(\,\overline{a} - \overline{aq}\,), \quad \text{where} \quad \overline{a} = \frac{1}{n}\sum_{i=1}^{n} a_i \quad \text{and} \quad \overline{aq} = \frac{1}{n}\sum_{i=1}^{n} a_i\,q_{i,0} \tag{19b}$$

Likewise, when selecting for reduced trait values, the total response is given by

$$R_L^{(\infty)} = 2n\,\overline{aq} \tag{19c}$$

From Equations 19a and 19c,

$$\frac{R_H^{(\infty)}}{R_L^{(\infty)}} = \frac{2n(\,\overline{a} - \overline{aq}\,)}{2n\,\overline{aq}} = \frac{\overline{a}}{\overline{aq}} - 1 \tag{19d}$$

where R_H and R_L are the upper and lower limits of selection response.

2. Simple Approximations. If we assume all loci have the same effect ($\overline{a} = a_i = a$), then (Dudley 1977) we can estimate the average starting allele frequency by

$$\widehat{\overline{q}}_0 = \frac{1}{R_H/R_L + 1}, \quad \text{where} \quad \overline{q} = \frac{1}{n}\sum_{i=1}^{n} q_{i,0} \tag{20}$$

Finally, note that the additive variation is given by

$$\sigma_A^2 = 2\sum_{i=1}^{n} a_i^2 q_i(1 - q_i) = 2n(\,\overline{a^2q} - \overline{a^2q^2}\,)$$

where

$$\overline{a^2q} = \frac{1}{n}\sum_{i=1}^{n} a_i^2 q_i \quad \text{and} \quad \overline{a^2q^2} = \frac{1}{n}\sum_{i=1}^{n} a_i^2\,q_i^2$$

Thus, the ratio of the total response to the initial additive variance is

$$\frac{R^{(\infty)}}{\sigma_A^2(0)} = \frac{2n(\,\overline{a} - \overline{aq}\,),}{2n(\,\overline{a^2q} - \overline{a^2q^2}\,)} = \frac{\overline{a} - \overline{aq}}{\overline{a^2q} - \overline{a^2q^2}} \tag{21a}$$

Equation 21a demonstrates that there is no simple relationship between the initial additive variance and the total response. If we are willing to assume that all loci have the same effect ($a_i = a$) and starting frequency ($q_{i,0} = q_0$), then

$$\frac{R^{(\infty)}}{\sigma_A(0)} = \frac{2na(1 - q_0)}{\sqrt{2na^2q_0(1 - q_0)}} = \sqrt{\frac{2n(1 - q_0)}{q_0}} \tag{21b}$$

This result was first given by Robertson (1970), and can be used to estimate the number of loci (provided we are willing to assume that all alleles have the same starting frequency).

C. Allele Frequency Change Required for Partial Response

The allele frequency q_β at which a preset fraction β of the total contribution (from a given locus) occurs is also of interest. This is determined by solving the quadratic equation

$$m(q_\beta) - m(q_0) = \beta\,[\,m(1) - m(q_0)\,] \tag{22}$$

A case of particular interest is $q_{1/2}$, the frequency at which half the response occurs ($\beta = 0.5$). Expressions for $q_{1/2}$ are given in Table 3 and plotted in Fig. 6. Rare recessives have to increase substantially in frequency to give half the response (e.g., if $q_0 = 0.1$ then $q_{1/2} \simeq 0.71$). Conversely, if alleles favored by selection are dominant, response slows down considerably as these alleles become common, reflecting the rarity of homozygous recessives. In such cases, response can be so slow that the population appears to be at a limit. However, reverse selection on these populations can result in a fairly rapid response.

V. SELECTION ON A QUANTITATIVE TRAIT LOCUS

A. Selection Coefficients on a QTL

In order to take the first steps beyond the infinitesimal model, we need to consider how selection changes the allele frequencies at a QTL underlying the trait under selection. For a locus of small effect, the change in allele frequency due to phenotypic selection on a normally-distributed trait is approximately

$$\Delta q \simeq i\,(\alpha^*/\sigma_z)\,q = \frac{a\,i}{\sigma_z}\,q(1-q)[\,1 + k(1-2q)\,] \tag{23}$$

where q and α^* are the frequency and average excess of allele $\mathbf{A}$ (Haldane 1931, Griffing 1960, Kimura and Crow 1978, Milkman 1978). This is a weak-selection approximation as it assumes that $|\,i\,\alpha^*/\sigma_z| << 1$. It also assumes that epistasis, gametic-phase disequilibrium, and genotype $\times$ environment interactions are negligible. Equation 23 is correct only to linear order (terms of a^2 and higher order are ignored, see Nagylaki 1984; Walsh 1990; Hastings 1990, 1992). Thus, there are potential pitfalls in applying Equation 23 when $i \simeq 0$.

To translate selection on a QTL into the standard single-locus selection model used in population genetics (e.g., Crow and Kimura 1970), recall that when the genotypes $\mathbf{aa} : \mathbf{Aa} : \mathbf{AA}$ have fitnesses $1 : 1 + s(1+h) : 1 + 2s$, the change in the frequency q of $\mathbf{A}$ under weak selection is

$$\Delta q \simeq s\,q\,(1-q)\,[\,1 + h\,(1-2q)\,]$$

Matching terms with Equation 23, we find that a QTL under directional selection behaves like a locus with fitnesses

$$s = \frac{a}{\sigma_z}\,i \qquad \text{and} \qquad h = k \tag{24}$$

Thus, as an initial approximation, the dynamics at a QTL with a small effect on the character follow those of a locus under these constant fitnesses. With gametic-phase disequilibrium and/or epistasis, these fitnesses change as the background genotype changes. Even without these complications, fitnesses still change as the phenotypic variance of the character under selection changes. This is especially a problem with major alleles. Even if the locus has a small effect, as other loci become fixed due to selection (and drift), σ_z^2 (generally) decreases as the genetic variance decreases, which increases $|\,s\,|$. Unless heritability is large, this effect is usually small.

The approximate fitnesses given by Equation 24 provide some insight into the behavior of an allele at a QTL under selection. For example, an additive QTL (of small effect) underlying a character under directional selection behaves approximately like a locus with an additive fitness

of $s = i\,a/\sigma_z$. Alternatively, if the locus displays overdominance in the character ($k > 1$), then under directional selection this locus displays overdominance in fitness and $\widehat{q} = (1+k)/(2k)$ is an equilibrium frequency. Thus, for this locus there is still genetic variation at the selective equilibrium, although none of it is expected to be additive under this simple model. The dynamics of a QTL under stabilizing selection are much more complicated, as the linear approximation given by Equation 23 fails near the equilibrium point (as $i \simeq 0$) and an approximation correct to (at least) quadratic order must be considered.

B. Half-Life of Deterministic Response

For weak selection, approximate expressions for the expected time for an allele to move from frequency q_o to q can be obtained (e.g., Crow and Kimura 1970). Assuming single-locus fitnesses of $1 : 1 + s(1+h) : 1 + 2s$, then if **A** is additive ($h = 0$),

$$t_{q_0,q} \simeq s^{-1} \ln\left(\frac{q\,(1-q_0)}{q_0\,(1-q)}\right) \tag{25a}$$

if **A** is recessive ($h = -1$),

$$t_{q_0,q} \simeq s^{-1}\,\frac{1}{2}\,\left[\ln\left(\frac{q\,(1-q_0)}{q_0\,(1-q)}\right) - \frac{1}{q} + \frac{1}{q_0}\right] \tag{25b}$$

while if **A** is dominant ($h = 1$),

$$t_{q_0,q} \simeq s^{-1}\,\frac{1}{2}\left[\ln\left(\frac{q\,(1-q_0)}{q_0\,(1-q)}\right) + \frac{1}{1-q} - \frac{1}{1-q_0}\right] \tag{25c}$$

These expressions, together the values for q_β obtained from solving Equation 22, allow us to obtain approximate expressions the expected time until β of the total contribution from a single locus occurs (the time for q to reach q_β). Note that the dynamics of evolutionary change scale as $s^{-1} = (\,i\,a/\sigma_z)^{-1}$ — the smaller the allelic effect, the slower the expected response time. Substituting $q_{0.5}$ values (Table 3) for q gives the expected half-life of response associated with the locus under consideration (Fig. 7). The half-life for rare recessives can be quite long. Note also that the half-life of response for dominant loci *increases* with allele frequency when **A** is common (although in such cases, the additional gain made by fixing **A** is typically very small).

—> Fig. SEVEN HERE <—

These results for locus-specific half-lives ignore the effects of gametic-phase disequilibrium. Negative disequilibrium generated by directional selection reduces the average effect of an allele (+ alleles are associated with an excess of − alleles, and vice versa, reducing allelic effects relative to a population in gametic-phase equilibrium). This results in weaker selection and a slower changes in allele frequency.

C. Increases in Variance and Accelerated Responses

Contrary to the expectations of idealized long-term response, phenotypic and additive genetic variance often *increase*, resulting in a burst of response. One obvious source for such a burst is the presence of favorable rare alleles in the base population (Fig. 8). Recombination generating new favorable gametes is another source. This can occur when recombination between tightly linked loci generates gametes with two favorable alleles in coupling (i.e., ++) when only repulsion

chromosomes (i.e. $+-$, $-+$) were initially present in the base population. Yet another source for a burst of response are new mutations of large effect.

—> Fig. EIGHT HERE <—

Scale effects can also result in increases in variances and/or response, for example if the variance increases with the mean. A possible example is Enfield's (1972) selection experiments for increased pupal weight in *Tribolium*. Both additive variance and total phenotypic variance increased over time while heritiability remained roughly constant (so that response was fairly constant). Comstock and Enfield (1981) suggest that a multiplicative model of gene action was more appropriate in this case than an additive model, and that this can account for the observed increases in variance. Variances can also increase due to environmental effects. For example, environmental variance can increase as genotypes become more homozygous, although this is not inevitable (Lynch and Walsh 1998). More interestingly, changes in the environment during the course of selection can also increase the additive variance. A possible example of this is long-term selection in milk yield in North American dairy cows. Additive variance in yield has been increasing rather than decreasing (Kennedy 1984). One explanation is changes in environmental effects, as improved management techniques likely allow for greater discrimination between genotypes, although scale effects may also play a role.

VI. SINGLE-LOCUS MODELS IN FINITE POPULATIONS

A. Fixation Probabilities of Favorable QTL Alleles

The above results (e.g.., Equations 19-21) for single loci assume infinite population size, so that all favorable alleles are fixed. Since the population sizes for selection experiments are typically very small, drift can have a significant effect on allele frequencies. The infinitesimal model allows for drift but not selection as it assumes alleles behave as if they are strictly neutral. A more exact treatment follows from standard population-genetics theory on the interaction of selection and drift at a single locus (e.g., Crow and Kimura 1970). When the genotypes $\mathbf{aa}:\mathbf{Aa}:\mathbf{AA}$ have additive fitnesses $(1:1+s:1+2s)$ the probability $u(q_0)$ that allele $\mathbf{A}$ is fixed given its starts at frequency q_0, was obtained by Kimura (1957) and is

$$u(q_0) \simeq \frac{1-e^{-4N_e s q_0}}{1-e^{-4N_e s}} \tag{26a}$$

$$\simeq q_0 + 2N_e s q_0(1-q_0) \qquad \text{when } 2N_e|\,s\,| \leq 1 \tag{26b}$$

Similar (but more complex) expressions exist for $u(q_0)$ under more general fitnesses ($1:1+s(1+h):1+2s$), see Crow and Kimura (1970). For weak selection,

$$u(q_0) \simeq q_0 + 2N_e s q_0(1-q_0)\left(1+\frac{h(1-2q_0)}{3}\right) \qquad \text{when } 2N_e|\,s\,| \leq 1 \tag{26c}$$

as obtained by Silvela (1980). Since the fixation probability for a neutral allele is q_0 (its starting frequency), selection dominates drift when $u(q_0)$ is significantly different from q_0, while drift dominates when $u(q_0) \simeq q_0$. Noting that $1-\exp(-x) \simeq x$ when $|\,x\,| << 1$ shows that drift dominates selection when $4N_e\,|\,s\,| << 1$, while selection dominates when $4N_e\,|\,s\,| >> 1$. Recalling Equation 24, selection dominates the fixation dynamics at a QTL when

$$4N_e\,|\,s\,| = 4N_e\frac{|\,i\,a\,|}{\sigma_z} >> 1 \tag{27}$$

or when

$$4N_e \,|\, i \,| >> \frac{\sigma_z}{|\, a \,|}$$

Even if selection dominates, the fixation probabilities can still be very small (for example, one might have $1 >> u(q_0) >> q_0$). From Equation 26, the probability of fixation exceeds 0.7 when

$$N_e s q_0 = N_e |\, i \,| \, q_0 \, \frac{|a|}{\sigma_z} \geq 1/2 \tag{28a}$$

and exceeds 0.93 when this quantity exceeds 1. We can rearrange Equation 28a to show that the fixation probability exceed 0.7 when the initial allele frequency is sufficiently large,

$$q_0 > \frac{\sigma_z}{|\, a \,| 2N_e |\, i \,|} \tag{28b}$$

Hence, if the product of initial allele frequency and the standardized allelic effect $q_0 |\, a \,| / \sigma_z$ is sufficiently small, the allele can easily be lost by drift, even when selection on the character is strong. With low values of $N_e \, i$, only alleles of large effect and/or at moderate to high initial frequencies are likely to be fixed. As $N_e \, i$ increases, favorable alleles with smaller effects and/or lower frequencies are increasingly likely to be fixed.

B. Limits Under Drift and Selection

The above fixation probabilities allow one to compute the expected contribution of a particular locus towards the selection limit in a finite population. Let Δ denote the contribution (at the selection limit) for a particular locus under consideration. If q_0 is the initial starting frequency of the favored allele at this locus, then

$$\Delta = m(q_\infty) - m(q_0) \tag{29a}$$

where m is given by Equation 18a and q_∞ is the final allele frequency. The expected contribution becomes

$$\begin{aligned} E[\,\Delta\,] &= E[\,m(q_\infty)\,] - m(q_0) \\ &= E[\,2aq_\infty(1+k) - 2aq_\infty^2 k\,] - m(q_0) \\ &= 2a(1+k)E[\,q_\infty\,] - 2akE[\,q_\infty^2\,] - m(q_0) \end{aligned} \tag{29b}$$

The expected allele frequency at the limit is easily obtained, as an allele is either fixed ($q_\infty = 1$) which occurs with probability $u(q_0)$, or it is lost. Hence, $E[\,q_\infty^k\,] = 1^k \cdot u(q_0) = u(q_0)$, giving the limiting expected contribution from a particular locus as

$$E[\,\Delta\,] = 2a\left[u(q_0) - q_0 - k\Big(q_0(1-q_0)\Big)\right] \tag{30a}$$

Two cases of special interest are when $\mathbf{A}$ is additive ($k = 0$), in which case

$$E[\,\Delta\,] = 2a\,[u(q) - q_0] \tag{30b}$$

and when $\mathbf{A}$ is recessive ($k = -1$),

$$E[\,\Delta\,] = 2a\left[u(q) - q_0^2\,\right] \tag{30c}$$

When **A** is additive, and there is weak selection on the locus (i.e., $2N_e|\,s\,| \leq 1$), substituting Equations 26b and 24 into Equation 30b gives the expected response from that locus as

$$\begin{aligned} E[\,\Delta\,] &= 2a\,[u(q) - q_0] = 2a2N_e s q_0(1-q_0) \\ &= 2N_e \frac{i\,2a^2}{\sigma_z} q_0(1-q_0) = 2N_e\, i\frac{\sigma_A^2(0)}{\sigma_z} \\ &= 2N_e\, iR(0) \end{aligned}$$

which recovers Robertson's (1960) selection limit without having to assume the infinitesimal model. The effects of drift can be quantified by considering the ratio of the expected response under drift with the deterministic response ($u(q) = 1$). For a single locus,

$$\frac{\text{expected response under drift}}{\text{deterministic response}} = \frac{u(q_0) - q_0 - k\Big(q_0(1-q_0)\Big)}{1 - q_0 - k\Big(q_0(1-q_0)\Big)}$$

Table 4 gives this fraction of the maximal response for certain some situations.

—> TABLE FOUR HERE <—

C. Variance In Response

Equation 30 gives the expected selection limit under drift, but there is also a variance about these expected values. The variance (and indeed all higher moments) of the total response at the selection limit is easily computed, as the single locus contribution Δ takes on only two values,

$$\Delta = \begin{cases} 2a - m(q_0) & \text{with probability } u(q_0) \\ 0 - m(q_0) & \text{with probability } 1 - u(q_0) \end{cases} \tag{31}$$

In particular, the variance in response contributed by a given locus is

$$\sigma^2\,[\,\Delta\,] = E\left[\,\Delta^2\,\right] - \Big(E\,[\,\Delta\,]\Big)^2 = 4a^2 u(q_0)\,[1 - u(q_0)] \tag{32}$$

With weak selection, $u_i(q_0) \simeq q_0$ (i.e., the allelic dynamics are governed by drift), implying

$$\sigma^2\left[\,R^{(\infty)}\,\right] \simeq 4\sum a^2 q_0(1-q_0) \tag{33}$$

If all loci are additive, this is simply $2\sigma_A^2(0)$, the expected between-line divergence under pure drift.

Under sufficiently strong selection, almost all favorable alleles are fixed and the variance is close to zero as $u(q_0) \simeq 1$. When selection is moderate to weak, then it is often the case that $u(q_0)[\,1 - u(q_0)\,] > q_0(1-q)_0$, as the function $x(1-x)$ is maximized (for $0 \leq x \leq 1$) when $x = 1/2$. If this condition holds over enough loci, then selection *increases* the between-line variance relative to drift.

The variance in the selection limit across replicate lines has a direct bearing on whether further response can occur by crossing plateaued lines and then reselecting. If drift has played a significant role in response, a line formed by crossing replicate plateaued lines should show further response to selection, as each line should be fixed for a considerable number of unfavorable alleles.

The variance in response at the selection limit is considered in more detail by Hill and Rasbash (1986a) and Zeng and Cockerham (1990).

VII. RESPONSE FROM MUTATIONAL INPUT

A. Contribution from New Mutation

As reviewed by Keightley (this volume) , there is strong evidence that new mutants contribute to response even over the short time scales of many "long-term" selection experiments. The limit resulting from drift and selection removing all initial genetic variation is thus an artifact of time scale as it ignores this mutational contribution. Even if an observed limit is due to a balance between natural and artificial selection, new mutations with less deleterious pleiotropic effects on fitness can arise, resulting in further response.

If a rare recessive is initially present at low frequency, the appearance of homozygotes involving this allele may been taken as new mutations. If a recessive is present as a single copy, then the expected time until the first appearance of a homozygote is approximately $2N^{1/3}$ generations, with the distribution of appearance time being nearly geometric (Robertson 1978; Karlin and Tavare' 1980, 1981a, 1981b; Santago 1989). Since for most selection experiments $N \leq 500$, any recessives initially present will be expresses as homozygotes by generation 15. For more typical values of population sizes, namely N = 20, 50, and 100, the expected time is 6, 8, and 10 generations (respectively).

B. Mutational Response Under the Infinitesimal Model

Let σ_m^2 be the mutational variance (the per-generation contribution by mutation to the additive variance). The equilibrium additive variance under drift and mutation becomes $\widetilde{\sigma}_A^2 = 2N_e\sigma_m^2$. Assuming the infinitesimal model, completely additive loci, and ignoring any effects of gametic-phase disequilibrium, the expected additive genetic variance at generation t is given by

$$\sigma_A^2(t) \simeq 2N_e\sigma_m^2 + \left[\sigma_A^2(0) - 2N_e\sigma_m^2\right]\, \exp(-t/2N_e) \tag{34}$$

Setting $\sigma_A^2(0) = 0$ gives the additive variance contributed entirely from mutation as

$$\sigma_{A,m}^2(t) \simeq 2N_e\sigma_m^2\,[\,1 - \exp(-t/2N_e)\,] \tag{35a}$$

Hence, the rate of response at generation t from mutational input is

$$r_m(t) = i\,\frac{\sigma_{A,m}^2(t)}{\sigma_z} \simeq 2N_e\,i\,\frac{\sigma_m^2}{\sigma_z}\,[\,1 - \exp(-t/2N_e)\,] \tag{35b}$$

where we have made the usual assumption that the phenotypic variance σ_z^2 does not significantly change over time (more generally, σ_z^2 can be replaced by $\sigma_z^2(t) = \sigma_A^2(t) + \sigma_E^2$). For $t >> 2N_e$, the per-generation response approaches an asymptotic limit of

$$\widetilde{r}_m = 2N_e\,i\,\frac{\sigma_m^2}{\sigma_z} = i\,\frac{\widetilde{\sigma}_A^2}{\sigma_z} \tag{36}$$

Assuming $\sigma_A^2(0) = 0$, half this rate occurs when $t \simeq 1.4N_e$ (Hill 1982a,b). One way to intuit the value of the asymptotic limit follows from Robertson's theory: we expect the final response to be $2N_e$ times the initial response $R(0)$, which for new mutants arising in any particular generation is $R(0) = i\,\sigma_m^2/\sigma_z$.

Summing over generations gives the cumulative response due to new mutation as

$$R_m^{(t)} = \sum_{\tau=1}^{t} r_m(\tau) \simeq 2N_e\,i\,\frac{\sigma_m^2}{\sigma_z}\left(t - 2N_e[\,1 - \exp(-t/2N_e)\,]\right) \tag{37a}$$

as found by Hill (1982c, 1990) and Weber and Diggins (1990). Combining the mutational response with the response due to genetic variation originally in the base population (Equation 11) gives an expected cumulative response of

$$R^{(t)} = 2N_e \frac{i}{\sigma_z} \left(t\,\sigma_m^2 + [\,1 - \exp(-t/2N_e)\,]\,[\sigma_A^2(0) - 2N_e\sigma_m^2]\,\right) \tag{37b}$$

The $t\sigma_m^2$ term, which represents the asymptotic response, will eventually dominate (i.e., for large t). The remaining term in the parentheses of Equation 37b represents the transient effect of the initial additive variance, and is zero if the population starts at the mutation-drift equilibrium (i.e., $\sigma_A^2(0) = 2N_e\sigma_m^2$).

Of some interest is the expected number of generations until response from mutational input exceeds that contributed by the initial variation. Let t^* be the generation when the per-generation response from both sources is equal. Here the initial additive variance remaining at generation t^* equals the new additive variance generated by generation t^*,

$$\sigma_A^2(0)\exp(-t^*/2N_e) = 2N_e\,\sigma_m^2\,[\,1 - \exp(-t^*/2N_e)\,] \tag{38}$$

This equation has the solution

$$t^* = 2N_e\,\ln(1+\phi) \tag{39a}$$

where $\phi = \sigma_A^2(0)/(2N_e\sigma_m^2)$ is the ratio of the initial to the equilibrium additive variance. Denoting the initial heritability by h^2, a little rearrangement gives

$$\phi = \frac{h^2}{(1-h^2)\,2N_e\,(\sigma_m^2/\sigma_E^2)} \tag{39b}$$

The average value of σ_m^2/σ_E^2 is approximately 0.005 (Lynch and Walsh 1998). Using this value, it is seen that t^* is only rather weakly dependent on N_e (see Fig. 9). If $\phi << 1$, so that the expected additive variance at the mutation-drift equilibrium exceeds the initial additive variance ($\sigma_A^2(0) << 2N_e\sigma_m^2$), then using the approximation $\ln(1+x) \simeq x$ for small $|x|$, we have

$$t^* \simeq 2N_e\phi = \frac{h^2}{(1-h^2)(\sigma_m^2/\sigma_E^2)} \tag{39c}$$

Again using $\sigma_m^2/\sigma_E^2 = 0.005$ gives $t^* \simeq 200h^2/(1-h^2)$. This translates into 11, 22, and 67 generations until the rate of response from mutational input exceeds the rate of response due to initial variation for h^2 values of 0.05, 0.10, and 0.25, respectively.

—> Fig. NINE HERE <—

It is important to stress that Equation 39 for mutational half-life of response assumes that drift dominates and thus tends to overestimate the half-life when selection is moderate to strong. Likewise, we expect that the infinitesimal model underestimates the changes in allele frequencies of new mutants under moderate to strong selection. Thus, our expression for t^* is very likely an overestimate and we should regard Equation 39 as an upper bound.

VIII. THE ILLINOIS LONG-TERM EXPERIMENT: WHICH MODELS FIT?

The Illinois long-term selection experiment for oil and protein content in maize (Dudley, this volume) is one of the classic experiments in all of science. It is certainly one of the longest on-going active biological experiments and its one hundredth generation is the inspiration for the conference from

which this volume derives. It is thus appropriate to compare the fit of these data with the simple theoretical models developed above. We focus on response in the High-Oil and High-Protein lines. Table 5 summarizes the results of the various analyses given below.

—> TABLE FIVE HERE <—

A. Effective Population Sizes of the Illinois Lines

The exact effective population size of the various Illinois lines is unclear, but we can provide some clear bounds. The initial generation started with 24 pollinated ears, bounding the effective population size at 96. The logic behind this number is that with unequal contribution from the two sexes, the effective population size is given by

$$N_e = \left(\frac{1}{4N_{e_m}} + \frac{1}{4N_{e_f}} \right)^{-1} \tag{40}$$

With $N_{e_f} = 24$ and an infinite effective number of males ($N_{e_m} = \infty$), $N_e = 96$. Dudley (personal communication) reports the average number of kernels per ear in generation zero was likely around 300-500, giving an upper bound of 89 to 92. These bounds are for the effective size of the founding population, but as mentioned above, selection reduces N_e below this initial value. While expressions like Equation 16 can provide some insight into the effects of selection, a more direct measure is available. East and Jones (1920) note that after 10 generations of selection, all descendants in the High Oil line could be traced back to just a few ancestors, as could all descendants of High Protein line. In particular, for generation 11 they note (pp. 553-554) that all 24 ears chosen for high protein trace back to a single ear (bounding N_e at 4!), while all ears selected for High Oil trace back to three founding ears (bounding N_e at 12). Given these Fig.s, we consider three effective population sizes in our discussion, 6, 12, and 24.

1. Reconciling the Observed Levels of Marker Polymorphism. Rocheford (this volume) presents marker data that is inconsistent with the above bounds. After 50 and 100 generations, 12% and 1.4% of the initial heterozygosity should be present (assuming $N_e = 12$). Assuming $N_e = 24$, these values are 34% and 12%, which may be more consistent with the marker data, but as discussed this high an effective population size is very unlikely. One possible explanation for regions of greater than expected heterozygosity in the face of inbreeding is the presence of alleles that improve the trait value but also decrease fitness. This creates selective overdominance, retaining heterozygosity (at least over short to moderate time scales) in the face of drift. One extreme case of this is often seen in *Drosophila* selection experiments where lethal alleles, that also contribute favorably to the character under artificial selection, arise. If such alleles have arisen in the Illinois lines, tightly linked markers are expected to show departures from Mendelian segregation.

2. Predicted Response under Robertson's Model. For our low (6), medium (12), and high (24) values for N_e, Robertson's theory predicts a selection limit of 12, 24, and 48 times the initial response. The ratio of the current (100 generation) response divided by the response in generation 1 is 259 for protein and 158 for oil. If the lines are at their limit and follow Robertson's theory, this ratio estimates $2N_e$ (provided no response from new mutations), implying N_e values of 130 for protein and 79 for oil. If the population is still responding, these are lower limits on N_e (again provided the assumptions of Robertson's theory hold, most notably that all the response is from the initial variation). It is perhaps a bit unfair to use the observed value of the response in the first generation, as there is a considerable variance around the expected response, and any particular realization is inflated by $2N_e$. Hence, a more reasonable approach is to uses the average response over the first few (we will use the first five) generations as the baseline. This gives responses of 33 and 50 times

the (average) initial response for effective populations sizes of 16 in protein and 25 in oil. While these values are a bit more consistent with the likely effective population size, they are still too large.

Robertson's theory also predicts that the time for half the response (from the initial variation) to occur is $1.4N_e$ or 8, 17, and 34 generations (for $N_e = 6$, 12, and 24, respectively). Clearly, these are not the half-lives of response, as they correspond to 15%, 19%, and 47% of the current total response for oil and 11%, 22%, and 51% for protein. While the half-times for the upper bound of N_e are consistent with Robertson's predictions, those under the more realistic values of N_e are not.

3. Mutational Response. Mutation contributes to on-going response, obscuring both the half-life and the limit of response attributable to initial variation in the base population. Taking the realized heritabilities over the first nine generations ($h_r^2 = 0.17$ for protein, $h_r^2 = 0.50$ for oil) as the actual heritabilities, Equation 39c gives the expected number of generations until half the response is due to mutation as 16, 24, and 30 generations for high oil (for $N_e = 6$, 12, and 24, respectively, assuming $\sigma_m^2/\sigma_E^2 = 0.005$). For protein, these values are 34, 54, and 79 generations. Clearly, under any of these effective population sizes, the current response is largely due to new mutations. Further, for the majority of generations, the majority of response has been due to the effects of new mutations not initially present in the base population.

B. Strictly Deterministic Predictions

Robertson's predictions are essentially driven by drift, making N_e the key predictive parameter. The complementary modeling assumption is that all the response is due to selection being the only force changing allele frequencies. We can examine the predicted response under determinstic single-locus modes by using the rough estimates of underlying genetic parameters obtained by Dudley (1977) and Dudley and Lambert (1992). Using the assumptions leading to Equation 20 (all loci have the same effect), the 100-generation total responses give estimated average starting frequencies of favorable alleles in the base population of 0.20 for oil and 0.24 for protein. Likewise, using estimates of the number of effective factors K (from a line cross analysis) and the total amount of response, estimates of the average effects of the underling loci are $2\,\overline{a}$ = 0.39 for oil and 0.21 for protein. Equation 24 allows us to translate these values into average selection coefficients. The typical amount of selection has been 20% on ears, for a selection intensity of $i_f = 1.4$. Since selection is only on the seed parent, the average selection intensity is $i = 1.4/2 = 0.7$, giving average selection coefficients of $s = 0.33$ (oil) and 0.07 (protein). Assuming additive loci (and the above values for q_0 and s), Equation 25a gives the expected time for half the response to occur at a given locus as 5 generations for oil and 25 generations for protein. These times, especially for oil, are so short that one would expect to see an initial burst of response followed by a lag in response until new variation is generated through mutation. The actual pattern has been a relatively smooth response, suggesting that at least some reasonable fraction of the underlying loci have much smaller effects (and hence much longer time scales for allele frequency change) than suggested by the average values of $\overline{a}$.

C. Does Selection on QTLs Overpower Drift?

We can take the above rough estimates for the average starting frequency of a favorable allele and its average selection intensity to compute fixation probabilities. For oil, these are 0.80, 0.96, and 1.00 for N_e of 6, 12, and 24 (respectively). The dynamics at average oil QTLs thus seem to be largely determined by deterministic forces. For protein, these values are 0.41, 0.57, and 0.80. As a comparison, note that under only drift, the fixation probabilities (for protein) are $q_0 = 0.24$. Thus while selection is more important than drift for protein QTLs (the fixation probabilities are 2 and 2.5 times the drift value under the small and moderate population sizes), many of the favorable protein alleles are expected to have become lost due to drift.

We can also examine the effects of drift another way: what starting allele frequency (q_o) is required to give a 90% fixation probability for fixing a favorable QTL allele (assuming its effect equals the average value given in Table 5)? Using Equation 26a, these required initial frequencies for oil are $q_0 = 0.29$, 0.14, and 0.07 (corresponding to N_e = 6, 12, and 24), and $q_0 = 0.79$, 0.60, and 0.34 for protein. For a fixation probability of 50%, these values become $q_0 = 0.09$, 0.04, and 0.02 (for oil) and $q_0 = 0.31$, 0.19, and 0.10. (for protein). Thus, even at very small population sizes, the average favorable oil gene is likely to contribute to selection response. For protein, favorable alleles at low or even modest frequencies can become lost and hence not contribute to the response. These dramatic differences in oil and protein are due to much larger estimated values of a/σ_z for oil compared to protein.

1. Between-replicate variance. To translate these fixation probabilities into an expected between-replicate-line variance, from Equations 32 and 33, the ratio of the between-line variance under selection with that expected under strict drift is

$$\frac{u(q_0)[1-u(q_0)]}{q_0(1-q_0)} \tag{41}$$

The significance this ratio is that the higher the between-line variance, the larger the response expected from a cross between replicate lines. With only alleles of large effect, replicate lines fix identical alleles and hence the resulting line cross shows little variation. Conversely, with alleles having low to moderate fixation probabilities, replicate lines may be fixed for different alleles, leading to considerable variation (and hence response) in the line cross.

A ratio value of one for Equation 41 implies the selected lines show the same between-line divergence as lines under drift. A value less than one implies less expected response from a line cross (relative to a cross between drift-divergent lines), while a value greater than one implies a large expected response. As shown in Table 5, for $N_e = 6$, the expected between-replicate variance for oil is the same as for two lines under only drift. With larger effective populations sizes, the expected variance becomes considerably less than under strict drift, and little additional response is expected in between replicate crosses. With protein, the between-line variance is greater than under drift for N_e = 6 and 12. For these settings, crosses between selected lines should show considerable variation.

D. What Can We Conclude ?

The observed amount of response is remarkable given the very low effective population sizes. Given the average estimated allelic effects, the initial variation for oil has been effectively used by selection, while favorable protein alleles are likely to have been lost. The observed pattern of response is not consistent with models assuming no mutational input, as under either a deterministic or finite-population infinitesimal analysis, the time scale and amount of response requires new mutation.

Table 1. Differences in short-term versus long-term response as a function of the number of adults saved N when the number of measured individuals $M = 50$. Initially $h^2 = 0.5$ and $\sigma_z^2 = 100$. The infinitesimal model is assumed and we further assume $N_e = N$. The selection intensity i was corrected for finite population size. From the breeders' equation $R(1) = 5\,i$, while the total response is obtained as $R^{(\infty)} = 2N\,R(1)$. The half-life of response ($t_{0.5}$) is obtained from Equation 13.

N	p	i	$R(1)$	$R^{(\infty)}$	$t_{0.5}$
25	0.5	0.8	4.0	200	35
10	0.2	1.4	7.0	140	14
5	0.1	1.8	9.0	90	7

Table 2. As selection intensity increases, N_e is increasingly less than the actual number of parents, further increasing drift. The reduction in effective population size due to selection is computed using Equation 16. Parameters and assumptions are as in Table 1 (e.g., $M = 50$, $h^2 = 0.5$).

N	i	N_e	N_e/N	$2N_e\,R(1)$	$t_{0.5}$
25	0.8	20.2	0.81	161	28
10	1.4	5.8	0.58	81	8
5	1.8	2.3	0.47	41	3

Table 3. Total contribution to the selection limit and the allele frequency ($q_{1/2}$) at which half this contribution occurs for a diallelic locus where the favorable allele **A** has initial frequency q_0.

Gene action	Total contribution	$q_{1/2}$
A additive ($k = 0$)	$2a(1 - q_0)$	$(1 + q_0)/2$
A dominant ($k = 1$)	$2a(1 - q_0)^2$	$1 - \sqrt{[1 - q_0(2 - q_0)\,]/2}$
A recessive ($k = -1$)	$2a(1 - q_0^2\,)$	$\sqrt{(1 + q_0^2)/2}$

Table 4. Effects of finite population size on the selection limit. The genetic model was the 250 locus model assumed for Fig. 5, where all loci are completely additive, each with an a values of 0.89 and an environmental variance of 100. When the starting frequency of all loci is $q_0 = 0.5$, this model gives an initial heritability of 0.5. For different effective population sizes and initial frequencies, the table gives the fixation probability $u(q_0)$ of a favorable QTL and the expected percentage of response relative to the response when the favorable locus is always fixed (the maximal possible response).

N_e	q_0	$u(q_0)$	% Maximal response
100	0.5	1.00	100
100	0.3	1.00	100
100	0.1	0.99	98
40	0.5	1.00	100
40	0.3	0.99	98
40	0.1	0.82	80
20	0.5	0.97	94
20	0.3	0.89	84
20	0.1	0.58	53
10	0.5	0.85	71
10	0.3	0.69	55
10	0.1	0.35	28

Table 5. Rough estimates of various parameters from the Illinois long-term selection experiment. For both traits, $i \simeq 1.4$ on seed parents, with no selection on pollen parents, giving an overall selection intensity of $i \simeq 0.7$.

Parameter	Oil	Protein	Remarks
Realized h^2	0.50	0.17	Estimated using the first 9 generations
σ_z	0.41	1.1	Phenotypic standard deviations
q_0	0.20	0.24	Using the assumptions leading to Equation 20
K	54	123	Estimated number of segregating factors (Dudley 1997)
$2\,\overline{a}$	0.39	0.21	Estimated as the total observed response divided by K
s	0.33	0.07	Selection coefficient on a typical QTL (Equation 24)
$t_{1/2}$	5	25	Generations for half the deterministic response to occur assuming the above s and q_0 at an additive QTL (Equation 25a)
For $N_e = 6$, Half-life of response under Robertson's model = $1.4N_e = 8$ generations			
$u(q_0)$	0.798	0.408	Fixation probability of a favorable allele (Equation 26)
t^*	34	18	Time until half the response from new mutations (Equation 39)
$\sigma^2\left[R^{(\infty)}\right]$	1.02	1.32	Expected between-replicate-line variance in response scaled by the expected drift variance (Equation 41)
For $N_e = 12$, Half-life of response under Robertson's model = 17 generations			
$u(q_0)$	0.959	0.573	
t^*	54	24	
$\sigma^2\left[R^{(\infty)}\right]$	0.25	1.34	
For $N_e = 24$, Half-life of response under Robertson's model = 34 generations			
$u(q_0)$	0.998	0.802	
t^*	79	30	
$\sigma^2\left[R^{(\infty)}\right]$	0.01	0.87	

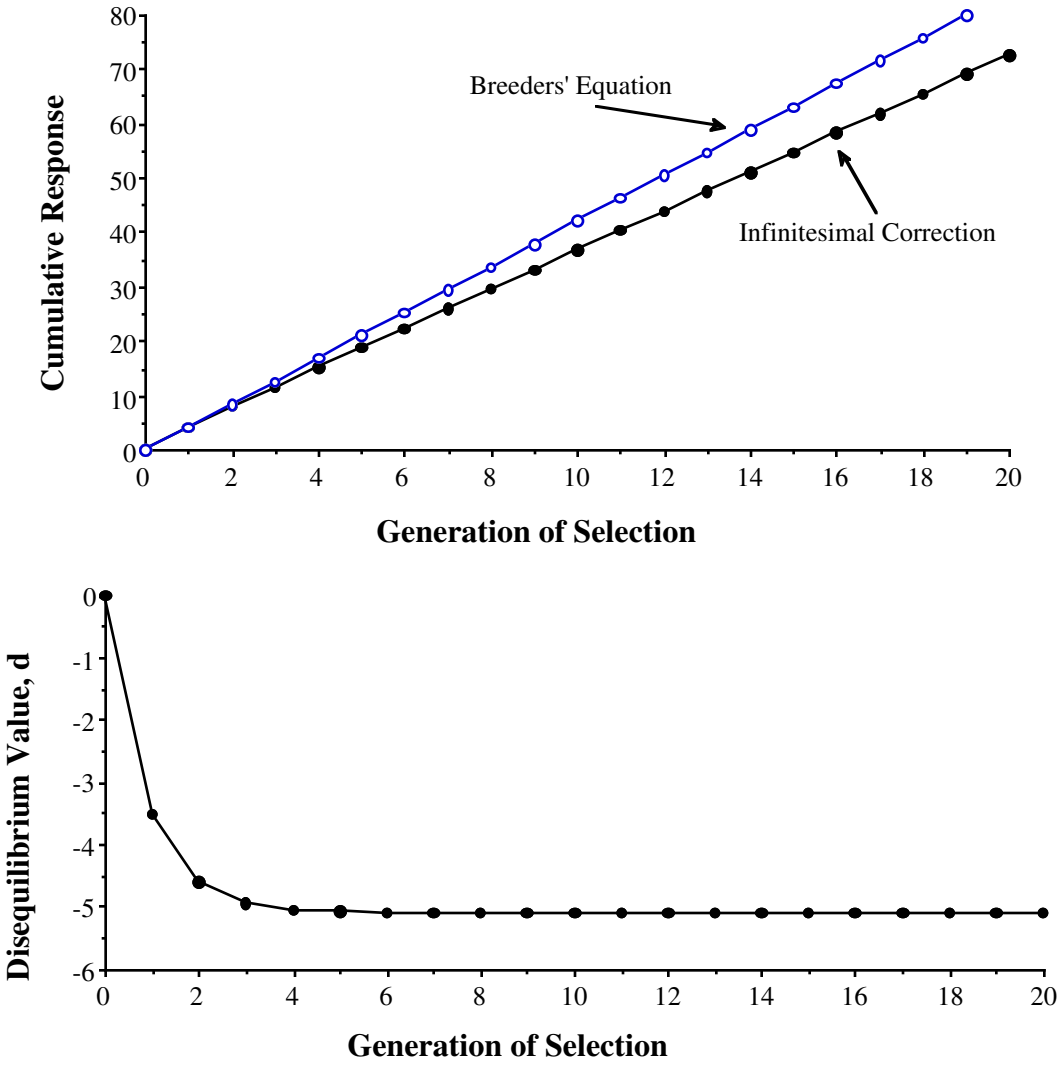

Fig. 1: **Upper :** The response to truncation selection, assuming the infinitesimal model in an infinite population. Here it assumed that the upper 20% of the population is saved ($p = 0.2$ and hence $i = 1.4$), with $h^2(0) = 0.3$ and $\sigma_z^2(0) = 100$. The equilibrium rate of response is 0.85 of the initial response. **Lower:** The dynamics of the disequilibrium $d(t)$. The equilibrium value of d is essentially reached after three generations.

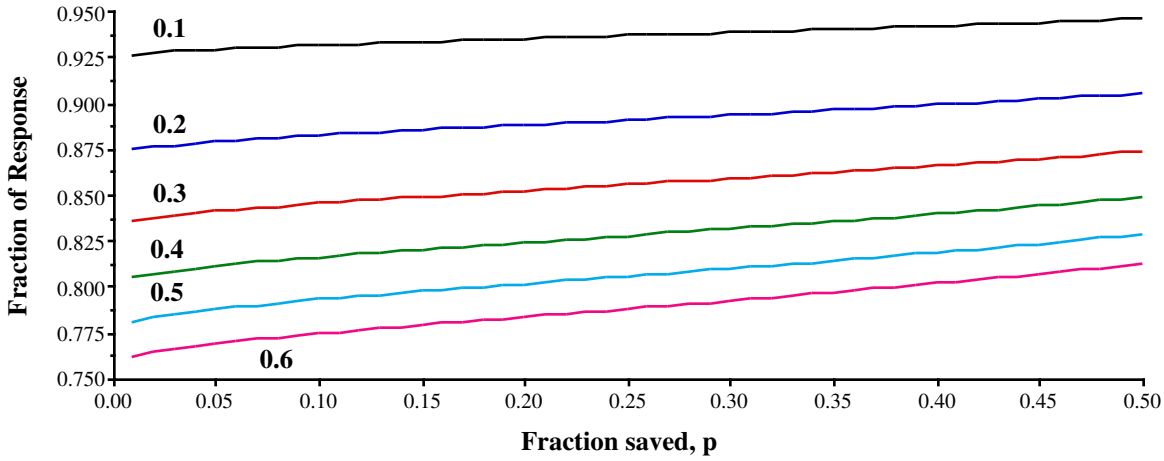

Fig. 2: The ratio $\widetilde{R}/R$ of the equilibrium rate of response $\widetilde{R}$ to the initial rate of response R as a function of the strength of truncation selection (smaller values of p imply stronger selection). The five curves correspond to initial heritabilities of 0.1 (uppermost) to 0.6 (lowermost).

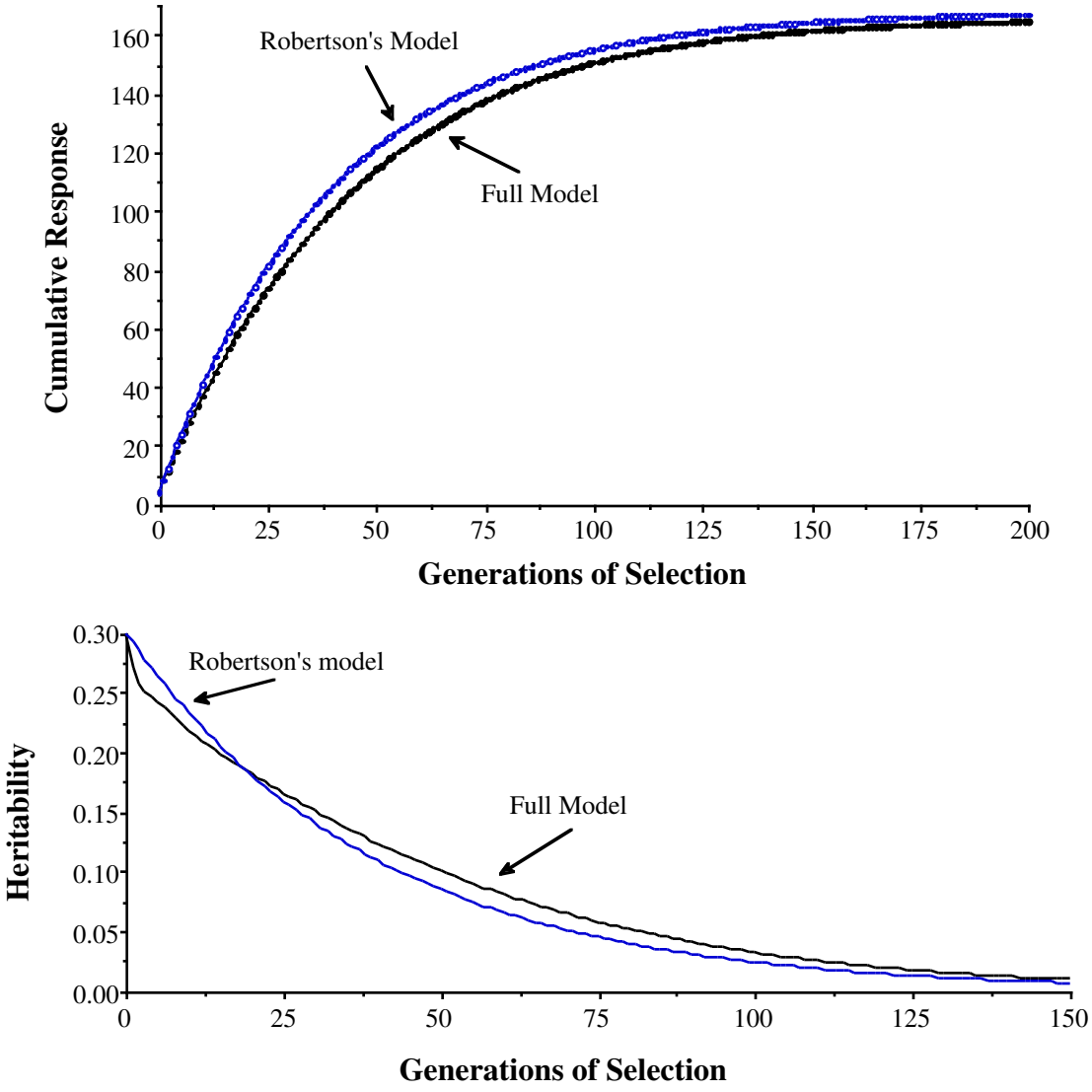

Fig. 3: The infinitesimal model with drift and disequilibrium. The cumulative response (top Fig.) and heritability (bottom Fig.) are plotted for Robertson's approximation (Equation 12a) and the full model based on jointly iterating Equations 11 and 14. The model parameters are as for Fig. 1 (truncation selection with $p = 0.2$, $h^2(0) = 0.3$, $\sigma_z^2(0) = 100$).

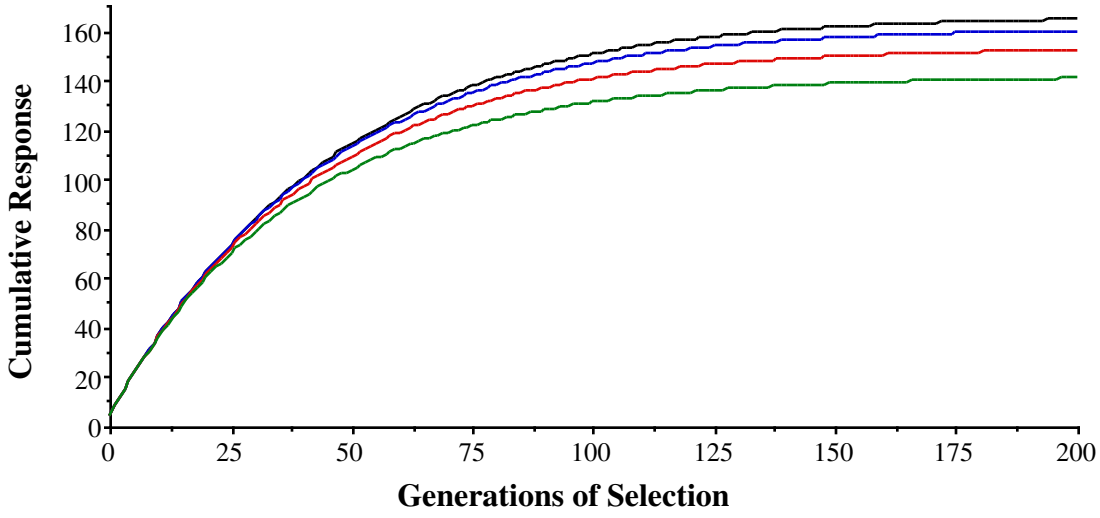

Fig. 4: The effects of a finite number of equal-effect loci, assuming the distribution of allelic effects at each locus is Gaussian (Normal). The upper curve corresponds to the response under an infinite number of loci, while the three lower curves (top to bottom) are for 50, 20, and 10 loci, respectively. The other model parameters are as for Fig. 1 (truncation selection with $p = 0.2$, $h^2(0) = 0.3$, $\sigma_z^2(0) = 100$).

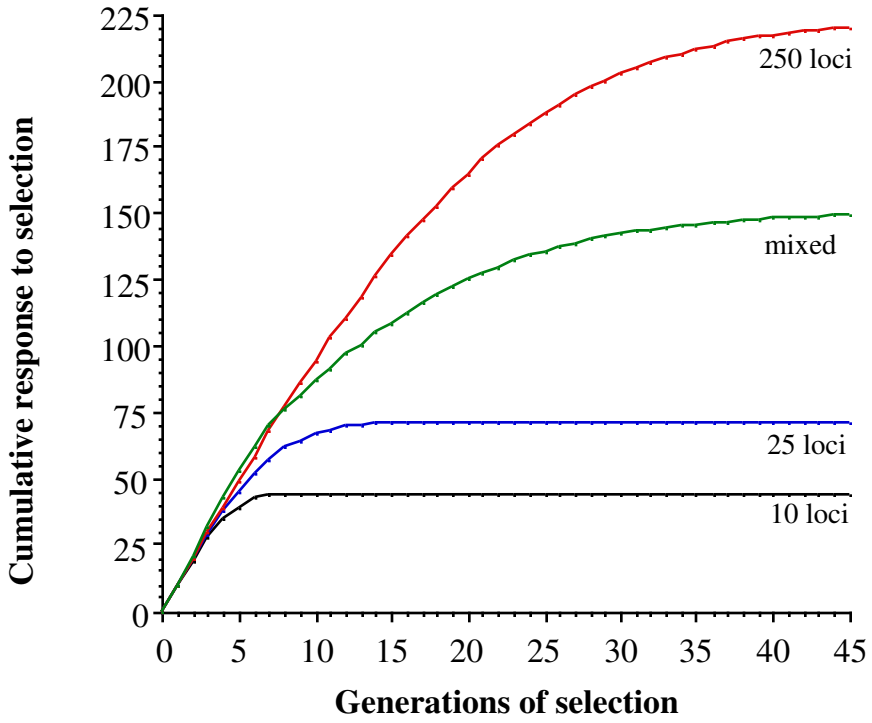

Fig. 5: Examples of the expected response to selection, assuming truncation selection (with the upper 20% saved), n identical diallelic loci (at each, the genotypes **AA** : **Aa** : **aa** have genotypic values $2a : a : 0$, and all loci have the same initial frequency q_0 for **A**). Results are for a population of infinite size (all favorable alleles increase in frequency) and we further assume no epistasis and ignore any effects of gametic-phase disequilibrium. All populations start with $\sigma_A^2(0) = 100$ and $h^2(0) = 0.5$. Curves marked 10, 25, and 250 loci correspond to populations with initial allele frequency $q_0 = 0.5$ and a values of 4.47, 2.82, and 0.89, respectively. The mixed population consists of 5 identical major loci (with $q_0 = 0.25$, $a = 5.16$) and 125 identical minor (loci with $q_0 = 0.5$, $a = 0.89$).

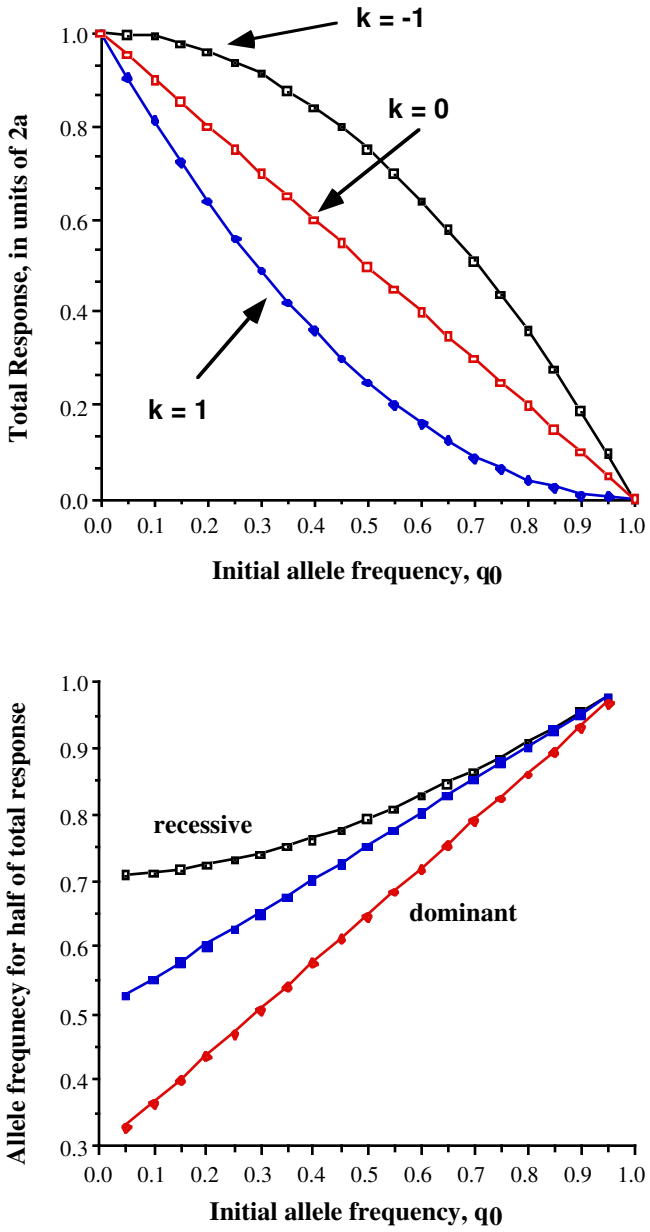

Fig. 6: **Top**: The contribution to total response from a diallelic locus assuming allele **A** (with initial frequency q_0) is fixed. The genotypes $\mathbf{AA}:\mathbf{Aa}:\mathbf{aa}$ have values $2a:a(1+k):0$. The three curves correspond to **A** being additive ($k=0$), dominant ($k=1$), and recessive ($k=-1$). The smallest contribution is made by dominant alleles at high frequencies, the largest is from recessive alleles at low frequencies. **Bottom**: The allele frequency ($q_{1/2}$) at which half the total response contributed by a locus occurs.

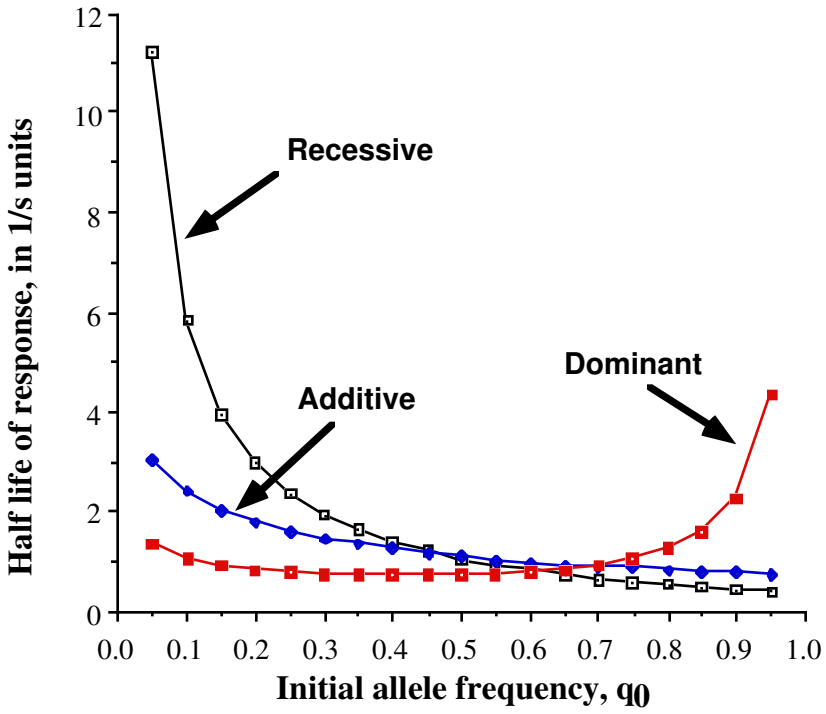

Fig. 7: The expected times for a diallelic locus to contribute half its total response, assuming **A** is eventually fixed. These curves are obtained by substituting $q_{0.5}$ from Table 3 into the appropriate version of Equation 25. Note that the time units for half-life scale as $s^{-1} = (i\,a/\sigma_z)^{-1}$.

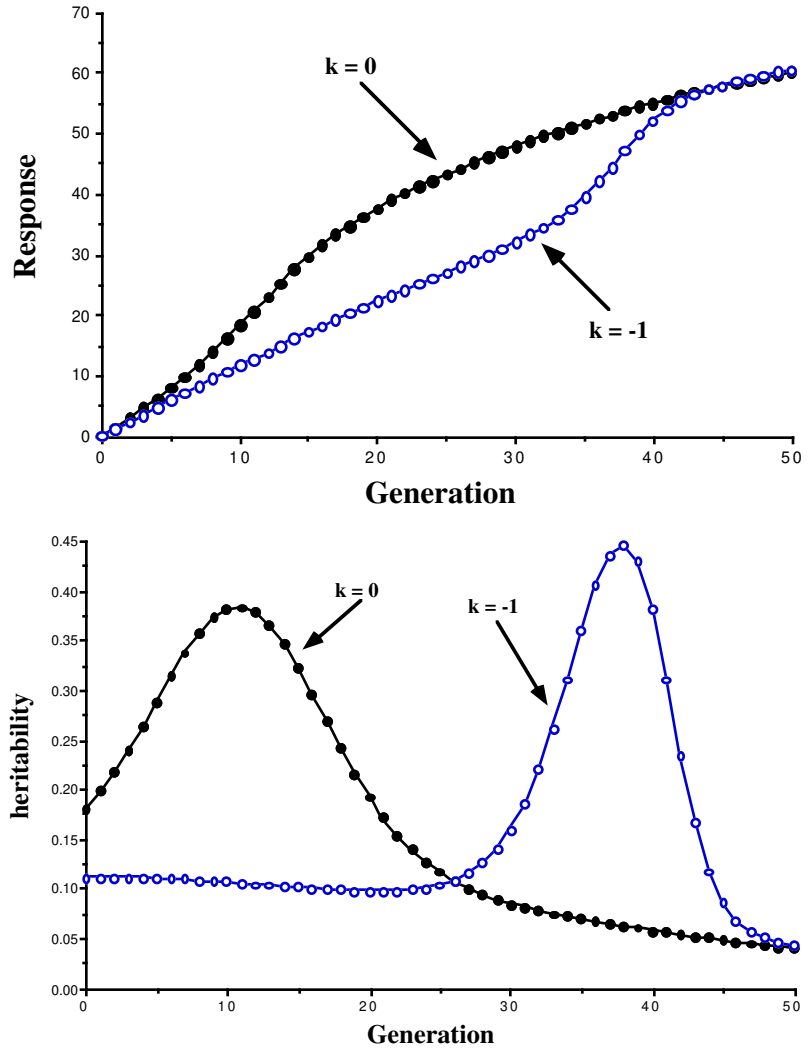

Fig. 8: Examples of a delayed accelerated response due to the increase of an initially rare allele of major effect. The character is determined by a polygenic background (100 completely additive dialleic loci, with $a = 0.5$ and $q_0 = 0.5$, so that the initially additive variance contributed by the polygenic background is $\sigma_A^2 = 9.5$) plus a major allele initially at low frequency ($a = 10$ and $q_0 = 0.05$). We assume that this locus is either additive ($k = 0$) or recessive ($k = -1$). **Top:** The response under the recessive model shows an accelerated response around generation 30, while the additive major gene results in an acceleration around generation 5. **Bottom:** The population heritabilities clearly show the acceleration.

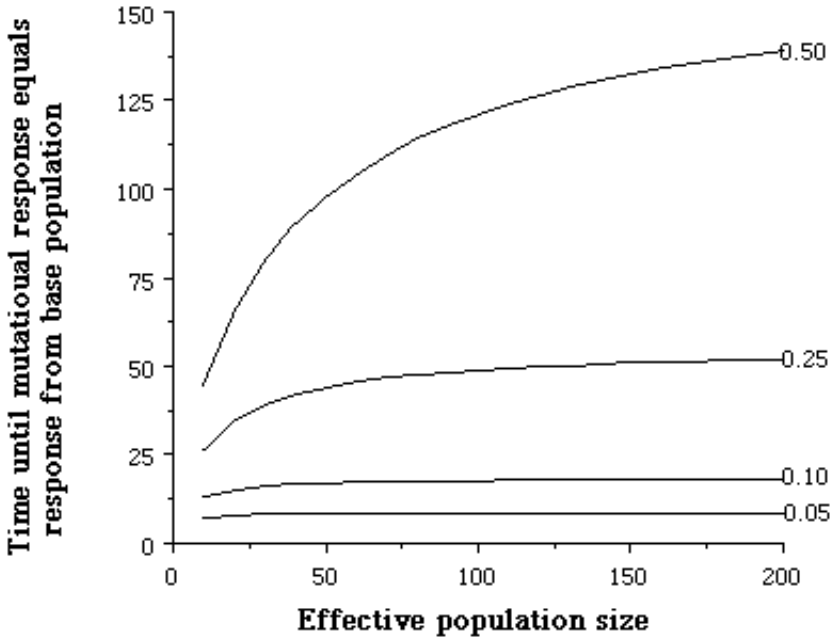

Fig. 9: The expected generation at which response due to mutational input equals the response due to initial variation in the base population, assuming $\sigma_m^2/\sigma_E^2 = 0.005$. The four curves correspond to initial heritabilities of 0.05, 0.10, 0.25 and 0.50.

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