Theoretical and Applied Genetics 48, 101-104 (1976)

# Forward and Reverse Response to Artificial Selection

F.W. Nicholas
Institute of Animal Genetics, Edinburgh (Scotland)

Summary. The effect of t' generations of reverse selection after t generations of forward selection can be described by expressing the change in the metric mean resulting from reverse selection (R) in terms of the change in the metric mean due to the previous forward selection ($\Delta x$). An additive model of artificial selection in a population of effective size N with no natural selection has been considered.

If reverse selection is continued for as many generations as the previous forward selection ($t' = t$), then the ratio $R/\Delta x$ equals $1 - F$ where F is the inbreeding coefficient for a neutral locus at generation t and is estimated as $[1 - (1 - 1/2N)^t]$. The result of a single generation of reverse selection ($t' = 1$) following t generations of forward selection can be described in terms of the ratio $NR_1/\Delta x$ where $R_1$ is the response to the first generation of reverse selection. The value of $NR_1/\Delta x$ is expected to be $(1 - F)/2F$.

For any period of reverse selection following any period of forward selection, the value of $R/\Delta x$ never exceeds $t'/t$, and tends to decrease exponentially from this value as t increases.

## Introduction

Reverse and relaxed selection have been used quite commonly in laboratory selection experiments as diagnostic tools, especially in situations where selection response seems to have plateaued. The results of such selection have usually been interpreted in the light of common sense arguments which say that any alteration in the metric mean after relaxation must be an indication of opposing natural selection, and that response to reverse selection indicates the remaining presence of at least some additive genetic variance.

What is lacking at present is a quantitative prediction as to what the results of reverse and relaxed selection at a particular stage of the selection programme might be, for specific models of artificial selection. One method by which some understanding of the problem can be obtained for various single locus models involves the use of a suitable transition probability matrix. Such an approach has already been used by Allan and Robertson (1964), but they were concerned specifically with the effects of initial reverse selection on the ultimate result of subsequent forward selection to the limit. In the present context, this amounts to a study of the total change in gene frequency or metric mean resulting from a given period of forward selection followed by reverse selection to the limit. In the present study, the methods and results of Allan and Robertson are extended to cover any number of generations of both forward and reverse selection.

## The additive model

Consider a single locus with two alleles $A_1$ and $A_2$, and following Haldane (1931) and Robertson (1960), assume the relative selective values of the three genotypes $A_2A_2$, $A_1A_2$ and $A_1A_1$ as a result of artificial selection are $1 - i\alpha/2$, 1, $1 + i\alpha/2$ respectively, where i is the standardized selection differential, and $\alpha$ is the difference (a) between the metric means of the two homozygotes, divided by the phenotypic standard deviation ($\sigma_P$).

For small $Ni\alpha$, the frequency of allele $A_1$ after t generations of forward selection in the absence of natural selection is

$$E[q_t] = q_0 + Ni\alpha\, q_0(1 - q_0)\left(1 - e^{-t/2N}\right) \qquad (1)$$

(Robertson 1960) where $q_0$ is the initial gene frequency. It is usually assumed that during this time the effect of finite population size is to reduce $q_0(1-q_0)$ by a fraction $1/2N$ per generation, in which case it will have the value $q_0(1 - q_0)e^{-t/2N}$ after t generations of forward selection. It is then possible to express the expected frequency of allele $A_1$ after t' subsequent generations of reverse selection $(i < 0)$ in a form analogous to that given above:

$$E[q_{t+t'}] = E[q_t] + N(-i\alpha)\left[q_0(1-q_0)e^{-t/2N}\right]\left(1-e^{-t'/2N}\right)$$
$$= q_0 + Ni\alpha q_0(1-q_0)\left(1-2e^{-t/2N}+e^{-(t+t')/2N}\right) \qquad (2)$$

The difference between the initial frequency $q_0$ and the ultimate frequency after $t + t'$ generations is then

$$E[q_{t+t'}] - q_0 = Ni\alpha q_0(1-q_0)\left(1-2e^{-t/2N}+e^{-(t+t')/2N}\right).$$

When $t' = \infty$, implying reverse selection to the limit, this expression reduces to

$$E[q_{t+\infty}] - q_0 = Ni\alpha q_0(1-q_0)\left(1-2e^{-t/2N}\right) \qquad (3)$$

which is analogous to the result obtained by Allan and Robertson (1964) who where studying the effect of t generations of initial reverse selection on the ultimate result of subsequent forward selection to the limit.

### A prediction for small $Ni\alpha$

A general description of the effects of reverse selection following forward selection can be achieved by considering the change in metric mean due to reverse selection (R) in terms of the change in metric mean resulting from the previous forward selection ($\Delta x$). From equations (1) and (2), it can be seen for an additive model that

$$\Delta x = a\{E[q_t] - q_0\}$$
$$= aNi\alpha q_0(1-q_0)\left(1-e^{-t/2N}\right) \qquad (4)$$

and

$$R = a\left\{E[q_{t+t'}] - E[q_t]\right\}$$
$$= -aNi\alpha q_0(1-q_0)e^{-t'/2N}\left(1-e^{-t'/2N}\right) \qquad (5)$$

which gives

$$\left|\frac{R}{\Delta x}\right| = \frac{e^{-t/2N}\left(1-e^{-t'/2N}\right)}{1-e^{-t/2N}} \qquad (6)$$

The ratio of reverse selection response to previous forward selection response is thus the same for all initial gene frequencies and is independent of the size of the gene effect $(a/\sigma_P = \alpha)$, and the intensity of articicial selection (i), so long as $Ni\alpha$ is small.

An even more simple prediction is obtained if reverse selection is carried out for the same number of generations as the previous forward selection, in which case $t' = t$, and equation (6) reduces to

$$\frac{R}{\Delta x} = e^{-t/2N}$$
$$= 1 - F$$

where F is the inbreeding coefficient at a neutral locus after t generations of random mating in a population of effective size N. Thus, if forward selection is followed by an equal number of generations of reverse selection, the response to reverse selection is never as great as the previous forward selection response. Furthermore, the effectiveness of reverse selection decreases as the period of previous forward selection is lengthened, as might be expected. It must be emphasised that these conclusion apply only to a model of additive gene action in the absence of natural selection.

The general relationship between $R/\Delta x$ and the length of forward and reverse selection is shown in Fig. 1, having been obtained from equation (6). The first point to note is that the time scale on the x-axis corresponds exactly to the time scale commonly used

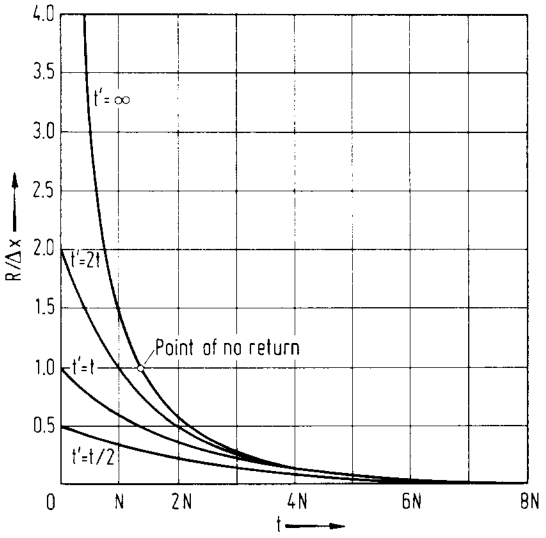

Fig. 1. The relationship between length of forward selection, t, and the ratio $R/\Delta x$ after various lengths of subsequent reverse selection, t', corresponding to t/2, t, 2t and $\infty$ generations, with t and t' being expressed in terms of effective population size N. Curves have been obtained from equation (6)

in the presentation of selection response curves. Thus all possible periods of initial forward selection are included, from $t = 0$ to $t = 8N$. Each curve in the figure represents the value of $R/\Delta x$ to be expected from a particular length of subsequent reverse selection. The curve for equal numbers of generations of forward and reverse selection ($t' = t$) is simply the plot of $1 - F$ for a neutral locus against time in units of N. It shows, for example, that an equal number of generations of reverse selection after forward selection of length equivalent to the half-life of the overall selection process (1.4N generations), results in the metric mean returning half way to its original level.

The circle in the figure represents the 'point of no return', a concept introduced by Allan and Robertson (1964) and which in this context can be defined as the number of generations of forward selection beyond which it is impossible for even an infinite number of generations of reverse selection to return the metric mean to its original level. For genes of small effect, Allan and Robertson found that the point of no return was 1.4N generations and indeed this conclusion derives directly from equation (3) by setting $E[q_{t+\infty}] - q_0 = 0$. The curve for $t' = \infty$ thus passes through the point of no return, and approaches asymptotically a value of $R/\Delta x = \infty$ as $t \rightarrow 0$. All other curves for all finite values of $t'$ will be situated to the left of this curve and will therefore always pass to the left of the point of no return. If $t < 1.4N$, the number of generations of reverse selection necessary to return the metric mean to its original value, (that is, to obtain $R/\Delta x = 1$) decreases as $t$ decreases. Beyond $t = 1.4N$, on the other hand, even reverse selection to the limit (complete fixation) will not return the metric mean to its original value.

Finally, it can be seen that the magnitude of $R/\Delta x$ approaches a limit of $t'/t$ as the number of generations of forward selection decreases. Forward selection for $t = 0.2N$ generations, for example, followed by $t' = 0.1N$ generations of reverse selection results in an $R/\Delta x$ value approaching 0.5, in this 0.47.

It is possible to obtain one more simple prediction from equation (6), in this case for a single generation of reverse selection ($t' = 1$) following $t$ generations of forward selection. If response to the first generation of reverse selection is denoted by $R_1$, then equation (6) reduces to

$$\frac{R_1}{\Delta x} = \frac{1}{2N} \; \frac{e^{-t/2N}}{1 - e^{-t/2N}}$$

or

$$\frac{NR_1}{\Delta x} = \frac{1 - F}{2F} \; .$$

Thus the results of a single generation of reverse selection following any period of forward selection can be described in terms of the parameter combination $NR_1/\Delta x$. It follows from the above expression that beyond $t = 1.4N$, $NR_1/\Delta x$ is less than $1 - F$, while if the single generation of reverse selection is carried out before the point of no return, then $NR_1/\Delta x$ is greater than $1 - F$.

All the conclusions so far reached refer to a specific model of additive gene action with no natural selection and $Ni\alpha < 1$, inferring genes of small effect and/or small population size. How will the conclusions be altered if the model is extended to include larger values of $Ni\alpha$?

## Stronger artificial selection

Since larger $Ni\alpha$ values tend to decrease genetic variance more quickly thus leaving relatively less genetic variance for subsequent reverse selection, it could be expected that the value of $\Delta x$ will be increased by a greater proportion than the value of R by larger values of $Ni\alpha$, for any particular $t$ and $t'$. Thus with equal periods of forward and reverse selection the ratio $R/\Delta x$ is expected to be less than the $1 - F$ predicted for $Ni\alpha < 1$. For $t = t'$ and $q_0 = 0.5$, Fig.2 shows this to be true.

The values of $R/\Delta x$ have been obtained from continued multiplication of the row vector of gene frequency distribution onto the appropriate transition probability matrix, and the subsequent determination of gene frequency, as described by Allan and Robertson (1964). All runs were actually carried out with $N = 10$, but results can be generalised to any value of N by describing the selection process in terms of the parameter combination $Ni\alpha$. Firstly, it can be seen that the points for $Ni\alpha = 1$ correspond very closely to the expectation of $e^{-t/2N}$ for small $Ni\alpha$. Increasing the strength of artificial selection reduces the value of $R/\Delta x$ for any particular $t$, until with say $Ni\alpha = 8$, forward selection for as little as 2N generations is sufficient to effectively prohibit any response to subsequent reverse selection.

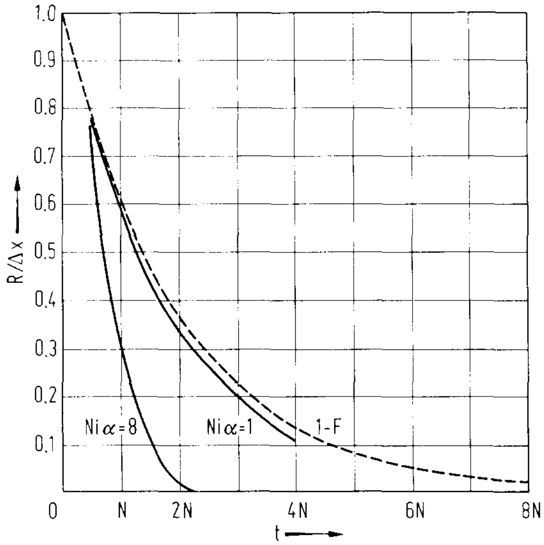

Fig.2. The relationship between length of forward selection, t, and the ratio $R/\Delta x$ after as many generations of reverse selection as previous forward selection ($t' = t$). Transition probability matrix results (solid lines) for relatively weak ($Ni\alpha = 1$) and relatively strong ($Ni\alpha = 8$) artificial selection with $q_0 = 0.5$ are compared with the prediction of $R/\Delta x = 1 - F$ (dotted line) from equation (6)

Similar conclusions in general have been obtained for all possible initial gene frequencies, with the exception that for $t' = t$ the value of $R/\Delta x$ may be slightly greater than $e^{-t/2N}$ if reverse selection is commenced after only a few generations of forward selection and if initial gene frequency is less than one half. The reason for this is simply that any forward selection favouring alleles with an initial frequency less than one half initially increases the genetic variance at that locus (until $q_t = 0.5$) thus enhancing the prospects of response to any reverse selection which occurs before $q_t$ has reached 0.5. More generally, it has been found that the value of $R/\Delta x$ observed from the matrix operations for any initial gene frequency and for any value of t' and t corresponds very closely to the value predicted from equation (6), if $Ni\alpha \leqslant 1$. Once again, the observed value of $R/\Delta x$ for any t' and any t tends to decrease below that predicted from equation (6) as $Ni\alpha$ increases, for all initial gene frequencies.

## Discussion

The results of this study provide a theoretical basis for the practical analysis of the nature of response in artificial selection lines. Thus if the results of reverse selection at any stage of the selection programme depart significantly from the expectations described above, then such a result may be an indication of nonadditive gene action for the metric character, or the presence of natural selection opposing forward artificial selection. Further work on departures from the simple additive model will provide a clearer indication of the effects of such other models on the expected value of $R/\Delta x$.

Relaxation of forward artificial selection can also be considered in this context. It is quite evident that no change in metric mean as a result of relaxation of selection is expected to occur with an additive model in the absence of natural selection. Matrix results have confirmed this expectation, and have shon that the only result of relaxation is a gradual widening and flattening of the gene frequency distribution, with fixation and loss occurring in the ratio $q_t/(1 - q_t)$ where $q_t$ is the frequency of the allele favoured by artificial selection at the final generation of forward selection. For additive artificial selection in the presence of natural selection, Robertson (1956) und Latter (1960) have already provided expectations of the value of $R_1/\Delta x$ for the homeostatic and optimum models of natural selection respectively.

Finally, it is evident that many relevant aspects of response to forward and reverse selection for the additive model have not been treated in detail here. However, it should be quite possible to use similar matrix operations to simulate a particular practical situation and consequently study it in more detail.

## Literature

Allan, J.S.; Robertson, A.: The effect of initial reverse selection upon total selection response. Genet. Res. 5, 68-79 (1964)

Haldane, J.B.S.: A mathematical theory of natural and artificial selection. VII. Selection intensity as a function of mortality rate. Proc. Cambridge Philos. Soc. 27, 131-136 (1931)

Latter, B.D.H.: Natural selection for an intermediate optimum. Austral. J. Biol. Sci. 13, 30-35 (1960)

Robertson, A.: The effect of selection against extreme deviants based on deviation or on homozygosis. J. Genet. 54, 236-248 (1956)

Robertson, A.: A theory of limits in artificial selection. Proc. Roy. Soc. (Series B) 153, 234-249 (1960)

Received April 4, 1976
Communicated by A. Robertson

F.W. Nicholas
Department of Animal Husbandry
University of Sydney
N.S.W. 2006 (Australia)