Changes in genetic parameters under restricted index selection

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Summary

The ability of restricted selection indices to prevent genetic change in a restricted trait over several generations of selection was studied using deterministic computer models. Four loci, two affecting each trait independently, and two pleiotropic loci, one affecting each trait in the same direction, and one with opposite effects, were modelled. In general, continued effectiveness of the restriction was achieved only when the restricted trait was affected by only one locus. In some conditions (equal gene frequencies), an independent locus and one pleiotropic locus affecting the restricted trait allowed maintenance of the restriction. The results suggest that long-term restriction may be very difficult without re-estimation of parameters.

1. Introduction

Restricted index selection may be viewed as a method of controlling correlated response to selection by 'breaking' the genetic correlations between the restricted trait and other selected traits. This effectively means choosing favourable genes for unrestricted traits which have little or no effect on the restricted trait (Famula, 1984), or selecting genes affecting the restricted trait in such a way that changes at different loci balance each other, with no resulting change in that trait.

Several restricted index selection experiments have shown discrepancies between predicted and observed responses. Eisen (1977), using bidirectional restricted index selection in an unreplicated experiment over ten generations, selected for maximal genetic change in post-weaning gain in mice while holding feed intake unchanged. Responses agreed with expectations for four generations, but thereafter feed intake tended to change in the same direction as post-weaning gain in both index lines, suggesting that genetic parameters may have altered during selection. Eisen (1977) suggested that restricted index selection may be more sensitive to such changes than other selection procedures. Abplanalp, Ogasawara & Asmundson (1963), Scheinberg, Bell & Anderson (1967) and McCarthy & Doolittle (1977) all noted that changes in genetic parameters due to selection may have been

a cause of disagreement between expected and observed responses to restricted index selection.

Bohren, Hill & Robertson (1966), in a theoretical examination of correlated selection responses, concluded that genetic covariances may be more sensitive than genetic variances to the changes in gene frequency produced by selection. Thus they suggested that initial genetic parameter estimates would give reasonable predictions over a shorter period for correlated than for direct responses. Accurate prediction of correlated responses over many generations would require knowledge of the composition of the genetic covariance.

An understanding of the patterns of change in genetic parameters under selection would be particularly pertinent in the case of restricted index selection, whose effectiveness depends on the balance of variance and covariance. Such understanding could permit identification of conditions under which restricted indices would be expected to function as predicted for a number of generations. The aim of this study was to apply the methods of Bohren *et al.* (1966) to restricted index selection, in order to establish the conditions in which response in the restricted trait could be held to zero, and to investigate the changes in genetic parameters in relation to that objective.

2. Method

A genetic model of the same type as that analysed by Bohren *et al.* (1966) was used, where four types of loci are considered, with gene action additive both within

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and between loci. The different loci have the following effects of gene substitutions on the two traits (X and Y):

Loci...	A	B	C	D
Trait X	α	β_X	γ_X	0
Trait Y	0	β_Y	$-\gamma_Y$	δ

Loci A and D affect the traits independently, while loci B and C affect both traits, making positive and negative contributions respectively to the genetic covariances. If p_A and q_A are the frequencies of the alleles at the A locus, with similar notation for other gene frequencies, the genetic variances and covariance are

$$V_{GX} = 2p_A q_A \alpha^2 + 2p_B q_B \beta_X^2 + 2p_C q_C \gamma_X^2,$$
$$V_{GY} = \qquad 2p_B q_B \beta_Y^2 + 2p_C q_C \gamma_Y^2 + 2p_D q_D \delta^2,$$
$$\text{cov}_G = \qquad 2p_B q_B \beta_X \beta_Y - 2p_C q_C \gamma_X \gamma_Y.$$

In our computations, environmental variances were set equal to the genetic variances, while the environmental covariance was set equal to zero.

If R denotes the restricted and U the unrestricted trait, the index for maintaining the restricted trait constant is (Morley, 1955)

$$I = P_U - bP_R$$

where P denotes phenotypic value and $b = -\text{cov}_G/V_{GR}$. Restriction was such that the covariance between the restricted trait and index was equal to zero. Selection on such an index will lead to changes in gene frequency which can be approximated by

$$\Delta p_A = \frac{ip_A q_A \dfrac{z_A}{\sigma_I}\left[1 + \dfrac{1}{2}\dfrac{z_A}{\sigma_I}\dfrac{x_0}{\sigma}(q_A - p_A)\right]}{1 + ip_A q_A \left(\dfrac{z_A}{\sigma_I}\right)^2 \dfrac{x_0}{\sigma}},$$

with similar expressions for gene frequency changes at other loci. In this equation, which is equation (4) of

Latter (1965) written in terms of average effect instead of difference between homozygotes, σ_I^2 is the variance of the index, I, for which the average effect of the locus is $z_A = \alpha_U - b\alpha_R$, ($\alpha_U$ and α_R being the average effect of a gene substitution on the unrestricted and restricted traits respectively), and x_0 is the truncation point. We first tried the simple linear term used by Bohren *et al.* (1966), but found that in some cases this resulted in impossible outcomes, so the more complex form had to be used.

Combinations of gene effects and initial gene frequencies used by Bohren *et al.* (1966) were examined, and are shown in Table 1. The computing procedure was as follows. For a given model, the genetic variances and covariances were calculated, and phenotypic variances were taken as twice the genetic variances ($h^2 = 0.5$). Then the restricted index coefficient was computed for holding each of the two traits constant. The expected gene frequency changes were then calculated, and used to compute the new set of genetic parameters, and the means of both restricted and unrestricted traits. Maintaining the restricted index coefficient at its initial value, this procedure was repeated to give a ten-generation selection experiment. Standardized selection differentials and truncation points were set to correspond to selection of the best 40, 20 and 5% in both high and low directions.

3. Results

For the restricted indices considered, the genetic gains in standardized units accumulated over the ten generations of selection are presented in Tables 2 and 3 for selection intensities of 20% in the high and low directions respectively. Only in the case of gene effect model 4 were the restricted indices able to attain the goal of no genetic change in the restricted trait. This was true for all selection intensities, in both high and

Table 1. *Gene effects and initial gene frequencies examined by model selection experiments*

	Gene effects Trait X α / Trait Y β_Y	β_X / γ_Y	γ_X / δ		Initial gene frequencies P_A	P_B	P_C	P_D
(1)	1 / 1	1 / 1	1	(a)	0·5	0·5	0·5	0·5
(2)	0 / 1	1 / 1	1 / 0	(b)	0·5	0·2	0·5	0·5
(3)	1 / 1	1 / 1	1 / 2	(c)	0·5	0·5	0·2	0·5
(4)	0 / 1	1 / 0	0 / 1	(d)	0·5	0·5	0·5	0·2
(5)	1 / 2	2 / 1	1 / 1	(e)	0·5	0·2	0·2	0·5
(6)	1 / 1	1 / 2	2 / 1	(f)	0·5	0·8	0·3	0·5
(7)	1 / 1	2 / 2	1 / 1	(g)	0·5	0·3	0·8	0·5

Table 2. *Genetic gains of traits X (TX) and Y (TY) after ten generations of selection on restricted indices restricting trait X (XR) and trait Y (YR) with a selection intensity of 1·4. Gene effects and initial gene frequencies as defined in Table 1*

Initial gene frequencies		Gene effects												
		(1)		(2)		(3)		(4)		(5)		(6)		(7)
		XR	YR	XR	YR	XR	YR	XR	YR	XR	YR	XR	YR	XR	YR
(a)	TX	2·00	3·00	2·00	2·00	2·00	3·00	0·0	1·00	2·00	3·92	3·95	4·00	3·00	4·00
	TY	3·00	2·00	2·00	2·00	4·00	2·00	1·00	0·0	3·92	2·00	4·00	3·95	4·00	3·00
(b)	TX	3·23	3·60	2·60	2·60	3·07	3·60	0·0	1·60	3·32	5·19	4·57	4·60	4·73	5·20
	TY	3·60	3·23	2·60	2·60	4·60	3·80	1·00	0·60	5·19	3·32	4·60	4·57	4·60	4·08
(c)	TX	1·98	3·60	2·60	2·60	2·12	3·60	0·0	1·00	2·10	4·05	5·09	5·20	3·12	4·54
	TY	3·60	1·98	2·60	2·60	4·59	1·41	1·00	0·0	4·05	2·10	5·20	5·09	5·20	3·58
(d)	TX	2·00	3·00	2·00	2·00	2·00	3·00	0·00	1·00	2·00	3·90	3·94	4·00	3·00	4·00
	TY	3·60	2·00	2·00	2·00	5·20	2·00	1·60	0·60	4·52	2·52	4·59	4·39	4·60	3·00
(e)	TX	3·20	4·20	3·20	3·20	3·20	4·20	0·0	1·60	3·71	5·65	5·75	5·89	4·80	5·80
	TY	4·20	3·20	3·20	3·20	5·20	3·20	1·00	0·60	5·65	3·71	5·80	5·75	5·80	4·80
(f)	TX	2·23	2·80	1·80	1·80	2·10	2·80	0·0	0·40	1·25	3·16	4·17	4·20	2·55	3·20
	TY	2·80	2·23	1·80	1·80	3·80	2·59	1·00	0·60	3·16	1·25	4·20	4·17	4·20	3·53
(g)	TX	1·37	2·80	1·80	1·80	1·50	2·80	0·0	1·40	2·21	4·17	3·12	3·20	2·86	4·20
	TY	2·89	1·37	1·80	1·80	3·80	1·01	1·00	0·40	4·17	2·21	3·20	3·12	3·20	1·85

Table 3. *Genetic gains of traits X (TX) and Y(TY) and Y(TY) after ten generations of selection on restricted indices restricting trait X (XR) and trait Y (YR) with a selection intensity of −1·4. Gene effects and initial gene frequencies as defined in Table 1.*

Initial gene frequencies		Gene effects												
		(1)		(2)		(3)		(4)		(5)		(6)		(7)
		XR	YR	XR	YR	XR	YR	XR	YR	XR	YR	XR	YR	XR	YR

|		(1) XR	(1) YR	(2) XR	(2) YR	(3) XR	(3) YR	(4) XR	(4) YR	(5) XR	(5) YR	(6) XR	(6) YR	(7) XR	(7) YR
(a)	TX	2·00	3·00	2·00	2·00	2·00	3·00	0·0	1·00	2·00	3·02	3·94	4·00	3·00	4·00
	TY	3·00	2·00	2·00	2·00	4·00	2·00	1·00	0·0	3·92	2·00	4·00	3·94	4·00	3·00
(b)	TX	2·05	2·40	1·40	1·40	1·88	2·40	0·0	0·40	0·91	2·79	3·37	3·40	2·30	2·80
	TY	2·40	2·05	1·40	1·40	3·40	2·63	1·00	0·60	2·79	0·91	3·40	3·37	3·40	2·90
(c)	TX	1·76	2·40	1·40	1·40	0·92	2·40	0·0	1·00	1·39	3·35	2·79	2·80	1·90	3·40
	TY	2·40	1·76	1·40	1·40	3·40	0·17	1·00	0·00	3·35	1·39	2·80	2·79	2·80	1·26
(d)	TX	2·00	3·00	2·00	2·00	2·00	3·00	0·0	1·00	2·00	3·90	3·95	4·00	3·00	4·00
	TY	2·40	2·00	2·00	2·00	2·80	2·00	0·40	−0·60	2·33	1·55	3·40	3·39	3·40	3·00
(e)	TX	0·80	1·80	0·80	0·80	0·80	1·80	0·0	0·40	0·24	2·20	2·16	2·20	1·20	2·20
	TY	1·80	0·80	0·80	0·80	2·80	0·80	1·00	−0·60	2·20	0·24	2·20	2·16	2·20	1·20
(f)	TX	2·62	3·20	2·20	2·20	2·50	3·20	0·0	1·60	2·88	4·79	3·77	3·80	4·15	4·80
	TY	3·20	2·62	2·20	2·20	4·20	2·98	1·00	0·60	4·79	2·88	3·89	3·77	3·89	3·12
(g)	TX	1·78	3·20	2·20	2·20	1·90	3·20	0·0	0·60	1·50	3·45	4·73	4·80	2·48	3·79
	TY	3·20	1·78	2·20	2·20	4·19	1·43	1·00	−0·40	3·45	1·50	4·89	4·73	4·89	3·44
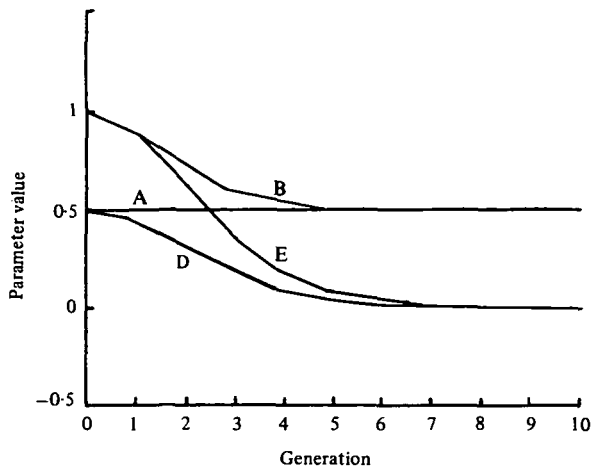
Fig. 1. Standard genetic covariances and variances under restricted index selection with intensity 20% in the high direction, using model 4a. Genetic variances for X and Y are the same. (A) Genetic variances, X restricted. (B) Genetic covariance, X restricted. (D) Genetic variances, Y restricted. (E) Genetic covariance, Y restricted.

low directions. For all combinations of initial gene frequencies, indices restricting trait X while trait Y was unrestricted were able to maintain zero response in X. However, indices restricting trait Y with trait X unrestricted were successful only for initial gene frequency combinations (*a*) and (*c*), which are identical for gene effect model 4, since locus C has no effect.

Figure 1 illustrates the changes in genetic covariance and genetic variances under restricted index selection for model 4a with a selection intensity of 20% in the high direction. For the index restricting trait X, the genetic variance of X and the genetic covariance remained constant over the ten generations, while the variance of Y decreased. For the index restricting trait Y, both the genetic variance of X and the genetic covariance decreased at the same rate to zero. The variance of Y decreased at a proportionate rate to zero. For all parameters, most change occurred during the first five generations.

For this gene effect model, restriction of trait X resulted in gene frequency change at the D locus only, where gene frequency finally reached unity for all initial gene frequency combinations. In contrast, restriction of trait Y caused gene frequency changes at both B and D loci; the B locus was fixed, while the gene frequency at the D locus decreased to near zero. These trends were for selection in the high direction, reverse trends occurring with low selection. This pattern of gene frequency changes was not observed in any of the other gene effect models, particularly at the B locus when trait X was restricted. In all six models, gene frequency changes occurred at all loci, except in model 2 which had zero gene effects for loci A and D. The patterns of change of genetic covariance and variances shown in Fig. 1 were typical of most combinations of initial gene frequencies examined for model 4.

Exceptions occurred where restriction of trait Y was not achieved, because the variance of trait Y changed at a proportionally different rate from that of the covariance and the variance of trait X.

For the other six gene-effect models there was considerable variation between models in the patterns of change of the genetic parameters. Generally, the genetic parameters decreased in absolute value, decreasing to zero over ten generations of selection. The variance of the restricted trait changed at a slower rate than the variance of the unrestricted trait, and at a proportionally different rate from the covariance.

Increasing the selection intensity generally increased the rate of change of genetic variances, while the rate of change of the genetic covariance was decreased. This was observed for both high and low directions of selection. The effect of selection intensity was particularly apparent for the models for which the restricted indices were ineffective. More detailed results are given by Mortimer (1984).

4. Discussion

The results of this study indicate that restricted index selection is particularly sensitive to changes in genetic parameters. Restriction of genetic change to zero is possible only if the genetic covariance and the variance of the restricted trait either remain unaltered or change in proportion to each other. Under these conditions, the index weighting factor estimated from initial genetic parameters would remain appropriate for the restriction during continued selection. Any disproportionate changes in initial genetic parameters due to movements in gene frequencies at independent and pleiotropic loci influencing the restricted trait lead to ineffective restriction.

This was illustrated by gene effect model 4, the only one for which restriction remained effective. When X is restricted, the variance of the restricted trait and the covariance are both given by $2p_B q_B$, so the index weighting factor remains appropriate as gene frequencies change. When Y is restricted, the variance of the restricted trait is $2p_B q_B + 2p_D q_D$, and since selection altered gene frequencies, the index weight would remain appropriate only with equivalent gene frequency changes at the two loci. Thus restriction was effective only for the two sets of initial gene frequencies where $p_B = p_D$.

The inability of the index to maintain zero genetic change in the restricted trait for the other models is not hard to explain. If the goal of selection is to alter Y while restricting X, b must remain constant, where

$$b = \frac{2p_B q_B \beta_X \beta_Y - 2p_C q_C \gamma_X \gamma_Y}{2p_A q_A \alpha^2 + 2p_B q_B \beta_X^2 + 2p_C q_C \gamma_X^2},$$

$$= \frac{\beta_Y}{\beta_X} \frac{1 - \dfrac{p_C q_C}{p_B q_B} \dfrac{\gamma_X}{\beta_X} \dfrac{\gamma_Y}{\beta_Y}}{1 + \dfrac{p_A q_A}{p_B q_B}\left(\dfrac{\alpha}{\beta_X}\right)^2 + \dfrac{p_C q_C}{p_B q_B}\left(\dfrac{\gamma_X}{\beta_X}\right)^2}.$$

For this expression to remain constant as gene frequencies change, it is necessary to have $p_A = p_B = p_C$ and $\alpha/\beta_X = \gamma_X/\beta_X = \gamma_Y/\beta_Y$. Other sets may exist which could keep b constant at some points, but as gene frequencies altered, the value of b would change. Furthermore, gene frequency changes at each locus are in the following proportions

$$\Delta p_A \propto b\alpha,$$
$$\Delta p_B \propto b\beta_X + \beta_Y,$$
$$\Delta p_C \propto b\gamma_X - \gamma_Y.$$

If changes in gene frequency are to be equal, so that $p_A q_A = p_B q_B = p_C q_C$ remains true, non-zero values of α or γ are not compatible with the assumption that β_X and β_Y are non-zero. Alternatively, if $\beta_X = \beta_Y = 0$ it is possible to have $\alpha = 0$, $\gamma_X \neq 0$, $\gamma_Y \neq 0$. α can be non-zero only if the traits are uncorrelated.

Therefore, only one locus can affect the restricted trait; this could be A, B or C, but not any two of them. If correlation exists, it must be due to B or C type loci, but not to both, and all variation in the restricted trait must be due to a pleiotropic locus. The progress in the unrestricted trait is due to change in frequency at a type D locus. The pattern of effective restriction in the computer runs is easily understood on this basis.

Re-estimation of parameters each generation, to obtain an index weight appropriate for the population under selection, would appear to offer a means of maintaining an effective restriction. The results are for the extreme cases of major genes where effects at individual loci are very large. Changes in gene frequency at loci with much smaller gene effects may be slower, which would reduce the rate of breakdown of restriction. When many loci of each type affect the traits, the pattern would certainly not be so clear.

However, it would seem that similar conclusions would hold, though because changes in frequency at each locus would be slower it would probably take longer for the effectiveness of restriction to break down.

References

Abplanalp, H., Ogasawara, F. X. & Asmundson, V. S. (1963). Influence of selection for body weight at different ages on growth of turkeys. *British Poultry Science* **4**, 71–80.

Bohren, B. B., Hill, W. G. & Robertson, A. (1966). Some observations on asymmetrical correlated responses to selection. *Genetical Research* **7**, 44–57.

Eisen, E. J. (1977). Restricted selection index: an approach to selecting for feed efficiency. *Journal of Animal Science* **44**, 958–972.

Famula, T. R. (1984). Restricted best linear unbiased prediction and a selection model. *Theoretical and Applied Genetics* **67**, 337–340.

Latter, B. D. H. (1965). The response to artificial selection due to autosomal genes of large effect. 1. Changes in gene frequency at an additive locus. *Australian Journal of Biological Sciences* **18**, 585–598.

McCarthy, J. C. & Doolittle, D. P. (1977). Effects of selection for independent changes in two highly correlated body weight traits of mice. *Genetical Research* **29**, 133–145.

Morley, F. H. W. (1955). Selection for economic characters in Australian Merino sheep. V. Further estimates of phenotypic and genetic parameters. *Australian Journal of Agricultural Research* **6**, 77–90.

Mortimer, S. I. (1984). Efficiency of multiple-trait selection methods with and without restrictions. Ph.D. Thesis. University of New South Wales.

Scheinberg, E., Bell, A. E. & Anderson, V. L. (1967). Genetic gain in populations of *Tribolium castaneum* under uni-stage tandem selection and under restricted selection indices. *Genetics* **55**, 69–90.