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Genetic improvement of production while maintaining fitness

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Abstract Selection for production tends to decrease fitness, in particular, major components such as reproductive performance. Under an infinitesimal genetic model restricted index selection can maintain reproductive performance while improving production. However, reproductive traits are thought to be controlled by a finite number of recessive alleles at low frequency. Culling for low reproduction may weed out the negative homozygous genotypes for reproduction in any generation, thus controlling the frequencies of alleles negative for reproduction. Restricted index selection, culling for low reproduction and a new method called empirical restricted index selection were compared for their efficiency in improving production while maintaining reproduction. Empirical restricted index selection selects animals that have on average the highest estimated breeding values for production and on average the same estimated breeding values for reproduction as the base population. An infinitesimal genetic model and models with a finite number of loci for reproduction with rare deleterious recessive alleles, which have additive, dominant or no pleiotropic effects on production, were considered. When reproduction was controlled by a finite number of loci with rare recessive alleles, restricted index selection could not maintain reproduction. The culling of 20% of the animals on reproduction maintained reproduction with all genetic models, except for the model where loci for reproduction had additive effects on production. Empirical restricted selection maintained reproduction with all models and yielded higher production responses than culling on reproduction, except when there were dominant pleiotropic effects on production.

Key words Genetic improvement · Fitness
Finite locus models · Production

Introduction

Animal breeders usually select for production while a negative correlated response on fitness is considered undesirable. Although not necessarily an economically optimum approach (Gibson and Kennedy 1990), a standard method for increasing one trait (production) without reducing another (fitness) is the use of restricted selection indices (Kempthorne and Nordskog 1959; Cunningham et al. 1970; Brascamp 1984). Under an infinitesimal genetic model (Bulmer 1980), these indices yield maximum response for production while maintaining fitness.

Genetic variation of major components of fitness (e.g. reproductive performance), however, is thought mainly to be due to deleterious recessive genes with low frequencies (Falconer 1989), and hence, the infinitesimal model does not hold. Experimental selection for metric characters (e.g. production) almost always results in a reduction in the major components of fitness (Falconer 1989). This is thought to occur because natural populations at or near maximal fitness are in equilibrium, with all genes affecting fitness being close to their optimal frequencies. If any of the fitness genes have a pleiotropic effect on the metric character, selection for the metric character will change their frequencies away from the optimum. Also, pleiotropic effects of fitness genes on metric characters may be more or less additive (Robertson 1956; Falconer 1989), and intermediate values of the metric character will yield maximum fitness.

Gowe (1983), Frankham et al. (1988) and Gowe et al. (1993) proposed culling a small fraction of the population based on reproductive performance while selecting the remainder for production. If genotypes for reproduction are determined by rare recessive genes, then only homozygotes for the rare recessive genes will have low genetic values. Hence, an obvious way to avoid a decrease in re-

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production is to try to weed out the homozygotes for the recessive genes, which may be achieved by culling a small fraction of the population for reproductive value, since few animals will be homozygote recessives.

The aim of this paper is to compare by means of computer simulation of various genetic models the efficiency of restricted selection indices with independent culling and alternative selection criteria for improving production while maintaining reproductive levels.

Genetic models for reproduction and production

Infinitesimal model

The infinitesimal model is often used in animal breeding because of its simplicity and because its input parameters are genetic and non-genetic variances and covariances, which are estimable (see, e.g. Bulmer (1980) for a description). Finite loci models depend on allele frequencies and effects, which are generally unknown. The following paragraph describes the Monte Carlo simulation of the infinitesimal model that was used to investigate the effects of various selection methods on production and reproduction.

Genotypic values of each founder animal for production and reproduction are simulated by two correlated infinitesimal genetic components, which are distributed as $N(0, V_a)$, where V_a = the additive (co)variance matrix of production and reproduction (dimensions: 2×2). The genotypic values of offspring are distributed as $N(1/2 u_s + 1/2 u_d, 1/4(2-F_s-F_d)V_a)$, where u_s (u_d) = (two-dimensional) vector with infinitesimal genetic components of production and reproduction of the sire (dam); and F_s (F_d) = the coefficient of inbreeding of the sire (dam). Environmental values for both traits of animal i were randomly distributed as $N(0, V_e)$, where V_e = (co)variance matrix of environmental components of production and reproduction. The environmental components of production and reproduction were assumed to be uncorrelated. Phenotypes were obtained as the sum of the genotypic and environmental values. Further, reproductive phenotypes were simulated only for female animals, i.e. reproduction was assumed to be a sex-limited trait.

Finite locus models for reproduction

Because the inheritance of reproduction is mainly due to deleterious recessives at low frequency (Falconer 1989) and because dominance (or recessiveness) of genes is not possible in the infinitesimal model (Robertson and Hill 1983), a finite locus model was adopted for the reproductive trait. Alleles that increase reproduction were assumed to have negative pleiotropic effects on production. Other alleles for reproduction would not cause reproductive problems if selection is for production. An independent infinitesimal genetic component for production was simulated to reduce the genetic relationship between the two traits.

Theoretically, all loci in a genome may affect a quantitative character. Many will have very small effects and some may have substantial effects. Shrimpton and Robertson (1988) suggest that the distribution of effects of genes can be approximated by a geometric series. In the present study, the genetic value for reproduction was determined by 100 loci with additive and dominance effects, loci without epistasis. It was assumed that the additive genetic variances of the 100 loci followed a geometric series (as by Lande and Thompson 1990), hence, the additive variance due to locus i is:

$$\sigma_{ri}^2 = c^{i-1} \sigma_{ra}^2 (1-c) / (1-c^{100}), \text{ for } 1 \leq i \leq 100,$$

where σ_{ra}^2 = total additive genetic variance of reproduction, and constant c determines the rate at which the variances of the loci decrease ($0 < c < 1$). Note that $\sum_{i=1}^{100} \sigma_{ri}^2 = \sigma_{ra}^2$. Lande and Thompson calculated the effective number of loci as:

$$N_E = (1+c)/(1-c).$$

The average effect of gene substitution, as defined by Falconer (1989), is calculated as:

$$\alpha_{ri} = (\sigma_{ri}^2 / (2pq)),$$

where p (q) is the frequency of the positive (negative) allele ($p=1-q$). This assumes that allele frequencies across loci are equal and that at each locus there are only two alleles, i.e. a positive allele, that increases reproduction, and a negative allele.

The genotypic values of the heterozygotes $A_{i1}A_{i2}$ at each locus were assumed to decrease proportionally the same as the variance at each locus:

$$d_{ri} = D / (2pq) c^{i-1} (1-c) / (1-c^{100}),$$

where D = the inbreeding depression of the reproductive trait with complete inbreeding. The genotypic value of the positive homozygote $A_{i1}A_{i1}$ is $a_{ri} = \alpha_{ri} - d_{ri}(q-p)$ and that of the negative homozygote $A_{i2}A_{i2}$ is $-a_{ri}$. It may be noted that the degree of dominance d_{ri}/a_{ri} decreases with decreasing variance of the locus and that loci with large effects may be overdominant. For instance, if $q=p$, d_{ri}/a_{ri} is directly proportional to $c^{1/2}$, with $0 < c < 1$.

An animal's genotype for reproduction equals the sum of the genotypic values of its 100 loci:

$$G_{ri} = \sum_j g_{rij},$$

where g_{rij} = the genotypic value for reproduction of animal i for locus j , which is a_{ri} , d_{ri} , or $-a_{ri}$ if the genotype is $A_{j1}A_{j1}$, $A_{j1}A_{j2}$, or $A_{j2}A_{j2}$, respectively. The reproductive phenotype is the sum of the genotype plus the environmental effect, which is modelled as: $p_{ri} = G_{ri} + e_{ri}$, where e_{ri} is sampled from $N(0, \sigma_{re}^2)$.

It was assumed that the ranking of the loci according to the size of their effects was the same for production and reproduction. The average effect for production was simulated as:

$$\alpha_{pi} = \alpha_{ri} r_a \sigma_{pa} / \sigma_{ra},$$

where r_a = additive genetic correlation between production

and reproduction, and σ_{pa}^2 =additive genetic variance of production. Values of $A_{i1}A_{i1}$, $A_{i1}A_{i2}$ and $A_{i2}A_{i2}$ were: $a_{pi}=\alpha_{pi} - d_{pi}(q-p)$, d_{pi} , and $-a_{pi}$, respectively, where $d_{pi}=0$ (additive gene effects) or $d_{pi}=a_{pi} d_{ri}/a_{ri}$ (degree of dominance is the same as that for reproduction). The situation with $d_{pi}=0$ may represent genes such as the Halothane gene in pigs, which has a negative recessive effect on stress susceptibility and an additive effect on leanness of the carcass (Forstein et al. 1981). The double muscling gene in cattle has a recessive effect on dystocia (negative effect) and on muscle content (positive effect), which may reflect the situation with $d_{pi}/a_{pi}\approx d_{ri}/a_{ri}$. In the absence of saturation of the enzymes with substrates and other non-linearities in fluxes through the metabolic pathways (i.e. to a first order approximation), variation in enzyme activity due to homozygosity or heterozygosity at a locus leads to identical degrees of dominance of the locus for each of the outputs of the pathway (Keightley and Kacser 1987). Hence, under these linearity assumptions $d_{pi}/a_{pi}=d_{ri}/a_{ri}$.

The total genotypic value for production was the sum of the effects of the 100 loci plus an (additive) infinitesimal component:

$$G_{pi}=u_{pi} + \sum_j g_{pij},$$

where g_{pij} =genotypic effect of locus j of animal i on production. The infinitesimal component u_{pi} was simulated as with the infinitesimal model described above except that there was no reproduction component simulated, and $\text{Var}(u_{pi})=(1-r_a^2)\sigma_{pa}^2$ in the base generation. Hence, only a small proportion of the total additive variance of production, namely r_a^2 , was due to the reproduction loci, and inheritance of initial production would still be observed as additive. Phenotypes were simulated from the genotypes as with the infinitesimal model.

Selection methods

Random selection (RS) was considered because changes in gene frequencies due to random drift will lead to changes in mean genotypic values. Random selection may be considered to be the equivalent of a control line in a selection experiment.

Unrestricted selection for production (USP) was considered where selection was only for production. Selection for production was based on a selection index (Hazel 1943) containing own, full-sib, half-sib and parental performance. Reproduction information was not used to improve the accuracy of selection.

Restricted index selection (RIS) (Cunningham et al. 1970) was considered where the index contained the same information sources as before plus reproductive information on female full-sib, half sibs and the dam, and also own performance if the animal was female.

The index weights b_{ris} for the restricted index are obtained from (Cunningham et al. 1970):

$$\begin{bmatrix} P & G_r \\ G_r' & 0 \end{bmatrix} \begin{bmatrix} b_{ris} \\ \lambda \end{bmatrix} = \begin{bmatrix} G_p \\ 0 \end{bmatrix},$$

where P =variance-covariance matrix of the sources of information, and G_x =vector of genetic covariances between the sources of information and the true breeding value for trait x . The first equation yields: $b_{ris}=b_p - \lambda b_r$, where $b_x=P^{-1}G_x$, which are the index weights for the selection index for trait x . Substitution into the second equa-

tion yields $\lambda=G_r'b_p/G_r'b_r=\text{Cov}(I_{ri},I_{pi})/\text{Var}(I_{ri})$, where $I_{xi}=b'_x p_i$, which is the estimated breeding value for trait x of animal i , and p_i is the phenotypic value of the information sources for animal i . Hence,

$$I_{ris,i}=I_{pi}-\lambda I_{ri},$$

where $I_{ris,i}$ =the restricted selection index value for animal i . From the second restricted index equation it follows that the covariance between $I_{ris,i}$ and true breeding values for reproduction is zero. With linearity of regression of breeding values on phenotypes, i.e. with normality of distributions, the average response of reproduction with selection for $I_{ris,i}$ will be zero. It may be noted that if,

$$I_{pi}=\lambda I_{ri} + \epsilon$$

is the linear regression of I_{ri} on I_{pi} , then $I_{ris,i}$ is equal to the error term. If the true regression of I_{ri} on I_{pi} is non-linear, due to non-normal distributions, this error term, i.e. $I_{ris,i}$, will depend on the level of I_{ri} . Hence, with non-normal distributions, selection for $I_{ris,i}$ may lead to reduced reproductive performance.

True breeding values for reproduction are obtained from (Falconer 1989):

$$TBV_i=\sum_j f_{ij}\alpha_{rj},$$

where f_{ij} is $2q_j$, q_j-p_j , or $-2p_j$, if the genotype of animal i for locus j is $A_{j1}A_{j1}$, $A_{j1}A_{j2}$, or $A_{j2}A_{j2}$, respectively, and summation is over all loci. The frequencies p_j and q_j were adjusted each generation for each locus.

Empirical restricted index selection (ERIS) was considered, in which selection was on an index of estimated breeding values of production and reproduction with the aim of always maintaining average estimated breeding value for reproduction of selected animals, \bar{I}_{ri} , at a desired value, G_r , which is the average genetic level of reproduction in the base population. The selection index is

$$I_{eris,i}=(1-\gamma) I_{pi} + \gamma I_{ri},$$

for $0 \leq \gamma \leq 1$,

where γ is obtained empirically.

The value of γ was calculated numerically for each round of selection and within each sex. The production and reproduction indices used for ERIS use the same sources of information as the restricted selection index. Three situations can result: (1) if $\gamma=0$, selection is solely for I_{pi} , and the average breeding value for reproduction of the selected animals \bar{I}_{ri} , will be above the desired G_r ; (2) if $\gamma=1$, selection is solely for I_{ri} , and \bar{I}_{ri} will be below G_r ; and (3) some intermediate value for γ will yield approximately $\bar{I}_{ri}=G_r$. The value of which yields $\bar{I}_{ri}=G_r$ will maximize \bar{I}_{pi} given the constraint on \bar{I}_{ri} .

Compared to the restricted index selection ERIS will (1) correct a decrease in reproduction that might have occurred during previous selection and (2) select animals with the desired average reproductive index even if the regression of the production index on the reproductive index is non-linear and if there are fluctuations in index values due to sampling.

Phenotypic culling (PC10 and PC20) was considered, where 10% and 20% of the animals were culled prior to selection. Females were culled on own reproductive performance, and males were culled on the average reproduction of their female full sibs. The remaining animals were selected for production as with USP.

Index culling (IC10 and IC20) was considered, where 10% and 20% of the animals were culled on the basis of a reproductive index. The reproductive index used all available information on full-sibs, half sibs, parents and own performance for both traits, production and reproduction. The index used this information to predict reproductive genotype G_{ri} , rather than breeding value, because it was meant to weed out the $A_{i2}A_{i2}$ genotypes. The remaining animals were selected for production as with USP.

Selection index weights were obtained from the empirical variances and covariances that were calculated from phenotypic and actual genetic values of selection candidates within each generation. Hence, optimal properties of selection indices were not affected by changes of variances and covariances due to selection, changes in gene frequencies or sampling.

Parameters of the breeding scheme are given in Table 1. In the founder generation, all animals were unrelated and, hence, there was

Table 1 Parameters of the breeding scheme

Total number of animals/generation:	256 ♂ + 256 ♀
Number of animals selected/generation:	8 ♂ + 64 ♀
Mating design:	Hierarchical (8 dams /sire)
Number of offspring per dam:	4 ♂ + 4 ♀
Production: additive genetic variance, σ_{pa}^2	0.25
environmental variance, σ_{pe}^2	0.75
Reproduction: additive genetic variance, σ_{ra}^2	0.10
environmental variance, σ_{re}^2	0.90
depression with complete inbreeding, D	$8 \sigma_{ra}$
effective number of loci, N_E	10 or 3
frequencies of deleterious recessive alleles, q	0.1 or 0.2
Additive correlation between production and reproduction, r_a	-0.25 or 0

no family information available. Therefore, first-generation animals were obtained by random selection. This was followed by nine discrete generations of selection in a closed nucleus until the tenth generation of animals was obtained. Differences in the reproductive performance of selected animals did not lead to differences in their number of offspring. It was assumed that increased management efforts would overcome they reduced reproduction of elite animals.

Depression of reproduction with complete inbreeding, D, was assumed to be $8\sigma_{ra}$. If δ is the inbreeding depression expressed as a percentage of the mean value of reproduction per percent of inbreeding and CV is the coefficient of variation of reproduction, then

$$D = \delta / (h_r CV) \text{ (in } \sigma_{ra} \text{-units)}$$

where h_r^2 = heritability of reproduction. Values of δ for reproductive traits vary from 0.5% to 1% depression per percent of inbreeding (e.g. Falconer 1989; Woodard et al. 1982; MacNeil et al. 1989; Wiener et al. 1992). Coefficients of variation and heritabilities of reproductive traits are 0.2–0.4 and about 0.1, respectively (Smith 1984). Hence, $D = 8\sigma_{ra}$ may represent a typical value for D.

Results

Infinitesimal model

Table 2 shows the results for the infinitesimal model with a genetic correlation of -0.25 between production and reproduction. Random selection did not change mean genetic values because the infinitesimal model is additive, with no depression due to inbreeding. The assumptions underlying restricted index selection, i.e. linearity of regressions and thus multi-variate normal distributions, are satisfied under the infinitesimal model, hence both types of restricted index selection gave a response in reproduction that did not differ significantly from zero. With RIS and ERIS, production responses were approximately equal and 8–10% less than that for unrestricted selection. The culling of candidates for the reproduction index led to a larger reduction in production response and culling for phenotype for reproduction could not maintain reproduction.

Finite locus model without pleiotropic effects ($r_a=0$)

Table 3 shows the results with the finite locus model for reproduction, when the correlation between production and

Table 2 Genetic gains for production and reproduction traits (in initial additive genetic standard deviation units) after ten generations of selection^a (mean of 100 replicated simulations)^b. The infinitesimal genetic model was assumed for production and reproduction with a genetic correlation of -0.25

Selection	Production	Reproduction
Random selection	0.00	0.00
Unrestricted selection for production	7.30	-1.90
Restricted index selection	6.70	-0.06
Empirical restricted index selection	6.60	+0.06
20% culled on reproductive phenotype	6.80	-0.85
20% culled on reproductive index	6.10	+0.32

^a In the first generation, selection was at random for all alternatives

^b Typical standard errors are 0.07 and 0.06 for production and reproduction, respectively

Table 3 Genetic gains for production and reproduction traits (in initial additive genetic standard deviation units) after ten generations of selection^a (mean of 100 replicated simulations)^b. Inheritance of production followed the infinitesimal model and that of reproduction the finite locus model with an effective number of loci of $N_E=10$ and initial frequencies of deleterious recessive genes of $q=0.1$. The genetic correlation between production and reproduction was 0

Selection	Production	Reproduction
Random selection	0.00	-1.23
Unrestricted selection for production	7.32	-2.81
Restricted index selection	7.18	-2.31
Empirical restricted index selection	6.98	-0.13
20% culled on reproductive phenotype	6.82	-0.22
20% culled on reproductive index	6.86	+0.03

^a In the first generation, selection was at random for all alternatives

^b Typical standard errors are 0.12 and 0.10 for production and reproduction, respectively

reproduction is zero and the effective number of loci is 10. With random selection and with unrestricted selection for production, the genetic level of reproduction decreases due to random drift of allele frequencies at reproductive loci, i.e. due to inbreeding depression. The greater reduction of reproduction with unrestricted selection than with random selection is due to the higher rate of inbreeding with non-

Table 4 Genetic gains for production and reproduction traits (in initial additive genetic standard deviation units) after ten generations of selection^a (mean of 100 replicated simulations)^b. Inheritance model as in Table 3 except that loci for reproduction have additive pleiotropic effects on production such that the genetic correlation is -0.25

	Production		Reproduction
	Total	Infinitesimal component	
Random selection	0.06	0.06	-1.23
Unrestricted selection for production	7.44	6.78	-13.47
Restricted index selection	6.98	6.82	-3.67
Empirical restricted index selection	5.84	6.02	-0.13
10% culled on reproductive phenotype	7.14	6.80	-5.98
20% culled on reproductive phenotype	6.62	6.44	-3.57
10% culled on reproductive index	6.94	6.70	-4.68
20% culled on reproductive index	6.56	6.46	-2.21

^a In the first generation, selection was at random for all alternatives.

^b Typical standard errors are 0.06, 0.05 and 0.26 for total production, its infinitesimal component and reproduction, respectively.

random selection (Wray and Thompson 1990). The restricted selection index failed to prevent a decline in reproduction, which was probably due to non-additive gene effects. Empirical restricted selection gave almost a zero response for reproduction and only 5% less production response than unrestricted selection for production. Culling for reproductive performance virtually prevented the decline in reproduction and gave higher reproductive performances than the control line (random selection) at a cost of only a 6% decrease in rate of gain for production.

Finite locus model with additive pleiotropic effects ($r_a = -0.25$)

For the situation where the genes for reproduction have additive pleiotropic effects on production and the effective number of loci equals 10, the results are given in Table 4. When selection was only for production, the decrease for reproduction was much larger than with the absence of pleiotropic effects or than with the infinitesimal model (Tables 3 and 2, respectively). About 9% of the increase in production was due to changes in frequencies of the 100 simulated loci, which inevitably led to decreased reproduction. The restricted selection index gave a 9% reduction in genetic gain for production compared to unrestricted selection. There was no reduction in genetic gain for the infinitesimal component of production, which is desirable because gain in the infinitesimal component is not accompanied by loss of reproductive value.

The restricted selection index resulted in a reduction of reproductive performance by $3.67\sigma_{ra}$ over 10 generations (Table 4). Although still negative, this response in reproduction is 73% lower than that with unrestricted selection for production. With empirical restricted index selection, reduction in response for reproduction was minimal and less than that with random mating. Response for production, however, was 22% lower than that with unrestricted selection for production.

With 10% of the animals culled on reproductive performance, the gains in the infinitesimal component of produc-

tion, which is the gain that is desired, were approximately equal to that with restricted index selection. However, 10% culling resulted in a greater reduction of reproductive performance than restricted index selection. RIS is therefore preferred over 10% culling. With 20% of the animals culled on the reproductive index, the total production gain and its infinitesimal component was respectively 6% and 5% less than that with restricted index selection. IC20 could not maintain reproduction, but reproduction decreased less than with RIS.

Table 5 shows the results for different initial frequencies and different effective number of loci. As the effective number of loci decreases, effects of the largest genes increase and those of the smallest genes decrease. Results were qualitatively the same as those in Table 4. Restricted index selection reduced the decrease in reproduction substantially without reducing the gain in the infinitesimal component. Culling of 20% of the animals on the reproductive index reduced the infinitesimal gain for production and reduced the loss in reproduction even further. Empirical restricted index selection resulted in little decline in reproduction but also yielded the lowest responses for production.

Finite locus model with dominant pleiotropic effects ($r_a = -0.25$)

Table 6 shows the results when the reproduction loci show identical degrees of dominance in their effects on reproduction and production. Unrestricted selection for production was more effective at increasing frequencies of the positive alleles for production, i.e. the negative alleles for reproduction, than if their effects on production were additive (result not shown). Although a σ_{ra} unit is small because of the small heritability of reproduction, USP resulted in a large reduction in reproduction (45 and 30 σ_{ra} units for $N_E = 3$ and 10, respectively). In real populations, such a reduction in reproduction would probably cause extinction. Generally, effects of intense selection on production have less drastic effects on reproduction, which prob-

Table 5 Genetic gains for production and reproduction traits (in initial additive genetic standard deviation units) after ten generations of selection^a (mean of 100 replicated simulations)^b. Reproduction loci had additive pleiotropic effects on reproduction as in Table 4, but the effective number of loci N_E and initial frequencies of detrimental alleles q are varied here

	Production		Reproduction
	Total	Infinitesimal component	
	$q=0.1; N_E=3:$		
Random selection	0.00	0.00	-1.14
Unrestricted selection for production	7.52	6.70	-28.02
Restricted index selection	7.08	6.82	-5.31
Empirical restricted index selection	5.66	5.70	-0.38
20% culled on reproductive index	6.64	6.44	-3.45
	$q=0.2; N_E=10:$		
Random selection	0.02	0.02	-1.14
Unrestricted selection for phenotype	7.36	6.76	-9.30
Restricted index selection	6.88	6.68	-3.10
Empirical restricted index selection	5.78	5.96	-0.28
20% culled on reproductive index	6.54	6.46	-2.09

^a In the first generation, selection was at random for all alternatives

^b With $N_E=3$ and $q=0.1$, typical standard errors are 0.06, 0.06 and 0.53 for total production, its infinitesimal component and reproduction, respectively, and with $N_E=10$ and $q=0.2$, standard errors are 0.06, 0.06 and 0.16, respectively

Table 6 Genetic gains for production and reproduction traits (in initial additive genetic standard deviation units) after ten generations of selection^a (mean of 100 replicated simulations)^b with effective number of loci, N_E , of 3 or 10. Reproduction loci had dominant pleiotropic effects on production, such that the additive genetic correlation is -0.25

	Production		Reproduction
	Total	Infinitesimal component	
	$N_E=3:$		
Random selection	0.42	0.10	-1.26
Unrestricted selection for phenotype	16.00	4.66	-45.51
Restricted index selection	8.46	4.12	-17.36
Empirical restricted index selection	4.58	4.54	-0.16
10% culled on reproductive phenotype	10.62	5.74	-19.57
20% culled on reproductive phenotype	8.74	5.70	-12.02
10% culled on reproductive index	6.62	6.28	-1.39
20% culled on reproductive index	5.86	5.82	-0.16
	$N_E=10:$		
Random selection	0.28	-0.02	-1.26
Unrestricted selection for phenotype	12.46	4.86	-30.33
Restricted index selection	7.50	5.06	-9.74
Empirical restricted index selection	5.60	5.54	-0.18
10% culled on reproductive phenotype	10.44	5.54	-19.70
20% culled on reproductive phenotype	8.98	5.72	-12.93
10% culled on reproductive index	7.34	6.04	-5.22
20% culled on reproductive index	6.08	5.88	-0.76

^a In the first generation, selection was at random for all alternatives

^b With $N_E=3$, typical standard errors are 0.29, 0.13 and 1.22 for total production, its infinitesimal component and reproduction, and with $N_E=10$, standard errors are 0.14, 0.09 and 0.51

ably implies that the model with dominant pleiotropic effects is not very realistic. The large increases in frequencies of rare recessive alleles also resulted in a large increase in production due to the large gene effects a_{pi} and d_{pi} . The gene effects on production were large because the initial additive variances of the genes were assumed to be identical and, relative to the size of their gene effects, rare recessive genes contribute less additive variance than additive genes.

Because much of the genetic gain in production was due to the increase in frequency of detrimental alleles for reproduction, all selection methods that tried to prevent such an increase reduced the gain in production substantially (Table 6). The infinitesimal genetic component, however, generally increased. The culling of 20% of the animals for the reproductive index was remarkably effective at preventing a reduction in reproduction. As before, empirical restricted selection virtually prevented the decline in re-

production. But in situations with few major loci ($N_E=3$), culling 20% of the animals on the reproductive index also prevented the decline in reproduction and yielded 28% more response in production than with empirical restricted selection indices.

Discussion

The simulations investigated methods of preventing a decline in a fitness trait while selecting for increased performance. The fitness trait was assumed to be a measure of reproduction, though the results would apply to any fitness trait exhibiting parameters similar to those used here.

Comparison with experimental results

Gowe et al. (1993) report a selection experiment in laying hens. In the control lines, selection was at random. The selection lines were selected for production and approximately 10% of the birds were culled on the basis of fertility and hatchability. After 30 years of selection, levels of fertility and hatchability of the selected lines were not less than those in the control lines. Although their experimental conditions differed from the present simulations with the infinitesimal model, the model without pleiotropic effects and the dominant pleiotropic model yielded similar results.

Frankham et al. (1988) selected *Drosophila* for time to reach inebriation. Their experiment included unselected control lines and selected lines with and without culling 20% of the females on reproductive performance. After 25 generations, fitness was reduced in all lines, but was reduced most in the selected lines without culling on reproduction. The reduction in fitness in the control lines suggests that the infinitesimal genetic model is not appropriate. The control lines and selected lines with culling had a similar fitness. Inebriation times in selected lines with and without culling were similar and were about twice that of the control lines.

Results for the model without pleiotropic effects ($r_a=0$) were similar to those of Frankham et al. (1988). Frankham et al. (1988) reported no reduction in 'production' response, but it seems unlikely that the decrease of only 6% found here (Table 3) would have been found by their experiment. With additive pleiotropic effects ($r_a=-0.25$), 20% phenotypic culling reduced production response by 11% and reduced the negative reproduction response to 27% of that for lines with unrestricted selection for production (Table 4). The randomly selected line had 9% of the reduction in reproduction exhibited by unrestricted selection. Given the differences in definition of fitness traits, whether this differs significantly from the results of Frankham et al. (1988) is questionable (Frankham et al. measured a competitive index that may inflate small reductions in fitness and moderate reductions may result in almost equal competitive index values, though differences may be

substantial on a linear scale). However, with a dominant pleiotropic model, phenotypic culling and unrestricted selection gave a pattern of results very different from that observed by Frankham et al. (1988). In agreement with the results of Li (1993), it is concluded that maintaining levels of reproduction without substantially reducing progress in production can be achieved only with a model without pleiotropic effects of genes for reproduction.

Comparison of selection strategies

As summarized by Falconer (1989), experimental results indicate that genetic variation for reproduction traits is mainly due to deleterious recessive genes at low frequencies. Such a model may, for instance, explain why selection to increase reproduction usually yields a much lower response than selection to decrease reproduction. When such a model was adopted, restricted index selection could not prevent a reduction of the reproduction trait (Tables 3–6). There was no attempt here to adjust the index weights of RIS to compensate for the decline in fitness resulting from previous selection. Such compensation would have maintained fitness better, but at the expense of the selection response for production. The following simple example shows that such an adjusted RIS procedure differs from ERIS. Suppose selection is for one animal only, it is possible for RIS to choose an animal with $I_{ri} < 0$. Provided there are animals with $I_{ri} \geq 0$, an animal with $I_{ri} < 0$ would not be chosen by ERIS.

With the infinitesimal model, the model without the pleiotropic effects of reproduction loci, and the dominant pleiotropic model, the culling of selection candidates for a reproductive index maintained levels of reproduction. If $r_a=0$, a decline in fitness may also be prevented by adopting an effective population size such that the depression due to inbreeding is offset by natural selection (Meuwissen and Woolliams 1994).

The effect of culling on genetic gains is highly non-linear. For instance, culling 0%, 10% and 20% of the animals on the reproductive index gave reproduction responses of -13.47 , -4.68 and $-2.21 \sigma_{ra}$ units, respectively (Table 4). The effect of culling on responses is also model-dependent and, in practice, the optimum fraction to be culled has to be found empirically (e.g. by looking at the shape of the distribution of reproduction phenotypes or indices).

With dominant pleiotropic effects, the culling of 20% of the animals on reproduction was effective at limiting the decrease in reproduction to less than that in the control lines. The reason for the success of this method may become clear after examining Fig. 1. Index culling probably removed most of the animals with homozygous recessive genotypes (point W in Fig. 1). With the pleiotropic dominance model, the loci with the largest effects are close to being fully dominant, so that animals with performance close to point Y in Fig. 1 remain after index culling. Point Y includes animals with heterozygous and positive homozygous genotypes for reproduction. Because their performances for production are similar, subsequent selection for

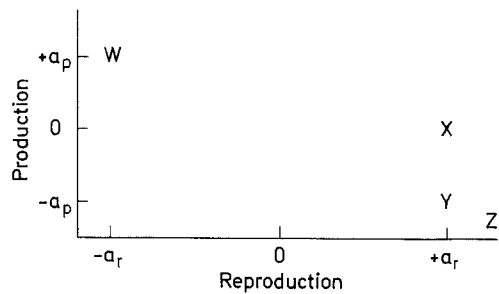


Fig. 1 Effects of (over) dominant reproductive genes with additive and (over) dominant pleiotropic effects on production. The average performances of the homozygotes are set to zero. *W* negative homozygote for reproduction, *X* heterozygote with additive pleiotropic effects on production, *Y* heterozygote with dominant pleiotropic effects on production and positive homozygote for reproduction, *Z* heterozygote with overdominance effects on production and reproduction

production will not favour any of these genotypes much and, thus, will not change gene frequencies much. Moreover, loci with the largest effects will exhibit slight overdominance (point *Z* in Fig. 1), and selection for production will avoid these heterozygotes, which will increase the frequency of the positive allele for reproduction. Phenotypic culling is probably less effective at removing recessive homozygotes for decreased reproduction (point *W* in Fig. 1), and subsequent selection for production will preferentially select the remaining homozygotes, which increases the frequency of the negative allele for reproduction. Thus, index culling is more effective than phenotypic culling at keeping the negative alleles for reproduction at low frequencies.

Even with an additive pleiotropic model, index culling will eliminate most of negative homozygous genotypes for reproduction (point *W* in Fig. 1). Subsequent selection for production, however, will then preferentially select heterozygous genotypes (point *X* in Fig. 1), which will increase the frequency of the negative allele for reproduction. Thus, culling will be less effective with the additive pleiotropic model.

Fitness traits such as survival, age at puberty and ovulation rate may be known before breeding. Juvenile predictors of fitness traits (from physiology or from DNA markers; Woolliams and Smith 1988) are also known before breeding. For many other traits information will not become available until after initial selection of breeding animals (e.g. litter size). This problem may be dealt with by selection of females after they are bred, which results in the selection or rejection of full-sibships of offspring. The situation becomes more complicated if full- and half-sib information is not available at the time of the selection of the sires, because a female may then be mated to a sire with too low a reproductive index. In such situations, culling could be based on matings instead of individual animals. Questions about optimum culling strategies arise. These and other complications that may arise when selecting for a reproduction trait will be examined in a subsequent paper.

ERIS uses all available information to estimate breeding values for production and fitness. Results indicate that this is more effective than a desired gains index in achieving the goal of maintaining fitness. This result is likely to hold even if desired gains index weights are modified every generation to allow for changes in mean fitness (see earlier discussion). The use of ERIS, or a desired gains index is, however, incompatible with the argument of Gibson and Kennedy (1990) that constrained indexes should not be used because they imply arbitrary economic values. Gibson and Kennedy (1990) did not consider the possibility of having to deal with non-additive variation and inbreeding depression. Also, in cases where estimates of economic values yield counter-intuitive selection responses, constrained indices are often used. Meanwhile, economic values should be more accurately evaluated or their counter-intuitive nature should be uncovered.

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