Inbreeding and its Impact on Design of Breeding Programs

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Inbreeding = mating of individuals that are related by ancestry

→ may carry alleles that are identical <u>by descent</u> (ibd) (vs. by state)

→ increases probability that progeny will by homozygous

Inbreeding coefficient = probability individual's pair of alleles at a locus are ibd

= coefficient of coancestry of parents

Coefficient of coancestry individuals *x* and *y*

= prob(a random allele from *x* (at a given locus) is ibd to a random allele from *y*)

Additive genetic relationship *x,y* = 2 x coefficient of coancestry between *x* and *y*

Effects of inbreeding → increased homozygosity

- Increased incidence of recessive disorders
- Inbreeding depression → reduced phenotypic performance
- Loss of genetic variance → reduction in rates of genetic improvement

Genotypic frequencies and mean performance in a population with inbreeding coefficient F for a single gene with 2 alleles with inbreeding coefficient F

$p=freq(A_1) \quad q=freq(A_2)$

Genotype	Frequency	Value	Frequency x value
A_1A_1	$p^2 \quad +pqF$	+a	$p^2a \quad +pqaF$
A_1A_2	$2pq -2pqF$	d	$2pqd -2pqdF$
A_2A_2	$q^2 \quad +pqF$	- a	$-q^2a \quad -pqaF$
		Sum = M_F	$= a(p-q)+2dpq-2dpqF$ $= a(p-q)+2dpq(1-F)$

Without inbreeding: mean = $M_0 = a(p-q)+2dpq$

Inbreeding depression = $M_0 – M_F = -2dpqF$

Summed over loci (no epistasis): $M_0 – M_F = -2F\Sigma dpq$

Impact of inbreeding on genetic variance:

Infinitesimal genetic model

No inbreeding: $\sigma^2_{g_{(t+1)}} = \frac{1}{4}(1-k_s r^2_{s_{(t)}})\sigma^2_{g_{(t)}} + \frac{1}{4}(1-k_d r^2_{d_{(t)}})\sigma^2_{g_{(t)}} + \frac{1}{2}\sigma^2_{g_{(o)}}$ $\sigma^2_{g_{(o)}}$ = base pop. var.

With inbreeding: Mendelian sampling variance = $(1-\bar{F}_{s(t)})\frac{1}{4}\sigma^2_{g_{(o)}} + (1-\bar{F}_{d(t)})\frac{1}{4}\sigma^2_{g_{(o)}}$

$= (1-\frac{1}{2}(\bar{F}_{s(t)} + \bar{F}_{d(t)}))\frac{1}{2}\sigma^2_{g_{(o)}}$

$$\sigma^2_{g_{(t+1)}} = \frac{1}{4}(1-k_s r^2_{s_{(t)}})\sigma^2_{g_{(t)}} + \frac{1}{4}(1-k_d r^2_{d_{(t)}})\sigma^2_{g_{(t)}} + (1-\frac{1}{2}(\bar{F}_{s(t)} + \bar{F}_{d(t)}))\frac{1}{2}\sigma^2_{g_{(o)}}$$

Only Mendelian sampling variance is affected by inbreeding, depending on inbreeding coefficient of parents, rather than inbreeding of the progeny

PREDICTION OF RATES OF INBREEDING

$$\Delta F = \frac{F_{t+1} - F_t}{1 - F_t} = \frac{1}{2N_e}$$

N_e = Effective population size = number of individuals that would give rise to a rate of inbreeding ΔF if bred as an idealized population

Idealized population
- **Random mating, including selfing**
- **No selection**
- **Discrete (non-overlapping) generations**
- **Random distribution of family size – each individual has equal probability of contributing progeny**

Factors affecting rate of inbreeding in a closed non-idealized population

In a population that is not under selection:

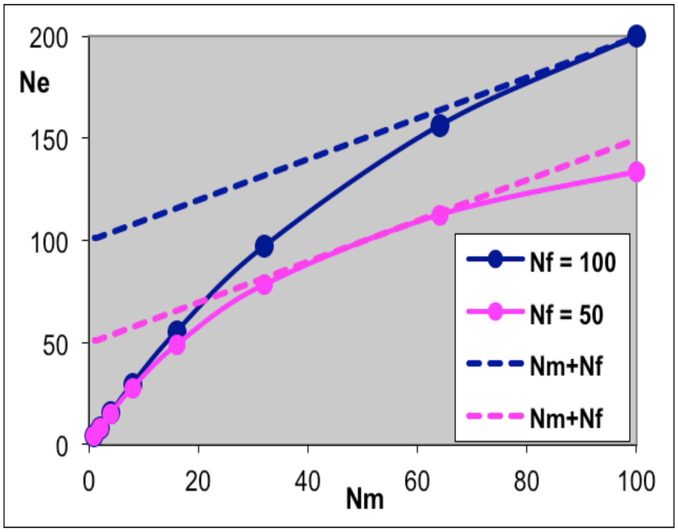
- **# males (N_m) and females (N_f) used for breeding** ←→ population size
  ←→ selection intensity

$$\frac{1}{N_e} = \frac{1}{4N_m} + \frac{1}{4N_f}$$

$$\Delta F = \frac{1}{8N_m} + \frac{1}{8N_f}$$

→ N_e is less than the # parents; $\leq N_m + N_f$

→ N_e is driven primarily by the smaller of N_m and N_f



- **Variance of family size** ←→ unequal use of parents (and their progeny)
  - family size = number of progeny that become breeding parents

(Hill, 1979 Genetics 92:317)

$$N_e \approx \frac{8N}{V_{km} + V_{kf} + 4} \quad ➔ \quad \Delta F = \frac{1}{2N_e} = \frac{V_{km} + V_{kf} + 4}{16N}$$

N = Total population size (½N males, ½N females)

V_{km} = Var(# progeny per male)

V_{kf} = Var(# progeny per female)

V_{km} and V_{kf} affected by unequal use of individuals for breeding

- **selection**
- **differential use of selected individuals**

Mean family size = 2 (each parent → 2 progeny to maintain population size)

Idealized population: distribution of family size = Binomial ≈ Poisson

$$\rightarrow V_{km} = V_{kf} = \text{ mean family size} = 2 \quad ➔ \quad N_e = \frac{8N}{2+2+4} = N$$

Variance of family size can be reduced (by the breeder) by ensuring that all selected parents equally contribute breeders for the next generation

- within family selection – select best male and best female from each fullsib family ➔ $V_k = 0$ ➔ $N_e \approx 2N$

- **Generation Interval** ←→ shorter → greater rate of inbreeding per year

$$N_e \approx \frac{8N_cL}{V_{km} + V_{kf} + 4} \quad ➔ \quad \Delta F/yr = \frac{1}{2N_e}/L = \frac{V_{km} + V_{kf} + 4}{16N_cL^2}$$

N_c = total # progeny per year
L = average generation interval (across males and females)

Selection increases inbreeding through: (Verrier et al. 1990)

- **Probability of co-selection of relatives** ←→ correlation of the selection criterion between relatives
- **Inheritance of selective advantage** – progeny of good parents are more likely to be selected themselves, as are their descendants ➔ increased variance of family size

More accurate methods to predict rates of inbreeding in populations under selection

In part based on notes from Bijma and van Arendonk

See Wray and Thompson (1990 Genet. Res. 55:41), Verrier et al. (1990)

Previous methods are ‘single generation’ methods

- account for differential contributions of ancestors to future generations through differential numbers of progeny that become breeding parents
- do not account for additional differences in an ancestral contributions through differential numbers of grand progeny that become breeding parents

Theory of long-term genetic contributions

Wray and Thompson 1990. Genet. Res. 55:41 Woolliams et al. 1999 Genetics 153:1009
Woolliams and Bijma 2000 Genetics 154:1851 Bijma and Woolliams 2000 Genetics 156:361
Bijma et al. 2000 Genetics 156:361

$r_{i,t_1}(j,t_2)$ = Genetic contribution of ancestor i born at generation t_1 to an individual j born at generation t_2 ($t_2 > t_1$)
= proportion of genes of j expected to derive by descent from ancestor i.

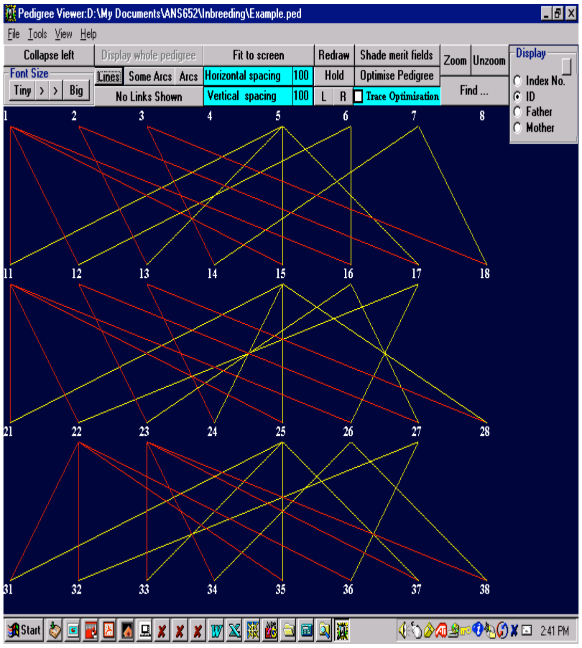
Note: Full-sibs share ½ of their genes but make no genetic contribution to each other.

$r_{i,t_1}(t_2)$ = Mean genetic contribution of ancestor i born at generation t_1 to generation t_2
= the average proportion of genes among individuals in generation t_2 that are expected to derive by descent from ancestor i

- $E(r_{i,t_1}(t_2)) = \frac{\mathbf{1}}{\mathbf{2N}_m}$ for male ancestors (N_m = # male ancestors)
  $= \frac{\mathbf{1}}{\mathbf{2N}_f}$ for female ancestors
- $r_{i,t_1}(t_2)$ differ between ancestors due to differences in use as parents and differences in selective advantage
- $\sum_i r_{i,t_1}(t_2) = 1$
- as t_2- t_1 increases, contributions from a given ancestor stabilize and become similar across individuals from generation t_2 $\underset{j}{\mathrm{Var}}(r_{i,t_1}(j,t_2)) \rightarrow 0$
- t_2- t_1→ infinity, genetic contributions from a given ancestor are the same for all individuals in time t_2 = **long-term genetic contribution** of ancestor i = r_i

Table 1: Pedigree to illustrate concept of genetic contributions in which each generation contains 4 males and 4 females.
The base population contains 8 individuals
(1-4: males and 5-8: females).

	Generation 1			Generation 2			Generation 3		
Sex	Ind	sire	dam	Ind	Sire	dam	Ind	sire	dam
Male	11	1	5	21	11	15	31	22	25
	12	1	6	22	11	17	32	22	27
	13	2	5	23	12	16	33	23	25
	14	3	7	24	13	15	34	23	26
Female	15	1	5	25	11	15	35	22	25
	16	1	6	26	11	17	36	22	27
	17	2	5	27	12	16	37	23	25
	18	3	7	28	13	15	38	23	26


Pedigree Viewer:D:\My Documents\ANS652\Inbreeding\Example.ped

Horizontal spacing 100

Vertical spacing 100

Display: ◉ ID

Contribution of ancestors to offspring ($r_{i,t_1}(j,t_2)$) and mean genetic contributions of each ancestor ($r_{i,t_1}(t_2)$).

	Ancestors							
***Offspring*[1]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
					Generation 1			
11/15	**0.5**	**0**	**0**	**0**	**0.5**	**0**	**0**	**0**
12/16	**0.5**	**0**	**0**	**0**	**0**	**0.5**	**0**	**0**
13/17	**0**	**0.5**	**0**	**0**	**0.5**	**0**	**0**	**0**
14/18	**0**	**0**	**0.5**	**0**	**0**	**0**	**0.5**	**0**
Mean contribution	***0.25***	***0.125***	***0.125***	***0***	***0.25***	***0.125***	***0.125***	***0***
					Generation 2			
21/25	**0.5**	**0**	**0**	**0**	**0.5**	**0**	**0**	**0**
22/26	**0.25**	**0.25**	**0**	**0**	**0.5**	**0**	**0**	**0**
23/27	**0.5**	**0**	**0**	**0**	**0**	**0.5**	**0**	**0**
24.28	**0.25**	**0.25**	**0**	**0**	**0.5**	**0**	**0**	**0**
Mean contribution	***0.375***	***0.125***	***0***	***0***	***0.375***	***0.125***	***0***	***0***
					Generation 3			
31/35	**0.375**	**0.125**	**0**	**0**	**0.5**	**0**	**0**	**0**
32/36	**0.375**	**0.125**	**0**	**0**	**0.25**	**0.25**	**0**	**0**
33/37	**0.5**	**0**	**0**	**0**	**0.25**	**0.25**	**0**	**0**
34/38	**0.375**	**0.125**	**0**	**0**	**0.25**	**0.25**	**0**	**0**
Mean contribution	***0.406***	***0.104***	***0***	***0***	***0.313***	***0.187***	***0***	***0***

[1] Each generation consisted of a full sib male and female, which have equal contributions

- **Use of long-term genetic contribution theory**

Asymptotic response to selection = sum of true breeding values weighted by long-term genetic contributions

$$\Delta G = \Sigma r_i g_i - \Sigma \frac{1}{N} g_i$$ = long-term impact of a single round of selection

- depends not only on selection in the initial generation but also on dissemination of genes from the selected parents in subsequent generations.

Rates of inbreeding are related to variation in long-term contributions between ancestors

- Asymptotic ΔF = ¼ * sum of squares of long-term contributions

$$\mathbf{\Delta F = \frac{1}{4} \Sigma r_i^2}$$

Example: 20 selected parents per generation (ignoring that there are two sexes).
Pedigree analysis quantifies the contribution of each parent to a particular generation.
Their contribution will sum to 1; genetic contributions always sum to 1 per generation.

Consider two extreme cases:

1) the contribution of each individual is the same, $r = 0.05$ for all individuals
   $\Delta F = \frac{1}{4}(0.05^2 + 0.05^2 + .. \; 0.05^2) = 0.0125 = 1.25\%$ per generation

2) contributions differ extremely between individuals:
   $r = 0.25$ for the 4 best parents $r = 0$ for the rest
   $\Delta F = \frac{1}{4}(0.25^2 + 0.25^2 + .. \; 0^2) = 0.0625 = 6.25\%$ per generation.

   ➔ variance in the contributions of ancestors causes higher inbreeding.

Example: If there were 2 male and 2 female ancestors in a generation with contributions 3/8, 1/8, 5/16 and 3/16 (note the 2 males sum to ½ and the two females sum to ½) then the estimate of ΔF attributed to that generation is

$$\Delta F = \frac{1}{4}\left\{\left(\frac{3}{8}\right)^2 + \left(\frac{1}{8}\right)^2 + \left(\frac{3}{16}\right)^2 \left(\frac{6}{16}\right)^2\right\} = 0.072$$

If the population were in a steady state we would expect approximately the same answer every generation and the average over generations would be the expected ΔF.

The importance of relationship $\Delta F = \frac{1}{4}\Sigma r_i^2$ is:

- It is general and applies to both selected and unselected populations.
- It relates ΔF to terms that can be found in the relationship (A) matrix.
- Predictive forms can be developed from the relationship.
- Strictly it is an approximation, but the proportional error (an underestimate) is of the same order as those previously developed for unselected populations.
- Its form will lead to insights into how optimal selection schemes work.

HOW TO USE THESE RELATIONSHIPS TO PREDICT RATES OF INBREEDING FOR A SPECIFIED BREEDING PROGRAM

Woolliams (1998): ΔF is related to squared *expected* long-term genetic contributions, making prediction of the variance of long term genetic contributions redundant.

Following Woolliams et al. (1998), the (long-term) genetic contribution of an ancestor can be predicted by regression on its breeding value, using the model:

$$E(r_i \mid g_i) = r_i = \alpha + \beta g_i$$

r_i = the expected genetic contribution of ancestor *i*

α = the expected genetic contribution for an average ancestor

ß = the regression coefficient of the genetic contribution on the breeding value (g_i) of the ancestor.

For discrete generations: α is determined by the number of parents.

For male ancestors, $\alpha = ½N_s$

For female ancestors $\alpha = ½N_d$

ß describes that selective advantage influences the selection decisions in the offspring generation but also that the selective advantage is inherited, i.e. it has an influence beyond the offspring generation.

The two mechanisms need to be described to enable the predictions:

1) better parents have on average more offspring that are selected as parents.
2) the selected offspring of better parents are on average better which also affect the genetic contributions.

In short, the procedure is as follows.

First, a regression model is used to predict the long-term contribution,

$$E(r) = \alpha + \beta(g - \bar{g})$$

E(r) = expected contribution given the true BV of an individual

α = the contribution of an individual with an average BV

β = increase of the contribution of parents with a higher BV.

Second term accounts for parents with high BV having more selected offspring.

Both α and β can be derived mathematically, but that is beyond the scope of this text.

The next step is to calculate the square of the expected contributions:

$$E(r)^2 = \alpha^2 + \beta^2 \sigma_A^2 (1 - k\rho^2)$$

The second term = genetic variance of the selected parents

So far we have calculated $E(r)^2$, but in fact we need to calculate $E(r^2)$.

$E(r)^2$ = the square of the expected contributions
$E(r^2)$ = the expectation of the squared (actual) contribution.

Under certain conditions $E(r^2) = 2E(r)^2$, leading to the result that the rate of inbreeding is

$$\Delta F = \tfrac{1}{2} N\mathrm{E}(\mathrm{r})^2$$

where N is the number of parents and $E(r)^2$ is the square of the expected contributions.

Note that the ¼ is replaced by ½ because we have replaced the square of the actual contributions Σr^2 by the square of the expected contributions, $N\mathrm{E}(r)^2$.

The above theory shows that selection strategies that increase the variance of contributions among parents lead to higher ΔF.

Selection strategies that rely heavily on family information are an example. If EBVs are largely based on family info, truncation selection on EBV → between family selection.

In that case parents of successful families will have a large contribution, whereas parents of non-successful families will have no contribution at all, which increases ΔF.

The expected long-term genetic contribution for a selected parent can be derived as a function of terms that are related to the Mendelian sampling component of the individual.

For mass selection and sib indices it is sufficient to consider only the genetic merit as a whole, but for selection methods utilizing BLUP the terms should include both the EBV and the prediction error (Woolliams, 1998). This has been implemented in SelAction.

For more complex breeding programs, the expected ΔF under random mating of selected animals can also be related to the sum of squared expected genetic contributions:

$$E(\Delta F) = \tfrac{1}{2}\sum_k X_k E\left(r_{i,k}^2\right)$$

where Σ_k = summation over all possible categories (e.g. sexes), X_k = # parents in the k^{th} category; $r_{i,k}$ = expected genetic contribution of the i^{th} selected individual in category k.

The expectation must include all the variables conferring selective advantage, such as the BV of mates. It has been shown that the expectation is tractable.

In the simplest case of random selection, the $r_{i,k}$ are simply $(2\mathrm{N}_s)^{-1}$ and $(2\mathrm{N}_d)^{-1}$ and the derivations lead to Wright's formula.

The genetic contributions can also be used to predict the rate of genetic gain (Woolliams, 1998),

$$E(\Delta G) = \sum_k X_k E\left(r_k g_k\right)$$

Woolliams et al. (1998) extended the method to situations with overlapping generations. When rates of inbreeding in selected populations can be predicted, predictions of long term response under the infinitesimal model become tractable.

Design of breeding programs with controls on inbreeding

Short-term response maximized by ($\Delta G = i\ r\ \sigma_g$) :

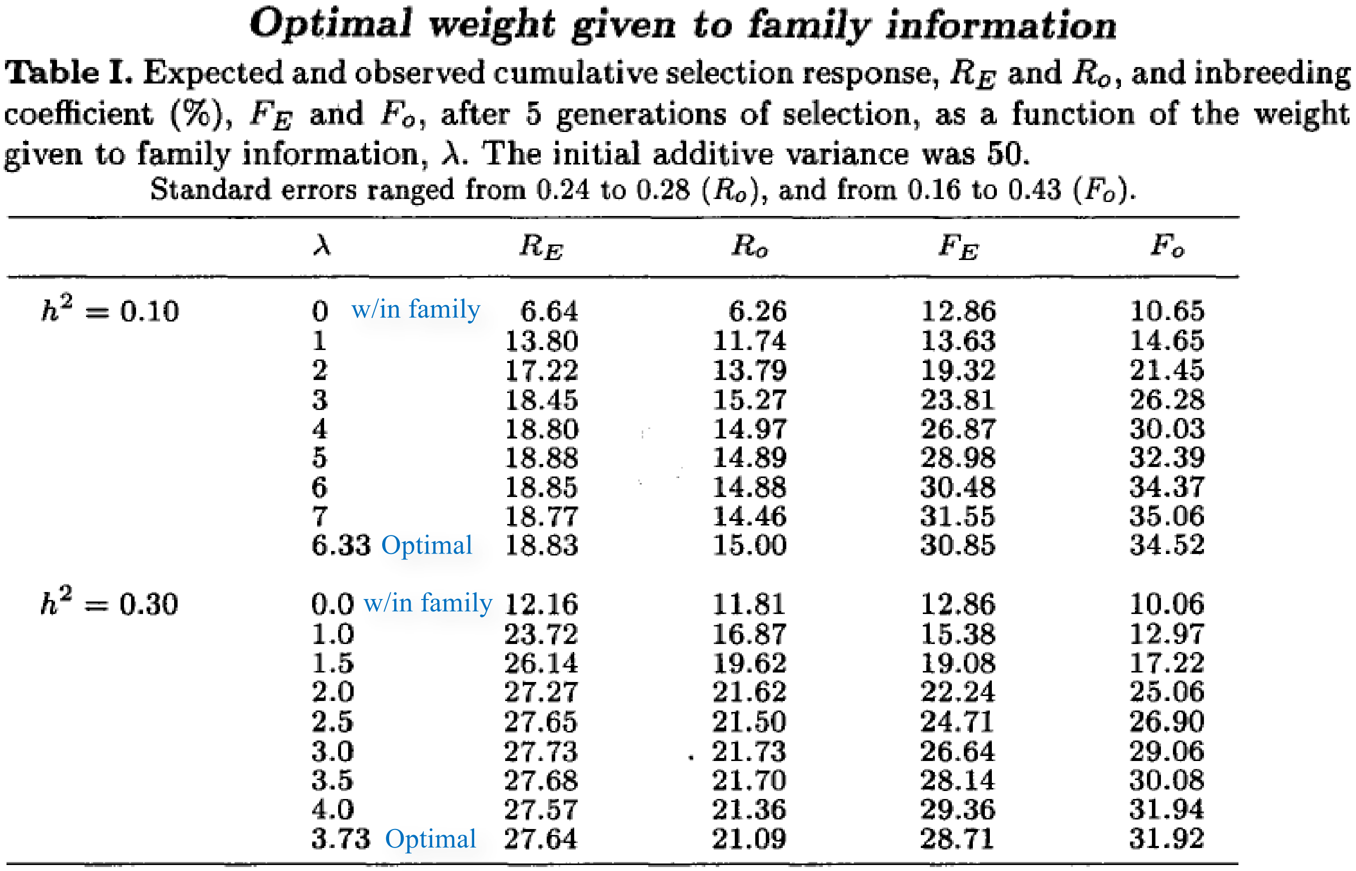
- select on BLUP EBV → maximum r
- select only the best individuals – maximize *i* - subject to reproduction rate constraints

But this may not maximize long(er)-term response because of higher ΔF.

Strategies to control inbreeding

- (Mate selected parents such that inbreeding of progeny is minimized)
  - has limited effect on long-term rates of inbreeding
- Select more animals
  - increase population size → increased costs
  - reduce selection intensity →reduced (short-term) response
- Reduce probability of co-selection of relatives
  - impose restrictions on selection of relatives (e.g. 1/full-sib family)
  - increase h^2 in genetic evaluation (affects both pedigree and progeny info)
    - decrease weight on pedigree information
    - control the average relationship among selected parents
      - cost factor on average relationship (Brisbane and Gibson 1994)
      - constraint on average relationship (Meuwissen 1997, JAS 75:934)
- Introduce outside genetics

Toro & Perez-Enciso 1990, GSE:



Optimal weight given to family information

Table I. Expected and observed cumulative selection response, R_E and R_o, and inbreeding coefficient (%), F_E and F_o, after 5 generations of selection, as a function of the weight given to family information, λ. The initial additive variance was 50. Standard errors ranged from 0.24 to 0.28 (R_o), and from 0.16 to 0.43 (F_o).

	λ	R_E	R_o	F_E	F_o
$h^2 = 0.10$	0 w/in family	6.64	6.26	12.86	10.65
	1	13.80	11.74	13.63	14.65
	2	17.22	13.79	19.32	21.45
	3	18.45	15.27	23.81	26.28
	4	18.80	14.97	26.87	30.03
	5	18.88	14.89	28.98	32.39
	6	18.85	14.88	30.48	34.37
	7	18.77	14.46	31.55	35.06
	6.33 Optimal	18.83	15.00	30.85	34.52
$h^2 = 0.30$	0.0 w/in family	12.16	11.81	12.86	10.06
	1.0	23.72	16.87	15.38	12.97
	1.5	26.14	19.62	19.08	17.22
	2.0	27.27	21.62	22.24	25.06
	2.5	27.65	21.50	24.71	26.90
	3.0	27.73	21.73	26.64	29.06
	3.5	27.68	21.70	28.14	30.08
	4.0	27.57	21.36	29.36	31.94
	3.73 Optimal	27.64	21.09	28.71	31.92

Restriction on the distribution of family size

Table II. Expected and observed cumulative selection response, R_E and R_o, and inbreeding coefficient (%), F_E and F_o, after 5 generations of selection, as a function of family size. The initial additive variance was 50, $h^2 = 0.10$.

Standard errors ranged from 0.21 to 0.32 (R_o), and from 0.16 to 0.43 (F_o).

Case	*Distribution of family size*	R_E	R_o	F_E	F_o
1	4 4 0 0 0 0 0 0	17.42	12.77	42.76	41.40
2	4 3 1 0 0 0 0 0	18.17	13.94	35.81	35.88
3	4 2 2 0 0 0 0 0	17.87	13.85	33.26	33.88
4	4 2 1 1 0 0 0 0	17.78	14.85	30.59	31.94
5	3 3 2 0 0 0 0 0	17.30	13.72	30.59	31.17
6	3 3 1 1 0 0 0 0	17.21	14.34	27.80	28.60
7	4 1 1 1 1 0 0 0	16.38	13.48	27.80	28.62
8	3 2 2 1 0 0 0 0	16.91	14.99	24.87	26.56
9	3 2 1 1 1 0 0 0	16.24	14.32	21.79	24.06
10	2 2 2 2 0 0 0 0	14.91	12.66	21.79	22.89
11	2 2 2 1 1 0 0 0	14.85	13.18	18.57	20.24
12	3 1 1 1 1 1 0 0	14.23	12.78	18.57	20.17
13	2 2 1 1 1 1 0 0	13.56	12.22	15.20	16.81
14	2 1 1 1 1 1 1 0	10.83	9.65	11.66	13.27
15	1 1 1 1 1 1 1 1	5.90	5.54	7.96	9.18
Opt.		18.83	15.00	30.85	34.52

Table III. Expected and observed cumulative selection response, R_E and R_o, and inbreeding coefficient (%), F_E and F_o, after 5 generations of selection, as a function of family size. The initial additive variance was 50, $h^2 = 0.30$.

Standard errors ranged from 0.17 to 0.27 (R_o), and from 0.16 to 0.43 (F_o).

Case	R_E	R_o	F_E	F_o
1	24.48	18.85	42.76	40.61
2	26.17	20.17	35.81	35.06
3	25.93	20.77	33.26	32.75
4	26.03	20.38	30.59	31.77
5	25.35	20.53	30.59	30.79
6	25.45	20.84	27.80	28.48
7	24.29	19.95	27.80	29.31
8	25.21	20.42	24.87	26.26
9	24.49	20.66	21.79	24.19
10	22.27	18.86	21.79	21.74
11	22.71	19.21	18.57	20.15
12	21.89	18.86	18.57	20.47
13	21.13	19.08	15.20	17.89
14	17.51	16.28	11.66	13.44
15	10.81	10.56	7.96	9.23
Opt.	27.64	21.09	28.71	31.92

Minimum coancestry matings

The observed genetic progress attained during the first 5 generations of selection, both with random, R_R, and minimum coancestry matings, R_{MC}, together with the corresponding inbreeding coefficients, F_R and F_{MC}, are shown in Table IV (λ_{op} was used). The selection response obtained was similar in both cases, as expected in a strictly additive model. However, minimum coancestry matings dramatically reduced inbreeding, compared with random mating. Nevertheless, it should be noted that this reduction was mainly due the one generation delay in the initial appearance of consanguinity.

Table IV. Observed cumulative selection response after 5 generations of selection with random mating, R_R, minimum coancestry mating, R_{MC}, and mate selection, R_{MS}, together with their respective inbreeding coefficient (%) F_R, F_{MC} and F_{MS}. The initial additive variance was 50.

Generation	R_R	R_{MC}	R_{MS}	F_R	F_{MC}	F_{MS}
$h^2 = 0.10$						
1	3.71	3.86	2.76	8.49	0.00	3.01
2	6.58	6.53	5.74	15.89	8.54	7.87
3	9.48	9.08	8.53	22.54	14.10	13.56
4	12.27	11.98	11.64	28.88	19.08	18.73
5	15.00	14.10	14.45	34.52	24.08	23.77
$h^2 = 0.30$						
1	5.26	5.65	4.96	7.87	0.00	3.03
2	9.54	9.64	9.90	14.44	7.21	8.00
3	14.51	16.68	14.38	21.01	12.48	13.19
4	17.43	17.79	18.49	26.43	17.03	17.81
5	21.09	21.34	22.31	31.92	21.78	22.92

Standard errors in the fifth generation ranged from 0.23 to 0.28 (R_R and R_{MC}), 0.80 (R_{MS}) and 0.40 (F_R, F_{MC} and F_{MS}).

Mates selection

Table IV shows the observed response, R_{MS}, and the inbreeding coefficient, F_{MS}. It can be seen that, while conforming with inbreeding restrictions, response was not smaller than that attained under the optimum unrestricted scheme, R_R.

Quinton, Smith, Goddard. 1992. Comparison of selection methods at the same level of inbreeding. J. Anim. Sci. 70: 1060.

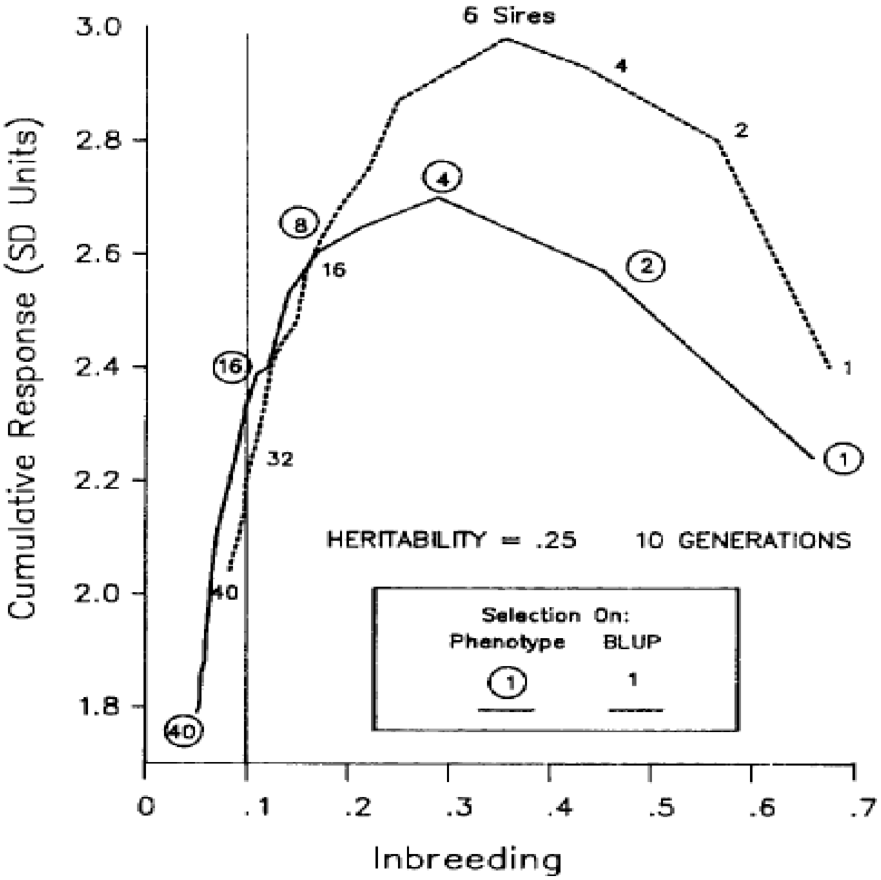


Figure 1. The average (100 replicates) simulated cumulative genetic response and inbreeding after 10 generations of phenotypic and best linear unbiased prediction (BLUP) selection for a range (1 to 40) in the number (S) of sires selected (heritability .25, S/100 males selected, 50/100 females selected). Numerical results are given in Table 2.

ABSTRACT: Animal geneticists predict higher genetic responses to selection by increasing the accuracy of selection using BLUP with information on relatives. Comparison of different selection methods is usually made with the same total number tested and with the same number of parents and mating structure so as to give some acceptable (low) level of inbreeding. Use of family information by BLUP results in the individuals selected being more closely related, and the levels of inbreeding are increased, thereby breaking the original restriction on inbreeding. An alternative is to compare methods at the same level of inbreeding. This would allow more intense selection (fewer males selected) with the less accurate methods. Stochastic simulation shows that, at the same level of inbreeding, differences between the methods are much smaller than if inbreeding is unrestricted. If low to moderate inbreeding levels are targeted, as in a closed line of limited size, then selection on phenotype can yield higher genetic responses than selection on BLUP. Extra responses by BLUP are at the expense of extra inbreeding. The results derived here show that selection on BLUP of breeding values may not be optimal in all cases. Thus, current theory and teaching on selection methods are queried. Revision of the methodology and a reappraisal of the optimization results of selection theory are required.

Villaneuva and Woolliams (1997). Optimization of breeding programmes under index selection and constrained inbreeding. Genet. Res. Camb. 69:145

Objective = maximize response (over planning horizon) with constraint on ΔF

Parameters to optimize:

- Population size
- # sires and dams to select
- Selection criterion to use (emphasis on family info)
- Mating strategy

Population size = 200

Maximize average response from 5 - 20 generations by optimizing

- # sires selected
- # dams/sire
- weight on family vs. own performance

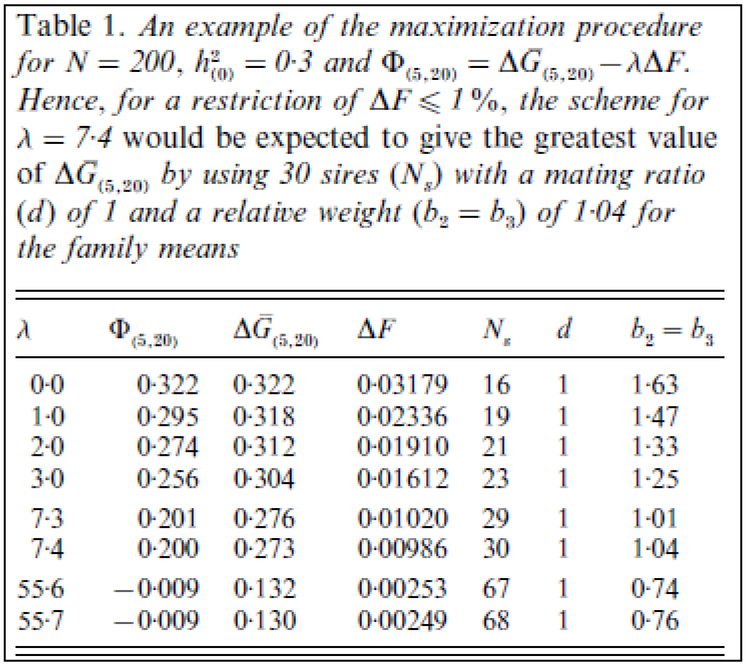


Table 1. *An example of the maximization procedure for* $N = 200$, $h^2_{(0)} = 0{\cdot}3$ *and* $\Phi_{(5,20)} = \Delta \bar{G}_{(5,20)} - \lambda \Delta F$. *Hence, for a restriction of* $\Delta F \leqslant 1\%$, *the scheme for* $\lambda = 7{\cdot}4$ would be expected to give the greatest value of $\Delta \bar{G}_{(5,20)}$ *by using 30 sires* (N_s) *with a mating ratio* (d) *of 1 and a relative weight* ($b_2 = b_3$) *of 1·04 for the family means*

λ	$\Phi_{(5,20)}$	$\Delta \bar{G}_{(5,20)}$	ΔF	N_s	d	$b_2 = b_3$
0·0	0·322	0·322	0·03179	16	1	1·63
1·0	0·295	0·318	0·02336	19	1	1·47
2·0	0·274	0·312	0·01910	21	1	1·33
3·0	0·256	0·304	0·01612	23	1	1·25
7·3	0·201	0·276	0·01020	29	1	1·01
7·4	0·200	0·273	0·00986	30	1	1·04
55·6	−0·009	0·132	0·00253	67	1	0·74
55·7	−0·009	0·130	0·00249	68	1	0·76

	h^2=0.1			**h^2=0.3**		
	Constraint on Inbreeding			**Constraint on Inbreeding**		
	None	**$\Delta F \leq 1\%$**	**$\Delta F \leq 0.25\%$**	**None**	**$\Delta F \leq 1\%$**	**$\Delta F \leq 0.25\%$**
ΔF/generation	**2.09**	**1.00**	**0.25**	**2.00**	**1.00**	**0.25**
ΔG in generation 20	**0.109**	**0.100**	**0.047**	**0.278**	**0.258**	**0.128**
# sires	**22**	**32**	**69**	**21**	**30**	**68**
# dams/sire	**1**	**1**	**1**	**1**	**1**	**1**
Relative weight on family info	**2.12**	**1.60**	**1.07**	**1.43**	**1.06**	**0.76**
Optimal weight based on sel. index	**9.6**					

Optimal Contribution Selection

Selection while Controlling Inbreeding in Operational Programs

Based on Meuwissen (1997). J. Anim. Sci. 75: 934.

Meuwissen (1997) developed a method to directly control long-term rates of inbreeding while maximizing response to selection by formulating selection as a constrained maximization program:

Max $\bar{g}_{t+1} = \mathbf{c}_t^{'}\hat{\mathbf{g}}_t$ Subject to $\mathbf{Q}'\mathbf{c}_t = \frac{\mathbf{1}}{\mathbf{2}}$

$\frac{1}{2}\mathbf{c}_t^{'}\mathbf{A}_t\mathbf{c}_t = \bar{C}_{t+1}$

$\bar{g}_{t+1}$ = mean BV in the next generation

$\hat{\mathbf{g}}_t$ = the vector of BLUP EBV of candidates for selection in generation *t*

$\mathbf{c}_t$ = a vector of contributions of selection candidates to the next generation

$\mathbf{Q}$ = a known incidence matrix for sex (the first column contains one for male candidates and the second column one for female candidates)

$\frac{\mathbf{1}}{\mathbf{2}} = \begin{bmatrix} 1/2 \\ 1/2 \end{bmatrix}$ and ensures that contributions of males and of all females sum to ½.

$\mathbf{A}_t$ = additive genetic relationship among selection candidates in generation *t*.

$\bar{C}_{t+1}$ = average coancestry among all progeny in generation *t*+1

= ½ weighted average genetic relationship among selected parents = $\frac{1}{2}\mathbf{c}_t^{'}\mathbf{A}_t\mathbf{c}_t$.

= set equal to ΔF(*t*+1) when objective is to restrict rate of inbreeding per generation to ΔF and generation 0 is non-inbred

⇨ Maximize $H_t = \mathbf{c}_\mathbf{t}^{'}\hat{g}_t - \lambda_0\left(\mathbf{c}_\mathbf{t}^{'}\mathbf{A}_\mathbf{t}\mathbf{c}_\mathbf{t} - 2\overline{\mathbf{C}}_{\mathbf{t+1}}\right) - \left(\mathbf{c}_\mathbf{t}^{'}\mathbf{Q} - \frac{1}{2}^{'}\right)\lambda_v$ for $\mathbf{c}_t$, λ_0, and λ

λ_0, and λ are LaGrangian multipliers, and $\boldsymbol{\lambda}_\mathbf{v}' = [\lambda_0, \lambda]$.

Solving this system for $\mathbf{c}_t$ results in: $\mathbf{c}_\mathbf{t} = \frac{\mathbf{A}_\mathbf{t}^{-1}\left(\hat{g}_\mathbf{t} - \mathbf{Q}\lambda_v\right)}{2\lambda_0}$

In order to obtain $\mathbf{c}_t$, values for λ_0 and λ are needed.

Constraint $\mathbf{Q}'\mathbf{c}_t = \frac{1}{2}$ → $\mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\mathbf{Q}\lambda_v = \mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\hat{g}_\mathbf{t} - \mathbf{1}\lambda_\mathbf{0}$

Constraint $\mathbf{c}_t'\mathbf{A}_t\mathbf{c}_t/2 = \bar{C}_{t+1}$ → $8\bar{C}_{t+1}\lambda_0^2 = \mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\hat{g}_\mathbf{t} - \mathbf{1}\lambda_0$

Solving for λ_0 → $\lambda_0^2 = \frac{\hat{g}_\mathbf{t}^{'}\left(\mathbf{A}_\mathbf{t}^{-1} - \mathbf{A}_\mathbf{t}^{-1}\mathbf{Q}\left(\mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\mathbf{Q}\right)^{-1}\mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\right)\hat{g}_\mathbf{t}}{8\bar{C}_{t+1} - \mathbf{1}'\left(\mathbf{Q}'\mathbf{A}_\mathbf{t}^{-1}\mathbf{Q}\right)^{-1}\mathbf{1}}$

The value for λ_0 is used in the previous equation to obtain the value for λ. These two values can now be used to obtain $\mathbf{c}_t$. This $\mathbf{c}_t$ may contain negative values for some animals with a poor EBV. Negative values of $\mathbf{c}_t$ can be constrained to zero by eliminating those animals.

A negative right hand sight for the last equation implies that $\mathbf{c}_t'\mathbf{A}_t\mathbf{c}_t/2 = \bar{C}_{t+1}$ cannot be met. So it is impossible to find a solution for $\mathbf{c}_t$ for which the average coancestry between parents is less or equal to the desired level. The minimum average relationship that can be obtained by minimizing $\mathbf{c}_t'\mathbf{A}_t\mathbf{c}_t$ under the constraint $\mathbf{Q}'\mathbf{c}_t = \frac{1}{2}$. This leads to the following minimum: $.25\mathbf{1}'(\mathbf{Q}'\mathbf{A}_t^{-1}\mathbf{Q})^{-1}\mathbf{1}$.

Table 1. The average coancestry of the parents of generation t, the inbreeding in generation t, and the genetic gain from generation t − 1 to t, when the average coancestry was limited to .025 (t − 1) and genetic contributions were optimized within each generation for both sexes[a]

Generation (t)	Coancestry parents	Inbreeding	Genetic gain
2	.025	0	.380
3	.050	.029	.322
4	.075	.052	.293
5	.100	.076	.318
6	.125	.100	.287
7	.150	.127	.303
8	.175	.150	.301
9	.200	.175	.311
10	.225	.202	.315

[a] Average of 100 replicated simulations of the breeding scheme. The standard errors of the inbreeding and genetic gain were approximately .0011 and .011, respectively. The coancestry did not vary, because it was constrained.

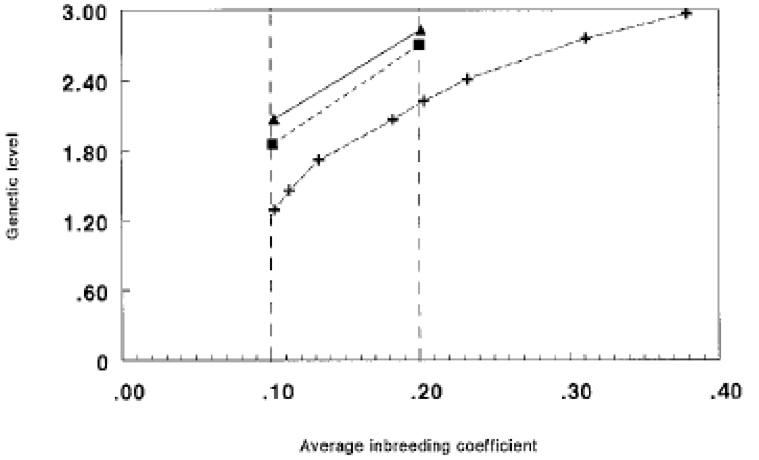


Figure 1. Genetic and inbreeding levels in generation 10 with inbreeding levels constrained to .1 and .2 and with optimal genetic contributions (▲), optimal selection of sires and dams but with equal contributions of selected sires and selected dams (■), and BLUP selection with selection of (from left to right) 32, 30, 26, 20, 18, 16, 12, and 10 sires and equal numbers of dams (+).

Table 2. Optimal numbers of parents selected when the number of offspring per sire and per dam are equal. For comparison, the numbers according to Wright's (1931) random mating formula are given

	$\Delta F_{init} = .025$[a]		$\Delta F_{init} = .0125$[a]	
Generation	Sires	Dams	Sires	Dams
2	10	10	21	20
3	10	10	19	19
4	10	10	18	19
5	9	9	18	18
6	9	9	18	17
7	9	9	17	17
8	8	8	17	17
9	8	8	16	17
10	8	8	17	16
Wright's formula	10	10	20	20[b]

[a] ΔF_{init} = the initial rates of inbreeding; in later generations ΔF increased to .0303 and .0137, respectively.

[b] Wright's formula is $\Delta F = 1/8n_s + 1/8n_d$, where the numbers of males (n_s) and females (n_d) are assumed equal.

Optimal contribution selection was extended to overlapping generations by Meuwissen and Sonesson (1998). J. Anim. Sci. 76: 2575.

Table 1. Parameters of the closed nucleus breeding schemes

Constraint on inbreeding	.5 or .25%/yr
No. of new progeny per yr (males and females)	256 or 512
Size of unrelated base population	5 × (No. of new progeny)
No. of years evaluated	20
Involuntary culling rate of males and females	.3
Voluntary culling rate	negligible
Age at which females completed lactation records	2, 3, and 4 yr[a]
No. of test daughters of bulls with unrelated cows outside the nucleus	0 or 100
Age at which progeny test became available	5 yr[a]
Reproductive rate of males and females within nucleus	unlimited
No. of sires and dams selected in BLUP selection schemes	equal and such that inbreeding constraint holds
Genetic, and permanent and temporary environmental variances	.3, .2, .5

[a] When the animals are selected for this information, the offspring are born 1 yr later (i.e., the generation interval is 1 yr longer than the age at which the information becomes available).

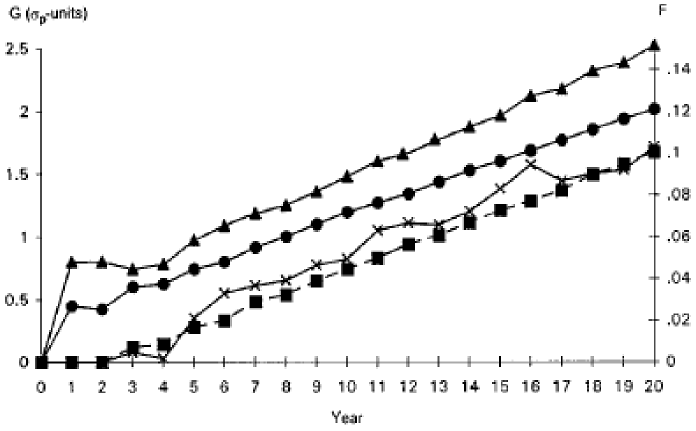


Figure 1. Genetic level (G) and inbreeding coefficient (F) for optimal contribution selection (OC) and BLUP-EBV selection of 64 sires and 64 dams. Averages of 50 simulations with 256 new progeny per year without progeny test of young bulls (G-OC = ▲; G-BLUP = ●; F-OC = ×; F-BLUP = ■).

Table 2. Genetic level (G) and inbreeding coefficients (F) at yr 20 when nucleus herds were selected with the optimal contribution method and with selection for BLUP-EBV[a]

New progeny per yr, no. of animals	Size of progeny test, no. of records	Optimal Contribution G, σ_p-units	Optimal Contribution F	BLUP G, σ_p-units	BLUP F
	Constraint on ΔF per year = .005				
256	0	2.52	.10	2.01	.10
	100	3.12	.08	2.30	.09
512	0	2.83	.11	2.43	.11
	100	3.46	.09	2.73	.09
	Constraint on ΔF per year = .0025				
256	0	2.24	.05	1.63	.05
	100	2.83	.04	1.97	.05
512	0	2.65	.05	2.05	.05
	100	3.27	.04	2.35	.05

Table 3. Number of animals selected and generation intervals at yr 20 with the optimal contribution and BLUP selection, where numbers selected were chosen to achieve the inbreeding constraint[a]

New progeny per yr, no. of animals	Size of progeny test, no. of records	Optimal Contribution Selected sires/dams, no. of animals	Optimal Contribution Gen. Interval sires/dams, yr	BLUP Selected sires/dams, no. of animals	BLUP Gen. Interval sires/dams, yr
	Constraint on ΔF per year = .005				
256	0	19.2/5.3	2.7/4.7	64/64	2.7/3.3
	100	2.8/4.5	6.2/4.5	64/64	3.2/3.1
512	0	24.6/5.3	2.9/4.5	80/80	2.5/3.2
	100	2.7/5.8	6.0/4.4	80/80	3.1/3.0
	Constraint on ΔF per year = .0025				
256	0	34.9/11.4	2.9/4.5	105/105	2.8/3.3
	100	7.6/10.1	6.0/4.4	95/95	3.1/3.1
512	0	45.2/13.2	2.6/4.5	130/130	2.6/3.2
	100	6.4/9.7	6.0/4.5	125/125	3.1/3.1