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Inbreeding[1]

9.1 Introduction

Optimization of the design requires that alternative breeding schemes can be compared and evaluated. Choosing the best breeding scheme among a number of alternatives requires yardsticks to measure the quality of breeding schemes. Such yardsticks can be developed only when there is a well-defined breeding goal. Given that the breeding goal is clearly defined, there are three criteria that summarize the quality of a breeding program. These are:

1. Selection response for the breeding goal.

2. Maintenance of genetic diversity as measured by the rate of inbreeding.

3. Costs of the breeding program.

Maintenance of biodiversity is an important element of sustainable animal breeding and reproduction. The loss of genetic diversity within a breed is related to the rate of inbreeding (ΔF). Factors influencing the maintenance of genetic variation in quantitative traits in populations undergoing artificial selection are recently reviewed by Hill (2000). He showed that genetic variation is lost by genetic drift and gained by mutation and therefore the minimum population size to maintain genetic variation is a function of mutation rate. From selection experiments in laboratory species Hill (2000) showed that substantial progress can be maintained for very many generations, even with populations of effective size well under 100, but that responses increase with population size.

The magnitude of inbreeding at the population level is measured by the rate of inbreeding (ΔF). Only in the absence of selection ΔF is related directly to the number of sires and dams. In selected populations, this equation is no longer valid because parents contribute unequally to the next generation. Recently, Woolliams et al. (1999) and Woolliams and Bijma (2000) developed a general theory to predict rates of inbreeding in populations undergoing selection. These methods facilitate a deterministic optimisation of short and long-term response of breeding schemes. Research on optimisation of breeding schemes has initially focused on genetic gain while little attention was paid to inbreeding (i.e. longer-term consequences of selection for genetic diversity). However, it is now well accepted that an evaluation of alternative breeding schemes should be based on genetic gain while constraining inbreeding. Background on prediction of rates of inbreeding are given in this chapter as well as description of software (SelAction) to predict rates of inbreeding in selected populations.

Meuwissen (1997) introduced a dynamic selection tool to maximise the genetic gain while restricting the rate of inbreeding. Given the available selection candidates, the method maximised the genetic level of the selected group of parents while constraining the average coefficient of coancestry. Implementation of this method results in a dynamic breeding program, where the number of parents and number of offspring per parent may vary, depending on the candidates available in a particular generation. This procedure will be described in more detail in this chapter.

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[1] In writing this chapter, we have used information from the notes prepaired by John Woolliams and Theo Meuwissen for a post-graduate course in The Netherlands in 2000.

9.2 Some parameters

Measures of relatedness are based upon the concept of identity by state. The inbreeding coefficient of an individual is the probability that the pair of alleles carried by the gametes that produced the individual were identical by descent (Wright, 1922). Computing the inbreeding coefficient involves tracing of the pedigree back to common ancestors of the parents and computing the probability of each segregation. Instead of thinking about the inbreeding of an individual, we can also think about the degree of relatedness of the two parents. This is called the coefficient of coancestry (sometimes also referred to coefficient of kinship, 'coefficiente de parente' or coefficient of consanguinity) The coefficient of coancestry between individuals is the probability that two alleles are identical by descent. The coefficient of coancestry of any two individuals is equal to the inbreeding coefficient of their progeny if they were mated. The additive genetic relationship or numerator relationship between two individuals is two times the coefficient of coancestry. For the calculation of genetic relationships and inbreeding coefficient there are now several public-domain algorithms (Tier, 1990; Meuwissen and Luo, 1992).

The degree of relationship between the individuals in a population depends on the size of the population which can be illustrated by considering the number of possible ancestors. In a population every individual has 2 parents, four grand-parents, and eight grand-grandparents. When we go back t generations each individual has 2^t ancestors. Not very many generations back, the number of individuals required to provide separate ancestors for all the individuals in the present population becomes larger than any real population could contain. As a consequence, any pair of individuals must be related to each other through one or more common ancestors in the more or less remote past.

In animal breeding practice the question is often asked: is a population with an average inbreeding coefficient of 10% too highly inbred? This question can not be answered as long as we do not know how many generations it took to reach this inbreeding coefficient. Inbreeding is inevitable in any closed population over a period of time. Therefore, any population will have inbred individuals.

The fact that one has to define a base population in order to calculate inbreeding coefficients implies that the inbreeding coefficient does not measure homozygosity in an absolute sense. In fact, it measures the decrease in heterozygosity relative to a base population in which all individuals are assumed to be unrelated and to have zero inbreeding. In other words, it measures the degree to which an individual is less heterozygous than individuals which are assumed to have zero inbreeding. When an individual has an inbreeding coefficient of 0.3, we know that the individual is 30% less heterozygous than the individual with an inbreeding coefficient of zero. The actual level of heterozygosity in both individuals depends on the heterozygosity in the base population.

The inbreeding coefficient of an individual is influenced by the number of ancestral generations which are considered in its calculation. In order to make a proper comparison between individuals it is important that there is a well defined base population and that the animals in the base population have similar dates of birth. In practice, a pedigree file might be incomplete which influences the inbreeding coefficients and complicates the comparison of inbreeding coefficients of animals.

Comparing inbreeding coefficients between populations has little value, unless the populations have a common base population or the information on the population spans a similar time period or generation number.

Message
It is important to realize that what has more relevance for a population and its genetic security is not the inbreeding coefficient itself but the rate t which it is changing in the population.

9.3 Rate of inbreeding

The principal parameter concerned with how fast inbreeding increases is the *rate of inbreeding*(ΔF). It is defined at time t+1 by:

$$\Delta F = (F_{t+1} - F_t)/(1 - F_t) \tag{9.1}$$

For populations of constant structure (such as number of parents, means and variances of family size, age structure, selection policy) the expected ΔF in the population is constant over time.

ΔF is a multiplicative measure and not an additive measure, i.e. the inbreeding coefficient is not expected to increase by a constant amount each generation, but rather a constant proportion of the heterozygosity present (measured by 1-F) is expected to disappear each generation.

9.4 Rate of inbreeding

The design of a breeding programs involves decisions on the number of animals to be used as parents which influences the expected rate of genetic progress as well as the expected rate of inbreeding in future generations. In the design of breeding programs involves finding the optimum balance between genetic progress and inbreeding. In order to find this optimum, there is a need to predict the expected rate of inbreeding for a given breeding program.

According to Wright (1922), the rate of inbreeding (ΔF) in a random mating, randomly selected population is obtained as

$$\Delta F = \frac{1}{8N_m} + \frac{1}{8N_f} \tag{9.2}$$

where N_m and N_f are the number of males and females used as parents in each generation. This equation holds when litter sizes are Poisson distributed.

The term 'effective populations size' is often used to describe the diversity in populations. The effective population size is defined by

$$N_e = \frac{1}{(2\Delta F)} \tag{9.3}$$

N_e individuals with random selection and mating and Poisson family sizes would have the same rate of inbreeding as the population in question.

From the above equation it appears that the rate of inbreeding is mainly determined by the numbers of the less numerous sex, i.e. the number of males used in most animal breeding situations. For example, a population of cattle which is maintained with one male only and a very large number of females would, according to the above equation, result in rate of inbreeding of 0.125. This rate of inbreeding corresponds with an effective number of approximately 4.

It is important to understand that the effective population size is not related directly to the actual number of parents, but that it is merely a way to express the rate of inbreeding on a different scale. The effective population size can be very different from the actual number of parents. The rate of inbreeding in the global dairy cattle population is approximately 1% per generation. The effective size of the global Holstein-Friesian dairy cattle population is therefore equal to $N_E = 1/(2\Delta F) = 1/(2\times0.01) = 50$ individuals. Thus though there are millions of diary cows, effectively the population consists of only ~50 individuals. The global Holstein-Friesian population clearly shows that a large actual number of animals by no means guarantees a large effective number of animals. In other words, populations consisting of many animals may still have high rates of inbreeding. The reason is that, by using artificial

insemination, a very small number of sires may contribute the majority of offspring to the next and later generation, whereas other sires contribute hardly any offspring to the next generation.

9.5 Prediction of inbreeding in selected populations

In designing breeding schemes that aim at controlling the rate of inbreeding, methods to predict the rate of inbreeding play an important role. In a previous section, methods to predict the rate of inbreeding in unselected populations have been described. *In selected populations the equation $\Delta F = 1/(8N_m) + 1/(8N_f)$ is invalid.* The reason is that with selection, parents contribute unequally to the next generation and also to further generations. For example, a superior sire will have more offspring selected and those offspring will be better than average. Therefore, the sire will also have more selected grand-offspring etc. This process continues until the breeding value of the sire is sufficiently diluted, which takes ~2-5 generations, depending on the selection strategy. In a selected population, therefore, there will be a systematic difference between the contribution of good *vs*. poor individuals. After a number of generations a superior individual will show up frequently in the pedigree of all individuals, whereas a poor individual will hardly show up in the pedigree. This difference in the contribution of ancestors has a booster effect on the rate of inbreeding. Therefore, in a selected population the rate of inbreeding can be much larger than $1/(8N_m) + 1/(8N_f)$. With most forms of selection, particularly with family indexes and BLUP of genetic merit, the rate of inbreeding in practice is more than double that predicted by Wright's formula for unselected populations.

Rates of inbreeding can be predicted using the concept of long-term genetic contributions. Rates of inbreeding are proportional to the sum of squared long-term genetic contributions of ancestors (Wray and Thompson, 1990). After a brief description of genetic contributions of ancestors in the next section, the prediction of rates of inbreeding using this second method will be described.

9.5.1 Genetic contributions

The genetic contribution of ancestor i in cohort t_1 is defined as the proportion of genes present in individuals in cohort t_2 deriving by descent from ancestor i. When a breeding program is in a steady state, genetic contributions reach an equilibrium over time. The long-term genetic contributions represent the values which correspond with $t_2-t_1 \rightarrow \infty$ (Woolliams, 1993). In words, the long-term genetic contribution of an ancestor is the contribution of the ancestor to the genetic make-up of future generations as a proportion of the total. By definition, genetic contributions sum to unity per generation. After several generations (5 to 10), genetic contributions of ancestors stabilize and become equal for all individuals in that generation while values differ between ancestors. Note that this is similar to what we discussed for geneflow in Chapter 8; the proportion of genes that are present in age groups at time t that can be traced back to a certain age group at time 0 initially varies but eventually stabilizes. Note that, in contrast to geneflow, here we will be modeling the contribution of genes held by a given ancestor to future generations, rather than the contribution of genes from a given (age) group of ancestors to (age) groups of descendants. The concepts are, however, very similar.

The small population in Table 9.1 will be used to illustrate the concept of genetic contributions. Sire 1 has 4 offspring in generation 1 while sires 2 and 3 have two offspring each. Sire 1 has a genetic contribution of .25 to generation 1 which reflects that .25 of the genes in generation 1 originate from sire 1. The sires 2 and 3 have a genetic contribution of .125 while the genetic contribution of sire 4 is zero. Six out of the eight individuals in

generation 2 result from a mating in which both the sire and the dam are an offspring of sire 1. This results in an contribution of .375 from sire 1 to generation 2.

Table 9.1: Pedigree to illustrate the 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).

Sex	Generation 1			Generation 2			Generation 3		
	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

Table 9.2 gives the contribution of animals in the base population to offspring in generations 1, 2, and 3. Each generation consisted of 4 full sib pairs consisting of one male and one female. Contributions of each ancestor are given for each full sib pair. In generation 3 contributions of two male and two female ancestors are found. Both ancestors have contributed to at least three out of the four animals for each sex. When the population would be followed for a larger number of generations, the contribution of a given ancestor would stabilize and the differences in genetic contributions of a given ancestor between animals within a generation would disappear.

Table 9.2: Contribution of ancestors to animals in subsequent generations and genetic contribution of each ancestor to generation.

	Ancestors							
	1	2	3	4	5	6	7	8
Generation 1								
11/15	.5	0	0	0	.5	0	0	0
12/16	.5	0	0	0	0	.5	0	0
13/17	0	.5	0	0	.5	0	0	0
14/18	0	0	.5	0	0	0	.5	0
Average	**.25**	**.125**	**.125**	**0**	**.25**	**.125**	**.125**	**0**
Generation 2								
21/25	.5	0	0	0	.5	0	0	0
22/26	.25	.25	0	0	.5	0	0	0
23/27	.5	0	0	0	0	.5	0	0
24/28	.25	.25	0	0	.5	0	0	0
Average	**.375**	**.125**	**0**	**0**	**.375**	**.125**	**0**	**0**
Generation 3								
31/35	.375	.125	0	0	.5	0	0	0
32/36	.375	.125	0	0	.25	.25	0	0
33/37	.5	0	0	0	.25	.25	0	0
34/38	.375	.125	0	0	.25	.25	0	0
Average	**.406**	**.104**	**0**	**0**	**.313**	**.187**	**0**	**0**

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

9.5.2. Prediction of rates of inbreeding

Rates of inbreeding are proportional to the sum of squared long-term genetic contributions of ancestors. For random mating:

$$\Delta F = \frac{1}{4} \sum r^2 \qquad (9.4)$$

where the sum is over a generation or cohort of ancestors; ΔF is per generation (cohort).

The long-term contribution is the proportional contribution of an individual to the genes in the population and can be calculated from the pedigree, but we will not go into that here. Consider an example with 20 selected parents per generation (ignoring that there are two sexes for simplicity). By analyzing the pedigree we can quantify the contribution of each of those 20 parents of a particular generation. Their contribution will sum to 1; genetic contributions always sum to 1 per generation. Consider two extreme cases, one where the contribution of each individual is the same, $r = 0.05$ for all individuals, and one where contributions differ extremely between individuals, $r = 0.25$ for the 4 best parents and $r=0$ for the rest. In the first case, the rate of inbreeding is $\frac{1}{4}(0.05^2 + 0.05^2 + .. \, 0.05^2) = 0.0125 = 1.25\%$ per generation. This is the lowest possible rate of inbreeding with 20 parents. In the second case the rate of inbreeding is $\frac{1}{4}(0.25^2 + 0.25^2 + .. \, 0^2) = 0.0625 = 6.25\%$ per generation. This example illustrates that 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, 5/15 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

$$\Delta F = \left(\frac{3}{8}\right)^2 + \left(\frac{1}{8}\right)^2 + \left(\frac{5}{16}\right)^2 \left(\frac{6}{16}\right)^2 = 0.072$$

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 (9.4) 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.

Further developments

Wray and Thompson (1990) obtained accurate predictions of rates of inbreeding for populations with discrete generations under mass selection, using iterative regression methods. For more complicated selection schemes, however, prediction became unmanageable due to the iterative nature of the procedure and the need for predicting the variance of long term genetic contributions. More recently, Woolliams (1998) showed that the rates of inbreeding are related to squared *expected* long-term genetic contributions, making a prediction of the variance of long term genetic contributions redundant. In the remainder, long-term genetic contributions of ancestors are referred to as "genetic contributions".

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

$$E(r_i \mid g_i) = r_i = \alpha + \beta g_i \qquad\qquad (9.5)$$

where r_i is the expected genetic contribution of ancestor i, α is the expected genetic contribution for an average ancestor, and ß is 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, α is equal to $\frac{1}{2}N_s$ and for female ancestors it is $\frac{1}{2}N_d$, where N_s and N_d is the number of male and female parents, respectively. The regression coefficient 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. First, better parents have on average more offspring that are selected as parents. Secondly, 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,

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

In this model E(r) is the expected contribution given that we know the true breeding value of an individual, α is the contribution of an individual with an average breeding value and β is a term that accounts for the increase of the contribution of parents with a higher breeding value. Thus the second term takes account of the fact that parents with high breeding values will have 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, by squaring the above equation

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

the right-most term is the genetic variance of the selected parents (see also the section about the Bulmer effect).

So far we have calculated E(r)^2, but in fact we need to calculate E(r^2). The difference is that E(r)^2 is the square of the expected contributions whereas E(r^2) is the expectation of the squared (actual) contribution. It can be derived that under certain conditions $E(r^2) = 2E(r)^2$, leading to the result that the rate of inbreeding is

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

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, NE(r)^2.

The above theory shows that selection strategies that increase the variance of contributions among parents lead to higher rates of inbreeding. Selection strategies that rely heavily on family information are an example. If estimated breeding values are largely based on family information, truncation selection on EBV will lead to 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 the rate of inbreeding substantially.

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 estimated breeding value and the prediction error (Woolliams, 1998).

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

$$E(\Delta F) = \tfrac{1}{2} \sum_k X_k E\!\left(r_{i,k}^2\right) \tag{9.6}$$

where Σ_k represents summation over all possible categories (e.g. sexes), X_k is the number of parents in the kth category and $r_{i,k}$ is the expected genetic contribution of the ith selected individual in category k. The expectation must include all the variables conferring selective advantage, such as the breeding value of mates. It has been shown that the expectation is tractable. In the simplest case of random selection the $r_{i,k}$ are simply $(2N_s)^{-1}$ and $(2N_d)^{-1}$ and the derivations lead to Wright's formula.

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

$$E(\Delta G) = \sum_k X_k E\!\left(r_k g_k\right) \tag{9.7}$$

The calculation of genetic progress is closely linked to the genetic contributions. The genetic merit of an animal can be decomposed into its own Mendelian sampling component plus the average of its parents. In turn, the genetic merit of its parents can be decomposed into their Mendelian sampling components plus the average genetic merit of its grandparents. This process can be applied recursively back through the pedigree. An individual's genetic merit is the weighed sum of the Mendelian sampling components of all its ancestors. A single round of selection then can be viewed as the joint process of initial selection among the current generation's Mendelian sampling components, making a second selection among the parental generation and so on. Selection alters the population mean through changing the contributions of an individual's Mendelian sampling component that is present in the population.

The theory of genetic contributions gave an approach towards prediction of rates of gain and inbreeding. Alternative options, in particular for the prediction of rate of inbreeding, are limited. For mass selection in discrete generations, the approach yielded answers for equilibrium rates of genetic gain that were identical to those derived from other methods (Woolliams and Thompson, 1994). The approach has been used to predict rates of inbreeding in selected populations with success in special cases of mass selection and sib indices. 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.

9.6 Maximizing genetic gain while constraining the rate of inbreeding

Maximising genetic gain while constraining the rate of inbreeding will change the layout of breeding schemes compared to simply maximising genetic gain. Following the pioneering work of Nicholas and Smith (26) and subsequently many others, breeding schemes for dairy cattle have moved towards selection based on sib information which enables higher short-term genetic gain. However, for species such as dairy cattle, where the trait of interest cannot be measured on the male selection candidate, maximising genetic gain while restricting inbreeding is likely to move optimum selection schemes back to progeny testing, in particular when population size is small and the constraint on ΔF is stringent (29). This situation changes when traits of interest can be measured early in life on both sexes, as is the case in beef cattle and pigs. The situation would also change when molecular information was available to predict the Mendelian-sampling component of selection candidates at an early age (e.g. 30). The combination of increased female reproductive rate and DNA markers offers good opportunities to increase gain while restricting inbreeding.

For illustration we give some results from a study by Villanueva and Woolliams(1997) who used the genetic contribution theory for the design of breeding schemes which maximize genetic gain with constraints on the rate of inbreeding. The selection index included information from the candidate and its sibs. The optimization involved determining the number of males and females and the index weights. Results for a population of 200 individuals are given in Table 9.3. Selection was for a trait with a base population heritability of 0.3 that was measured on both sexes prior to selection. The maximization procedure involved a comparison of all combinations of number of parents and index weights and that set giving the best value was defined as optimum. This optimization procedure is facilitated by the fact that computing time involved in evaluating a single set is very limited.

The weight given to family information when maximizing response after 20 generations of selection under unrestricted inbreeding were considerably lower than the classical index weights which maximize one-generation gain. The classical weight for the family information (full-sib mean) was 9.60. The value that results in the optimum response after 20 generations is equal to 2.97. Index weights are closer to those for mass selection (weight for own and family information equal to 1) when selection is for longer-term genetic response, even when there is no restriction on inbreeding. Restricting the rate of inbreeding results in the selection of a larger number of parents and a reduction in the index weight family information. The optimum number of parents selected increases with the severity of the restriction on ΔF.

Table 9.3: Optimum number of sires and dams under index selection, and optimum index weight for maximizing genetic gain after 20 generations under unrestricted inbreeding and two different constraints on the rate of inbreeding (ΔF) (from Villanueva and Woolliams, 1997)

	restriction		
	no	$\Delta F \leq 1\%$	$\Delta F \leq 0.25\%$
Number of sires	21	30	68
Number of dams	68	68	68
Index weight[1]	1.43	1.06	0.76
ΔF	2.00	1.00	0.25
$\Delta G_{(20)}$	0.278	0.258	0.128

[1] Index weight for mean of full-sib records, the weight for the own record is 1 in all cases.

9.7 Methods to reduce inbreeding

Modern breeding schemes tend towards smaller effective population sizes because selection decisions are based on estimates of genetic merit (EBV) which include family information, the generation interval tends to be shorter and the use of reproductive techniques. The use of family information in EBV increases the correlations between the EBV of relatives and increases the probability of co-selection of relatives which results in inbreeding. Effective population size has a direct relation with rate of inbreeding and is highly related to the variance in the selection response (Meuwissen and Woolliams, 1994). Selection on EBV from the animal model will maximize the genetic level of the next generation of animals. It, however, does not necessarily lead to the highest longer-term genetic response. This can be illustrated by the fact that with unlimited reproductive capacity the selection of the male and female with the highest EBV will result in the highest response in the first generation. This scheme reduces the opportunities for selection in their offspring, i.e. they all belong to the same full sib family. On the longer term, this scheme will lead to a high rate of inbreeding. In all breeding schemes more than one sire and more than one dam are selected, which demonstrates that breeding organizations do account for inbreeding and the longer term

genetic response. In order to achieve a higher longer-term genetic gain, breeding organizations sacrifice some short-term genetic gain. In most breeding schemes too close relationships between the selected animals are avoided. Furthermore, matings between close relatives are avoided.

9.7.1 Selection of more animals

The effective population size can be increased by using more sires and dams. As we have seen earlier, especially increasing the number for the sex with the smallest number affects the effective population size. Selection of more parents also leads to a reduction of the selection intensity. The relationship between selection intensity and selected fraction is not linear. The reduction in selection intensity, therefore, depends on the current level. If the selected fraction is large, for example due to low reproductive rates, the intensity of selection will be markedly increased. However, species with low reproductive rates are likely to have small effective population sizes unless their actual number is also small.

9.7.2 Increasing emphasis on within family deviation

When selection is for BLUP-EBV, the rate of inbreeding decreases with increasing heritability (Wray and Thompson, 1990). With increasing heritability, the weight of the own performance in the EBV increases relative to that of the pedigree information. The lower weight on the pedigree information reduces the correlation between EBV of relatives which results in a lower probability of co-selection of relatives.

Grundy and Hill (1993) suggested to increase the heritability above it's true value in the calculations of EBV such that the correlations between EBV of relatives are reduced. This leads to lower rates of inbreeding but also to lower selection response on the short term. Simulations showed that the rate of inbreeding was markedly reduced while the reduction in longer term selection response was small. The number of animals to be selected is not optimized by this method. In situations with a sex-limited trait, the effect of changes in heritability on selection in the sex (usually males) on which phenotypes are not observed can be limited. In the absence of progeny information, all males within a full sib family have the same EBV irrespective of the level of the heritability. Progeny information will reduce the correlations between EBV of full sibs. The heritability in that case influences the relative importance of pedigree information on the one hand and progeny information on the other.

The BLUP-EBV can be written as a sum of the pedigree index and the within family deviation. Verrier et al. (1993) suggested to decrease the weight on the pedigree index which results in selection of fewer relatives. Setting the weight on pedigree index to zero leads to within family selection, which was proposed by Dempfle (1975) to increase long term genetic response.

9.7.3. Selection while controlling inbreeding

BLUP automatically places large emphasis on family information in cases where individual or progeny information is lacking. Examples are MOET breeding schemes in dairy cattle where EBV are largely based on performance of female full-sibs; selection of boars for litter size in dam lines of pig-breeding programs, selection of roosters for egg number based on female full sibs etc. However, the fact that BLUP puts large emphasis on family information does not mean that BLUP breeding value estimation should be avoided. BLUP yields the most accurate method for breeding value estimation and properly corrects for fixed effects. Therefore, BLUP is the method of choice for breeding value estimation. If EBVs are largely based on family information one needs to include a restriction on the rate of inbreeding in the selection step, EBVs can still be based on BLUP. An excellent method to include a restriction

on the rate of inbreeding in the selection step is developed by Meuwissen (1997). In order to maximize the genetic selection differential but restrict the rate of inbreeding, Meuwissen's method calculates the optimum number of offspring of each parent. At present this method is the method of choice to maximize response to selection while restricting the rate of inbreeding.

Meuwissen (1997) developed a method that maximizes genetic level of selected animals while constraining their average relationship to a predefined value. The average relationship of the selected parents equals two times the inbreeding level in the next generation, so the rates of inbreeding are controlled. The dynamic rules optimize selection of the actual available candidates and takes advantage of opportunities which were unforeseen when the breeding program was designed.

Within every round of selection, we want to maximize the genetic level of the generation of animals $\overline{g}_{t+1}$:

$$\overline{g}_{t+1} = \mathbf{c}'_t \hat{g}_t$$

where $\hat{g}_t$ is the vector of BLUP estimated breeding values of the candidates for selection in generation t and $\mathbf{c}_t$ is the vector of contributions of the selection candidates to generation $t+1$. The problem is to find an optimum $\mathbf{c}_t$. The contributions of all males sum to ½, and likewise for all female candidates:

$$\mathbf{Q}'\mathbf{c_t} = \frac{1}{2}$$

where $\mathbf{Q}$ is a known incidence matrix for sex (the first column contains one for males and zeros for females, and the second column contains ones for females and zeros for males); and ½ is a vector of halves of order two.

The average coancestry between parents ($\overline{C}_{t+1}$), which equals half the additive genetic relationship, can be calculated as:

$$\overline{C}_{t+1} = \frac{1}{2} \mathbf{c}'_t \mathbf{A_t} \mathbf{c}_t$$

where $\mathbf{A}_t$ is the matrix of additive genetic relationships among the selection candidates in generation t. In order to constrain the increase in rate of inbreeding, we need to find a solution for $\mathbf{c}_t$ which maximizes the genetic level in the next generation and for which the average coancestry between parents is equal to the desired level. The desired level for the average coancestry between parents is equal to the current average coancestry between parents plus ΔF, where ΔF is the desired rate of inbreeding per generation. When generation 0 is noninbred ($F_0 = 0$), the desired level for $\overline{C}_{t+1}$ can be set equal to $\Delta F(t+1)$.

The optimal solution of this optimization problem can be found using the Lagrangian multiplier method. We would like to maximize H_t for $\mathbf{c}_t$, λ_0, and λ, with

$$H_t = \mathbf{c}'_t \hat{g}_t - \lambda_0 \left(\mathbf{c}'_t \mathbf{A_t} \mathbf{c}_t - 2\overline{C}_{t+1} \right) - \left(\mathbf{c}'_t \mathbf{Q} - \frac{1}{2}' \right) \lambda_v$$

where λ_0, and λ are LaGrangian multipliers, and λ_v is a vector with the two LaGrangian multipliers, i.e. $\lambda_v' = [\lambda_0, \lambda]$.

Solving this system for $\mathbf{c}_t$ results in:

$$\mathbf{c_t} = \frac{\mathbf{A_t^{-1}}\left(\hat{g}_t - \mathbf{Q}\lambda_v \right)}{2\lambda_0}$$

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

From the constraint $\mathbf{Q}'\mathbf{c}_t$ follows an equation for λ

$$\mathbf{Q}'\mathbf{A_t^{-1}}\mathbf{Q}\lambda_v = \mathbf{Q}'\mathbf{A_t^{-1}}\hat{g}_t - \mathbf{1}\lambda_0$$

and from the constraint $\mathbf{c}_t'\mathbf{A_t}\mathbf{c}_t/2 = \overline{C}_{t+1}$ it follows

$$8\overline{C}_{t+1}\lambda_0^2 = \mathbf{Q}'\mathbf{A_t^{-1}}\hat{g}_t - \mathbf{1}\lambda_0$$

Solving these two equations for λ_0 results in:

$$\lambda_0^2 = \frac{\hat{g}_t' \left(A_t^{-1} - A_t^{-1} Q \left(Q' A_t^{-1} Q \right)^{-1} Q' A_t^{-1} \right) \hat{g}_t}{8\overline{C}_{t+1} - 1' \left(Q' A_t^{-1} Q \right)^{-1} 1}$$

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 c_t. This c_t may contain negative values for some animals with a poor estimated genetic merit. Negative values of c_t can be constrained to zero by eliminating those animals from the optimization process.

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

Meuwissen (1997) showed that the application of this method for several generations, resulted in stable rates of genetic gain and the desired level of inbreeding. This indicates that the method is able to control the short- and long-term effects of selection on inbreeding. The method implicitly optimizes the number of sires and dams to be selected. Simulation showed that at equal rates of inbreeding, genetic gains were 21 to 60% greater than when selection was on estimated genetic merit. In the latter method, the animals with the highest merit were selected and all had equal contributions. The desired level of inbreeding in that case was achieved by varying the number of selected parents. The superiority of the optimum contribution method increased when smaller rates of inbreeding are required.

The average coancestry of the selected parents was constrained instead of the average inbreeding coefficient of their offspring. In the latter case, one sire and one dam would be selected from an unrelated base population yielding full sib offspring with an inbreeding coefficient of 0. In selecting parents from this generation of full siblings, only full sibs can be selected as parents and the rate of inbreeding cannot be lower than 0.25. This shows that a direct constraint on the level of inbreeding cannot effectively control rates of inbreeding. Selection of a single sire and dam would result in an average coancestry between selected parents of ¼. When the desired rate of inbreeding is lower than ¼, more parents will be selected with the optimum contribution method.

So far, discrete generations have been assumed here, but in practice generations overlap. Extensions of the algorithm are possible as discussed by Meuwissen (1997). Software has been developed to implement this algorithm in practice (Gencont).