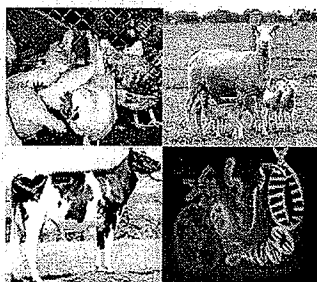


Inbreeding & optimal contribution theory



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Inbreeding

Due to the mating of relatives

Has a number of effects including:

- ❖ Increased expression of recessive genes
- ❖ Loss of performance & viability termed F depression
- ❖ Loss of genetic variation *within* the inbred population

Inbreeding

Inbreeding increases expression of recessive alleles

Genotype frequencies

- ❖ Non-inbred: q^2 $2pq$ p^2
- ❖ Inbred: q^2+pqF $2pq-2pqF$ p^2+pqF

Example, $q=0.02$ (2%)

| | | | | |
|----------------------------------|-------------|-------------|-------------|--------------|
| F | 0 | 0.125 | 0.25 | 0.50 |
| Prob. aa (recessive genotype) | 0.4 in 1000 | 2.9 in 1000 | 5.3 in 1000 | 10.2 in 1000 |

Inbreeding

Change in genotype frequencies in response to inbreeding

For example, $p=q=0.5$

| Genotype | aa | Aa | AA |
|-----------------|-----------|------------|-----------|
| Frequency | q^2+pqF | $2pq-2pqF$ | p^2+pqF |
| At F=0 | 0.25 | 0.50 | 0.25 |
| At F=0.5 | 0.375 | 0.25 | 0.375 |
| At F=1.0 | 0.5 | 0 | 0.5 |

Note that allele frequencies do not change

Inbreeding

Inbreeding depression reduces productivity & viability

Inbreeding depression

- ❖ Results in lowered performance and viability
 - especially reproductive fitness
- ❖ Primarily due to loss of dominance

Level of trait depression is variable

- ❖ Often 2-20% decrease in the trait per 10% F

Inbreeding

Inbreeding depression

F depression expressed as change in trait per 1% increase in F (from Simm, 2000)

| Animal | Breed | Trait | Inbreeding depression |
|--------------|----------|---------------|-----------------------|
| Dairy Cattle | Holstein | Milk yield | -29.6kg |
| | Holstein | Fat yield | -1.08kg |
| | Holstein | Protein yield | -0.97kg |
| Beef | Hereford | Weaning rate | -1.24% |
| Sheep | Many | GFW | -0.017kg |

Inbreeding

Inbreeding reduces genetic variance

Genetic variance in a population = variance in parents + mendelian sampling variance

❖ With no F $V_{MS} = \frac{1}{2}\sigma_g^2$

❖ With F $V_{MS} = \frac{1}{2}(1 - \frac{1}{2}(F_{sire} + F_{dam}))\sigma_g^2$

As individuals become more alike, the *within* population genetic variance decreases

Inbreeding

Case study

Authors: Evans, F; Matson, S; Brake, J; Langdon, C

Title: The effects of inbreeding on performance traits of adult Pacific oysters

Source: AQUACULTURE, 230 (1-4): 89-98 FEB 16 2004

Abstract

Understanding the effects of inbreeding is critical to the long-term viability of shellfish breeding programs.

Families were created with expected inbreeding coefficients (F) of 0, 0.0625, and 0.203. Average family yield, individual growth rate, and survival were recorded

After two growing seasons, significant inbreeding depression of yield and individual growth rate was observed in families with F = 0.0625 (P < 0.01) and F = 0.203 (P < 0.001).

Significant depression of survival at harvest was observed only in families with F = 0.203 (P = 0.009).

These results emphasize the importance of maintaining pedigree records in shellfish breeding programs to help avoid the deleterious effects of inbreeding depression.

Inbreeding

Case Study

Authors: Wu, HX; Matheson, AC; Abarquez, A

Title: Inbreeding in *Pinus radiata*. IV: the effect of inbreeding on wood density

Source: ANNALS OF FOREST SCIENCE, 59 (5-6): 557-562 Sp. Iss. SI JUL-OCT 2002

Abstract

The effects of inbreeding on basic wood density in a 17-year-old radiata pine trial were studied using five populations, each inbred to one of five inbreeding levels: $F=0$, 0.125, 0.25, 0.50, 0.75

Although inbreeding resulted in slightly depressed wood density (inbreeding depression was 1.47%, 2.50%, 1.65%, 0.02%, respectively at $F = 0.125$, 0.25, 0.50 and 0.75), the effects were not significant.

However, the variation of wood density among trees was increased by inbreeding, by 3.70%, 3.40%, 15.74%, and 29.01% respectively for populations at $F = 0.125$, 0.25, 0.5, and 0.75.

A lack of inbreeding depression for wood density makes radiata pine a species ideally suited for the use of inbreeding as a breeding tool.

Inbreeding

Coefficient of inbreeding

- ❖ The *coefficient of inbreeding* (F) is the probability that two alleles at a randomly chosen locus are identical by descent,
- ❖ F ranges from 0 to 1
- ❖ A measure of relatedness within an individuals
- ❖ Is relative to a base population, not absolute
 - e.g. $F=0.25$ means the animal is 25% less heterozygous than an $F=0$ base animal.

Inbreeding

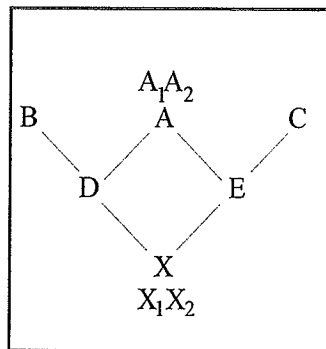
IBD versus IBS

- ❖ IBD (identical by descent) means that alleles are identical and derived from the same common ancestor
- ❖ IBS (identical by state) means that alleles are identical by chance

Why does the distinction matter?

Inbreeding

Inbreeding coefficient



The *coefficient of inbreeding (F)* is the probability of the 2 alleles at a randomly chosen locus being *identical by descent*

$$P_{A_1A_1} = \left(\frac{1}{2} \times \frac{1}{2}\right) \times \left(\frac{1}{2} \times \frac{1}{2}\right) = \frac{1}{16} \quad F_x = \frac{1}{8}$$

$$P_{A_2A_2} = \left(\frac{1}{2} \times \frac{1}{2}\right) \times \left(\frac{1}{2} \times \frac{1}{2}\right) = \frac{1}{16}$$

Shortcut: $n = 3$ descendants (D, A, E) in the closed loop -

$$F_x = \left(\frac{1}{2}\right)^3 = 1/8$$

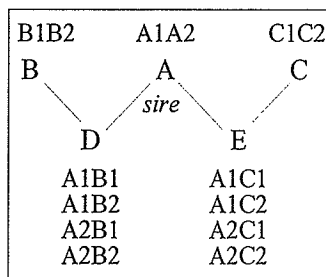
Inbreeding

Coancestry

- ❖ The *coancestry* (f_{ij}) is the probability that two gametes taken at random from two individuals (i & j) carry alleles that are IBD
- ❖ A measure of relatedness between two individuals
- ❖ The coancestry of two individuals is equal to the F of their progeny
- ❖ f ranges from 0 to 1

Inbreeding

Coancestry coefficient



The *coancestry* (f) is the probability of that 2 gametes taken at random from 2 individuals carry alleles *identical by descent*

Pick an allele in D and an allele in E.
Chances of being IBD are 2/8 if an paternal allele was picked, and 0 otherwise.

$$f = \frac{1}{8}$$

The coancestry of i & j (f_{ij}) is equivalent to the F of their progeny

Inbreeding

The rate of inbreeding

A simple formula for inbreeding at generation t , with no selection and random mating:

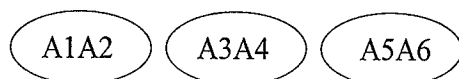
$$F_t = 1 - \left[1 - \frac{1}{2N_e} \right]^t$$

where t is number of generations and N_e the effective population size

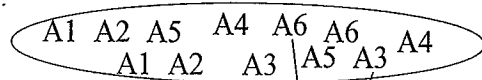
F rate in selected populations can be predicted using the concept of long-term genetic contributions (Wray and Thompson, 1990)

Inbreeding

Generation 0



Gene pool: 2N alleles



Generation 1



$$\frac{1}{2N}$$

$$1 - \frac{1}{2N}$$

F rate

$$F_t = \frac{1}{2N} + \left[1 - \frac{1}{2N} \right] F_{t-1}$$

$$F_t = 1 - \left[1 - \frac{1}{2N_e} \right]^t$$

Sample with replacement. The probability of sampling 2 copies of the same allele is $1/(2N)$. The probability of sampling 2 different alleles is $1-1/(2N)$ - in later gen's x by F as some alleles will be IBD. Assumes no selection and random mating.

Inbreeding

Ne

The size of the idealized population with the same inbreeding rate as the actual population

The idealized population has 'simplified' properties:

- ❖ Closed
- ❖ Random mating
- ❖ Discrete generations
- ❖ Constant population size
- ❖ Equal sex ratios
- ❖ Poisson distribution of family size

Inbreeding

Calculating Ne

Assume an unequal sex ratio, but all else as per an idealised population

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

| | | | | | | |
|----------------------|---|-----|-----|------|------|---------|
| Males / generation | 2 | 2 | 2 | 5 | 20 | 1 |
| Females / generation | 2 | 20 | 200 | 200 | 200 | 99999 |
| N | 4 | 22 | 202 | 205 | 220 | 100,000 |
| Ne | 4 | 7.3 | 7.9 | 19.5 | 72.7 | 4 |

Effective pop'n size (Ne) reduces towards sex with fewer breeding individuals

Inbreeding

Calculating Ne for non-idealised populations

- If variance in family sizes exist (often due to selection of more individuals from the better families), N_e becomes:

$$N_e = \frac{8N}{V_{km} + V_{kf} + 4}$$

For an idealised population, with random variation in family size V_{km} and $V_{kf}=2$, and thus $N_e=N$. Otherwise variance in family size is >2

- If the number of parents fluctuates over time, the smaller numbers will become more influential. An approximation of the average N_e for t generations becomes:

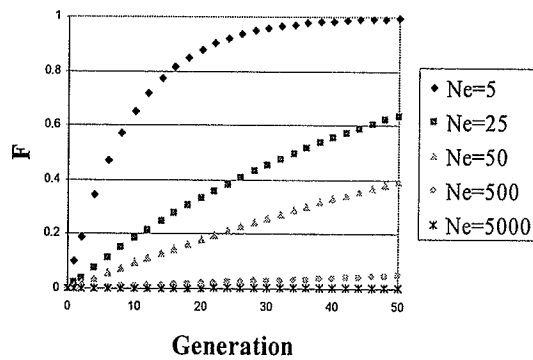
$$\frac{1}{N_e} = \frac{1}{t} \sum_{k=1}^t N_{e,k}$$

(where $N_{e,k}$ is the effective size in generation k)

- For overlapping generations see Hill 1979

Inbreeding

F rate



$$F_t = 1 - \left[1 - \frac{1}{2N_e} \right]^t$$

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

Inbreeding

Inbreeding rate in breeding schemes

Breeding schemes may have high F rates due to:

- ❖ Use of BLUP EBVs
 - Use of family information in EBVs increases the correlation of EBVs between relatives, and thus the probability of co-selection of relatives
- ❖ Short generation intervals
- ❖ Use of reproductive technologies

Inbreeding

Constraining inbreeding rate

- ❖ At equilibrium, under constant selection and with random mating, ΔF is equal to Δf
- ❖ Constraining Δf is likely the most effective way to constrain ΔF
- ❖ Select parents so that the mean f (of all mating pairs) is restricted to an acceptable level
- ❖ This principle is applied in 'optimal contribution theory'

Inbreeding

Truncation vs optimal selection

Truncation selection

- ❖ Select all animals above a cut-off for genetic merit
- ❖ May result in over-representation of some families
 - particularly if information from relatives was used
- ❖ Increases rate of F over a random selection policy

Optimal selection

- ❖ Can consider 'select best animal on merit, select 2nd animal based on merit and low coancestry with the 1st animal, etc.'
- ❖ Balances genetic gain and coancestry

Inbreeding

Optimal contribution theory

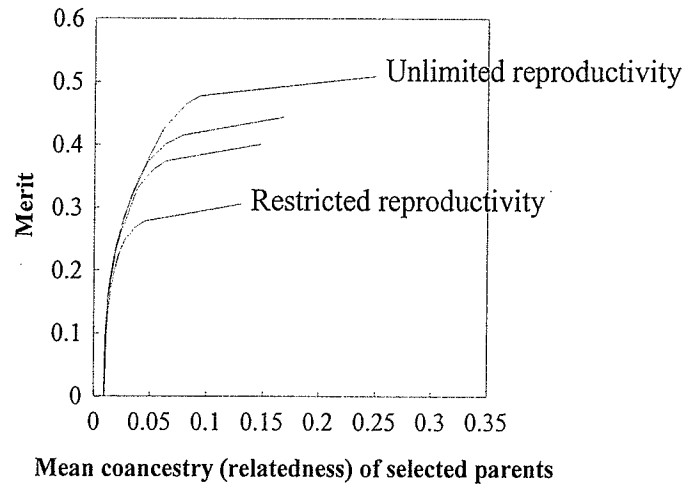
Aimed at maximising long-term response by weighting genetic response against future contributions to inbreeding

Maximise an objective function of: $\Delta G - b\Delta f$

- ❖ where G is genetic merit, b is a weight, and f is coancestry

Inbreeding

The relationship between merit and coancestry



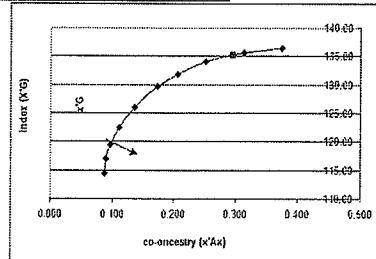
Inbreeding

Small weight on F → single sire selected

| X | nmales | nfeemales | G | Relationships Matrix | | | | | | | |
|----------------|-----------------------------|-----------|-----|----------------------|------|------|------|------|------|------|------|
| Male 1 0.000 | 4 | 4 | 127 | 1.00 | 0.00 | 0.50 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 |
| Male 2 0.000 | | | 122 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Male 3 0.500 | | | 150 | 0.50 | 0.00 | 1.00 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 |
| Male 4 0.000 | | | 109 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Female 1 0.043 | Final optimal contributions | | 120 | 0.50 | 0.00 | 0.50 | 0.00 | 1.00 | 0.50 | 0.00 | 0.00 |
| Female 2 0.343 | | | 123 | 0.00 | 0.00 | 0.50 | 0.00 | 0.50 | 1.00 | 0.00 | 0.00 |
| Female 3 0.000 | | | 89 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 |
| Female 4 0.114 | | | 113 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 |

| | |
|---------------------|--------|
| xG | 135.23 |
| Inbreeding weight λ | -10.0 |
| xAx | 0.295 |
| crit | 132.28 |
| ngens | 400 |

| λ | xG | xAx |
|----------|--------|-------|
| 0.00 | 138.50 | 0.375 |
| -8.77 | 135.58 | 0.314 |
| -18.10 | 134.11 | 0.251 |
| -28.69 | 131.66 | 0.205 |
| -41.65 | 129.68 | 0.173 |
| -59.05 | 125.97 | 0.136 |
| -85.54 | 122.51 | 0.112 |
| -134.74 | 119.51 | 0.097 |
| -272.16 | 116.86 | 0.080 |
| -6211.29 | 114.39 | 0.088 |
| | 135.23 | 0.295 |



Inbreeding

Moderate weight on F → two sires selected

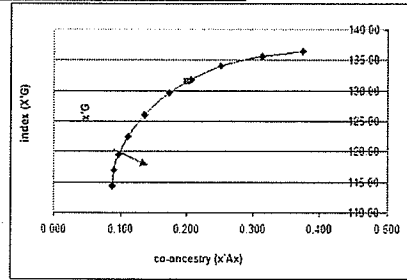
| X | | nmales | nfemales | G | | Relationships Matrix | | | | | | | | |
|----------|-------|--------|----------|-----|------|----------------------|------|------|------|------|------|------|------|------|
| Male 1 | 0.000 | 4 | 4 | 127 | 1.00 | 0.00 | 0.50 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 | 0.00 | 0.00 |
| Male 2 | 0.078 | | | 122 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Male 3 | 0.422 | | | 160 | 0.50 | 0.00 | 1.00 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 | 0.00 | 0.00 |
| Male 4 | 0.090 | | | 109 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Female 1 | 0.073 | | | 120 | 0.50 | 0.00 | 0.50 | 0.00 | 1.00 | 0.50 | 0.00 | 0.00 | 0.00 | 0.00 |
| Female 2 | 0.173 | | | 123 | 0.00 | 0.00 | 0.50 | 0.00 | 0.50 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Female 3 | 0.000 | | | 89 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 |
| Female 4 | 0.254 | | | 113 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 |

Find optimal contributions

| | |
|-----------------------------|--------|
| xG | 131.55 |
| Inbreeding weight λ | 30.0 |
| xAx | 0.200 |
| crit | 125.55 |

| | | |
|-----------|--------|-------|
| ngens | 400 | |
| λ | xG | xAx |
| 0.00 | 136.50 | 0.375 |
| -8.77 | 135.58 | 0.314 |
| -18.10 | 134.11 | 0.251 |
| -28.69 | 131.86 | 0.205 |
| -41.65 | 129.68 | 0.173 |
| -59.05 | 125.97 | 0.136 |
| -85.54 | 122.51 | 0.112 |
| -134.74 | 119.51 | 0.097 |
| -272.16 | 116.86 | 0.090 |
| -621.29 | 114.39 | 0.088 |
| | 131.55 | 0.200 |

Draw Graph



Inbreeding

Larger weight on F → all sires selected

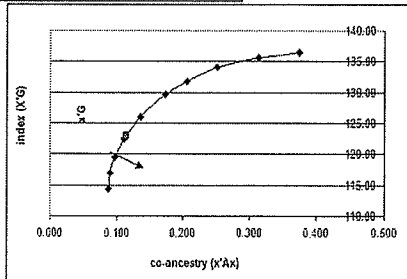
| X | | nmales | nfemales | G | | Relationships Matrix | | | | | | | | |
|----------|-------|--------|----------|-----|------|----------------------|------|------|------|------|------|------|------|--|
| Male 1 | 0.010 | 4 | 4 | 127 | 1.00 | 0.00 | 0.50 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 | 0.00 | |
| Male 2 | 0.168 | | | 122 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | |
| Male 3 | 0.235 | | | 160 | 0.50 | 0.00 | 1.00 | 0.00 | 0.50 | 0.50 | 0.00 | 0.00 | 0.00 | |
| Male 4 | 0.087 | | | 109 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | |
| Female 1 | 0.081 | | | 120 | 0.50 | 0.00 | 0.50 | 0.00 | 1.00 | 0.50 | 0.00 | 0.00 | 0.00 | |
| Female 2 | 0.124 | | | 123 | 0.00 | 0.00 | 0.50 | 0.00 | 0.50 | 1.00 | 0.00 | 0.00 | 0.00 | |
| Female 3 | 0.072 | | | 89 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | 0.00 | |
| Female 4 | 0.222 | | | 113 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 1.00 | 0.00 | |

Find optimal contributions

| | |
|-----------------------------|--------|
| xG | 123.09 |
| Inbreeding weight λ | 80.0 |
| xAx | 0.115 |
| crit | 113.88 |

| | | |
|-----------|--------|-------|
| ngens | 400 | |
| λ | xG | xAx |
| 0.00 | 136.50 | 0.375 |
| -8.77 | 135.58 | 0.314 |
| -18.10 | 134.11 | 0.251 |
| -28.69 | 131.86 | 0.205 |
| -41.65 | 129.68 | 0.173 |
| -59.05 | 125.97 | 0.136 |
| -85.54 | 122.51 | 0.112 |
| -134.74 | 119.51 | 0.097 |
| -272.16 | 116.86 | 0.090 |
| -621.29 | 114.39 | 0.088 |
| | 123.09 | 0.115 |

Draw Graph



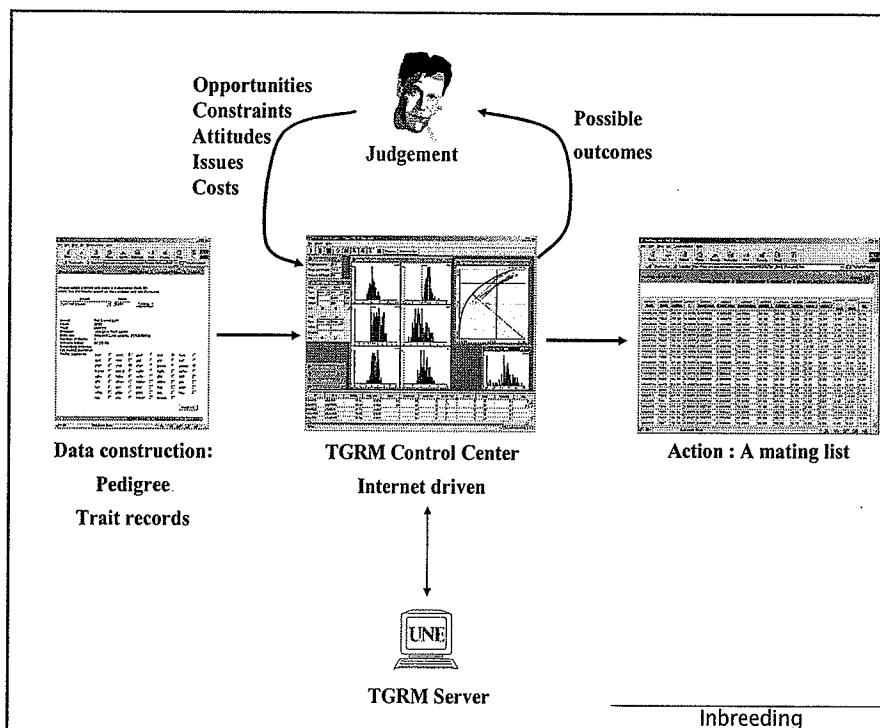
Inbreeding

Balancing merit and diversity

'Total Genetic Resource Management' (TGRM)

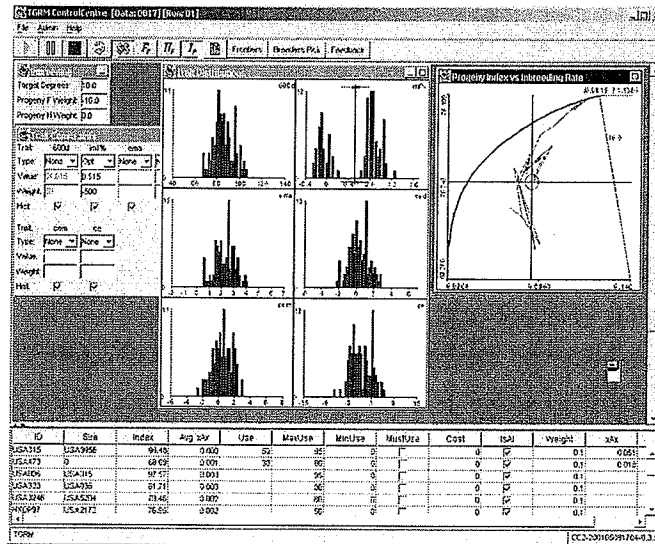
- ❖ a software program (not free)
- ❖ simultaneously determines which animals to select for breeding, and how these animals should be mated to each other 'mate selection'
- ❖ balances genetic merit & *f*, but also handles logistical and other constraints
- ❖ driven by an evolutionary algorithm

Inbreeding



Inbreeding

TGRM interface



Inbreeding

Mate selection index

A genetic algorithm is used to maximise an objective function, referred to as the mate selection index (MSI)

$$MSI = x'G - b_1 \frac{x'Ax}{2} - b_2 F - b_3 \text{cost}$$

Where

- ❖ x is a vector of contributions from candidates
- ❖ G is a vector of genetic merit
- ❖ x'G is the mean genetic merit of progeny
- ❖ A is the numerator relationship matrix
- ❖ x'Ax/2 is the mean coancestry of the selected parents
- ❖ F is progeny inbreeding
- ❖ Cost is the cost implied by the mating program
- ❖ b are weights

Inbreeding

Summary and useful concepts

- ❖ Inbreeding is due to mating of relatives, and may have undesirable consequences
- ❖ The inbreeding coefficient is relative to some base population, and thus it is more useful to consider the rate of F rather than the absolute value
- ❖ Theories exist to balance rates of F and genetic gain

Inbreeding