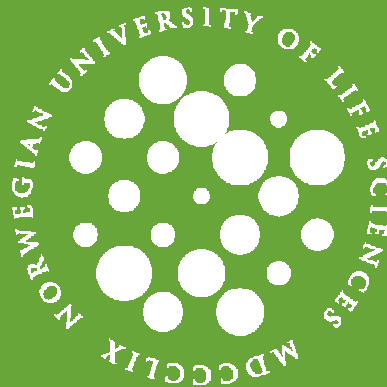


Genetic management of small populations: from theory to practice

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Introduction

- World population in 2050: 9 million
 - Requires ~50% increase in food production
 - few commercial breeds replace many locals
 - few commercial companies manage these commercial breeds
- Loss of genetic diversity
 - Both within and between breeds
 - Loss of historical values
 - Loss of typical landscapes
- High risk strategy
 - Holsteins are being crossed with red cattle now

Aim of genetic conservation :

- Maintain within and across breed diversity
 - Within breeds (management of 1 population)
 - Across breeds (management of several pops)

Aim of talk:

- Review methods for conservation
- Strategy: make local breeds profitable

Principles of the management of genetic variation

- $V_{gt} = (1 - F_t)Vg_0 \Rightarrow$ need control of F or ΔF
- $F_t = C_{t-1} \Rightarrow$ need control of Coancest.
- $C_t = \frac{1}{2}\bar{A}_t \Rightarrow$ need control of \bar{A}
- $A_{ij} = \frac{1}{4}(A_{S_i S_j} + A_{S_i D_j} + A_{D_i S_j} + A_{D_i D_j})$
- \bar{A} equals average relationship of parents
 - Weighted by number of offspring
 - Including self relationships
- Control of \bar{A} controls F_t and V_{gt}

Optimum Contribution Selection

(Meuwissen, '97)

- Maximises ΔG
- While restricting

$$\bar{A}_t = 2C_t = 2[C_{t-1} + \Delta F(1 - C_{t-1})]$$

- Maximises genetic gain and controls ΔF

Minimisation of inbreeding

- Minimise \bar{A}
- Flexible:
 - May correct previous unequal contributions
 - implementable in practical schemes

Mating

- Less important than selection
 - Random mating is generally quite OK
- Avoid mating of close relatives
 - Avoids highly inbred offspring
 - Delays the inbreeding; does not affect ΔF
- Factorial mating
 - Make maternal HS instead of FS families
 - Makes contributions of sires and dams less related

The critical effective population size?

- Or: what rate of inbreeding is acceptable?
- Approaches to assess $N_{e_{crit}}$:
 - Mutation meltdown : survival over 500 generations:
 - $N_{e_{crit}} \sim 500$ (Lynch et al., 1995)
 - Balancing natural selection vs. inbr. depression
 - $50 < N_{e_{crit}} < 100$ (Meuwissen & Woolliams, 1994)
 - Balancing 'old' vs. 'new' inbreeding
 - 'New F' is first 20 gens., (Hinrichs et al., 2007)
 - 'New F' < 10% if $N_e \sim 100$
 - Long term selection experiments: $N_e = 100$ is OK

The critical effective population size?

Conclusions:

- Not ONE answer possible
- Inbreeding is a chance process
- But consensus : $50 < Ne_{crit} < 100$
 - To be on safe side: $Ne_{crit} \sim 100$

Use of other breed to reduce ΔF

1. Population in bottleneck

- Use as much as possible related breed
- Stop using 2nd breed as soon as possible
- OR: create 'meta-population' from the two breeds

(Bennewitz et al., 2008)

2. Increase competitiveness

- Introgress desirable traits
 - Use genetic markers
 - Use phenotypes to maintain traits
- Merge with other related breeds
 - Try to have one breeding goal

Integrating live and cryo-conservation

1. Cryo-back-up

- In case of natural disaster
 - Need embryos and semen to restore population
- In case of genetic problems
 - Genetic defect can be removed by selection
 - Cryo stored animals may have higher EBV
 - Inbreeding depression problem:
 - Use Cryo stored animals to reduce general F

Integrating live and cryo-conservation

2. Cryo-aided live conservation

- Prolong generation interval by storing embryos:
 - more animals /gen
 - $L=1 \Rightarrow L=25$: 25 times bigger N_e
- Prolong L by storing semen:
 - Infinite use of founder semen: $\Delta F = 0$
 - Finite storage time: generation interval effect as before
 - Large number of founder males to keep F low

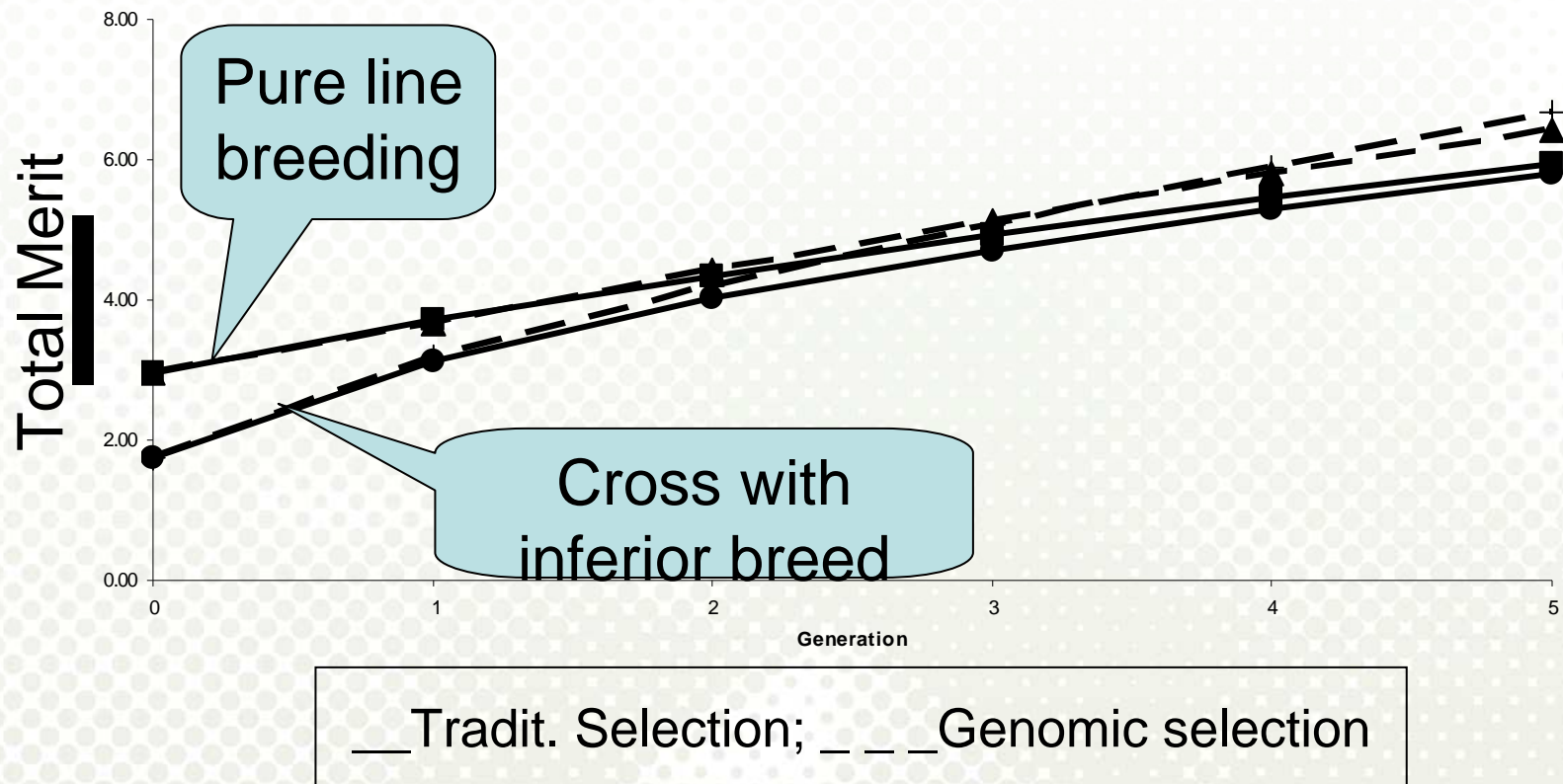
Rotational breeding schemes

- Do not require pedigree recording
 - E.g. several sire lines
 - Mated to the commercial dams in turn
 - Keep inbreeding of commercial animals low
 - Requires big population
 - Need several sire lines
 - Rotate individual cryo-conserved sires over time
- (Colleau & Avon, '08)

Get trait from conserved into commercial line

- Introgression scheme: continuous backcross
 - Use markers to maintain desirable trait
 - Successful QTL detection
 - Fine mapping of QTL
 - Introgression
 - Simultaneous detection and introgression (Yazdi et al.'08)
 - Use phenotype to maintain desirable trait
 - More difficult to maintain the trait
- Crossbreed, select over cross and purebred
 - Crossbreeding increases the variation

Upgrading using 'inferior' breeds



High density genotyping: SNP chips

$$E(\mathbf{X}\mathbf{X}') = \mathbf{A} * (1 - Hom) + \mathbf{1}\mathbf{1}' * Hom$$

(Habier et al., 2007)

- No pedigree recording required:
 - Can estimate accurate **A** matrix from SNPs
 - At least linear function of **A**
- Accurate **A** matrix of breeds
 - Across and within breed **A** matrix

High density SNP chips (cont.)

- Which chromosomal regions are related
- Can we pick interesting traits from conserved breeds by only genotyping them?
 - Requires across breed LD between SNPs and QTL
 - E.g., suppose we know:
 - Gene J may be involved in 'disease resistance'
 - Breed A has a very different haplotype for gene J
 - investigate 'disease resistance' effect of the gene J haplotype of breed A

SNP chip : estimate historical N_e

$$LD = R^2 = \frac{1}{4N_e c + 1}$$

- So linear regression of $1/R^2$ on c gives N_e
- estimate N_e at different times in the past:
 - look at different distances, c (Tenesa et al., '07)
 - Detect bottle necks
- More accurate estimates of N_e :
 - Model multi-locus LD as function of past N_e
- Model LD as function of Time since breeds splitted from each other => separation time

Conclusions

- Try to make endangered breed profitable
- Try to achieve $N_e=100$, $\Delta F=0.5\%$
- OC selection can:
 - Restrict ΔF , maximise ΔG
 - Requires **A** matrix (pedigree or dense SNPs chips)
- In absense of A (pedigree)
 - Rotational breeding schemes
- Selection more important than mating

Conclusions (cont.)

- Traits from inferior breeds can be used
 - Genomic selection makes it profitable
- High density SNP chips
 - Can make pedigree recording redundant
 - May reveal historical structure of the population