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

- $V_{gt}=(1-F_t)Vg_0$ => need control of F or ΔF
- $F_t = C_{t-1}$ => need control of Coancest.
- $C_t = \frac{1}{2}\bar{A}_t$ => need control of $\bar{A}$
- $A_{ij} = \frac{1}{4}(A_{S_iS_j} + A_{S_iD_j} + A_{D_iS_j} + A_{D_iD_j})$

- $\bar{A}$ 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 Ne_{crit}:
  - Mutation meltdown : survival over 500 generations:
    - Ne_{crit}~500 (Lynch et al., 1995)
  - Balancing natural selection vs. inbr. depression
    - $50<Ne_{crit}<100$ (Meuwissen & Woolliams, 1994)
  - Balancing ’old’ vs. ’new’ inbreeding
    - ’New F’ is first 20 gens., (Hinrichs et al., 2007)
    - ’New F’ <10% if Ne~100
  - Long term selection experiments: Ne=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 => L=25 : 25 times bigger Ne
- 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

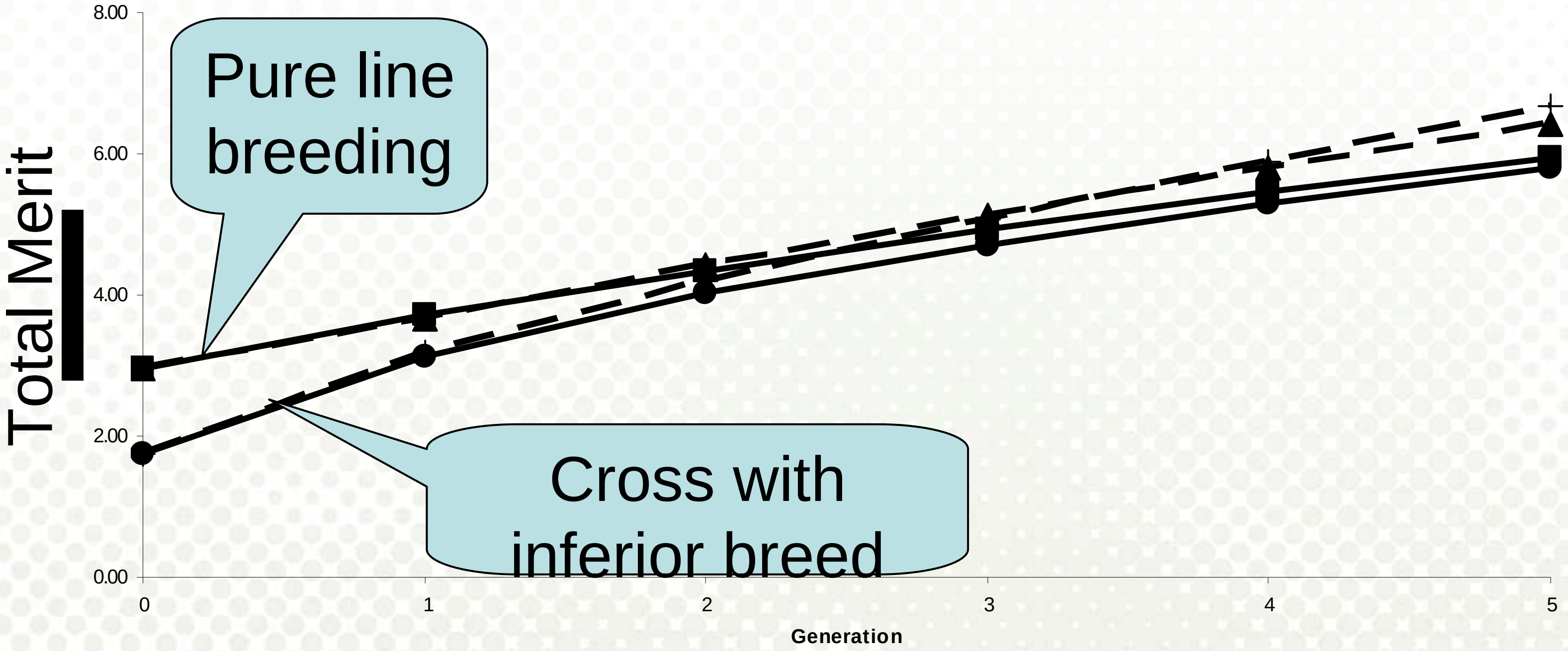
- Do not require pedigree recording
- E.g. several sire lines
  - – Mated to the commercial dams in turn
  - – Keep inbreeding of commercial animals low
  - – Requires big population
    - Need several sire lines
  - – Rotate individual cryo-conserved sires over time

(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



__Tradit. Selection; _ _ _Genomic selection

Odegard et al. 2008

High density genotyping: SNP chips

$$E(\mathbf{XX}') = \mathbf{A} * (1 - Hom) \quad + \quad \mathbf{11}' * Hom$$

(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 Ne

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

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

Conclusions

- Try to make endangered breed profitable
- Try to achieve Ne=100, ΔF=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