Genetic management of small populations

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Animal Breeding & Genomics Centre

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Agrobiodiversity

- **Worth to conserve**
  - Cultural Heritage
  - Rare breeds harbour unique genetic variation
  - Convention on Biological Diversity (Rio)
- **Conservation Genetics similar to wild biodiversity**

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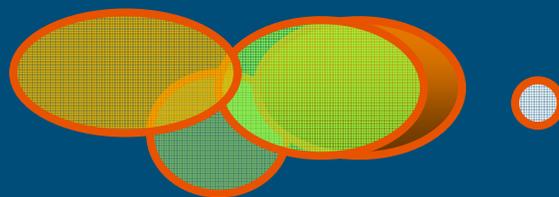WAGENINGEN UR

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What to do?

- Genetic management
- Conserve different populations (=breeds)
  - Prioritize populations for conservation
- Manage diversity within populations
  - Maximize N_e

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Prioritizing populations for conservation

- Maximise total genetic variation in set of conserved populations

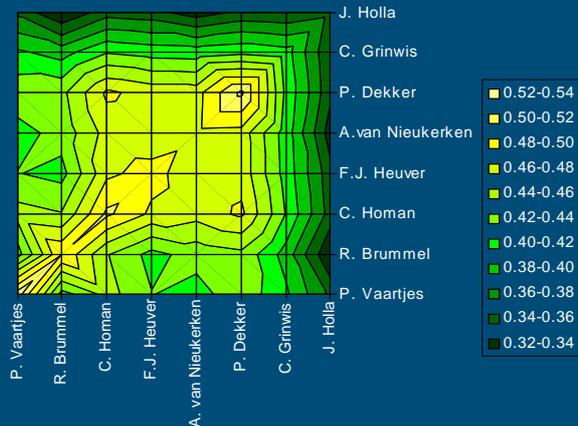- Quantitative genetics: Variance-Covariance Matrix

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Total genetic variance

- $G = A\sigma^2_A$
  - G = variance covariance matrix
  - A = relationship matrix
  - $\sigma^2_{A \ =\ Additive\ variance}$
- Infinitesimal model
  - A is the same for all traits
- Total genetic variance of all traits can be evaluated by the relationship matrix

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Marker Estimated Kinships (Eding)

- f_{ij} = probability that an allele of i is identical by descent (IBD) to an allele of j
- Pedigree
  - Rarely known for breeds
- DNA (e.g. micro-satellites)
  - Correction needed for alleles similar in state but not IBD
  - $S_{ij} = f_{ij} + (1-f_{ij})\, s_L$
  - S_{ij} = known
  - f_{ij} = constant over loci, different over populations
  - s_L = constant over populations, different over loci
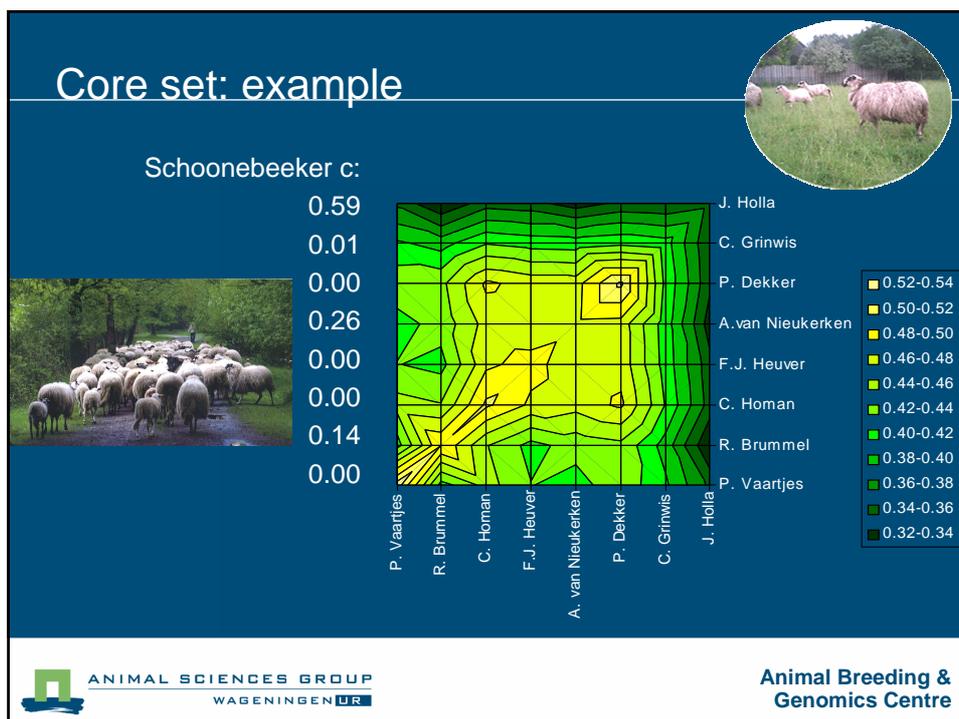 - can be solved in a set of equations

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Kinship matrix F: example

- Schoonebeeker: 8 herds typed for 20 micro-satellites across genome
- 4 herds high f
- 1 herd low f

| | 0.52-0.54 |
| 0.50-0.52 |
| 0.48-0.50 |
| 0.46-0.48 |
| 0.44-0.46 |
| 0.42-0.44 |
| 0.40-0.42 |
| 0.38-0.40 |
| 0.36-0.38 |
| 0.34-0.36 |
| 0.32-0.34 |

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P. Vaartjes, R. Brummel, C. Homan, F.J. Heuver, A. van Nieukerken, P. Dekker, C. Grinwis, J. Holla

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From kinship to genetic diversity

- **Genetic variance in set of populations**
  - $1 - \overline{f} \approx \sigma^2_G$
  - If populations contribute differentially:
    $\overline{f}(\text{set}) = c'Fc$
    - c = contribution vector summing to 1

- **Maximum genetic variation in set**
  - Minimizing f maximises genetic diversity
  - $c_{min} = (F^{-1}1_n)/(1_n'F^{-1}1_n)$ = core set

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Core set: example

Schoonebeeker c:

0.59
0.01
0.00
0.26
0.00
0.00
0.14
0.00

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C. Grinwis
P. Dekker
A. van Nieukerken
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- 0.52-0.54
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- 0.38-0.40
- 0.36-0.38
- 0.34-0.36
- 0.32-0.34

P. Vaartjes · R. Brummel · C. Homan · F.J. Heuver · A. van Nieukerken · P. Dekker · C. Grinwis · J. Holla

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Prioritizing populations for conservation

- Priority according to contribution to core set

  or

- Safe + 1 set
  - Safe set: breeds that are and will not be endangered
    - e.g Holstein, Texelaar etc.
  - Calculate diversity safe set
  - Add 1 breed and recalculate diversity
  - Difference is additional diversity
  - Repeat for all non-safe breeds
  - Rank breeds according to their additional diversity

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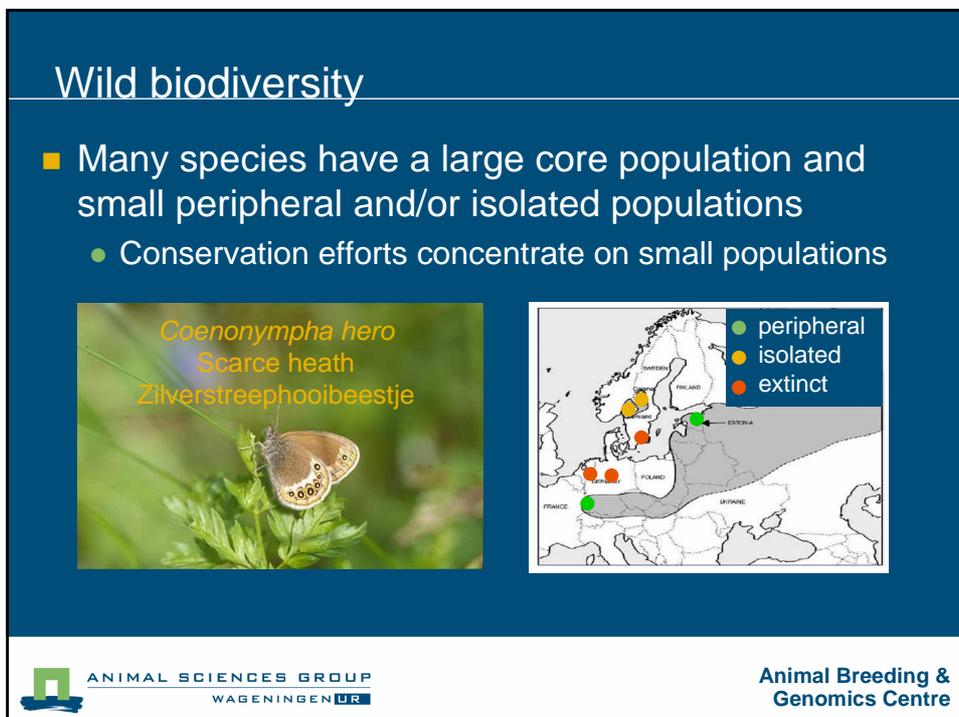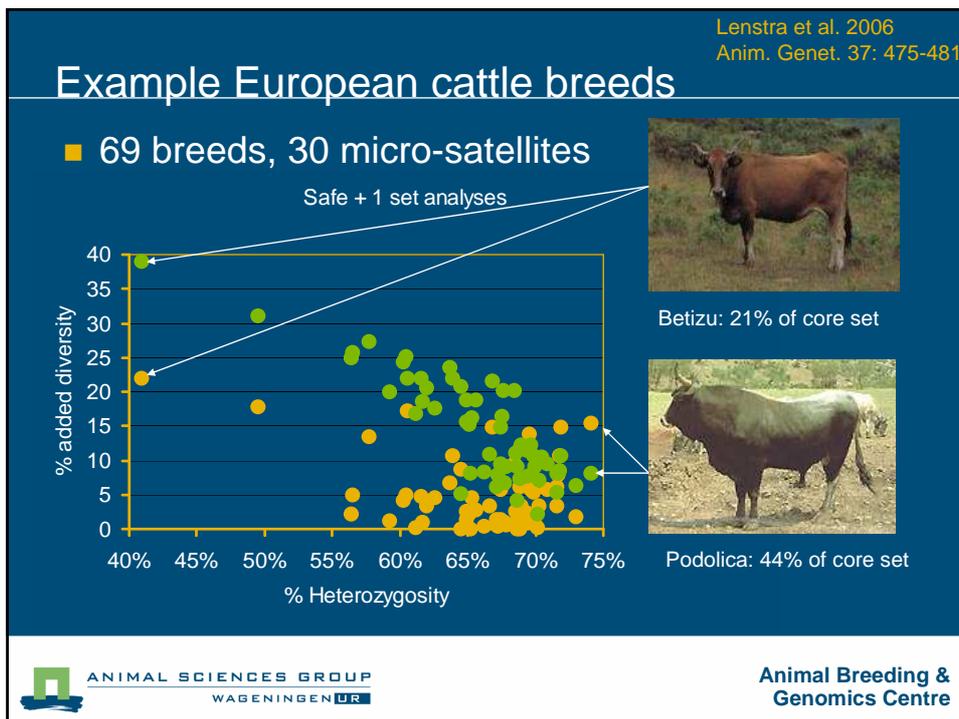**Animal Breeding &
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Example European cattle breeds (Engelsma 2005)

- 69 breeds typed for 30 micro-satellites

- Core set:
  - 22% Chianina (I)
  - 19% German Shorthorn (D)
  - 18% Normand (F)
  - 15% Red Danish (DK)
  - 10% Friesian-Holland (NL)
  - 8% Guernsey (GB)
  - 8% 6 other breeds

- Safe +1
  - 22% Betizu (E)
  - 19% Mallorquina (E)
  - 18% German Shorthorn (D)
  - 15% Podolica (I)
  - 10% Chianina (I)
  - etc.
- Safe set > 1 million
  - Holstein, Limousin Simmental etc.

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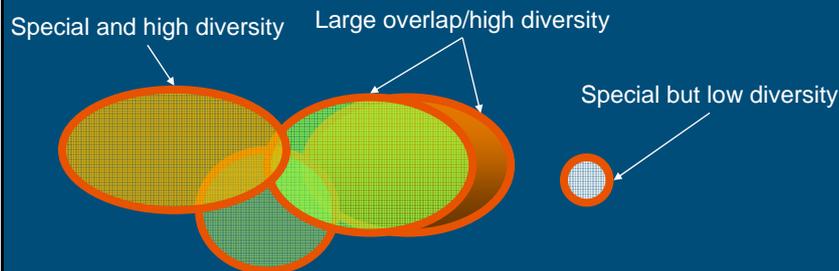
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Quantitative and Molecular genetics

- Molecular Geneticists: allelic diversity
  - Heterozygosity, Genetic distance
  - Weitzman
- Quantitative Geneticists: Additive variance
  - Eding
  - Takes within population variation into account
  - Takes variation in similarity between loci into account
  - Connects neutral genetic variance with additive variance of traits

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Lenstra et al. 2006
Anim. Genet. 37: 475-481

Example European cattle breeds

- 69 breeds, 30 micro-satellites

Safe + 1 set analyses

Betizu: 21% of core set

Podolica: 44% of core set

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Wild biodiversity

- Many species have a large core population and small peripheral and/or isolated populations
  - Conservation efforts concentrate on small populations

Coenonympha hero
Scarce heath
Zilverstreephooibeestje

- peripheral
- isolated
- extinct

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Summing up

Special and high diversity   Large overlap/high diversity

Special but low diversity

- **Marker estimated Kinships (Eding method)**
  - Weighs populations according to both within and across population diversity
  - Safe + 1 set analysis for prioritizing
  - Connects neutral variation to adaptive variation

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Managing diversity within populations

- **Small populations loose diversity**
  - $\sigma^2_{A,t}/\sigma^2_{A,0} = 1 - F$
  - $\Delta F = 1/2N_E$
  - N_E depends on population size, but also on mating structure
- **Maximizing diversity**
  - Maximizing N_E (=Minimizing ΔF)
  - Enlarge population size
  - Minimize relationship (=kinship, coancestry)

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Minimizing coancestry / inbreeding

- c = contribution each parent to next generation

$$c'Ac$$

- With overlapping generations

$$r_1^2 c'Ac + 2r_1 c'AJr_2 + r_2'\overline{A_{22}}r_2$$

- However, 50% female, 50% male

$$Q'c = \begin{bmatrix} \dfrac{1}{2} & \dfrac{1}{2} \end{bmatrix}$$

- Function

$$H = r_1^2 c'Ac + 2r_1 c'AJr_2 + r_2'\overline{A_{22}}r_2 - \lambda\,(c'Q - s')$$

- 1ste derivative = zero -> minimum coancestry

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Solution

$$c = \frac{A^{-1}Q\left(2r_1\left(Q'A^{-1}Q\right)^{-1}\left(r_1 s + Q'Jr_2\right)\right)}{2r_1^2} + \frac{Jr_2}{r_1}$$

- c = list of individual contributions to next year cohort
- A = relationship matrix
- Software programme available

  GENCONT

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Advantages GENCONT

- Gives best solution
- Flexible
  - Adjusts solution each generation to optimum
  - Optional: equal or variable contribution of selected parents, (possible per sexe)
  - Fixed contribution of particular parent possible
  - Fixed number of parents possible
  - Can also optimise selection at the same time

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Example: Stichting Ark: Galloway herd in Millingerwaard

- About 75 animals
- Known pedigree
- 2001: 21 calves of 7 fathers
- 2002 17 calves of 4 fathers

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Solution

A-matrix

Gencont
- 10 bulls
- 25 cows
- Equal contributions
- F = 0.87%

All animals
- F = 3.60%

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Disadvantages GENCONT

- A-matrix needed
  - Pedigree required
  - Or DNA typing
- Control over mating required
  - Many populations animals decide themselves
  - Not all matings successful
- Herd structure not taken into account
  - Animals of 1 herd (zoo, populations) may not be used in another herd
- Complex
  - Specialist needed for operation
  - Difficult to explain

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A matrix from DNA

Oliehoek et al. 2006
Genetics 173: 483-496

- Different estimators are around
- New estimators based on MEK developed
- Precision depends on population structure
  - Panmictic -> Lynch & Ritland
  - Structured (e.g. herds) -> WEDS
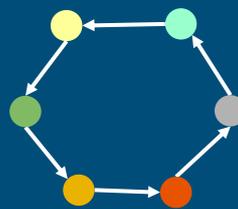- Wrong estimator -> decrease in genetic diversity
- Use > 20 markers

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Simpler solution: Rotational mating schemes
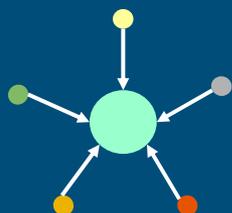
Pool -
sire lines
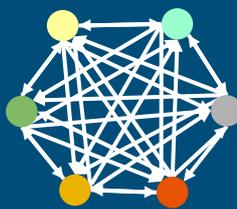
Postponed
inbreeding

Ram circle

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Rotational mating schemes 1: Sire lines

Pool of commercial females crossed with sire lines

Year 1   Year 2   Year 6

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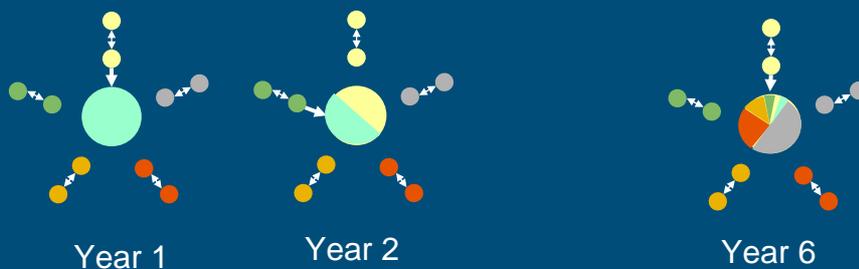
Rotational mating scheme 2 postponed inbreeding

Each flock provides rams for the next flock

Year 1   Year 2   Year 5

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Rotational mating scheme 3 ram circle

Each flock provides rams for the next flock

Year 1   Year 2   Year 3

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Kempisch Heideschaap

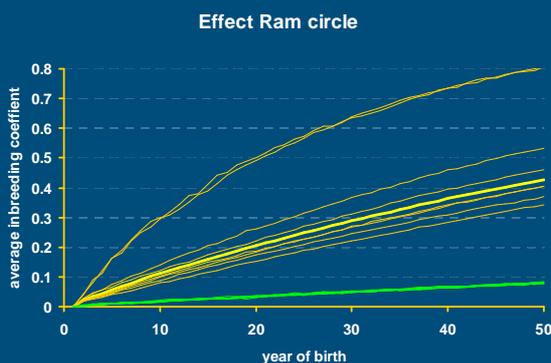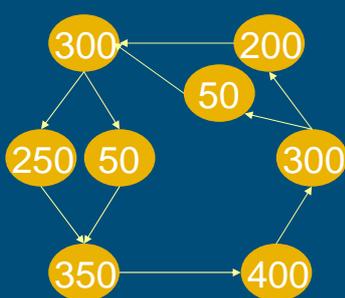■ 8 flocks varying from 50 to 400 sheep

50
50
200
250
300
300
350
400

■ Grazing on poor soils in S Netherlands
■ Replaced by Texel breed after introduction of artificial fertilizers

■Rams generally provided by own herd
■No pedigree records

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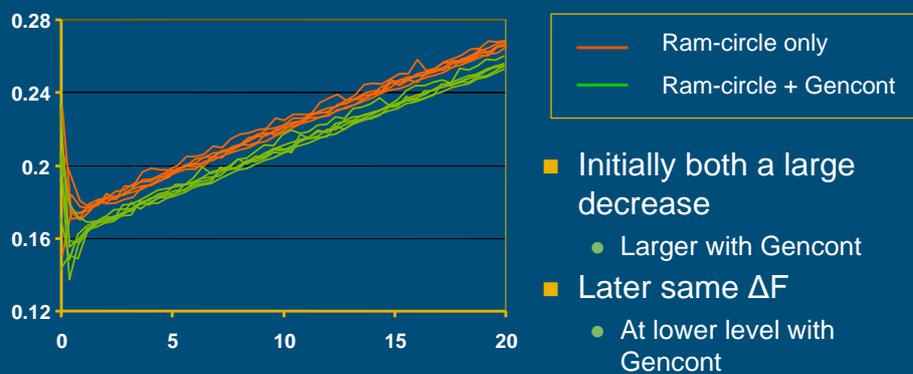## Breeding programme options

- No special program
  - Each breeder decides individually
- Optimal contribution
  - GENCONT
- Inbreeding restriction scheme
  - Ram circle
- Computer simulation
  - Herd, age structure, mating patterns etc. from 2004
  - A-matrix marker estimated

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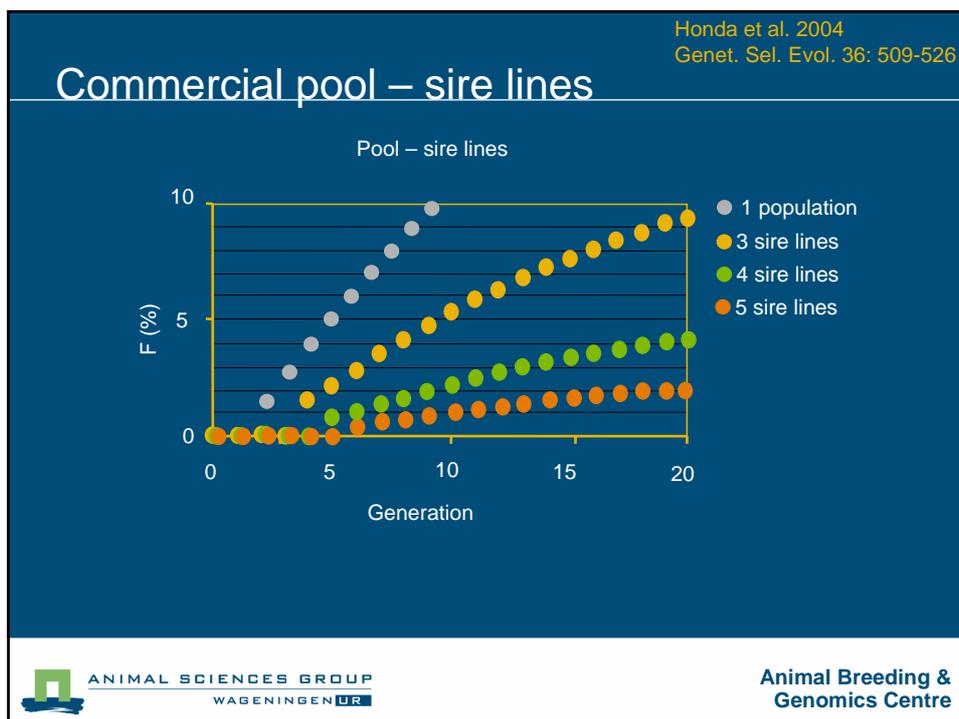
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No inbreeding restriction vs. Ram–circle

Effect Ram circle

300 ← 200
50
250 50   300
350 → 400

ΔF (within herds) : 1.5 – 4.3% vs. 0.2 – 0.4%

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Combining gencont and ram-circle

Legend:
- Ram-circle only
- Ram-circle + Gencont

- Initially both a large decrease
  - Larger with Gencont
- Later same ΔF
  - At lower level with Gencont

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Results with estimated A-matrix

ΔF	No special programme	Gencont
	1.5% (1.0% - 4.3%)	-6.7% (-9.2 - -0.4%)

	Ram-circle	Gencont + Ram-circle
Year 1	-3.5% (-11.1% - 4.0%)	-8.6% (-13.5% - 1.1%)
Year 4	0.2% (0.1% - 0.4%)	0.2% (0.1% - 0.4%)

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Commercial pool – sire lines

Pool – sire lines

- 1 population
- 3 sire lines
- 4 sire lines
- 5 sire lines

F (%) vs Generation

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Which genetic management strategy?

- Optimal contribution (Gencont) most effective
  - Not always possible (complexity)
- All three rotational schemes are effective in reducing inbreeding rates
  - Exact comparison never made
- Choise can be guided by practical considerations
  - Control over mating
  - Possibility of exchange of individuals between subpopulations

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Wild biodiversity

- No control over mating
- Sometimes control over interpopulation movement
- Reintroduction
  - From which population(s)?
  - Genetic diversity of introduced animals
- Supportive breeding
  - Manage inbreeding and diversity in breeding program
  - How? For example, release each year animals from different sire lines?

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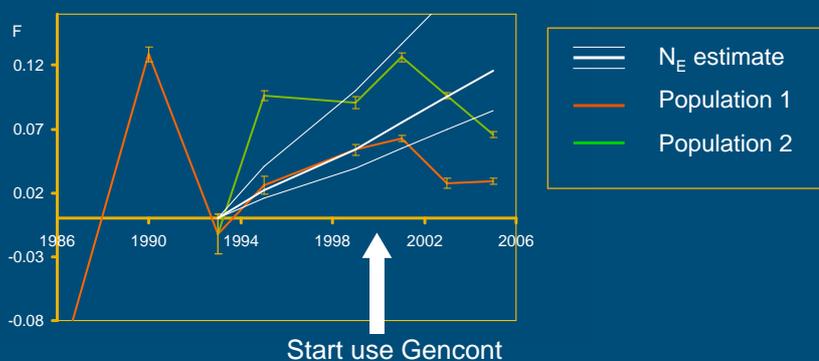**Animal Breeding & Genomics Centre**

Heck cattle

- Two populations SBB in SW-Netherlands
  - Regularly animals removed from populations
  - Relationships determined with micro-satellites
  - Gencont for advice for removing animals

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Results

F

0.12

0.07

0.02

-0.03

-0.08

1986 1990 1994 1998 2002 2006

N_E estimate

Population 1

Population 2

Start use Gencont

- Increase of F stopped after use of Gencont

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Conclusions

- Genetic management can be important for conservation
- Marker estimated kinships (Eding method) is the method of choice for prioritizing populations based on genetic diversity
- Optimal contribution maximises diversity within populations
- Rotational mating schemesgood alternative if optimal contribution not possible
- Conservation of wild biodiversity may benefit from these tools

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