

# Genetic diversity issues in animal populations in the genomic era

First chapter in the book:

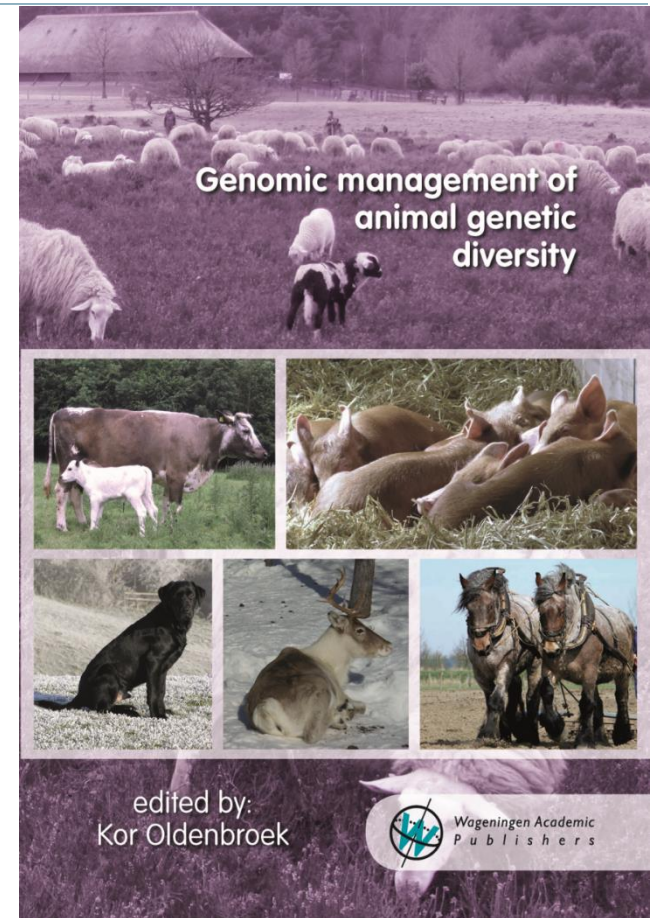
**"Genomic management of animal genetic diversity"**

Kor Oldenbroek



# Content of the presentation

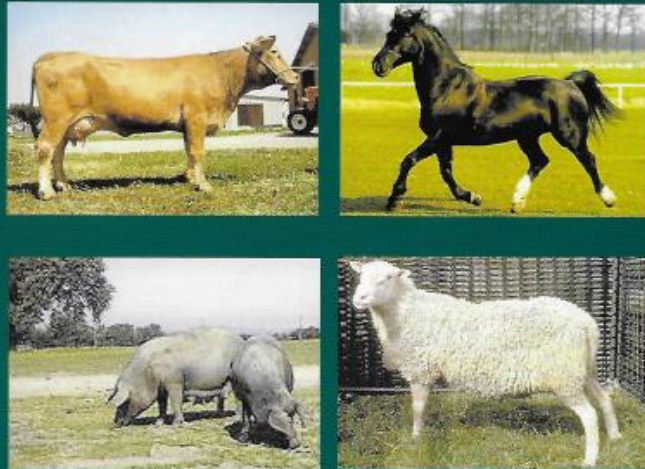
- Background of our new book
- Importance of genetic diversity
- Genomic opportunities and threats
- *In situ* and *ex situ* conservation
- Dutch examples of genomic research with breeds





# Population genetic tools to ...

## Genebanks and the conservation of farm animal genetic resources



J.K. Oldenbroek (ed.)

## Utilisation and conservation of farm animal genetic resources



edited by:  
Kor Oldenbroek



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Centre for Genetic Resources, the Netherlands

# Chapters in “Genomic management of animal genetic diversity”

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- Genetic diversity issues in animal populations in the genomic era: John Woolliams and Kor Oldenbroek
- Defining genetic diversity based on genomic tools: Jesús Fernández and Jörn Bennewitz
- Genomic diversity in the domestication process: Miika Tapio and Saber Qanbari
- Tracing domestication and selection in animal genomes: Saber Qanbari and Miika Tapio
- Management of genetic diversity including genomic selection in small *in vivo* populations: Theo Meuwissen and Kor Oldenbroek
- Management of cryo-collections with genomics tools: Peer Berg and Jack Windig
- Dog breeds: towards genomic management of populations with a high incidence of genetic defects: Tom Lewis and Jack Windig

# Definitions

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- **Genomics** is the detailed analysis of the DNA of an animal with high-throughput techniques (DNA-chips) from 10.000 SNPs (10k) > Whole Genome Scan (WGS)
- **Management** (in animal breeding) is: 1) the choice of the animals as parents for the next generation, 2) the choice of the sires and of dams for the individual matings and 3) the number of offspring each parent may produce
- **Genetic diversity** is the set of differences between species, breeds within species, and individuals within breeds expressed as a consequence of differences in their DNA

# Genetic diversity is important .....

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- Within a species and within a breed for **natural selection** that leads to adaptation to climate change, higher disease resistance and results in robust and fertile animals
- Between breeds for the choice of the right breed in the right livestock system and of efficient crossbreeding
- Within breeds it determines the efficiency of **artificial selection** and will diminish the occurrence of inbreeding effects: the expression of genetic defects and the decrease in health and fertility traits

# Role of breeds and definition of breeds

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## Emphasis on the conservation of breeds

On average, the genetic variance within a species =  
 $0.5 \times \text{variance between breeds} + 0.5 \times \text{variance within breeds}$

**> Conservation and use has two important aspects!**

## Definition of breeds:

A breed is a population of animals that, through selection and breeding, have come to resemble one another and pass those traits uniformly to their offspring

# Reasons for maintaining genetic diversity

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## **Between breeds (breeds are set aside):**

- In farm animal production intensification still takes place, started after World War II: leading to breeding of high input – high output breeds
- Role of species may change: e.g. sheep from wool > meat and horses from draught > sport
- Breeding programmes are expensive > mergers of breeding companies with loss of breeds or selection lines e.g. in pigs in 2000 25 Dutch lines; 2015 discussion about 5 or 3 lines for the future





# Reasons for maintaining genetic diversity

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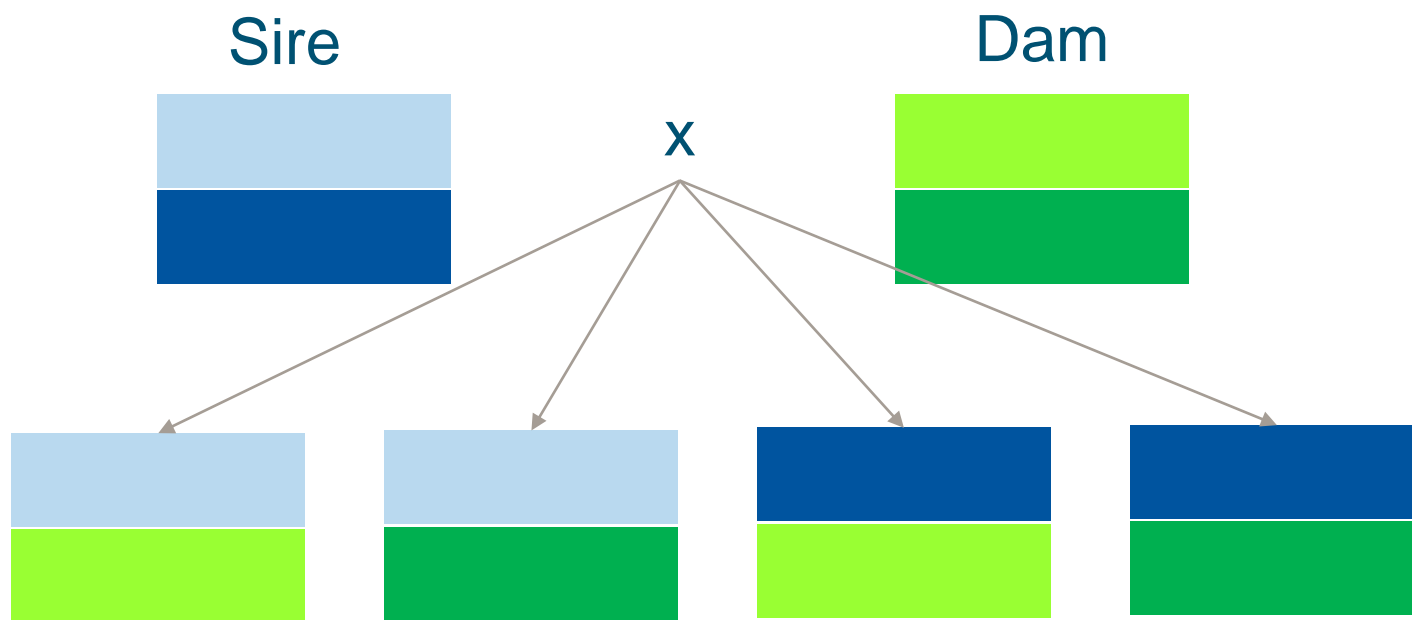
## **Within a breed (intense selection and drift):**

- To prevent inbreeding depression (decreased fitness)
- To maintain adaptability (large genetic variance needed)
- To preserve alleles that may be useful in the future
- To limit the occurrence of recessive genetic defects

# Genomics: determination and tracing of alleles by DNA analysis

## DNA

- Present in two copies (pairs of chromosomes)
- Always 50% submitted by the dam and 50% by the sire
- A random process (Mendelian sampling) determines the 50% DNA content



Genomics determines which part from the sire and which part from the dam!

# Opportunities of genomics

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- Improving pedigree quality (verifying pedigrees)
- More effective use of genetic variation to obtain genetic gain
- Better optimisation of genetic gain and inbreeding
- Identifying carriers of deleterious alleles to be purged
- Identifying carriers of interesting alleles or QTLs for introgression

# Conservation of genetic diversity: past and future

- **Past:** Decisions based on pedigree and phenotypic information

Genebank collections optimised based on pedigrees

- **Genomics era:** Decisions based on DNA information (SNPs en WGS) and phenotypic information

Genebank collections optimised based on DNA-relationships

Detection of interesting QTL's (link with QTL databases)

>> Compose core collection more efficient and is better characterised

# Animal QTL databases under development

Species	Number of QTL's	Publications	Traits
Cattle	81652	710	519
Pig	16033	557	627
Chicken	5683	250	335
Horse	1197	66	41
Sheep	1336	119	212



# Utilisation of genetic diversity: past and future

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- **Past:** BV estimated based on pedigree and phenotypic information

Selection based on estimated breeding values (EBV)

- **Genomics era:** BV estimated based on DNA information (SNPs)

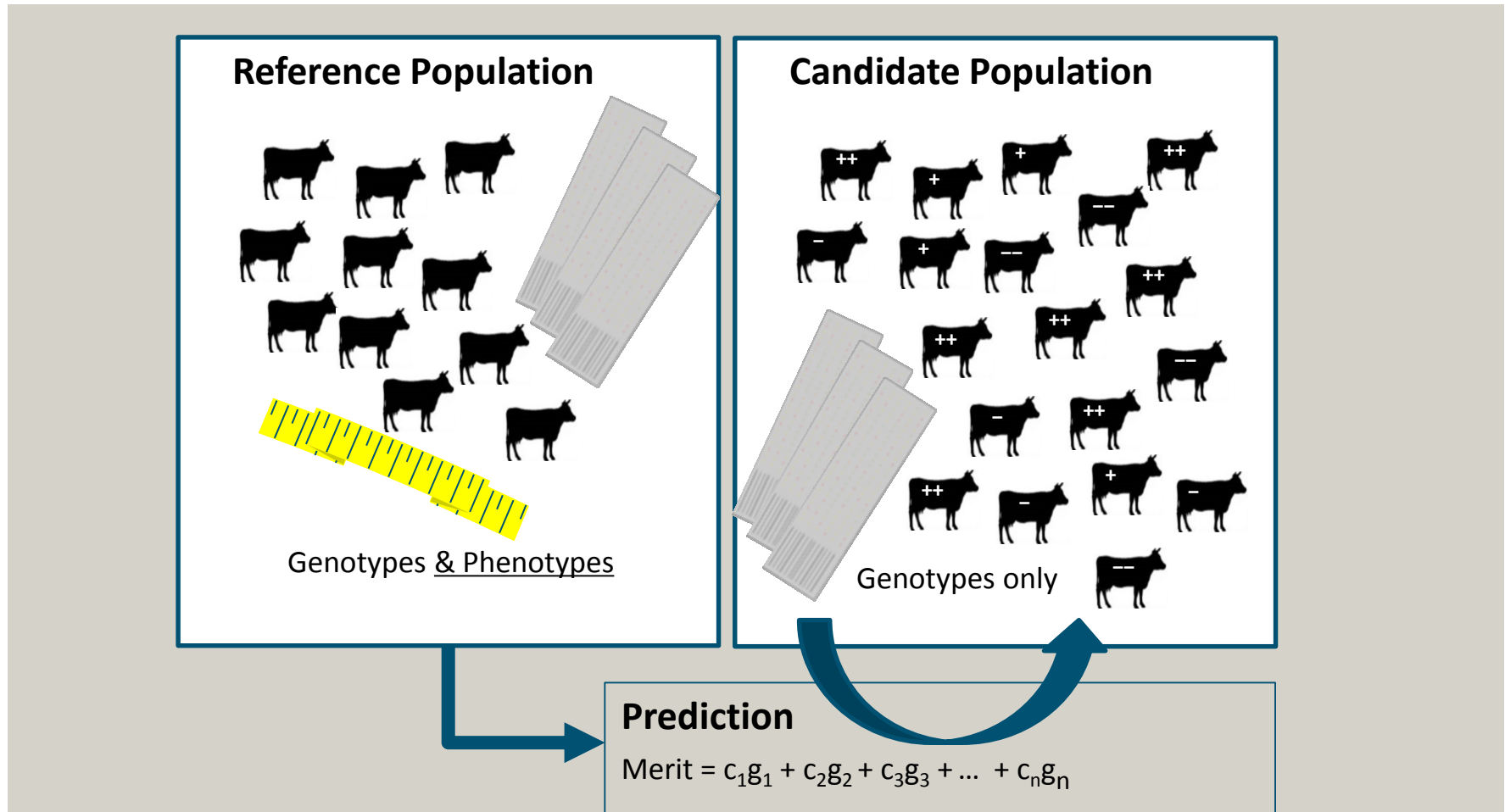
Phenotypic information still required!

Selection based on prediction formula with SNP-input

Detection of heterozygous carriers of recessive lethal alleles

>> Genomic selection possible at a young age of the animals

# Genomic selection



# Genetic defects: source OMIA,



- Genomics: carriers of recessive genetic defects can be detected

Species	Total defects	Monogenic	Mutation known
Dog	686	285	211
Horse	226	51	37
Cattle	502	231	132
Pig	247	66	31
Sheep	241	100	47
Goat	81	16	10
Chicken	212	129	43

# Threats of genomics to genetic diversity

- Concentration on mainstream breeds through GS
- Achieving a high accuracy in genomic selection: this accuracy depends of the relationship between the reference population (past parents) and the population of candidates (future parents) > less diversity > higher accuracy
- (Too) strict definitions of breeds based on SNP info
- Intense selection against genetic disorders

# Objectives conservation genetic diversity

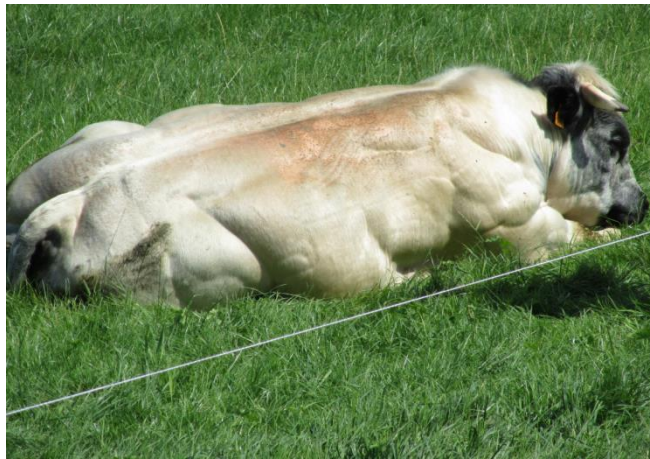


## **Sustainable use in the rural area:**

Economic potential

Social cultural role

Environmental services



## **Conservation of the flexibility of the genetic system: food security**

Risk of change  
environment

Risk of change in demand

Disasters (diseases)

Research and training



# Comparison of conservation methods (complementary)

## ■ *In situ* conservation

Active breeding

Used (short term)

Adaptation possible



## ■ *Ex situ* conservation

*in vivo*

Small numbers (zoos)

*in vitro*

Cryoconservation in  
liquid nitrogen



# Examples of use of rare breeds



## High quality products for niche markets:

- Breed specific products based on unique characteristics
- Produced with traditional techniques for regional markets with premium
- Collaboration between producers

# Ecological functions: nature management

- Herbivore species differ in grazing behaviour
- Breeds also and differ in robustness
- Large numbers required > great opportunity



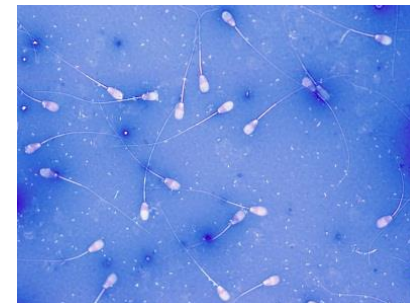
# Potential societal/cultural functions



- Attractive elements rural area (tourists)
- Cultural services (ceremonies, games)
- Sport or hobby function

# Purposes of Animal Gene Banks (*in vitro*)

- Preserve the present wealth of genetic diversity → Secure it for future generations
- To be able to recreate extinct breeds or breeding lines
- As a back-up in case genetic problems would occur
- To allow development of new lines or breeds
- To support *in situ* conservation
- For research and genetic characterisation purposes





# Aim of Dutch AnGR Gene Bank

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## *Long term*

- To safeguard all rare/native/endangered breeds of farm animals in the gene bank
- To promote and facilitate conservation of back-up samples of all (commercial) breeds in the gene bank

## *Short term*

- To support breeding programs of endangered breeds - by distribution of gene bank semen



# The CGN semen collection

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- Stored at two places: Wageningen – Utrecht (50 kms)
- Cattle: > 1960; >1990 unproven bulls; selected bulls from native breeds sampled at the farm (strict conditions)
- Pigs: 2001 16 different lines from industry; 5 > 3 in use now!
- Horses: stallions from native breeds (>1960)
- Poultry: semen from 20 native breeds collected at CGN
- Sheep and goat: collected at farms or at slaughter

# Semen collection CGN 2016

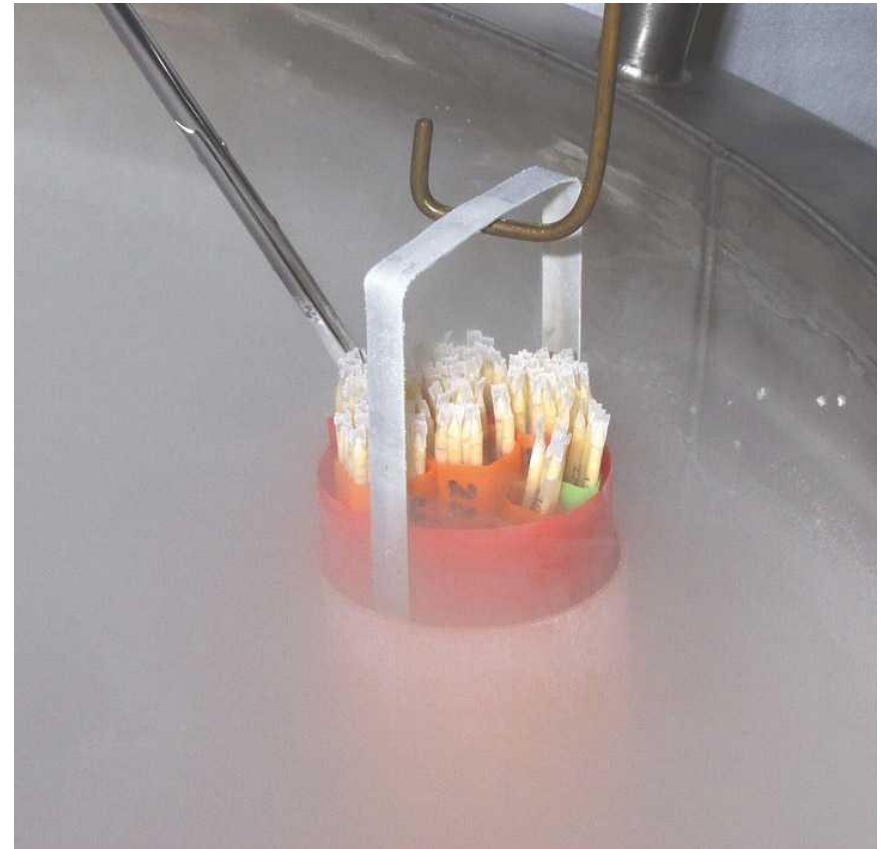
Species	# Breeds	# Males per breed	# Doses
Cattle	18	1 – 5,223	239,793
Sheep	10	8 – 71	31,154
Goat	5	5 – 33	6,590
Horse	9	1 – 41	3,307
Pig	28	1 – 56	20,464
Chicken	31	1 – 20	18,828
Duck	3	14 – 34	1,588
Dog	5	1 – 8	410
Rabbit	8	3-12	1,957

# Conservation of breeds within species

## Core collection per breed:

To be able to reconstitute a breed with semen only with 50 sires per breed

- Doses of semen: species dependent (Breeding success; litter size). It varies per breed from 600 (pigs and poultry) up to 5000 (sheep and goats)



# Genomics example for background of a unique trait

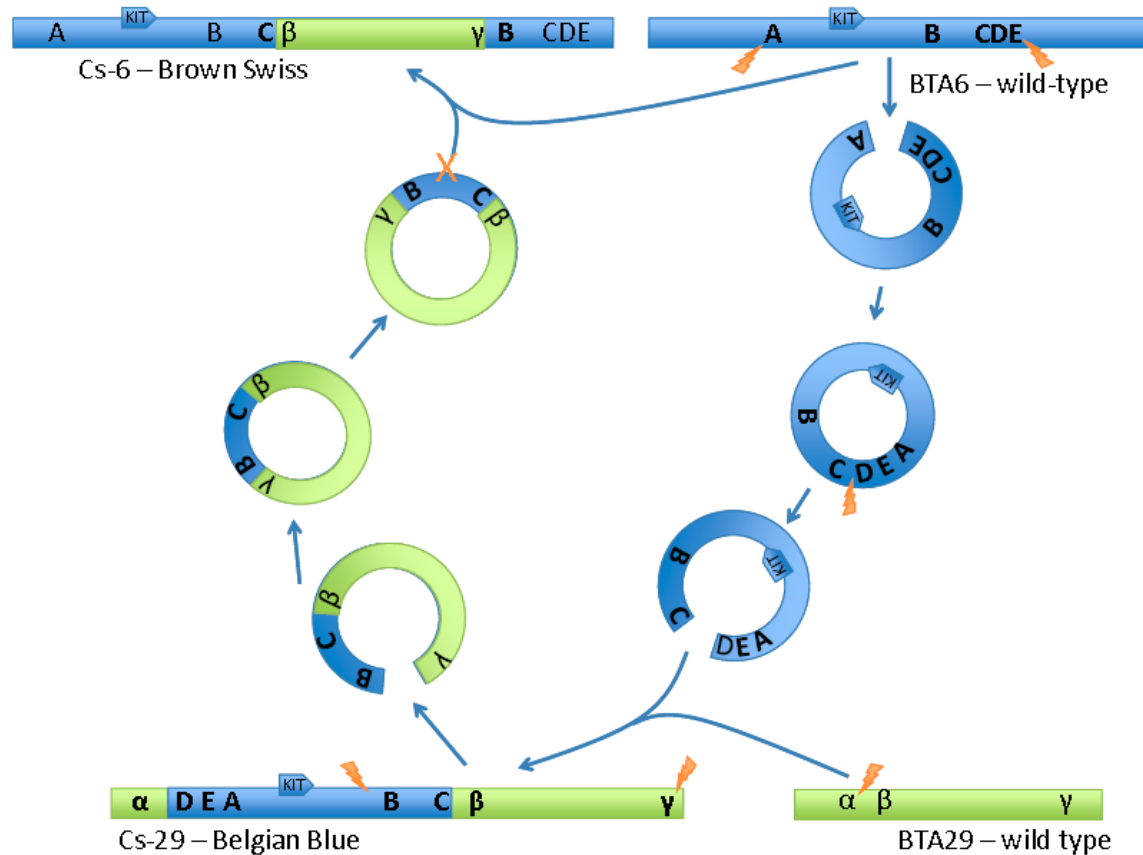
## *Color sided cattle*

- Locus for spotted is located on chromosome 6
- Long ago: during meiosis part of chromosome 6 created a circle and was incorporated (other sequence) in chromosome 29
- Color sided locus is on chromosome 29
- Epistasis with spotted
- WW = nearly white
- W/- = color sided
- -/- = spotted

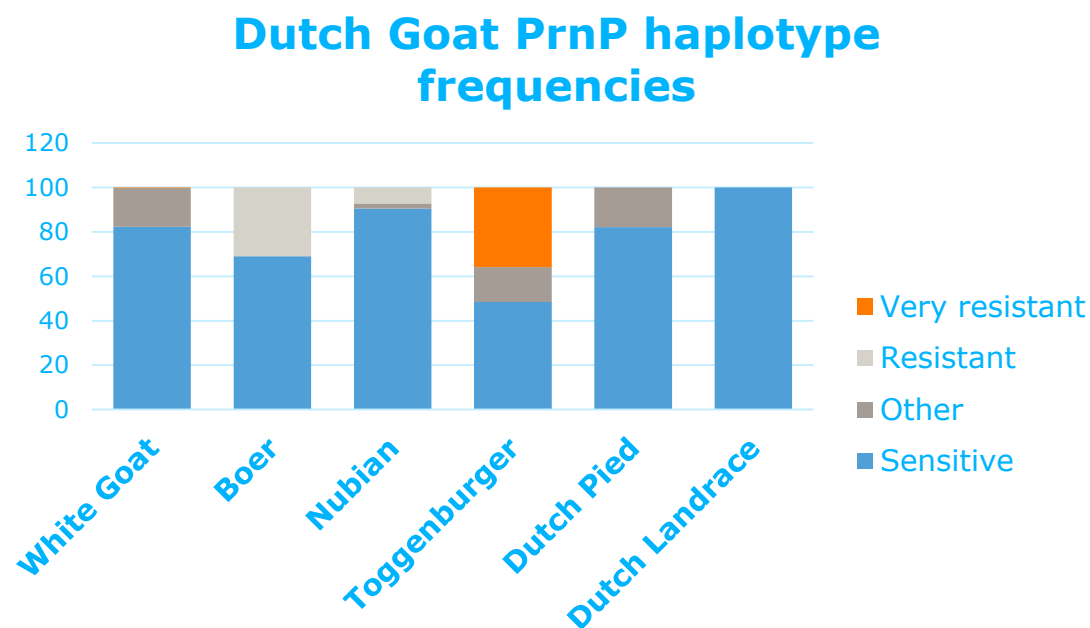




# Recombination of circles between different chromosomes, Nature (2010)



# Positive characteristic for introgression: PrnP haplotypes (scrapie resistance) in Dutch goats



Modified from Windig et al. 2016

# History of the Dutch Red Friesian Cattle breed

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- Herdbook established 1879
- Bottleneck in 1990 ( $n < 20$ )
- Genebank sires 1960-1970
- Regenerated in 25 years
- > 600 females; > 50 sires



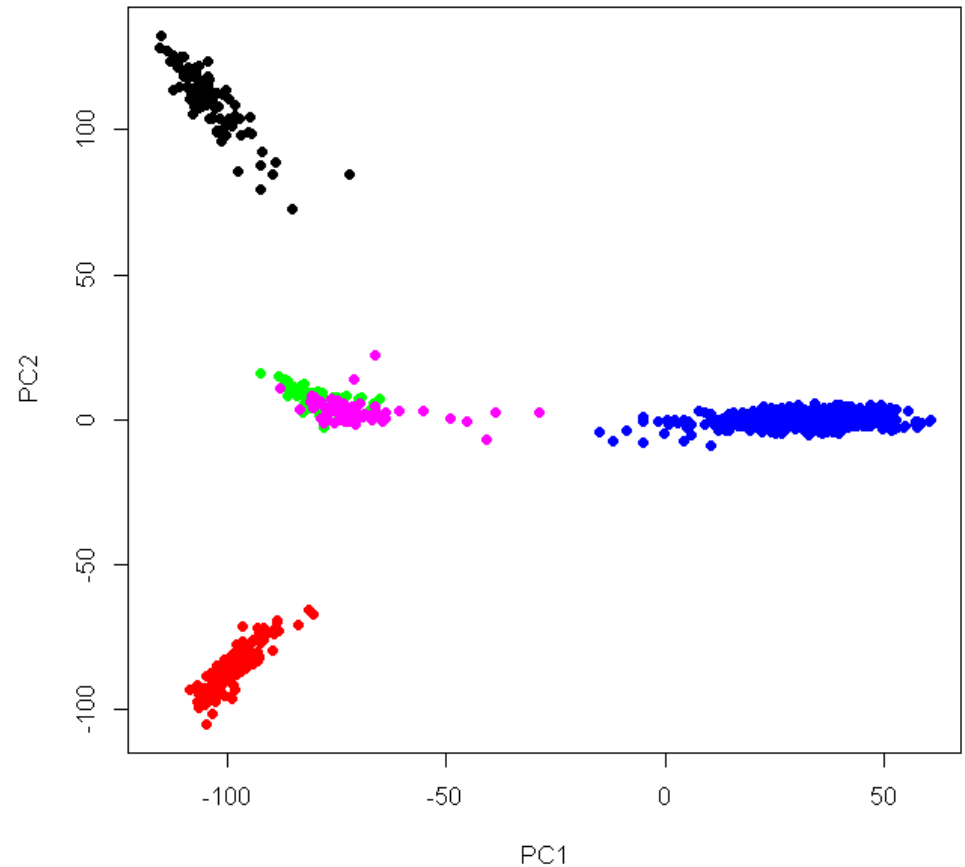
# Three questions of the breeding organization

1. Is the Dutch Red Friesian Cattle breed a unique breed or a strongly related to the Dutch Black and White breed?
2. Is it relevant to distinguish five different sire lines within the breed?
3. Are two herds of non-registered Dutch Red Friesian Cattle related to the registered population?

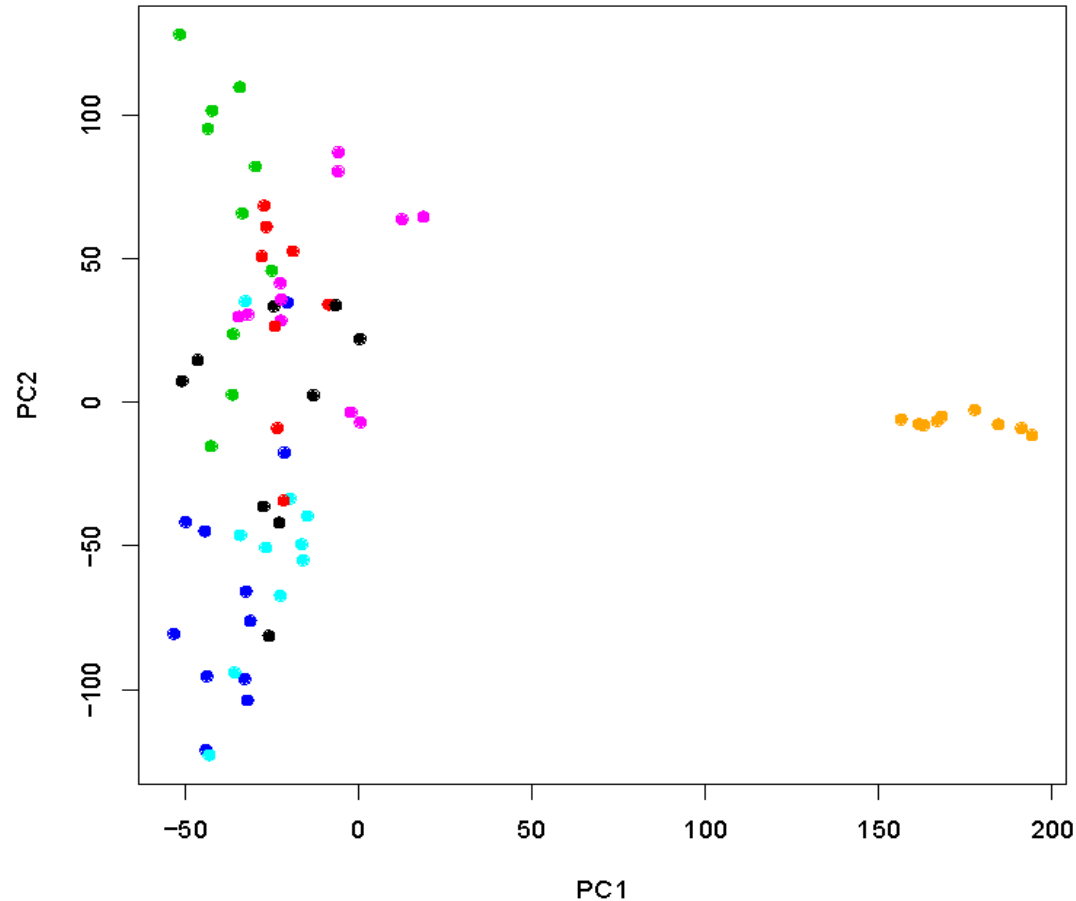


# Clusteranalysis of the Dutch cattle breeds

- Black = GWH
- Red = MRIJ
- Green = DBWF
- Blue = HF
- Magenta = DRF



# Clusteranalysis of the 7 lines of DRF-cattle



- PCA evidently distinguished DFR line 7 (orange) from the other lines

# Conclusions for the 7 lines

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- Line 6 and 7 related to DRF
- Line 6 and 7 some unique diversity
- Line 6 small HF influence
- Line 7 unique DRF diversity
- Much overlap among the lines





# Conclusions Red and White Friesian cattle

1. The Dutch Red Friesian Cattle breed is a unique breed strongly related to the Dutch Black and White breed.
2. It is not relevant to distinguish five different sire lines within the breed, but it can be used in an effective conservation programme.
3. Two herds of non-registered Dutch Red Friesian Cattle can be added to the registered population.



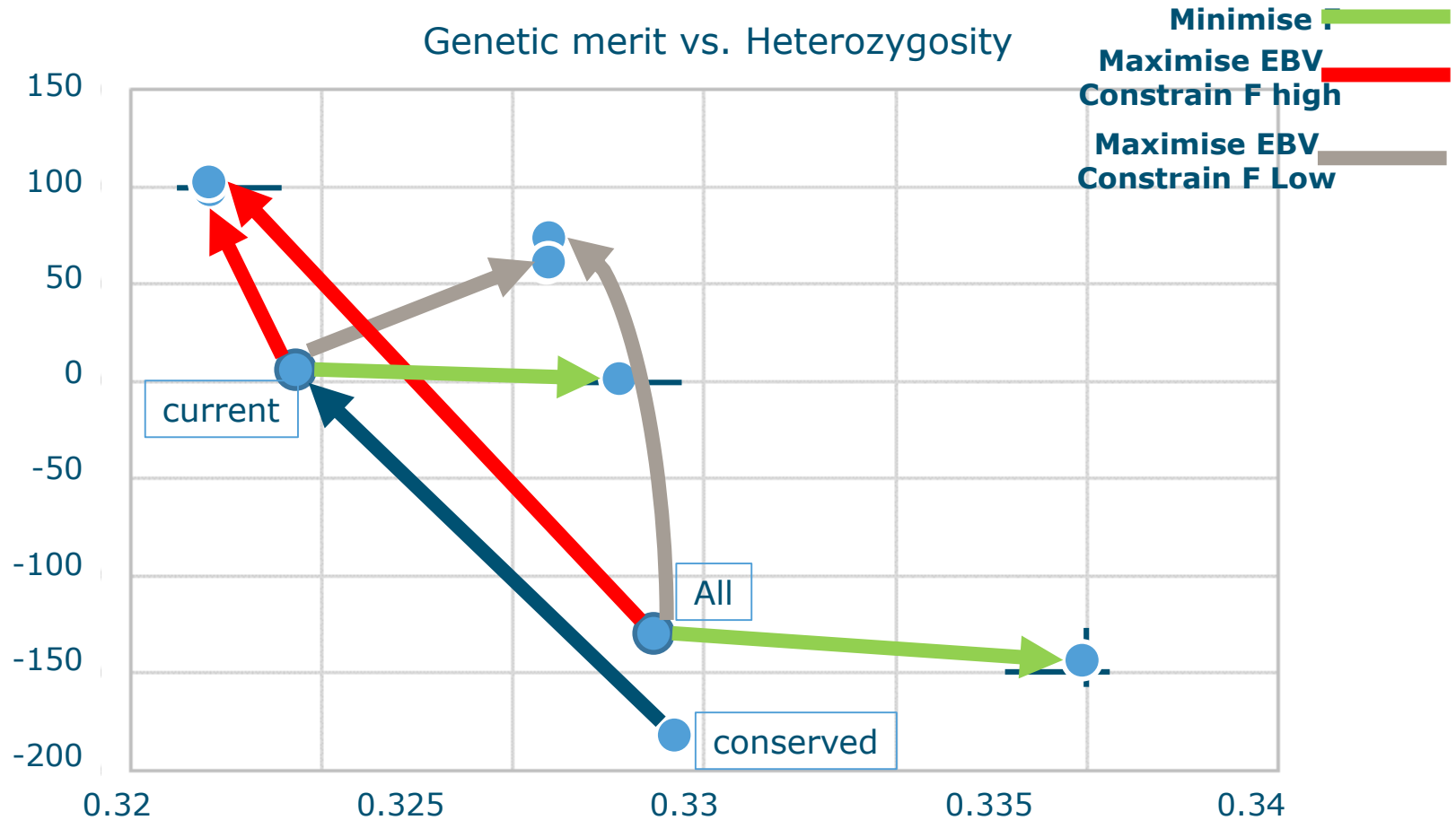


# Use of genebank sires to increase genetic diversity before genomic selection (MRIJ)

- Decrease in numbers from 160000 > 4000 females/year
- Founders and traits lost
- 294 sires born < 2000
- 119 sires born > 1999



## Genetic merit vs. Heterozygosity



# Increase in genetic gain and restoration of genetic diversity is possible in MRIJ!

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- Conserved sires > higher genetic diversity
- Only minimise F > much higher genetic diversity
- Only maximise EBV > lower genetic diversity
  
- Maximise EBV + accept high F > high gain + lower diversity
  
- Maximise EBV + accept low F > slightly lower gain + higher diversity

# In progress: DNA analysis (50k) rare breeds

- All bulls in the gene bank have been typed recently:

Breed	Analysed 50 k-chip	Time period up to now	Breed since
Dutch Friesian	198	50 years	1874
Dutch Red and White	302	50 years	1874
Groningen White Headed	94	50 years	1874
Deep Red	24	15 years	2001
Friesian Red and White	56	50 years	1957
Colour-sided (crosses)	34	15 years	Colour pattern
Dutch Belted	39	25 years	1997
Improved Red and White	26	15 years	1988

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# Work package 1: breed differences

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- Relationships between breeds and genetic history
- Contribution to genepool and prioritisation conservation
- Population structure within breeds
- Relationship with HF-breed
- Heterosis to be expected in crossbreeding with HF
- Relationship and inbreeding per period of 5 years
- Estimation of effective population size
- Prediction of the extinction rate
- Identification of bottle necks, founders lost and loss of SNP's and haplotypes

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## Workpackage 2: Positive and negative characteristics of genebank material

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- SNP's and haplotypes not present in HF
- Unique sequences of SNPs in QTL Databases
- Which sires can be used for introgression in HF?
- Which part of the genome is always homozygous?
- Which part of the genome is always heterozygous?
- Detection of colour loci and related genetic defects
- Carriers of genetic defects known in OMIA database

# Conclusions

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- Genomics offers great opportunities to make the *in situ* and *ex situ* conservation of animal genetic diversity more efficient and more effective
- Conservation and breeding strategies need to be in place to avoid the threats of genomics for the genetic diversity.