ICAR keynote presentations

Genomic selection and its potential to change cattle breeding

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Outline

- Where we come from

- New opportunities due to genomics

- Challenges for breeding programs

- Outlook

Selection from about 1960 to ~ 2009

- Quantitative-genetic concepts
    - (Wright, Lush, Henderson)
      -> additiv genetic model

- Genetic evaluation
    - Separate phenotypic observations (eg 9850 kg milk) in
        - additiv genetic effect → estimated breeding value (eg. + 1430 kg M)
        - Systematic environmental effect
        - Residual effect

- Ranking based on estimated breeding values (EBVs)

Selection on EBVs in AI breeding programs

A large proportion of genetic gain is achieved by a very high selection intensity on the male side (one bull returning to service out of ~10-15 test bulls → with 60.000 to 100.000 doses of semen per proven bull and year)

- Necessary elements for this ‚traditional breeding program'
    - Phenotypic observations
        - Milk yield, somatic cell counts, type traits, etc.
    - Pedigree data
    - Data structure (across herds/environments)
        - Artificial insemination gives optimal structure to estimate EBVs that rank the animals best and unbiased in many environments
    - Algorithms (Henderson, Schaeffer&Kennedy, Misztal, etc) and computing power
        - → BLUP methodology, which result in highly reliable EBVs (85-99%) for bulls with a **progeny test of 100-150 daughters**
        - → Transformation of these EBVs since 15 years via Interbull MACE
            - → **Bulls that are marketed worldwide**

Portfolio of Interbull evaluations

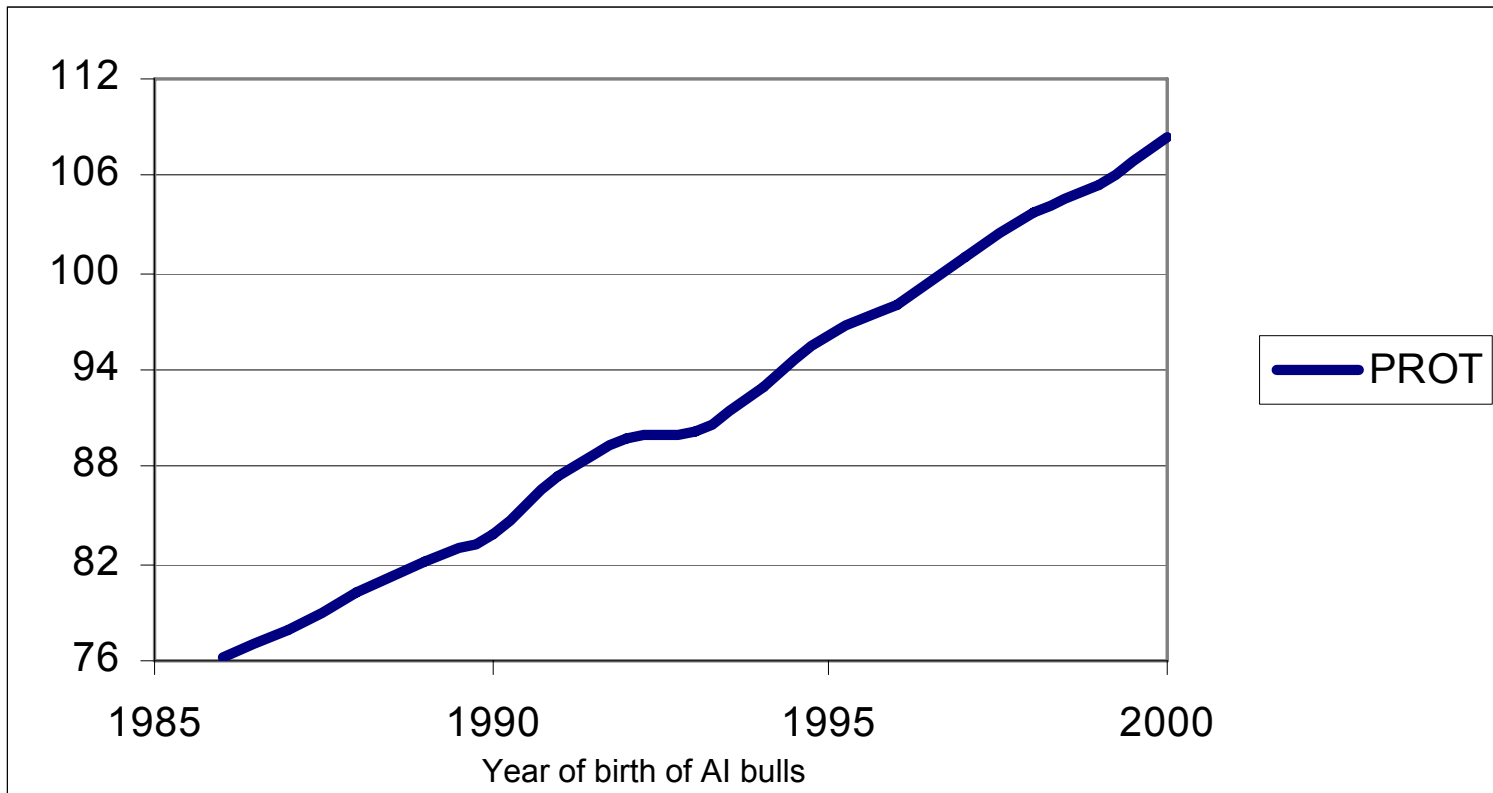| Year							
1995	Production						
1999	Production	Type					
2001	Production	Type	Cellcount				
2004	Production	Type	Cellcount	Longevity			
2005	Production	Type	Cellcount	Longevity	Calving		
2007	Production	Type	Cellcount	Longevity	Calving	Fertility	
2008	Production	Type	Cellcount	Longevity	Calving	Fertility	Workability

Genetic trend in Holstein bulls

(MACE Evaluation Interbull, Holstein AI bulls (50,000);
Mean = 100, SD = 10; Data Sept. 2007, Berglund, 2008)

EBV

PROT=Protein yield   Jorjani, 2008

but

- Genetic gain / costs
    - High generation interval due to progeny test
        - → Expensive, due to keeping of many waiting bulls
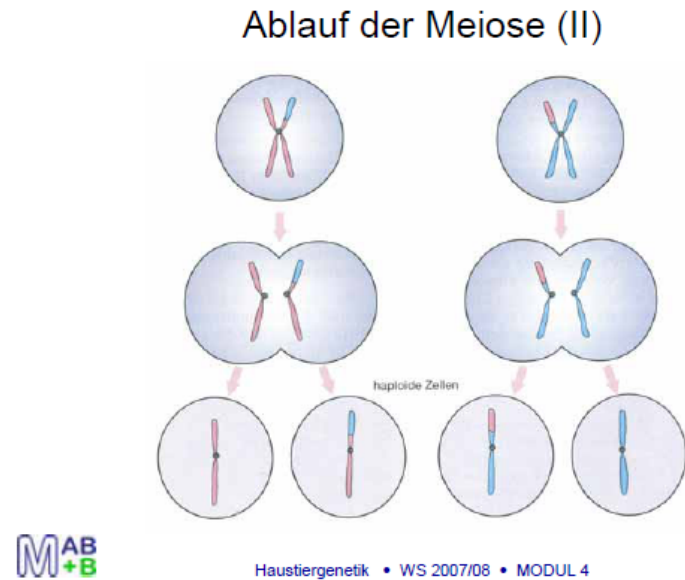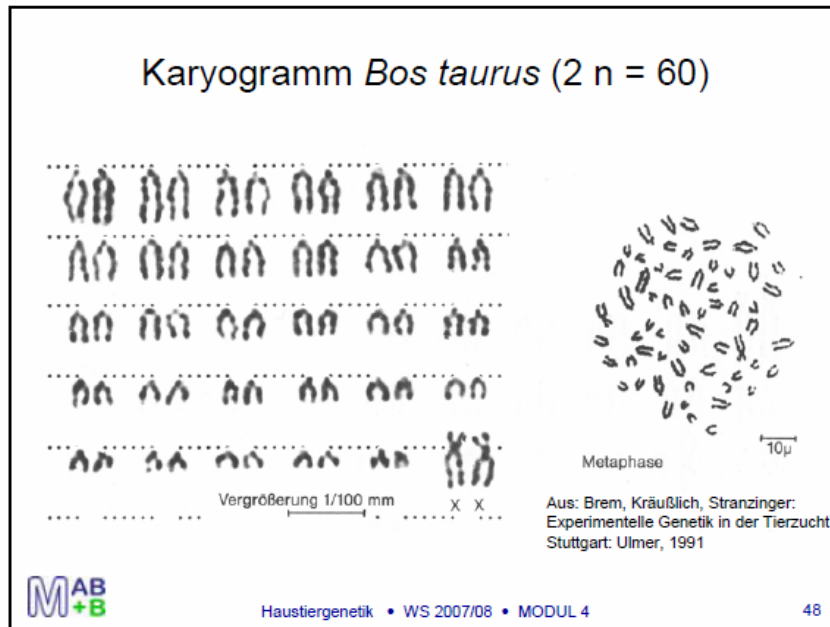   - → Genetic gain per year not very high

- Reasons for this:
    - Although one can select young bulls for progeny test on very reliable EBVs
        - (bull dams ~60% r^2 and bull sires ~95% r^2)

    reliability of a pedigree index =0,5 EBV sire + 0.5 EBV dam + MS
    is as low **as 25-35%**
        - MS = Mendelian sampling in the Meiosis

Meiosis (simplified)

- Recombination of chromosome fragments during Meiosis (I)
- Random allocation of the chromosomes, that were inherited from sire and dam, to the gametes

→ Large number of different zygotes (offspring) from the same pair of parents
  → Superior sires could only be identified by generating and testing ~ 100 daughters

Karyogramm *Bos taurus* (2 n = 60)

Vergrößerung 1/100 mm   x x

Metaphase

10µ

Aus: Brem, Kräußlich, Stranzinger:
Experimentelle Genetik in der Tierzucht
Stuttgart: Ulmer, 1991

Haustiergenetik • WS 2007/08 • MODUL 4   48

Ablauf der Meiose (II)

haploide Zellen

Haustiergenetik • WS 2007/08 • MODUL 4   47

New opportunities: SNP - genotyping

- SNP = Single-nucleotide polymorphism
- Genotype = Which alleles of the nucleotides **A-T,C-G** an animal carries
- Genome = contains 3 billion base pairs
- Ca. 50.000 SNPs at a cost of about 200 EUR

Genotype**:**

Anim. 1:
```
...AGGCACC GCAATCCACG GAGGCTACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
...AGGCACC GCAATCCACG GAGGCTACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
```
TT

Anim. 2:
```
...AGGCACC GCAATCCACG GAGGCAACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
...AGGCACC GCAATCCACG GAGGCAACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
```
AA

Anim. 3:
```
...AGGCACC GCAATCCACG GAGGCTACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
...AGGCACC GCAATCCACG GAGGCAACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
```
AT

Anim. n:
```
...AGGCACC GCAATCCACG GAGGCAACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
...AGGCACC GCAATCCACG GAGGCAACGC CCTCACCGGA GGTTTCGCTC TCCACGG...
```
AA

Eg position on chromosome 6 # 43.675.239

Use in practical application

- Lab is an important part, BUT
  SNP data has per se no information on 'traits'

Steps (eg Meuwissen et al 2001):

- Genotype animals that have reliable EBVs from 'conventional' genetic evaluation
- Calculate regression formulas from a 'reference population' so that SNPs explain well the conventional EBV
- Use the regression formulas derived by historic data to evaluate young animals
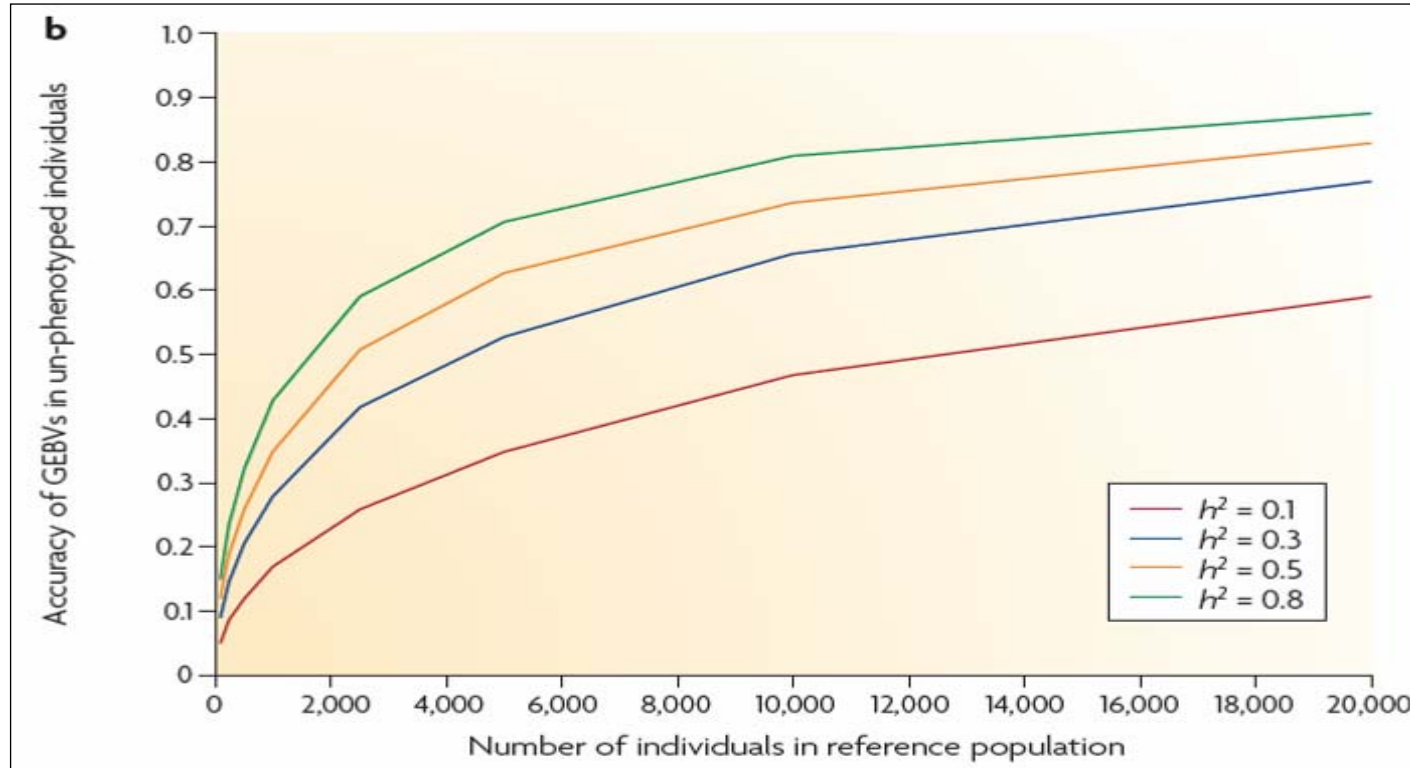- Select among these young animals
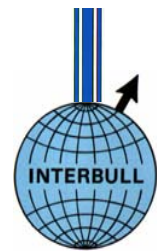
Key factor in application: Size of reference population

- Need for collaboration
  - US / CAN
  - Eurogenomics (Hol: DEU, FRA, NLD, DFS)
  - Intergenomics (BS: **AUT, CHE, DEU, FRA, ITA, SLO, USA**)

Goddard
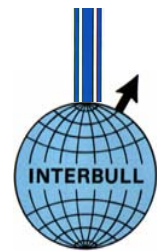
Genomic EBVs

- Statistical models work well

- Difficult to have same ranking for cows and bulls with
  - only phenotypic data
  - Genomic plus phenotypic data
  - → **Importance of Interbull validation procedure**

- Implemented in various countries
  - Need for converting GEBVs across countries
  - Interbull activities
    - **GMACE**

- Intense use of GEBVs can significantly increase genetic gain
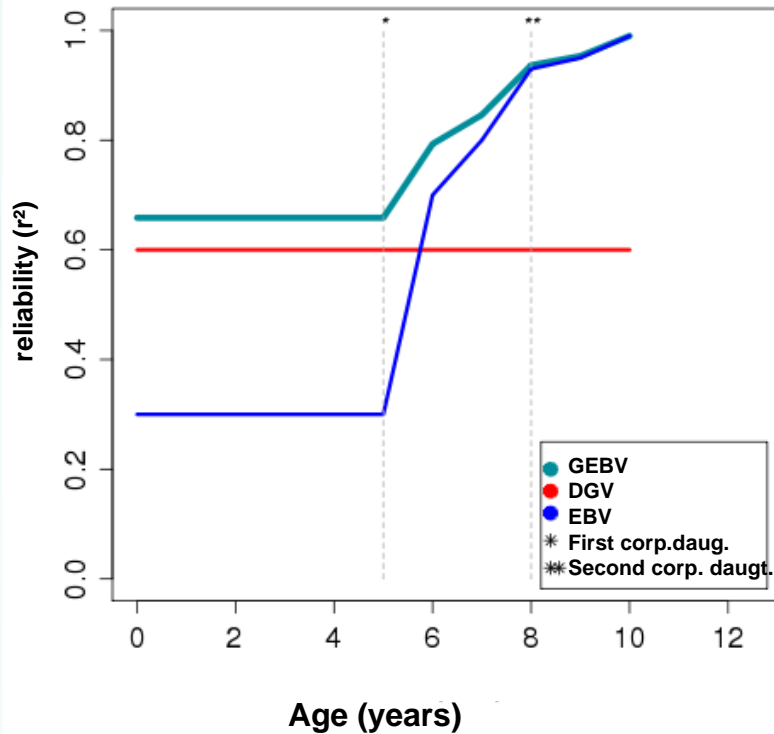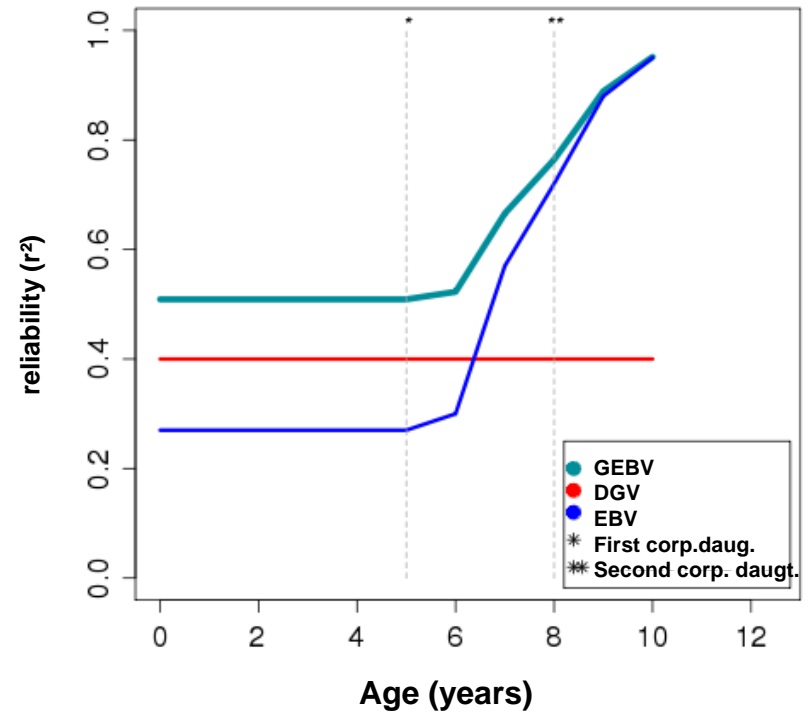 → **Genetic gain doubled (eg Schaeffer 2006)**

Increase in reliability of the BVs for AI bulls

AI Bull Milk Yield
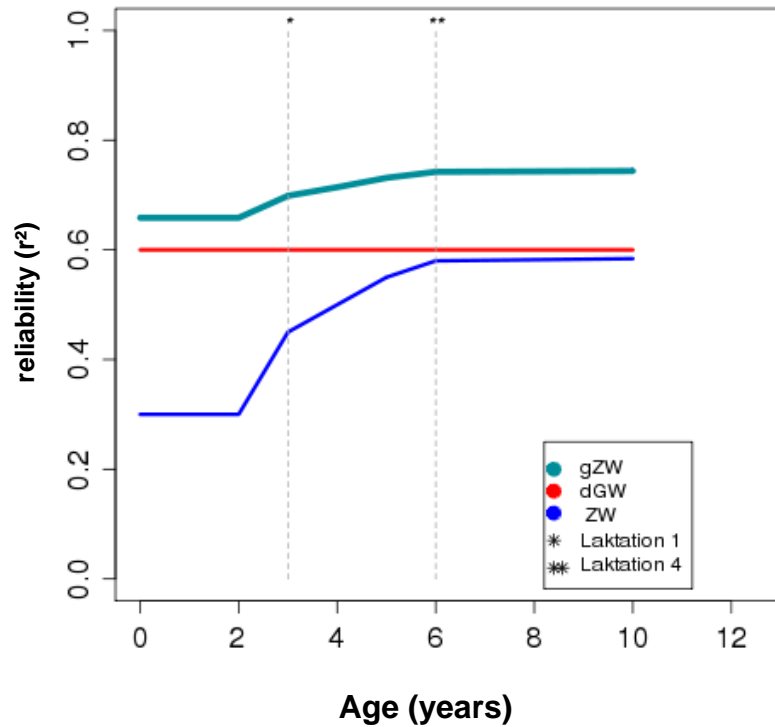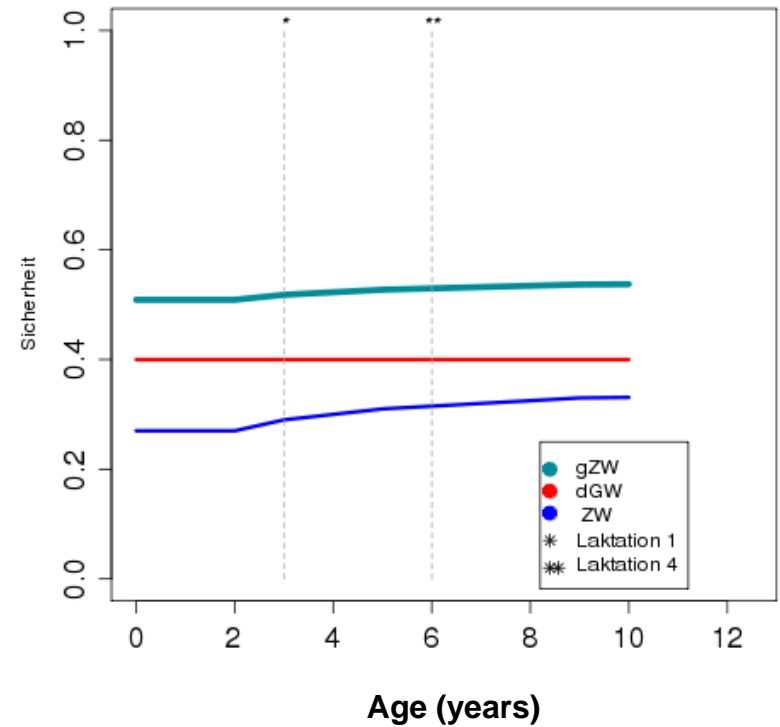
AI Bull longevity

Increase in reliability of the BVs: cows

Cow Milk Yield

Cow Longevity

Practical implementation in breeding programs

■ **GEBVs allow to select on the Mendelian sampling term of young animals (without own phenotypes or progeny with phenotypes)**
GEBV = 0,5 EBV sire + 0.5 EBV dam + MS

   ▪ This is very good approximated by Σ SNP effects

■ Strategy old:
Identify superior parents
→ mate them
     → progeny test (with 100 daughters) the highest young candidates
       → Select among bulls with highest EBVs from progeny test
         → Wide use of these bulls

  Success of a breeding program was closely linked to population size (test population) of cows under milk recording

Practical implementation in breeding programs

- Strategy new:
  Identify superior animals (r² ~ 75%)
  → mate them
    → progeny test (100 daughters) the highest young candidates
      → Select among bulls with highest EBVs from progeny test
        → Wide use of these bulls ??

- Success of a breeding program is closely linked to
  - Genomic evaluation system → ability to calculate GEBVs with high r²
  - Sourcing of promising candidates to calculate GEBVs on them
  - Optimised breeding program to have the
    - Optimal number of candidates for genotyping
    - Optimal selection intensity on them
    - Number of insemintations per young bull
    - Etc. (see presentation of Meuwissen in joint ICAR / IB session on genomics)

  - Success of breeding program is **not directly** linked to population under milk control any more
    - Entry for new players in the field

Challenges for breeding programs and herd recording

- **Rapid developments cause large challenges for cooperative breeding programs**
  - **Technological issues**
  - **Interaction with the breeders**
    - **As providers of superior genetics eg for AI centres**
    - **As users of semen**

- **Availability of phenotypic data**
  Standard traits:
  - **Necessary for updating the genomic prediction formula**
  - **Not directly needed for individual animals breeding value (different to old situation)**

  New traits
  - **Functional traits (eg as defined by the ICAR WG ‚Functional Traits')**
  - **New traits → e.g. composition of milk**
    have to be collected on a large number of animals (mostly cows) to first calculate EBVs for these traits and derive prediction formulas for GEBVs

- **Commercial companies may try to take over part of the cattle breeding industry**
  - **Issues**
    - **Technology**
    - **Patents**
    - **Data availability**

# Areas for future research

- **Optimal statistical model**
  - **Structure and size of reference population**
    - **Incl. Pooling of reference samples across countries**
  - **Bias due to preselection of bulls on GEBVs in conventional genetic evaluation**

- **Different SNP chips**
  - **3 K chip available**
    - **Impute from 3 K to 50K
      → use 50 K prediction formula**
    - **Large potential for cows and screening of bulls**
  - **HD Chip**
    - **Potential for higher reliability (see presentation of A. Eggen)**

- **Best use of GEBVs in breeding programs**
  - **Incorporation of international genetics in domestic selection decisions (see presentation of J. Dürr about Interbull plans)**
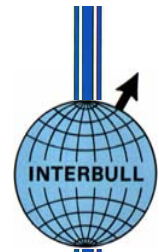
Summary

- Genomics leads to significant changes in genetic evaluation

- Significant changes also in structure of breeding programs

- Clear need for more collaboration
  - Best done in the Interbull/ICAR framework

- Breeding organisation and herd recording organisations will have to adapt their services and structure to the new opportunities

Thank you for your attention