AARHUS
UNIVERSITY

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Genomic selection – importance of size of reference population and SNP density

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Behind the scenes

AARHUS UNIVERSITET

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- Guosheng Su

SLU

- Freddy Fikse
- Elisenda Rius Vilarrasa

MTT

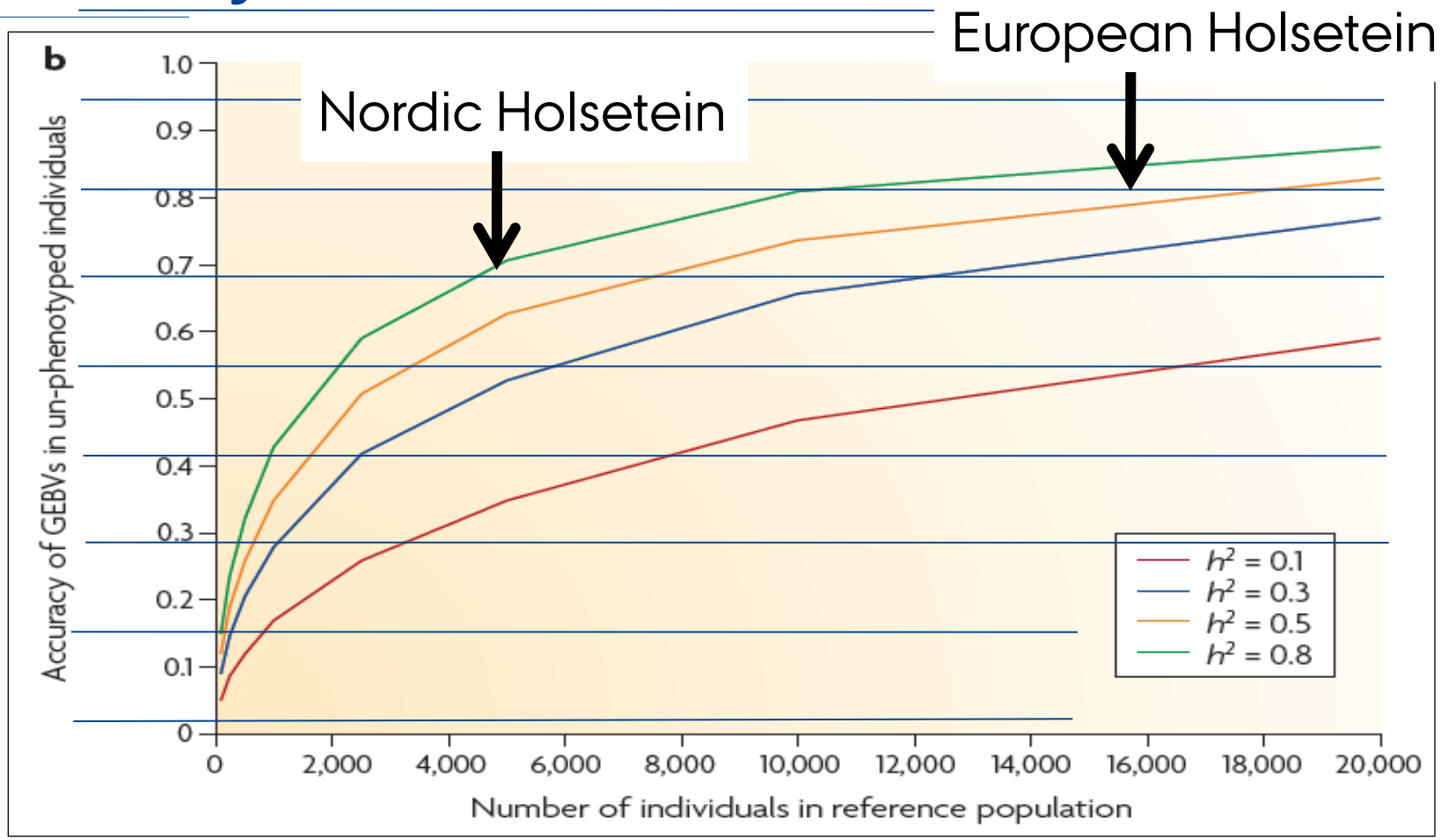
- Ismo Strandén
- Nina Schulman

Genomic selection

- Using dense SNPset på predict breeding values
  - Markers/haplotypes in close linkage disequilibrium with QTL
  - Many ”phenotypes” for each marker/haplotype to estimate effects accurately

- Critical factors
  - SNP density
  - Size of reference population (and effective population size)
  - Interplay between these factors in our breeds?

Accuracy increase with reference size



Goddard & Hayes, 2008

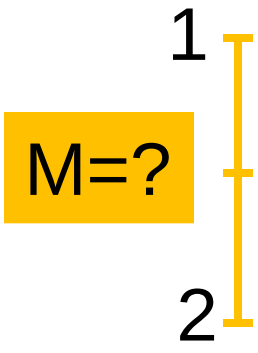
Improving genomic prediction by EuroGenomics collaboration

- Exchange genotypes between VikingGenetics, CRV, UNCEIA, DHV-VIT
- Increase reference from 4500 to 16.000
- Three different SNPsets used
- Initial imputation step to predict unobserved SNPs for CRV bulls

Imputation using LD and LA information

USDA chip

CRV chip



Imputation using LD and LA information

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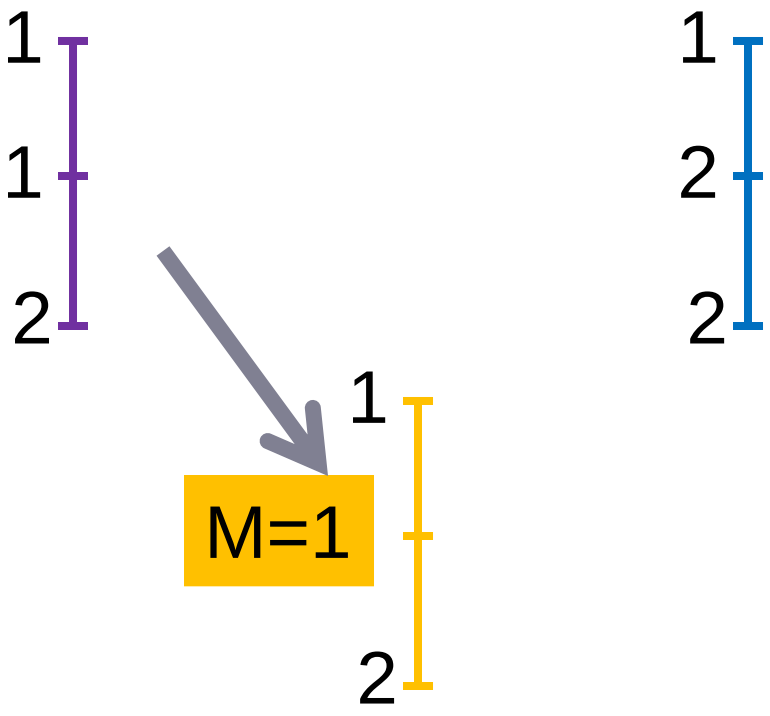
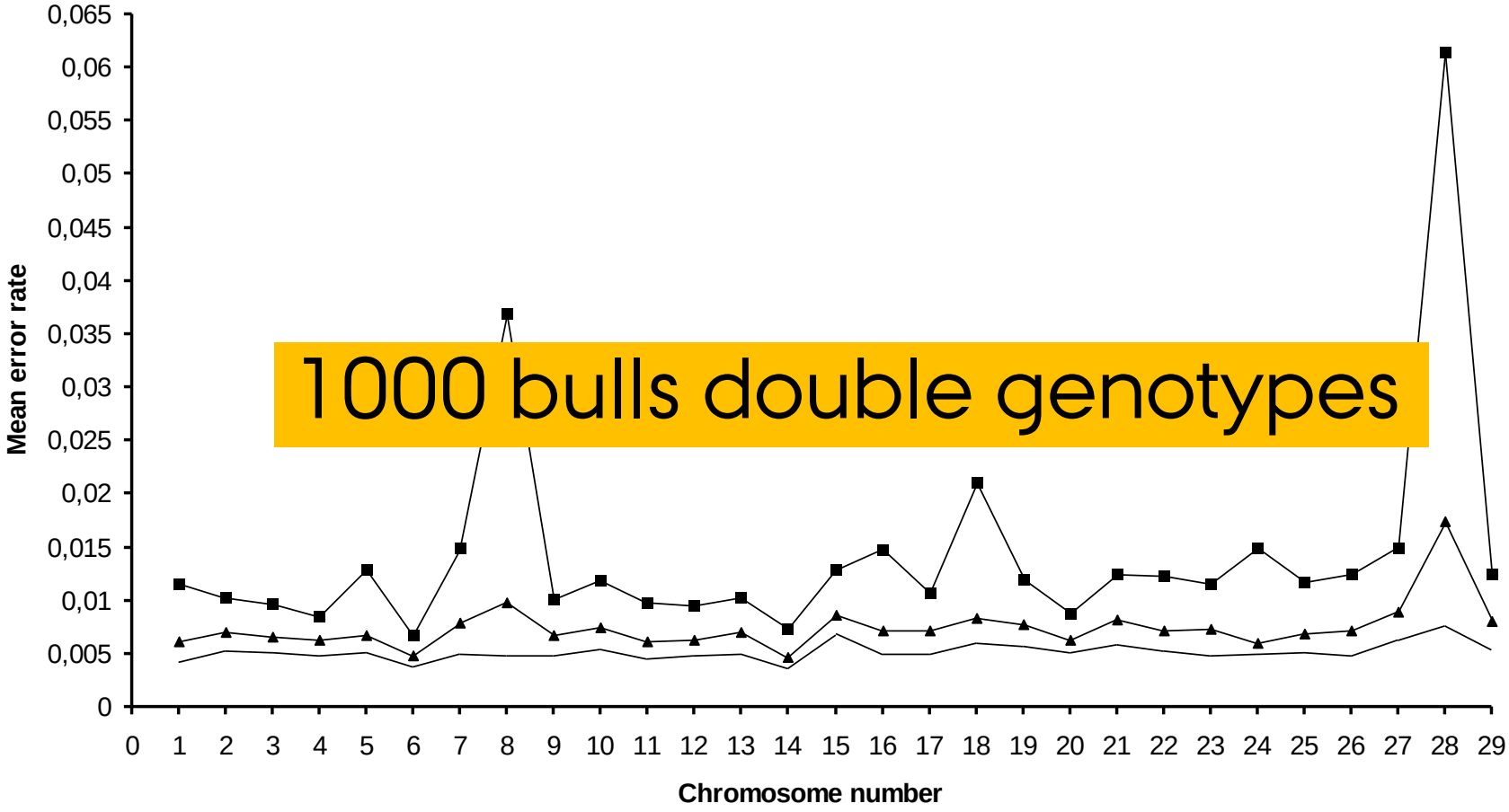


Imputation of USDA chip from CRV (Tom Druet)

› To study imputation (prediction of missing genotypes) across CRV 60K SNP panel and Illumina Bovine SNP50™ SNP chip («USDA» chip)

Double genotyping 500, 1000, or 2000 bulls



Improving genomic prediction by EuroGenomics collaboration

- Objective: Increase reliabilities of genomic breeding values by combining reference populations

- Hypothesis: Reliability increase 10-15% by using combined european reference compared to a purely Nordic reference

Joint EuroGenomics dataset

- 15,966 EuroGenomics bulls
- 19.4 million daughters
- 939 bulls with daughters in multiple countries
- Median number of daughters were:
  - DHV-VIT(117), UNCEIA (85), VikingGenetics (117), CRV (153)

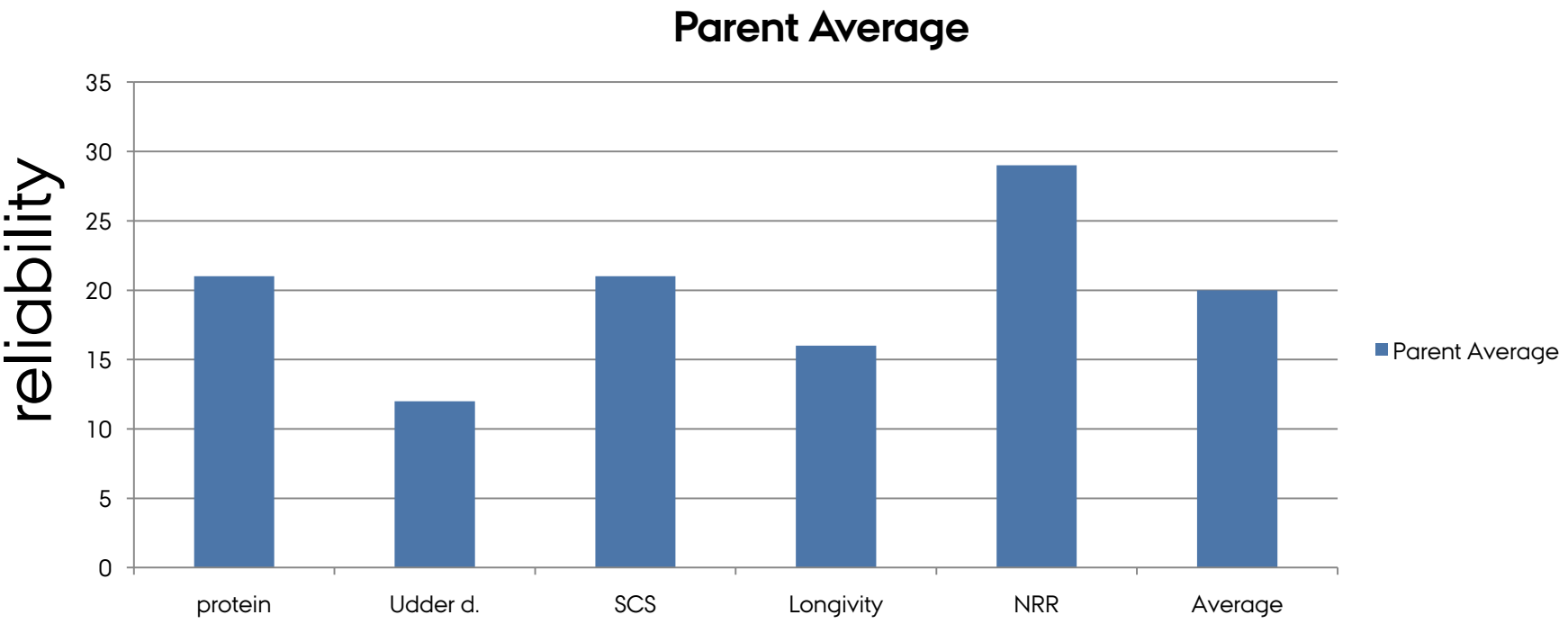
Reference and test population

- Nordic reference population
  - 75% of domestic population (oldest bulls)
- EuroGenomics reference population
  - all bulls born before same date as for domestic
- Test population
  - 25% yongest bulls
  - Sire in reference
  - EDC min. 20

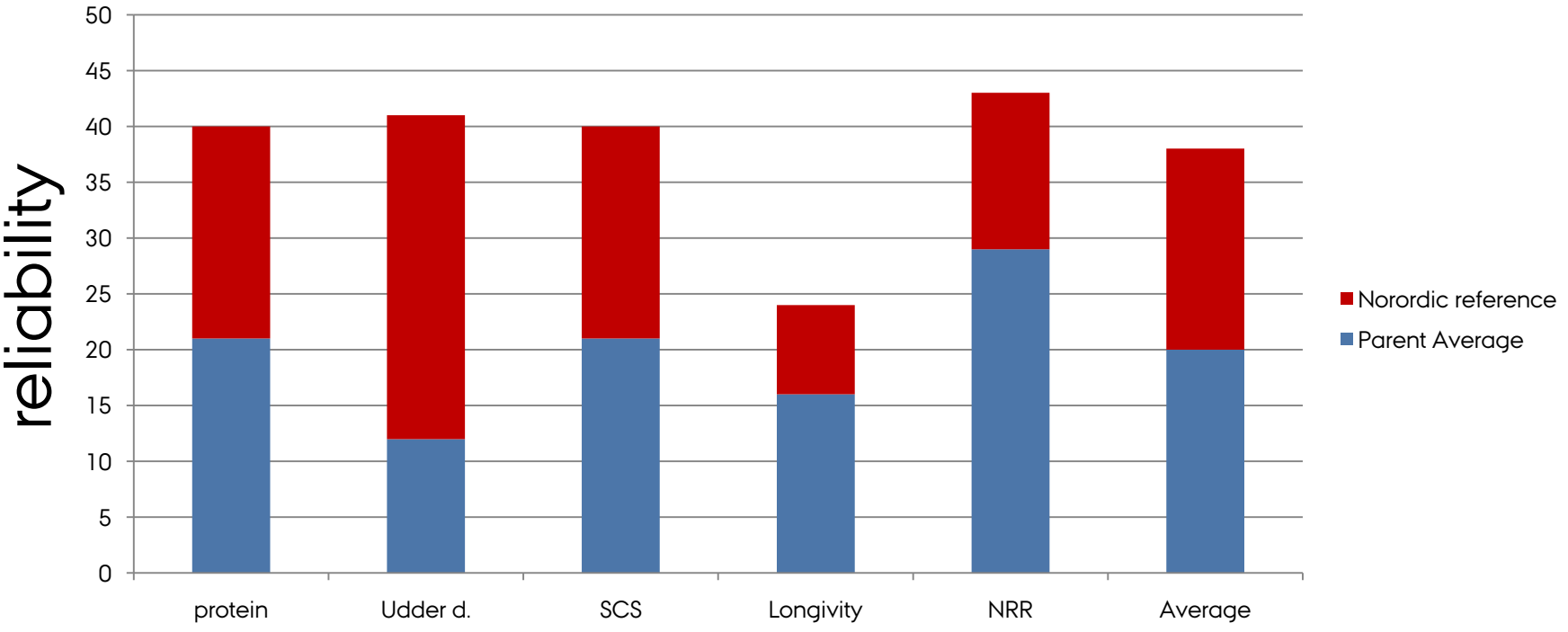
Data

- SNP data
  - DSF, Fr, Deu: USDA Illumina 50K
  - Holland: Imputed from costum 50K Illumina chip
- Phenotypes
  - Deregressed proofs of Interbull jan. 2010 (domestic scale)
- Traits
  - protein, udder deapth, SCS, Longivity, NRR

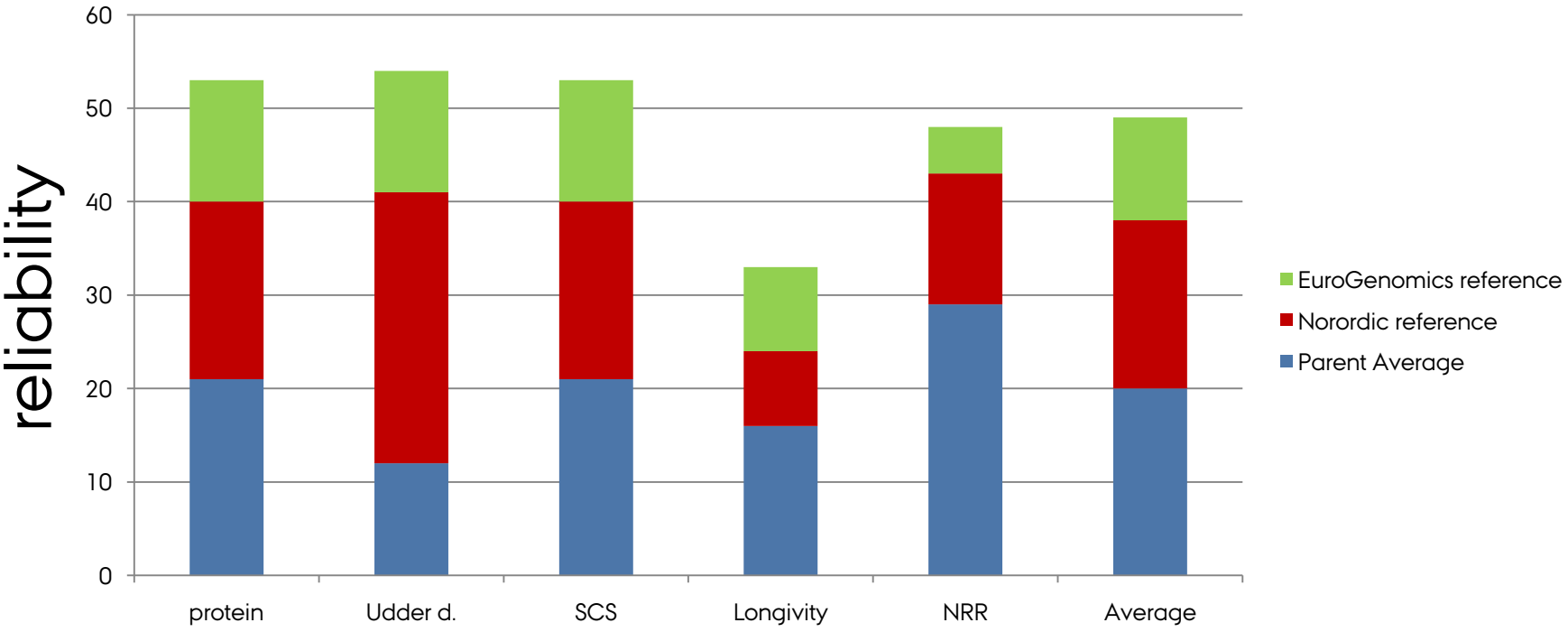
Reliability of parent average



Reliability of GEBVs using Nordic reference



Reliability of GEBVs using European reference



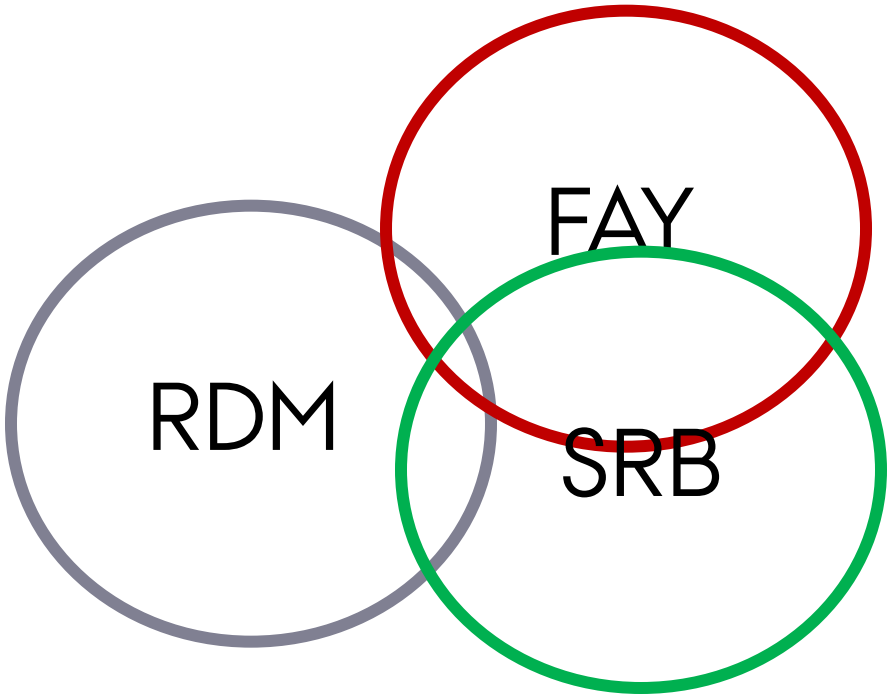
Conclusions

- Reliability increased by 11% (less than expected?)
- Starting point higher than expected
- Genetic correlation between traits less than 1 over the 4 countries

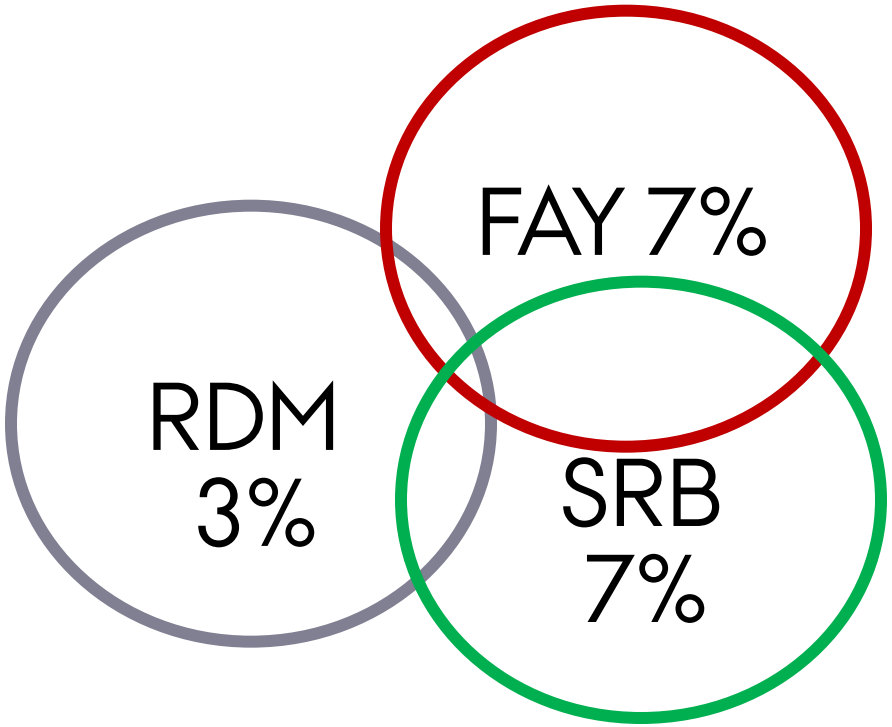
What about the other breeds?

- Jersey
- Red Nordic breeds
  - RDM
  - SRB
  - FAY

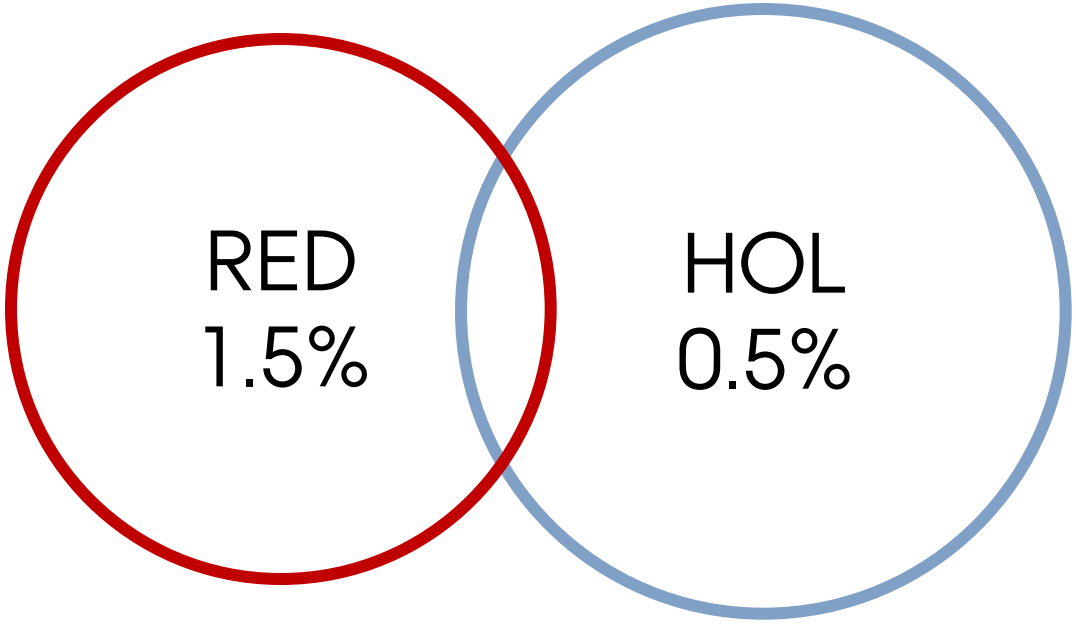
Clustering of the red breeds?



Increase in accuracy by common reference (SLU,AU, MTT)



Increase in accuracy by common reference with Holstein



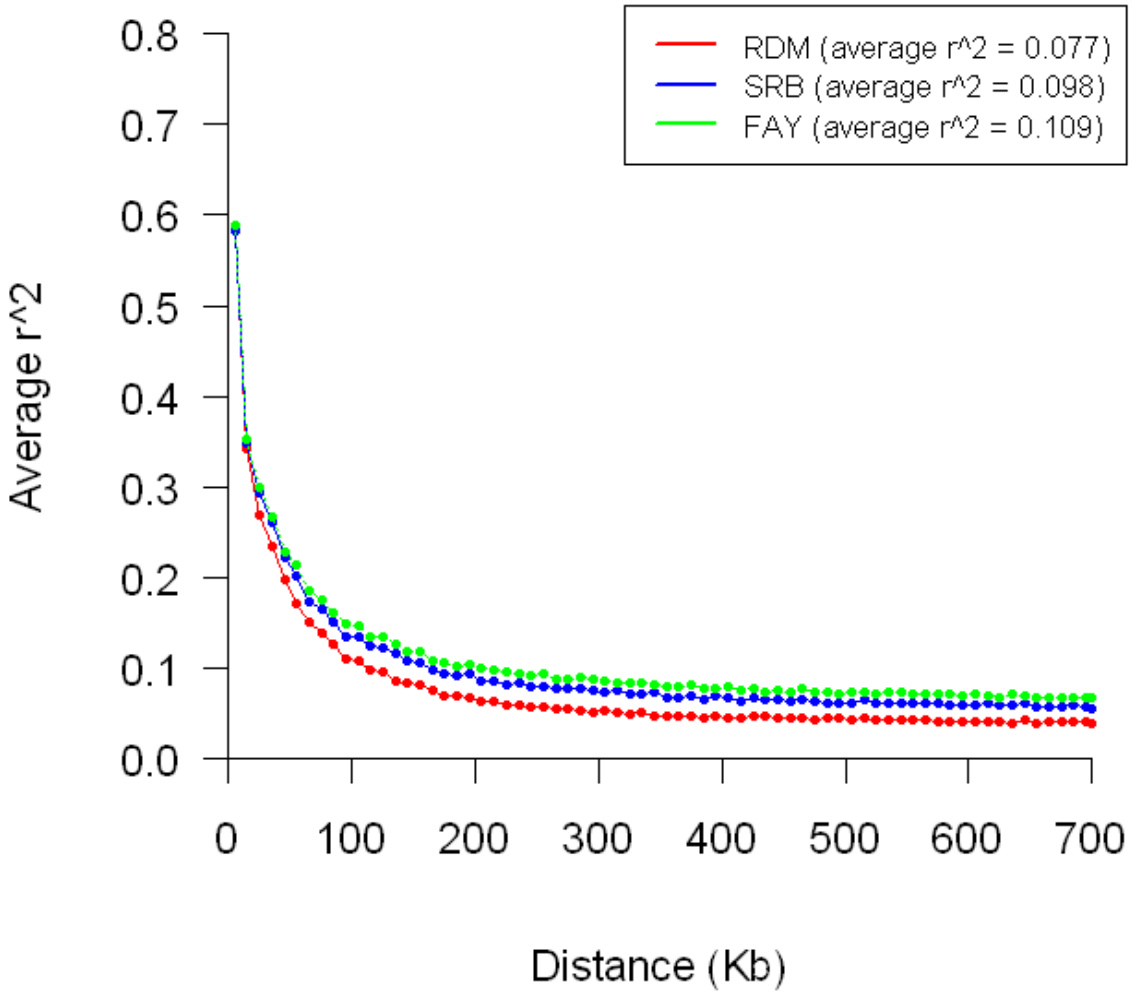
Reliability affected by:

✚ More bulls with sire in reference
✚ Better estimation of SNP effects

− Several (related) breeds
− Relationships within breed

Some effects cancel out !

Strength of Associations



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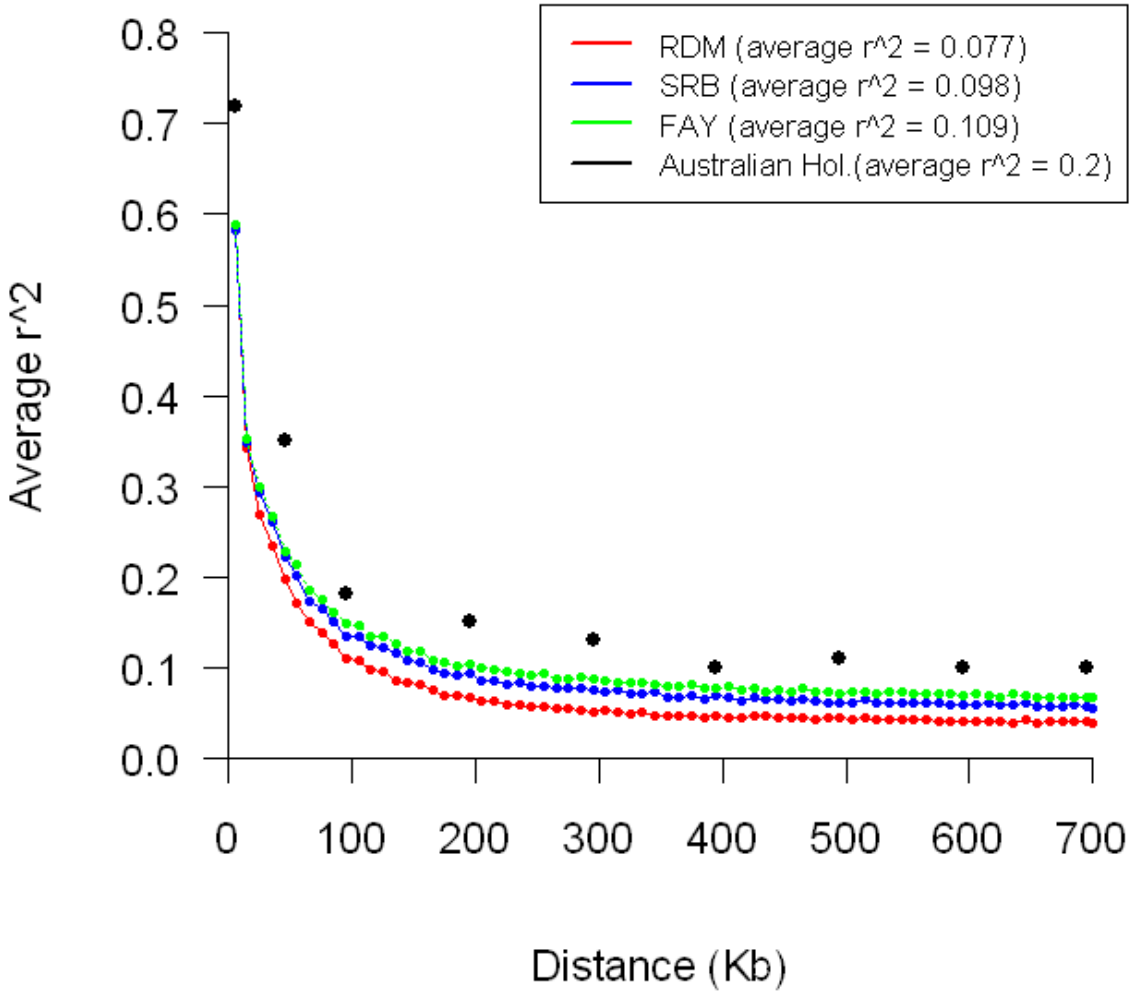
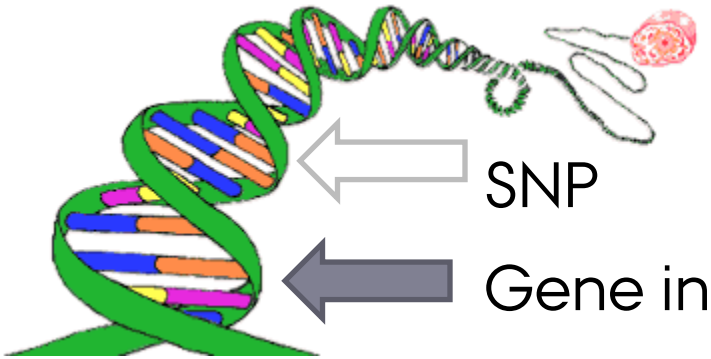


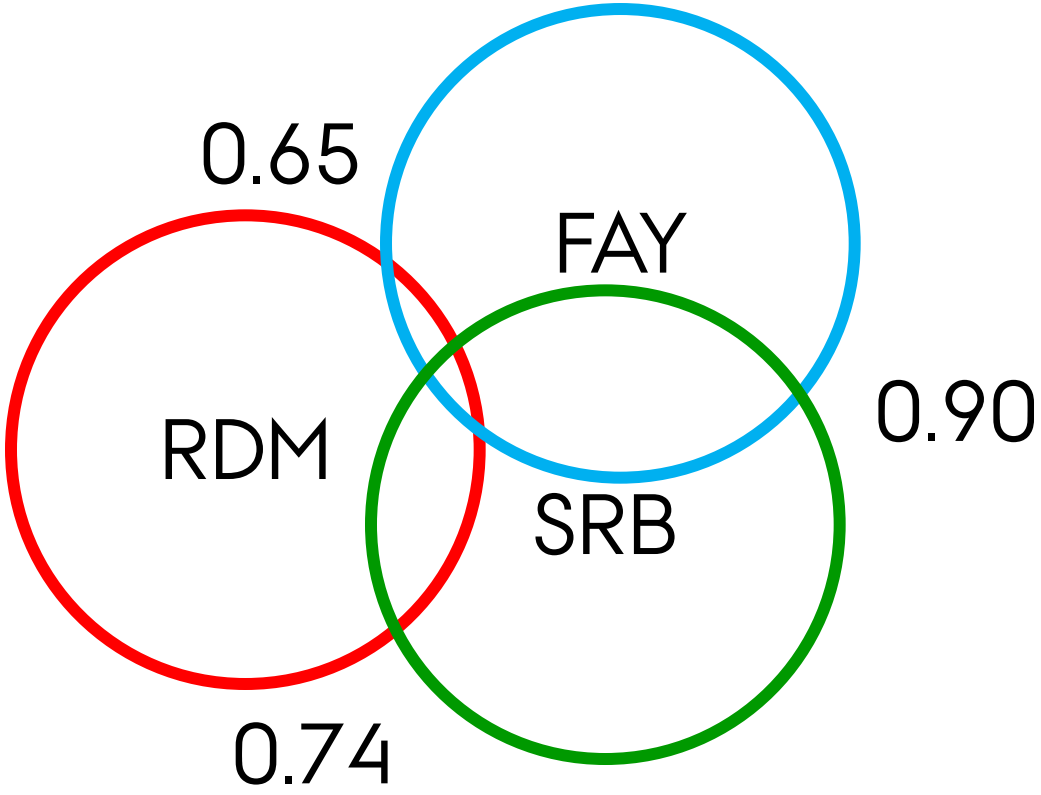
“Direction” of Association

Persistency of Phase

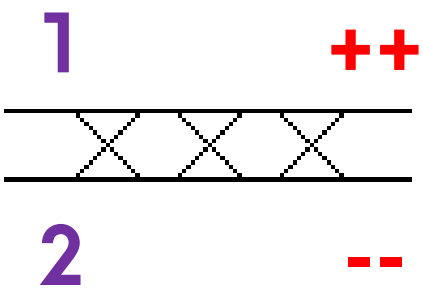


SNP Allele	Effect on Mastitis Resistance
1	++
2	--

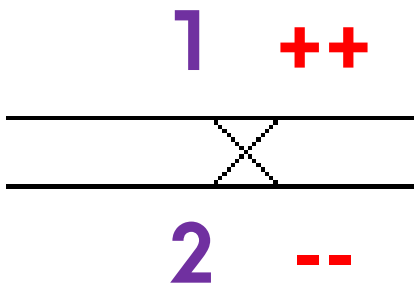
Persistency of Phase



SNP Density and Associations



More crossing over possible for genes far apart



Fewer crossing over possible for genes close together

Improvements with BovineHD

- Distance between SNP and QTL becomes much shorter
  - Stronger associations within breed

    (Marginal effect)
  - Direction of association more similar across breed

    (Large effect, especially for RDM ⇔ SRB&FAY and HOL ⇨ RED)
- Benefits greater when more data is added

Imputation to Combine

› <1% error rate for Bovine SNP50K & CRV50K

› ~3% error rate for Bovine SNP50K & 3k

? Error rates for Nordic Red

Available SNP-chips

Illumina

- Bovine SNP50K
- Bovine HD
- Bovine 3K panel
- Customized chips (CRV)

} Subsets of each other

Affymetrix

- Bovine 25K SNP Kit

…more to come …

Upgrade SNP50K ⇨ BovineHD

- Need to genotype *some* bulls in the reference population with BovineHD
  - Only influential bulls
- Holstein
  - Reduce costs through EuroGenomics
    - 500+500
- Nordic Red
  - Evaluate how much re-genotyping is needed
  - Second half of 2010

Opportunities with 3K

- Large scale screening of potential bull dams
  - Contract matings
  - Embryo flushing

- Cows comprise the future reference population ?!
  - Tendency to reduce number of bulls

New data sources and traits

- Recording devices
  - Milk flow meters
  - Voluntary Milking systems
  - Activity meters
  - Herd navigator
  - …

- Collect phenotypic data
- Genotype cows with 3K panel

} Genomic selection for new traits

Summary

- Reliability of GEBVs depend strongly on reference size
- Large increase for HOL in EuroGenomics
- Smaller increase for Nordic Red breeds
- High density SNP set will be important
- Low density SNP set for screening and reference
- Imputation techniques are crucial