Characterization of Linkage disequilibrium in a Danish, Swedish and Finnish Red Breed Cattle Population

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Background

- Multi-breed genomic predictions in the Nordic Red dairy cattle populations, are influenced by the genetic ties between breeds.

- Linkage disequilibrium and persistency of marker-QTL phase might differ between populations.

- This can compromise the effectiveness of pooling genetic data together in a multi-breed genomic prediction analysis.

- Assessing the differences in the patterns of LD between populations can contribute to:
  - The information on the marker density requirements (de Roos *et al.* 2008)
  - The optimization of the genomic prediction models for multi-breed reference populations .

Aims

Explore linkage disequilibrium (LD) and persistency of phase

Estimate the effective population size

Materials and Methods

- Genotypes
  - Illumina 50K SNP array → 38.647 SNPs after editing (MAF>5%)
  - 6,107 bulls (RDM = 21%, SRB = 32% and FAY = 47%)

- LD measures *(Lewontin, 1964; Hill & Robertson 1968)*

$$r^2 = \frac{D^2}{p_{A1} p_{A2} p_{B1} p_{B2}} \qquad r = \frac{D}{\sqrt{p_{A1} p_{A2} p_{B1} p_{B2}}}$$

  - $D = p_{A1B1} p_{A2B2} - p_{A1B2} p_{A2B1}$ and p_{A1}, p_{A2}, p_{B1} and p_{B2} are the frequencies of alleles *A1, A2, B1* and *B2*, respectively.

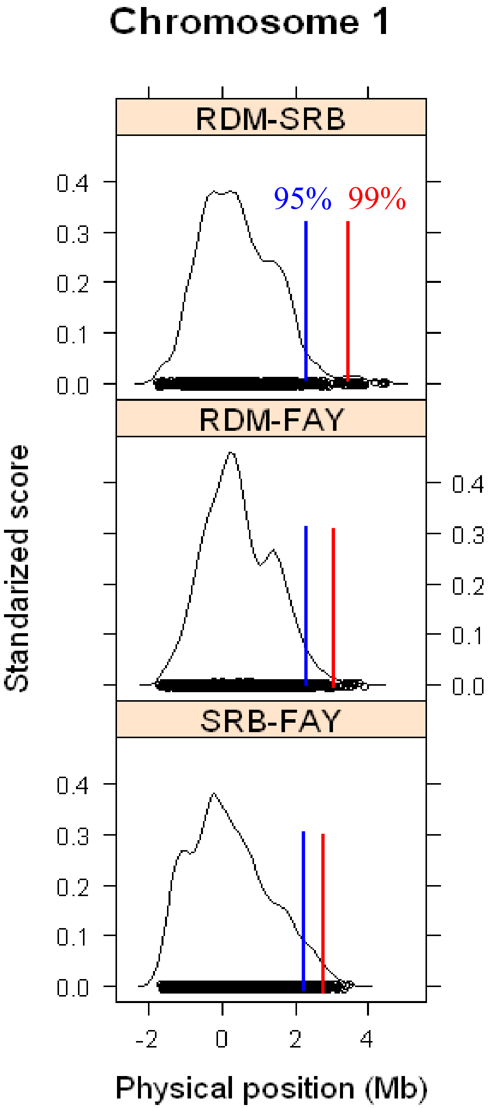
  - varLD program *(Ong and Teo 2010, Gen. Res.)*

VarLD program

- Identify genomic regions with LD difference between populations
    - *Calculate the extent of LD (r^2) between every pair of SNP of pre-defined sliding windows → LD matrix for each window/population.*
    - *varLD scores: comparing the extent of departures between the eigenvalues of the two matrix*
    - *The magnitude of the varLD scores as a measure of dissimilarity between populations*

varLD program

- *Candidate regions displaying significant LD difference between populations are obtained by truncation of the distribution of scores at 95% and 99% percentiles.*



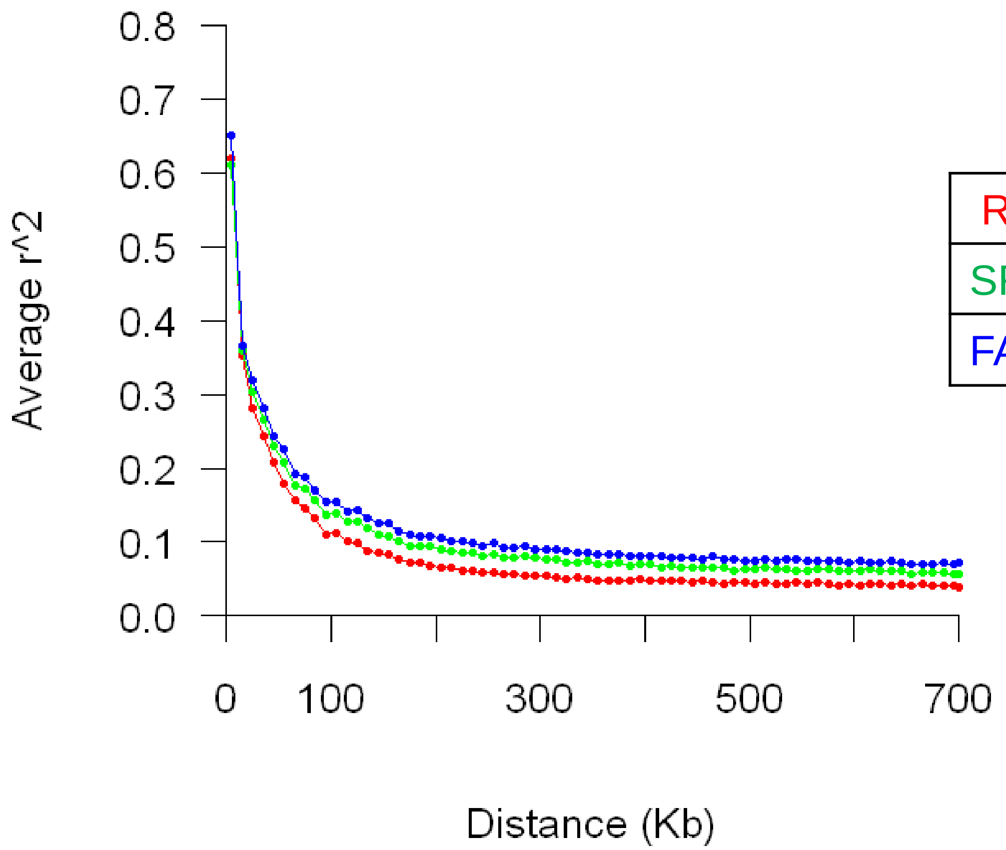
Effective population size: Ne

- Equations *(Hill W. 1975, Hayes et al. 2003; Goddard et al. 2006)*

$$E(r^2) = 1 / (4Ne_t c+2) \qquad Ne_t = (4\bar{c})^{-1}\left[(\bar{r}_c^{\,2})^{-1} - 2\right]$$

  - ***c*** is the marker distance, assuming that 1Mb ≈ 1cM
  - $\boldsymbol{r^2}$ is the average LD at different marker distances
  - $\boldsymbol{Ne_t}$ is the effective population size, *T* generations ago, where *T* = 1/(2***c***)

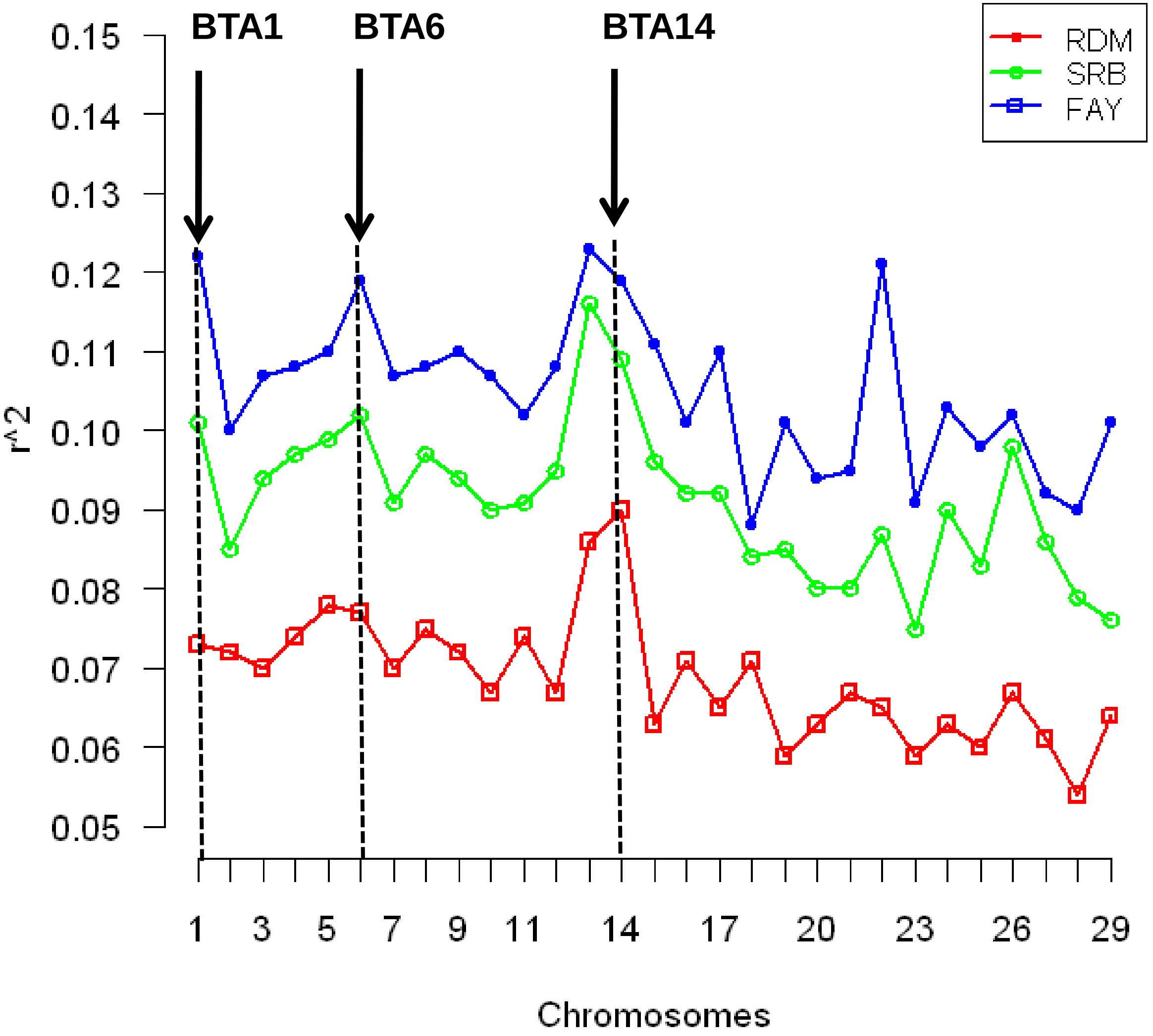
Results$_{(1)}$ - Average r^2 across marker distance



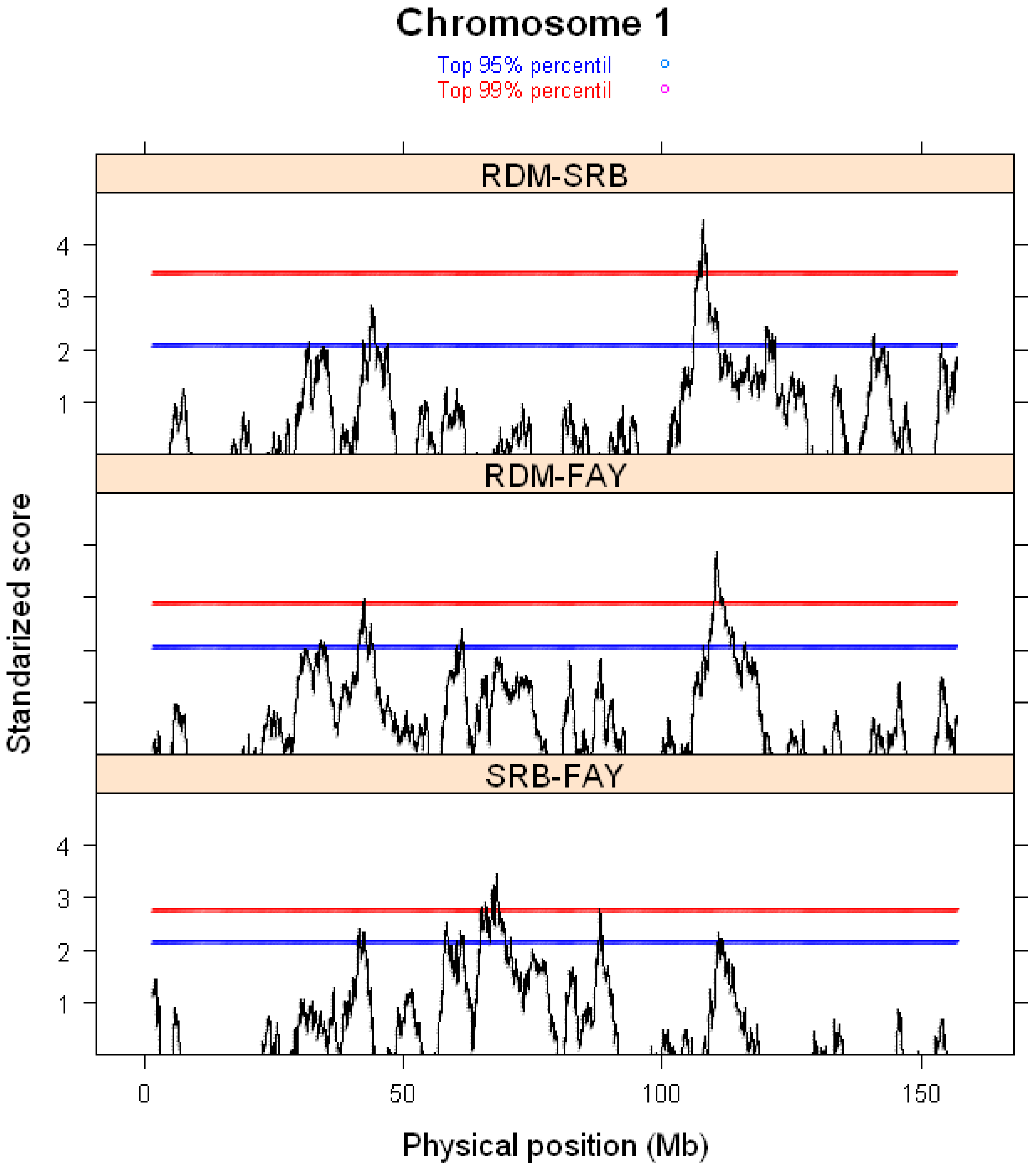
	Average LD (r^2)	
	>0 – 700 Kb	**>0 – 100 Kb**
RDM	0.07	0.22
SRB	0.091	0.24
FAY	0.11	0.25

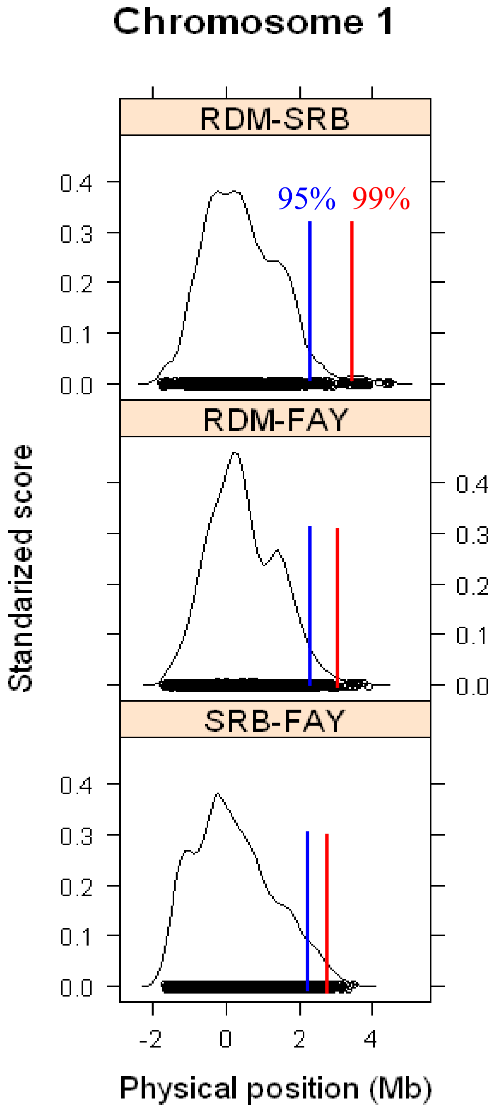
Useful LD of 0.20 → 54,000 SNPs (SRB/FAY) and 75,000 SNPs (RDM) to achieve accuracies from genomic prediction models of ≥ .85 *(Meuwissen et al. 2001)*

Results$_{(2)}$ – Average r^2 per chromosome

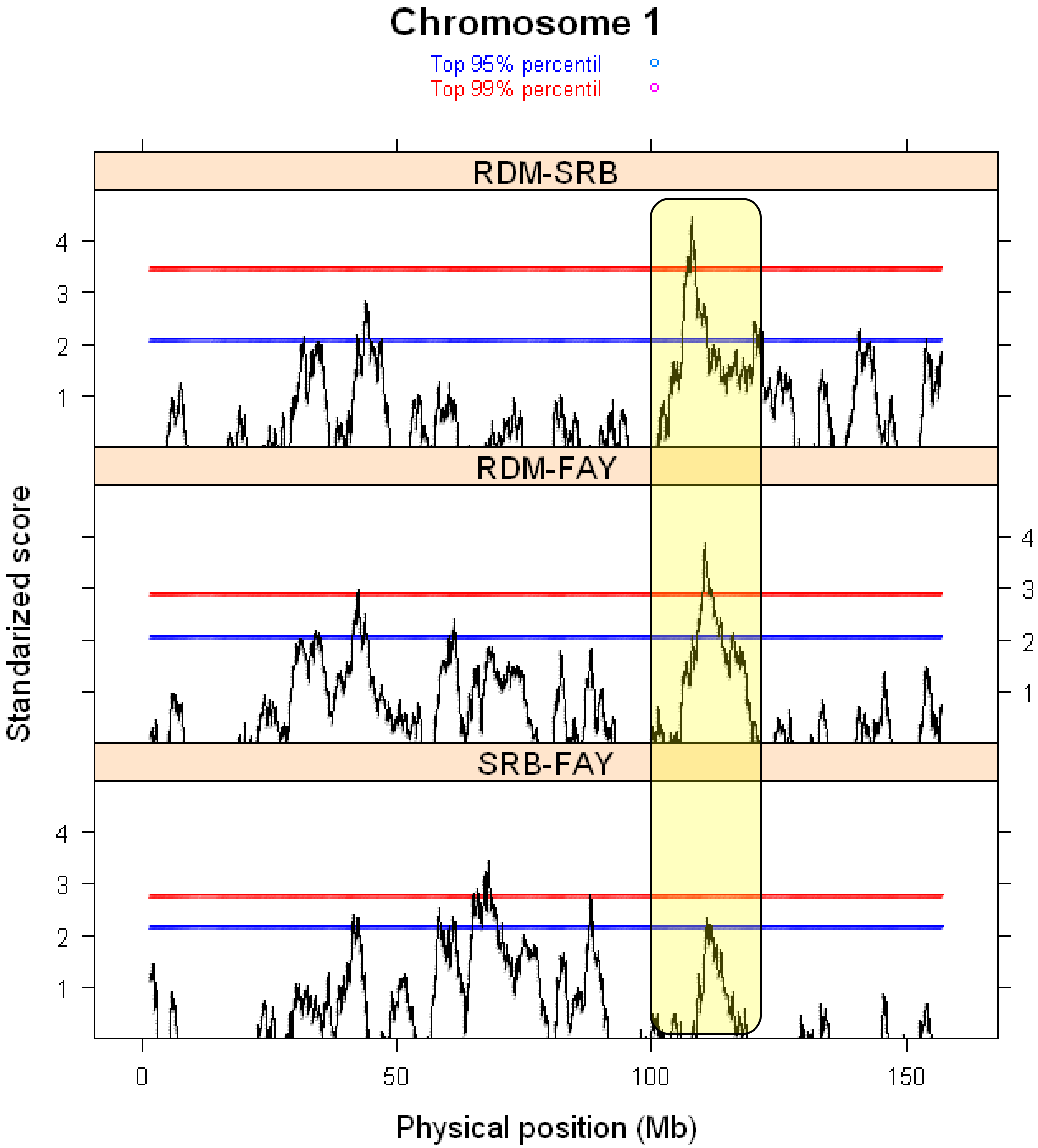


Results$_{(3)}$ – Patterns of LD between populations





Results$_{(3)}$ – Patterns of LD between populations

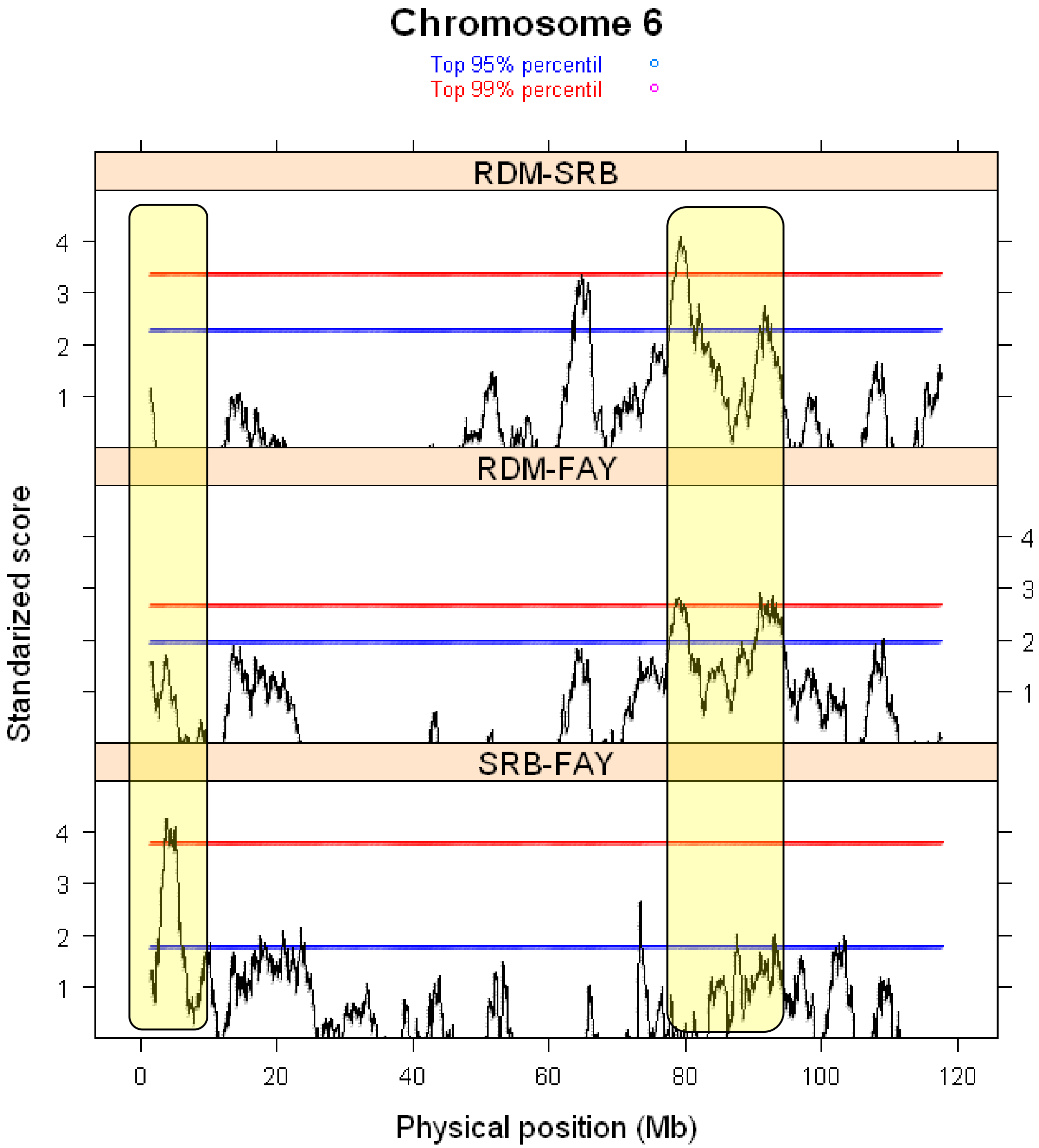


QTL

Milk yield (FAY)

(Viitala S.M et al. 2003, J Dairy Sci.)

Results$_{(4)}$ – Patterns of LD between populations

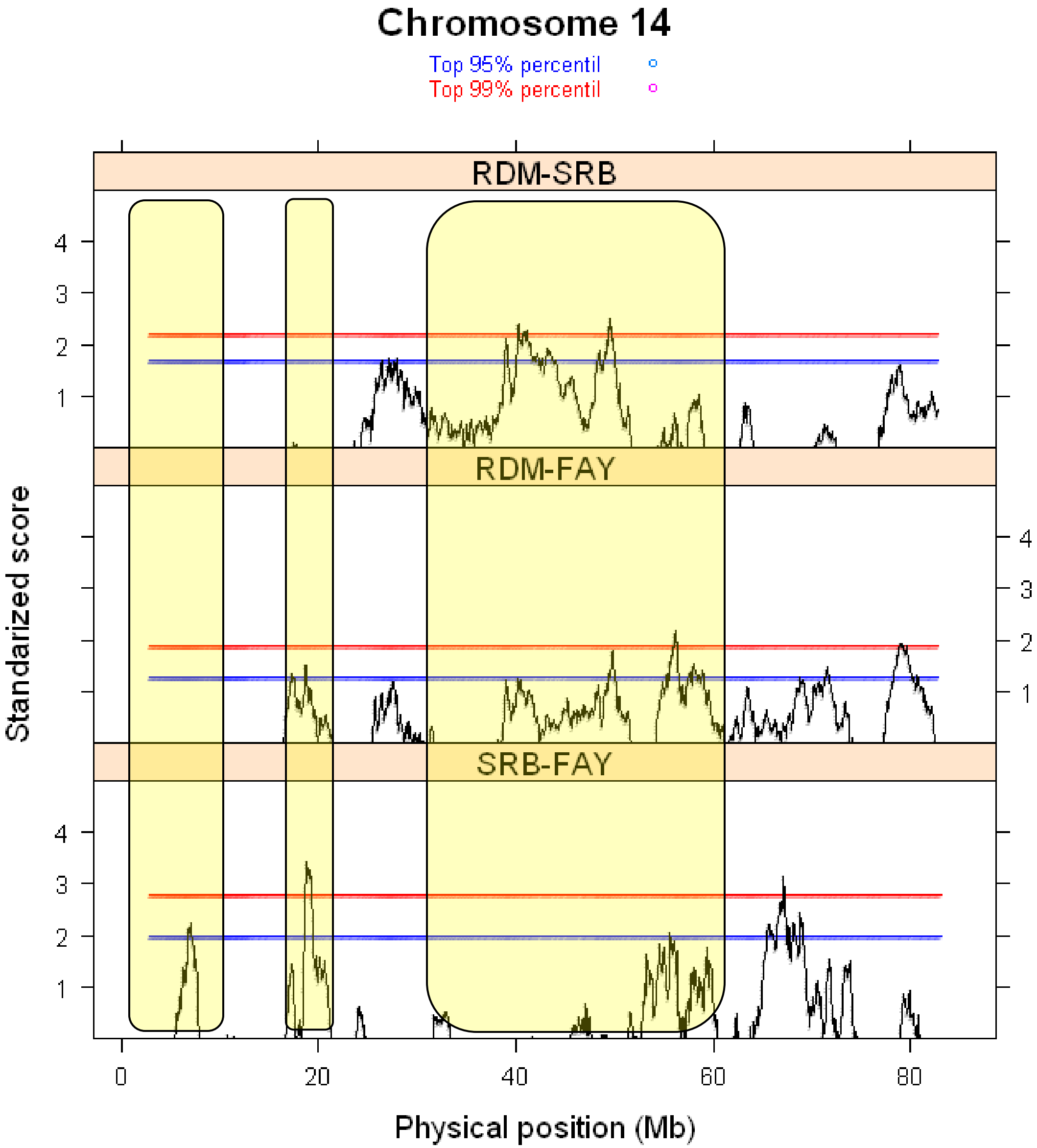


QTLs:

Somatic cell count (NRF) *(Klungland H. et al. 2001 Mamm. Genome)*

Milk protein % (FAY) *(Velmala R.J et al. 1999, Animal Genetics)*

Results$_{(5)}$ – Patterns of LD between populations



QTLs:

Milk fat yield (FAY)

(Viitala S.M et al. 2003, J. Dairy Sci.)

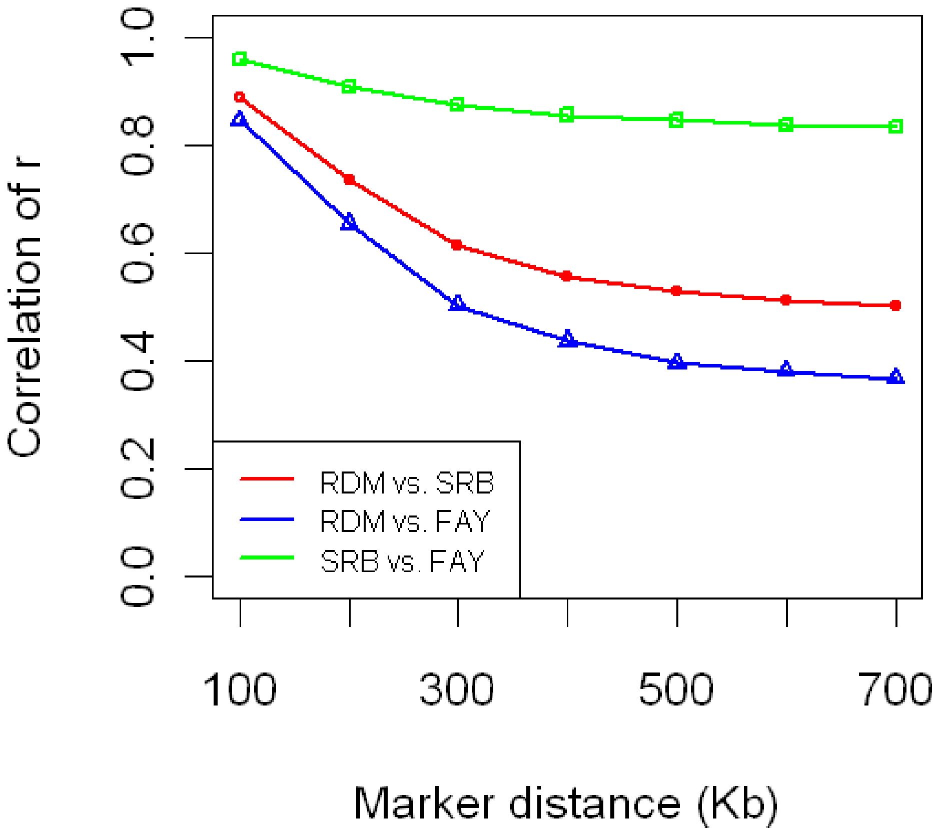
Non-return rate (FAY)

(Shulman N. et al 2008, GSE)

Somatic cell score (RDM, SRB and FAY)

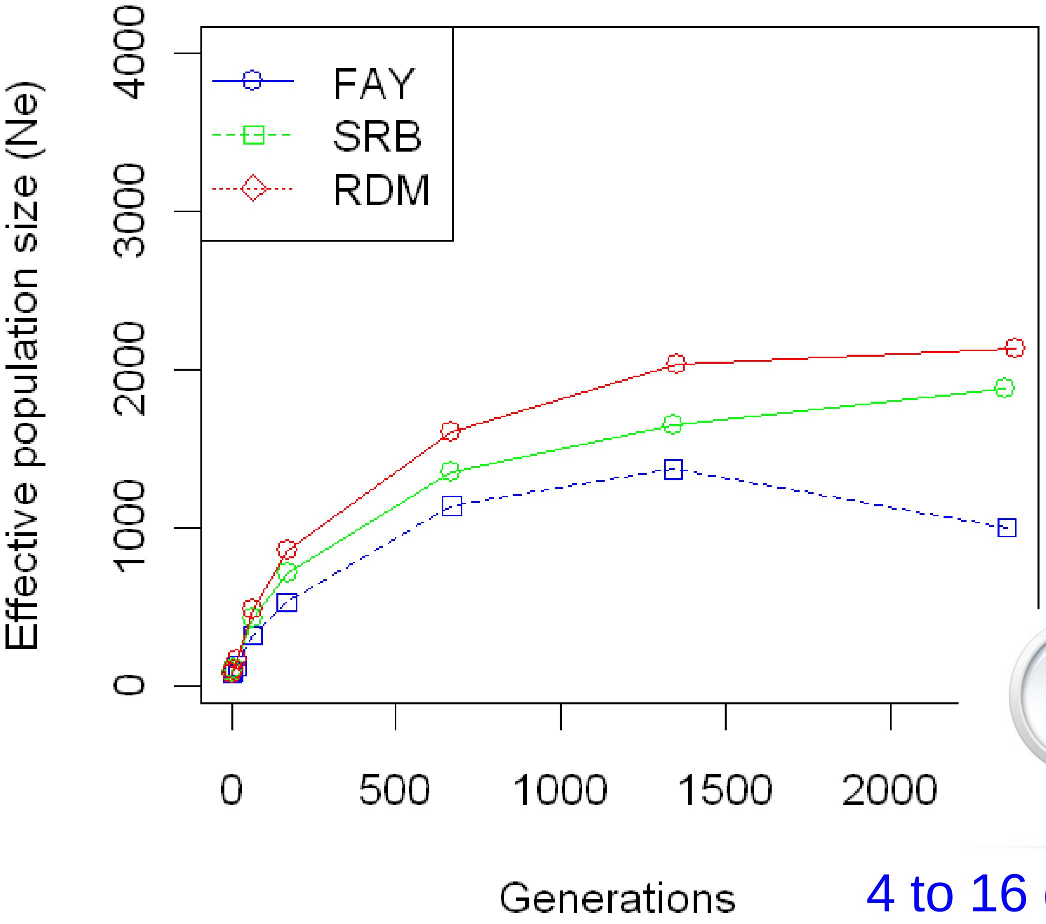
(Lund M. S et al. 2007, J. Dairy Sci.)

Results$_{(6)}$ – Persistency of marker phase



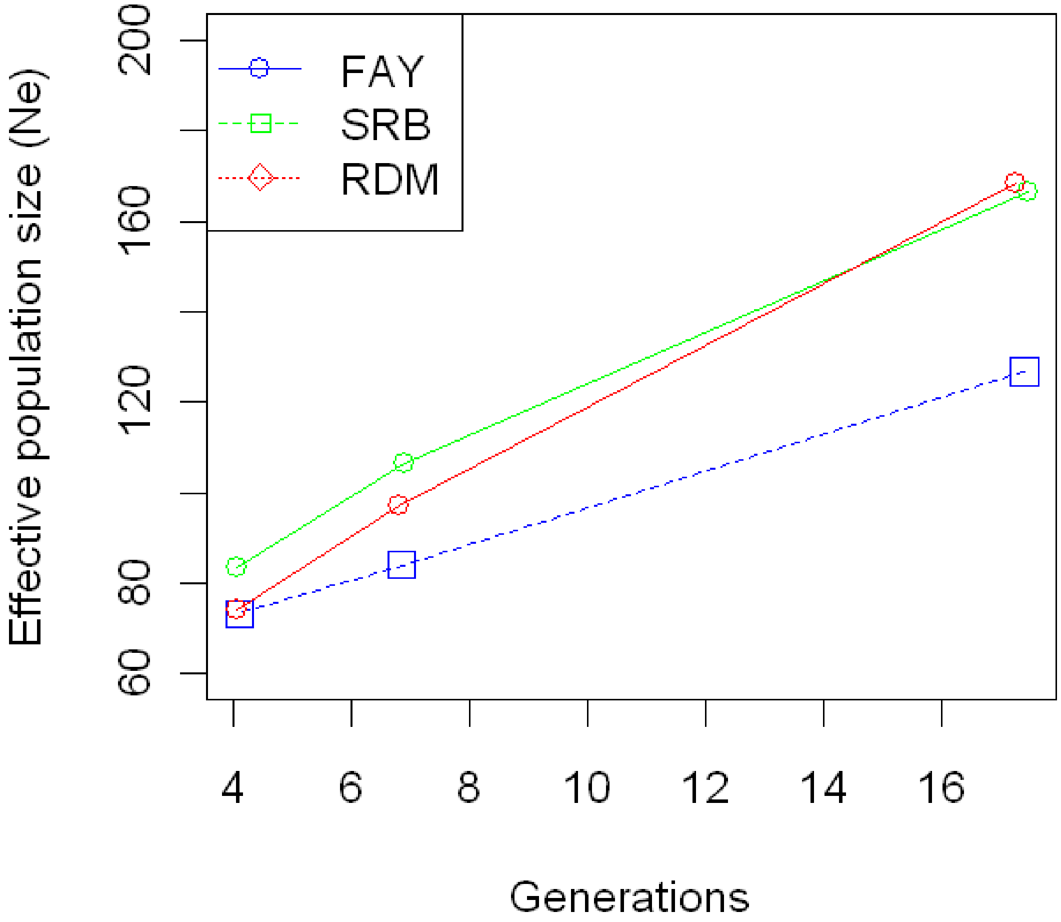
	RDM-SRB	RDM-FAY	SRB-FAY
P. Phase (0-100kb)	29.1% (16.5%)	33.2% (19.0%)	15.6% (9.1%)
Corr. of r (0-100kb)	0.68 (0.89)	0.58 (0.85)	0.89 (0.96)

Results$_{(7)}$ – Estimates of Ne



4 to 16 generations

Results$_{(7)}$ – Estimates of Ne of recent generations



Holstein < 50

Summary

- Average LD was lowest for RDM (0.07) and highest for FAY (0.11)
  - North American Holstein $r^2 > 0.20$, (Bohmanova J. et al. 2010)
- More markers to increase accuracies from genomic prediction models.
- Regional LD differences within reported QTL positions.
- Quantify regional LD variation to help:
  - Imputation strategies.
- The loss of persistency was highest between RDM-FAY and lowest between SRB-FAY
- Ne up to 4 generations ago was 84 for SRB, 74 for RDM and 73 for FAY.

Thank you