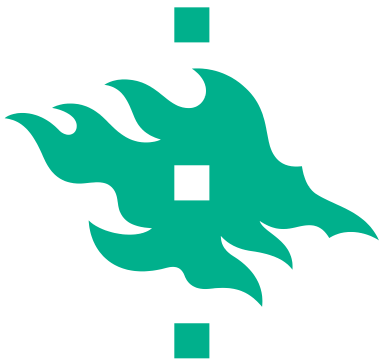


Single step evaluations using haplotype segments

M. L. Makgahlela, T. Knürr, G. P. Aamand, I. Strandén
& E. A. Mäntysaari



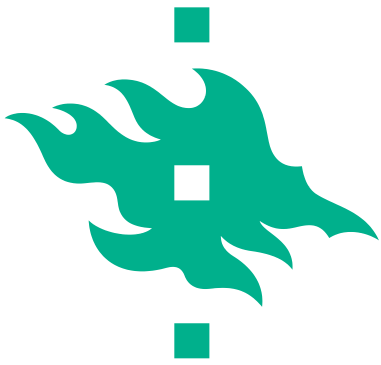


Introduction



- Genomic evaluations, as originally proposed, were based on haplotype segments, which are;
 - closely located allele combinations that tend to be jointly inherited

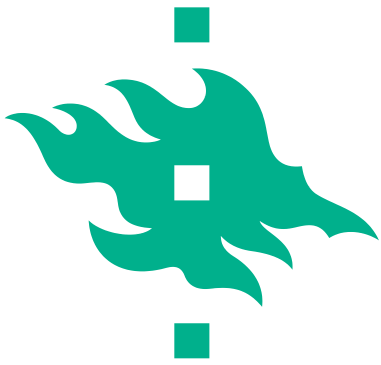
- Many current evaluations however, use large number of SNP markers in models that are;
 - simplified and less computationally demanding



Introduction



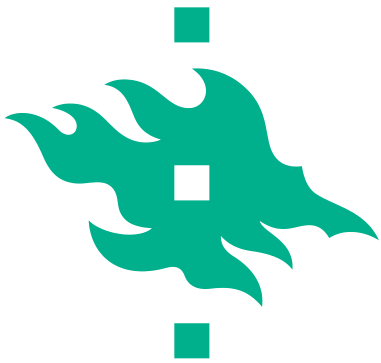
- If the observed reliabilities are low, haplo-block models may improve evaluations
 - 1) They were found to be more reliable than single markers
 - Because ancestral haplotypes may capture greater linkage disequilibrium (LD) with QTL than single markers
 - 2) They could greatly reduce the number of markers for genomic evaluations
 - 3) There are many free haplotyping software available



Objectives



- Examine the reliability of single step with genomic relationship matrix (**G**) constructed using haplotype segments in the Nordic Red dairy cattle (RDC)
- Compare the haplo-block model with standard single-step GBLUP



Data provided by NAV

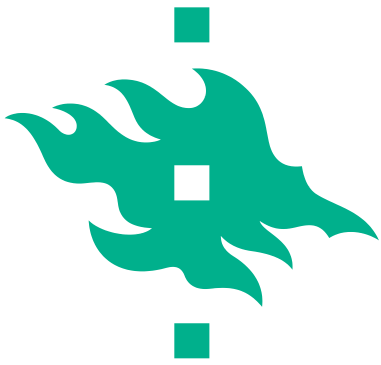
Genotypes

- After editing, there were 38,194 informative SNPs available for 4,727 bulls born between 1971-2008

Phenotypes

- Deregressed Proofs (DRP) of cows for milk, protein and fat
 - Full data (DRP_F) → 3,633,481 cows
 - Reduced data (DRP_R) i.e., discard cows born after > 2005 → 3,146,448 cows

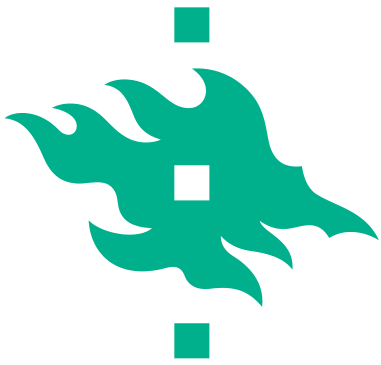
 Full RDC pedigree (n=4,873,703)



For validation



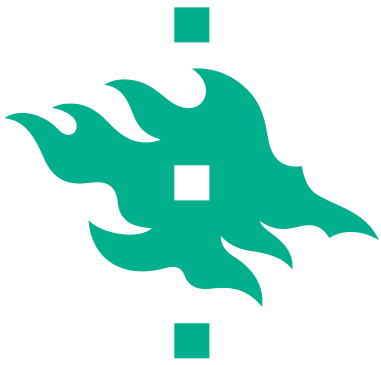
- ApaX in Mix99 program was used for calculating EDCs
- 2 runs of animal model were used to solve deregressed bull EBVs as follows;
 - 1st full run → with DRP_F → generate DRP for 519 validation bulls born between 2002-2008 with $EDC \geq 20$
 - 2nd reduced run → with DRP_R → daughters of 4,208 training bulls born between 1971-2005



Construction of Haplotype blocks



- 1) BayesB fitting joint estimation of SNP effects in multilocus model
- 2) Rank SNPs by the absolute effect $\hat{\beta}_g$
- 3) Haplotype (phase) genotypes using Beagle software
- 4) Construct **5-SNP** haplotypes (i.e., 2 SNPs before and after the one with the highest $\hat{\beta}_g$)
- 5) Estimate haplotype variances
- 6) Number of haplotype segments → 750 and 1500

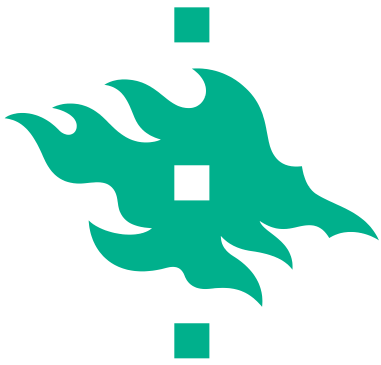


Single step model



$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} \mathbf{G}\mathbf{w}^{-1} - \mathbf{A}_{22}^{-1} & 0 \\ 0 & 0 \end{bmatrix}, \text{ where}$$

- \mathbf{A}^{-1} includes all animals and \mathbf{A}_{22}^{-1} is a sub-matrix for genotyped bulls
- $\mathbf{G}\mathbf{w} = (1 - w)\mathbf{G}\mathbf{k} + w\mathbf{A}_{22}$
 - ✓ $\mathbf{k} = \frac{\text{trace}\mathbf{A}_{ii22}}{\text{trace}\mathbf{G}_{ii}}$; w values were varied at 0.10, 0.20 or 0.40



Single step model

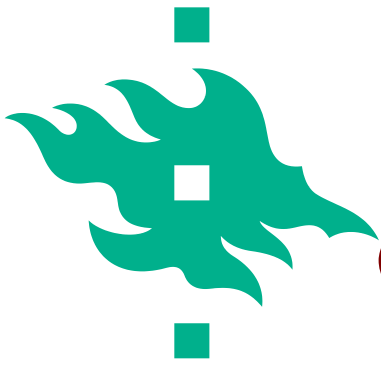
- Haplo-block \mathbf{G}

$$\mathbf{G} = \mathbf{ZDZ}' ; \quad \mathbf{Z}_{i,j} \leftarrow (0 - 2p_j); (1 - 2p_j); (2 - 2p_j),$$

- 0,1 or 2 is the number of 2nd allele
- p_j is the frequency for the 2nd allele
- \mathbf{D} is a diagonal of the estimate of haplotype variances
- Haplo-block \mathbf{G} was constructed with segments length 750 (HAP750) and 1500 (HAP1500)

- Regular SNP-based \mathbf{G} :

$$\mathbf{G} = \mathbf{ZZ}' / \sum 2pq$$



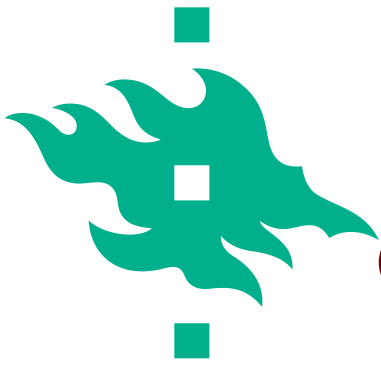
GEBV evaluation



$$\text{DRP}_{\text{R}_{\text{cow}}} = \mathbf{1}_n \mu + \mathbf{Za} + e,$$

➤ where:

- ✓ $\text{var}(\mathbf{a}) = \mathbf{H}\sigma^2_a$ with variances from NAV routine evaluations
- ✓ $\text{DRP}_{\text{R}_{\text{cow}}}$ is the deregressed proof of the daughter of training bulls in the reduced data
- ✓ Reliability of DRP was used as weight



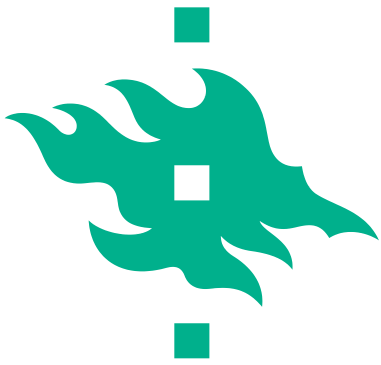
GEBV validation



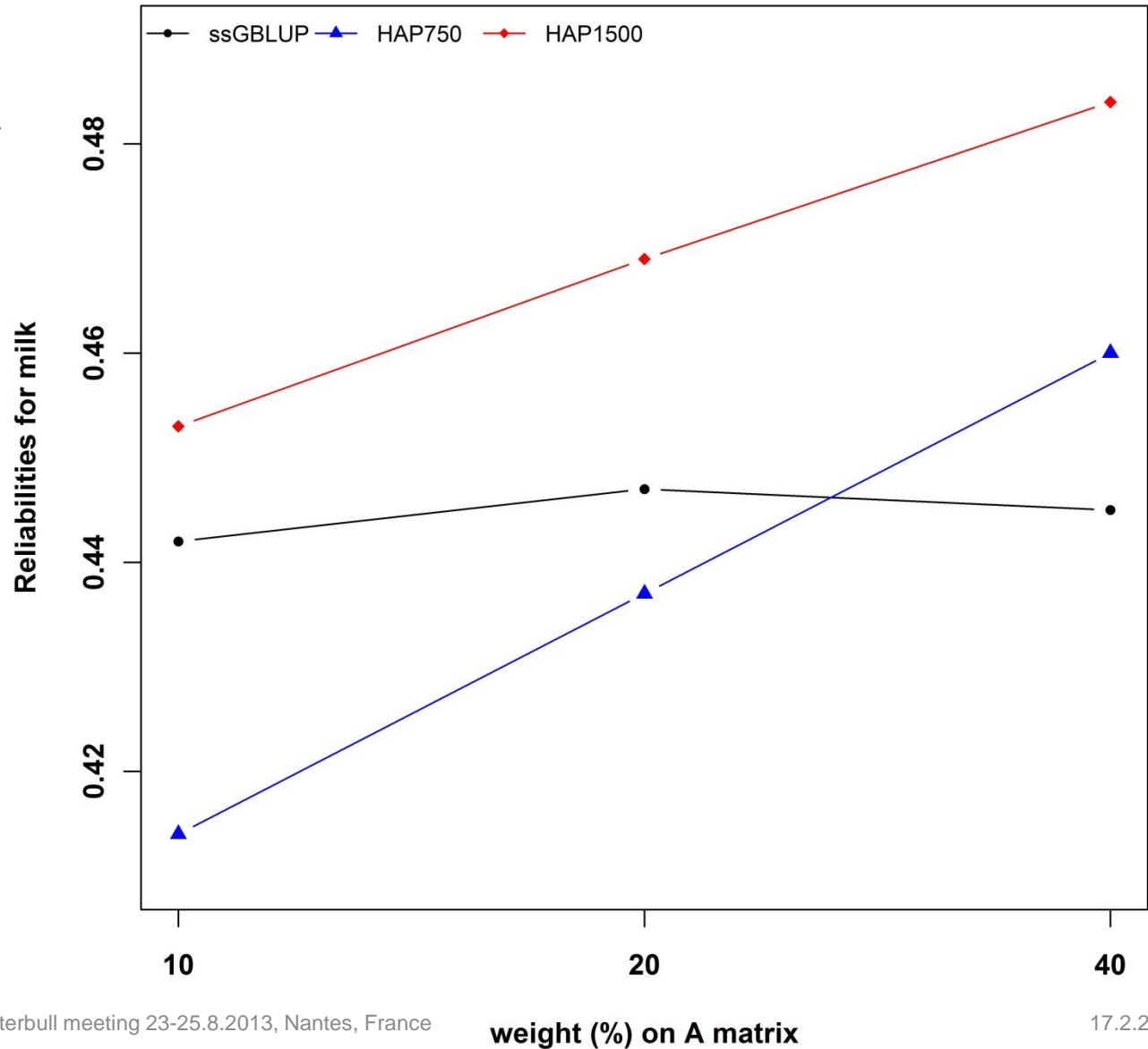
$$\text{DRP}_{F_{\text{bull}}} = b_0 + b_1 \text{GEBV} + e,$$

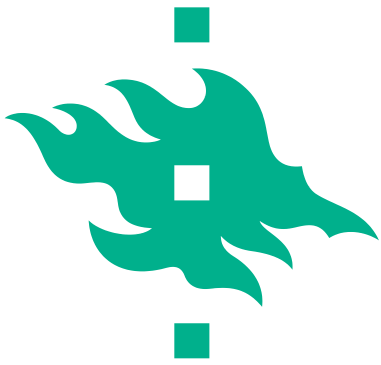
➤ where:

- ✓ $\text{DRP}_{F_{\text{cow}}}$ is the deregressed proof of the candidate from the full data run
- ✓ Reliability of DRP was used as weight

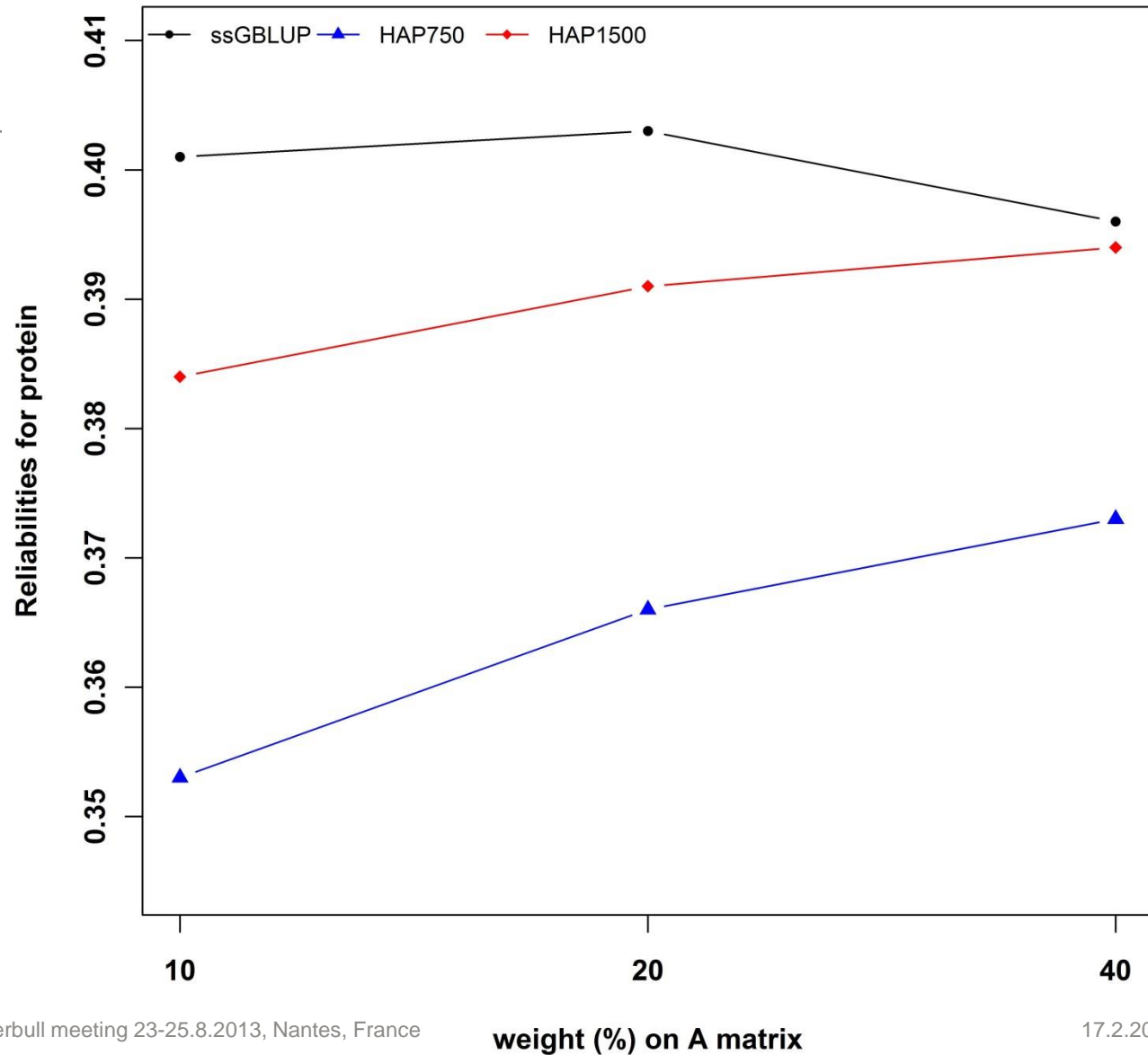


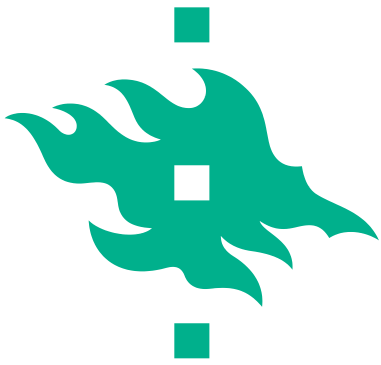
Validation reliabilities for milk



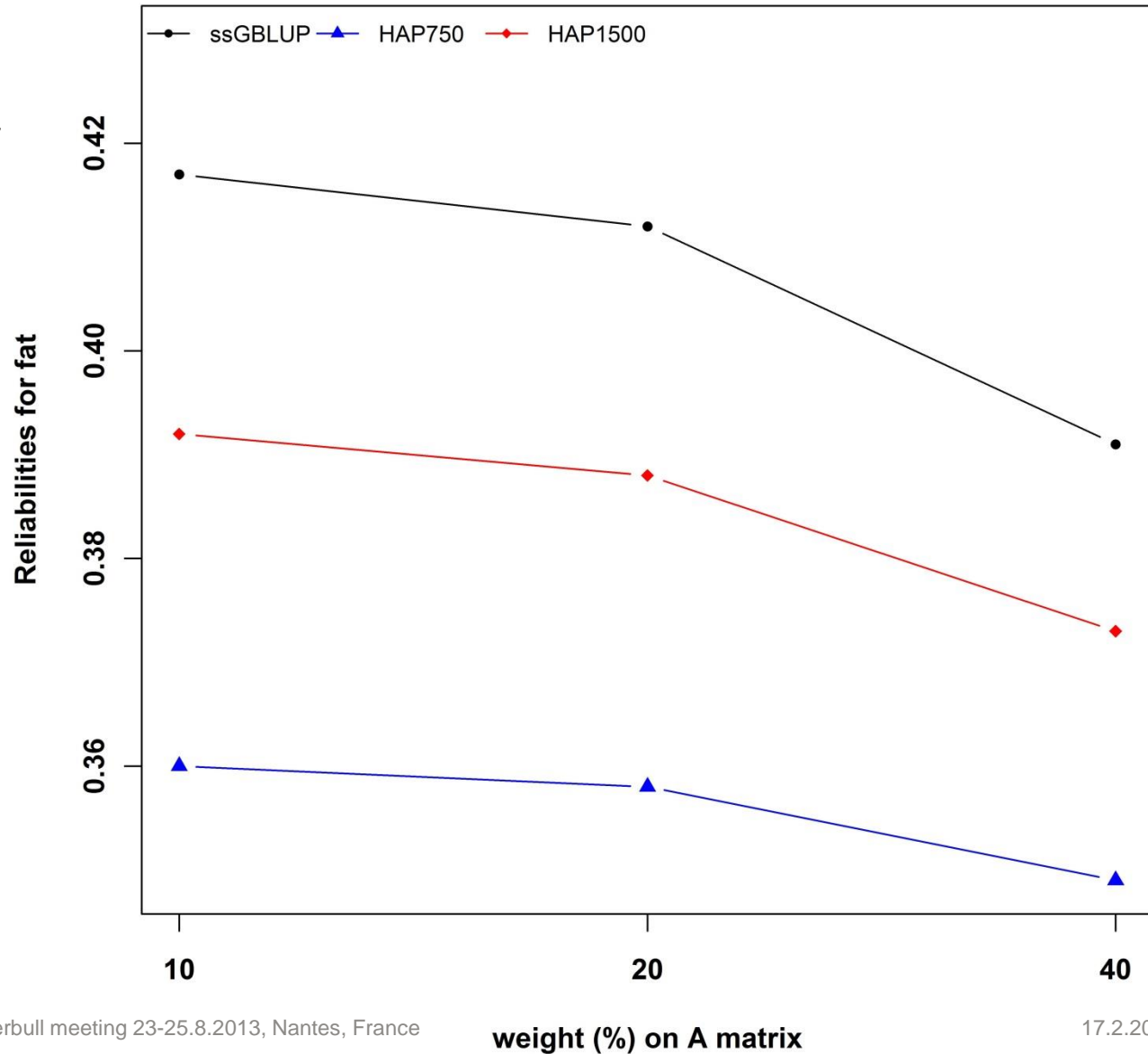


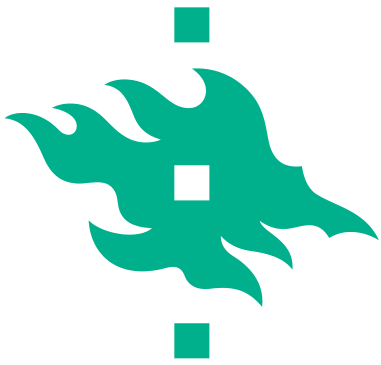
Validation reliabilities for protein



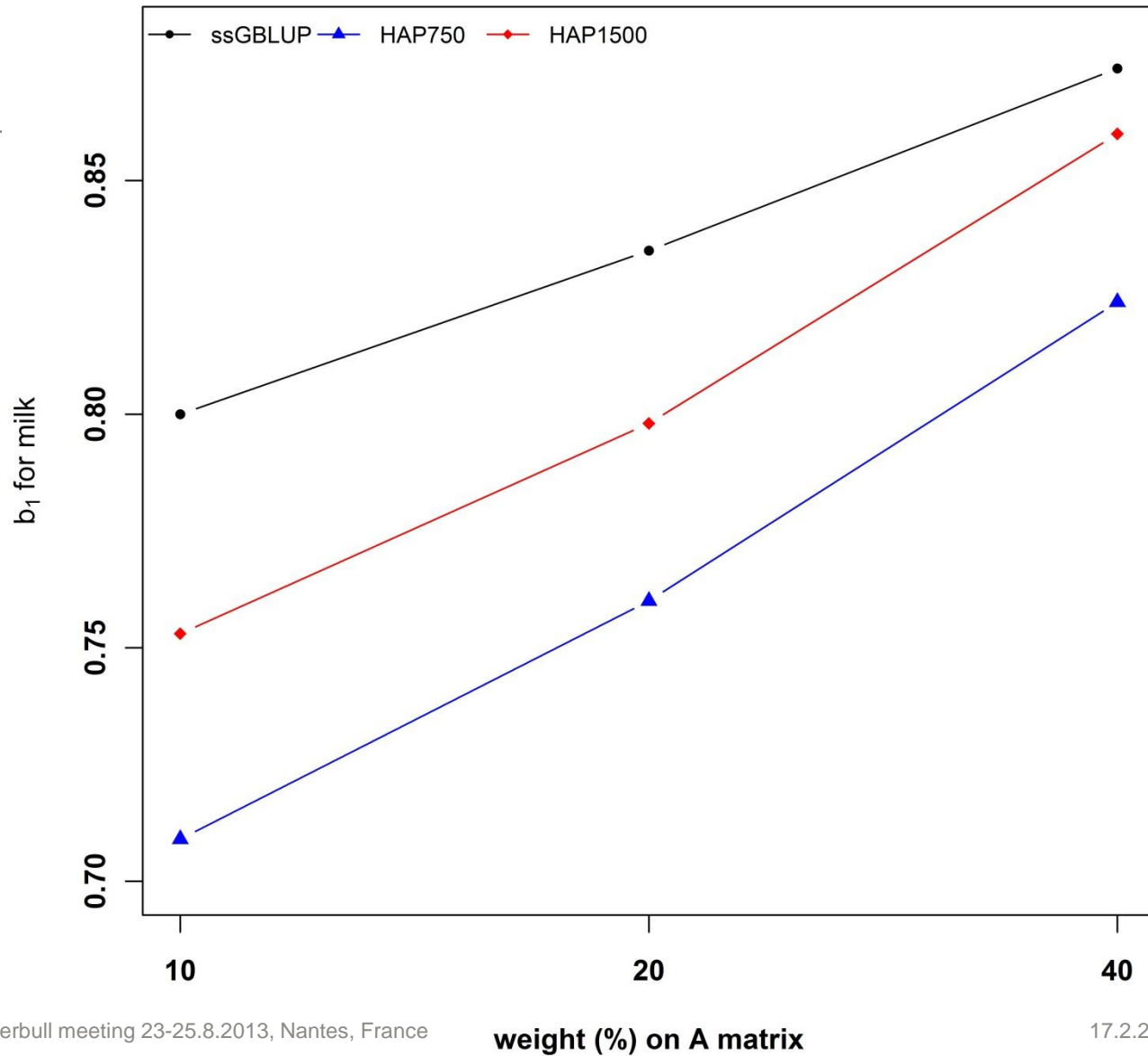


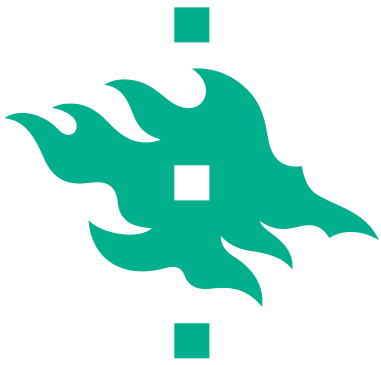
Validation reliabilities for fat



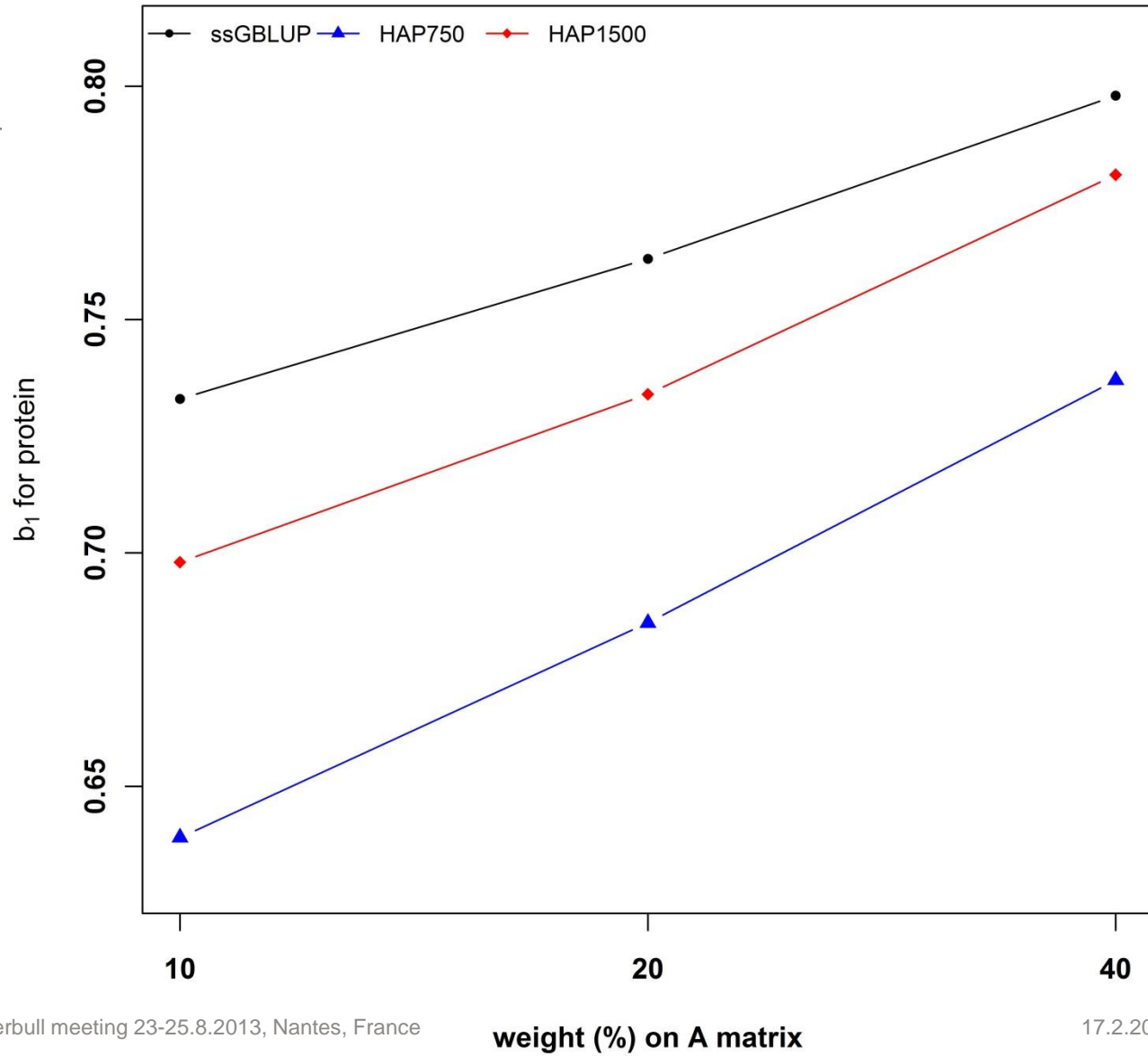


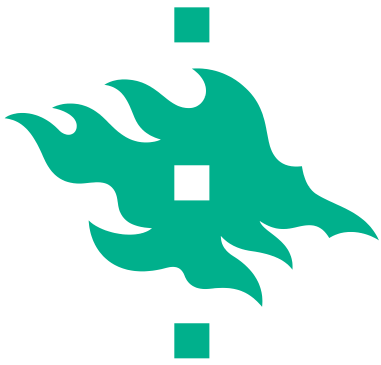
Inflation for milk



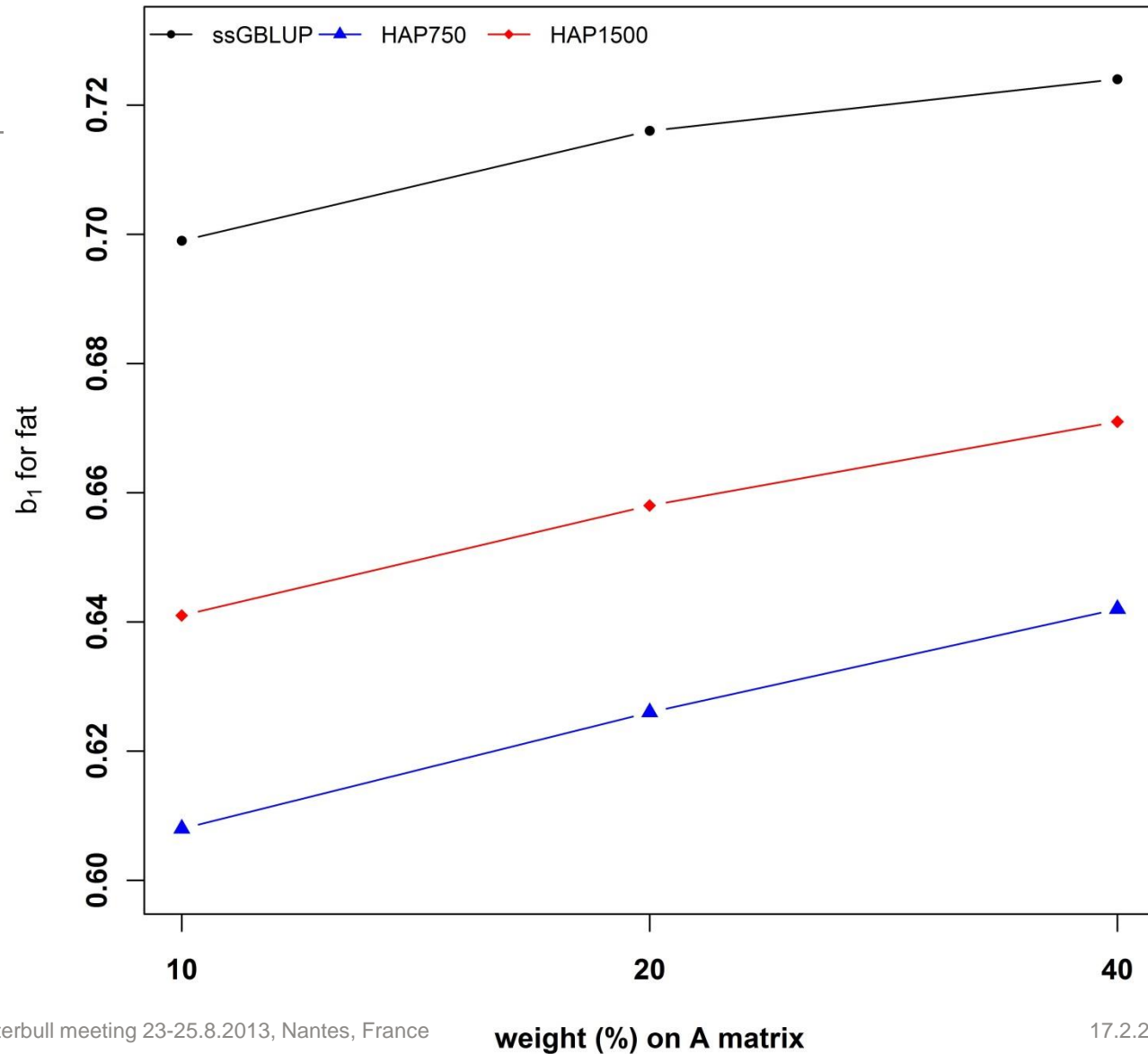


Inflation for protein





Inflation for fat



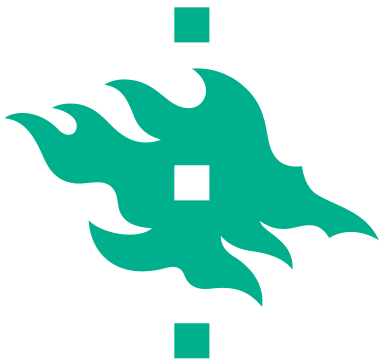
Validation reliabilities of GEBV

Method	Milk	Protein	Fat
w_A=0.1			
ssGBLUP	0.442	0.401	0.417
HAP750	0.414	0.353	0.360
HAP1500	0.453	0.384	0.392
w_A=0.2			
ssGBLUP	0.447	0.403	0.412
HAP750	0.437	0.366	0.358
HAP1500	0.469	0.391	0.388
w_A=0.2			
ssGBLUP	0.445	0.396	0.391
HAP750	0.460	0.373	0.349
HAP1500	0.484	0.394	0.373



Inflation of GEBV

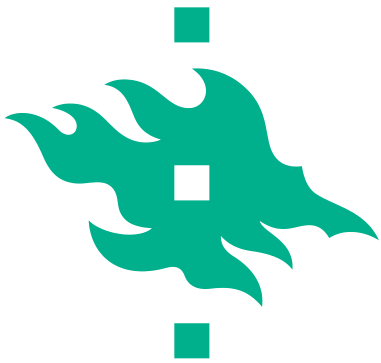
Method	Milk	Protein	Fat
wA=0.1			
ssGBLUP	0.800	0.733	0.699
HAP750	0.709	0.639	0.608
HAP1500	0.753	0.698	0.641
wA=0.2			
ssGBLUP	0.835	0.763	0.716
HAP750	0.760	0.685	0.626
HAP1500	0.798	0.734	0.658
wA=0.2			
ssGBLUP	0.874	0.798	0.724
HAP750	0.824	0.737	0.642
HAP1500	0.860	0.781	0.671



Conclusions



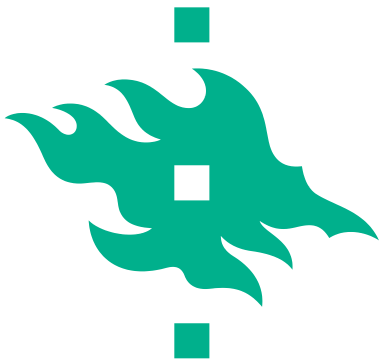
- The validation reliability for milk was clearly increased when using more haplotype segments → HAP1500
 - 1, 2 and 4 % when the weight on **A** was 0.1, 0.2 and 0.4, respectively
- Reliability for milk with HAP750 was increased by 2% when the weight on **A** was 40%
- These improvements however, were not achieved for protein and fat as reliabilities were low
- Reliabilities of haplo-block models for milk and protein tended to increase with increasing weight on **A** but the opposite was true for fat



Conclusions



- For all traits, the inflation levels of GEBV were greater with haplo-block models
 - In all cases, inflation intervals with standard single step reduced as the amount of pedigree increased
- The use of haplotype segments appeared to be very promising provided there is balance between the number of haplotypes and optimal scaling with pedigree information



THANK YOU !!!