Haplotype-assisted genomic evaluations in Nordic Red Dairy Cattle

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NAV Nordic Cattle Genetic Evaluation

Background

- Poor predictive ability of genomic data in admixed populations like Nordic Red Dairy Cattle originating from numerous base breeds
  - inability of SNP to trace genetic relationships (IBS≠IBD) in heterogeneous populations
  - inconsistencies of LD between SNP and QTL
- Haplotypes may be more useful than SNP to recover genetic relationships and LD

Goals of the study

- Improve the prediction accuracy by use of IBD information in haplotypes of chromosomal segments
    - Criterium: validation test reliability

- Optimize use of genomic information and statistical procedure

Outline of statistical procedure

Pre-selection of markers

- Bayes B-type model to detect QTL signals
- Using SNP genotypes

Construction of haplotype blocks

- Around pre-selected SNP
- Using flanking markers in chromosomal segments

Estimation of haploblock variances

- Bayes A-type model
- To achieve correct weighting in multilocus model

Estimation of haplotype effects for prediction

- Solutions of MME
- A proportion of genetic variance assigned to pedigree
- Rest of genetic variance assigned to weighted haplotypes

Methods: Pre-selection of markers and construction of haplotypes

- Simultaneous scan of all SNP markers via Bayes B

- Ranking of signals using the estimates of the absolute effect size

- 750/1500 SNP with strongest signals chosen as the centers of haplotype blocks spanning 3/5 neighbouring SNP

Methods: Estimation of haploblock variances

$$\mathrm{DRP} = \mu + \sum_{m=1}^{750/1500} \left(\underbrace{g_{m,1}^{\mathrm{hap}}}_{\text{paternal}} + \underbrace{g_{m,2}^{\mathrm{hap}}}_{\text{maternal}} \right) + \varepsilon$$

- Outcome: here deregressed proofs (DRP)
- Estimation of haploblock variances $\sigma_{gm}^2 = Var(g_m^{\mathrm{hap}})$ by Bayes A
- Weights: effective daughter contributions (EDC)

Methods: Estimation of haplotype effects and predictions

$$\mathrm{DRP} = \mu + a + \sum_{m=1}^{750/1500} \left(g_{m,1}^{\mathrm{hap}} + g_{m,2}^{\mathrm{hap}} \right) + \varepsilon$$

- Solutions of MME with fixed $\mathrm{Var}(a) = \omega \hat{\sigma}_a^2 \mathbf{A}$ and $\mathrm{Var}(g_m^{\mathrm{hap}}) = (1-\omega)\hat{\sigma}_a^2 \cdot \hat{\sigma}_{gm}^2 / S$
- Proportion ω of additive variance assigned to pedrigee and $1-\omega$ to haplotype segments
- Weighted by EDC

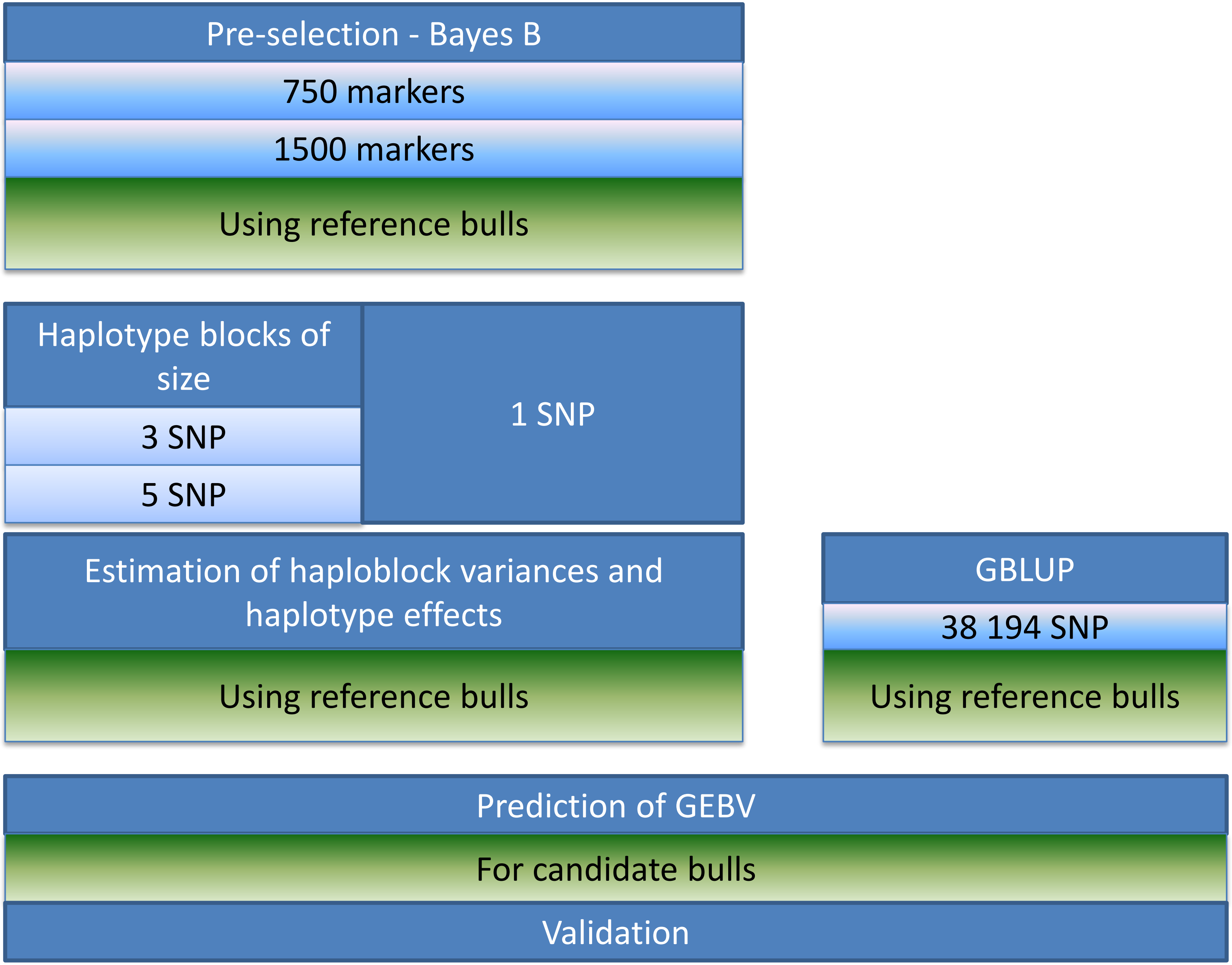
Evaluation: $\mathrm{GEBV} = \hat{a} + \sum_{m=1}^{750/1500} \left(\hat{g}_{m,1}^{\mathrm{hap}} + \hat{g}_{m,2}^{\mathrm{hap}} \right)$

Data

	Production traits: milk, protein, fat	Fertility
Reference bulls (born 1971-2005)	4250	4422
Candidate bulls (born 2006-2008)	516	551
Total	**4766**	**4973**

- DRP and EDC from Nordic Cattle Genetic Evalution (February 2013)

- 38 194 SNPs (after editing) on autosomes from Illumina Bovine SNP50 BeadChip - imputation of missing genotypes and phasing with BEAGLE v3.3 (Browning & Browning 2009)



Pre-selection - Bayes B

750 markers

1500 markers

Using reference bulls

Haplotype blocks of size

3 SNP

5 SNP

1 SNP

Estimation of haploblock variances and haplotype effects

Using reference bulls

GBLUP

38 194 SNP

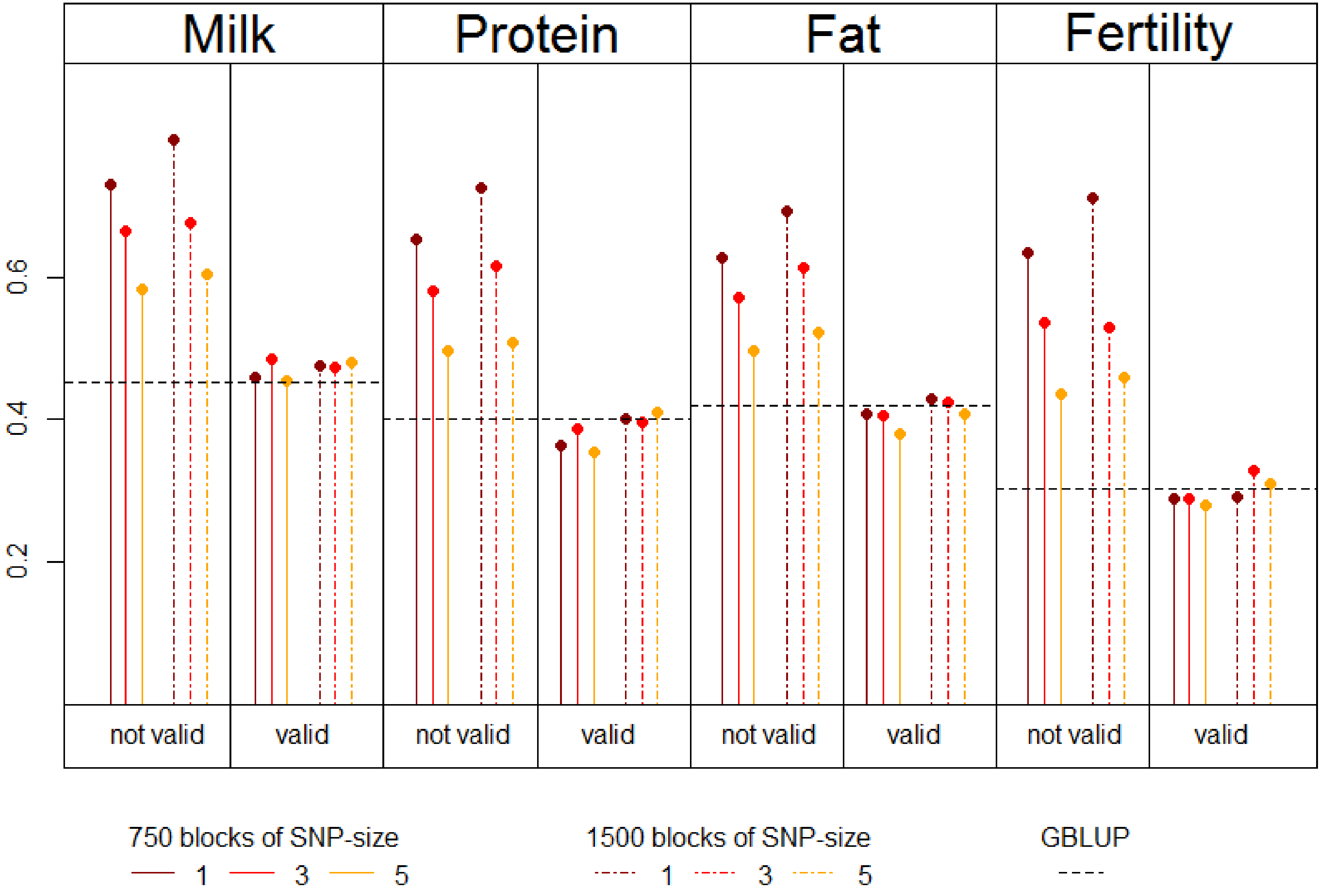
Using reference bulls

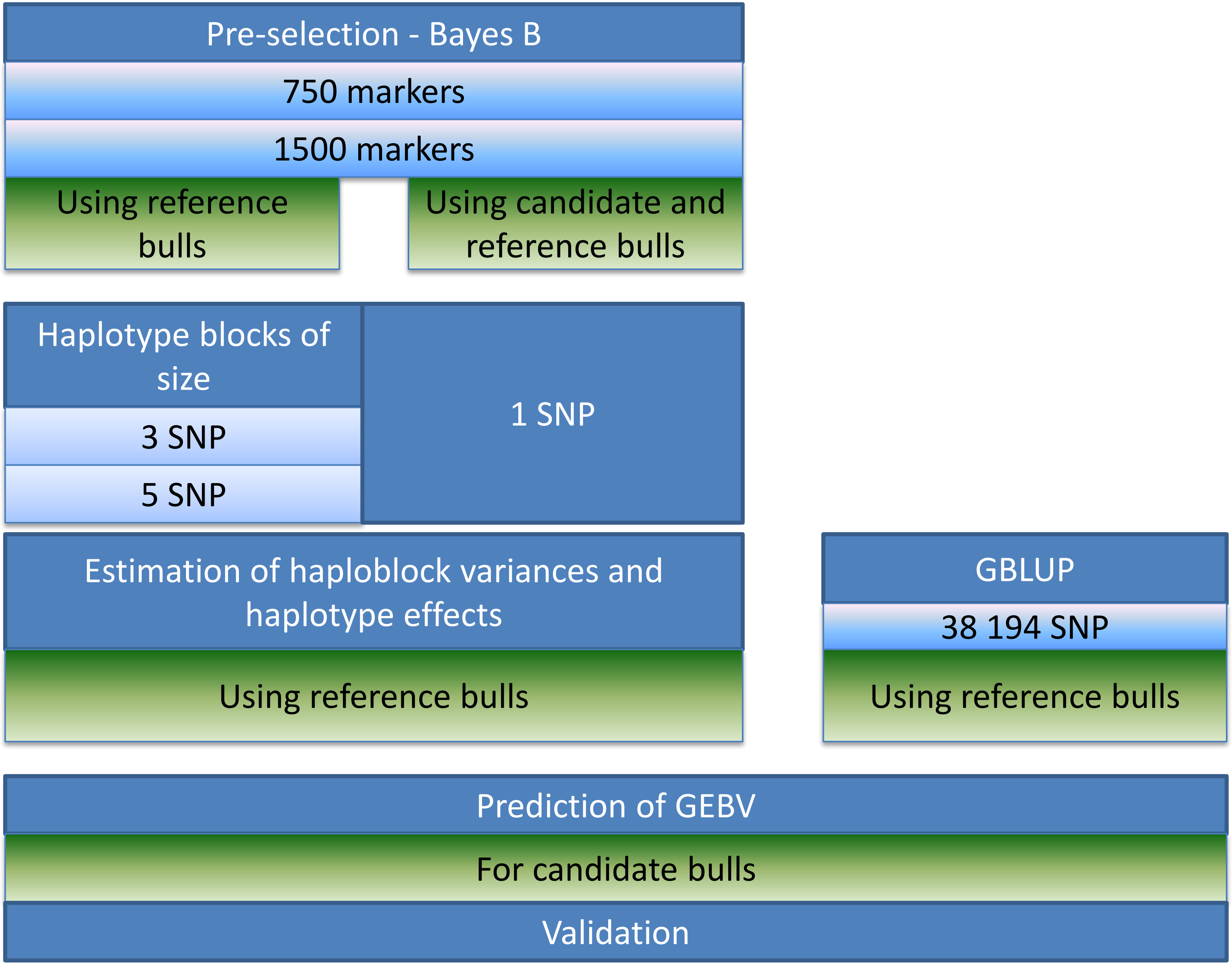
Prediction of GEBV

For candidate bulls

Validation

Results – Validation test reliabilities





Pre-selection - Bayes B

750 markers

1500 markers

Using reference bulls

Using candidate and reference bulls

Haplotype blocks of size

3 SNP

5 SNP

1 SNP

Estimation of haploblock variances and haplotype effects

Using reference bulls

GBLUP

38 194 SNP

Using reference bulls

Prediction of GEBV

For candidate bulls

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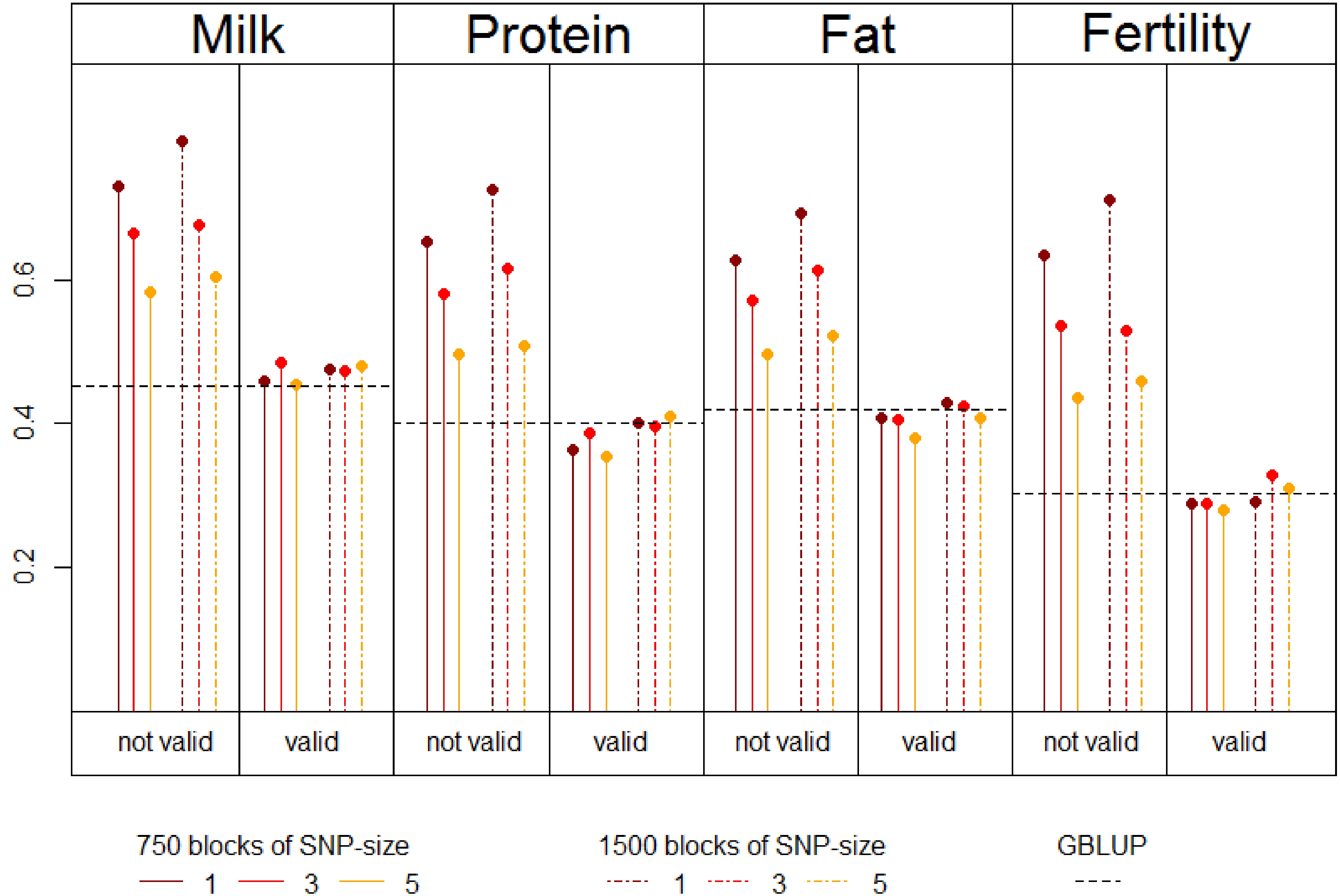

Conclusions

Acknowledgements