Biology informed genomic predictions for mastitis in Danish Jersey and Nordic Red cattle

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BovReg WP7: Models for biology driven genomic selection

Task 7.2: Validating biology-driven genomic selection within and across small breeds

Sub-task (AU&LUKE):
Incorporating biological information (QTL, mQTL, ATAC-seq etc.) generated in BovReg, into models of genomic prediction for mastitis, in Nordic breeds.

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50K → HD → WGS

- Little or no improvement by using HD instead of 50K SNPs
- Little or no improvement by using WGS instead of HD SNPs
- 50K already captures most of the genetic variation
- WGS data is better utilized if selected SNPs are added to standard 50K chip
    - It maybe relatively easy to include QTL and eQTL SNPs etc., but not those from ATACseq results

Our approach

- Enrich 50K SNPs with results of “-omics” studies
- Can be implemented in routine as weighted GBLUP
- Additional analysis to obtain SNP variances is needed

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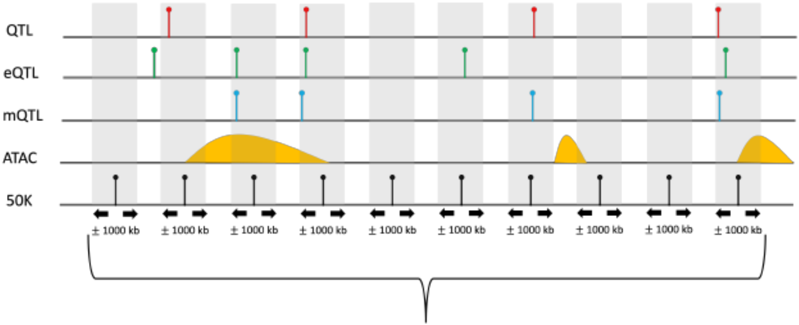
Data sets: Phenotypes and genotypes

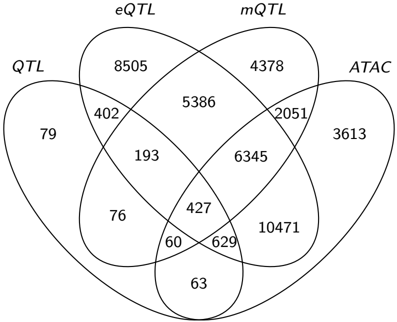
- Danish Jersey (JER) and Nordic Red Cattle (RDC)
- DRPs for mastitis, derived by LUKE were used as phenotypes
- 9,939 JER and 34,394 RDC cows with DRPs
  - Cows born in 2017 or before → reference population (JER: 8,737, RDC: 31,101)
  - Cows born in and after 2018 → validation population (JER: 1,202, RDC: 3,293)
- SNPs on 50K chip were extracted

Data sets: Annotations



$$\mathbf{Q} \rightarrow \begin{array}{l} \text{QTL} \\ \text{eQTL} \\ \text{mQTL} \\ \text{ATAC} \\ \text{50K} \end{array} \begin{bmatrix} 0 & 1 & 0 & 1 & 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 1 & 1 & 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 1 & 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 1 & 1 & 1 & 0 & 0 & 0 & 1 & 0 & 1 \\ 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \end{bmatrix}$$

Data sets: Annotations



Method: BayesLV

$$\beta_j \sim N(0, exp(\mathbf{Q}_j\mathbf{q} + \epsilon_j)$$

- $\mathbf{Q}$ is a matrix of known covariates to model the SNP-variances, $\mathbf{Q}_j$ is the j'th row of $\mathbf{Q}$ with covariates for SNP j.
- $\mathbf{q}$ is a vector of effects on the SNP log-variance scale.
- ϵ_i is a residual in the SNP variance model with $\epsilon_j \sim N(0, \sigma^2_\epsilon)$.
- This modelling of SNP variances allows for incorporation of additional biological information, such as genomic annotation groups and QTL information, in genomic predictions. The noise variance σ^2_ϵ is set fixed to a relatively small noise level.
- This forces SNPs that have the same annotations to have close to the same prior Normal distribution ($\mathbf{Q}_j\mathbf{q}$ terms are identical).

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Reliabilities

	GBLUP	BayesLV				
	50K	+QTL	+eQTL	+mQTL	+ATAC	+All
JER	0.164	0.178	0.173	0.181	0.176	0.187
RDC	0.145	0.139	0.131	0.131	0.135	0.140

The + stands for additional information used on 50K data.

Conclusions

- Enriching 50K SNPs with the prior information from "-omics" analysis, improved reliabilities for JER but not for RDC
- It should be noted that the choice of 1,000 kb for extending SNP region downstream and upstream was arbitrary,
  - Large values may cause a large set of overlapping SNPs across different categories.
  - Small values may cause some important WGS SNPs to be missed, and thereby may lead to loss of information.
- Need further look into the analysis pipelines, to make the approach work also for RDC
- The statistical method (BayesLV) used, and its implemented sampling algorithm has not been thoroughly investigated in such a data integration study for genomic prediction, and they may be improved

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