

Genome-wide associations for feed utilisation complex in primiparous Holstein-Friesian dairy cows from experimental research herds in four European countries

Veerkamp, R.F., Wall, E., Berry, D.P., De Haas, Y., Coffey, M.P., Strandberg, E., Bovenhuis, H., Calus, M.P.L.



Aim

- Investigate genetics underlying feed utilisation complex; important components of robustness.
- "What is new"
 - Combine data across countries
 - High density SNP & Bayesian stochastic search variable selection
 - How to come to useful inferences?



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Data

- Research herds: Teagasc, Ireland; SAC, Scotland; 2x Dutch; SLU, Sweden.
- 1,804 first lactation Holstein-Friesian cows with 66,116 test-week records collected up to 315 DIM
- Live-weight (LW), body condition score (BCS), dry matter intake (DMI) and fat and protein corrected milk yield (FPCM).
- Genotypes: Illumina BovineSNP50 BeadChip (QC: Calus et al GSE 2011)



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Step 1: smoothing and homogenising data

- predict full lactation curve for each animal to use average of week 3-15 (when at least 10 records)

Model:

- Random polynomial for each animal (sixth order)
- Fixed effects:
 - mean lactation curve by management group (10x)
- Time dependant random effects:
 - year-month of test by management group (353)
 - experimental treatment Ireland (81)



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Step 2: Persistency of LD

- Persistency of the linkage disequilibrium (LD) across subpopulations (de Roos et al 2008):
 - LD as r^2 between all neighbouring SNP as a function of distance
 - Correlation between groups for r was calculated across all marker distances



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Step 3: Estimate SNP effects

- Bayesian Stochastic Search Variable Selection (Calus et al)

$$y_i = \mu + a_i + \sum_{j=1}^n \sum_{k=1}^2 SNP_{ijk} + e_i$$

- Interpret SNP effects:

- Bayes factor

$$BF = \frac{Pr(H_1|y)}{1 - Pr(H_1|y)} \div \frac{Pr(H_1)}{1 - Pr(H_1)}$$

- Variance explained

$$\sigma_{ik}^2 = 2p_k q_k \times a_{ik}^2$$



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Step 4: Biological function

- Use Biomart (R) to identify genes:
 - positional close to SNP (500 kb)
 - genes in which significant SNP are located
- David: Bioinformatics enrichment tools, functional analysis of large gene lists



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Results: smoothing

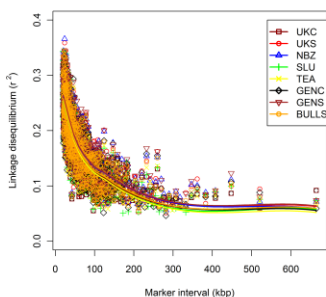
	N	Heritability and genetic correlation			
		FPCM	DMI	BCS	LW
Milk yield (FPCM)	1629	0.37			
Dry matter intake (DMI)	970	0.41	0.53		
Body condition score (BCS)	564	-0.09	0.39	0.58	
Live weight (LW)	1416	0.39	0.68	0.52	0.47

s.e.: 0.07 – 0.14



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Results: Linkage disequilibrium

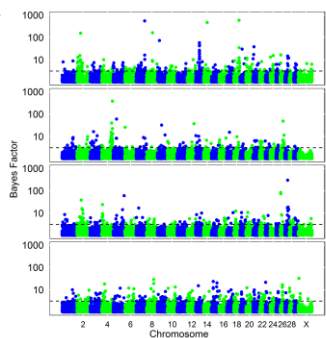


Correlations between r across the genome were 0.95 and 0.97; exception Langhill control 0.92



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Results: Individual SNP



36, 18, 19 SNP BF>10 for LW, BCS and DMI, 2.5%, 1.2%, 0.8% of the genetic variance.

31 SNP associated two traits 1 was associated with three



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Results: Variance by chromosome

Chr.	LW	BCS	DMI	FPCM	Chr.	LW	BCS	DMI	FPCM
1	5.8%	6.0%	6.0%	6.1%	16	3.0%	3.0%	3.1%	3.0%
2	5.3%	5.1%	5.3%	5.2%	17	2.9%	2.9%	2.9%	2.9%
3	4.6%	4.8%	4.7%	4.7%	18	3.1%	2.5%	2.5%	2.5%
4	4.6%	5.6%	4.7%	4.7%	19	2.6%	2.6%	2.6%	2.6%
5	4.0%	4.1%	4.1%	4.0%	20	2.8%	2.8%	2.8%	2.8%
6	4.6%	4.7%	4.7%	4.8%	21	2.7%	2.7%	2.7%	2.7%
7	4.7%	4.1%	4.1%	4.2%	22	2.4%	2.5%	2.5%	2.5%
8	4.3%	4.1%	4.2%	4.3%	23	2.0%	2.1%	2.1%	2.1%
9	3.8%	3.8%	3.8%	3.9%	24	2.3%	2.3%	2.3%	2.3%
10	4.0%	4.1%	4.0%	4.1%	25	2.0%	2.0%	2.0%	2.0%
11	4.1%	4.2%	4.2%	4.2%	26	1.9%	2.1%	2.1%	2.0%
12	3.1%	3.2%	3.1%	3.2%	27	1.8%	1.8%	2.3%	1.8%
13	3.7%	3.5%	3.5%	3.5%	28	1.7%	1.8%	1.8%	1.8%
14	3.8%	3.4%	3.4%	3.4%	29	2.1%	2.1%	2.1%	2.1%
15	3.1%	3.1%	3.1%	3.3%	X	1.9%	1.9%	1.9%	1.9%



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Results: Biology

- 500 unique genes were found within 500 kbp flanking the SNPs bf>10 associated with LW, DMI or BCS
- Three functional groups overrepresented
 - 16 kallikrein, peptidase and trypsin genes
 - 5 genes involved with cystan
 - 32 olfactory, taste receptor, and pheromone receptor genes
- 22 SNPs that were identified with Bayes factor >3.1 and located in known genes: insulin, epidermal growth factor and tryptophane



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Conclusions

- Were able of combining data across herds
- Identified biological interesting SNP & genes & processes: olfactory, taste receptor, and pheromone receptor; Tryptophan; Insulin; Leptin
- Each single SNP explained little variation (using BSSVS).

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R. F. Veerkamp¹, M. P. Coffey², D. P. Berry³, Y. de Haas¹, E. Strandberg⁴, H. Bovenhuis⁵, M. P. L. Calus¹ and E. Wolf¹



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