GenomeWide Association Study for Milk and Fat / Protein Ratio in Dairy Cattle

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Introduction

- The Robustmilk project
    - Develops new practical technologies for selection on milk quality and dairy cow robustness
    - Brings together resources from 5 European countries

- This study : Combine data from 4 research herds and discover genomic regions that are associated with :
    - Milk production
    - Fat / Protein ratio

Materials - Phenotypes

- Holstein cows from 4 countries :
  - 546 : Ireland
  - 653 : Scotland
  - 144 : Sweden
  - 590 : The Netherlands

- Weekly test day milk records during 1st lactation :
  - Milk (kg)
  - Fat (kg)
  - Protein (kg)
- 305 day yields calculated from Wilmink curve (Wilmink, 1987)

Fat / Protein ratio deviation

- Negative Energy Balance is common in early lactation
  - Demands for milk production increase
  - Feed intake levels lag behind
  - Slow return to homeostasis

- Fat / Protein Ratio averages
  - 305 day lactation : 1.19
  - Early lactation, week 2-5 : 1.30
  - Maximum in early lactation, week 2-5 : 1.45

- Fat / Protein Ratio deviation

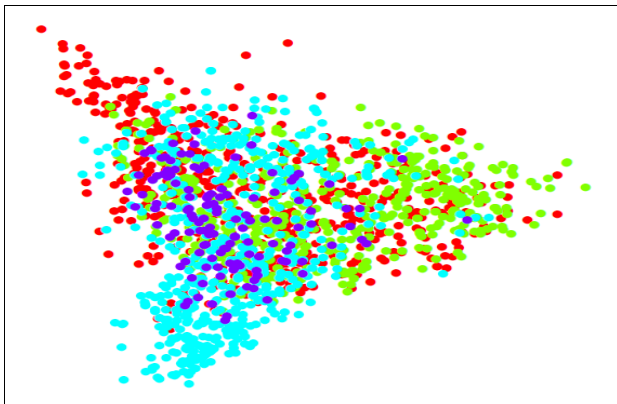$$(\text{Maximum Ratio week } 2-5) - (\text{Average Ratio 305 days}) \qquad (1)$$

Materials - Genotypes

- Cow genotypes from Illumina BovineSNP50 BeadChip

- 54 samples (2.8%) were removed :
  - Call rate ≤ 0.95

- 18,577 SNPs (34%) were removed :
  - GC score ≤ 0.20
  - GT score ≤ 0.55
  - Call rate ≤ 0.95 in one or more countries
  - χ^2 for HWE ≤ 600
  - Minor Allele Frequency
    - ≤ 0.01 in one or more countries
    - ≤ 0.05 overall

Results : Combining data

► Calculate IBS distances between all pairs

► Apply standard metric 2 dimensional scaling

► No separation of clusters by country

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Association analyses

▶ Adjusted phenotypes

$$Y = CHYS + \beta_1 age + \beta_2 age^2 + e \qquad (2)$$

▶ Regression analysis including individual SNP and Y adjusted from model 2
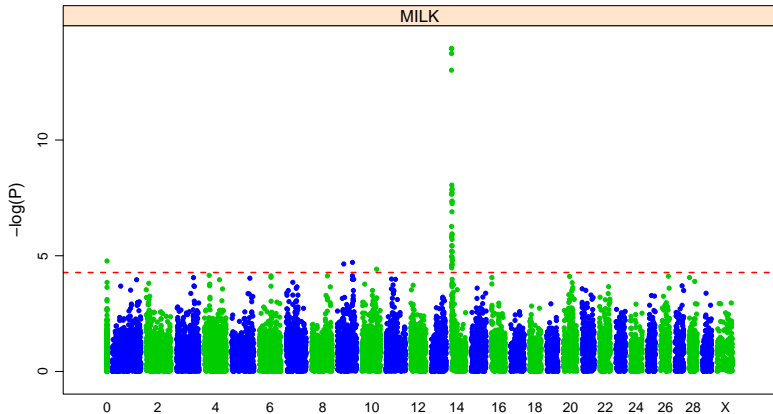
$$Y^* = SNP + e \qquad (3)$$

▶ False Discovery Rate adjustment
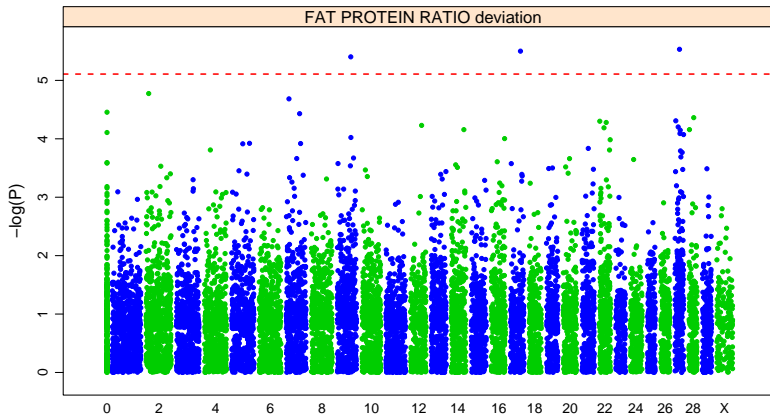
(Storey and Tibshirani, 2003)

    ▶ 0.05 FDR level

Results : GWAS Milk

- Plot of $-log_{10}(P)$ against genome position : MILK

Results : GWAS Fat / Protein ratio

- Plot of $-log_{10}(P)$ against genome position : FPR deviation

FAT PROTEIN RATIO deviation

Associations with Fat / Protein Ratio

- Details of associated SNPs

Chr.	Mb	MAF	Effect	Genes $\leq 500kb$
9	75	0.12	0.035	HBSL1 / MYB
17	56	0.35	0.043	PSMD9
27	26	0.27	0.036	

- HBSL1 / MYB region associated with hemoglobin levels and platelet count
- PSMD9 involved in Insulin regulation

Results

- ▶ Associations with milk on chromosomes 9, 10 and 14
  - ▶ Chromosome 14 as expected near DGAT
  - ▶ Milk yield QTL have been reported on all cow chromosomes

- ▶ Associations with FPR deviation on chromosomes 9, 17 and 27
  - ▶ Feed intake QTL reported on chromosome 17
    (Nkrumah et al., 2007)
  - ▶ Fat% QTL have been reported on all cow chromosomes

Conclusions

- Combining genotypes from multiple European cow populations
  - No substructure detected from genotypes
  - Known QTL detected by simply accounting for herd year and season effects

- QTL are detected for FPR deviation on chromosomes 9, 17 and 27
  - Feed intake QTL and PSMD9 candidate gene on chromosome 17

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Citations

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