



Sustainable Solutions for Small Ruminants

Loci underlying variation in nematode resistance in three European sheep populations: a joint-analysis



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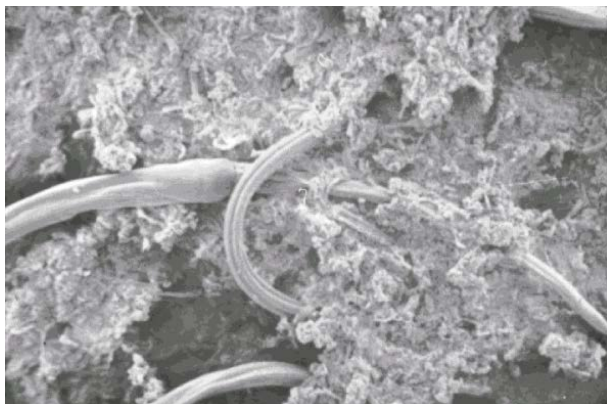


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Introduction

- **Gastrointestinal nematode infections large impact on the sheep industry:**
 - Anthelmintic treatment
 - Production losses
- e.g. €100 million/year in UK



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- **Gastrointestinal nematode infections large impact on the sheep industry:**
 - Anthelmintic treatment
 - Production losses

e.g. €100 million/year in UK
- **Anthelmintic resistance has developed fast in many nematode populations:**
 - Need for new control measures

Introduction

- **Selection for increased resistance to nematodes has often been suggested**



Introduction

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- **Nematode resistance is a complex trait:**
 - **Large number of physiological pathways involved**
 - **Indicator traits (i.e. Faecal Egg Count) are time specific**

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- **Selection for increased resistance to nematodes has often been suggested**
- **Nematode resistance is a complex trait:**
 - **Large number of physiological pathways involved**
 - **Indicator traits (i.e. Faecal Egg Count) are time specific**
- **Advantageous to select directly for resistance:**
 - **Several QTL studies addressed nematode resistance**

Introduction

- **Little overall consensus has emerged from these studies in terms of resistance loci:**
 - **Apparent genetic complexity of the trait**
 - **Variety of sheep breeds, nematode species and experimental approaches**
- **Do common regions exist? → meta (or joint) analysis**
 - **Tool for aggregating information from multiple independent studies**

Aim

Identify genomic regions underlying FEC variation in a joint analysis of three European sheep populations



Material and Methods

- **Data**

- **Average animal effect for *Strongyles* FEC on 4123 individuals from the three populations**

- **752 Scottish Blackface (SBF) lambs**

- **2371 Sarda x Lacaune backcross (SAR) ewes**

- **1000 Martinik Black-Belly x Romane backcross (MBR) lambs**

Material and Methods

- **Data**
 - **Different *Strongyles* species and challenges:**
 - natural (mixed species) challenge at pasture for SBF
 - mainly *Teladorsagia*
 - natural (mixed species) challenge at pasture for SAR
 - changes through the year
 - artificial challenge with *Haemonchus* for MBR

Material and Methods

- **Data**

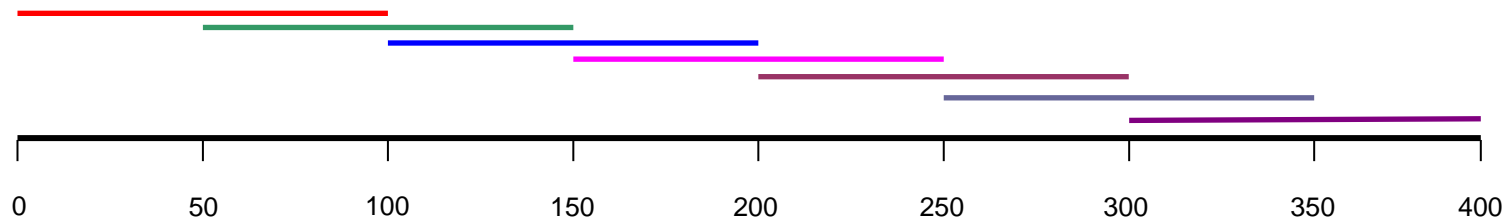
- **Fixed effects specific for each population**
- **Animals genotyped with the 50k SNPchip**
- **QC specific for each population:**
 - **38,991 SNPs in common after QC**
- **SNP positions from Sheep Genome browser v2.0**

Material and Methods

- QTL found in previous population-specific analyses:
 - **SBF:**
 - Chr 3 & 6
 - **SAR:**
 - Chr 7, 12 & 20
 - **MBR:**
 - Chr 5, 12 & 13

Material and Methods

- **Regional Heritability Mapping (RHM)**
 - Variance component approach
 - Fit joint effects of all loci within a genomic region
 - Each chromosome is divided into windows of a pre-defined number of SNPs:
 - In our case, 100 SNPs and window shifted every 50 SNPs



Material and Methods

- Regional Heritability Mapping (RHM)

$$y = Xb + Za + Zw + e$$

overall genetic effect

regional combined genetic effect

$$h^2 = \frac{(\sigma_a^2 + \sigma_w^2)}{(\sigma_a^2 + \sigma_w^2 + \sigma_e^2)}$$

Total h^2

$$h_w^2 = \frac{\sigma_w^2}{(\sigma_a^2 + \sigma_w^2 + \sigma_e^2)}$$

Regional h^2

Material and Methods - Issues

- **Problem 1:**
 - **Unrelated populations and therefore IBS relationships uninformative**
- **Problem 2:**
 - **few sire families and therefore long chromosome segments inherited intact → long stretches of LD**

Material and Methods - Solutions

- **Problem 1**
 - **Unrelated populations and therefore IBS relationships uninformative**
- **Genomic relationship matrix (G) set to block diagonal \rightarrow covariance between populations = 0**

Material and Methods - Issues

- **Problem 2**

**Region of
interest**



Material and Methods - Issues

- **Problem 2**

Random population

LD



Region of interest



Material and Methods - Issues

- **Problem 2**

Random population



Region of interest



Our population



Material and Methods - Solutions

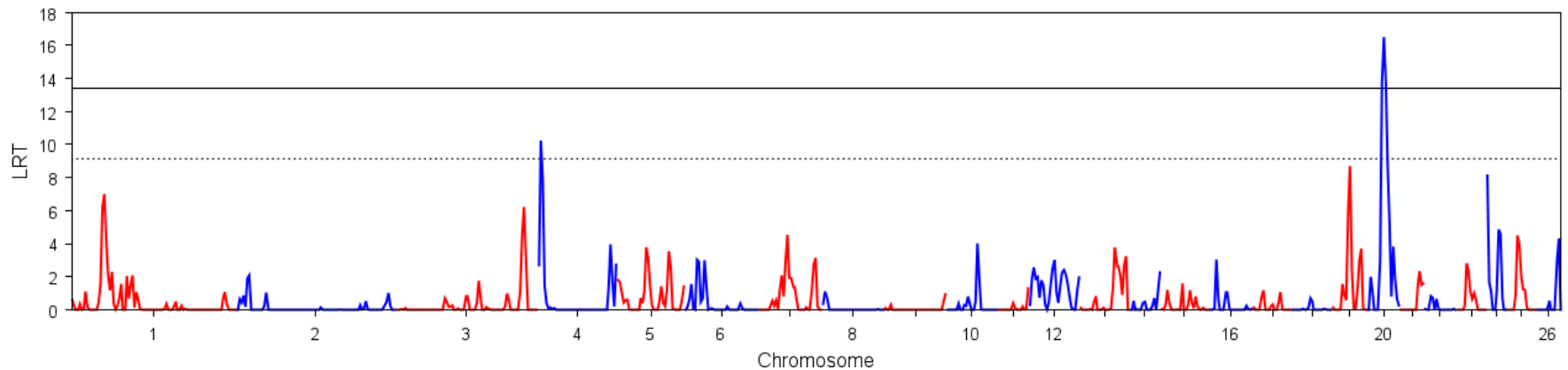
- Problem 1
- Problem 2
 - few sire families and therefore long chromosome segments inherited intact → long stretches of LD
- Two different G matrices:
 - **whole** → using all SNPs across the genome
 - **n-1** → created separately for each chromosome excluding the chromosome being interrogated

Material and Methods

- **Model tested by Likelihood Ratio Test (LRT):**
 - compared to LogL of model with no QTL
- **Correction for multiple testing required:**
 - threshold for genome-wide ($p < 0.05$) significance **13.38**
 - threshold for suggestive significance **9.11**

Results

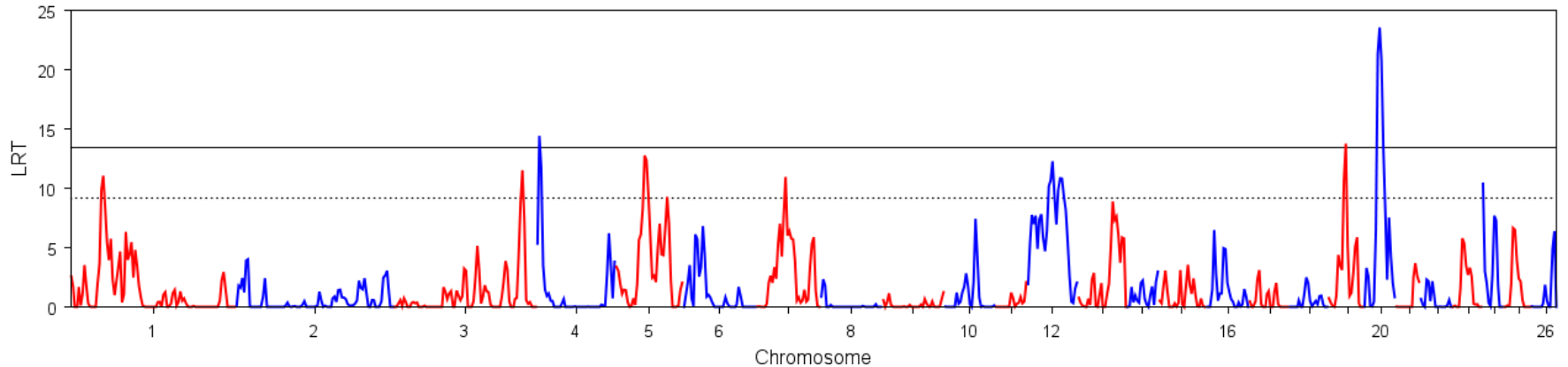
Plot of all genome using the **whole** genomic relationship matrix



OAR	window	LRT	h^2_w
20	8	13.78	0.02
20	9	16.50	0.02
20	10	13.88	0.02
4	2	10.24	0.01

Results

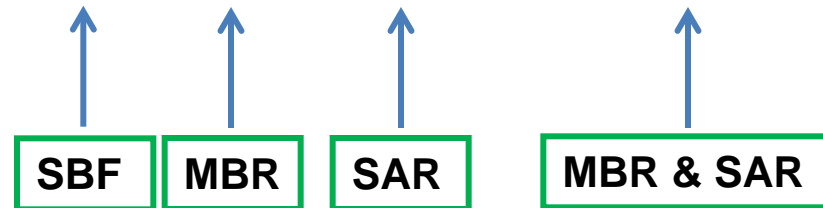
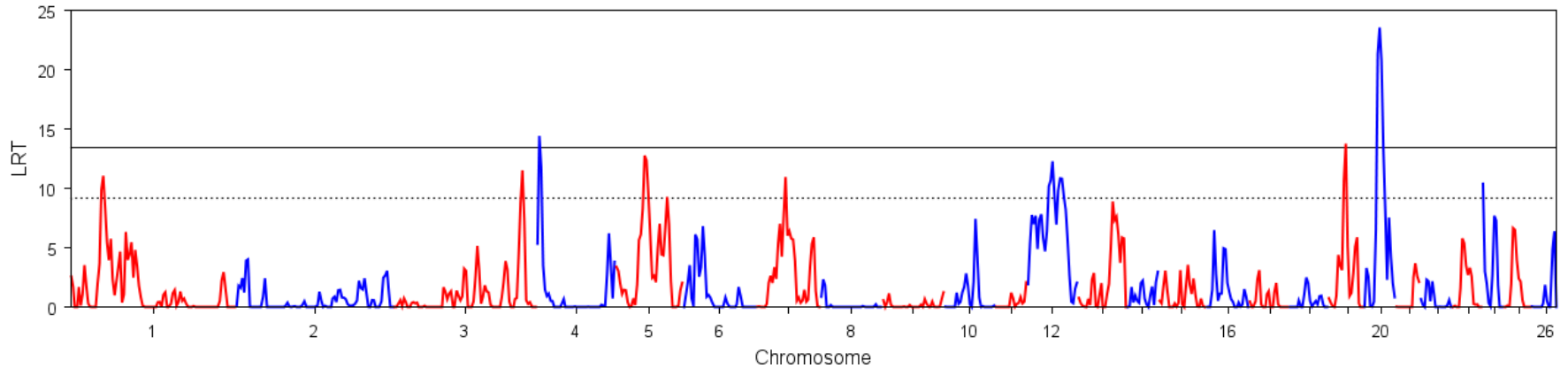
Plots of all genome using the **n-1** genomic relationship matrix



OAR	window	LRT	h^2_w
20	8	21.28	0.02
20	9	23.52	0.02
20	10	20.74	0.02
4	2	14.40	0.02
19	10	13.74	0.02

Results

Plots of all genome using the **n-1** genomic relationship matrix



Considerations on data structure

- The **n-1 G** partially overcomes problem of long stretches of LD
- RHM can detect different types of QTL architecture from LA or LD methods:
 - does not require large differences between contrasting loci in same population
- MHC was most significant region:
 - Region characterised by extreme complexity

Conclusions

- Despite heterogeneity of data, joint-analysis allowed identification of common regions
- Using a **whole** (block diagonal) G , some QTL significant in individual datasets were lost
- Using the **$n-1$** G , the QTL from individual studies reappeared, and those already found become more significant



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Thank you



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