GWAS for genotype by lactation stage interaction for milk production traits

Haibo Lu, Yachun Wang, Henk Bovenhuis

WAGENINGEN
UNIVERSITY & RESEARCH

Acknowledgements

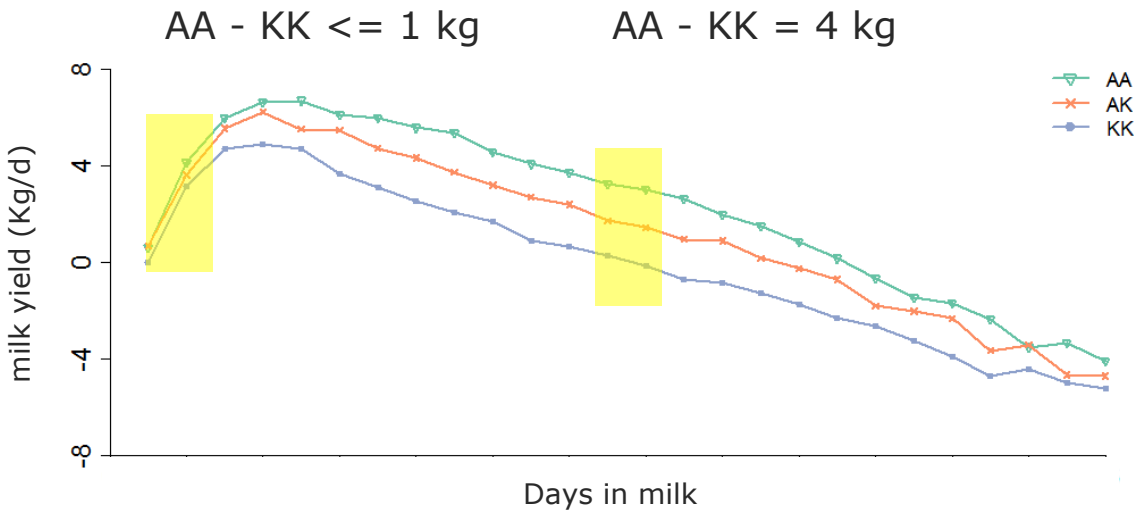
Dutch Milk Genomics Project

Sino-Dutch Dairy Development Centre

Introduction

Most GWAS assume SNP effects to be constant during lactation

DGAT1 effects on milk yield -- effects change during lactation

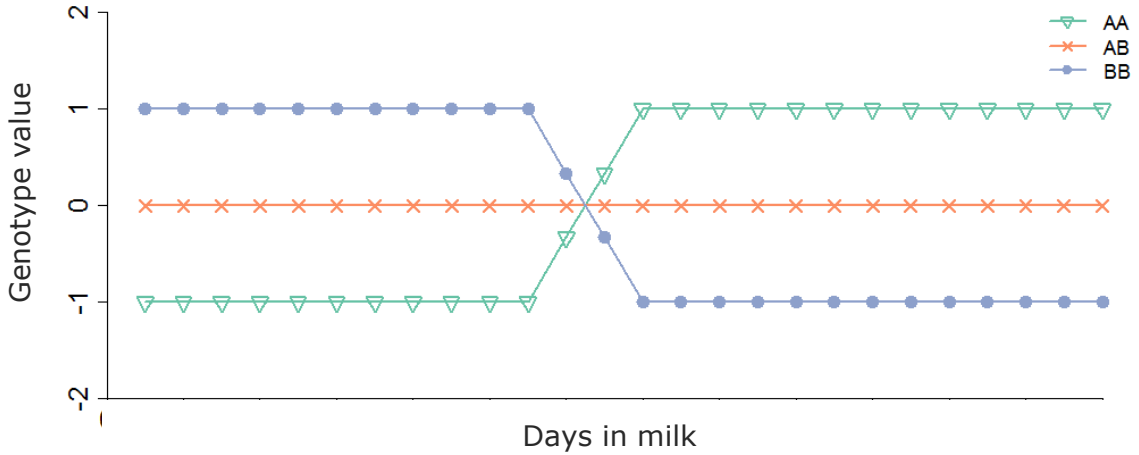


WAGENINGEN
UNIVERSITY & RESEARCH

QTL detection

True: SNP*lact interaction

Model assumes constant effects



$\overline{AA} = 0$

$\overline{AB} = 0$

$\overline{BB} = 0$

QTL will remain undetected

Objective

Identify SNP whose effects **change** during lactation

Phenotypes and Genotypes

- 1,829 first-parity Dutch Holstein cows on 400 farms
- 8 milk production traits (KgMilk, KgLact, KgFat, KgProt, Lact%, Fat%, Prot%, SCS)
- 26 lactation stages (15 days each stage)
- 19,593 test-day records per trait; 10.7 test-day records per cow per trait
- 30,348 SNP after quality control

WAGENINGEN
UNIVERSITY & RESEARCH

Statistical Models

"Traditional" GWAS -- constant SNP effects:

$$Y = \mu + b_1 * C\_age + C\_season + S\_code + herd + animal + permanent + lact\_stage + SNP + residual$$

GWAS for SNP*lact:

$$Y = \mu + b_1 * C\_age + C\_season + S\_code + herd + animal + permanent + lact\_stage + SNP + (SNP*lact) + residual$$

WAGENINGEN
UNIVERSITY & RESEARCH

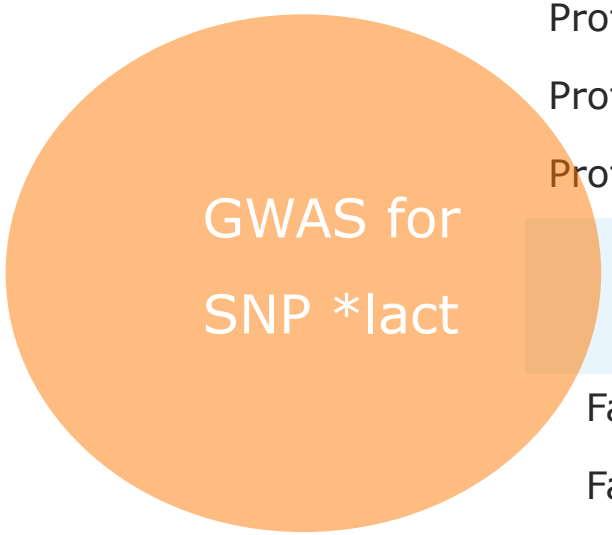
Significance thresholds

- "Traditional" GWAS -- FDR < 0.01

- GWAS for SNP*lact -- Permutation
    - all 30,348 SNPs randomly reassigned to other individuals
    - smallest genome-wide P value was stored in each permutation
    - repeat permutation 100 times
    - 1% quantile as significance threshold

Significant regions

Traits	BTA
Lactose content	19
Milk yield Lactose yield Fat content Protein content	14
Protein content	10

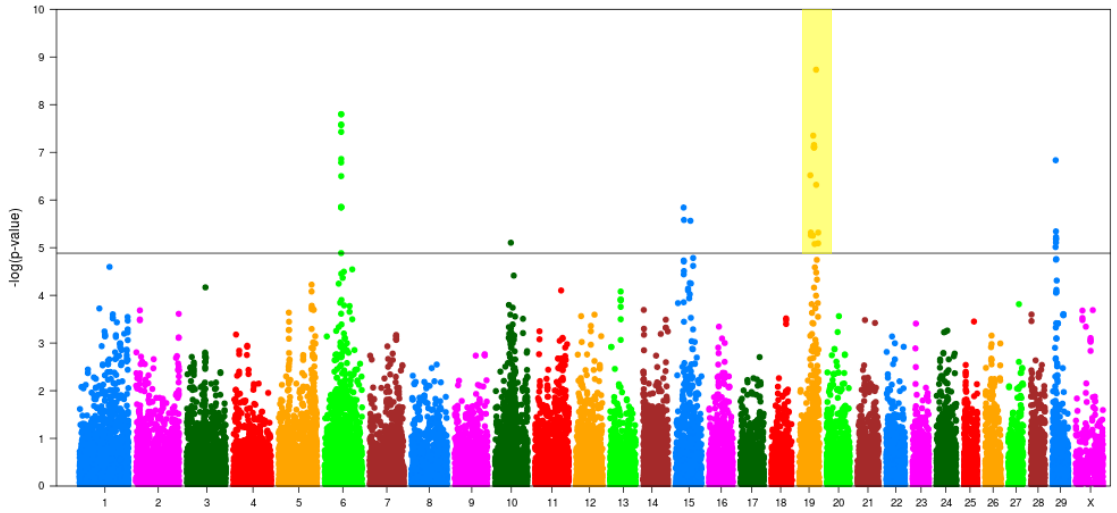


Traits	BTA
Protein content	3
Protein content	9
Protein content	27
Fat yield	4
Fat yield	16
Fat content	10
Fat content	11
Fat content	23

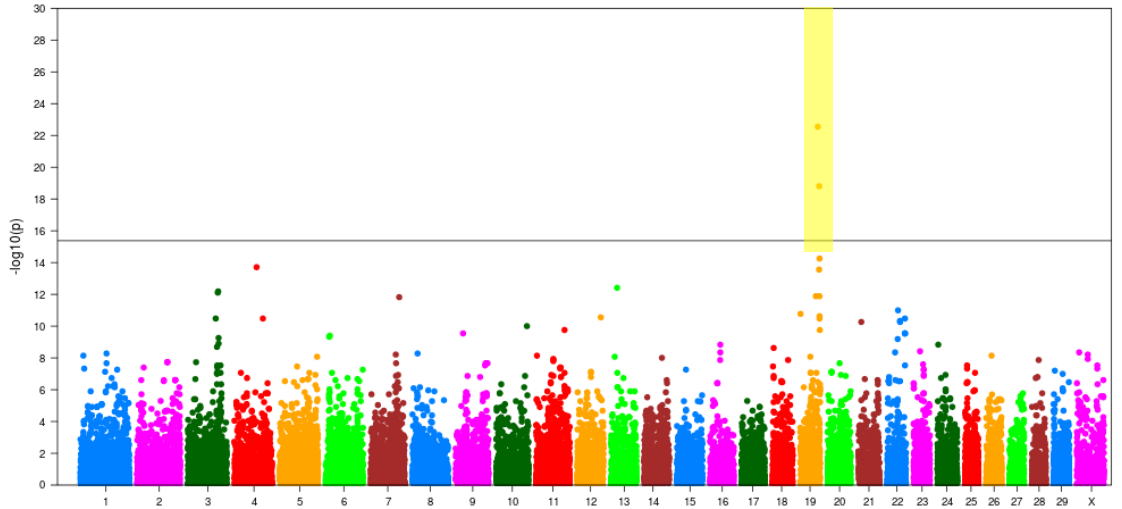
WAGENINGEN
UNIVERSITY & RESEARCH

Lactose content

"Traditional" GWAS



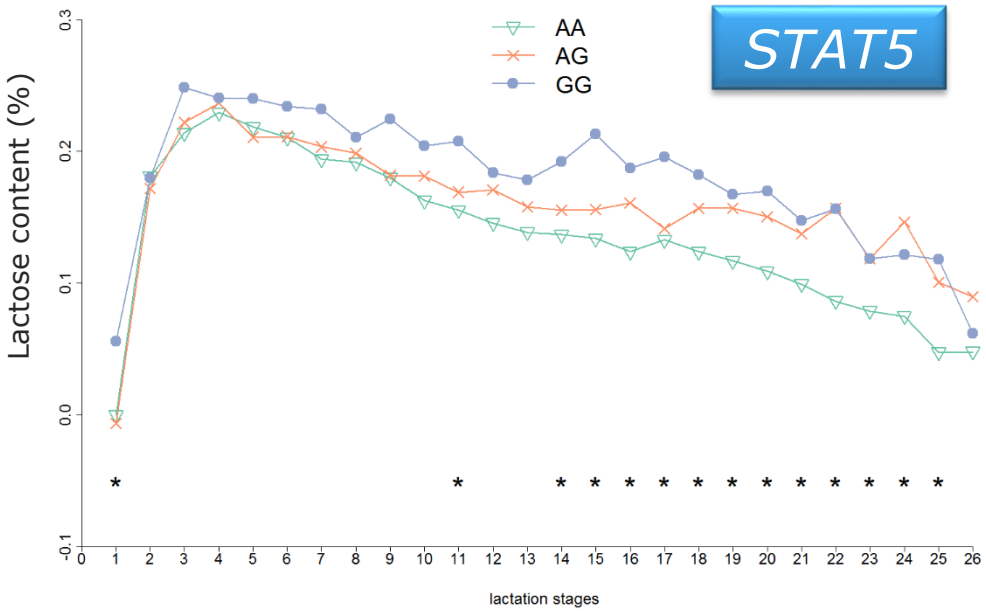
GWAS for SNP*lact

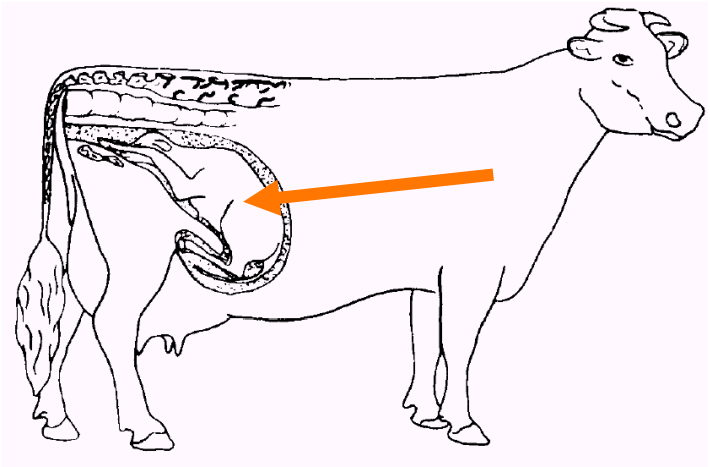


Lactose content – BTA 19

Biological explanation?

- Milk osmosis
- Mastitis
- Fatty acid
- Reproduction



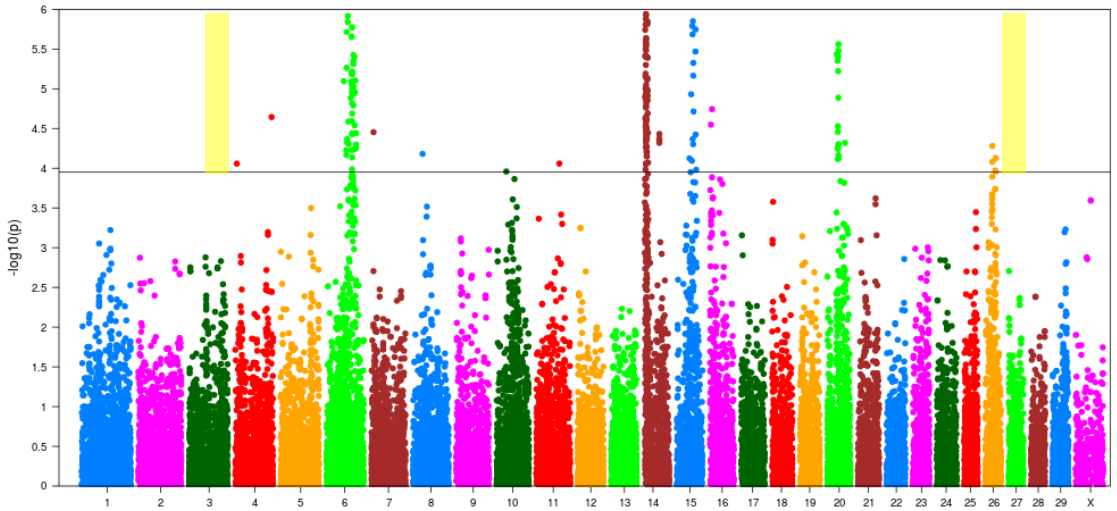


Effect of pregnancy

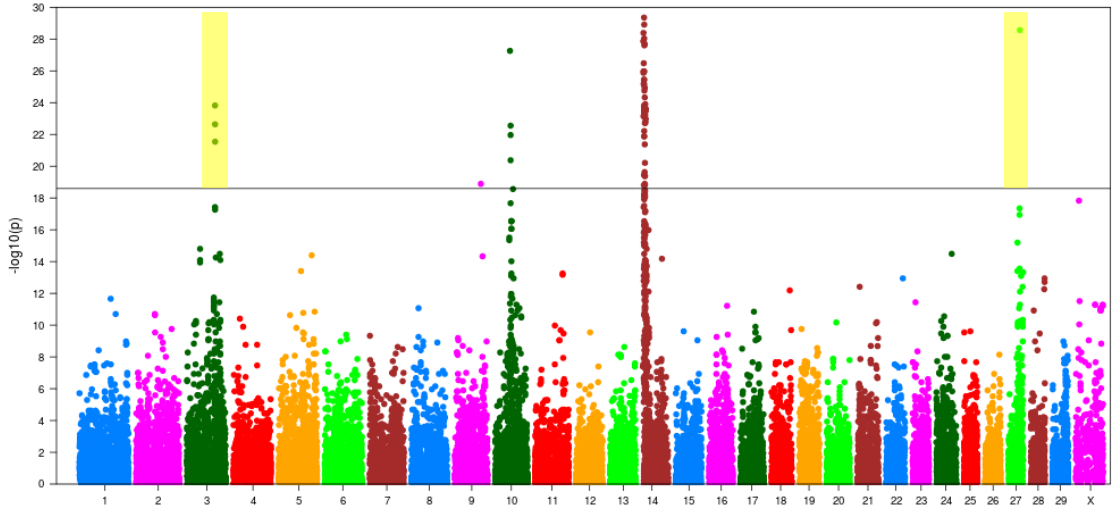
on milk production?

Protein content

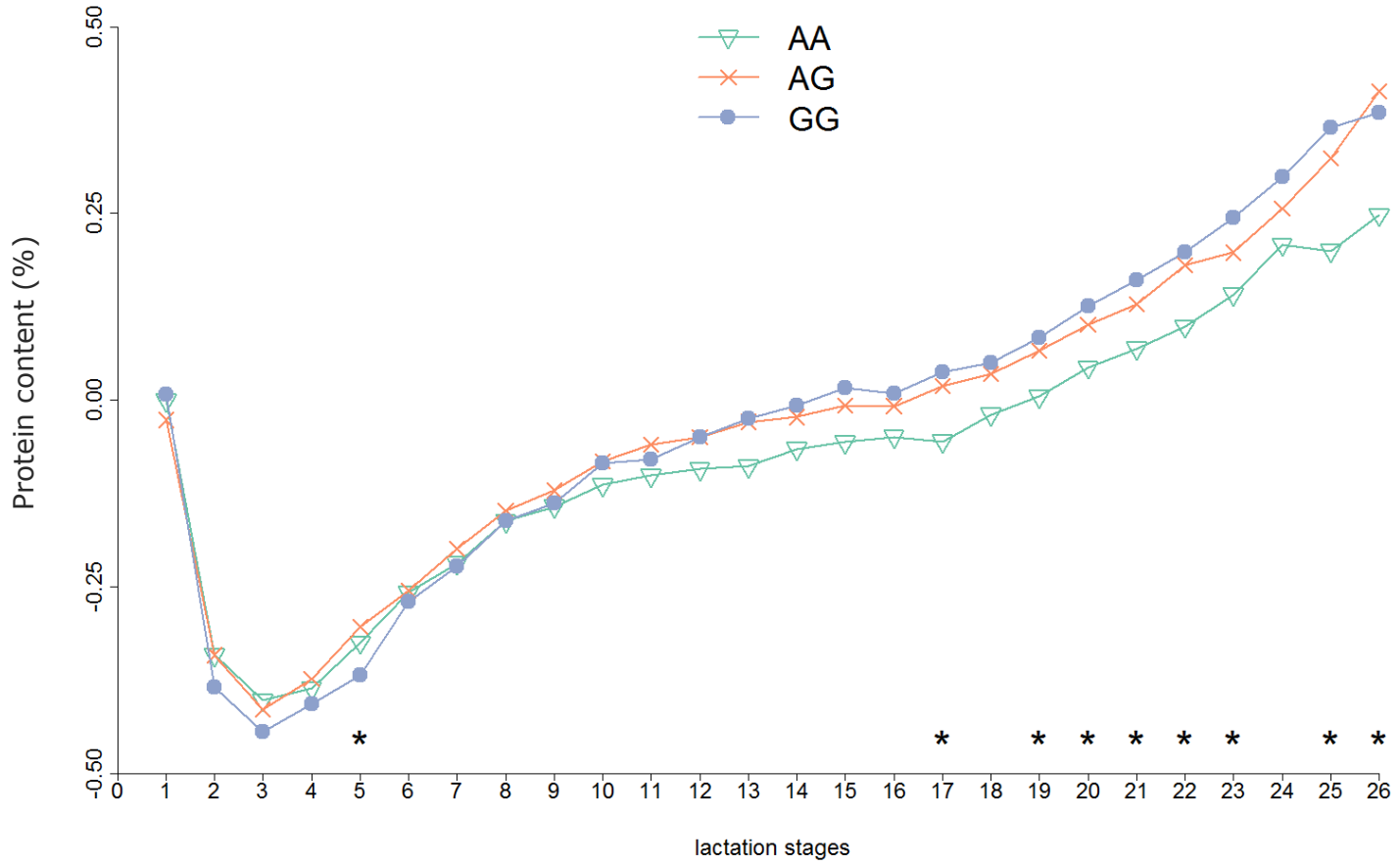
"Traditional" GWAS



GWAS for SNP*lact



Protein content – BTA 27



$\overline{AA}$

$\overline{AG}$

$\overline{GG}$

Potential other applications

- Milk production traits:

  SNP * pregnancy stage interaction

  SNP * Environment interaction

- Other longitudinal traits:

  Body weight, egg production

Take-home messages

- GWAS for (SNP*lact) identified additional regions affecting milk production traits
- Change of SNP effects in late lactation: effect of pregnancy ?
- Methods may be used in GWAS for SNP*Environment or other longitudinal traits

Thank you for your attention

WAGENINGEN UNIVERSITY & RESEARCH

haibo.lu@wur.nl