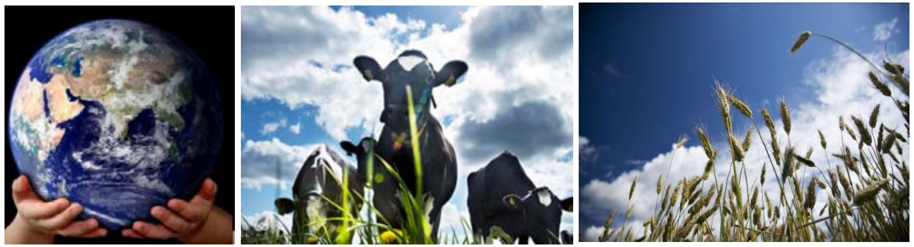
Estimation of non-additive variance components and SNP effects in five dairy cattle breeds

Andrew G. Marete
INRA / AgroParisTech, France
Aarhus University, Denmark



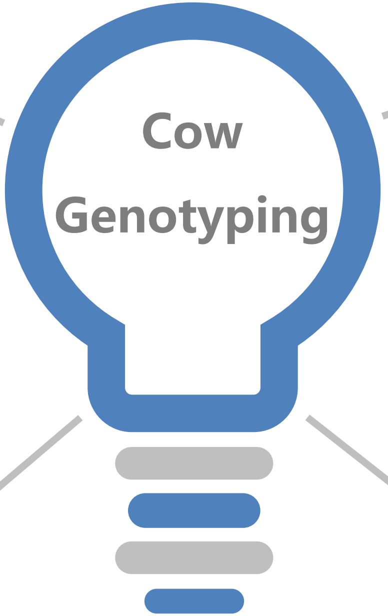
Premise

- Milk production traits are affected by many genes, many with a small effect and some with a major effect, thus complex traits
- Complex traits are regulated by complex interplay between multiple genes
- Theoretically, these genes can interact
- Interaction can be explained as non-additive genetic variance (NAGV)
    1. same locus interaction (dominance deviation)
    2. different loci interaction (epistatic variance)

Challenge

- Non-additive genetic variance (NAGV) is usually omitted in Genomic Selection (GS) and when estimating life-time merit of cows
- GS is based on additive effects of sire
- Especially the case when reference population is made of progeny tested bulls
- But cows with own performances are becoming more popular as a resource of choice for GS
- If NAGV is substantial, it can augment the GRM based solely on the additive genetic variance

Opportunity



Cow Genotyping

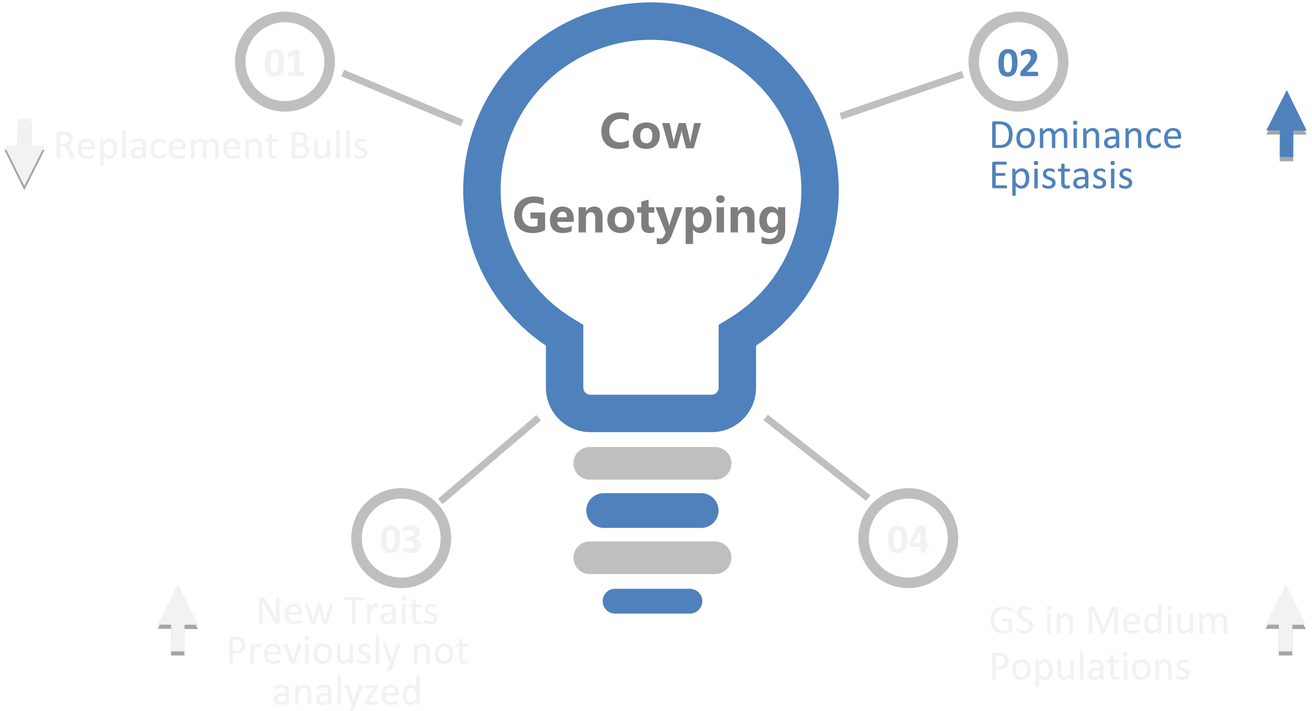
01 ↓ Replacement Bulls

02 Dominance Epistasis ↑

03 ↑ New Traits Previously not analyzed

04 GS in Medium Populations ↑

Opportunity



Cow Genotyping

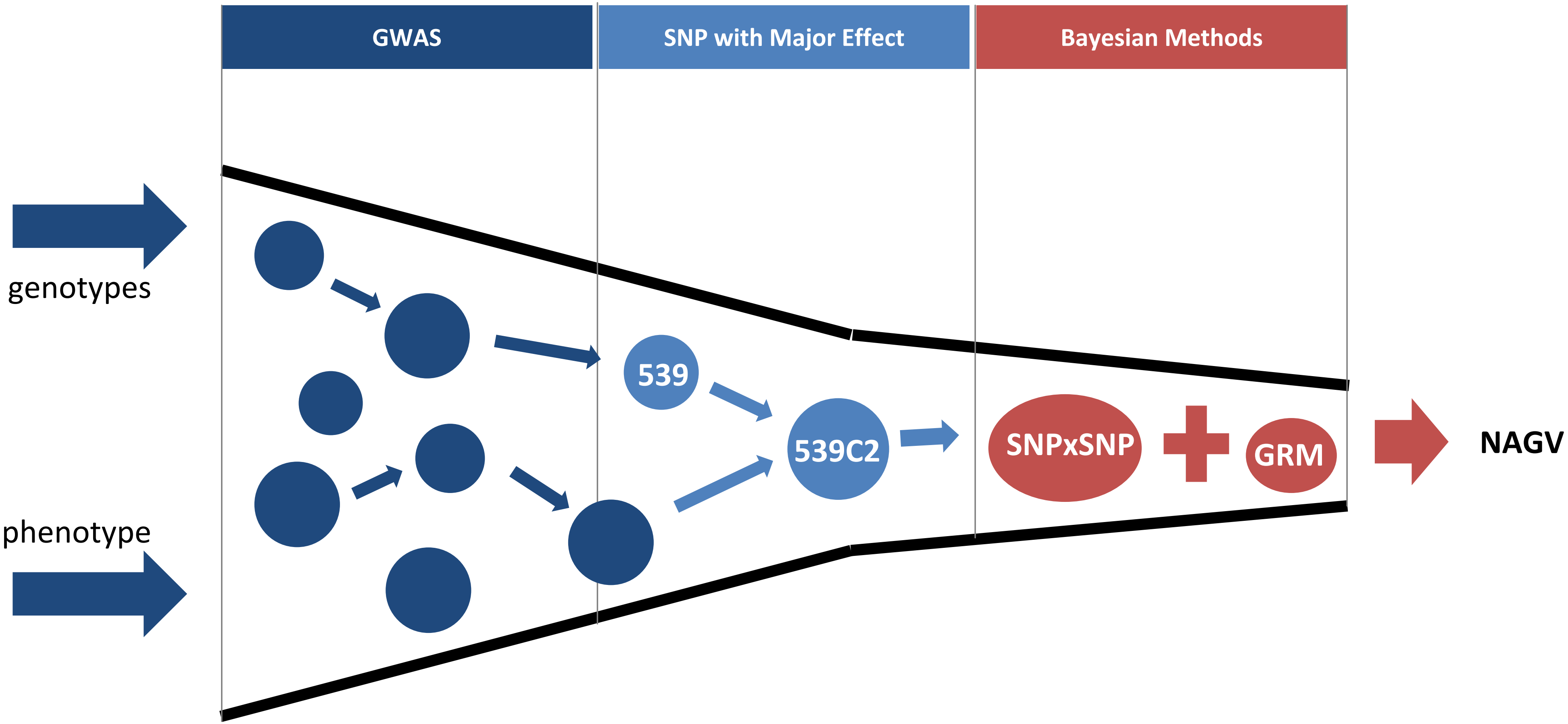
01 ↓ Replacement Bulls

02 Dominance Epistasis ↑

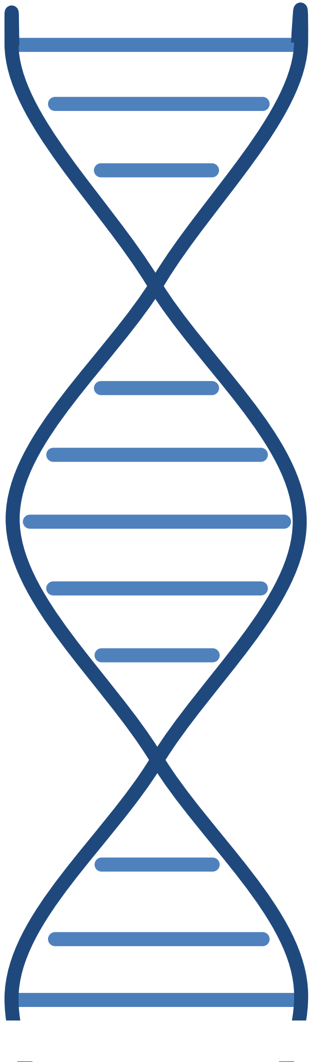
03 ↑ New Traits Previously not analyzed

04 GS in Medium Populations ↑

Workflow


GWAS
SNP with Major Effect
Bayesian Methods
genotypes
phenotype
539
539C2
SNPxSNP
GRM
NAGV

Data



Study animal

- Approximately 100K dairy cows from five French and Danish populations

Phenotypes

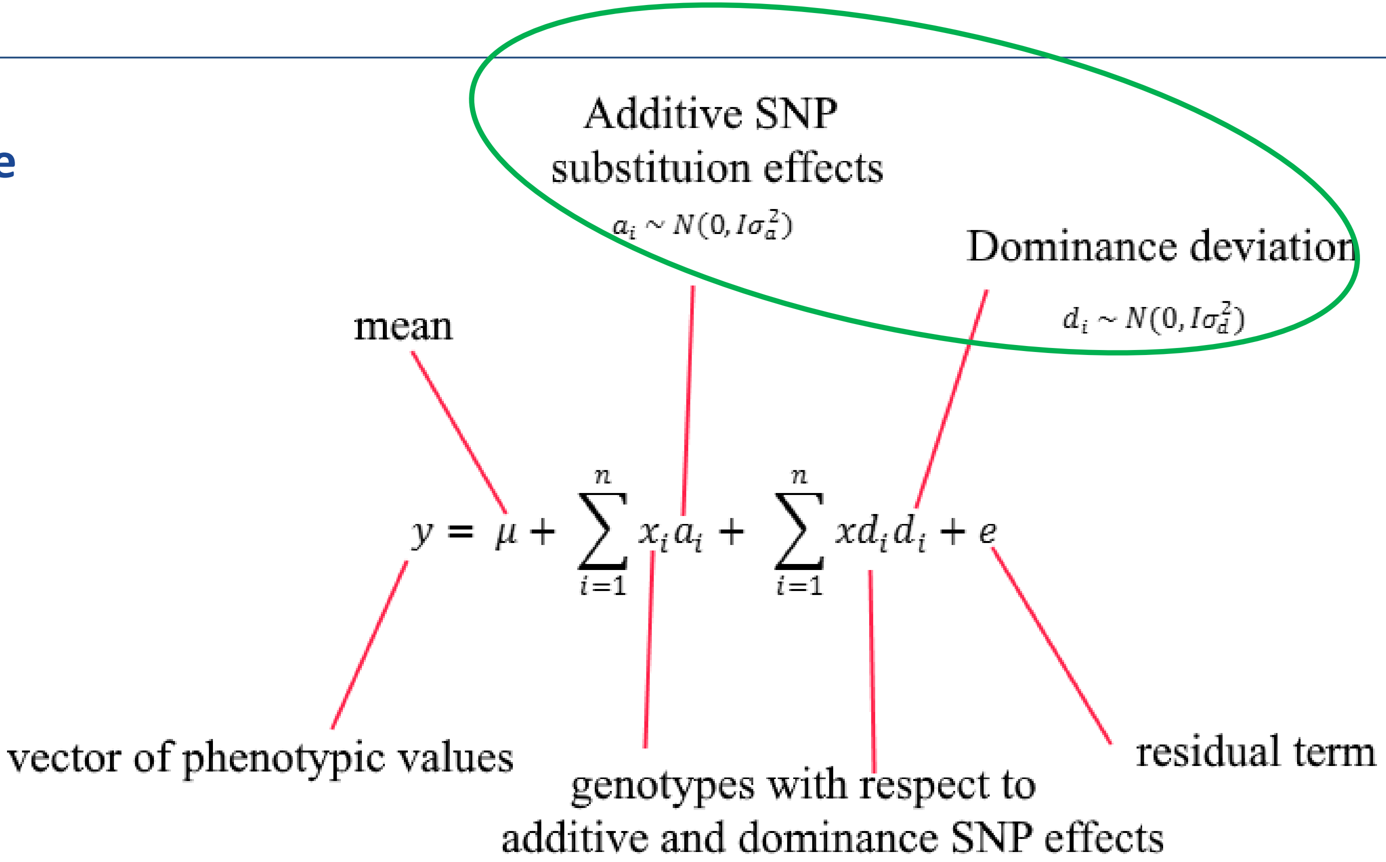
- Three milk production traits expressed as yield deviations
- Milk Yield, protein yield and fat yield

Genotypes

- Genotyped with 50K Illumina Infinium bead chip
- 7K SNP selected from Whole Genome Sequence
- Imputed to 50K to obtain similar genotype for all cows

Models

(a) Dominance



Additive SNP substituion effects

$a_i \sim N(0, I\sigma_a^2)$

Dominance deviation

$d_i \sim N(0, I\sigma_d^2)$

mean

$$y = \mu + \sum_{i=1}^{n} x_i a_i + \sum_{i=1}^{n} xd_i d_i + e$$

vector of phenotypic values

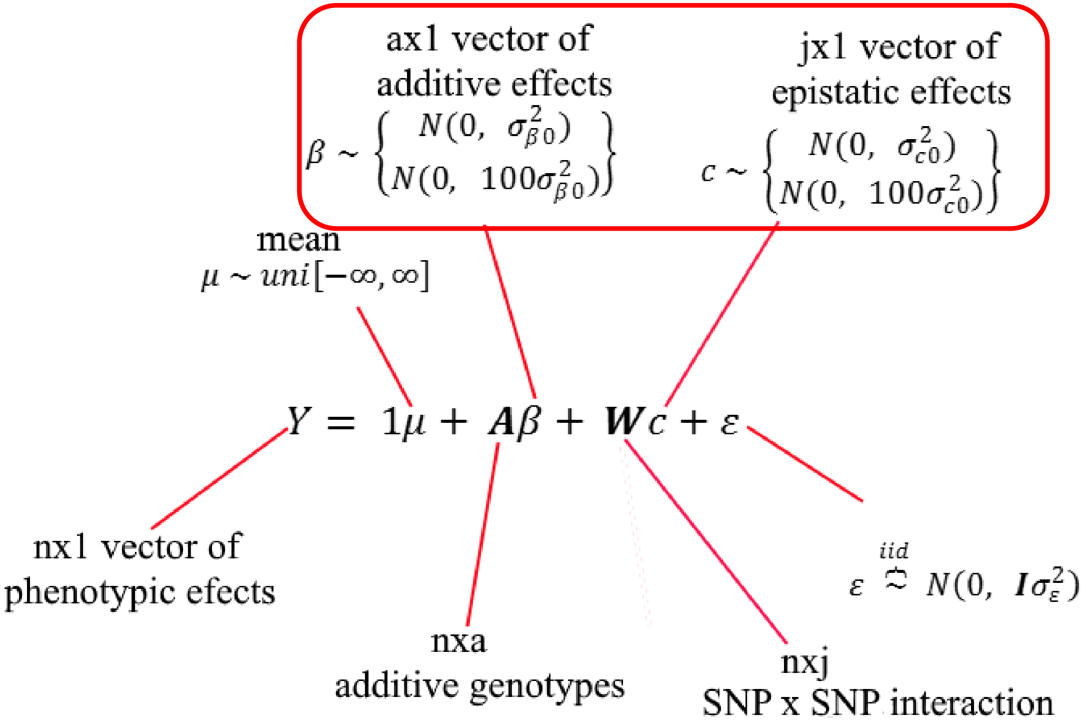
genotypes with respect to additive and dominance SNP effects

residual term

- **Chain=200k, burn=50k, skip=0.5k**
- **Metropolis-Hastings sampler with acceptance between 0.3 – 0.8**

Models

(b) SNP x SNP



ax1 vector of additive effects

$\beta \sim \begin{cases} N(0,\ \sigma^2_{\beta 0}) \\ N(0,\ 100\sigma^2_{\beta 0}) \end{cases}$

jx1 vector of epistatic effects

$c \sim \begin{cases} N(0,\ \sigma^2_{c0}) \\ N(0,\ 100\sigma^2_{c0}) \end{cases}$

mean

$\mu \sim uni[-\infty, \infty]$

$$Y = 1\mu + \boldsymbol{A}\beta + \boldsymbol{W}c + \varepsilon$$

nx1 vector of phenotypic efects

nxa additive genotypes

nxj SNP x SNP interaction

$\varepsilon \overset{iid}{\sim} N(0,\ \boldsymbol{I}\sigma^2_{\varepsilon})$

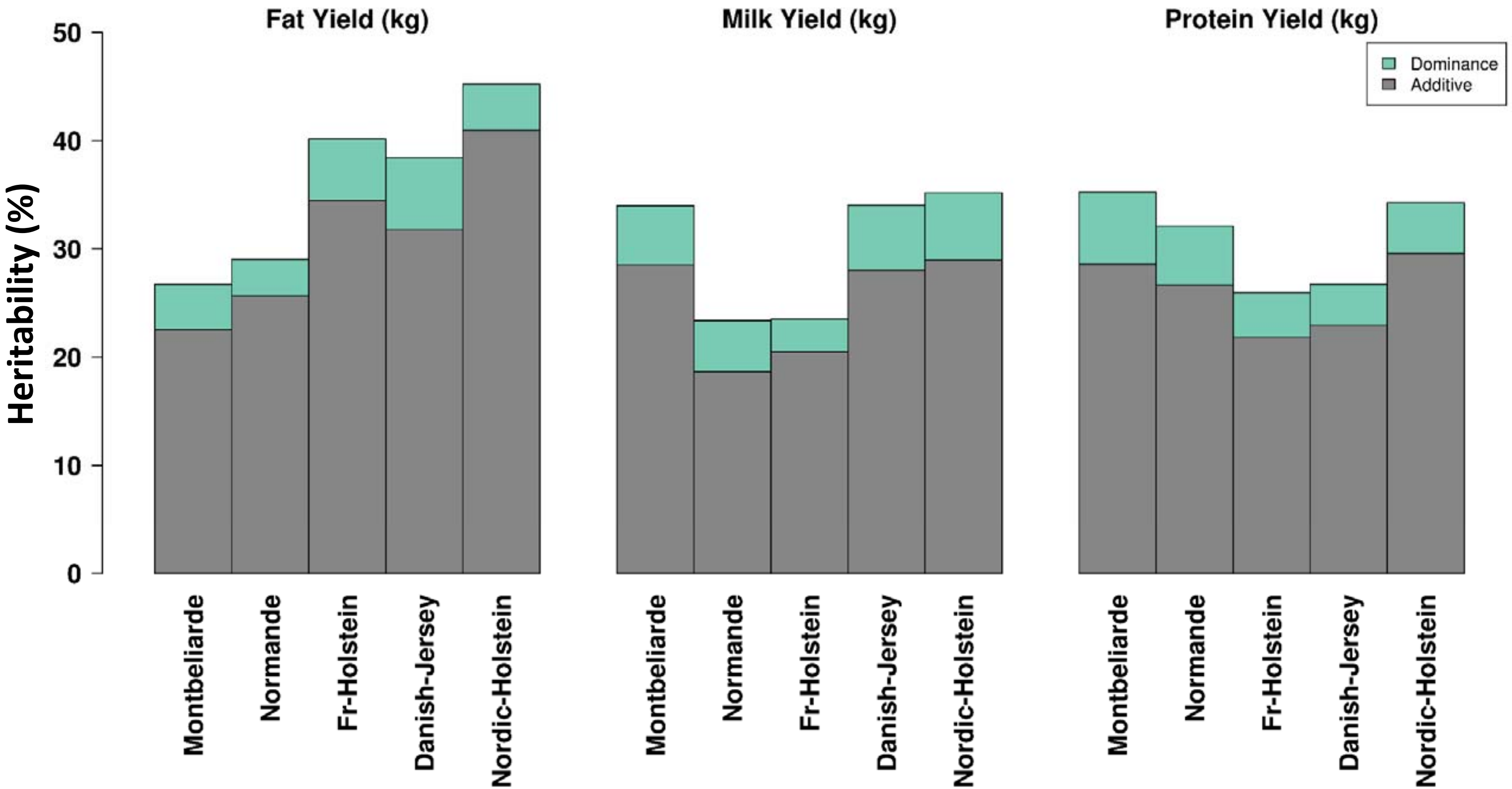
$$(\pi\beta_0, \pi 100\beta_0) \sim beta(10,1)\ and\ \ (\pi c_0, \pi 100 c_0) \sim beta(10,1)$$

$$\sigma^2_{\beta 0}, \sigma^2_{c0}, \sigma^2_{\varepsilon 0} \sim uni[0, \infty]$$

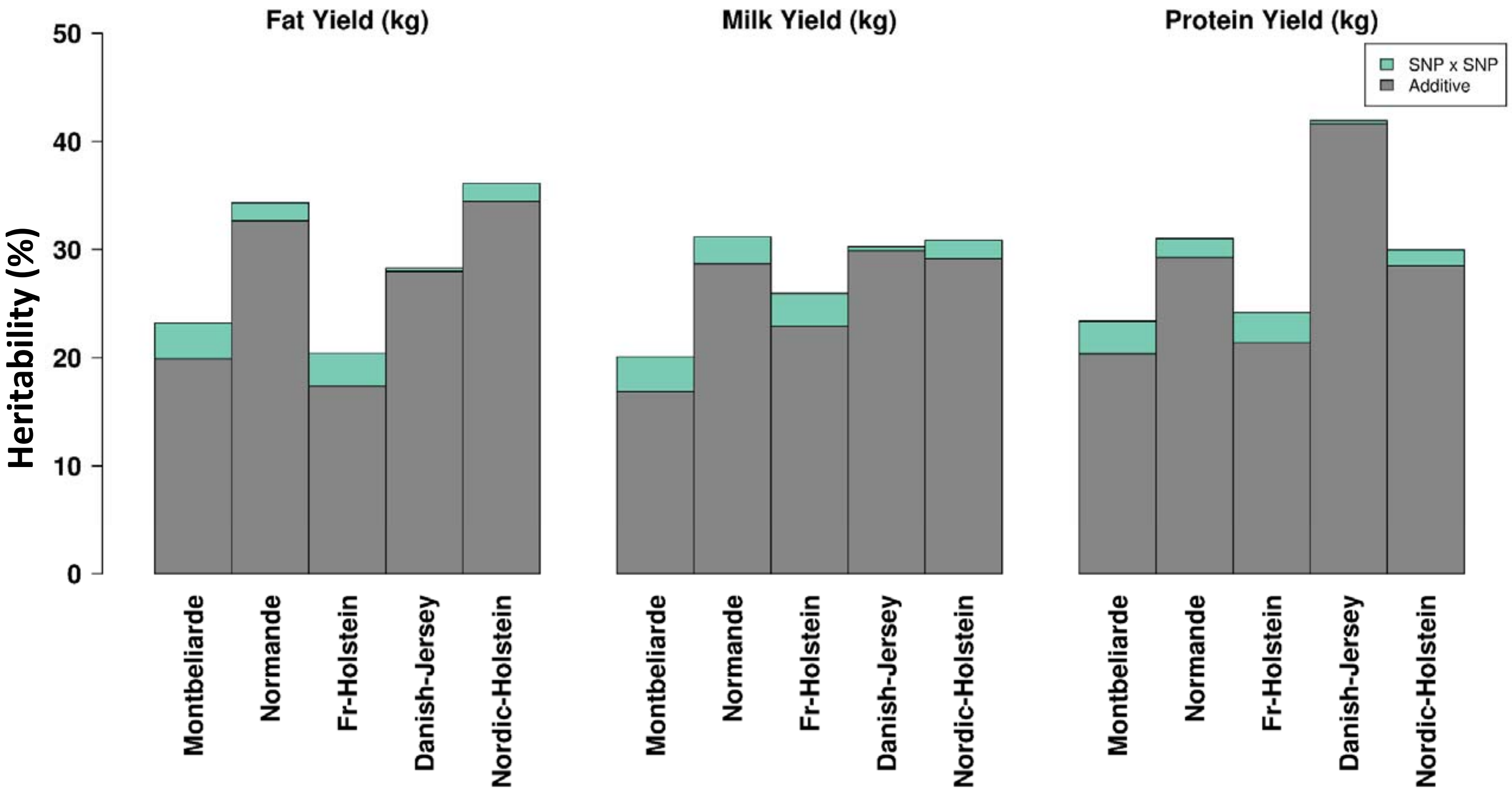
- **Chain=200k, burn=50k, skip=0.5k**
- **Bernoulli distribution**

W_{ij}	**Locus k**		
Locus j	AA	AB	BB
AA	1	0	-1
AB	0	0	0
BB	-1	0	1

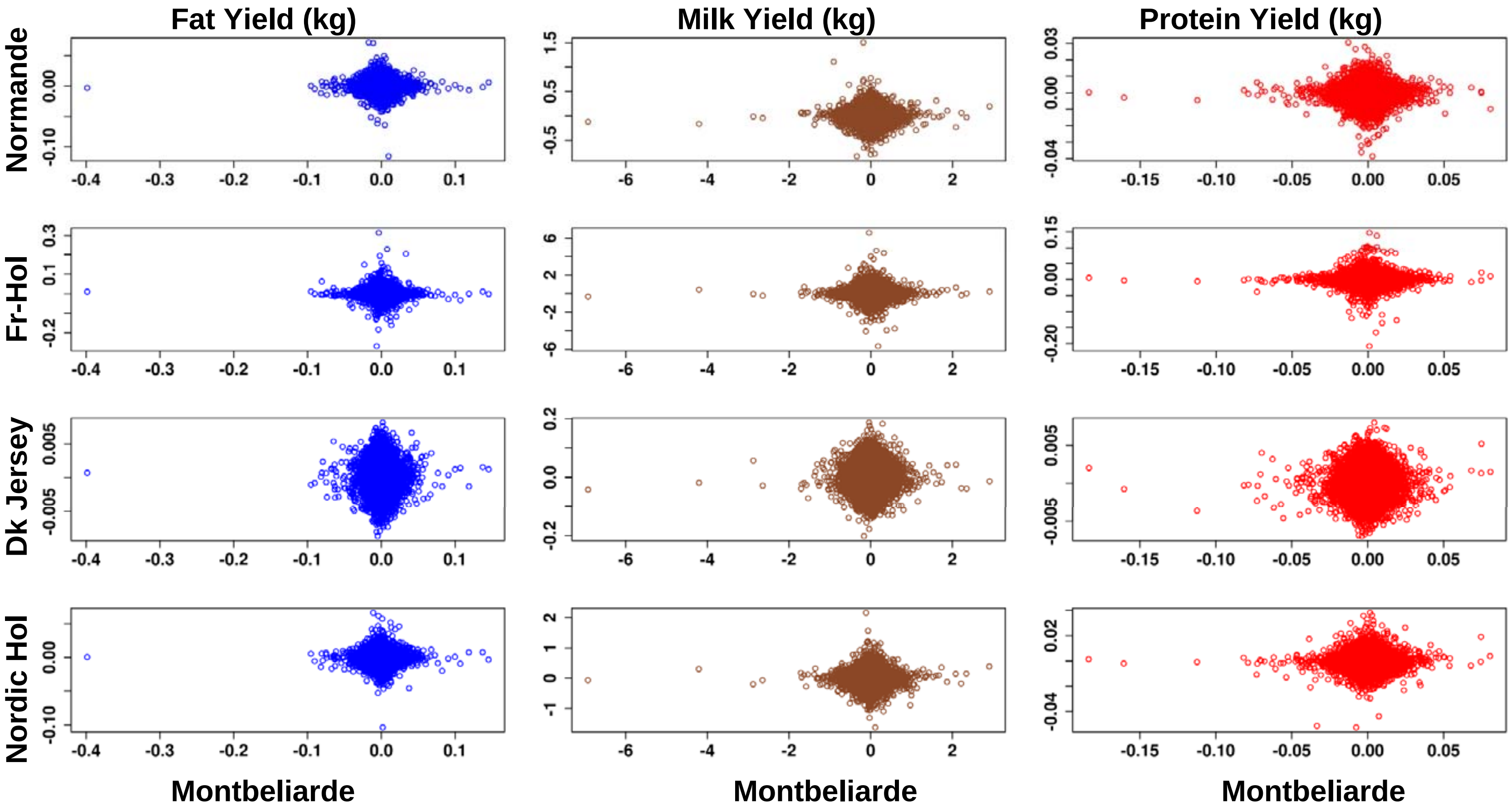
Heritability: Broad and Narrow sense



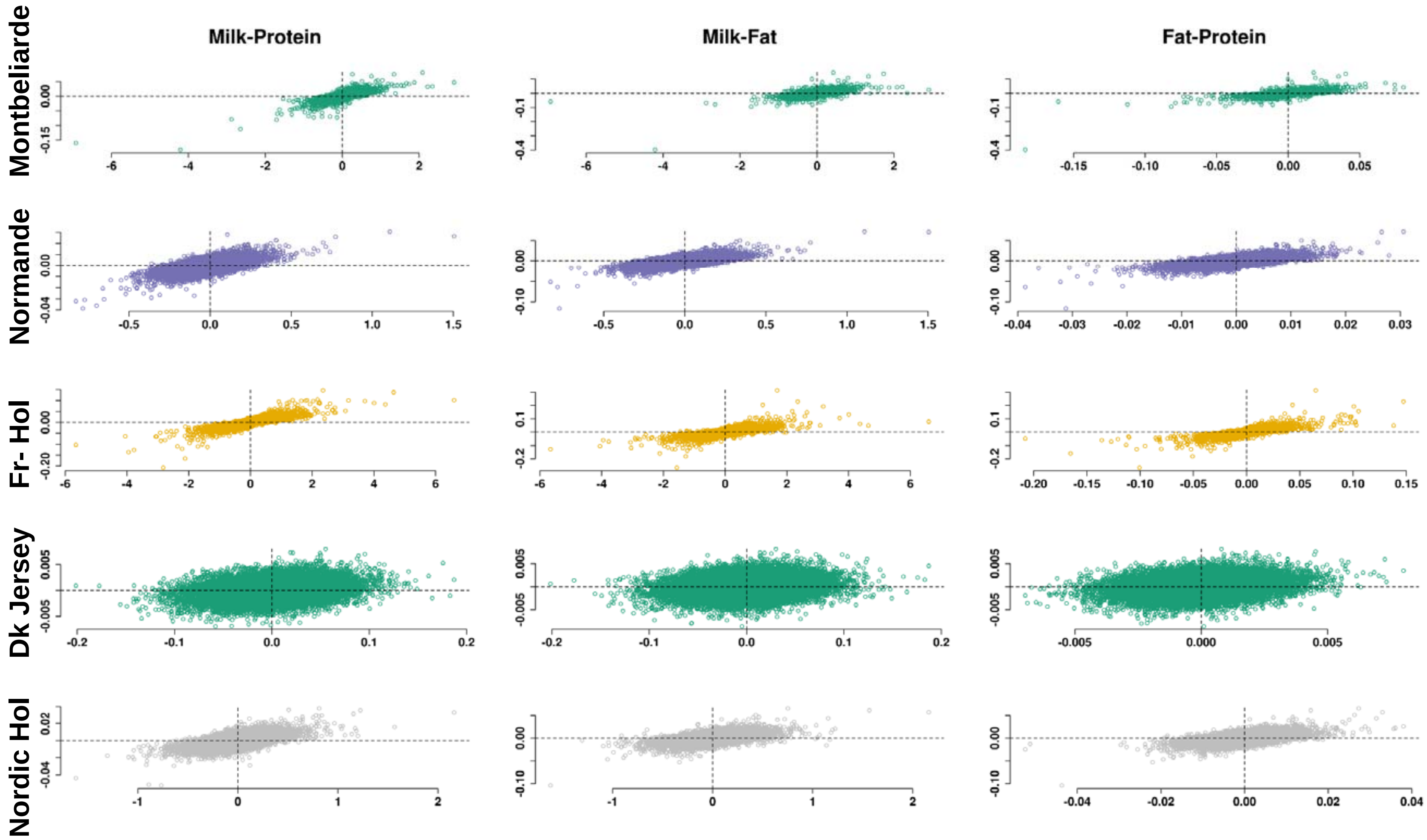
Heritability: SNPxSNP



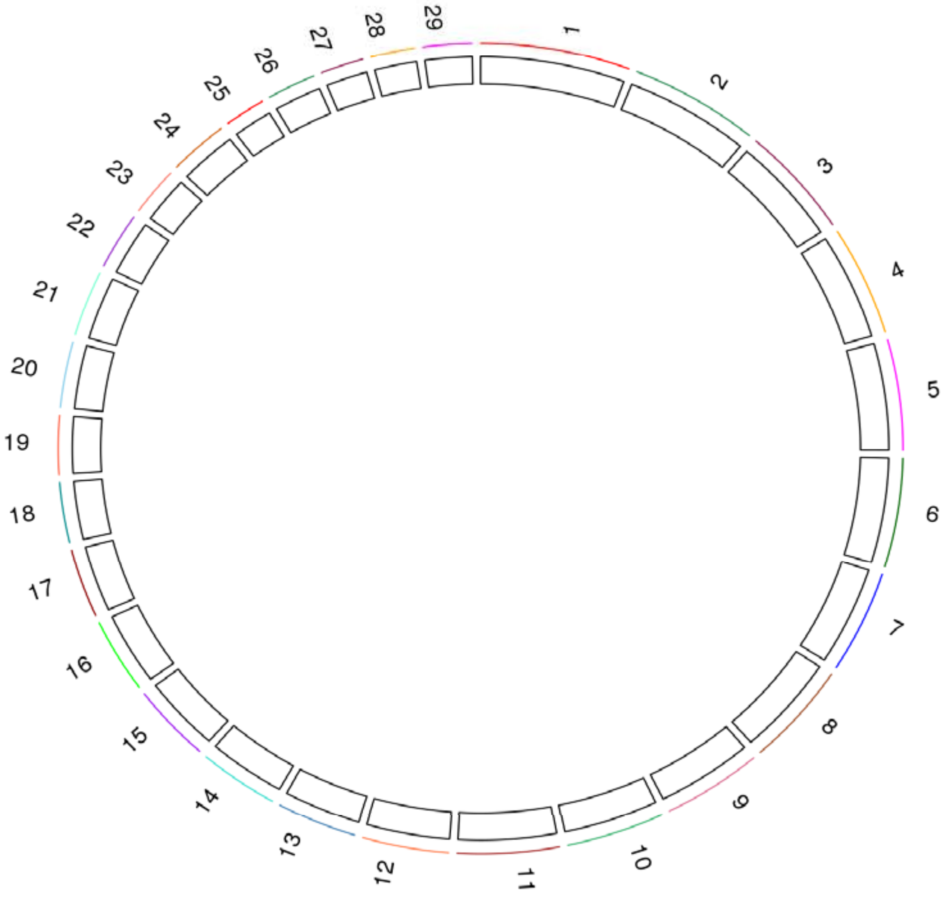
SNPxSNP: Allele Substitution Effects



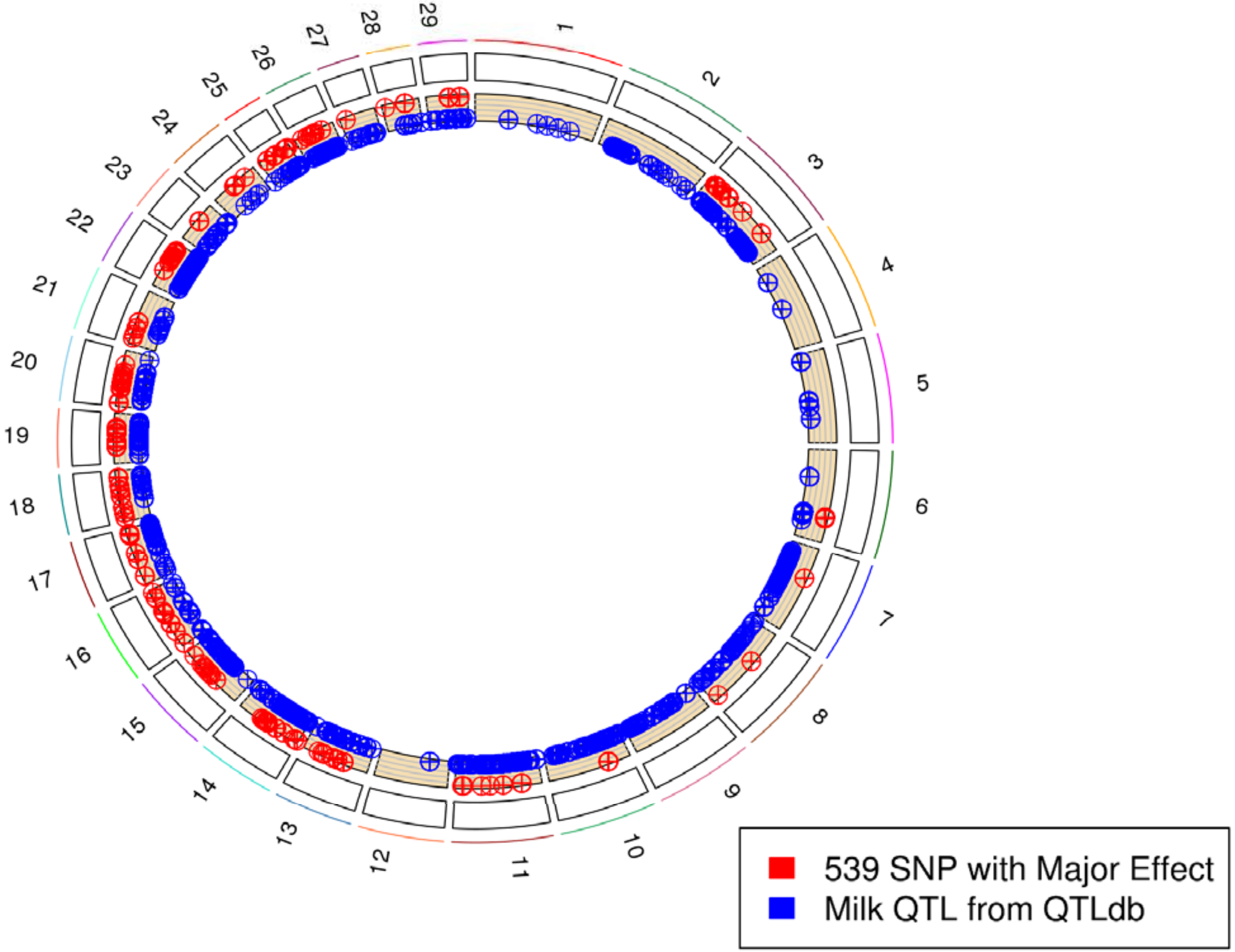
SNPxSNP: Allele Substitution Effects



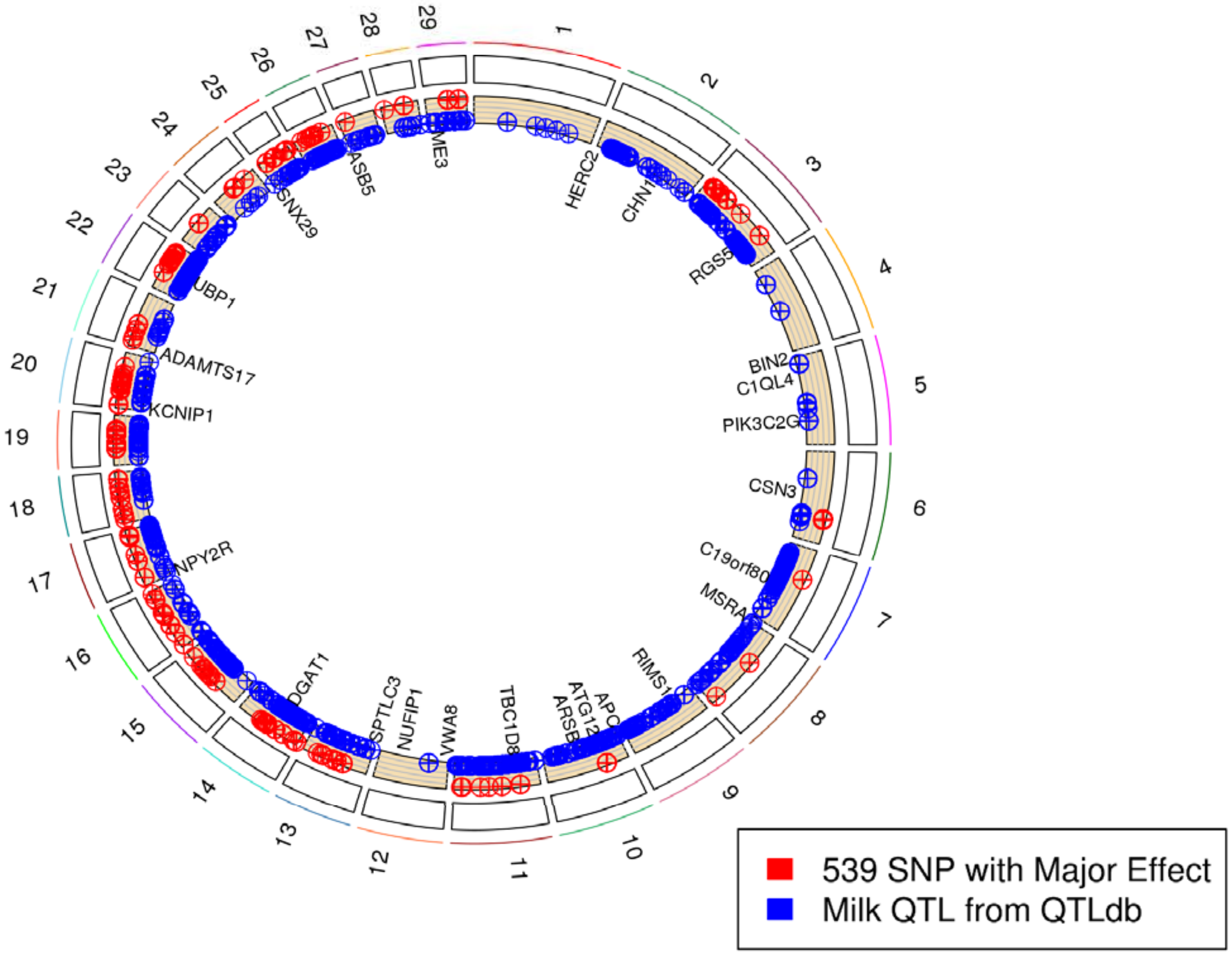
Summary: Milk yield (Kg) in Holstein



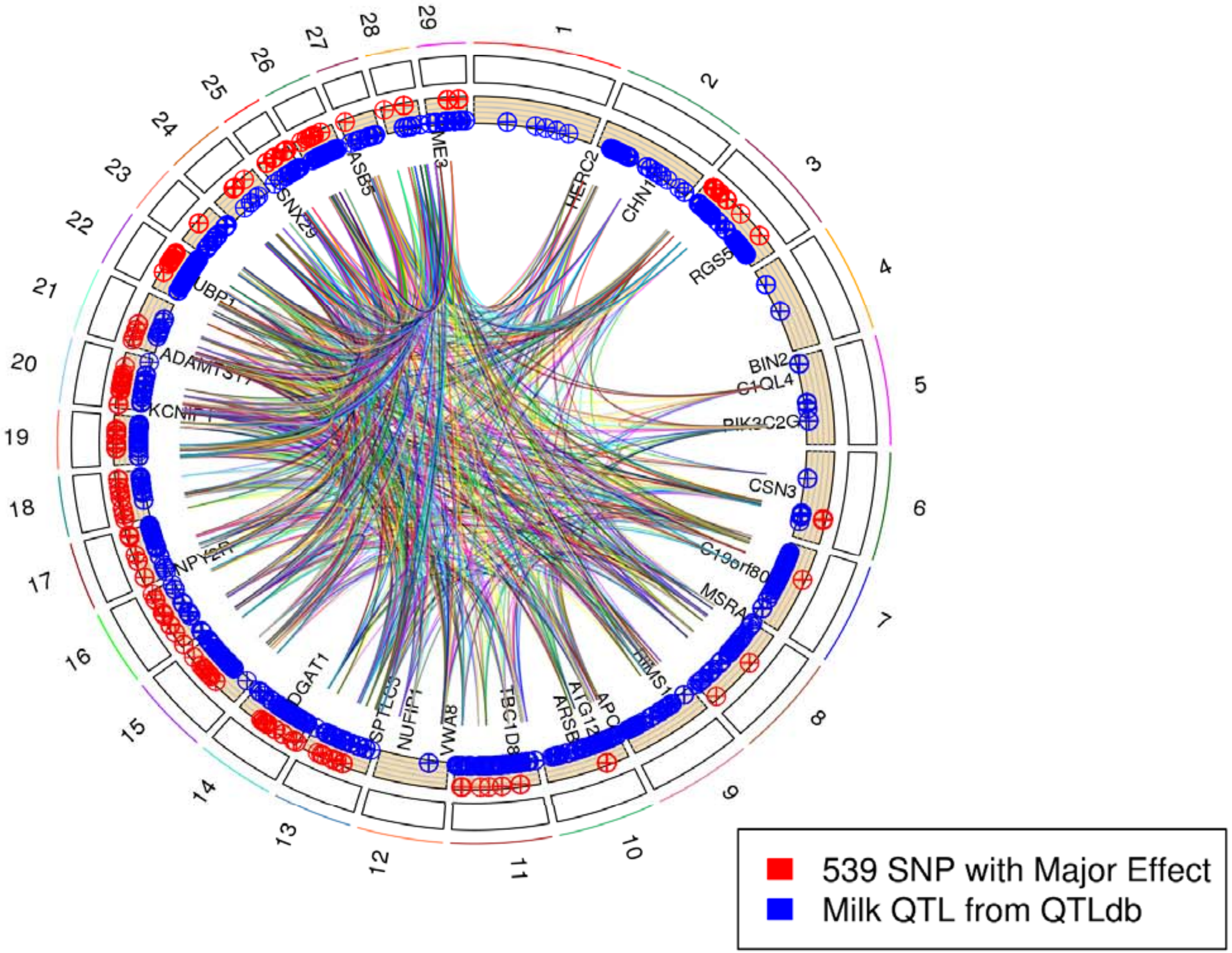
Summary: Milk yield (Kg) in Holstein



Summary: Milk yield (Kg) in Holstein



Summary: Milk yield (Kg) in Holstein



Conclusion

SNP with major effect including those selected from whole genome sequence explain non-additive variation

This interaction matrix can augment the normal GRM when predicting breeding accuracies

Thank you for your attention

Any questions?