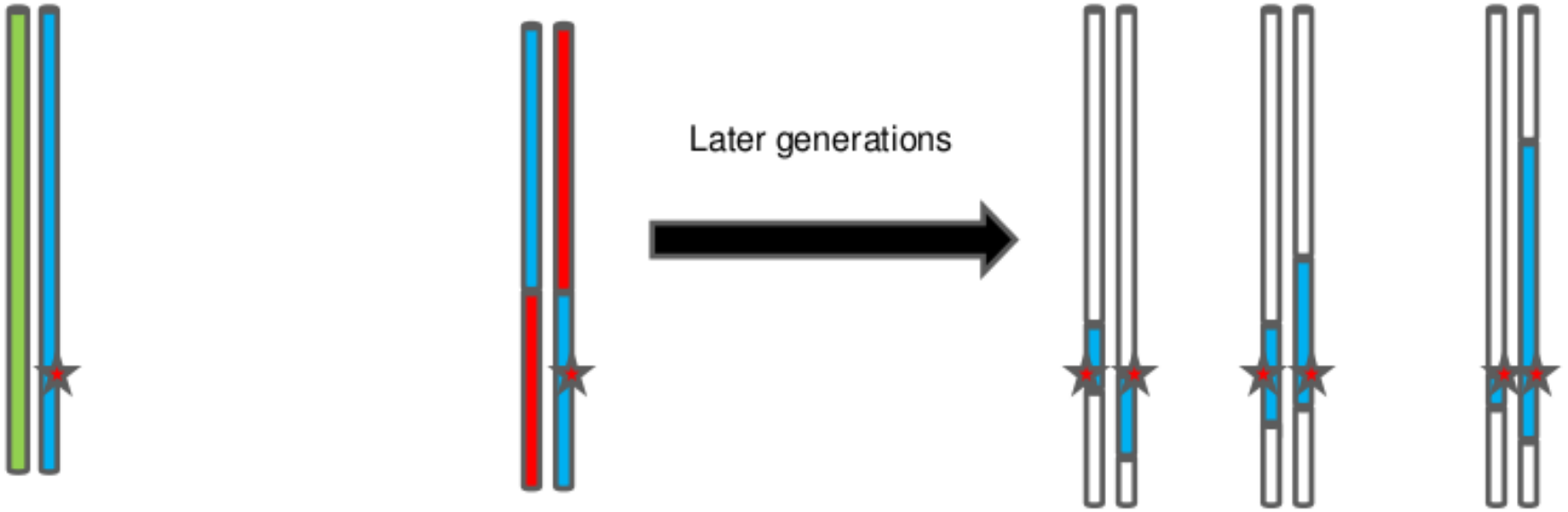
Parco Tecnologico Padano

Filippo Biscarini

Dep. of Bioinformatics

CAN RUNS OF HOMOZYGOSITY BE USED AS AN ALTERNATIVE OR COMPLEMENT TO GWAS?

What are ROHs?



- stretches of homozygous SNP genotypes
- autozygosity (IBD vs IBS)

Case/control studies et similia

HOMOZYGOSITY

- > in cases vs controls
- > around the mutation

RECESSIVE DISEASES

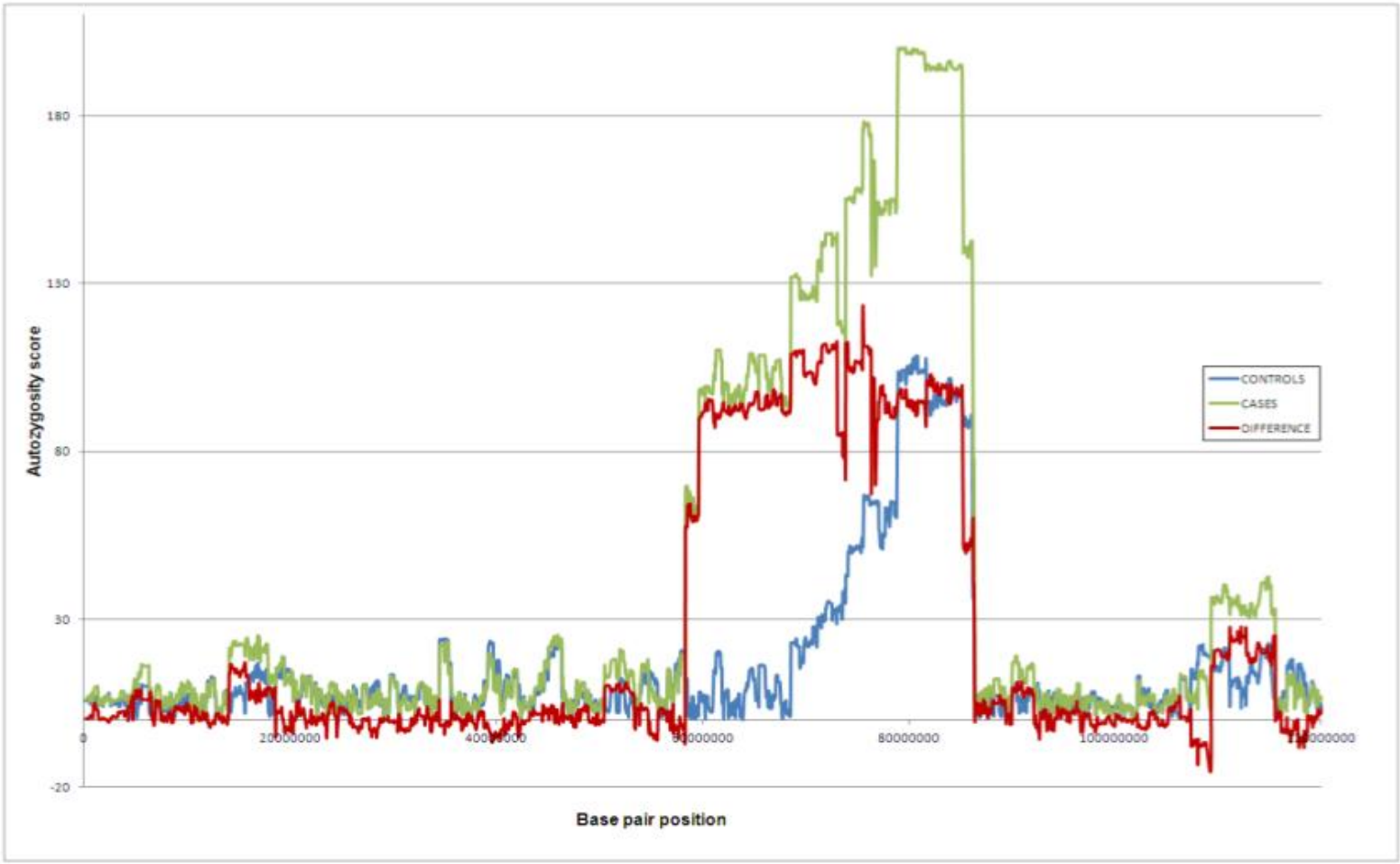
- Identify mutation
- Identify carriers

ROH in stead of (or in addition to) GWAS?

GWAS LIMITS

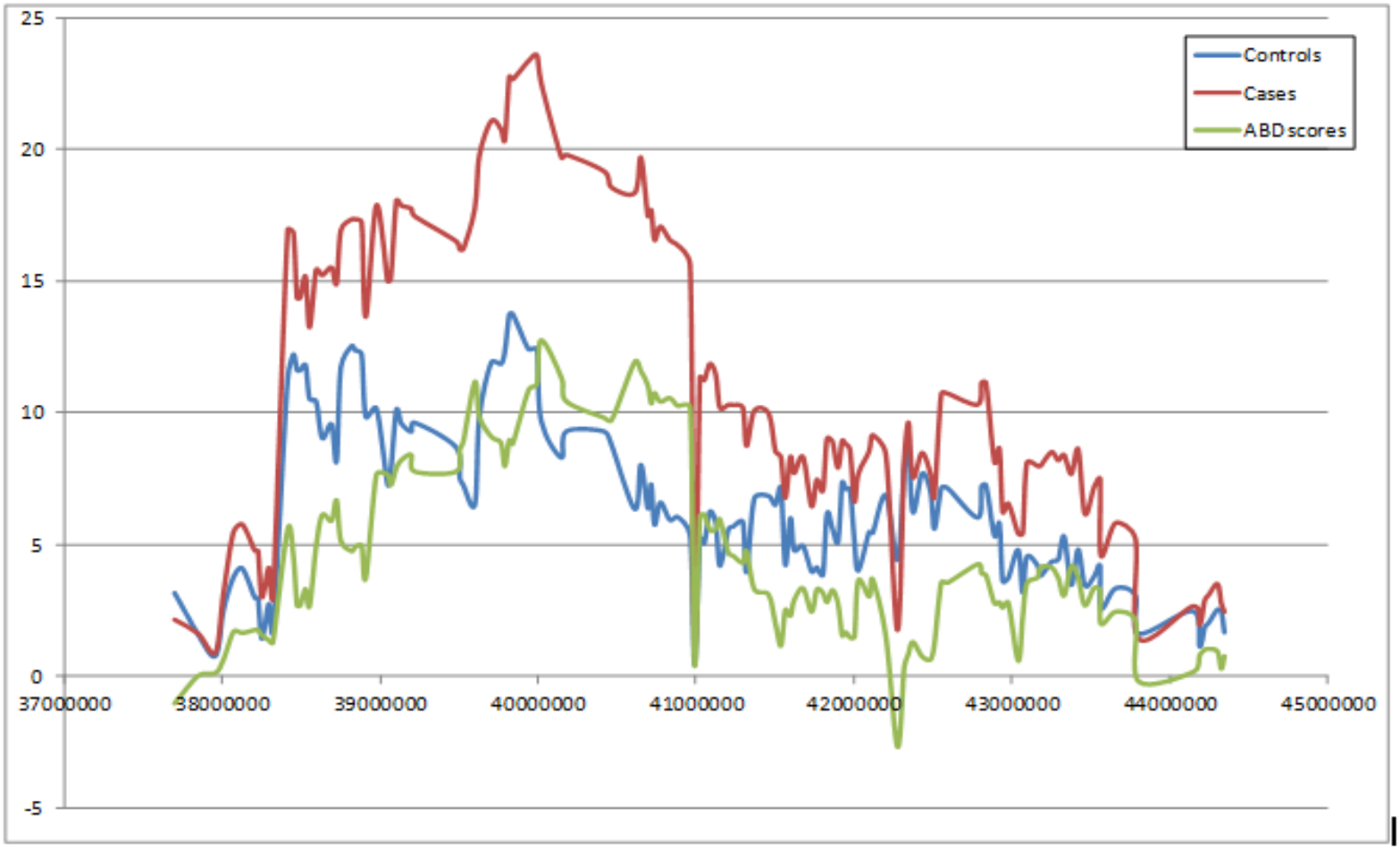
- one locus at a time
- spurious associations
- ambiguous interpretation

Perinatal mortality calves – BTA 4



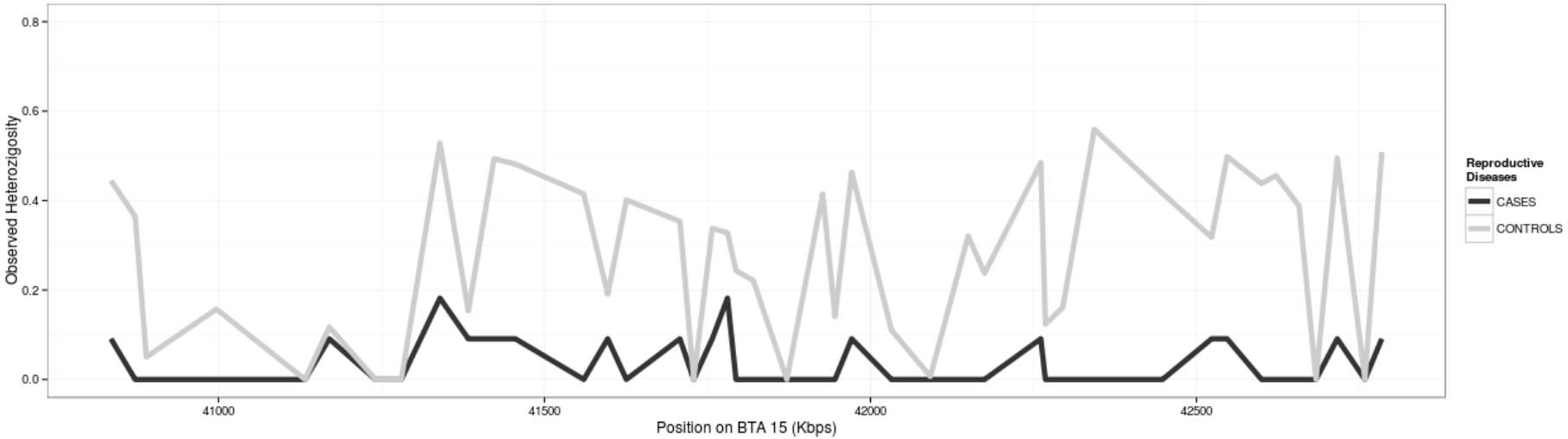
[Pollot, 2012]

Arthrogryposis Piedmontese cattle – BTA 6



[Biscarini et al., 2013]

Reproductive diseases Holsteins – BTA 15



[Biscarini et al., 2014]

ROH for GWAS?

Statistical issues

- **model-free technique**
- **no direct modeling of the phenotype**
- **no direct association**

Testing for significance

Homozygosity difference b'een cases and controls

$$H_0 : \mu_{cases} = \mu_{controls}$$

$$H_1 : \mu_{cases} > \mu_{controls}$$

Non-inferiority trial

Performance of ROH relative to the current standard (single-SNP GWAS)

$$H_0 : FDR_{ROH} - FDR_{GWAS} > M$$

$$H_1 : FDR_{ROH} - FDR_{GWAS} \leq M$$

Systematic effects

MODELING

$$CH = C + S + CxS$$

STRATIFICATION

ROH analysis within class of effect

Accounting for population structure and systematic effects

RESIDUALS

obs are pre-corrected for systematic effects

Conclusions