

The Impact of Selection on the Genome

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Introduction



Rationale



- Historically pedigree used to manage genetic diversity
 - Assumes selection-free, neutral loci
- Loci close to QTL will have higher loss of diversity

Roughsedge et al. (2008) *Genetics Research*, 90:199-208

Sonesson et al. (2012) *Genetics Selection Evolution*, 44:27



Aims



- With high density data we can:
 1. Identify regional variations in selection
 2. Examine level of conformity with pedigree model





Materials & Methods



Data



- Line A
 - Reproductive traits & growth rate
 - 1,551 genotyped individuals over 6 generations
 - 39,377 SNPs
- Line B
 - Reproductive traits
 - 4,889 genotyped individuals over 6 generations
 - 40,396 SNPs
- Illumina PorcineSNP60 Beadchip

Model



- Fit a regression for each SNP :

$$\ln(H_{ij}) = \beta_j + \gamma_j \ln(1-F_i) + \mu_{ij}$$

Model



- Fit a regression for each SNP :

$$\ln(H_{ij}) = \pm_j + {}^2_j \ln(1-F_i) + \mu_{ij}$$

Where,

H = Observed heterozygosity

$1-F$ = Expected heterozygosity

\pm = Intercept

μ = Error term

2 = Slope of the regression

Model



- Fit a regression for each SNP :

$$\ln(H_{ij}) = \beta_j + \gamma_j \ln(1-F_i) + \mu_{ij}$$

Where,

H = Observed heterozygosity

$1-F$ = Expected heterozygosity

β = Intercept

μ = Error term

γ = Slope of the regression

Model

- Fit a regression for each SNP :

$$\ln(H_{ij}) = \pm_j + \textcolor{red}{\alpha_j} \ln(1-F_i) + \mu_{ij}$$

Where,

H = Observed heterozygosity

$1-F$ = Expected heterozygosity

\pm = Intercept

μ = Error term

$\textcolor{red}{\alpha}$ = Slope of the regression

Regression slope, $\hat{\beta}_j^2$



- Fit a regression for each SNP :

$$\ln(H_{ij}) = \beta_j + \hat{\beta}_j^2 \ln(1-F_i) + \mu_{ij}$$

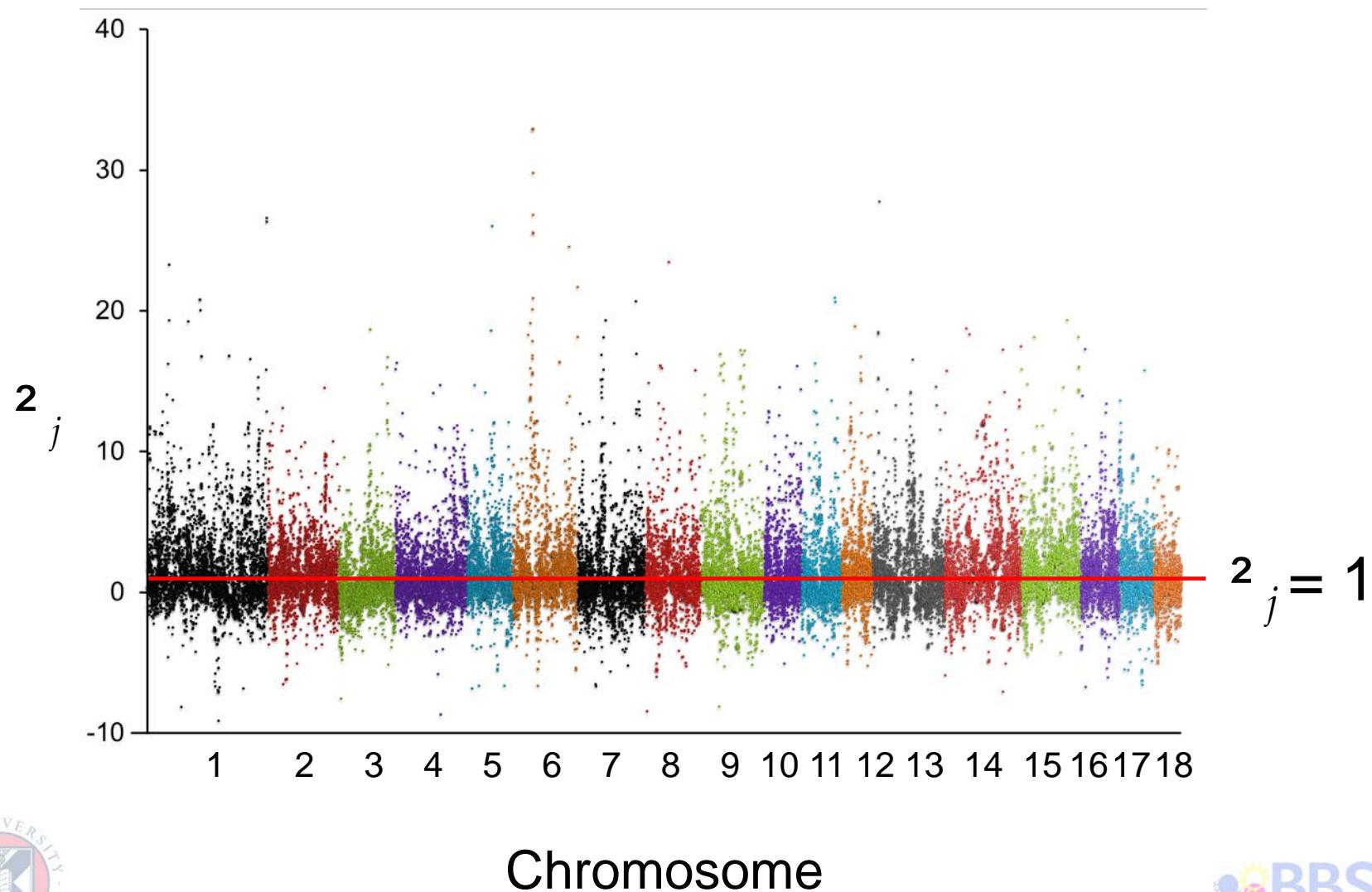
$\hat{\beta}_j^2 = 1$, Loss of heterozygosity equals expectation

$\hat{\beta}_j^2 > 1$, Loss is greater than expected

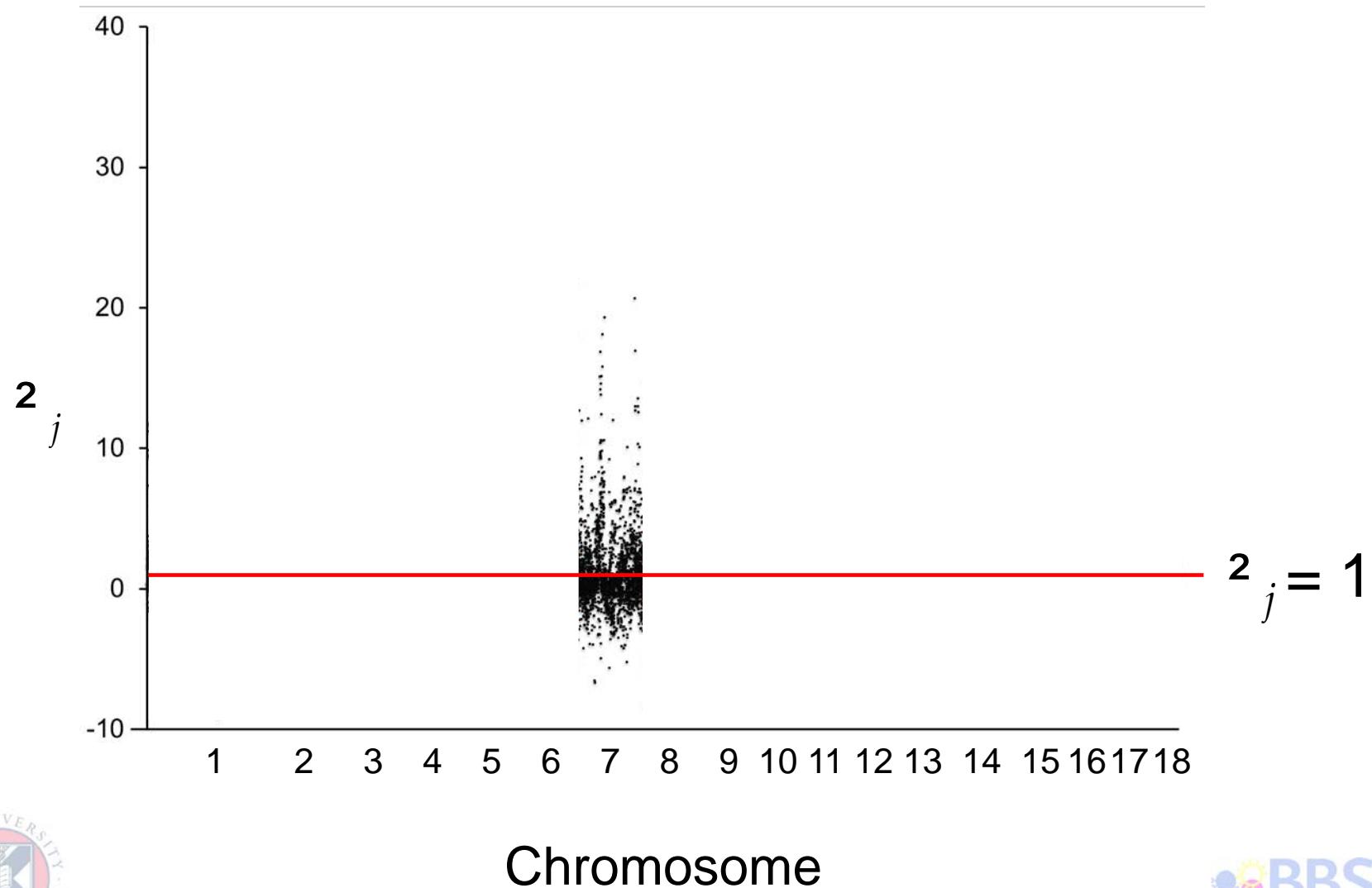
$\hat{\beta}_j^2 < 1$, Loss is less than expected



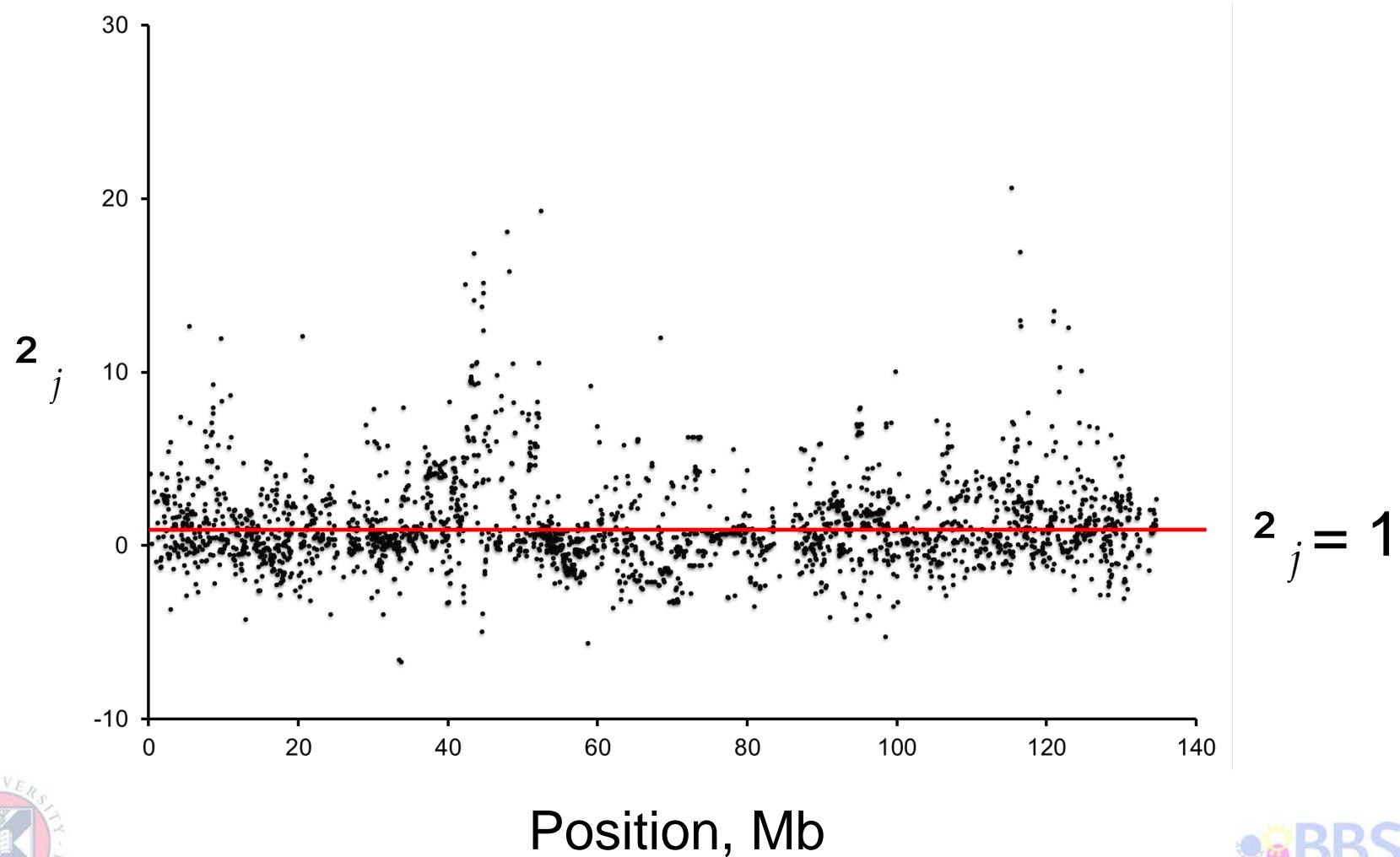
Line A, Genome Wide



Line A, Genome Wide



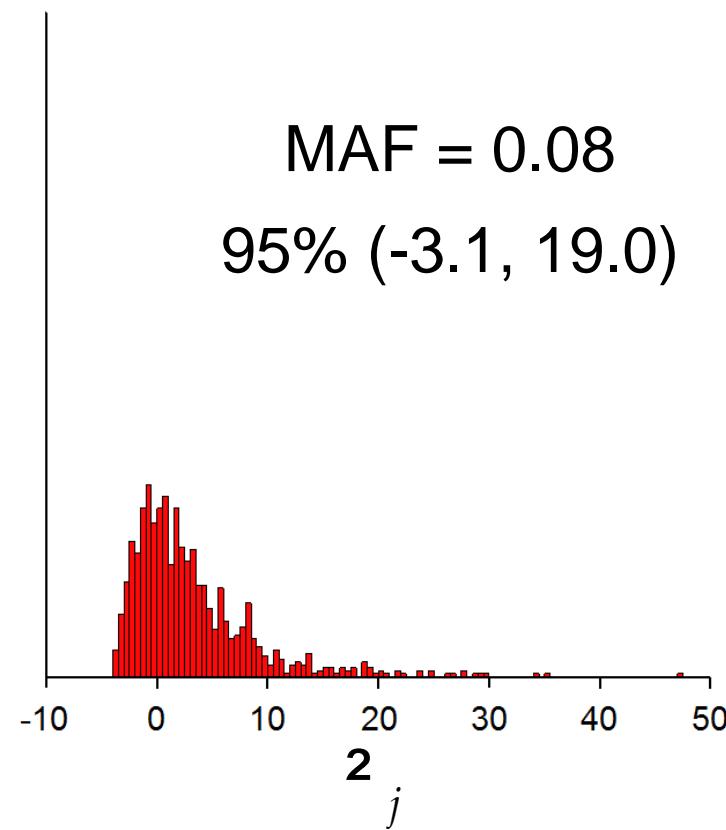
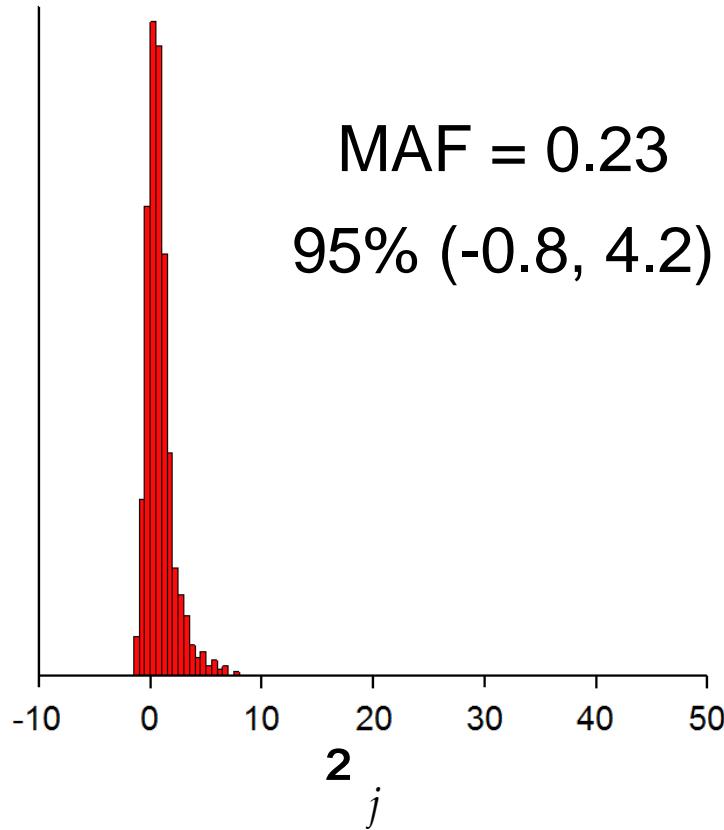
Line A, SSC07



Confidence Intervals



- Bootstrap using gene-dropping for every SNP
- Use distribution of iterations to form confidence intervals

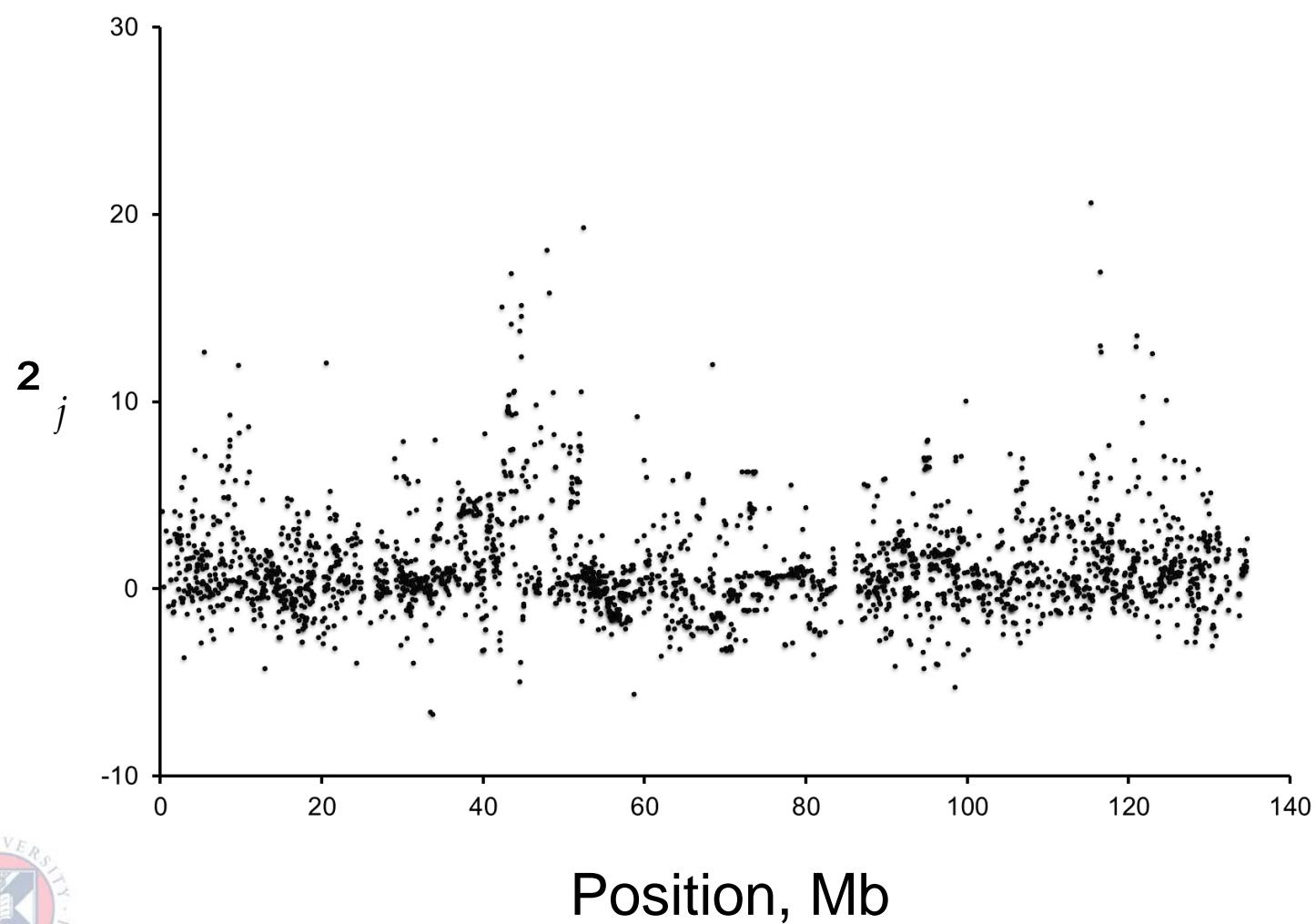




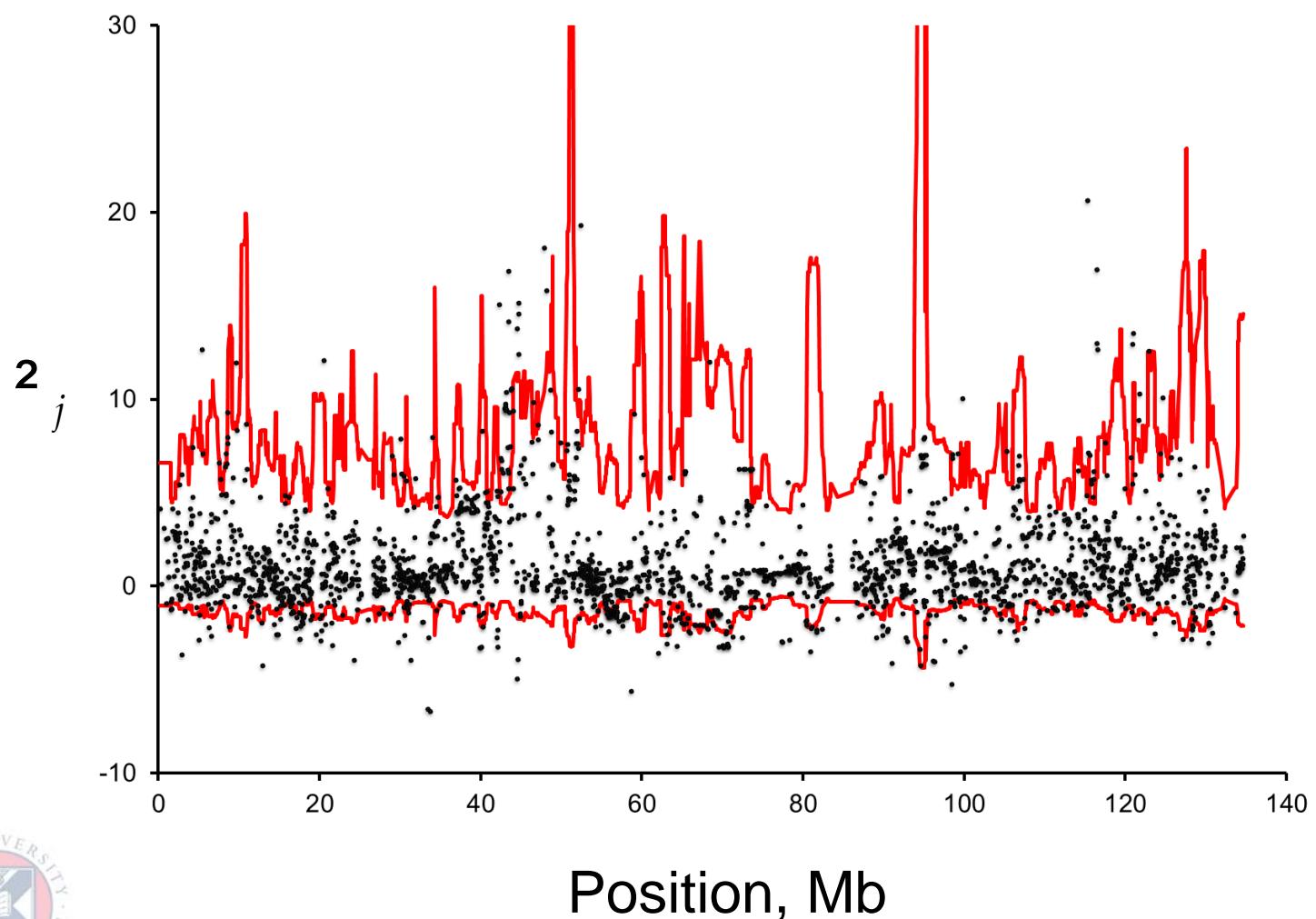
Results



Line A, SSC07



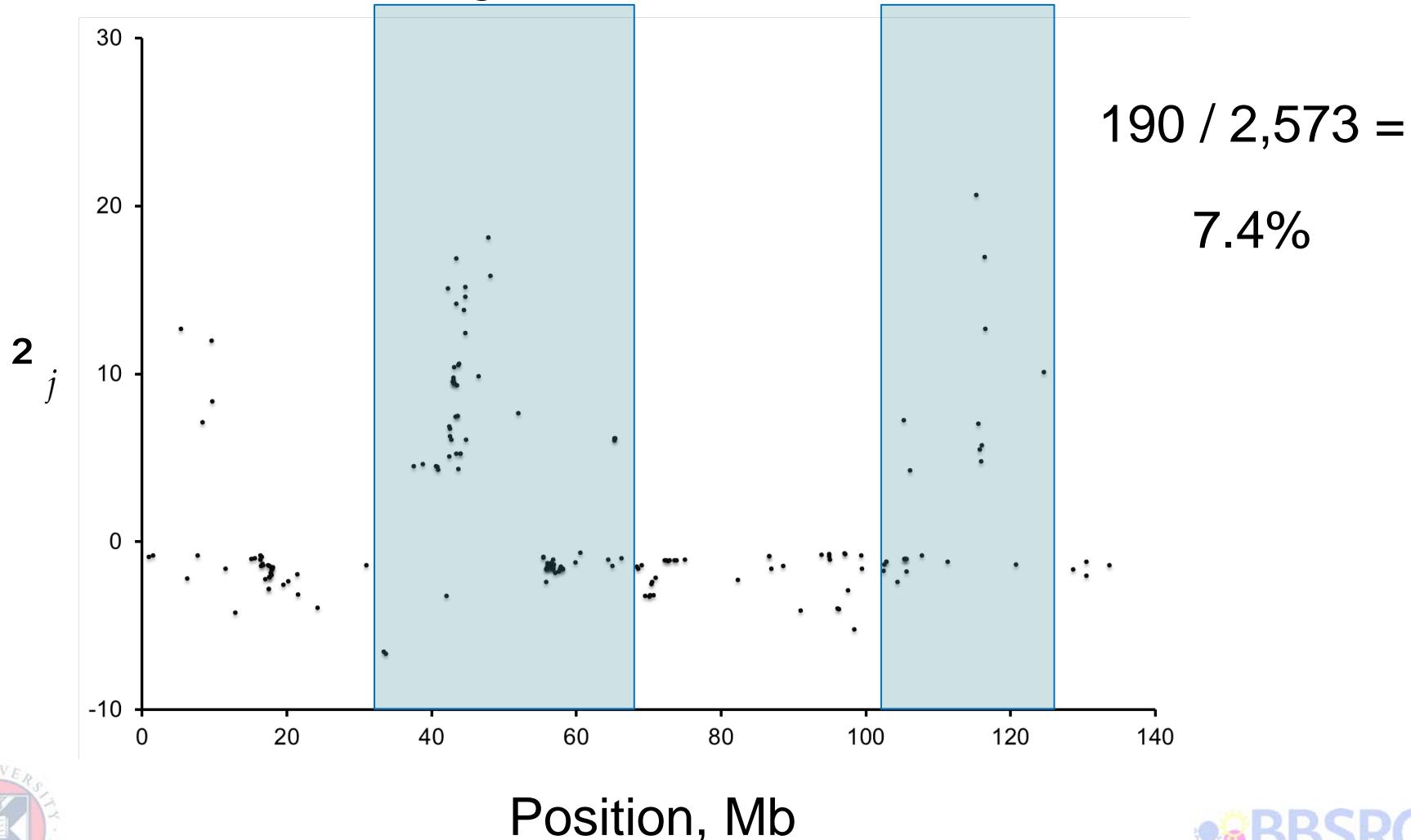
95% Confidence Interval



Line A, SSC07



Significant at 5% level



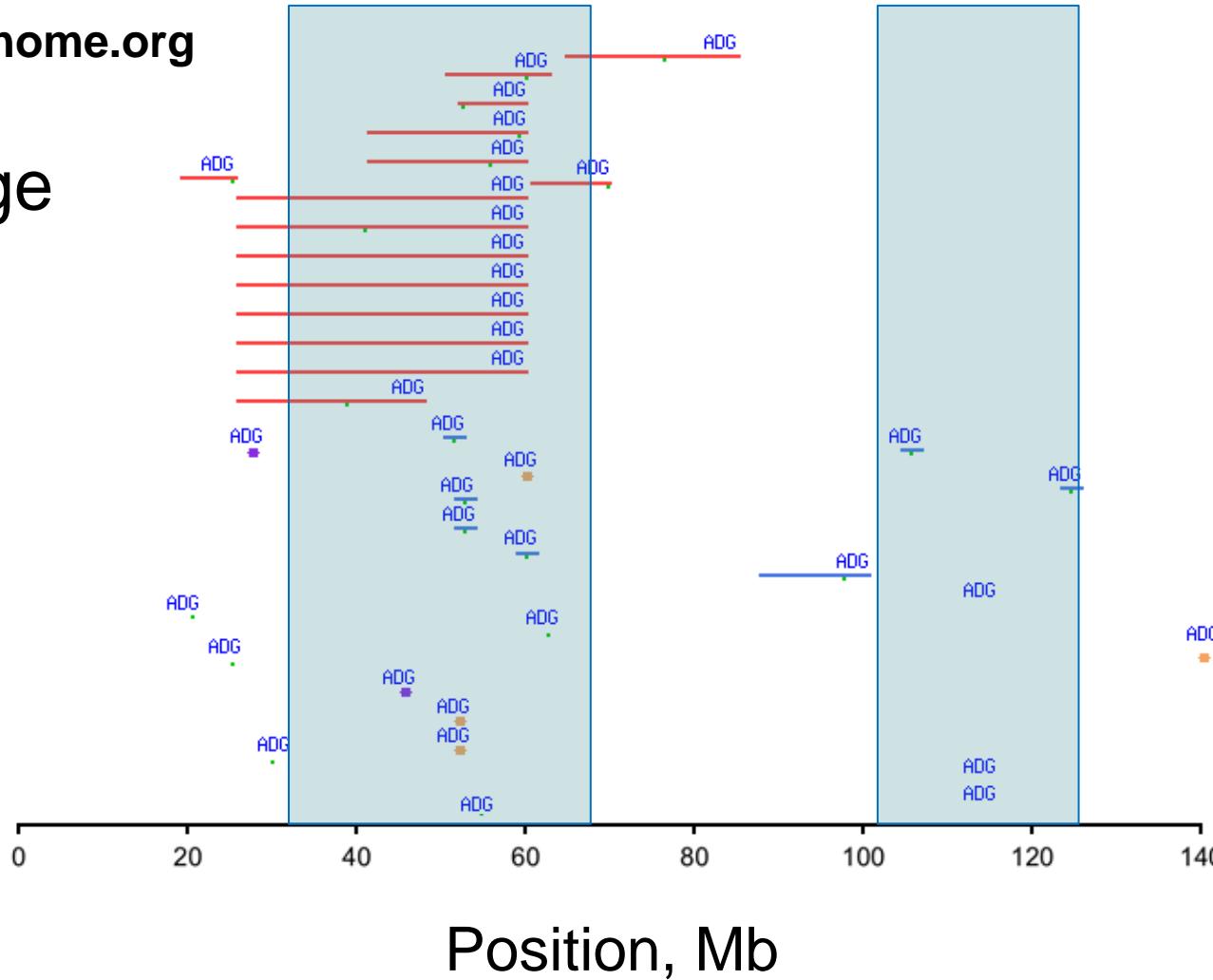
Putative QTL, SSC07



PigQTLdb

animalgenome.org

Average
Daily
Gain

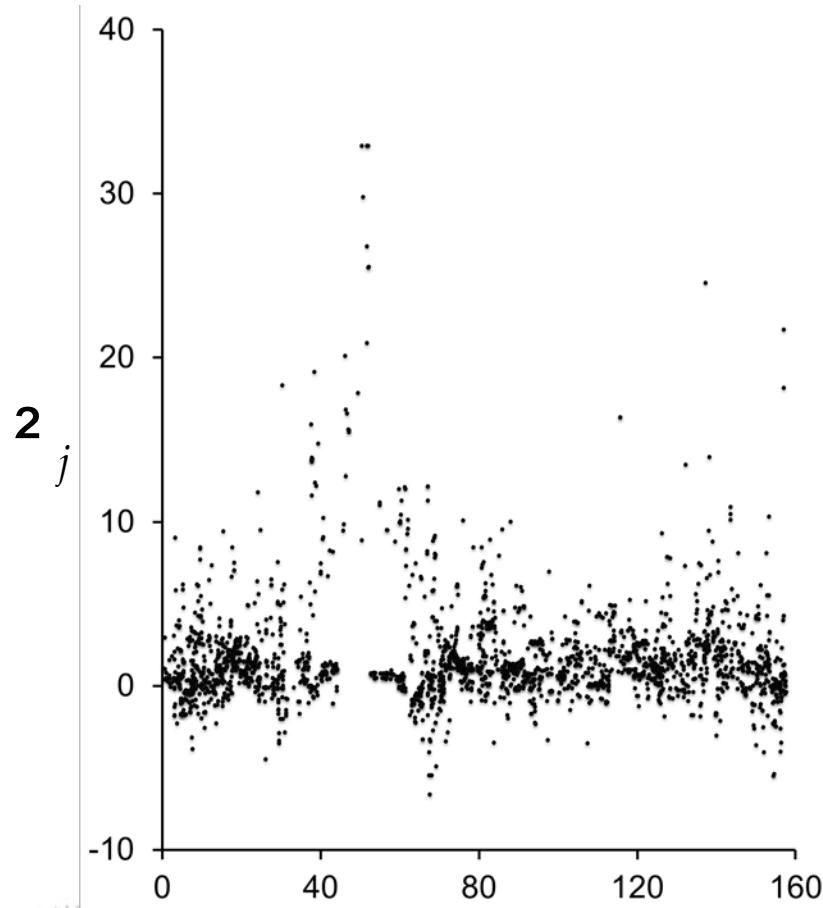


BBSRC

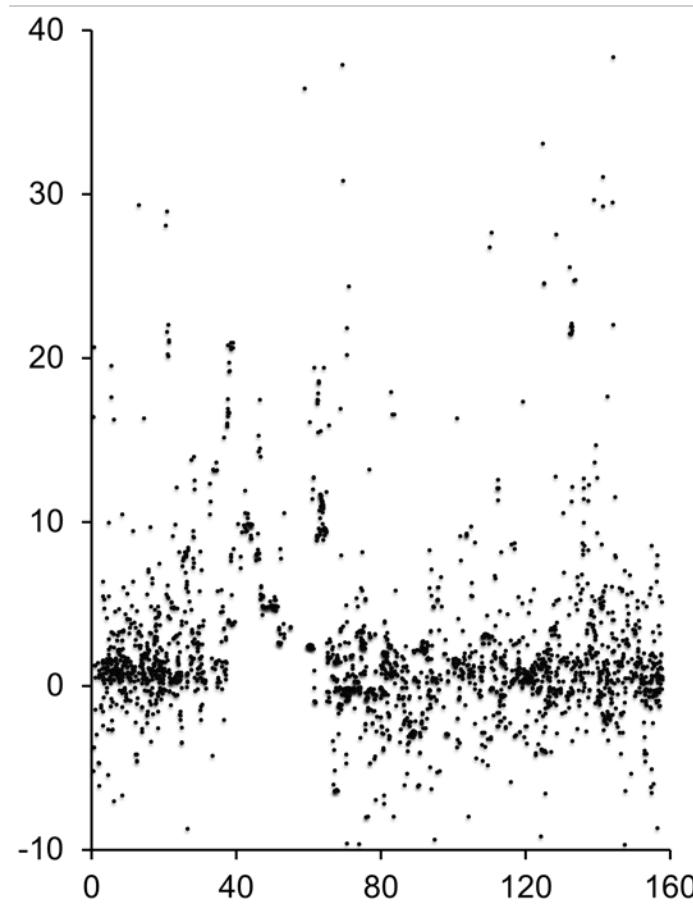
Line Comparison, SSC06



Line A



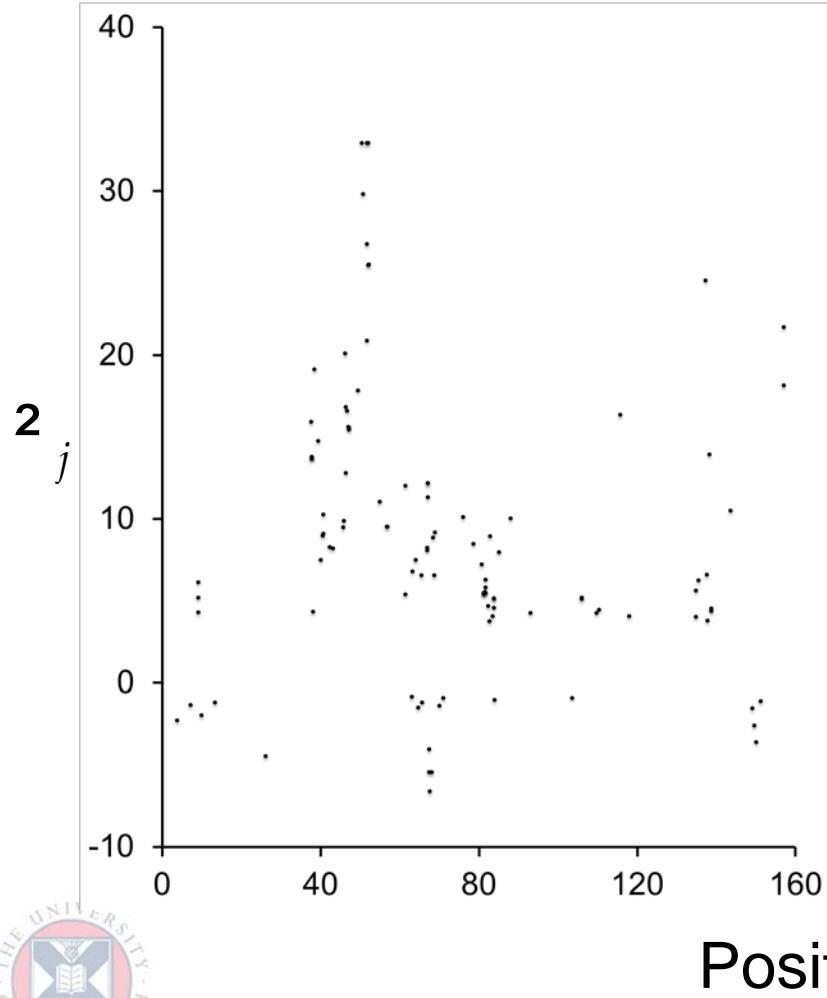
Line B



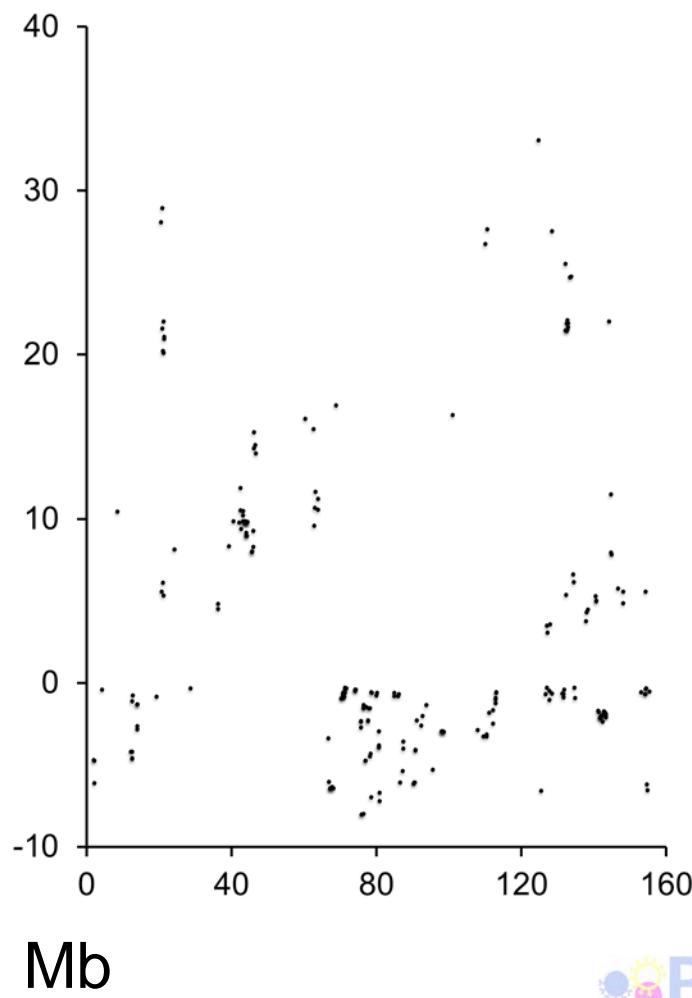
Significant at 5% level



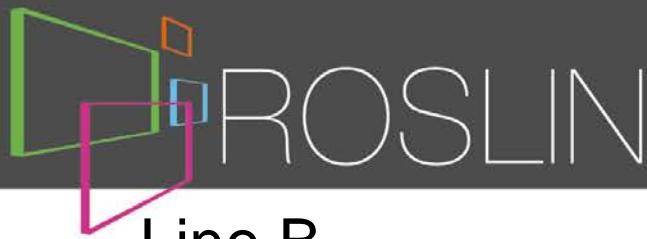
Line A



Line B



Changes in Heterozygosity



Line A

	Confidence Intervals					
	1%	5%	Upper 0.5%	Upper 2.5%	Lower 0.5%	Lower 2.5%
Whole Genome	0.86%	4.05%	0.33%	1.59%	0.53%	2.46%
SSC01						
SSC02						
SSC03						
SSC04						
SSC05						
SSC06						
SSC07		7.4%				
SSC08						
SSC09						
SSC10						
SSC11						
SSC12						
SSC13						
SSC14						
SSC15						
SSC16						
SSC17						
SSC18						

	Confidence Intervals					
	1%	5%	Upper 0.5%	Upper 2.5%	Lower 0.5%	Lower 2.5%
Whole Genome	1.70%	6.14%	0.65%	2.66%	1.05%	3.48%
SSC01						
SSC02						
SSC03						
SSC04						
SSC05						
SSC06						
SSC07						
SSC08						
SSC09						
SSC10						
SSC11						
SSC12						
SSC13						
SSC14						
SSC15						
SSC16						
SSC17						
SSC18						



= Evidence for excessive change in heterozygosity



Summation



Aims



- With high density data we can:
 1. Identify regional variations in selection
 2. Examine level of conformity with pedigree model



Conclusions



- Evidence of diversity loss at specific regions
 - Putative QTL identification (Line A, SSC07)
- Varying impact between lines (SSC06)
 - Trait Architecture
 - Power
 - Future - Haplotyping



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- With high density data we can:
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Implications



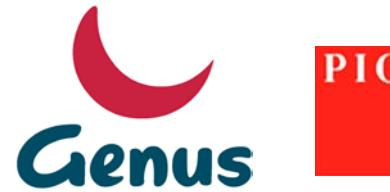
- Evidence for inadequacy of pedigree model (Line B)
- Genomic Optimal Contributions
- Precision inbreeding at SNP level
- ‘‘ Regional loss of diversity, provided maintained elsewhere



Acknowledgements



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Dave McLaren
Olwen Southwood
Nan Yu

