Genetic variants underlying hoof diseases in Braunvieh and Fleckvieh cattle

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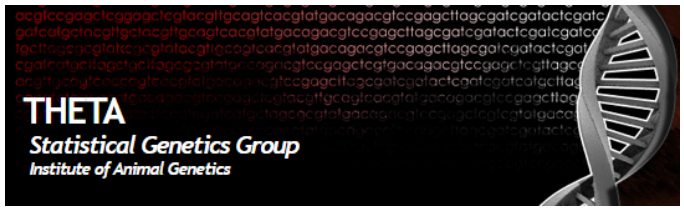


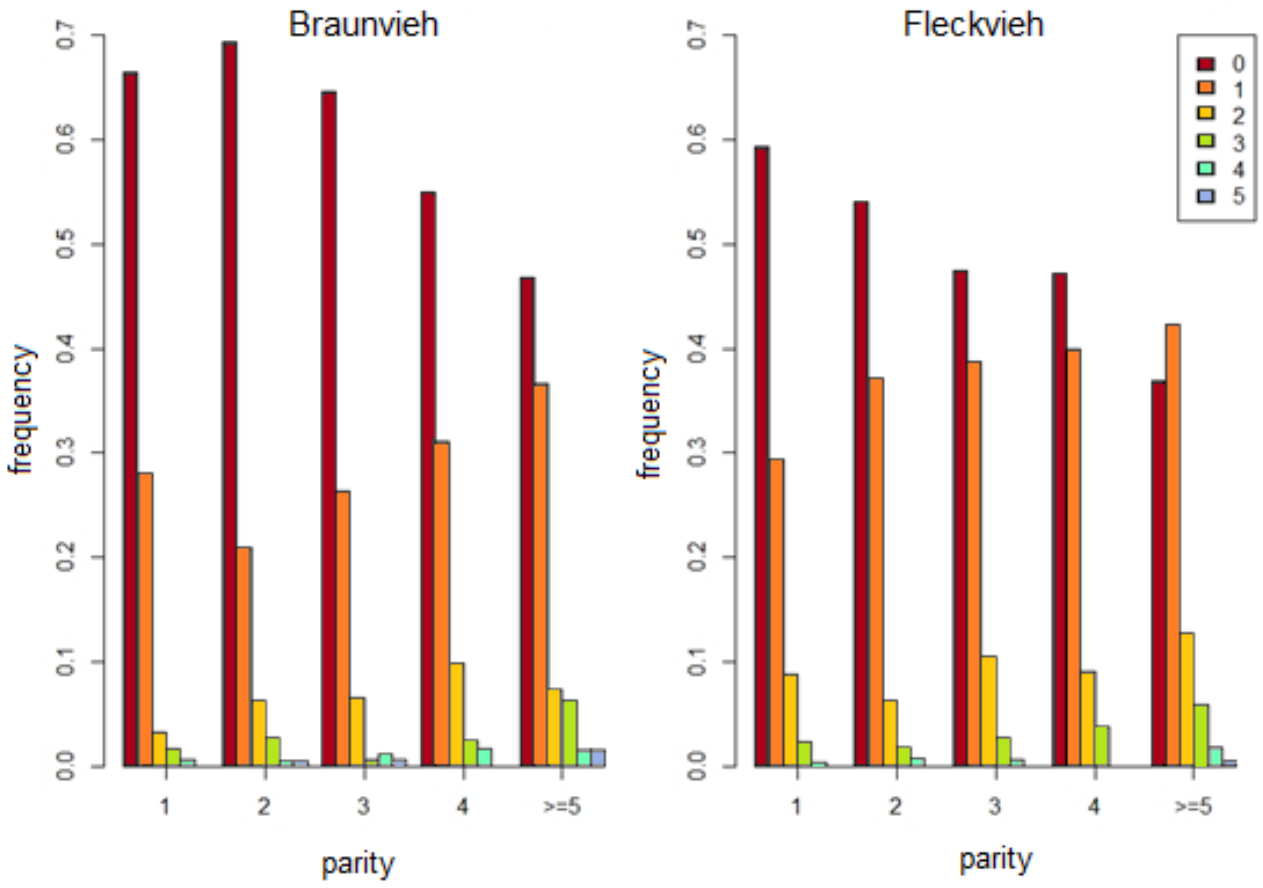
Objectives

Better understanding of genetics background underlying **hoof diseases and lameness**

Material

1. Cows
   - 1 999 Fleckvieh (FLV), 985 Braunvieh (BSW)
2. SNPs
   - Geneseek Genomic Profiler HD BeadChip
   - 76 932 SNPs
   - 74 762 SNPs (MAF 0.01; call rate 99 %)
3. Phenotype
   - total number of leg disorders until DIM 300^{th}
   - EBV

Material



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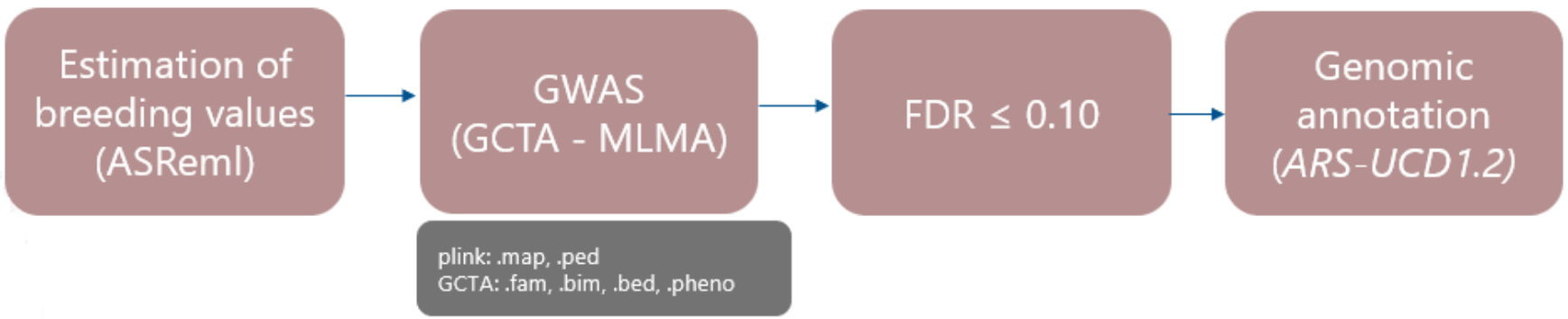
Methods/genome-wide association study (GWAS)



Methods/EBV prediction

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Z_u u} + \boldsymbol{Z_v v} + \boldsymbol{Z_p p} + \boldsymbol{\varepsilon}$$

$\boldsymbol{y}$	total number of leg disorders scored till DIM 300
$\boldsymbol{\beta}$	fixed effects : a general mean, breed (Braunvieh or Fleckvieh), parity (1,2,3,4 or >4), calving year-season, hoof status recording code (four levels)
$\boldsymbol{u}$	$\sim N(0, \boldsymbol{A}\sigma_u^2)$ EBV
$\boldsymbol{v}$	$\sim N(0, \boldsymbol{I}\sigma_v^2)$ random veterinarian effect
$\boldsymbol{p}$	$\sim N(0, \boldsymbol{I}\sigma_p^2)$ random permanent environmental effect
$\boldsymbol{\varepsilon}$	$\sim N(0, \boldsymbol{I}\sigma_\epsilon^2)$ residual

Methods/GWAS model

$$\boldsymbol{u} = \mu + \boldsymbol{X}\boldsymbol{b} + \boldsymbol{Z}\boldsymbol{g} + \boldsymbol{e}$$

$\boldsymbol{u}$ EBV

$\boldsymbol{\mu}$ general mean

$\boldsymbol{b}$ additive effect of all single SNP

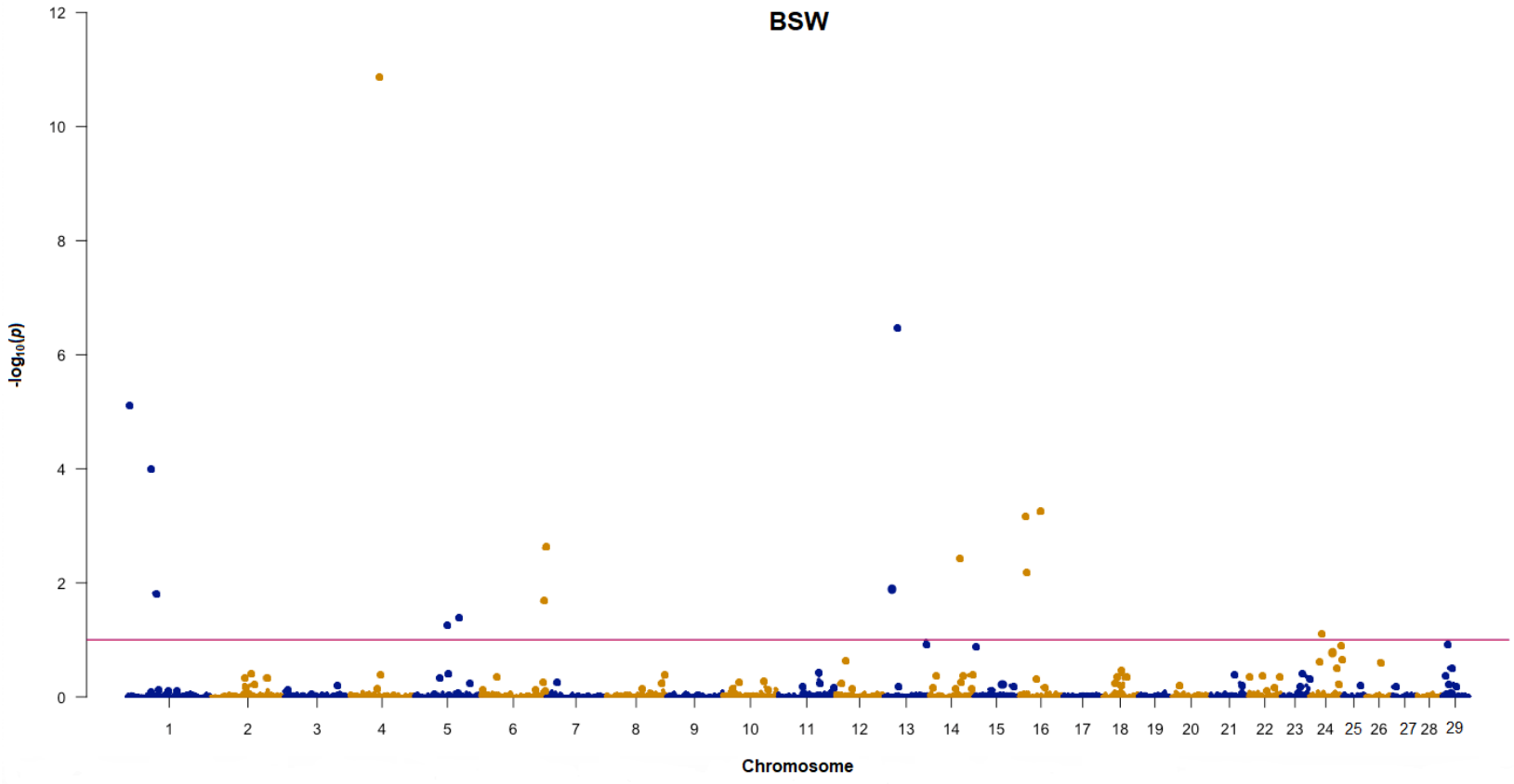
$\boldsymbol{X}$ design matrix {0, 1, 2}

$\boldsymbol{g} \sim N(0, \boldsymbol{G}\sigma_g^2)$ cumulated effect of all remaining SNPs,

$\boldsymbol{G}$ corresponds to the genomic covariance matrix between cows calculated based on SNPs.

$\boldsymbol{e} \sim N(0, \boldsymbol{I}\sigma_e^2)$ residual

Results/GWAS



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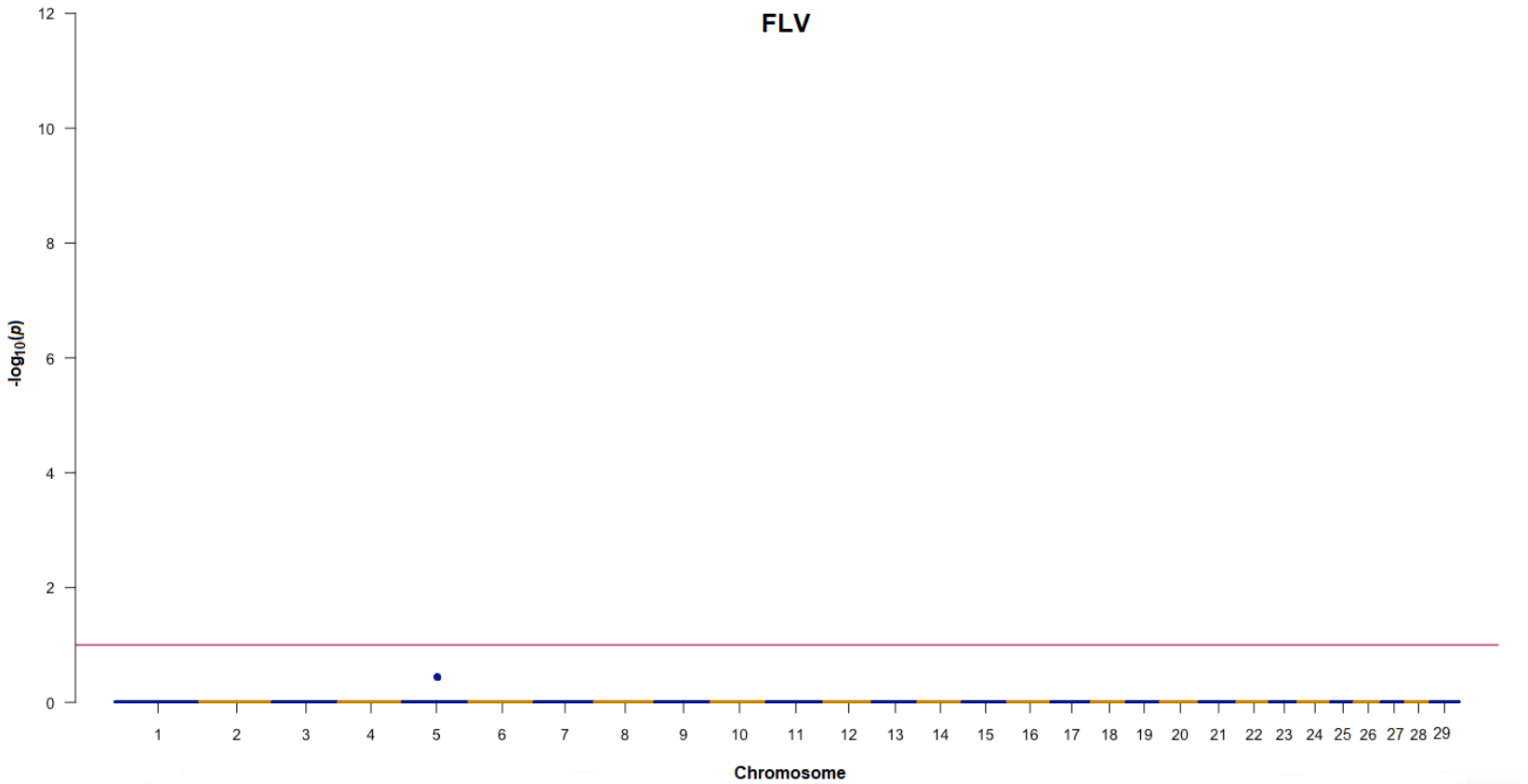
Results/GWAS



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Results/GWAS

SNP	Position [bp]**	Additive effect	FDR*	Annotation**
ARS-BFGL-NGS-92033	1:3,303,269	0.018	$7.5 \cdot 10^{-6}$	intergenic, between MIS18A and HUNK
BTA-89698-no-rs	1:43,542,488	0.012	0.0001	intergenic, between DCBLD2 and COL8A1
ARS-BFGL-NGS-6521	1:50,767,507	0.007	0.0150	intergenic, between CBLB and CCDC54
BovineHD0400014448	4:52,028,036	0.029	$1.4 \cdot 10^{-11}$	intergenic, between CAV2 and TES
BovineHD0400014458	4:52,079,221	0.029	$1.4 \cdot 10^{-11}$	
Hapmap48066-BTA-73690	5:61,220,624	0.010	0.0530	intergenic, closest to NEDD1
ARS-BFGL-NGS-85328	5:81,769,685	0.008	0.0430	intergenic, between CCDC91 and PTHLH
ARS-BFGL-NGS-103113	6:115,208,599	0.016	0.0210	intergenic, between ADRA2C and LRPAP1
ARS-BFGL-NGS-100768	6:114,116,280	0.010	0.0020	intron of SORCS2
ARS-BFGL-NGS-25175	13:13,590,662	0.008	0.0120	intergenic, closest to CELF2
ARS-BFGL-NGS-101509	13:23,590,146	0.019	$3.3 \cdot 10^{-7}$	intergenic, between SPAG6 and PIP4K2A
ARS-BFGL-NGS-63852	14:55,768,446	0.010	0.0040	intergenic, between TMEM74 and EMC2
Hapmap55901-rs29024589	16:12,125,227	0.010	0.0007	intergenic between B3GALT2 and GLRX2
ARS-BFGL-NGS-109246	16:12,280,122	0.008	0.0060	intergenic, between UCHL5 and RGS2
Hapmap51828-BTA-38538	16:36,037,389	0.007	0.0006	intergenic, between RGS7 and XCL1
BovineHD2400006669	24:24,273,191	0.002	0.0820	intergenic, between CCDC178 and KLHL14

*False Discovery Rate

**ARS UCD1.2.assembly

Results/ GWAS

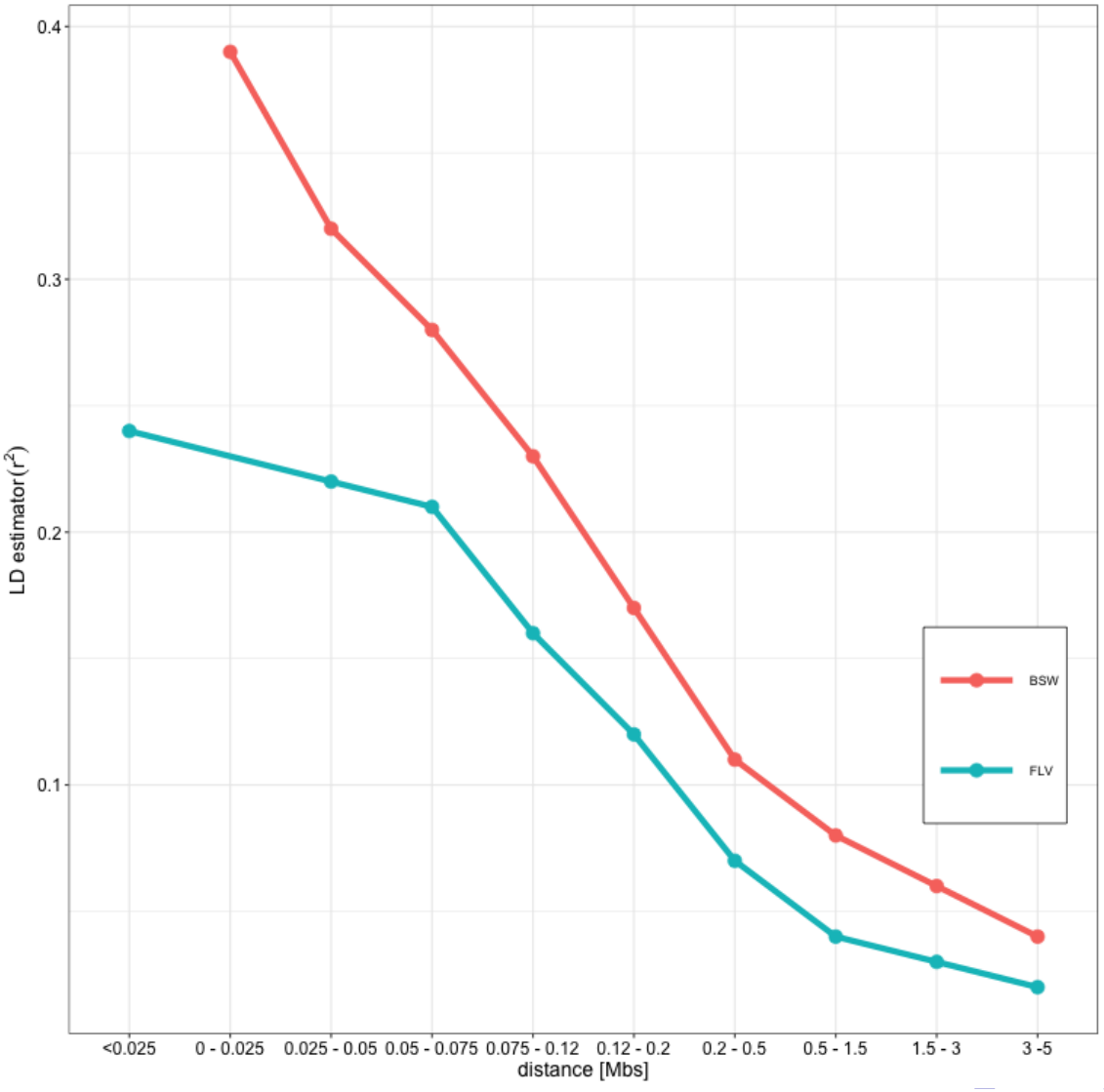
CBLB

CAV2

PTHLH

SORCS2

Comparison of LD patterns



Methods/Differences in pairwise LD structure between breeds

$$S = \left[\sum_{i=1}^{n}[(v_{i21} + v_{i22}) - (v_{i12} + v_{i21})]^2\right] + \left[\sum_{i=1}^{n}[(v_{i11} + v_{i12}) - (v_{i21} + v_{i22})]^2\right]$$

S – general meausure of variability

v_{ij} – product of linkage disequilibrium covariance matrix of breed$_i$ and the vector of eigenvectors corresponding to breed$_j$

(Garcia, 2012)
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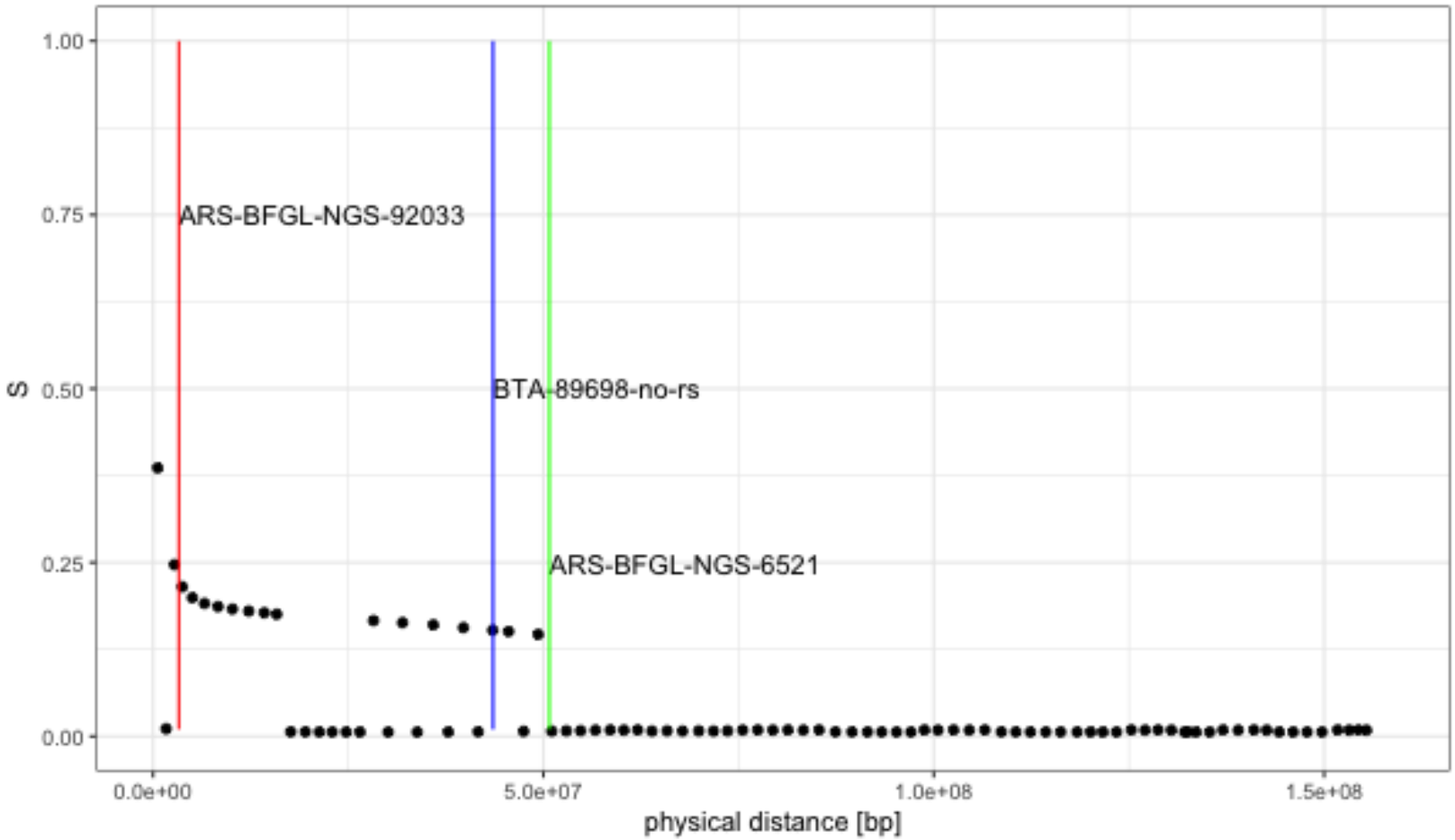
Results/PCA/BTA1



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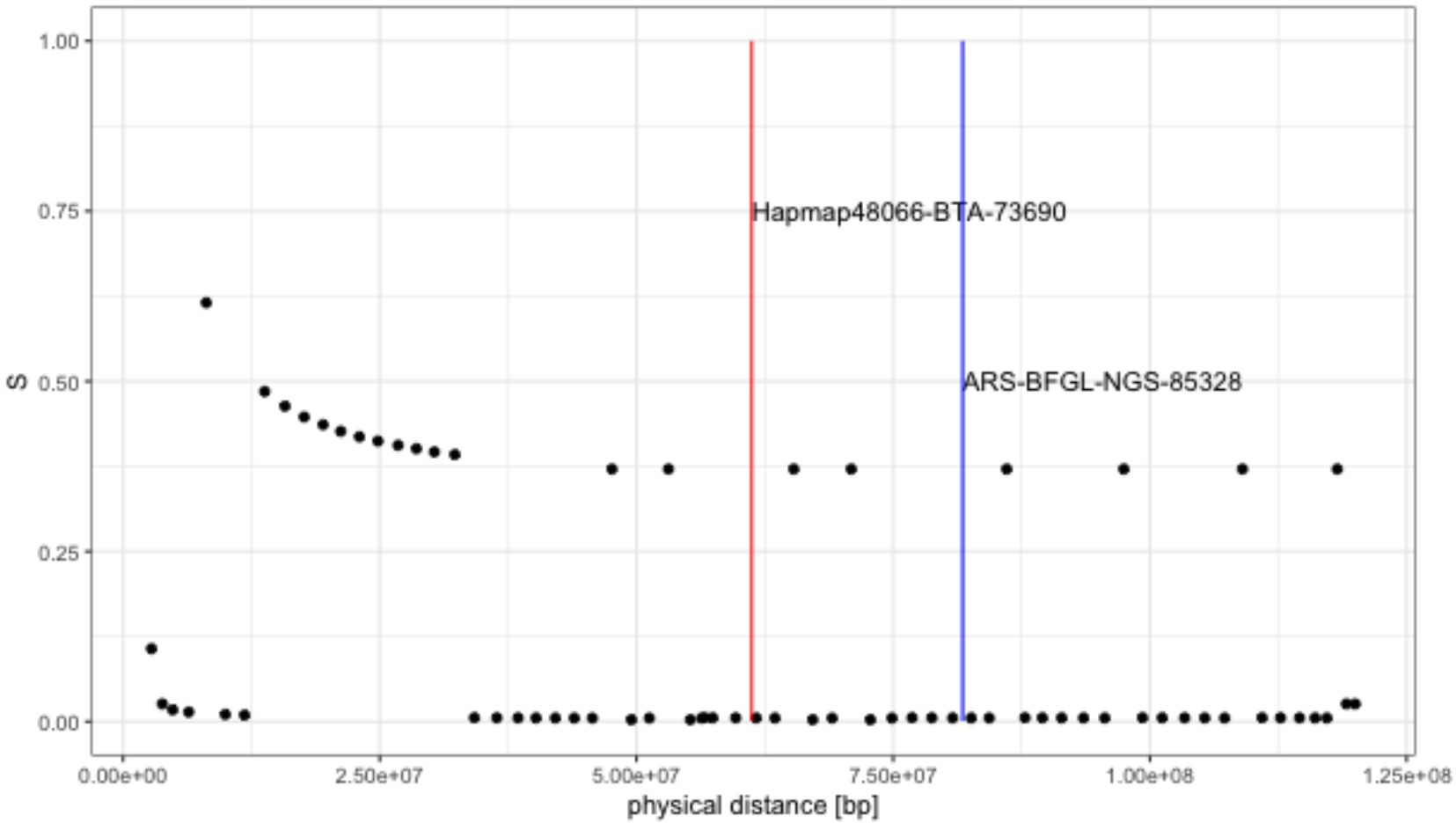
Results/PCA/BTA5



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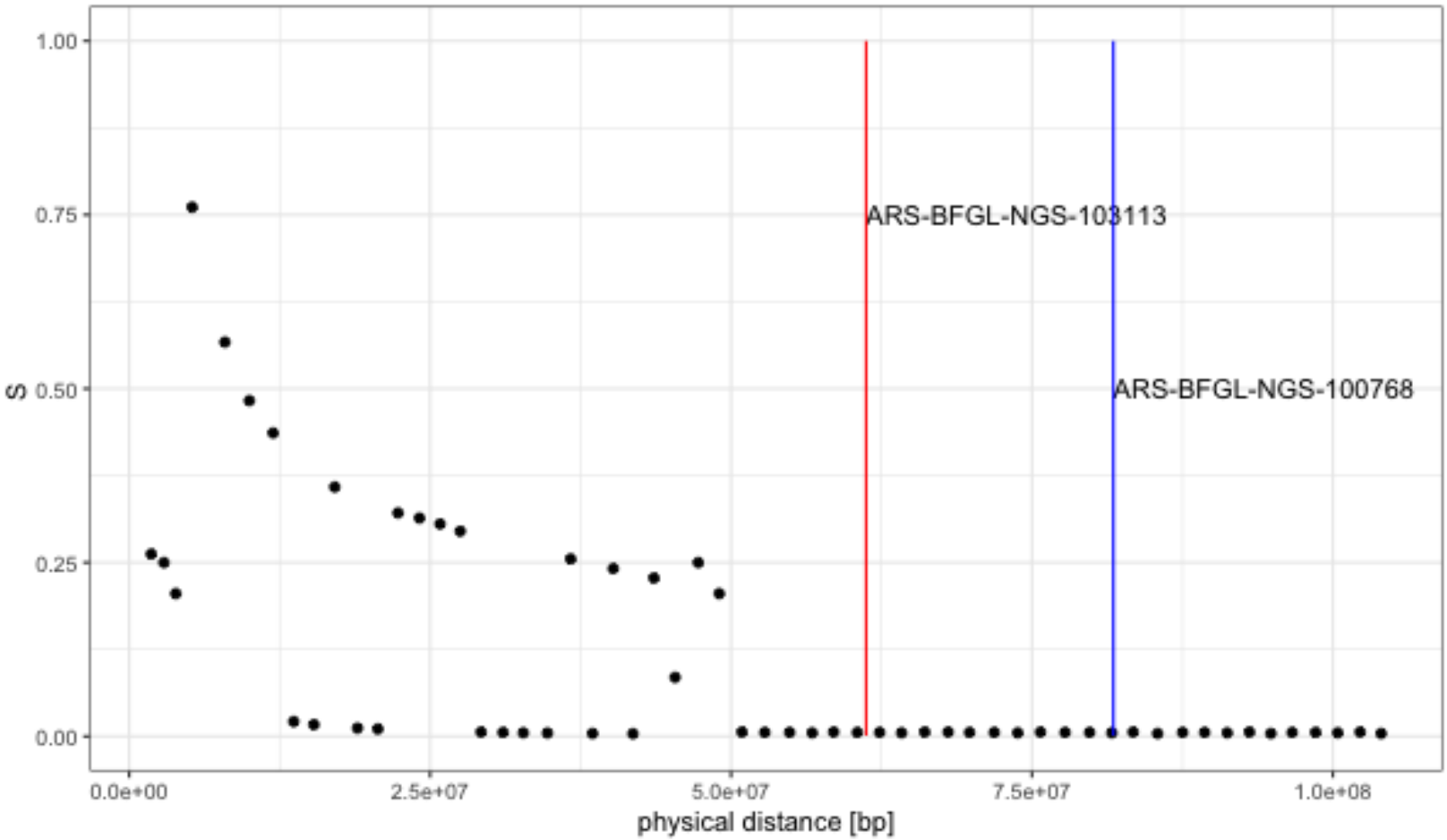
Results/PCA/BTA6



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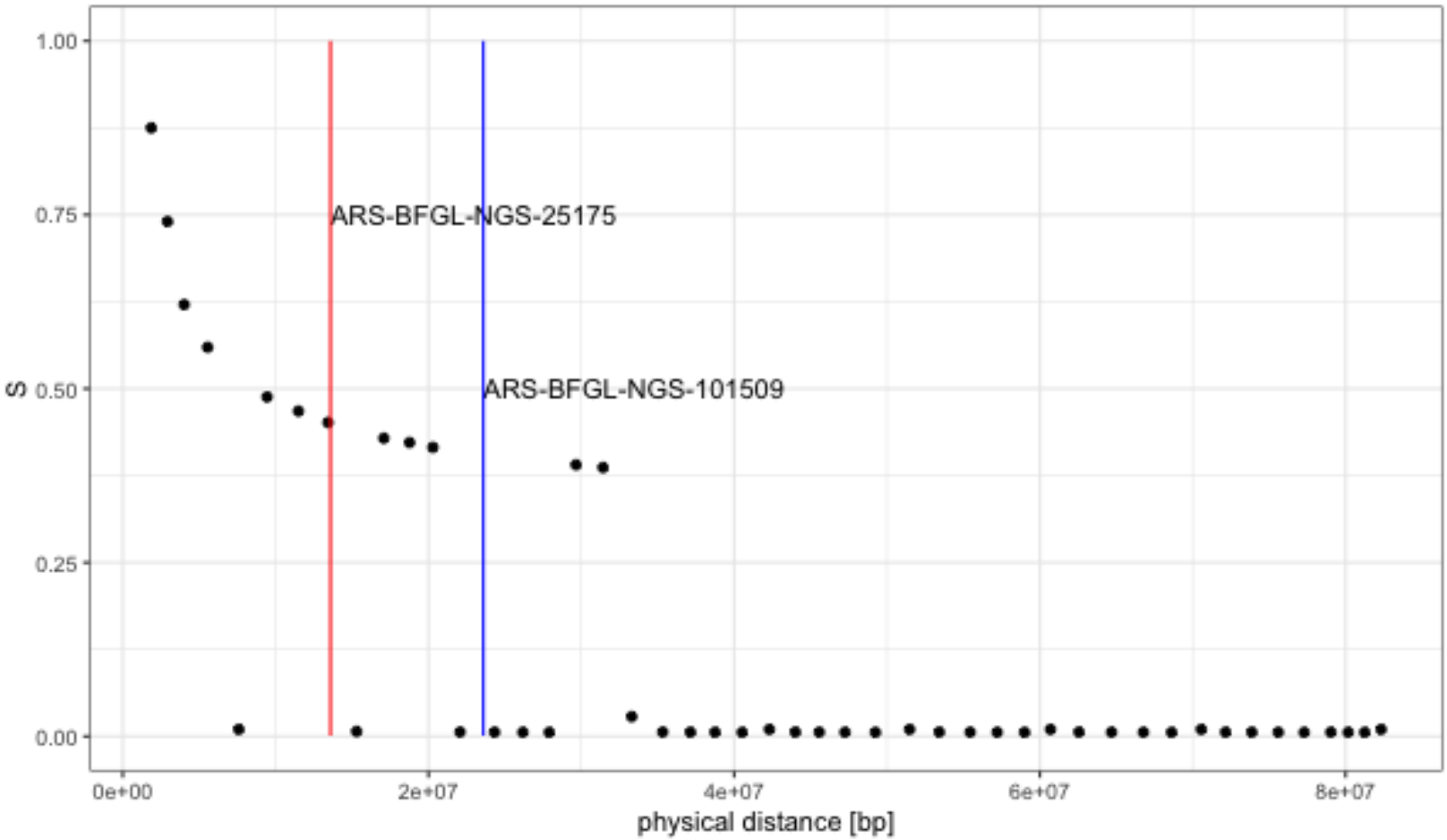
Results/PCA/BTA13



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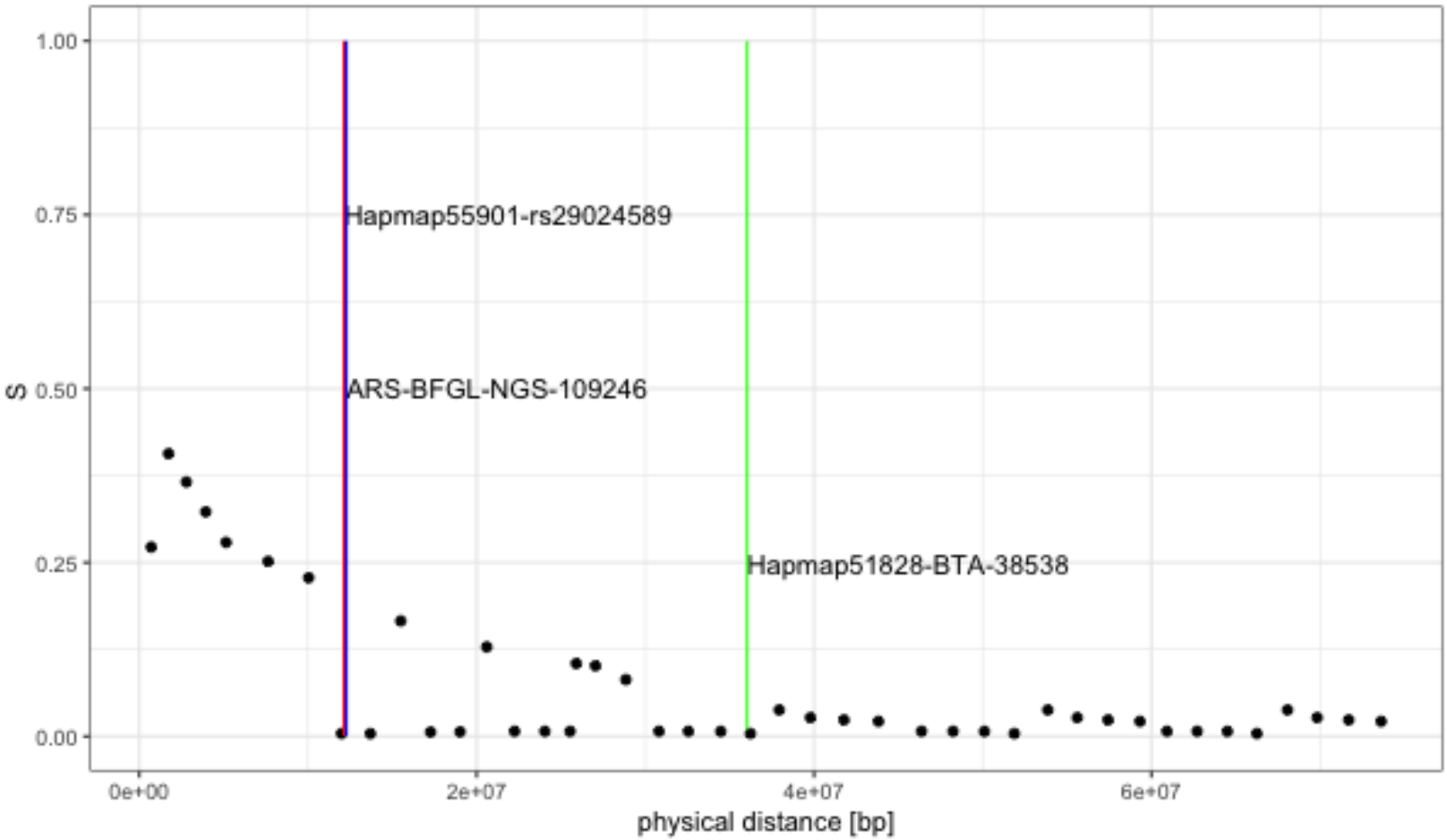
Results/PCA/BTA16



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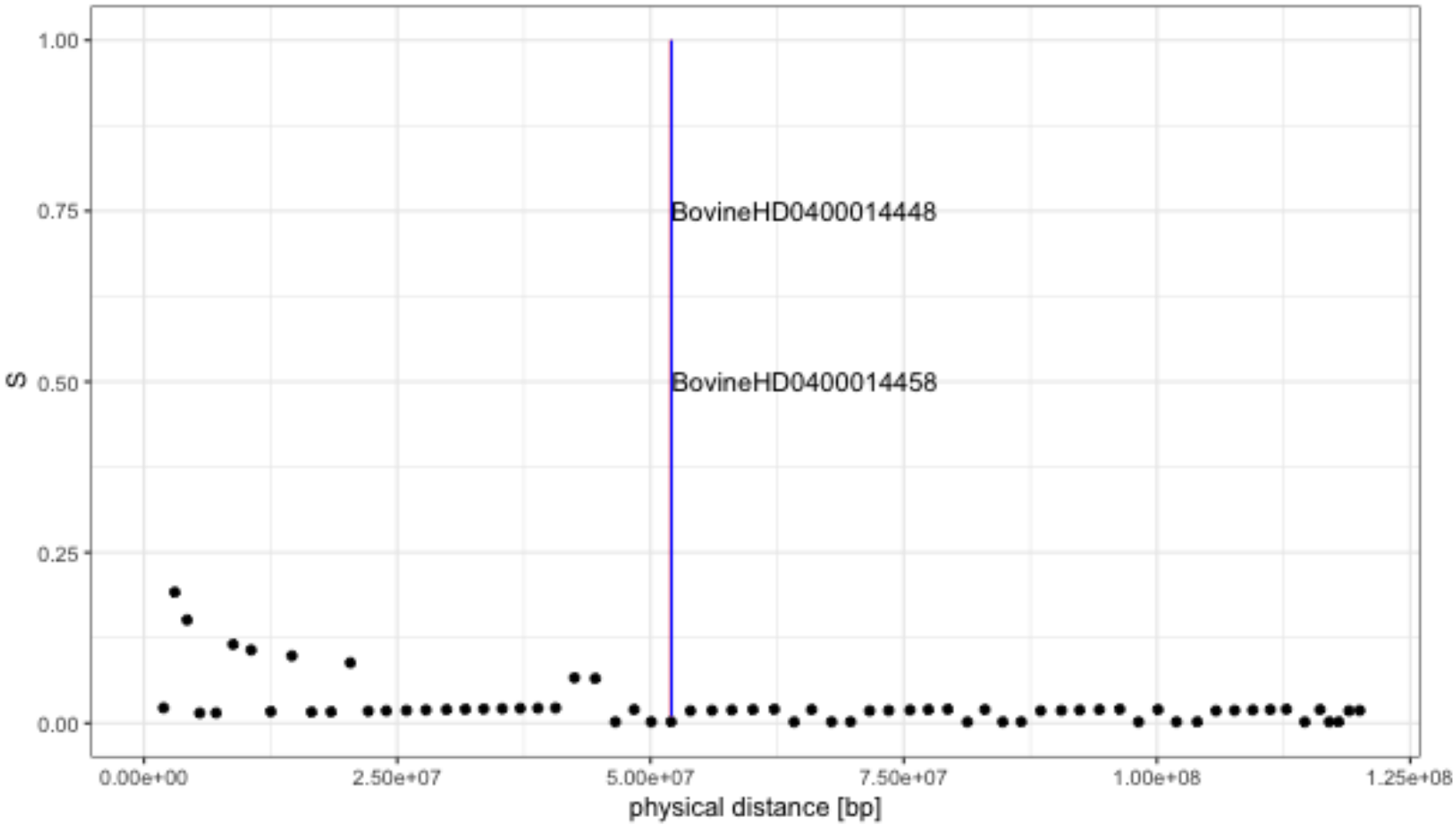
Results/PCA/BTA4



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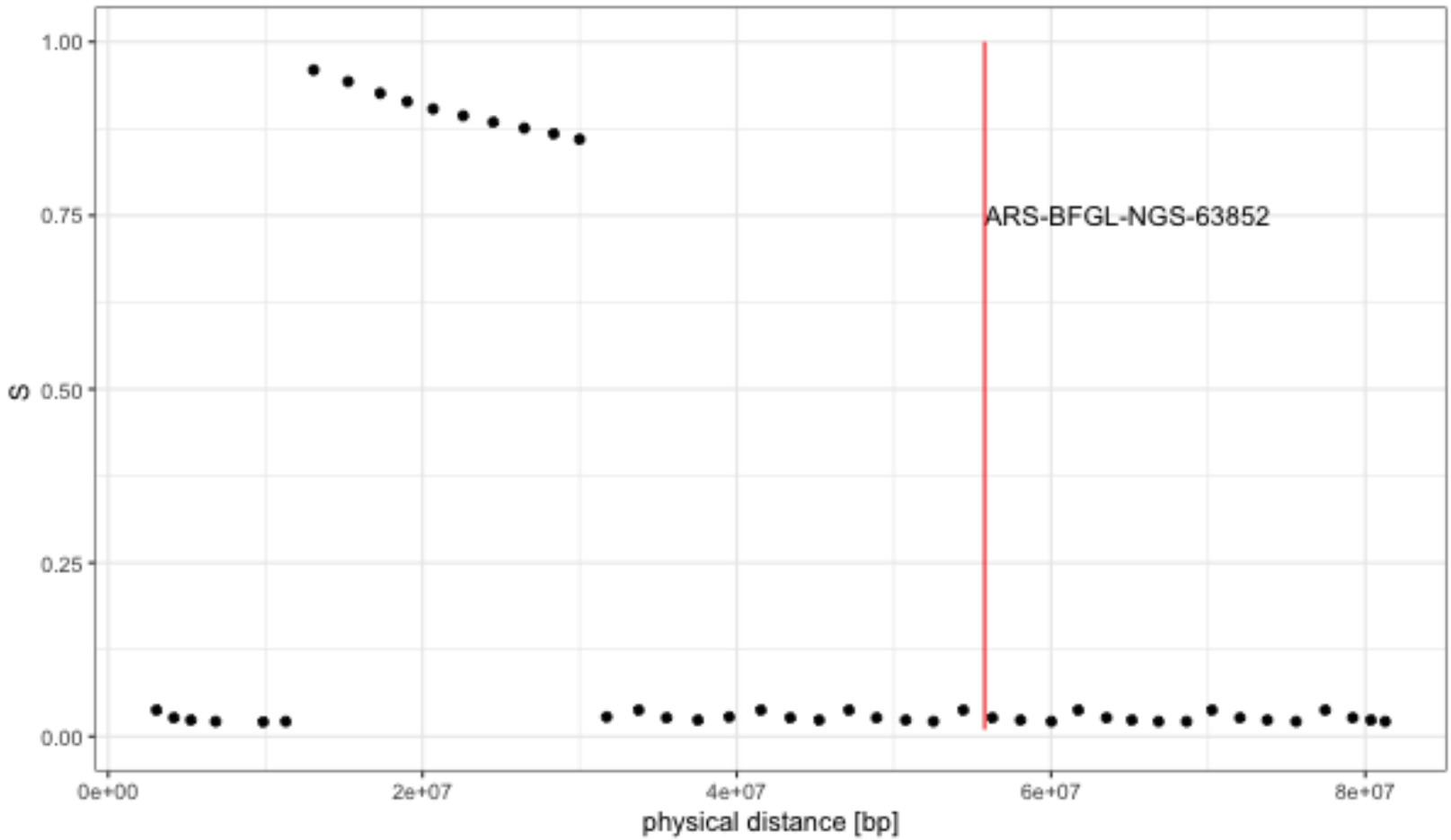
Results/PCA/BTA14



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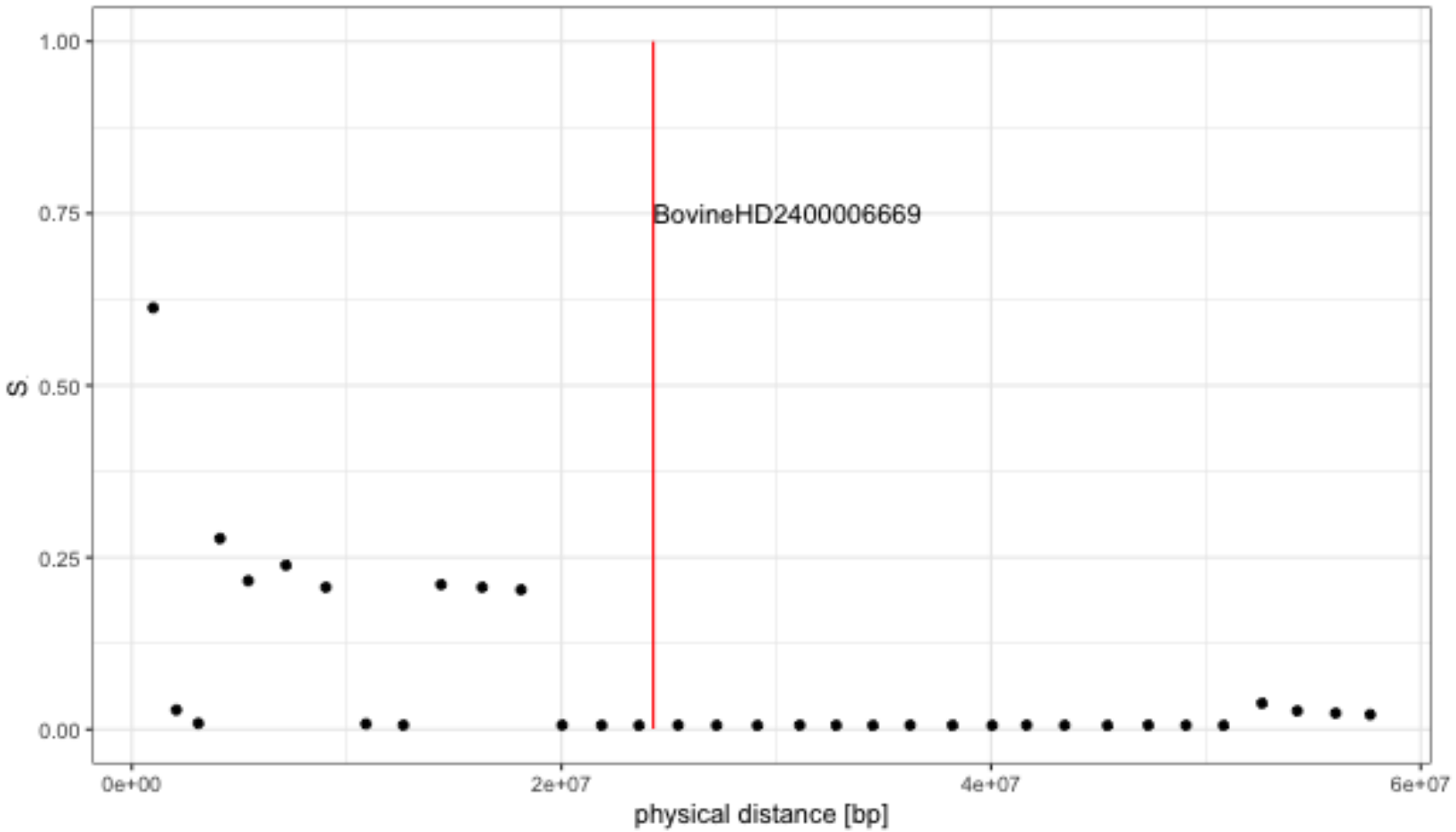
Results/PCA/BTA24



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Conclusions

1. GWAS allow to identify SNPs that are related to number of leg disorders
2. Differences in LD structure between Fleckvieh and Braunvieh in some genomic regions
3. Differences in LD structure partially explain genetic heterogeneity

Acknowledgement

1. NCN grant No. 2015/19/B/NZ9/03725 as well as by the Efficient Cow and the Gene2Farm projects

2. Biostatistics group, Department of Genetics, Wroclaw University of Environmental and Life Sciences
   - Magdalena Fraszczak
   - Joanna Szyda
   - Tomasz Suchocki

3. ZuchtData, Vienna, Austria
   - Christa Egger-Danner,
   - Hermann Schwarzenbacher