



Current projects at ETH

*SABRE TP Meeting
05 June 2019*

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Ongoing projects at ETH

- Sequencing of Original Braunvieh cattle
- Fine-mapping of QTL underlying impaired male fertility
- Construction of a Brown Swiss haplotype reference panel
- BovReg - Identification of functionally active genomic features relevant to phenotypic diversity and plasticity in cattle
- Integrating breed-specific haplotype-resolved genome assemblies in a bovine pangenome

Sequencing of Original Braunvieh cattle

- 83 OB cattle sequenced at ETH
- Graph-based sequence variant genotyping

Crysnanto *et al. Genet Sel Evol* (2019) 51:21
<https://doi.org/10.1186/s12711-019-0462-x>

GSE Genetics
Selection
Evolution

RESEARCH ARTICLE

Open Access

Accurate sequence variant genotyping in cattle using variation-aware genome graphs

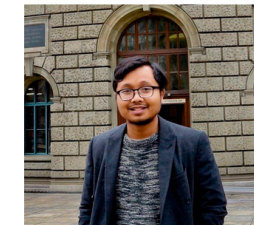


Danang Crysnanto^{1*}, Christine Wurmser² and Hubert Pausch¹

Abstract

Background: Genotyping of sequence variants typically involves, as a first step, the alignment of sequencing reads to a linear reference genome. Because a linear reference genome represents only a small fraction of all the DNA sequence variation within a species, reference allele bias may occur at highly polymorphic or divergent regions of the genome. Graph-based methods facilitate the comparison of sequencing reads to a variation-aware genome graph, which incorporates a collection of non-redundant DNA sequences that segregate within a species. We compared the

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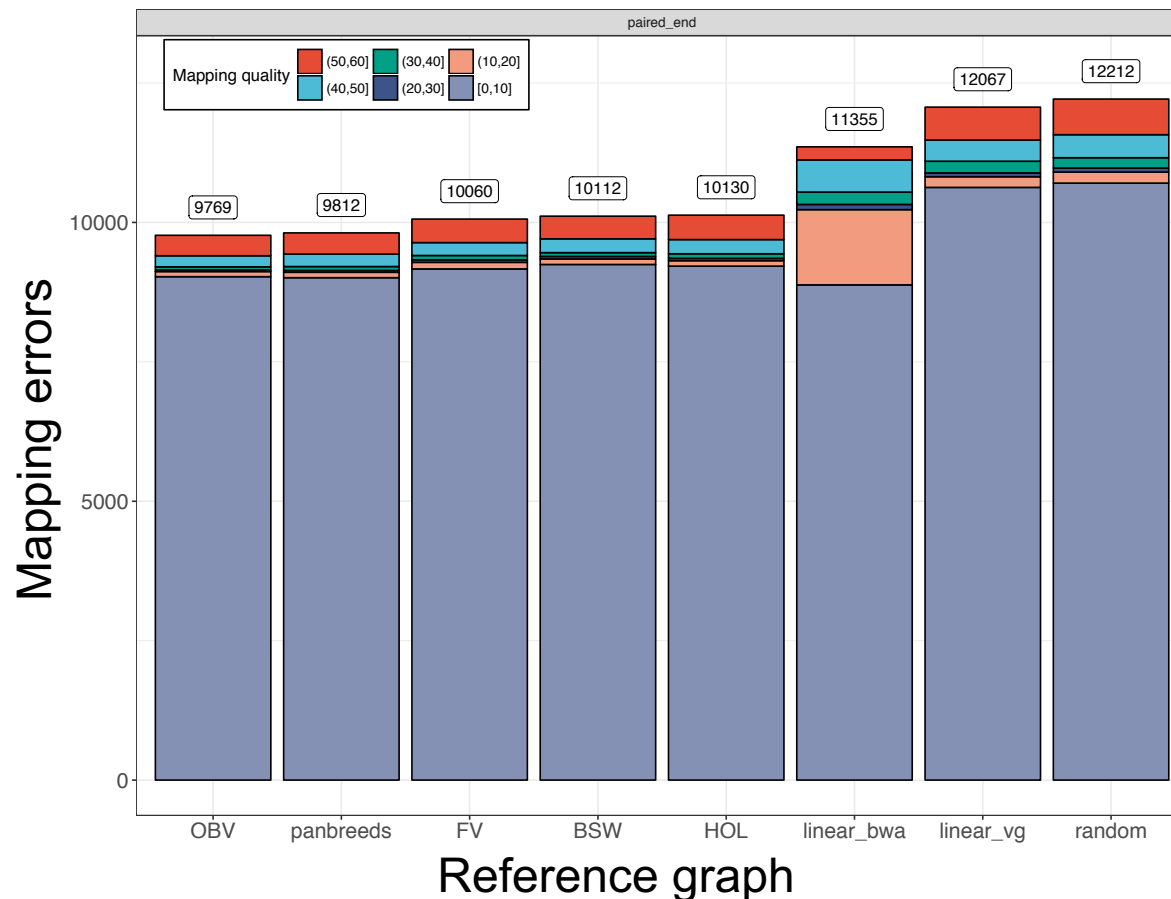
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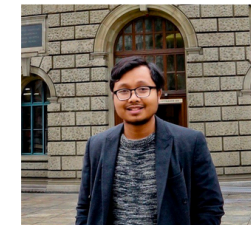
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Sequencing of Original Braunvieh cattle

■ Graph-based sequence read mapping



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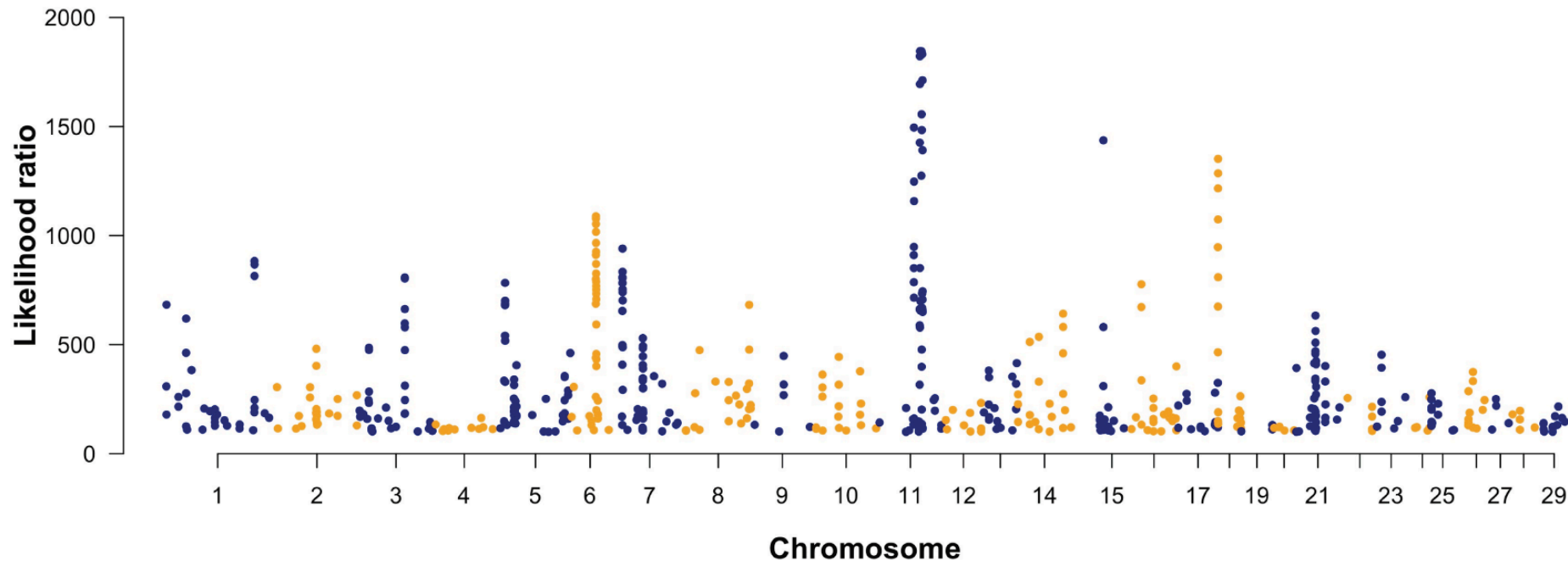
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Sequencing of Original Braunvieh cattle

■ Genomic characterization of OB



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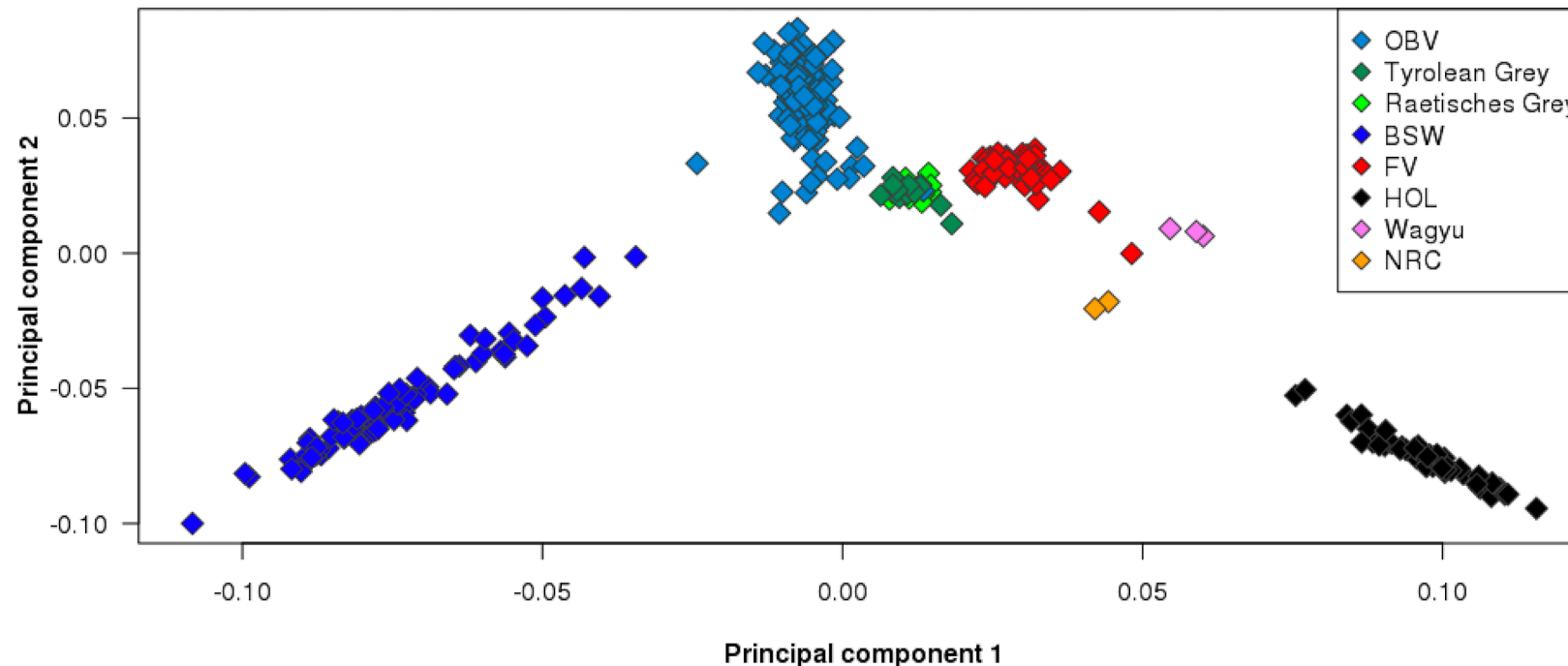
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Sequencing of Original Braunvieh cattle

- Genomic differentiation within and between brown and grey cattle breeds (CH/DEU/AUT Original Braunvieh, Brown Swiss, Tyrolean Grey, Rätisches Grauvieh)



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Identification and fine-mapping of QTL underlying impaired male reproductive performance in BSW cattle

- Joint endeavor of ETH, Swissgenetics, QualitasAG & UZH
- 935 BSW bulls from Swissgenetics with (partly imputed) genotypes at 600'000 SNPs
 - Semen quality data from 75'000 ejaculates
 - Insemination success (non-return rate)
- 2600 BSW bulls from the Austrian and German populations with (partly imputed) genotypes at 600'000 SNPs
 - Insemination success

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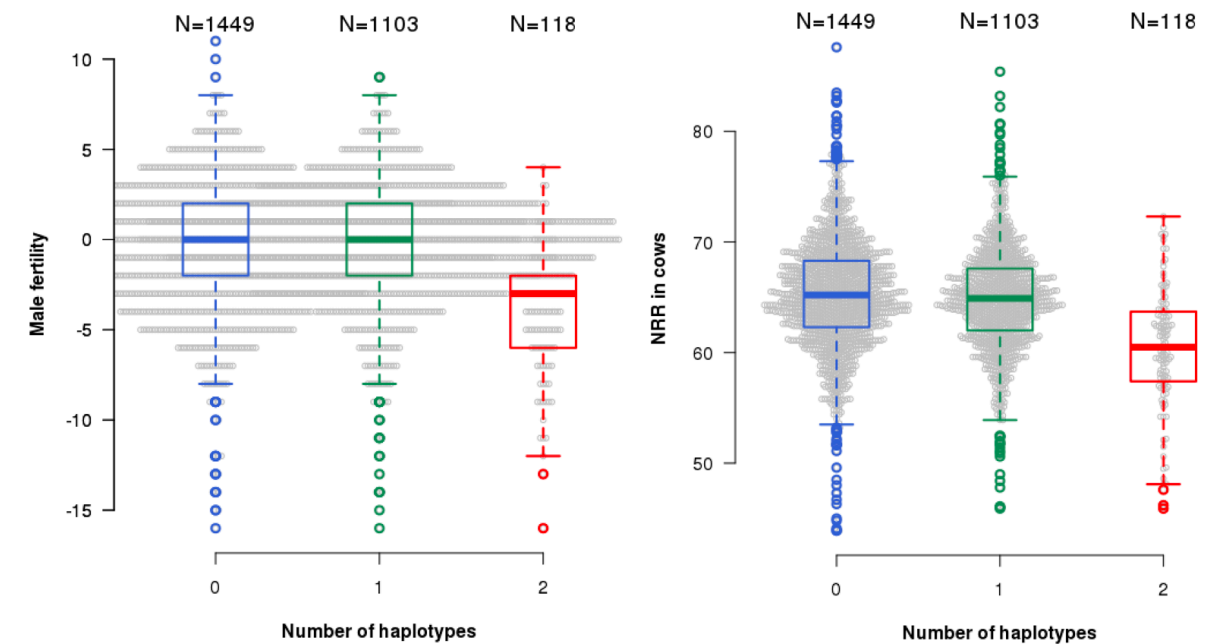
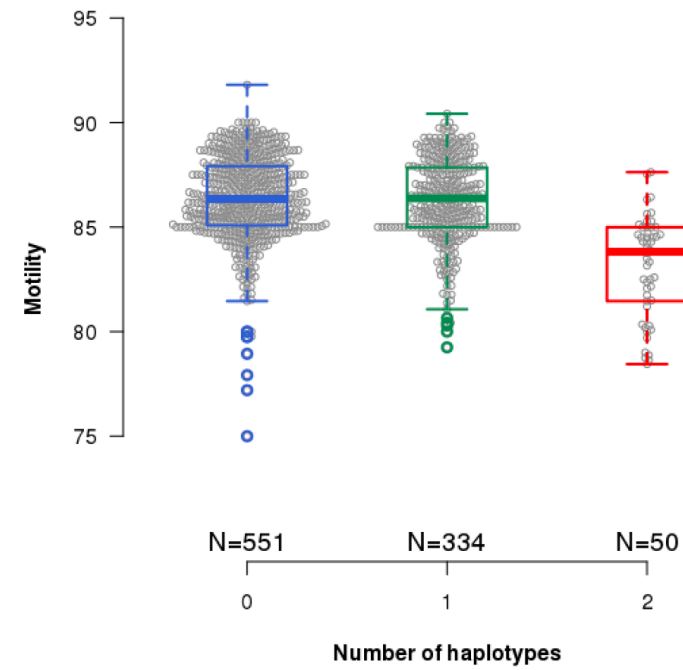
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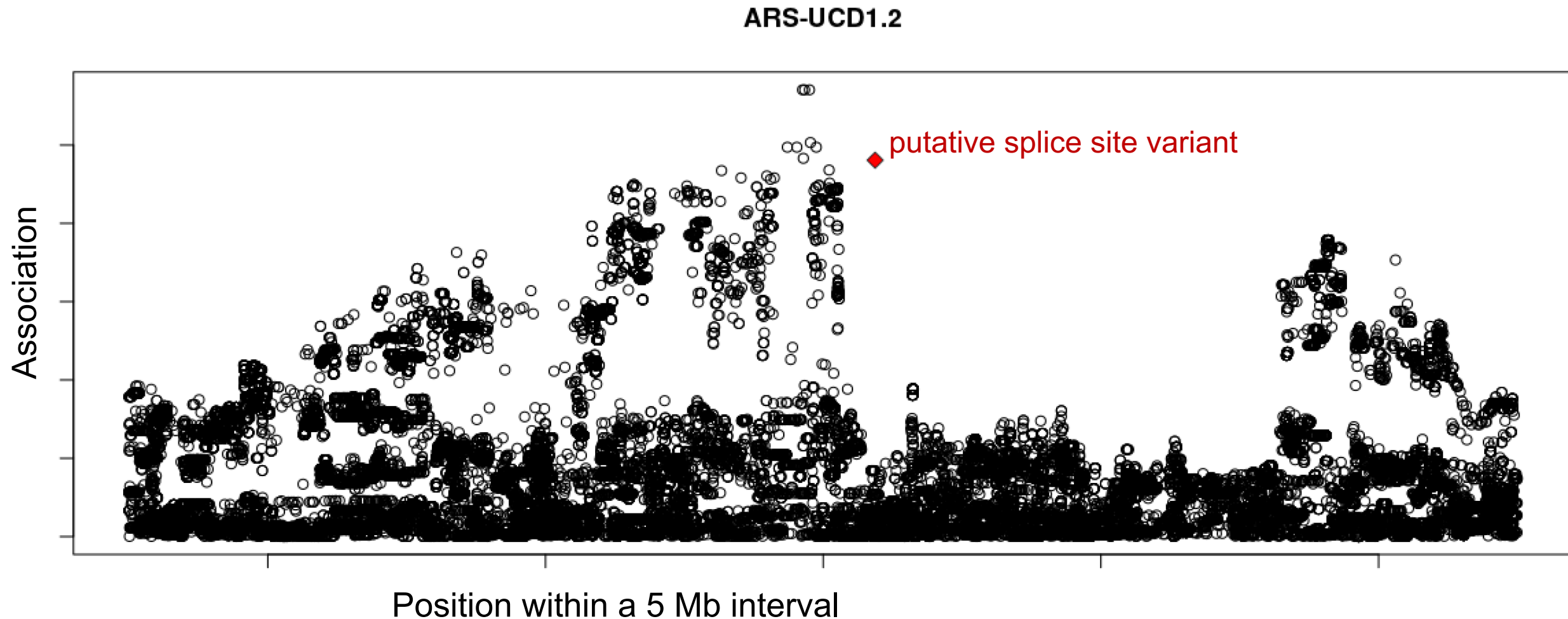
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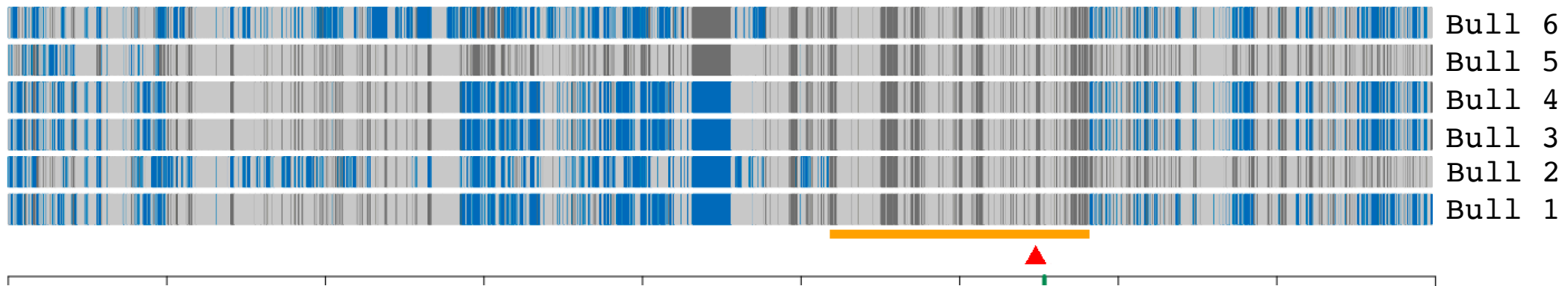
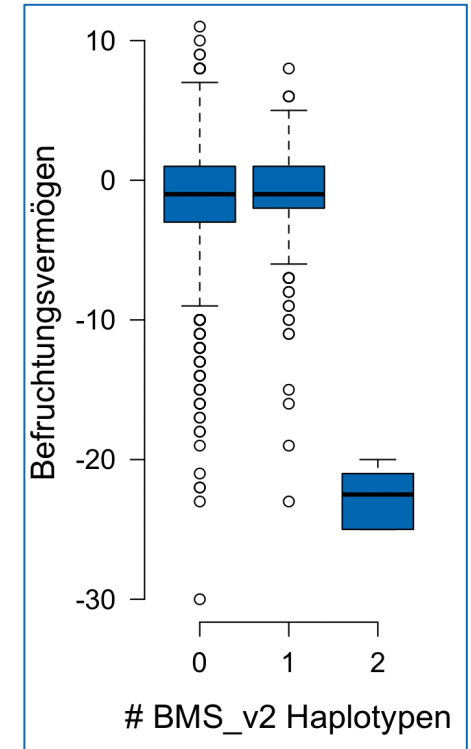
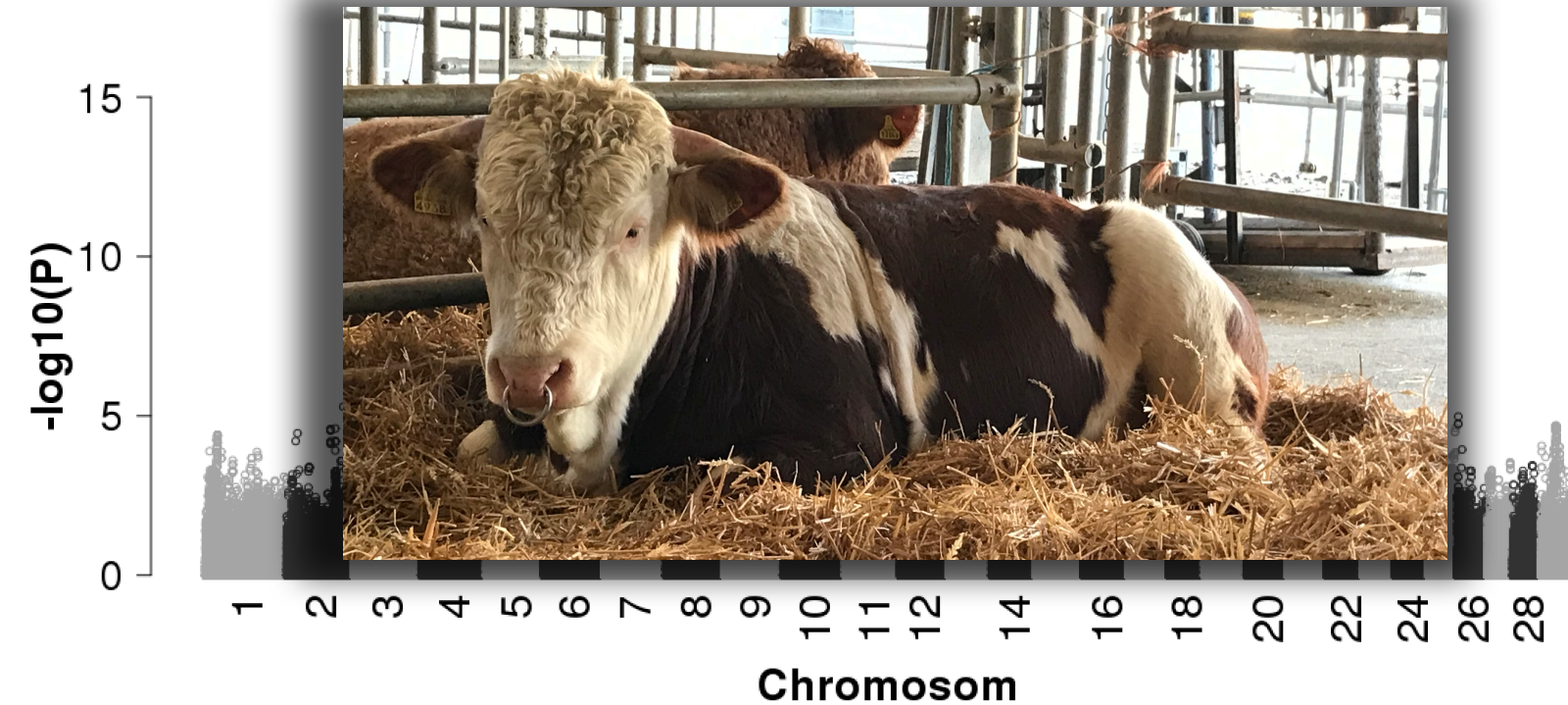
Identification and fine-mapping of QTL underlying impaired male reproductive performance in BSW cattle

- A QTL on chromosome 6 affects sperm motility and male fertility
- Reproductive performance is reduced only in homozygous animals
- The haplotype occurs at a frequency of 27%
- Impaired motility is only the tip of the iceberg...

Missing homozygosity at the fertility-associated QTL



Identification and fine-mapping of QTL underlying impaired male reproductive performance in Fleckvieh cattle



Compilation of a Brown Swiss haplotype panel

- PhD student will start 1st September 2019
- Our aim is to sequence ~500 animals at 2-5x coverage
 - All Swiss BSW bulls that were used in AI in the past 2 years
 - A number of informative cows
- Can we call sequence variants reliably at very low sequencing coverage?
- Does a highly informative breed specific haplotype reference panel increase accuracy of imputation?

BovReg - Identification of functionally active genomic features relevant to phenotypic diversity and plasticity in cattle

- H2020-funded project coordinated by Christa Kühn (FBN Dummerstorf)
- Postdoc will start 1st September 2019
- >15 project partners including FBN, GIGA, Roslin, INRA, Aarhus, Wageningen, University of Alberta, AgriBio, ...
- ETH leads a WP where we'll carry out meta-analyses between imputed sequence variants and a number of economically important traits in >50'000 animals
- ETH and GIGA will identify insertion sites of mobile genetic elements and estimate phenotypic effects associated with these insertion sites
- ETH will map recombination hotspots in Brown Swiss cattle

Towards breed-specific haplotype-resolved genome assemblies

- « *Trio-binning* » (Koren et al., Nat Biotechnology 2018)

~40x Illumina short reads on both parents

- *identify kmers that are specific to each parent*

~80x PacBio on the F1

- *partition reads into paternal and maternal sets based on the kmers from the parents*

