



DEPARTMENT OF
**ANIMAL
BIOSCIENCES**



Identification of unfavourable homozygous haplotypes associated with milk and fertility traits in Holsteins

Gabriele Marras¹, J. Howard², P. Martin¹, A. Fleming¹, K. Alves¹, B. Mankanjuola¹,
F. Schenkel¹, F. Miglior^{1,3}, C. Maltecca⁴ & C.F. Baes¹

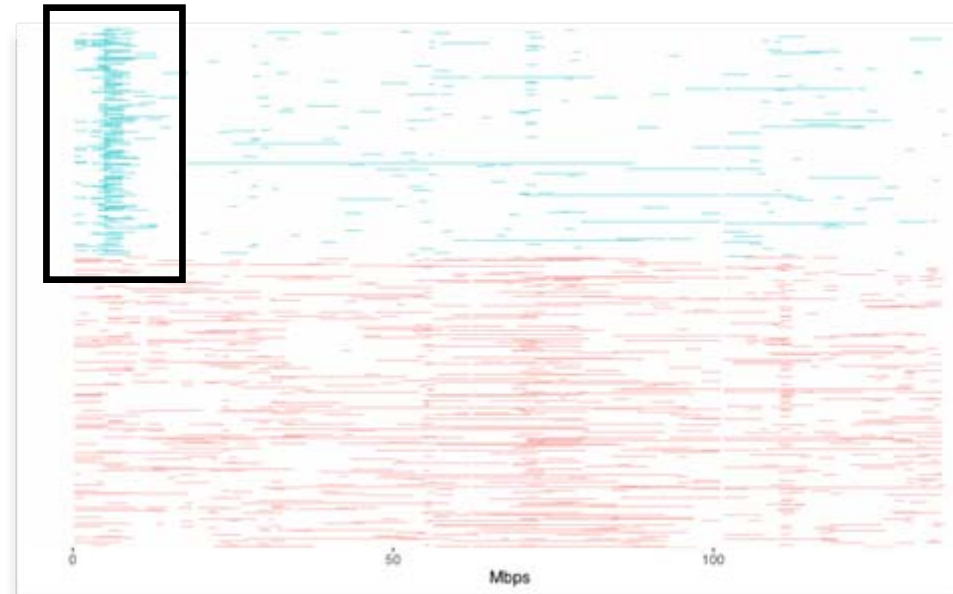
¹Centre for Genetic Improvement of Livestock (CGIL), University of Guelph, Canada,

²Department of Animal Science, University of Nebraska, USA, ³Canadian Dairy Network (CDN), Canada,

⁴Department of Animal Science, North Carolina State University, USA

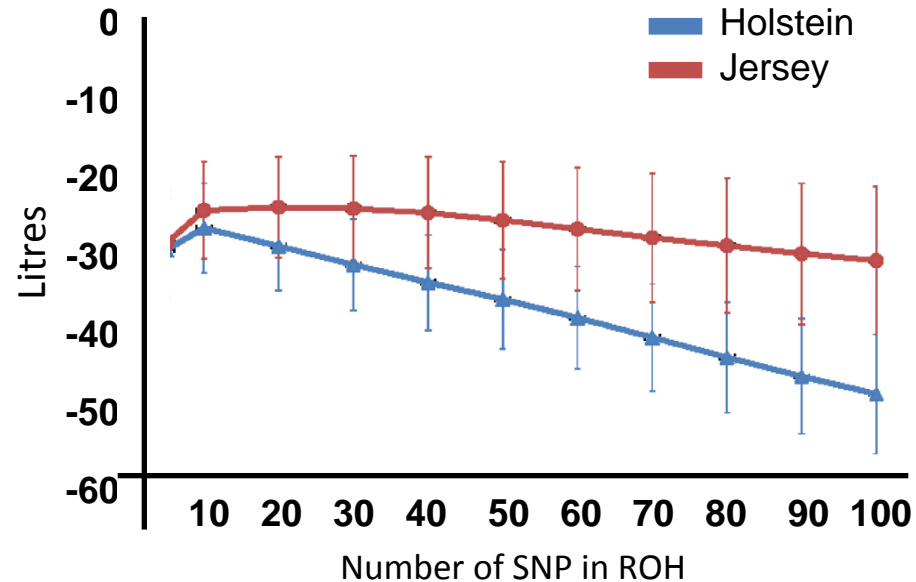
Introduction

- Runs of homozygosity (ROH) are a result of the transmission of identical haplotypes from related parents to the offspring
- Breeding programs can increase the frequency of favourable/unfavourable alleles in the population



Introduction

- ROH have an impact on the genetic architecture
- The presence of ROH at site-specific locations of the genome have been associated with milk yield in dairy cattle breeds



Objective

Identify regions of homozygosity in the genome associated with:

- Reproduction traits
- Milk production traits



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Data

- 6,849 cows genotyped with a 50K SNP chip panel. Missing genotypes were imputed using FImpute v2.2*
- Quality control parameters:
 - Minor allele frequency less than 5%
 - SNP call rate lower than 95%
 - Animal call rate lower than 95%
 - Hardy-Weinberg equilibrium with p-value smaller than 1×10^{-5}
- After filtering, **40,874 SNP** genotypes were used

Phenotypes

Production (305-days)

Milk yield

Fat yield

Protein yield



Total number of individuals
with all phenotypes **3,289**



Reproduction

Traits	Heifer	First Parity
Age at first service	✓	
Age at calving	✓	
Number of services	✓	✓
First service to conception	✓	✓
Calving to first insemination		✓
Days open		✓
Gestation length	✓	✓
Calf size	✓	✓

Haplofinder algorithm

Step 1: Find unique ROH in the genome associated with unfavourable phenotype below given threshold

Step 2: Test each window for significance using a standard linear mixed model

Step 3: Report the nested significant unfavourable haplotype

Chromosome	StartPos	EndPos	StartIndex	EndIndex	Genotype	PhenoMean	BetaEffect	LSM T-Stat
1	6187555	9114098	111	158	0202222200200020000200002000200020002202	8872.05	-392.31	8915.19 -2.45206
1	6623322	9900095	119	168	0020020002000020000200002000200020002202	8854.45	-420.277	8886.69 -2.56377
1	6674252	9072009	121	157	20020002000020002000200020002202	8866.98	-397.813	8907.87 -2.50106
1	6882069	9900095	124	168	200020000200020002000200022022022020020	8852.44	-424.984	8882.61 -2.60853
1	6967148	9798988	125	166	0002000020002000200020002202202202002	8891.56	-372.949	8934.11 -2.34498
1	7013625	8998063	126	156	002000020002000200020002202	8864.93	-402.327	8903.02 -2.54417
1	7260284	9852144	128	167	20000200020002000200022022022020020	8882.19	-395.52	8912.11 -2.45934
1	7260284	9072009	128	157	2000020002000200020002202	8886.79	-380.046	8925.39 -2.41865
1	7344117	10776728	130	179	0002000200020002000220220220220002000000222	8764.04	-514.801	8794.36 -3.13211
1	7344117	10182749	130	173	0002000200020002000220220220220002000000	8839.65	-435.328	8872.66 -2.69824
1	7370460	9114098	131	158	0020002000200020002202202	8874.09	-390.471	8915.57 -2.49745
1	7627111	9942902	135	170	20020002000200022022022020002	8848.38	-426.824	8881.25 -2.65999
1	7669386	8963404	136	155	00200200020002202	8881.81	-382.047	8923.23 -2.45604
1	7706031	11221889	137	183	0200200020002000220220220200002000000222000	8859.42	-421.629	8886.32 -2.63075
1	7782816	10776728	140	179	0202020200200022022022020002000000222	8857.44	-444.672	8864.92 -2.79908
1	7782816	9940497	140	169	02020202000200022022022020000	8924.41	-372.125	8935.98 -2.38845
1	8054589	12223821	142	195	020202200200020022022022020002000002220002202000000	8818.72	-505.953	8802.45 -2.9
1	8148041	11845279	143	190	202020002002202202202000000002200002202000	8896.92	-489.227	8819.26 -3.03276
1	8217339	10776728	145	179	20220020022022022020002000000222	8887.88	-407.945	8899.88 -2.60254
1	8240375	11158004	147	182	22002002202202202000200000022200	8886.64	-409.926	8898.01 -2.61545
1	8437530	10776728	150	179	02022022022022020002000000222	8898.37	-397.281	8910.52 -2.56221
1	8627862	12172404	152	193	002220220220002000000022200022202000020	8804.65	-508.648	8800.48 -3.14058
1	8627862	11603310	152	186	0022202202200020000000222000222	8806.24	-473.215	8836.5 -3.10759
1	8627862	11221889	152	183	0022202202200020000000222000	8892.16	-387.117	8921.12 -2.59537
1	8963404	13089432	155	199	220220220020002000000222000220200020002020	8875.78	-432.969	8874.34 -2.58726
1	8963404	10776728	155	179	220220220020002000000222	8906.07	-377.836	8930.9 -2.56863
1	9323844	11845279	160	190	02220020002000000222000220200	8829.56	-452.039	8856.91 -2.99968
1	9323844	11603310	160	186	02220020002000000222000222	8835.45	-445.613	8863.79 -2.97098
1	9323844	10776728	160	179	02220020002000000222	8927.15	-356.207	8952.28 -2.44588
1	9601018	14417802	163	208	200200020000002222000220200020002000000220	8725.05	-586.902	8722.32 -3.20113
1	9601018	12172404	163	193	200200020000002222000220200020	8840.1	-480.164	8829.21 -3.02616

Haplotype impact in % of SD

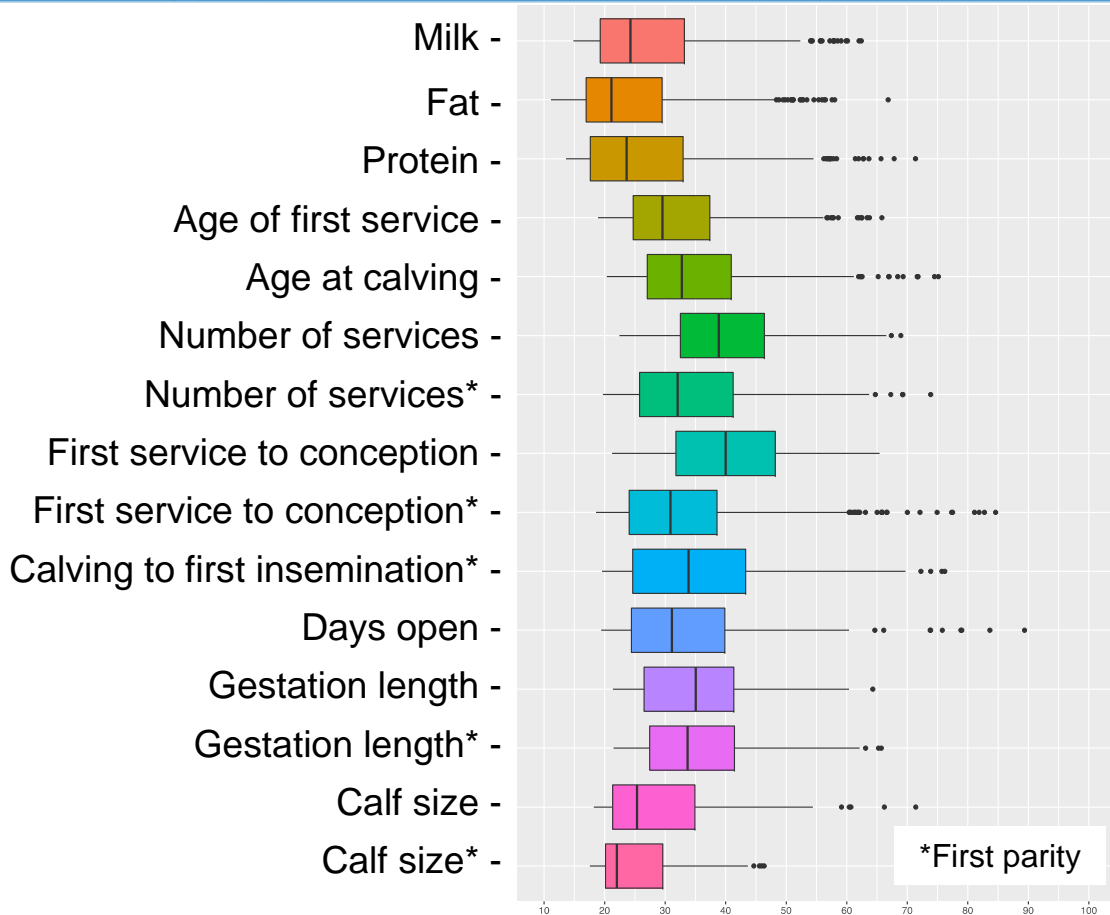
$$Z = \frac{x - \mu}{\sigma} * 100$$

z = standard score

x = raw score

μ = phenotypic mean

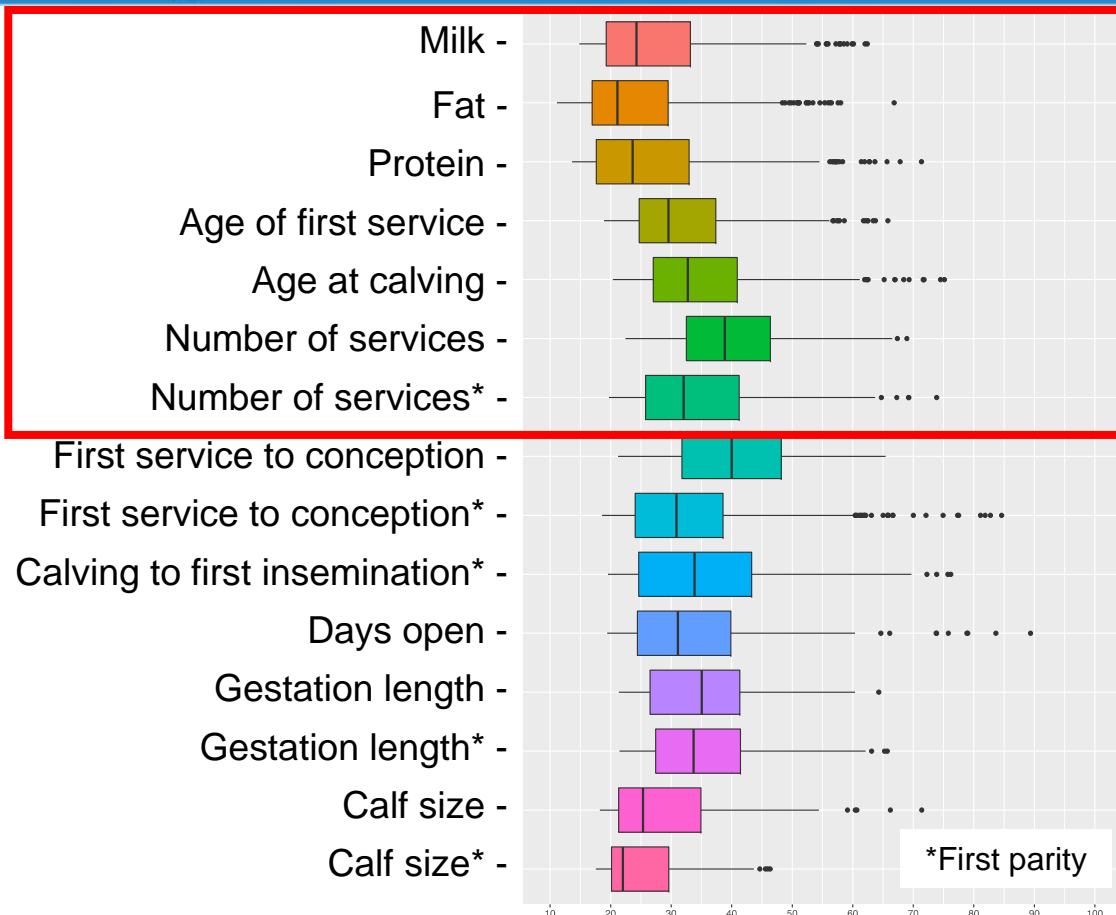
σ = phenotypic standard deviation



Haplotype impact in % of SD

Most extreme unfavourable haplotype effect

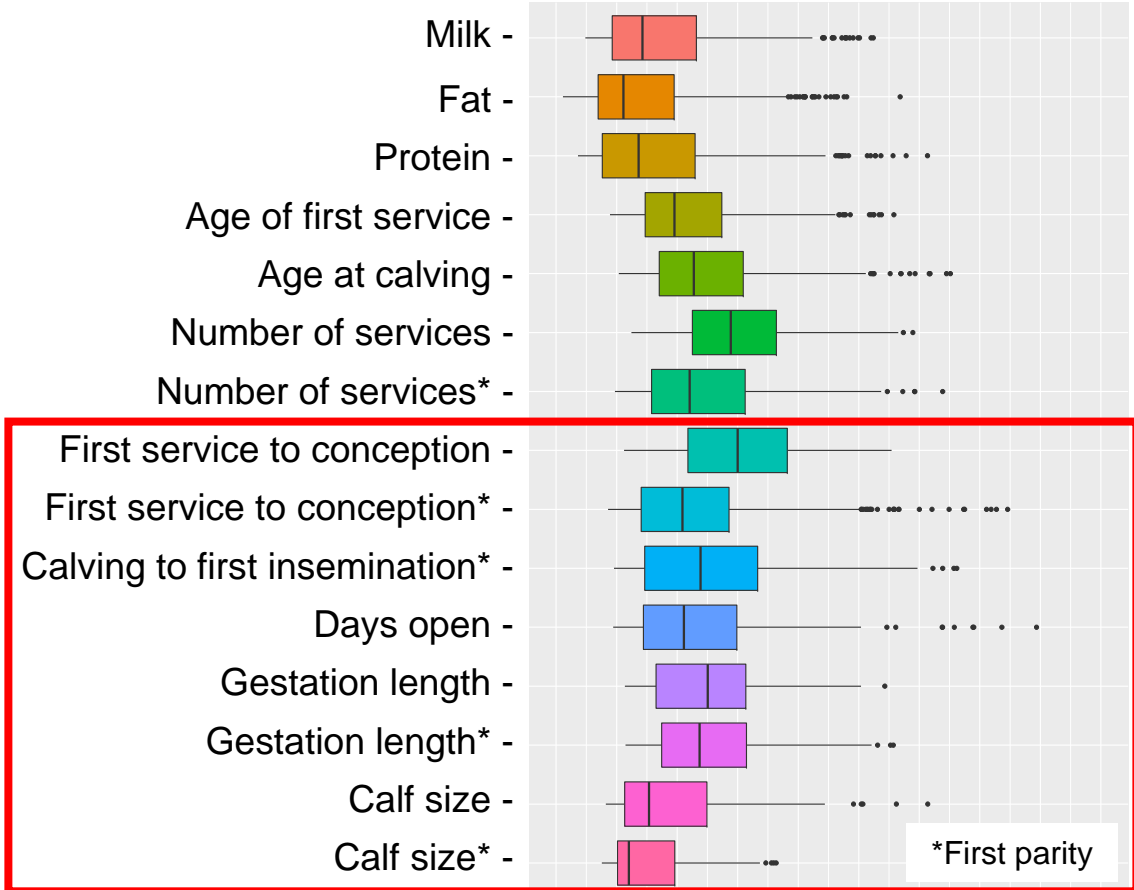
Trait	Value	BTA
Milk (kg)	-684.05	3
Fat (kg)	-28.83	5
Protein (kg)	-22.34	21
Age at first service (day)	17.03	9
Age at calving (mo)	0.98	12
Number of services	0.57	3
Number of services*	0.63	1



Haplotype impact in % of SD

Most extreme unfavourable haplotype effect

Trait	Value	BTA
First service to conception (day)	14.47	14
First service to conception* (day)	22.92	11
Calving to first insemination* (day)	10.49	14
Days open	25.93	28
Gestation length (day)	3.46	15
Gestation length* (day)	3.79	3
Calf size	0.36	5
Calf size*	0.33	26



Common haplotypes

Type of cluster		Total number of haplotypes within trait group	Number of haplotypes across multiple traits
Production	Milk, Fat and Protein	388	48
Fertility1	Age at first insemination Age at calving	247	49
Fertility2	Number of services First service to calving Calving to first service Days open	750	1
Calving	Gestation length Calf size	275	1

Unfavourable haplotypes

Production

- Milk, Fat and Protein

Fertility1

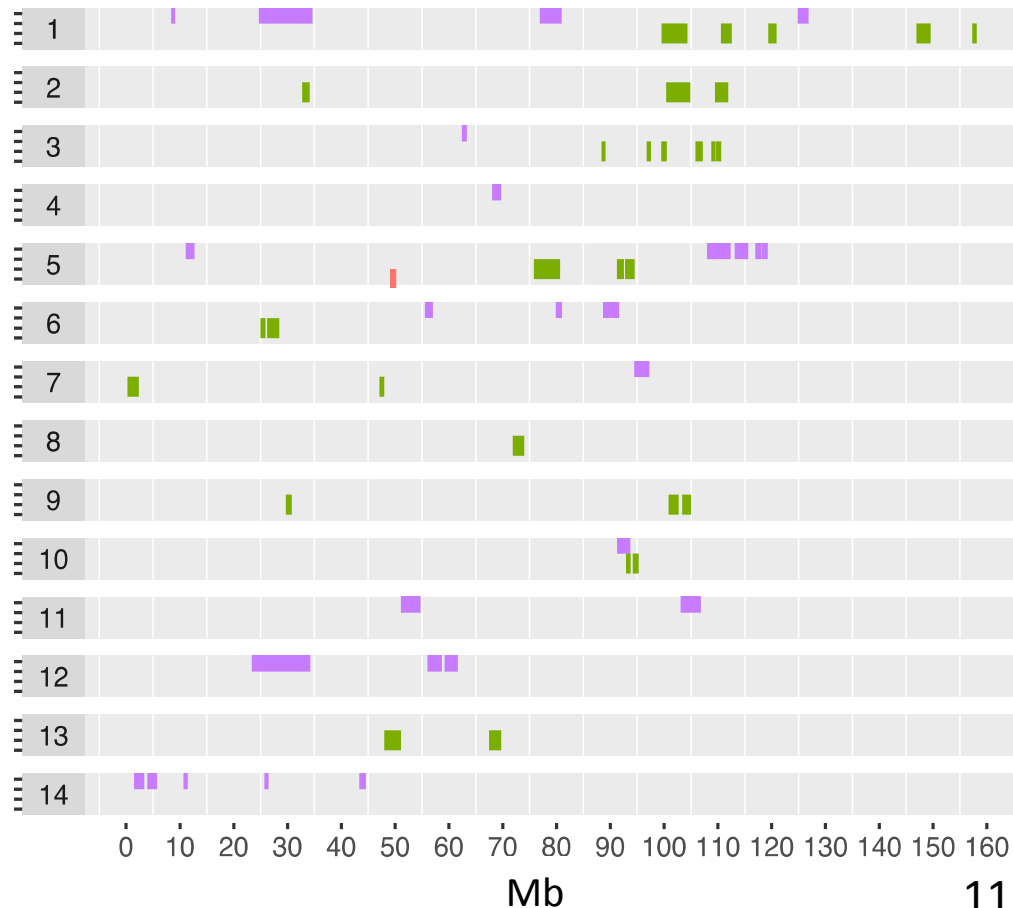
- Age at first insemination
- Age at calving

Fertility2

- Number of services
- First service to conception
- Calving to first insemination
- Days open

Calving

- Gestation length
- Calf size



Unfavourable haplotypes

Production

- Milk, Fat and Protein

Fertility1

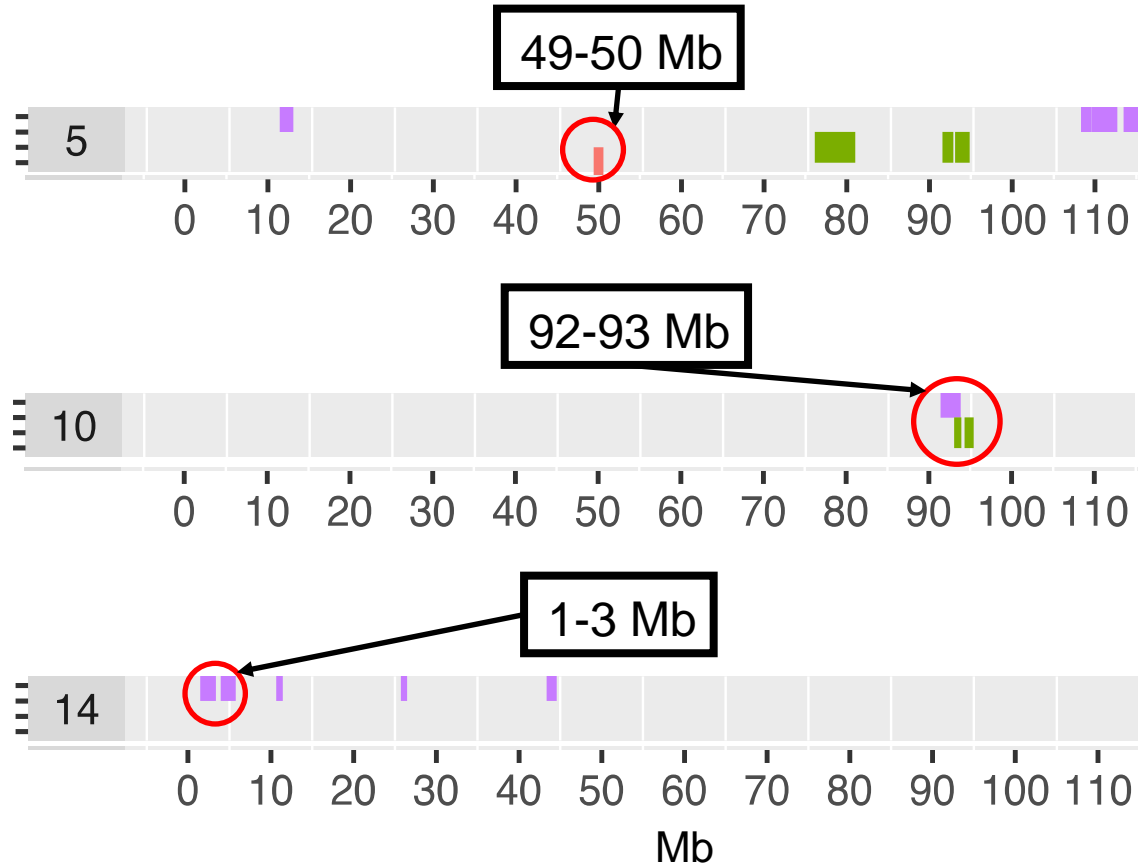
- Age at first insemination
- Age at calving

Fertility2

- Number of services
- First service to conceptio
- Calving to first inseminati
- Days open

Calving

- Gestation length
- Calf size



Unfavourable haplotypes

Production

- Milk, Fat and Protein

Fertility1

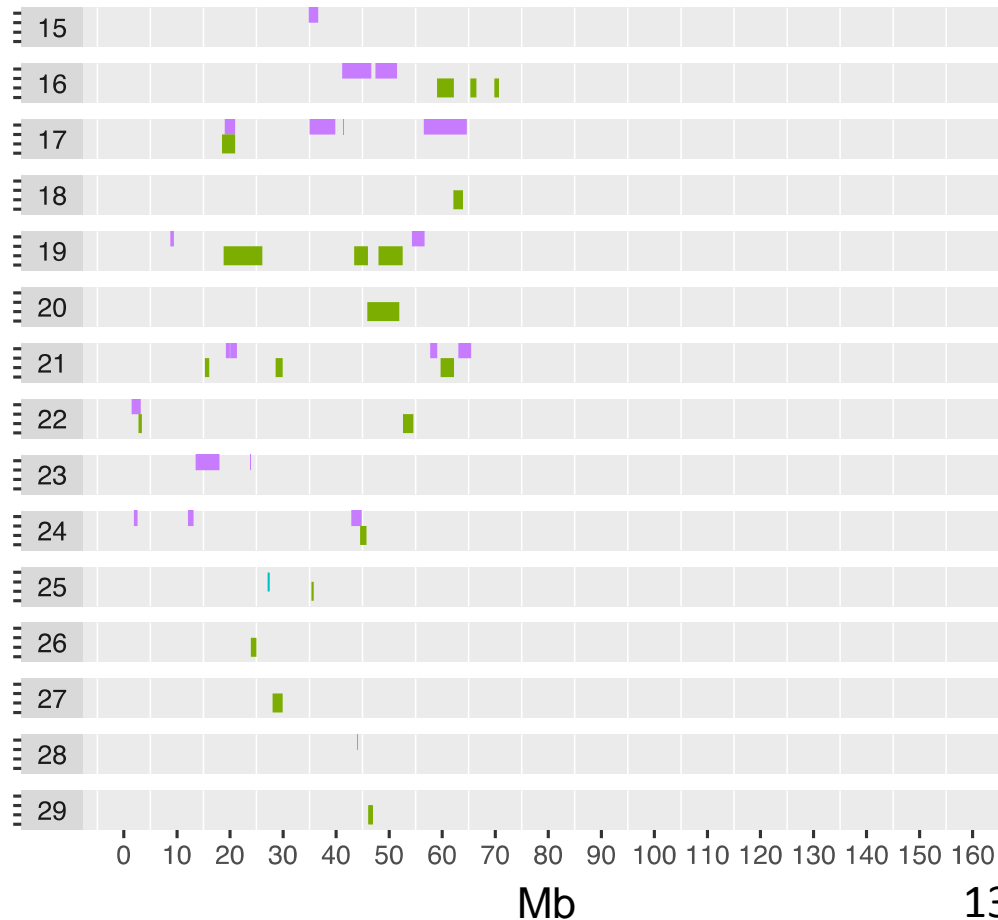
- Age at first insemination
- Age at calving

Fertility2

- Number of services
- First service to conception
- Calving to first insemination
- Days open

Calving

- Gestation length
- Calf size



Unfavourable haplotypes

Production

- Milk, Fat and Protein

Fertility1

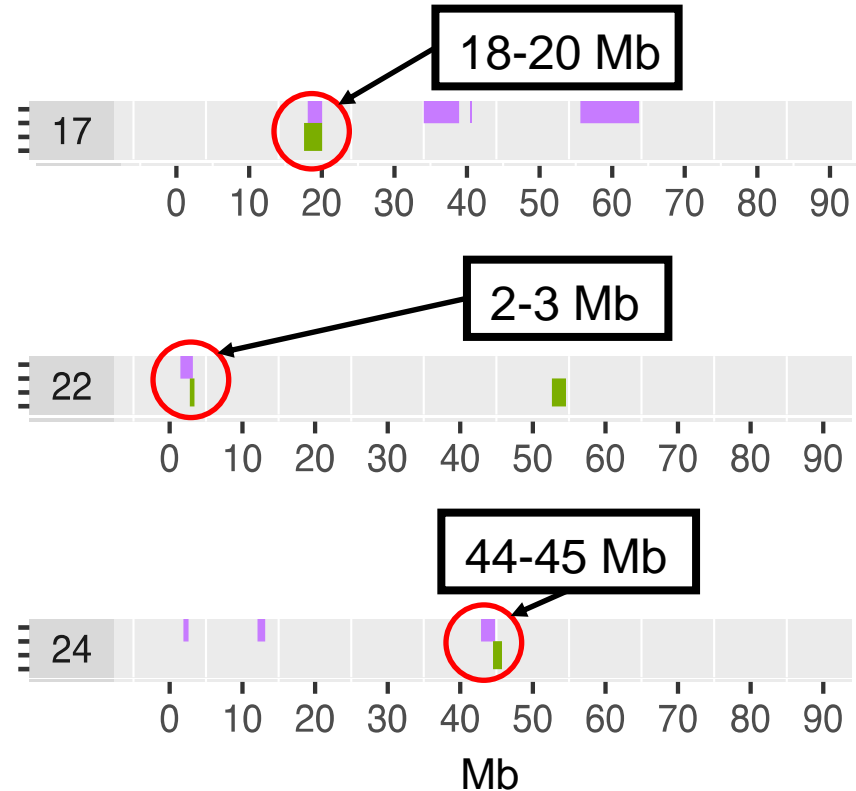
- Age at first insemination
- Age at calving

Fertility2

- Number of services
- First service to conception
- Calving to first insemination
- Days open

Calving

- Gestation length
- Calf size



Conclusions

- Runs of homozygosity can be associated with with traits of interest
- Homozygous regions associated with milk production and fertility were identified

Conclusions

- Multiple unfavourable haplotypes were identified within and across trait groups
- Detrimental effects of homozygosity in dairy populations can be further investigated

Acknowledgements

Funding from NSERC of Canada and a grant from the Dairy Cattle Genetics Research and Development (DairyGen) Council of Canadian Dairy Network

