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Genetic Diversity in 5 North American Dairy Breeds

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Managing Genetic Diversity in Dairy Cattle Workshop
14th of July 2022 Cremona, Italy

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Consequences of Genomic Selection on Genetic Diversity

- Genomic selection has become the standard approach in US dairy cattle breeding.
- Increased rates of genetic gain through improved accuracy of prediction and reduced generation intervals.
- Faster accumulation of homozygosity under genomic selection.

Are there methods that can be utilized to monitor the accumulation of inbreeding?

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Topics

1. Genome-wide and region-specific autozygosity.

2. Pedigree *vs* genomic inbreeding.

3. Understanding historical and recent changes in genetic diversity.

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Genomic Dairy Breeds in the US

Ayrshire

Holstein

Brown Swiss

Jersey

Guernsey

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Animals

Breed	Acronym	Pedigree	Genotyped
Holstein	**HO**	6,725,679	3,649,734
Jersey	**JE**	985,959	459,784
Brown Swiss	**BS**	208,219	49,360
Ayrshire	**AY**	33,975	9,442
Guernsey	**GU**	45,792	5,359

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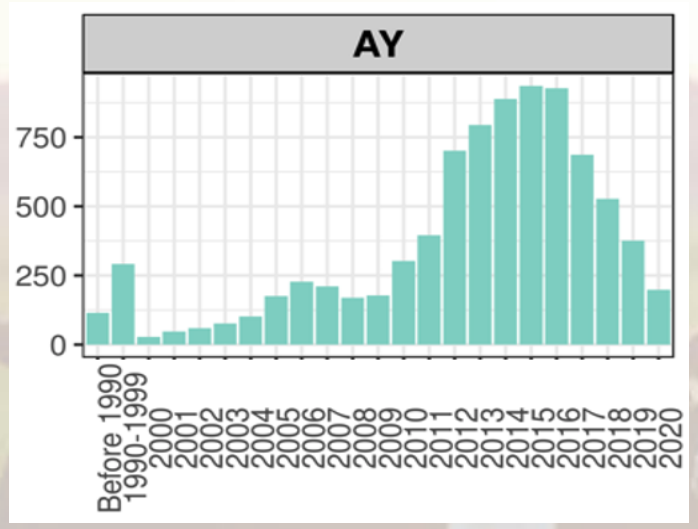
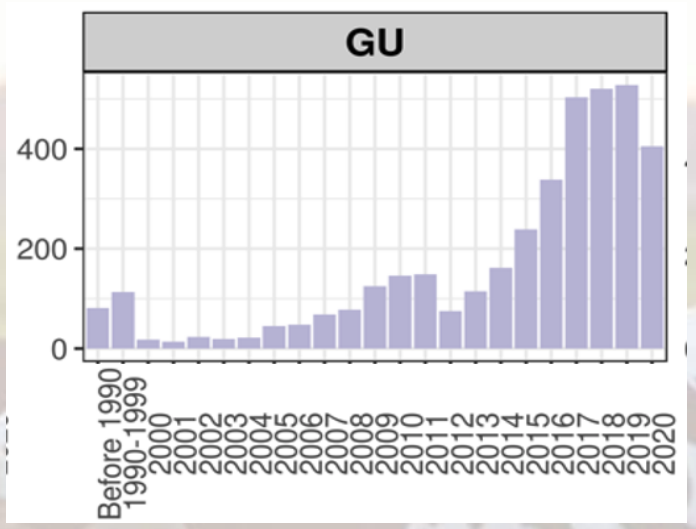
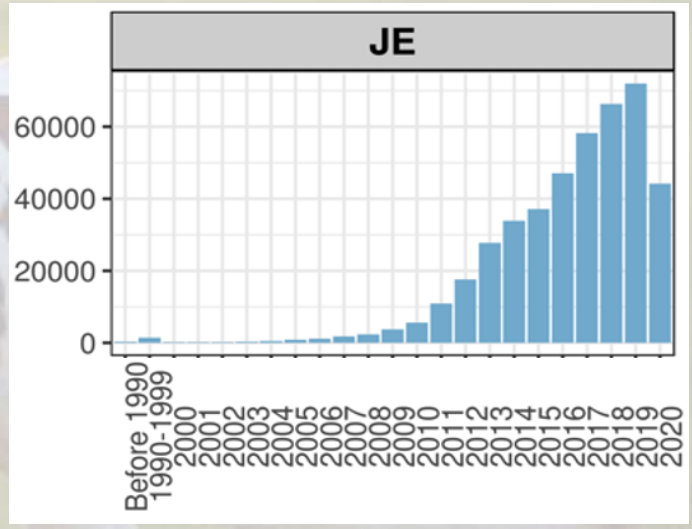
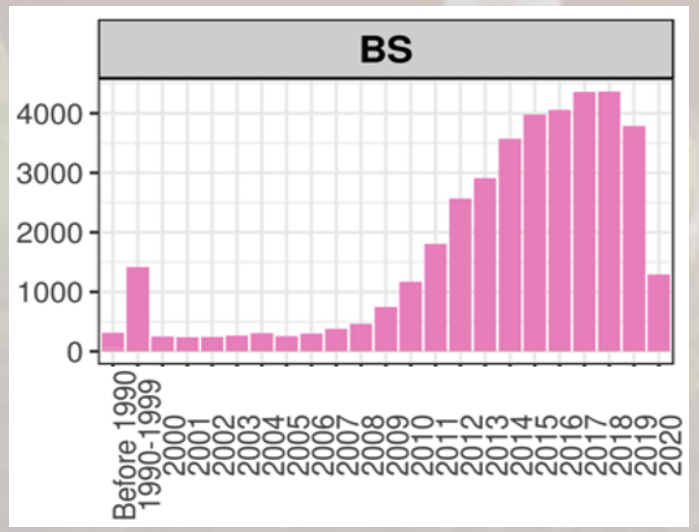
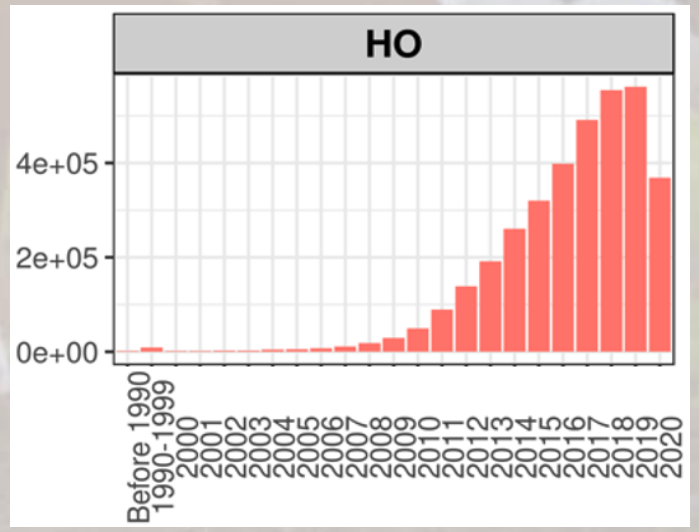
Number of animals by year of birth











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Detection of ROH

- Runs of homozygosity were detected using PLINK 1.9

- Parameters used to detect ROH were:
  1. Window size = 20 SNPs
  2. At most one heterozygote call in a window
  3. At most two missing calls in a window
  4. Minimum physical length of an ROH of 2 Mb
  5. A maximum gap of 500 Kb between consecutive SNPs
  6. A minimum SNP density of at least 1 SNP per 100kb
  7. A minimum number of 60 SNPs to declare an ROH

Parameter	AY	BS	GU	HO	JE
Number of ROH					
Mean	37.24	47.69	54.40	40.39	62.66
Standard Deviation	8.27	8.59	7.48	8.49	8.29
Minimum	4	6	20	1	24
Maximum	68	91	81	94	105
Average ROH length (Mb)					
Mean	7.04	7.54	6.74	7.46	6.80
Standard Deviation	1.40	1.10	1.07	1.19	0.94
Minimum	3.01	3.02	4.20	2.56	3.76
Maximum	17.95	16.57	16.92	22.91	18.48

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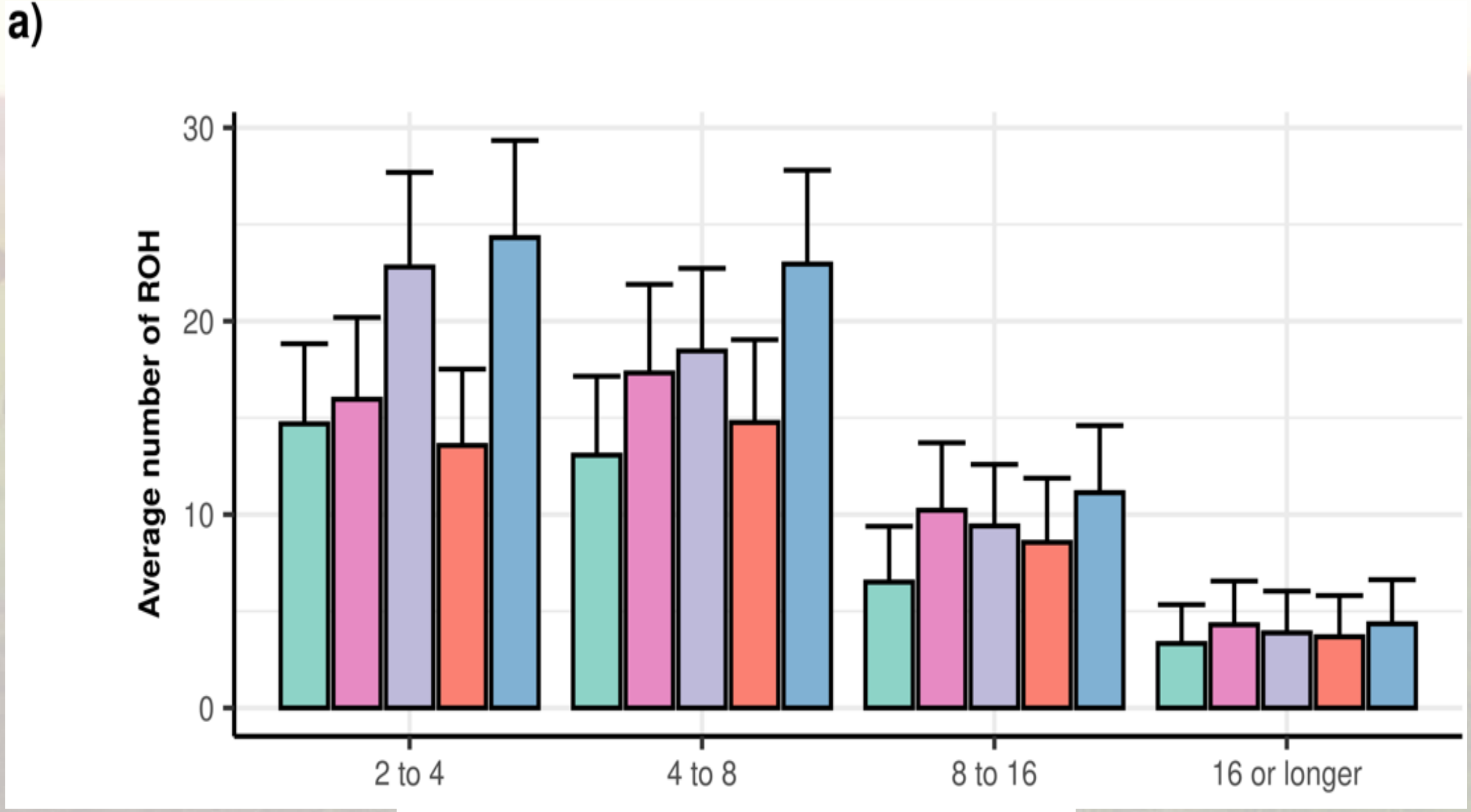
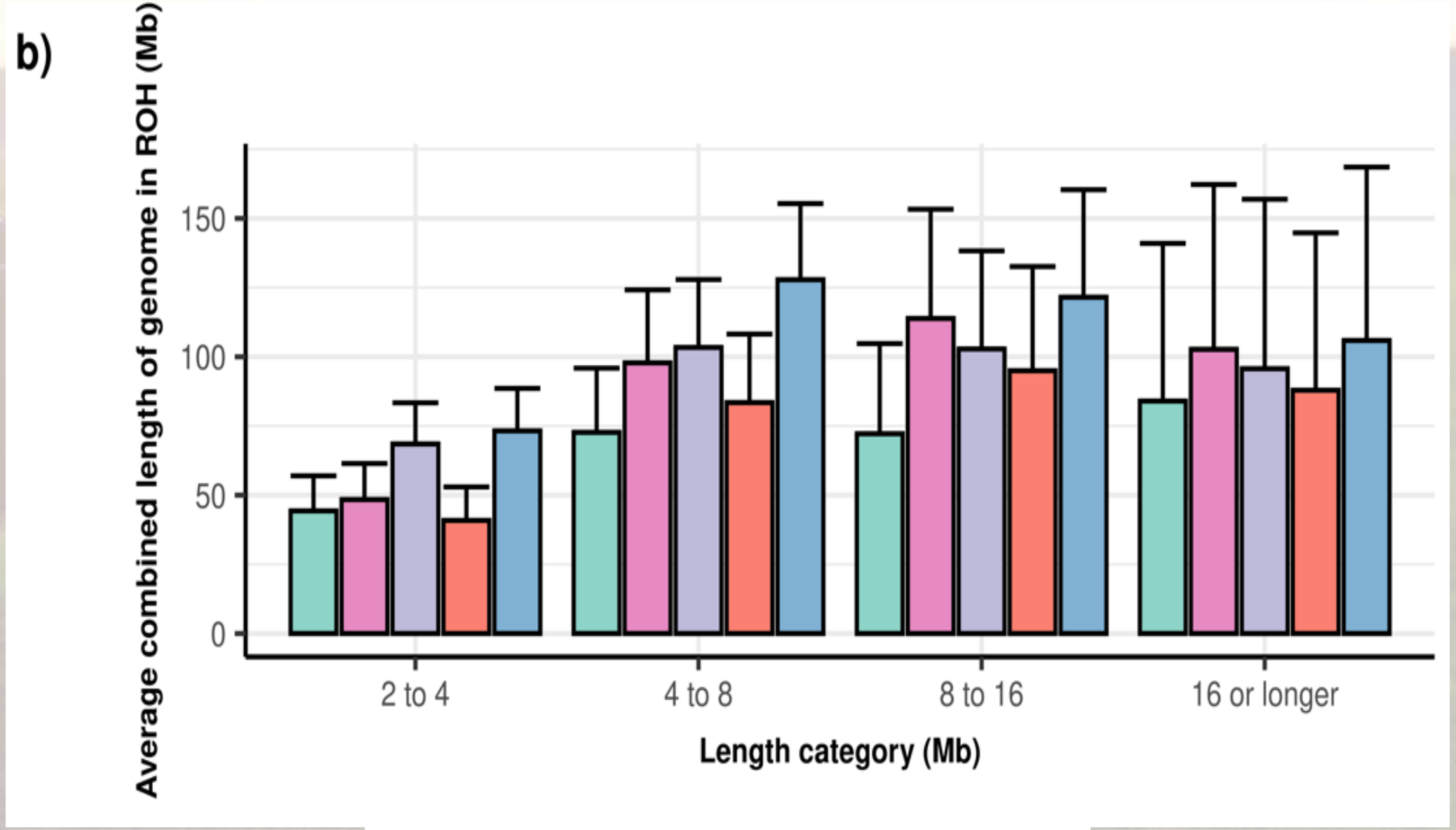
a)




b)
Average combined length of genome in ROH (Mb)
150
100
50
0
2 to 4
4 to 8
8 to 16
16 or longer
Length category (Mb)
Breed
Ayrshire
Brown Swiss
Guernsey
Holstein
Jersey

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Region-specific autozygosity

- Within breed, a coefficient of autozygosity for every marker (F_L) was calculated as the proportion of animals in which the marker was located inside an ROH.
- We identified significant SNP as those with F_L at or above the 99.5th percentile for all genome-wide markers.
- Adjacent significant SNP were joined into larger segments known as ROH islands. ROH islands represent regions of reduced local variability that serve as genomic signatures of past selective history.

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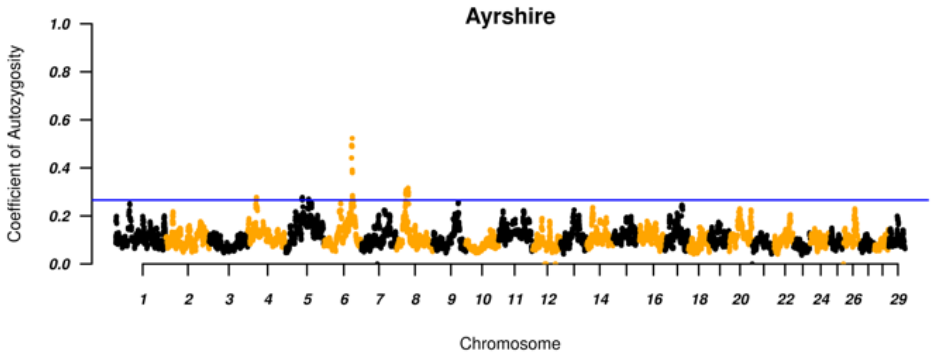

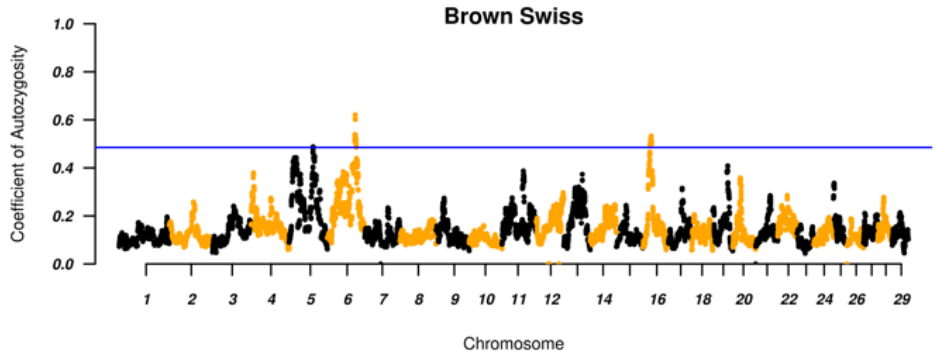

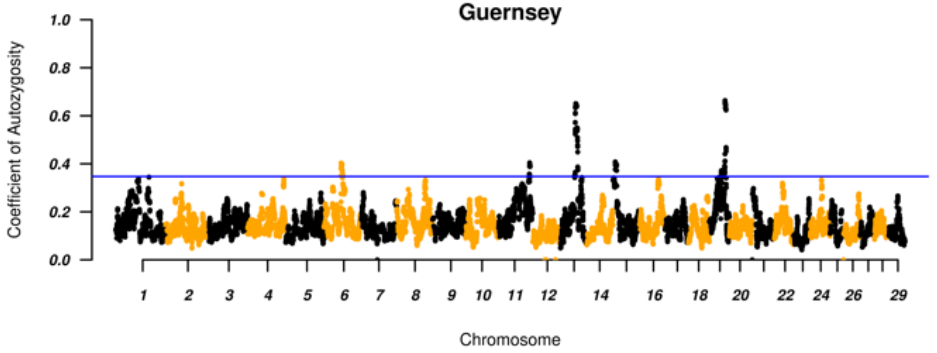

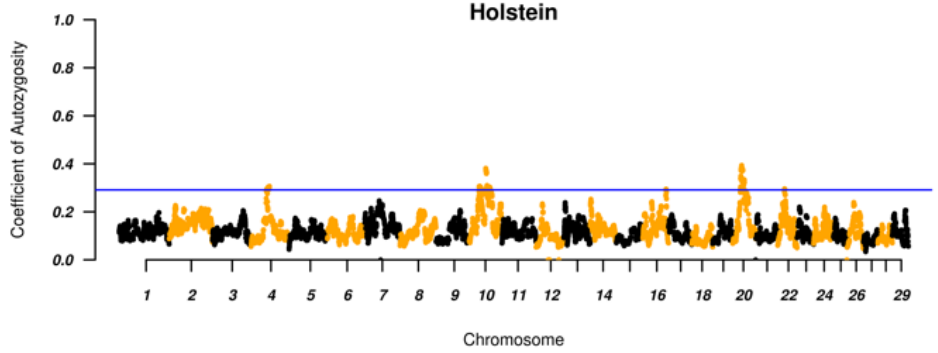

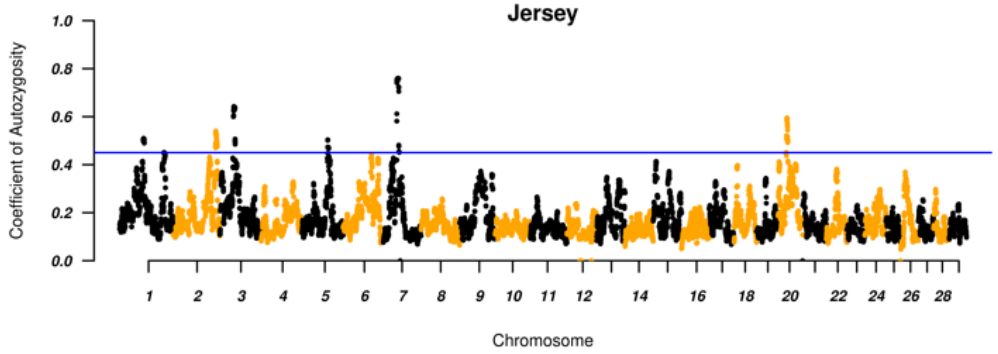

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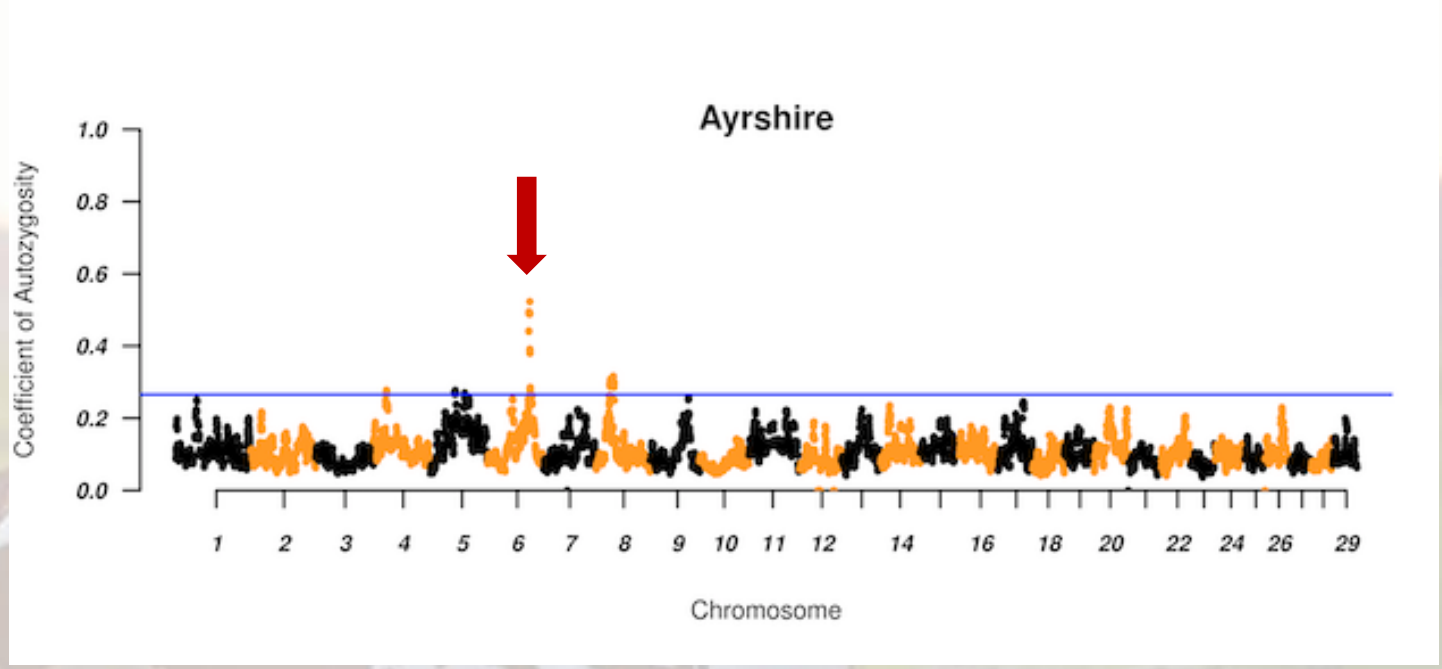
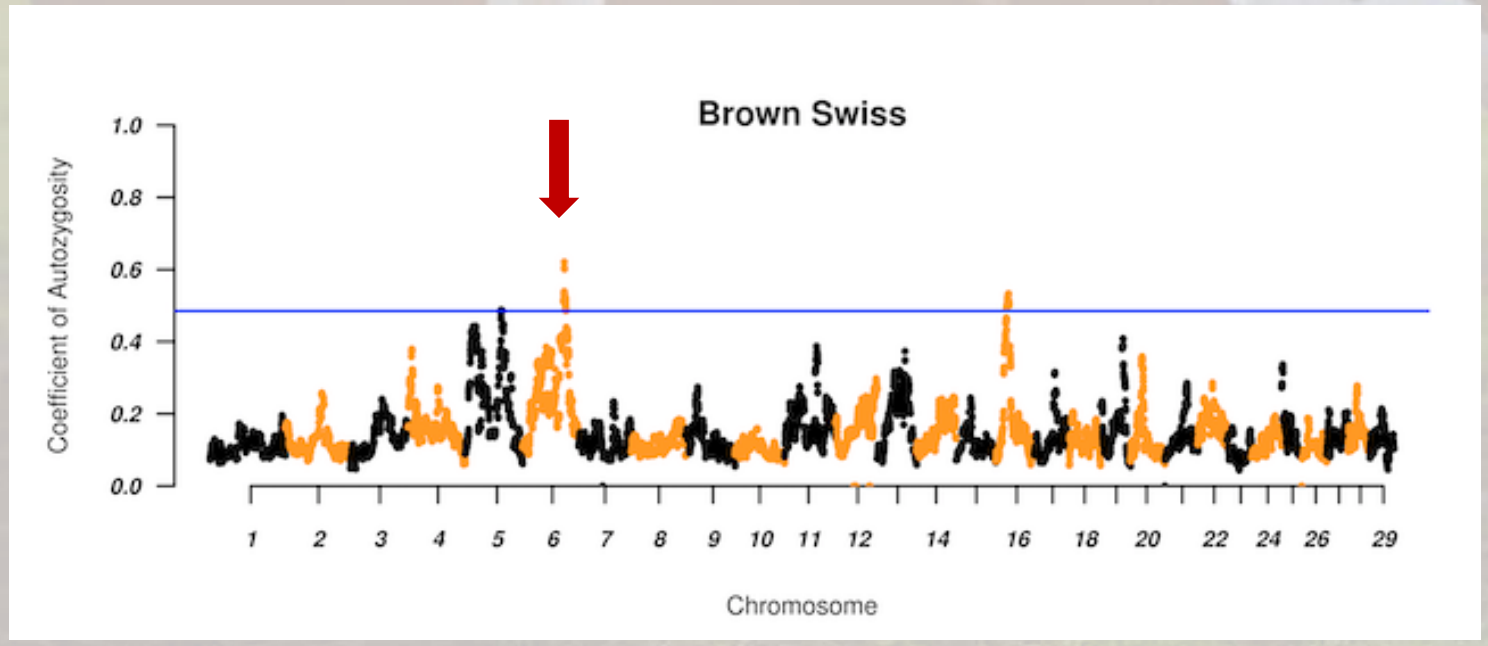
Overlapping region between AY and BS





Notable genes:

- ADAMTS3
- ANKRD17
- GC
- NPFFR2

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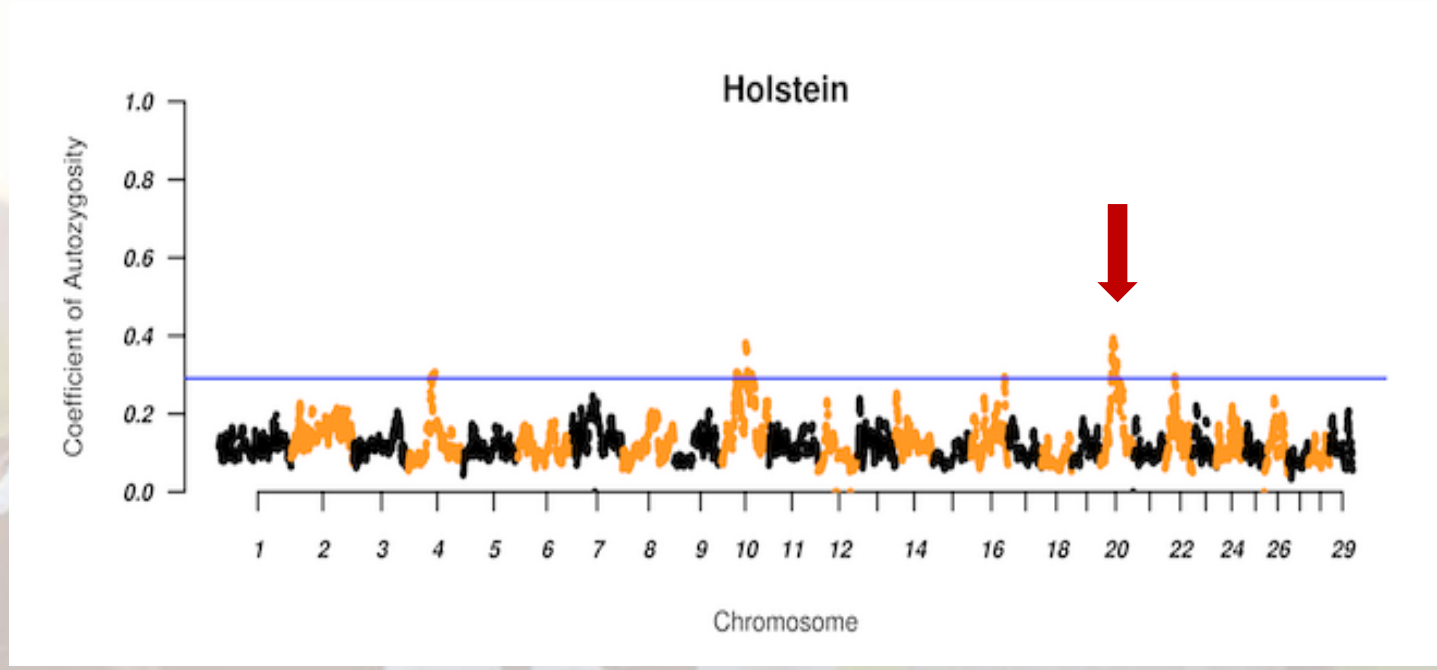
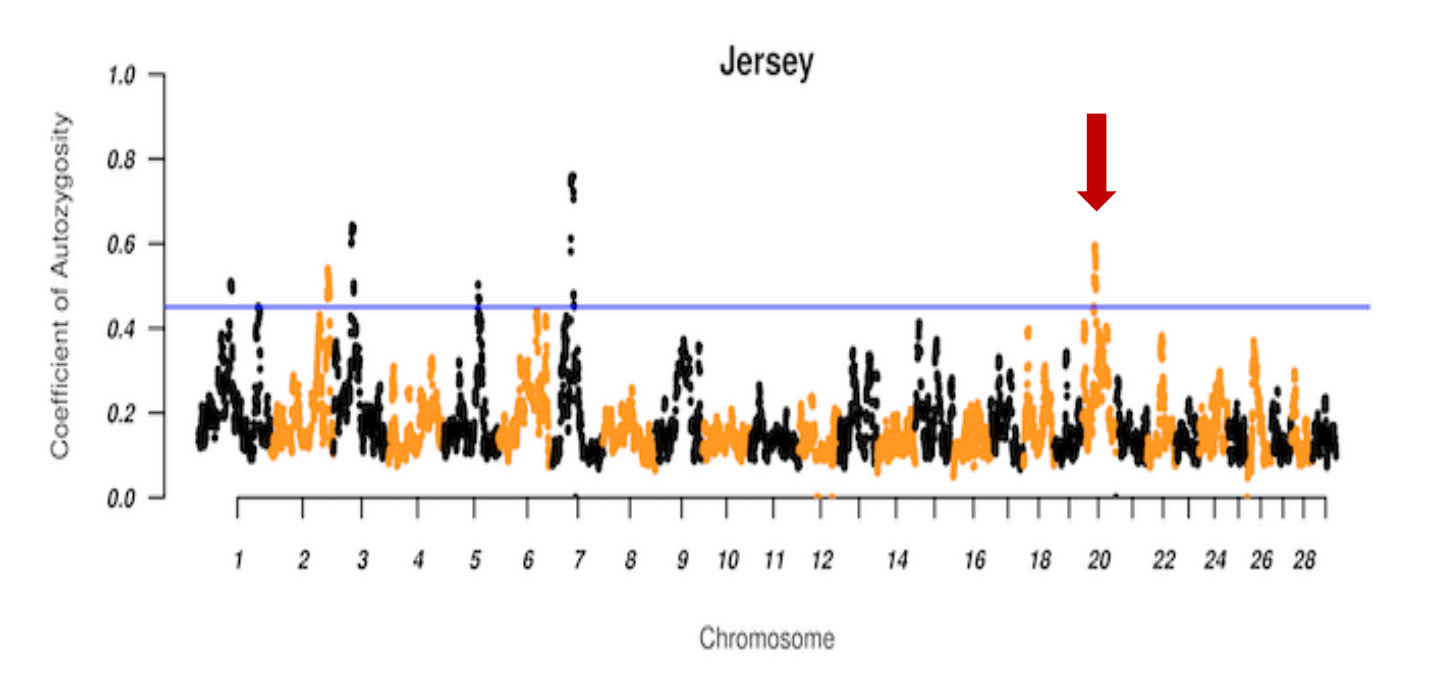
Overlapping region between HO and JE





Notable genes:

- ISL1
- PELO

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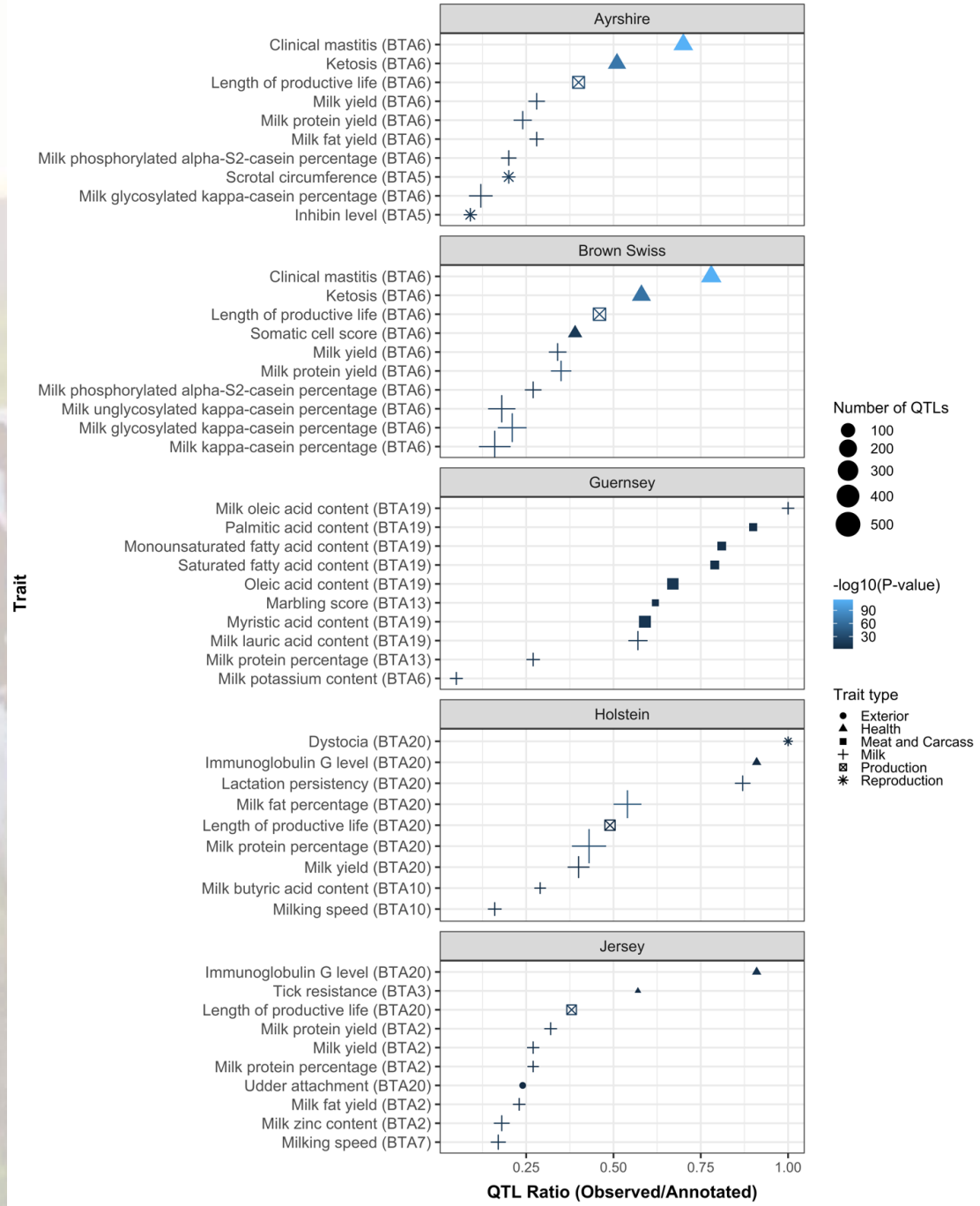
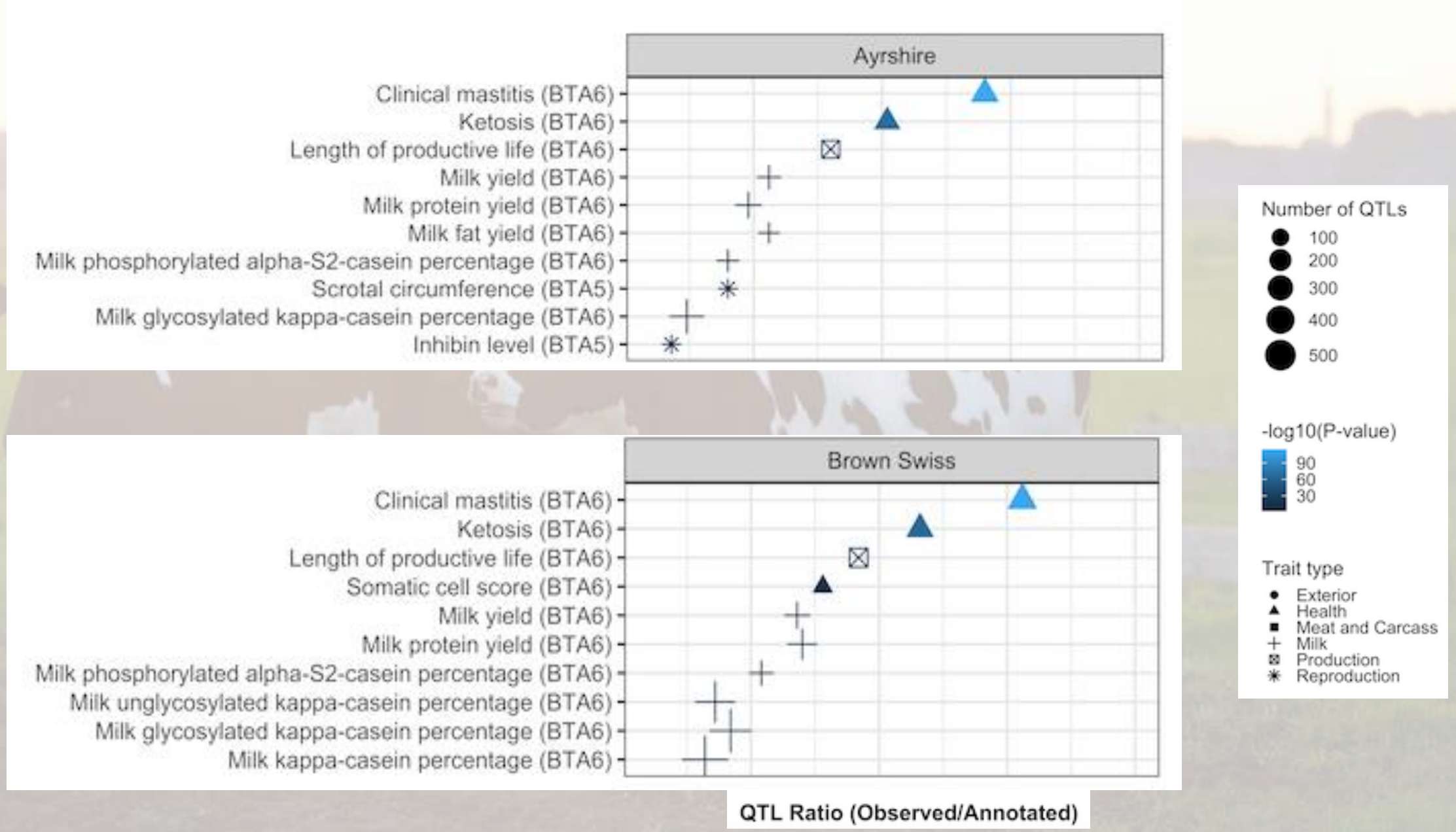
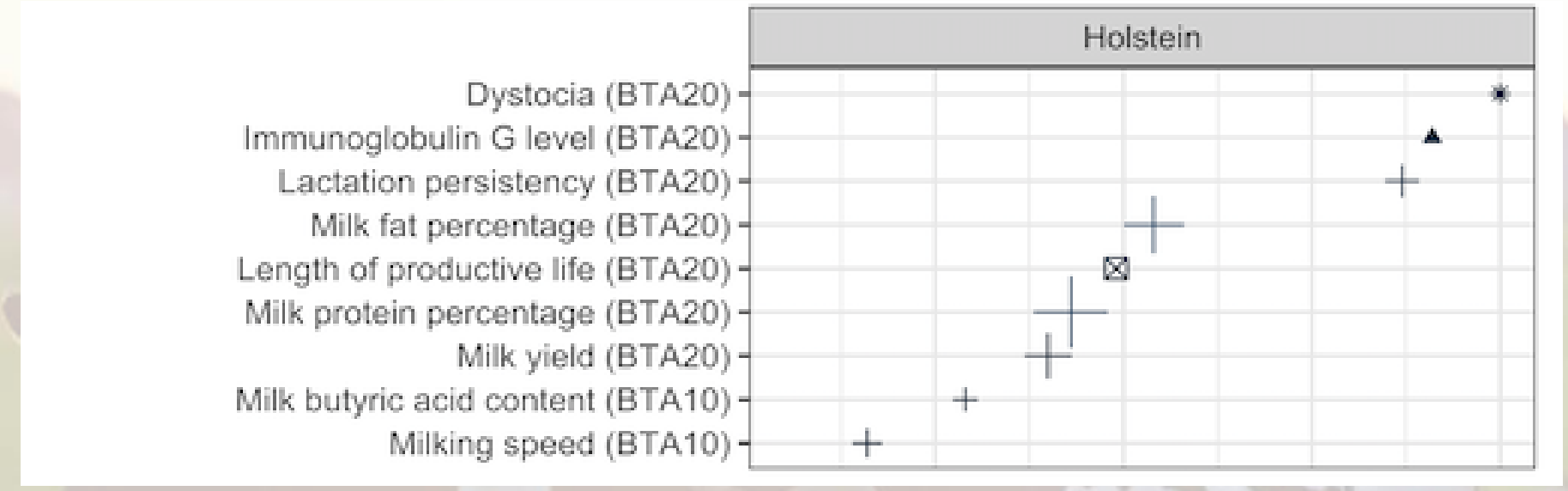
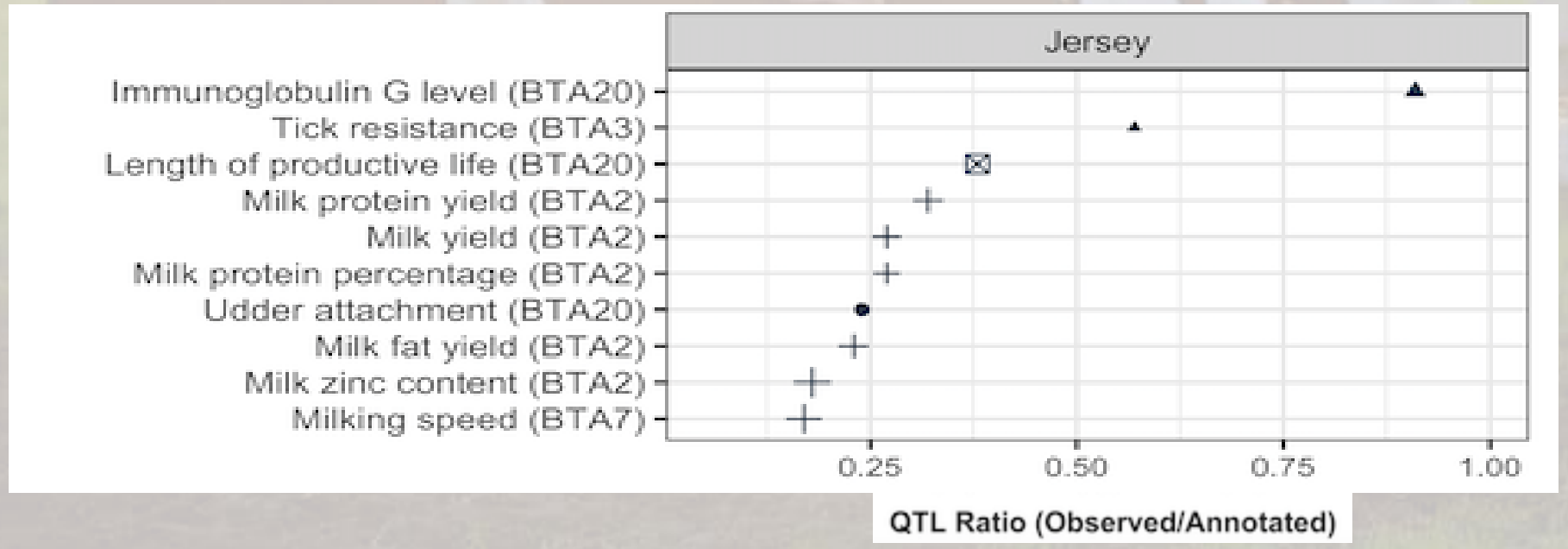
QTL annotation and trait enrichment

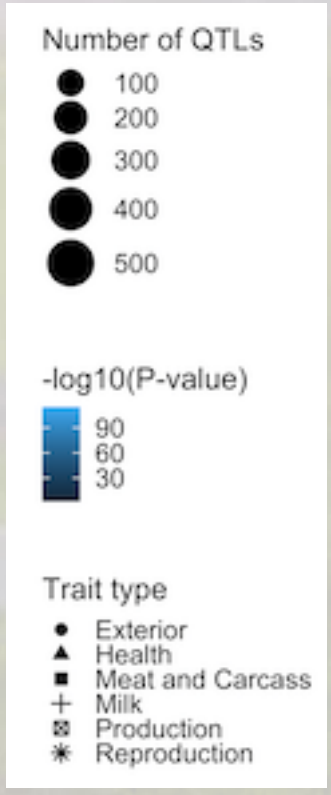
- We utilized the GALLO R package to query the Animal QTLdb for quantitative trait loci (QTL) that have been previously identified in the regions of interest.
- Trait enrichment analysis was performed on the annotated QTL by chromosome.
- Significantly enriched traits had an FDR adjusted P-value lower than 0.05.

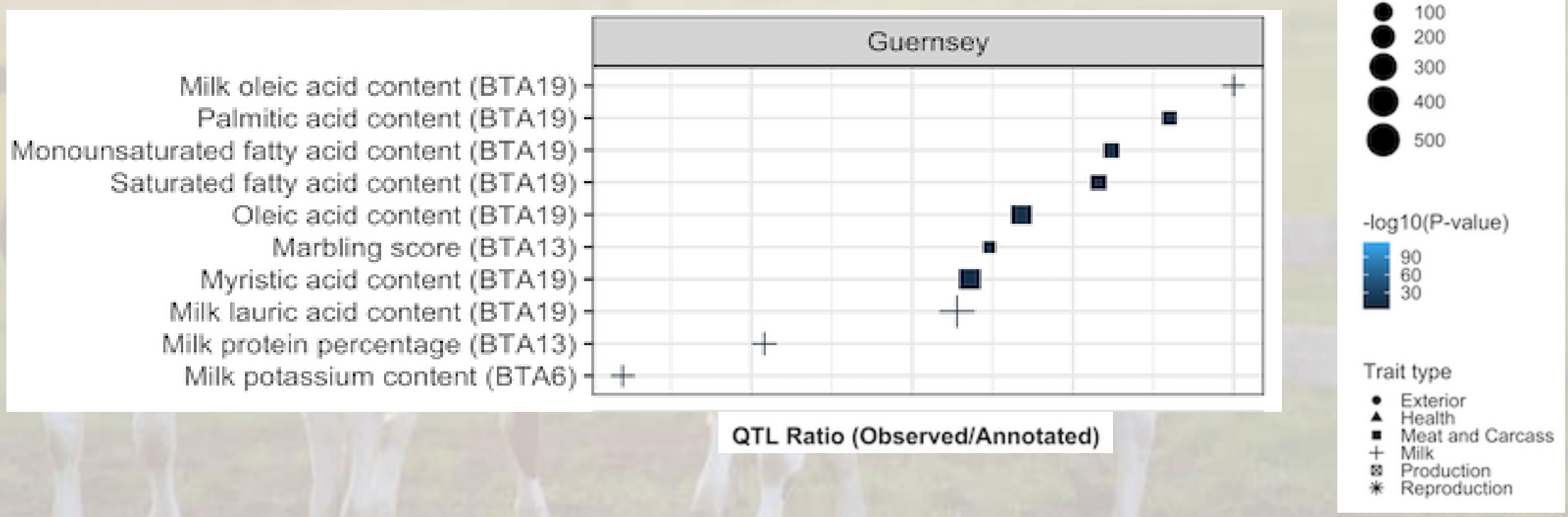



Ayrshire
Clinical mastitis (BTA6)
Ketosis (BTA6)
Length of productive life (BTA6)
Milk yield (BTA6)
Milk protein yield (BTA6)
Milk fat yield (BTA6)
Milk phosphorylated alpha-S2-casein percentage (BTA6)
Scrotal circumference (BTA5)
Milk glycosylated kappa-casein percentage (BTA6)
Inhibin level (BTA5)
Brown Swiss
Clinical mastitis (BTA6)
Ketosis (BTA6)
Length of productive life (BTA6)
Somatic cell score (BTA6)
Milk yield (BTA6)
Milk protein yield (BTA6)
Milk phosphorylated alpha-S2-casein percentage (BTA6)
Milk unglycosylated kappa-casein percentage (BTA6)
Milk glycosylated kappa-casein percentage (BTA6)
Milk kappa-casein percentage (BTA6)
QTL Ratio (Observed/Annotated)
Number of QTLs
100
200
300
400
500
-log10(P-value)
90
60
30
Trait type
Exterior
Health
Meat and Carcass
Milk
Production
Reproduction


Holstein
Dystocia (BTA20)
Immunoglobulin G level (BTA20)
Lactation persistency (BTA20)
Milk fat percentage (BTA20)
Length of productive life (BTA20)
Milk protein percentage (BTA20)
Milk yield (BTA20)
Milk butyric acid content (BTA10)
Milking speed (BTA10)


Jersey
Immunoglobulin G level (BTA20)
Tick resistance (BTA3)
Length of productive life (BTA20)
Milk protein yield (BTA2)
Milk yield (BTA2)
Milk protein percentage (BTA2)
Udder attachment (BTA20)
Milk fat yield (BTA2)
Milk zinc content (BTA2)
Milking speed (BTA7)
0.25
0.50
0.75
1.00
QTL Ratio (Observed/Annotated)


Number of QTLs
100
200
300
400
500
-log10(P-value)
90
60
30
Trait type
Exterior
Health
Meat and Carcass
Milk
Production
Reproduction


Guernsey
Milk oleic acid content (BTA19)
Palmitic acid content (BTA19)
Monounsaturated fatty acid content (BTA19)
Saturated fatty acid content (BTA19)
Oleic acid content (BTA19)
Marbling score (BTA13)
Myristic acid content (BTA19)
Milk lauric acid content (BTA19)
Milk protein percentage (BTA13)
Milk potassium content (BTA6)
QTL Ratio (Observed/Annotated)
Number of QTLs
100
200
300
400
500
-log10(P-value)
90
60
30
Trait type
Exterior
Health
Meat and Carcass
Milk
Production
Reproduction

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Inbreeding

- We calculated pedigree and genomic inbreeding coefficients.
  - Pedigree Inbreeding (F_{PED})
  - Genomic Inbreeding
    - Using genomic relationship matrix (F_{GRM})
    - Using proportion of genome in ROH (F_{ROH})

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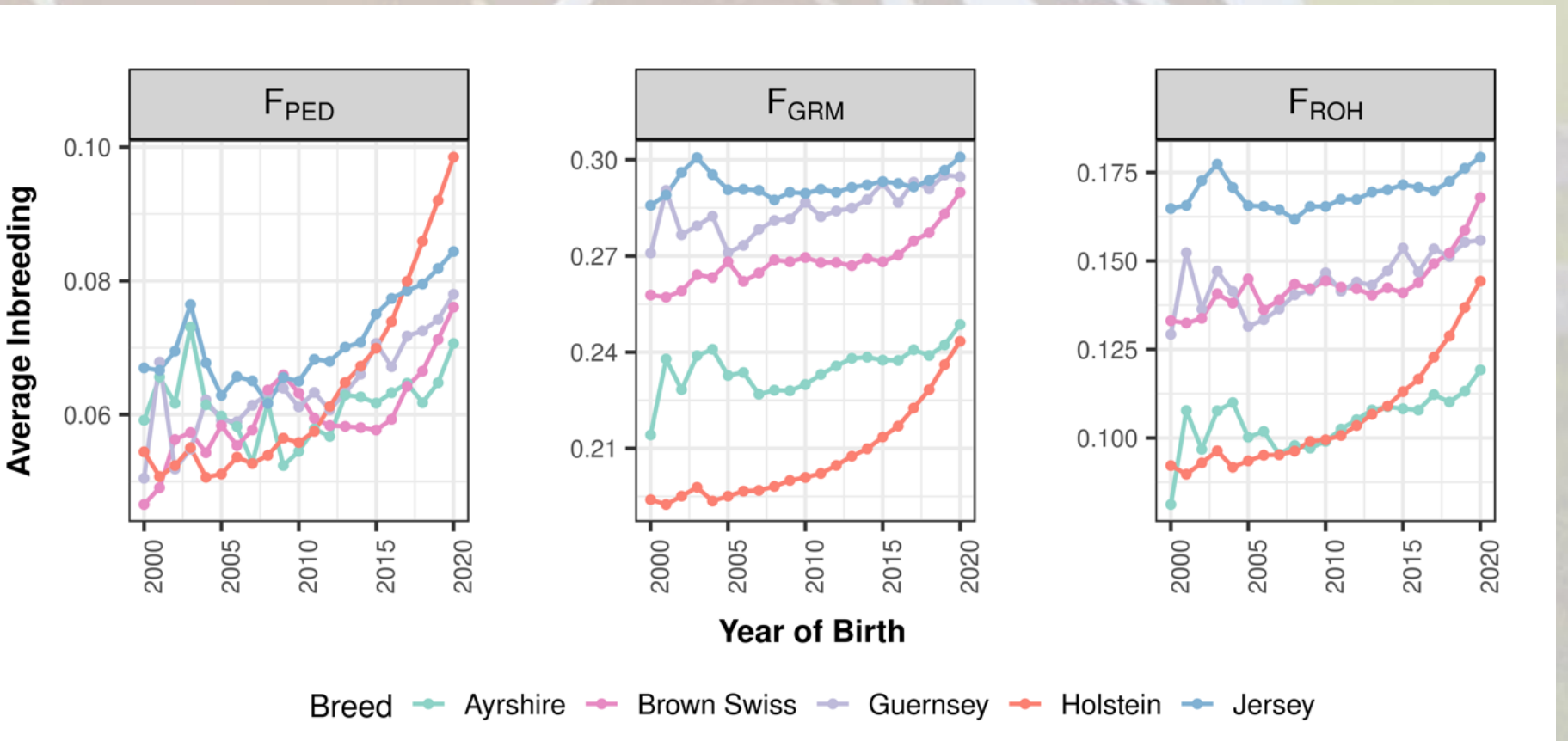
Breed	F_{PED}	F_{GRM}	F_{ROH}
AY	0.06 ± 0.02	0.24 ± 0.03	0.11 ± 0.03
BS	0.06 ± 0.03	0.27 ± 0.03	0.15 ± 0.04
GU	0.07 ± 0.02	0.29 ± 0.03	0.15 ± 0.03
HO	0.08 ± 0.03	0.22 ± 0.03	0.12 ± 0.04
JE	0.08 ± 0.02	0.29 ± 0.03	0.17 ± 0.03



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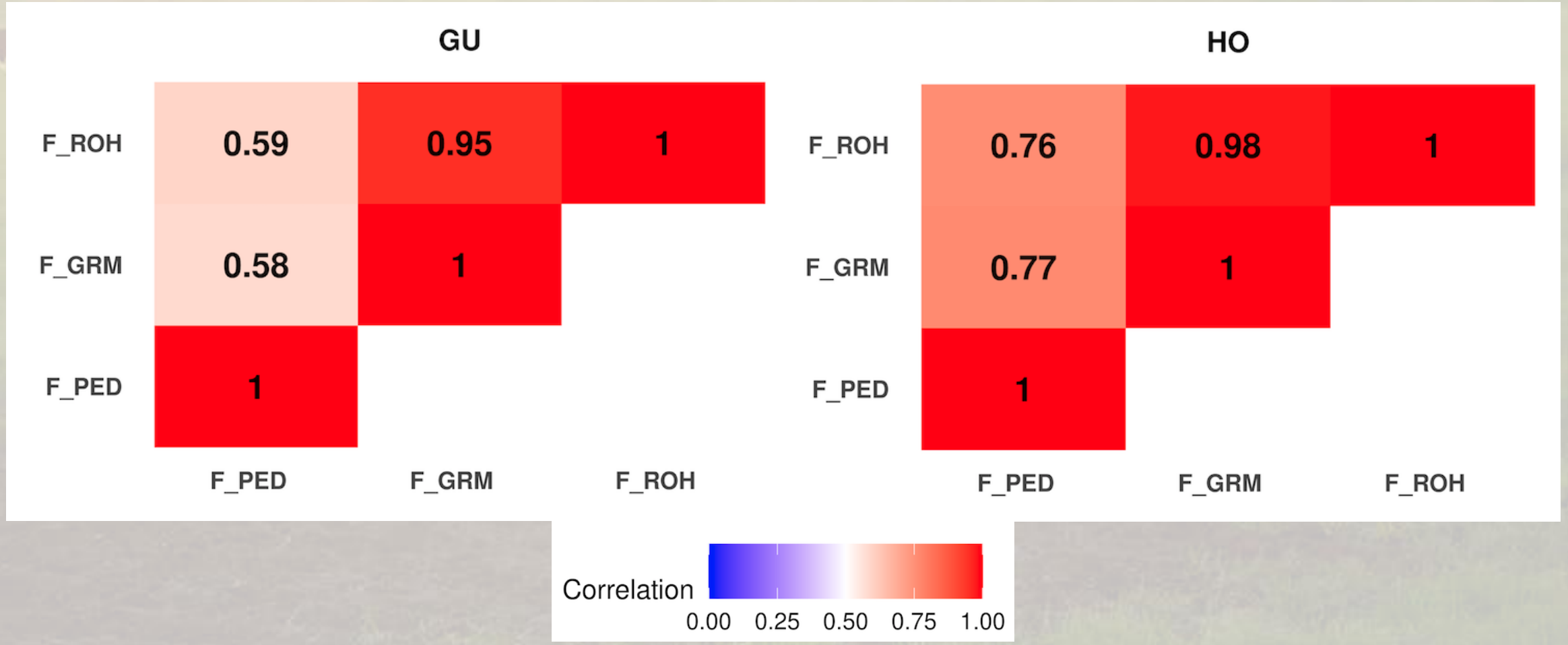
Pearson Correlations



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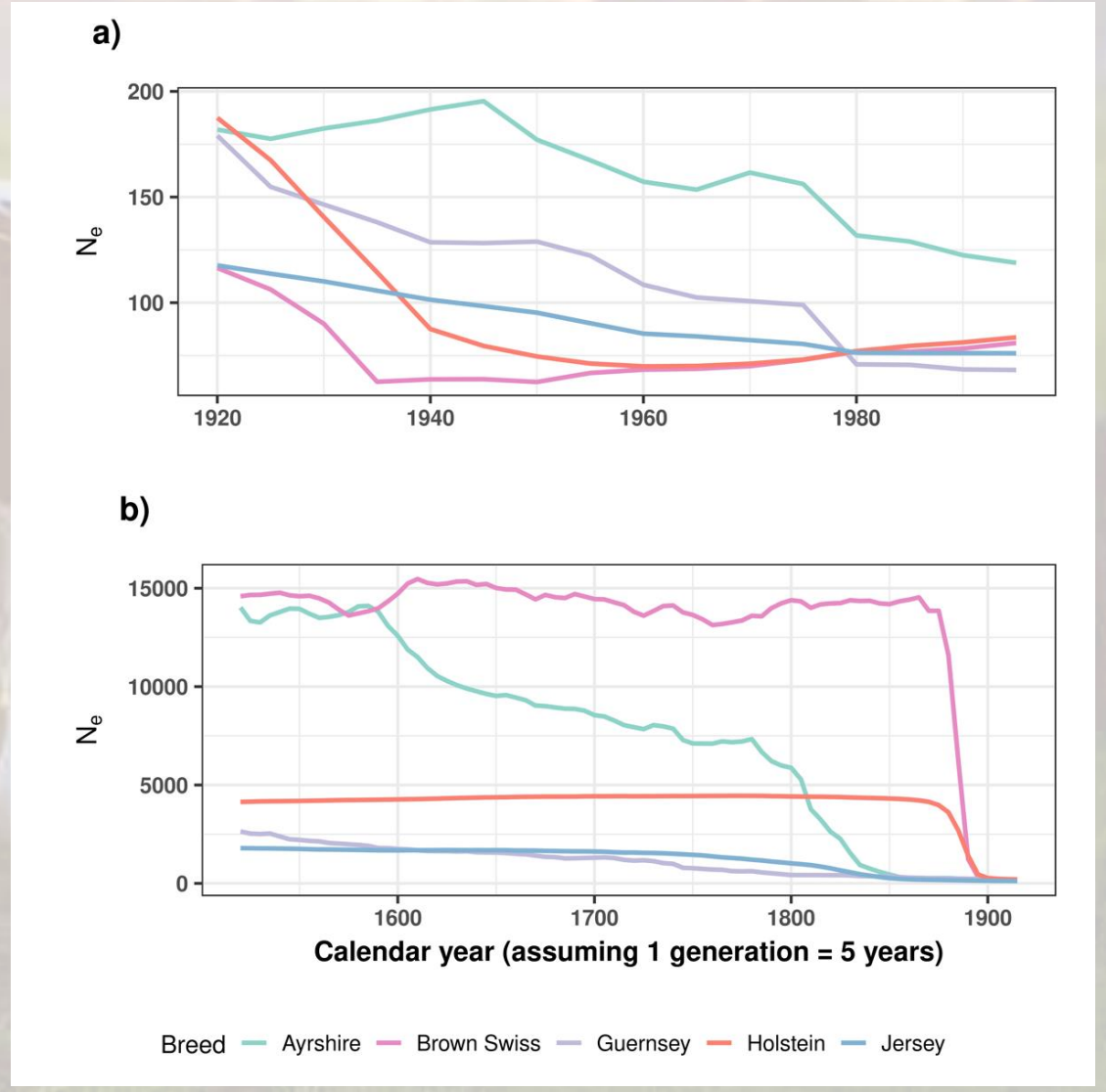
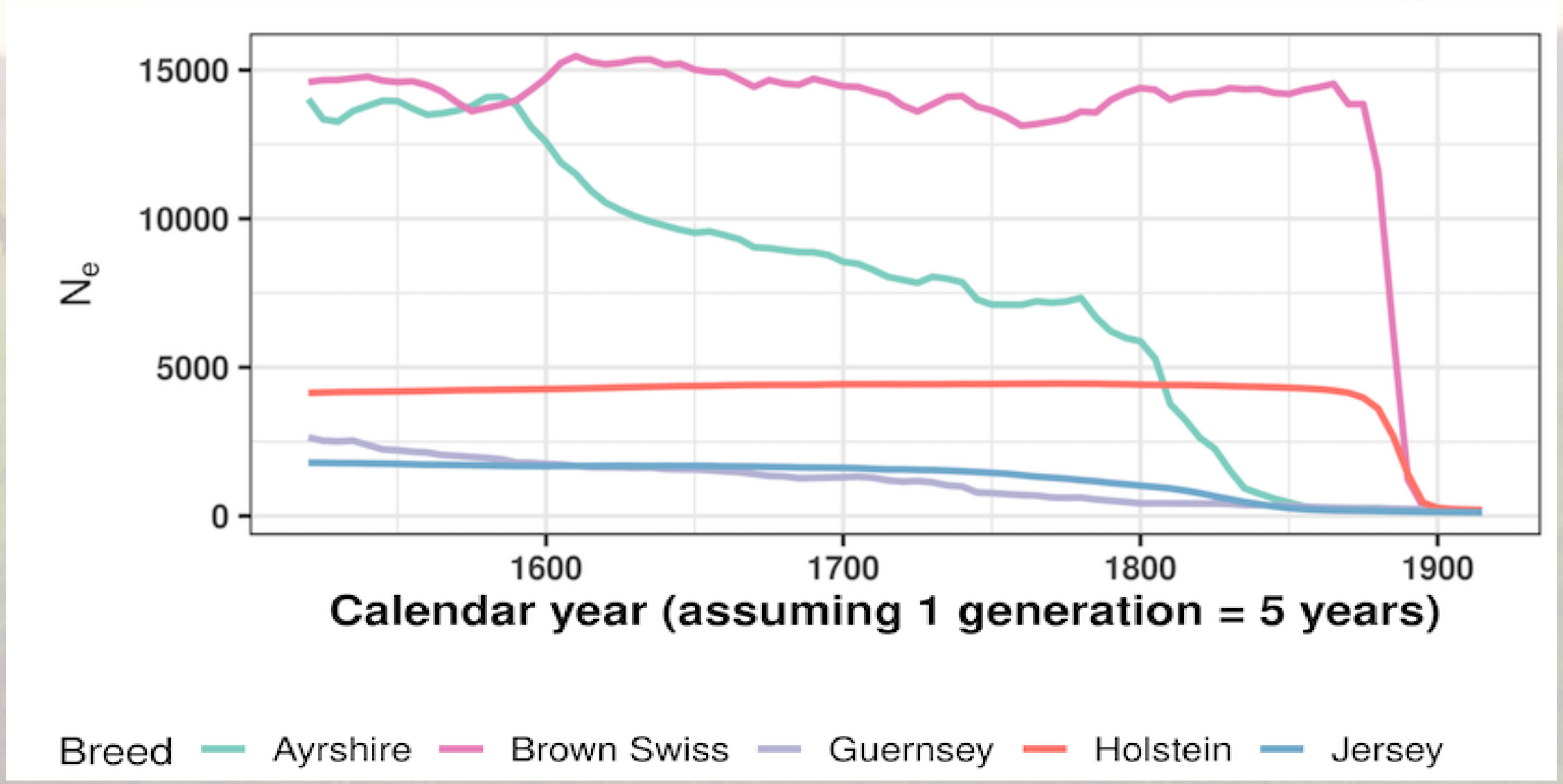
Past effective population size (N_e)

- Effective population size 5 to 100 generations ago was estimated using the GONE software.
- The program was run with default parameters.




15000
10000
5000
0
N_e
1600
1700
1800
1900
Calendar year (assuming 1 generation = 5 years)
Breed
Ayrshire
Brown Swiss
Guernsey
Holstein
Jersey

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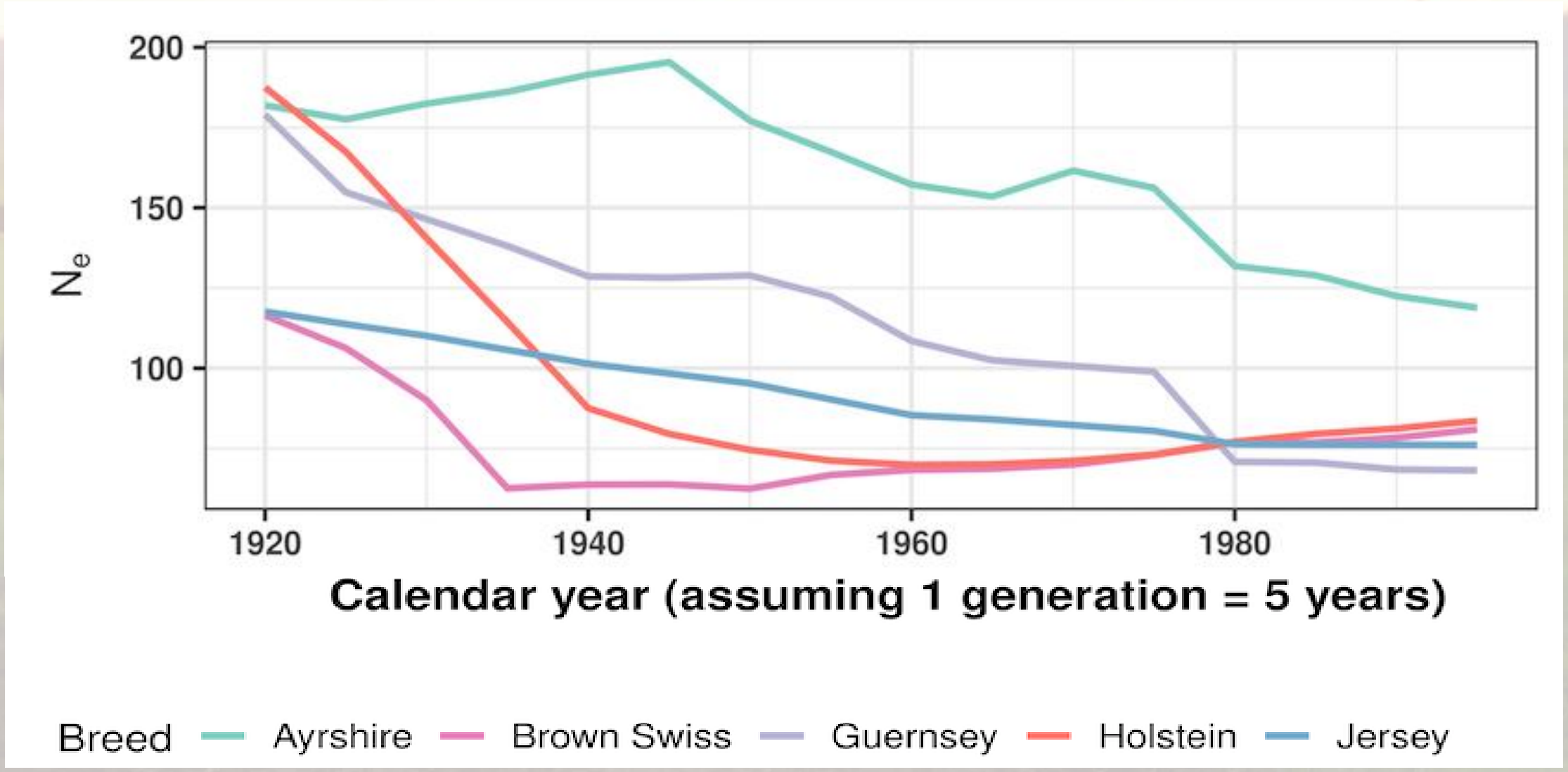

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What role is genomic selection playing in the current levels of genetic diversity?

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Yearly rates of inbreeding (ΔF_{yr})

- ΔF_{yr} was calculated for each inbreeding measure ($\Delta F_{PED_{yr}}$, $\Delta F_{GRM_{yr}}$, $\Delta F_{ROH_{yr}}$) in sires and dams of each breed for three periods of interest:

1. Before the advent of GS (P1 = 2000 to 2009)
2. During the initial implementation of GS (P2 = 2010 to 2014)
3. After the widespread adoption of GS (P3 = 2015 to 2018)

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Effective population size in the three periods

- We used the estimates of the yearly rate of inbreeding coupled with the generation intervals calculated at each period to estimate each population's effective population size in the three recent time periods (P1, P2, and P3)

$$N_e = \frac{1}{2L\Delta F_{yr}}$$

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ΔF_{yr} in sires

Measure	Period	AY	BS	GU	HO	JE
ΔF_{PED} (CI) (%)	P1	-0.12 (-0.25, 0.01)	0.08 (0.00, 0.16)	0.23 (0.09, 0.36)	0.03 (0.01, 0.04)	-0.18 (-0.24, -0.13)
	P2	0.15 (-0.15, 0.44)	0.05 (-0.13, 0.22)	-0.01 (-0.32, 0.30)	0.66 (0.63, 0.69)	0.31 (0.22, 0.40)
	P3	0.19 (-0.45, 0.83)	0.65 (0.26, 1.03)	0.52 (-0.03, 1.07)	1.09 (1.02, 1.16)	0.29 (0.10, 0.48)
ΔF_{GRM} (CI) (%)	P1	0.14 (-0.09, 0.36)	0.05 (-0.07, 0.16)	0.21 (-0.02, 0.44)	0.07 (0.05, 0.09)	-0.19 (-0.27, -0.10)
	P2	0.03 (-0.43, 0.48)	0.36 (0.09, 0.64)	-0.14 (-0.59, 0.30)	1.01 (0.96, 1.06)	0.34 (0.19, 0.50)
	P3	0.52 (-0.64, 1.68)	1.03 (0.44, 1.63)	0.76 (-0.07, 1.59)	1.50 (1.40, 1.60)	0.28 (-0.01, 0.57)
ΔF_{ROH} (CI) (%)	P1	0.15 (-0.06, 0.36)	0.02 (-0.09, 0.14)	0.24 (0.03, 0.45)	0.08 (0.06, 0.10)	-0.18 (-0.27, -0.10)
	P2	0.08 (-0.37, 0.52)	0.26 (-0.04, 0.56)	-0.30 (-0.75, 0.15)	0.97 (0.92, 1.01)	0.42 (0.27, 0.57)
	P3	0.52 (-0.59, 1.64)	1.00 (0.41, 1.59)	0.60 (-0.23, 1.42)	1.41 (1.31, 1.51)	0.33 (0.05, 0.61)

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ΔF_{yr} in sires

Measure	Period	AY	GU
ΔF_{PED} (CI) (%)	P1	-0.12 (-0.25, 0.01)	0.23 (0.09, 0.36)
	P2	0.15 (-0.15, 0.44)	-0.01 (-0.32, 0.30)
	P3	0.19 (-0.45, 0.83)	0.52 (-0.03, 1.07)
ΔF_{GRM} (CI) (%)	P1	0.14 (-0.09, 0.36)	0.21 (-0.02, 0.44)
	P2	0.03 (-0.43, 0.48)	-0.14 (-0.59, 0.30)
	P3	0.52 (-0.64, 1.68)	0.76 (-0.07, 1.59)
ΔF_{ROH} (CI) (%)	P1	0.15 (-0.06, 0.36)	0.24 (0.03, 0.45)
	P2	0.08 (-0.37, 0.52)	-0.30 (-0.75, 0.15)
	P3	0.52 (-0.59, 1.64)	0.60 (-0.23, 1.42)

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ΔF_{yr} in sires

Measure	Period	BS	HO	JE
ΔF_{PED} (CI) (%)	P1	0.08 (0.00, 0.16)	0.03 (0.01, 0.04)	-0.18 (-0.24, -0.13)
	P2	0.05 (-0.13, 0.22)	0.66 (0.63, 0.69)	0.31 (0.22, 0.40)
	P3	0.65 (0.26, 1.03)	1.09 (1.02, 1.16)	0.29 (0.10, 0.48)
ΔF_{GRM} (CI) (%)	P1	0.05 (-0.07, 0.16)	0.07 (0.05, 0.09)	-0.19 (-0.27, -0.10)
	P2	0.36 (0.09, 0.64)	1.01 (0.96, 1.06)	0.34 (0.19, 0.50)
	P3	1.03 (0.44, 1.63)	1.50 (1.40, 1.60)	0.28 (-0.01, 0.57)
ΔF_{ROH} (CI) (%)	P1	0.02 (-0.09, 0.14)	0.08 (0.06, 0.10)	-0.18 (-0.27, -0.10)
	P2	0.26 (-0.04, 0.56)	0.97 (0.92, 1.01)	0.42 (0.27, 0.57)
	P3	1.00 (0.41, 1.59)	1.41 (1.31, 1.51)	0.33 (0.05, 0.61)

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ΔF_{yr} in dams

Measure	Period	AY	BS	GU	HO	JE
ΔF_{PED} (CI) (%)	P1	-0.17 (-0.28, -0.06)	0.26 (0.15, 0.37)	0.02 (-0.15, 0.19)	0.11 (0.10, 0.12)	-0.01 (-0.06, -0.03)
	P2	0.25 (0.14, 0.36)	0.01 (-0.08, 0.09)	0.09 (-0.04, 0.22)	0.27 (0.26, 0.27)	0.10 (0.08, 0.12)
	P3	0.08 (-0.11, 0.26)	0.18 (0.06, 0.30)	-0.07 (-0.26, 0.11)	0.55 (0.54, 0.56)	0.15 (0.13, 0.17)
ΔF_{GRM} (CI) (%)	P1	-0.19 (-0.34, -0.04)	0.23 (0.08, 0.38)	0.18 (-0.04, 0.40)	0.17 (0.16, 0.19)	-0.11 (-0.17, -0.05)
	P2	0.28 (0.16, 0.41)	0.06 (-0.07, 0.18)	0.11 (-0.10, 0.32)	0.27 (0.26, 0.27)	0.06 (0.03, 0.09)
	P3	0.11 (-0.13, 0.35)	0.37 (0.20, 0.54)	-0.11 (-0.40, 0.18)	0.70 (0.69, 0.70)	0.05 (0.03, 0.08)
ΔF_{ROH} (CI) (%)	P1	-0.13 (-0.26, 0.01)	0.28 (0.13, 0.43)	0.17 (-0.04, 0.38)	0.21 (0.20, 0.23)	-0.05 (-0.11, 0.01)
	P2	0.26 (0.15, 0.38)	0.07 (-0.05, 0.19)	0.07 (-0.13, 0.28)	0.26 (0.25, 0.27)	0.11 (0.09, 0.14)
	P3	0.15 (-0.07, 0.38)	0.35 (0.19, 0.51)	-0.06 (-0.34, 0.22)	0.66 (0.66, 0.67)	0.07 (0.05, 0.10)

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N_e in sires

Measure	Period	HO	JE	BS
N_{ePED} (CI)	P1	344 (172, 518)	NA	93 (3, 184)
	P2	20 (19, 21)	36 (25, 46)	NA
	P3	18 (17, 19)	51 (18, 84)	18 (8, 29)
N_{eGRM} (CI)	P1	124 (88, 161)	NA	NA
	P2	13 (13, 14)	32 (18, 47)	24 (6, 42)
	P3	13 (12, 14)	NA	12 (5, 18)
N_{eROH} (CI)	P1	113 (82, 144)	NA	NA
	P2	14 (13, 14)	26 (17, 36)	NA
	P3	14 (13, 15)	46 (7, 85)	12 (5, 19)

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N_e in dams

Measure	Period	HO	JE	BS
N_{ePED} (CI)	P1	82 (75, 89)	NA	32 (18, 45)
	P2	42 (41, 43)	113 (92, 134)	NA
	P3	25 (25, 26)	99 (87, 110)	64 (20, 107)
N_{eGRM} (CI)	P1	55 (50, 59)	NA	36 (13, 59)
	P2	42 (41, 44)	195 (103, 286)	NA
	P3	20 (20, 20)	276 (148, 403)	31 (17, 44)
N_{eROH} (CI)	P1	44 (41, 47)	NA	30 (13, 46)
	P2	44 (42, 45)	104 (78, 129)	NA
	P3	21 (21, 21)	199 (135, 263)	32 (17, 48)

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Take-home Message

- Differences across breeds in terms of:
  - Pedigree and genomic inbreeding levels
  - Rates of inbreeding accumulation
  - Past and present effective population sizes

- The adoption of genomic selection has brought with it increased levels of inbreeding and has decreased the genetic diversity within breeds.

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Implications

- More detailed analysis must be conducted to census the genetic diversity available for selection in US dairy breeds.

- Strategies to curb the accumulation of inbreeding in these populations need to be continuously investigated and implemented.

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Thank you for your attention!

Questions?