

At Anafibj, a procedure was developed to estimate an Runs-Of-Homozygosity (ROH) style genomic inbreeding coefficient using an output file of our imputation software `pedimpute.f90` (Nicolazzi et al., 2013), where haplotype segments are numbered. Using numbered haplotype segments, we could directly compare the segments by their number rather than using time-consuming SNP-by-SNP comparisons. The fraction of autosomal haplotypes with the same number (i.e., identical) on a pair of homologous chromosomes is an estimate of the Froh. A Froh is an identity-by-descent (IBD) type of inbreeding coefficient. We computed the own as well as the future inbreeding coefficients. Our genomic expected future inbreeding coefficient was named Gefi. An advantage of an IBD type of inbreeding measure is that values are within the probability space $[0,1]$, which avoids negative values that are more difficult to understand.

A comparison was undertaken between the Gefi estimated by Anafibj and the genomic future inbreeding coefficients (GFI) estimated by CDCB using the diagonal from the genomic relationship matrix, which is an identity-by-state (IBS) measure with values within the correlation space $[-1,1]$. This Pearson correlation was computed based on 38,280 genotyped proven bulls covering 70 years (born 1951-2020), which had both estimates available.

Inbreeding depression standardized effect size across traits

In the literature, a number of articles showed results of genomic inbreeding depression using ROH-based inbreeding coefficients (Froh) in Holsteins. In order to compare traits and to understand which traits had a larger inbreeding depression, we standardized the inbreeding depression effects so that they became comparable across traits. We computed the standardized effect size as the inbreeding depression estimate (b) multiplied by the standard deviation of the genomic inbreeding

coefficient (SD(F)) used to estimate the inbreeding depression. We then divided this by the observed standard deviation of the trait (SD(y)). Estimates from the following papers were included: Ablondi et al., 2023; Bjelland et al., 2013; Doekes et al., 2019; Makanjuola et al., 2020; Mugambe et al., 2023. Also, new unpublished results from Ablondi et al. were included.

Results & Discussion

Issue of declining genetic variation

Figure 1 shows the annual trend in SNP heterozygosity before and during the genomics era.

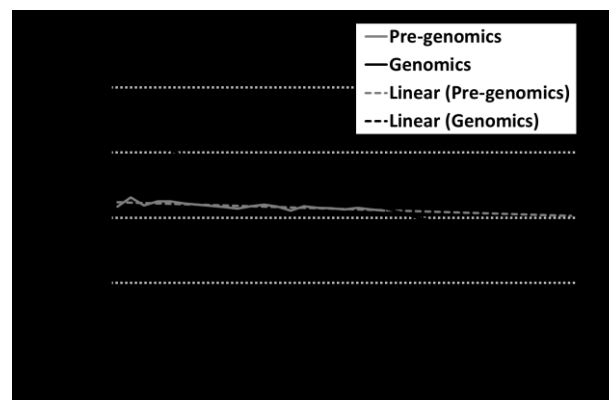


Figure 1. Pre- and post-genomic trends of SNP heterozygosity by birth year

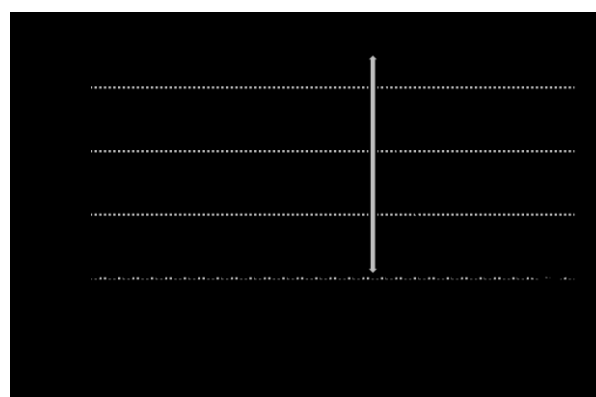


Figure 2. Decline of effective population size (N_e) during the most recent 16 birth years

Genomic inbreeding coefficients from imputed data

Table 1 shows different types of correlation coefficients between the genomic inbreeding

coefficients of the samples in the imputed downgraded set with their fully genotyped (i.e. not downgraded) samples.

In the same manner Table 2 and 3 show the correlation coefficients for the subsets 1 and 2.

Table 1. Correlations of inbreeding coefficients entire downgraded set (N=329)

Downgrade	Correlation	GRM	ROH	ROH
			27	80
GGP3 (26K)	Spearman	0.85	0.85	0.90
	Pearson	0.43	0.48	0.89
	Concordance	0.26	0.39	0.87
Labogena MD (62K)	Spearman	0.93	0.96	0.96
	Pearson	0.65	0.97	0.98
	Concordance	0.55	0.97	0.96

Table 2. Correlations of inbreeding coefficients downgraded set (N=266) with info on both parental sides

Downgrade	Correlation	GRM	ROH	ROH
			27	80
GGP3 (26K)	Spearman	0.93	0.96	0.96
	Pearson	0.89	0.96	0.96
	Concordance	0.82	0.96	0.94
Labogena MD (62K)	Spearman	0.98	0.99	0.98
	Pearson	0.97	0.99	0.98
	Concordance	0.95	0.99	0.97

Table 3. Correlations of inbreeding coefficients downgraded set (N=63) without info on one or both parental sides

Downgrade	Correlation	GRM	ROH	ROH
			27	80
GGP3 (26K)	Spearman	0.68	0.54	0.67
	Pearson	0.65	0.34	0.65
	Concordance	0.14	0.10	0.55
Labogena MD (62K)	Spearman	0.83	0.77	0.83
	Pearson	0.72	0.82	0.90
	Concordance	0.27	0.79	0.84

Correlation between Gefi and GFI

Summary statistics from Gefi and GFI are presented in Table 4 based on 38,280 proven bulls. The Pearson correlation between Gefi and GFI was 0.959.

Table 4: Summary statistics of Gefi and GFI

	Gefi	GFI
Average	6.9	7.2
Standard deviation	2.6	2.6
Maximum	15.3	13.5
Minimum	0.1	-3.1

Inbreeding depression standardized effect size across traits

Table 5 shows the average standardized effect size of the inbreeding depression per trait based on the estimates in literature. For all traits the effect was in the undesirable direction.

Table 5. Standardized effect size of the inbreeding depression

Trait	Standardized effect size
Milk kg	-.068%
Fat kg	-.063%
Protein kg	-.084%
Fat %	-.015%
Protein %	-.013%
SCS*	.020%
SCS5-150	.006%
SCS151-400	.017%
Age at 1 st calving	.007%
Heifer interval 1 st -last insemination	.022%
Heifer NR56	-.009%
Heifer conception rate	-.022%
Cow interval 1 st -last insemination	.016%
Cow NR56	-.019%
Cow conception rate	-.028%
Interval calving to 1st insemination	.008%
Days open	.060%
Calving interval	.018%

*SCS: Somatic Cell Score

A further condensed overview of the standardized effect size of the inbreeding depression is given in Table 6. Here the average value per trait group is given.

Table 6. Average across trait standardized effect size of the inbreeding depression per trait group

Trait	Standardized effect size
Yields	-.072%
Contents	-.014%
SCS*	.014%
Fertility	-.019%

*SCS: Somatic Cell Score

Conclusions

Regarding genomic inbreeding coefficients from imputed data, we can conclude:

- The 62K chip outperforms the 26K chip.
- Froh exhibits stronger correlations than Fgrm0.5.
- Longer Froh segments demonstrate higher correlations than shorter segments.
- Spearman rank correlations > Pearson correlations > Concordance correlations
- Results are satisfactory when both parental sides have genotypes.
- In 2023, >97.3% of animals have genotypes on both parental sides, so for recent animals the results based on imputed data should be fine.

The high correlation between Gefi and GFI shows that they are both measuring future inbreeding producing very similar results.

For the inbreeding depression per trait group, we can conclude that by far the largest impact is on the yield traits. Fertility, contents and SCS all have an undesirable inbreeding depression of around 20% from the inbreeding depression on yields.

Overall take-home messages are:

- There has been a rapid increase in inbreeding since the advent of genomic selection.
- Inbreeding detrimentally affects nearly all traits, with the most pronounced impact seen in yield traits.
- Anafibj intends to introduce a premium/penalty for expected future inbreeding later this year.

- We will use genomic estimates when possible and otherwise pedigree-based estimates on a comparable scale.
- It is important to give a signal regarding the impact of inbreeding.

Acknowledgments

This study was supported by “Latteco2 project, sottomisura 10.2 of the PSRN-Biodiversity 2020–2023” (MIPAAF. D.M. no. 465907 del 24/09/2021, project unique code J12C21004080005).

References

- Ablondi, M., Summer, A., Stocco, G., Finocchiaro, R., Van Kaam, J.-T., Cassandro, M., Dadousis, C., Sabbioni, A., and Cipolat-Gotet, C., 2023. The role of inbreeding depression on productive performance in the Italian Holstein breed. *J. Anim. Sci.* 101:1–10. <https://doi.org/10.1093/jas/skad382>.
- Bjelland, D.W., Weigel, K.A., Vukasinovic, N., and Nkrumah, J.D., 2013. Evaluation of inbreeding depression in Holstein cattle using whole-genome SNP markers and alternative measures of genomic inbreeding. *J. Dairy Sci.* 96:4697–4706. <https://doi.org/10.3168/jds.2012-6435>.
- Doekes, H.P., Veerkamp, R.F., Bijma, P., De Jong, G., Hiemstra, S.J., and Windig, J.J., 2019. Inbreeding depression due to recent and ancient inbreeding in Dutch Holstein–Friesian dairy cattle. *Genet. Sel. Evol.* 51:54. <https://doi.org/10.1186/s12711-019-0497-z>.
- Makanjuola, B.O., Maltecca, C., Miglior, F., Schenkel, F.S., and Baes, C.F., 2020. Effect of recent and ancient inbreeding on production and fertility traits in Canadian Holsteins. *BMC Genomics* 21:605. <https://doi.org/10.1186/s12864-020-07031-w>.

- Mugambe, J., Ahmed, R., Thaller, G., and Schmidtman C., 2024. Impact of inbreeding on production, fertility, and health traits in German Holstein dairy cattle utilizing various inbreeding estimators. *J. Dairy Sci.* TBC.
<https://doi.org/10.3168/jds.2023-23728>.
- Nicolazzi, E.L., Biffani, S., and Jansen, G., 2013. Short communication: Imputing genotypes using PedImpute fast algorithm combining pedigree and population information. *J. Dairy Sci.* 96:2649–2653.
<https://doi.org/10.3168/jds.2012-6062>.
- Van Kaam, J-T., Ablondi, M., Maltecca, C., and Cassandro, M., 2023. Inbreeding Becomes a Serious Issue. *Interbull Bulletin.* 59:101-104.