SEGES INNOVATION

STØTTET AF
Mælkeafgiftsfonden

Report on systematic call errors on certain SNP markers

Andreas Bøgh Poulsen Trine Andersen Ulrik Sander Nielsen

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Introduction

During the transition to Single-step evaluations, some traits exhibited a ubelievable genetic genetic development. Traits like Longevity saw a a development of more than 20 index points in 10 years. While it would be amazing if this was actually the case, it raised suspicion. The cause was found to be certain SNP markers, which had an outsized influence on the genetic breeding values. When investigated further, these markers turned out to be called wrongly from the laboratory on some versions of the genotyping chips. This lead to the Minor Allele Frequency (MAF) changing drastically over years, which in turn meant that animals tested on the same chip appeared more closely related than they actually are.

This document is an attempt to document these findings and our current understanding of the problem.

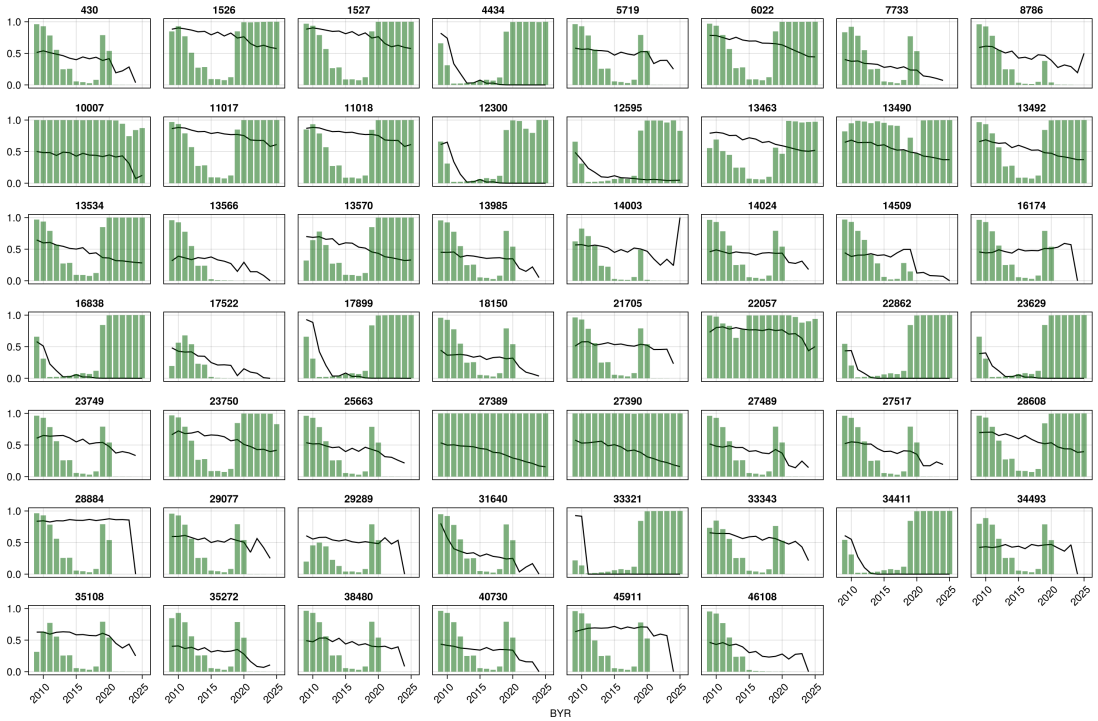
Problematic markers

So far, we've found 3 ways of detecting problematic markers: 1. Unrealisticly strong development in Minor Allele Frequency 2. Sharp year-to-year changes in Minor Allele Frequency 3. Large number of mendelian errors.

Strong development in MAF

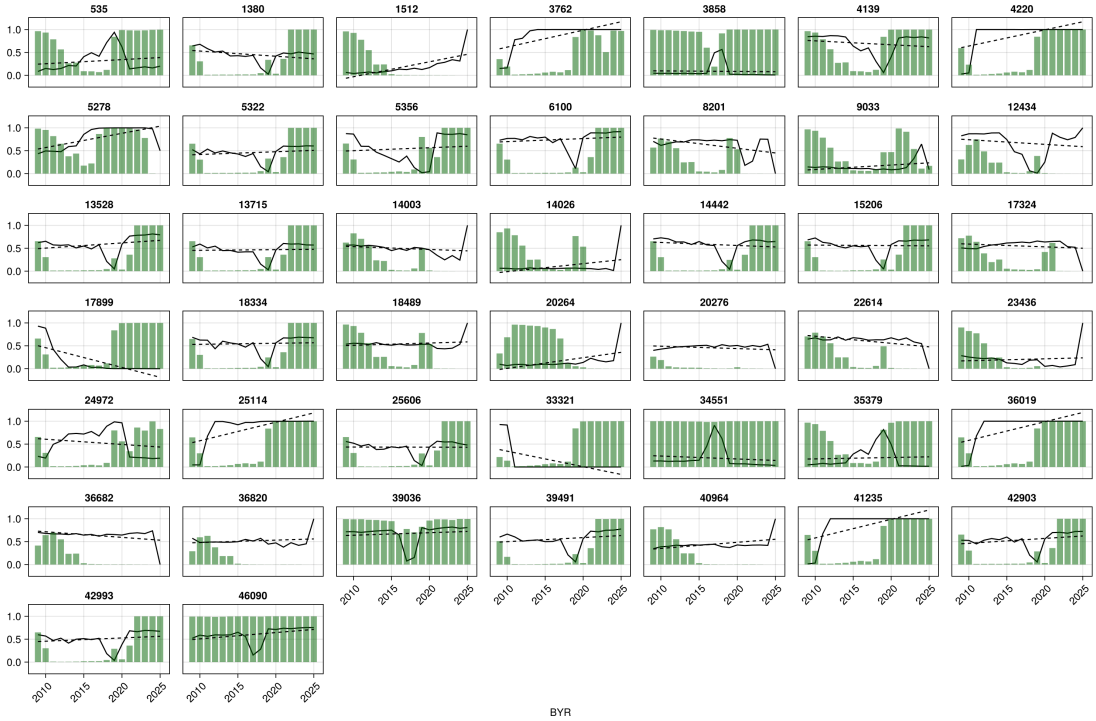
Some markers exhibit a remarkably strong development in Minor Allele Frequency. Given that none of these are specific targets of selection, we find it hard to believe that the distribution would change drastically over few years. The following plot shows those markers whose MAF changed by more than 30 percentage points from 2010 to 2024. The line represents the MAF and the bars in the background represents the fraction of genotyped animals with a call for that marker. It should be noted, that a marker not being called in a given year can have many reasonable explanations. Between 2012 and 2018, most cows were genotyped on a 10K chip

instead of a 50K chip, so many markers will show low call rates in these years. Also, markers are sometimes removed from chips due to quality assurance issues.



Sharp changes in MAF

Some markers exhibit extrme fluctuations certain years, before either settling into a new level or returning to its original level. We saw some of them in the previous section. We detect these markers by fitting a linear trend line to each marker and measure deviations from this line. The following plots shows those markers that deviate more than 40 percentage points from this plotted trend. Again, the solid line shows the MAF, the bars in the background shows the callrate for that marker, and the dotted line shows the fitted trend line.



Many mendelian errors

During imputation, our software collects statistics on how many times the SNP value for an individual is impossible given the call for the parents. For example, the offspring of two homozygous parents with the same allele can never be heterozygous. The following plot displays the development of markers where more than 2,5 percent of called values give rise to a mendelian error.

As we can see, not all markers caught by this filter is found with the other two methods.

Impact on genomic evaluations

This problem of systematic genotype markers was discovered due a number of our traits exhibiting problems when moved to a single-step model. For example, the following table shows genetic trends of a single-step model of birth traits with all markers included (old), a single-step model with the problematic markers removed (new), and the official EBVs from NAV pedigree-based evaluation (off) for nordic bulls with progeny test. The table shows means, standard deviations and correlations between the single step evaluations and the official evaluation. As can be seen, the correlation between the official EBVs and the naive single-step EBVs is quite bad in recent years.

BYR	trait	n	old_m	new_m	off_m	old_s	new_s	off_s	cor_old	cor_new
2009	nysb1	251	95.05	99.2	96.87	9.15	9.15	9.62	0.96	0.96
2010	nysb1	226	96.23	99.87	97.83	7.57	7.69	8.17	0.95	0.95
2011	nysb1	186	97.25	100.19	98.23	6.8	6.93	7.01	0.95	0.95
2012	nysb1	205	97.1	99.17	97.62	7.84	7.86	8.31	0.95	0.95
2013	nysb1	184	100.91	102.13	100.94	7.01	7.13	7.27	0.94	0.94
2014	nysb1	149	99.64	100.09	99.45	6.98	7.11	7.27	0.96	0.94
2015	nysb1	118	101.67	101.27	101.05	6.98	7.13	7.28	0.96	0.95
2016	nysb1	97	99.77	98.73	98.75	7.65	8.02	7.67	0.95	0.95
2017	nysb1	118	100.76	99.18	99.16	7.36	7.4	7.65	0.94	0.93

BYR	trait	n	old_m	new_m	off_m	old_s	new_s	off_s	cor_old	cor_new
2018	nysb1	126	101.79	99.7	99.87	6.16	6.34	6.46	0.92	0.93
2019	nysb1	83	102.3	99.23	100.26	6.65	6.53	6.36	0.9	0.93
2020	nysb1	74	102.12	98.58	99.99	6.32	6.35	6.42	0.94	0.96
2021	nysb1	71	103.21	99.61	100.85	4.87	5.1	5.05	0.76	0.9
2022	nysb1	61	102.81	97.52	98.46	5.1	5.65	6.41	0.51	0.94

For the Youngstock survival trait, we saw the same low correlations in recent years and additionally an inflated genetic trend compared to the EBVs.

BYR	trait	n	old_m	new_m	off_m	old_s	new_s	off_s	cor_old	cor_new
2009	HP1	246	93.43	95.18	97.09	10.67	10.76	10.82	0.93	0.93
2010	HP1	215	91.39	92.73	94.48	11.75	11.54	11.46	0.95	0.95
2011	HP1	183	94.59	94.81	96.29	11.28	11.47	11.55	0.93	0.94
2012	HP1	196	98.66	98.37	99.38	11.49	11.52	11.12	0.94	0.95
2013	HP1	183	98.21	97.26	97.73	11.01	11.09	11.32	0.94	0.95
2014	HP1	148	100.81	99.7	100.49	12.04	12.2	12.14	0.95	0.96
2015	HP1	105	100.0	98.51	99.02	10.61	10.92	10.63	0.95	0.96
2016	HP1	99	100.59	99.65	99.58	9.84	10.11	10.18	0.95	0.95
2017	HP1	106	99.92	98.69	98.57	9.52	9.97	10.53	0.92	0.93
2018	HP1	115	104.13	101.58	101.4	9.92	10.13	10.11	0.94	0.95
2019	HP1	82	108.39	104.98	103.7	9.61	9.56	9.44	0.88	0.9
2020	HP1	71	109.11	104.06	102.51	9.84	10.25	10.39	0.88	0.93
2021	HP1	61	107.66	105.21	103.07	11.7	11.63	11.55	0.85	0.96
2022	HP1	57	109.51	105.53	103.15	8.45	10.48	10.06	0.58	0.94

In the marker set used for the evaluation above, we used only markers with a deviation from a fitted MAF trend line of less than 0.1 and less than 200 mendelian errors. These values were loosely chosen, an will be refined in a future NAV project.

For mendelian errors specifically, we should move to checking the rate of mendelian errors, i.e. the number of mendelian errors divided by the number of calls. A priliminary test showed that the distribution mendelian error rate has a very fat tail (some markers have mendelian errors on 10% of all called individuals). Hence, we should use the median instead of mean and median absolute deviation instead of standard deviation to detect outliers.