Genomic selection and inbreeding and kinship in Dutch-Flemish Holstein Friesian cattle

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Introduction

Holstein-Friesian (HF) dairy cattle have been artificially selected for many decades. Previously, we observed that changes in the HF breeding program have largely affected genetic diversity trends. For example, we found that the introduction of optimal contribution selection and the major shift in breeding goal, which both occurred around the year 2000, have been accompanied by a strong reduction in the rate of inbreeding and by a shift in the direction of allele frequency changes (Doekes et al., submitted). More recently, around 2009, genomic selection (GS) has been widely implemented in HF selection schemes. Since then, animals have been selected based on genomic estimated breeding values (GEBVs), thereby accelerating genetic progress (Hayes et al., 2009; Meuwissen et al., 2013; García-Ruiz et al., 2016) and changing the selection process. Although the effect of GS on diversity across the genome has been investigated in various simulation and experimental studies (Sonesson et al., 2012; Heidaritabar et al., 2014; Liu et al., 2014), results from real life populations are scarce.

The objective of this study was to assess how the implementation of GS in the Dutch-Flemish HF breeding program has affected genome-wide and region-specific inbreeding and kinship in artificial insemination (AI) bulls and in the cow population.

Material and methods

Animals and data

A total of 2,761 HF AI-bulls and 5,770 HF cows were included in this study. Bulls were born in 2003-2015 and comprised the vast majority of AI-bulls in the Dutch-Flemish breeding program. Cows were born in 2003-2017 and were a random sample from farms with a data-agreement with the Dutch-Flemish cattle improvement co-operative (CRV).

Pedigree and genotype data were provided by CRV and the pedigree for AI-bulls was extended with publicly available information (CDN, 2017). The average number of complete generation equivalents (CGE) for bulls and cows equalled 14.7 and 12.0, respectively. Since the implementation of GS in 2009, the generation interval () has decreased for both bulls and cows, with the most pronounced decrease for bull sires (Figure 1).

Genotypes were obtained from various SNP-panels and imputed to ~76 k following Druet *et al.* (2010). The final datasets included 75,538 autosomal SNPs. Haplotypes were

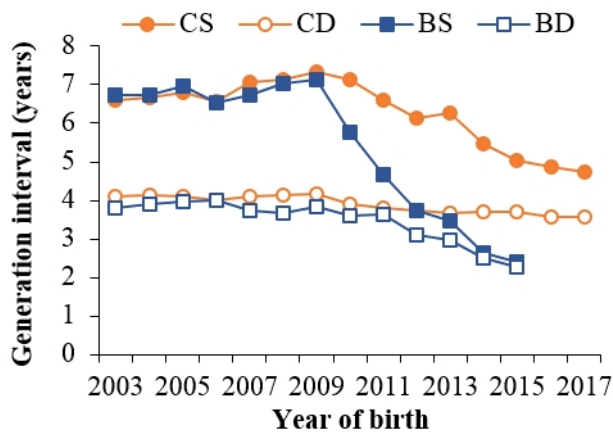constructed with a combination of Beagle and PHASEBOOK (Druet & Georges, 2010).

Figure 1. Generation interval for cow sires (CS), cow dams (CD), AI-bull sires (BS) and AI-bull dams (BD) by year of birth.

Genome-wide inbreeding and kinship
Recent inbreeding and kinship were quantified with identical by descent (IBD) probabilities and more distant relationships were evaluated with identical by state (IBS) measures. Note that the latter also include IBD. The following measures were used: genealogical inbreeding () and kinship (), marker-by-marker homozygosity () and similarity (), and segment-based inbreeding () and kinship (). The and were defined as the pedigree-based probabilities that two alleles at a selection-free locus, sampled within individual i or between individuals i and j, were IBD. The and were the probabilities that two alleles at a random marker, sampled within i or between i and j, were IBS. The was the proportion of the genome of i that was in regions of homozygosity (ROHs), and the was the expected for an offspring of i and j (McQuillan et al., 2008; de Cara et al., 2013). The following criteria were used to define ROHs and IBD-segments: i) a minimum physical length of 3.75 Mb, ii) a minimum of 38 consecutive homozygous SNPs, and iii) a maximum gap of 500 kb between two consecutive SNPs. Considering the inverse exponential distribution for the length of autozygous segments (Fisher, 1954), the and were expected to capture realised IBD over 13.3 ancestral generations.

For each genome-wide parameter , the annual rate of change was computed as the opposite of the slope of the regression of) on year of birth. The annual rate was multiplied by to obtain the rate per generation.

Region-specific inbreeding
Region-specific inbreeding was quantified with positional inbreeding coefficients (), following Kim et al. (2013). The was calculated per period of three years and was defined as the proportion of animals in the period for which marker k was encompassed by a ROH.

Results and discussion

Genome-wide inbreeding and kinship
Inbreeding and kinship levels for AI-bulls steeply increased since 2011 and 2009, respectively (Figure 2). Despite the reduction in generation interval, inbreeding and kinship rates increased from 0.11-0.72% in 2003-2009 to 1.58-2.52% in 2009-2015 (Table 1). Inbreeding

and kinship rates for cows also increased with GS (to 0.79-1.14% in 2009-2017), although the increase was less pronounced than for AI-bulls. The increase for cows was also more gradual than that for AI-bulls and occurred a few years after the increase for AI-bulls.
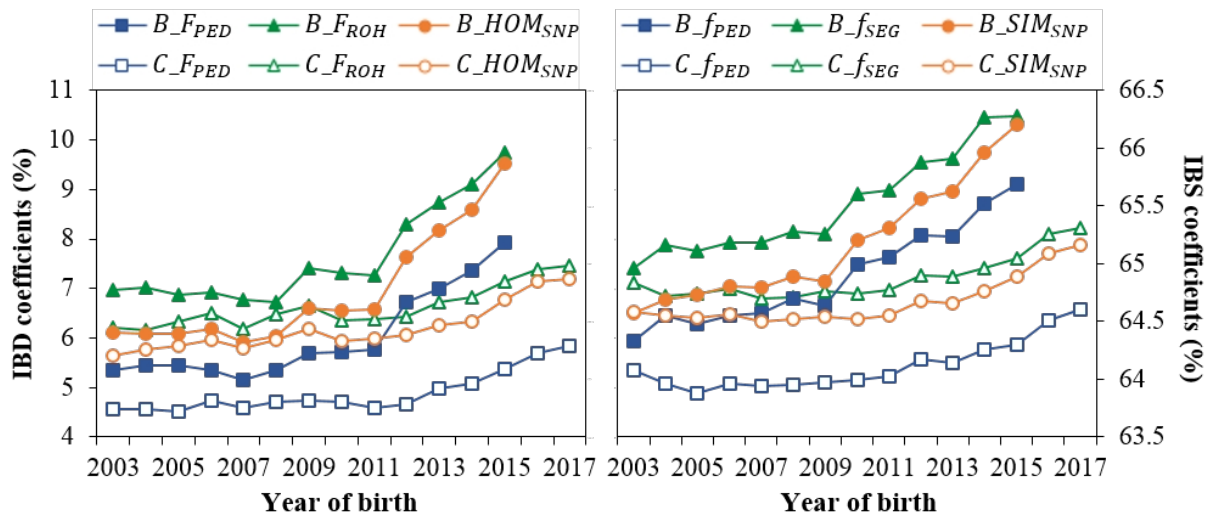

Figure 2. *Average genome-wide inbreeding (left) and kinship (right) for AI-bulls (B) and cows (C) by year of birth. and : genealogical inbreeding and kinship (expected IBD); and : segment-based inbreeding and kinship (realised IBD); and : marker-by-marker homozygosity and similarity (IBS).*

Table 1. *Rates of change per generation before and after 2009 for AI-bulls and cows.*

	AI-bulls		Cows	
Parameter	'03-'09	'09-'15	'03-'09	'09-'17
	0.11	1.70	0.19	0.79
	0.15	1.85	0.39	0.71
	0.28	2.52	0.48	0.93
	0.62	1.58	-0.13	0.95
	0.58	1.70	-0.14	0.89
	0.72	2.42	-0.11	1.14

Years are abbreviated (e.g.'09 = 2009). and : genealogical inbreeding and kinship; and : segment-based inbreeding and kinship; and : marker-by-marker homozygosity and similarity.

Rates of IBS (i.e. and) were higher than rates of IBD, especially since the introduction of GS for AI-bulls (Table 1). This suggests that relationships due to more distant common ancestors are increasing faster with GS than inbreeding and kinship due to more recent common ancestors. The relatively fast increase in IBS could be explained by the fact that selection in the current scheme is based on GEBVs, while inbreeding is restricted using genealogical coefficients. As demonstrated by Sonesson et al. (2012), the rate of genomic inbreeding - quantified in their study with IBS corrected for allele frequencies in the base population - may largely exceed the genealogical restriction in such a scheme.

Region-specific inbreeding

There was substantial variation in levels of across the genome. The most pronounced peaks were observed on chromosome 10, with values of up to 34% and 28% for AI-bulls in 2012-2014 and cows in 2015-2017, respectively (Figure 3). Not only levels, but also rates of inbreeding showed heterogeneity across the genome. Interestingly, there were various regions (e.g. around 50-60 Mb on chromosome 4) that showed a striking increase in since the introduction of GS, especially in AI-bulls. These peaks could be the result of a more localized selection pressure with GS compared to traditional BLUP selection (Sonesson et al., 2012; Heidaritabar et al., 2014). As the pattern of for cows follows the pattern for AI-bulls, the peaks observed in AI-bulls may be used to predict future peaks in the cow population.
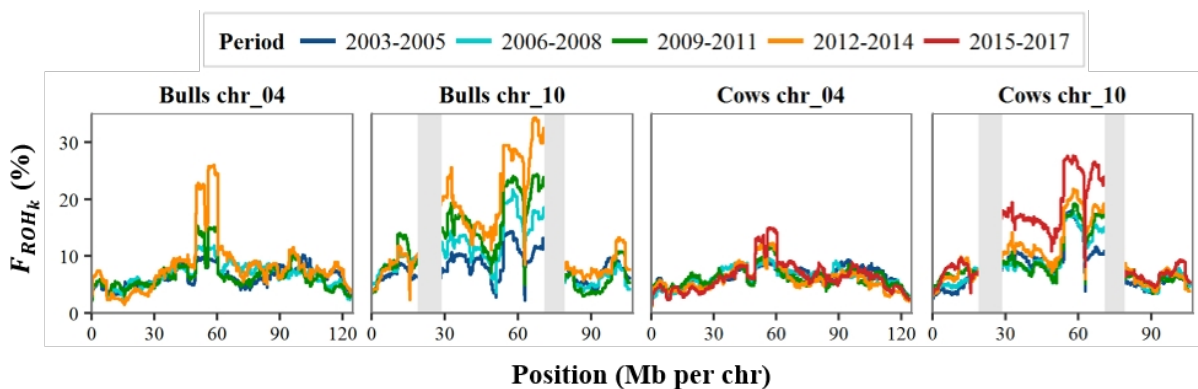

Figure 3. *Positional ROH-based inbreeding () across three-year periods for chromosome 4 and 10 in AI-bulls and cows. Grey bars cover gaps between consecutive markers of >500 kb with an additional 3.75 Mb on both sides of the gap.*

Conclusions

The introduction of GS has been accompanied by a substantial increase in rates of inbreeding and kinship in the Dutch-Flemish HF breeding program and cow population. Levels of IBS, which include both recent and distant relatedness, increased faster with GS than levels of IBD, which include only recent inbreeding and kinship. Substantial heterogeneity in accumulation of inbreeding across the genome over time was observed, with specific regions showing a strikingly fast increase in inbreeding since the implementation of GS. These findings emphasize the need for efficient genomic management of inbreeding in GS-schemes.

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