GENOMIC ANALYSIS OF THE EFFECTS OF INBREEDING ON SIZE AND REPRODUCTIVE TRAITS ACROSS FOUR GENERATIONS OF NELLORE-ANGUS CROSSBRED CATTLE

A Thesis

by

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ABSTRACT

The objective of the study was to evaluate genomic based inbreeding within a closed population of Nellore-Angus crossbred cows and the effect it has on growth and reproductive traits. From 2003 to 2018, cows were evaluated for heifer weight (649 heifers averaging 354.11 (SD = 40.366) kg), cow weight (1,460 records averaging 470.09 (SD = 57.527) kg), and weaning rate (1,647 records averaging 0.79 (SD = 0.407)). Inbreeding coefficients (F) were derived from the genomic relationship matrix (GRM) and runs of homozygosity (ROH). Average F_{ROH} and F_{GRM} across all cows was 0.064 and 0.046 respectfully. There was a moderate correlation between F_{ROH} and F_{GRM} (r = 0.416) with a 95% confidence interval of (0.347, 0.481). When heifer weight was regressed on F_{GRM}, estimates of regression coefficients indicated inbreeding depression (0.727 ± 0.3491 kg and 1.020 ± 0.3210 kg with every 1% increase in inbreeding from models that included pedigree matrix or the GRM, respectively). When regressed on F_{ROH}, a 1% increase in inbreeding showed a depression of 0.316 ± 0.0073 kg without inclusion of additive genetic effects. There was no significant inbreeding depression indicated by regression of cow weight on either form of inbreeding coefficient. Most importantly, there was a 0.05 ± 0.01 decrease in cow weaning rate through 5 years of age corresponding to a 1% increase in $F_{ROH.}$ When regressed on F_{GRM}, there was no depression in weaning rate due to inbreeding. The inclusion of inbreeding within a herd can increase uniformity but could be at the cost of herd performance which was significantly impacted by weaning rate.

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The analyses depicted in the Materials and Methods were conducted with the guidance of Dr. Romdhane Rekaya and Dr. Pattarapol Sumreddee of the Department of Animal and Dairy Science at the University of Georgia.

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1. INTRODUCTION

The use of inbreeding has occurred throughout many livestock operations to establish uniformity and fix desirable characteristics; however, there is often a corresponding loss of fitness and performance. This is due to an increase in homozygosity throughout the genome and the accumulation of detrimental alleles. This increase in homozygosity is due to an animal receiving the same genomic material (DNA) from each parent. In order to assess the level of inbreeding, Wright (1922) proposed a method to determine the relatedness of an individual's parents based on pedigree, that is, twice the inbreeding coefficient (*F*). However, the accuracy of this method corresponds to the completeness of pedigree information. An alternative way to determine inbreeding coefficient is through the use of an individual's genomic information. This is done through the use of single nucleotide polymorphism (SNP) markers identifying the autozygosity of an animal, which is also considered alleles that are identical by decent (IBD). This autozygosity is the loci that are homozygous within an individual due to being IBD. Animal autozygosity can then be assessed to identify segments that exceed a preset limit of autozygosity which supports estimation of inbreeding (Broman and Weber, 1999; McQuillan et al., 2008). These segments of autozygosity are referred to as runs of homozygosity (ROH). Characterization of the variation in length and distribution of ROH segments within and across chromosomes in the genome may permit a better understanding of the occurrence and purging of deleterious alleles, and could lead to a more comprehensive dissection and understanding of the depression of reproductive traits due to inbreeding. The objectives of this project are to: 1) characterize runs of homozygosity of a closed Nellore-Angus population, 2) quantify and compare estimates of genomic relationship matrix based inbreeding coefficients with estimates of inbreeding though runs of homozygosity, and 3)

evaluate the correspondence of runs of homozygosity with weight of cow one year post weaning, weight of cow at weaning of her calf, and cow weaning rates.

2. LITERATURE REVIEW

2.1 Inbreeding and Inbreeding Depression

Inbreeding is defined as the mating of two related individuals (Wright, 1922). The inbred offspring will have many alleles that are IBD due to transmitting the same alleles by related parents. Homozygosity is not entirely due to inbreeding. This autozygosity can be due to many different effects such as genetic drift, bottlenecks, natural and artificial selection, as well as inbreeding (Curik et al., 2014). Wright (1922) stated that if the percentage of homozygosis can be calculated, the most natural coefficient of inbreeding can be derived. Presently, the standard calculation of inbreeding is through the use of Wright's inbreeding coefficient. Charlesworth and Charlesworth (1987) stated that Wright's inbreeding coefficient was originally used to express the correlation of additive genetic values between the uniting of two gametes; however, the use of this coefficient has changed in that it determines the probability of an individual having two alleles that are IBD. Wright's inbreeding coefficient, however, is just an estimate of the probability alleles are IBD since it does not include identification of transmitted alleles (Hedrick and Kalinowski, 2000). Hedrick and Kalinowski (2000) stated that this coefficient requires the knowledge of certain relatedness among the founders of an animal's pedigree that most of the time is unknown. It is assumed that these founders are non-inbred animals as well as unrelated, both of which are likely incorrect. Inbred animals tend to have more detrimental alleles in homozygous genotypes which can cause phenotype alterations and even death (Charlesworth and Willis, 2009). When closely related animals are mated, there are more alleles that are IBD, which can result in a loss of performance and fitness as possible detrimental alleles begin to accumulate. It has been shown that in humans, the degree of homozygosity across the genome is greatly increased in individuals that

are born of consanguineous marriages being second cousins or closer (Broman and Weber, 1999; Woods et al., 2006). Wright (1922) stated that there are two effects of inbreeding which need to be noted: a decline in all vigor and an increase in uniformity of the inbred herd. The decline in vigor and corresponding loss of performance is known as inbreeding depression. In populations of finite size under selection, inbreeding is unavoidable, and results many times in consequences such as decrease in performance traits, accumulation of recessive lethal alleles, and the decrease in genetic variation (Bjelland et al., 2013; Kim et al., 2015). Hedrick and Kalinowski (2000) stated that inbreeding is a major concern in endangered species due to finite or small population size. With lower genetic variation between animals due to inbreeding, the mean fitness of populations is decreased causing decreased population growth rates as well as long-term adaptability (Lacy, 1997). These populations with low genetic variation have increased homozygosity across the genome, and in some cases this results in lower fitness. McQuillan et al. (2008) also stated that the mechanism of these detrimental effects is due to the autozygosity across the genome increasing from related mating. In any population where consanguinity is normal or population sizes are small or isolated, such as endangered species or humans, the frequency of deleterious alleles are increased through the rising level of homozygosity (Hedrick and Kalinowski, 2000; McQuillan et al., 2008). Charlesworth and Willis (2009) reported that increases in homozygosity can cause a decrease in fitness in two distinct ways. The first is due to increased recessive lethal alleles in homozygous genotypes throughout the genome, and the second is due to increased homozygosity at loci where there is overdominance as the heterozygote has an advantage. Lacy (1997) stated that there is no evidence that there are any mammalian species that do not suffer the consequences of inbreeding. Dickerson (1973) developed animal breeding theory that mathematically predicted the inbreeding depression across a variety of traits.

2.2 Runs of Homozygosity

McQuillan et al. (2008) explained that pedigree based inbreeding coefficients have a disadvantage for two reasons: 1) meiosis is an extremely random event where on average half the genetic material is maternal and the other half is paternal, 2) inbreeding coefficients based on pedigree are estimates of alleles that are IBD assuming the founding generation is unrelated. A genomic determination of inbreeding is through the evaluation of runs of SNP homozygosity. Runs of homozygosity are uninterrupted segments of homozygous loci that occur throughout a genome (Gomez-Raya et al., 2015). Runs of homozygosity can be used to estimate inbreeding coefficients of animals; this may be more reliable than utilizing incomplete pedigrees in pedigree-based inbreeding (McQuillan et al., 2008). Purfield et al. (2012) found that across many different Bos taurus bovine breeds, ROH are persistent and correspond with the degree of pedigree consanguinity. Even though loci can be homozygous through many forces that change allele frequencies, high density SNP arrays are extremely effective in discriminating loci that have identical alleles due to outside forces from loci that have alleles that are identical by decent (Howrigan et al., 2011). Gibson et al. (2006) explained that in certain individuals, long segments of uninterrupted homozygous markers can be found, and this is due to parents passing the same chromosomal segment to their offspring.

It is well understood that autozygosity occurs within the genome through the inheritance of identical alleles by related parents, but it is also important to consider the result of linkage disequilibrium, which can also lead to homozygosity (Broman and Weber, 1999). Linkage disequilibrium is the inheritance of alleles together more often than expected under independent and random allelic segregations (Lewontin and Kojima, 1960). It is important to note that

homozygous segments resulting from linkage disequilibrium are not considered IBD, thus not autozygous (Broman and Weber, 1999). This was deduced by Broman and Weber (1999) when they found that homozygosity in linkage disequilibrium transpires as the result of ancestral haplotypes occurring in a finite population, due to the result of mating very distantly related individuals. Broman and Weber (1999) also stated that linkage disequilibrium only causes short segments of homozygosity; this was consistent with the results of Purfield et al. (2012), who stated that the smaller ROH segments may suggest relatedness of ancient populations that is unaccounted for in pedigree based inbreeding due to the lack of information on these older animals.

2.3 Relationship of ROH and Inbreeding

The variation of length in the ROH provides a way to assess the level of inbreeding in the animal or reference population (Curik et al., 2014), as well as infer the number of generations of inbreeding that has occurred (Marras et al., 2014). Inbreeding coefficients based on ROH may compensate or offset the incompleteness of pedigrees. However, short homozygous segments that are not IBD can occur by chance; this may result in some estimation error (Marras et al., 2014). There is a strong correlation between the inbreeding coefficient based on ROH (F_{ROH}) and the inbreeding coefficient based on pedigree (F_{PED}) (Purfield et al., 2012; Sumreddee et al., 2019b). Through analyzing different lengths of ROH, Marras et al. (2014) observed that correlations are stronger for F_{ROH} with F_{PED} than F_{ROH} with inbreeding coefficients calculated from the diagonal elements of the genomic relationship matrix (F_{GRM}). Estimates of F_{GRM} were in general larger than F_{PED} or F_{ROH}. Through the increased use of larger marker density arrays, inbreeding coefficients based on ROH will be more precisely estimated to determine alleles that are IBD from recent to ancient inbreeding.

Inbreeding coefficients are a proportion of the heterozygosity that is reduced in an individual through inbreeding, with a parameter space of 0 to 1 (Wright, 1922). Inbreeding coefficients based on ROH can be estimated as the total length of ROH in the genome divided by the total length of the autosomal genome (Dixit et al., 2020). The lengths used in this calculation are the physical distance in millions of base pairs (Dixit et al., 2020). The lengths used may also be the number of continuous homozygous SNP (Gomez-Raya et al., 2015). These measurements are highly correlated allowing them to be used interchangeably (Gomez-Raya et al., 2015).

Inbreeding coefficients estimated with ROHs may provide information for management of inbreeding as genome-assisted breeding (Pryce et al., 2012). Through the use of assisted breeding schemes, Pryce et al. (2012) determined in a herd of Australian dairy sires, that controlling the inbreeding of progeny has an economic impact that far exceeds the penalty of the reduction of the estimate of genetic merit (Australian Profit Ranking index). This economic impact is because ROH can detect inbreeding at different time periods, for example, recent or ancient. This information may enhance decision-making strategies to control the herd's autozygosity (Pryce et al., 2012).

3. MATERIALS AND METHODS

3.1 Animals

All animal procedures were approved by the Texas A&M University Institutional Animal Care and Use Committee in multiple Animal Use Protocols, and previously collected data were utilized for this thesis. The data used in this project encompass four generations of a closed population of primarily Nellore-Angus crossbred cattle (Riley et al., 2014). Briefly, the first generation of cattle (Cycle 1) was produced by embryo transfer with the mating of five F_1 sires with 14 F_1 dams. All founders were sired by Nellore bulls and out of Angus cows. Four of the five sires, one sire only had 2 calves used for the project, were also mated with Brahman-Hereford crossbred cows (natural mating) to produce an additional group of Cycle 1 animals. The Cycle 1 cows (n = 302), approximately two-thirds of the calves were out of the embryo transfer matings and one-third were out of the natural mating, were fall- and spring-born from 2003 through spring 2007. All females (and those in subsequent generations) were exposed for mating with Angus bulls as yearlings. Cycle 1 females from two of the four sires were exposed to Cycle 1 bulls out of the other two sires from 2008 to 2012 to produce second generation animals, and either Angus or Hereford bulls thereafter. Second generation cows (Cycle 3; n = 285) were spring-born from 2009 through 2013. Cycle 3 females were mated to Cycle 3 bulls in 2013 and 2014 to produce the third generation (Cycle 4) females (n = 105). Cycle 4 females were exposed for breeding to Cycle 4 males in 2017 and 2018, and the fourth generation (Cycle 5) animals were produced from those matings. Only Cycle 5 females born in 2018 (n = 29) were old enough to contribute records to this study; only their first calving data recorded for this study as offspring were spring-born in 2020.

The Cycle 1, 3, and 4 bulls used in this project were chosen based on pedigree (sire information was not always available in later generations) to avoid inbreeding as much as possible.

3.2 Traits

The traits analyzed in this study were weight at one year after weaning, cow weight at weaning, and cow weaning rate. In this study, heifer weight is defined as one year post weaning. This is due to most of the cows being born in the spring, weaned in the fall, and have yearly weights taken each fall. A total of 4,029 weight measurements were taken from 721 cows across all generations. The heifer weight analysis consisted of 588 females ranging in age from 500 to 650 days, with mean of 578 days, or approximately 1 year 7 months. Cow weights (excluding that first weight) consisted of 503 cows with records for the next 3 years, that is, at approximately 3.5, 4.5, and 5.5 years of age. The Cycle 5 cows had only heifer weights available at the time of analyses. Summary statistics for these weight traits are shown in Table 1.

Weaning rate was created by assigning values of 0 and 1 to cows exposed to bulls for breeding in the most recent breeding season that failed to wean or weaned a calf, respectively. The first three opportunities to conceive were analyzed; records from any animal with less than three production years were removed. Cycle 5 animals were not included as there were not 3 records to be analyzed. Cows were culled after two failures to wean a calf. Average weaning rates of cows in each cycle are shown in Table 1, and phenotypic records based on year are shown in Table 2.

Table 1. Average weights, kg (SD), of females per cycle at production timepoints and weaning rates

Cycle	Heifer wt	Average cow weight	Weaning rate
1	371.2 (42.01)	505.5 (62.38)	0.82 (0.382)
3	348.4 (34.49)	464.5 (54.67)	0.78 (0.414)
4	330.6 (37.97)	470.8 (55.36)	0.72 (0.451)
5	339.6 (28.43)		

Table 2. Cow production value as number of calves weaned per year per cow birth year

Cycle	N*	Birth yr	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
1	38	2003	21	31	35	33	28	28	27	26	24	15	16	5	6	5	4	304
	74	2004		42	57	62	54	57	54	45	46	26	34	20	19	16	10	542
	81	2005			55	68	61	66	67	61	57	36	48	23	18	14	10	584
	76	2006				37	47	54	51	50	46	41	35	18	14	13	10	416
	34	2007					17	24	24	24	20	18	18	8	6	7	6	172
Total	**303**		**21**	**73**	**147**	**200**	**207**	**229**	**223**	**206**	**193**	**136**	**151**	**74**	**63**	**55**	**40**	**2018**
3	40	2009							31	32	28	28	29					148
	82	2010								68	44	52	26					190
	78	2011									51	58	45					154
	78	2012										27	43	15	16	14	12	127
	18	2013																0
Total	**296**								**31**	**100**	**123**	**165**	**143**	**15**	**16**	**14**	**12**	**619**
4	71	2014												35	33	47	37	152
	41	2015													26	33	30	89
Total	**112**													**35**	**59**	**80**	**67**	**241**

*Number of cows exposed

3.3 Genotypes

Across all generations 1,752 animals (including males) were genotyped using low and medium density single nucleotide polymorphism (SNP) arrays (26K and 50K). All 417 Cycle 1 males and 317 Cycle 1 females had genotypes from version 1 of the BovineSNP50 array (Illumina Inc., San Diego, CA) with approximately 53,000 SNP. Cows from Cycles 3 (n = 358 females and 49 males) and Cycle 4 (n = 124 females and 66 males) had genotypes from the IDB V.3 array with approximately 54,000 SNP (Weatherbys Scientific, Newhall, Naas, Co. Kildare, Ireland). Cycle 3 males (n = 223) and Cycle 4 males (n = 65) had genotypes from the Illumina GGP Bovine LD 26K Array (Illumina, Inc., San Diego, CA). All Cycle 5 animals, including 59 females and 74 males, were genotyped using the GGP 50K array (Neogen Genomics, Lincoln, NE). Genotypes were removed for markers and animals with call rates less than 90%, markers with a minor allele frequency less than 5%, and deviations ($P < 0.0001$) from Hardy-Weinberg proportions (Wigginton et al., 2005). The SNP across these arrays that were in common positions were kept to combine the genotype files. Animals with the low-density genotypes, as well as missing genotypes, were imputed to the 50K SNP chip panel using the software FImpute version 3 (Sargolzaei et al., 2014). This program imputes the SNP that are not in the reference, higher density panel, while keeping the common SNP in the lower density panel. After imputation and quality control, a total of 1,728 animals (including males) with 28,133 SNP remained. Genetic information on these animals was used to calculate two different estimates of inbreeding. The first used the identification of autozygosity across chromosomes, ROH, to estimate genomic inbreeding. The ROH of each individual were estimated with PLINK v 1.9 (Purcell et al., 2007). Parameters in PLINK v1.09 were set as: (1) only autosomal chromosomes (--chr-set 29), (2) a minimum density of 1 SNP per 500 kb (--homozyg-density 500), (3) maximum gap of 500 kb between consecutive

SNP (--homozyg-gap 500), (4) minimum length of 0.5 Mb for ROH segments (--homozyg-kb 500), (5) minimum of 10 SNP in ROH (--homozyg-snp 10), (6) allow maximum of 2 heterozygote SNP within ROH sliding window for any genotyping errors or recent mutations of alleles (--homozyg-window-het 2). These parameter settings accomplish the removal of short, non-autozygous ROH (< 0.5 Mb) caused by linkage disequilibrium (Purfield et al. 2012; Ferenčaković et al, 2013). The inbreeding coefficient based on ROH was then calculated for each animal by dividing the total length of homozygosity ($\sum L_{\mathrm{ROH}}$) by the total length of the genome assessed (L_{TOTAL}) through the genotyped autosomal SNP (McQuillan et al., 2008):

$$F_{\mathrm{ROH}} = \frac{\sum L_{\mathrm{ROH}}}{L_{\mathrm{TOTAL}}}$$

The total length of the genome assessed was 2,542,303 kb.

Inbreeding was also calculated using the covariance of an animal with itself, the variance of the animal as diagonal elements of the genomic relationship matrix (GRM) computed as:

$$GRM = \frac{ZZ'}{2\Sigma p(1-p)}$$

where p is the allelic frequency of the genotyped population, and Z is the incidence matrix for markers (VanRaden et al., 2008). This inbreeding coefficient, F_{GRM}, is obtained by subtracting 1 from the diagonal elements of this matrix. Estimation of this matrix was done with the BLUPF90 family programs (Misztal et al., 2002).

3.4 Statistical Analyses

Associations of inbreeding coefficients estimated the two ways, F_{ROH} and F_{GRM}, were assessed with Pearson correlation coefficients. The association of inbreeding coefficients with the evaluated traits was assessed by inclusion of each inbreeding coefficient estimate (separate

analyses, that is not together) as a linear covariate in distinct analyses, including a fixed model, and when modeling the genetic covariances as A (pedigree based relationship matrix) or G (GRM) as described by VanRaden (2008).

The model for cow weight included year of record, parity number, and pregnancy status. Year of record ranged from 2006 to 2019. Parity consisted of 3 categories consistent with the 3 record of weights. Pregnancy status was broken into 6 categories and were constructed using the actual birth dates of calve using 283 days as standard gestation length: 1) non-pregnant (n = 115), 2) less than 100 days (n = 127), 3) between 100 to 150 days (n = 783), 4) greater than 150 days (n = 151), 5) unknown status (no birth date recorded for offspring) in 4.5-year-olds (n = 99), 6) unknown status (no birth date recorded for offspring) in 5.5-year-olds (n = 77). The animals in the categories of unknown status for 4.5- and 5.5- year-olds gave birth to a calf the next year, but the birth date of the calf was unknown, therefore estimation of days bred could not be calculated. There were no unknown statuses for the 3.5-year-old group. In this study, 87% of all weight records were in categories 1 through 4.

A Bayesian threshold model was employed in analyses of weaning rate with the effects of birth year of cow, production year (first, second, or third, corresponding to heifers, 3-, and 4-year-olds, respectively), breeding value, and permanent environmental effect. The threshold model used a Markov chain Monte Carlo algorithm, Gibbs sampling, to estimate variances. Variances were estimated using 150,000 samples, with a burn-in of 50,000 samples discarded, and thereafter keeping every 100th sample. Estimates of regression coefficients were based on Gibbs sampling with 30,000 samples, with a burn-in of 10,000 samples discarded, and keeping every 20th sample thereafter. Analyses were additionally conducted regressing weaning rate on F_{ROH} calculated based upon the ROH unique to each chromosome. Analyses were conducted using various

packages and functions of R Statistical Software (R Core Team, 2018) and BLUPF90 family of programs (Misztal et al., 2002). Phenotypic records were recorded for weaning rate as number of calves weaned and are shown in Table 2.

4. RESULTS

4.1 Inbreeding Coefficients

The inbreeding coefficients estimated in this study based on ROH, GRM, and pedigree (F_{PED}), are shown in Table 3, and the correlations between the three estimates in Table 4. Overall, the average F_{ROH} and F_{GRM} were 0.064 and 0.046, respectively. The negative inbreeding coefficients for F_{GRM} were set to zero before all analyses due to animals being less inbred than the average of the population. The estimated Pearson correlation coefficient between F_{ROH} and F_{GRM} indicated a positive, moderate correlation of 0.416 ($P \leq 0.01$) with a 95% confidence interval of (0.347, 0.481).

Table 3. Summary of all inbreeding coefficients

Group	Inbreeding coefficient	N	Mean (SD)	Min	Max
Cycle 1		734			
	F_{ROH}		0.039 (0.0229)	0.000	0.122
	F_{GRM}		–0.002 (0.0422)	–0.117	0.136
	F_{PED}		0.001 (0.0051)	0.000	0.078
Cycle 3		613			
	F_{ROH}		0.068 (0.0285)	0.000	0.217
	F_{GRM}		0.022 (0.0416)	–0.090	0.444
	F_{PED}		0.006 (0.0163)	0.000	0.096
Cycle 4		251			
	F_{ROH}		0.106 (0.0382)	0.016	0.244
	F_{GRM}		0.062 (0.0556)	–0.059	0.514
	F_{PED}		0.009 (0.0257)	0.000	0.148
Cycle 5		129			
	F_{ROH}		0.108 (0.0425)	0.030	0.247
	F_{GRM}		0.404 (0.0463)	0.318	0.580
	F_{PED}		0.004 (0.0184)	0.000	0.137
All		1727			
	F_{ROH}		0.064 (0.0391)	0.000	0.247
	F_{GRM}		0.046 (0.1130)	–0.117	0.580
	F_{PED}		0.004 (0.0154)	0.000	0.148

Table 4. Correlations of inbreeding coefficients

	F_{ROH}	F_{GRM}	F_{PED}
F_{ROH}	1.000	0.416	0.184
F_{GRM}		1.000	0.032
F_{PED}			1.000

4.2 Weight Traits

The variance components estimated in analyses of both traits, and the repeatability of the cow weight model, are shown in Table 5. The regression coefficient of heifer weight on F_{GRM} ($P \leq 0.05$) suggested inbreeding depression (Table 6) as a reduction in weight of 0.727 ± 0.3491 kg and 1.020 ± 0.3210 kg with 1% increase in F_{GRM} when including the A matrix (pedigree relationships) and the G matrix (GRM), respectively. These estimates of regression coefficients were similar to that estimated from the fixed model (–0.316 ± 0.007; Table 6); however, the regression of heifer weight on F_{ROH} using additive genetic effects was not different from 0 ($P > 0.05$). The regressions of cow weight on both F_{ROH} and F_{GRM} were not significant (Table 7).

Table 5. Variance components (SE) for heifer weight and weight as cows

Trait	**Genetic variance**	**Permanent Environmental variance**	**Residual variance**	**Heritability**	**Repeatability**
Heifer Weight	553.0 ± 160.76		307.3 ± 112.23		
Cow Weight	295.5 ± 17.40	1,824.0 ± 140.14	595.1 ± 27.44	0.11 ± 0.008	0.78 ± 0.014

Table 6. Inbreeding depression (estimates of regression coefficients) on heifer weight (kg)

Inbreeding	Number of records	Model	Estimate ($\widehat{\boldsymbol{\beta}}$)	SE	$\widehat{\boldsymbol{\beta}}$ / SE[1]
F_{ROH}	588	Fixed	–0.316*	0.0073	–43.29
		Mixed (A^2)	–0.347	0.4908	–0.71
		Mixed (G^3)	–0.299	0.4048	–0.74
F_{GRM}	588	Fixed	–1.023*	0.0057	–179.47
		Mixed (A^2)	–0.727*	0.3491	–2.08
		Mixed (G^3)	–1.020*	0.3210	–3.18

[1]*t*-statistic = estimated regression coefficient divided by SE.
*$P < 0.05$ when t ($|\hat{\beta}/ SE|$) > 2
[2]A = pedigree-based relationship matrix for breeding effect
[3]G = genomic relationship matrix (GRM) for breeding effect based on VanRaden (2008)

Table 7. Inbreeding depression (estimates of regression coefficients) on cow weight (kg)

Inbreeding	Model	Estimate ($\widehat{\boldsymbol{\beta}}$)	SE	$\widehat{\boldsymbol{\beta}}$ / SE[1]
F_{ROH}	Mixed (A)	1.234	0.8323	1.48
	Mixed (G)	1.314	0.8220	1.60
F_{GRM}	Mixed (A)	–0.442	1.0909	–0.40
	Mixed (G)	–0.544	1.0772	–0.50

[1]*t*-statistic = estimated regression coefficient divided by SE.
*$P < 0.05$ when t ($|\hat{\beta}/ SE|$) > 2

4.3 Reproduction Traits

The overall weaning rate for the 538 cows in this study was 79.3% (1,280 calves weaned of 1,614 cows exposed). The posterior variances estimated with the threshold model are shown in Table 8 along with the trace plots shown in Figure 1. These variances were calculated using Gibbs sampling from the THRGIBBS1F90 program. Estimates of regression coefficients of weaning rate on F_{ROH} were significant and substantially larger than estimates of regression coefficients on F_{GRM},

which did not differ from 0 (Table 9). Estimates of regression coefficients on F_{ROH} were similar for analyses including pedigree based, genomic, or no modeling of genetic relationship. Estimated regression coefficients for chromosomal level F_{ROH} did not differ from 0 for any chromosome with either pedigree-based or genomic based genetic covariance structures.

Table 8. Estimates of variances for weaning rate

Parameter	**Posterior mean (SD)**
Genetic variance	0.016 (0.0148)
Permanent environmental variance	0.012 (0.0115)
Residual variance	1.008 (0.0499)
Heritability	0.016 (0.0138)
Repeatability	0.027 (0.0168)

Sampling criteria used was 150,000 sample, burn-in of 50,000 samples, with every 100th sample kept (n = 1,000)

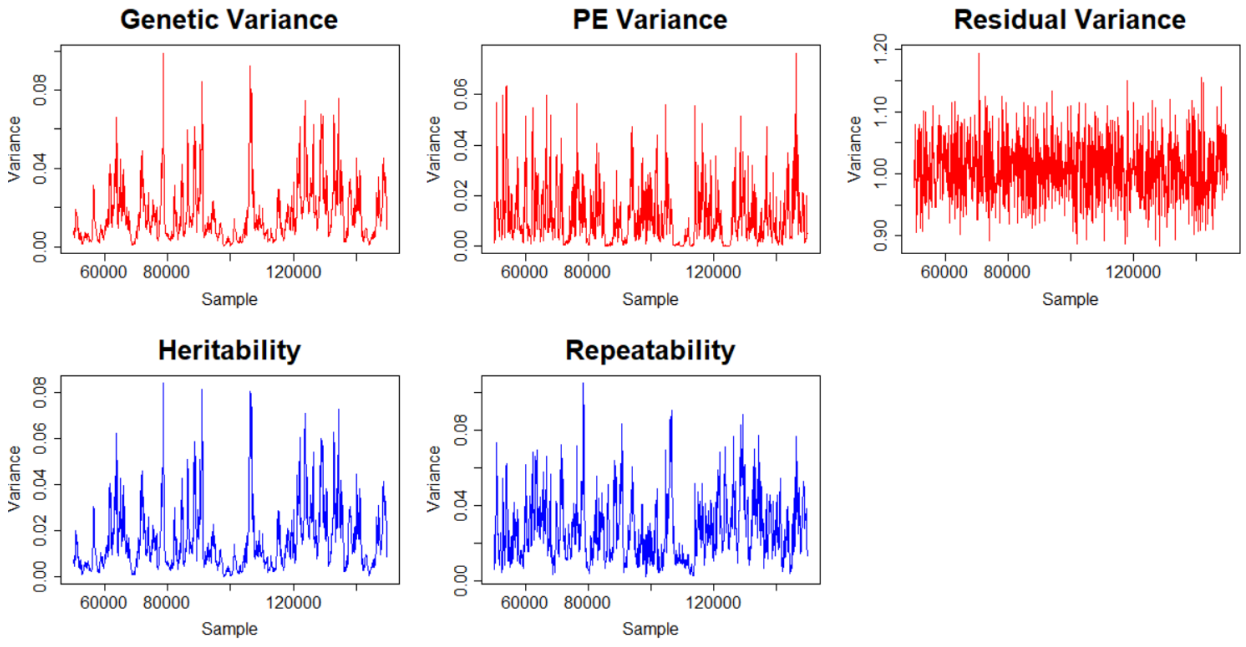

Figure 1. Trace plots of variance components for weaning rate estimated in threshold model. PE Variance = variance of permanent environmental effects.

Table 9. Estimates of regression coefficients on weaning rate

Inbreeding	**Model**	**Posterior mean (SD)**	**Posterior SD 95% CI[1]**
F_{ROH}	Fixed	–0.048* (0.0145)	(–0.0764, –0.0196)
	Mixed (A)	–0.049* (0.0147)	(–0.0779, –0.0203)
	Mixed (G)	–0.047* (0.0144)	(–0.0750, –0.0185)
F_{GRM}	Fixed	0.004 (0.0100)	(–0.0158, 0.0235)
	Mixed (A)	0.004 (0.0102)	(–0.0163, 0.0236)
	Mixed (G)	0.004 (0.0107)	(–0.0170, 0.0250)

[1] 95% confidence interval of posterior standard deviation

5. DISCUSSION

5.1 Inbreeding Coefficients

Much like in previous studies, the correlation between F_{ROH} and F_{GRM} in this study was moderate (Pryce et al., 2014; Sumreddee et al., 2019b). Forutan et al. (2018) reached the same conclusion about correlations between F_{ROH} and F_{GRM} which showed an extremely strong correlation (r = 0.94) in Holsteins. However, Marras et al. (2014) demonstrated that the use of different minimum lengths of ROH used for inbreeding can impact the correlation of F_{ROH} between F_{GRM}. It was concluded that the use of ROH inbreeding coefficients of greater than 8 Mb best represents F_{PED}; however, correlations between F_{ROH} and F_{GRM} were significant for ROH lengths greater than 1 Mb, 4 Mb, and 8 Mb ($P < 0.001$) and 16 Mb ($P < 0.05$; Marras et al., 2014). Sumreddee et al. (2019a) stated that inbreeding can be analyzed by ancient, intermediate, and recent inbreeding by increasing the minimum length of ROH segments and concluded that most of the damaging effects occur with recent inbreeding. The use of a minimum ROH of 0.5 Mb for estimating F_{ROH} in the current study reflect the significance in correlation with F_{GRM} in past studies. (Pryce et al., 2014; Sumreddee et al., 2019b; Marras et al., 2014; Forutan et al., 2018). Mastrangelo et al. (2016) also reported a significance in inbreeding correlation using ROH and GRM in two dairy cattle breeds ($P < 0.001$ and $P < 0.01$), Cinisara and Reggiana respectfully, but concluded that there was no significance in correlation in the dairy breeds Modicana and Italian Holstein. Pryce et al. (2014) and Yoshida et al. (2020) reported that longer ROH indicated more recently inbreeding. Peripolli et al. (2017) concluded that inbreeding estimations based on ROH are more accurate that pedigree-based estimates due to the better detection of recent and past inbreeding along with alleles that are IBD. In the absence of pedigree information, ROH has been proven to be an accurate predictor of inbreeding based on pedigree (Purfield et al., 2012; McQuillan et al., 2008). Thus, the

use of F_{ROH} and F_{GRM} within the study accurately represent the animals inbreeding coefficient without the use of pedigree-based inbreeding (Purfield et al., 2012).

5.2 Weight Traits

Heifer weight decreased as inbreeding (F_{GRM}) increased across generations, as well as regressing on F_{ROH} without the modeling of genetic relationship; however, there was no significant depression when regressing on F_{ROH} when genetic relationship was modeled. Reverter et al. (2017) showed that across 2 different SNP arrays (70K, and 19K) and 2 breeds (Australian Brahman and Tropical Composite), there was a significant decrease in yearling weight as F_{GRM} increased. Reverter et al. (2017) reported inbreeding depression on yearling weight in Brahman and Tropical Composite of 0.514 and 0.579 kg, respectively, when using the 70K SNP panel modeling F_{GRM}. Sumreddee et al. (2019b) reported a depression in yearling weight of 0.458 kg in Hereford cattle when inbreeding was modeled with F_{GRM}, which was slightly lower than results in the present study (1.020 kg depression in heifer weight with 1% increase in F_{GRM}). Although the only detected relationship of F_{ROH} with heifer weight in the present study was without the modeling of genetic relationship (0.316 kg depression in heifer weight with 1% increase in F_{ROH}), Sumreddee et al. (2019b) reported a decrease in yearling weight of 0.923 when regressing on F_{ROH}. However, when limiting their analyses to the low density, 19K array in Tropical Composite cattle, Reverter et al. (2017) reported no relationship of F_{ROH} with yearling weight. The results using the 28K SNP evaluated in this study were reasonably consistent with those of Reverter et al. (2017), despite the differences in breed composition between cows in the current study and the Tropical Composite breed.

No depression on cow weight due to inbreeding using ROH and GRM was detected (Table 6). Burrow (1998) conducted a similar study using Hereford, Shorthorn, Brahman, and Africander

crosses, where cow weight was separated into these categories: first (33 mo), second (45 mo), third (57 mo), and fourth through sixth records (69 – 93 mo). Burrow (1998) reported regression coefficients of –0.52, –1.52, and –0.73 (none significantly different from 0), across second (45 mo), third (57 mo), and fourth through sixth records (69 – 93 mo), respectively, and this appeared to be consistent with results for cow weight in Table 6. However, in the first category, 33 mo, Burrow (1998) reported a significant regression of –2.07 ± 0.882 of weight on a pedigree based inbreeding coefficient. Carolino and Gama (2008) evaluated cow weights in the Portuguese breed Alentejana meeting the criteria of at least 3.5 years of age and at least 3 weights recorded. These were similar criteria used in the present study; however, they reported a significant depression of 0.962 kg corresponding to a 1% increase in inbreeding coefficient based on pedigree.

5.3 Reproduction

The significance of the posterior mean F_{ROH} indicated inbreeding depression of weaning rate of almost 0.05 with each 1% increase in F_{ROH}. When using pedigree to determine inbreeding coefficients, MacNeil et al. (1989) reported a smaller decrease of 0.0124 ($P < 0.05$) in weaning rate of Hereford cows. When analyzing conception rate, Bjelland et al. (2013) reported that for every 1% increase in F_{ROH} and F_{GRM}, there was a decrease of 0.82% and 0.53% respectfully in Holstein cows. Sumreddee et al. (2019b) reports that ROH can be used to find chromosomes that impact the production of an animal based on traits, and has concluded that birth weight, weaning weight, yearling weight, and average daily gain all had at least one chromosome that caused a significant depression on these traits. Martikainen et al. (2018) also reported a significance of chromosomal level inbreeding based on ROH through interval from first to last insemination, nonreturn rate, and interval from calving to first insemination in Finnish Ayrshire heifers and cows using first 3 parities.

However, in the present study there was no significant evidence that a specific chromosome impacted the weaning rate of cows.

6. SUMMARY AND CONCLUSION

Understanding the effects of inbreeding is important in livestock production. As inbreeding is increased, often a loss of performance is observed. The analyses in this project showed the inbreeding levels in a herd of crossbred Nellore-Angus cattle evaluated through the use of ROH had some detrimental impacts on growth and reproductive traits. Heifer weight was decreased by 0.727 and 1.020 kg when regressed on F_{GRM} with inclusion of pedigree matrix and GRM, respectfully, and a decrease of 0.316 kg when regressed on F_{ROH} without modeling additive effects. Weaning rate also had a decrease of approximately 0.05 with a 1% increase in F_{ROH}. As genomic information is becoming more useful and widely used, inbreeding estimates based on ROH could become an important component of genetic management decisions of an operation.

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