Effect of inbreeding in productive traits in Nellore cattle

G. Mamani\(^1\), B.F. Santana\(^1\), G. Oliveira Jr\(^2\), E.C. Mattos\(^3\), R. Ventura\(^1\), J.P. Eler\(^1\), G. Morota\(^1\) & J.B.S Ferraz\(^1\)

\(^1\)Universidade de São Paulo, Departamento de Medicina Veterinária, Av. Duque de Caxias Norte 225 - Campus da USP, 13635-900, Pirassununga, São Paulo, Brazil
gerardo.mamani@usp.br (Corresponding Author)
\(^2\)CRV Lagoa, Rod. Carlos Tonani, km 88, Sertãozinho, São Paulo, Brazil
\(^3\)University of Nebraska-Lincoln, Department of Animal Science, Lincoln, NE 68583-0908 USA

Summary

Inbreeding coefficients were estimated using the diagonal elements of genomic matrix (F\(_{GRM}\)), runs of homozygosity (F\(_{ROH}\)), and pedigree data (F\(_{PED}\)) of a Nellore cattle population. Genotypic data were obtained using a panel of 700,000 SNPs, out of a total of 2,569 animals. The genomic matrix was calculated using the VanRaden (2008) formula and the runs of homozygosity were calculated using the Plink program. The noticeable peaks on chromosome 7, 12, and 21 present hotspots of autozygosity (> 40%) putatively hovering selective pressure. The pedigree had 1,535,678 animals. The mean values for F\(_{PED}\), F\(_{ROH}\) and F\(_{GRM}\) were 0.48%, 6.05% and 0.96% respectively. Indicating that the pairings between relatives is reduced in this population. Using one mixed model we found a negative effect of F\(_{ROH}\) on postweaning weight gain, muscul arity and conformation and a negative effect of F\(_{PED}\) in the postweaning weight gain. In the rest of the studied traits, we found no effect.

Keywords: inbreeding depression, genomic relationship matrix, pedigree, runs of homozygosity.

Introduction

Nellore cattle (Bos indicus) make up 90% of the Zebu cattle population in Brazil, which is the second largest beef cattle producer in the world. Inbreeding is the result of matings between related individuals, resulting in progeny with less heterozygosity. This creates more pairs of homozygous genes than the average population (Lush, 1945). In a population subject to selection or a conserved population with a smaller effective population size, levels of inbreeding tend to increase in each generation. Therefore, it is necessary to monitor inbreeding levels to establish the management criteria in the population. Increased inbreeding in the population lead to the presentation of prepotency, recessive genetic defects, and inbreeding depression. Inbreeding depression is the decrease in the average of productive, reproductive and survival traits in a population due to inbreeding.

The measure of inbreeding, the inbreeding coefficient, refers to the probability that an individual inherits the same ancestral alleles at a given locus (Wright, 1922). It can be estimated through pedigree data, which is an estimator of identical alleles by descent (IBD). Inbreeding coefficients calculated in this way are called pedigree inbreeding coefficients (F\(_{PED}\)). However, pedigree inbreeding coefficient have several disadvantages. First, they fail to grasp the influence of relationship among the founders of the population base. Second, they are equal to the expected proportion of the genome that is IBD and do not take into
account the nature of random recombination. Third, pedigree errors are common due to misinterpretation, misidentification, and incorrect data recording. Finally, they assume that the entire genome is a neutral selection and does not take into account potential biases resulting from selection (Ferenčaković et al., 2011). These problems restrict the use of pedigree inbreeding coefficients to populations with large amounts of data accumulated by several generations, which is not common in livestock populations.

In this situation, inbreeding coefficients can be estimated using either the genomic matrix (VanRaden, 2008) or runs of homozygosity (McQuillan et al., 2008), which are realized values of homozygosity instead of probabilities as with pedigree inbreeding coefficients. This can elucidate the genetic basis of inbreeding depression that until now was not clear. In Nellore cattle there is literature with different values of the impact of inbreeding on the traits of economic importance. However, studies based on genomic inbreeding coefficients are few. The objective of this work is to estimate the effect of inbreeding through inbreeding coefficients calculated by pedigree and genomic data on Nellore cattle.

**Material and methods**

**Phenotypic and genotypic data**

We analyzed 8 traits to investigate the impact of inbreeding depression: Birth weight (BW), weaning weight (WW, measured at 210 days of age), postweaning weight gain (PWG, weight gain from weaning to 18 months old), hip height (HH, measured at the croup at 15 months of age), scrotal circumference (SC, measured at 550 days of age), yearling visual scores like conformation at 18 months of age (CON, evaluate the development of the round, back, and shoulder, with scores varying from 1 to 6), finishing at 18 months of age (FIN, evaluate the capacity of animal to reach to minimal degree of carcass ), musculature at 18 months of age (MUS, the development of muscle mass observed in point such a forearm, crops, loin and the especially in the quarter, with score varying from 1 to 6 ). The structure of data is summarized in the Table 1.

A total of 2,569 Nellore cattle were provided by the Genetic Breeding Program of Agro-Pecuaria CFM Ltda. located in São Paulo, Mato Grosso, and Goiás in Brazil. These herds have commercial purposes for sale of both meat animals and genetically-evaluated sires, raised under a pasture system without supplementation. These animals were genotyped with 770K BovineHD Genotyping BeadChip assay (Illumina Inc., San Diego, CA). Missing genotypes were imputed by the program FIImpute (Sargolzaei et al., 2014). Genotypes with call rates lower than 95% for both marker and sample were discarded in the quality control process. In addition, removing monomorphic SNPs and ones that deviated from Hardy Weinberg equilibrium (Fisher's exact test p-value<1x10-9) resulted in 663,545 SNPs on autosomes left for the subsequent analysis.

**Detecting runs of homozygosity**

Segments of ROH were computed by PLINK software (Purcell et al., 2007) and defined as follows: SNP threshold to call a ROH (50 SNPs), minimum segment length (1Mb), the minimum SNP density (1 SNP for every 50 kb), allowable maximum gap between two consecutive SNPs (500 kb), heterozygote allowance (n=1), missing SNP allowance (n= 0), and window threshold to call a ROH (0.05). We computed a locus specific autozygosity score for each SNP, which is defined as a proportion of animals carrying at least one ROH at that
locus. This is given by: , where \( n \) is the total number of animals and \( m \) is the 0 or 1 indicator variable expressing absence or presence of ROH at that locus (Kim et al., 2013).

**ROH derived estimates of genomic inbreeding coefficient (\( F_{ROH} \))**

Macquillan et al. (2008) proposed to estimate each individual’s inbreeding coefficient from the fraction of one’s genomic region encompassed by ROH. Hereinafter this is referred as \( F_{ROH} \) and for each animal this is given by: , whereas the total number of ROH segment for animal, is the length of \( j_h \) ROH, and \( 7 \) is the total coverage of the genome given by the SNPs.

**Genomic relationship matrix derived estimates of genomic inbreeding coefficient (\( F_{GRM} \))**

The genomic relationship matrix (G) was used for estimating the inbreeding coefficient using the formula of VanRaden (2008). This matrix was calculated by: , where is the genotype matrix containing the values for homozygotes, for heterozygotes, or for opposites homozygotes, and is the reference allele frequency at locus . The inbreeding coefficient was estimated using the diagonal elements of G minus one.

**Pedigree derived estimates of pedigree inbreeding coefficient (\( F_{PED} \))**

The pedigree data of 1,599,222 animals was used to compute the pedigree inbreeding coefficients using the CFC program (Sargolzaei et al., 2006).

**Model and analysis**

We evaluated the impact of the three types of inbreeding coefficients on the traits, including separately. The model fitted for BW and WW was: , and for PWG, HH, SC, CO, FIN and MUS was: , where \( y \) is the vector of observations, \( b \) is the vector of fixed effects, \( u \) the vector of additive genetic effects, \( m \) the vector of maternal genetic effects, \( e \) the vector of residuals; \( X, Z \), and \( W \) are the incidence matrices for fixed, direct genetic and maternal genetic effects, respectively. The fixed effects for all traits included the contemporary group (farm, year of birth, sex and management group), linear effect of age at measurement (covariable), quadratic effect of age of dam at calving (covariable) and inbreeding coefficients, either \( F_{PED} \), \( F_{ROH} \) or \( F_{GRM} \). The analysis was realized by the Bayesian approach using the R package MCMCglmm (Hadfield, 2016). The analysis consisted of a single chain of 50,000 cycles discarding the first 5,000 cycles, and keeping a sample at every 10 iterations. Convergence of the Markov Chain Monte Carlo was verified by visual inspection.

**Results**

The mean, median, and maximum ROH lengths across the entire genome were 3,405, 1,779, and 104,221 Mb, respectively. Totals of 89%, 62%, and 39% of animals presented at least one ROH segments larger than 10 Mb, 15 Mb, and 20 Mb, respectively. The presence of these long ROH segments imply that increase of inbreeding is due to recent ancestors (Howrigan et al., 2011). Figure 1 shows a Manhattan plot of genome-wide locus autozygosity estimated from ROH. The noticeable peaks on chromosome 7, 12, and 21 present hotspots of autozygosity (> 40%) putatively hovering selective pressure. These regions correspond to 7:51607797-52994652, 12:28428128-29572256, and 21:5191-1526125.
The means of inbreeding coefficients in the population were 0.48%, 6.05% and 0.96% for \( F_{\text{PED}} \), \( F_{\text{ROH}} \) and \( F_{\text{GRM}} \) respectively. The correlation was 0.14 between \( F_{\text{PED}} \) and \( F_{\text{ROH}} \), 0 between \( F_{\text{PED}} \) and \( F_{\text{GRM}} \) and 0.32 between \( F_{\text{ROH}} \) and \( F_{\text{GRM}} \). The impact of the inbreeding coefficients in the traits is summarized in the Table 2. The regression coefficients \( F_{\text{ROH}} \) were significant for the PWG, MUS, and CON and the \( F_{\text{PED}} \) was significant for PWG. The \( F_{\text{GRM}} \) was not significantly associated with any traits.

**Discussion**

The locus autozygosity regions on chromosomes 7 and 12 agree with the findings from previous studies based on divergent selection analysis between Bos taurus and Bos indicus cattle (Porto-Neto et al., 2013) and ROH analysis in Nellore cattle (Zavarez et al., 2015).

The correlation between inbreeding coefficients obtained in the present study was lower than that reported by Martikainen et al. (2017) of 0.71 for \( F_{\text{ROH}} \) and \( F_{\text{GRM}} \) in Finnish Ayrshire cattle. No significant effects were found in most of the traits, which could be due to our small population relative to the others like to Pereira et al., (2016), which used pedigree data. We analyzed animals with pedigree and genotypic data. Reverter et al. (2017) showed that negative effects of a 1% increase in genomic inbreeding in Brahman and Tropical Composite populations were associated with yearling body weight decrease of 0.51 and 0.58 kg, respectively. Pereira et al., (2016), using the individual inbreeding increase instead of the traditional individual inbreeding coefficient, found impacts of -0.07 cm, -0.38 kg and -1.00 kg for each 1% increase in inbreeding for scrotal circumference, weaning weight (measured at about 201 days of age) and for yearling weight in Nellore cattle. These differences may be caused by segregation of alleles in each population, diversity of the founders or genetic variation in the base population.

**Conclusions**

We characterized inbreeding levels in Nellore cattle using the three inbreeding metrics: pedigree, genomic relationship matrix, and ROH. We found a negative effect of genomics inbreeding on traits such as postweaning weight gain, muscularity and conformation and a negative effect of pedigree inbreeding in postweaning weight gain. In the rest of the analyzed traits we found no effect. We believe that more observations are necessary to detect inbreeding effect.

**List of References**


Table 1. Descriptive statistics of traits in Nellore cattle.

<table>
<thead>
<tr>
<th>Trait</th>
<th>Mean</th>
<th>N of records</th>
<th>N Contemporary Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (kg)</td>
<td>33.4</td>
<td>2019</td>
<td>140</td>
</tr>
<tr>
<td>Weaning weight (kg)</td>
<td>207.1</td>
<td>2221</td>
<td>152</td>
</tr>
<tr>
<td>Postweaning weight gain(kg)</td>
<td>119</td>
<td>2049</td>
<td>31</td>
</tr>
<tr>
<td>Hip height (cm)</td>
<td>138.9</td>
<td>2056</td>
<td>31</td>
</tr>
<tr>
<td>Scrotal circumference (cm)</td>
<td>27.7</td>
<td>1678</td>
<td>31</td>
</tr>
<tr>
<td>Muscularity (score)</td>
<td>3.3</td>
<td>2054</td>
<td>31</td>
</tr>
<tr>
<td>Finishing (score)</td>
<td>3.5</td>
<td>2054</td>
<td>31</td>
</tr>
<tr>
<td>Conformation (score)</td>
<td>3.3</td>
<td>2054</td>
<td>31</td>
</tr>
</tbody>
</table>

Table 2. Posterior mean and highest posterior density interval (HDP) for inbreeding depression per 1% derived from genomic relationship matrix ($F_{GRM}$), inbreeding coefficient by runs of homozygosity ($F_{ROH}$) and pedigree inbreeding coefficients ($F_{PED}$) in Nellore cattle traits.

<table>
<thead>
<tr>
<th>Trait</th>
<th>$F_{GRM}$</th>
<th>$F_{ROH}$</th>
<th>$F_{PED}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>HPD$_{95%}$</td>
<td>Mean</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>0.01</td>
<td>-0.05 to 0.07</td>
<td>-0.05</td>
</tr>
<tr>
<td>Weaning weight (kg)</td>
<td>0.02</td>
<td>-0.32 to 0.28</td>
<td>-0.17</td>
</tr>
<tr>
<td>Postweaning weight gain (kg)</td>
<td>-0.23</td>
<td>-0.68 to 0.21</td>
<td>-0.71</td>
</tr>
<tr>
<td>Hip height (cm)</td>
<td>-0.05</td>
<td>-0.12 to 0.01</td>
<td>-0.06</td>
</tr>
<tr>
<td>Scrotal circumference (cm)</td>
<td>0.01</td>
<td>-0.06 to 0.07</td>
<td>-0.02</td>
</tr>
<tr>
<td>Muscularity (score)</td>
<td>-0.01</td>
<td>-0.03 to 0.01</td>
<td>-0.02</td>
</tr>
<tr>
<td>Finishing (score)</td>
<td>-0.01</td>
<td>-0.03 to 0.01</td>
<td>-0.02</td>
</tr>
<tr>
<td>Conformation (score)</td>
<td>0.00</td>
<td>-0.02 to 0.02</td>
<td>-0.02</td>
</tr>
</tbody>
</table>
Figure 1. Genome-wide locus autozygosity in high density panel of Nellore cattle population.