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QUANTITATIVE GENETIC STUDY OF NOVEL ECONOMIC PHENOTYPES IN NELORE CATTLE

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Letícia Silva Pereira
Orientador: Dr.Cláudio Ulhoa Magnabosco

Goiânia
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LETÍCIA SILVA PEREIRA

QUANTITATIVE GENETIC STUDY OF NOVEL PHENOTYPES AND THEIR RELATIONSHIPS WITH TRAITS OF ECONOMIC IMPORTANCE IN NELORE CATTLE

Thesis presented to obtain the degree of *Doctor in Animal Science* in the Postgraduate Program in Animal Science at the School of Veterinary Medicine and Animal Science of the Federal University of Goiás.

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Ata número **83** da sessão de Defesa de Tese de **Letícia Silva Pereira** que confere o título de **Doutora em Zootecnia** pelo Programa de Pós-Graduação em Zootecnia, na área de concentração em Produção Animal.

Aos **nove dias do mês de maio de dois mil e vinte e quatro (09/05/2024), às 14h00min,** na Escola de Veterinária e Zootecnia, Departamento de Zootecnia, Sala de Reuniões, realizou-se a sessão pública de Defesa de Tese intitulada "**Estudo genético quantitativo de novos fenótipos e suas relações com características de importância econômica em bovinos Nelore**". Os trabalhos foram instalados pelo Orientador e Presidente da Banca Examinadora **Claudio Ulhoa Magnabosco** com a participação dos demais membros da Banca Examinadora: **Arthur dos Santos Mascioli - EVZ/UFG; Leonardo de França e Melo – EVZ/UFG; Rafael Espigolan - UNESP/FCAV Campus Jaboticabal e Marcos Fernando Oliveira e Costa - Embrapa Cerrados**, membros titulares externos. Durante a arguição os membros da banca **fizeram** sugestão de alteração do título do trabalho conforme explicitado abaixo. A Banca Examinadora reuniu-se em sessão secreta a fim de concluir o julgamento da Tese tendo sido a candidata **Aprovada** pelos seus membros. Proclamados os resultados pelo Orientador e Presidente da Banca Examinadora **Claudio Ulhoa Magnabosco**, foram encerrados os trabalhos e, para constar, lavrou-se a presente ata que é assinada pelos Membros da Banca Examinadora.

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DEDICATION

This thesis is dedicated to my dear mother Maria and my unforgettable uncle Zeca (i*n memoriam*). My mother, you have always been my greatest supporter and source of inspiration. Your unconditional love and wisdom are what kept me strong during difficult times and guided me through life's paths. My uncle, even though no longer physically present, has left an indelible mark on my life. His wise words and captivating presence have always inspired me to pursue my dreams and never give up, you will always be alive in my heart. To both of you, my eternal gratitude and affection for you existing in my life. I dedicate this to you with all my love.

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May our journey be characterized by constant evolution, both personal and professional, learning from the lessons of mistakes and successes along our paths, and always treading the path of goodness. And may we always keep in our minds and express our gratitude for everything and everyone who crosses our path.

EPIGRAPH

"Find a group of people who challenge and inspire you,
spend a lot of time with them, and it will change your life."
Amy Poehler

Perseverance

"If in your harsh life, happiness
Seems to be a far-off place,
Your determination needs to be greater
To pursue it until you find it.

And never fear a storm,
Do not let anything discourage you,
The greater the difficulty,
The harder you must fight.

Move forward with humility,
Seeking to respect others,
Spread justice and truth,
And thus, you will make the world better.

Be faithful to your principles,
Love and faith can change everything,
Your dream will become a reality
If you don't stop believing in it."
Dennys Távora

SUMMARY

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LIST OF ACRONYMS AND ABBREVIATIONS

ACP	- Accumulated cow productivity
ADG	- Average daily gain
AFC	- Age at first calving
ANCP	- Associação Nacional de Criadores e Pesquisadores
APF	- Accumulated profitability
APM	- Age at puberty in males
BLUP	- Best Linear Unbiased Prediction
BTA	- Bos taurus autosomes
CEPEA	- Centro de Estudos Avançados em Economia Aplicada
CEUA	- Animal Ethics Committee
CG	- Contemporary group
Chr	- Chromosome
CMS	- Consumo de matéria seca
CONCEA	- National Council for Animal Experimentation Control
CVS	- Computer vision system
DIT	- Days in teste
DM	- Dry matter
DMI	- Dry matter intake
EBV	- Estimated breeding value
FE	- Feed efficency
FRAME	- Frame score
GEBV	- Genomic Estimated Breeding Value
GO	- Gene Ontology Terms
GS	- Genomic Selection
GWAS	- Genome wide Association Studies
HPD	- High probability density
HTP	- High-Throughput Phenotyping
KEGG	- Kyoto Encyclopedia of Genes and Genomes
LD	- Linkage disequilibrium
LPT	- Livestock Profit Tool
MAF	- Minor allele frequency
MAS	- Marker-assisted selection
$MW^{0.75}$	- Metabolic body weight
PFT	- Profit per kilogram of liveweight gain
PL	- Precision Livestock
PLF	- Precision Livestock Farming
PPC30	- Probability of precocious calving at 30 months of age
QC	- Quality control
QTL	- Quantitative trait loci
REA	- Rib eye area
RFI	- Residual feed intake
RFT	- Rump fat thickness
SC365	- Scrotal circumference at 365 days of age

SD	- Standard deviation
SNPs	- Single nucleotide polymorphism
ssGBLUP	- Single-step Genomic Best Linear Unbiased Prediction
STAY	- Stayability
UFG	- Universidade Federal de Goiás
Var %	- Additive genetic variance
W450	- Adjusted weight at 450 days of age
WssGBLUP	- Weighted single-step Genomic Best Linear Unbiased Prediction

RESUMO

O objetivo deste estudo foi estimar os componentes de (co)variâncias e parâmetros genéticos de novas características indicadoras de lucratividade e suas associações com características de carcaça, fertilidade, crescimento e eficiência alimentar em bovinos Nelore. Adicionalmente, objetivou-se realizar análises de seleção genômica para avaliar diferentes modelos de predição, e conduzir um estudo de associação genômica ampla ponderada de passo único e análises de enriquecimento para características relacionadas à lucratividade. As características analisadas foram lucratividade acumulada (APF), lucro por arroba (PFT), peso ajustado aos 450 dias de idade (P450), circunferência escrotal ajustada aos 365 dias de idade (PE365), idade ao primeiro parto (IPP), probabilidade de parto precoce (3P), idade à puberdade nos machos (IPM), produtividade acumulada da vaca (PAC), área de olho de lombo (AOL), espessura de gordura subcutânea (EGS), consumo alimentar residual (CAR), consumo de matéria seca (CMS) e frame score (FRAME). Foram utilizados dados fenotípicos de 3614 de animais fenotipados para APF e PFT. Os componentes de (co)variância e parâmetros genéticos foram estimados sob inferência bayesiana em modelo animal multicaracterística. Os animais foram genotipados com o painel SNP Clarifide® Nelore 3.0. Um modelo animal unicaracterístico foi aplicado para estimar os parâmetros genéticos e realizar o GWAS ponderado linear de etapa única (WssGWAS) para identificar regiões genômicas associadas a APF e PFT. Janelas genômicas de 10-SNP que explicaram mais de 0,5% da variância genética aditiva foram selecionadas para investigar potenciais regiões e genes candidatos. Nove modelos foram implementados para predizer os valores genéticos genômicos (GEBV) utilizando as abordagens de melhor preditor linear não viesado passo único (ssGBLUP) e melhor preditor genômico ponderado linear e não linear de passo único (WssGBLUP). A capacidade de predizer o desempenho futuro foi calculada como a correlação entre o GEBV e os fenótipos ajustados. A APF e PFT apresentaram estimativas de herdabilidade de moderada a baixa, 0.18 e 0.02, respectivamente. APF e PFT tiveram correlação genética moderada a alta com crescimento (0,51 a 0,64), eficiência alimentar (-0.23 a 0.72), carcaça (-0.68 a 0.43) e frame (0.44 a 0.77), e moderada a baixa com reprodução (-0.47 a 0.20). As correlações residuais entre APF e PFT foram baixas com crescimento, reprodução, carcaça, eficiência alimentar e frame, variando de -0.05 a 0.18, exceto para as correlações entre APF com P450 e DMI (0.21 e 0.21, respectivamente). Na análise de GWAS, foram identificados um total de 83 genes em 21 janelas para APF e 268 genes em 52 janelas associados ao PFT. Maiores ganhos na habilidade preditiva para APF e PFT foram obtidos ao utilizar o modelo multicaracterística e o modelo bicaracterístico quando adicionadas características correlacionadas, com valores de acurácia variando de 0.556 a 0.665. Para predição da fração fenótipo, os modelos unicaracterísticos WssGBLUP linear obtiveram as maiores estimativas de predição, com valores variando de 0.65 a 0.94. Os resultados do GWAS contribuem para um maior entendimento dos mecanismos biológicos e genéticos, identificando os genes e vias metabólicas envolvidas na regulação da lucratividade e do lucro por arroba. Vários genes relacionados à fertilidade, eficiência alimentar, características de carcaça, desenvolvimento e metabolismo muscular e de tecido adiposo e metabolismo de lipídios e carboidratos foram identificados, juntamente com genes associados ao comportamento animal. Os resultados sugerem que a precisão da predição de características com baixa herdabilidade, como APF e PFT, aumentou

consideravelmente quando foram combinadas com características de alta correlação genética em uma predição multicaracterística. Essas duas novas características podem ser incluídas como uma ferramenta complementar de seleção e manejo para identificar animais com maior retorno econômico em termos genéticos, oferecendo insights aos produtores sobre o retorno econômico esperado da seleção dos animais mais produtivos.

Palavras chaves: *Bos indicus*, Lucratividade acumulada, Parâmetros genéticos, Predição genômica, WssGWAS

ABSTRACT

This study aimed to estimate the components of (co)variance and genetic parameters of new profitability-indicating traits and their associations with carcass, fertility, growth, and feed efficiency in Nelore cattle. Additionally, we aimed to perform genomic selection analyses to evaluate different prediction models and conduct a single-step nonlinear weighted genome-wide association study and enrichment analyses for profitability-related traits. The traits analyzed were accumulated profitability (APF), profit per kilogram of liveweight gain (PFT), weight at 450 days of age (W450), scrotal circumference at 365 days of age (SC365), age at first calving (AFC), probability of precocious calving at 30 months of age (PPC30), age at puberty in males (APM), accumulated cow productivity (ACP), rib eye area (REA), rump fat thickness (RFT), residual feed intake (RFI), dry-matter intake (DMI), and frame score (FRAME). Phenotypic data from 3614 animals phenotyped for APF and PFT were used. The (co)variance components and genetic parameters were estimated under Bayesian inference in a multi-trait animal model. The animals were genotyped with the Clarifide® Nelore 3.0 SNP panel. A single-trait animal model was applied to estimate genetic parameters and perform single-step linear weighted GWAS (WssGWAS) to identify genomic regions associated with APF and PFT. 10-SNP genomic windows that explained more than 0.5% of the additive genetic variance were selected to investigate potential candidate regions and genes. Seven models were implemented to predict genomic breeding values (GEBV) using the best linear unbiased genomic prediction (ssGBLUP) and single-step linear and nonlinear weighted best genomic prediction (WssGBLUP) approaches. The ability to predict future performance was calculated as the correlation between GEBV and fitted phenotypes. APF and PFT showed moderate to low heritability, 0.18 and 0.02, respectively. APF and PFT had moderate to high genetic correlation with growth (0.65 to 0.64), feed efficiency (-0.23 to 0.72), carcass (-0.68 to 0.43), and frame (0.44 to 0.77), and moderate to low with reproduction (-0.47 to 0.20). Residual correlations of profitability-related traits were low with growth, reproduction, carcass, feed efficiency, and frame, ranging from -0.05 to 0.18, except for the correlations between APF with w450 and DMI (0.21 and 0.21, respectively). In the GWAS analysis, a total of 83 genes in 21 windows for APF and 268 genes in 52 windows associated with PFT were identified. Greater gains in predictive ability for APF and PFT were obtained when using the multi-trait model and the two-trait model when genetically correlated traits were added, with accuracy values ranging from 0.556 to 0.665. The linear single-trait WssGBLUP models obtained the highest prediction estimates for phenotype prediction, with values ranging from 0.65 to 0.94. GWAS results contribute to a greater understanding of biological and genetic mechanisms, identifying the genes and metabolic pathways involved in regulating accumulated profitability and profit per kilogram of liveweight gain. Several genes related to fertility, feed efficiency, carcass traits, muscle and adipose tissue development and metabolism, and lipid and carbohydrate metabolism have been identified, along with genes associated with animal behavior. The results suggest that the prediction accuracy of traits with low heritability, such as APF and PFT, increased when they were combined with traits with high genetic correlation in a multi-trait prediction. These two new traits can be included as a complementary selection and management tool to identify animals with greater economic returns in genetic terms,

offering insights to producers on the expected economic returns from selecting the most productive animals.

Keywords: Accumulated profitability, *Bos indicus*, Genetic parameters, Genomic prediction, WssGWAS

CHAPTER 1 – INITIAL CONSIDERATIONS

1. INTRODUCTION

The estimates of global population growth are consistently highlighted as one of the main challenges global food production faces. With the population steadily increasing, the demand for food also grows exponentially, which means there is a need to produce more animals with limited natural resources. It is estimated that by 2050, to meet the increasing demands for animal products worldwide, producers will need to increase their production by 70%[1]. Traditional production practices may no longer suffice[2] , and systems that allow for greater productivity per unit area will need to be explored. This implies the utilization of tools that can maximize the outcomes of meat production systems. In this context, finding sustainable and technological solutions to ensure food security while preserving natural resources for future generations is essential.

The efficiency of production systems is crucial for enhancing productivity, ensuring greater availability of animal protein for more people, supporting sustainable initiatives[3] and promoting good management practices to ensure animal welfare. Additionally, this can be achieved through animal selection by identifying animals with higher genetic potential for the trait of interest[4]. Sustainable genetic improvement can only be attained through accurate and frequent phenotypic records, along with the appropriate utilization of this information[4]. Therefore, genetic improvement will be one of the technologies applied in this scenario[5] to intensify animal protein production sustainably.

Simultaneously, precision livestock farming could provide tools to enhance the phenotyping of existing traits[6] and expand possibilities for phenotyping traits that were previously unavailable, thus opening up new selection opportunities[7]. The integration of new phenotypes alongside the automatic collection of traits is a powerful tool to optimize herd management and breeding programs[8], enabling decision-making tailored to the specific needs of each meat production segment[9].

In this context, this research proposes the study of two new phenotypes obtained in confinement through precision livestock farming technologies: accumulated profitability (APF) and profit per kilogram of liveweight gain (PFT). Especially in the last phase of the production cycle, feedlot operators face a series of challenges during finishing or fattening, including market volatility, fluctuations in feed prices, competition with other animal protein sources, and primarily, underperformance due to low genetic

potential regarding performance traits. All these factors still contribute to making this phase less profitable than expected[10].

The sustainability of beef industries requires high production and farm efficiency indicators[11]. The sustainability of beef industries requires high production and farm efficiency indicators. Within this perspective, these two new phenotypes can contribute as complementary tools for feedlot operators and commercial herd producers, aiming to optimize production efficiency. Using this tool to identify animals with greater genetic potential for economic return can directly impact decision-making, herd management, finishing time, and consequently increase the profit margin of operations. Additionally, it will facilitate the quick turnover of animals in the production area, resulting in greater environmental sustainability and increased meat production per area.

The quantitative genetic study of these emerging traits constitutes the first step, as knowledge of genetic parameters will support the design of selection programs. Therefore, it is important to explore the variance components and heritability of these new traits to understand the proportion of their total phenotypic variation due to genetic variation. Additionally, knowledge of genetic associations with other traits is necessary to successfully incorporate a new trait into selection objectives[12].

Genomics will also be important in integrating these new phenotypes into selection programs. Emerging traits now being evaluated commonly exhibit low heritability, require significant financial resources[13], or are difficult to phenotyping. However, even in a small reference population, genomics will enable the selection of these new traits[14].

The progress of genomic technologies has enabled the genotyping of hundreds of thousands of DNA markers distributed throughout the genoma[15]. The effects of thousands of DNA markers are estimated simultaneously by associating phenotypic information in a reference population and are used to estimate genetic values of animals under selection. Different methods have been extensively studied and compared to identify the most appropriate approach for genomic prediction for various traits[16].

In addition to genomic selection, genome-wide association studies (GWAS) have been conducted to identify candidate genes related to interest traits[17]. The identification of these genes and understanding their function in phenotype expression are important resources that can contribute to the implementation of genomic selection[18]. GWAS studies the existence of linkage disequilibrium (LD) between SNPs and causal variants [19]. In general, GWAS aims to detect SNPs related to the traits under study and explore

regions where these SNPs are located to investigate genes and further study biological functions, with the goal of better understanding the genetic influence on trait expression[20].

In this sense, it is essential to estimate variance components and genetic parameters to understand the association with other traditional traits already used in breeding programs. Conducting GWAS and GS studies to deepen knowledge about potential genomic regions or genes, physiological processes that influence these new traits,[21] and including them in genomic evaluation through more accurate genomic value predictions[22] for precision selection.

Therefore, this study aimed to estimate the variance components and genetic parameters of profitability-indicating traits and investigate their associations with growth, fertility, carcass, and feed efficiency traits in Nelore cattle. Weighted genomic association studies will be conducted to identify genomic regions associated with profitability traits and candidate genes involved in biological processes related to the expression of these phenotypes. Additionally, this study aimed to compare the accuracy of genomic predictions using single-step GBLUP (ssGBLUP) and weighted ssGBLUP (WssGBLUP) methods under single and multi-trait models.

1.1 OBJECTIVES

1.1.1 General Objective

This study aims to estimate the variance components and genetic parameters, conduct wide genomic selection studies, and compare different genomic prediction methods for accumulated profitability and profit per kilogram of liveweight gain.

1.1.2 Specific objectives

- Estimate the (co)variance components and genetic parameters (heritability, genetic, and residual correlations) for accumulated profitability and profit per kilogram of liveweight gain through Bayesian inference using multi-trait analysis.
- Conduct wide genomic wide association studies for profitability related traits using the WssGWAS approach.
- Compare the predictive ability of ssGBLUP and WssGLUP methods (linear and non-linear) in single-, two-, three-, and multitrait models related-traits accumulated.

2. LITERATURE REVIEW

2.1 Profitability

Typically, global indices of genetic merit have been used to predict total profit and associate weighted genetic values with their respective economic values[23]. However, a new approach involves calculating and using the animal's profitability as a phenotype[23]. This direct animal profit prediction approach has been predominantly applied in dairy cattle. About two decades ago, several studies calculated the profit phenotype in dairy cattle. These calculations involved cost information, revenues, reproductive indicators, and milk production indicators, among others. Additionally, some of these studies incorporated the slaughter weight of the dairy cow into the profit prediction equation.

These studies showed that profitability for cattle could be calculated and used to directly estimate the genetic value of the animal based on the profit phenotype. Despite the different methodologies employed in these studies regarding the variables used for the phenotype calculation, this trait exhibited genetic variability. The heritabilities reported in these studies ranged from 0,09 to 0,25[24 25 26 27].

Recently, Canadian DHI organizations, for example, calculated the accumulated profit per cow until the cow was slaughtered; variables such as milk and component prices, maintenance and feeding costs, and heifer rearing costs were considered[28]. In beef cattle, few studies have been conducted in this direction. Dunner et al. (2020) developed the Beef Female's Profit Potential (BFPP), which represents the expected profitability over the cow's lifetime. For this, data from both the cow and its progeny were considered. However, this tool was developed as an aid for culling decisions of cows for slaughter, based on reproductive indicators and their respective economic weights[9].

Although meat production has experienced rapid growth in the past five decades, fueled by the development of various techniques, economic indicators show that the fattening sector still generates returns below expectations[10], or operates with narrow margins of financial return. The cost and management of production inputs are routinely cited as important variables impacting financial gains; however, factors affecting the profitability of cattle fattening operations are numerous and often interconnected[10] .

Emerging measurement technologies, such as electronic sensors and automatic scales, have the potential to improve the development of decision-support technological solutions, aiming to achieve meat industries with greater sustainability, productivity, profitability, and high standards of animal welfare[11]. In this context, these technologies, such as artificial intelligence algorithms, can be employed to measure various

confinement metrics in more detail and in real-time, such as performance and consumption, costs, and market data. These integrated data can be used to calculate the direct profit phenotype of animals more accurately, becoming a strategic genetic tool in identifying those with the highest potential for economic return. Genetic evaluation focusing on profit, as an individual trait, can provide producers with information about economic gains based on their genetic choices, serving as complementary tools to selection indices[24].

2.2 Precision Livestock

Digital tools have influenced a large part of society over the past twenty years, with rapid growth in internet access, computing autonomy, and automation in the use of smartphone applications. This change has been termed Industry 4.0 or the Fourth Industrial Revolution[29]. Despite this revolution having gained a plurality of names[31], it has currently been termed Agriculture 4.0 to integrate into a fourth agricultural revolution driven by developing technologies grounded in information and communication and the large volume of data collected[32] both in agriculture and animal production[33]. In animal production, various terms have been used, such as precision livestock farming, smart farming, and smart animal agriculture. And they all refer to the same goal: to increase food production sustainably while preserving animal welfare and reducing environmental impact. This is achieved through the collection of information via sensors, storage, and processing of this data, as well as predictive analysis using artificial intelligence tools[34] [35] [35].

Precision livestock farming tools are gradually becoming more common in contemporary livestock farming. According to Wathes et al.[36] these tools are based on process engineering for the automation of livestock farming, enabling farmers to monitor many animals, their health, and environment, identifying individual disturbances in a timely manner and even anticipating them[37]. The use of technologies can assist in the development of production systems such as selection and management techniques, where there is still potential to be explored in associating precision livestock farming metrics, resulting in the generation of refined and biologically relevant phenotypes. Precision livestock farming can still be classified as first-generation livestock farming, similar to what currently exists[37]. And high-throughput phenotyping, or phenomics is the second generation, which faces a bottleneck for its advancement, which is evolving from monitoring a single phenomenon to monitoring associated phenomena, and thus

progressing to precision phenotyping, which refers to the speed and quantity at which digital sensor devices can transmit information[37] .

2.3 Phenomics

Current developments in precision livestock farming tools, such as sensors for data collection, automation and robotics, cloud computing, big data analysis, machine learning, nanotechnology, genomics, and gene editing[38] will provide solutions for advancing phenomics programs, encompassing phenotyping, data acquisition, and computation[39]. The purpose of these applications is not necessarily to replace existing phenotypes with new ones but to detect new associated sources of information that allow for large-scale data collection10 and to obtain measurements with greater reliability[37].

The phenotype represents the most complex expression of biological organization at the individual level, encompassing a wide diversity of observable traits in organisms[40]. Phenotypes can be measured continuously or categorically. When these phenotypic data are measured and recorded, this technique is called phenotyping[36]. Phenomics, therefore, is based on obtaining high-dimensional phenotypes in real-time, aiming at improving animal performance through precise increments and reproducible traits, whether traditional or incorporating new economically important traits, which have become available in precision livestock farming and were otherwise inaccessible[41].

This new perspective requires the use of new technologies and the management of a large amount of information, thus, phenotyping becomes essential in beef cattle farming and other areas of animal production, given the demands of the new society and the challenges in research that will need to be addressed to ensure sustainable livestock farming[42]. The first phenotyping platforms were developed in crop production, where numerous individuals were constantly involved in genetic improvement programs, the image analysis devices, for example, are commonly used in plant breeding programs[43].

Phenotyping programs make measuring traits faster and more economical, rendering phenotypic information more precise across all biological stages and preventing, where possible, the vulnerability associated with traditional methods of collecting phenotypic data[44]. Unlike studies focusing on human genetics and crops, animal phenomics has received less attention[9], thus limiting the use of new tools that assess a greater number of phenotypes demanded by society, such as animal welfare, disease incidence, or efficient resource utilization[45].

However, current studies show that phenomics in animal production is also becoming common in the scientific community, as demonstrated by Koltes et al.[46], Baes, et al.[47], Rexroad, et al[48] e Cole, et al[49]. The use of big data techniques is an important tool for the analysis and interpretation of data generated by phenomics. The utilization of big data can aid in the analysis and interpretation of large volumes of information generated by phenomics, enabling the identification of patterns and trends in data that would be very difficult or impossible to analyze manually.

The development of these new sensors, technologies, and methodologies to automate the collection of phenotypes related to disease resistance, animal welfare, fertility, feed efficiency, and animal product quality will contribute to the definition of management techniques and result in the improvement of genetic improvement programs and, consequently, the optimization of the production cycle[48]. In summary, phenomics offers many promising possibilities for enhancing production in beef cattle farming, but still faces significant challenges. As technology evolves and costs decrease, it is likely that more producers will adopt phenomics to improve production efficiency, sustainability, and animal welfare.

The precision of measurement and the reproducibility of traits or phenotyping are essential for the progress of phenomics programs in livestock farming, as they will enable detailed phenotypic information currently inaccessible[41]. Furthermore, they will ensure advancements in performance and productivity of the production system through genetics, genomics, and other 'omic' sciences, better animal handling management, and optimization of natural resources, such as pastures[50].

2.3.1 Perspectives of phenomics use in beef genetic breeding

Selection programs have been essential for increasing gains in the genetic evolution of productive traits in livestock farming, as well as the use of genomic selection, which has significantly accelerated genetic gain in some populations in recent decades[51]. This growth has been assisted by the maximization of production systems, the use of numerous precision tools in routine management activities, and high-performance phenotyping[52].

The success of quantitative trait selection largely depends on available and reliable phenotypic information[43]. However, phenotyping systems have been established for many years as a key factor in genetic evaluation, precision of statistical models, and predictions through molecular markers[43], especially in recent years with the progress

achieved in genomics[44]. The understanding that phenotyping can be a limiting factor for genetic gain[53] in selection programs has motivated many researchers in the field of animal production to develop new approaches[54], such as genome sequencing[9], adaptation to challenging environments[55] and the development of innovative and economically accessible tools for phenotyping[56].

Phenomics is constantly justified as providing us with the ability to delineate causal associations between genotypes and environmental factors and phenotypes[40]. Phenotypic variation is shaped through a complex interplay between genotype and environment, and this genotype-phenotype map is intangible in the absence of detailed phenotypic information that enables these interactions to be elucidated[40]. Phenomics should be understood as an interdisciplinary field to facilitate the advancement and use of high-performance and high-dimensional phenotyping[40]. At present, one of the indispensable goals is to determine increasingly detailed functional relationships between animal genotypes and phenotypes and develop precision livestock farming with greater long-term sustainability[42].

Phenomics integrated with high-performance phenotyping directly contributes to three relevant components of genetic improvement through a selection program[53]: enhancing selection accuracy, aiding in the efficient identification of genetic variation, and increasing the robustness of decision support software[39]. According to Miller et al.[57] the possibilities of driving genetic evolution include increasing selection accuracy, reducing generation interval, and intensifying selection. These opportunities also enhance the ability to measure certain traits, such as opportunities for changes, like new traits. Phenotyping in animal production aims to transform traits that are difficult to measure into easily measurable ones. The benefits of this approach lie in its high capacity to generate a large volume of phenotypic data of the quality required for strategically precise prediction, thus overcoming the major limitation to progress through genomics[42].

In quantitative genetics, an essential concept is genetic gain. Genetic gain can be determined by the increase in performance achieved per unit through selection[58]. When placed in this scenario, to enhance genetic gain, phenotyping can assist in improving selection intensity, selection accuracy, and even characterizing new genetic changes. Obtaining estimates with greater reliability and precise genetic value is an essential goal for producers, and for this purpose, phenotyping is a crucial point[59].

The selection rate determines selection intensity, the portion of the selected population from the total population[58]. Increasing the volume and optimizing the costs of

phenotyping can lead to an increase in selection intensity. Increasing the volume and optimizing the costs of phenotyping can lead to an increase in selection intensity[59] of higher genetic merit. Therefore, high-performance methodologies are indispensable when implementing phenotyping to efficiently pursue larger population sizes[53].

The large volume of phenotypic data currently accessible through the deployment of high-throughput phenotyping systems related to enhancing the accuracy of measured traits results in better estimates of heritability and productivity indices[40]. Another important aspect is that high-throughput phenotyping in animal production comes under two perspectives: new traits can be determined and measured, which could not be recorded previously, and traditional traits can be monitored almost constantly without interfering with a significant volume of animals under normal production conditions.

The selection of superior phenotypes, standardization of methods, development of techniques for high-throughput data collection, systematic recording of environmental variables, and the incorporation of informatics are some challenges in advancing an animal phenomics program. Precision livestock farming aims to implement uninterrupted and automatic real-time monitoring systems to enhance management and productivity throughout the production cycle. This perspective requires the use of new technological tools and the management of large volumes of information.

In beef cattle production, several traits are of great economic relevance. First and foremost, fertility traits stand out, followed by weight gain, meat quality, and feed efficiency. Different technologies and sensors have already been adopted or can monitor these important individual traits[60]. There are several challenges to the widespread use of phenotyping techniques in beef cattle, however, simultaneously, current technologies are becoming more available, and producers are increasingly encouraged to use these tools[61]. Thus, integrating phenomics in animal production concerning genetic improvement and precision livestock farming approaches will result in accelerated progress in these two areas and optimization of resource utilization[62].

Phenomics, along with phenotyping, is therefore an indispensable tool for precision livestock farming, as it allows for a more accurate understanding of genotype-environment interaction and, consequently, the selection of animals with high genetic potential. Through phenotyping, precise information about economically important traits can be obtained, enabling the rapid identification of the best animals for reproduction, and thus improving the efficiency of livestock production. Thus, phenotyping is a key

component for advancing precision livestock farming and for the sustainable production of high-quality food[63].

2.4 Genomic studies applied to animal breeding

The genetic advancement through selection and mating is based on predicting the ability of parents to produce offspring with higher performance[64]. This method is known as genetic evaluation or prediction[64]. Genetic evaluation in plants and animals has been based, for the last 100 years, on the use of phenotypes related to desirable traits, along with pedigree information. Genetic evaluations, for the most part, did not take into account the physical basis of heredity, i.e., DNA, and used a simplified conception of genetic information transmission from parents to progeny, in which each parent contributes, on average, half of their genetic constitution[64]. In this conception, selection is based on the total predicted effect of the genes an individual carries or their estimated genetic values (EBVs)[65].

Recently, a paradigm shift in technology has paved the way towards a systems biology approach and its related disciplines[66], to unravel the previously adopted 'black box' by quantitative geneticists, which considers that each quantitative trait results from the interaction of an infinite number of genes, each with an infinitesimally small effect (infinitesimal genetic model outlined by Fisher)[66]. This new paradigmatic approach focuses on the investigation of actual genomic regions and their effects or associations with performance, as opposed to contemporary methods that rely on the statistical analysis of extensive sets of phenotypic data.

Most economically important traits in classical genetics are quantitative or complex[68], where the phenotype is influenced by an infinite number of genes, each with an extremely small effect, resulting in a small proportion of variance explained by each gene[65], in addition to non-genetic environmental factors. This leads to the involvement of multiple genes, whose effects are often small and, therefore, difficult to estimate accurately[65].

In the early years of the last decade, simultaneous developments in molecular genetics and bioinformatics paved the way for the establishment of genomic selection as a new approach to enhance genetic gain in animal breeding[69]. Since the late 1960s, there have been studies on the application of genomic data to improve selection in animal breeding[71], and it became feasible with the identification of genes or genetic markers linked to loci of quantitative traits[69]. Especially for traits that were challenging to improve

in traditional breeding programs due to low heritabilities or costly phenotypic data collection, marker-assisted selection (MAS) emerged as a promising strategy to enhance selection response[69].

According to Hayes et al.[72], the revolution of genomic selection was driven by two significant advancements. Firstly, the recent sequencing of the bovine genome allowed the discovery of thousands of DNA markers known as SNPs (Single Nucleotide Polymorphisms). Simultaneously with this discovery, there was a reduction in the cost of genotyping these markers across the entire bovine genome. The second advancement was proof that it was feasible to make very precise selections based on predicted breeding values from dense marker data using an approach called genomic selection[73].

With the emergence of genomic panels containing single nucleotide polymorphisms (SNPs), these markers have been extensively employed to detect and locate loci of complex traits in various species[74]. Additionally, they have proven effective and relevant in identifying causal mutations associated with economically relevant traits in livestock[75]. The introduction of SNP panels has enabled the conduct of various studies, such as association studies, prediction studies, and population studies, which have been implemented in different species. Markers associated with economically important traits can play a significant role in genetic advancement, especially when their information is incorporated into models to estimate genomic breeding values for such traits.

Among the tools employed for genomic evaluation, genomic selection (GS) and genome-wide association study (GWAS) stand out as the primary methods for predicting genomic breeding values (GEBV) and identifying and associating molecular markers with the phenotype of interest. Both methodologies complement each other. Additionally, both GS and GWAS have enabled researchers to explore and quantify the genetic and phenotypic variations of quantitative traits.

For all sectors of the livestock industry, genomics is expected to increase efficiency and productivity throughout the production cycle. Regarding consumers and the processing industry, genomics is expected to enhance the safety and quality of animal-derived products. Furthermore, it is anticipated to provide new insights into growth, nutrition, health, and animal welfare, enabling a deeper understanding of the molecular mechanisms underlying the traits of interest. Thus, genomics offers new perspectives for more precise selection, cost reduction, shortened generation intervals, and exploration of new sources of genetic variability[76].

2.4.1 Genomic Selection

According to Meuwissen and Goddard (2016), three developments have been responsible for the widespread current adoption of DNA information: 1) the GS approach[73], 2) the discovery of numerous SNP markers, and 3) the emergence of genotyping technologies through SNP chips, which made the genotyping of all these SNPs economically feasible[77].

Genomic selection was first introduced by Meuwissen et al.[73] based on the principle that information from many markers can be used to estimate genetic values, even without precise knowledge about the exact location of genes in the genome. By selecting thousands of SNPs to represent the entire genome, it is assumed that there is always an SNP near a specific gene or DNA segment of interest[78]. The linkage disequilibrium between one (or several) SNP and a causal mutation is crucial, allowing for explaining a significant portion of the observed variation in the trait under analysis[78].

To comprehend how GS can accelerate the speed of genetic progress, it is essential to understand some of the fundamental principles of animal breeding[79]. The optimal design of any selection program involves the integration of various disciplines, including genetics, statistics, computer science, physiology, molecular biology, logistics, economics, and social sciences[80]. The breeder's equation provides a framework through which the impact of each of these areas and their technologies and decisions regarding their applications can be evaluated[81]. This equation models the expected variation in a trait in response to selection, and its description can be expressed according to Falconer[82] as:

$$\Delta G = \frac{i\, r \sigma_A}{L}$$

Where: ΔG is the expected genetic gain , i is the selection intensity (the proportion of animals in a population that are selected to become parents of the next generation), r is the selection accuracy (correlation between the estimated breeding value (EBV) and the true breeding value), σ_A is the additive genetic standard deviation of the trait of interest (genetic variation in the population available for selection), and L is the generation interval (average age of parents when their offspring are born).

Genomic selection directly addresses the four factors that affect the rate of genetic progress in animal and plant breeding[80]. Firstly, the reproductive process is accelerated, as breeders can renew individuals more quickly if selection is guided by the estimated genomic estimated breeding values (GEBV), which typically proves to be more effective

than phenotype-based selection[80]. Secondly, the selection intensity is expanded, as breeders can choose more individuals based on genotypes rather than phenotypes: the cost of genotyping is commonly lower than that of phenotyping, thus enabling the evaluation of a larger number of candidates for selection[80].

And thirdly, GEBV can offer higher precision than the breeding value estimated solely based on phenotype and pedigree[80]. Lastly, genomic selection tools can also optimize the incorporation of new genetic material more efficiently[83], through the utilization of the three factors described above, in crossings and pre-breeding programs, as well as the utilization of the ideal contribution theory driven by genomic information[80]. In practical terms, genomic selection involves making selection decisions based on the estimated genetic values of an individual[72]. These GEBVs are obtained by summing the effects of dense genetic markers, or haplotypes formed by these markers, spanning the entire genome, making it possible to potentially capture all loci of quantitative traits (QTLs) contributing to the variation of a particular trait[72].

The implementation of genomic selection accelerates genetic progress while reducing the costs associated with progeny testing[73 84] while simultaneously enhancing the gains from other reproductive technologies such as artificial insemination, sexed semen, bovine semen, or in vitro embryo fertilization, which also contribute to selection intensity[8586]. This approach allows breeders to pre-select animals that have inherited chromosomal segments of higher genetic value[73 84], thus optimizing the efficiency of the breeding program. The effects of achieving these accuracies for newborn animals are significant. Findings from simulation studies indicate that the accuracy of GEBV for a calf can be as high as the accuracy of an EBV after progeny testing[84]. The generation interval was approximately five years because young animals exhibit higher average merit and now also have high reliability[87]

2.4.2 Implementation and methods of genomic prediction

According to Hayes e Goddard, 2010[88], genomic selection aims to utilize genotypic, phenotypic, and pedigree information to predict genomic GEBVs within a specific population[73]**.** In the implementation of genomic selection, three steps are carried out: estimation and validation of the prediction model, prediction of the genetic values of selection candidates, and selection of genotypes based on the predictions[73 89]. For this, three populations must be defined for this: estimation population (training or reference), validation, and selection population[73].

The training population with known phenotypic and genotypic information is employed to develop a prediction model of DNA marker effects simultaneously[68 67]. These models integrate phenotypic information to establish predictive equations of genomic values[68 67]. Such equations are constructed through regressions between phenotypes and genotypes, allowing the estimation of the effect of allele substitution at each marker[6867]. This equation, constituted by the combination of SNP genotypes and the estimated marker effects, is then used to predict the GEBVs of animals from the validation population, which possess genotypic information but not necessarily phenotypic data[24,25].

Once validated, this equation can be used to predict the GEBVs of animals considered for selection[24,25]. Thus, the summation of the effects of all SNPs is adopted as a predictor of the genetic merit of animals under evaluation[73 24 25]. Therefore, different efficient methods for processing genomic data have been developed to increase the reliability of estimated genetic values and to estimate thousands of marker effects simultaneously[89].

According to Gianola et al.,[90] these methods encompass a multiple regression on marker genotypes, best linear unbiased prediction (BLUP) including effects of a single-marker locus, ridge regression, Bayesian procedures, and semiparametric specifications[90]. Bayesian methods, Bayes A, Bayes B, and Lasso, and the GBLUP method are widely employed to predict genetic merit, with the main distinction among them being the assumed distribution of SNP effects[90]. The GBLUP method assumes that the trait under study has a polygenic structure and takes into account the contribution of all genotyped markers when constructing the genomic relationship matrix (G). This is in contrast to the Bayesian approach, which assumes that the genetic variability of a trait is influenced by a small number of markers[91 92].

Recently, the GBLUP method has been enhanced into the single-step GBLUP method, which allows for the inclusion of pedigree and genomic relationships in a single relationship matrix[89], and has become one of the main approaches for genomic evaluation currently[93]. In this methodology, when phenotype and genotype data are simultaneously available, ssGBLUP emerges as a practical alternative[94]. These pieces of information are pooled together to generate an overall relationship matrix (H)[96] which can then be used for BLUP of genetic values. This matrix was proposed by Misztal et al.[97] who suggested that a numerator relationship matrix (A) can be adapted to a matrix (H) that encompasses both pedigree-based relationships and differences between pedigree and genomic relationships (A_Δ) $H = A + A_\Delta$ [97].

However, ssGBLUP assumes that variances are identical for all SNPs, which may not be the most appropriate assumption from a biological perspective[73 89 92]. As a result, another approach based on the structure of ssGBLUP, called weighted ssGBLUP (WssGBLUP), was proposed by Zhang et al. WssGBLUP is an expanded method of ssGBLUP that considers weights for SNP variations used in constructing the genomic relationship matrix[98]. WssGBLUP can assign more weight to SNPs in high LD with a causal mutation or associated with QTLs with a comparatively significant effect. These weights are estimated based on the variance explained by each SNP, as demonstrated by Wang et al[99].

The success of genomic selection is influenced by the accuracy of GEBVs, which are greatly affected by the prediction methods employed, the size of the reference population, the heritability of the traits in question, and the magnitude of linkage disequilibrium between SNPs and QTLs[72], including the size of the training population, the effective population size[65], the genetic relationship between the target population and the training population, marker density, statistical modeling employed, heritability, and genetic structure of the trait[65].

Thus, the selection of the most appropriate method for each trait in each population depends on the specificities of each scenario and can directly influence the accuracy of genomic predictions, with this choice being conditioned by the distribution of QTL effects, which are not known[100]. Therefore, the primary purpose of these methods is to enhance the prediction capacity of GEBVs by employing computationally efficient tools that can be easily incorporated into commercial selection programs[22].

2.4.3 Genome-Wide Association Study

The discovery of QTLs is a significant advancement for the identification and understanding of genetic variants linked to economically important phenotypes, and in this regard, genome-wide association study (GWAS) has been extensively employed as a strategy to identify QTLs and genomic regions associated with phenotypes[21]. This approach has been used to map traits such as meat quality and quantity, sensory panel evaluation, ease of calving, milk production, fat and protein percentage, fertility traits, egg production, etc[101].

In general, due to differences in the genetic architecture of breeds and the polygenic nature of complex traits, different genes and regions are associated with the same trait in different breeds of the same species. When conducted carefully, GWAS has

proven to be an efficient method for detecting genes associated with various phenotypes and elucidating the underlying mechanisms of these traits[101] as well as subsequent studies of biological functions aimed at increasing the understanding of the genetic component of phenotype expression[20]. These studies have being conducted using SNPs from panels of different densities, aiming to identify QTLs to elucidate biological functions and genetic structure.

The advancements in the development of dense panels of SNP markers have enabled the analysis of numerous SNPs collectively, allowing genomic analyses of genetic architecture, inbreeding, estimation of diversity and genetic divergence within and between populations, and detection of regions under selection[102 103]. These markers are then important for understanding the genetic architecture of traits of interest and are subsequently applied in genomic selection[104] This way, a better understanding of the genetic bases of the evaluated breeds can be obtained with greater accuracy, and young animals with high genetic value can be identified early on[105].

GWAS investigate linkage disequilibrium (LD) between SNPs and causal variants[106], assuming that at least one SNP is in LD with genes or genomic regions associated with the phenotype and is in sufficient frequency to be identified[107]. Thus, the identification of genome regions where these SNPs are present is sought, detecting genes and/or QTL associated with the phenotypic expression of the trait under study[1918]. With the identification of genes or genomic regions of interest, this information can be useful for breeding programs through genomic selection, directing attention to important genomic regions[108].

2.5 A brief overview of integrating phenomics and genomics to improve precision selection

The integration of phenomics and genomics is already underway and is progressing due to the acquisition of large-scale data through high-throughput phenotyping (HTP) and next-generation sequencing techniques[109]. The rapid development of phenomic technologies and methodologies is already reshaping the landscape of breeding programs, as evidenced by the continuous flow of genomic data[110]. These high-throughput phenotyping methodologies are not just complementary to genomic selection, but they also reinforce it, leading to the revolutionary concept of 'phenomic selection' and GS + HTP methodologies. These innovative approaches,

coupled with advanced prediction models, are poised to revolutionize breeding programs[111 112].

These new strategies that concurrently use available genomic and phenomic information are being presented/studied in selection programs and demonstrate great potential to enhance prediction accuracy and/or increase yield for selection (through prediction) in the early stages of the breeding program[113 114 115]. This new modeling perspective is highly favorable for accelerating genetic gain, as they can increase predictions of selection for new generations, expand the size of the population that can be effectively evaluated, and offer complementary data that will contribute to improvements in genomic predictions, resulting in more efficient models and precise selection[110].

Another critical point is that new traits are emerging through these PL technologies applied to phenomics, and most of them now evaluated generally have low heritability or require considerable investments in the early stages to obtain phenotypes[13]. However, they can be measured in a small reference population.[116]. Examples include new traits such as methane emission reduction[117], energy balance[118], and progesterone profiles as indicators of fertility[119]. Genetics plays an important role, as a strategy for effective selection of these new traits may lie in cost-effective ways to increase DGV prediction, such as incorporating a trait that correlates with a multi-trait genomic selection approach[116] that has large reference populations in the study population[14].

Advances in genetic improvement have been largely promoted by the use of genomics, which has enabled the integration between genomics and phenomics in GWAS studies and contributed to the prediction of the phenotype from the genotype in genomic selection[120]. In this sense, GWAS will also provide important insights into new traits, including their genetic architecture, biological processes, potential regions, and candidate genes associated with these traits. This complementary information will help breeding programs select new traits, providing a greater understanding of their genetic basis and assisting in the precise selection of animals with desirable traits. Therefore, the use of cutting-edge technologies, such as genomics, combined with phenotyping, will further facilitate the selection of animals with high productive performance and greater efficiency in the use of resources[63].

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CHAPTER 2: GENETIC PARAMETERS FOR NOVEL FEEDLOT PROFITABILITY-RELATED TRAITS IN NELORE CATTLE

Abstract: This study aimed to estimate (co)variance components and genetic parameters for accumulated profitability (APF) and profit per kilogram of liveweight gain (PFT), as well as their relationships with adjusted weight at 450 days of age (W450), scrotal circumference adjusted at 365 days of age (SC365), age at first calving (AFC), probability of precocious calving at 30 months of age (PPC30), age at puberty in males (APM), accumulated cow productivity (ACP), rib eye area (REA), rump fat thickness (RFT), residual feed intake (RFI), dry-matter intake (DMI), and frame score (FRAME). Data of profitability from 3,614 Nelore (*Bos indicus*) animals were used. The (co)variance components and genetic parameters were estimated using Bayesian inference in multiple-trait animal model. The posterior means of heritability estimates for APF and PFT were 0.18 and 0.02, respectively. APF and PFT exhibited moderate to high genetic correlations with growth traits (0.64 to 0.65), carcass (0.43 to 0.44), feed efficiency (0.72), and frame (0.44 to 0.77), except for the correlation with RFT (-0.10 to -0.68), RFI (-0.23 to 0.28), and between PFT and DMI (0.26). APF and PFT showed moderate to low genetic correlations (-0.48 to -0.01) with female reproductive traits and low correlations (-0.03 to -0.21) with male reproductive traits. These results offer important information to improve productive and economic performance when considering the inclusion of APF and PFT complementary tools in the selection criteria. Such traits can be strategic tools for producers by identifying animals with more significant genetic potential for profitability supporting decision-making in genetic planning and herd management.

Keywords: Genetic parameters, Livestock precision, Phenotyping, Profit phenotype, Zebu cattle

1. Introduction

The beef production sector faces ongoing challenges across various aspects of the production chain, encompassing management, global trade, animal health and welfare concerns, consumer preferences (Tonsor & Schroeder, 2006), pressures resulting from population growth, limited availability of productive lands for cattle rearing (Greenwood, 2021), and environmental sustainability. As resources become scarcer and environmental concerns grow, the search for increased productivity and efficiency in beef production through genetic improvement and precision livestock farming has become increasingly relevant (Reynolds et al., 2011; Scollan et al., 2011). In this context, innovations in genetic breeding are important to address and attempt to resolve these issues, aiming to contribute towards more sustainable, efficient, and profitable beef production.

Models of extensive production of red protein commonly include the raising of cows and their progeny on pasture, while the rearing and finishing phase of the steers occur on pasture based intensive or in feedlot conditions (Greenwood et al., 2021). The finishing phase of cattle in the feedlot is a strategy that primarily aims to intensify the production of kilograms of meat per unit area (Pacheco et a., 2014). However, feedlot operators have faced ongoing difficulties such as price fluctuations, feed costs, and fluctuations in market demand. Achieving satisfactory profit margins in feedlot operations presents a challenge, as margins are typically narrow and require economies of scale to ensure an adequate economic return. Therefore, it becomes relevant to identify and select individuals capable of achieving superior performance in productivity and profitability during the rearing and finishing phases, as well as reducing feedlot period length.

In this context, Precision Livestock Farming (PLF) enables a strategic approach to optimize the management of large herds, resulting in improved profitability, efficiency, and reduction of environmental impacts related to livestock systems (Kaur et al., 2023). Additionally, PLF technological solutions can enhance production system efficiency, enabling opportunities to select animals more efficiently through automated phenotyping (Brito et al., 2021). Advances in precision livestock farming have fostered the use of high-throughput phenotyping, facilitating enhanced monitoring in animal improvement, research, and genetic applications (Silva et al., 2021). These phenotypes obtained through PLF can be utilized as indicators or even introduce new traits for the genetic progress of herds (Silva et al., 2021).

Given the complexity of challenges breeders face in feedlot finishing systems, carefully selecting the most suitable animals becomes fundamental importance. Thus, including new traits or phenotypes associated with productivity and profitability has become a promising strategy in breeding programs, complementing conventional traits in beef cattle. It is important to emphasize that these new traits are as important for genetic improvement programs as those linked to (re)production (Knap et al., 2020). In this scenario, this study proposes the investigation of two novel phenotypes: accumulated profitability and profit per kilogram of liveweight gain in feedlot.

The availability of genetic Information and the integration of these traits as a complementary tool in the selection process enables breeders to evaluate the feedlot profitability potential of animals from the initial stages of development. This enables early identification of individuals with superior genetic merit for feedlot profitability, allowing producers to adjust their management strategies within their operations. This tool avoids investing resources in animals with lower economic potential, optimizes management practices, and reduces production-related risks, including the environmental impact of meat production.

It is important to highlight that beef cattle genetic breeding programs often do not consider traits directly related to performance in feedlots. Furthermore, few studies relate the feedlot traditionally evaluated in selection programs with those measured directly in confinement environments. This study is initially justified by the need to understand how the traditional traits established in breeding programs correlate with the economic performance of animals in feedlots environments. Understanding the genetic relationships between the novel profitability phenotypes in feedlot and the criteria traditionally used in breeding programs, such as traits related to carcass, growth, fertility, and feed efficiency, is of paramount importance.

This study would identify the most relevant traits to improve the feedlot profitability, thus facilitating the implementation of the most appropriate strategies and selection criteria for each production system. Furthermore, this approach favors a more balanced and holistic selection, optimizing the efficiency of breeding programs. The need for higher efficiency in productivity motivates the implementation of strategies and the use of new precision livestock technologies applicable to genetic improvement. Thus, the objectives of this study were to estimate the (co)variance components and genetic parameters for novel feedlot profitability-related traits and their genetic and residual correlations with growth, reproduction, carcass, and feed efficiency traits in Nelore cattle.

2. Materials and methods

This study was exempt from evaluation by the Animal Ethics Committee (CEUA), as established by Law No. 11,794 of 08/10/2008 and Normative Resolution No. 51 of 05/19/2021 from the National Council for Animal Experimentation Control (CONCEA) because the data were obtained from an existing database.

2.1 Dataset

The dataset used in this study, related to growth, reproduction, carcass, and feed efficiency, originates from 27 herds participating in the Nelore Brazil Improvement Program, coordinated by the National Association of Breeders and Researchers (ANCP, Ribeirão Preto, São Paulo, Brazil) located in four Brazilian geographical regions (Midwest, Southeast, Northeast, and North). Data regarding accumulated profitability and Profit per kilogram of liveweight gain were provided by the company @tech (Piracicaba, São Paulo, Brazil). The @tech is a startup that develops technological solutions in software and research, employing artificial intelligence in beef cattle, broiler poultry, and cultivated fish chains to support producers in decision-making. For further information about the company, please refer to the website https://techagr.com/beeftrader. The relationship matrix contained 116,815 animals, including 4,248 sires and 49,106 dams. The animals constituted the database had an average inbreeding coefficient of 1.11% and a proportion of 1.75% of inbred individuals in the total population.

2,127 animals were genotyped with the low-density panel (Clarifide® Nelore 3.0) containing more than 70,000 markers. The genotype quality control (QC) excluded animals and SNPs from the dataset with call rates <0.90. Additionally, SNPs with a minor allele frequency (MAF) <0.05, Mendelian conflicts >1%, monomorphic SNPs with redundant positions, SNPs deviating from Hardy-Weinberg equilibrium expectations, and those located on non-autosomal chromosomes were also excluded. After QC, 2,127 genotyped animals and 35,658 SNPs remained in the database for analysis.

2.2 Traits analyzed

Growth: A growth trait considered in this study was adjusted weight at 450 days of age (W450, kg). The calculation of standardized weight was conducted through linear

regression, considering the average daily gain assessed between days 405 and 495 of age for the variable P450 (Negreiros et al., 2022).

Carcass: The carcass traits considered were ribeye area (REA, cm^2) and rump fat thickness (RFT, mm). To obtain carcass phenotypes, ultrasound images were taken of the *Longissimus dorsi* muscle among the 12th and 13th ribs (REA) and in the rump region, between the ilium and ischium at the intersection of the *Gluteus medius* and *Biceps femoris muscles* (RFT), using the ALOKA 500V equipment with a 3.5 MHz linear probe.

Fertility*:* The age at first calving (AFC, months), probability of early calving (PPC30, %), accumulative cow productivity (ACP, kg weaned calf/cow/year), age at puberty for males (APM), and scrotal circumference at 365 days of age (SC365) were considered in this study. All heifers that underwent the sexual precocity program were exposed to reproduction during the weaning year as part of the early calving probability (PPC30) determination process. Those females that confirmed pregnancy and gave birth to a live calf by 30 months of age received a score of 2 (success), while the others that failed received a score of 1 (failure).

The age at first calving (AFC) was defined as the age, in months, of the heifer at her first calving. Annual cow productivity (ACP) was calculated based on the average weight of weaned calves over time, considering sexual precocity, maternal ability, and the cow's reproductive regularity. The animals underwent testicular ultrasonography and andrological clinical examination to determine the males' puberty age. According to the assessment, the animals were categorized as super-early (pubertal at ≤ 14 months of age), early (puberty between 14 and 17 months of age), or traditional (puberty >17 months of age) (Silva et al., 2020). Scrotal circumference at 365 days of age was adjusted according to age.

Feed Efficiency: The feed efficiency traits were obtained through Intergado® and GrowSafe electronic systems. Feed efficiency tests followed the guidelines established by Mendes et al., (2020), for assessing individual feed intake in beef cattle using both electronic systems. Animals were kept in collective or individual pens and subjected to a 21-day adaptation period followed by a valid 70-day testing phase. Throughout this period, each animal's average weight was recorded via manual weighing every 14 days or through automated weighing platforms (Intergado®).

To obtain residual feed intake (RFI, kg of dry matter/day), the average daily gain (ADG) (kg/day) and metabolic live weight ($MW^{0,75}$) were calculated. Daily dry matter intake (DMI, kg/day) was derived from the mean of all valid individual daily intake values electronically recorded by the Intergado and GrowSafe systems during the test period. ADG was estimated using the linear regression coefficient of weight concerning the days in the test for the animals (DIT) using the lm function in the R program with the following equation (Koch et al., 1963):

$$y_i = \alpha + \beta * DIT_i + \varepsilon_i$$

Where: y_i represents the weight of the animal; α is the intercept of the regression equation representing the initial weight; β is the linear regression coefficient representing ADG; DIT_i represents the day in the test for the nth observation; e ε_i is the error associated with each observation.

Considering live weight, the metabolic weight ($MW^{0,75}$), was calculated using the formula below (Koch et al., 1963):

$$PV^{0,75} = \left[\alpha + \beta * \left(\frac{DET_j}{2}\right)\right]^{0,75}$$

Em que: α represents the live weight at the beginning of the feed efficiency test; β stands for average daily weight gain, and DET_j represents the days in test.

Residual feed intake (RFI) was calculated as the difference between predicted and observed dry matter intake, using a regression equation based on live weight ($MW^{0,75}$), and average daily weight gain (ADG), following the methodology proposed by Koch et al., in 1963.

$$Y = \beta0 + \beta1\ (ADG) + \beta2\ (MW^{0,75}) + \varepsilon$$

Where: Y individual feed intake; β0 intercept; β1 partial regression coefficient of daily dry matter intake on average daily weight gain; β2 partial regression coefficient of dry matter intake on live weight; and ε: residual error of the regression, i.e., residual feed intake.

Body composition: the calculation for the frame score was performed based on the equation developed by Guimarães et al. (2020), using the method of multiple linear regression prediction applying different equations for males (1) and females (2):

FRAME MALES = −20.35 + 0.1305 × REA + 0.2633×BFT – 0.5901 × RFT + 0.1139 × HH+0.0056 × AGE (1)
FRAME FEMALES = −11.87 + 0.1316 × REA – 0.2457×BFT – 0.6218 × RFT + 0.1139 × HH+0.0009507 × AGE (2)

Where: REA, BFT, RFT, HH and AGE are ribeye area (cm2), subcutaneous backfat thickness (cm), rump fat thickness (cm), hip height (cm) and age (days) at ultrasound measurement, respectively.

Novel phenotypes: The new phenotypes analyzed were accumulated feedlot profitability (APF) and feedlot profit per kilogram of liveweight gain (PFT). @Tech's algorithms are designed to make full use of this data, ideally collected within a standardized 80-day trial period for running in the BeefTrader Decision Support System generating the phenotypes used by the Livestock Profit Tool (LPT) profitability. For trials that do not meet this 80-day standard, our system employs Artificial Intelligence and advanced growth modeling techniques to set the standard. This approach considers historical data to produce estimates that align with the 80-day prediction requirements of the LPT, ensuring robust and reliable analytics across varying trial durations.

The BeefTrader algorithm uses animal traits as input variables (gender, breed, body condition score, initial weight, initial date, among other exogenous factors that impact on growth dynamics), daily weights individually collected through a weighing sensor (daily basis), and information on the nutritional composition of the diets. The records for obtaining the new phenotypes were collected from animals participating in feed efficiency trials, following the same guidelines as Mendes et al., (2020), as mentioned in the section on feed efficiency traits. Based on this information, adjusted for local conditions, weight prediction is carried out in two steps: based on the biology of each animal and with the nutritional data and animal daily weight profile (observed or predicted), it is possible to estimate an optimal growth function for the animals (Step 1); from there, a dynamically adjusted linear or non-linear regression is performed using the least squares method on the weights to fit the predicted growth curve (Step 2). From the predicted growth curve, it is possible to find other variables required by the model, including animal performance in terms of growth and composition of gain, as well as economic and environmental factors. The profitability is the central trait used by LPT, as

commented, thus the next topics the @Tech intention is to present the equations related to this core phenotype.

Accumulated kilograms*

$$(sbw * cdf/100) \,/\, 15$$

Where:

sbw: Shrunk Body Weight (kg) - 96% of the Body Weight

cdf: Carcass Dressing (%)

kilograms $*$ Gain

$$initial\ gain = acum\ kilograms\ [2] - acum\ kilograms\ [1]$$

$$initial\ gain = acum\ kilograms\ [d] - acum\ arroba\ [1] + initial\ gain$$

Where:
Acum $kilograms$ = accumulated $kilograms$ $(15kg)$ on a specific day
d = Day
gain initial = gain to be considered on the first day since it is unknown. This value becomes a constant.
Note: The correct procedure for the first day would be to calculate based on the corral weight and remove the constant from the subsequent days.

Daily Cost

$$DMI * diet\ price\ (kg) + feedlot\ daily\ overhead$$

Where:
dmi = Dry Matter intake (kg)
diet_price_kg = diet cost ($/kg)
feedlot_daily_overhead = non-feed cost ($)

Daily Revenue

$$kilograms\ \ price * kilograms\ \ gain$$

Where,
kilograms price = price of the arroba ($/$kilograms$)
Gain kilograms = arroba* gain ($kilograms$ /day)

Daily Profit

$$revenue\ daily - cost\ daily$$

Where,
Revenue daily = daily revenue ($)

Cost daily = daily cost ($)

Total Revenue, Cost and Profit

$$\sum_{time} daily\ revenue$$

$$\sum_{time} daily\ cost$$

$$\sum_{time} daily\ profit$$

Where,
revenue_daily= see section 4
cost_daily = see section 3
profit_ddaily = see section 5

Cost and Profit per kilograms *

$$\text{total cost}/kilograms\ \ gain_t$$

$$total\ profit/kilograms\ \ gain_t$$

Where,
Total profit = see section 6
Total cost = see section 6
$arroba\ gain_t$ = $kilograms$ gain over time, see section 2

* To assess the profit obtained by meat producers, it is common to use the unit of measurement 'arroba' in Brazil. In this study, the 'arroba' unit is defined as equivalent to 15 kilograms, following the standard practice in the national livestock industry. Therefore, for the purposes of this study, the term 'arroba' in this equation will be used to represent the profit obtained per each 15 kilograms of meat produced.

Standardization of Costs and Arroba Pricing

i. Food cost:

Even considering the effect of the batch (animals evaluated by farm) in the analyses, all common foods between batches, especially among farms, had their prices standardized to

set up the food cost (for example, for corn silage, the price was always the same for the different batches). Based on the cost of natural matter and the percentage of dry matter (DM), from the measurement of each animal's daily individual intake, the food cost for everyone was imputed over the 80-day evaluation period. It is important to note that after a seven-day adaptation period, there were 80 days of data collection on weight, DM intake (DMI), and food and non-food costs (operational cost), all individual, to obtain the measure of accumulated profit and profitability per arroba gained by the evaluated animal.

ii. Non-food cost (operational cost):
The non-feed cost was also set at the same value for all evaluated batches with the aim of standardizing this cost source in the process, and it's a source that doesn't affect the animals' performance.

iii. Price paid per kilograms (arroba*):
The arroba price for all batches was standardized to the prices at the time of data collection, with the aim of ensuring that the revenue per arroba was equal for all animals. The prices followed those indicated by Center for Advanced Studies in Applied Economics (CEPEA, https://www.cepea.esalq.usp.br/br/indicador/boi-gordo.aspx)* - University of São Paulo (USP).

2.3 Data structuring

The contemporary groups (CG) for profitability, growth, fertility, carcass, and feed efficiency traits were formed by farm, management lot, sex, year, and birth season (dry season: April-September and rainy season: October-March). For the profitability and feed efficiency traits, the identification of the feed efficiency test was also considered to form the CG. Animals belonging to the CG with fewer than four individuals, as well as those without identification of sire and dam or those lacking phenotypic records within ±3.5 standard deviations from the mean of the CG, were excluded from the analyses. The number of records and the descriptive statistics for the studied traits are presented in Table 1.

Table 1. Descriptive statistics and number of animals with phenotypic records (N) and contemporary groups for growth, reproduction, carcass, feed efficiency, and profitability-related traits in Nelore cattle.

TRAIT (unit)	N	MEAN	SD	MIN	MAX	CV	MODA	MEDIAN	NCG
APF ($)	3.614	151.84	66.45	-17.98	420.06	43.76	81.45	155.50	226
PFT ($/kg)	3.614	36.21	9.75	-13.33	51.23	26.93	19.38	39.82	226
W450 (kg)	55.952	289.97	62.70	119.00	592.00	21.62	254.00	278.00	2181
DMI (kg/day)	9.910	8.06	1.87	3.18	18.74	23.21	7.15	7.82	219
RFI (kg of DM/day)	9.910	0.00	0.67	-4.93	4.69	-	-0.15	0.00	219
REA (cm^2)	36.170	57.20	12.70	20.45	116.35	22.21	60.00	56.19	1496
RFT (mm)	361.15	4.28	2.70	0.13	24.39	63.24	2.54	3.56	1496
FRAME	10.567	5.36	2.16	-6.34	15.58	40.38	2.76	5.23	425
PPC30 (%)	7.116	1.48	0.50	1.00(30,12%)	2.00 (69,8%)	33.60	1.00	1.00	126
AFC (month)	27.457	35.26	7.17	21.00	49.00	20.33	36.00	36.00	463
ACP (kg/cow/year)	14.983	140.86	33.34	45.00	331.00	23.67	143.00	137.00	286
SC365 (cm)	19.300	21.46	2.97	12.90	34.70	13.84	20.00	21.10	2303
APM (months)	3.422	16.62	3.89	8.73	22.00	23.45	22.00	15.00	32

APF, accumulated profitability in dollars; PFT, profit per kilogram of liveweight gain in dollars; W450, weight at 450 days of age; DMI, dry-matter intake; RFI, residual feed intake; REA, rib eye area; RFT, rump fat thickness; FRAME, frame score; PPC30, probability of precocious calving at 30 months of age; AFC, age first calving; ACP, accumulated cow productivity; SC365, scrotal circumference at 365 days of age; APM, age at puberty in males.

2.4 Variance components and genetics parameters estimation

The (co)variance components and genetic parameters were estimated using a multiple-trait animal model through Bayesian inference. This approach employed the Gibbs sampling algorithm implemented in the GIBBSF90+ software (Misztal et al., 2014) for both linear and categorical traits. Two groups of mult-trait models were constructed, as follows: 1) Model 1 (n = 8) considered the traits APF, PFT, and W450, DMI, RFI, REA, RFT and FRAME; 2) Model 2 (n = 7), the traits APF, PFT, and reproductive traits PPC30, AFC, ACP APM and SC365 were considered. The general animal model used was:

$$y = X\beta + Za + e$$

where y is the vector of observations; β is the vector of fixed effects; a is the vector of direct additive genetic effects, and e is the vector of random residual effects associated with the observations. X and Z are incidence matrices relating b and a to y. The

assumptions made in the model were: $E[y] = X\beta;\ Var(a)A\otimes G\ e\ Var(e) = I\otimes R$, where G is the direct genetic (co)variance effects; *A is the* relationship matrix; I is the identity matrix; *NR* is the number of animals with records; R is the residual (co)variance matrix, and $\otimes$ is the direct product of matrices. The general structure of the variance and covariance matrices of the random effects in the models was:

$$\begin{bmatrix} a \\ e \end{bmatrix} \sim N\,(0, V); V = \begin{bmatrix} G\otimes H & 0 \\ 0 & R\otimes I \end{bmatrix}$$

Where G is the (co)variance matrix of the direct additive genetic effects, H is a combined matrix from A (pedigree relationship matrix) and G (genomic relationship matrix); R is the residual (co)variance matrix, I is the identity matrix, and $\otimes$ is the direct product of the matrices.

As the multi-trait model comprised both categorical and linear traits, it was assumed that the initial distributions of the genetic and residual random effects followed a multivariate normal distribution, according to the Bayesian approach, as described below (adapted from Bonamy et al., 2019):

$$p\left(\begin{bmatrix} \alpha_1 \\ \vdots \\ \alpha_n \end{bmatrix} |G\right) \sim N = \left(\begin{bmatrix} 0 \\ \vdots \\ 0 \end{bmatrix}, G = G_0 \otimes H\right), P\left(\begin{bmatrix} e_1 \\ \vdots \\ e_n \end{bmatrix} |R\right) \sim N\left(\begin{bmatrix} 0 \\ \vdots \\ 0 \end{bmatrix}, R = R_0 \otimes I\right)$$

Where: G_0 is the genetic (co)variance matrix; R_0 is the residual variance matrix; $\otimes$ direct product; H is a combined matrix from A (pedigree relationship matrix) and G (genomic relationship matrix); I is the identity matrix. The inverse of the H matrix (H^{-1}) was constructed according to Aguilar et al. (2010) as:

$$H^{-1} = A^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & G^{-1} - A_{22}^{-1} \end{bmatrix}$$

where G^{-1} is the inverse of the genomic relationship matrix and A_{22}^{-1} is the inverse of numerator relationship matrix (the block of A for genotyped animals). The genomic relationship matrix (G) is the submatrix of the direct additive genetic and was built as per VanRaden (2008), in which $G = ZZ'/2\Sigma p_k q_k$ with p and q being the allele frequencies of marker K.

In the Gibbs Sampling implementation, 600,000 iterations were employed, with an initial burn-in of 100,000 iterations and a sampling interval of 100 iterations (thin). Convergence of the Monte Carlo Markov Chain (MCMC) was assessed using the Geweke Test (Geweke, 1992), available in the R package Bayesian Output Analysis Program (BOA) (Smith, 2007), as well as through visual evaluation using trace-plot graphs.

The estimated heritability coefficients were categorized following the guidelines established by Bourdon (1997), classifying them as low (below 0.20), moderate (ranging from 0.20 to 0.40), and high (above 0.40). For genetic and phenotypic correlations, the recommendation of Hill et al., (2013) was adhered to, considering them as low (less than 0.30), moderate (ranging from 0.30 to 0.70), and high (greater than 0.70).

3. Results and Discussion

The variance components and heritability estimates for accumulated profitability, profit per kilogram of liveweight gain, growth, carcass, reproduction, and feed efficiency are presented in Table 2. The heritability estimate was moderate to low (0.18), suggesting that genetic gains can be expected through selection for APF. The estimated heritability for PFT was low (0.02). PFT is an economic measure that reflects the relationship between two variables: the economic component, composed of the financial return per produced arroba, and the biological components involving different traits, for example carcass weight and feed conversion. In other words, it is directly affected by a complex interaction between economic and biological variables. Thus, the variance components partition or the estimation of the additive genetic component fraction contributing to the phenotype is difficult for complex traits calculated as a relationship of other traits.

Currently, there is no available knowledge regarding genetic parameter estimates for feedlot profitability-related traits in beef cattle. Nevertheless, with advancements in phenotyping technologies, we can identify and quantify new traits and potential environmental variables influencing phenotypic variation (Berry, 2023). This novel perspective underscores the importance of considering new traits, in addition to conventional ones, in the selection process, demonstrating the ongoing evolution of research and industry efforts toward improved economic indicators and sustainability.

Table 2. Posterior mean and high probability density (HPD[a]) for direct additive genetic (σ_a^2), residual (σ_e^2) variances and heritability (SD, standard deviation) for growth, carcass, feed efficiency, reproductive and feedlot profitability related traits in Nelore cattle.

Trait	σ_a^2	σ_e^2	h^2	± SD	HPD
APF	6321.23	28687.29	0.18	0.04	0.095 to 0.255
PFT	10.42	448.46	0.02	0.00	0.020 to 0.026
W450	292.87	539.77	0.35	0.01	0.326 to 0.375
DMI	0.23	0.62	0.27	0.03	0.231 to 0.316
RFI	0.07	0.41	0.15	0.02	0.113 to 0.185
REA	11.81	26.02	0.31	0.01	0.287 to 0.339
RFT	0.52	1.13	0.31	0.01	0.292 to 0.337
FRAME	0.55	1.17	0.32	0.02	0.291 to 0.351
PPC30	0.40	1.00	0.28	0.05	0.181 to 0.387
AFC	2.36	20.77	0.10	0.01	0.078 to 0.125
ACP	162.28	514.36	0.24	0.02	0.195 to 0.283
SC365	1.15	1.96	0.36	0.02	0.322 to 0.413
APM	5.79	7.51	0.43	0.05	0.326 to 0.535

[a]Credibility intervals at 95%; APF, accumulated profitability; PFT, profit per kilogram of liveweight gain ; W450, weight at 450 days of age; DMI, dry-matter intake; RFI, residual feed intake; REA, rib eye area; RFT, rump fat thickness; FRAME, frame score; PPC30, probability of precocious calving at 30 months of age; AFC, age first calving; ACP, accumulated cow productivity; SC365, scrotal circumference at 365 days of age; APM, age at puberty in males.

The estimated heritability for W450 was moderate (0.35), like previous findings in Nelore breed animals, as reported by Bonamy et al., 2019, Negreiros et al., 2022, and Silva Neto et al., 2023, ranging between 0.26 and 0.37. The heritability estimates for SC365, and APM were moderate to high, being 0.36 and 0.43, respectively, and were like the findings reported by Silva Neto et al., 2020, which were 0.33 and 0.30, respectively. The PPC30 heritability estimate obtained in this study was moderate, 0.28, and like those reported by Bonamy et al., 2019, and Negreiros et al., 2022, in Nelore animals, whose values were 0.29 and 0.28, respectively.

For AFC and ACP, the estimated heritability estimates were low to moderate (0.10 and 0.24, respectively; Table 2), indicating a considerable environmental influence on these traits. Similar estimates for AFC and ACP were also reported in Nelore animals by Costa et al., 2020, Van Mellis et al., 2010, and Kluska et al., 2018, ranging from 0.08 to 0.16, closely aligned with those described.

The heritability estimates for REA (0.31) and RFT (0.31) obtained in this study suggest that these traits are highly responsive to selection. These findings align with previous reports (Silva Neto et al., 2023; Londoño-Gil et al., 2022), which ranged from 0.28 to 0.33. Concerning feed efficiency traits, the heritability estimate for RFI (0.15) was lower than that reported by Kava et al., 2023 and like that obtained by Gomes et al., 2023, both in Nelore cattle (0.55 and 0.37, respectively). For DMI, the heritability estimate was moderate (0.27), similar with literature estimates also for Nelore cattle ranging from 0.29 to 0.45 (Kava et al., 2023; Gomes et al., 2023; Ceacero et al., 2016).

The genetic correlations between APF, PFT and growth, reproduction, carcass, and feed efficiency -related traits are presented in Table 3. The estimated genetic correlations between APF and PFT with W450 were favorable and moderate to high, 0.65 and 0.64, respectively. These results suggest that selecting animals with higher W450 would also increase APF and PFT. Growth traits evaluated after weaning are often used in breeding programs as selection criteria (Pinheiro et al., 2012), since post-weaning growth traits are favorable genetic correlated with liveweight gain efficiency and final carcass weight at slaughter (Abreu Silva et al., 2018; Pinheiro et al., 2012).

The genetic correlation between PFT and DMI was moderate (0.72) and low with PFT (0.26). These results suggest that selection for higher profitability would increase the DMI. DMI is closely associated with feed efficiency, body weight, and growth in cattle (Herd et al., 2014; Donoghue et al., 2016). Animals with higher dry matter intake typically exhibit higher average daily gain resulting in better feed conversion (Ceacero et al., 2016). The results of these studies pointed out that genetically more profitable animals have higher feed intake and better feed efficiency.

The genetic correlation between APF and PFT with RFI were low, 0.28 and -0.23, respectively. These results suggest that selection to improve RFI would not influence feedlot profitability. It is important to highlight that RFI is closely related to the maintenance of energy in cattle (Herd & Bishop, 2000). It is an important measure to identify animals that differ in the efficiency of using energy for maintenance, as reported by Archer et al. 1999. More efficient animals, i.e., low RFI, are due to their higher metabolic efficiency, reducing the energy cost of maintenance (Tempelman & Liu, 2020), which reduces demand for food without compromising the growth or size of adult animals Koch et al., 1963. Furthermore, many studies have reported the low genetic association of RFI with output traits, such as reproduction (Bonamy et al., 2019), growth, and carcass (Ceacero et al., 2016). RFI is more related to metabolizable energy efficiency than to

direct results in the production system, such as weight, weight gain, and rib eye area, which directly influence the profitability potential of the animals, which corroborates the low genetic correlation between RFI, and profitability obtained in this study.

Moderate and favorable genetic correlation estimates between APF and PFT with REA (0.43 and 0.44, respectively) were obtained, suggesting that selection to increase REA would likely result in higher feedlot profitability. The favorable genetic correlation between profitability and REA can be a relevant parameter for selection in production systems during the rearing and finishing phases, particularly within the beef industry. The REA is associated with the degree of muscling, edible mass, and yield of high-value meat cuts (Malheiros et al., 2020).

When breeders select animals with a larger ribeye area, they tend to choose animals with higher APF and PFT. This suggests that animals with greater muscularity, reflected by the ribeye area, can produce a larger quantity of higher-quality meat. As a result, these animals are generally more valued in the industry and generate higher profits per animal. Therefore, by focusing on the selection of animals with a higher ribeye area, producers can expect an increase in the profitability of beef production, as these traits are positively correlated.

The genetic correlations between APF and PFT with RFT were negative, low and moderate, -0.10 and -0.68, respectively, implying that selection for higher carcass fatness degree would not lead to more profitable animals in the feedlot. To obtain animals with greater APF, PFT, and finishing, these traits must be selected simultaneously in genetic improvement programs. Subcutaneous fat thickness is essential in determining meat product quality, as it shields the carcass from fiber shortening during the cooling process (Malheiros et al., 2015).

The moderate to low genetic correlation (0.20 and 0.48, respectively) obtained between APF and PFT with female sexual precocity indicator trait (PPC30) indicates that selection to improve PPC30 would also improve feedlot profitability. The results suggest that including profitability in selection identifies females with economic potential and productivity, improving the herd's reproductive performance and increasing financial returns, especially in commercial herds.

Table 3. Posterior mean and high probability density (HPD[a]) for genetic correlations between traits related to feedlot profitability with growth, reproduction, carcass, and feed efficiency in Nelore cattle.

Trait	Mean	± SD	HPD
Genetic correlation with Accumulated Profitability			
W450	0.65	0.08	0.512 to 0.812
DMI	0.72	0.09	0.546 to 0.866
RFI	0.28	0.15	-0.005 to 0.544
REA	0.43	0.09	0.263 to 0.620
RFT	- 0.10	0.07	-0.246 to 0.041
FRAME	0.44	0.08	0.284 to 0.592
PPC30	0.20	0.18	-0.141 to 0.538
AFC	-0.19	0.20	-0.811 to 0.188
ACP	-0.14	0.19	-0.498 to 0.216
SC365	-0.05	0.12	-0.297 to 0.168
APM	-0.21	0.18	-0.547 to 0.229
Genetic correlation with Profit per kilogram of liveweight gain			
W450	0.64	0.05	0.549 to 0.734
DMI	0.26	0.08	0.116 to 0.405
RFI	-0.23	0.08	-0.373 to -0.067
REA	0.44	0.07	-0.329 to 0.584
RFT	-0.68	0.04	-0.757 to -0.596
FRAME	0.77	0.44	0.692 to 0.869
PPC30	0.48	0.178	-0.112 to 0.792
AFC	-0.47	0.08	-0.621 to -0.304
ACP	-0.01	0.09	-0.208 to 0.178
SC365	-0.06	0.08	-0.210 to 0.095
APM	-0.03	0.13	-0.294 to 0.219

[a] Credibility interval at 95%; W450, weight at 450 days of age; DMI, dry-matter intake; RFI, residual feed intake; REA, rib eye area; RFT, rump fat thickness; FRAME, frame score; PPC30, probability of precocious calving at 30 months of age; AFC, age first calving; ACP, accumulated cow productivity; SC365, scrotal circumference at 365 days of age; APM, age at puberty in males.

Similarly, the estimates of genetic correlation between APF and PFT with AFC were also favorable and low to moderate, -0.19 and -0.47, respectively. Therefore, the negative yet favorable correlations indicate that an earlier age at first calving may be associated with higher APF and PFT. Although sexual precocity and age at first calving are not directly associated with meat production in the finishing phase, they can indirectly impact the quantity of calves produced over time, contributing to the availability of animals ready for slaughter and, consequently, to the total meat production. On the other hand, genetic correlations estimates between ACP, SC365, APM, APF, and PFT were

close to zero, ranging from -0.01 to -0.21 (Table 3), indicating that selection to increase scrotal circumference, reduce male age at puberty age, or cow accumulated productivity would not increase or affect the feedlot profitability.

The genetic correlation estimates between APF and PFT with FRAME (0.44 and 0.77, respectively) pointed out a moderate to high and favorable association. Therefore, selecting for higher FRAME would increase the feedlot profitability. Animals with a balanced body structure, that is, medium-sized, tend to convert feed into weight gain more efficiently, with adequate fat deposition. This contributes to quicker readiness for slaughter. Breeders can use this information to select animals better suited to the specific conditions of the environment and management conditions in which they will be raised, which can lead to higher productivity and, consequently, increased profit per unit of weight.

The residual correlations between APF, PFT and growth, reproductive, feed efficiency, and carcass traits are described in Table 4. In general, residual correlations for most traits with APF, and PFT were low and close to zero, suggesting a low association between traits relative to non-additive components (Falconer & Mackay, 1996). This suggests that shared environmental factors and non-additive genetic effects do not strongly influence the traits under study. However, except for the moderate residual correlation between profitability and W450 and DMI (0.21 and 0.21, respectively), it is indicated that variations similarly influence these traits in environmental conditions and favor these traits in the same direction.

Table 4. Posterior mean and high probability density (HPD[a]) for residuals correlations between feedlot profitability related traits with growth, reproduction, carcass, and feed efficiency in Nelore cattle.

Trait	Mean	± SD	HPD
Residual correlation with Accumulated Profitability			
W450	0.21	0.03	0.146 to 0.276
DMI	0.21	0.03	0.150 to 0.262
RFI	-0.05	0.03	-0.098 to 0.011
REA	0.12	0.03	0.063 to 0.170
RFT	0.13	0.03	0.073 to 0.177
FRAME	0.03	0.04	-0.0.53 to 0.107
PPC30	0.02	0.10	-0.179 to 0.211
AFC	0.02	0.07	-0.121 to 0.157
ACP	0.17	0.33	-0.397 to 0.764
SC365	0.18	0.05	0.083 to 0.282
APM	0.07	0.08	-0.101 to 0.235
Residual correlation with Profit per kilogram of liveweight gain			
W450	0.09	0.03	0.029 to 0.161
DMI	0.06	0.02	0.014 to 0.104
RFI	0.07	0.21	0.032 to 0.115
REA	0.05	0.02	0.008 to 0.097
RFT	0.07	0.03	0.029 to 0.112
FRAME	0.01	0.03	-0.442 to 0.066
PPC30	0.03	0.10	-0.160 to 0.224
AFC	0.02	0.07	-0.126 to 0.159
ACP	0.11	0.35	-0.480 to 0.733
SC365	0.15	0.05	0.015 to 0.206
APM	0.01	0.08	-0.135 to 0.164

W450, weight at 450 days of age; DMI, dry-matter intake; RFI, residual feed intake; REA, rib eye area; RFT, rump fat thickness; FRAME, frame score; PPC30, probability of precocious calving at 30 months of age; AFC, age first calving; ACP, accumulated cow productivity; SC365, scrotal circumference at 365 days of age; APM, age at puberty in males.

Based on the results, these two new novel traits (APF and PFT) can be used as support tools for efficiently managing feedlot operators' daily operations and as selection criteria for intensive beef cattle systems. Applying APF and PFT in commercial herds allow to classify the animals that would have a lower return than expected from those with higher genetic potential for profitability The animals with higher genetic potential for feedlot profitability are genetic associated with greater weight gain, carcass muscle deposition, and carcass yield. These animals, which require shorter feedlot duration length, can be identified early, and allocated differently from animals with lower returns,

enabling precise and more efficient management of resources. This approach contributes to optimizing business operations and promoting sustainability. For breeding herds, genetic evaluation focused on profit, as a trait, could be employed to provide producers with information about economic gains based on their genetic choices, being complementary tools to the selection index (Hassanvand - Javanmard et al.,2017).

4. Conclusion

This study shows that APF and PFT are heritable and can be improved through selection, although the response to selection for PFT is low. The results revealed that W450, REA, FRAME and DMI were the most informative traits associated with feedlot profitability, while W450, FRAME and REA were the most relevant for PFT, given the moderate to high and favorable genetic correlations. In practical terms, animal breeders can identify and select animals with higher P450, DMI, carcass and REA, resulting in higher feedlot accumulated profitability and profit per kilogram of live weight gain in the feedlot.

Thus, this study suggests that these novel new traits can be included as complementary tools in selection criteria, as they provide additional tools to classify animals based on expected feedlot profit, which is essential for management decision-making. Additionally, with recent advancements in high-throughput phenotyping tools, it is possible to significantly expand the collection of new phenotypes and incorporate them as support in the selection process, aiming to make livestock farming increasingly productive, efficient, and sustainable.

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CHAPTER 3: GENOME-WIDE ASSOCIATION ANALYSIS OF NOVEL FEEDLOT PROFITABILITY-RELATED TRAITS IN NELORE BEEF CATTLE

Abstract: This study aimed to conduct a genome-wide association study (GWAS) to identify genomic regions associated with profitability traits in Nelore beef cattle. The dataset included 3,614 phenotypic records of accumulated profitability (APF) and profit per kilogram of liveweight gain (PFT) from animals born between 2020 and 2022, participating in the Nelore Brazilian breeding program from the National Association of Breeders and Researchers (ANCP). From this total, 2,127 animals were genotyped with the Clarifide® Nelore 3.0 SNP panel. After quality control, 2,127 genotyped animals and 35,658 SNPs remained in the dataset for analysis. The weighted single-step approach for genome-wide association (WssGWAS) methodology was used to identify genomic regions associated with APF and PFT. A single-trait animal model was applied to predict genetic values, and SNP effect solutions were obtained from these values. Genomic windows of 10–SNP sliding windows that explained more than 0.5% of the additive genetic variance of each trait were selected to investigate potential candidate genes. A total of 83 genes within 21 windows and 268 genes within 52 windows associated with the APF and PFT were identified, respectively. Several genes related to fertility, feed efficiency, carcass traits, muscle and adipose tissue development and metabolism, and lipid and carbohydrate metabolism were identified, along with genes associated with animal behavior. The results revealed that identifying genomic regions and their respective candidate genes contributes substantially to a better understanding of the genetic mechanisms regarding these novel profitability-related phenotypes in Nelore beef cattle.

Keywords: Accumulated profitability, *Bos indicus*, Profit per kilogram of liveweight gain, Single nucleotide polymorphism, WssGWAS

1. Introduction

Sustainable agricultural practices and improving production efficiency go side by side (Mueller & Van Eenennaam, 2022). As improvements occur in sustainable production practices in this sector, results are automatically generated that serve as inputs for the production system, contributing to increased availability of resources, both in terms of quality and quantity. Efficiency is determined by attaining the highest achievable production capacity while minimizing waste and increasing production using the same or fewer resources (Mueller & Van Eenennaam, 2022). For example, over the past 50 years, the evolution of genetic improvement in livestock through selection and crossbreeding has brought about significant changes in animal performance (Simm, 1998; Haskell et al., 2014). Economically important traits, such as milk production, feed efficiency, reproductive and carcass traits, disease resistance, and adaptation to local environmental conditions, have been improved in several livestock species (Pramod et al., 2023).

The modern livestock industry consistently pursues innovative solutions and advanced strategies to tackle challenges in beef production. In this scenario, there is a demand for new traits/phenotypes to manage animal breeding and handling (Egger-Danner et al., 2015). The emergence of new technologies in precision livestock farming has considerably expedited phenotyping programs, enabling the identification of previously unexplored phenotypes (Berckmans, 2017). These emerging phenotypes play a significant role in the genetic progress of beef herds, reshaping how we perceive efficiency and profitability in beef production.

Despite the relatively slow evolution in generating and adopting new phenotypes within the selection process, several research studies and reviews have tackled emerging phenotypes such as those related to meat quality, fertility, and growth in beef cattle, aiming to enhance productivity sustainably (Greenwood et al., 2016; Ventura et al., 2020). However, facing these novel technologies capable of capturing and measuring numerous variables that contribute to the desired phenotypes, it is highly fundamental to delve into understanding the genetic component in economic terms, transcending beyond the production phenotype.

In this context, new traits or phenotypes that can be incorporated into selection program (Merkes et al., 2011) and commercial farms, especially those related to the genetic component of the animal that can predict individuals' genetic profitability potential, are needed. This includes novel phenotypes that indicate economic return, such as accumulated feedlot profitability (APF) and profit per kilogram of liveweight gain

(PFT) in feedlot, which are important in management and decision-making. Both feedlot APF and PFT traits are innovative and are obtained through advanced data analysis and processing techniques used in precision livestock technologies.

Given the increase in the world population, the advancement of urbanization, and economic growth, along with changes in consumer preferences (Delgado et al., 2020), a significant impact on the demand for meat is expected. In view of this perspective and the need to maintain productivity in the face of high production costs, especially in feedlots, it is opportune to consider the inclusion of these two new profitability-related traits in addition to conventional ones.

The advancement of molecular techniques, including the mapping and identification of quantitative trait loci (QTLs), has resulted in a considerable paradigm shift in the field of livestock farming (Pramod et al., 2023). Additionally, current innovations in high-throughput and high-dimensional genotyping and phenotyping technologies enable the identification of the causal networks within the 'black box' between genotype-phenotype through the principles of genome-wide association studies (GWAS) (Chen et al., 2013).

The GWAS has been applied in cattle to identify regions or genetic variants associated with several traits of interest, mainly for polygenic and complex phenotypes (Schaid et al., 2018), enabling the understanding of underlying biological processes (Luo et al., 2022) and facilitating the definition of selection strategies aimed at increasing the frequency of favorable alleles (Carreño et al., 2019). The tool in question has proven particularly useful for selecting new traits that are difficult, costly, or time-consuming to measure (Calus et al., 2013; Oliveira Silva et al., 2017). In this sense, GWAS becomes an important tool for identifying genes or regions associated with these novel traits related to profitability. This study will thus provide opportunities to understand how biological processes are involved in these traits.

Therefore, the main objectives of this study were to identify genomic regions associated with feedlot APF and PFT in Nelore beef cattle through weighted single-step genome-wide association study (WssGWAS) to identify potential candidate genes within QTL regions that explain more significant proportions of the additive genetic variance for each studied trait. Additionally, a functional gene enrichment analysis was conducted to enhance our understanding of the genetic interaction, biological processes, and metabolic pathways associated with APF and PFT in Nelore cattle.

2. Materials and methods

This study was exempt from evaluation by the Animal Ethics Committee (CEUA), as established by Law No. 11,794 of 08/10/2008 and Normative Resolution No. 51 of 05/19/2021 from the National Council for Animal Experimentation Control (CONCEA) as all the analyses were performed using pre-existing databases.

2.1 Data source

The dataset used in this study was provided by the National Association of Breeders and Researchers (ANCP, São Paulo, Brazil) in collaboration with @Tech (Piracicaba, São Paulo, Brazil). ANCP provided the pedigree information and genotypes, and novel profitability-related phenotypes were provided by @Tech. For further information about the company, please refer to the website https://techagr.com/beeftrader. The animals belonged to 27 different herds located in the Southeast, Northeast, and Midwest regions of Brazil. The data set contained pedigree information of 38,930 animals, born from 1998 and 2016, comprising 2,691 sires and 19,884 dams.

2.2 Phenotypic Data

The new phenotypes analyzed were accumulated feedlot profitability (APF) and feedlot profit per kilogram of liveweight gain (PFT). @Tech's algorithms are designed to make full use of this data, ideally collected within a standardized 80-day trial period for running in the BeefTrader Decision Support System generating the phenotypes used by the Livestock Profit Tool (LPT) profitability. For trials that do not meet this 80-day standard, our system employs Artificial Intelligence and advanced growth modeling techniques to set the standard. This approach considers historical data to produce estimates that align with the 80-day prediction requirements of the LPT, ensuring robust and reliable analytics across varying trial durations.

The BeefTrader algorithm uses animal traits as input variables (gender, breed, body condition score, initial weight, initial date, among other exogenous factors that impact on growth dynamics), daily weights individually collected through a weighing sensor (daily basis), and information on the nutritional composition of the diets. The records for obtaining the new phenotypes were collected from animals participating in feed efficiency trials, following the same guidelines as Mendes et al., 2020, as mentioned in the section on feed efficiency traits. Based on this information, adjusted for local conditions, weight prediction is carried out in two steps: based on the biology of each

animal and with the nutritional data and animal daily weight profile (observed or predicted), it is possible to estimate an optimal growth function for the animals (Step 1); from there, a dynamically adjusted linear or non-linear regression is performed using the least squares method on the weights to fit the predicted growth curve (Step 2). From the predicted growth curve, it is possible to find other variables required by the model, including animal performance in terms of growth and composition of gain, as well as economic and environmental factors. The profitability is the central trait used by LPT, as commented, thus the next topics the @Tech intention is to present the equations related to this core phenotype.

Accumulated kilograms*

$$(sbw * cdf/100) \,/\, 15$$

Where:

sbw: Shrunk Body Weight (kg) - 96% of the Body Weight

cdf: Carcass Dressing (%)

kilograms $*$ Gain

$$initial\ gain = acum\ kilograms\ [2] - acum\ kilograms\ [1]$$

$$initial\ gain = acum\ kilograms\ [d] - acum\ arroba\ [1] + initial\ gain$$

Where:
Acum $kilograms$ = accumulated $kilograms$ $(15kg)$ on a specific day
d = Day
gain initial = gain to be considered on the first day since it is unknown. This value becomes a constant.
Note: The correct procedure for the first day would be to calculate based on the corral weight and remove the constant from the subsequent days.

Daily Cost

$$DMI * diet\ price\ (kg) + feedlot\ daily\ overhead$$

Where:
dmi = Dry Matter intake (kg)
diet_price_kg = diet cost ($/kg)
feedlot_daily_overhead = non-feed cost ($)

Daily Revenue

$$kilograms\ \ price * kilograms\ \ gain$$

Where,
arroba_price = price of the arroba (\$/$kilograms$)
gain_arroba = arroba gain ($kilograms$ /day)

Daily Profit

$$revenue\ daily - cost\ daily$$

Where,
Revenue daily = daily revenue (\$)

Cost daily = daily cost (\$)

Total Revenue, Cost and Profit

$$\sum_{time} daily\ revenue$$

$$\sum_{time} daily\ cost$$

$$\sum_{time} daily\ profit$$

Where,
revenue_daily= see section 4
cost_daily = see section 3
profit_ddaily = see section 5

Cost and Profit per kilograms $*$

$$\text{total cost}/kilograms\ \ gain_t$$

$$total\ profit/kilograms\ \ gain_t$$

Where,
Total profit = see section 6
Total cost = see section 6
$arroba\ gain_t$ = $kilograms$ gain over time, see section 2

Standardization of Costs and Arroba Pricing

i. Food cost:

Even considering the effect of the batch (animals evaluated by farm) in the analyses, all common foods between batches, especially among farms, had their prices standardized to set up the food cost (for example, for corn silage, the price was always the same for the different batches). Based on the cost of natural natter and the percentage of dry matter (DM), from the measurement of each animal's daily individual intake, the food cost for everyone was imputed over the 80-day evaluation period. It is important to note that after a seven-day adaptation period, there were 80 days of data collection on weight, DM intake (DMI), and food and non-food costs (operational cost), all individual, to obtain the measure of accumulated profit and profitability per arroba gained by the evaluated animal.

ii. Non-food cost (operational cost):
The non-feed cost was also set at the same value for all evaluated batches with the aim of standardizing this cost source in the process, and it's a source that doesn't affect the animals' performance.

iii. Price paid per kilograms (arroba*):
The arroba price for all batches was standardized to the prices at the time of data collection, with the aim of ensuring that the revenue per arroba was equal for all animals. The prices followed those indicated by Center for Advanced Studies in Applied Economics (CEPEA, https://www.cepea.esalq.usp.br/br/indicador/boi-gordo.aspx)* - University of São Paulo (USP).

* To assess the profit obtained by meat producers, it is common to use the unit of measurement 'arroba' in Brazil. In this study, the 'arroba' unit is defined as equivalent to 15 kilograms, following the standard practice in the national livestock industry. Therefore, for the purposes of this study, the term 'arroba' in this equation will be used to represent the profit obtained per each 15 kilograms of meat produced.

2.3 Data structuring

The contemporary groups (CGs) were composed considering the farm, year, and season of birth (dry: March to August; rainy: September to February), management group and sex. The phenotypic quality control removed records that deviated 3.5 standard deviations from the overall mean of the CG and those with fewer than four records.

Descriptive statistics for the APF and PFT traits after quality control are summarized in Table 1.

Table 1. Number of records and descriptive statistics for the studied traits in Nelore breed.

TRAIT	N	MEAN	SD	MIN	MAX	CV (%)	CG
APF ($)	3614	151.84	66.45	-17.98	420.06	43.76	226
PFT ($/kg)	3614	36.21	9.75	-13.33	51.23	26.93	226

APF, accumulated profitability in dollars; PFT, profit per kilogram of liveweight gain in dollars; N, number animals with records; SD, standard deviation; MIN, minimum; MAX, maximum; CV, coefficient of variation; CG, number contemporary group.

2.4 Genotyping and quality control

A total of 2,127 animals were genotyped with the Clarifide® Nelore 3.0 low-density SNP panel, containing more than 70,000 markers. The genotype quality control (QC) was performed by the PREGSF90 package (Aguilar et al., 2014), where animals and SNPs from the dataset with call rates < 0.90 were excluded. Additionally, SNPs with a minor allele frequency (MAF) < 0.05, Mendelian conflicts >1%, with redundant positions, SNPs deviating from Hardy-Weinberg equilibrium expectations, and those located on non-autosomal chromosomes were also excluded. After QC, 2,127 genotyped animals and 35,658 SNPs remained in the dataset for analysis.

2.5 Genome-wide association study

The genome-wide association analysis for APF and PFT was performed using the methodology proposed by Wang et al. (2012), known as the weighted single-step genome-wide association study (WssGWAS). Briefly, the variance components were estimated using the restricted maximum likelihood method, using software BLUPF90+ through a single-trait model, and the genomic estimated breeding values (GEBVs) were estimated using the single-step genomic BLUP (ssGBLUP) approach (Aguilar et al., 2010). SNP effects were subsequently calculated using the postGSf90 software. A single-trait animal model was applied to estimate the variance components and perform the WssGWAS. In matrix notation, the model is described as:

$$y = Xb + Za + e$$

where *Y* is the vector of phenotypic observations; *X* the incidence matrix that relates the phenotypes to the fixed effects; *b* the vector of fixed effects of the CG and covariates (linear and quadratic effects of age of the animal); *Z* is an incidence matrix relating the animal to the phenotype, *a* is the vector of effects of the animals, and *e* is the vector of residual effects. The variances of *a* and *e* are given by:

$$Var\begin{bmatrix} a \\ e \end{bmatrix} = \begin{bmatrix} H\sigma_a^2 & 0 \\ 0 & I\sigma_e^2 \end{bmatrix}$$

where $\sigma_a^2\sigma$ is the additive genetic variance and σ_e^2 is the residual variance. *H* is the matrix that combines the relationship matrix and genomic information matrix as described by Aguilar et al. (2010), and *I* is an identity matrix. The inverse of matrix *H* is:

$$H^{-1} = A^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & G^{-1} - A_{22}^{-1} \end{bmatrix}$$

where *A* denoted the numerator relationship matrix based on the pedigree for all individuals; A_{22} was the numerator relationship matrix for the genotyped animals; and the *G* matrix was a genomic relationship matrix that was constructed as described by Vanraden et al. (2009).

Table 2. Additive genetic variance (σ_a^2); residual variance (σ_e^2), heritability (h^2) and standard deviation (SD) estimates for accumulated profitability (APF) and profit per kilogram of liveweight gain (PFT) in Nelore breed.

TRAIT	$\boldsymbol{\sigma_a^2}$	$\boldsymbol{\sigma_e^2}$	$\boldsymbol{h^2 \pm SD}$
APF	8548.70	27081	0.24 ± 0.04
PFT	21.88	439.17	0.05 ± 0.02

For the derivation of SNPs effects and weights, the animal effect was decomposed into genotyped (a_g) and not genotyped animals (a_n), as described by Wang et al. (2012). The animal effect of the genotyped animals is a function of the SNP effects (Wang et al., 2012):

$$a_g = Z_g u$$

where $\mathbf{Z_g}$ represents the relationship matrix of the genotypes of each locus, and **u** is a vector of the SNPs effects. The variance of animal effects was assumed as:

$$\mathrm{var}\left(a_g\right) = \mathrm{var}\left(\mathrm{Z}_g\mathrm{u}\right) = \mathrm{Z}_g\mathrm{DZ}_g{}'\sigma_{\mathrm{u}}^2 = G^*\sigma_a^2$$

where ***D*** is a diagonal matrix of weights for variances of SNP variances (**D** = **I** for GBLUP), σ_{u}^2 is the variance of the additive genetic effect obtained from each SNP when the same variance is assumed for all SNPs, σ_a^2 is the additive genetic variance, and G^* is the weighted genomic relationship matrix.

The ratio of covariance of additive genetic (a_g) and SNPs (***u***) effects is:

$$var_u^{a_g} = \begin{bmatrix} ZDZ' & ZD' \\ DZ' & D \end{bmatrix}\sigma_u^2$$

Sequentially:

$$G^* = \frac{var(a_g)}{\sigma_a^2} = \frac{var(Zu)}{\sigma_a^2} = ZDZ'\lambda$$

where $\boldsymbol{\lambda}$ is a normalizing constant described by VanRaden et al. (2009) as:

$$\lambda = \frac{\sigma_{\mathrm{u}}^2}{\sigma_{\mathrm{a}}^2} = \frac{1}{\sum_{i=1}^{m} 2p_i(1-p_i)}$$

where ***m*** is the number of SNPs and $\boldsymbol{p_i}$ is the frequency of the second allele in the ***i***-th SNP. The SNP effects was described by Wang et al. (2012), as:

$$\hat{u} = \lambda \mathrm{D}Z'G^{*-1}\hat{a}_g = DZ'[ZDZ']^{-1}\hat{a}_g$$

The estimated SNP effects can be used to calculate the variance of each individual SNP (Zhang et al., 2010), which can be used as different weighting for each SNP:

$$\sigma^2_{u,i} = u_i^2 2p_i(1-p_i)$$

WssGWAS is an iterative process with several steps, considering t as the iteration number, the steps are (Wang et al., 2012):

1. Let D = I in the first step.
2. Calculate G = $\mathbf{Z_g D Z_g' \lambda}$.
3. Calculate GEBVs for the entire data set using the ssGBLUP.
4. Convert GEBVs to SNP effects ($\hat{u}$): $\hat{u} = \boldsymbol{\lambda}\, DZ' (\mathbf{Z_g} D \mathbf{Z_g}' \boldsymbol{\lambda})^{-1} \hat{a}_{\mathbf{g}}$, where $\hat{a}_{\mathbf{g}}$ is the GEBVs of animals which were also genotyped.
5. Calculate weight for each SNP for linear model (Zhang et al., 2010):
$$d_i = \hat{a}_i^2 2p_i(1-p_i)$$
6. Normalize SNP weights to remain the total genetic variance constant.
7. Back to step 2.

In this study, the procedure was executed in three iterations, following the approach employed by Wang et al. (2012), and the effects of the markers obtained in the third iteration were used to calculate proportions of genetic variances explained by subsets of consecutive SNPs. The results were presented as the proportion of the additive genetic variance explained by windows of 10 adjacent SNPs, as below:

$$\frac{\mathrm{Var}(a_i)}{\sigma_a^2} \mathrm{x}100 = \frac{\mathrm{Var}(\sum_{j=1}^{10} Z_j\, \hat{u}_j)}{\sigma_a^2} \mathrm{x}100$$

where, a_i is the genetic value of the *i*-th region that consists of continuous 10 SNPs, σ_a^2 is the additive genetic variance; Z_j is the vector of gene content of the *j*-th SNP for all individuals; and $\hat{u}_j$ is the marker effect of the *j*th SNP within the *i*-th region.

2.6 Gene prospection and functional enrichment analysis

The Ensembl Biomart tool with the Genes 111 database and Cow genes ARS-UCD1.3 dataset was used to identify the gene content of significant genomic regions of each studied trait. The search for significant ($P < 0.05$) Gene Ontology terms (biological processes, cellular components and molecular functions) and pathways (KEGG) was

performed by DAVID v.2023q4 tool (Sherman et al., 2022) using the bovine genome as background.

3 Results and Discussion

The proportion of additive genetic variance explained by windows of 10 adjacent SNPs for APF and PFT from single-trait WssGWAS can be visualized in the Manhattan plots present in Fig. 1 and Fig. 2, respectively**.** The Manhattan plots from the 1st and 2nd iterations of WssGWAS, along with the respective percentages of additive genetic variance explained by 10-SNP windows for APF and PFT, are presented in supplementary material. The proportions of additive genetic variances explained by the windows of Figures 1 and 2 indicate the polygenic nature of APF and PFT, suggesting that probably many genes with small effect likely influence these analyzed traits.

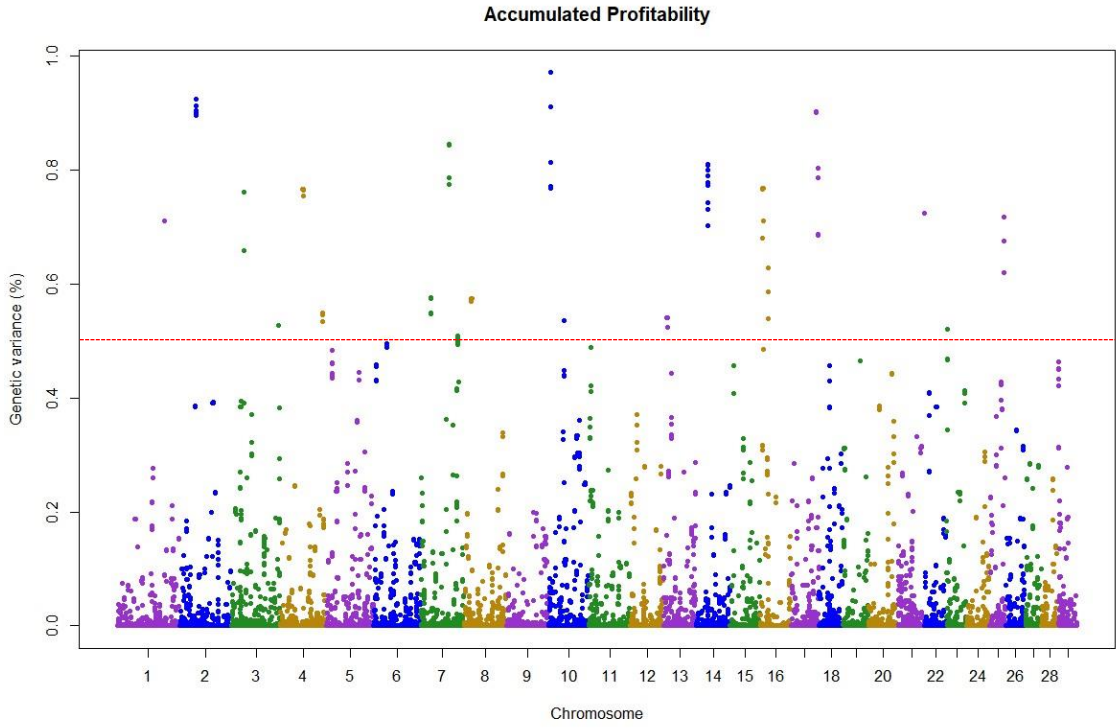

Figure 1. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 3nd iteration of the WssGWAS for accumulated profitability in Nelore cattle. The dot above the red line indicates the 21 genomic regions explaining together 14.67% of the additive genetic variance for APF in Nelore beef cattle.

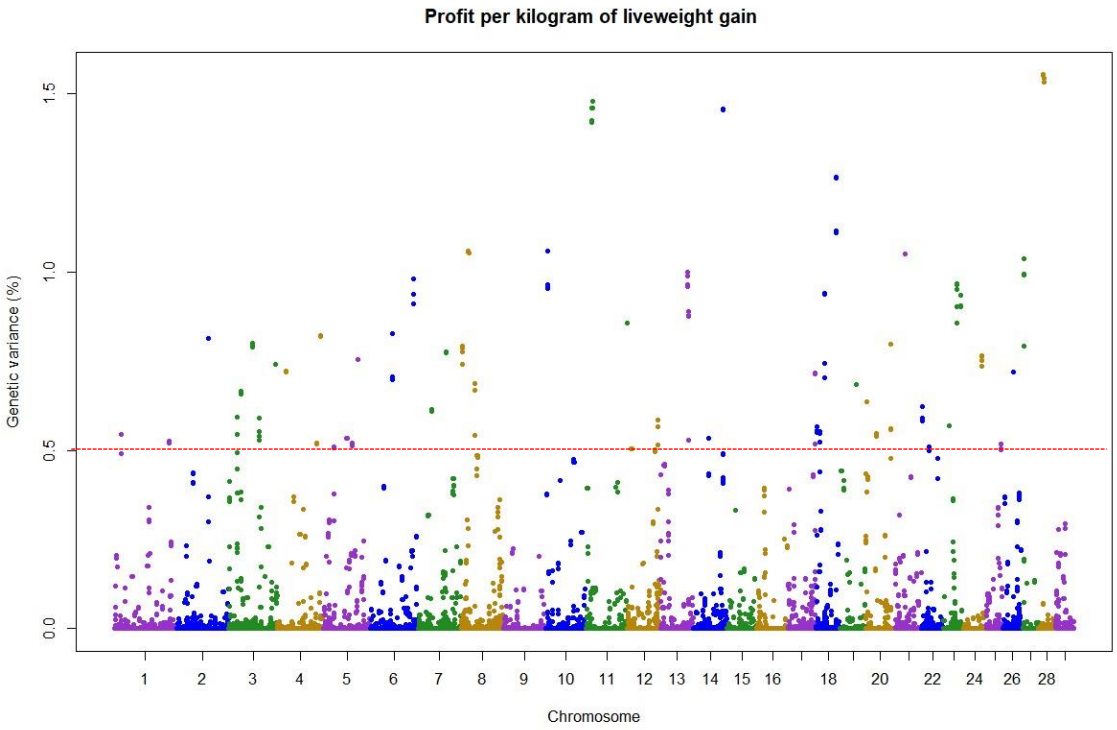

Figure 2. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 3nd iteration of the WssGWAS for profit per kilogram of liveweight gain in Nelore cattle. The dot above the red line indicates the 52 genomic regions explaining together 38,11% of the additive genetic variance for PFT in Nelore beef cattle.

A total of 21 genomic regions explaining more than 0.5% of the additive genetic variance for APF were identified on chromosomes 1, 2, 3, 4, 7, 8, 10, 13, 14, 16, 17, 21, 23, and 25, which encompasses 83 genes (47 protein-coding genes and 5 non-coding RNA) (Table 3).

Table 3. Potential candidate genes based on the proportion of the additive genetic variance explained by windows of 10 adjacent SNPs (Var %) obtained in the 3nd iteration of the WssGWAS for accumulated profitability in Nelore cattle.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
1	122665580	122970921	-	0.71182
2	41647204	42042712	*GALNT13*[1]	0.92468
3	115957406	116233438	*CHI3L2*[1], *DENND2D*[1], *CEPT1*[1], *DRAM2*[1], *ACKR3*[1], *ENSBTAG00000066299*[1], *ENSBTAG00000050725*[1], *IQCA1*	0.52799
	32178026	32406998		0.76174
4	110884207	111245497	*CNTNAP2*[1]	0.54940
	58883457	59154008		0.76754
7	98757265	98907404	*GRAMD2B*[1], *MIR2458*[2], *ENSBTAG00000068092*[2], *ENSBTAG00000055597*[2], *ENSBTAG00000060037*[2], *ENSBTAG00000059942*[2],	0.50930
	27361086	27661808		0.57638
	76689716	77004653		0.84567
8	20507980	20885550	*ENSBTAG00000067218*[2], *ENSBTAG00000067020*[1], *ENSBTAG00000066014*[1]	0.57502
10	40483645	40939069	*HRH2*[1], *SFXN*[1], *DRD1*[1], *ENSBTAG00000060352*[2], *ENSBTAG00000057676*[2], *ENSBTAG00000061410*[2], *ENSBTAG00000057850*[2], *ENSBTAG00000067561*[2], *MDGA2*[1],	0.53580
	5437359	5794507		0.97162
13	7792833	8069828	*FLRT3*[1], *MACROD2*[1]	0.54132
14	24573257	24710609	*UBXN2B*[1], *CYP7A1*[1], *U1*[2], *ENSBTAG00000061529*[1], *ENSBTAG00000067760*[1]	0.81010
16	25915302	25935999	-	0.62888
	9778896	10182016		0.76919

Continued Table 3.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
17	72729254	73183467	*LIF*[1], *OSM*[1], *CASTOR1*[1], *TBC1D10A*[1], *CCDC157*[1], *RNF215*[1], *SEC14L2*[1], *MTFP1*[1], *SEC14L3*[1], *SEC14L4*[1], *CDC45*[1], *CLDN5*[1], *SEPTIN5*[1], *GP1BB*[1], *TBX1*[1], *GNB1L*[1], *TXNRD2*[1], *COMT*[1], *ARVCF*[1], *TANGO2*[1], *MIR185*[2], *DGCR8*[1], *MIR3618*[2], *MIR1306*[2], *TRMT2A*[1], *RANBP1*[1], *ZDHHC8*[1], *CCDC188*[1], *RTN4R*[1], *PRODH*[1], *DGCR6L*[1], *SF3A1*[1], *ENSBTAG00000067193*[2], *ENSBTAG00000064410*[2], *ENSBTAG00000056180*[2], *ENSBTAG00000066914*[2], *ENSBTAG00000067425*[2], *ENSBTAG00000068969*[2], *ENSBTAG00000042154*[2], *ENSBTAG00000065648*[2], *ENSBTAG00000064523*[2], *ENSBTAG00000065346*[1], *ENSBTAG00000049878*[1]	0.80385
	69246711	69459128		0.90250
21	71412000	71412000	-	0.72480
23	4040152	4359518	*COL21A1*[1]	0.52107
25	37799150	38003995	*LMTK2*[1], *CCZ1*[1], *RSPH10B*[1], *ENSBTAG00000046943*[1]	0.71717

protein-coding gene[1]; non-coding RNA[2].

For PFT, 52 regions on chromosomes 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28 were identified explaining more than 0.5% of the additive genetic variance, encompassing 268 genes (187 protein-coding, 79 non-coding RNA and two pseudogenes) (Table 4).

Table 4. Potential candidate genes based on the proportion of the additive genetic variance (Var %) explained by windows of 10 adjacent SNPs obtained in the 3nd iteration of the WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
1	141205936	141713896	*BACE2*[1], *FAM3B*[1], *MX1*[1], *MX2*[1], *C1H21orf91*[1], *TMPRSS2*[1], *ENSBTAG00000060761*[2], *ENSBTAG00000067615*[1], *ENSBTAG00000066992*[1], *ENSBTAG00000069934*[1]	0.52606
	18843649	19231564		0.54430
2	85493604	86006315	*PGAP1*[1], *ANKRD44*[1], *SF3B1*[1], *SNORA70*[2], *ENSBTAG00000058339*[1]	0.81517
3	78644818	79069350	*PDZK1*[1], *DENND2D*[1], *DRAM2*[1], *SGIP1*[1], *PDE4B*[1], *ACKR3*[1], *ASB18*[1], *CEPT1*[1], *GJA8*[1], *GPR89A*[1], *IQCA1*[1], *ENSBTAG00000055369*[2], *ENSBTAG00000066299*[1], *ENSBTAG00000050725*[1], *ENSBTAG00000056285*[3]	0.59149
	21640254	21869985		0.59332
	32178026	32406998		0.66478
	115730569	116035968		0.74251
	61630774	61947686		0.80003
4	102525893	102774902	*ETV1*[1], *DGKB*[1], *TTC26*[1], *IFT56*[1] *KIAA1549*[1], *ZC3HAV1*[1], *ZC3HAV1L*[1]	0.52033
	22180214	22588568	*KRBA1*[1], *SSPO*[1], *ZNF862*[1], *ENSBTAG00000062759*[2]	0.72227
	112529847	112756381	*ATP6V0E2*[1], *LRRC61*[1], *RARRES2*[1], *ZNF467*[1], *ENSBTAG00000067250*[2], *ENSBTAG00000064227*[2], *ENSBTAG00000068937*[1]	0.82340
5	24960637	25217149	*USP44*[1], *MUCL1*[1], *CDK17*[1], *MB*[1], *METAP2*[1], *ENSBTAG00000069851*[2], *ENSBTAG00000062636*[2], *ENSBTAG00000056536*[1], *ENSBTAG00000049200*[1], *ENSBTAG00000010711*[1], *ENSBTAG00000062967*[1], *ENSBTAG00000057023*[1],	0.50864
	73664348	74010148	*RBFOX2*[1], *PDE3A*[1], *RASD2*[1]	0.52112
	60604166	60985883	*CFAP54*[1], *ENSBTAG00000064001*[2], *ENSBTAG00000064878*[2], *ENSBTAG00000057831*[1]	0.53433

Continued Table 4.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
5	60604166	60985883	*ENSBTAG00000057741*[2]	0.53433
	89193101	89472174	-	0.75480
6	56419575	56639531	*FGFBP1*[1], *PROM1*[1], *U6*[2], *CD38*[1], *ENSBTAG00000056148*[1], *ENSBTAG00000068440*[2], *ENSBTAG00000058952*[2], *ENSBTAG00000059226*[2], *ENSBTAG00000067563*[2], *ENSBTAG00000065702*[2]	0.82805
	110983795	111321399		0.98191
7	37076940	37364183	*SEMA6A*[1], *ENSBTAG00000067375*[2], *ENSBTAG00000055768*[2], *ENSBTAG00000059150*[2], *ENSBTAG00000056595*[2], *ENSBTAG00000062478*[2], *ENSBTAG00000055597*[2], *ENSBTAG00000060037*[2]	0.61589
	76719459	77011685		0.77686
8	35996382	36293755	*PTPRD*[2], *bta-mir-2285bg*[2], *ENSBTAG00000067020*[1], *ENSBTAG00000066014*[1],	0.68703
	3258367	3663959		0.79303
	20535633	20906765		1.05777
10	5502939	5822775	*DRD1*[1], *SFXN1*[1], *ENSBTAG00000061410*[2], *ENSBTAG00000057850*[2]	1.05901
11	106094470	106396975	*UAP1L1*[1], *MAN1B1*[1], *GRIN1*[1], *bta-mir-12014*[2], *SSNA1*[1], *NDOR1*[1], *CYSRT1*[1], *RNF224*[1], *SLC34A3*[1], *TUBB4B*[1], *STPG3*[1], *NELFB*[1], *TOR4A*[1], *ANAPC2*[1], *CIMIP2A*[1], *DPP7*[1], *LRRC26*[1], *NRARP*[1], *RNF208*[1], *SAPCD2*[1], *EXD3*[1], *TGFA*[1], *TMEM210*[1], *TPRN*[1], *UAP1L1*[1], *ENSBTAG00000058667*[2], *ENSBTAG00000053827*[1], *ENSBTAG00000061834*[2], *ENSBTAG00000059218*[3], *ENSBTAG00000068829*[2], *ENSBTAG00000065600*[2], *ENSBTAG00000067502*[2], *ENSBTAG00000056166*[2], *ADD2*[1], *ENSBTAG00000051045*[2]	0.85735
	13730813	13993403		1.47951

Continued Table 4.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
12	78879934	78914611	*bta-mir-759*, *PCDH8*[1], *COL4A1*[1], *IRS2*[1], *TPP2*[1], *ENSBTAG00000058337*[2], *ENSBTAG00000060184*[2], *CNMD*[1], *ENSBTAG00000061417*[2], *ENSBTAG00000064577*[2], *ENSBTAG00000067735*[2],	0.50067
	10719656	11096637		0.50393
	84500786	84882391		0.58411
13	72638085	72997024	*OSER1*[1], *FITM2*[1], *SERINC3*[1], *GDAP1L1*[1], *HNF4A*[1], *JPH2*[1], *PKIG*[1], *PTPRT*[1], *R3HDML*[1], *TTPAL*[1], *U6*[2], *ENSBTAG00000062014*[2], *ENSBTAG00000066052*[2]	0.88883
	71271729	71544363		0.99982
14	32977353	33372261	*SULF1*[1], *ENSBTAG00000064289*[1], *ENSBTAG00000056677*[2], *ENSBTAG00000063436*[2]	0.53475
	71025573	71256147	*ENSBTAG00000056366*[2], *ENSBTAG00000067399*[2], *ENSBTAG00000061994*[2]	1.45630
17	73206420	73511787	*MORC2*[1]	0.71746
18	9328369	9622822	*RPL18*[1], *DBP*[1], *CA11*[1], *NTN5*[1], *MAMSTR*[1], *RASIP1*[1], *IZUMO1*[1], *FUT1*[1], *BCAT2*[1], *HSD17B14*[1], *PLEKHA4*[1], *TULP2*[1], *GYS1*[1], *LHB*[1], *NTF4*[1], *KCNA7*[1], *BCAT2*[1], *CDH13*[1], *DHDH*[1], *FGF21*[1], *FTL*[1], *FUT2*[1], *IRX6*[1], *NUCB1*[1], *PPP1R15A*[1], *RUVBL2*[1], *SAXO*[1], *SEC1*[1], *SPHK2*[1], *ENSBTAG00000066099*[2], *ENSBTAG00000062913*[2], *ENSBTAG00000056750*[2], *ENSBTAG00000012131*[1], *ENSBTAG00000058064*[2], *ENSBTAG00000068021*[2], *ENSBTAG00000068980*[2], *ENSBTAG00000069233*[2], *ENSBTAG00000056999*[2], *ENSBTAG00000068160*[2], *ENSBTAG00000058911*[1]	0.55219
	3940271	4373037		0.56773
	23363011	23662224		0.94004
	55262498	55590144		1.26496

Continued Table 4.

Chr	Start position (bp)	End position (bp)	Gene symbol/ENSEMBL ID	Var (%)
19	44174487	44547216	*ITGA2B*[1], *GPATCH8*[1], *CCDC43*[1], *GJC1*[1], *ADAM11*[1], *DBF4B*[1], *FZD2*[1], *MEIOC*[1], *ENSBTAG00000064367*[2], *ENSBTAG00000060869*[2]	0.68536
20	24744585	25028988	*ARL15*[1], *CTNND2*[1], *FGF18*[1], *U6*[2], *ENSBTAG00000068631*[2], *ENSBTAG00000055331*[2],	0.54638
	3253977	3532931		0.63697
	61537001	61834994		0.79704
21	25792494	26146591	*ZFAND6*[1], *FAH*[1], *BCL2A*[1], *MTHFS*[1], *ENSBTAG00000065309*[1], *ENSBTAG00000068050*[2], *ENSBTAG00000060444*[1]	1.05007
22	20686811	20984209	*SEC61G*[1], *U6*[2], *NEK10*[1]	0.51086
	1426126	1741940		0.62315
23	14935852	15276599	*UNC5CL*[1], *OARD1*[1], *TREML1*[1], *TREM2*[1], *TREML2*[1], *TREM1*[1], *NEDD9*[1], *APOBEC2*[1], *NFYA*[1], *ENSBTAG00000021359*[1], *ENSBTAG00000060030*[2], *ENSBTAG00000050887*[1], *ENSBTAG00000061826*[2], *ENSBTAG00000064702*[1], *ENSBTAG00000062933*[1], *ENSBTAG00000055384*[2], *ENSBTAG00000057654*[2], *ENSBTAG00000065527*[2], *ENSBTAG00000064351*[2],	0.56817
	44876806	45125767		0.93532
	38412668	38891267		0.96628
24	51371971	51846761	*DCC*[1], *ENSBTAG00000049503*[1], *ENSBTAG00000066760*[1],	0.76479
25	37501749	37799150	*NPTX2*[1], *BRI3*[1], *BHLHA15*[1], *BAIAP2L1*[1], *TECPR1*[1], *ENSBTAG00000069291*[2], *ENSBTAG00000060002*[2], *ENSBTAG00000066747*[2], *ENSBTAG00000060317*[2], *ENSBTAG00000066438*[1]	0.51895
26	30168678	30504596	*XPNPEP1*[1], *ENSBTAG00000068792*[1], *ENSBTAG00000067787*[2]	0.72092
27	3243779	3783637	*CSMD1*[1], *ENSBTAG00000065138*[1]	1.03616
28	13995887	14338094	*BICC1*[1], *ENSBTAG00000069738*[2], *ENSBTAG00000058304*[2]	1.55328

protein-coding gene[1]; non-coding RNA[2]; pseudogene[3].

The functional enrichment analysis for APF revealed eight significant Gene Ontology terms, in which we highlighted the negative regulation of hormonal secretion (GO:0046888) biological process (Table 5), with the *OSM* and *LIF* genes participates. The *OSM* and *LIF* genes encodes cytokines belonging to the interleukin 6 family and are intrinsically associated with the structures and functions of this cytokine family (Tanaka & Miyahima, 2003). Cytokines influence virtually all cell types, termed pleiotropic, as a single cytokine can influence the activity of several distinct cells (Dinarello, 2007).

Table 5. Significant (P < 0.05) Gene Ontology terms revealed by DAVID for accumulated profitability in Nelore cattle.

GO terms	N	Genes	P-value
Biological process			
GO:0046888 - negative regulation of hormone secretion	2	*OSM, LIF*	0.006
GO:0046604 - positive regulation of mitotic centrosome separation	2	*RANBP1, UBXN2B*	0.006
GO:0010646 - regulation of cell communication	2	*OSM, LIF*	0.008
GO:0023051 - regulation of signaling	2	*OSM, LIF*	0.016
Cellular component			
GO:0005739 - mitochondrion	6	*TXNRD2, TANGO2, SFXN1, ZDHHC8, PRODH, MTFP1*	0.042
GO:0005829 - cytosol	12	*CASTOR1, TXNRD2, TANGO2, DENND2D, COMT, FLRT3, DGCR8, TBC1D10A, LIF, LMTK2, RANBP1, UBXN2B*	0.025
GO:0044295 - axonal growth cone	2	*FLRT3, RTN4R*	0.025
GO:0005794 - Golgi apparatus	6	*TANGO2, ZDHHC8, LMTK2, CEPT1, DRAM2, GALNT13*	0.016

The *LIF* gene is involved in a variety of physiological and biological processes, including an important function in the early stage of embryonic development and in regulating endometrial function during implantation and placentation in various species (Campanile et al., 2021), suggesting its relevance as a potential gene associated with female fertility (Cai et al., 2019). The *OSM* gene is structurally, genetically, and functionally associated with *LIF*. However, the specific biological functions of *OSM* have

been documented in the process of blood cell formation, liver development, nervous system (Morikawa, 2005), and insulin metabolism (Komori et al., 2014).

Many important genes were identified in the genomic regions associated with APF (Table 3); however, the functional enrichment analysis not revealed biological process or cellular component relevant to APF trait, probably due to the small number of genes detected. These genes were highlighted according their functions and categorized into seven groups, as following: lipid and cholesterol metabolism (*GALNT13, CEPT1*, *GRAMD2A, SEC14L2* and *PRODH*), carbohydrate metabolism (*CHI3L2*), muscular development and growth (*CASTOR1* and *MIR1306*), fertility and reproductive traits (*ACKR3, CDC45, RANBP1, TANGO2, DGCR8, SFXN, RNF215* and *ARVCF*), carcass traits (*IQCA1, MACROD2* as *IQCA1, ASB18* and *MACROD2*), feed efficiency (*UBXN2B, CYP7A1, DGCR6L* and *TBC1D10A*), homeostasis (*TXNRD2* and *TCAF1*), gastrointestinal regulation (*HRH2)* as well as genes related to the nervous system and behavior (*GNB1L, COMT, FLRT3, SEPTIN5, RTN4R* and *LMTK2*) (Table 3).

Regarding lipid and cholesterol metabolism genes, the *GALNT13* gene is among the 20 enzymes identified to initiate O-glycosylation, a process with multiple functions in organisms (Van Den Steen et al., 1998; Goettig, 2016). Although the functions of *GALNTs* are not fully understood, the targets regulated by them (Schjoldager et al., 2012; Katrine et al., 2010) may influence lipoprotein metabolism and fat deposition in the intramuscular space (Anton et al., 2018). In cattle, Abo-Ismail et al. (2018) reported the *GALNT13* association with metabolic weight and dorsal fat deposition, using models that considered genotypic, additive, and dominance effects in Angus, Hereford, and Angus-Hereford crossbreeds.

The *CEPT1* gene responsible for encoding the choline/ethanolamine phosphotransferase enzyme, which acts on choline- and ethanolamine-containing phospholipids (Wright et al., 2002) and may also play an essential role in lipid metabolism regulation in the large intestine (Chao et al., 2017). The *GRAMD2A* gene encodes a protein involved in regulation of store-operated calcium entry and has shown consistent and favorable associations with genes related to lipid metabolism in both humans and mice (Besprozvannaya et al., 2018).

SEC14L2 encodes the SEC14-like protein 2, a cytosolic protein which belongs to a family of lipid-binding proteins in which studies suggest its participation as a potential transporter of lipophilic molecules between various cellular compartments and is closely linked to regulating the availability of vitamin E (Panagabko et al., 2003). *PRODH*

encodes the enzyme proline dehydrogenase, which is responsible for catalyzing the first phase of the proline degradation (Wang et al., 2020), which is essential for energy metabolism (Amorim et al., 2022) and has been associated with lipid metabolism (Murakami et al., (2017). The *CHI3L2* gene encodes a protein involved in cartilage biogenesis, and it is known for its association with carbohydrate metabolism (Cunningham et al., 2015; Yates et al., 2016), as well as has been correlated with comprehensive metabolic processes in cattle, such as carbohydrate, lipid, and protein metabolism (Chen et al., 2021)

CASTOR1 encodes a cytosolic arginine sensor that is involved in cellular response to L-arginine and regulation of mTOR signalling pathway (Xia et al., 2016). L-arginine plays a central role in the nitrogen metabolism (e.g., syntheses of protein, polyamines, creatine and nitric oxide), nutrient utilization, blood flow, and health of ruminants (Wu et al., 2022). mTOR is the primary regulator of growth (mass accumulation) in animals that controls most anabolic and catabolic processes in response to nutrient signals such as insulin (Sabatini et al., 2017). Lastly, the *MIR1306* gene encodes a miRNA that may regulate the synthesis of growth hormone, as described in a Holstein cattle study (Mullen et al., 2010).

The BTA14:24573257-24710609 bp genomic region revealed the presence of several relevant genes associated with economically important traits such as feed efficiency and carcass. The *UBXN2B* and *CYP7A1* genes, associated with feed efficiency. The *UBXN2B* gene encodes a protein involved in the Golgi complex and endoplasmic reticulum biogenesis (Luca et al., 2013) and has been associated with metabolic weight during feed efficiency testing in Angus, Hereford, and SimAngus cattle breeds (Seabury et al., 2017). *CYP7A1* gene encodes the cholesterol 7α-hydroxylase, member of the cytochrome P450 superfamily, which catalyze several reactions involved in synthesis of steroids, cholesterol, and other lipids.

Cholesterol 7α-hydroxylase acts as a key enzyme to catalyzes the cholesterol to bile acids conversion in the liver, which is the main mechanism for the regulation of bile acid synthesis and removal of cholesterol from the body (Qi et al., 2015; Han et al., 2016), which was associated with residual feed intake in Nordic dairy cattle (Salleh et al., 2017). These enzymes play important roles in nutrient absorption and digestion, as well as in regulating lipid homeostasis, glucose metabolism, and energy (Ferrell et al., 2016). Two other genes, *DGCR6L* and *TBC1D10A*, located on BTA17, were previously associated with high-gain-low-intake and low-gain-high-intake traits (Kern et al., 2017; Kern et al.,

2016). Other genes such as *IQCA1, ASB18* and *MACROD2* were also reported as associated with rib eye area and carcass weight traits (Niu et al., 2021),

Genes related to fertility in both males and females were also found in this study. Previous studies have shown that the *ACKR3* gene performs critical functions in reproductive physiology, acting as the alternative receptor for the inflammatory chemokine C-X-C motif ligand 12 (stromal cell-derived factor 1) and adrenomedullin (Quinn et al., 2018). Studies suggest that the protein encoded by *ACKR3* also significantly regulates lipid levels in adipose tissue, indeed, this gene has been associated with controlling systemic lipid levels by lipid uptake in adipose tissue (Gencer et al., 2021).

The *CDC45* gene has been described as an important component in the development process of sperm cells and embryogenesis, necessary for initiating chromosomal DNA replication (Owens et al., 1997; Özbek et al., 2021). Özbek et al. (2021) reported that sperm from bulls with high fertility showed increased expression of the *CDC45* gene. *RANBP1* participates in the regulation of the cell cycle by controlling transport of proteins and nucleic acids into the nucleus, and transcription process in both oocyte and cumulus cells. This network induces biological pathways that activate primary follicles, follicular secretion, and cell migration (Tavana et al., 2021).

The *TANGO2* gene was associated with Holstein' fertility traits, such as daughters' pregnancy rate (Cochran et al., 2013). *DGCR8* gene encodes a subunit of the microprocessor complex that mediates the biogenesis of microRNAs, which acts in the regulation of stem cell proliferation and appears to be associated with the transition from morula to blastocyst in cattle (Paulson et al., 2013). The *SFXN* gene was identified as positively regulated with the multipotent trophoblast cell mass of bovine blastocysts (Ozawa et al., 2012).

ARVCF gene encodes a member of the catenin family that plays an important role in the formation of adherent junction complexes, which facilitates communication between the inside and outside cellular environments. Kiser et al. (2019) reported a list positional candidate gene, among which includes the *ARVCF* gene, along with binding sites for conception-associated transcription factors in first service and services per conception in primiparous Holstein cows in the United States.

Of the six genes related to the nervous system and behavior, one gene associated with behavior also had its function linked to an economically important trait, such as the *COMT* gene. The *GNB1L* and *COMT* genes have previously been associated with animal behavior (Qayyum et al., 2015). In addition to the mentioned function, the *COMT* gene

is vital in estrogen metabolic pathways (Worda et al., 2003). Activation of *COMT* during the estrous cycle and pregnancy has led researchers to hypothesize that *COMT* activity is sensitive to estrogen levels (Jiang et al., 2003). Interestingly, this gene has also been associated with growth traits in Montana breed animals, such as weaning and yearling weight (Grigoletto et al., 2019). The *SEPTIN5* gene in transgenic cattle may be related to enhancing olfactory and visual sensory functions (Malnic et al., 2004; Xin et al., 2007). The *FLRT3* gene is linked to the Unc-5 family of receptor proteins involved in multiple physiological interactions in the developing mammalian nervous system (Yamagishi et al., 2011).

The *RTN4R* gene encodes the reticulon-4 receptor, also known as nogo receptor, is suggested to regulate axonal regeneration and plasticity in the adult central nervous system (Bianco et al., 2017). *LMTK2* gene encodes aserine/threonine-protein kinase, where its biological functions are notably observed in neuronal and muscular tissues, where it plays a role in intracellular trafficking (Luz et al., 2014).

According to Ghaffari et al. (2023), the positive regulation of the *TCAF1* gene has been associated with cellular motility, which may influence increasing nutrient uptake and utilization in NBCS-PN cows (High Body Condition Score predicted Normal Body Condition Score) due to optimal ECC (Energy Corrected Milk). *TXNRD2*, thioredoxin reductase 2, participates in controlling levels of reactive oxygen species, playing a key role in mitochondrial redox homeostasis, and is considered to function in cell signaling controlled by the redox state (Alexandre et al., 2020). Inhibiting *TRXR2* affects redox homeostasis, increasing H_2O levels, which may compromise cellular functions (Prasad et al., 2014).

Concerning *HRH2* encodes the histamine H2 receptor, an integral membrane protein that stimulates gastric acid secretion and regulates gastrointestinal motility and intestinal secretion (Fernández-Novoa et al., 2017). Another study reported that this gene was also identified in the 'signal transduction' category during the analysis of differentially expressed genes between pregnant and non-pregnant heifers (Moorey et al., 2020).

Regarding the functional enrichment analyses for PFT trait, a total of 14 Gene Ontology terms and seven KEGG pathways were found as significant (Table 6), in which we emphasized the glucose homeostasis (GO:0042593), lipid homeostasis (GO:0055088), proteolysis (GO:0006508), PI3K-Akt signaling pathway (bta04151), calcium signaling (bta04020) and metabolic pathways (bta01100) terms.

Table 6. Significant (P < 0.05) Gene Ontology terms and KEGG pathways revealed by DAVID for profit per kilogram of liveweight gain in Nelore cattle.

Terms	N	Genes	P-value
Biological process			
GO:0036065 - fucosylation	3	*SEC1, FUT1, FUT2*	0.0026
GO:0042593 - glucose homeostasis	5	*HNF4A, CSMD1, FAM3B, BHLHA15, BACE2*	0.0068
GO:0007267 - cell-cell signaling	4	*BHLHA15, GJA8, GJC1, FGFBP1*	0.0076
GO:0005975 - carbohydrate metabolic process	5	*SEC1, FUT1, FUT2, A0A3Q1NNK3_BOVIN, MAN1B1*	0.0145
GO:0001936 - regulation of endothelial cell proliferation	2	*FUT1, FUT2*	0.0381
GO:0055088 - lipid homeostasis	3	*TREM2, HNF4A, FITM2*	0.0455
GO:0006508 - proteolysis	5	*PDZK1, XPNPEP1, DPP7, TPP2, METAP2*	0.0471
Cellular component			
GO:0016020 -membrane	15	*MX2, PPP1R15A, RUVBL2, COL4A1, MAN1B1, SPHK2, BACE2, SERINC3, MX1, CNMD, NUCB1, PDE3A, A0A3Q1NNK3_BOVIN, PTPRT, BAX*	0.0096
GO:0032580 - Golgi cisterna membrane	4	*SEC1, FUT1, FUT2, GPR89A*	0.0024
Molecular function			
GO:0008107 -galactoside 2-alpha-L-fucosyltransferase activity	3	*SEC1, FUT1, FUT2*	0.0001
GO:0031127 -alpha-(1,2) -fucosyltransferase activity	3	*SEC1, FUT1, FUT2*	0.0001
GO:0045296 - cadherin binding	4	*CDH13, PROM1, PTPRT, CTNND2*	0.0068
GO:0005042 - netrin receptor activity	2	*DCC, UNC5CL*	0.0401
GO:0042803 - protein homodimerization activity	9	*HNF4A, ADD2, CDH13, BCL2A1, XPNPEP1, PTPRT, RUVBL2, BAX, RASIP1*	0.0472
KEGG_Pathway			
bta04151: PI3K-Akt signaling pathway	7	*NTF4, TGFA, ITGA2B, GYS18, FGF21, FGF18, COL4A1*	0.0394
bta05202: Transcriptional misregulation in cancer	5	*TMPRSS2, BCL2A1, PROM1, BAX, ETV1*	0.0395
bta00601: Glycosphingolipid biosynthesis - lacto and neolacto series	3	*SEC1, FUT1, FUT2*	0.0154
bta04024: cAMP signaling pathway	6	*LHB, GRIN1, DRD1, PDE3A, LOC531747, PDE4B*	0.0227
bta00603: Glycosphingolipid biosynthesis - globo and isoglobo series	3	*SEC1, FUT1, FUT2*	0.0061
bta04020:Calcium signaling pathway	7	*GRIN1, TGFA, CD38, FGF21, DRD1, FGF18, SPHK2*	0.0072
bta01100:Metabolic pathways	19	*SEC1, DHDH, DGKB, FAH, GYS1, CD38, PGAP1, BCAT2, LOC531747, CEPT1, PDE4B, MAN1B1, ATP6V0E2, SPHK2, MTHFS, FUT1, FUT2, PDE3A, UAP1L1*	0.0118

The biological process of glucose homeostasis (GO:0042593) is extremely important for the body's cells and the central nervous (SNC) system since glucose is the main source of energy for both (Thorens, 2005). Due to its function in cellular and brain energy, blood glucose concentration levels are continuously controlled to adapt cellular and whole-body physiology and regulate blood glucose levels at normal levels (Thorens, 2005). Glucose originates from three different sources: intestinal absorption of food, glycogenolysis, the breakdown of glycogen in the liver, and gluconeogenesis, which involves the production of glucose in the liver and kidneys from different precursors such as lactate, pyruvate, amino acids, and glycerol (Bano, 2013).

The main factors that control glucose levels include immediate response hormones: insulin, glucagon, and catecholamines; sympathetic nervous system activity; the concentration of free fatty acids (FFA); prolonged response hormones: cortisol and growth hormone; and nutritional factors, exercise, and physical fitness (Bano, 2013). Two important genes in this pathway were identified in this study: *BHLHA15* and *BACE2*.

The *BHLHA15* gene, also known as *MIST1*, acts in several processes, including glucose homeostasis, cellular response to glucose starvation and mitochondrial calcium ion transmembrane transport. *BHLHA15* has a critical function during the embryonic development of mice, specifically in gastrulas, plantules, and skeletal muscle (Pin et al., 2000). The *BACE2* gene encodes a transmembrane protease that catalyzes the proteolysis of amyloid precursor protein to produce amyloid beta peptide. Mice lacking this protease exhibit. *BACE2* suppression in mice leads to excessive body weight gain, hyperinsulinemia, insulin resistance and improved glucose tolerance due to increased insulin secretion (Díaz-Catalán et al., 2021). *BACE2* gene has been linked to bovine muscle formation, and its expression has been observed in adipocytes (Lee et al., 2012).

Lipid homeostasis (GO:0055088) is an essential biological process for normal cells to ensure their physiological functioning (Zhao et al., 2024). In terms of quantity, the main way of storing energy is represented by lipids in adipose tissue (Ferré et al., 2007), and the liver is the primary organ for lipid metabolism (Ipsen et al., 2018). As the primary regulator of lipid homeostasis, the liver is responsible for coordinating the production of new fatty acids, their transport and subsequent redistribution to other organs, and their use as an animal energy source (Nguyen et al., 2008). Complex interactions between hormones, nuclear receptors, and transcription factors control these activities, strictly preserving lipid homeostasis (Bechmann et al., 2012).

Diverse groups of lipids, encompassing energy storage lipids, structural lipids, and signaling lipids, are closely related through the lipid homeostasis system (Vendruscolo et al., 2022). Any alteration of these pathways results in an imbalance between the uptake and output of lipids, which is controlled by four important pathways, such as uptake of circulating lipids, de novo lipogenesis (DNL), fatty acid oxidation (FAO), and export of lipids at deficient levels lows density lipoproteins (VLDL) (Ipsen et al., 2018). Among the three genes identified in this biological process (Table 6), the *FITM2* gene is involved in many biological processes, such as fatty-acyl-CoA catabolic process, diacylglycerol and triglyceride binding activities, cellular triglyceride homeostasis, lipid droplet formation and lipid homeostasis (Miranda et al., 2014; Pan et al., 2022).

Proteolysis (GO:0006508) is a biological process that regulates the progression of the cell cycle in the manipulation of proteins and is essential for several phases of mitosis and the beginning of DNA replication (King et al., 1996); this process is not only relevant for maintenance but is also responsible for regulating critical cellular activities, such as homeostasis and survival (Chondrogianni et al., 2014). Protein degradation occurs constantly in all tissues throughout the animals' lives (Baracos et al., 2005). Proteolytic degradation is coordinated by two central systems, the lysosome and proteasome (Chondrogianni et al., 2014).

The absence/decrease or increase in the function of the two systems is linked in all directions to the complex cellular metabolic networks associated with physiological and pathological processes (Chondrogianni et al., 2014). Furthermore, proteolysis has a vital role in the post-mortem phase, as in cattle, these proteolytic processes originate mainly from studies of skeletal muscle, covering techniques and strategies for their determination, addressing proteolytic enzymes and regulators, as well as controls—physiological and post-mortem proteolytic transformations that influence meat quality (Baracos et al., 2005). Five genes were identified participating in the proteolysis (GO:0006508), in which we highlighted the *PDZK1.*The *PDZK1* gene encodes a PDZ domain-containing scaffolding protein that plays a pivot role in cholesterol metabolism through regulation of HDL receptor, scavenger receptor class B type 1. It acts as an adaptor protein for the Scavenger Receptor Class B Type I (SR-BI), with high expression in the placenta, enabling the developing fetus to acquire a significant portion of its cholesterol from maternal lipoproteins (Kocher et al., 2003).

The PI3K-Akt signaling pathway (bta04151) has been extensively studied and considered a key regulator of diverse cellular functions, including cell migration,

mitogenesis, differentiation, and cell survival (Vara et al., 2004). Furthermore, it plays a central role in regulating skeletal muscle mass and metabolism, promoting protein synthesis and inhibiting protein degradation (Glass, 2005). In this signaling route, a relevant gene, FGF18, was identified.

The *FGF18* gene encoded the fibroblast growth factor 18, a member of the fibroblast growth factor (FGF) family, which members are involved many biological processes, such as cell growth, morphogenesis, tissue repair, embryonic development and skeletal system development (Ornitz et a., 2001). Studies in mouse suggested its pleiotropic growth factor function that stimulates proliferation in several tissues, most notably the small intestine and liver (Ornitz et a., 2001).

The calcium signaling pathway (bta04020) is important in regulating the growth, development, and function of skeletal muscle in beef cattle (Sadkowski et al., 2009; Liu et al., 2022). Additionally, calcium exhibits relevant roles in meat tenderness, feed efficiency, and muscle contraction, and numerous genes participating in processes associated with calcium also influence meat quality in cattle (Mateescu et al., 2017; Rolf et al., 2012). Among the seven genes identified in the calcium signaling pathway (bta04020), we highlighted the *TGFA and DRD1*. *TGFA* gene encodes the transforming growth factor alpha, a protein that participates in signaling events that results in cellular proliferation, mucous production, or inhibition of gastric acid secretion. *FGF21*encodes a secreted endocrine factor member of the fibroblast growth factor (FGF) family, that acts as a major metabolic regulator and stimulates the uptake of glucose in adipose tissue. *TGFA* and *FGF21* are associated with adipose tissue metabolism (Singh et al., 2014; Sun et al.,2013).

The *DRD1* gene encodes the most abundant dopamine receptor in the central nervous system, named D(1A) dopamine receptor, which is highly characterized for its association with cattle temperament (Garza-Brenner et al., 2017). Dopamine receptors (DRDs) are major candidates in regulating energy homeostasis, have been linked to the modulation of feeding behavior (Martel & Fantino, 1996; Lutz et al., 2001) and linked to reducing feeding duration (Szczypka et al., 1999).

The metabolic pathway (bta01100) plays crucial roles in regulating the metabolism of carbohydrates, energy, glucose, lipids, nucleotides, amino acids, glycans, vitamins, xenobiotics, oxidative stress, and inflammation (Abdalla et al., 2021; Veshkini et al., 2022). In beef cattle, this pathway has been identified as associated with primary beef cuts (Naserkheil et al., 2021), subcutaneous fat (Muroya et al., 2021), feed efficiency

(Abo-Ismail et al., 2014; Fonseca et al., 2019) and was associated with body size in Holstein cattle (Abdalla et al., 2023). Among the 19 genes detected in metabolic pathway (bta01100), we highlighted the *DHDH, DGKB, GYS1* and *BCAT2* genes. *DHDH* encodes an enzyme that from dihydrodiol dehydrogenases family, which are involved in the metabolism of xenobiotics and sugars. The *DHDH* and *IRX6* genes were described in the literature as being associated with metabolic live weight (Hardie et al., 2017). Gan et al. (2020) reported that *DGKB* is closely related to insulin secretion in cattle. Variation in an SNP located within *DGKB* likely affects signal transduction, cell proliferation, development, glucose sensing, and circadian regulation (Gan et al., 2020).

The glycogen synthase 1 (*GYS1*) gene, responsible for encoding an enzyme that mediates glycogen synthesis in skeletal muscles, suggests that this gene is an important biological candidate for production traits (Wang et al., 2012b) and have been associated with meat quality traits in pigs (Zuo et al., 2007). The *BCAT2* gene is involved in the metabolism of branched-chain amino acids in peripheral tissues, acting on the catabolism of these amino acids and the regulation of *BCKDHA* and *BCKDHB* genes during pre-adipocyte differentiation (Shi et al., 2018).

Other important genes have been identified in genomic regions associated with PFT trait, but they were not related to any significative biological processes, molecular function, or pathway, probably due to the small number of genes detected to perform the functional enrichment analysis. Among these genes, 70 were highlighted according their functions and also classified into seven groups: lipid metabolism (*BCAT2, CDK17, RUNX1T1, BRI3* and *PDE4B*), muscle development and growth (*MAMSTR, SEC61G, ETV1, FGFBP1, PROM1, USP4, PREX2, BICC1, CCDC43* and *GJC1*), fertility and reproductive traits (*NTN5, IZUMO1, FUT1, TULP2, LHB, HSD17B14, PDZK1, PDE3A, PGAP1, ANKRD44, ZFAND6, FAH, ADD2* and *MBD1*), carcass traits (*COL11A1, SLC34A, TUBB4B, ITGA2B, RBFOX2, C1H21orf91, PTPRD and MORC2*), feed efficiency (*PCDH8, RPL18, CA11, RASIP1, NTF4, KCNA7, SNORA70, NEDD9,* and *NEK10*), insulin (*CDK17, RARRES2*), behavior (*DRD1, DBP, SGIP1* and *NPTX2*), immune system (*MX1, MX2, OARD1, TREML1, TREM2, TREML2, TREM1, SSNA1* and *UNC5CL*) and genes related to multiple traits (*TOR4A, NELFB, RNF224, CYSRT1, RNF224, NDOR1* and *MUCL1*).

In the analysis of this study, important genes related with muscular development and growth were identified. The gene *MAMSTR* is a member of the myomodulins family (Swärd et al., 2016) and is associated with muscular development in various species,

including cattle (Jing et al., 2023). The *SEC61G* gene was associated with musculoskeletal development and growth (Adamson et al., 2016). The *ETV1* gene encodes a member of the E twenty-six family of transcription factors that regulate several target genes that modulate many biological processes such as angiogenesis, cell growth, migration, proliferation, and differentiation. *ETVI* gene has also been reported as essential in muscular organ development (Ben-Jemaa et al., 2021).

The fibroblast growth factor binding protein 1 (*FGFBP1*) interacts with fibroblast growth factors, which are essential for skeletal muscle development, stimulating myoblast proliferation and differentiation into mature muscle cells (Beer et al., 2005). The *FGFBP1* gene was initially identified in chickens and associated with carcass quality and muscular growth (Nassar et al., 2012). On the other hand, the gene *PROM1* was reported as a candidate gene for birth weight in Simental and Simbrah breed animals (Calderón-Chagoya et al., 2023).

The *USP44* gene encodes a protease that acts as a deubiquitinating enzyme and showed positive regulation during skeletal muscle development in pigs (Jiang et al., 2010). The *PREX2* gene was associated with genomic regions within a QTL related to musculature in Charolais cattle (Doyle et al., 2020). *BICC1* encodes an RNA-binding protein that regulates gene expression during embryonic development, which is maternally provided in mouse. Some studies have indicated the *BICC1* gene's relation to muscle mass, metabolic body weight (Mukiibi et al., 2019), and carcass traits such as marbling (Li et al., 2017). Notably, the epigenetic regulation of *BICC1* in muscle hypertrophy suggests its potential contribution to feed efficiency, encompassing both food intake and body development (Seaborne et al., 2018). The *GJC1* gene, responsible for encoding a member of the connexin gene family, is a component of gap junctions that is involved in bone tissue development (Chaible et al., 2011) and has been identified as a potential candidate for stature in Holstein cows (Sassi et al., 2016).

Regarding the genes associated with carcass traits, the *COL11A1, SLC34A, TUBB4B* and *ITGA2B* genes has been described as potential candidates for meat quality traits, such as tenderness in Nelore cattle (Berton et al., 2021; Leal-Gutiérrez et al., 2020). Myoglobin (*MB*) is a monomeric heme protein predominantly expressed in skeletal and cardiac muscles, which has been considered a potential marker for meat tenderness in Nelore cattle, as reported by Muniz et al. (2021) and Gonçalves et al. (2018). The *ARL15* gene has been associated with carcass conformation in a study conducted with multi-breed beef cattle (Purfield et al., 2019), carcass weight in Limousin and Charolais cows

(Keogh et al., 2021), and subcutaneous fat deposition in Nelore cattle (Carvalho et al., 2020). The *BRI3* was previously reported by Arikawa et al. (2022), establishing its association with subcutaneous fat deposition in Nelore cattle.

The *RBFOX2* gene encodes a key regulator of alternative exon splicing in the nervous system and other cell types, which also regulates estrogen receptor 1 transcriptional activity. *RBFOX2* has been pinpointed as a relevant candidate for carcass traits such as loin eye area and meat color in Nelore cattle (Junior et al., 2016; Marín-Garzón et al., 2021), as well as in crossbred animals of Angus, Simmental, and Hereford breeds associated with ribeye, loin, rib, and whole carcass side (Sood et al., 2023). Sood et al. (2023) reported the association of the *C1H21orf91* gene with the primary carcass cuts traits. The *PTPRD* gene encodes a tyrosine phosphatase protein involved in signaling receptor binding and cell adhesion molecule binding activities, regulation of immune response and regulation of receptor signaling pathway through JAK-STAT. *PTPRD* has been previously identified as a potential candidate for intramuscular fat and carcass weight, in Nelore and Limousin cattle, respectively (Ariwaya 2022; Keogh et al., 2021). The *MORC2* gene, which regulate the condensation of heterochromatin in response to DNA damage and play a role in repressing transcription (Li et al., 2013), has been associated with marbling (Li et al., 2017). The *GPR89A* gene is associated with visual precocity scores (Machado et al., 2022).

Other genes, even if not directly related to PFT, have been reported to be associated with other reproductive and fertility traits in males and females. The izumo sperm-egg fusion protein 1 (*IZUMO1*), belonging to the immunoglobulin family, plays an essential role in fertilization due its pivot role in binding and fusion of sperm to egg plasma membrane (Kim et al., 2015). *FUT1* was reported to be associated with reproductive traits in dairy cows, such as pregnancy rate (Cochran et al., 2013), services per conception, and days open (Ortega et al., 2017).

The *LHB* encodes the luteinizing hormone beta subunit, which promotes ovulation and spermatogenesis by stimulating ovaries and testes to synthesize steroids (Degani et al., 2003; Junior et al., 2017), as well as its involvement in male sexual behavior (Degani et al., 2003). The 17β-hydroxysteroid dehydrogenases, such as the encoded by *HSD17B14*, acts primarily on metabolism of steroids and of other substrates, such as prostaglandins, fatty acids, and xenobiotics (Gao et al., 2022). In cattle, *HSD17B14* has been associated with early pregnancy in Nelore heifers (Junior et al., 2017). The *ADD2*

gene was also identified in regions associated with the probability of early calving in Nelore heifers (Mota et al., 2022).

The FAH gene is associated with days from calving to first service in Holstein cows (Mohammadi et al., 2022). The *PGAP1* gene was associated with male infertility and autocephaly in mice (Ueda et al., 2007). *PDE3A*, a phosphodiesterase family member, exhibits role in regulation of oocyte development and maturation and regulation of meiosis. *PDE3A* has been reported to have high expression in oocytes and the post-acrosomal segment of the sperm head (Qin et al., 2017). The *ZFAND6* gene has been linked to reproductive traits in Holstein cows, such as days from calving to first service (Mohammadi et al., 2022).

Another significant group of genes related to feed efficiency, associated with PFT, was also found in this study. The *PCDH8*, *NEK10* and *SNORA70* genes were associated with residual feed intake, residual gain, and feed efficiency in Charolais, Brown Swiss, Red Angus, and Creole cattle (Taussat et al., 2020; Manca et al., 2021; Pitt et al., 2019, Smith et al., 2022). The *CA11*, *RASIP1, NTF4* and *KCNA7* genes have also been reported in the literature as associated with body metabolic weight in dairy cows (Hardie et al., 2017). *CA11* encodes a member of carbonic anhydrases (CAs) family, which is formed by zinc metalloenzymes that participate in several biological processes, including calcification, acid-base balance, bone resorption, respiration, and the formation saliva and gastric acid.

KCNA7 encodes a member of potassium voltage-gated ion channels that play several functions including regulating of insulin secretion and smooth muscle contraction. The *NEDD9* gene encodes a focal adhesion protein that regulates signaling complexes crucial in cell attachment, migration and as apoptosis, which has been related to phenotypic variation between high and low RFI animals in pigs (Wang et al., 2022). The bta-*mir-2285bg* was associated as a positive regulator in cattle with low residual feed intake (Mukiibi et al., 2020).

Some genes related to immune function were identified in genomic regions associated with PFT trait, some of which are associated with potential mechanisms of bovine immune response and others with immunological functions in the reproductive system. The *MX1* and *MX2* genes encodes members of the Mx protein family of large GTPases, which acts in the immune system (Davoodi et al., 2016). The *MX1* gene is recognized for its well-characterized antiviral properties (Lee & Vidal, 2002), while the MX*2* is a possible reliable marker for predicting pregnancy (Yoshino et al., 2018).

The genes *OARD1, TREML1, TREM2, TREML2*, and *TREM1* located on chromosome 23 are also related to bovine immune functions (Elsik et al., 2009; Otto et al., 2018; Goszczynski et al., 2018). The *TREML1, TREM2, TREML2*, and *TREM1* genes belong to the family of triggering receptors expressed on myeloid cells (TREM). This family of immune receptors encompasses both inhibitory and activating receptors, which regulate the development and function of myeloid cells (Colonna, 2003). Colonna (2003) reported that TREM is associated with granulocytic and monocytic inflammatory responses during infections and in the differentiation of osteoclasts and glial cells from monocytic precursors. The *SSNA1* and *RASD2* genes are widely described in the literature for its roles in the immune system (Goszczynski et al., 2018; Rocha et al., 2020) and the *UNC5CL* gene is involved in the positive regulation of I-kappaB kinase/NF-kappaB signaling and JNK cascade (Goszczynski et al., 2018).

Several genes widely known in the literature related to behavior were also identified genomic regions associated with PFT trait, such as *DRD1, DBP,* and *SGIP1*. The *DBP* gene acts in the circadian rhythym transcriptional regulation of various metabolic enzymes (Reppert & Weaver, 2002; Lowrey & Takahashi, 2004). Daily cycles of hormones and metabolites may contribute to coordinating the timing of ingestion with metabolism (Plaut & Casey, 2012). Additionally, this gene was associated with variations in residual feed intake phenotype in cattle (McKenna et al., 2021).

The *SGIP1* gene has been reported as an essential regulator of food intake, fat mass, energy balance, and energy homeostasis (Trevaskis et al., 2005; Cummings et al., 2012). Its function as a regulator of feeding behavior can affect any process that activates or increases the frequency, rate, or extent of feeding behavior (Trevaskis et al., 2005; Cummings et al., 2012). Khansefid et al. (2015), identifying variants associated with complex traits, suggest that *SGIP1* gene may affect residual feed intake in Angus cattle. The *NPTX2* gene's function depends on activity-dependent exocytosis and dynamic elimination at synapses, and it is associated with the circadian behavior pattern (Xiao et al., 2021). Concerning genes associated with lipid metabolism, the gene *FZD2* exhibits high expression in adipose cells (Miranda et al., 2014; Pan et al., 2022).

The *CDK17* gene, belonging to the cyclin-dependent kinase (CDK) family, primarily regulates vital cellular processes such as the cell cycle and transcription (Pan et al., 2021). CDK family genes regulate adipocyte differentiation (Pan et al., 2021). The *RARRES2* gene is involved in the regulation of fat cell differentiation, protein

phosphorylation, and insulin receptor signaling pathway. Acts upstream of or within brown fat cell differentiation (Coppack, 2001).

Also, in genomic regions associated with PFT trait, a group of genes related to various traits was also identified (*TOR4A, NELFB, NDOR1, MUCL1, DCC* and *IRS2*. Pitt et al. (2019) associated the genes *TOR4A, NELFB, RNF224, CYSRT1,* and *NDOR1* with a QTL related to milk traits, reproduction, conformation, and fatty acids. *MUCL1*, a gene linked to several traits, was identified in a QTL related to daughter pregnancy rate, milk fat yield, and milk production in Charolais cattle (Olšanská et al., 2020). *DCC* is related to body depth as pointed out by Abdalla et al. (2023). *IRS2* encodes the insulin receptor substrate 2, a signaling protein that mediates effects of insulin, insulin-like growth factor 1, and other cytokines. Some studies have reported that *IRS2* has crucial roles in regulating cellular processes, such as growth, development, survival, and metabolism (Zhang et al., 2023).

4. Conclusions

The results presented in this study provide new insights into the biological and molecular mechanisms underlying the novel phenotypes of APF and PFT in feedlot. This study showed that the genetic architecture of these phenotypes demonstrates a polygenic inheritance pattern, with several genomic regions exhibiting small effects. Different candidate regions for APF and PFT were identified, which are associated with traits of economic importance such as growth, feed efficiency, fertility, and carcass. Several genes involved in biological processes related to the metabolism of carbohydrates, proteins and lipids and immunological functions and behavior were also identified. In this way, these findings provide us with a better understanding of the biological and genetic control of the expression of APF and PFT.

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6. Supplementary material

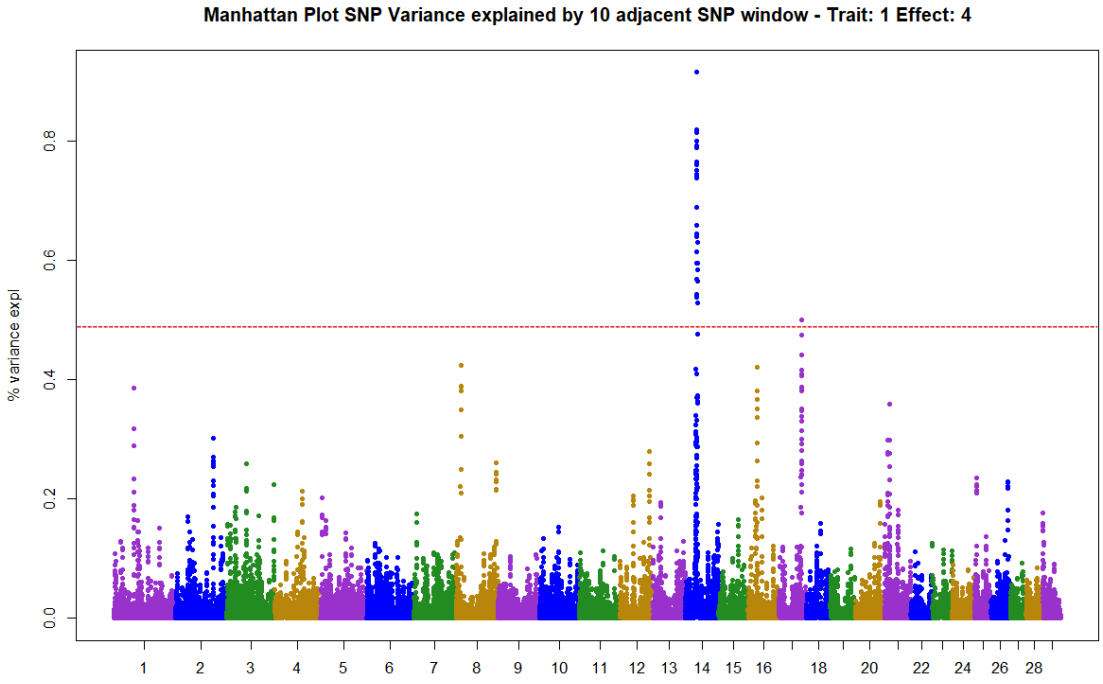

Figure S1. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the WssGWAS for accumulated profitability in Nelore cattle.

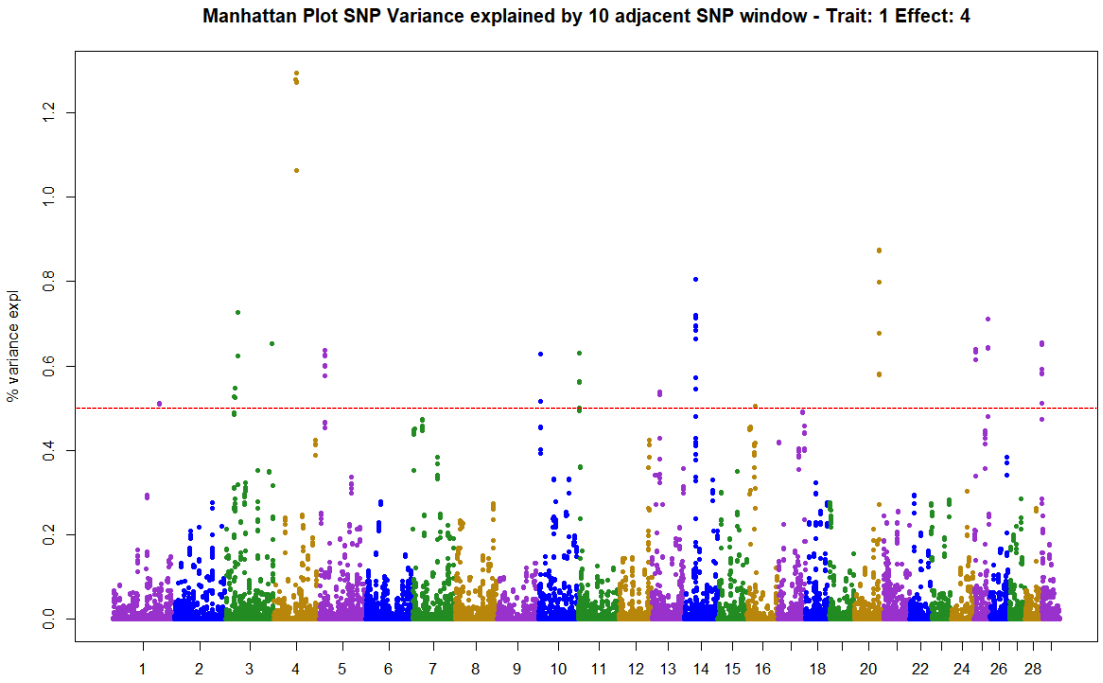

Figure S2. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the WssGWAS for accumulated profitability in Nelore cattle.

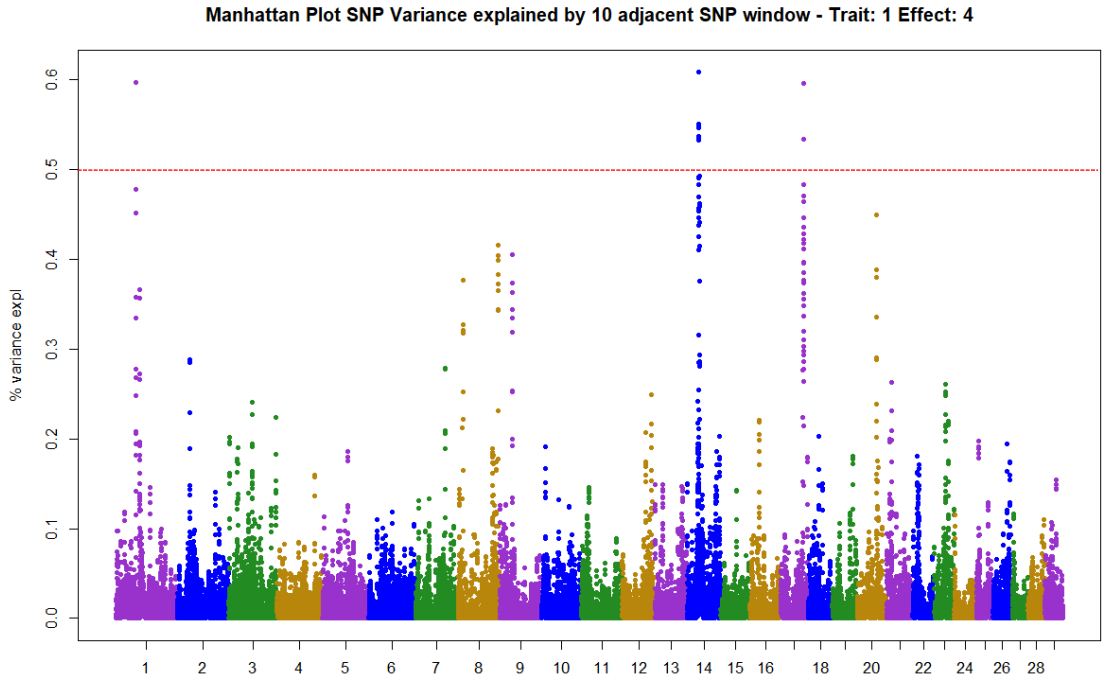

Figure S3. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

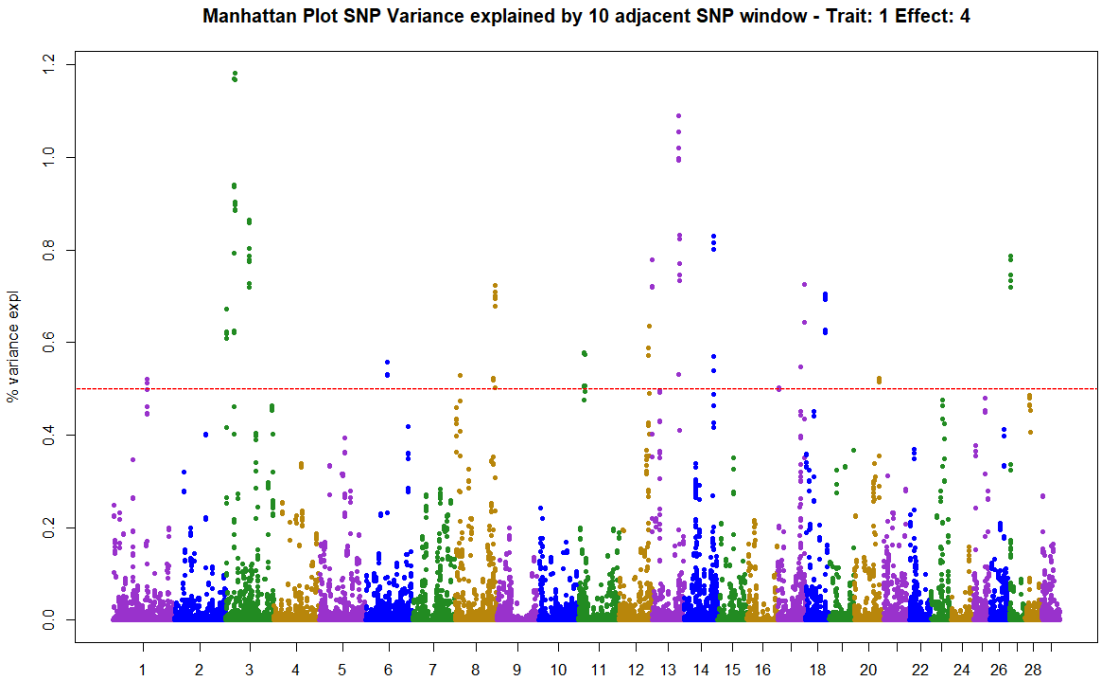

Figure S4. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

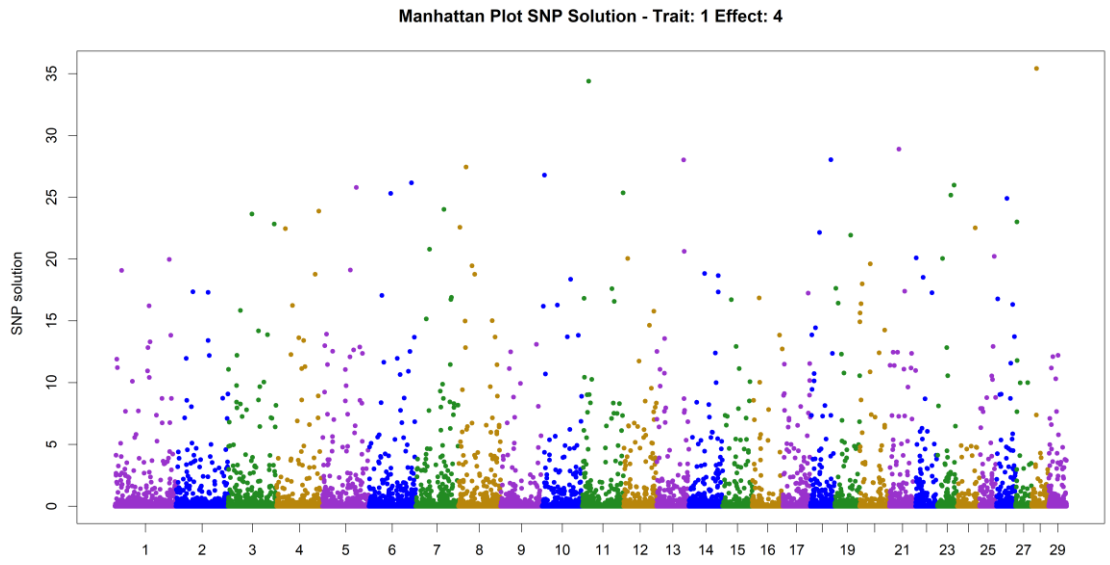

Figure S5. Manhattan plot of absolute values of SNP effects estimated obtained in the 3nd iteration of the WssGWAS for accumulated profitability in Nelore cattle.

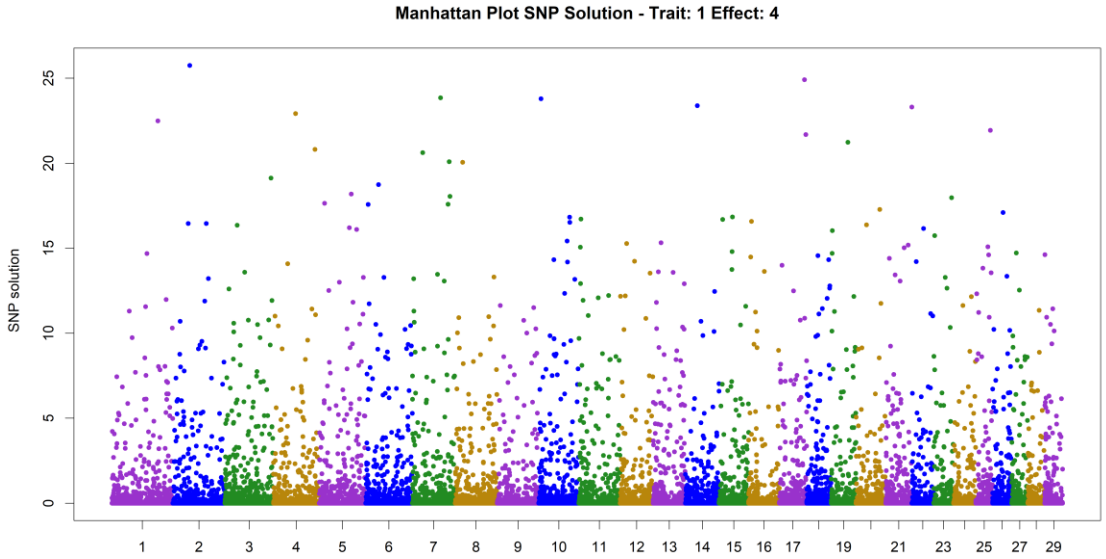

Figure S6. Manhattan plot of absolute values of SNP effects estimated obtained in the 3nd iteration of the WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

CHAPTER 4: GENOMIC PREDICTION FOR NOVEL FEEDLOT PROFITABILITY RELATED-TRAITS IN NELORE CATTLE

Abstract: The aim of this study was to assess the accuracy, bias, and dispersion of genomic predictions accumulated profitability (APF) and profit per kilogram of liveweight gain (PFT) in Nelore cattle using different prediction approaches. Data set consisted of 3,969 phenotypic records for each trait. The pedigree harbored information from 38,930 animals born between 1998 and 2016, 2,691 sires and 19,884 dams. A total of 2,449 animals were genotyped with the Clarifide® Nelore 3.0 SNP panel. Nine models for genomic prediction were evaluated: a linear animal model was applied to estimate the genetic parameters and to perform the genomic single-trait best linear unbiased prediction (ST_ss - default), bi-trait ssGBLUP (TT_CAR, TT_W450, and TT_DMI), and multi-trait ssGBLUP (MT_ss), and finally, two models using the weighted linear (ST_sswl1 and ST_sswl2) and non-linear (ST_sswnl1 and ST_sswnl2) single-step genomic approach (WssGBLUP) were implemented to predict genomic breeding values (GEBV). The ability to predict future performance was calculated as the correlation between GEBV and adjusted phenotypes. The average prediction accuracy of the GEBV of the models ranged from 0.345 to 0.665 for PFT and from 0.425 to 0.603 for APF. The predictive capability of the MT_ss model (0.665) was significantly higher than that of the other models for PFT, except for the TT_CAR model (0.604), which also showed improvements in predictive capacity. For APF, the MT_ss (0.561) and TT_W450 (0.556) models demonstrated improvements in genomic prediction accuracy compared to the other models. In general, the single trait ssGBLUP (ST_ss – default) models and the nonlinear weighting did not increase the accuracy of predictions for both traits. For the phenotypic prediction ability of PFT, the linear WssGBLUP models ST_sswl1 (0.65) and ST_sswl2 (0.70), TT_W450 W450 (0.64), and ssGBLUP-M (0.66) demonstrated the highest prediction abilities. Similar results were observed for the phenotypic prediction ability of APF for both models. However, the linear WssGBLUP model ST_sswl1 (0.84) and ST_sswl2 (0.94) provided higher prediction compared to the bi-trait and multi-trait models. The results indicate that the multi-trait model achieved better predictive ability for the new traits of PFT and APF. Multi-trait genomic selection may provide greater genetic gains than other models for these new economically important traits in breeding programs.

Keywords: Genomic selection, multi-trait model, prediction accuracy, phenotypes of profit.

1. Introduction

Beef cattle genetic breeding has proven and will continue to be an essential driver of sustainability in the livestock industry worldwide (Mueller & Van Eenennaam, 2022). Selective breeding for economically important traits has been performed typically based on phenotypic observations (Meuwissen et al., 2016). In the last decades, significant advances in the tools and methods used in genetic improvement occurred, increasing the speed of the rate of genetic change (Van Eenennaam et al., 2017). Objective measurements replaced subjective records, and more refined statistical methods were adopted to separate heritable genetic effects from environmental factors (Van Eenennaam et al., 2014). Among these methods, the application of genomic selection stands out as the strategy with the highest potential to increase the rate of genetic progress in livestock breeding (Weigel et al., 2010).

Genomic selection has been advancing rapidly, and even after a decade since its initial implementation, various innovative resources continue to be incorporated (VanRaden et al., 2020). Despite this progress, it is becoming increasingly challenging to meet the needs of the market and livestock producers, in addition to the expectations of consumers (Merks et al., 2012). Livestock farming is facing new challenges regarding sustainability, considering its three main components: social, environmental, and economic (Boichard & Brochard, 2012).

In the current "phenomic era," it is crucial to have access to robust phenotypes to address these new concerns (Boichard et al., 2016). In livestock farming, new possibilities are emerging using precision data (Boichard et al., 2016). Technological innovation and the ability to handle large volumes of data play a significant role in this scenario (Seidel et al., 2020). Considering current and future perspectives, selection goals should incorporate new phenotypes and additional traits (Merks et al., 2012), supported by high-precision or large-scale technological tools (Seidel et al., 2020).

One of these new phenotypes includes the ability to predict an animal's profitability and utilize this prediction to assist in identifying and selecting high-performance animals based on their genetic potential for economic return. Additionally, this tool aims to be a management strategy and decision-making tool that directly impacts

productivity and sustainability. These phenotypes encompass accumulated feedlot profitability (AFP) and profit per kilogram of liveweight gain (PFT), measurements obtained in the context of precision livestock techniques, which are proposed in this study as a strategy considering current trends.

In this regard, genomic selection brings new possibilities to initiate the selection of emerging traits, which ones often have reference populations with a limited number of animals, as phenotyping large volumes still needs to be feasible due to the cost and challenges of practical measurement (Calus et al., 2013). Therefore, genomic selection has proven to be an advantageous resource for increasing genetic gains, especially for complex traits, challenging, or costly-to-measure traits with low heritability (Alvarenga et al., 2020).

In this scenario, different methodologies have been proposed to estimate Genomic Estimated Breeding Values (GEBVs), such as the single-step Genomic Best Linear Unbiased Prediction (ssGBLUP) (Misztal et al., 2009; Aguilar et al., 2010; Christensen & Lund, 2010). The ssGBLUP combines phenotype, pedigree, and genomic information simultaneously in individuals with phenotypic but no genotypic information and individuals with only genotypic information through a pedigree-based relationship matrix (A) with the genomic relationship matrix (G) into a hybrid matrix (H) (Legarra et al., 2009; Christensen & Lund, 2010). However, this approach assumes that the effects of single nucleotide polymorphisms (SNPs) have equal variance, which may not be the most appropriate assumption biologically (Meuwissen et al., 2001; VanRaden, 2008; Goddard & Hayes, 2009). As a result, approaches that consider locus-specific variance have been proposed, such as the weighted single-step GBLUP method (WssGBLUP), proposed by Zhang et al., 2016, which is an extended method of ssGBLUP that assigns different weights to SNPs used in the calculation of matrix G.

Most of the current genomic prediction models have been supported by univariate analyses (Mehrban et al., 2021). However, this analysis may need to adequately reproduce the complex interactions among the analyzed traits, as it does not capture the flow of information between them through available information on genetic (co)variances (Gaire et al., 2022). These (co)variances result from pleiotropy and linkage disequilibrium, which are involved in complex relationships among quantitative traits (Lynch, 1998). Therefore, the multi-trait model adopted in genomic selection has demonstrated efficiency in integrating information and identifying the effect of association among traits, resulting in more precise GEBV predictions than univariate analysis models (Calus &

Veerkamp, 2011; Guo et al., 2014; Wang et al., 2017). Thus, it is presumed that the multi-trait model enhances gains by increasing the predictive capacity of GEBVs through the incorporation of records of genetically correlated traits, especially for traits with low heritability or limited number of phenotypes (Song et al., 2019), such as the feedlot profitability-related traits proposed in this study.

In this context, the present study aimed to assess the predictive ability for novel feedlot profitability-related traits in Nelore cattle. For this purpose, seven models were evaluated, as follow: Best linear unbiased genomic prediction of single-step (ssGBLUP) and genomic single-step Weighted Linear and Non-linear approaches (WssGBLUP) under single-, two- and multi-trait models. The model comparison was based on the bias, dispersion, and accuracy of genetic values for profitability-related traits.

2. Materials and methods

This study was exempt from evaluation by the Animal Ethics Committee (CEUA), as established by Law No. 11,794 of 08/10/2008 and Normative Resolution No. 51 of 05/19/2021 from the National Council for Animal Experimentation Control (CONCEA) because all the analyses were performed using pre-existing databases.

2.1 Data source

The dataset used in this study was provided by the National Association of Breeders and Researchers (ANCP, São Paulo, Brazil) in collaboration with @Tech (Piracicaba, São Paulo, Brazil). The ANCP provided the pedigree information and genotypes, and novel feedlot profitability-related phenotypes were provided by @tech. For further information about the company, please refer to the website https://techagr.com/beeftrader. The animals belonged to 26 different herds located in the Southeast, Northeast, and Midwest regions of Brazil. The pedigree contained information of 38,930 animals, born from 1998 to 2016, comprising 2,691 sires and 19,884 dams.

2.2 Phenotyping

Novel phenotypes: The new phenotypes analyzed were accumulated feedlot profitability (AFP) profit per kilogram of liveweight gain (PFT) in feedlot. @Tech's algorithms are designed to make full use of this data, ideally collected within a standardized 80-day trial period for running in the BeefTrader Decision Support System generating the phenotypes

used by the Livestock Profit Tool (LPT) profitability. For trials that do not meet this 80-day standard, our system employs Artificial Intelligence and advanced growth modeling techniques to set the standard. This approach considers historical data to produce estimates that align with the 80-day prediction requirements of the LPT, ensuring robust and reliable analytics across varying trial durations.

The BeefTrader algorithm uses animal traits as input variables (gender, breed, body condition score, initial weight, initial date, among other exogenous factors that impact on growth dynamics), daily weights individually collected through a weighing sensor (daily basis), and information on the nutritional composition of the diets. The records for obtaining the new phenotypes were collected from animals participating in feed efficiency trials, following the same guidelines as Mendes et al., 2020, as mentioned in the section on feed efficiency traits. Based on this information, adjusted for local conditions, weight prediction is carried out in two steps: based on the biology of each animal and with the nutritional data and animal daily weight profile (observed or predicted), it is possible to estimate an optimal growth function for the animals (Step 1); from there, a dynamically adjusted linear or non-linear regression is performed using the least squares method on the weights to fit the predicted growth curve (Step 2). From the predicted growth curve, it is possible to find other variables required by the model, including animal performance in terms of growth and composition of gain, as well as economic and environmental factors. The profitability is the central trait used by LPT, as commented, thus the next topics the @Tech intention is to present the equations related to this core phenotype.

Accumulated kilograms*

$$(sbw * cdf/100) \,/\, 15$$

Where:

sbw: Shrunk Body Weight (kg) - 96% of the Body Weight

cdf: Carcass Dressing (%)

kilograms $*$ Gain

$$initial\ gain = acum\ kilograms\ [2] - acum\ kilograms\ [1]$$

$$initial\ gain = acum\ kilograms\ [d] - acum\ arroba\ [1] + initial\ gain$$

Where:
Acum $kilograms$ = accumulated $kilograms$ $(15kg)$ on a specific day
d = Day
gain initial = gain to be considered on the first day since it is unknown. This value becomes a constant.
Note: The correct procedure for the first day would be to calculate based on the corral weight and remove the constant from the subsequent days.

Daily Cost

$$DMI * diet\ price\ (kg) + feedlot\ daily\ overhead$$

Where:
dmi = Dry Matter intake (kg)
diet_price_kg = diet cost ($/kg)
feedlot_daily_overhead = non-feed cost ($)

Daily Revenue

$$kilograms\ \ price * kilograms\ \ gain$$

Where,
arroba_price = price of the arroba ($/$kilograms$)
gain_arroba = arroba gain ($kilograms$ /day)

Daily Profit

$$revenue\ daily - cost\ daily$$

Where,
Revenue daily = daily revenue ($)

Cost daily = daily cost ($)

Total Revenue, Cost and Profit

$$\sum_{time} daily\ revenue$$

$$\sum_{time} daily\ cost$$

$$\sum_{time} daily\ profit$$

Where,

revenue_daily= see section 4
cost_daily = see section 3
profit_ddaily = see section 5

Cost and Profit per kilograms *

$$\text{total cost}/kilograms\ \ gain_t$$

$$total\ profit/kilograms\ \ gain_t$$

Where,
Total profit = see section 6
Total cost = see section 6
$arroba\ gain_t$ = $kilograms$ gain over time, see section 2

* To assess the profit obtained by meat producers, it is common to use the unit of measurement 'arroba' in Brazil. In this study, the 'arroba' unit is defined as equivalent to 15 kilograms, following the standard practice in the national livestock industry. Therefore, for the purposes of this study, the term 'arroba' in this equation will be used to represent the profit obtained per each 15 kilograms of meat produced.

Standardization of Costs and Arroba Pricing

i. Food cost:

Even considering the effect of the batch (animals evaluated by farm) in the analyses, all common foods between batches, especially among farms, had their prices standardized to set up the food cost (for example, for corn silage, the price was always the same for the different batches). Based on the cost of natural natter and the percentage of dry matter (DM), from the measurement of each animal's daily individual intake, the food cost for everyone was imputed over the 80-day evaluation period. It is important to note that after a seven-day adaptation period, there were 80 days of data collection on weight, DM intake (DMI), and food and non-food costs (operational cost), all individual, to obtain the measure of accumulated profit and profitability per arroba gained by the evaluated animal.

ii. Non-food cost (operational cost):

The non-feed cost was also set at the same value for all evaluated batches with the aim of standardizing this cost source in the process, and it's a source that doesn't affect the animals' performance.

iii. Price paid per kilograms (arroba*):

The arroba price for all batches was standardized to the prices at the time of data collection, with the aim of ensuring that the revenue per arroba was equal for all animals. The prices followed those indicated by Center for Advanced Studies in Applied Economics (CEPEA, https://www.cepea.esalq.usp.br/br/indicador/boi-gordo.aspx)* - University of São Paulo (USP).

For the two- and multi-trait genomic prediction models, the following traits were included in the analyses along with AFP and PFT:

Growth: A growth trait considered in this study was adjusted weight at 450 days of age (W450, kg). The calculation of standardized weight was conducted through linear regression, considering the average daily gain assessed between days 405 and 495 of age for the variable P450 (Negreiros et al., 2022).

Carcass: The carcass traits considered were ribeye area (REA, cm2) and rump fat thickness (RFT, mm). To obtain carcass phenotypes, ultrasound images were taken of the *Longissimus dorsi* muscle among the 12th and 13th ribs (REA) and in the rump region, between the ilium and ischium at the intersection of the *Gluteus medius* and *Biceps femoris muscles* (RFT), using the ALOKA 500V equipment with a 3.5 MHz linear probe.

Feed Efficiency: The feed efficiency trait considered was DMI. This trait was obtained through Intergado® and GrowSafe electronic systems. Feed efficiency tests followed the guidelines established by Mendes et al., 2020, for assessing individual feed intake in beef cattle using both electronic systems. Animals were kept in collective or individual pens and subjected to a 21-day adaptation period followed by a valid 70-day testing phase. Throughout this period, each animal's average weight was recorded via manual weighing every 14 days or through automated weighing platforms (Intergado®). Daily dry matter intake (DMI, kg/day) was derived from the mean of all valid individual daily intake values electronically recorded by the Intergado and GrowSafe systems during the test period.

2.4 Statistical and quality control analyses

The contemporary groups (CG s) were composed considering the effect of farm, year, and season of birth (dry: March to August, and rainy: September to February), management group and sex. For the feed efficiency trait, the identification of the feed

efficiency test was also considered to form the CG. The phenotypic quality control removed records that deviated 3.5 standard deviations from the overall mean of the CG and those with fewer than four records. The descriptive statistics for APF, PFT, and carcass, growth, and feed efficiency related-traits used in the two- and multi-trait analyses after quality control are summarized in Table 1.

Table 1. Descriptive statistics for profitability, growth, feed efficiency, and carcass-related traits in Nelore cattle.

TRAIT	N	MEAN	SD	MIN	MAX	CV (%)	CG
APF ($)	3969	157.71	67.18	-17.98	420.06	42.60	252
PFT ($/kg)	3969	36.65	9.54	-13.33	51.23	26.04	252
W450 (kg)	55052	289.96	63.23	119.00	592.00	21.81	2211
DMI (kg/day)	11169	8.17	2.06	3.18	20.66	25.23	251
REA (cm^2)	37091	57.55	12.85	20.45	114.97	22.33	1559
RFT (mm)	37003	4.35	2.74	0.13	24.39	62.94	1559

APF, accumulated profitability; PFT, Profit per each 30 kilograms; BW450, weight at 450 days of age; DMI, dry-matter intake; REA, rib eye area; RFT, rump fat thickness; N, number animals with records; SD, standard deviation; MIN, minimum; MAX, maximum; CV, coefficient of variation; CG, number contemporary group.

2.5 Genotyping

Genotypes were provided by the National Association of Breeders and Researchers (ANCP), Ribeirão Preto, Brazil. A total of 2,449 animals were genotyped with the low-density panel (Clarifide® Nelore 3.0). The genotype quality control (QC) was performed by the PREGSF90 package (Aguilar et al., 2014), excluding both animals and SNPs from the dataset with call rates < 0.90. Additionally, SNPs with a minor allele frequency (MAF) < 0.05, Mendelian conflicts > 1%, monomorphic SNPs with redundant positions, SNPs deviating from Hardy-Weinberg equilibrium expectations, and those located on non-autosomal chromosomes were also excluded. After QC, 2,449 genotyped animals and 35,658 SNPs remained in the database for analysis.

2.6 Genomic prediction models

Genomic prediction models for APF and PFT was performed using nine genomic models applying the ssGBLUP methodology as follows: single-trait model, three two-trait models, and multi-trait model. Additionally, in the case of the single-trait model, the weighted linear and non-linear single-step genomic approach (WssGBLUP) was also applied in the analyses. The analyses were performed using the BLUPF90 family (Misztal et al., 2002). The general model can be defined as:

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e} \qquad (1)$$

where $\boldsymbol{y}$ is a vector of phenotypic records; $\boldsymbol{\beta}$ is a vector of fixed effects; $\boldsymbol{X}$ is a design matrix associating $\boldsymbol{\beta}$ with $\boldsymbol{y}$; $\boldsymbol{u}$ is a vector of random effects of the direct additive genetic effects; $\boldsymbol{Z}$ is the incidence matrix associating $\boldsymbol{u}$ with $\boldsymbol{y}$; $\boldsymbol{e}$ is the residual effect. Assumptions for residual effects are described below:

$$\boldsymbol{e} \sim \boldsymbol{N}(\boldsymbol{0}, \boldsymbol{I}\boldsymbol{\sigma}_{\boldsymbol{e}}^{\boldsymbol{2}}),$$

where $\boldsymbol{\sigma}_{\boldsymbol{e}}^{\boldsymbol{2}}$ is the residual variance, and $\boldsymbol{I}$ is an identity matrix with a dimension equal to the number of animals with records.

The description of the genomic prediction models is presented in Table 2.

Table 2. Genomic prediction models for feedlot profitability-related traits in Nelore cattle.

Model	Description
Single-trait	
ST_ss (default)	ssGBLUP based on genotypic records (default)
ST_sswl1	ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 1st iteration of the WssGWAS for nonlinear model
ST_sswl2	ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 2nd iteration of the WssGWAS for linear model
ST_sswnl1	ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 1st iteration of the WssGWAS for nonlinear model
ST_sswnl2	ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 2st iteration of the WssGWAS for nonlinear model
Two-trait	
TT_CAR	ssGBLUP based on genotypic records + carcass records
TT – W450	ssGBLUP based on genotypic records + BW450 records
TT_DMI	ssGBLUP based on genotypic records + DMI records
Mult-trait	
MT_ss	ssGBLUP based on genotypic records + W450, DMI, REA and RFT records

Single-Trait prediction model

The ssGBLUP single-trait model using information of both genotyped and non-genotyped phenotype information and using both marker and pedigree information for genetic evaluations were performed. The ssGBLUP is a modification of the BLUP model, in which the inverse of the numerator relationship matrix A^{-1} is replaced by H^{-1} (Aguilar et al., 2010), which is given by:

$$\mathbf{H^{-1}} = \mathbf{A^{-1}} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G^{-1}} - \mathbf{A_{22}^{-1}} \end{bmatrix}$$

where H is the relationship coefficient matrix between the animals; *A* is the (numerator) additive relationship matrix; $\mathbf{A_{22}^{-1}}$ is a partition of *A* corresponding to the genotyped animals and $\boldsymbol{G^{-1}}$ is the genomic relationship matrix as described by VanRaden (2008), where:

$$G = ZZ'$$

Where,

$$Z = (M - P) / \left[2 \sum_{j=1}^{K} p_j (1 - p_j) \right]^{1/2}$$

in which M is the matrix of *K* SNP genotype for each animal, and P is the matrix of frequency of the second allele *p* in the locus *j* (p_j) multiplied by two.

Two-trait and multi-trait prediction model

In the analysis of two or three traits and multi-trait models, carcass traits (REA and RFT), growth (W450), and feed efficiency (DMI) were identified as those genetically correlated with APF and PFT in feedlot, being used as predictors in genomic prediction. The covariances and genetic correlations are presented in the supplementary material section, completing Table S2, and further details about the datasets used in this study are described in Pereira et al. (2024). Regarding the construction of the models, for the two-trait analysis, the traits W450 and DMI were considered alongside APF and PFT in feedlot, leading to the following combinations: APF-W450, APF-DMI, PFT-W450, and PFT-DMI. The three-trait analysis combined carcass traits with APF and PFT, resulting in APF-REA-RFT and PFT-REA-RFT combinations. In the multi-trait analysis, the traits W450, DMI, REA, and RFT were considered in the APF and PFT models.

The two, three-trait and multi-trait models was applied to estimate genomic breeding values for traits through the realized matrix (H) as follows (adapted from Guo et al., 2014):

$$\begin{matrix} y_1 \\ \vdots \\ y_n \end{matrix} = \begin{bmatrix} I_1 & 0 \\ \vdots & \vdots \\ 0 & I_N \end{bmatrix} \begin{bmatrix} \mu_1 \\ \vdots \\ \mu_n \end{bmatrix} + \begin{bmatrix} Z_1 & 0 \\ \vdots & \vdots \\ 0 & Z_n \end{bmatrix} \begin{bmatrix} g_1 \\ \vdots \\ g_n \end{bmatrix} + \begin{bmatrix} e_1 \\ \vdots \\ e_n \end{bmatrix}$$

Where y is the vector that includes each of the n type traits. In these two-trait and multi-trait model, it was assumed that the genomic effects ~N ($\boldsymbol{0}$, $\boldsymbol{G} \otimes \boldsymbol{H}$) and the residuals ($e$) ~$N$ ($\mathbf{0}$, $\boldsymbol{R} \otimes \boldsymbol{I}$) where $\otimes$ is the Kronecker direct product, $\boldsymbol{G}$ and $\boldsymbol{R}$ are the genetic and residual covariance matrices, respectively and $\boldsymbol{I}$ is an identity matrix. The assumed co-variance structure is:

$$Var \begin{bmatrix} g \\ e \end{bmatrix} = \begin{bmatrix} G \otimes \mathrm{H} & 0 \\ 0 & I\sigma_e^2 \end{bmatrix}$$

Single-trait WssGBLUP linear and nonlinear

Before performing weighted genomic prediction, a single-step weighted GWAS (WssGWAS) was conducted to identify SNPs and their respective weights. To perform the ssGWAS a single-trait animal model was applied. The effects and variances of the SNPs were estimated following the methodology proposed by Wang et al. (2012). In this methodology, SNP effects are obtained from the genomic values estimated by the ssGBLUP model, where SNP weights are iteratively obtained. The iterative process increases the weights of SNPs with large effects and decreases those with small effects, essentially regressing them towards the mean. The equation 1 was employed to construct the WssGBLUP model. For the derivation of SNPs effects and weights, the animal effect was decomposed into genotyped animals (a_g) and not genotyped (a_n), as described by Wang et al. (2012). The animal effect of the genotyped animals is a function of the SNP effects (Wang et al., 2012):

$$a_g = Z_g u$$

where $\boldsymbol{Z_g}$ represents the relationship matrix of the genotypes of each locus, and $\boldsymbol{u}$ is a vector of the SNPs effects. The variance of animal effects was assumed as:

$$var\left(a_g\right) = var\left(Z_g u\right) = Z_g D Z_g{}' \sigma_u^2 = G^* \sigma_a^2$$

where $\boldsymbol{D}$ is a diagonal matrix of weights for variances of SNP variances ($\boldsymbol{D} = \boldsymbol{I}$ for GBLUP), σ_u^2 is the variance of the additive genetic effect obtained from each SNP when the same variance is assumed for all SNPs, σ_a^2 is the additive genetic variance, and G^* is the weighted genomic relationship matrix.

The ratio of covariance of additive genetic (a_g) and SNPs ($\boldsymbol{u}$) effects is:

$$var_u^{a_g} = \begin{bmatrix} ZDZ' & ZD' \\ DZ' & D \end{bmatrix} \sigma_u^2$$

Sequentially:

$$G^* = \frac{var(a_g)}{\sigma_a^2} = \frac{var(Zu)}{\sigma_a^2} = ZDZ'\lambda$$

where $\boldsymbol{\lambda}$ is a normalizing constant described by VanRaden et al. (2009) as:

$$\lambda = \frac{\sigma_u^2}{\sigma_a^2} = \frac{1}{\sum_{i=1}^{m} 2p_i(1-p_i)}$$

where $\boldsymbol{m}$ is the number of SNPs and $\boldsymbol{p_i}$ is the frequency of the second allele in the $\boldsymbol{i}$-th SNP. The SNP effects can be described by Wang et al. (2012):

$$\hat{u} = \lambda DZ'G^{*-1}\hat{a}_g = DZ'[ZDZ']^{-1}\hat{a}_g$$

The estimated SNP effects can be used to calculate the variance of each individual SNP (Zhang et al., 2010), which can be used as different weighting for each SNP:

$$\sigma_{u,i}^2 = \widehat{U}_i^2 2p_i(1-p_i)$$

Where $\sigma_{u,i}^2$ is the j SNP weight (equivalent to j SNP variance); û is a vector of estimated j SNP effect; and p is the allele frequency of j SNP.

Two strategies were used to weight SNPs and perform genomic prediction: linear and non-linear methodology. Weighted ssGWAS is an iterative process with several steps, considering t as the iteration number, the steps are (Wang *et al*., 2012):

8. Let D = I in the first step.
9. Calculate G = $\mathbf{Z}_g\mathbf{D}\mathbf{Z}_g'\boldsymbol{\lambda}$.
10. Calculate GEBVs for the entire data set using the ssGBLUP.
11. Convert GEBVs to SNP effects ($\hat{u}$): $\hat{u} = \boldsymbol{\lambda}\, DZ' (\mathbf{Z}_g D \mathbf{Z}_g' \boldsymbol{\lambda})^{-1}\hat{\mathbf{a}}_\mathbf{g}$,
    where $\hat{\mathbf{a}}_\mathbf{g}$ is the GEBVs of animals which were also genotyped.
12. Calculate weight for each SNP for linear model (Zhang et al., 2010):
    $$d_i = \hat{a}_i^2 2p_i(1-p_i) \text{ (default)}$$
    For the non-linear weighted model, using similar approach to VanRaden (2008), SNP-specific weights were calculated as:
    $$d_i = 1.125^{\frac{|\hat{a}_i|}{sd\,(\hat{a})}-2}$$
13. Normalize SNP weights to remain the total genetic variance constant.
14. Back to step 2.

A total of two iterations (i.e., using the identity matrix plus one iteration using the D matrix derived from SNP solutions) were used in the WssGBLUP because the second iteration provided higher GEBV accuracies in the preliminary analysis. The SNP solutions were estimated using the POSTGSF90 software (Aguilar et al., 2014). The genomic association analyses were performed using the BLUPF90 software family (Misztal et al., 2002) including the genomic information (Aguilar et al., 2010).

2.7 Prediction accuracy, bias, and dispersion

To conduct the prediction analyses, the data set was divided into whole (*w*, training) and partial (*p*, validation) subsets, which initially requires evaluations with a partial dataset where the phenotypic records of target validation animals are removed. Thus, the partial GEBV (GEBV*p*) is calculated from relatives and genomic information. Then, the phenotypes of validation animals are included for further evaluation, and the whole genomic breeding value (GEBV*w*) is achieved. Animals born in 2022 and 2023 belonged to six herds were selected as the target validation group for being the young selection candidates. This validation methodology simulates the practical situation of genomic selection, where the estimate of GEBV prediction of younger animals (i.e., those

candidates for selection) is based on phenotypic and genotypic information from proven or older animals in the total population. Table 3 presents the descriptive statistics of the traits for the whole and partial datasets.

Table 3. Number of animals with phenotypic records in the whole and partial subsets for profitability-related traits in Nelore cattle.

Dataset	Trait	N	Mean	SD	Min	Max	CV (%)	CG
Training	APF	3478	160.26	62.54	-17.98	420.06	39.02	242
	PFT	3478	37.62	8.83	-13.34	51.23	23.47	242
Validation	APF	502	139.64	91.75	-6.59	374.61	65.70	28
	PFT	502	29.76	11.39	-3.49	48.57	38.28	28

APF, accumulated profitability; PFT, Profit per each 30 kilograms; N, number animals with records; SD, standard deviation; MIN, minimum; MAX, maximum; CV, coefficient of variation; CG, number contemporary group.

Prediction accuracy, bias, and dispersion were calculated according to the methodology proposed by Legarra and Reverter (2018). The prediction accuracy (acc_p^2) was calculated as a direct estimate of squared population accuracy of the estimated genomic breeding value (GEBV) based on partial dataset. In this methodology, the covariance of GEBV based on partial and whole data ($\rho^2_{Cov_{w,p}}$) is a function of the squared accuracy (reliability) of the partial GEBV, as follows:

$$acc_p^2 = \rho^2_{Cov_{w,p}} = \sqrt{\frac{cov(\hat{u}_w, \hat{u}_p)}{(1-\bar{F})\sigma_a{}^2}}$$

where $\hat{u}_w$ is the GEBV estimated with genomic and phenotypic information; $\hat{u}p$ is the (G)EBV considering the partial dataset; F is the average inbreeding coefficient estimated for the animals included in the validation dataset; and $\sigma_u{}^2$ is the additive genetic variance for APF and PFT.

The averages of the estimated breeding values were used to estimate bias. It has an expected value of 0 if the evaluation is unbiased.

$$\mu_{wp} = \bar{\hat{u}}_p - \bar{\hat{u}}_w$$

The dispersion was obtained through the regression of EBV from whole data on EBV from partial data. The $b_{w,p}$ has an expectation, $E(b_{w,p}) = 1$ if there is not over/under dispersion:

$$b_{w,p} = \frac{cov(\hat{u}_w, \hat{u}_p)}{var(\hat{u}_p)}$$

To assess the predictive capacity of the phenotypes in the different models, the Pearson's correlation between the o GEBV and the adjusted phenotype for the fixed effects (Yc) was used (Legarra et al., 2008). The phenotype adjustment was performed using the PREDICTF90 software (BLUPF90 family) (Misztal et al., 2002). This correlation was calculated between a GEBV and the adjusted phenotype (y*; phenotype y adjusted for fixed effects) for individuals in the validation population, and divided by the square root of heritability (h^2):

$$ACC_P = \frac{r(\hat{u}_p, y^*)}{\sqrt{h^2}}$$

3. Results and Discussion

The prediction accuracy, bias, and dispersion of genomic prediction for PFT and APF using different prediction models are described in Table 4. The prediction accuracy results obtained through the different models demonstrate their dependency on the ability to capture and evaluate the genetic architecture of the studied traits, as well as the effects of the present polymorphisms, regardless of their magnitude, whether they are of minor or significant effect (Terakado et al., 2021).

The results revealed that the prediction accuracy of the ST_sswl1 (0.587) and ST_sswl2 (0.528) models was higher to that of the ST_ss model (0.345) for PFT. A significant gain of 59% in prediction accuracy was observed using the WssGBLUP method. A similar trend was observed concerning APF, where the prediction accuracy of ST_sswl1 (0.575) and ST_sswl2 (0.603) models was higher to that of the ssGBLUP single-trait model (0.425). On the other hand, the results obtained with the ST_sswnl1 (0.365 and 0.443, respectively) and ST_sswnl2 (0.365 and 0.442, respectively) nonlinear models did not indicate improvements compared to the ssGBLUP model in terms of prediction accuracy for both traits.

These results pointed out that the ST_sswnl1 and ST_sswnl2 nonlinear models did not contribute to improvements in prediction accuracy for both PFT and APF traits. This considerable increase observed in prediction accuracy of the ST_sswl1 and ST_sswl2 linear models compared to the nonlinear can be attributed to the polygenic

nature of the analyzed trait, where several small-effect SNPs probably explained most of the genetic additive variation for feedlot profitability-related traits in Nelore cattle.

Concerning the two- and three-trait models, when incorporating information from correlated traits, such as W450 and carcass traits with PFT, an improvement in the accuracy of the GEBVs obtained was observed, 0.604 and 0.523 (TT_CAR and TT_W450), respectively. However, the PFT benefited less from the two-trait analysis with DMI (TT_ DMI), which can be attributed to the low genetic correlation between these traits and the lower number of records for DMI, reducing accuracy to 0.372. Likewise, it was observed that in the two- and three-trait models for APF with W450, DMI, and carcass traits, there were also improvements in predictive ability, with values of 0.503, 0.505, and 0.556 for TT_DMI, TT_CAR and TT_W450, respectively.

The differences observed, therefore, in the precision of GEBVs between the two- and three-trait models can be explained by the fact that the traits that contributed more information to the models, as well as those that showed higher genetic correlation with PFT, such as W450 and carcass traits, and APF with DMI, W450, and carcass, resulted in improvements in the predictive ability of GEBVs.

According to results obtained here, the MT_ss model showed the highest prediction accuracy (0.665) than all evaluated models for PFT, meaning that prediction accuracy increased using the multi-trait model compared to the single and two-trait models. In contrast, the prediction accuracy of GEBV using the MT_ss model (0.561) for APF showed little improved predictive ability compared to the values obtained from the WssGBLUP single-trait linear model, ssGBLUP two-trait model, and three models. These results align with those reported by Guo et al. (2014), and Song et al. (2019), where the two-trait and multi-trait genomic models proved more effective for traits with a smaller set of phenotypic data. This observation is relevant for livestock breeding programs, as often, no phenotypes are available for all traits of interest in all individuals of a reference population Guo et al. (2014). According to Guo et al. (2014), incorporating phenotypic data from correlated and easily measurable traits through the multi-trait model improved the accuracy of GEBVs.

Table 4. Genomic prediction accuracy, bias, and dispersion of genomic prediction for feedlot accumulated profitability and profit per kilogram of liveweight gain in Nelore cattle based on different models.

Trait	Model	Accuracy	Bias	Dispersion
Profit per kilogram of liveweight gain	*Single-trait*			
	ST_ss	0.345 (0.000)	-0.771 (0.250)	1.124 (0.043)
	ST_sswl1	0.587 (0.000)	-0.792 (0.242)	0.713 (0.013)
	ST_sswl2	0.528 (0.000)	-0.746 (0.234)	0.470 (0.014)
	ST_sswnl1	0.365 (0.000)	-0.770 (0.249)	1.111 (0.038)
	ST_sswnl2	0.365 (0.000)	-0.770 (0.249)	1.120 (0.038)
	Two-trait			
	TT_CAR	0.604 (0.005)	-1.230 (0.345)	0.969 (0.019)
	TT_W450	0.523 (0.000)	-1.031 (0.349)	1.063 (0.019)
	TT_ DMI	0.372 (0.000)	-1.075 (0.346)	1.122 (0.034)
	Mult-trait			
	MT_ss	0.665 (0.00)	-1.111 (0.344)	0.982 (0.016)
Accumulated Profitability	*Single-trait*			
	ST_ss	0.425 (0.000)	0.002 (0.018)	1.104 (0.045)
	ST_sswl1	0.575 (0.000)	0.049 (0.017)	0.739 (0.023)
	ST_sswl2	0.603 (0.000)	0.033 (0.024)	0.556 (0.022)
	ST_sswnl1	0.443 (0.000)	0.001 (0.017)	1.084 (0.040)
	ST_sswnl2	0.442 (0.000)	0.001 (0.017)	1.093 (0.040)
	Two-trait			
	TT_CAR	0.505 (0.000)	0.096 (0.015)	1.068 (0.032)
	TT_W450	0.556 (0.000)	0.002(0.015)	1.087 (0.028)
	TT_ DMI	0.503 (0.000)	-0.003 (0.016)	1.065 (0.034)
	Mult-trait			
	MT_ss	0.5612 (0.000)	0.004 (0.015)	1.049 (0.027)

ST_ ss, ssGBLUP (default) based on genotypic records; ST_sswl1, ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 1st iteration of the WssGWAS for nonlinear model; ST_sswl2, ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 2nd iteration of the WssGWAS for linear model; ST_sswnl1, ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 1st iteration of the WssGWAS for nonlinear model; ST_sswnl2, ssGBLUP weighting the diagonal of D matrix with the λ values obtained in the 1st iteration of the WssGWAS for nonlinear model; TT_CAR, ssGBLUP based on genotypic records + carcass records; TT_W450, ssGBLUP based on genotypic records + BW450 records; TT_ DMI, ssGBLUP based on genotypic records + DMI records; MT_ss, ssGBLUP based on genotypic records + BW450, DMI, REA and RFT records; λ, lambda (proportion of the additive genetic variance explained by each SNP).

Regarding bias, it was observed to be low and followed the same trends for all prediction models of the PFT. Different variables may limit the response of prediction accuracy and reduce the bias of genomic predictions, as reported by Lund et al. (2009), Zhang et al. (2011), and Goddard (2009), where the genetic structure of the traits in focus

can be characterized by heritability and the number of associated QTLs. This report is consistent with the biases found in our results, which may be due to the low genetic variance and heritability of the PFT trait. In contrast, the observed values for bias in PFT were close to zero for all models, ranging from -0.003 to 0.096.

The dispersion values varied for PFT and APF among the different models, as illustrated in Table 4. These values indicated variation in predictive ability, showing both inflation and deflation of the estimated GEBVs. Values below 1 indicate overdispersion (inflation) of the estimated genetic values, while values above 1 imply underdispersion (deflation) (Himmelbauer et al., 2023). The single-trait models ssGBLUP, nonlinear models (ST – sswnl1 and ST - sswnl2), and the bi-trait models TT_CAR, TT_W450, and TT_DMI obtained slightly higher slopes, ranging from 1.063 to 1.124 for PFT and from 1.065 to 1.104 for PFT, respectively, suggesting a slight tendency towards inflation and more significant variability in predictions. The ST_sswl1 and ST_sswl2 single-trait models exhibited the lowest dispersions, with values of 0.713 and 0.470 for PFT and 0.556 and 0.739 for APFT, respectively. However, it is important to note that although the predictive ability of these models was high compared to other single-trait models and like two- and multi-trait models, these values showed greater underdispersion and indicated possible deflation in the estimated genetic values.

The models that showed dispersions with values closer to 1 were the multi-trait models (MT_ss), with values of 0.982 and 1.049 for PFT and APF, respectively. When predictions are deflated and greater than one, in practical terms, the difference between the progenies of selected sires is expected to be greater than predicted by the GEBV. In contrast, the opposite occurs when the predictor is inflated (Chiaia et al., 2017). Although the predictive ability between multi-trait and bi-trait models is similar, the dispersion of multi-trait predictions was close to one, demonstrating the consistency of this model for better prediction of GEBVs. In other words, this model was more effective in predicting the absolute differences between individuals under evaluation (Rezende et al., 2012) for the two traits evaluated in this study.

Regarding the accuracies of prediction of the fraction of additive genetic variance that explains the phenotype, the accuracy was calculated by dividing the correlation between the partial GEBV and the phenotype adjusted for fixed effects by the square root of the heritability. The weighted models ST_sswl1 and ST_sswl2 presented the highest estimate of the accuracy of the genetic fraction that explains the phenotype, 0.65 and 0.70, respectively for PFT. Similarly, for APF, the ST_sswl1 and ST_sswl2 models showed

high accuracy, 0.84 and 0.94, respectively, which was significantly higher compared to the other models. In the two-, three-, and multi-trait scenarios, accuracy ranged from 0.46 to 0.57. For this dataset, it was observed that the weighted WssGBLUP linear model was more efficient in predicting the fraction of additive genetic variance responsible for explaining the phenotype. These results also showed that incorporating information from weighted regions of GWAS into genomic prediction models, through the weighted linear WssGBLUP approach, can be an efficient strategy to improve the accuracy of predicting the fraction of additive genetic variance for the traits under study.

Regarding the predictive accuracy of the fraction of additive genetic variance explaining the adjusted phenotype for PFT, weighted linear model demonstrated the highest predictive abilities, ST_sswl2 (0.70), followed by MT_ss (0.66), ST_sswl (0.65), and TT_W450 (0.64). Conversely, models ST_sswnl1 (0.58) and ST_sswnl2 (0.55) exhibited slightly lower predictive abilities, while models TT_CAR (0.41), TT_DMI (0.38), and ST_ss (0.33) displayed the lowest predictive abilities.

For APF, the same trend was observed for weighted linear models, where ST_sswl (0.84) and ST_sswl2 (0.94) showed substantially higher predictive accuracies of the fraction of additive genetic variance explaining the adjusted phenotype for APF compared to other models, such as TT_W450 (0.57), MT_ss (0.56), ST_sswnl1 (0.54), ST_sswnl2 (0.54), TT_DMI (0.52), TT_CAR (0.46), and ST_ss (0.46).

These results suggest that the analyses of two- and three-multi-trait models and nonlinear weighted models did not contribute to the predictive accuracies of the adjusted phenotypes. On the other hand, weighted regions, where weighted linear models used their own QTL information, contributed to a better predictive capacity of the fraction of additive genetic variance explaining the adjusted phenotypes for PFT and APF. This indicates that these models were more effective in capturing the additive genetic variation that genuinely contributes to each trait.

4. Conclusions

The multi-trait model increased the genomic prediction accuracy of feedlot profitability related traits. Genomic prediction using multi-trait models is particularly relevant when the trait is complex and the number of phenotypes is limited, as is the case for novel traits. This strategy is more accurate for improving genomic prediction estimates of these traits and integrating them efficiently into genetic improvement programs. These results would provide additional support to breeders to improve management and

selection decision in order to enhance the feedlot profitability operations. In the weighted linear single-trait model, incorporating weighted regions for GEBV prediction showed adequate predictive ability, but resulted in a dispersion below 1 and yielded more biased predictions.

For commercial herds, feedlot operators, and buyers of calves for rearing and fattening, for example, the models in general demonstrated adequate predictive ability of the phenotype. The results obtained in predicting future performance (phenotype) can assist these producers in making more assertive management decisions, aiming to optimize productivity efficiency and maximize profitability per animal in their operations. This would enable producers to prioritize animals with greater genetic potential for higher economic returns based on feedlot profitability-related traits.

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6. Supplementary material

Table S1. Covariance components and genetic and residual correlations between accumulated profitability (APF), profit per kilogram of liveweight gain (PFT) and e adjusted weight at 450 days of age (W450), dry matter intake (DMI), ribeye area (REA) and rump fat thickness (RFT).

Trait	Components	W450	DMI	REA	RFT
PFT	Cov_a	35.78	0.47	5.13	-1.19
	Cov_e	43.99	0.92	5.17	1.49
	r_a	0.64 ±0.05	0.26 ±0.08	0.44 ±0.07	-0.68 ±0.04
	r_e	0.09 ±0.03	0.06 ±0.02	0.05 ±0.02	0.07 ±0.03
APF	Cov_a	35.78	0.47	5.13	-1.19
	Cov_e	43.99	0.92	5.17	1.49
	r_a	0.64 ±0.05	0.26 ±0.08	0.44 ±0.07	-0.68 ±0.04
	r_e	0.09 ±0.03	0.06 ±0.02	0.05 ±0.02	0.07 ±0.03

Cov_a, additive genetic covariance; Cov_e, residual covariance; r_a additive genetic correlation; r_e, residual correlation.

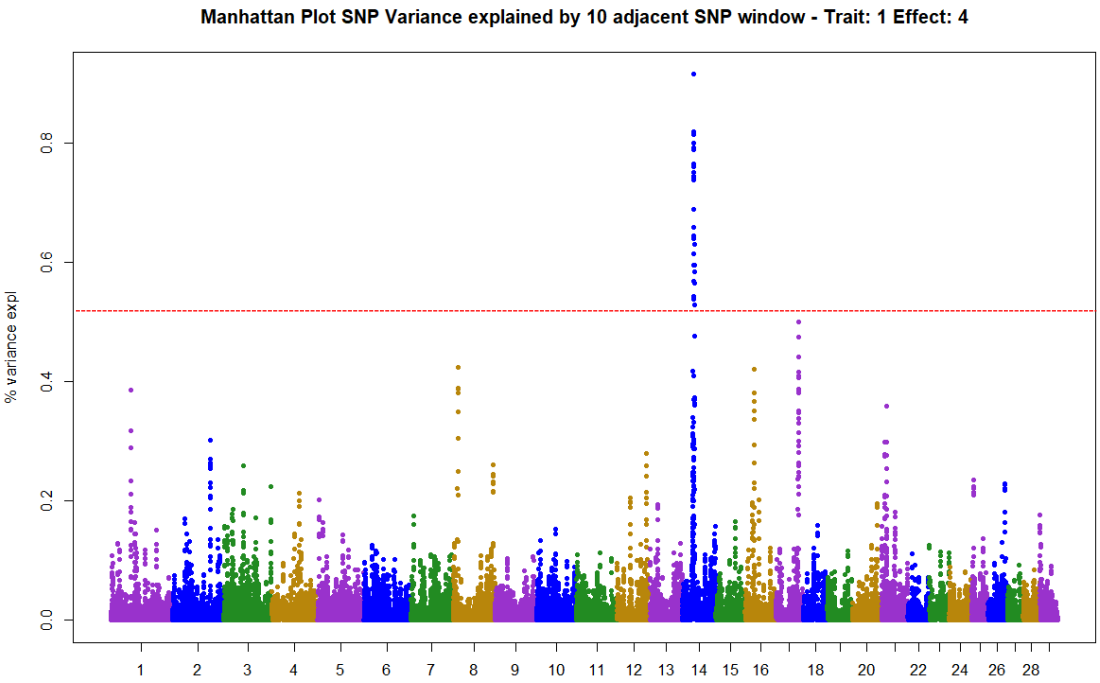

Figure S1 Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the linear WssGWAS for accumulated profitability in Nelore cattle.

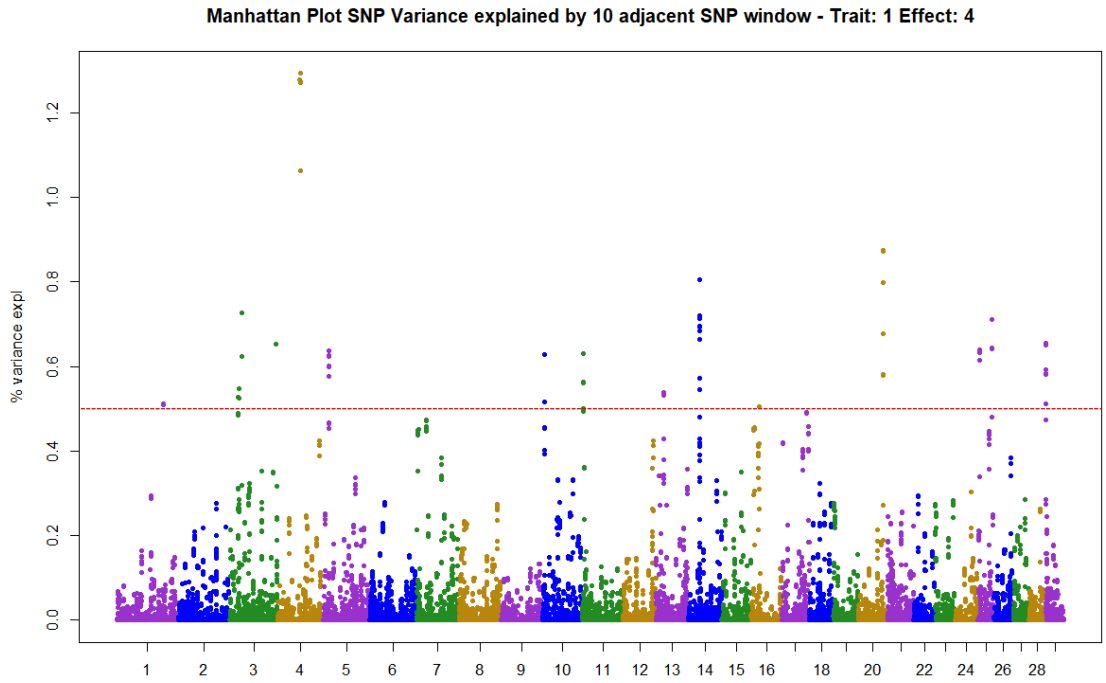

Figure S2. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the linear WssGWAS for accumulated profitability in Nelore cattle.

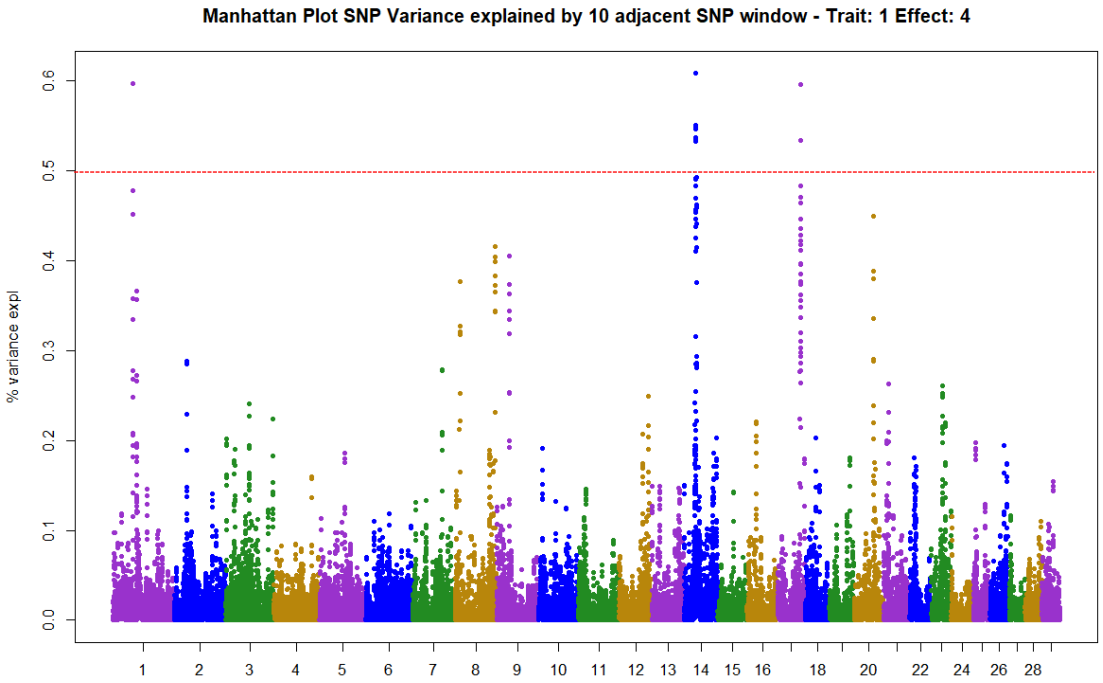

Figure S3. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the linear WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

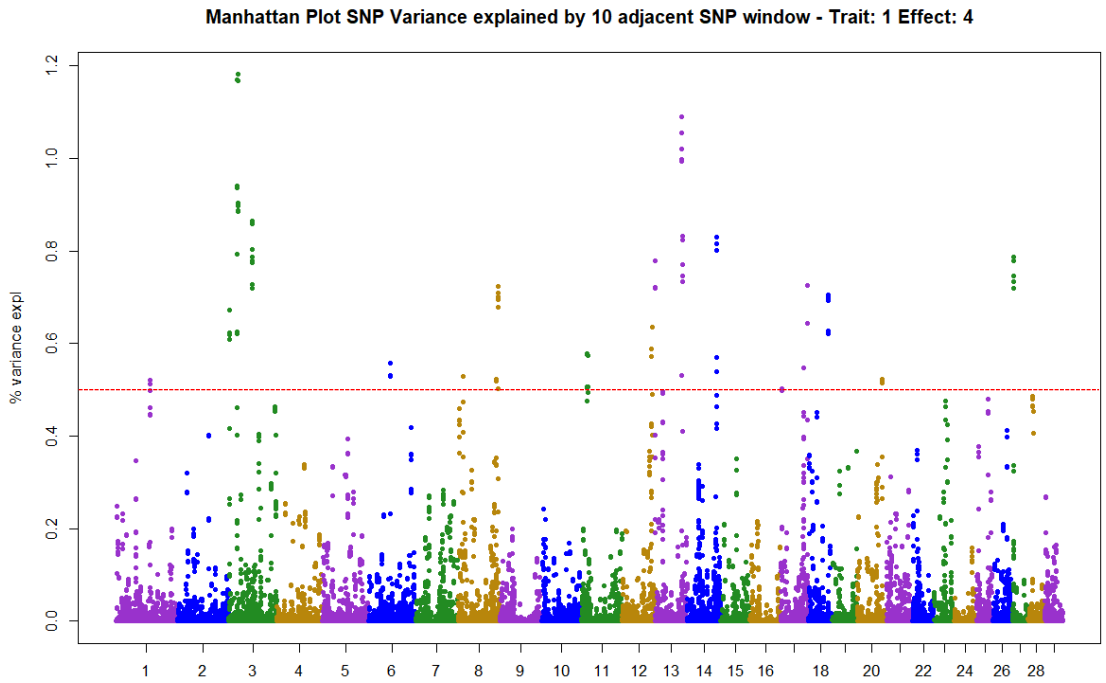

Figure S4. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the linear WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

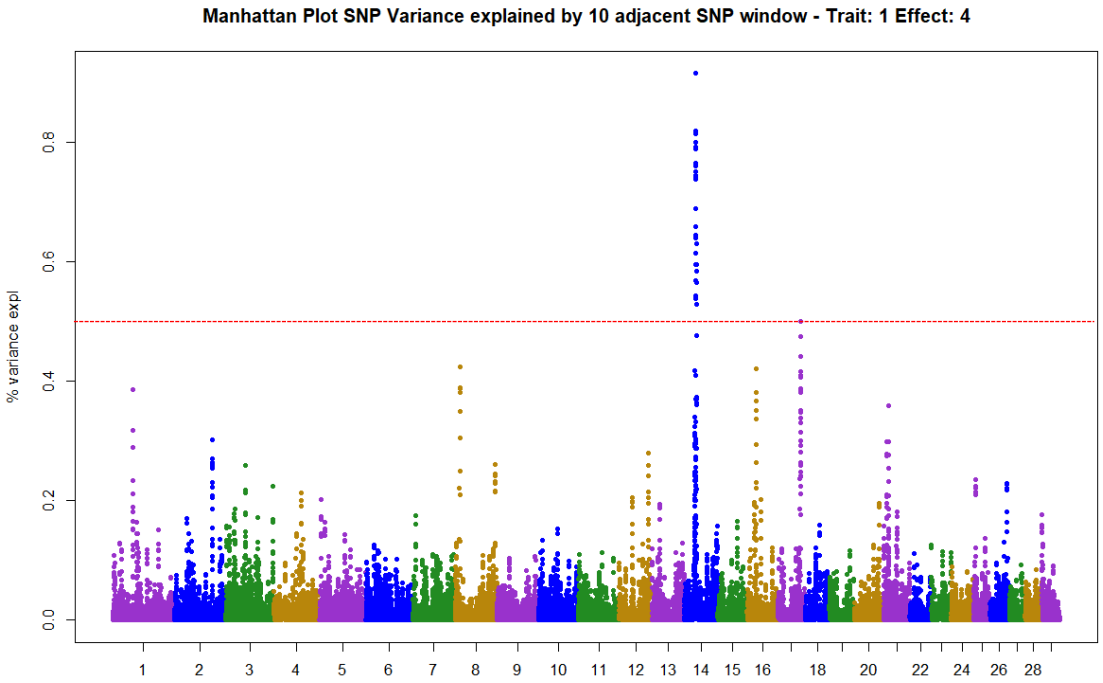

Figure S5. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the nonlinear WssGWAS for accumulated profitability in Nelore cattle.

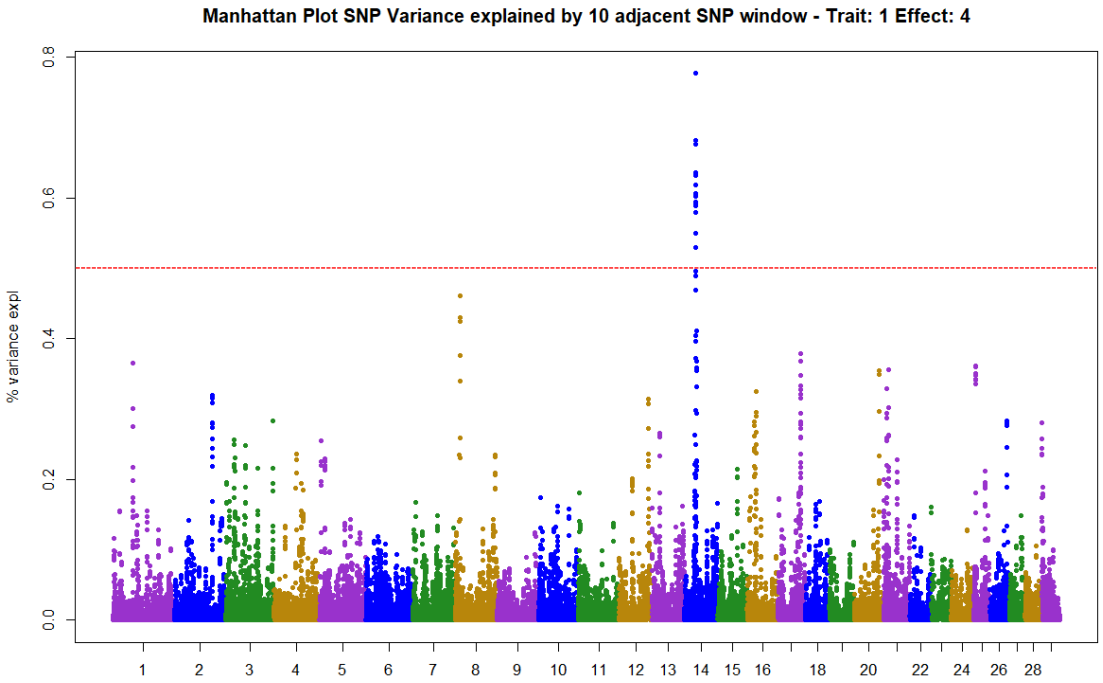

Figure S6. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the nonlinear WssGWAS for accumulated profitability in Nelore cattle.

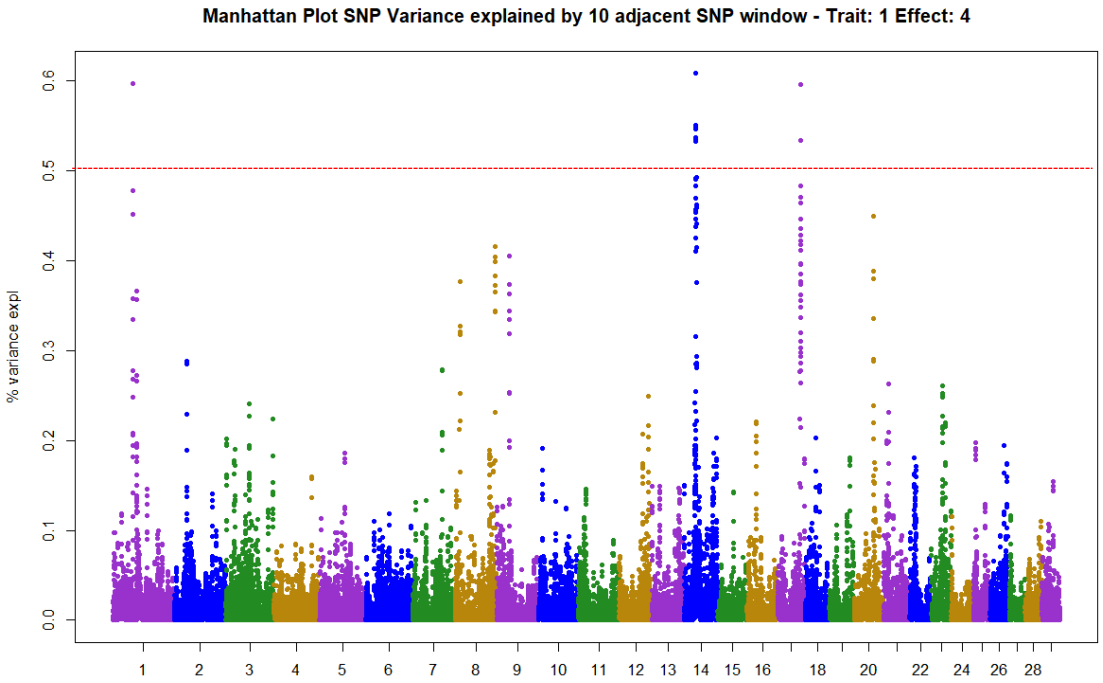

Figure S7. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 1nd iteration of the nonlinear WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

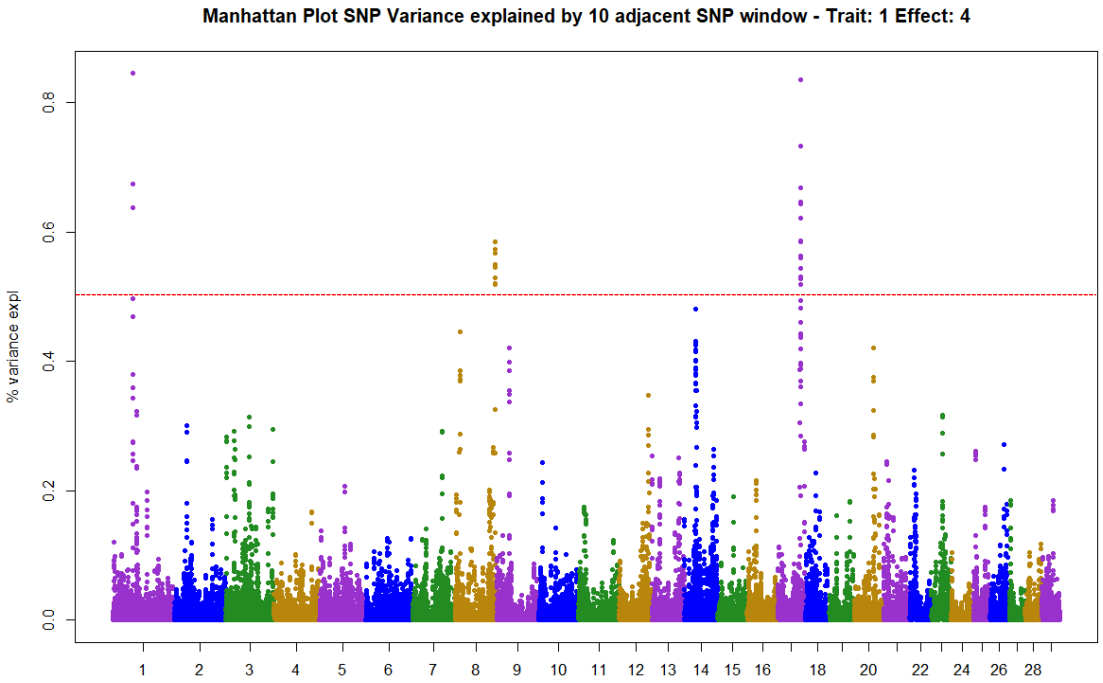

Figure S8. Manhattan plot of the genomic regions of 10 adjacent SNPs that explain more than 0.5% of the additive genetic variance (Var) obtained in the 2nd iteration of the nonlinear WssGWAS for profit per kilogram of liveweight gain in Nelore cattle.

CHAPTER 5: FINAL CONSIDERATIONS

The beef cattle industry plays an important role in the global economy, food security, and the agribusiness economy, and is essential to develop strategies and technological solutions that promote its long-term sustainability. Genetic improvement is an efficient tool that contributes to the increase of sustainable production in livestock due to its ability to generate continuous and cumulative productive and economically improvements over time. The use of new measurement technologies in precision livestock farming, promoting phenotyping through phenomics, has provided new opportunities for genetic improvement.

Among them, it highlights the more precise and large volumes of measurement of traditional traits, such as carcass, weight, feed efficiency, and reproduction, and introducing new traits into selection programs. These new traits can be considered technological solutions resulting from the synergy between genetics, precision livestock farming, and phenomics, aiming to complement the already used selection criteria and enhance the outcomes of economic, productive, and sustainable indicators. And, through genomics, these traits have the potential to be explored and incorporated into selection programs, thus accelerating the genetic gain of herds.

Finishing is recognized as a strategic and determining phase within the beef cattle production cycle, representing all the work carried out from the breeding phase to the moment of slaughter. At this stage, attention and appropriate investments are necessary to ensure the success and profitability of the business. Producers often focus on carcass traits and growth to obtain high performance from animals in feedlot. Despite significant advances, there is still room for further growth in terms of productivity. In this sense, this study investigated two novel traits: profit per kilogram of liveweight gain (PFT) and accumulated profitability (APF) in feedlot.

The variance components and genetic parameters for these traits were estimated, showing genetic variability and moderate to low heritability. The results provided important information on the relationship of these traits with carcass, reproduction, feed efficiency, growth, and body composition. Including these traits as selection criteria can improve performance and economic indicators due to the observed associations with dry matter intake, body composition, rib eye area, and yearling weight. Furthermore, it is important to highlight that, despite being traits measured in feedlot, a favorable relationship with sexual precocity indicators traits was observed.

These two traits are recommended for both rearing and finishing. Feedlot operators will have at their disposal two new tools that can assist in managing the animals during lot formation along with selection indices, considering the expected economic return. Based on this, breeders can make more informed decisions, as animals with more significant genetic potential for profitability will be prioritized to exit the feedlot earlier. This allows for developing specific strategies for each lot, considering the expected productive and economic performance. Identifying animals with higher economic return potential reduces production costs and minimizes resource wastage, such as unnecessary feeding for animals that will not achieve the expected performance in the feedlot. This increases meat production efficiency and contributes to reducing environmental impact.

Concerning the favorable association between APF, PFT gain, and indicators traits of sexual precocity, it is important to highlight that sexual precocity is closely related to herd productivity and the overall efficiency of the production system, which can have a considerable impact on production costs and economic returns. The ability to produce sexually precocious animals is especially relevant in breeding herds, where age at first calving is a performance indicator. The identification and selection of females based on profitability traits, along with genetic and reproductive indicators, can lead to improvements in the economic outcomes of this phase. This represents another metric for selecting females that produce calves with higher growth rates, better carcass conformation, and greater feed conversion efficiency. Furthermore, including these traits as selection criteria can contribute to reducing the costs associated with maintaining economically unproductive dams in the herd.

Detecting causal genetic variability is one of the main objectives of bovine genetic improvement, as understanding the genetic architecture of the characteristics of interest is fundamental to efficiently direct genetic variants in the selection process. In this context, Genome-Wide Association Studies (GWAS) represent an important approach to identifying genomic regions and the genetic basis of complex traits, elucidating the associations between genotype and phenotype in each study population. To better understand and elucidate the genetic and biological mechanisms associated with regulating APF and PFT gain, this study conducted a GWAS analysis using the weighted single-step approach and a functional enrichment and metabolic pathway analysis.

As a result, it was revealed that these traits are controlled by many genes of small effect. A total of 21 genomic regions collectively explains 14.67% of the additive genetic variance for APF, while 52 genomic regions collectively explain 38.11% of the additive

genetic variance for PFT in Nelore cattle. Different candidate genomic regions have been associated with biological processes such as carbohydrate, protein, and lipid metabolism, as well as physiological processes regulating ingestive behavior and the immune system. Several candidate genes located in these genomic regions associated with growth, feed efficiency, carcass traits, and fertility were also identified.

In practical terms, these biological and molecular processes play roles in expressing traits that make an animal more profitable. For example, genes in genomic regions associated with growth can regulate the expression of growth and growth-related hormones, influencing weight gain. Similarly, processes or genes regulating feed efficiency or ingestive behavior affect the efficiency of converting feed into body weight, such as nutrient absorption and degradation. Additionally, regions associated with carcass conformation, fat deposition, and muscle development directly impact the determination of the quantity of meat produced.

As shown in the results of genetic parameter estimation, all these traits are associated with the animal's profitability genetic potential. These results contribute to a better understanding of the genetic architecture and the identification of molecular markers for the new traits proposed in this study, enabling more precise and targeted genetic improvement, which may help accelerate genetic gains in Nelore cattle.

The use of genomic selection in breeding programs has contributed to increasing genetic progress, owing to the greater precision of estimated breeding values (EBVs), thereby reducing the generation interval. Different methods have been introduced in the literature to perform genomic prediction of genetic values. The accuracy, bias, and dispersion of genomic predictions are influenced by the trait of interest, the number of animals and markers, reference population size, and the trait's heritability. Additionally, another critical aspect is the relationship between animals in the reference population and the evaluated animals.

There is generally not a large population of animals with genotypes and phenotypes available simultaneously for novel and difficult-to-measure traits. Multi-trait models have emerged as a strategy to improve the prediction capacity of these traits. Multi-trait models can potentially increase genetic gain for profitability-related traits, as they benefit from relationships between traits, such as additional information from genetic covariances. These covariances arise from pleiotropy and linkage disequilibrium, resulting in complex relationships between traits.

The multi-trait model demonstrated to be the most appropriate for estimating genomic values for profitability-related traits in Nelore cattle. This study revealed that genomic prediction for APF and PFT had a better predictive ability of GEBVs when incorporating correlated traits, such as carcass, weight, and dry matter intake. This model, therefore, can be used to obtain the most accurate genomic values in young animals. Genomic prediction for APF and PFT in young animals can serve as an additional tool to distinguish between more and less profitable groups of animals, enabling early decision-making.

The predictive ability of the fraction of genetic variance explaining the phenotype, using the weighted single-trait linear method, also yielded high accuracy values. This predictive capacity is essential for anticipating the future performance of animals regarding profitability indicators in selection programs, translating into substantial gains in greater economic returns from the animals.

The results presented are innovative for the new traits evaluated in Nelore cattle in feedlot, which have potential as profitability indicators. These traits can assist producers and breeding programs identify and select animals with high genetic potential for profitability. They can be widely integrated as selection criteria, enabling more informed decision-making when selecting individuals based on their productive performance and economic return. The integration of genomic regions associated with these traits identified by GWAS provides valuable insights into the underlying genetic basis and offers opportunities for more effective selection. Genomic predictions would significantly contribute to the early identification of the most profitable animals at the expense of those with lower-than-expected economic returns, thus accelerating genetic progress for these traits through more precise selection.