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REVIEW

Genotype-by-environment interactions in beef and dairy cattle populations: A review of methodologies and perspectives on research and applications

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Abstract

Modern livestock production systems are characterized by a greater focus on intensification, involving managing larger numbers of animals to achieve higher productive efficiency and animal health and welfare within herds. Therefore, animal breeding programs need to be strategically designed to select animals that can effectively enhance production performance and animal welfare across a range of environmental conditions. Thus, this review summarizes the main methodologies used for assessing the levels of genotype-by-environment interaction (G × E) in cattle populations. In addition, we explored the importance of integrating genomic and phenotypic information to quantify and account for G × E in breeding programs. An overview of the structure of cattle breeding programs is provided to give insights into the potential outcomes and challenges faced when considering G × E to optimize genetic gains in breeding programs. The role of nutrigenomics and its impact on gene expression related to metabolism in cattle are also discussed, along with an examination of current research findings and their potential implications for future research and practical applications. Out of the 116 studies examined, 60 and 56 focused on beef and dairy cattle, respectively. A total of 83.62% of these studies reported genetic correlations across environmental gradients below 0.80, indicating the presence of G × E. For beef cattle, 69.33%, 24%, 2.67%, 2.67%, and 1.33% of the studies evaluated growth, reproduction, carcass and meat quality, survival, and feed efficiency traits, respectively. By contrast, G × E research in dairy cattle populations predominantly focused on milk yield and milk composition (79.36% of the studies), followed by reproduction and fertility (19.05%), and survival (1.59%) traits. The importance of G × E becomes particularly evident when considering complex traits such as heat tolerance, disease resistance, reproductive performance, and feed efficiency, as highlighted in this review. Genomic models provide a valuable avenue for studying these traits in greater depth, allowing for the identification of candidate genes and metabolic pathways associated with animal fitness, adaptation, and environmental efficiency. Nutrigenetics and nutrigenomics are emerging fields that require extensive investigation to maximize our understanding of gene–nutrient interactions. By studying various transcription factors, we can potentially improve animal metabolism, improving performance, health, and quality of products such as meat and milk.

KEYWORDS
animal adaptability, *Bos taurus indicus*, *Bos taurus taurus*, environmental sensitivity, resilience

INTRODUCTION

The accurate identification of genetically superior individuals for economically relevant traits is crucial for the success of animal breeding programs (Goddard, 2009; Hayes et al., 2007). This involves assessing the genomic background of populations and evaluating the phenotypic variability from interactions between genetic and environmental factors using classical animal models (Burrow, 2012; Dickerson, 1962). The environmental effect encompasses non-genetic factors that contribute differentially to phenotypic variability. Several studies have consistently shown that most traits of economic relevance to cattle breeding are complex traits largely influenced by a large number of genes and environmental conditions (Carvalho Filho et al., 2022; Mota, Fernandes Jr, et al., 2020; Santana Jr et al., 2017). To achieve successful production intensification, it is important to identify and select animals with lower environmental sensitivity and enhanced adaptive traits (Brito et al., 2021; Henry et al., 2018). Typically, less environmentally sensitive genotypes are preferred, although, in some contexts (e.g., more environmentally controlled production systems), more productive and probably more sensitive may be more advantageous. Investigating the implications of genotype-by-environment (G × E) is essential for designing mating strategies and selection decisions to increase productivity across diverse production systems.

In traditional breeding programs, animals are often selected under more favorable or less stringent environmental conditions (e.g., nucleus breeding farms), allowing them to express more of their genetic potential. However, the offspring of the selected animals are frequently raised under more challenging conditions. As a result, in situations where G × E occurs, the reproductive and productive performance of specific genotypes may become unpredictable in certain environments, potentially impacting the overall genetic progress of the population (Cardoso & Tempelman, 2012; Rauw & Gomez-Raya, 2015). Thus, to minimize these effects, breeding programs should focus on selecting animals that are more adapted to various environmental and management conditions (Hermesch et al., 2015; Kolmodin & Bijma, 2004; Nirea & Meuwissen, 2017) or select animals that perform better in the environmental conditions where they will be raised.

A key goal of breeding programs is to comprehensively characterize and understand the impact of G × E to minimize or even eliminate the unpredictability associated with such interactions. The occurrence of G × E can introduce challenges in the design of breeding programs. However, it also presents opportunities to strategically identify and combine the most appropriate genotypes for given production systems aiming to optimize the industry profitability and improve animal health and welfare. Despite being a significant source of variation in production systems, often leading to reduced responses to selection (Hayes et al., 2016; Mota, Fernandes Jr, et al., 2020), G × E is often ignored in routine genetic and genomic evaluations. One of the primary challenges in G × E modeling lies in disseminating and effectively implementing the results at the producer level. Furthermore, fitting G × E leads to additional complexity in the statistical models, particularly when relying solely on pedigree information. This is due to the increased number of parameters needed to account for interaction effects, the heterogeneous variance caused by different environments, the need for including environmental covariates, and the creation of complex correlation structures among traits. Additionally, G × E may exacerbate non-additive effects, which are already present in the population, making them more challenging to model accurately with pedigree data alone. This often results in less accurate genetic evaluations, especially in more extreme environmental conditions (De Leon et al., 2016; Mulder, 2016; Sae-Lim et al., 2016; Tiezzi et al., 2017).

G × E can be broadly categorized into two main types: (1) changes in the ranking of genotypes across different environments; and (2) variations in the dispersion of genetic values across environments without a simultaneous shift in the ranking of genotypes (Falconer, 1990; Lynch & Walsh, 1998). The impact of G × E is typically quantified based on the genetic correlation of a given trait measured in different environmental conditions (and considered as a separate trait depending on the environmental category). Genetic correlation values falling below 0.80 are considered as an indication of substantial G × E effects on animal performance (Robertson, 1959).

The occurrence of G × E, particularly when there is a reranking of genotypes, has been documented for several traits in cattle (Raidan et al., 2016; Ruiz-Sánchez et al., 2007; Santana Jr et al., 2017, 2018; Tsuruta et al., 2015). In such cases, substantial discrepancies in the genetic variance and shifts in the estimated breeding values (EBVs) of the selection candidates are observed (Mota et al., 2019). In other words, the genotypes that perform best in one environment may not necessarily maintain better performance in other environments (Mulder & Bijma, 2005). Advancements in omics technologies and statistical methods, particularly with the implementation of genomic selection, have significantly enhanced the performance of genetic evaluations, leading to increased selection accuracy, especially for young animals (Misztal et al., 2020; Mrode et al., 2019; Silva Neto, Peripoli, et al., 2023). Adding genomic information to the analyses plays a pivotal role in increasing the accuracy of genetic variation and breeding value estimates across environmental conditions (Carvalheiro et al., 2019; Mota et al., 2018; Mota, Fernandes Jr, et al., 2020; Mota, Lopes, et al., 2020; Oliveira et al., 2018).

This review exploits the main methods used to quantify G×E levels and their implications for important traits within cattle breeding programs. We aimed to discuss the implications of the reported findings for breeding programs and identify possible knowledge gaps. Additionally, we discuss the contribution of genomic information when estimating and accounting for G×E in cattle breeding schemes. Before doing so, we provide an overview of the cattle breeding program structure and their relationship with key challenges associated with harnessing G×E to optimize genetic progress in cattle populations. We also summarize key contributions of the nutrigenomics field and the role of nutritional strategies in the phenotypic variability of complex traits. We explore the relationship between resilience and productivity in livestock production systems and outline potential opportunities for future research and practical applications.

STRUCTURE OF CATTLE BREEDING PROGRAMS

Most cattle breeding programs are structured hierarchically, with the most intensive genetic selection of animals performed in *nucleus* or elite herds. Subsequently, the superior genetic material is disseminated to commercial herds through artificial insemination or other reproductive technologies (Raidan et al., 2016; Schenkel, 2000; Simm, 1998) (Figure 1). In nucleus herds, animals are selected under more favorable conditions, including better nutritional and management practices, enabling them to express their genetic potential fully (Raidan et al., 2016). However, this scenario contrasts with the reality of most commercial herds, where significant variation in environmental conditions exists, including factors related to nutritional practices, climatic conditions, and incidence of diseases. Consequently, the average performance of the offspring sired by the bulls selected in more favorable environmental conditions may deviate from expectations, especially when the commercial conditions differ from those where the sires were initially evaluated (Burrow, 2012).

A study by Raidan et al. (2016) evaluating the performance of young Nellore bulls in both nucleus and commercial herds for reproductive and growth traits, revealed significant variations in the estimates of genetic parameters. The highest additive genetic variance and heritability estimates were observed in more favorable environmental conditions. Haile-Mariam et al. (2008) reported evidence of G×E interaction in calving to first service interval and nonreturn rate in Australian dairy cattle considering different calving systems and regions. Some studies evaluating African Holstein cattle also observed G×E interaction for age at first calving and milk production, considering the performance of daughters of bulls raised in intensive and extensive production systems (Neser et al., 2014). The substantial differences between selection and breeding conditions often lead to genetic correlations between the same trait measure in different environments being close to or below 0.80, indicating a substantial G×E effect on the trait evaluated.

Dairy cattle breeding programs face a major challenge when using genetic material imported from countries with different environmental conditions and production systems. The market for artificial insemination is dominated by companies from the USA, Europe, and Canada (Araújo et al., 2016; Santos et al., 2020). In Brazil, around 80% of the semen used by farmers is imported into the country (Araújo et al., 2016). Studies investigating G×E in dairy cattle populations in Brazil have confirmed that

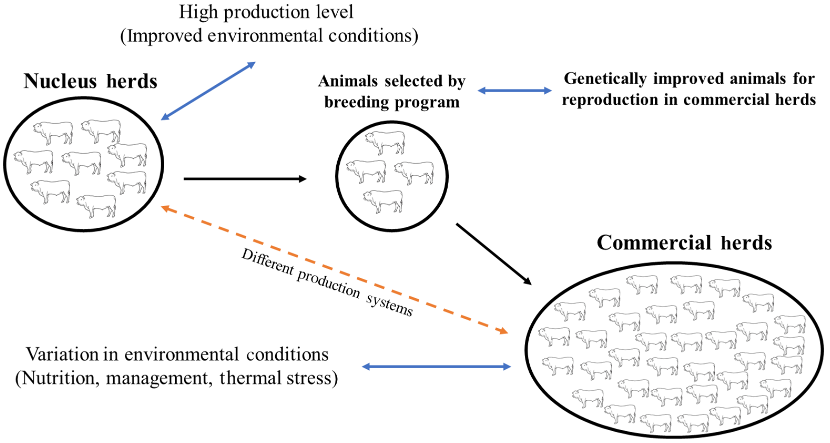

FIGURE 1 Hierarchical structure of cattle improvement programs with selection is usually done in elite herds with better nutritional and management conditions for later dissemination of the superior genetic material in commercial herds with less ideal environmental conditions.

these animals are more environmentally sensitive. This is expected given the countries' production system differences (Cardoso & Tempelman, 2012; Cooke et al., 2020). For instance, Sub-Saharan Africa smallholder dairy cattle farmers rely on the importation of sire semen (Chawala et al., 2021). This dependence contributes to slower genetic progress, partly due to the effects of G × E interactions.

To minimize the G × E effect, the Interbull organization conducts an international genetic evaluation of dairy bulls based on specific procedures (www.interbull.org; Philipsson, 1987, 2011). In these multi-trait across-country genetic evaluations, traits such as milk yield and milk composition, are fitted as different traits across countries, and bulls have EBV for different countries participating in the genetic evaluations. This approach is feasible in dairy cattle due to the reduced number of breeds used and high level of genetic connectedness in worldwide dairy cattle populations due to the widespread use of a small number of sires (Hayes et al., 2016).

The impact of choosing sires for different production systems from where their offspring will be raised depends on their genetic potential and adaptability to the environment. Breeders must carefully assess the performance of sires and their offspring in the target environmental conditions before making selection or semen purchase decisions to avoid adverse effects. By considering G × E interaction in breeding programs, breeders can select more adapted genotypes that perform well in diverse environments and production systems. Nonetheless, genetic evaluations that consider G × E have yet to be adopted in commercial breeding companies. This is because the G × E effects vary significantly across breeds, strains, and production systems, making it challenging to generalize genetic models for all situations. Additionally, accurate breeding values require substantial amounts of well-structured phenotypic and environmental data recorded across environmental levels. As more environmental variables and phenotypic traits are included in the models, the analyses become more parameterized, and convergence issues may arise in multivariate evaluations. As a result, livestock breeding programs typically use simpler genetic evaluation models and only consider G × E in specific situations.

GENETIC ASPECTS OF UNIFORMITY OF PRODUCTION

The demand for enhanced productive efficiency and more uniform animal performance is essential for the profitability of livestock production systems (Júnior et al., 2022). Given that uniformity holds great importance in various stages of animal production, any lack of homogeneity within the production chain can directly impact the producers' profitability. In intensive production systems, such as group-housed pigs, poultry, and fish, variability in size and growth rate among animals can increase competition for resources, such as space, feed, and water. This excessive competition can lead to agonistic interactions, resulting in social stress, which in turn can negatively affect growth, increase mortality and morbidity, reduce milk production in dairy species, and impair feed intake in group-housed animals (Gilmour et al., 2005; Janhunen et al., 2012; Milligan et al., 2002). Therefore, a lack of uniformity impacts both meat and milk production, as it can result in lower production efficiency and higher management costs. One practical approach to address this need for greater uniformity is through genetic improvement, considering G × E and selecting more robust animals, i.e., animals that adapt and perform more consistently across environments.

The primary focus of this review was related to factors associated with macro-environmental effects, which are regular, persistent, and global factors (e.g., climatic conditions, average herd production, heat stress, and varying nutritional levels) that can lead to G × E interactions (Berghof et al., 2019). However, there are micro-environmental factors that are sporadic, conditional, and specific to the individual, such as animal age, health status, and social hierarchies. Although these micro-environmental factors can influence production uniformity and contribute to G × E interactions, few studies have evaluated their potential impact on G × E, with most focusing on the variance of genotypes in a common environment (Mulder et al., 2013; Neves et al., 2012).

Production homogeneity in livestock is somewhat influenced by genetic factors (Hill & Mulder, 2010; Iung et al., 2018; Mulder, 2016; Mulder et al., 2007; Sell-Kubiak et al., 2015). This genetic variability can be used to enhance animal uniformity through genetic selection. In traditional quantitative genetics, models often assume that the residual variance is homogeneous, implying that genotypes primarily differ in their average effect (Falconer, 1996; Lynch & Walsh, 1998). However, genetic heterogeneity indicates how animals respond to environmental disturbances and their environmental sensitivity as reported in beef cattle studies (Iung et al., 2018; Mulder et al., 2013; Neves et al., 2011).

Differences in animal uniformity for a specific trait can be characterized as variations in residual variance (Iung et al., 2020). The genetic heterogeneity of residual variance has been examined through two primary methods. Mulder et al. (2009) employed a two-step approach to estimate the genetic heterogeneity component of residual variance in female and male broiler chickens. Several studies have used this methodology to evaluate G × E in cattle (Berghof et al., 2019; Ehsaninia et al., 2020). In the first step, they assessed the variance components for the trait's mean and subsequently employed a log transformation on the squared residuals, using these as the response variable in their analyses. Alternatively, Rönnegård et al. (2010) and Felleki et al. (2012) introduced the Hierarchical Dual Generalized Linear Model, which concurrently fits two sets of mixed model equations, one for the mean level and another one for the residual variance level. Elucidating the relationship between uniformity of production and G×E is crucial for advancing our understanding of the genetic mechanisms influencing integrated production systems' performance. This knowledge, in turn, can aid in developing or enhancing selection and mating schemes in the cattle industry.

G × E INTERACTIONS

G×E refers to the phenomenon in which genotypes exhibit varying phenotypic responses due to variations in environmental conditions (Falconer, 1996). In the context of breeding programs, two primary forms of G×E are of major importance, given their far-reaching implications for selecting superior genotypes for performance in target environments (Figure 2b,c).

The first G×E scenario is typically considered nonsignificant, occurring only as an additional effect of the environment on the phenotypic response that can be adjusted for in the classical model of genetic evaluation (BLUP, Best Linear Unbiased Prediction; Figure 2a). The second type of G×E is characterized by variations in the magnitude of the genetic additive variance across the environments evaluated, as shown in Figure 2b.

The accuracy of selection in breeding programs can be affected by changes in genetic variance across environments, leading to more biased EBV when G×E is ignored in the genetic models, mainly due to the selection of sires from herds with high phenotypic variability (Meuwissen et al., 1996). This means that the selection of animals in one environment does not guarantee the desired improvement in other environments. The genetic parameters of the trait may differ between environments, which may affect the correlation between phenotypic values and EBV when G×E is ignored. This is due to changes in additive genetic (σ_a^2) and/or residual (σ_e^2) variances.

G×E can differently affect the phenotypic expression of complex traits, in which genotypes may have different responses when exposed to contrasting environmental conditions (Figure 2). In situations where genotypes exhibit differences in EBV between environmental conditions, yet without re-ranking, the environmental effect can result in an EBV scale adjustment when G×E is ignored (Figure 2b). G×E plays a substantial role in this scale change, even though the best-performing genotype in one environment remains the best in other environments. However, when genotypes exhibit different degrees of response according to the environmental conditions, re-ranking of animals based on their EBV can occur (Figure 2c). This significant G×E effect highlights that the evaluated trait expression cannot be considered the same across environmental conditions (Strandberg et al., 2002). For animal breeding purposes, the reclassification of animals based on their EBV across environments represents the most critical form of G×E. In other words, there may not be a single superior genotype that stands out in all environments, and selection for performance in one environment may result in smaller genetic gains than anticipated in other environments (Mulder & Bijma, 2005).

Robertson (1959) suggested that a genetic correlation for the same trait evaluated in different environments lower than 0.80 indicates potential reclassification of animals and the need for selection schemes tailored to specific environments (Mulder & Bijma, 2005, 2006). However, given the current structure of cattle genetic evaluations, breeding programs with specialized selection schemes for each distinct production environment are not anticipated to be widely implemented in the near future. Nonetheless, the evaluation of G×E remains a crucial element in cattle breeding and management.

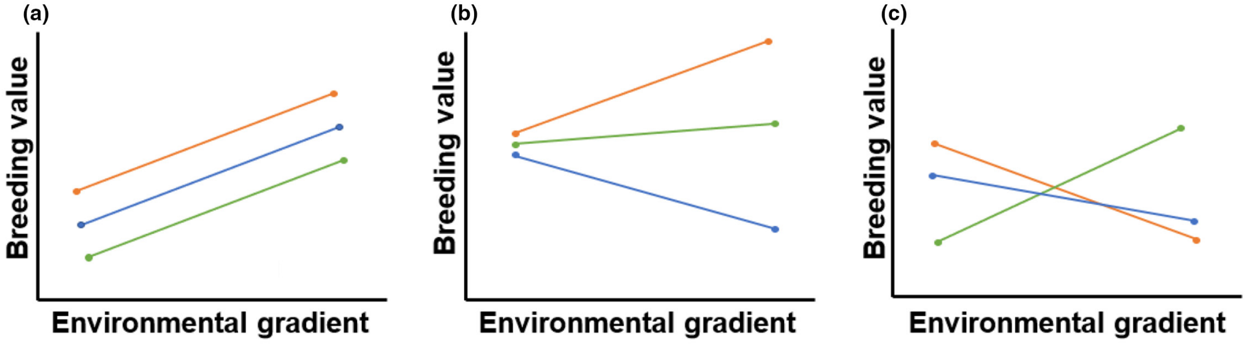

FIGURE 2 Environmental effect on genotype variation, breeding value can change depending on environment, often leading to complex interaction between genotype and environment. (a) Additive effect of environment on phenotypic response, genotype by environment interaction (G×E), not significant; (b) example of environmental effect leading to scale effect on the genetic value of the genotype; and (c) significant rearrangement of genetic value in response to environmental change.

ENVIRONMENTAL SENSITIVITY AND PHENOTYPIC PLASTICITY

Environmental sensitivity or reaction norms can be defined based on differences in a genotype's or population's performance across environments (Falconer, 1990). This sensitivity can be assessed using reaction norm models (RNMs), employing random regression models to estimate how each individual responds to environmental changes. These models map trajectories influenced by a continuous environmental descriptor (Carvalheiro et al., 2019; Kirkpatrick et al., 1990; Mota et al., 2019; Schaeffer, 2004). Random regression models (RRMs) for reaction norms began to gain prominence in the 1990s (Oliveira et al., 2019). Henderson (1984) established the theoretical foundation with his mixed models. The direct application of RRMs to reaction norms was first demonstrated by Kirkpatrick et al. (1990). In 2004, Schaeffer (2004) further advanced the field by refining and expanding the use of RRMs in genetic evaluation, enhancing their effectiveness across various environmental conditions. These developments were pivotal for advancing the modeling of G × E using reaction norms.

In general, the sensitivity of animals to environmental changes is assessed using linear models, as higher-order polynomials can be more complex to estimate and make biological interpretations. However, higher-order RNM may be indicated when changes in phenotypic expression do not exhibit a linear pattern along the environmental gradient (Hayes et al., 2016; Schaeffer, 2004). Animals with a steeper slope in their reaction norms are more sensitive to environmental changes, leading to greater variations in phenotypes. Conversely, animals with flatter slopes exhibit lower sensitivity to environmental variations, resulting in smaller phenotypic differences across diverse environmental conditions (Carvalho et al., 2019; Oliveira et al., 2018). Consequently, more resilient animals, i.e., those with a greater ability to be minimally affected by environmental variations or rapidly return to the unperturbed state (Colditz & Hine, 2016), are particularly valuable for breeding purposes in more challenging conditions.

Understanding the genetic factors that underlie the sensitivity of the animals to environmental variations holds significant importance in optimizing cattle breeding programs. In this context, incorporating genomic data in the analyses has expanded the application of RNM, transitioning from individual-level analyses to the level of single nucleotide polymorphisms (SNPs). This can be achieved by leveraging extensive genotypic data from animals exposed to diverse environmental conditions that might not be necessarily connected at the pedigree level (Carvalho et al., 2019; Hayes et al., 2009; Mota, Lopes, et al., 2020; Silva et al., 2014).

An important term to be addressed is phenotypic plasticity, defined by De Jong and Bijma (2002) and Sommer (2020) as the ability of a genotype to exhibit different phenotypic responses in different environments. This includes morphological, physiological, and behavioral variations of an animal's phenotype (Pelster & Burggren, 2018; Sommer, 2020) and is considered a fundamental mechanism for animal adaptation to environmental changes (Murren et al., 2015). Although genotype and gene expression determine an individual's phenotype, phenotypic plasticity allows the same genotypes to present considerable variation in their performance (West-Eberhard, 2003). Like environmental sensitivity, phenotypic plasticity can be measured by RNM, and factor-analytic (FA) models can also be used. As the multi-trait animal model that will be covered in the next session, the FA model is limited to discrete environments and does not assume a scaled classification of environments or physiological continuity across different environments (De Jong & Bijma, 2002).

Although we focused on exploring genotype plasticity in macro-environments, Pelster and Burggren (2018) highlight that the conventional definition of phenotypic plasticity typically overlooks 'response time.' This refers to the period required for a phenotypic modification to manifest, with time intervals for these changes varying significantly, from minutes to years. Furthermore, the authors highlighted that when considering the temporal aspect of phenotypic plasticity, it must be clear whether the observed change is a real change in phenotype or a change in performance due to homeostatic adjustment.

ASSESSING THE RELATIONSHIP BETWEEN RESILIENCE AND PRODUCTIVITY IN LIVESTOCK SYSTEMS

It has been known for a long time that the environment can influence the phenotype of animals (Lamarck, 1914). However, as suggested by Lerner (1954), populations can balance their genetic background and resist environmental changes. In livestock production systems, there has been an emphasis on animal resilience, which involves both crossbreeding to introduce suitable genetic variations and selecting animals with higher genetic potential for desired traits, as well as the ability to adapt to environmental conditions.

Resilience, understood as an animal's ability to adapt and maintain its performance in the face of challenges or environmental changes, is critical in ensuring productive stability (Berghof et al., 2019; Colditz & Hine, 2016). Resilient animals are characterized by their ability to recover from a disturbance quickly. Despite experiencing a sharp initial decline in productivity, these animals demonstrate a remarkable ability to return to pre-disturbance levels swiftly, while less resilient animals may take longer to recover and may not fully return to their previous state (Berghof et al., 2019). Thus, the intrinsic relationship between animal resilience and productivity in agricultural systems is a fundamental element of sustainability. Resilient animals have shown a remarkable ability to adapt to climate variations, resource scarcity, and environmental stress, maintaining productivity or minimizing losses (Poppe et al., 2021, 2022; Poppi et al., 2018). This adaptive capacity provides a more favorable scenario for maintaining consistent production levels in agro-industrial systems. Furthermore, animal resilience has a genetic correlation with the efficiency in resource use, health, fertility, and longevity of animals (Chen et al., 2023; Poppe et al., 2020).

Measuring resilience can be difficult, and the mechanisms involved strongly depend on the nature of the disturbance, that is, the results are dependent on the disturbance investigated in the study (Berghof et al., 2019; Colditz & Hine, 2016). Colditz and Hine (2016) proposed a diverse set of response variables that enables the measurement of resilience for disturbance events. These variables encompass deviations between expected and observed production over the duration of the disturbance, aiming to assess animals' response after a severe drop in production (Van der Waaij et al., 2000).

Precision livestock farming technologies, such as automated feeding systems and automated milk sensors in milking parlors, have emerged as a strategic solution for longitudinal data sampling to assess resilience indicators based on variability in animal performance (Brito et al., 2020). With repeated records of frequently measured traits, estimating an individual's performance without environmental challenges is possible using linear and nonlinear statistical models (the differences between expected and observed production yield contain valuable information about the animal's adaptability to known and unknown macro- and micro-environmental disturbances). Based on these deviations, Berghof et al. (2019) suggested using skewness, residual variance, and autocorrelation of deviations in productive performance as resilience indicators in livestock production systems. This finding is based on the aspect that repeated measures over time for the same production trait contain relevant insights into an animal's ability to cope with micro-environmental challenges.

Residual variance is a measure calculated based on the analysis of variability patterns originating from repeated measurements over time, reflecting the impact of environmental disturbances at an individual level (Berghof et al., 2019; Chen et al., 2023; Elgersma et al., 2018; Poppe et al., 2020, 2021, 2022; Rodrigues et al., 2024; Scheffer et al., 2018). Animals lowly affected by environmental fluctuations tend to have low residual variance, while the opposite is observed in animals more susceptible to environmental disturbances. The autocorrelation (Lag-one) of the deviations signals the duration of the impact of the disturbances (Chen et al., 2023). For animals without disturbances or with rapid recovery, the autocorrelation approaches zero. For animals influenced by disturbances, with a slower recovery, the autocorrelation approaches +1, indicating that subsequent deviations are similar. In cases of rapid and overcompensation responses to perturbations, such as compensatory growth, the autocorrelation approaches −1, indicating that subsequent deviations are the opposite (Berghof et al., 2019; Chen et al., 2023). In turn, the deviations' skewness highlights the direction of these variations. For animals without disturbances or with little influence, the asymmetry approaches zero. However, a positive skewness suggests positive deviations, mainly due to favorable responses to environmental improvements, while a negative skewness indicates predominantly negative deviations resulting from disturbances (Poppe et al., 2020).

In a study conducted by Chen et al. (2023) to assess resilience indicators based on daily milk yield variability, moderate genetic correlations were found between residual variance and cow's productive life in months, with estimates of −0.30. This suggests that more resilient cows (i.e., less affected by environmental challenges) tend to have a longer productive life. The same authors also reported genetic correlations of −0.20 between the autocorrelation of deviations and productive life in months. However, Poppe et al. (2020), evaluating the skewness of deviations, found insufficient genetic variability for this indicator. Furthermore, the authors also did not identify any significant genetic correlation between skewness and health, longevity, fertility, or metabolic traits.

Efficient adaptation to variable environments is an intrinsic characteristic of resilient animals, positively impacting agricultural production's sustainability (Berghof et al., 2019). Resilience is also closely related to animals' welfare and tolerance to disease and stress (Doeschl-Wilson et al., 2021). The animals' ability to quickly recover after stressful events contributes to maintaining productivity, as it reduces the duration of periods of production loss (Colditz & Hine, 2016; Doeschl-Wilson et al., 2021). This relationship between welfare, tolerance, and resilience emphasizes the importance of these attributes in the sustainability of agro-industrial production systems.

STATISTICAL MODELS FOR QUANTIFYING G × E

The analysis of G×E interactions has undergone significant evolution over time. Initially, these interactions were primarily examined through analysis of variance (ANOVA) in experiments with small, balanced datasets, focusing on the identification of simple interaction effects. As statistical analysis advanced, the introduction of mixed models in animal breeding (Henderson, 1984) laid the foundation for more sophisticated methods. In the 1990s, Kirkpatrick et al. (1990) pioneered the application of RRMs to capture the nuances of reaction norms, overcoming the limitations of traditional ANOVA methods. Subsequently, Jensen (2001) further advanced the application of RRMs in dairy cattle breeding, while Schaeffer (2004) refined and expanded these models for genetic evaluations under diverse environmental conditions. The transition from basic analyses to more complex and precise models has significantly enhanced the understanding of G × E interactions, enabling a more detailed analysis of genotypic responses to varying environmental contexts.

The models for assessing G × E include two main components, the genotype (G) and environmental (E) effects, as well as the interactions among them (Falconer, 1996; Lynch & Walsh, 1998). To evaluate a trait and obtain (G) EBV across environments, three main statistical models can be used: (1) analytical factorial mixed models; (2) multi-trait models (MMs); and (3) RNMs (or RRMs). Among these options, 2 and 3 are the most used methods for assessing G × E in beef and dairy cattle populations (Crossa et al., 2022; Hayes et al., 2016; Mota, Fernandes Jr, et al., 2020; Mota, Lopes, et al., 2020; Santana Jr. et al., 2014). Each of these models has unique characteristics, which will be discussed in detail below.

FA mixed models

FA models were initially proposed for analyzing multi-environment trials in plant breeding (Li et al., 2017). Meyer (2009), when examining FA models in a standard linear mixed model framework, showed that the models are applicable in animal breeding. FA models can identify environmental factors that cause G × E by structuring the genetic (co)variance matrix into two main components, i.e., common factor and specific effect. Common factors establish correlations between variables, whereas specific factors aim to identify those factors that explain the maximum variation (Meyer, 2009). Factor analysis is a valuable multivariate tool for assessing interrelated traits and streamlining redundant information inherent in multiple variables (Corrales et al., 2011; Vukasinovic et al., 1997; Xu et al., 2022). This, in turn, enhances the accuracy of variance estimates and reduces computational demands, especially when working with large-scale datasets (Mazza et al., 2015; Olasege et al., 2019).

The mixed animal FA model can be described as (Meyer, 2009; Sae-Lim et al., 2014):

$$\boldsymbol{P_{ijk}} = \boldsymbol{\mu} + \boldsymbol{ef_k} + \boldsymbol{a_{c,i}} + \boldsymbol{a_{s,ik}} + \boldsymbol{e_{ijk}},$$

where, $\boldsymbol{P_{ijk}}$ is the phenotypic record of the ith individual of the jth genotype in kth environment, $\boldsymbol{\mu}$ is the overall trait mean, $\boldsymbol{ef_k}$ is the fixed environmental effect, $\boldsymbol{a_{c,i}}$ and $\boldsymbol{a_{s,ik}}$ are the random additive genetic effects of the i-th individual due to the common factor(s) and specific effects for the k-th environment, respectively, and $(a_c, a_s) \sim \mathrm{MVN}\left(\mathbf{0}, \mathbf{A} \otimes \mathbf{G_{FA}}\right)$. The $\mathbf{G_{AF}} = \boldsymbol{\Gamma}\boldsymbol{\Gamma}' + \Psi$ is the matrix of genetic (co)variance for common and specific additive genetic effects; $\boldsymbol{\Gamma}$ is the matrix of factor loadings; and $\boldsymbol{\Psi}$ is the diagonal matrix of the specific variances ($\boldsymbol{\Psi_k}$), accounting for the additional variance, i.e., the variation that is not explained by the common factor(s) of the $\boldsymbol{k}$-th environment. This additive genetic variance not explained by the common latent factor is captured by the specific effects. The matrix of loading factors, Γ, is obtained from the analysis of the environmental variables, and its interpretation depends on the relationship of these loadings with the environmental gradients studied.

When the common factor delineates different proportions of genetic variance across different environments, it indicates the existence of G × E. The environmental factor responsible for G × E can be identified by correlating the estimated factor loadings with the observed environmental variables. For the FA model to adequately capture G × E interactions, it is essential that the animals are evaluated in multiple environments, allowing genetic and environmental variations to be captured in a multivariate way. Despite the possibility of using the FA model in livestock G × E studies, no studies using this methodology were found in the literature. One of the explanations for this scenario may be due to the greater complexity of animal data, involving a wider range of variables to be evaluated, making FA modeling more challenging to implement and interpret the results. For example, in plants, genetic structure often follows simpler patterns of inheritance, which can facilitate G × E modeling. In contrast, factors such as sex-linked inheritance, epistatic interactions, and more significant genetic variability can make modeling more challenging in animals.

MMs

In MMs in the context of G × E, the same trait recorded under different environmental conditions is considered as a potentially different trait (Falconer & Latyszewski, 1952). The MM is well-suited for situations where the environmental effects are considered to be categorical factors (Calus et al., 2002; Hayes et al., 2016; Kolver et al., 2002; Mulder et al., 2004). Such factors include diets, production systems, milking type, production levels, and geographical region. This model is a reliable tool for analyzing data containing multiple variables and can effectively capture their relationships. Therefore, the MM allows for quantifying the genetic variance of the trait and ranking of genotypes in each pair of environments. In livestock production, the genotype is usually defined as the individual animal, given that the same animals are not recorded across multiple environments. Consequently, the genetic performance of an animal can be defined based on the degree of relatedness among related animals raised in different environments (Hayes et al., 2016; Henderson, 1984).

For two environments (two traits), the MM can be described as (Hayes et al., 2003, 2016; Mulder et al., 2004):

$$\begin{bmatrix} \mathbf{y_1} \\ \mathbf{y_2} \end{bmatrix} = \begin{bmatrix} \mathbf{I_1} & \mathbf{0} \\ \mathbf{0} & \mathbf{I_2} \end{bmatrix} \begin{bmatrix} \boldsymbol{\mu}_1 \\ \boldsymbol{\mu}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{Z_1} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z_2} \end{bmatrix} \begin{bmatrix} \mathbf{g_1} \\ \mathbf{g_2} \end{bmatrix} + \begin{bmatrix} \mathbf{e_1} \\ \mathbf{e_2} \end{bmatrix},$$

where, $\mathbf{y_1}$ and $\mathbf{y_2}$ are the phenotypic records for a certain trait in environments 1 and 2, respectively; $\mathbf{I_1}$ and $\mathbf{I_2}$ are identity matrices, $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are the phenotypic means for the trait in environments 1 and 2; $\mathbf{Z_1}$ and $\mathbf{Z_2}$ are the incidence matrices relating the (G)EBV (additive genetic values) to the response variables; $\mathbf{g_1}$ and $\mathbf{g_2}$ are the additive genetic values for the genotypes in environments 1 and 2, and $\mathbf{e_1}$ and $\mathbf{e_2}$ are the residual vectors for environments 1 and 2. The residuals are assumed $\begin{bmatrix} \mathbf{e_1} \\ \mathbf{e_2} \end{bmatrix} \sim \mathrm{N}(\mathbf{0}, \mathbf{I} \otimes \mathbf{R})$, where, $\mathbf{R} = \begin{bmatrix} \boldsymbol{\sigma}^2_{e_1} & \boldsymbol{\sigma}_{e_{12}} \\ \boldsymbol{\sigma}_{e_{12}} & \boldsymbol{\sigma}^2_{e_2} \end{bmatrix}$ is the matrix of residual variances and covariances for environments 1 and 2 and $\otimes$ is the Kronecker product (Hayes et al., 2016).

The genetic values based on the relationship between the animals can be assumed through the pedigree-based relationship matrix **A** (Henderson, 1984) as follows:

$$\begin{bmatrix} \mathbf{g_1} \\ \mathbf{g_2} \end{bmatrix} \sim \mathrm{N}(\mathbf{0}, \mathbf{A} \otimes \mathbf{T}),$$

where $\mathbf{T} = \begin{bmatrix} \boldsymbol{\sigma}^2_{g_1} & \boldsymbol{\sigma}_{g_{12}} \\ \boldsymbol{\sigma}_{g_{12}} & \boldsymbol{\sigma}^2_{g_2} \end{bmatrix}$ is the genetic variance and covariance matrix for environments 1 and 2.

The estimates of genetic correlations between phenotypic performance in two environments can be calculated as (Falconer & Latyszewski, 1952; Gilmour et al., 2006):

$$\mathbf{r}_{g_{12}} = \frac{\widehat{\boldsymbol{\sigma}}g_{12}}{\widehat{\boldsymbol{\sigma}}g_1 \widehat{\boldsymbol{\sigma}}g_2},$$

where, $\widehat{\boldsymbol{\sigma}}g_{12}$ is the genetic covariance between the same trait measured in environments 1 and 2; $\widehat{\boldsymbol{\sigma}}g_1$ is the square root of genetic variance for trait measured in environment 1; and $\widehat{\boldsymbol{\sigma}}g_2$ is the square root of genetic variance for trait measured in environment 2.

Genomic-based MM can also be obtained by replacing the **A** by the **G** or **H** matrices, which enables the calculation of GEBV for each environment. The **H** matrix was defined by Legarra et al. (2009) and its inverse $\mathbf{H}^{-1}$ can be calculated as (Aguilar et al., 2010):

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

where $\mathbf{A}^{-1}$ is the inverse of the pedigree-based relationship matrix; $\mathbf{A}^{-1}_{22}$ represents the inverse of the pedigree-based relationship matrix for the genotyped animals, and $\mathbf{G}^{-1}$ is the inverse of the genomic relationship matrix obtained according to VanRaden (2008).

An illustration of the use of MM for the estimation of EBV across environments was demonstrated by Williams et al. (2012) for the growth of Angus cattle at high and low altitudes. The authors evaluated the weaning weight of over 77000 cattle raised in Colorado (USA) farms located at different altitudes as two traits: (1) weaning weight at high altitudes; and (2) weaning weight at low altitudes. The genetic correlation for growth at high and low altitudes was 0.74±0.07, suggesting a re-ranking of genotypes raised on farms located at different altitudes. Therefore, the authors recommended that genetic evaluations for growth in Angus cattle raised on farms located at different altitudes consider the influence of G×E within their statistical modeling. For Holstein cows raised in 805 Chilean herds, Chuma-Alvarez et al. (2021) reported genetic correlations of 0.73±0.06 between milk yield measured in the central region (low production technology level) and the southern region (high production technology level). This finding suggests a re-ranking of genotypes of animals raised in different locations in Chile.

RNMs

The RNM is an alternative to MM when the environmental gradients are described on a continuous scale (Hayes et al., 2016). These aspects are often referred to as *infinite dimensional* resources because they allow for an infinite number of values along the environmental gradient trajectories and because these values are considered different (Meyer, 1998). G×E in beef and dairy cattle for several traits has been widely described in the literature (Calus et al., 2006; Corrêa et al., 2010; Pegolo et al., 2011; Santana Jr. et al., 2014; Nguyen et al., 2016; Silva Neto, Mota, et al., 2023).

The expression of genotypes across different environmental conditions is often modeled as a linear function (reaction norm) of an environmental value or gradient (Kirkpatrick et al., 1990). RNM assumes that the phenotypic value is expressed as a polynomial function associated with the environmental gradient. In this framework, the polynomial coefficients indicate the average EBV of the animal (intercept), while the slope coefficient represents the animal's response to environmental changes (de Jong, 1995). The covariance estimates between the random regression coefficients yield estimates of covariance functions (Kirkpatrick et al., 1990). In this context, a covariance function describes the covariance between measurements obtained in given environments as a function of those environmental conditions (Figure 3).

The RNM can be applied in two steps (Calus & Veerkamp, 2003; Mota, Fernandes Jr, et al., 2020). In the first step, BLUE (Best Linear Unbiased Estimates)

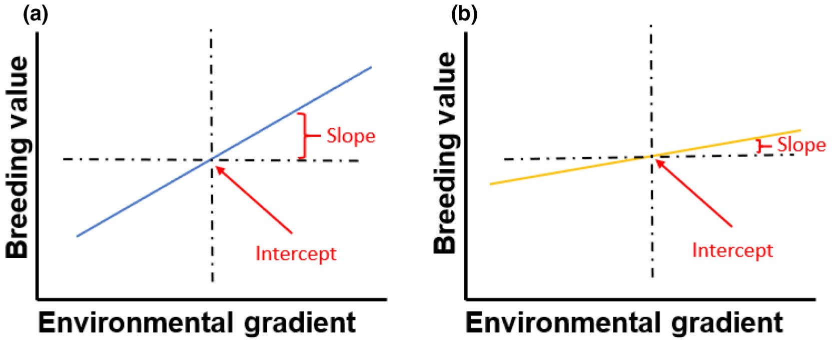

FIGURE 3 Reaction norms for genetic values in relation to environmental conditions. (a) The polynomial intercept and slope coefficients of an animal with lower resilience to variations in environmental conditions (higher slope coefficient). (b) The polynomial intercept and slope coefficients of an animal with higher resilience to variations in environmental conditions (lower slope coefficient).

solutions are obtained from an animal model and subsequently used to define the environmental conditions. In the second step, the general RNM can be used to estimate genetic parameters across environments conditions (EC):

$$y = \mathbf{Xb} + \mathbf{Za} + \mathbf{e},$$

where, ***y*** represents the phenotypic information recorded at different EC; ***b*** is a vector of the fixed effects to adjust the phenotypic information; ***X*** is an incidence matrix linking the fixed effects to the phenotypic information (y); **a** is the vector of random animal additive genetic effects of RN parameters (intercept and slope) corresponding to the EC levels; ***Z*** is the incidence matrix relating the records to additive genetic effects of RN parameters and **e** is the random residual (Mota, Lopes, et al., 2020). In RNM, RN parameters (intercept and slope) on phenotypic information can also be included as fixed effects.

In RNMs, the EC levels can be modeled using different polynomials such as ordinary, Legendre, or spline polynomials. Details about each of these models are presented in Table S1. Ordinary polynomials are simple algebraic expressions of variables, often used as a linear form using directly EC information. Ordinary polynomials are typically used in simple models to establish an understanding of how an environmental variable affects a trait. For example, they can be used to model growth rates or milk yield as a function of temperature humidity index (THI). By contrast, Legendre orthogonal polynomials are a specific type of orthogonal polynomial, useful in RNM due to their mathematical properties. These properties reduce the correlation between polynomial terms, meaning that the different polynomial terms are uncorrelated with each other (Meyer, 1998). This reduces the multicollinearity problems in the model, which leads to more reliable estimates of coefficients and better model interpretation. Legendre orthogonal polynomials are often better at generalizing beyond the range of observed data compared to ordinary polynomials, particularly when the reaction norm must be extrapolated.

Spline polynomials consist of segmented functions that are connected at specific points known as knots, for modeling segmented regressions, where each segment are smoothly linked (Meyer, 2005). Splines provide high flexibility as they enable the model to adjust to local changes in the data (Misztal, 2006). This is particularly valuable when the relationship between the environment and the trait shows multiple inflection points offering local control (Carvalheiro et al., 2019; Carvalho Filho et al., 2022). Splines are especially beneficial in situations where the reaction norm is expected to vary nonlinearly across a range of environmental conditions. RNM can also be used in sire models, which can facilitate the selection of the most adaptable and efficient sires across various environments, particularly in systems where the available data are predominantly paternal.

The genetic correlation between EC levels ($r_{\mathrm{EC_j,EC_k}}$) can be calculated as:

$$r_{\mathrm{EC_{j},EC_{k}}} = \frac{\sigma_{\mathrm{EC_{j},EC_{k}}}}{\sqrt{\sigma^2_{\mathrm{aEC_j}} * \sigma^2_{\mathrm{aEC_k}}}},$$

where, $\sigma_{\mathrm{EC_{j},EC_{k}}}$ is the covariance between the level of EC $_{\mathrm{j}}$ and the level of $\mathrm{EC_k}$; $\sigma^2_{\mathrm{aEC_j}}$ and $\sigma^2_{\mathrm{aEC_k}}$ are the genetic variance for the trait at each level of $\mathrm{EC_j}$ and $\mathrm{EC_k}$. These variances can be obtained through various modeling techniques, which may include the use of transformed covariates, such as orthogonal polynomials, or untransformed covariates, depending on the approach used to capture genetic variation across different environmental levels.

The EBVs associated with each level of EC are obtained using the following equation: $\hat{g}_{\mathrm{jEC_j}} = \hat{\alpha}_i \phi_{\mathrm{j}}$; where $\widehat{\alpha_i}$ is the estimated additive genetic value for intercept and slope estimates of animal *i* and ϕ_{j} is the vector representing the specific characteristics of the $\mathrm{EC_j}$. Genomic information can also be considered into RNM by replacing the **A** matrix with a genomic (**G**) or hybrid genomic relationship matrix such as **H** (Aguilar et al., 2010;

Legarra et al., 2009), resulting in GEBV for each individual and environment.

Cheruiyot et al. (2020) presented an application of RNM to explore G × E, specifically in relation to heat tolerance in milk yield and composition in Australian Holstein cattle. The study incorporated a large dataset, encompassing 6.7 million milk production records from 491 562 cows across three lactations and 6410 sires with offspring across multiple environments. The authors used the THI derived from climate data obtained from 163 meteorological stations as the environmental gradient. As a result, the authors observed that the heritability estimates decreased as THI increased throughout the trajectory for fat and increased for THI > 70 for milk and protein yield. The correlation estimates between the 5th and 95th THI percentiles (extremes) for milk, protein, and fat yield were close to 0.80, with values of 0.88 ± 0.01, 0.79 ± 0.02, and 0.86 ± 0.02, respectively. The percentage of bulls with EBV with a lower slope, with at least 100 daughters with multi-parity records, was 65%, 57%, and 64%, respectively, demonstrating the presence of G × E in that population.

Silva Neto, Mota, et al. (2023) and Mota, Fernandes Jr, et al. (2020) applied RNMs in Nellore cattle to investigate G × E interactions, observing significant genetic reranking across different environmental gradients. Silva Neto, Mota, et al. (2023) identified G × E interactions for dry matter intake and residual feed intake using contemporary group solutions for average daily gain as the environmental gradient. The lowest genetic correlations between extreme environmental levels were 0.22 for residual feed intake and 0.26 for dry matter intake, resulting in selection coincidences of 53.3% and 40.0%, respectively. Mota, Fernandes Jr, et al. (2020) reported G × E interactions for early pregnancy and scrotal circumference, using yearling weight as the environmental gradient, with genetic correlations of 0.30 and −0.12 between more favorable and more unfavorable environments. Both studies confirmed variability in genetic variance and reranking of selection candidates, highlighting the importance of considering G × E in breeding programs.

The clear and comprehensive definition of the environmental gradient plays a crucial role in G × E analysis, significantly influencing the results obtained in scientific studies (Fikse et al., 2003; Freitas et al., 2021). When the definition of the environmental gradient is inadequate or imprecise, distortion can occur in G × E analyses (Fikse et al., 2003). If environmental variations are not correctly identified or quantified, the real effects of genotypes can be misinterpreted, resulting in mistaken conclusions about the adaptability or resilience of different genotypes across environments (Freitas et al., 2021). Therefore, a precise definition of the environmental gradient is essential to obtain accurate estimates of G × E.

G × E INTERACTION STUDIES PUBLISHED FROM 1967 TO 2023

To evaluate trends over time and the degree of G × E interaction for traits measured in cattle breeding programs, we performed a literature search from October to December 2023 in six electronic databases (Scielo, PubMed, Google Scholar, Scopus, Science Direct, and Web of Sciences). A total of 116 beef and dairy cattle articles published from 1967 to 2023 were identified [see Tables S2 and S3]. The success of breeding programs hinges upon identifying the best-performing animals for the target production systems and environmental conditions. In the G × E studies summarized, various definitions of environmental gradients were used, including diets (Hay & Roberts, 2018), temperature and humidity indices (Santana Jr et al., 2018), weight gain (Santana Jr et al., 2015), somatic cell count (Calus et al., 2006), productive indices (Lillehammer et al., 2009), production systems (Raidan et al., 2016), milking type (Hammami et al., 2015), geographical regions (Fennewald et al., 2018), and countries (Hammami et al., 2009). Hence, the G × E levels were presented based on the magnitude of genetic correlations. Among the 116 studies (60 in beef cattle and 56 in dairy cattle, see Tables S2 and S3, respectively), a total of 97 studies (83.62%) reported genetic correlations below 0.80, indicating the presence of G × E. Furthermore, differences in protocols for measuring traits may result in lower genetic correlations.

The variability in the estimates of genetic correlation for the same trait evaluated in different environments could be due to the genetic differences between the herds evaluated; the models used to quantify G × E, and the definitions of the environmental gradients (Araujo Neto et al., 2018; Calus et al., 2004). Approximately 69.33% of the 60 studies on beef cattle (see Table S2) focused on growth traits, 24% on reproductive and fertility traits, 2.67% on carcass and meat quality traits, 2.67% on survival traits, and 1.33% on feed efficiency traits. In contrast, 79.36% of the 56 studies on dairy cattle (see Table S3) focused on milk production and quality traits, 19.05% on fertility and reproduction traits, and 1.59% on survival and productive life traits. A notable divergence was evident in the geographical regions of the G × E studies, in which 25.33% of the G × E studies in beef cattle were published using datasets from countries with a more temperate climate, while 74.67% of the studies were conducted in tropical countries, in which there is more significant variability in nutritional practices, management, and weather and/or geographical conditions. In contrast, for the dairy G × E studies, 66.67% of the studies were performed in countries with more temperate climatic conditions and 33.33% in countries with more tropical climate conditions. RNMs and MMs were used most to evaluate G × E, which was approximately 50% for each model. More beef cattle studies applied RNM

(~60%) than MM (~40%) to assess G × E. Conversely, the reverse trend was observed for dairy cattle, with MM being used more than RNM. Among the traits evaluated in the studies listed in Tables S2 and S3, traits with lower heritability estimates, such as reproduction, displayed a more pronounced effect of the G × E.

Although most of the traits recorded in breeding programs have been used to assess the effect of the G × E (see Tables S2 and S3), one study has evaluated feed efficiency traits in beef cattle and none in dairy cattle populations. This is a notable knowledge gap, considering that 55% to 80% of the total cost of cattle production is related to feeding, especially in more intensive production systems (Anderson et al., 2005; Herd et al., 2003; Ramsey et al., 2005; Rolf et al., 2010). Therefore, there is a need to investigate G × E on feed efficiency traits in cattle populations, especially in herds raised in countries with large variations in soil, climate, or other sources of heterogeneity in production environments. In such conditions, nutrition level and quality may restrict the expression of the full genetic potential of an animal, and this is even more pronounced in extensive production systems, particularly in tropical regions where animal diets may be suboptimal. In these situations, even if management is ideal for the environmental conditions, the lack of adequate nutrients can prevent the expression of superior alleles. Thus, it is crucial to clearly define the production system in question and assess whether the environment and management are optimized for animals to reach their full genetic potential.

According to the Food and Agricultural Organization (FAO, 2009), global meat consumption is expected to increase by 30% until 2050. To meet this demand, beef production needs to increase by approximately 72%. Beef represents a quarter (25%) of the overall global meat production and consumption is projected to rise from 60 million to 130 million tons. At least 70% of the anticipated rise in beef production essential to meet the escalating demand is projected to come from subtropical and tropical regions (FAO, 2009). In this context, G × E emerges as a critical factor, especially in subtropical and tropical regions where climatic and breeding conditions vary considerably and animals are raised in more extensive production systems. As ~80% of the world's livestock population is concentrated in these locations (Cooke et al., 2020), identifying genotypes adapted to these specific climatic contexts is essential to maximize production efficiency. Breeds and lineages genetically adapted to such environments have the potential to offer superior performance in animal production in these regions. Therefore, understanding the complex interaction between the genotype and the environment is fundamental in optimizing livestock production, ensuring an efficient response to growing global food needs, particularly in places where climatic conditions favor food production.

INCLUSION OF GENOMIC INFORMATION IN THE ASSESSMENT OF G × E

The integration of genomic information into genetic evaluations has resulted in major advancements in animal breeding. Genomic evaluations result in more accurate breeding values for younger animals and enable a considerable reduction in generation interval, to name some of the benefits of genomics (Oliveira et al., 2018; Silva Neto, Peripoli, et al., 2023). By including genomic information in G × E studies, researchers have better understood the genetic factors contributing to variation in complex traits across environmental conditions (Carvalheiro et al., 2019; Mota, Lopes, et al., 2020; Oliveira et al., 2018). Quantifying and modeling the G × E in the context of genomic selection is a valuable approach for addressing the impact of G × E on selection decisions and investigating the genetic basis of animal adaptation and environmental sensitivity (Carvalheiro et al., 2019; Mota, Lopes, et al., 2020; Oliveira et al., 2018).

Understanding the genomic background of G × E for traits under selection is highly relevant and contributes to improving the robustness of genetic evaluations. This is because an animal can have a reasonably accurate GEBV in an environment where they have not been measured yet based on information from their relatives (Cao et al., 2020; Hayes et al., 2016). However, one of the main challenges in implementing genomic selection is the development of a reference population consisting of genotyped animals with phenotypic records in a wide range of environmental conditions (Mota, Fernandes Jr, et al., 2020). Hence, genotyping and phenotyping animals widely distributed across environmental conditions can lead to more accurate GEBV predictions.

Incorporating genomic information into models for evaluating G × E can enhance breeding schemes by contributing to a more accurate selection of the most resilient animals based on genotypic performance consistency across environments. In addition to greater selection accuracy, genomic information also enable the identification of genomic regions that influence plasticity or stable phenotypic performance across environments (Mulder, 2016). The evaluation of G × E effects has been deepened by including genomic information combined with pedigree information for several traits evaluated in cattle breeding programs, such as body weight (Oliveira et al., 2018), tick resistance (Mota et al., 2016), traits related to sexual precocity (Mota, Fernandes Jr, et al., 2020), and milk production (Toro-Ospina et al., 2023).

Genome-wide association studies in the identification of G × E

In the context of G × E, the single-step genome-wide association study (GWAS) approach has been used to detect SNP markers and genomic regions associated with resilience and environmental sensitivity in animals (Carvalheiro et al., 2019; Mota et al., 2018; Mota, Lopes, et al., 2020). An important question in the G × E is whether the quantitative trait loci (QTL) that control a trait show consistent effects across different environments, varying only in magnitude and direction as environmental conditions vary, or whether these QTL change in each specific environment (Lillehammer et al., 2008, 2009). Certain QTL might be more favorable for particular environments. As a result, we expect a higher prevalence of these QTL in comparable environments (i.e., genetic correlations >0.80), while in more divergent environments, others have a greater effect on the trait (i.e., genetic correlations <0.80).

Mota, Fernandes Jr, et al. (2020), using genomic RNM to assess G × E in traits related to sexual precocity in Nellore cattle, reported dependent SNPs of some environments, indicating strong SNP-by-environment interaction with changes in the magnitude and direction of the SNP effects on the trait. The authors suggested the use of these genomic regions and SNPs in statistical models so that the process of genetic selection could obtain animals with greater genetic potential for sexual precocity and tolerance to variations in environmental conditions. For example, the weighted single-step genomic BLUP model can highlight regions that explain a large proportion of the genetic variance of the trait (Wang et al., 2012). This approach would allow the weighting of SNPs adjacent to these regions, informing the model about their greater relevance for the trait in a specific environment allowing adjustments in the weightings according to the interactions between SNP and environment. Lillehammer et al. (2008), using random regression models to identify QTL related to production traits in Australian dairy cattle, reported that the greatest variation in SNP effects occurred when environmental conditions became less restrictive. In addition, the authors observed that those genomic regions with the higher effect on the trait were not equally significant across environments.

Mota et al. (2018), evaluating the genomic background of tick resistance in Hereford and Braford cattle using reaction norms, observed that an allele can additively increase the value of the trait as much as decrease it in different environments. This is because gene expression can vary and, therefore, the function of a gene and the percentage of genetic variance explained by the SNP marker near this gene is expected to change (Des Marais et al., 2013; El-Soda et al., 2014; Gibson, 2008; Hayes et al., 2009; Mota, Fernandes Jr, et al., 2020).

Oliveira et al. (2018) and Carvalheiro et al. (2019), using the intercept and slope of the RNM as the target traits for the GWAS analyses, identified SNP markers corresponding to different types of biological functions and regulatory genes associated with environmental plasticity. Biological mechanisms associated with animal environmental sensitivity depend on the extent of the environmental effect on the trait (Lillehammer et al., 2007; Streit et al., 2013). Lillehammer et al. (2009) reported that some QTL were not reported in previous GWAS that did not consider G × E interactions. They suggested that SNP-by-environment interaction effects could explain inconsistencies between QTL mapping studies, particularly when a QTL in one environment is not detected in another or has different effects.

Among the effects of G × E, the variation in SNP marker effects represents one of the main challenges for performing more accurate genomic selection in cattle. This is because the best subset of SNP markers might differ across environments (Des Marais et al., 2013; Mota, Lopes, et al., 2020; Nirea & Meuwissen, 2017; Oliveira et al., 2018). This variation in SNP effects underscores the importance of considering G × E in breeding programs, as the animals' ability to adapt to adverse conditions in production systems can be strongly influenced by these interactions. Therefore, it is crucial that breeding programs include strategies that integrate G × E to ensure that genetic selection is adaptive and effective under different environmental conditions.

A practical approach to addressing G × E in animal breeding programs is through progeny tests, which involve collecting data on animal performance in different locations, management systems, and climatic conditions. From these data, statistical models can be used to estimate the specific genetic effects of each environment, allowing a more precise understanding of how genotypes behave under different circumstances. However, it is crucial to keep it simple to make it easier for breeders to understand and make decisions. A viable strategy for this simplification is the development of selection indices that incorporate G × E (Mulder & Bijma, 2006). These indices would combine EBV from different environments into a single measurement, considering how animals respond in varying conditions (Mulder, 2016; Mulder & Bijma, 2006). This simplified approach can assist breeders in making more informed selection decisions, contributing to improved animal adaptation and performance in diverse environments.

NUTRIGENETICS, NUTRIGENOMICS, AND G × E IN LIVESTOCK PRODUCTION

With advances in nutrition, biochemistry, molecular biology, and genomics are transforming nutritional studies into an integrated science (Osorio et al., 2017; Sato, 2016), where we are now better able to understand how nutrients interact with the animal genome, which is crucial to understanding G × E in animal production systems. Nutrition evaluates the effects of nutrients on animal physiology (Osorio et al., 2017). Nutrigenomics and nutrigenetics are new research approaches that aim to study the interaction between food nutrients and gene expression in individual animals (Neibergs & Johnson, 2012). Nutrigenetics focuses on the study of genetic variations in a genome and the response of those organisms to a given diet (Neibergs & Johnson, 2012). Nutrigenomics, in turn, investigates the relationship between nutrition and the genome at the molecular, cellular, and systemic levels. In other words, it focuses on how the nutrients present in the diet interact with genes and their effects on gene regulation processes, such as transcription factors, RNA, protein expression, and metabolite production (Benítez et al., 2017; Gonçalves et al., 2009; Osorio et al., 2017; Trujillo et al., 2006).

There are various databases useful in these fields, including the dbSNP database (www.ncbi.nlm.nih.gov/projects/SNP), gene ontology (www.geneontology.org), the Kyoto Encyclopedia of Genes and Genomes (www.genome.jp/kegg), carbohydrate-active enzymes (www.cazy.org), peptidase database (http://merops.sanger.ac.uk), gene cards (www.genecards.org), and the bovine gene atlas (http://bovineatlas.msstate.edu), as well as websites hosting the cattle genome sequences (Neibergs & Johnson, 2012). These resources can enable the assessment of the impact of different dietary environments on gene expression levels, offering a better understanding of G × E in livestock.

The possibility of adapting the diet to the individual's genome has encouraged researchers worldwide to develop studies in this research area. According to Trujillo et al. (2006), nutrigenomics presents four basic premises: (1) diet and dietary components can alter the risk of disease development by modulating multiple processes involved with onset, incidence, progression, and severity of disease; (2) food components can act on the genome, either directly or indirectly, to alter the expression of genes and gene products; (3) diet could potentially compensate or accentuate the effects of genetic polymorphisms; and (4) the consequences of diets are dependent on the balance of health and disease states and on an individual's genetic background. These premises illustrate how diet, part of the environment, interacts with the genome to influence the phenotype, exemplifying the importance of G × E in animal performance and environmental adaptation. Thus, knowing that the diet and the nutrients present in the food are an important part of the environment in which the animals are raised and greatly affects variations in performance. Using new tools and results obtained in nutrigenomics would make it possible to understand how the genes of animals respond to different diets and how this interaction can influence their performance, health, and adaptation to the environment in which they are raised. This knowledge is valuable for developing schemes for specific diets or more efficient nutritional strategies and for selecting more genetically suitable animals for given production systems or environments.

DNA methylation is one of the most studied forms of epigenetics, which involves adding methyl groups to certain DNA regions, inhibiting or activating gene expression (Lesta et al., 2023; Xue et al., 2023). These epigenetic changes can be, in some cases, heritable, affecting gene expression in future generations (Fitz-James & Cavalli, 2022; Van Cauwenbergh et al., 2020). Epigenetic changes, resulting from interactions between genes and the environment, are an essential component of G × E, showing how the environment can have lasting effects on gene expression and, consequently, on phenotype. Thus, environmental effects can permanently influence the animal's genotype, changing how genes are expressed and its impact on the target phenotype. This complex interaction between the environment and the genotype is fundamental for the adaptation of animals to different environmental conditions and for developing genetic improvement strategies that consider these epigenetic influences.

Several studies conducted in humans and mice have focused on exploring the molecular basis of multifactorial diseases, such as obesity, cardiovascular diseases, and cancer, interpreting them as a result of interactions between genes and diet (Ferguson et al., 2009; Ordovas & Corella, 2004; Šedova et al., 2004; Trujillo et al., 2006). Notably, they revealed significant interactions resulting from combining specific foods or dietary components. These studies demonstrate clearly the G × E, where different genotypes respond differently to the same nutritional conditions. For example, combined consumption of soy with black or green tea has demonstrated greater efficacy in preventing the growth and metastasis of prostate cancer in men than alone consumption (Gonçalves et al., 2009; Lyn-Cook et al., 1999; Zhou et al., 2003). Furthermore, in humans, an understanding of the implications of early maternal nutrition on epigenetic changes and how they translate into phenotypic changes has already been clarified (Burdge & Lillycrop, 2010).

In domestic animals, although part of the information about the genes that make up the genome and their respective locations on the chromosome, structure, and function have been identified (Barbosa et al., 2023; Marti et al., 2005), there are still scarce studies on how genes act in animal metabolism. Recent studies investigating the molecular interactions of dietary nutrients have revealed that gene expression undergoes modifications due to various nutritional elements. These include carbohydrates, proteins, fatty acids, vitamins, minerals, and phytochemicals such as flavonoids and isothiocyanates (Abete et al., 2012; Benítez et al., 2017; Mutch et al., 2005; Raqib & Cravioto, 2009).

In cattle, variations in dietary mineral requirements between breeds indicate that genetic factors influence the individual requirements of each animal. An example of this is the study carried out by Mullis et al. (2003) with Angus and Simmental heifers housed together during pregnancy and early lactation, in which the authors observed differences in plasma concentrations between breeds, with Angus heifers having higher plasma copper concentrations, suggesting a lower copper requirement compared to Simmental heifers (Mullis et al., 2003). In a study conducted by Joseph et al. (2010), they examined the impact of diverse dietary supplements on the expression of genes associated with lipid metabolism in Angus steers. The study compared several animal groups: those solely consuming grass, pasture-fed steers supplemented with soy hulls and corn oil, pasture-fed steers supplemented with corn grain, and a group on a high-concentrate diet. The findings highlighted that alterations in diet, mainly through high-concentrate supplementation, influenced the transcription of genes linked to fat metabolism. This, in turn, impacted the fatty acid composition in carcass tissues, thereby influencing carcass quality. Notably, supplementing with corn, whether in oil or grain, influenced the expression of genes associated with fatty acid synthesis.

It has long been agreed that nutrition and genetic predisposition significantly influence reproductive performance and fertility in dairy cattle (Butler, 1998; Roche, 2006; Sammad et al., 2022). This association becomes particularly crucial during transitional phases and early lactation when the animals are highly sensitive to nutritional fluctuations (Laible, 2009). Du et al. (2010) state that adequate maternal nutrition during gestation increases the Wingless and Int (Wnt). This pathway, responsible for bolstering myogenesis and curbing adipogenesis in skeletal muscle, regulates body fat levels and reduces susceptibility to obesity. It facilitates heightened myogenesis during early and mid-gestation through an epigenetic mechanism (Yan et al., 2013).

Among livestock species, cattle have one of the most complete and detailed sets of comparative SNP arrays, mainly due to their economic relevance (Seo et al., 2013). Databases and livestock-specific web-based pathway genomics tools (cited earlier), facilitate the functional analysis of diverse 'omics' data types, such as transcriptome, proteome, and metabolome (Seo et al., 2013). For beef and dairy cattle production, the overall efficiency of nutrient use during growth and lactation hinges on a combination of management practices and environmental factors, which influence metabolic responses through an integrated system of genetics, nutrition, immunity, and physiological processes (Berry et al., 2011; Hocquette et al., 2010; Loor, 2010). Hence, information from nutrigenomics studies has the potential to guide the formulation of more specific diets, taking into account the health status of the animals and the nutritional composition of the feed, which may result in improved metabolic responses and, therefore, higher production.

PERSPECTIVES ON RESEARCH AND APPLICATION

G×E interaction is relevant for production and many other complex traits such as heat tolerance, disease resistance, reproductive and feed efficiency, as demonstrated in this review. With the use of omics data, it is possible to advance significantly in researching these traits identifying genes and metabolic pathways associated with animal adaptation. It is expected that the results obtained in the present and those that will be obtained in the future directly benefit the genetic improvement programs in livestock production. Evaluating and elucidating the G×E in feed efficiency traits will provide knowledge of the complex genetic background regarding feed efficiency in cattle, allowing the selection of animals with greater genetic potential for feed efficiency under different production conditions. In addition, the results from GWAS for these traits in contrasting environments (low, medium, and high environmental gradient levels) can be used to identify important genomic regions associated with these traits. This information can then contribute to the development of more comprehensive SNP panels that cover all relevant genomic regions, improving the accuracy of genomic evaluations by focusing on genomic regions with significant associations. Ultimately, advancements in omics technologies will support the creation of more efficient selection strategies and tools, aiming to enhance production sustainability.

Studies on nutrigenetics and nutrigenomics are expanding areas of science that still require many studies to maximize the benefits of understanding gene–nutrient interactions. There are several transcription factors with great potential to be studied to improve animal metabolism for greater performance, health, and the quality of the inputs produced, such as meat and milk. Nutrigenomic analyses can prevent diseases linked to the individual's nutritional condition, formulating diets based on gene mapping. Diseases such as ketosis, a metabolic disease that mainly affects dairy herds with a body condition above that recommended at the time of parturition (Goodacre, 2007; Ingvartsen, 2006), can be partially prevented, reducing its incidence. The general results of the nutrigenomic experiments produced so far seem promising. However, practical applications are not yet available, partly due to the complexity of the systems under study. The discoveries to be made in the coming decades using molecular tools will revolutionize our basic understanding of the physiology of herds and will help in the improvement and development of new methods for the nutritional control of animals.

CONCLUSIONS

Based on the literature results presented in this review, it is clear that G×E is a reality in cattle breeding programs leading to a loss in selection response, especially when genetic evaluations of sires are performed in different environments. In most studies, the genetic correlations were below 0.80, demonstrating the significant effect on the genetic reranking of the selection candidate, which results in changes in the residual and additive genetic variance of the traits. Consequently, there are expected changes in heritability estimates and breeding value across environments, which decreases the expected genetic gain. It is necessary conduct studies to understand the relationship between differences in animal performance and the effects of the G × E, as well as the best way to include them in the statistical models used in genetic evaluations. In the face of climate change, monitoring the G × E is essential, aiming to select resilient animals to ensure the sustainability of production systems.

AUTHOR CONTRIBUTIONS

João B. Silva Neto: carried out the literature review; contributed to the preparation of the manuscript; drafted the manuscript. **Lucio F. M. Mota:** carried out the literature review; contributed to the preparation of the manuscript; drafted the manuscript. **Marisol Londoño-Gil:** contributed to the critical review of the manuscript. **Patricia I. Schmidt:** contributed to the critical review of the manuscript. **Gustavo R. D. Rodrigues:** drafted the manuscript. **Viviane A. Ligori:** drafted the manuscript. **Leonardo M. Arikawa:** drafted the manuscript. **Claudio U. Magnabosco:** contributed to the critical review of the manuscript. **Luiz F. Brito:** drafted the manuscript; contributed to the critical review of the manuscript. **Fernando Baldi:** carried out the literature review; contributed to the critical review of the manuscript. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data were shown in the main manuscript and available to readers.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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