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## Estimation of genetic parameters for feed efficiency traits using random regression models in dairy cattle

K. Houlahan,<sup>1</sup> F. S. Schenkel,<sup>1</sup> F. Miglior,<sup>12</sup> J. Jamrozik,<sup>12</sup> R.B. Stephansen,<sup>3</sup> O. González-Recio,<sup>4</sup> N. Charfeddine,<sup>5</sup> D. Segelke,<sup>6</sup> A. M. Butty,<sup>7</sup> P. Stratz,<sup>7</sup> M. J. VandeHaar,<sup>8</sup> R. J. Tempelman,<sup>8</sup> K. Weigel,<sup>9</sup> H. White,<sup>9</sup> F. Peñaricano,<sup>9</sup> J. E. Koltjes,<sup>10</sup> J. E. P. Santos,<sup>11</sup> R.L. Baldwin VI<sup>12</sup> and C. F. Baes<sup>113\*</sup>

<sup>1</sup>Centre for Genetic Improvement of Livestock, Department of Animal Biosciences, University of Guelph, Guelph, Ontario, Canada, N1G 2W1

<sup>2</sup>Lactanet, Guelph, Ontario, Canada, N1K 1E5

<sup>3</sup>Center for Quantitative Genetics and Genomics, Aarhus University, Blichers Alle 20, 8830 Tjele, Denmark

<sup>4</sup>Departamento de Producción Animal, E.T.S.I. Agrónomos, Universidad Politécnica, Ciudad Universitaria s/n, 28040 Madrid, Spain

<sup>5</sup>CONAFE, Valdemoro, 28340, Madrid, Spain

<sup>6</sup>Vereinigte Informationssysteme Tierhaltung w.V. 27283 Verden / Aller

<sup>7</sup>Qualitas AG, 6300 Zug, Switzerland

<sup>8</sup>Department of Animal Science, Michigan State University, East Lansing, Michigan, United States of America, 48824

<sup>9</sup>Department of Animal and Dairy Sciences, University of Wisconsin-Madison, Madison, WI, United States of America, 53706

<sup>10</sup>Department of Animal Science, Iowa State University, Ames, IA, United States of America, 50011

<sup>11</sup>Department of Animal Sciences, University of Florida, Gainesville, FL, United States of America, 32611

<sup>12</sup>Animal Genomics and Improvement Lab, USDA, Beltsville, MD, 207052350

<sup>13</sup>Institute of Genetics, Vetsuisse Faculty, University of Bern, 3012 Bern, Switzerland

### ABSTRACT

Feed efficiency has become an increasingly important research topic in recent years. As feed costs rise and the environmental impacts of agriculture become more apparent, improving the efficiency with which dairy cows convert feed to milk is increasingly important. However, feed intake is expensive to measure accurately on large populations, making the inclusion of this trait in breeding programs difficult. Understanding how the genetic parameters of feed efficiency and traits related to feed efficiency vary throughout the lactation period is valuable to gain understanding into the genetic nature of feed efficiency. This study used 121,226 dry matter intake (DMI) records, 120,500 energy corrected milk (ECM) records, and 98,975 metabolic body weight (MBW) records, collected on 7,440 first lactation Holstein cows from 6 countries (Canada, Denmark, Germany, Spain, Switzerland, and United States of America), from January 2003 to February 2022. Genetic parameters were estimated using a multiple-trait random regression model with a fourth order Legendre polynomial for all traits. Weekly phenotypes for DMI were re-parameterized using linear regressions of DMI on ECM and MBW, creating a measure of feed efficiency that was genetically corrected for ECM and MBW, referred to as genomic

residual feed intake (gRFI). Heritability (SE) estimates varied from 0.15 (0.03) to 0.29 (0.02) for DMI, 0.24 (0.01) to 0.29 (0.03) for ECM, 0.55 (0.03) to 0.83 (0.05) for MBW, and 0.12 (0.03) to 0.22 (0.06) for gRFI. In general, heritability estimates were lower in the first stage of lactation compared with the later stages of lactation. Additive genetic correlations between weeks of lactation varied, with stronger correlations between weeks of lactation that were close together. The results of this study contribute to a better understanding of the change in genetic parameters across the first lactation, providing insight into potential selection strategies to include feed efficiency in breeding programs.

Key Words: dry matter intake, energy corrected milk, metabolic body weight, feed efficiency

### INTRODUCTION

As the global population expands and consumer awareness of animal production practices grows, the importance of sustainable dairy production is increasingly emphasized. Improving feed efficiency is one way to increase sustainability and reduce the environmental impact of dairy farms. Feed efficiency is defined as the ability of a cow to convert feed to milk; therefore, an efficient cow is one that consumes less feed while maintaining milk production. Feed is a major expense for the dairy industry, and it accounts for over half of the total cost of farm operations (Connor, 2015; Van Biert, 2019). Previous studies have shown that genetic selection for improved feed efficiency directly impacts

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\*Corresponding authors: C.F. Baes, Centre for Genetic Improvement of Livestock, Department of Animal Biosciences, University of Guelph, 50 Stone Road East, Guelph N1G 2W1, Ontario, Canada, [cbaes@uoguelph.ca](mailto:cbaes@uoguelph.ca)

operational farm costs (Beever et al., 2007; Hemme et al., 2014; Tempelman et al., 2015).

In the context of genetic selection for feed efficiency, many accurate records for dry matter intake (DMI) are required (Seymour et al., 2019; Brito et al., 2020). However, acquiring records for DMI is expensive and time-consuming, making it challenging to include this trait in selection programs (Negussie et al., 2019). Moreover, the inclusion of DMI alone is not sufficient for improving feed efficiency, as it does not account for energy sinks. Several measures of feed efficiency have been discussed as potential traits to include in breeding programs, including residual feed intake (Koch et al., 1963). Residual feed intake is usually defined as the residual of a fixed linear regression of DMI on energy sinks, such as energy corrected milk (ECM) and metabolic body weight (MBW) (Kennedy et al., 1993; Veerkamp et al., 1998; Li et al., 2018). An alternative way of calculated feed efficiency was proposed by Lu et al. (2015), Tempelman et al. (2020), Jamrozik et al. (2021), and Martin et al. (2021), where estimated breeding values for DMI were re-parameterized using linear regressions of DMI on ECM and MBW, to create a measure of Feed efficiency that was genetically uncorrelated to ECM and MBW. Improving knowledge about the genetic relationship between feed efficiency indicator traits is critical when defining the optimal traits to be included in the selection program (Liinamo et al., 2012; Berry et al., 2014).

Most studies have used only a few time points to analyze feed efficiency indicator traits (e.g., Connor et al., 2013; Tempelman et al., 2015; Li et al., 2016). However, considering dynamic changes in physiology over entire lactation might have a substantial influence on accurate estimation of genetic parameters for these traits. For instance, the lactation peak normally occurs between 6 to 8 weeks after calving, and during this phase the cows are usually in negative energy balance (Connor et al., 2013). On the other hand, after the lactation peak there is an excess of energy consumed compared with energy output in the milk. Moreover, it has been suggested that feed intake is dynamic throughout the lactation (e.g., Seymour et al., 2020; Martin et al., 2021), further emphasizing the need to analyze feed efficiency and its underlying traits across the entire lactation.

Random regression is a powerful tool to take into account the genetic variation of a trait over time, which allows estimation of variance components and breeding values for all time points evaluated (Schaeffer, 2004; Oliveira et al., 2019). In addition, the random regression model (RRM) can account for changing environmental effects over a complete lactation cycle, which can improve the accuracy of breeding values (Jamrozik and Schaeffer, 1997). In summary, additive genetic

and permanent environmental effects are predicted as deviations from a fixed curve, allowing animals to have differently shaped curves over the lactation for feed intake, body weight, milk yield, etc. (Jamrozik and Schaeffer, 1997). Therefore, the main objective of this study was to estimate variance components and genetic parameters over days in milk (DIM) of first lactation cows for DMI, ECM, MBW, and genomic residual feed intake (gRFI), using RRM

## MATERIALS AND METHODS

### *Ethics and Animal Care*

All data was obtained from pre-existing databases through studies performed in accordance with the legislation and institutional guidelines in each country.

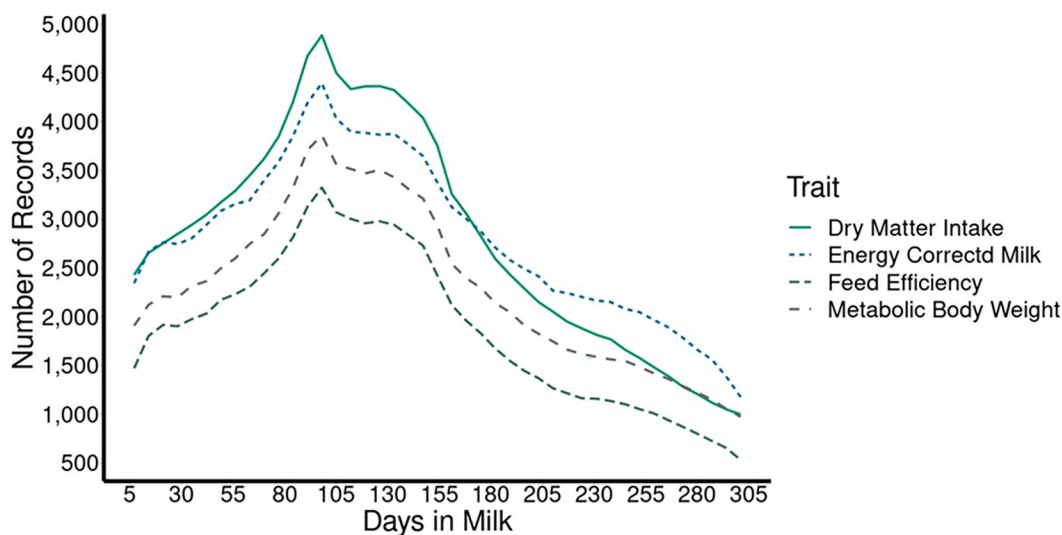
### *Data and Quality Control*

The data set used in this study was provided through the Resilient Dairy Genome Project (<http://www.resilientdairy.ca/>). The data consisted of 121,226 DMI, 120,500 ECM records, and 98,975 MBW records, collected on 7,440 first lactation Holstein cows from 6 countries, namely Canada, Denmark, Germany, Spain, Switzerland and United States of America. Data were collected over a 305-d lactation, with the number of records from each source varying. All records were collected between January 2003 and February 2022 on animals with the first calving before 40 mo of age. Data were collected on a daily, weekly, or monthly basis, depending on the trait and country. For more details on the methodology of data collection please refer to van Staaveren et al. (2022). The pedigree file included information up to 10 generations for phenotyped cows, resulting in a file with 30,776 animals, where there were 5,410 sires and 22,399 dams. Ten generations were used as this captured founder animals and maintained a manageable pedigree size for computation.

Phenotypic data recorded from 5 to 305 DIM were used to create weekly phenotypes. In total 43 weeks of lactation (WOL) were defined based on DIM, as (DIM-4)/7. Weekly phenotypes were then computed as averages of daily measures within a WOL. The MBW was calculated as body weight<sup>0.75</sup> and ECM was calculated following the formula presented by Sjaunja et al. (1990):

$$\text{ECM}_{(\text{kg})} = (0.25 \times \text{milk kg}) + (12.2 \times \text{fat kg}) + (7.7 \times \text{protein kg}).$$

Data editing was performed based on biological limitations. Before the calculation of ECM, records of milk



**Figure 1.** Number of records for dry matter intake, energy corrected milk, metabolic body weight, and feed efficiency across the first lactation.

yield less than 4kg were removed and fat and protein yield were required to be greater than zero. The MBW was required to be at least  $50\text{kg}^{0.75}$  and DMI needed to be between 4kg and 50kg. In addition, animals were required to have at least 3 WOL records for a given trait (DMI, ECM or MBW) and to have at least 2 daily records in a given WOL. It was also required that each year-season ( $YS$ ) model factor had a minimum of 5 animals. On average a single animal had 17.5 weeks' worth of data. Due to a lack of homogeneity between the countries (van Staaveren et al., 2022), the data were standardized to the mean and standard deviation of the Canadian data. Descriptive statistics of the data are presented in Table 1. Figure 1 indicates the number of records per WOL.

### Variance Component Estimation

Additive genetic, permanent environmental (PE), and residual variances were estimated for DMI, ECM, and MBW using a multiple-trait random regression animal model. The variance components were estimated using the Average Information Restricted Maximum Likeli-

hood (AIREML) algorithm implemented in WOMBAT (Meyer, 2007). A fourth order Legendre polynomial was used for all analyses, as it was the best fit of orders one through 4. It is worth noting that Legendre polynomials above the fourth order were not analyzed due to convergence issues. All parameters in the model were tested and found to be significant for the data analyzed. The general model used for all traits is described as follows:

$$y_{ijklm} = \mu + YS_k + AC_l + \sum_{n=0}^3 HY_{mn} \phi_n(t_j) + \sum_{n=0}^3 a_{in} \phi_n(t_j) + \sum_{n=0}^3 pe_{in} \phi_{ln}(t_j) + e_{ijklm},$$

where  $y_{ijklm}$  is the observation of the  $i$ th cow in the  $j$ th WOL;  $\mu$  is the overall mean;  $YS_k$  is the fixed effect of  $k$ th year-season of calving (77 levels for DMI, 72 levels for ECM and MBW);  $AC_l$  is the fixed effect of  $l$ th class of age at calving (5 classes: < 22, 23, 24, 25, and > 26 mo);  $HY_{mn}$  is the  $n$ th coefficient of the fixed regression on WOL of the  $m$ th herd-year of calving to represent the average curves;  $a_{in}$  is the  $n$ th random regression coefficient for the additive genetic effect of the  $i$ th cow;

**Table 1: Descriptive statistics for dry matter intake (DMI), energy corrected milk (ECM), metabolic body weight (MBW) and genomic residual feed intake (gRFI) for first lactation Holsteins, standardized to the mean and standard deviation of Canada**

Trait	Number of records	Number of animals	Mean	SD	Minimum	Maximum	CV(%)
DMI (kg)	121,544	6,889	20.76	4.00	2.11	40.67	19.28
ECM (kg)	121,271	7,489	32.43	5.19	11.10	56.20	15.99
MBW (kg)	99,540	6,416	127.54	9.28	90.88	170.69	7.27
gRFI (kg)	80,633	6,242	20.80	3.39	-0.57	38.62	16.30

$pe_m$  is the  $n$ th random regression coefficient for the PE effect of the  $i$ th cow with record;  $t_{ij}$  is the  $j$ th WOL of the  $i$ th cow standardized from  $-1$  (WOL 1) to  $1$  (WOL 43);  $\varphi_n(t_{ij})$  is the Legendre polynomial coefficient (Kirkpatrick et al., 1990) for the parameter  $n$  evaluated at standardized WOL of the  $i$ th cow at  $t_{ij}$ , and  $e_{ijklm}$  is the residual for each observation. In matrix notation, the previous single trait RRM is described as:

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{pe} + \mathbf{e},$$

where  $\mathbf{y}$  is the vector of phenotypic records;  $\mathbf{X}$ ,  $\mathbf{Z}$ , and  $\mathbf{W}$  are the incidence matrices for the vectors of fixed ( $\mathbf{b}$ ), additive genetic ( $\mathbf{a}$ ), and PE ( $\mathbf{pe}$ ) effects; and  $\mathbf{e}$  is the vector of random residuals. The model assumptions are:

$$E[\mathbf{y}] = \mathbf{X}\mathbf{b}$$

$$\text{Var} \begin{bmatrix} \mathbf{a} \\ \mathbf{pe} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{G}_0 \otimes \mathbf{A} & 0 & 0 \\ 0 & \mathbf{P}_0 \otimes \mathbf{I} & 0 \\ 0 & 0 & \sigma_e^2 \mathbf{I} \end{bmatrix},$$

Where  $\mathbf{G}_0$  and  $\mathbf{P}_0$  are the additive genetic and PE variance-covariance matrices for the random regression coefficients, respectively;  $\sigma_e^2$  is the residual variance for WOL (assumed homogenous across WOL);  $\mathbf{A}$  is the numerator relationship matrix;  $\mathbf{I}$  is the identity matrix. The  $\mathbf{G}_0$  and  $\mathbf{P}_0$  covariance matrices were used to calculate the additive genetic and PE (co)variances for all WOL (G and P, respectively) as (Kirkpatrick et al., 1990):

$$\mathbf{G} = \phi^t \mathbf{G}_0 \phi \text{ and } \mathbf{P} = \phi^t \mathbf{P}_0 \phi,$$

Where  $\phi$  is a matrix of orthogonal coefficients associated with the Legendre polynomial function; and  $\mathbf{G}$  and  $\mathbf{P}$  are the additive genetic and PE covariance matrices. Heritability estimated for the different WOL were calculated using the diagonal elements of  $\mathbf{G}$  and  $\mathbf{P}$  associated with the corresponding WOL analyzed and the homogeneous  $\sigma_e^2$  of each trait.

The residual covariance structure for the multiple trait analysis was as follows, assuming correlated residuals between traits:

$$\text{ECOV} = \begin{bmatrix} \sigma_{eECM}^2 & \sigma_{eECM,MBW}^2 & \sigma_{eECM,DMI}^2 \\ \sigma_{eECM,MBW}^2 & \sigma_{eMBW}^2 & \sigma_{eMBW,DMI}^2 \\ \sigma_{eECM,DMI}^2 & \sigma_{eMBW,DMI}^2 & \sigma_{eDMI}^2 \end{bmatrix} \ddot{\mathbf{A}}\mathbf{I}.$$

Approximate standard errors for the additive genetic, PE, and phenotypic correlations between WOL were estimated using the methodology described in Robertson (1959):

$$SE_{j,j'} = \left[ 1 - \left( \frac{r_{o_{jj'}} \times r_{o_{jj'}}}{\sqrt{2}} \right) \right] \times \left( \sqrt{\frac{se_{q_j} \times se_{q_{j'}}}{q_j \times q_{j'}}} \right).$$

where  $r_{o_{j,j'}}$  is the additive genetic, permanent environmental, or phenotypic correlation between WOL  $j$  and  $j'$  for trait  $o$ ;  $se_{y_j}$  and  $se_{y_{j'}}$  are the standard errors for the heritabilities for WOL  $j$  and  $j'$  (in the case of additive genetic correlation), PE ratio  $\left( \frac{\sigma_{pe}^2}{\sigma_{total}^2} \right)$  (pe correlation), or the phenotypic variance (phenotypic correlation) for WOL  $j$  and  $j'$ ; and  $q_j$  and  $q_{j'}$  are the heritabilities (used for the additive genetic correlation), PE ratio (pe correlation), or phenotypic variance (phenotypic correlation) for WOL  $j$  and  $j'$ .

### Calculation of Feed Efficiency

Using the genetic (co)variance components from the multiple-trait random regression model, partial regression coefficients for ECM and MBW were calculated for each WOL as described by Jamrozik et al. (2017) and Jamrozik et al. (2021). In brief, the partial regression coefficients were calculated based on elements of the genetic covariance for each  $j^{\text{th}}$  WOL.

$$\mathbf{GCOV}_j = \begin{bmatrix} \sigma_{aECM}^2 & \sigma_{aECM,MBW} & \sigma_{aECM,DMI} \\ \sigma_{aECM,MBW} & \sigma_{aMBW}^2 & \sigma_{aMBW,DMI} \\ \sigma_{aECM,DMI} & \sigma_{aMBW,DMI} & \sigma_{aDMI}^2 \end{bmatrix}$$

The elements of the genetic covariance matrix ( $\mathbf{GCOV}_j$ ), for each WOL are used as shown in the equations below, where,  $PC_{ECM}$  and  $PC_{MBW}$  are the partial regression coefficients of ECM and MBW respectively, for the  $j^{\text{th}}$  WOL.

$$PC_{ECM} = \frac{(\mathbf{GCOV}_{12} \times \mathbf{GCOV}_{23}) - (\mathbf{GCOV}_{13} \times \mathbf{GCOV}_{22})}{(\mathbf{GCOV}_{12} \times \mathbf{GCOV}_{12}) - (\mathbf{GCOV}_{11} \times \mathbf{GCOV}_{22})}$$

$$PC_{MBW} = \frac{(\mathbf{GCOV}_{12} \times \mathbf{GCOV}_{13}) - (\mathbf{GCOV}_{11} \times \mathbf{GCOV}_{23})}{(\mathbf{GCOV}_{12} \times \mathbf{GCOV}_{12}) - (\mathbf{GCOV}_{11} \times \mathbf{GCOV}_{22})}$$

The partial regression coefficients were used in a linear transformation on the phenotype of DMI. Adjusted



DMI, which will be referred to hereafter as gRFI, can be interpreted as DMI adjusted for energy sinks based on their genetic relationship. The linear transformation was as follows:

$$gRFI_{ij} = DMI_{ij} - PC_{ECMj} \times ECM_{ij} - PC_{MBWj} \times MBW_{ij},$$

where,  $DMI_{ij}$ ,  $ECM_{ij}$  and  $MBW_{ij}$  are the phenotypes of the  $i$ th cow in the  $j^{th}$  WOL,  $PC_{ECMj}$ , and  $PC_{MBWj}$  are the partial regression coefficients for ECM and MBW, respectively, in the  $j^{th}$  WOL. Accordingly,  $ECM_{ij}$  and  $MBW_{ij}$  were pre-adjusted with their respective fixed effects before multiplying with the partial regression coefficients and subtracting from  $DMI_{ij}$  to create the  $gRFI_{ij}$ . This method was performed following the proposition of Kennedy et al. (1993).

Variance components of gRFI were obtained using the previously described random regression methodology, where bivariate analyses between gRFI and the other traits were performed. Final variance components for gRFI were obtained as averages of the estimates obtained from the bivariate analyses.

## RESULTS AND DISCUSSION

### Heritability Estimates

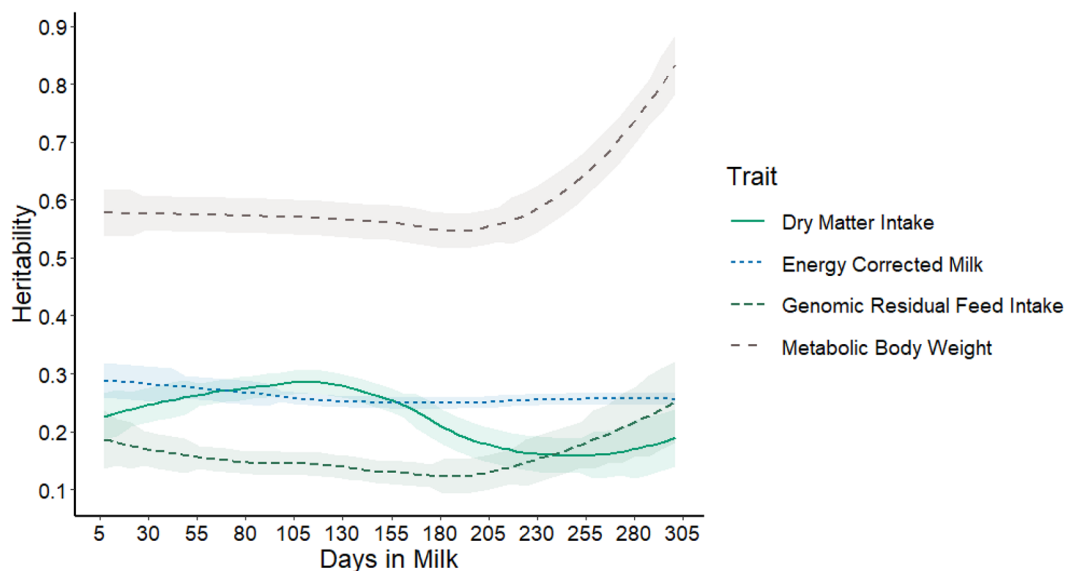
Heritability estimates for DMI, ECM, MBW, and gRFI are shown in Figure 2. All variance component estimates (additive genetic variance, PE variance, residual error variance, phenotypic variance), heritability and their corresponding standard errors are presented in Supplementary Material Tables S1 to S4. In general, moderate heritability estimates were observed for DMI, ranging from 0.15 (0.03) at WOL 33 to 36 (231 to 252 DIM), to 0.29 (0.02) at WOL 16 to 20 (112 to 140 DIM). Heritability estimates for ECM remained fairly stable across the lactation, ranging from 0.24 (0.01) to 0.29 (0.03). The highest heritability estimates were observed for MBW, with estimates ranging from 0.55 (0.03) in 28 to 32 WOL (196 to 224 DIM) to 0.83 (0.05) in the final WOL. Heritability estimates for gRFI were moderate, ranging from 0.12 (0.03) in WOL 26 to 31 (182 to 217 DIM) to 0.22 (0.06) in WOL 41 and 42 (287 to 305 DIM). A substantial increase in estimates was observed for MBW at the end of lactation, which could be related to the smaller number of records available in later stages of lactation and the known behavior of Legendre polynomials under this situation (Misztal, 2006; Oliveira et al., 2019). It is also worth noting that the PE was also dynamic over the course of the lactation, indicating that the changes in the PE effect also need to be considered.

Early lactation (WOL 1 to 8; ~5 to 56 DIM) heritability estimated for DMI (0.24 (0.03) to 0.25 (0.04)) were similar to heritabilities reported by Byskov et al., (2017), Li et al., (2018), and Krattenmacher et al., (2019). The heritabilities estimated in the mid and late lactation (0.15 (0.03) to 0.29 (0.02)) were also similar to previous studies (Spurlock et al., 2012; Li et al., 2016; Manzanilla-Pech et al., 2016; Byskov et al., 2017). Heritabilities reported by Li et al., (2018) were slightly higher (0.30 to 0.55) than the heritabilities estimated in this study, but the pattern of heritabilities over the lactation was similar.

Heritability estimates for ECM in this study (0.24 to 0.29 (0.04)) were within the range of those previously estimated (Spurlock et al., 2012; Li et al., 2018). Byskov et al., (2017) compared genetic parameters estimated for a research herd and a commercial farm, and they found slightly higher heritabilities for mid and late lactation for the commercial herd (0.53 (0.08) to 0.70 (0.08)), and similar heritabilities for the research herd (0.23 (0.06) to 0.35 (0.08)) compared with this study (0.28 (0.03) to 0.44 (0.06)). The pattern of the heritability curve estimated for ECM in our study (slightly parabolic) has also been reported in previous studies (Li et al., 2018; Krattenmacher et al., 2019), in which a quadratic polynomial was used.

The heritability estimates observed in previous studies for MBW were reported between 0.17 (0.05) and 0.53 (0.07) (Manzanilla-Pech et al., 2016; Hurley et al., 2017), which were similar to the lactation heritability estimates found in this study (0.60 (0.03)). Most notably, Manzanilla-Pech et al., (2016) found heritability estimates of 0.53 (0.07) and 0.43 (0.06) for Holstein animals from the Netherlands and the United States, respectively. The heritability estimates found in Manzanilla-Pech et al., (2016) had the same pattern as those in our study, which ranged from 0.53 (0.05) in early lactation to 0.79 (0.12) in later lactation. In addition to MBW, Manzanilla-Pech et al. (2016), Li et al. (2018) and Spurlock et al. (2012) also investigated the heritability of body weight, which ranged from 0.49 (0.08) to 0.74 (0.12). Heritabilities estimated for body weight by Manzanilla-Pech et al. (2016) were similar to those estimated for MBW in our study. Similarities between heritability estimates for body weight and MBW are expected, as MBW is a function of body weight ( $MBW = \text{body weight}^{0.75}$ ).

The heritability estimates observed in this study for gRFI ranged from 0.12 (0.02) to 0.23 (0.07). This is in line with previous studies (Tempelman et al., 2015; Li et al., 2017), which estimated heritabilities for gRFI ranging from 0.10 to 0.25. In this context, it is important to highlight that previous studies used slightly different energy sinks compared with this



**Figure 2.** Heritabilities estimated for dry matter intake, energy corrected milk, metabolic body weight, and feed efficiency over the first lactation. Shadowing indicates the standard error of the estimates.

study, which included change in body weight, body weight, fat-protein corrected milk, and milk energy. Li et al. (2018) found a tertiary shape in the heritability curve for gRFI throughout a 305-d lactation using a fifth-order Legendre polynomial, whereas Tempelman et al. (2015) showed varying shapes in the heritability curve, depending on the data considered using a third-order Legendre polynomial. The heritability curve in this study was similar to the curve based on data from the Netherlands presented in Tempelman et al. (2015).

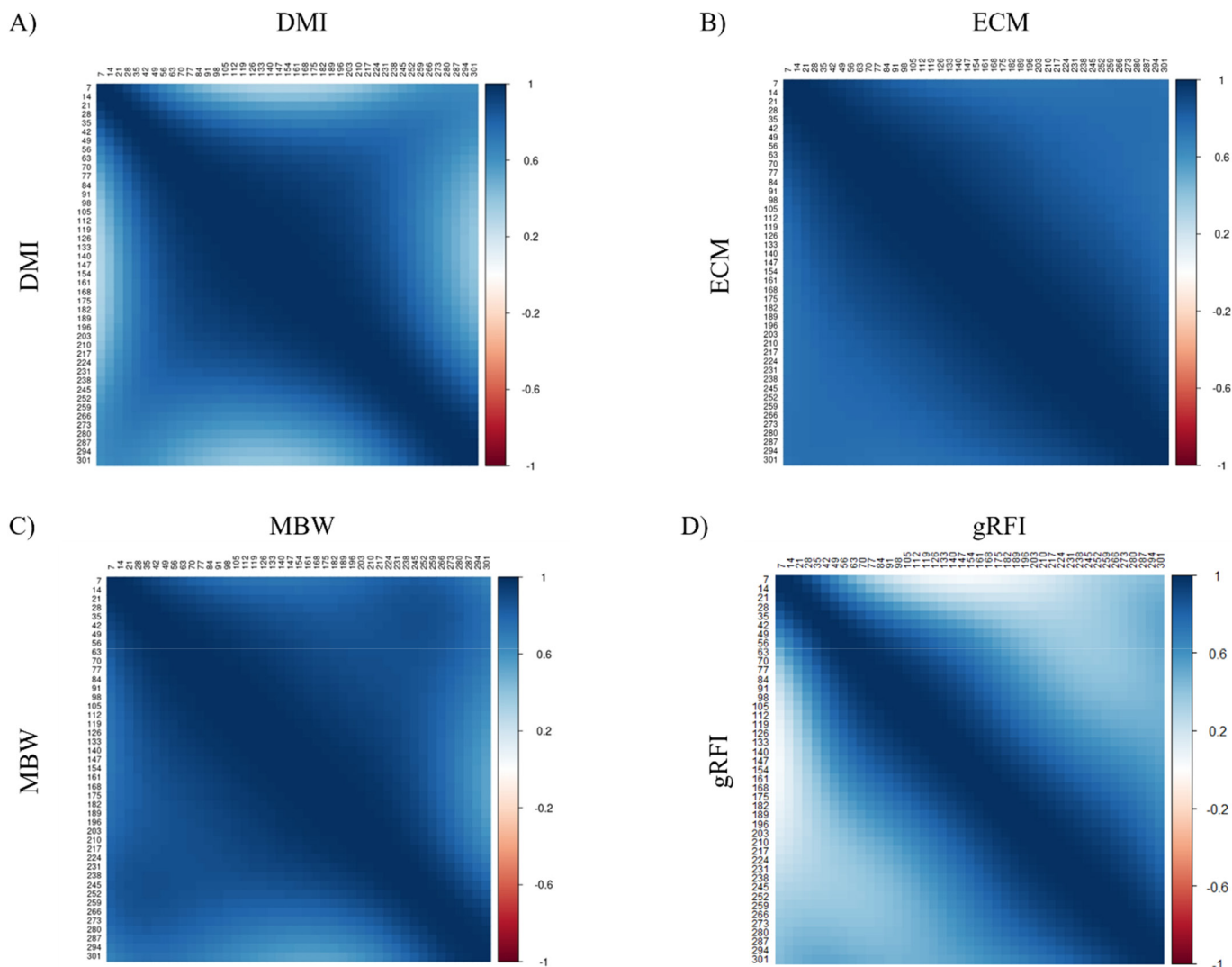
### Correlations

All traits within this study are controlled by biological processes, with some evidence that these traits have different regulatory control affecting them through lactation, leading to a change in the observed phenotype across lactation stages (Strucken et al., 2015; Krattenmacher et al., 2019). Most notably, it has been suggested that feed intake is a genetically different trait at various stages of lactation (Liinamo et al., 2012; Li et al., 2018). To identify these biological patterns across the lactation, we investigated the changes in genetic and phenotypic correlations over time within a trait. Due to the large standard errors of the estimated correlations between-traits, only their trends and potential biological reasons will be discussed.

### Within Trait Correlations

**Additive Genetic Correlations.** The current study found variation within DMI when comparing

early (WOL 1 to 8; ~5 to 56 DIM), mid (WOL 9 to 23; ~70 to 154 DIM), and late lactation (WOL 24 to 43; ~168 to 305 DIM) (Figure 3A). Additive genetic correlations for DMI were, as expected, stronger for WOL close to each other. For instance, correlations ranged between 0.31 (0.17) for weeks far apart (e.g., WOL 1 (5 DIM) and WOL 43 (305 DIM)) to 0.99 (<0.01) for weeks close together (e.g., WOL 6 and WOL 7; 42 to 49 DIM). When comparing the genetic correlations between early lactation and mid and late lactation, correlations decreased as cows moved through the lactation. This decrease of genetic correlations from early to late lactation, especially moderately low genetic correlations between early and late lactation for DMI, has been reported in previous studies (Karacaören et al., 2006; Manzanilla-Pech et al., 2014a; Li et al., 2018). Similar to the results presented by Krattenmacher et al. (2019), genetic correlations between early and mid-lactation were moderate, with an average correlation of 0.66 (0.06). The results of this study supported the concept that DMI is a genetically different trait at various stages of lactation (Berry et al., 2007; Liinamo et al., 2012; Li et al., 2018). Multiple measures of DMI should be taken throughout the lactation, either directly or using proxies, to allow including this trait in the breeding goal and to ensure accurate predictions (Liinamo et al., 2012; Krattenmacher et al., 2019). Results of this study are in line with previous studies; however, it is important to use caution when interpreting the results at the extremes of the lactation period (very early and very late lactation), due to the limited amount of data at these time points. Further to this point, relationship



**Figure 3.** Heat map of within-trait genetic correlations over the first lactation for: A) dry matter intake (DMI; standard errors between  $< 0.01$  and  $0.17$ ); B) energy corrected milk (ECM; standard errors between  $< 0.01$  and  $0.10$ ); C) metabolic body weight (MBW; standard errors between  $< 0.01$  and  $0.04$ ); and D) feed efficiency (gRFI; standard errors between  $< 0.01$  and  $0.22$ ) across the lactation. Axes labels run from 7 to 301 DIM (each pixel represents one week of lactation).

between the extremes of the lactation had standard errors upwards of  $0.17$ . Nevertheless, it is still relevant to observe the relationship of gRFI and its underlying traits throughout lactation when implementing gRFI into breeding programs, as also reported by Khanal et al. (2022).

Like DMI, variation in correlation between stages of lactation were observed for gRFI (Figure 3D), ranging from  $0.04$  ( $0.16$ ) to  $0.99$  ( $0.01$ ). The lowest correlations were observed between early and mid-lactation. Linamo et al. (2015) reported similar results, where the lowest correlations were observed within mid-lactation, however strong correlations were observed in the later stages of lactation. Li et al. (2017) reported a more uni-

form pattern of correlations throughout the lactation, although weaker correlations were observed between early and mid to late lactation, which is in line with the results of the current study. The results of this study are further supported by Nehme Marinho et al. (2021).

The genetic correlation estimates over lactation for ECM did not have the same variation as those observed for DMI or gRFI, being relatively stable across the lactation (Figure 3B). Correlations ranged from  $0.72$  ( $0.06$ ) between mid and late lactation to  $0.99$  ( $<0.01$ ) between close WOL. Li et al. (2018) reported moderate correlation ( $0.50$ ) between early and late lactation, and Krattenmacher et al. (2019) reported  $0.59$  as the lowest correlation between all weeks in early to mid-lactation.

Manzanilla-Pech et al. (2014) reported correlations  $> 0.80$  between most of the weeks of lactation, with some negative correlations reported in early (before 50 d in milk) and very late (after 300 d in milk) lactation. The negative correlations reported in Manzanilla-Pech et al. (2014) at the extreme ends of the lactation were not found in the current study. While there is more uniformity in correlations across the lactation compared with DMI, ECM still showed variation within the lactation. It is important to consider how ECM changes with various stages of lactation, as timing of trait assessment within the lactation could have important implications in selection to improve milk production and gRFI.

Like ECM, MBW had more consistent correlations throughout the lactation compared with DMI (Figure 3C). Genetic correlations between stages of lactation were between 0.53 (0.04) and 0.99 ( $<0.01$ ). The minimum correlation observed (0.53 (0.04)) was estimated between WOL 23 and the last WOL. Previous studies considered body weight instead of MBW, with similar estimates reported. For instance, Li et al. (2018) reported the correlation for body weight between WOL as the most consistent when compared with DMI and ECM. They reported the genetic correlation equal to or greater than 0.74 (0.08) for time points throughout the lactation. More in line with the results presented in our study, Liinamo et al. (2012) and Manzanilla Pech et al. (2014) also found body weight to be a more uniform trait across lactation, where the minimum genetic correlations observed were 0.60 and 0.69, respectively. Since MBW has moderate to strong genetic correlations across the lactation, the need for measurements at multiple time points is not as critical as for DMI. However, it is important to consider that a change in body weight across the lactation can have implications regarding gRFI, animal health, and performance.

**Phenotypic Correlations.** Phenotypic correlations estimated between WOL varied across lactation for all traits (Figure 4). Phenotypic correlations ranged from 0.21 (0.02) to 0.84 (0.01) for DMI, 0.25 (0.02) to 0.81 (0.01) for ECM, 0.53 (0.02) to 0.96 (0.01) for MBW, and  $-0.05$  (0.03) to 0.75 (0.01) for gRFI. Following the trends observed for the additive genetic correlations, and as expected, phenotypic correlations were strongest between WOL closest together and weakest between WOL far apart. Phenotypically, DMI appears to be related through low to moderate correlations throughout the lactation, which supports that DMI should be considered as different traits at various lactation stages. This phenomenon was also reported by Seymour et al. (2020), as they observed that feed intake is dynamic and changes daily. This dynamic behavior of DMI can also be extrapolated to gRFI, as the phenotypic behavior of DMI influences phenotypic behavior of gRFI. As

expected, the phenotypic correlations between WOL for ECM and MBW had weaker correlations in the early part of lactation with the end of lactation.

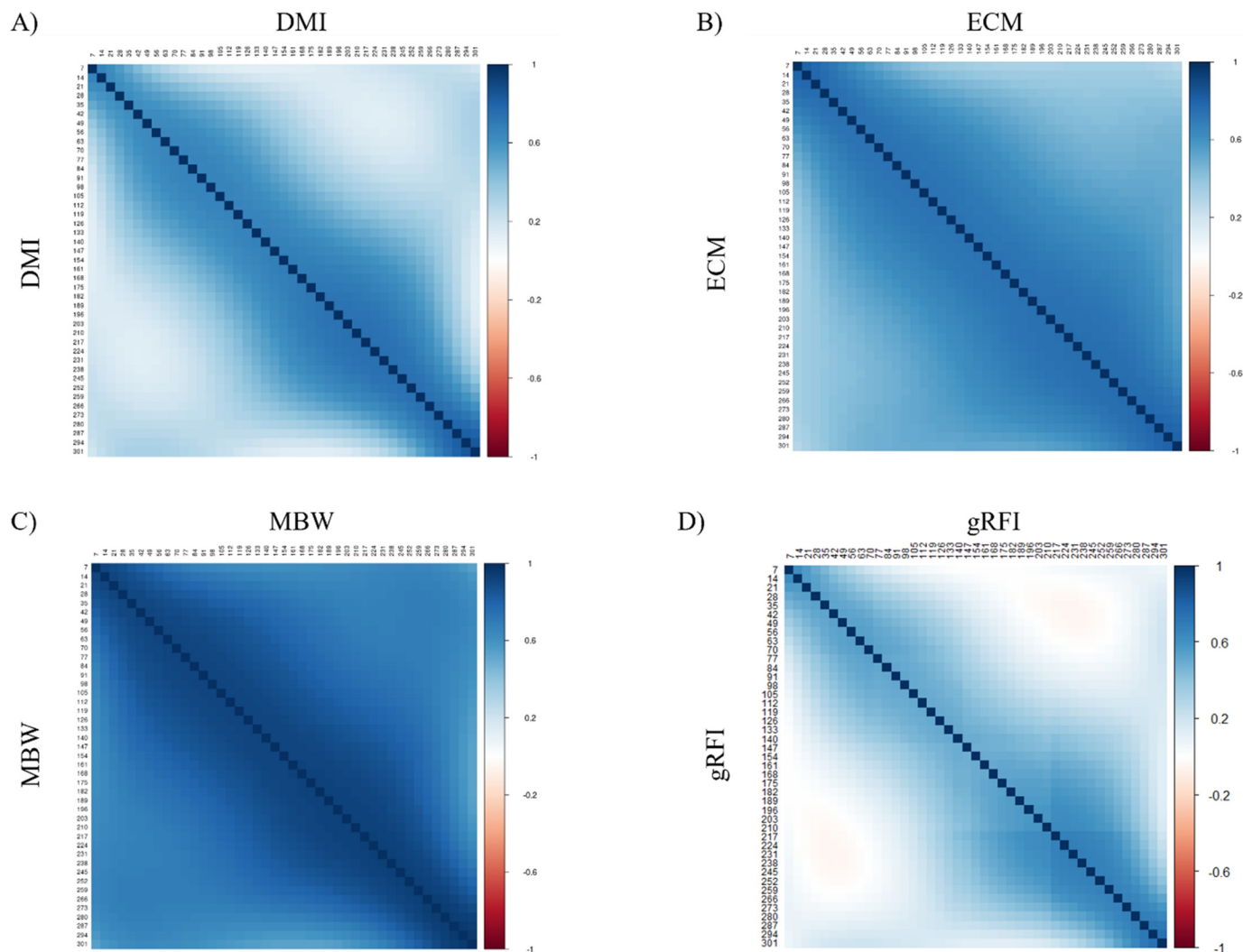
### Between-Trait Correlations

**Additive Genetic Correlations.** Additive genetic correlations estimated between traits varied in different stages of lactation (Figure 5). The trend of weak correlations between feed intake (DMI) and production (ECM) in early lactation (Figure 5A), increasing to moderate or high correlations by mid to later lactation, has been shown in other studies (Liinamo et al., 2012; Manzanilla-Pech et al., 2014a; Li et al., 2018; Krattenmacher et al., 2019). These same trends were observed between ECM and gRFI (Figure 5E) in this study. It is important to note that the genetic correlations between ECM and gRFI within a given week were zero, which was expected based on the definition of gRFI. These weak correlations within the early part of lactation can be due to feed intake not meeting the demand for milk production. The transition to stronger positive correlations as the lactation progresses coincided with the points of lactation where the intake meets production demand (Liinamo et al., 2012). Additionally, the correlations observed in early lactation suggest that selecting to increase ECM would have a small change on DMI and gRFI. However, an increase in production without an increase in DMI, especially in early lactation, has the potential to extend negative energy balance (Buttchereit et al., 2011; Li et al., 2018). An extension of negative energy balance has many unfavorable effects, most notably related to health and fertility (Veerkamp et al., 2000; Banos and Coffey, 2010). Therefore, selecting to improve feed efficiency while increasing milk production should be avoided in early lactation.

The genetic correlation between MBW and ECM (Figure 5D) further highlights the change in the allocation of energy throughout lactation. In this study, the genetic correlations between MBW and ECM ranged from  $-0.19$  (0.11) to 0.21 (0.13), with low positive correlations in early lactation moving to low negative correlations in late lactation. Li et al. (2018) also reported low positive correlations in early lactation, suggesting that larger cows have a greater capacity for milk production in early lactation. The rapid change in correlations to weak negative correlations observed in this study might suggest that the animals' metabolism changes to put on weight during the later stages of lactation, as milk production declines and pregnancy.

The genetic relationship between DMI and MBW (Figure 5B) varies throughout lactation. The correlations ranged from  $-0.01$  (0.13) in late lactation to 0.69



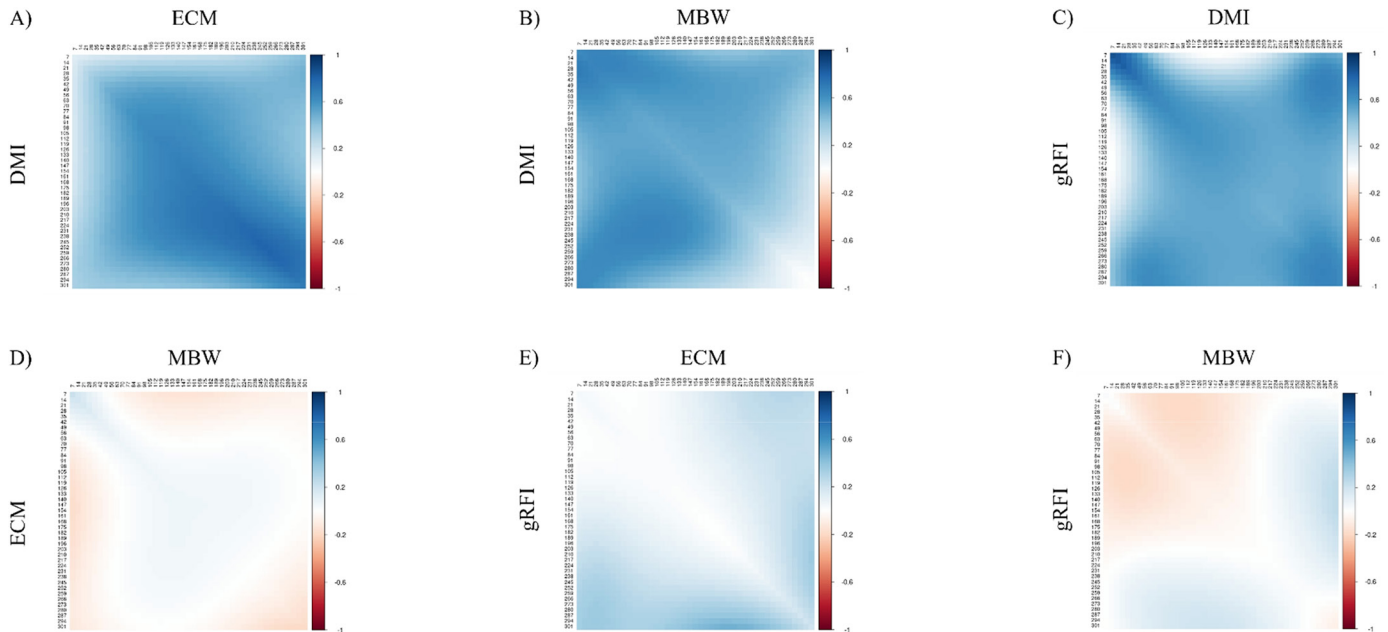


**Figure 4.** Heat map of the within-trait phenotypic correlations over the first lactation for: A) dry matter intake (DMI; standard errors between 0.01 and 0.05); B) energy corrected milk (ECM; standard errors between 0.01 and 0.03); C) metabolic body weight (MBW; standard errors between 0.01 and 0.06); and D) feed efficiency (gRFI; standard errors between 0.01 and 0.10) across the lactation. Axes labels run from 7 to 301 DIM (each pixel represents one week of lactation).

(0.13) in early to mid-lactation. A similar pattern was observed with correlations between gRFI and MBW, which ranged from  $-0.20$  (0.11) in early to mid-lactation, to  $0.26$  (0.13) late-lactation. Again, it is important to note that the genetic correlations between gRFI and MBW within each WOL were zero, which was as expected due to the definition of gRFI. Hüttmann et al. (2009) found weak correlations after calving with a slight increase throughout lactation, while Manzanilla-Pech et al. (2014) and Li et al. (2018) reported the highest correlation in early lactation (wk 4 and 7, respectively), and correlations weakening throughout the lactation. These changes in correlations suggest that increasing intake in the early stages of lactation will improve MBW in the early part of lactation, however,

it may have negative implications in the later stages of lactation.

The genetic correlations estimated between traits over time indicate that potentially different metabolic mechanisms are active between stages of lactation (Linamo et al., 2012; Manzanilla-Pech et al., 2014a; Li et al., 2018). Due to the changes in these correlations throughout lactation, it is important to consider different stages of lactation separately, and to consider all traits simultaneously in a selection program. Understanding the relationship between DMI, MBW, ECM, and gRFI and traits such as energy balance and body condition score is important for an integrated and successful approach to breeding for gRFI.



**Figure 5.** Heat map of the genetic correlations between traits over the first lactation (days in milk from 1 to 305 running left to right and top to bottom). Pair of traits analyzed are: A) dry matter intake and energy corrected milk (DMI and ECM; standard errors between 0.04 and 0.17); B) dry matter intake and metabolic body weight (DMI and MBW; standard errors between 0.05 and 0.14); C) dry matter intake and feed efficiency (DMI and gRFI; standard errors between 0.05 and 0.17); D) energy corrected milk and metabolic body weight (ECM and MBW; standard errors between 0.05 and 0.17); E) energy corrected milk and feed efficiency (ECM and gRFI; standard errors between 0.02 and 0.20); and F) metabolic body weight feed efficiency (MBW and gRFI; standard errors between 0.07 and 0.19). Axes labels run from 7 to 301 DIM (each pixel represents one week of lactation).

### Phenotypic Correlations

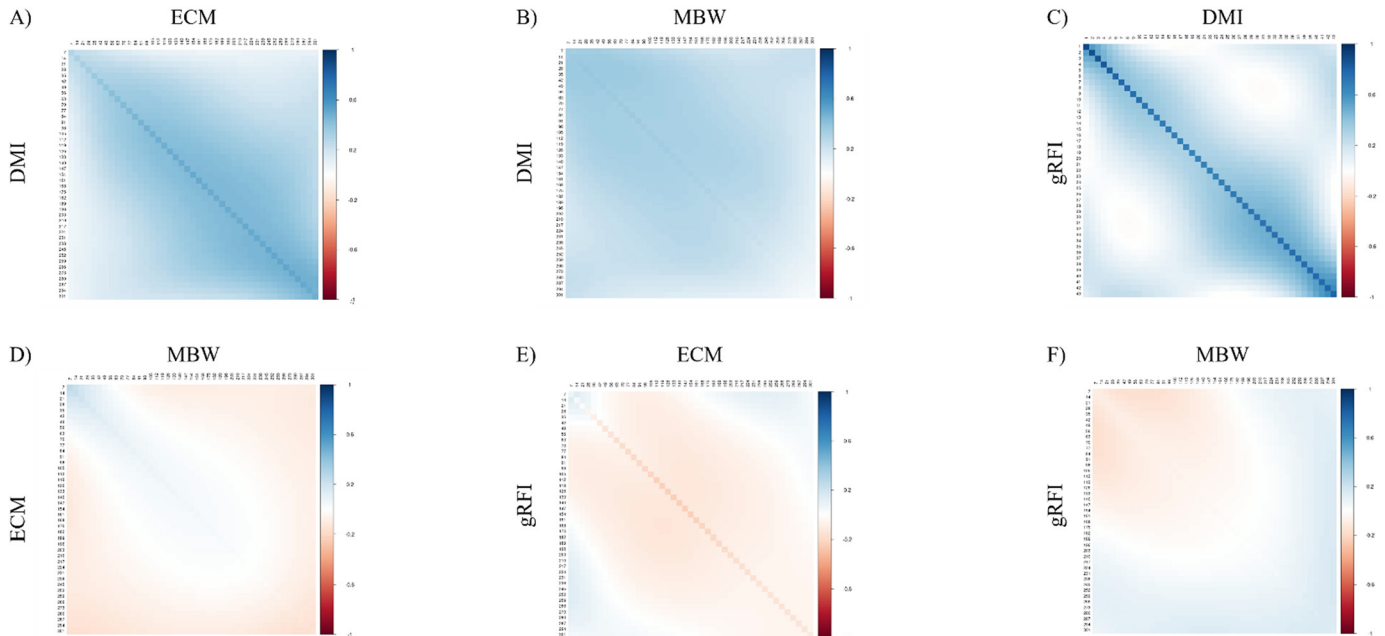
Between-trait phenotypic correlations were low over lactation for all traits. Correlations estimated between DMI and ECM (Figure 6A) ranged from 0.06 (0.10) in early lactation to 0.52 (0.06) in late lactation. The low phenotypic correlations observed in early lactation may suggest that intake does not meet demands for milk production in early lactation. Phenotypic correlation estimates between MBW and ECM (Figure 6D) ranged from  $-0.16$  (0.18) to  $0.25$  (0.13); indicating that these traits are generally unrelated phenotypically. Phenotypic correlations between DMI and MBW (Figure 6B) ranged from  $0.04$  (0.13) to  $0.38$  (0.05). Phenotypic correlations between gRFI and MBW, and between gRFI and ECM were relatively low for all WOL, ranging from  $-0.17$  (0.10) to  $0.16$  (0.14) for gRFI and MBW and  $-0.24$  (0.08) to  $0.14$  (0.11) for gRFI and ECM. However, DMI and gRFI (Figure 6C) had strong positive correlations in the same and similar WOL, but all other WOL had weak correlations. This could reflect the dynamic phenotypic behavior of DMI and its influence on gRFI.

The results of this study provide a deeper look into how the genetic parameters of traits associated with gRFI change over time. That said, it is important to

note that more data from first lactation and from later lactations should be included in subsequent analyses. Additional traits, such as change in body weight, should also be considered in the definition of gRFI to provide a more complete picture of the biology behind the trait, as also suggested in Islam et al. (2020) and Khanal et al. (2022). As research continues, the data available for these types of analyses will continue to grow. This study provides the groundwork for these methods to be developed further as the database expands.

### CONCLUSIONS

The results presented in this study provide an insight into the dynamic behavior of phenotypic and genetic parameters of DMI, ECM, MBW, and gRFI when assessed throughout lactation. Genetic parameters estimated in this study changed over time, highlighting the need to consider how the traits change throughout lactation and consider multiple time points when collecting data and performing genetic evaluations. To validate the results of this study and gain a deeper understanding of the changes that happen within DMI, ECM, MBW, and gRFI throughout a lactation, future studies with a larger population should be conducted exploiting available genomic information.



**Figure 6.** Heat map of the phenotypic correlations between traits over the first lactation (days in milk from 1 to 305 running left to right and top to bottom). Pair of traits analyzed are: A) dry matter intake and energy corrected milk (DMI and ECM; standard errors between 0.06 and 0.18), B) dry matter intake and metabolic body weight (DMI and MBW; standard errors between 0.07 and 0.19), C) dry matter intake and feed efficiency (DMI and gRFI; standard errors between 0.05 and 0.20), D) energy corrected milk and metabolic body weight (ECM and MBW; standard errors between 0.07 and 0.16), E) energy corrected milk and feed efficiency (ECM and gRFI; standard errors between 0.01 and 0.29), and F) metabolic body weight and feed efficiency (MBW and gRFI; standard errors between 0.02 and 0.17). Axes labels run from 7 to 301 DIM (each pixel represents one week of lactation).

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