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Multiple-trait random regression modeling of feed efficiency in US Holsteins

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ABSTRACT

Residual feed intake (RFI) and feed saved (FS) are important feed efficiency traits that have been increasingly considered in genetic improvement programs. Future sustainability of these genetic evaluations will depend upon greater flexibility to accommodate sparsely recorded dry matter intake (DMI) records on many more cows, especially from commercial environments. Recent multiple-trait random regression (MTRR) modeling developments have facilitated days in milk (DIM)-specific inferences on RFI and FS, particularly in modeling the effect of change in metabolic body weight (MBW). The MTRR analyses, using daily data on the core traits of DMI, MBW, and milk energy (MilkE), were conducted separately for 2,532 primiparous and 2,379 multiparous US Holstein cows from 50 to 200 DIM. Estimated MTRR variance components were used to derive genetic RFI and FS and DIM-specific genetic partial regressions of DMI on MBW, MilkE, and change in MBW. Estimated daily heritabilities of RFI and FS varied across lactation for both primiparous (0.05–0.07 and 0.11–0.17, respectively) and multiparous (0.03–0.13 and 0.10–0.17, respectively) cows. Genetic correlations of RFI across DIM varied (>0.05) widely compared with FS (>0.54) within either parity class. Heritability estimates based on average lactation-wise measures were substantially larger than daily heritabilities, ranging from 0.17 to 0.25 for RFI and from 0.35 to 0.41 for FS. The partial genetic regression coefficients of DMI on MBW (0.11 to 0.16 kg/kg$^{0.75}$ for primiparous and 0.12 to 0.14 kg/kg$^{0.75}$ for multiparous cows) and of DMI on MilkE (0.45 to 0.68 kg/Mcal for primiparous and 0.36 to 0.61 kg/Mcal for multiparous cows) also varied across lactation. In spite of the computational challenges encountered with MTRR, the model potentially facilitates an efficient strategy for harnessing more data involving a wide variety of data recording scenarios for genetic evaluations on feed efficiency.

Key words: residual feed intake, feed saved, multiple trait, random regression

INTRODUCTION

Residual feed intake (**RFI**) has been included in the lifetime net merit index used to evaluate US dairy cows for total genetic merit. Genetic evaluations for feed saved (**FS**) which combines RFI with feed intake due to differences in BW are also now provided (Gaddis et al., 2021). These evaluations have benefited from large and ongoing research investments made into the recording of DMI at various US dairy research facilities. The primary RFI input into these national genetic evaluations are generally based on 42 d, and less often 28 d (VanRaden et al., 2021), of almost continuously recorded DMI and milk yields along with less frequently recorded milk components, and, typically, even less frequently recorded BW.

Sustained recording of DMI is required to ensure future reliable genetic evaluations for RFI and its continued incorporation in net merit. Recently, Negussie et al. (2019) determined that sparse recording scenarios, such as recording DMI much less frequently throughout a lactation on individual cows, might be effectively used to provide reliable genetic evaluations for DMI and RFI on sires, provided that more cows are recorded for DMI relative to scenarios based on more intensive recording. Although it is not the intent of this paper to speculate how many more current or future cows sparsely recorded for DMI could be used, future genetic evaluations should flexibly allow the incorporation of as many available records on DMI as possible on cows from other research stations or representative commercial dairy farms.

A clear statistical modeling strategy for flexibly modeling repeated records from various stages of lactation

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involves the use of random regression models (Negussie et al., 2019). The use of random regression models flexibly allows genetic parameters (e.g., heritabilities, genetic correlations) to vary across lactation. However, even then, such a strategy requires the specification of key energy sinks needed to define RFI, namely milk energy (**MilkE**), metabolic BW (**MBW** = $BW^{0.75}$) and change in BW (**dBW**) or, equivalently, change in MBW (**dMBW**). A classical regression-based approach is typically used to derive RFI based on the estimated residuals from fitting weekly DMI as a linear function of averages of MilkE and MBW as well as dBW over a week (Tempelman et al., 2015; Li et al., 2017) or even over longer intervals of time (Lu et al., 2018). This RFI is typically referred to as phenotypic RFI (**pRFI**). Although daily continuous recording of DMI can be readily averaged to provide weekly DMI data, BW, and milk components required to determine MilkE are often measured less frequently and thereby require interpolation to obtain RFI for weekly or longer time frames. Furthermore, because of less frequent recording of BW at some research stations relative to others, it is unclear how to properly weight the varying sparsity of recording on (M)BW, and hence dBW, accordingly when estimating partial regressions between DMI and the energy sinks in the determination of RFI. This will likely be an even greater issue if data from commercial dairies is used in the future.

Recently, Islam et al. (2020) demonstrated how multiple-trait random regression (**MTRR**) model analyses involving MBW could be adapted to dynamically determine the genetic component of dBW as required to derive genetic RFI (**gRFI**) across various stages of lactation. Here gRFI is defined by partial regression relationships between DMI and the energy sink traits at the genetic, rather than phenotypic, level. Because any available daily records can be readily incorporated into a MTRR analysis and do not need to match up by DIM between the various component traits in a MTRR, this development from Islam et al. (2020) avoids the need for interpolated records to determine weekly (or from other broader timeframes) records as required to derive a dBW. Furthermore, the uncertainty due to differences in recording frequencies is formally accounted for in a MTRR when genetically evaluating dBW and, hence, gRFI. A multiple-trait model also avoids the biases implicit with regression on covariates that are potentially characterized by substantial measurement error, especially dBW (Lu et al., 2015; Tempelman and Lu, 2020).

Several studies have used single-trait random regression models or MTRR to dynamically model heritabilities of DMI or RFI across lactation; however, to our knowledge, most studies have focused on data from primiparous cows. Exceptions have been studies which combine both primiparous and multiparous cows together into one analysis, including those that involve a subset of the data used in the current study (Spurlock et al., 2012; Tempelman et al., 2015) or studies that have not considered genetic effects (Martin et al., 2021).

The primary objective of this study was to use the recent MTRR developments provided in Islam et al. (2020) to determine stage of lactation specific genetic parameters for day-specific heritabilities, partial regression relationships, and genetic correlations involving RFI, FS, and their core traits with separate analyses conducted for primiparous and multiparous cows. We also set out to use MTRR models to more reliably estimate genetic parameters for lactation-wise measures of these traits.

MATERIALS AND METHODS

Data Sources, Recording, and Editing

Records on DMI, milk yields (**MY**), fat (**F%**), protein (**P%**), and lactose (**L%**) components of milk, and BW were collected from Holstein cows at 5 different research stations from 50 to 200 DIM between 2007 and 2020. These research stations were the Animal Genomics and Improvement Laboratory (**AGIL**; Beltsville, MD), Iowa State University (**ISU**; Ames, IA), Michigan State University (**MSU**; East Lansing, MI), University of Florida (**UF**; Gainesville, FL), and the University of Wisconsin-Madison (**UW**; Madison, WI). Recording frequencies on DMI and MY were typically daily whereas recording frequencies for all other traits (BW, F%, P%, and L%) varied among different research stations. The MilkE was calculated as a function of MY, F%, P%, and L% using the expression provided in Tempelman et al. (2015). Given that L% was not recorded at AGIL, all missing L% values were set to 4.85%. Although the emphasis in this paper is on the use of daily data, the data on MBW, DMI, and MilkE were edited and also converted to weekly records using procedures outlined in Tempelman et al. (2015). A detailed summary of number of cows and number of daily records on each trait across the 5 research stations is provided in Table 1. There were a total of 37,268 and 46,283 daily records on BW, 165,445 and 154,270 daily records on DMI, 170,990 and 157,542 daily records on MY, and 32,238 and 39,656 records on F% recorded on 2,532 primiparous and 2,379 multiparous cows, respectively. The number of P% and L% records were within 0.01% of the total number of F% records with the exception of L% for AGIL as previously noted. Across both primiparous and multiparous cows, there were a total of 4,233 unique cows. Sum-

mary statistics for both daily MBW, DMI, and MilkE are presented in Table 2. Here, 312 multiparous cows had records across multiple lactations beyond first lactation and 1,024 cows had multiple lactations across all lactations including first lactation. Pedigrees going back 4 generations and genotypes were obtained from Council of Dairy Cattle Breeding (Bowie, MD) for all cows with records. No animals were used in this study, and ethical approval for the use of animals was thus deemed unnecessary.

Statistical Analysis

The software WOMBAT (Meyer, 2007) was used for all quantitative genetic analyses. To explore the appropriate degree of the polynomial to specify for the random effects specifications within the MTRR model for each particular core trait (i.e., MBW, MilkE, and DMI), we first fitted univariate random regression models to each individual trait, separately for primiparous and multiparous animals.

We defined 19 environmental subclasses based on the intersection of 4 time blocks, 2007 to 2010, 2011 to 2013, 2014 to 2016, and 2017 to 2020, with the 5 research stations (no data were available from MSU during 2007–2010). The statistical model used for primiparous cows was as in Equation [1].

$$y_{ijklm} = env_j + b_{AC}AC_i + \sum\nolimits_{s=1}^{5} b_{sj} z_{sim} + \sum\nolimits_{s=0}^{q} a_{si} z_{sim} + \sum\nolimits_{s=0}^{q} p_{si} z_{sim} + r_{k(j)} + d_{l(j)} + \varepsilon_{ijklm}. \quad [1]$$

Here y_{ijklm} is the response at DIM m on cow i on ration k during testdate (i.e., recording date) l within environment j, whereas z_{sim} is the Legendre polynomial on DIM m on cow i for random intercept or polynomial s such that $s = 0$ denotes the intercept. Also env_j is the fixed effect of environmental subclass j, b_{AC} is the regression coefficient on AC_i or age at calving for cow i, and b_{sj} is the sth order fixed regression coefficient on Legendre polynomial z_{sim} specified up to fifth order for the jth environment.

For random effects, a_{si} and p_{si} are the sth order random regression coefficients of additive and within-lactation permanent environmental effects, respectively, for cow i specified up to order q. Furthermore, $r_{k(j)}$ is the random effect of diet or ration k nested within environment j whereas $d_{l(j)}$ is the random effect of testdate l nested within environment j. Finally, ε_{ijklm} is the random residual effect at DIM m on cow i eating ration k during testdate l within environment j. Note that the additive random regression coefficients across all cows are specified to be multivariate normal with null mean

Table 1. Number of cows and number of records of DMI, BW, and milk yields and fat percentages for primiparous and multiparous cows by research station

	Number of cows		DMI records		BW records		Milk yield records		Fat percentage records	
Station[1]	Primiparous	Multiparous	Primiparous	Multiparous	Primiparous	Multiparous	Primiparous	Multiparous	Primiparous	Multiparous
AGIL	663	416	45,643	23,912	3,719	2,316	47,603	25,060	6,714	4,099
ISU	767	347	52,174	26,153	8,130	4,248	55,419	28,560	6,712	3,763
MSU	261	249	17,839	18,521	7,666	8,302	17,738	18,544	6,401	7,132
UF	309	430	16,267	25,580	12,668	21,753	16,405	25,423	6,177	12,093
UW	532	937	33,522	60,104	5,085	9,664	33,825	59,955	6,234	12,569
TOTAL	2,532	2,379	165,445	154,270	37,268	46,283	170,990	157,542	32,238	39,656

[1] AGIL = Animal Genomics Improvement Laboratory; ISU = Iowa State University; MSU = Michigan State University; UF = University of Florida; UW = University of Wisconsin.

Table 2. Station-specific means (SD) of DMI, milk yield (MY), BW, and fat, protein, and lactose percentages across 50 to 200 DIM for primiparous and multiparous Holstein cows

	Daily records											
	Primiparous cows						Multiparous cows					
Station[1]	BW, kg	Milk yield, kg	DMI, kg	Fat %	Protein %	Lactose %	BW, kg	Milk yield, kg	DMI, kg	Fat %	Protein %	Lactose %
AGIL	560.50	40.41	21.55	3.87	2.91	—	636.09	49.06	25.45	3.86	2.85	—
	(49.48)	(5.69)	(3.36)	(0.57)	(0.25)	—	(60.78)	(8.32)	(3.93)	(0.65)	(0.31)	—
ISU	573.25	37.68	22.37	3.67	2.95	4.95	637.52	46.84	26.40	3.87	2.88	4.83
	(52.28)	(6.07)	(3.23)	(0.72)	(0.26)	(0.17)	(59.53)	(8.39)	(4.13)	(0.87)	(0.27)	(0.19)
MSU	607.82	35.00	21.89	3.59	3.06	5.02	708.81	46.69	27.55	3.47	3.01	4.87
	(52.28)	(6.10)	(3.09)	(0.60)	(0.26)	(0.14)	(67.60)	(9.20)	(3.85)	(0.65)	(0.28)	(0.18)
UF	558.62	34.90	22.06	3.42	3.62	4.87	650.60	42.89	25.91	3.44	2.81	4.78
	(53.38)	(6.66)	(3.01)	(0.51)	(0.24)	(0.28)	(66.77)	(7.29)	(4.09)	(0.52)	(0.25)	(0.27)
UW	621.93	37.57	23.29	3.68	3.68	5.01	720.68	49.52	28.99	3.45	3.01	4.89
	(52.48)	(5.95)	(3.66)	(0.64)	(0.64)	(0.18)	(73.62)	(8.36)	(4.64)	(0.65)	(0.25)	(0.20)

[1] AGIL = Animal Genomics Improvement Laboratory, ISU = Iowa State University, MSU = Michigan State University, UF = University of Florida, UW = University of Wisconsin.

and variance-covariance matrix $\mathbf{A} \otimes \mathbf{G}$. Here $\mathbf{A}$ is the pedigree relationship matrix and $\mathbf{G}$ is the $(q + 1) \times (q + 1)$ genetic covariance matrix between the Legendre polynomial coefficients with $\otimes$ being the Kronecker product. Similarly, the within-lactation permanent environmental regression coefficients are specified to be multivariate normal with null mean and variance-covariance matrix $\mathbf{I}_{n_c} \otimes \mathbf{P}$, where $\mathbf{I}_{n_c}$ is an identity matrix of order n_c for n_c being the number of cows and $\mathbf{P}$ being a $(q + 1) \times (q + 1)$ covariance matrix between the corresponding random regression coefficients. Both $\{r_{k(j)}\}$ and $\{d_{l(j)}\}$ were treated as homoscedastic independent random effects whereas residuals $\{\varepsilon_{ijklm}\}$ were also specified to be independent but heteroskedastic across 6 different DIM subclasses: (1) 50 to 69 d, (2) 70 to 89 d, (3) 90 to 109 d, (4) 110 to 129 d, (5) 130 to 159 d, and (6) 160 to 200 d.

Consider trait 1 (MBW), trait 2 (MilkE), and trait 3 (DMI) as being the core traits of feed efficiency. Separate multiple-trait model analyses were conducted for each parity class on the 3 core traits specifying $q = 2$ for both random additive and permanent environmental effects in both instances. The model for each trait for primiparous cows was based on Equation [1], whereas the following extensions for Equation [1] were specified for multiparous animals. First, a fixed classification effect for parity (2, 3, and 4+) was considered. Second, a random between-lactation permanent environmental effects term was specified as independent cow effects to accommodate multiple lactations on cows (Tempelman et al., 2015) recognizing that permanent environmental effects are more strongly correlated within lactation than between different lactations on the same cow.

We specify the additive genetic effects on any cow i for trait t as $\mathbf{a}_{it}$ being a 3 × 1 vector of random intercept, linear and quadratic coefficients on trait t, $t = 1, 2, 3$. Hence, the variance-covariance matrix of all genetic effects $\mathbf{a}_i = \left[\mathbf{a}'_{i1}\ \mathbf{a}'_{i2}\ \mathbf{a}'_{i3}\right]'$ on all 3 traits for any cow i is $\mathbf{G}$ where $\mathbf{G}$ is now a 9 × 9 matrix of genetic variances and covariances for the intercept, linear and quadratic coefficients on each of MBW, MilkE, and DMI. Across all cows then, the variance-covariance matrix of genetic effects is $\mathbf{A} \otimes \mathbf{G}$. Similarly, the variance-covariance matrix for the within-lactation permanent environmental effects for all 3 core traits on any cow i is $\mathbf{P}$, where $\mathbf{P}$ is the 9 × 9 matrix of permanent environmental (co)variances for the intercept, linear and quadratic coefficients on each of MBW, MilkE, and DMI. Across all cows then, the variance-covariance matrix of the within-lactation permanent environmental effects is $\mathbf{I}_{n_c} \otimes \mathbf{P}$.

Because of the large number of estimated variance-covariances already defined in $\mathbf{G}$ and $\mathbf{P}$, the between-

trait covariances for ration effects $\mathbf{r} = \left[\mathbf{r}_1' \; \mathbf{r}_2' \; \mathbf{r}_3'\right]'$ and for testdate effects $\mathbf{d} = \left[\mathbf{d}_1' \; \mathbf{d}_2' \; \mathbf{d}_3'\right]'$ were set to zero. For multiparous cows, a 3 × 3 (co)variance matrix $\mathbf{C}$ was specified for the between-lactation permanent environmental effects for the 3 traits at all DIM (i.e., random intercepts only). We similarly extended the heteroskedastic residuals from the univariate models to specify heterogeneous residual (co)variances for the 3 traits where the residual (co)variances were $\mathbf{R}_v$, $v = 1, 2, \ldots, 6$ for the same 6 DIM subclasses as the univariate models: 50–69 d, 70–89 d, 90–109 d, 110–129 d, 130–159 d, and 160–200 d.

Derivation of (Co)variances for BW Change for Each Day of Lactation. The genetic and permanent environment (co)variance components of dMBW with other traits for each day were obtained from the cow-specific changes of the fitted MBW curve using first differences (Islam et al., 2020). First, the Legendre polynomial coefficients were used to define the DIM-specific genetic merit of MBW, MilkE, and DMI. Noting that $\mathbf{G}$ and $\mathbf{P}$ are each 9 × 9 matrices ordered by degree of polynomial (intercept = 0, linear = 1, and quadratic = 2) within each trait (MBW, MilkE, and DMI, respectively), the contrast matrix ($\boldsymbol{\Phi}_{(\mathrm{m})}$) containing Legendre polynomials coefficients for DIM m were defined as

$$\Phi_{(\mathbf{m})} = \begin{bmatrix} z_{(m).0} & z_{(m).1} & z_{(m).2} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & z_{(m).0} & z_{(m).1} & z_{(m).2} & 0 & 0 & 0 \\ 0 & z_{(m).1} - z_{(m-1).1} & z_{(m).2} - z_{(m-1).2} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & z_{(m).0} & z_{(m).1} & z_{(m).2} \end{bmatrix}. \qquad [2]$$

Here $z_{(m).0}$, $z_{(m).1}$, and $z_{(m).2}$ are, respectively, the Legendre intercept, linear, and quadratic coefficients for DIM m. Note that rows 1, 2, and 4 of $\boldsymbol{\Phi}_{(\mathrm{m})}$ in Equation [2] are used to define the genetic merit of MBW, MilkE, and DMI, respectively, for animal i at DIM m when multiplied by the corresponding solutions for animal i in $\mathbf{a}$. The third row of $\boldsymbol{\Phi}_{(\mathrm{m})}$ is used to derive the DIM-specific genetic merit of dMBW based on the first differences (Islam et al., 2020) in the respective coefficients between DIM m and $m - 1$ with the exception of DIM 50, which was specified to be the same as that for DIM 51. Hence, there were 151 DIM-specific $\boldsymbol{\Phi}_{(\mathrm{m})}$ matrices (i.e., from DIM 50–200).

The genetic (co)variance matrix $[\mathbf{G}_{(\mathrm{m})}]$ at DIM m was then calculated to be

$$\mathbf{G}_{(\mathrm{m})} = \boldsymbol{\Phi}_{(\mathrm{m})}\mathbf{G}\boldsymbol{\Phi}_{(\mathrm{m})}',$$

where

$$\mathbf{G}_{(\mathbf{m})} = \begin{bmatrix} \sigma^2_{\mathrm{g,MBW(m)}} & \sigma_{\mathrm{g,MBW,MilkE(m)}} & \sigma_{\mathrm{g,MBW,dMBW(m)}} & \sigma_{\mathrm{g,MBW,DMI(m)}} \\ \sigma_{\mathrm{g,MBW,MilkE(m)}} & \sigma^2_{\mathrm{g,MilkE(m)}} & \sigma_{\mathrm{g,MilkE,dMBW(m)}} & \sigma_{\mathrm{g,MilkE,DMI(m)}} \\ \sigma_{\mathrm{g,MBW,dMBW(m)}} & \sigma_{\mathrm{g,MilkE,dMBW(m)}} & \sigma^2_{\mathrm{g,dMBW(m)}} & \sigma_{\mathrm{g,dMBW,DMI(m)}} \\ \sigma_{\mathrm{g,MBW,DMI(m)}} & \sigma_{\mathrm{g,MilkE,DMI(m)}} & \sigma_{\mathrm{g,dMBW,DMI(m)}} & \sigma^2_{\mathrm{g,DMI(m)}} \end{bmatrix} \qquad [3]$$

defines the DIM m specific genetic (co)variances between the 4 traits MBW, MilkE, dMBW, and DMI, respectively. In a virtually identical manner, the 4 × 4 permanent environmental (co)variance matrix between these 4 traits and specific to DIM m was obtained as $\mathbf{P}_{(m)} = \boldsymbol{\Phi}_{(\mathrm{m})}\mathbf{P}\boldsymbol{\Phi}_{(\mathrm{m})}'$.

The contrast matrix used to convert DIM subclasses specific between-trait residual (co)variance matrices

is provided as $\mathbf{T}$ in Equation [4] as per Islam et al. (2020):

$$\mathbf{T}=\begin{bmatrix}1&0&0&0&0&0\\0&1&0&0&0&0\\-1&0&0&1&0&0\\0&0&1&0&0&0\end{bmatrix}. \qquad [4]$$

That is, $\mathbf{R}_{(m)}=\mathbf{T}\mathbf{R}_{m-1,m}\mathbf{T}'$ was used to derive the residual (co)variance matrix for the 4 traits MBW, MilkE, dMBW, and DMI, respectively, at DIM m by defining $\mathbf{R}_{m-1,m}=\mathrm{diag}[\mathbf{R}_{v'(m-1)},\ \mathbf{R}_{v(m)}]$ as a block diagonal matrix whereby DIM $m-1$ and m defines which subclass(es) v' and v, respectively, of the 6 possible residual (co)variance subclasses for the 3 core traits are defined as the first and second blocks, respectively, in $\mathbf{R}_{m-1,m}$.

For the multiparous cow analyses, only random intercepts were specified for the covariance matrix $\mathbf{C}$ between the core traits. The between-lactation permanent environmental (co)variance matrix $\mathbf{C}^*$ for the 4 traits MBW, MilkE, dMBW, and DMI, respectively, at DIM m, was then also constant such that zero (co)variances were specified for any term involving dMBW with the remaining components (rows and columns 1, 2, and 4) being the elements of $\mathbf{C}$:

$$\mathbf{C}^*=\begin{bmatrix}\sigma^2_{\mathrm{c,MBW}}&\sigma_{\mathrm{c,MBW,MilkE}}&0&\sigma_{\mathrm{c,MBW,DMI}}\\\sigma_{\mathrm{c,MBW,MilkE}}&\sigma^2_{\mathrm{c,MilkE}}&0&\sigma_{\mathrm{c,MilkE,DMI}}\\0&0&0&0\\\sigma_{\mathrm{c,MBW,DMI}}&\sigma_{\mathrm{c,MilkE,DMI}}&0&\sigma^2_{\mathrm{c,DMI}}\end{bmatrix}. \qquad [5]$$

We derived the phenotypic (co)variance matrix $[\mathbf{V}_{(m)}]$ for DIM m as follows: $\mathbf{V}_{(m)}=\mathbf{G}_{(m)}+\mathbf{P}_{(m)}+\mathbf{R}_{(m)}$ for primiparous cows and $\mathbf{V}_{(m)}=\mathbf{G}_{(m)}+\mathbf{P}_{(m)}+\mathbf{R}_{(m)}+\mathbf{C}^*$ for multiparous cows. We included neither testdate nor ration variance components in the specification of $\mathbf{V}_{(m)}$ to facilitate more straightforward comparisons with other studies as dairy breeders historically have treated management effects as fixed.

Estimation of DIM-Specific Regression Coefficients. We partition the matrix $\mathbf{G}_{(m)}$ from Equation [3] into a scalar $g^{(\mathrm{m})}_{\mathrm{source,source}}$ due to the source trait (DMI), a 3 × 3 matrix $\mathbf{G}^{(\mathrm{m})}_{\mathrm{sink,sink}}$ due to the sink traits (MBW, MilkE, dMBW), and a 3 × 1 covariance component $\mathbf{g}^{(\mathrm{m})}_{\mathrm{sink,source}}$ between source and sink traits. In other words, we rewrite $\mathbf{G}_{(m)}$ as in Equation [6]:

$$\mathbf{G}_{(\mathrm{m})}=\begin{bmatrix}\mathbf{G}^{(\mathrm{m})}_{\mathrm{sink,sink}}&\mathbf{g}^{(\mathrm{m})}_{\mathrm{sink,source}}\\\mathbf{g}'^{(\mathrm{m})}_{\mathrm{sink,source}}&g^{(\mathrm{m})}_{\mathrm{source,source}}\end{bmatrix}, \qquad [6]$$

such that, for example, $g^{(\mathrm{m})}_{\mathrm{source,source}}=\sigma^2_{\mathrm{g,DMI(m)}}$ from Equation [3]. We also partition $\mathbf{V}_{(m)}$ in a similar manner:

$$\mathbf{V}_{(\mathrm{m})}=\begin{bmatrix}\mathbf{V}^{(\mathrm{m})}_{\mathrm{sink,sink}}&\mathbf{v}^{(\mathrm{m})}_{\mathrm{sink,source}}\\\mathbf{v}'^{(\mathrm{m})}_{\mathrm{sink,source}}&v^{(\mathrm{m})}_{\mathrm{source,source}}\end{bmatrix}. \qquad [7]$$

Because RFI and FS are linear functions of energy sink traits and DMI, Tempelman and Lu (2020) demonstrate how both FE traits can be derived from a multiple-trait analysis involving the core traits although their original derivation did not address MTRR involving records across different DIM nor a formal incorporation of dMBW as illustrated later for gRFI by Islam et al. (2020). A first step is to derive the corresponding partial regression coefficients required to determine either genetic or phenotypic versions of those traits. The DIM-specific partial genetic $\left(\mathbf{b}^{(\mathrm{m})}_{\boldsymbol{g}}\right)$ and phenotypic regression $\left(\mathbf{b}^{(\mathrm{m})}_{p}\right)$ coefficients were obtained as follows:

$$\mathbf{b}^{(\mathrm{m})}_{\mathbf{g}}=\left[\mathbf{G}^{(\mathrm{m})}_{\mathrm{sink,sink}}\right]^{-1}\mathbf{g}^{(\mathrm{m})}_{\mathrm{sink,sink}} \qquad [8]$$

and

$$\mathbf{b}^{(\mathrm{m})}_{p}=\left[\mathbf{V}^{(\mathrm{m})}_{\mathrm{sink,sink}}\right]^{-1}\mathbf{v}^{(\mathrm{m})}_{\mathrm{sink,source}} \qquad [9]$$

for $m = 50, 51, \ldots, 199, 200$, where

$$\mathbf{b}^{(\mathrm{m})}_{\boldsymbol{g}}=\left[b^{(\mathrm{m})}_{g,MBW}\quad b^{(\mathrm{m})}_{g,MilkE}\quad b^{(\mathrm{m})}_{g,dMBW}\right]'$$

and

$$\mathbf{b}^{(\mathrm{m})}_{p}=\left[b^{(\mathrm{m})}_{p,MBW}\quad b^{(\mathrm{m})}_{p,MilkE}\quad b^{(\mathrm{m})}_{p,dMBW}\right]'$$

are 3 × 1 vectors of genetic and phenotypic partial regression coefficients, respectively, of the source trait DMI on the key sink traits MBW, MilkE, and dMBW, respectively, at DIM m.

The corresponding DIM-specific genetic variance-covariance matrix $\mathbf{G}_{(m)}$ was then augmented to a 6 × 6 matrix $\mathbf{K}_g^{(m)}\mathbf{G}_{(m)}\mathbf{K}_g^{(m)}$, where the contrast matrix $\mathbf{K}_g^{(m)}$ includes the partial regression coefficients to derive gRFI and genetic FS (**gFS**) at DIM m within its fifth and sixth rows, respectively (Tempelman and Lu, 2020), as per Equation [10].

$$\mathbf{K}_g^{(m)} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ -b_{g,MBW}^{(\mathrm{m})} & -b_{g,MilkE}^{(\mathrm{m})} & -b_{g,dMBW}^{(\mathrm{m})} & 1 \\ 0 & -b_{g,MilkE}^{(\mathrm{m})} & -b_{g,dMBW}^{(\mathrm{m})} & 1 \end{bmatrix}. \quad [10]$$

In other words, $\mathbf{K}_g^{(m)}\mathbf{G}_{(m)}\mathbf{K}_g^{(m)\prime}$ defines the genetic variance-covariance matrix for MBW, MilkE, dMBW, DMI, gRFI, and gFS, respectively, at DIM m.

Estimation of Overall Genetic Parameters from 50 to 200 DIM. We also used another contrast matrix $\mathbf{\Phi_T}$ to determine genetic parameters for all these traits summed across the entire 50 to 200 DIM as traits defined on an average or lactation-wise basis would more likely be a focus of selection and incorporated into selection indexes. The genetic (co)variance matrix $(\mathbf{G_T})$ for the total genetic merit of MBW, MilkE, DMI, and dMBW across 50 to 200 DIM was written as $\mathbf{G_T} = \mathbf{\Phi_T G \Phi_T'}$, where $\mathbf{G}$ is the same as before and

$$\mathbf{\Phi_T} = \begin{bmatrix} z_{T,0} & z_{T,1} & z_{T,2} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & z_{T,0} & z_{T,1} & z_{T,2} & 0 & 0 & 0 \\ 0 & z_{200.1} - z_{50.1} & z_{200.2} - z_{50.2} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & z_{T,0} & z_{T,1} & z_{T,2} \end{bmatrix}. \quad [11]$$

Here $z_{T,0} = \sum_{m=50}^{200} \mathrm{z}_{(m).0}$, $z_{T,1} = \sum_{m=50}^{200} \mathrm{z}_{(m).1}$, and $z_{T,2} = \sum_{m=50}^{200} \mathrm{z}_{(m).2}$ represent the sum of the Legendre polynomial coefficients for intercept, linear trend, and quadratic trend, respectively, from DIM 50 to 200. In a similar manner, we obtained the (co)variance matrix for the lactation-wise within lactation permanent environmental effects of MBW, MilkE, DMI, and dMBW across the entire period as $\mathbf{P_T} = \mathbf{\Phi_T P \Phi_T}'$.

For multiparous cows across the entire range of DIM, the variance-covariance matrix for the lactation-wise between-lactation permanent environmental effects is $\mathbf{C_T} = \mathbf{LC^*L'}$, where $\mathbf{C^*}$ is as defined in Equation [5] and $\mathbf{L}=151\mathbf{I}_4$. Here, $\mathbf{R^*} = d_1\mathbf{R}_1 + d_2\mathbf{R}_2 + d_3\mathbf{R}_3 + \ldots + d_6\mathbf{R}_6$, where $\mathbf{R}_1$, $\mathbf{R}_2, \ldots,$ $\mathbf{R}_6$ are the 6 different subclasses of residual (co)variances for the core traits MBW, MilkE, and DMI as characterized previously with d_1, d_2, …, d_6 being the number of days within the 6 residual subclasses, respectively. We write the components of $\mathbf{R^*}$ as follows:

$$\mathbf{R^*} = \begin{bmatrix} \mathrm{r}_{\mathrm{MBW}}^2 & \mathrm{r}_{\mathrm{MBW,MilkE}} & \mathrm{r}_{\mathrm{MBW,DMI}} \\ \mathrm{r}_{\mathrm{MBW,MilkE}} & \mathrm{r}_{\mathrm{MilkE}}^2 & \mathrm{r}_{\mathrm{MilkE,DMI}} \\ \mathrm{r}_{\mathrm{MBW,DMI}} & \mathrm{r}_{\mathrm{MilkE,DMI}} & \mathrm{r}_{\mathrm{DMI}}^2 \end{bmatrix}. \quad [12]$$

The first, second, and fourth rows and columns of the residual (co)variance $(\mathbf{R_T})$ between the lactation-wise residual effects of MBW, MilkE, dMBW, and DMI are composed of the elements of $\mathbf{R^*}$, whereas the third row and column for lactation-wise dMBW are simply functions of the residual (co)variances for the first $(\mathbf{R}_1)$ and last $(\mathbf{R}_6)$ subclasses:

$$\mathbf{R_T} = \begin{bmatrix} \mathrm{r}_{\mathrm{MBW}}^2 & \mathrm{r}_{\mathrm{MBW,MilkE}} & \delta_{11} - \sigma_{11} & \mathrm{r}_{\mathrm{MBW,DMI}} \\ \mathrm{r}_{\mathrm{MBW,MilkE}} & \mathrm{r}_{\mathrm{MilkE}}^2 & \delta_{12} - \sigma_{12} & \mathrm{r}_{\mathrm{MilkE,DMI}} \\ \delta_{11} - \sigma_{11} & \delta_{12} - \sigma_{12} & \sigma_{33} + \delta_{33} & \delta_{13} - \sigma_{13} \\ \mathrm{r}_{\mathrm{MBW,DMI}} & \mathrm{r}_{\mathrm{MilkE,DMI}} & \delta_{13} - \sigma_{13} & \mathrm{r}_{\mathrm{DMI}}^2 \end{bmatrix}. \quad [13]$$

Here,

$$\mathbf{R}_1 = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \sigma_{13} \\ \sigma_{12} & \sigma_{22} & \sigma_{23} \\ \sigma_{31} & \sigma_{32} & \sigma_{33} \end{bmatrix}$$

is the residual variance-covariance matrix for the first subclass, whereas

$$\mathbf{R}_6 = \begin{bmatrix} \delta_{11} & \delta_{12} & \delta_{13} \\ \delta_{12} & \delta_{22} & \delta_{23} \\ \delta_{13} & \delta_{23} & \delta_{33} \end{bmatrix}$$

is the residual variance-covariance matrix for the last or sixth subclass. In this way, the phenotypic (co)variance matrix ($\mathbf{V}_\mathbf{T}$) was calculated for primiparous cows as $\mathbf{V}_\mathbf{T} = \mathbf{G}_\mathbf{T} + \mathbf{P}_\mathbf{T} + \mathbf{R}_\mathbf{T}$ whereas for multiparous cows it was determined as $\mathbf{V}_\mathbf{T} = \mathbf{G}_\mathbf{T} + \mathbf{P}_\mathbf{T} + \mathbf{C}_\mathbf{T} + \mathbf{R}_\mathbf{T}$. Furthermore, the lactation-wise genetic and phenotypic partial regression coefficients were computed using Equations [8] and [9] but this time using the corresponding partitions of $\mathbf{G}_\mathbf{T}$ and $\mathbf{V}_\mathbf{T}$, respectively. Finally, the resulting genetic regression coefficient estimates were used in an expression identical to that provided in Equation [10], which we label as $\mathbf{K}_g^T$. Hence, the lactation-wise genetic variance-covariance matrix of the 6 traits (MBW, MilkE, dMBW, DMI, gRFI, and gFS) was defined as $\mathbf{K}_g^T\mathbf{G}_\mathbf{T}\mathbf{K}_g^{T\prime}$. Note then that the breeding values of cow i for the 6 traits on a lactation-wise basis can be defined as $\mathbf{K}_g^T\boldsymbol{\Phi}_\mathbf{T}\boldsymbol{a}_i$.

Estimating Standard Errors. The software WOMBAT is based on the AIREML algorithm (Meyer, 2007), which provides the average information matrix for the estimates of **G**, **P**, $\mathbf{R}_1$–$\mathbf{R}_6$, and additionally **C** for the multiparous analysis. The asymptotic variance-covariance (**AVC**) matrix of these (co)variance estimates is thereby based on the inverse of the average information matrix. In a manner similar to Meyer and Houle (2013), a total of 100 multivariate normal random vectors were drawn from a multivariate normal distribution with mean vector based on the estimated (co)variance components and (co)variances based on the AVC matrix, ensuring that all random draws lead to positive definite random draws for **G**, **P**, $\mathbf{R}_1$–$\mathbf{R}_6$, and additionally **C** for the multiparous analyses. These random draws were transformed into elements of $\mathbf{G}_{(m)}$, $\mathbf{V}_{(m)}$, $\mathbf{b}_g^{(\mathrm{m})}$, and $\mathbf{b}_p^{(\mathrm{m})}$, for example, to determine approximate standard errors of their elements and any other derivative expressions from them such as lactation-wise or DIM-specific genetic correlations and heritabilities.

RESULTS

A characterization of the number of records by DIM is provided in Figure 1. Quite clearly, the bulk of the data on all traits was collected in the first half of the 50 to 200 DIM test period with a substantial drop-off in number of records, especially for DMI and MY, beyond 150 DIM.

A representative example WOMBAT "par" file used for conducting the multiple-trait analysis for multiparous cows is provided in Supplemental File S1 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022). We focus the presentation of our results from a pedigree-based analyses on the use of daily data, given that it was not possible to fit all 3 core traits simultaneously in a genomic-based analysis. However, we also conducted a genomic-based analysis based on a series of bivariate MTRR as we further describe later. We later briefly characterize the differences between the genomic- and pedigree-based analyses.

There were a total of 158 and 210 different rations defined for primiparous and multiparous cows, respectively, across the 19 environmental subclasses, in part because much of the data was generated from nutritional trials as described in Tempelman et al. (2015). As a proportion of total random effects variability at DIM = 125d, ration effects accounted for less than 0.3% for

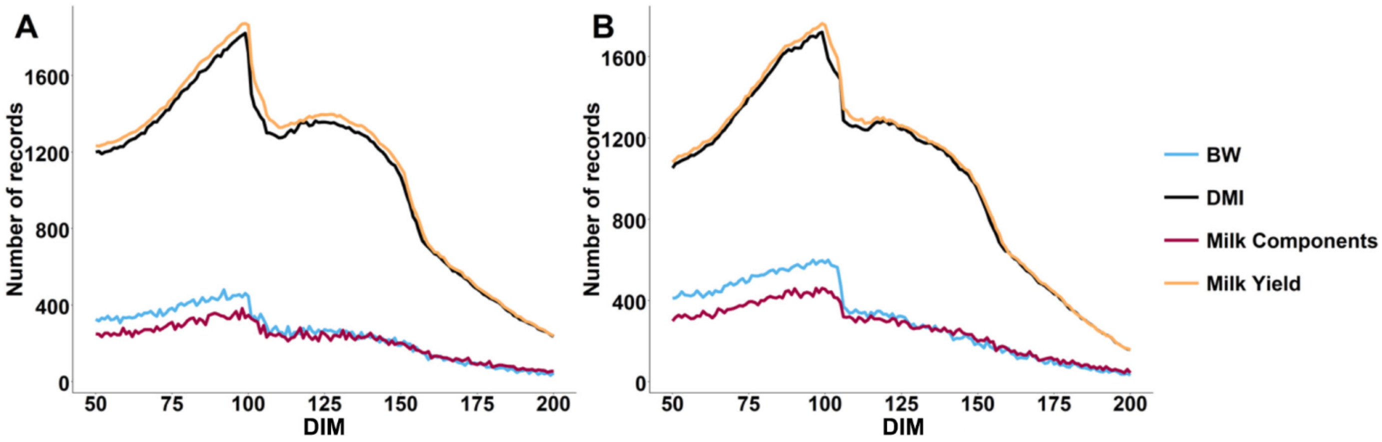

Figure 1. Frequency distribution of the number of records for BW, DMI, milk components, and milk yield by DIM for primiparous (A) and multiparous cows (B).

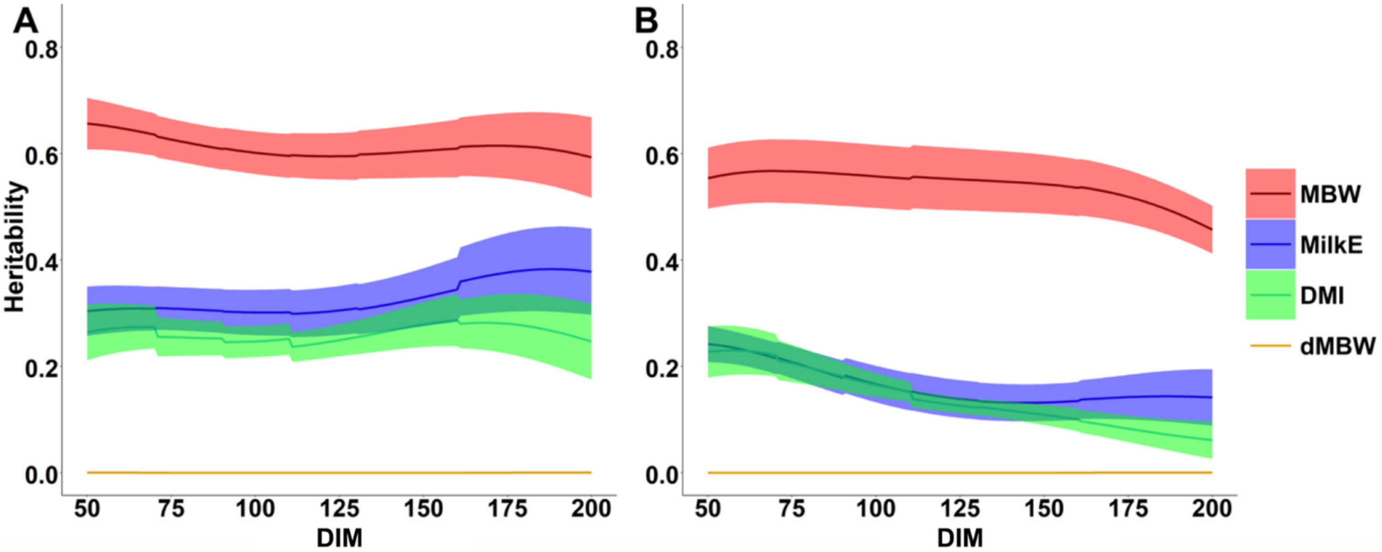

Figure 2. Day-specific estimated heritabilities of metabolic BW (MBW), milk energy (MilkE), DMI, and change in MBW (dMBW) between 50 and 200 DIM for primiparous (A) and multiparous (B) cows. Lines represent REML estimates with bands representing asymptotic sampling-based SE on those estimates.

MBW, between 2 and 3% for MilkE, and between 5 and 8% for DMI across both parities.

Heritability Estimates

The heritability estimates for the energy sink traits (MBW, MilkE, and dMBW) and DMI using daily data are presented in Figure 2. The estimated heritabilities for MBW were consistently high across DIM ranging rather narrowly between 0.59 to 0.65 in primiparous cows and from 0.46 to 0.57 in multiparous cows. Both MilkE and DMI had somewhat lower yet moderate heritabilities that closely tracked each other within the 2 parity classes throughout lactation although MilkE had slightly higher heritability estimates ranging from 0.30 to 0.38 in primiparous and from 0.13 to 0.24 in multiparous animals. What seemed particularly intriguing was that heritability estimates for both these traits gradually increased from 50 to 200 DIM in primiparous cows whereas they decreased for both traits in multiparous cows. The estimated heritabilities for daily dMBW were close to 0 throughout the entire test period.

Estimated heritabilities for the 2 feed efficiency traits, gRFI and gFS, are provided in Figure 3. The

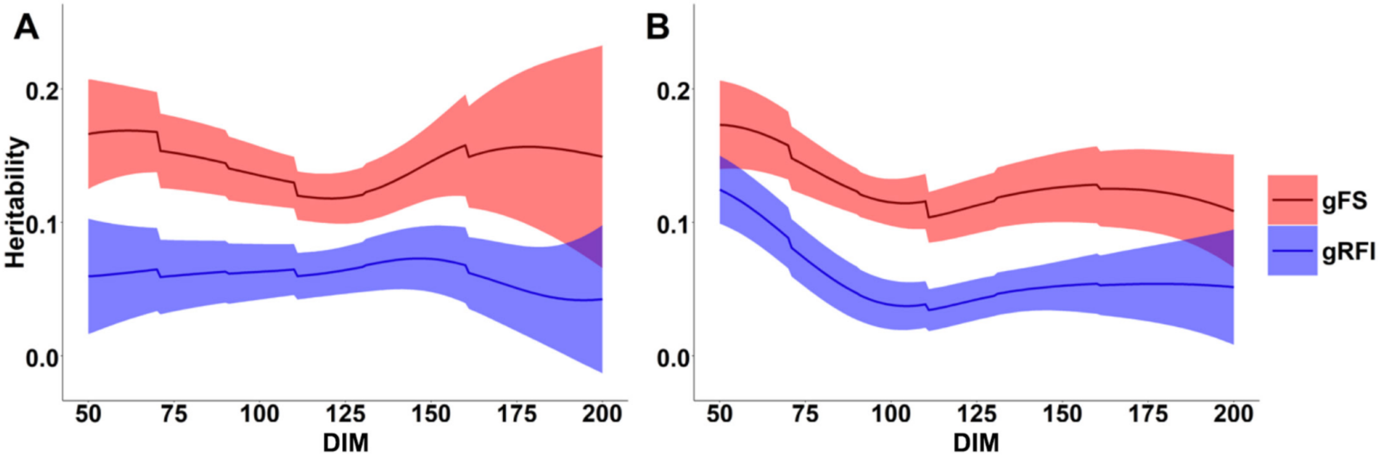

Figure 3. Day-specific estimated heritabilities of residual feed intake and feed saved between 50 and 200 DIM for primiparous (A) and multiparous (B) cows. Lines represent REML estimates with bands representing asymptotic sampling-based SE on those estimates. gFS = genetic feed saved; gRFI = genetic residual feed intake.

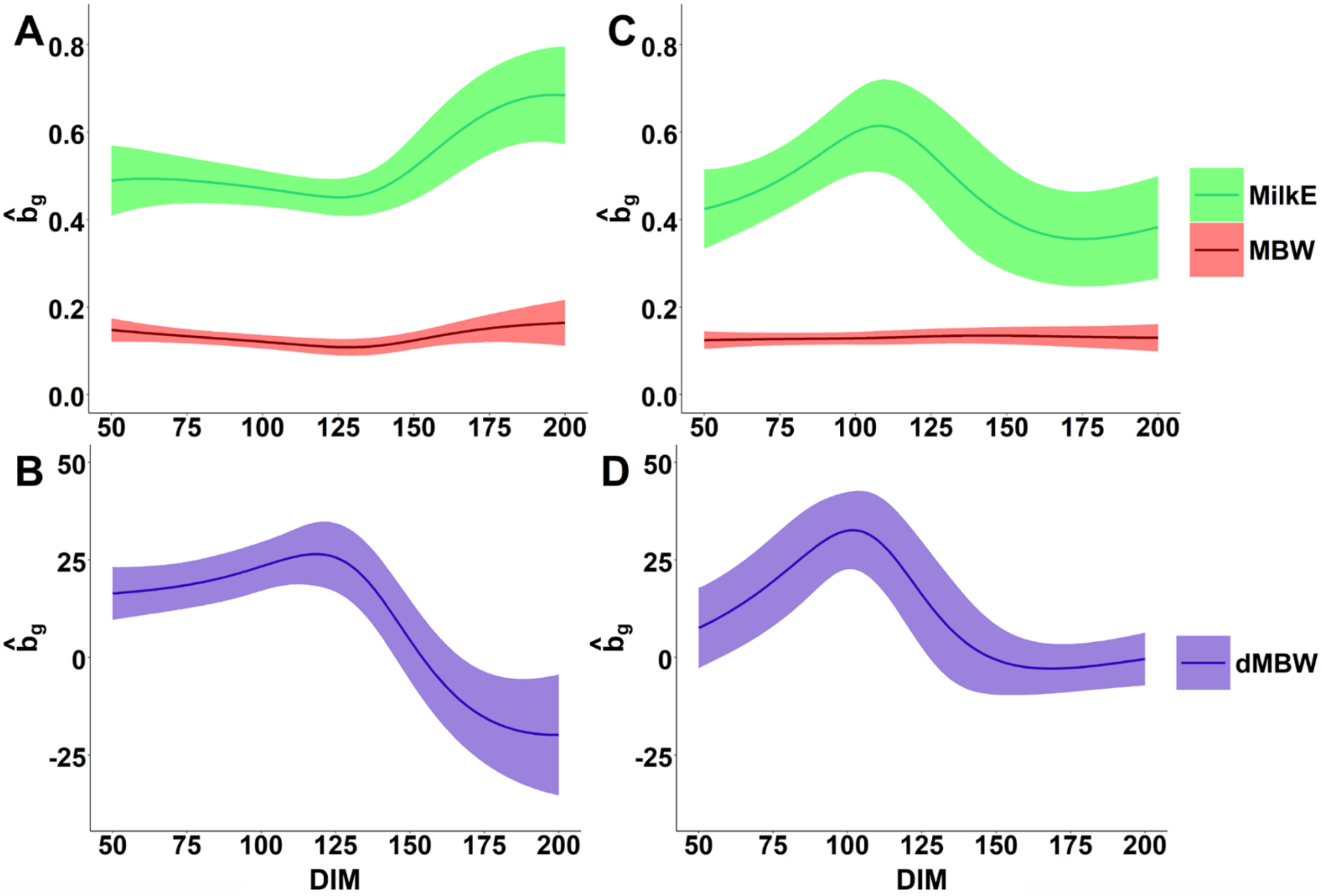

Figure 4. Day-specific estimated genetic partial regression coefficients $\left(\hat{b}_g\right)$ of DMI on metabolic weight (MBW; kg/kg$^{0.75}$), DMI on milk energy (MilkE; kg/Mcal), and DMI on change in metabolic BW (dMBW; kg/kg$^{0.75}$) between 50 and 200 DIM for primiparous (A and B) and multiparous (C and D) cows. Lines represent REML estimates with bands representing asymptotic sampling-based SE on those estimates.

heritabilities for gRFI ranged from 0.05 to 0.07 in primiparous cows and from 0.03 to 0.13 in multiparous cows. Whereas heritabilities for gRFI were relatively constant across DIM in primiparous cows, they were higher in early lactation for multiparous cows. The estimated heritabilities for gFS ranged from 0.11 to 0.17 for primiparous cows and from 0.10 to 0.17 for multiparous cows.

Estimated Partial Regression Coefficients

Genetic. Estimated genetic partial regression coefficients of DMI on MilkE and on MBW are provided for primiparous cows in Figure 4A whereas that of DMI on dMBW are provided in Figure 4B. Analogous plots are provided for multiparous cows in Figure 4C and 4D, respectively. The estimated partial regression coefficients on MBW were more stable across DIM in multiparous cows (0.12–0.14 kg/kg$^{0.75}$) than in primiparous cows (0.11–0.16 kg/kg$^{0.75}$) with no obvious trend across DIM. For partial regressions of DMI on MilkE, the estimated coefficients varied from 0.45 to 0.68 kg/Mcal in primiparous cows, abruptly increasing after 130 DIM. The corresponding estimated coefficients in multiparous cows changed more erratically across lactation, varying from 0.36 to a peak of 0.61 kg/Mcal near 110 DIM. Finally, the estimated genetic partial coefficients of DMI on dMBW were also erratic ranging from -19.8 to 26.5 kg/kg$^{0.75}$ in primiparous animals, generally decreasing with advancing DIM whereas the corresponding range for multiparous cows was from -2.8 to 32.6 kg/kg$^{0.75}$, peaking near 100 DIM. These estimated genetic regression coefficients of DMI on dMBW should be interpreted with caution because the estimated heritabilities for dMBW were near zero for all DIM, as previously indicated. Hence, the cor-

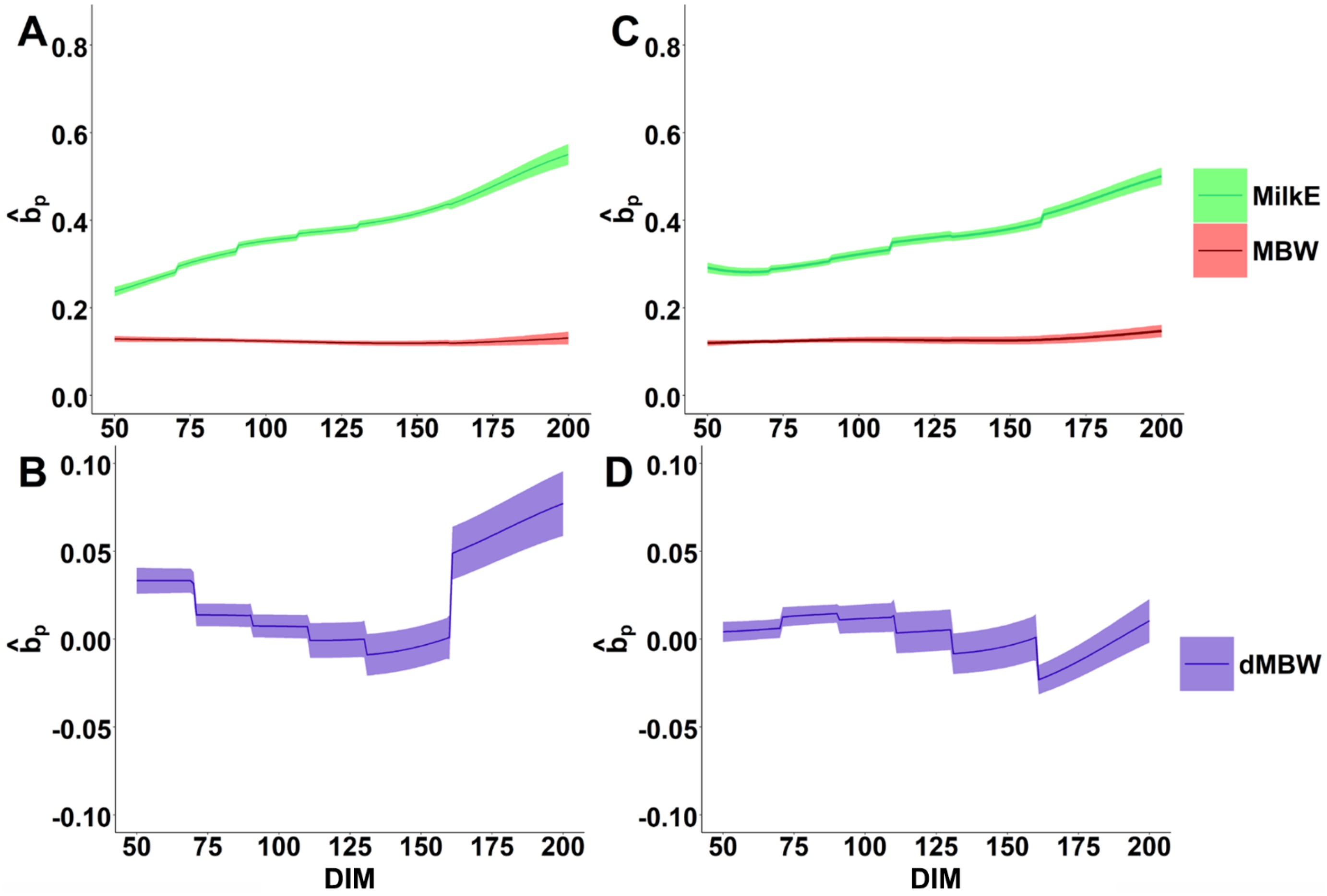

Figure 5. Day-specific estimated phenotypic partial regression coefficients $\left(\hat{b}_p\right)$ of DMI on metabolic BW (MBW; kg/kg$^{0.75}$), DME on milk energy (MilkE; kg/Mcal), and DMI on change in MBW (dMBW; kg/kg$^{0.75}$) between 50 and 200 DIM for primiparous (A and B) and multiparous (C and D) cows. Lines represent REML estimates with bands representing asymptotic sampling-based SE on those estimates.

responding animal specific genetic effects for dMBW, which effectively serve as "covariates" for those partial genetic regressions, were tightly varying around 0.

Phenotypic. Estimated phenotypic partial regression coefficients of DMI on MilkE and on MBW are provided in Figure 5A and of DMI on dMBW are provided in Figure 5B for primiparous cows. Similar plots are provided for multiparous cows in Figure 5C and D, respectively. In general, these phenotypic partial regression coefficients were more stable than the corresponding genetic regression coefficients in Figure 4. For DMI on MBW, the partial phenotypic regression coefficients had averages across DIM that were similar to but less variable relative to the partial genetic coefficients. This similarity may be expected given the large heritability for MBW; i.e., any genetic versus phenotypic partial relationships involving MBW are likely to closely mirror each other relative to other less heritable traits. For DMI on MilkE, the partial phenotypic regression coefficients steadily increased from 50 to 200 DIM, ranging from 0.22 to 0.55 kg/Mcal for primiparous cows and from 0.28 to 0.50 kg/Mcal for multiparous cows. The estimated phenotypic partial regression coefficients of DMI on dMBW were very stable and close to zero ranging from −0.009 ± 0.001 to 0.07 ± 0.01 kg/kg$^{0.75}$ for primiparous cows and from −0.02 ± 0.008 to 0.02 ± 0.005 kg/kg$^{0.75}$ for multiparous cows. It is important to note that these coefficients are expressed relative to the overall positive regression relationships generally inferred between DMI on dMBW when fixed effects such as those in Equation [1] (e.g., environmental subclass specific intercepts and regressions on DIM) are not typically adjusted for. That is, the "covariate" for dMBW is based on differences involving a smaller range of random effects relative to phenotypic differences driven by fixed effects. Hence these estimates

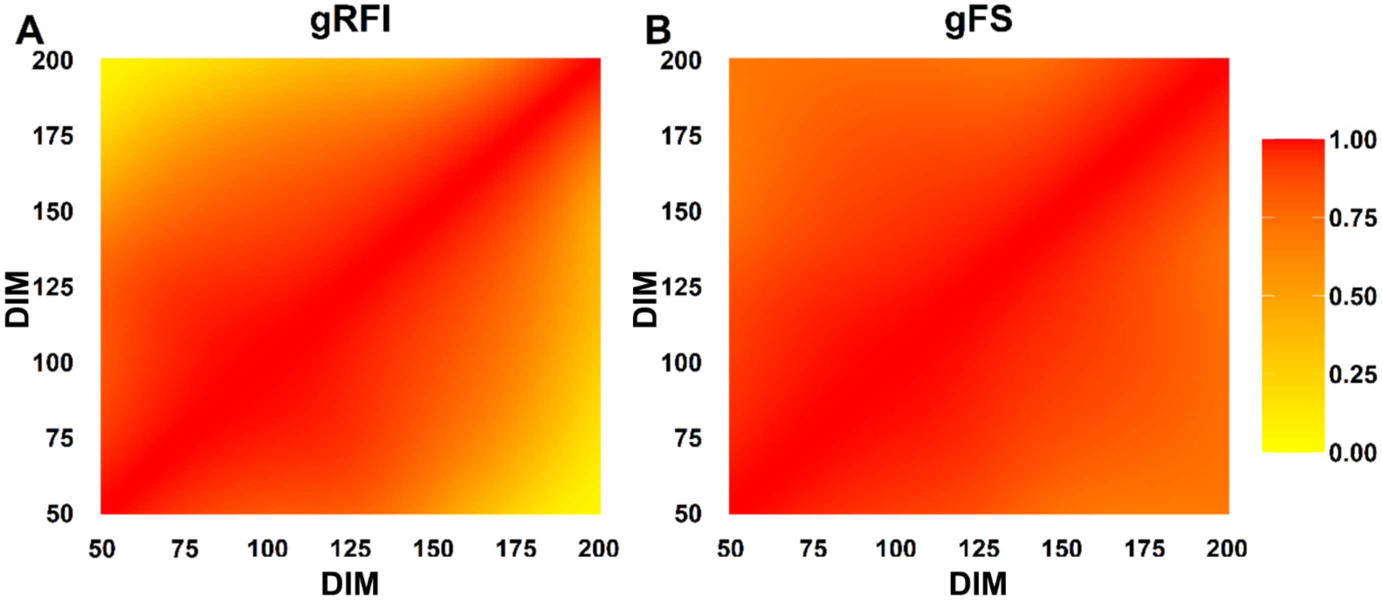

Figure 6. Estimated genetic correlations between days for genetic residual feed intake (gRFI; A) and genetic feed saved (gFS; B) for primiparous cows between 50 and 200 DIM.

should not be interpreted in the same way as classically determined partial regression coefficients on dMBW per Tempelman et al. (2015), for example.

Estimated Genetic Correlations Within Lactation

Estimated genetic correlations between DIM within 50 to 200 d for the core traits of gRFI and gFS, namely DMI, MBW, and MilkE, are provided as heat maps for primiparous cows in Supplemental Figure S1, included in Supplemental File S2 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022), and for multiparous cows in Supplemental Figure S2 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022). As expected, genetic correlations generally decreased as intervals between corresponding DIM increased. These correlations were consistently high (>0.9) between DIM for both MBW and DMI within either parity class. Genetic correlations between distant DIM for MilkE were lower, being as low as 0.75 for primiparous cows and 0.50 for multiparous cows between 50 and 200 DIM. Estimated genetic correlations between DIM for gRFI and gFS for primiparous and multiparous cows are provided in Figures 6 and 7, respectively. Genetic correlations between DIM for gRFI fell to as low as 0.05 in primiparous cows and as low as 0.25 in multiparous cows. Genetic correlations between DIM for gFS were generally higher than they were for gRFI, falling to as low as 0.68 in primiparous cows and as low as 0.54 in multiparous cows. The higher within lactation genetic correlations observed for gFS relative to gRFI was likely due to the contributing effect of MBW. Estimated genetic correlations between the 3 core traits across the test period are provided in Supplemental Figure S3 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022), and genetic correlations between gFS and gRFI with MBW and DMI are provided in Supplemental Figure S4 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022). Here, DMI had consistently large positive genetic correlations with both MBW and MilkE throughout the test period. Estimated genetic correlations between MilkE and DMI hovered just above 0 in primiparous cows and declined from slightly positive to moderately negative values over the 50 to 200 DIM test period in multiparous cows.

Genetic Parameters for Lactation-Wise Measures

Although MTRR models allow the determination of DIM-specific genetic parameters, the total or lactation-wise genetic merit of gRFI, gFS, and the core traits across the 50 to 200 DIM test period might be considered to be a primary focus for genetic selection. The estimated lactation-wise heritabilities of these traits are provided in Table 3. These estimates for MBW did not change substantially from their respective day-specific heritabilities, ranging from 0.59 for multiparous cows to 0.67 for primiparous cows. However, for MilkE and DMI, there were substantial increases from DIM-specific to lactation-wise heritabilities as well as substantial differences in lactation-wise heritabilities

Table 3. Estimated heritabilities of lactation-wise (50–200 DIM) genetic residual feed intake and genetic feed saved and their component traits

Trait	Heritability	
	Primiparous	Multiparous
Metabolic BW	0.67 ± 0.05	0.59 ± 0.07
Milk energy	0.43 ± 0.06	0.22 ± 0.04
Change in metabolic BW	0.11 ± 0.05	0.13 ± 0.05
DMI	0.57 ± 0.05	0.28 ± 0.05
Genetic residual feed intake	0.25 ± 0.08	0.17 ± 0.05
Genetic feed saved	0.41 ± 0.06	0.35 ± 0.06

between primiparous and multiparous cows. For example, we estimated a heritability of 0.43 ± 0.06 for MilkE in primiparous cows whereas the corresponding estimate for multiparous cows was 0.22 ± 0.04. Similarly, the heritability estimate for DMI was 0.57 ± 0.05 for primiparous cows versus 0.28 ± 0.05 for multiparous cows. A substantial contributor to the lower heritability estimates in multiparous versus primiparous cows was the additional variation due to between-lactation permanent environmental effects modeled for multiparous cows, accounting for anywhere between 0.13 (for DMI) to 0.23 (for MilkE) of the total phenotypic variance (results not reported). A particularly intriguing result in Table 3 was that the estimated heritabilities for lactation-wise dMBW were substantial, being 0.11 ± 0.05 for primiparous cows and 0.13 ± 0.05 for multiparous cows suggesting that genetic variation for dMBW across a broad period of lactation is important in sharp contrast to the near-zero daily heritabilities for dMBW previously reported in this paper.

We also estimated genetic correlations of DIM-specific genetic merit with lactation-wise genetic merit for both gRFI and gFS between 50 and 200 DIM. These correlations are illustrated in Figure 8. In general, correlations were consistently greater than 0.9 for both traits up until 125 DIM although they tended to drop sharply after 140 d in primiparous cows and after 130 d in multiparous cows. These genetic correlations dropped to as low as 0.66 for gRFI and to 0.75 for gFS, both at 200 DIM.

Summary of Analyses Based on the Use of Weekly Data and Genomic Information

We briefly summarize similar analyses based on the use of weekly interpolated data, again using only pedigree information for genetic modeling, in Supplemental Figures S5 to S12 provided in Supplemental File S3 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022). In general, heritabilities for MilkE and DMI were slightly higher for analyses of weekly (Supplemental Figure S5) as opposed to daily data for primiparous cows whereas weekly based estimates for gRFI were substantially higher ranging from 0.05 to 0.22 in primiparous cows and from 0.12 to 0.18 in multiparous cows (Supplemental Figure S6). Similarly, weekly gFS had higher heritabilities, ranging from 0.15 to 0.32 in primiparous cows and from 0.23 to 0.25 in multiparous cows. Trajectories on estimated herita-

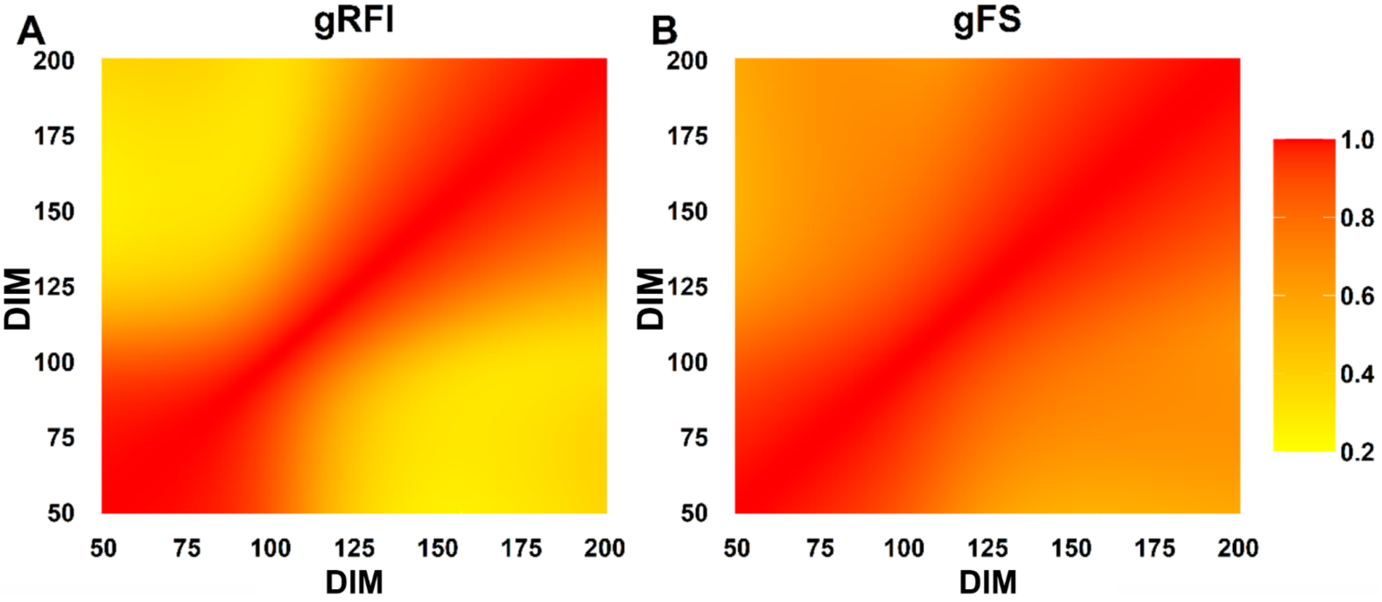

Figure 7. Estimated genetic correlations between days for genetic residual feed intake (gRFI; A) and genetic feed saved (gFS; B) for multiparous cows between 50 and 200 DIM.

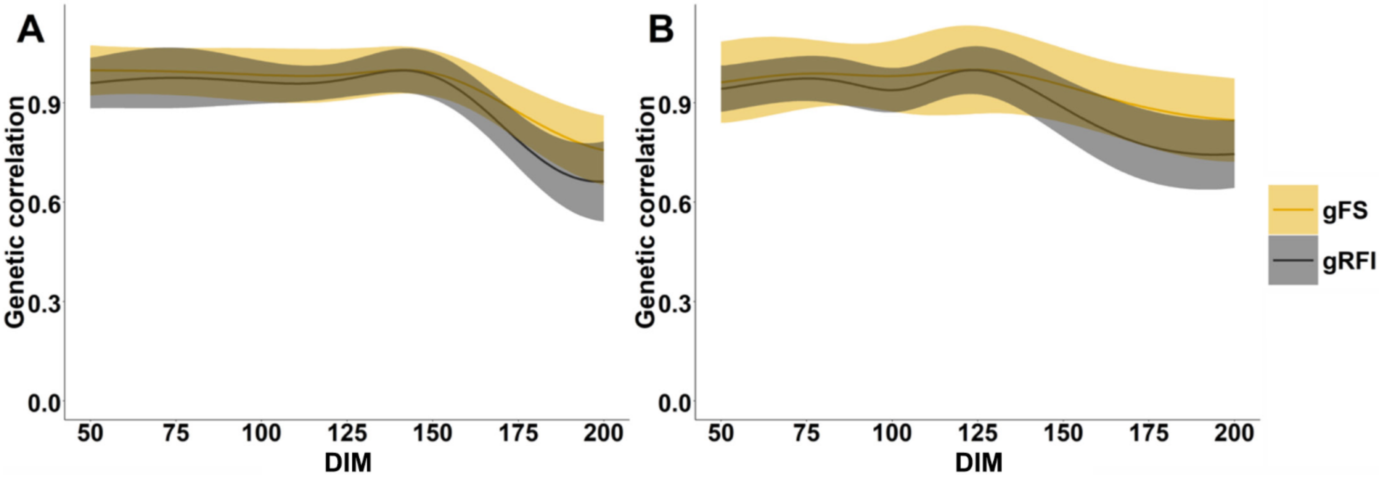

Figure 8. Estimated genetic correlation of genetic feed saved (gFS) and genetic residual feed intake (gRFI) with average residual feed intake and feed saved over 50 to 200 DIM for primiparous (A) and multiparous (B) cows. Lines represent REML estimates with bands representing asymptotic sampling-based SE on those estimates.

bilities across DIM were particularly different for DMI, gRFI, and gFS, all showing a downward trend with weekly data as opposed to daily data. Partial genetic regression coefficients involving MBW were slightly higher using weekly as opposed to daily data whereas partial genetic regression coefficients involving analysis of weekly MilkE were of comparable magnitude to those based on daily data (Supplemental Figure S7). Inferences on partial genetic regressions involving dMBW using weekly data were rather erratic whereas partial phenotypic regression coefficients were similar to those determined for daily data (Supplemental Figure S8). Genetic correlations between DIM for the 3 core traits tended to be substantially higher with weekly data (Supplemental Figures S9 and S10) compared with daily data with similar observations being made for gRFI and gFS (Supplemental Figures S11 and S12).

We also used pairwise bivariate genomic analyses to determine the same genetic parameters as we did with the pedigree analysis. Key results from those analyses along with the brief description of methods are presented in Supplemental File S4 (https://doi.org/10.6084/m9.figshare.17291225; Khanal et al., 2022). In all cases, estimated genetic parameters were remarkably similar to those provided based on the pedigree-based analysis. Due to the increased complexity of averaging estimates and hence, average standard errors across the various pairwise bivariate analyses, approximate standard errors were not provided in the corresponding figures.

DISCUSSION

The use of RFI in genetic evaluations has been typically determined using a 2-stage modeling process (Tempelman et al., 2015) whereby DMI is regressed on energy sinks (MilkE, MBW, dMBW, or dBW) to derive a pRFI. This process typically requires continuous recording of these traits over various periods of time (e.g., weekly, monthly) or the use of interpolated data for traits (e.g., BW) that are recorded much less frequently. Any use of interpolated data potentially leads to a differential understating of uncertainty for RFI determinations. Furthermore, the 2-stage classical regression approach to RFI modeling (Tempelman et al., 2015) does not facilitate the use of data on cows when one or more of the core traits defining RFI is completely missing.

To sustain reliable future genetic evaluations of RFI or FS, it is important to develop quantitative genetic analyses strategies that use as much reliable DMI data as are available under a wide range of representative production environments. We have pursued a MTRR analysis in this paper to model genetic variability in feed efficiency traits such as gRFI and gFS, as well as its core traits, DMI, MBW, and MilkE, across a lactation. From a modeling perspective, the MTRR model has a substantial advantage over the classical regression approach in that it more elegantly incorporates the use of sparsely recorded daily data. The recent modeling developments outlined in Islam et al. (2020) further facilitate the direct incorporation of instantaneous dMBW or dBW, at least from a genetic regression perspective, while accounting for the uncertainty due to highly variable differences in recording frequencies for BW. Whether the model includes dMBW or dBW is inconsequential because MBW is almost a linear function of BW over the normal range of Holstein cow BW (Tempelman and Lu, 2020).

The genetic regression implied with the use of the MTRR is more appealing than phenotypic regression used to derive pRFI for several reasons. First, gRFI is a trait constructed to be genetically uncorrelated with MBW, MilkE, and dMBW such that direct selection on gRFI should not lead to unintended consequences on these energy sinks. Furthermore, phenotypic regression used to derive pRFI conflates nongenetic relationships with genetic relationships between traits whereas we are only concerned with the latter for genetic selection.

The use of MTRR modeling requires special care and relatively large data sets to be able to ensure convergence and reliable estimates. As one example, an earlier analysis of a subset of the data set used in this study was provided in Tempelman et al. (2015) whereby only a random intercept for additive genetic effects was fitted. In other recent cases, only random intercept and linear coefficients have been fitted (e.g., Islam et al., 2020). The true genetic variability across lactation for some traits might be simple enough to capture with random intercepts or with random intercepts plus random linear regressions. Higher-order random regressions are often not fitted because of convergence problems or because these terms are deemed to be not significant in small data sets. Based on likelihood ratio tests involving univariate analyses on our own data (results not reported), we determined that up to second-order random regression specifications were sufficient for additive genetic effects on all 3 core traits but that third-order random regression specifications for permanent environmental effects might be worth pursuing. However, we were not able to successfully able to model beyond second order for both sets of random effects in a multiple-trait setting.

If one specified only up to a linear random coefficient on genetic effects for MBW, the genetic merit for dMBW on a cow would be defined to be the same for any interval of the same length because of the use of first differences. Specifying only random intercepts for MBW would not allow modeling of dMBW. Although we were able to fit up to a second-order random regressions on both additive and permanent environmental effects for all 3 core traits, the implications of specifying only up to first order terms are probably less serious for more "linear" portions of the lactation curve (i.e., 50–200 DIM) or if primary attention is focused on lactation-wise genetic merit across the test period. Another often overlooked aspect of MTRR is the asymptotic correlations of the variance component estimates as derived from the average information matrix. For example, we discovered (results not reported) using the AVC matrix that the asymptotic correlations between the additive genetic (**a**) with the permanent environmental effects (**p**) for their respective variance component estimates of intercept, linear, and quadratic terms for MBW as well as of intercepts for MilkE and DMI were all less than −0.80. This implies, for example, that if one failed to model the quadratic variance component for **p** on a particular trait, the corresponding quadratic variance component estimate for **a** would likely be inflated for that same trait. Other energy sinks (e.g., BCS and its change) might be accounted for in deriving gRFI although that would also potentially exacerbate convergence problems in a MTRR.

Our estimates for heritabilities for the component traits of gRFI and gFS are well within the range of other recent feed efficiency studies conducting various forms of random regression analyses even though such studies typically involved substantially smaller numbers of cows from other breeds or countries. For example, weekly heritability estimates of BW are typically moderate to high (0.49–0.72) as previously reported by Li et al. (2018) and Islam et al. (2020) although Manzanilla Pech et al. (2014) reported lower estimates ranging from 0.25 to 0.48. Similarly, our range of heritability estimates (0.23–0.28) for DMI fell well within the range (0.18–0.40) reported in recent previous studies (Manzanilla Pech et al., 2014; Liinamo et al., 2015; Negussie et al., 2019; Islam et al., 2020). Finally, our heritability estimates (0.30–0.38) for MilkE in primiparous cows not only fell within the range of those recently reported (Islam et al., 2020; Manzanilla Pech et al., 2014; Negussie et al., 2019) but also generally demonstrated a similar trajectory with a slight rise in estimates from earlier to later stages of lactation. Our near-zero estimates of daily heritabilities for dMBW agreed with conclusions drawn from Lu et al. (2015) and from Islam et al. (2020) although the latter did report estimates of weekly heritabilities approaching as high as 0.05.

Our heritability estimates for the analysis of daily gRFI were slightly lower compared with those previously reported (Islam et al., 2020) including an earlier study using a subset of our own data (Tempelman et al., 2015). Yet all of these studies were based on the use of weekly data which we have demonstrated tends to lead to somewhat higher heritability estimates compared with the use of daily data. Although analyzing daily data from a substantially smaller data set involving Nordic Red cows, Negussie et al. (2019) determined that estimated heritabilities of pRFI can approach as low as 0.07. Our estimated heritabilities for gRFI based on the use of weekly data closely followed estimates on pRFI from Li et al. (2017) also derived from weekly data. To our knowledge, nobody has previously conducted a study involving a random regression analysis involving FS.

Our daily data-based estimates for within-trait genetic correlations between DIM for the core traits of

feed efficiency were generally rather high relative to previous studies. Negussie et al. (2019) found that genetic correlations for each of DMI, MilkE, and RFI across DIM deviated substantially from unity. Negussie et al. (2019) specifically found that genetic correlations between early and later lactation DMI became negative after DIM 160 and onwards, suggesting that DMI at the early stages of lactation is a weak predictor of the trait at mid or late stages of lactation. Manzanilla Pech et al. (2014) determined that DMI within early lactation tended to have low genetic correlations with DMI in mid to late lactation with correlations being as low as −0.5. In spite of what we observed for the core traits, our estimates of genetic correlations between gRFI across DIM suggest that gRFI may be a different trait between 50 and 200 DIM given a near-zero genetic correlation, especially for primiparous cows. Our results also agree with those provided by Li et al. (2017), in which they determined genetic correlations between DIM approaching as low as −0.29 for gRFI in Danish Holstein cows although their study involved a wider range of DIM than what we studied.

Our genetic regression coefficients were rather erratic compared with those previously reported in Islam et al. (2020). A couple of reasons may explain these differences. First, our estimated heritabilities for DIM-specific dMBW were very close to zero whereas Islam et al. (2020) estimated heritabilities for dBW as high as 0.05. A higher heritability on dMBW should lead to a more stable and less erratic genetic partial regression coefficients on dMBW. Second, Islam et al. (2020) did not model variance components for quadratic coefficients on **p** but did so for **a** which could have contributed to the larger heritability, given the strongly negative asymptotic correlation between estimates of quadratic variance components of **a** and **p** as previously noted from our own analyses. Our estimated phenotypic partial regression coefficients of DMI on MilkE were remarkably similar in trend to those reported both by Li et al. (2017) and Islam et al. (2020) for energy corrected milk whereby the coefficients monotonically increased from earlier to later stages of lactation. Both studies partly attributed this trend to the potential effect of pregnancy which should be modeled in future studies. The partial phenotypic regression coefficients for MBW and for MilkE were comparable in magnitude to those based on a classical regression approach (Tempelman et al., 2015). However, those for dMBW are not comparable since, as noted previously, the dMBW “covariates” are expressed relative to average trends modeled by the fixed effects (i.e., environmental subclasses and fifth order polynomial on DIM) on MBW. This is further illustrated in results from Islam et al. (2020) who also estimated negative albeit small partial phenotypic regression coefficients on dBW at various stages of lactation, again because of the adjustment for fixed effects.

Given the heterogeneity in heritabilities, genetic correlations, and partial genetic regression coefficients across the test period, it seems prudent to focus attention on selection for lactation-wise genetic merit. The lactation-wise heritabilities were generally substantially greater than the corresponding DIM-specific heritabilities. Even dMBW was estimated to have a substantial heritability exceeding 0.10 such that it would have a meaningful effect in determining lactation-wise gRFI or gFS. Heritabilities of lactation-wise (or averaged) measures should be greater than heritabilities of their individual daily components, as we noted for comparing weekly to daily data, especially if the genetic and permanent environmental correlations between different DIM for the corresponding trait deviate substantially from unity. Negussie et al. (2019) similarly estimated a lactation-wise heritability of 0.33 for DMI in Nordic Red cows, whereas Manzanilla Pech et al. (2014) reported a lactation-wise heritability of 0.46 for DMI on Dutch Holsteins which was also much higher than their corresponding weekly heritabilities. Given the low genetic correlations involving individual days between 150 and 200 DIM with the remainder of the 50 to 200 DIM test period for gRFI and the low numbers of records within the later DIM range in our study, more data should be collected within later stages of lactation.

We focused the presentation of our results using only pedigree information given that we were not able to fit more than 2 traits at one time using genomic information in a MTRR. Nevertheless, based on the remarkable similarity between the pedigree- and genomic-based results, the estimated variance components from a pedigree-based analysis could be readily ported over to a genomics based analyses thereby avoiding computationally intensive genomics based variance component estimation. Forni et al. (2011) generally found little difference in estimated variance components using pedigree versus genomics information, but determined that standard errors for pedigree-based estimates would be slightly larger than those based on genomics. Hence our genomic-based estimates in Supplemental File S4 should be anticipated to have smaller standard errors than the pedigree-based standard errors reported in this paper. The APY algorithm (Misztal, 2016) may also provide an option for computationally feasible estimation of variance components using genomics in MTRR.

To obtain more data from commercial dairy environments, we anticipate that sensor information may someday be used as a proxy for individual cow intakes. Sensor data might be down-weighted accordingly rela-

tive to actual DMI measurements, similar to what is currently done for MY based on different DHIA sampling protocols in the United States. From a national genetic evaluation perspective, implementation of a modified best prediction strategy (VanRaden, 1997) may be a suitable alternative to MTRR in developing a more stable gRFI and gFS that best reflects the heterogeneity in genetic parameters across a lactation yet recognizes the heterogeneity between different sampling protocols for the core traits and their generally higher heritabilities on a lactation-wise basis. Heterogeneity of variances and partial regression coefficients does exist across environments (Tempelman et al., 2015) and may need to be additionally accounted for by first standardizing the data in some manner or pursuing computationally intensive analyses to take account for such heterogeneities (Lu et al., 2017). It may be more feasible to alter the best prediction strategy accordingly based on inferring environment-specific regression relationships between DMI and energy sink traits.

CONCLUSIONS

We conducted a MTRR analysis involving the core traits of feed efficiency, namely DMI, MBW, and MilkE, to dynamically determine genetic parameters for these traits as well as gRFI and gFS separately for primiparous and multiparous cows. This analysis also facilitates a more elegant strategy for estimating lactation-wise heritabilities across the 50 to 200 DIM test period, taking into account the heterogeneity in parameters across lactation. The MTRR model not only allows for a formal inquiry into changes in genetic parameters (i.e., heritabilities) across lactation but will potentially allow the use of sparsely recorded data on DMI which may need to be increasingly used to sustain future genetic evaluations of RFI and FS. Although estimated heritabilities of lactation-wise gRFI were near those of previous studies (0.25 for primiparous cows and 0.17 for multiparous cows), genetic correlations were estimated to be as low as 0.05 between 50 and 200 DIM for gRFI in primiparous cows. Nevertheless, genetic correlations between any daily gRFI with lactation-wise gRFI were never less than 0.66. Greater effort should be made to collect records on DMI on cows across broader periods of the lactation.

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