

# Genetic properties of feed efficiency and related traits in dairy cattle

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## Abstract

Feed accounts for the largest part of operating costs in dairy production. Improving feed efficiency (FE) is expected to increase the profits of dairy farmers and to reduce the ecological footprint of dairy production. The aim of the thesis was to study the genetic properties of alternative FE definitions and FE-related traits in several dairy breeds, to investigate the possibility of including FE into Nordic dairy cattle breeding.

In Papers I-IV, two important FE traits, dry matter intake (DMI) and residual feed intake (RFI), were studied to investigate the genetic properties of these traits across lactation and across breeds. In Paper I and II, genetic parameters for DMI, energy-corrected milk (ECM) and body weight (BW) across lactation were studied for Holstein, Nordic Red (RDC), and Jersey cows. The genetic heterogeneity of DMI, ECM and BW across lactation and the genetic correlations between these traits were studied by random regression models in Paper II. Paper III and Paper IV focused on alternative modelling methods for RFI. In Paper III, the influence of lactation stages in modelling RFI was investigated. In Paper IV, multivariate analyses were used as a novel way to derive RFI in dairy cattle.

We found moderate heritability for DMI in Holstein, RDC and Jersey cows. The heritability for DMI was in a similar range to that for ECM and was lower than that for BW. DMI was in positive genetic correlations with ECM and BW across lactation. Cows of different breeds generally shared a similar pattern of genetic parameters of DMI. Different modelling strategies for RFI affected the genetic properties of RFI and gave different rankings of animals for efficiency. The genetic variance and heritability for RFI were lower than those for DMI. Genetically, DMI or RFI was not the same trait across lactation. The genetic heterogeneity for DMI and RFI across lactation should be carefully considered in the recording and selection for FE in dairy cattle.

*Keywords:* feed efficiency, dairy cattle, genetic heterogeneity, genetic parameter, random regression model

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## Genetic properties of feed efficiency and related traits in dairy cattle

### Sammendrag

Foder udgør den største del af driftsomkostningerne i mælkeproduktionen. Forbedring af fodereffektiviteten (FE) forventes at øge mælkeproducenternes overskud og reducere mælkeproduktionens klima og miljøbelastning. Formålet med afhandlingen var at studere de genetiske parametre ved alternative FE-definitioner og FE-relaterede egenskaber hos flere malkekvægracer for at undersøge muligheden for at inddrage FE i nordisk kvægavl.

I artiklerne I-IV blev to vigtige FE-egenskaber, tørstofindtag (DMI) og residual-foderoptagelse (RFI) undersøgt for genetiske variation i og mellem egenskaber på tværs af laktation og på tværs af racer. I artikel I og III blev genetiske parametre for DMI, energikorrigeret mælkeydelse (ECM) og legemsvægt (BW) på tværs af laktation undersøgt hos Holstein, Nordic Red (RDC) og Jersey køer. Udviklingen i den genetiske variation af DMI, ECM og BW på tværs af laktation og de genetiske korrelationer mellem disse egenskaber blev undersøgt ved hjælp af modeller med tilfældige regressioner i artikel III. Artikel II og artikel IV fokuserede på alternative statistiske modeller for RFI. I artikel II blev indflydelsen af laktationsstadier på RFI varianskomponenter undersøgt. I artikel IV blev multivariate analyser brugt som en ny måde at udlede RFI i malkekvæg.

Vi fandt moderat arvelighed for DMI i Holstein, RDC og Jersey køer (Artiklerne I-IV). Arvbarheden for DMI var i et lignende område som for ECM og var lavere end for BW. DMI var positivt genetisk korreleret med ECM og BW på tværs af laktationsstadie. Køer af forskellige racer viste generelt et lignende mønster af genetiske parametre af DMI. Forskellige modelleringsstrategier for RFI påvirkede RFI's genetiske egenskaber og gav forskellige rangeringer af køer i forhold til effektivitet. Den genetiske varians og arvelighed for RFI var lavere end for DMI. Genetisk var DMI eller RFI ikke den samme egenskab på forskellige laktationsstadier. Den genetiske heterogenitet for DMI og RFI på tværs af laktationen bør inddrages ved avlsværdiurdering for FE hos malkekvæg.

*Nøgleord:* foder effektivitet, malkekvæg, genetisk heterogenitet, genetisk parameter, tilfældig regression model

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# Dedication

To all who has helped me on my way to grow up, especially to my father.

*This is the short and long of it.*

William Shakespeare

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## List of publications

This thesis is based on the work contained in the following papers, referred to by Roman numerals in the text:

- I Li, B. \*, Fikse, W. F., Lassen, J., Lidauer, M. H., Løvendahl, P., Mäntysaari, P., Berglund, B. (2016). Genetic parameters for dry matter intake in primiparous Holstein, Nordic Red, and Jersey cows in the first half of lactation. *Journal of Dairy Science*, 99(9), pp. 7232–7239.
- II Li, B. \*, Fikse, W. F., Løvendahl, P., Lassen, J., Lidauer, M. H., Mäntysaari, P., Berglund, B. (2018). Genetic heterogeneity of feed intake, energy-corrected milk and body weight across lactation in Holstein, Nordic Red, and Jersey cows (Accepted in *Journal of Dairy Science*, June 25<sup>th</sup>, 2018)
- III Li, B. \*, Berglund, B., Fikse, W. F., Lassen, J., Lidauer, M. H., Mäntysaari, P., Løvendahl, P. (2017). Neglect of lactation stage leads to naive assessment of residual feed intake in dairy cattle. *Journal of Dairy Science*, 100 (11), pp. 9076-9084.
- IV Li, B. \*, Berglund, B., Løvendahl, P., Lassen, J., Lidauer, M. H., Mäntysaari, P., Fikse, W. F. Deriving residual feed intake from covariance functions of dry matter intake, energy corrected milk, and metabolic body weight in Holstein dairy cattle across lactation (manuscript)

Papers I-III are reproduced with the permission of the publishers.

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The contribution of Bingjie Li to the papers included in this thesis was as follows:

- I Contributed in data collection and management, performed the statistical analyses, and wrote the paper with regular input from the co- authors.
- II Contributed in data management, performed the statistical analyses, and wrote the paper with regular input from the co-authors.
- III Contributed in data management, performed the statistical analyses, and wrote the paper with regular input from the co-authors.
- IV Contributed in data collection and management, performed the statistical analyses, and wrote the paper with regular input from the co-authors.

## Abbreviations

BCS	body condition score
BW	body weight
$\Delta$ BW	change of body weight
DM	dry matter
DMI	dry matter intake
EB	energy balance
EBV	estimated breeding value
ECM	energy-corrected milk
FE	feed efficiency
GBLUP	genomic best linear unbiased prediction
MBW	metabolic body weight
MY	milk yield
RDC	Nordic Red cattle
REI	residual energy intake
RFI	residual feed intake



# 1 Introduction

Improving feed efficiency (FE) of dairy cattle has been a major interest of dairy farmers and researchers over decades. Increasing the FE of dairy cattle needs to be achieved by an interdisciplinary effort of animal genetics and breeding, nutrition, and management. The FE of a dairy cow is influenced by diet, genetic ability and physiological state of the cow. Among all these factors, genetic abilities of cows for FE are expected to play an important part in improving efficiency for the whole dairy cattle population and also for the next generations of dairy cows. In this thesis, we will focus on the genetic aspects of improving FE of dairy cattle.

One of the first reports on the inheritance of the efficiency of feed utilization in dairy cattle was published in the 1930s with 42 Holsteins and Jersey (Smith and Rice, 1934). After 1950s, several papers on the genetic aspects of FE were published, aiming to estimate genetic parameters for gross efficiency (ratio of milk yield per unit of feed intake). In general, these earlier genetic studies on FE were limited to very small data sets, due to the difficulty in recording feed intake for individual animals.

Over the last 60 years, milk production per unit of body weight (BW) has doubled, so efficiency has been improved because of the dilution of the maintenance requirements (Pryce et al., 2018). Meanwhile, the number of FE records in dairy cattle has been gradually accumulated within each country, mainly in research herds, making it possible to launch genetic analyses for FE with larger data sets. Recent studies on FE in dairy cattle have covered several important topics, including genetic variation and genetic parameter estimation, genomic evaluation, and genome-wide association study for FE (e.g., Berry et al., 2014; de Haas et al., 2015; Lu et al., 2018). Alternative FE definitions have been investigated in order to properly define FE in dairy cattle (Lu et al., 2015; Pryce et al., 2015; Hurley et al., 2017; Li et al., 2017). However, it still remains controversial on which trait should be used to properly represent or measure FE in practice.

Another challenge is to obtain sufficient genetic information in non-Holstein populations for FE. Recent genetic studies of FE have mostly focused on Holstein cows (Berry et al., 2014; de Haas et al., 2015). Breeds other than Holstein, e.g., Jersey and Nordic Red (RDC), are economically important breeds globally and locally, and may offer important genetic information with respect to FE. Studies of the genetics of FE in the 1980s demonstrated between-breed or selection-line variation in feed intake as the first impression of genetic differences in feed consumption (Korver, 1988). Due to considerable genetic progress, the results from old studies may no longer be fully relevant to modern high-genetic-merit dairy populations (Liinamo, Mäntysaari and Mäntysaari, 2012). Good knowledge of the genetic variation for FE-related traits in multiple dairy breeds would benefit diverse selection purposes in dairy production, e.g., multi-breed genetic evaluation.

Facing the importance, opportunities as well as the challenges of improving FE in dairy cattle breeding, international collaborations have been established in order to set up joint data sets for genetic studies of FE (Berry et al., 2014; de Haas et al., 2015; Manzanilla-Pech et al., 2016). In Nordic countries, a joint data set of feed efficiency in dairy cattle has been established since 2013, aiming to investigate the genetic variation for FE in dairy cattle and to assess the possibility of including FE in the Nordic genetic evaluation of dairy cattle.

## 1.1 Importance of feed efficiency in dairy breeding

Feed efficiency has implications for farm profitability and the environment. In recent years, the topic of FE is on the tip of every dairy producer's tongue, since the feed accounts for the largest part of operating costs in dairy production (European Commission, 2014). Improving FE in dairy production is expected to increase the profits of dairy farmers without sacrificing milk production or animal health. In addition, improving FE in cattle is also expected to help lower methane emission (de Haas et al., 2011). Methane (CH<sub>4</sub>) contributes to global warming, being one of the most important greenhouse gas (Knapp et al., 2014). Improving FE in dairy production could have implications for greenhouse gas mitigation (Wall, Simm and Moran, 2010).

## 1.2 Definitions of feed efficiency in dairy cattle

Feed efficiency in dairy cattle is a broad concept with multiple definitions. In general, defining FE in lactating dairy cows is more complicated than defining

FE in growing animals due to the metabolic changes that occur during lactation cycles (Berry and Crowley, 2013). In early lactation, the milk production of dairy cows increases more sharply than feed intake, and body reserves need to be mobilized to meet the energy demand (Berglund and Danell, 1987; Banos and Coffey, 2009; Roche et al., 2009). After the early lactation stage, the feed intake of cows is kept at a relatively high level and body reserves are gradually restored (Mao et al., 2004; Vallimont et al., 2010). During lactation cycles, the complexity of metabolic change in dairy cows needs to be considered in defining FE of dairy cattle.

In this thesis, three categories of FE definition traits are mainly studied and discussed: Feed intake, gross efficiency, and residual feed intake.

### 1.2.1 Feed intake

Feed intake is the key component of all available FE traits in dairy cattle. Feed intake can be defined as the mass of dry matter intake, feed energy intake, and possibly a form of feed costs, and so on. Feed intake has been proposed as a FE candidate trait in the breeding goal (Veerkamp et al., 2014). Ideally, we would like to select for efficient animals that have less feed intake compared to inefficient animals for a certain level of production and a certain cow size, and without sacrificing the fertility and health of the efficient animals. Currently, measurement of feed intake for individual cows is mainly available in research or nucleus herds. Insufficient recording of feed intake, in large part due to high cost, has hindered accurate genetic analyses for feed intake.

### 1.2.2 Gross efficiency

In gross efficiency, a cow's efficiency is calculated from the ratio of milk output to feed intake input (i.e. milk output / feed input). For several years, gross efficiency has been widely studied as a definition of FE in dairy cattle. Cows with higher gross efficiency are considered as efficient animals that are able to efficiently convert feed nutrients into milk production. How to define milk outputs and intake inputs leads to several definitions of gross efficiency. Milk outputs can be defined as milk yields, milk energy, milk fat or protein yields, or can be directly defined as a certain form of milk income, and so on. Feed inputs can be defined as the mass of dry matter intake, feed energy intake, and possibly a form of feed costs, and so on. There are several limitations of using gross efficiency as a FE trait in dairy cattle breeding, which will be discussed in detail in the general discussion section of this thesis.

### 1.2.3 Residual feed intake

Residual feed intake (RFI) has been widely studied in pig, chicken, beef cattle, and dairy cattle as one proposed FE trait (Berry and Crowley, 2013; Wolc et al., 2013; Patience, Rossoni-Serão and Gutiérrez, 2015; Tempelman et al., 2015). RFI is defined as the difference between an animal's actual feed intake and its expected feed intake based on energy requirements for production and maintenance (Koch, Chambers and Gregory, 1963). Animals with low RFI values are considered as more efficient animals. Residual energy intake (REI) is a similar concept to RFI, but REI is derived based on the energy intake of the feed instead of dry matter intake (DMI).

In dairy cattle, RFI can be defined in several different ways. A popular way of defining RFI in dairy cattle is based on an energy sink model where cows' actual feed intake is linearly regressed on cows' energy sinks (e.g., milk production, body weight (BW), change of BW ( $\Delta$ BW)) (VandeHaar et al., 2016). The residuals from the energy sink model are the phenotypes for RFI that are used in genetic analyses for RFI. This definition of RFI is based on linear regressions of DMI on energy sinks, where feed intake is phenotypically adjusted for energy sink traits. However, RFI defined in this way is still genetically correlated with energy sink traits (e.g., milk production, BW,  $\Delta$ BW), because the adjustment of energy sinks is only done at phenotypic level. In addition, the commonly used RFI model employs constant partial regressions of feed intake on energy sinks. Considering the complexity of the metabolic changes of cows across lactation, it is possible that the partial regression coefficients of feed intake on milk production, body maintenance, and  $\Delta$ BW could vary across lactation. Therefore, the general RFI model with constant partial regression coefficients of feed intake on energy sinks might not always hold for the entire lactation period, which might influence the estimation of RFI. Most previous studies corrected for the influence of lactation stages on RFI by using a systematic effect of days in milk (DIM) or lactation week on feed intake, or by including random regression terms in the model for the influence of lactation stage on cow random variances (Mäntysaari et al., 2012; Hardie et al., 2015; Tempelman et al., 2015). However, these commonly-used corrections of lactation stages on RFI have ignored the potential influence of lactation stage on the partial regression coefficients of feed intake on energy sinks. It is then interesting to investigate if the partial regression coefficients of feed intake on milk production, body maintenance, and  $\Delta$ BW could vary across lactation, and its potential influence in modelling RFI in dairy cattle.

An alternative definition of RFI is to derive RFI that is genetically adjusted for the major energy sinks (e.g., milk yield, BW), so that RFI is genetically



uncorrelated with major energy sink traits. In dairy cattle breeding, it is of interest to define RFI that is genetically uncorrelated with the major energy sink traits (e.g., milk yield, BW). Milk production traits and BW-related traits are often part of the total merit index traits in dairy cattle evaluation. After removing the genetic correlations of RFI with milk production and BW, RFI becomes a more independent trait representing FE in the selection index. In pig breeding, Strathe et al., (2014) proposed a method of deriving RFI from covariance functions of DMI, BW, and rate of gain from multivariate random regression analyses, where they genetically adjusted DMI for BW and rate of gain. Lu et al., (2015) applied a similar method of multivariate modelling for RFI to dairy cattle, where random regression analyses were not applied to model RFI since they assumed a constant genetic variance for RFI across lactation.

### 1.3 Genetic variation and parameters for feed efficiency in dairy cattle

Genetic variation for feed intake has been widely studied in dairy cattle (e.g., Korver, 1988; Berry et al., 2014; Manzanilla-Pech et al., 2016). In Holstein cows, heritability estimates for DMI were reported ranging from 0.04 to 0.54 (e.g., Veerkamp and Thompson, 1999; Butchereit et al., 2011; Berry et al., 2014). Heritability was found to vary along lactation, and a low genetic correlation was reported for DMI between early lactation and the rest of lactation (e.g., Huttmann et al., 2009; Manzanilla Pech et al., 2014; Tetens, Thaller and Krattenmacher, 2014). Feed intake was found to be positively correlated with milk yield (Veerkamp, 1998; Vallimont et al., 2010; Manzanilla-Pech et al., 2016). Apart from Holsteins, genetic studies on DMI in other dairy cattle breeds are relatively rare and based on small data sets (Sondergaard et al., 2002; Liinamo, Mäntysaari and Mäntysaari, 2012). Nordic Red was studied by Liinamo, Mäntysaari and Mäntysaari (2012) using 291 primiparous cows, and the heritability for DMI was estimated to range from 0.18 to 0.33 within lactation week 2 to 30, with large standard errors of estimates. Gaps remain in the genetic parameter estimation for DMI in other dairy cattle breeds (e.g., Jersey).

For RFI, evidence from previous studies suggests that some variation in residual feed intake is under genetic control (Veerkamp, 1998; Coleman et al., 2010). Heritability estimates for RFI in dairy cattle were reported ranging widely from 0.00 to 0.38 (Berry and Crowley, 2013; Tempelman et al., 2015; Manzanilla-Pech et al., 2016; Li et al., 2017). A recent study showed a low genetic correlation for residual energy intake between early lactation and

lactation week 20 in Nordic Red cows (Liinamo et al., 2015). When RFI was derived from linear regressions of DMI on milk production, MBW and  $\Delta$ BW, RFI was reported to be in positive genetic correlations with milk production and BW (Manzanilla-Pech et al., 2016). When RFI was derived from multivariate analyses of DMI, milk energy and MBW, RFI was genetically uncorrelated with milk energy and MBW (Lu et al., 2015).

The heritability of gross feed efficiency was reported ranging from 0.14 to 0.47 (Vallimont et al., 2011; Manafiazar et al., 2015; Lidauer et al., 2018). The genetic correlation between gross efficiency and milk production is higher than 0.6 (Vallimont et al., 2011; Manafiazar et al., 2015; Lidauer et al., 2018). Negative genetic correlations were reported for gross efficiency with BW and with BCS (Vallimont et al., 2011; Manafiazar et al., 2015; Lidauer et al., 2018).

## 1.4 Progress and applications of feed efficiency in dairy cattle breeding

Including FE into dairy cattle breeding is of great interest globally. Due to insufficient FE data within each country, international collaborations for FE studies have been established to combine data sets for FE. Joint data sets across countries made it possible to initiate genetic and genomic evaluation for FE (e.g., de Haas et al., 2015). Since genomic selection is well-suited for difficult-to-measure traits, like FE in dairy cattle, genomic selection has been used as an important tool to introduce FE into dairy breeding (Pryce et al., 2018). Different FE definition traits have been studied or applied for FE in dairy cattle in different countries, in order to suit to the specific breeding goals of the country.

In Australia, a trait of “feed saved” has been included as a FE trait for dairy cattle in the national selection indices of Australia since 2015 (Pryce et al., 2018, 2015). Feed saved is defined as the amount of feed that is saved through improved metabolic efficiency and reduced maintenance requirements (Pryce et al., 2015). The breeding value (EBV) of “feed saved” includes a genomic component for RFI combined with an EBV for BW predicted from type traits (Pryce et al., 2015). The mean reliability of the feed saved EBV was reported to be 37% in 4,416 genotyped Holstein sires without phenotypes (Pryce et al., 2018).

The Netherlands is the second country after Australia that have published breeding values for FE in dairy cattle genetic evaluation (Jong et al., 2016). In the Netherlands and Flanders a genetic evaluation for DMI was developed using observations on 3200 cows of which 1300 were genotyped (Jong et al.,

2016). The breeding value for DMI was based on DMI and indicator traits (milk, fat and protein yield, BW) (Jong et al., 2016). Using information of indicator traits together with DMI, reliability of breeding value for DMI for bulls was reported to be on average 59% (Veerkamp et al., 2014).

In US, RFI genetically adjusted for milk energy and BW is proposed as an FE candidate trait in selection, where EBV of milk energy and EBV of BW were used to adjust RFI. The resulting RFI is genetically uncorrelated with milk energy and BW. This definition for RFI was reported with a heritability of 0.14 (VanRaden et al., 2018). Around 4,000 US Holstein cows from research herds with RFI phenotypes were included in the national genomic evaluation for RFI, and the average theoretical reliability of genomic EBV was around 31% for the cows with phenotypes (unpublished results). The EBV for FE in dairy cattle has not been published due to the low prediction reliability.

In Nordic countries, a joint data set of feed efficiency in dairy cattle has been established among Nordic countries since 2013, aiming to investigate the genetic variation for FE in several dairy breeds in Nordic countries and to assess the possibility of including FE into Nordic dairy cattle breeding. Several genetic studies have been carried out recently in Nordic countries for FE in dairy cattle, including genetic studies on alternative FE traits, genetic parameter estimation, accuracy of genomic evaluation for DMI, and economic values for FE traits, in several dairy breeds. The current thesis work is part of the joint project “Feed Utilization in Nordic Cattle (FUNC)” among the Nordic countries (Denmark, Finland, Norway, and Sweden), aiming to investigate the genetic properties of alternative FE definitions and the possibility of including FE into Nordic dairy cattle breeding.

## 2 Aims of the thesis

The overall aim of the thesis was to study the genetic properties of alternative feed efficiency (FE) definitions and FE-related traits in dairy cattle, in order to investigate the possibility of including FE into Nordic dairy cattle breeding. More specifically, the aims of the thesis were to investigate:

- genetic parameters of dry matter intake (DMI) in Holstein, Nordic Red, and Jersey cows across lactation (*Paper I, Paper II*)
- genetic relationships of DMI with milk production and body weight (BW) in dairy cattle (*Paper II*)
- genetic heterogeneity of DMI, energy-corrected milk (ECM), and BW across the entire lactation in dairy cattle (*Paper II*)
- genetic properties of residual feed intake (RFI) and the influence of lactation stages on estimating RFI (*Paper III, Paper IV*)
- alternative modelling strategies for RFI in dairy cattle (*Paper III, Paper IV*)

### 3 Summary of Investigations

This thesis consists of four studies presented in Papers I-IV. The animals included in Papers I-IV were from the Nordic joint data set of FE recordings in dairy cattle. The original data set consisted of 199,645 weekly records of DMI, ECM, and BW across lactation for 3,258 dairy cows across breeds and lactations. The data sizes of FE were larger in Paper II and Paper IV, compared to Paper I and Paper III, since more FE data were recorded and included over time. The studied cows came from six research herds in Denmark, Finland, and Sweden, located at the Danish Cattle Research Center (DCRC, Foulum) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle) in Denmark; at the Natural Resources Institute Finland previous research herd (Rehtijärvi, Jokioinen) and current research herd (Minkiö, Jokioinen) in Finland; and at the Swedish University of Agricultural Sciences previous research herd Kungsängen (Kungsängen, Uppsala), and the current research herd Lövsta (Lövsta, Uppsala), and Öjebyn research herd (Öjebyn) in Sweden. The studied cows calved between 1991 and 2015 for Holstein cows, between 1994 and 2015 for RDC cows, and between 1995 and 2015 for Jersey cows. The cows were involved in some nutrition experiments within research herds. The feeding and milking information in the trials have been described in detail in previous studies (Mäntysaari, Nousiainen and Huhtanen, 2003; Mäntysaari and Mäntysaari, 2015; Nielsen et al., 2003; Løvendahl, Ridder and Friggens, 2010; Løvendahl and Chagunda, 2011; Andrée O'Hara et al., 2018). Feed offered to cows and feed refusals were measured individually to calculate the feed intake per cow. The DM contents in forage and concentrates were analysed regularly, and the compositions were aligned and merged with feed intake records to obtain daily DMI values per cow. A weekly average DMI per cow was calculated as the average of daily DMI records in each lactation week. A weekly observation of average daily milk yield per cow was also obtained from the average of daily milk yield records per cow in each week. Milk samples were taken regularly for analyses of fat, protein, and lactose content

(Mäntysaari, Nousiainen and Huhtanen, 2003; Løvendahl, Ridder and Friggens, 2010; Andrée O'Hara et al., 2018). The average daily ECM (kg) per cow in each lactation week was calculated from average daily milk yield (kg) and milk composition (g/kg) using the formula by Sjaunja et al. (1990):  $ECM (kg) = \text{milk yield (kg)} \times [(38.30 \times \text{fat content (g/kg)} + 24.20 \times \text{protein content (g/kg)} + 16.54 \times \text{lactose content (g/kg)} + 20.7)/3,140]$ . Cows were weighted on a weekly basis in some research herds. In other research herds cows were automatically weighted at each milking so that BW records were averaged to obtain a weekly record of BW per cow in each week (Mäntysaari, Nousiainen and Huhtanen, 2003; Mäntysaari and Mäntysaari, 2015; Nielsen et al., 2003; Løvendahl, Ridder and Friggens, 2010; Andrée O'Hara et al., 2018).

In Papers I-IV, two important FE candidate traits, DMI and RFI, were studied to investigate the genetic properties of these FE traits across lactation and across breeds. In Paper I and Paper II, genetic parameters for DMI, ECM, and BW were studied across lactation for primiparous cows of three dairy breeds: Holstein, Nordic Red (RDC), and Jersey. The genetic heterogeneity of the traits of DMI, ECM, and BW across lactation, and the genetic correlations between DMI, ECM, and BW were studied in Paper II. Paper III and Paper IV focused on alternative modelling methods for RFI, using only Holstein cows in the studies. In Paper III, the influence of lactation stages in modelling RFI was investigated. In Paper IV, a multivariate modelling strategy for deriving RFI was studied, as a novel way of deriving RFI in dairy cattle.

The detailed information on the material and methods, and the main findings for each paper are described below.

### 3.1 Genetic parameters for dry matter intake in primiparous Holstein, Nordic Red, and Jersey cows in the first half of lactation (Paper I)

The objective of this paper was to estimate the genetic parameters for DMI in primiparous Holstein, Nordic Red, and Jersey cows in different lactation periods within the first 24 lactation weeks.

#### 3.1.1 Data

Data for this study consisted of 32,929 weekly DMI records from 1,656 primiparous cows (717 Holstein, 663 Nordic Red, and 276 Jersey). Cows' first calving ages ranged from 22 to 36 months. The pedigree information included 9,612, 12,762, and 2,810 individuals for Holstein, Nordic Red, and Jersey, respectively, by tracing back as many generations as possible for cows with

DMI records. Weekly DMI records for the first 24 lactation weeks were included in this study, and were grouped into six consecutive lactation periods of four weeks in length (Table 1). The number of animals and the number of DMI observations in each period are shown in Table 1.

Table 1. Description of the number of cows and the number of records in six consecutive lactation periods of four weeks in length within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Lactation week	Number of cows			Number of records		
		HOL	RDC	JER	HOL	RDC	JER
1	1 - 4	670	583	274	2,569	1,965	1,046
2	5 - 8	687	602	275	2,655	2,287	1,057
3	9 -12	670	586	262	2,572	2,199	1,013
4	13 -16	636	523	254	2,431	1,987	986
5	17 - 20	617	501	241	2,364	1,891	935
6	21 - 24	593	486	230	2,286	1,788	898

### 3.1.2 Methods

The weekly DMI from the different periods were considered as different traits. Within a period, the weekly DMI observations were considered as repeated measures of DMI for individual animals in the period. The analyses were carried out separately for each breed. Within each breed, variance components for DMI were estimated for each lactation period, using the following repeatability animal model:

$$y_{j\text{mnp}sq} = \mu + \text{Herd}_j + \mathbf{b} * \text{CalvAge} + \text{Trial}_m + \text{YS\_Rec}_n + \text{LacWk}_p + \text{Trial}_m * \text{YS\_Rec}_n + \mathbf{a}_s + \mathbf{p}_s + \mathbf{e}_{j\text{mnp}sq}$$

where  $y_{j\text{mnp}sq}$  is the weekly DMI observation within a period, where a period included up to four DMI observations for each individual cow;  $\mu$  is the overall intercept;  $\text{Herd}_j$  is the fixed effect of herd, where Holstein cows were from two herds, Jersey cows were from one herd, and Nordic Red cows were from four herds;  $\mathbf{b}$  is the regression coefficient of a linear regression on the covariable  $\text{CalvAge}$  for calving age, where the calving age ranged from 664 to 1,065 days in Holstein, from 658 to 992 days in Jersey, and from 674 to 1,094 days in

Nordic Red;  $\text{Trial}_m$  is the fixed effect of the trial where the data originated from, to adjust for the feeding difference between trials, where Holstein were in 25 trials, Jersey were in 15 trials, and Nordic Red were in 16 trials;  $\text{YS\_Rec}_n$  is the fixed effect of year-season of recording, where four seasons were defined (March to May; June to August, September to November; and December to February) ( $n= 1$  to 70 in Holstein, 1 to 48 in Jersey, and 1 to 60 in Nordic Red);  $\text{LacWk}_p$  is the fixed effect of the lactation week within period ( $p=1$  to 4);  $\text{Trial}_m * \text{YS\_Rec}_n$  is the fixed effect of the interaction between trial and year-season of recording;  $\mathbf{a}_s$  is the random additive genetic effect with  $\text{var}(\mathbf{a}) \sim \mathbf{N}(\mathbf{0}, \mathbf{A}\sigma_a^2)$ , where  $\sigma_a^2$  is the additive genetic variance and  $\mathbf{A}$  is the relationship matrix;  $\mathbf{p}_s$  is the random permanent environmental effect with  $\text{var}(\mathbf{p}) \sim \mathbf{N}(\mathbf{0}, \mathbf{I}\sigma_p^2)$ , where  $\sigma_p^2$  is the permanent environmental variance and  $\mathbf{I}$  is the identity matrix;  $\mathbf{e}_{j\text{mnp}sq}$  is the random residual with  $\text{var}(\mathbf{e}) \sim \mathbf{N}(\mathbf{0}, \mathbf{I}\sigma_e^2)$ , where  $\sigma_e^2$  is the residual variance.

The fixed effects included in the repeatability animal model were tested for significance for DMI ( $P < 0.05$ ) by PROC MIXED in SAS 9.3 (SAS Institute Inc., Cary, NC), using a mixed model including these fixed effects and a random animal effect without using pedigree relationship. Variance components, heritability and repeatability of DMI for each breed within each lactation period were estimated using the repeatability animal model by restricted maximum likelihood (REML) by ASReml 3.0 (Gilmour et al., 2009). Bivariate analyses were carried out to estimate genetic correlations for DMI between different lactation periods in each breed.

### 3.1.3 Main findings

#### *Breed Characteristics in DMI*

The shape of the mean DMI profiles within the first 24 weeks of lactation was similar between breeds (Figure 1). The DMI of cows increased after calving until around lactation week 12, and then it remained at a relatively stable level during lactation weeks 12 to 24. Holstein and Nordic Red cows had similar levels of DMI at the beginning of lactation, but later in lactation Holstein cows had a slightly higher DMI than Nordic Red cows (Figure 1). In comparison, Jersey cows had a much lower DMI than Holstein and Nordic Red cows within the first 24 lactation weeks (Figure 1).



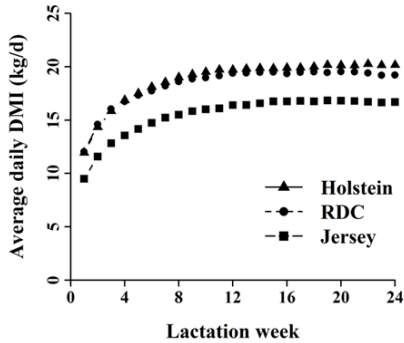


Figure 1. Average daily Dry Matter Intake (DMI, kg/d) within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows.

### *Variance Components, Heritability, and Repeatability for DMI*

For the first 24 lactation weeks, genetic and phenotypic variances for DMI tended to vary along lactation (Table 2). Comparing the three breeds, Nordic Red and Jersey tended to have the highest and the lowest genetic variance for DMI, respectively. The difference in genetic variances between breeds was not statistically significant due to the large standard errors ( $P > 0.05$ ; Table 2). Phenotypic variances increased along the lactation in all breeds. Nordic Red had significantly higher phenotypic variance for DMI than the other two breeds, and Jersey had the lowest phenotypic variance among the breeds (Table 2).

In the first 24 lactation weeks, heritability estimates for DMI ranged from 0.20 to 0.40 in Holstein, 0.25 to 0.41 in Nordic Red, and 0.17 to 0.42 in Jersey (Table 3). The difference between breeds in the heritability for DMI was not significant ( $P > 0.05$ ). The repeatability was high in all periods for each breed, and the repeatability increased from around 0.68 in the first period of lactation to around 0.80 in later periods (Table 3).

Table 2. Genetic variance ( $\sigma_a^2$ ) and phenotypic variance ( $\sigma_p^2$ ) (standard errors in subscript) for Dry Matter Intake (DMI, kg/d) in six consecutive lactation periods of four weeks in length within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Genetic variance <sup>1</sup> ( $\sigma_a^2$ )			Phenotypic variance <sup>2</sup> ( $\sigma_p^2$ )		
	HOL	RDC	JER	HOL	RDC	JER
1	1.2 <sub>0.4</sub>	1.9 <sub>0.6</sub>	0.8 <sub>0.3</sub>	4.4 <sub>0.2</sub>	5.0 <sub>0.3</sub>	2.6 <sub>0.2</sub>
2	1.3 <sub>0.4</sub>	1.6 <sub>0.7</sub>	0.8 <sub>0.4</sub>	4.6 <sub>0.2</sub>	6.0 <sub>0.3</sub>	3.3 <sub>0.3</sub>
3	1.0 <sub>0.4</sub>	3.0 <sub>0.9</sub>	0.6 <sub>0.4</sub>	5.1 <sub>0.3</sub>	7.3 <sub>0.4</sub>	3.4 <sub>0.3</sub>
4	1.3 <sub>0.5</sub>	1.9 <sub>0.8</sub>	1.1 <sub>0.5</sub>	5.3 <sub>0.3</sub>	7.3 <sub>0.4</sub>	3.6 <sub>0.3</sub>
5	1.7 <sub>0.5</sub>	1.9 <sub>0.9</sub>	1.8 <sub>0.7</sub>	5.0 <sub>0.3</sub>	7.8 <sub>0.5</sub>	4.4 <sub>0.4</sub>
6	2.1 <sub>0.6</sub>	2.1 <sub>1.0</sub>	1.5 <sub>0.9</sub>	5.3 <sub>0.3</sub>	8.0 <sub>0.5</sub>	5.3 <sub>0.5</sub>

<sup>1</sup>All  $\sigma_a^2$  estimates, except for one  $\sigma_a^2$  estimate in Period 3 in Jersey, deviate more than  $1.645 \times \text{SE}$  from 0 ( $P < 0.05$ ).

<sup>2</sup>All  $\sigma_p^2$  estimates deviate more than  $1.645 \times \text{SE}$  from 0 ( $P < 0.05$ ).

Table 3. Heritability ( $h^2$ ) (standard errors in subscript) and repeatability (standard errors in subscript) for Dry Matter Intake (DMI, kg/d) in six consecutive lactation periods of four weeks in length within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Heritability <sup>1</sup>			Repeatability <sup>2</sup>		
	HOL	RDC	JER	HOL	RDC	JER
1	0.26 <sub>0.08</sub>	0.37 <sub>0.10</sub>	0.29 <sub>0.12</sub>	0.68 <sub>0.02</sub>	0.68 <sub>0.02</sub>	0.67 <sub>0.03</sub>
2	0.29 <sub>0.08</sub>	0.26 <sub>0.11</sub>	0.25 <sub>0.12</sub>	0.74 <sub>0.02</sub>	0.79 <sub>0.01</sub>	0.78 <sub>0.02</sub>
3	0.20 <sub>0.08</sub>	0.41 <sub>0.11</sub>	0.17 <sub>0.11</sub>	0.78 <sub>0.01</sub>	0.79 <sub>0.01</sub>	0.75 <sub>0.02</sub>
4	0.25 <sub>0.08</sub>	0.26 <sub>0.11</sub>	0.31 <sub>0.13</sub>	0.80 <sub>0.01</sub>	0.81 <sub>0.01</sub>	0.79 <sub>0.02</sub>
5	0.34 <sub>0.09</sub>	0.25 <sub>0.11</sub>	0.42 <sub>0.14</sub>	0.78 <sub>0.01</sub>	0.85 <sub>0.01</sub>	0.79 <sub>0.02</sub>
6	0.40 <sub>0.10</sub>	0.26 <sub>0.12</sub>	0.29 <sub>0.15</sub>	0.83 <sub>0.01</sub>	0.83 <sub>0.01</sub>	0.77 <sub>0.02</sub>

<sup>1</sup>All heritability estimates, except for one heritability estimate in Period 3 in Jersey, deviate more than  $1.645 \times \text{SE}$  from 0 ( $P < 0.05$ ).

<sup>2</sup>All repeatability estimates deviate more than  $1.645 \times \text{SE}$  from 0 ( $P < 0.05$ ).

### 3.2 Genetic heterogeneity of feed intake, energy-corrected milk, and body weight across lactation in primiparous Holstein, Nordic Red, and Jersey cows (Paper II)

The objectives of this study were to estimate and compare the genetic parameters of DMI, energy-corrected milk (ECM), and BW across the entire first lactation in three dairy breeds. The genetic heterogeneity of DMI, ECM, and BW across lactation was investigated by calculating the genetic

correlations for the traits across different lactation weeks. The genetic correlations between each pair of the three traits (DMI, ECM, and BW) were also estimated across lactation.

### 3.2.1 Data

A total of 30,717 records of 842 primiparous Holstein cows from 3 research herds in Denmark and Sweden (DCRC, Skovgaard, and Öjebyn herds), 21,279 records of 746 primiparous RDC cows from 5 research herds from all three countries (Rehtijärvi, Minkiö, Kungsängen, DCRC, and Skovgaard herds), and 14,021 records of 378 primiparous Jersey cows from 2 research herds in Denmark (DCRC and Skovgaard herds) were included in the statistical analyses. Cows were recorded with weekly records of DMI, ECM, and BW across lactation (Table 4). For Holstein and Jersey, cows' weekly records from lactation weeks 1 to 44 were included in the analyses, corresponding to the typical 305-day lactation. For RDC, cows' weekly records from lactation weeks 1 to 32 were studied, due to sparse records in later lactation weeks in some research herds. The age at first calving ranged from 24 to 38 months, 25 to 38 months, and 24 to 36 months for Holstein, RDC, and Jersey cows, respectively.

Table 4. *Descriptive statistics of dry matter intake (DMI, kg/d), energy-corrected milk (ECM, kg/d), and body weight (BW, kg) for 842 primiparous Holstein (HOL) cows in 44 lactation weeks, 746 primiparous Nordic Red cows (RDC) in 32 lactation weeks, and 378 primiparous Jersey (JER) cows in 44 lactation weeks*

	<b>Mean</b>	<b>SD</b>	<b>Min</b>	<b>Max</b>
<b>DMI (kg/d)</b>				
<b>HOL</b>	19.4	3.2	3.8	40.9
<b>RDC</b>	18.5	3.3	4.1	39.1
<b>JER</b>	15.8	2.9	5.5	34.5
<b>ECM (kg/d)</b>				
<b>HOL</b>	29.1	6.0	1.2	57.9
<b>RDC</b>	26.9	5.5	1.6	49.0
<b>JER</b>	24.6	5.3	2.8	48.6
<b>BW (kg)</b>				
<b>HOL</b>	601.2	63.8	387.0	869.0
<b>RDC</b>	575.1	61.0	396.0	857.5
<b>JER</b>	433.0	47.9	253.5	630.7

### 3.2.2 Methods

The analyses were carried out separately for each breed. Within each breed, variance components for weekly observations of DMI, ECM, and BW across lactation were estimated using the following random regression model for each trait:

$$y_{jklmp} = \mathbf{u} + \mathbf{Herd-Trial}_j + \mathbf{CA}_k + \mathbf{YSC}_l + \mathbf{Lactwk}_m + \sum_{n=0}^2 \mathbf{a}_{np} \Phi_n + \sum_{n=0}^2 \mathbf{pe}_{np} \Phi_n + e_{jklmp},$$

where  $y_{jklmp}$  is the weekly observation of DMI, ECM, or BW in lactation week (Lactwk)  $m$  for cow  $p$ , where cow  $p$  is in herd and trial (Herd-Trial)  $j$ , at calving age (CA)  $k$ , and in the year-season of calving (YSC)  $l$ .  $\mathbf{u}$  is the intercept for DMI, ECM, or BW;  $\mathbf{Herd-Trial}_j$  is the fixed effect of herd and trial for the cow; the trials were herd-specific ( $j = 1$  to 29 for Holstein cows;  $j = 1$  to 16 for RDC cows;  $j = 1$  to 14 for Jersey cows);  $\mathbf{CA}_k$  is the fixed effect of calving age in months, where the calving age of Holstein, RDC, and Jersey cows ranges from 24 to 38 months, 25 to 38 months, and 24 to 36 months, respectively;  $\mathbf{YSC}_l$  is the fixed effect of year-season of calving, where four seasons were defined (March to May, June to August, September to November, and December to February) ( $l = 1$  to 22 for Holstein cows;  $l = 1$  to 45 for RDC cows;  $l = 1$  to 39 for Jersey cows); and  $\mathbf{Lactwk}_m$  accounts for the fixed effect of lactation week ( $m = 1$  to 44 for Holstein and Jersey cows;  $m = 1$  to 32 for RDC cows). Random regression terms were used to describe the cows' additive genetic effect and permanent environmental effect. The  $\mathbf{a}_{np}$  and  $\mathbf{pe}_{np}$  are the  $n^{\text{th}}$  regression coefficients of the Legendre polynomial for the random additive genetic effect and the random permanent environmental effect, respectively, for cow  $p$ ;  $\Phi_n$  is the  $n^{\text{th}}$  covariable of the second-order Legendre polynomial for the week of lactation; The analyses failed to converge when higher order polynomials were fitted for animal and permanent environmental effects;  $e_{jklmp}$  is the random residual, which was assumed to have heterogeneous variances across lactation (every 4 consecutive lactation weeks was set as one class).

The variance components were estimated by an average information-restricted maximum likelihood algorithm (Jensen et al., 1997) implemented in the software DMU (Madsen and Jensen, 2013). Within each breed, estimates of variance components were used to calculate heritability for DMI, ECM, and BW for each trait in each lactation week. Genetic correlations for each trait between different lactation weeks were calculated for DMI, ECM, and BW

across lactation. In addition, genetic correlations between DMI, ECM, and BW at the same lactation week were estimated in Holstein and RDC cows using bivariate analyses by applying the same random regression model as for single trait analyses. The bivariate analyses between DMI, ECM, and BW were not performed for Jersey cows due to the small amount of data available.

### 3.2.3 Main findings

#### *Phenotypic means of DMI, ECM, and BW in Holstein, RDC, and Jersey cows*

Cows of different breeds had a similar pattern of phenotypic means of daily DMI over lactation, and the breed difference was at the level of phenotypic means (Figure 2). Generally, the average daily DMI in all three breeds increased from the beginning of lactation until reaching a relatively steady level not earlier than lactation week 11. Holstein cows had the highest level of average daily DMI among the three breeds, and Jersey cows had the lowest level of DMI, in according to what we found in Paper I.

The pattern of average daily ECM over the course of lactation was similar in three breeds (Figure 2). The ECM yield increased in early lactation and peaked in week 7 (for RDC and Jersey cows) or week 8 (for Holstein cows), followed by a gradual decrease in yield. Among the three breeds, Holstein and Jersey had the highest level and lowest level of average daily ECM over lactation, respectively.

As to BW, Holstein and RDC cows had a similar level of average BW, compared to Jersey cows with a significantly lower level (Figure 2). Loss of BW occurred at the beginning of lactation in all three breeds, and the nadir of BW curve appeared in week 5 in Holstein cows, in week 6 in RDC cows, and in week 7 in Jersey cows. The total loss of BW from week 1 to the nadir was on average 23.4, 17.1 and 22.1 kg for Holstein, RDC and Jersey cows, respectively. After the nadir point, the cows' BW were regained gradually to the original level of BW (i.e., BW in week 1) in week 16 for all breeds, and followed by continuous BW gains.

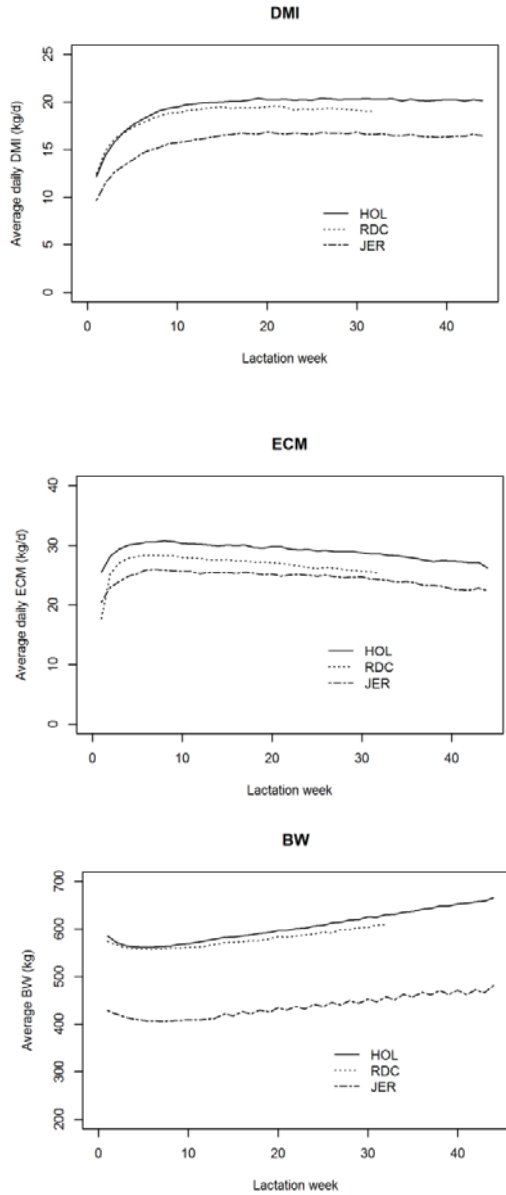


Figure 2. Phenotypic means of daily DMI (kg/d), daily ECM (kg/d), and BW (kg) for Holstein cows (HOL) in 44 lactation weeks, for Nordic Red cows (RDC) in 32 lactation weeks, and for Jersey cows (JER) in 44 lactation weeks.

### *Variance Components and Heritability of DMI, ECM, and BW across Lactation*

The genetic variances for DMI tended to increase over lactation, whereas the permanent environmental variances were relatively stable over lactation. The residual variance for DMI was slightly higher at the beginning of lactation than later in the lactation. The heritability for DMI followed a similar trajectory over lactation for the three breeds and tended to increase from early lactation to later lactation stages (Figure 3). The heritability estimates ranged from 0.30 to 0.55 (Mean SE = 0.06) in Holstein cows across 44 weeks, 0.20 to 0.48 (Mean SE = 0.08) in RDC cows across 32 weeks, and 0.17 to 0.52 (Mean SE = 0.10) in Jersey cows across 44 weeks. There was no significant breed difference in heritability for DMI ( $P > 0.05$ ).

The genetic variance and the residual variance for ECM were higher at the beginning of lactation than at later lactation stages. The permanent environmental variance for ECM tended to increase over lactation. The heritability for ECM was moderate and tended to differ among breeds (Figure 3). However, differences in heritability estimates between breeds were not statistically significant in this study due to large standard errors ( $P > 0.05$ ). In Holstein and RDC cows, the heritability of ECM was relatively stable over lactation, ranging from 0.26 to 0.37 (Mean SE = 0.06) in Holstein cows across 44 weeks and from 0.33 to 0.49 (SE=0.08) in RDC cows across 32 weeks. The heritability of ECM in Jersey cows showed a tendency of increase over lactation (from 0.14 to 0.53) but with fairly large standard errors (Mean SE = 0.11).

The genetic variances for BW increased over lactation, whereas the permanent environmental variances were relatively stable over lactation. The residual variance for BW was higher at the beginning of lactation than at later lactation. The heritability for BW was higher than the heritability for DMI or ECM in all three breeds (Figure 3). Heritability for BW in Holstein and Jersey cows was fairly similar and stable across lactation, ranging from 0.49-0.63 in Holstein (Mean SE = 0.08) and 0.46-0.61 in Jersey (Mean SE = 0.12). The heritability of BW in RDC was from 0.32 to 0.53 over 32 weeks (Mean SE = 0.10), which was not significantly different from the heritability for BW in Holstein or Jersey breed ( $P > 0.05$ ).

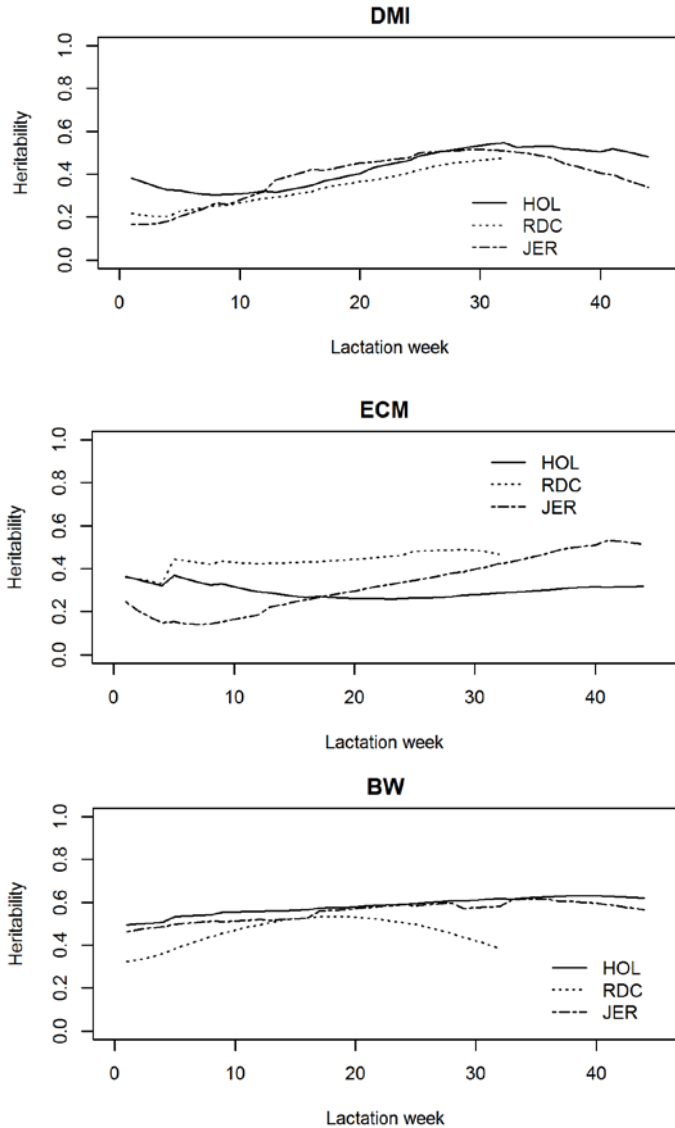
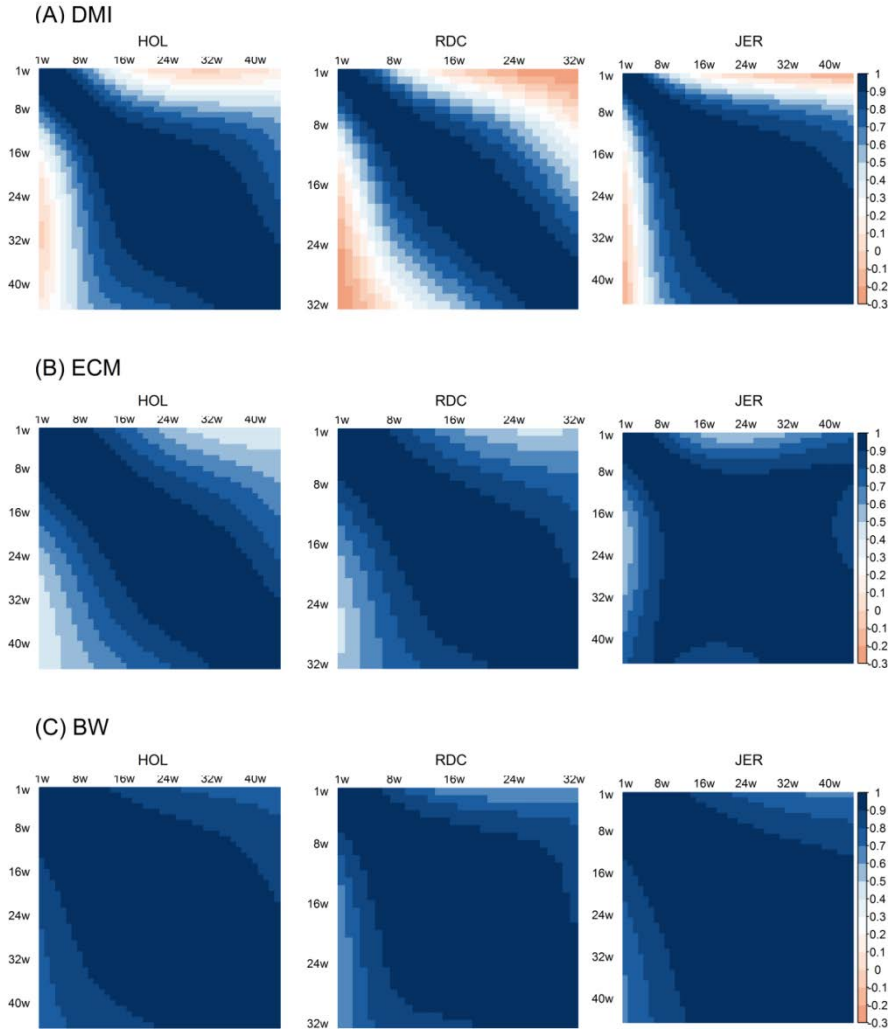


Figure 3. Heritability estimates of average daily DMI (kg/d), average daily ECM (kg/d), and average BW (kg) in Holstein cows (HOL) in 44 lactation weeks, in Nordic Red cows (RDC) in 32 lactation weeks, and in Jersey cows (JER) in 44 lactation weeks. The mean SE of heritability for DMI were 0.06, 0.08, and 0.10 in HOL, RDC, and JER, respectively; The mean SE of heritability for ECM were 0.06, 0.08, and 0.11 in HOL, RDC, and JER, respectively; The mean SE of heritability for BW were in 0.08, 0.10, and 0.12 in HOL, RDC, and JER, respectively.



*Genetic Correlations within DMI, ECM, and BW across Lactation in Three Dairy Breeds*

The genetic correlations between DMI at different lactation stages were less than unity (Figure 4A), indicating a genetic heterogeneity of feed intake across lactation. Low or even negative genetic correlations were observed for DMI between early lactation and the mid or late lactation stage, with the lowest values for Holstein, RDC and Jersey of 0.0, -0.27 and -0.15, respectively. However, DMI in middle and late lactation stages generally showed a high genetic correlation. Compared to DMI, ECM showed less genetic heterogeneity across lactation in all breeds, although ECM in early and later lactation stages were still shown to be genetically different, with the lowest genetic correlation at approximately 0.5 (Figure 4B). In contrast, BW was shown to be the most consistent trait across lactation for all breeds, where BW in all weeks was highly correlated (Figure 4C). The genetic correlations for BW across lactation were higher than 0.74, 0.61 and 0.67 in Holstein, RDC, and Jersey cows, respectively.



*Figure 4.* Genetic correlations for (A) DMI, (B) ECM, and (C) BW across 44 lactation weeks in Holstein cows (HOL), across 32 lactation weeks in Nordic Red cows (RDC), and across 44 lactation weeks in Jersey cows (JER). The mean SE of genetic correlations for DMI were 0.09, 0.12, 0.14 in HOL, RDC, and JER, respectively; The mean SE of genetic correlations for ECM were 0.09, 0.12, 0.15 in HOL, RDC, and JER, respectively; The mean SE of genetic correlations for BW were 0.11, 0.13, 0.17 in HOL, RDC, and JER, respectively.

### *Genetic Correlations between DMI, ECM, and BW in the Same Week of Lactation*

Genetic correlations between DMI, ECM, and BW changed over lactation (Figure 5), and the correlations changed considerably more in early lactation compared to mid and late lactation. The trajectories of the correlations over lactation followed similar patterns in Holstein and RDC cows. In both breeds, cows' DMI and ECM were genetically weakly correlated at the beginning of lactation (0.24 for Holstein cows and 0.16 for RDC cows). After the beginning of lactation the correlation between DMI and ECM increased to 0.80 in week 14 in Holstein cows, and remained above 0.80 until the end of lactation. Similarly, in RDC cows, the genetic correlation between DMI and ECM continued to increase from early lactation and peaked in week 16 with a correlation of 0.67; the correlation remained above 0.50 until week 32.

The genetic correlation between cows' BW and ECM was low but positive at the beginning of lactation, and decreased to become slightly negative in later lactation stages in both Holstein and RDC (Figure 5).

In both breeds, the correlation between DMI and BW increased from the beginning of lactation and peaked in week 7 (with correlation at approximately 0.7), followed by a gradual decrease (Figure 5). The correlations remained positive in the entire lactation.

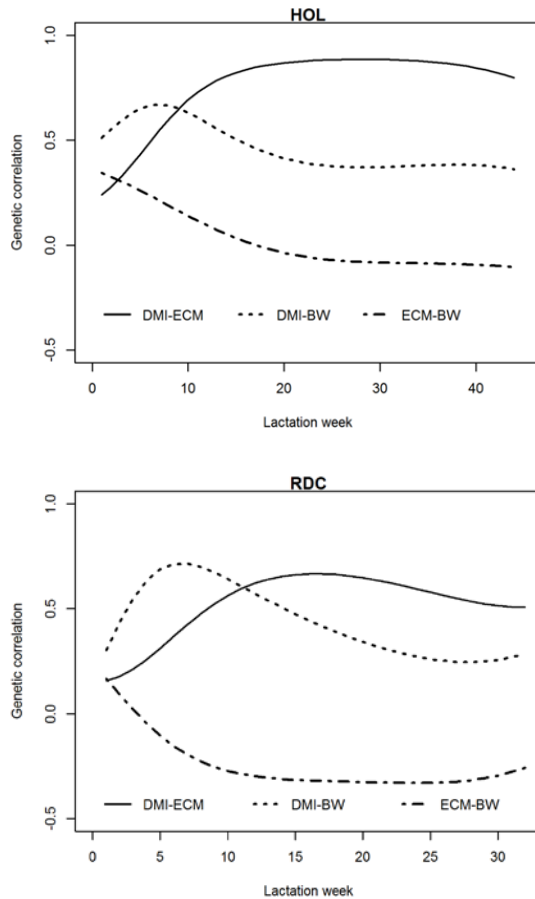


Figure 5. Genetic correlations between DMI, ECM, and BW in the same week of lactation in Holstein cows (HOL) across 44 lactation weeks and in Nordic Red cows (RDC) across 32 lactation weeks. The mean SE of genetic correlations among DMI, ECM, and BW ranged from 0.09 to 0.11 in HOL cows, and from 0.12 to 0.13 in RDC cows.

### 3.3 Neglect of lactation stage leads to naive assessment of residual feed intake in dairy cattle (Paper III)

The objectives of this study were to investigate the influence of lactation stage on estimating RFI, and also to estimate the genetic parameters for RFI across lactation in dairy cattle. Two RFI models were studied, in which regression coefficients of feed intake on energy sinks were allowed or not allowed to change across lactation. Genetic parameters for RFI were estimated across lactation and were compared between the two RFI models.

### 3.3.1 Data

A total of 747 primiparous Holstein cows with 24,993 weekly records on DMI, milk yield (MY), milk composition (fat%, protein%, lactose%), and BW were used for the statistical analyses (Table 5). The studied cows were from the Danish Cattle Research Center (Foulum, Denmark) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle, Denmark). Cows' weekly records from lactation weeks 1 to 44 were included in the analyses, corresponding to the typical 305-day lactation. Cows' age at first calving was from 24 to 36 months. Pedigree information was extracted from the Nordic Cattle Genetic Evaluation Database (NAV, Skejby, Denmark), by tracing back as many generations as possible for cows with records.

Table 5. Descriptive statistics of dry matter intake (DMI), milk yield, milk composition, and body weight (BW) during 44 lactation weeks in 747 primiparous Holstein cows.

Item	Mean	SD	Minimum	Maximum
<b>DMI (kg/d)</b>	19.63	2.97	5.72	40.48
<b>Milk yield (kg/d)</b>	28.55	6.39	2.50	47.00
<b>Milk composition (%)</b>				
<b>Protein</b>	3.51	0.35	2.35	4.70
<b>Fat</b>	4.15	0.65	2.04	6.37
<b>Lactose</b>	4.96	0.26	3.97	5.96
<b>BW (kg)</b>	601.0	62.2	396.5	867.1

### 3.3.2 Methods

Energy-corrected milk (ECM), metabolic BW (MBW), and  $\Delta$ BW were calculated individually in each lactation week. The weekly BW per cow over 44 lactation weeks was modelled by a third-order Legendre polynomial function of lactation weeks. The  $\Delta$ BW per cow at each lactation week was obtained from the first derivative (i.e., the slope) of the fitted BW curve of each cow. MBW was computed as  $BW^{0.75}$  (McDonald et al., 2011).

Two RFI models were considered. Model [1] is a One-Step RFI model that combines the energy sink model for estimating RFI and the genetic model (Lu et al., 2015; Tempelman et al., 2015). In Model [1], the partial regression coefficient of DMI on each energy sink (ECM, MBW, and  $\Delta$ BW) was considered to be constant over lactation. RFI Model [2] considered period-specific partial regressions of DMI on ECM, MBW, and  $\Delta$ BW for each lactation period, with the whole lactation (44 lactation weeks) being divided into 11 consecutive 4-week lactation periods. The two models were identical

except for the period-specific partial regressions of DMI on energy sinks in Model [2].

$$\begin{aligned} \text{DMI}_{jklmp} = & b_1 * \text{ECM} + b_2 * \text{MBW} + b_3 * \Delta \text{BW} + \text{Herd-Trial}_j + \text{CA}_k + \text{YS}_l \\ & + \text{Lactwk}_m + \sum_{n=0}^2 a_{np} \Phi_n + \sum_{n=0}^2 pe_{np} \Phi_n + e_{jklmp}, \end{aligned} \quad [1]$$

$$\begin{aligned} \text{DMI}_{ijklmp} = & b_{1i} * \text{ECM} + b_{2i} * \text{MBW} + b_{3i} * \Delta \text{BW} + \text{Herd-Trial}_j + \text{CA}_k + \text{YS}_l \\ & + \text{Lactwk}_m + \sum_{n=0}^2 a_{np} \Phi_n + \sum_{n=0}^2 pe_{np} \Phi_n + e_{ijklmp}, \end{aligned} \quad [2]$$

where  $\text{DMI}_{jklmp}$  and  $\text{DMI}_{ijklmp}$  are the weekly records of DMI in Lactation week  $m$  for cow  $p$  in Model [1] and Model [2], respectively, where cow  $p$  is in calving age  $k$  in the year-season of calving  $l$  and from Herd-Trial  $j$ . In Model [1],  $b_1$ ,  $b_2$ , and  $b_3$  are the partial regression coefficients of DMI on ECM, MBW and  $\Delta \text{BW}$  over lactation, respectively. In Model [2],  $b_{1i}$ ,  $b_{2i}$ , and  $b_{3i}$  are the period-specific partial regression coefficients of DMI on ECM, MBW, and  $\Delta \text{BW}$ , respectively, in lactation period  $i$  ( $i = 1$  to 11).  $\text{Herd-Trial}_j$  is the fixed effect of herd and trial in which the cows were involved ( $j = 1$  to 25), where the cows were from two research herds and the trials were herd-specific.  $\text{CA}_k$  is the fixed effect of calving age in the month of cows' first calving ( $k = 24$  to 36).  $\text{YS}_l$  is the fixed effect of year-season of calving, where the year of calving is from 1995 to 2015 and four seasons were defined (March to May, June to August, September to November, and December to February) ( $l = 1$  to 64).  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week on DMI ( $m = 1$  to 44).  $a_{np}$  and  $pe_{np}$  are the  $n^{\text{th}}$  regression coefficients of the Legendre polynomial for the random additive genetic effect and for the random permanent environmental effect, respectively, of the cow  $p$ .  $\Phi_n$  is the term of the second-order Legendre polynomial for  $a_{np}$  and  $pe_{np}$ , where the time variable is the week of lactation.  $e_{jklmp}$  and  $e_{ijklmp}$  are random residuals for Model [1] and Model [2], respectively, which were assumed to be with heterogeneous variances along lactation and were divided into 11 classes of heterogeneous residual variances (every 4 consecutive weeks of the 44 lactation weeks was set as one class).

We initially tested the significance of the period-specific partial regressions of DMI on energy sinks (ECM, MBW, and  $\Delta \text{BW}$ ) by using PROC MIXED in SAS 9.3 (SAS Institute Inc., Cary, NC), and the period-specific partial regressions of DMI on energy sinks (ECM, MBW, and  $\Delta \text{BW}$ ) were shown to be significant ( $P < 0.05$ ). In this test, we used a mixed model that

included the same fixed effects as Model [2] and a random cow effect with a third-order Legendre polynomial of lactation weeks but without using pedigree relationships. Thereafter, we carried out a genetic analysis for RFI with Model [1] and Model [2] with pedigree information, using the restricted maximum likelihood (REML) in DMU 5.2 (Madsen and Jensen, 2013). Period-specific partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW were estimated with Model [2] and compared with the partial regression coefficients estimated from Model [1]. Variance components and genetic parameters for RFI across lactation were estimated from both Model [1] and Model [2] and were compared with each other.

### 3.3.3 Main findings

#### *Effects of Energy Sinks on DMI in Different Lactation Periods*

Period-specific partial regressions of DMI on ECM (Figure 6A), on MBW (Figure 6B), and on  $\Delta$ BW (Figure 6C) from RFI Model [2] varied across lactation. From the genetic analysis using RFI Model [1], the partial regression coefficient of DMI on ECM over lactation was close to 0.15 kg DMI per kg ECM (SE = 0.004; Figure 6A). When the period-specific effect of ECM on DMI was considered in Model [2], the effect of ECM on DMI changed significantly across lactation (Figure 6A). In early lactation (Periods 1–2), the estimated regression coefficients of DMI on ECM were significantly lower than later lactation periods. The regression coefficients of feed intake on ECM increased from the beginning of lactation until Period 4 (Figure 6A). From Period 4 until the end of lactation, partial regression coefficients of DMI on ECM were relatively stable.

When Model [1] was used, the estimated partial regression coefficient of DMI on MBW over lactation was around 0.08 kg DMI per kg<sup>0.75</sup> MBW (SE = 0.005; Figure 6B). In Model [2], the estimated partial regression coefficients of DMI on MBW were generally stable across periods (Figure 6B), but tended to be greater in Period 1, 2, and 6, compared to other periods. For the partial regression coefficient of DMI on  $\Delta$ BW, when Model [1] was used, the partial regression coefficient was 0.57 kg DMI per kg  $\Delta$ BW over lactation (SE = 0.06; Figure 6C). When Model [2] was used, partial regression coefficients of DMI on  $\Delta$ BW were significantly lower than 0.57 kg DMI per kg  $\Delta$ BW at the beginning of lactation (Period 1) and in the end of lactation (Periods 9–11), and tended to be higher than 0.57 kg DMI per kg  $\Delta$ BW from Periods 2 to 8 (Figure 6C).

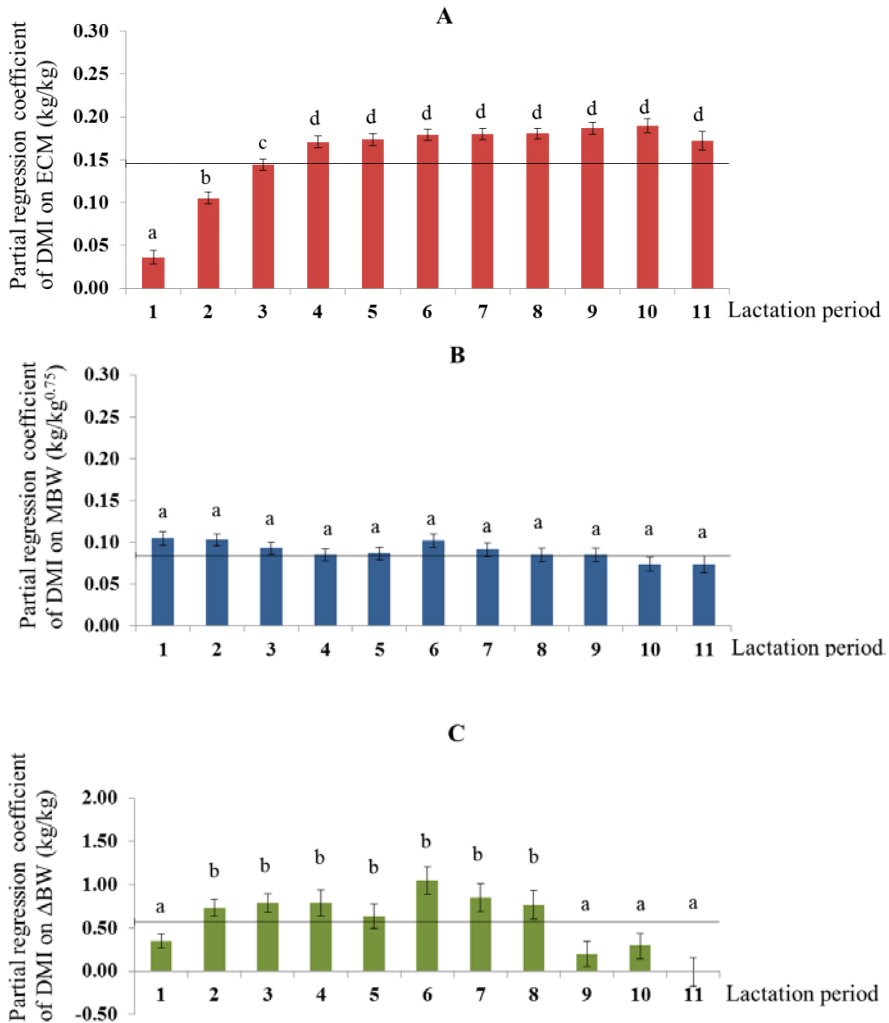


Figure 6. Partial regression coefficients of DMI on (A) Energy-corrected milk (ECM), (B) metabolic BW (MBW), and (C) change in BW ( $\Delta$ BW) in each lactation period estimated from residual feed intake (RFI) Model [2]. Error bars are standard errors. Bars not sharing the same letter within (A), (B), and (C) are significantly different ( $P < 0.05$ ). Horizontal lines in (A), (B), and (C) are the partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW across 44 lactation weeks estimated from Model [1], respectively.

### Variance Components and Heritability for Two RFI Models

Variance components estimated from two RFI models followed similar patterns (Figure 7). In RFI Model [2], where the partial regression coefficients



of DMI on energy sinks were allowed to change over lactation, lower and more stable genetic variances for RFI along lactation were observed compared to the genetic variances estimated from Model [1]. The permanent environmental variances estimated from both models were similar. The residual variance from Model [2] was slightly lower than Model [1]. The phenotypic variance from RFI Model [2] was lower than the total variance from Model [1] in most of the lactation. Additionally, in most of the lactation weeks, the correlations between observed DMI and predicted DMI were higher in Model [2] than in Model [1], especially in the first 3 weeks when the correlations between predicted and observed DMI were on average 2% higher in Model [2] than in Model [1].

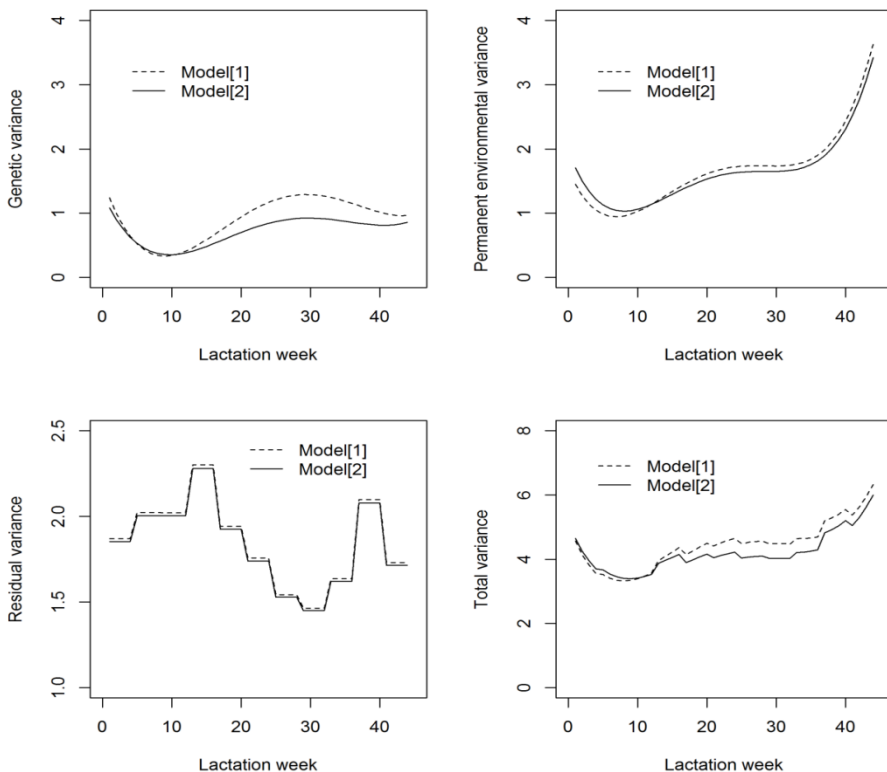


Figure 7. Genetic variances, permanent environmental variances, residual variances, and total variances for residual feed intake (RFI) across 44 lactation weeks estimated from RFI Model [1] (dashed lines) and RFI Model [2] (solid lines).

The heritability for RFI estimated from two RFI models followed a similar trajectory (Figure 8). The heritability for RFI estimated from Model [1] ranged from 0.10 to 0.29 across lactation (mean SE = 0.05), whereas the heritability

from Model [2] was slightly lower and more stable over lactation, ranging from 0.10 to 0.23 across lactation (mean SE = 0.05; Figure 8).

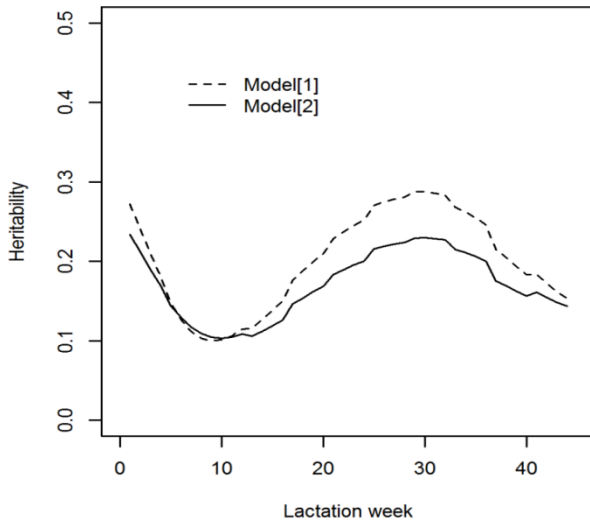
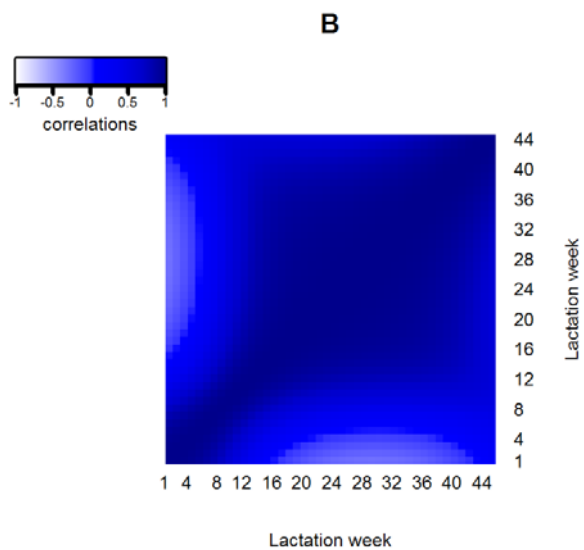
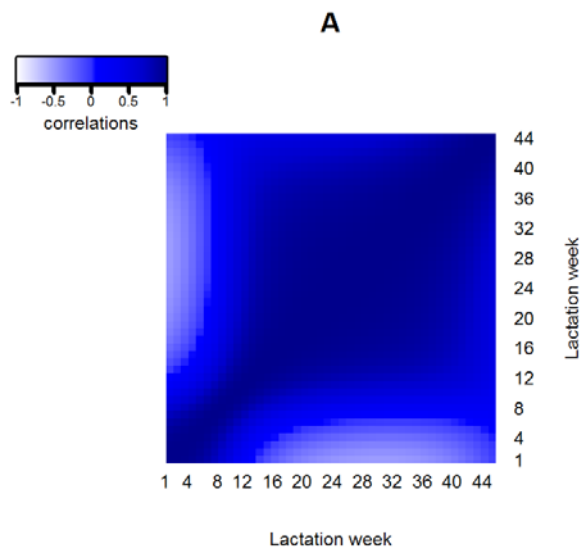


Figure 8. Heritability for residual feed intake (RFI) across 44 lactation weeks estimated from RFI Model [1] (dashed line) and RFI Model [2] (solid line).

#### *Genetic Correlations for RFI across Lactation*

RFI in middle and late lactation were genetically highly correlated, whereas RFI in early lactation was negatively correlated with RFI in later lactation weeks (Figure 9). Genetic correlations for RFI across 44 lactation weeks estimated from Model [1] and Model [2] ranged from -0.51 to 1 and from -0.29 to 1, respectively. Genetic correlations for RFI were shown to be negative between early and middle lactation weeks from both models. However, the most extreme negative genetic correlation for RFI between early and middle lactation was reduced to -0.29 in RFI Model [2] (Figure 9B), compared to -0.51 from Model [1] (Figure 9A).



*Figure 9.* Genetic correlations for residual feed intake (RFI) across 44 lactation weeks estimated from (A) RFI Model [1] and (B) RFI Model [2].

### 3.4 Deriving residual feed intake from genetic covariance functions of dry matter intake, energy-corrected milk, and metabolic body weight in Holstein dairy cattle across lactation (Paper IV)

In this study, we applied a multivariate modelling strategy for RFI (denoted as “genetic RFI”) in Nordic Holstein dairy cows in a random regression analysis, where genetic RFI was defined as DMI conditional on energy sinks (ECM and BW). In addition, RFI was also derived from DMI phenotypically adjusted for energy sinks (denoted as “phenotypic RFI” in this study). Two ways of defining RFI were compared in this study. The objective of this study was (1) to derive genetic RFI from genetic covariance functions of DMI, ECM and MBW by multivariate analyses, (2) to estimate genetic parameters for genetic RFI across the whole lactation, (3) to compare the variance components, genetic parameters, and breeding value estimation between the two definitions of RFI (i.e., genetic RFI and phenotypic RFI).

#### 3.4.1 Data

A total of 34,675 records of 963 primiparous Holstein cows from 4 research herds in Denmark and Sweden (DCRC, Skovgaard, Lövsta, and Öjebyn herds) were included in the study. The studied cows calved between 1991 and 2015. Cows’ ages at first calving ranged from 24 to 38 months. Pedigree information was extracted from the Nordic Cattle Genetic Evaluation (NAV, Skejby, Denmark) database, by tracing back as many generations as possible for cows with records. Cows’ weekly records of DMI, ECM, and BW from lactation weeks 1 to 44 were included in the analyses (Table 6). Metabolic BW (MBW) was computed as  $BW^{0.75}$  (McDonald et al., 2011).

*Table 6. Descriptive statistics of dry matter intake (DMI, kg/d), energy-corrected milk (ECM, kg/d), and body weight (BW, kg) for 963 primiparous Holstein cows in 44 lactation weeks*

	Mean	SD	Min	Max
DMI (kg/d)	19.5	3.3	1.3	40.9
ECM (kg/d)	29.1	6.1	1.1	57.9
BW (kg)	602.2	63.4	306.0	869.0

#### 3.4.2 Genetic RFI

The first way of modelling RFI, denoted as “genetic RFI” in this study, was to derive RFI from genetic covariance functions of DMI, ECM and MBW by

multivariate random regression analyses (Strathe et al., 2014). In genetic RFI, DMI was genetically adjusted for ECM and MBW through decomposition of (co)variances among DMI, ECM, and MBW (Strathe et al., 2014; Lu et al., 2015).

### *Multivariate Random Regression Analyses*

Multivariate random regression analyses for DMI, ECM, and MBW across lactation were applied to model “genetic RFI”. The random regression model, which was the same for each trait in the multivariate analyses, was as follows in [3]:

$$y_{ijklm} = u + \text{Herd-Trial}_j + \text{CA}_k + \text{YS\_Country}_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{ni} \Phi_n + \sum_{n=0}^2 p e_{ni} \Phi_n + e_{ijklm}, \quad [3]$$

where  $y_{ijklm}$  is the weekly observation of DMI, ECM, or MBW in lactation week (Lactwk)  $m$  for cow  $i$ , where cow  $i$  is in herd and trial (Herd-Trial)  $j$ , at calving age (CA)  $k$ , and in the year-season of recording and country (YS\_Country)  $l$ .  $u$  is the intercept for DMI, ECM, or BW; Herd-Trial $_j$  is the fixed effect of herd and trial for the cow, where the trials were herd-specific ( $j = 1$  to 37);  $\text{CA}_k$  is the fixed effect of calving age in months, where the calving age of primiparous Holstein cows ranges from 24 to 38 months;  $\text{YS\_Country}_l$  is the fixed effect of year-season of recording for each country, where the year of recording is from 1991 to 2016 and 4 seasons were defined (March to May, June to August, September to November, and December to February, for two countries (Denmark and Sweden) ( $l = 1$  to 117)); and  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week ( $m = 1$  to 44). Random regression terms were used to describe the cows’ additive genetic effect and permanent environmental effect. The  $a_{ni}$  and  $p e_{ni}$  are the  $n^{\text{th}}$  regression coefficients of the Legendre polynomial for the random additive genetic effect and the random permanent environmental effect, respectively, for cow  $i$ ;  $\Phi_n$  is the  $n^{\text{th}}$  covariable of the second-order Legendre polynomial on the weeks of lactation;  $e_{ijklm}$  is the random residual, whose variance was assumed to be constant across lactation.

The variance components were estimated by an average information-restricted maximum likelihood algorithm (Jensen et al., 1997) implemented in the software DMU (Madsen and Jensen, 2013). The genetic (co)variance matrix

among the three traits across 44 lactation weeks ( $G_0$ ) was derived in the random regression setting as follows in [4]:

$$G_0 = MK_a M', \quad [4]$$

where  $G_0$  is the genetic (co)variance matrix across traits and weeks. Matrix  $K_a$  contains the estimated covariance function describing the genetic variance components for the random regression coefficients across three traits, estimated with DMU using Model [3]. Matrix  $M$  is a block-diagonal matrix containing the Legendre polynomials for 44 weeks for three traits. Likewise, the permanent environmental (co)variance matrix across traits and week ( $PE_0$ ) was calculated by  $PE_0 = MK_{pe} M'$ , where matrix  $K_{pe}$  contains the estimated covariance function describing the permanent environmental variance components for the random regression coefficients across three traits, estimated with DMU using Model [3]. The residual variance matrix across traits ( $E_0$ ) is not with a random regression setting, and is a  $3 \times 3$  matrix containing residual (co)variances across three traits.

#### *Derivation of RFI*

In the next step,  $G_0$  was partitioned into 4 blocks as shown in [5] to derive RFI:

$$G_0 = \begin{bmatrix} G_{11} & G_{12} \\ G_{21} & G_{22} \end{bmatrix} \quad [5]$$

where  $G_0$  is the genetic (co)variance matrix across weeks and across three traits (DMI, ECM, and MBW), as described previously;  $G_{11}$  corresponds to the (co)variance matrix for DMI across 44 lactation weeks;  $G_{22}$  corresponds to (co)variance matrix for two energy sink traits (ECM and MBW), which contains the (co)variance matrix for ECM across 44 weeks, the (co)variance matrix for MBW across 44 weeks, and the covariance matrix between ECM and MBW across 44 lactation weeks;  $G_{12}$  corresponds to the covariance matrix between DMI and energy sink traits (ECM and MBW) across 44 weeks; and  $G_{21}$  is the transpose of  $G_{12}$ . Likewise, the same partitioning was also applied to the permanent environmental variance matrix ( $PE_0$ ) and the residual variance matrix ( $E_0$ ).

The genetic (co)variance matrix for genetic RFI ( $G_{1|2}$ ) was then derived as the genetic (co)variances of DMI conditional on energy sink traits (ECM and MBW) as shown in [6] (Strathe et al., 2014):

$$G_{1|2} = G_{11} - G_{12}G_{22}^{-1}G_{21}, \quad [6]$$

where  $G_{1|2}$  is the genetic (co)variance matrix for genetic RFI across 44 lactation weeks;  $G_{11}$ ,  $G_{22}$ ,  $G_{12}$ ,  $G_{21}$  are the decomposed genetic (co)variance matrices from  $G_0$  as described before in [5]. In this way, the genetic (co)variance matrix for genetic RFI ( $G_{1|2}$ ) was derived as the conditional (co)variance of DMI given the energy sink traits (ECM and MBW). The same method was applied to obtain the permanent environmental variance for genetic RFI across 44 weeks ( $PE_{1|2}$ ) and for the residual variance for genetic RFI ( $E_{1|2}$ ).

Based on the variance components estimates for genetic RFI across lactation weeks, the heritability for genetic RFI was calculated for each week. The proportion of genetic variance of RFI out of DMI was calculated through computing the ratio of genetic variance of RFI to genetic variance of DMI. The genetic correlations for genetic RFI across 44 lactation weeks were also computed. SE of parameters are mathematically intricate to calculate and were not available.

#### *Calculation of EBV for genetic RFI*

The EBV for genetic RFI were calculated for all animals in each lactation week by the following formula [7] (Strathe et al., 2014). Afterwards, the overall EBV of the entire lactation for animal  $i$  was calculated as the sum of the EBVs of each week for animal  $i$ .

$$a_{im}^{RFI} = a_{im}^{DMI} - b_{1m} * a_{im}^{ECM} - b_{2m} * a_{im}^{MBW}, \quad [7]$$

where  $a_{im}^{RFI}$ ,  $a_{im}^{DMI}$ ,  $a_{im}^{ECM}$ , and  $a_{im}^{MBW}$  are the EBVs for  $i$ th animal for RFI, DMI, ECM, and MBW in lactation week  $m$ , respectively;  $a_{im}^{DMI}$ ,  $a_{im}^{ECM}$ , and  $a_{im}^{MBW}$  were calculated as  $\sum_{n=0}^2 a_{ni} \Phi_n$  for  $i$ th animal in week  $m$ , where  $\hat{a}_{ni}$  are the solutions for the additive genetic effect for animal  $i$  from the random regression model [3].  $b_{1m}$  is the ratio of genetic covariance between DMI and ECM to the genetic variance of ECM (i.e.,  $b_1 = \text{cov}(\text{DMI}, \text{ECM})/\text{var}(\text{ECM})$ ) for lactation week  $m$ ;  $b_{2m}$  is the ratio of genetic covariance between DMI and MBW to the genetic variance of MBW (i.e.,  $b_2 = \text{cov}(\text{DMI}, \text{MBW})/\text{var}(\text{MBW})$ ) for lactation week  $m$ ;  $b_{1m}$  and  $b_{2m}$  were derived from the  $G_0$  matrix (i.e., the genetic (co)variance matrix across traits and weeks).

### 3.4.3 Phenotypic RFI

The second way of modelling RFI, denoted as “phenotypic RFI” in this study, was based on a one-step RFI model (Tempelman et al., 2015; Lu et al., 2015; Li et al., 2017), already studied in Paper III. In the one-step RFI model, DMI was phenotypically adjusted for energy sink traits by partial linear regressions of DMI on energy sink traits (Tempelman et al., 2015; Lu et al., 2015). In the current study, 11 lactation periods were defined during 44 lactation weeks (every 4 consecutive weeks of the 44 lactation weeks was set as one period). Period-specific partial regressions of DMI on ECM and on MBW were considered in the random regression analysis for phenotypic RFI (as in Paper III). The random regression model was as follows in [8]:

$$\text{DMI}_{ijklms} = u + b_{1s} * \text{ECM} + b_{2s} * \text{MBW} + \text{Herd-Trial}_j + \text{CA}_k + \text{YS\_Country}_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{ni} \Phi_n + \sum_{n=0}^2 pe_{ni} \Phi_n + e_{ijklms}, \quad [8]$$

where  $\text{DMI}_{ijklms}$  is the weekly records of DMI in lactation week (Lactwk)  $m$  for cow  $i$ , where cow  $i$  is in calving age (CA)  $k$ , in the year-season of recording and country (YS\_Country)  $l$ , and from Herd-Trial  $j$ .  $b_{1s}$  is the period-specific partial regression coefficient of DMI on ECM in lactation period  $s$  ( $s = 1$  to  $11$ );  $b_{2s}$  is the period-specific partial regression coefficient of DMI on MBW in lactation period  $s$  ( $s = 1$  to  $11$ ).  $\text{Herd-Trial}_j$  is the fixed effect of herd and trial in which the cows were involved ( $j = 1$  to  $37$ ), where the trials were herd-specific;  $\text{CA}_k$  is the fixed effect of calving age in the month of cows' first calving ( $k = 24$  to  $38$ );  $\text{YS\_Country}_l$  is the fixed effect of year-season of recording for each country, where the year of recording is from 1991 to 2016 and 4 seasons were defined (March to May, June to August, September to November, and December to February, for two countries (Denmark and Sweden) ( $l = 1$  to  $117$ ); and  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week on DMI ( $m = 1$  to  $44$ ). Random regression terms were used to describe the cows' additive genetic effect and permanent environmental effect. The  $a_{ni}$  and  $pe_{ni}$  are the  $n^{\text{th}}$  regression coefficients of the Legendre polynomial for the random additive genetic effect and the random permanent environmental effect, respectively, for cow  $i$ ;  $\Phi_n$  is the  $n^{\text{th}}$  covariable of the second-order Legendre polynomial on weeks of lactation.  $e_{ijklms}$  is the random residual, whose variance was assumed constant across lactation for this study.

The variance components for phenotypic RFI were estimated by an average information-restricted maximum likelihood algorithm (Jensen et al., 1997)



implemented in DMU (Madsen and Jensen, 2013). Variance components and heritability for phenotypic RFI were calculated for each week, and the genetic correlations for RFI across lactation were also computed. EBV for phenotypic RFI for each individual in each lactation week was obtained from  $\sum_{n=0}^2 \hat{a}_{ni} \Phi_n$  for animal  $i$  in week  $m$ , where  $\hat{a}_{ni}$  are the solutions for the genetic effect for animal  $i$  from the random regression model [8]. The overall EBV for animal  $i$  in the entire lactation was calculated as the sum of the EBVs of each week for animal  $i$ .

#### 3.4.4 Comparison between genetic RFI and phenotypic RFI

The variance components and genetic parameters were compared between genetic RFI and phenotypic RFI across lactation. When it comes to comparing EBVs between the two RFI definitions, firstly, the correlation was calculated between animals' overall EBVs (EBV of the entire lactation) for genetic RFI and animals' overall EBVs for phenotypic RFI, among all the animals with phenotypes. The correlations for EBVs between the two RFI definitions were also computed across 44 lactation weeks. Secondly, among all the animals with phenotypes, the 10% of animals that had the lowest overall EBVs for RFI (i.e., the most desirable animals) were selected from genetic RFI and phenotypic RFI, respectively. The selected animals from genetic RFI and phenotypic RFI were compared to see how many of the selected animals were the same between the two RFI definitions. Accordingly, the 10% of animals that had the highest EBVs for RFI (i.e., undesirable animals) were also selected from genetic RFI and phenotypic RFI, respectively. Animals with lowest EBV (i.e., desirable animals) and animals with highest EBV (i.e., undesirable animals) were compared for their average DMI, ECM, BW, and the ratio of ECM to DMI (i.e., gross efficiency, kg ECM / kg DMI) across lactation.

#### 3.4.5 Main findings

##### *Variance components and heritability for genetic RFI and phenotypic RFI*

The genetic variance of phenotypic RFI was higher than that of genetic RFI (Figure 10). In phenotypic RFI, DMI was only phenotypically corrected for ECM and MBW, and the resulting RFI was still genetically correlated with ECM and MBW. In contrast, in genetic RFI, RFI was derived as DMI conditional on ECM and MBW, where DMI was genetically uncorrelated with ECM and MBW. The higher estimate of genetic variance for phenotypic RFI could be partly attributed to the genetic covariance between DMI and the

energy sink traits (ECM and MBW) that was not removed in phenotypic RFI, but was adjusted for in genetic RFI.

Based on our results, the genetic variance for RFI was higher at the beginning of lactation compared to later lactation stages in both two RFI definitions, which is probably due to ignoring the change of BW ( $\Delta$ BW) in both RFI models. In early lactation changes in BW are common for lactating cows (Li et al., 2017). Cows'  $\Delta$ BW is associated with feed intake, so that  $\Delta$ BW could explain part of the variance for feed intake (Li et al., 2017). Variance components estimates for RFI could be affected by adjusting for  $\Delta$ BW in RFI models or not. As in Lu et al. (2015), we tried but failed to include  $\Delta$ BW in the multivariate modelling for genetic RFI due to convergence problems. Accordingly, we did not apply  $\Delta$ BW to phenotypic RFI in order to compare the two RFI definitions in the same level. In Paper III, phenotypic RFI was derived with the adjustment of ECM, MBW, and also  $\Delta$ BW in the model, positive partial regression coefficients of DMI on  $\Delta$ BW were seen over lactation. The genetic variance for phenotypic RFI in Paper III (where  $\Delta$ BW was considered) was lower than the genetic variance for the phenotypic RFI in this study where  $\Delta$ BW was not modeled. In future investigation for RFI,  $\Delta$ BW would be recommended to be included in the RFI model as one important energy sink for feed intake and also as a factor to reduce the risk of selecting for negative energy balance of the animals.

The permanent environmental variance for genetic RFI was lower compared to that for phenotypic RFI, and the residual variance for genetic RFI was higher than that for phenotypic RFI (Figure 10). Lu et al. (2015) used very similar modelling methods to derive genetic RFI and phenotypic RFI to what we used in this study but without the random regression setting. They also found lower genetic variance and lower permanent environmental variance for genetic RFI compared to those for phenotypic RFI, but they found equal residual variances between two RFI definitions (Lu et al., 2015).

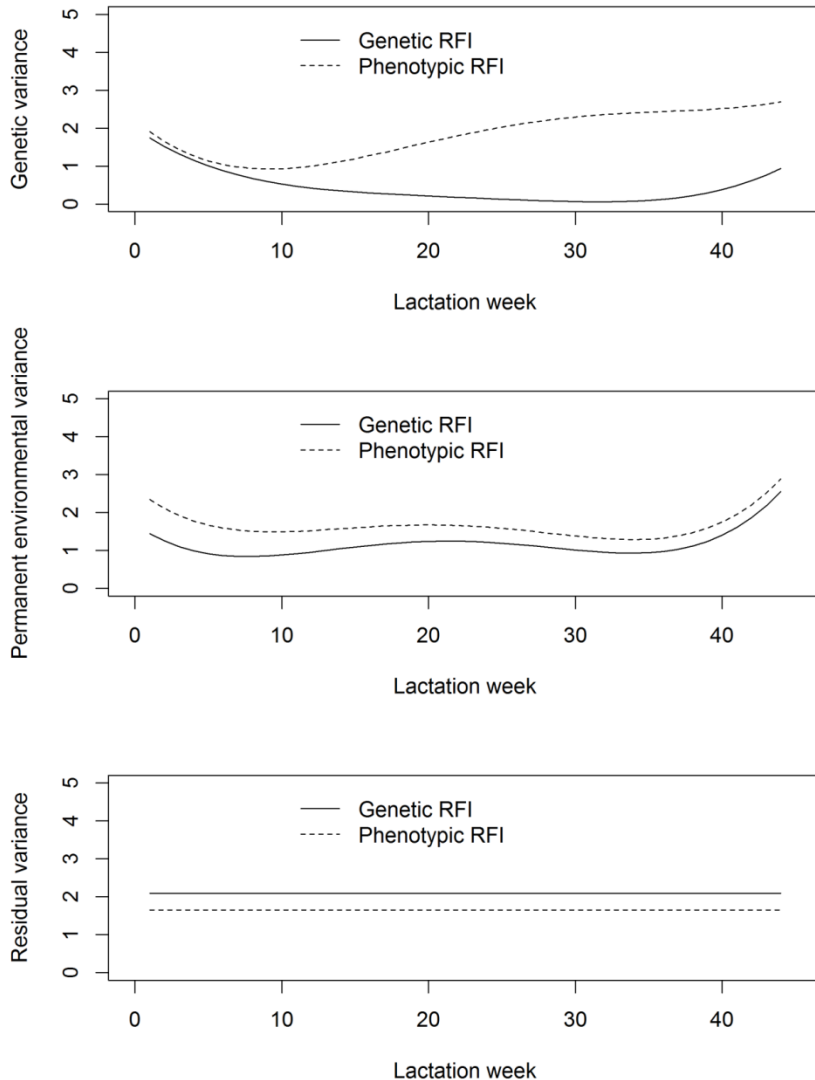


Figure 10. Genetic variances, permanent environmental variances, and residual variances across 44 lactation weeks for two definitions of residual feed intake (RFI) in Holstein dairy cattle. The estimates for genetic RFI are in solid lines, and the estimates for phenotypic RFI are in dashed lines.

The heritability for genetic RFI and for phenotypic RFI showed different patterns across lactation (Figure 11). The mean heritability across lactation was 0.11 for genetic RFI, and 0.35 for phenotypic RFI. The lower heritability for genetic RFI compared to that for phenotypic RFI was due to the lower genetic variance and higher residual variance for genetic RFI. Our

heritability estimate for genetic RFI was close to the estimate of 0.14 found by Lu et al. (2015). The proportion of genetic variance for DMI explained by the genetic variance of RFI was 17% on average across 44 lactation weeks (Figure 12). The proportion was highest at the beginning of lactation (64% in week 1) and was lowest in week 32 (1%). In early lactation, the high proportion of the genetic variance for DMI explained by RFI was partly due to the fact that  $\Delta BW$  was not modeled in the multivariate analyses for RFI.

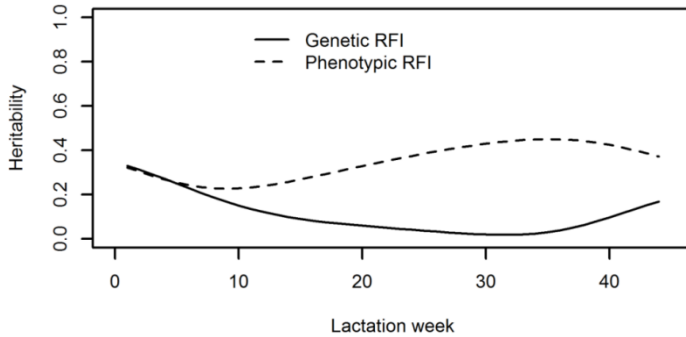


Figure 11. Heritability estimates across 44 lactation weeks for genetic residual feed intake (RFI) and for phenotypic RFI in Holstein dairy cattle. The estimates for genetic RFI are in solid line, and the estimates for phenotypic RFI are in dashed line.

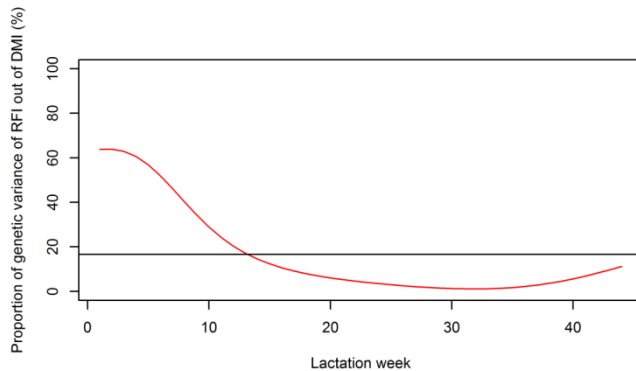


Figure 12. Proportion of genetic variance for dry matter intake (DMI) explained by the genetic variance for RFI in the multivariate analyses for RFI (i.e., genetic RFI) across 44 lactation weeks in Holstein dairy cattle. The horizontal line shows the average of the ratio across lactation.

### *Genetic correlations for RFI across lactation*

For genetic RFI, the genetic correlations for RFI ranged from -0.24 to 1 across lactation, where genetic RFI in early, middle, and late lactation stages were shown to be genetically different from each other (Figure 13A). The non-unity genetic correlations for genetic RFI across lactation suggest a changing genetic background of RFI efficiency in dairy cattle. For phenotypic RFI, the genetic correlation for RFI across lactation ranged from 0.01 to 1, where RFI in early lactation was genetically not the same trait as RFI in middle and late lactation (Figure 13B). Generally, genetic RFI and phenotypic RFI tended to show different patterns of genetic correlations across lactation, but in both cases RFI in early lactation was genetically different from RFI in later lactation stages.

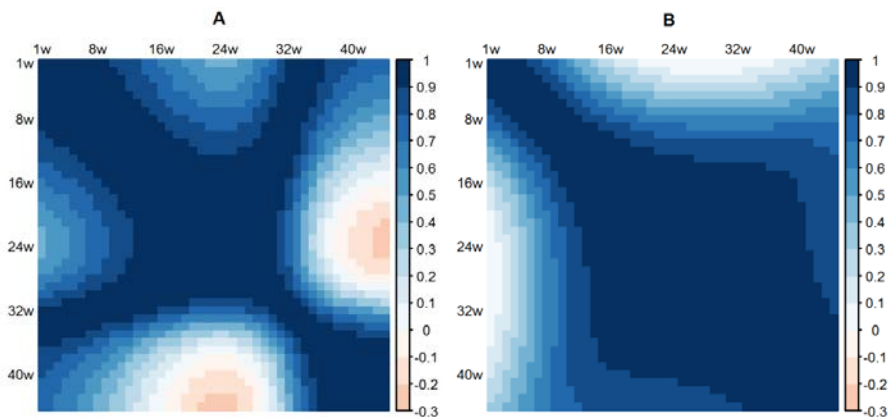


Figure 13. Genetic correlations across 44 lactation weeks for two definitions of residual feed intake (RFI): (A) genetic RFI, (B) phenotypic RFI.

### *Correlations between cows' EBVs for genetic RFI and EBVs for phenotypic RFI*

For the overall EBVs (i.e., EBV of the entire lactation) for all the animals with phenotypes, the Pearson correlation between animals' EBVs for genetic RFI and EBVs for phenotypic RFI was only 0.47. If we further looked at the EBV correlations across all 44 lactation weeks (Figure 14), the EBV correlations between genetic RFI and phenotypic RFI ranged from -0.18 to 0.80 across lactation. In general, the observed EBVs from two definitions of RFIs were moderately correlated, indicating different rankings of the animals by using different RFI definitions for selection.

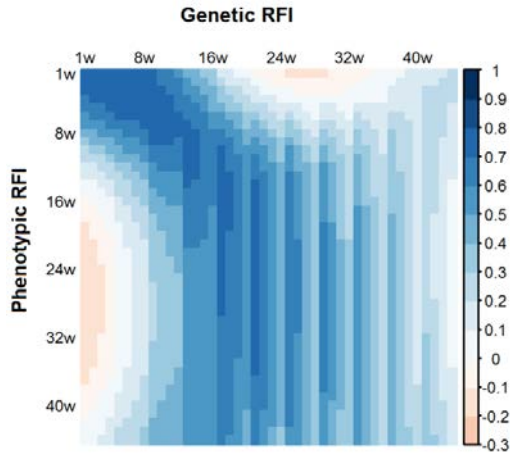


Figure 14. The correlations between animals' EBVs calculated from genetic RFI and those calculated from phenotypic RFI across 44 lactation weeks in Holstein dairy cattle.

#### *Comparison between Animals with Highest and Lowest EBVs for RFI*

The 10% of the animals with the lowest (i.e., most desirable) EBVs for RFI were selected from genetic RFI and phenotypic RFI, respectively, and only 37% of these selected animals were the same between genetic RFI and phenotypic RFI. We further compared the average DMI, ECM, BW, and gross efficiency (kg ECM / kg DMI) between the animals with the lowest EBVs and the animals with the highest EBVs for RFI, genetic RFI and phenotypic RFI tended to show more differences in the direction of selection for RFI efficiency (Figure 15). Specifically, when phenotypic RFI was used for selection, animals with the lowest EBVs (i.e., most desirable) for RFI had lower DMI, lower ECM, and higher BW compared to animals with the highest EBVs (Figure 15A, 15B, 15C). When genetic RFI was used for selection, cows with the lowest EBVs for RFI had similar DMI (or slightly lower in some weeks), higher BW, and higher ECM compared to cows with the highest EBVs (Figure 15A, 15B, 15C). Comparing the gross efficiency (i.e., kg ECM per kg DMI), when genetic RFI was used, cows with low EBVs for RFI had a slightly higher gross efficiency than cows with high EBVs (Figure 16). However, when the selection was based on phenotypic RFI, cows with low EBVs tended to have lower gross efficiency than cows with high EBVs for RFI.

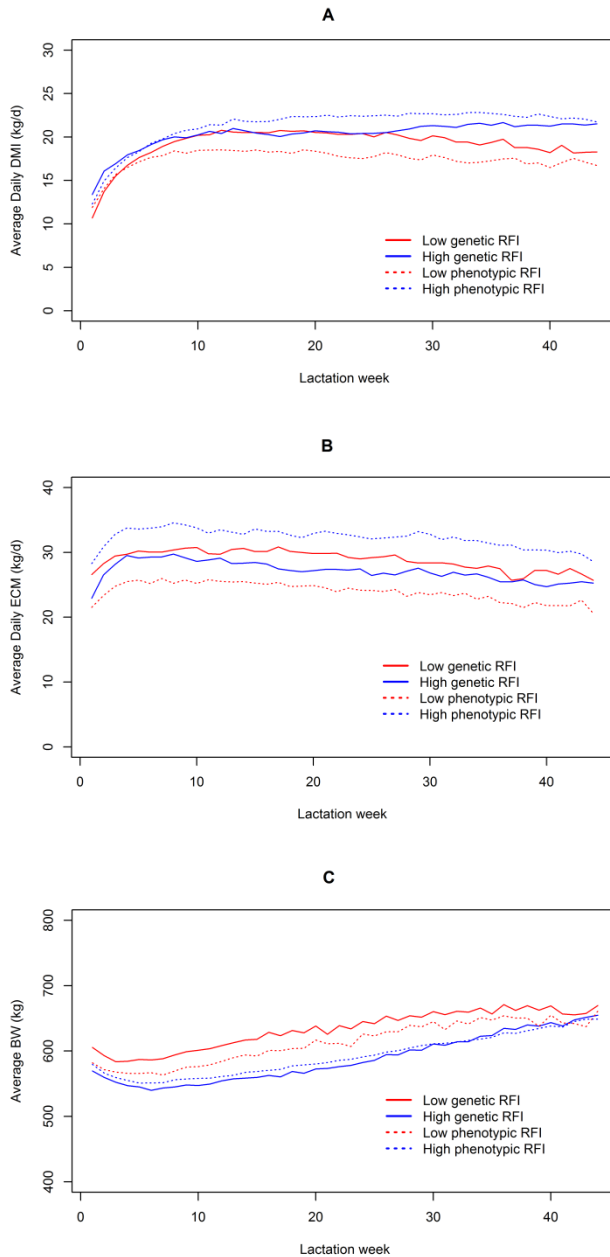
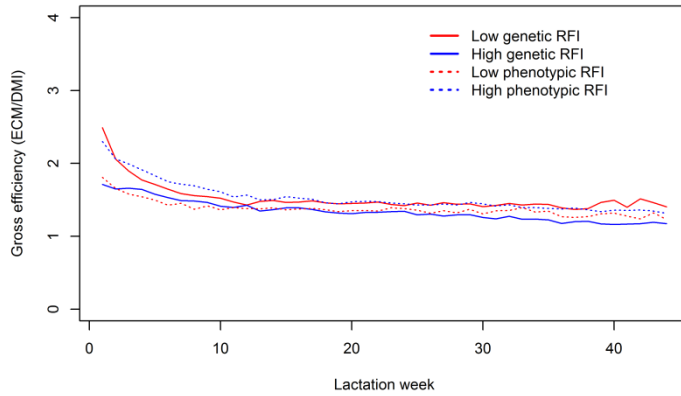


Figure 15. (A) Average daily dry matter intake (DMI, kg/d), (B) average daily energy-corrected milk (ECM, kg/d), and (C) average body weight (BW, kg) across 44 lactation weeks for (1) the 10% of cows with the lowest EBVs for genetic RFI, as “Low genetic RFI”, (2) the 10% of cows with the highest EBVs for genetic RFI, as “High genetic RFI”, (3) the 10% of cows with the lowest EBVs for phenotypic RFI, as “Low phenotypic RFI”, (4) the 10% of cows with the highest EBVs for phenotypic RFI, as “High phenotypic RFI”.



*Figure 16.* Gross efficiency (kg ECM/kg DMI) across 44 lactation weeks for (1) the 10% of cows with the lowest EBVs for genetic RFI, as “Low genetic RFI”, (2) the 10% of cows with the highest EBVs for genetic RFI, as “High genetic RFI”, (3) the 10% of cows with the lowest EBVs for phenotypic RFI, as “Low phenotypic RFI”, (4) the 10% of cows with the highest EBVs for phenotypic RFI, as “High phenotypic RFI”.



## 4 General discussion

### 4.1 Considerations on alternative FE definitions in dairy cattle

Defining feed efficiency in lactating animals is more complicated than defining feed efficiency in growing animals due to the metabolic changes that occur during lactation cycles (Berry and Crowley, 2013). Nutrient intake of the dairy cow is used for different biological processes such as milk production, maintenance, growth and pregnancy. Milk production and maintenance are important factors for the dairy cow in energy utilization. Dairy cows experience rapid metabolism of body reserves immediately postpartum for milk production, and the body reserves are gradually restored in later lactation stages and during the non-lactating period (Mao et al., 2004; Roche et al., 2009; Vallimont et al., 2010). Considering the metabolic complexity of FE in dairy cows, defining FE in dairy cattle should properly take account of the physiological bases of feed utilization, the genetic variation and parameters for FE, and the correlated responses for selecting for FE.

Recent genetic studies on FE focused on DMI and RFI, as two important FE candidate traits. The genetic properties for DMI and RFI were discussed in detail below. In addition, some other FE definitions (e.g., gross efficiency) were also briefly discussed.

#### 4.1.1 Feed intake

Genetic variation for feed intake exists in multiple dairy cattle breeds. Based on the results from Paper II, the heritability estimates for DMI ranged from 0.30 to 0.55 in Holstein cows across 44 weeks, 0.20 to 0.48 in RDC cows across 32 weeks, and 0.17 to 0.52 in Jersey cows across 44 weeks. In most

studies, including ours, the heritability estimates for feed intake in dairy cattle were moderate and in the same range as the heritability for milk yield, but were lower than the heritability for BW of dairy cattle (Karacaoren, Jaffrezic and Kadarmideen, 2006; Vallimont et al., 2010; Spurlock et al., 2012).

Positive genetic correlations were found between DMI and ECM across the entire lactation, which were consistent with previous studies (Veerkamp, 1998; Vallimont et al., 2010; Manzanilla-Pech et al., 2016), indicating that selection for milk yield would concurrently increase DMI. However, recent studies, including our results in Paper II, showed that the genetic correlation between DMI and ECM in early lactation is low (Huttman et al., 2009; Spurlock et al., 2012). The low correlation between DMI and ECM in early lactation indicated that selection for higher milk yield may only lead to a small genetic change in cows' feed intake in the initial period of lactation, and vice versa. This indicates an increased negative EB in the case of exclusive breeding for milk yield (Huttman et al., 2009). A negative EB has been reported to have an unfavourable genetic correlation with dairy cattle fertility and health (Collard et al., 2000; Veerkamp et al., 2000; Banos and Coffey, 2010). In this case, EB itself or an EB indicator trait (i.e., BCS) for early lactation should be considered in dairy cattle breeding to avoid a more severe negative EB when selecting for higher yield or FE (e.g., Veerkamp, 1998; Coffey, Simm and Brotherstone, 2002; Liinamo, Mäntysaari and Mäntysaari, 2012).

The genetic correlation between cows' DMI and BW was found to be positive in Paper II and also in previous studies (Liinamo, Mäntysaari and Mäntysaari, 2012; Spurlock et al., 2012; Manzanilla Pech et al., 2014b), indicating that bigger cows tend to have higher feed intake due to the higher energy required for body maintenance. Generally, high BW of cows could indicate low FE of cows due to the high energy requirement for body maintenance. Therefore, including maintenance requirement in selection has a potential to improve FE in dairy cattle (Lidauer et al., 2018). Metabolic body weight (MBW) is an indicator of cows' energy required for body maintenance. Lidauer et al. (2018) reported an improved gross efficiency of dairy cattle by including a candidate FE trait of maintenance requirement ratio (MRR,  $MRR = MBW / ECM$ ) into the selection index (Lidauer et al., 2018).

In addition, feed intake has been recently reported to be in positive genetic correlations with energy balance (EB), body condition score (BCS), and conformation traits (Vallimont et al., 2010; Liinamo et al., 2015; Manzanilla-Pech et al., 2016). There is also a study reporting slightly negative genetic correlation between feed intake and somatic cell score (SCS) (Vallimont et al., 2010). When breeding for FE with feed intake, the correlated responses for fertility and health traits should be carefully considered.

In practice, when DMI is used as a FE trait, it is important to be aware that DMI is hard to value on its own, because a higher producing cow or a heavier cow eats more. To improve efficiency of cows should not unlimitedly minimize the feed intake of cows at risks of decreasing milk production or sacrificing cows' fertility and health. In the Netherlands, DMI has been applied as a FE definition trait in dairy cattle breeding, by combing EBVs of DMI with EBVs of indicator traits (i.e., milk, fat and protein yield, and BW) from the breeding value estimation of the whole population (Jong et al., 2016). Using breeding value for feed intake in relation to the breeding values for milk production and BW would be an option to avoid selecting for cows that become too skinny or have low milk production (Veerkamp et al., 2014).

Last but not least, energy intake could be used as an alternative for DMI. Applying energy content of DM to DMI for a standard energy intake might increase the accuracy of calculating FE and could eliminate the variability associated with the energy density of the feed. Accurate FE data, in one way or another, is vital for accurate genetic evaluation of FE.

#### 4.1.2 Residual feed intake

As one important FE candidate trait in dairy cattle, RFI has been studied widely and has been applied as a FE definition trait in selection index in some countries, e.g., Australia (Pryce et al., 2015). Compared with feed intake, the general benefit of using RFI is that RFI adjusts for the important energy sinks for feed intake, so that RFI itself is defined in a way relative to milk production, BW, and the change of BW. The challenge is how to properly model RFI so that RFI can make good sense to stand for efficiency physiologically and be easy for implementation. Alternative ways of modelling RFI have been studied recently, including our studies in Paper III and Paper IV. In Paper IV, RFI derived from linear regression of DMI on energy sink traits was denoted as “phenotypic RFI”, and RFI derived from multivariate analyses was denoted as “genetic RFI”. Phenotypic RFI and genetic RFI showed differences in variance components, genetic parameters, and rankings of animals in selecting for FE in dairy cattle.

Phenotypic RFI had higher genetic variance and heritability than genetic RFI. The heritability of phenotypic RFI in dairy cattle ranged from 0.10 to 0.23 across lactation in Paper III, where DMI was phenotypically adjusted for ECM, MBW, and  $\Delta$ BW. The result was consistent with the heritability for RFI reported by Tempelman et al. (2015) (i.e., 0.10–0.25). The mean heritability for genetic RFI across lactation was found to be 0.11 across lactation in Paper IV, similar to the estimate of 0.14 found by Lu et al. (2015) for genetic RFI.

The difference in genetic variance and heritability for the two RFI definitions comes from the different modelling strategies of RFI. Phenotypic RFI was based on phenotypic adjustment for milk production and BW, so that phenotypic RFI was still in low but positive genetic correlations with milk production and BW (Manzanilla-Pech et al., 2016; Liinamo et al., 2015). Genetic RFI was derived as DMI conditional on ECM and MBW, where the resulting RFI was genetically independent from ECM and MBW. Defining RFI genetically independent from production traits makes FE a relatively independent trait in the selection index, which could lead to easily interpretable breeding values for FE in the selection index.

Using genetic RFI or phenotypic RFI tends to give different rankings for RFI efficient animals. Selection for FE based on genetic RFI and phenotypic RFI could also lead to different directions of selection for efficient cows. In Paper IV, favored animals for phenotypic RFI tended to have lower DMI, lower ECM, and higher BW compared to un-favored animals. In contrast, favored animals for genetic RFI tended to have similar DMI, higher ECM, and higher BW compared to un-favored animals. The current comparison was based on differences in the phenotypic level of DMI, ECM, and BW between favored and un-favored animals. It would be interesting to see if the difference in phenotypic performances between the two groups could still be seen among the offspring of these animals. In addition, no matter which RFI definition (genetic RFI or phenotypic RFI) was applied in Paper IV, favored cows for RFI tended to have higher BW compared to un-favored cows. Generally, high BW of cows could indicate relatively low FE due to the high energy requirement for body maintenance. Therefore, BW could be needed to be put together with RFI in the selection index to limit the increase of BW if RFI is applied to the selection for FE in dairy cattle.

In practice, the application of phenotypic RFI and genetic RFI to dairy cattle breeding has both been seen recently. In Australia, the FE trait of “feed saved” in the selection index is based on animals’ phenotypic RFI and breeding values for BW. In US, the idea of “genetic RFI” is planned to be used as a FE trait in dairy cattle breeding, where genetic RFI is genetically uncorrelated with milk production and BW. In US the genetic RFI is derived by a slightly different way compared to what we did in paper IV (VanRaden et al., 2018). In VanRaden et al. (2018), the breeding value for FE was derived from phenotypic RFI linear regressed on EBVs for milk production and EBVs for BW.

### 4.1.3 Other feed efficiency definitions

#### *Gross efficiency*

In gross efficiency, a cow's efficiency is calculated from the ratio of milk output to feed intake input (i.e. milk output / intake input). Although the definition of gross efficiency sounds simple, the actual situation is not. Selection for higher gross efficiency is not always a favoured strategy because it may not increase the physiological efficiency of cows (i.e. reduce heat loss, increase digestive efficiency) even though there can be a reduction in the feed required to produce milk (Dechow, 2013). Body condition mobilization can inflate gross efficiency for early lactation cows, so that evaluation of gross efficiency in early lactation without factoring body condition changes can lead to misleading conclusions (Dechow, 2013). Furthermore, direct selection on gross efficiency could have some limitations because gross efficiency is defined as a ratio trait of milk output to intake input. The nominator of the trait (i.e., milk output) is a composite of milk production traits which are included in the total merit index with different weights (Lidauer et al., 2018). Gross efficiency is still in positive correlation with milk production traits phenotypically and genetically (e.g., Manafiazar et al., 2015; Lidauer et al., 2018). The relationship between gross efficiency and production traits would need to be carefully taken care of, if gross efficiency is used in the selection index.

#### *Herd efficiency*

We can also define dairy cattle feed efficiency at the level of dairy herds, denoted as "herd efficiency" here. The feed input to the herd includes the feed for lactating cows, but also includes feed for the dry cows and feed used to raise replacement animals. Since dairy farms can be dual-purpose with income from both milk production and salvage value of cows at the end of productive life, the output of feed input in the herd could include mainly milk production but also the value of culling cows. This is just a simple example of how dairy cattle FE can be defined on the level of dairy herds, and there can be alternative definitions of herd-level FE considering the diverse herd structures and conditions.

## 4.2 Influence of lactation stages on feed efficiency

### 4.2.1 Genetic heterogeneity of FE traits across lactation stages

#### *Feed intake*

Feed intake for dairy cows was genetically not the same trait across lactation, where the genetic correlations for DMI between early lactation and later lactation stages were found to be far from unity (Koenen and Veerkamp, 1998; Berry et al., 2007; Liinamo, Mäntysaari and Mäntysaari, 2012). Our study confirmed the genetic heterogeneity of DMI across lactation in Holstein and RDC dairy cows, and observed the same phenomenon across lactation in Jersey cows. In all three breeds, DMI in middle and late lactation was generally highly correlated, similar to findings of previous studies on the Holstein breed (Manzanilla Pech et al., 2014b).

In practice, the genetic heterogeneity of DMI across lactation needs to be carefully considered in any recording and selection strategy for FE. Due to the low genetic correlation for DMI between early and later lactation stages, DMI measurements in middle or late lactation cannot be strong predictors of DMI in early lactation, and vice versa. To improve FE across lactation, it might be necessary to take DMI records from separate time points across all lactation stages. Apart from recording in middle and late lactation, a few DMI records in early lactation would also be recommended, because DMI in early lactation is a different trait from DMI in later lactation. Manzanilla Pech et al. (2014a) estimated the accuracy of DMI breeding values using various different recording schemes for DMI, and found that higher accuracy was achieved when DMI was recorded at several lactation stages, when the number of measurements was limited across lactation (Manzanilla Pech et al., 2014a).

The genetic heterogeneity of DMI across lactation should also be considered when joining data from different sources. To accumulate sufficient data for genetic and genomic evaluation for FE, feed intake data were usually collected or combined from several herds and experiments within or across countries (e.g., Berry et al., 2014; de Haas et al., 2015). The joint data for FE could be heterogeneous in many aspects, for example due to the difference in feeding systems, recording periods, or the number of repeated measurements (Hardie et al., 2015; Tempelman et al., 2015; Veerkamp et al., 2015). When joint data come from different lactation periods, the heterogeneity of feed intake across lactation stages may need to be considered before genetic evaluation. Data standardization might be needed in this situation to calibrate data from different lactation periods (Veerkamp et al., 2015). One method of

standardization could be based on a random regression prediction of records for a cow using the cow's own repeated records and the covariance structure in the population (Banos et al., 2012; Berry et al., 2014; Veerkamp et al., 2015). Alternatively, feed intake from different lactation stages could also be defined as different traits, where a multiple-trait model could be applied in the genetic analyses.

### *Residual feed intake*

In Paper III and Paper IV, RFI was found to be genetically different across lactation. For phenotypic RFI, RFI in early lactation was genetically different compared to RFI in middle and late lactation stages. Liinamo et al. (2015) reported a similar finding of the genetic heterogeneity of residual energy intake during 30 weeks of lactation in Nordic Red dairy cattle. For genetic RFI, genetic RFI in early, middle, and late lactation stages were shown to be genetically different from each other. Generally, genetic RFI and phenotypic RFI tended to show different patterns of genetic correlations across lactation, but in both cases RFI in early lactation were genetically different from RFI in the rest of the lactation.

The non-unity genetic correlations for RFI across lactation suggest a changing genetic background of RFI efficiency in dairy cattle, for both genetic RFI and phenotypic RFI. The heterogeneity of RFI across lactation could stem from the basic definition of RFI. Basically, RFI is defined based on the phenotypes of DMI, milk yield, and BW. From the findings of Paper II and several previous studies, milk yield (MY) and DMI are genetically different traits across lactation, especially between early and later lactation stages (Veerkamp and Thompson, 1999; Manzanilla Pech et al., 2014b; Li et al., 2016). BW tended to be a more consistent trait across lactation, but the genetic correlation of BW between early and later lactation was still not unity (Veerkamp and Thompson, 1999; Manzanilla Pech et al., 2014b). Properties of component traits of RFI (DMI, MY, and BW) across lactation influence the genetic properties of RFI across lactation.

#### 4.2.2 Influence of lactation stage on estimating RFI

Neglect of lactation stages in modeling RFI influenced the assessment of RFI and the variance component estimation for RFI, based on results from Paper III. In Paper III, the partial regression coefficients of DMI on energy sinks changed across lactation, when period-specific regressions were allowed for in modeling RFI. The assumption of constant partial regressions of feed intake on ECM, MBW, and  $\Delta$ BW over lactation was not always sufficient to explain the

feed utilization for energy sinks in RFI model and tended to result in roughly average information of all period-specific effects. More specifically, the partial regression coefficients of DMI on ECM were significantly different between early and later lactation stages, with the effect of ECM on DMI being much lower in early lactation compared with later lactation. This result could partly reflect the change of metabolic condition in dairy cows during lactation. A cow's MY increases sharply after calving, and feed intake peaks no earlier than lactation week 10 to 12 (e.g., Gravert, 1985; Berry et al., 2014). In early lactation, the energy intake from diet cannot meet the energy demand for rapidly increased MY, and part of the required energy comes from the mobilization of body reserves (Berglund and Danell, 1987; Mao et al., 2004; Banos and Coffey, 2010). After early lactation, the feed intake of cows remains at a relatively high level to provide energy for milk production, and body reserves are gradually restored (Mao et al., 2004). The potential change in the relationship between feed intake and milk production could also be reflected by a varying genetic correlation between DMI and milk production traits across lactation from findings in Paper II and previous studies, where feed intake in early lactation was weakly genetically correlated with milk production traits (Veerkamp and Thompson, 1999; Huttman et al., 2009; Manzanilla Pech et al., 2014b).

The partial regression coefficients of DMI on  $\Delta$ BW were also found to be significantly influenced by the lactation period, based on results from Paper III. Generally, lactating cows lose BW at the beginning of lactation and gradually gain BW in later lactation (Vallimont et al., 2010). The catabolism and anabolism of body tissues correspond to different energy values, such that the energy generated from a 1-kg loss in BW is less than the energy required for a 1-kg gain (O'Mara, 1996; Coleman et al., 2010). Therefore, the effect of  $\Delta$ BW on feed intake in early lactation (mostly BW loss) would be expected to differ from the effect in middle and late lactation (mostly BW gain). The feed intake of cows could hardly follow a constant partial regression of the cows'  $\Delta$ BW over the whole lactation.

The variance component and genetic parameters for RFI were influenced if period-specific effects of energy sinks were allowed. In Paper III, after accounting for the period-specific effects of energy sinks, the genetic variance and heritability for RFI were slightly lower but more stable over lactation, compared to those from a RFI model without period-specific effects on energy sinks. The higher genetic variance from the RFI model without period-specific effects might partly come from the unexplained variance in the period-specific effects of energy sinks. In addition, when period-specific partial regressions of DMI on energy sinks were included in RFI model, the extreme negative



genetic correlations for RFI between early and middle lactation tended to be mitigated.

### 4.3 Genetics of feed efficiency in diverse dairy breeds

Feed efficiency in three dairy breeds (Holstein, RDC, and Jersey) was studied in Paper I and II. Based on the findings from our papers and previous studies, the phenotypic observations and genetic parameters for DMI and its related traits (ECM and BW) followed similar patterns between breeds.

#### 4.3.1 Phenotypic observations

Cows of different breeds shared very similar patterns of lactation trajectories for phenotypic means of DMI, ECM, and BW. Immediately after calving, cows' average daily DMI and ECM both increased, but at different rates. The average daily ECM increased sharply to peak at lactation week 7 or week 8 in all three breeds, whereas DMI reached a relatively high stable level no earlier than week 11 and peaked even later. In dairy cattle, the slower increase in feed intake relative to milk yield in early lactation has been widely recognized, and it explained the deficiency of energy intake for milk production in early lactation as well as the body reserve mobilization of dairy cows (Berglund and Danell, 1987; Mao et al., 2004; Banos and Coffey, 2010). Cows of different breeds differed in the amount of BW loss from the beginning of lactation to the nadir of BW. Our study showed that Holstein cows and RDC cows had the highest and lowest BW loss, respectively, which was in agreement with Sondergaard et al. (2002).

#### 4.3.2 Genetic parameters

Cows of different breeds followed similar patterns of genetic parameters for DMI. In most studies, including ours, the heritability estimates for DMI in Holstein, RDC, and Jersey cows were moderate and in the same range as the heritability for milk yield, whereas heritability for BW was moderate to high and was higher than the heritability for DMI or yield (Karacaoren, Jaffrezic and Kadarmideen, 2006; Vallimont et al., 2010; Spurlock et al., 2012). Feed intake in early lactation was genetically different from that in mid and late lactation stages, no matter in which breed. The genetic correlations of DMI with ECM and with BW in RDC cows followed a similar pattern as those in Holstein cows, as shown in Paper II.

There are some limitations of our studies in understanding the breed similarity and difference in the genetic parameters for FE, due to the small data sizes for cows in each breed. Feed intake is costly and difficult to measure, making it very difficult to have sufficient data from multiple breeds. Our current data set for RDC cows came from Denmark, Finland, and Sweden. RDC cows could be genetically diverse between countries (Lidauer et al., 2015), which may affect our variance component estimation for RDC. The genetic parameters for DMI in Jersey cows across the whole lactation was to our knowledge first addressed in our studies, where our results indicated similar genetic parameters for DMI in Jersey cows and Holstein cows. However, more accurate genetic parameter estimates for FE in Jersey need to be addressed in future studies considering the fairly large standard errors of estimates in Jersey cows in our studies due to the small data sizes.

## 5 Conclusions

Dry matter intake (DMI) and residual feed intake (RFI) are important candidate traits for feed efficiency in dairy cattle. The recognized genetic variation in DMI and RFI has opened up possibilities for genetically improving FE of dairy cattle to increase the profitability of dairy production and to reduce the ecological footprint. We found moderate heritability for DMI in primiparous Holstein, Nordic Red, and Jersey cows across lactation. The heritability for DMI is in a similar range to the heritability for ECM and is lower than the heritability for BW in dairy cattle. The heritability for DMI is higher than that for RFI. Cows from different breeds shared a similar pattern of genetic parameters for DMI and RFI across lactation, and the breed difference in genetic parameters for DMI and RFI was not significant in our studies.

Dry matter intake is in positive genetic correlations with milk production and BW across lactation. The genetic correlation between DMI and ECM is low in early lactation, but keeps higher than 0.8 in middle and late lactation stages. In practice, when DMI is used as a FE trait, it is important to be aware that DMI is hard to value on its own, because a higher producing cow or a heavier cow eats more. Selecting for FE based on DMI should consider cows' milk yield and maintenance requirement together with DMI.

There are alternative ways of modelling RFI in dairy cattle. RFI is usually modelled by linear regression of DMI on energy sink traits (e.g., milk production, BW,  $\Delta$ BW), denoted as “phenotypic RFI” in our studies. Phenotypic RFI is still genetic correlated with energy sink traits. RFI that is derived from multivariate analyses (denoted as “genetic RFI” in our studies) was genetically uncorrelated with energy sink traits. Genetic RFI and phenotypic RFI showed differences in variance component estimates, genetic parameters across lactation, and also in the ranking of efficient animals. On one hand, phenotypic RFI has higher genetic variance and heritability than genetic RFI. On the other hand, genetic RFI is genetically independent from milk production and BW in selection. In addition, when modelling phenotypic

RFI, the partial regression coefficients of cows' feed intake on energy sinks were found to vary across lactation, especially for ECM in early lactation. Neglect of lactation stages in modelling RFI could lead to naïve assessment of RFI and affect the genetic parameter estimates for RFI.

DMI is genetically not the same trait across lactation stages, especially between the early and later lactation stages. The genetic heterogeneity across lactation was also found for RFI, indicating a changing genetic background of FE in dairy cattle. Compared to DMI and RFI, ECM and BW showed much less genetic heterogeneity across lactation in all three breeds. In practice, the genetic heterogeneity of DMI across lactation needs to be carefully considered in the recording and selection strategy for FE. Due to the low genetic correlation for DMI between early and later lactation stages, DMI measurements in middle or late lactation cannot be strong predictors of DMI in early lactation, and vice versa. To improve FE for the entire lactation, it is recommended to take DMI records from separate time points across all lactation stages.

## 6 Future research

Genomic selection is well-suited to difficult-to-measure traits, such as feed efficiency in dairy cattle (Pryce et al., 2018). Genomic evaluation for FE in dairy cattle has been started recently in Australia and the Netherlands. Future research in the possibility of using genomic evaluation for FE will be further studied in Nordic dairy cattle breeding. Single-step GBLUP method could be helpful for genomic evaluation for FE given that some animals with phenotypes may be not genotyped. The challenge remains in the limited data size for FE for genomic evaluation. International collaboration for joining data for large reference population and regular refreshment of the reference population could be one efficient solution to obtain acceptable prediction reliabilities for FE in dairy cattle genomic evaluation.

In addition, the expected genetic responses for FE and production when using different FE traits in selection should be further investigated, to help making decisions on how to define FE in Nordic total merit index. Improving FE of dairy cattle by limiting the maintenance requirement for dairy cows could be one interesting topic to study on.

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## Popular science summary

Feed efficiency (FE) of dairy cows is an important concept in dairy production. Feed accounts for the largest part of operating costs in dairy production. Improving FE in dairy production is expected to increase the profits of dairy farmers. Feed efficient cows are expected to require less feed intake than the inefficient cows for a certain amount of milk yield and for a certain cow size. Meanwhile, selecting for efficient cows should not decrease the fertility or health of cows.

Feed efficiency in dairy cattle is influenced by diet and other environmental factors, genetic ability and physiological state of the cow. Selecting for the cows with better genetic ability for efficiency plays an important part in improving efficiency for the whole dairy cattle population and also for the next generations of dairy cows. Recent genetic studies on FE in dairy cattle have found evidence of genetic variation for FE in several dairy breeds, making it possible to improve FE of cows through genetics and breeding.

Feed intake and FE are difficult and costly to measure in large scale for individual cows. The data are mostly available in research herds with limited data size. International collaborations have been established to join FE data across countries for genetic studies on FE. In Nordic countries, a joint data set of feed efficiency in dairy cattle has been established among Nordic countries since 2013, aiming to investigate the genetic variation for FE in several dairy breeds in Nordic countries and to assess the possibility of including FE into Nordic dairy cattle breeding. The current thesis work is part of the Nordic collaborative project of “Feed Utilization in Nordic Cattle (FUNC)” among Denmark, Finland, Norway, and Sweden. The aim of the thesis was to study the genetic properties of alternative FE definitions and FE-related traits (milk production, and body weight) in several dairy cattle breeds, in order to properly define FE in dairy cattle for breeding.

Four papers were included in the thesis work. Two important FE traits for dairy cattle, dry matter intake (DMI) and residual feed intake (RFI), were

studied to investigate the genetic properties of these traits across lactation and across breeds.

In Paper I-IV, genetic variation for DMI was shown for all studied dairy breeds. Cows of different breeds shared a similar pattern of genetic parameters for DMI. We found moderate heritability for DMI in Holstein, RDC and Jersey cows. The heritability for DMI was in a similar range to the heritability for ECM and was lower than that for BW. Feed intake was in positive genetic relationships with ECM and BW across lactation, indicating that heavier cows eat more feed and high-yielding cows eat more feed, genetically. Therefore, defining FE based on DMI of cows should consider cows' production and BW as well. In the Netherlands, FE of cows is defined using the DMI of cows combined with milk production and BW in breeding.

As an important FE candidate trait in dairy cows, RFI was defined based on cows' DMI adjusted for milk production, BW, and the change of BW. The heritability for RFI was lower than that for DMI. There are alternative ways of defining RFI by different models. Different definitions of RFI influence the assessment of RFI and have different genetic properties of describing efficiency of cows. In Australia, RFI is used as a FE definition in their dairy cattle breeding for efficiency.

Last but not least, cows' DMI or RFI is genetically not the same trait across lactation stages, especially between early and later lactation stages. Cows' feed intake information in early lactation is not a good indicator of feed intake in mid or late lactation, and vice versa. This phenomenon should be considered in recording and selection for efficiency in dairy cows. In order to improve FE for the entire lactation, it is recommended to take DMI measurements from separate time points across all lactation stages.

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Bingjie Li  
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# Appendix





## Genetic parameters for dry matter intake in primiparous Holstein, Nordic Red, and Jersey cows in the first half of lactation

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### ABSTRACT

Dry matter intake (DMI) is a key component of feed efficiency in dairy cattle. In this study, we estimated genetic parameters of DMI over the first 24 lactation weeks in 3 dairy cattle breeds: Holstein, Nordic Red, and Jersey. In total, 1,656 primiparous cows (717 Holstein, 663 Nordic Red, and 276 Jersey) from Denmark, Finland, and Sweden were studied. For each breed, variance components, heritability, and repeatability for weekly DMI were estimated in 6 consecutive periods of the first 24 lactation weeks based on a repeatability animal model. Genetic correlations for DMI between different lactation periods were estimated using bivariate models. Based on our results, Holstein and Nordic Red cows had similar DMI at the beginning of lactation, but later in lactation Holstein cows had a slightly higher DMI than Nordic Red cows. In comparison, Jersey cows had a significantly lower DMI than the other 2 breeds within the first 24 lactation weeks. Heritability estimates for DMI ranged from 0.20 to 0.40 in Holsteins, 0.25 to 0.41 in Nordic Red, and 0.17 to 0.42 in Jerseys within the first 24 lactation weeks. Genetic and phenotypic variances for DMI varied along lactation within each breed and tended to be higher in the middle of lactation than at the beginning of the lactation. High genetic correlations were noted for DMI in lactation wk 5 to 24 in all 3 breeds, whereas DMI at early lactation (lactation wk 1 to 4) tended to be genetically different from DMI in the middle of lactation. The 3 breeds in this study might differ in their genetic variances for DMI, but the differences were not statistically significant in most of the studied periods. Breed differences for the genetic variance tended to be more obvious than for heritability. The potential breed differences in genetic variation for DMI should be considered in a future study using feed intake information from multiple breeds.

**Key words:** feed efficiency, dry matter intake, dairy cattle, heritability, genetic correlation

### INTRODUCTION

Feed accounts for the largest part of operating costs in dairy production (European Commission, 2013; USDA, 2016), and feed intake is the key component of all available measures of feed efficiency. Currently, measurement of feed intake for individual cows is available only in research or nucleus herds. Insufficient recording of feed intake, in large part due to high cost, has hindered accurate estimation of genetic parameters as well as accurate selection of feed-efficient dairy cattle. Genetic studies on feed intake in dairy cattle call for larger data sets using information from multiple data sources (e.g., multiple countries or breeds).

Genetic variation for feed intake in the Holstein breed has been widely studied (e.g., Korver, 1988; Berry et al., 2014; Manzanilla Pech et al., 2016). In Holsteins, heritability estimates for DMI were estimated to range from 0.04 to 0.54 (e.g., Veerkamp and Thompson, 1999; Buttchereit et al., 2011; Berry et al., 2014). Heritability was found to vary along lactation, although the trajectory of heritability along lactation is still controversial (e.g., Karacaören et al., 2006; Manzanilla Pech et al., 2014a; Tetens et al., 2014). Large standard errors in most of the previous studies make it difficult to compare and differentiate the heritability estimates to clarify the trajectory. In addition, a low genetic correlation was reported for DMI between early lactation and the rest of lactation in Holstein (e.g., Hüttmann et al., 2009; Manzanilla Pech et al., 2014a; Tetens et al., 2014).

Apart from Holsteins, genetic studies on DMI in other dairy cattle breeds are rare and based on very small data sets (Søndergaard et al., 2002; Liinamo et al., 2012). Nordic Red was studied by Liinamo et al. (2012) using 291 primiparous cows, in which the heritability for DMI was estimated to range from 0.18 to 0.33 within lactation wk 2 to 30, with large standard errors of estimates. They reported low but positive genetic correlations for DMI between lactation wk 2 and

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the middle of lactation. In addition, Søndergaard et al. (2002) reported the heritability for daily energy intake to be 0.14 based on a combined population of 293 lactating Jersey, Nordic Red, and Holstein cows in total.

The main limitations of previous studies on DMI in dairy cows are the uncertainty of estimates due to large standard errors and the domination by studies on the Holstein breed (e.g., Berry et al., 2014; Manzanilla Pech et al., 2014a). Larger data sets are necessary for accurate estimation of genetic parameters for DMI, and gaps remain in estimates of the genetic parameters for DMI in other dairy cattle breeds (e.g., Jersey, Nordic Red). One solution could be to join DMI data from multiple countries or breeds. Some international collaborative studies have been completed using feed intake in Holsteins, which made it possible to develop genetic and genomic evaluations of feed intake in Holstein through joining multiple-country data (Berry et al., 2014; de Haas et al., 2015; Manzanilla Pech et al., 2016). Feed intake information from multiple breeds, however, has not been used in previous studies. To assess the possibility of future genetic evaluation using DMI data from multiple breeds, information on the genetic variation and genetic parameters for DMI in the particular dairy cattle breeds is needed.

The objective of our study was to estimate the genetic parameters for DMI in primiparous Holstein, Nordic Red, and Jersey in different lactation periods within the first 24 lactation weeks. Heritability estimates and genetic variances for DMI as well as the genetic correlations for DMI between different lactation periods were compared within and between breeds along lactation.

## MATERIALS AND METHODS

### *Animals, Feeding, and Data Recording*

A total of 2,109 cows from 3 dairy breeds (905 Holstein, 872 Nordic Red, and 332 Jersey) were included in the original data set. The cows were from the Danish Cattle Research Center (<http://www.KFC-Foulum.dk>), Natural Resources Institute Finland Rehtijärvi research herd (Jokioinen, Finland) and Minkiö research herd (Jokioinen, Finland), and Swedish University of Agricultural Sciences Kungsängen research herd (Uppsala, Sweden) and Öjebyn research herd (Öjebyn, Sweden). The 291 Nordic Red cows studied by Liinamo et al. (2012) were from the Rehtijärvi research herd (Jokioinen, Finland) and were part of our data set. The cows calved between 1991 and 2014 for Holstein, between 1994 and 2013 for Nordic Red, and between 2002 and 2014 for Jersey. The cows were involved in several trials where feeding conditions were slightly different between trials (Åkerlind et al., 1999; Mäntysaari et al.,

2003, 2004, 2005, 2012; Patel, 2012; Berry et al., 2014; Mäntysaari and Mäntysaari, 2015). In most of the trials included in our study the cows were fed a TMR plus a fixed amount of concentrate, but there were also trials in which cows were fed forage and concentrate separately to fulfill specific feeding conditions. The feed offered to cows was measured individually and feed refusals were recorded to calculate the feed intake of individual cows. The DM contents in TMR, concentrates, and forages were analyzed regularly and the compositions were aligned and merged with feed intake records to obtain daily DMI values for individual cows.

### *Data Editing*

The original data set consisted of 111,129 records of weekly DMI from 2,109 cows of the 3 breeds, where a weekly DMI was the average of 7 daily DMI measurements from a particular lactation week of an individual cow. The cows were from parity 1 to 8. In our study, only DMI records of the primiparous cows within the first 24 lactation weeks were included, resulting in a total of 33,311 weekly DMI records from 1,751 primiparous cows (771 Holstein, 696 Nordic Red, and 284 Jersey). Cows with less than 5 DMI records within the first 24 wk were removed from the data set. Cows with ages at first calving of more than 36 mo were also removed from the data set, resulting in a data set with the cows' calving ages ranging from 22 to 36 mo. For each breed, those trials with less than 10 records per trial were removed from the data set.

After editing, the final data set of our study consisted of 32,929 weekly DMI records from 1,656 primiparous cows (717 Holstein, 663 Nordic Red, and 276 Jersey). Among all the studied cows, the Holstein cows were from Denmark (572 cows) and Sweden (145 cows); the Nordic Red cows were from Denmark (138 cows), Finland (446 cows), and Sweden (79 cows); the Jersey cows were from Denmark only.

The pedigree information was extracted from the Nordic Cattle Genetic Evaluation Database (NAV, Skejby, Denmark) by tracing back as many generations as possible for cows with DMI records. The number of animals within each pedigree was 9,612, 12,762, and 2,810 for Holstein, Nordic Red, and Jersey, respectively.

### *Statistical Analysis*

The weekly DMI in the first 24 lactation weeks were grouped into 6 consecutive lactation periods of 4 wk in length (Table 1). The number of animals with DMI observations differed across periods due to missing observations of some cows in some periods (Table 1). Generally, the number of DMI records increased from

**Table 1.** Description of the number of cows and the number of records in 6 consecutive lactation periods of 4 wk within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Lactation week	Number of cows			Number of records		
		HOL	RDC	JER	HOL	RDC	JER
1	1–4	670	583	274	2,569	1,965	1,046
2	5–8	687	602	275	2,655	2,287	1,057
3	9–12	670	586	262	2,572	2,199	1,013
4	13–16	636	523	254	2,431	1,987	986
5	17–20	617	501	241	2,364	1,891	935
6	21–24	593	486	230	2,286	1,788	898

period 1 to 2, mainly because DMI recording in the first lactation week was not available in some of the recording schemes.

The weekly DMI from different periods were considered as different traits. Within a period, the weekly DMI observations were considered as repeated measures of DMI for individual animals. In each breed, variance components for DMI of a particular lactation period were estimated using the following repeatability animal model:

$$y_{j\text{mnp}sq} = \mu + \text{Herd}_j + b \times \text{CalvAge} + \text{Trial}_m \\ + \text{YS\_Rec}_n + \text{LacWk}_p + \text{Trial}_m \times \text{YS\_Rec}_n \\ + a_s + p_s + e_{j\text{mnp}sq}$$

where  $y_{j\text{mnp}sq}$  is the weekly DMI observation within a period, where a period included up to 4 DMI observations for each individual cow;  $\mu$  is the overall intercept;  $\text{Herd}_j$  is the fixed effect of herd, where Holstein cows were from 2 herds, Jersey cows were from 1 herd, and Nordic Red cows were from 4 herds;  $b$  is the regression coefficient of a linear regression on the covariable CalvAge for calving age, where the calving age ranged from 664 to 1,065 d in Holstein, from 658 to 992 d in Jersey, and from 674 to 1,094 d in Nordic Red;  $\text{Trial}_m$  is the fixed effect of the trial where the data originated from, to adjust for the feeding difference between trials where Holstein were in 25 trials, Jersey were in 15 trials, and Nordic Red were in 16 trials;  $\text{YS\_Rec}_n$  is the fixed effect of year-season of recording, where 4 seasons were defined (March to May, June to August, September to November, and December to February), and the level of year-season of recording with less than 10 records was regrouped to the level of its nearest year-season of recording based on its recording date ( $n = 1$  to 70 in Holstein, 1 to 48 in Jersey, and 1 to 60 in Nordic Red);  $\text{LacWk}_p$  is the fixed effect of the lactation week within period ( $p = 1$  to 4);  $\text{Trial}_m \times \text{YS\_Rec}_n$  is the fixed effect of the interaction between trial and year-season of recording;  $a_s$  is the random additive ge-

netic effect with  $\text{var}(a) \sim N(0, \mathbf{A}\sigma_a^2)$ , where  $\sigma_a^2$  is the additive genetic variance and  $\mathbf{A}$  is the relationship matrix;  $p_s$  is the random permanent environmental effect with  $\text{var}(p) \sim N(0, \mathbf{I}\sigma_p^2)$ , where  $\sigma_p^2$  is the permanent environmental variance and  $\mathbf{I}$  is the identity matrix;  $e_{j\text{mnp}sq}$  is the random residual with  $\text{var}(e) \sim N(0, \mathbf{I}\sigma_e^2)$ , where  $\sigma_e^2$  is the residual variance.

The fixed effects included in the repeatability animal model were tested for significance for DMI ( $P < 0.05$ ) by PROC MIXED in SAS 9.3 (SAS Institute Inc., Cary, NC), using a mixed model including these fixed effects and a random animal effect without using pedigree relationship. Within each breed, the residuals of weekly DMI observations generated from this mixed model were tested following the normal distribution by PROC UNIVARIATE in SAS 9.3 (SAS Institute Inc.).

Variance components, heritability, and repeatability of DMI for each breed within each lactation period were estimated using the repeatability animal model by restricted maximum likelihood (REML) by ASReml 3.0 (Gilmour et al., 2009). Bivariate analyses were carried out to estimate genetic correlations for DMI between different lactation periods in each breed.

## RESULTS

### Breed Characteristics in DMI

The shape of the mean DMI profiles within the first 24 wk of lactation was similar between breeds (Figure 1). The DMI of cows increased after calving until around lactation wk 12, and then it remained at a relatively stable level during lactation wk 12 to 24. Holstein and Nordic Red cows had similar levels of DMI at the beginning of lactation, but later in lactation Holstein cows had a slightly higher DMI than Nordic Red cows (Figure 1; Table 2). In comparison, Jersey cows had a much lower DMI than Holstein and Nordic Red cows within the first 24 lactation weeks (Figure 1). Despite the differences in DMI, the 3 breeds had relatively con-

**Table 2.** Descriptive statistics of average daily DMI (kg/d) with SD (kg/d), and the CV for DMI in 6 consecutive lactation periods of 4 wk length within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Average daily DMI (kg/d)			SD (kg/d)			CV (%)		
	HOL	RDC	JER	HOL	RDC	JER	HOL	RDC	JER
1	14.80	15.23	11.95	3.07	2.90	2.37	21	19	20
2	18.29	17.95	14.89	2.52	2.67	2.07	14	15	14
3	19.55	19.08	16.08	2.54	2.94	2.10	13	15	13
4	19.85	19.42	16.61	2.61	2.97	2.06	13	15	12
5	20.04	19.48	16.80	2.63	3.13	2.30	13	16	14
6	20.17	19.33	16.70	2.73	3.24	2.49	14	17	15

sistent coefficients of variation (CV) for DMI in each period (Table 2). For all 3 breeds CV for DMI in period 1 was around 20% and then decreased to around 15% in later lactation periods (Table 2).

In addition, the effect of year-season of recording significantly affected DMI in all 6 lactation periods in all 3 breeds. The effects of the age of first calving, lactation week, trial, and the interaction between trial and year-season of recording significantly affected DMI in only some of the lactation periods.

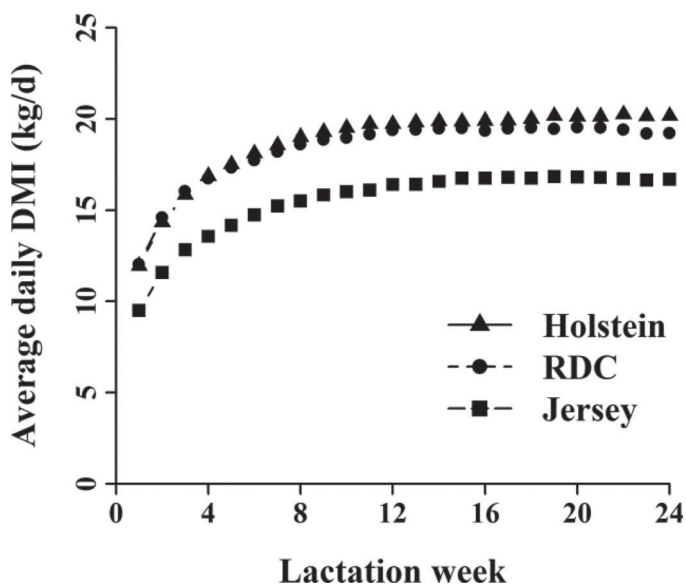
#### Heritability, Repeatability, and Variance Components

For the first 24 lactation weeks, heritability estimates for DMI ranged from 0.20 to 0.40 in Holstein, 0.25 to 0.41 in Nordic Red, and 0.17 to 0.42 in Jersey (Table 3). The difference between breeds in the heritability for DMI was not significant due to large standard errors (Table 3). The repeatability was high in all periods for each breed, and the repeatability increased from around 0.68 in the first period of lactation to around 0.80 in later periods (Table 3).

Genetic and phenotypic variances for DMI varied along lactation (Table 4). The tendency of increased genetic variance from early to mid lactation was shown in Holstein and Jersey cows, whereas the tendency was not obvious in Nordic Red cows. Comparing the 3 breeds, Nordic Red and Jersey tended to have the highest and the lowest genetic variance for DMI, respectively. The potential breed difference was more obvious for genetic variances than for the heritability estimates. However, due to the large standard errors, the difference in genetic variances between breeds was not statistically significant in most of the periods, except for period 3 between Nordic Red and Jersey (Table 4). Phenotypic variances increased along the lactation in all 3 breeds. Nordic Red had significantly higher phenotypic variance than the other 2 breeds. Jersey had the lowest phenotypic variance among the 3 breeds, but Jersey also had the lowest mean DMI and a similar CV for DMI with Holstein and Nordic Red, which are larger-sized breeds (Table 2; Table 4).

#### Genetic Correlations for DMI Between Lactation Periods

Generally for all 3 breeds, DMI between adjacent periods were highly genetically correlated, and DMI for periods 2 to 6 were highly genetically correlated (Table 5). In Holstein, the genetic correlations for DMI between period 1 and mid-lactation periods (periods 3 to 6) were significantly different from unity ( $P < 0.05$ ; Table 5). A significant difference was also found for DMI between periods 1 and 5 in Jersey. In Nordic Red, the differences for DMI between period 1 and later periods were not statistically significant, but DMI in period 1 tended to have weaker genetic correlations with periods 3 to 6 compared with the genetic correlations within periods 3 to 6.

**Figure 1.** Average daily DMI (kg/d) within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows.

**Table 3.** Heritability (SE in subscript) and repeatability (SE in subscript) for DMI (kg/d) in 6 consecutive lactation periods of 4 wk within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Heritability <sup>1</sup>			Repeatability <sup>2</sup>		
	HOL	RDC	JER	HOL	RDC	JER
1	0.26 <sub>0.08</sub>	0.37 <sub>0.10</sub>	0.29 <sub>0.12</sub>	0.68 <sub>0.02</sub>	0.68 <sub>0.02</sub>	0.67 <sub>0.03</sub>
2	0.29 <sub>0.08</sub>	0.26 <sub>0.11</sub>	0.25 <sub>0.12</sub>	0.74 <sub>0.02</sub>	0.79 <sub>0.01</sub>	0.78 <sub>0.02</sub>
3	0.20 <sub>0.08</sub>	0.41 <sub>0.11</sub>	0.17 <sub>0.11</sub>	0.78 <sub>0.01</sub>	0.79 <sub>0.01</sub>	0.75 <sub>0.02</sub>
4	0.25 <sub>0.08</sub>	0.26 <sub>0.11</sub>	0.31 <sub>0.13</sub>	0.80 <sub>0.01</sub>	0.81 <sub>0.01</sub>	0.79 <sub>0.02</sub>
5	0.34 <sub>0.09</sub>	0.25 <sub>0.11</sub>	0.42 <sub>0.14</sub>	0.78 <sub>0.01</sub>	0.85 <sub>0.01</sub>	0.79 <sub>0.02</sub>
6	0.40 <sub>0.10</sub>	0.26 <sub>0.12</sub>	0.29 <sub>0.15</sub>	0.83 <sub>0.01</sub>	0.83 <sub>0.01</sub>	0.77 <sub>0.02</sub>

<sup>1</sup>All heritability estimates, except for one heritability estimate in period 3 in Jersey, deviate more than  $1.645 \times SE$  from 0 ( $P < 0.05$ ).

<sup>2</sup>All repeatability estimates deviate more than  $1.645 \times SE$  from 0 ( $P < 0.05$ ).

**Table 4.** Genetic variance ( $\sigma_a^2$ ) and phenotypic variance ( $\sigma_p^2$ ; SE in subscript) for DMI (kg/d) in 6 consecutive lactation periods of 4 wk within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Period	Genetic variance <sup>1</sup>			Phenotypic variance <sup>2</sup>		
	HOL	RDC	JER	HOL	RDC	JER
1	1.2 <sub>0.4</sub>	1.9 <sub>0.6</sub>	0.8 <sub>0.3</sub>	4.4 <sub>0.2</sub>	5.0 <sub>0.3</sub>	2.6 <sub>0.2</sub>
2	1.3 <sub>0.4</sub>	1.6 <sub>0.7</sub>	0.8 <sub>0.4</sub>	4.6 <sub>0.2</sub>	6.0 <sub>0.3</sub>	3.3 <sub>0.3</sub>
3	1.0 <sub>0.4</sub>	3.0 <sub>0.9</sub>	0.6 <sub>0.4</sub>	5.1 <sub>0.3</sub>	7.3 <sub>0.4</sub>	3.4 <sub>0.3</sub>
4	1.3 <sub>0.5</sub>	1.9 <sub>0.8</sub>	1.1 <sub>0.5</sub>	5.3 <sub>0.3</sub>	7.3 <sub>0.4</sub>	3.6 <sub>0.3</sub>
5	1.7 <sub>0.5</sub>	1.9 <sub>0.9</sub>	1.8 <sub>0.7</sub>	5.0 <sub>0.3</sub>	7.8 <sub>0.5</sub>	4.4 <sub>0.4</sub>
6	2.1 <sub>0.6</sub>	2.1 <sub>1.0</sub>	1.5 <sub>0.9</sub>	5.3 <sub>0.3</sub>	8.0 <sub>0.5</sub>	5.3 <sub>0.5</sub>

<sup>1</sup>All estimates, except for one in period 3 in Jersey, deviate more than  $1.645 \times SE$  from 0 ( $P < 0.05$ ).

<sup>2</sup>All estimates deviate more than  $1.645 \times SE$  from 0 ( $P < 0.05$ ).

**Table 5.** Genetic correlations<sup>1</sup> (above diagonal, SE in subscript) and phenotypic correlations (below diagonal, SE in subscript) for DMI (kg/d) between 6 consecutive lactation periods of 4 wk within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows

Breed	Period	Period					
		1	2	3	4	5	6
HOL	1		1.00 <sub>0.04</sub>	0.78* <sub>0.13</sub>	0.70* <sub>0.15</sub>	0.69* <sub>0.15</sub>	0.63* <sub>0.15</sub>
	2	0.58 <sub>0.02</sub>		0.98 <sub>0.04</sub>	0.89 <sub>0.09</sub>	0.88 <sub>0.10</sub>	0.85 <sub>0.10</sub>
	3	0.46 <sub>0.03</sub>	0.68 <sub>0.02</sub>		0.99 <sub>0.05</sub>	0.98 <sub>0.08</sub>	0.97 <sub>0.09</sub>
	4	0.35 <sub>0.03</sub>	0.57 <sub>0.02</sub>	0.72 <sub>0.02</sub>		0.98 <sub>0.03</sub>	1.00 <sub>0.03</sub>
	5	0.31 <sub>0.04</sub>	0.51 <sub>0.03</sub>	0.64 <sub>0.02</sub>	0.73 <sub>0.02</sub>		0.99 <sub>0.03</sub>
	6	0.28 <sub>0.04</sub>	0.47 <sub>0.03</sub>	0.57 <sub>0.03</sub>	0.68 <sub>0.02</sub>	0.73 <sub>0.02</sub>	
RDC	1		0.86 <sub>0.11</sub>	0.96 <sub>0.11</sub>	0.77 <sub>0.17</sub>	0.90 <sub>0.17</sub>	0.78 <sub>0.22</sub>
	2	0.57 <sub>0.02</sub>		0.99 <sub>0.06</sub>	0.82 <sub>0.16</sub>	0.91 <sub>0.18</sub>	0.90 <sub>0.20</sub>
	3	0.46 <sub>0.03</sub>	0.65 <sub>0.02</sub>		0.87 <sub>0.09</sub>	0.84 <sub>0.13</sub>	0.93 <sub>0.12</sub>
	4	0.45 <sub>0.03</sub>	0.54 <sub>0.03</sub>	0.66 <sub>0.02</sub>		0.98 <sub>0.07</sub>	0.99 <sub>0.13</sub>
	5	0.42 <sub>0.03</sub>	0.48 <sub>0.03</sub>	0.60 <sub>0.03</sub>	0.73 <sub>0.02</sub>		0.95 <sub>0.10</sub>
	6	0.36 <sub>0.04</sub>	0.44 <sub>0.04</sub>	0.55 <sub>0.03</sub>	0.64 <sub>0.02</sub>	0.73 <sub>0.02</sub>	
JER	1		0.85 <sub>0.14</sub>	0.96 <sub>0.16</sub>	0.98 <sub>0.16</sub>	0.52* <sub>0.25</sub>	0.80 <sub>0.30</sub>
	2	0.62 <sub>0.03</sub>		1.00 <sub>0.11</sub>	0.93 <sub>0.18</sub>	0.97 <sub>0.19</sub>	0.99 <sub>0.21</sub>
	3	0.50 <sub>0.04</sub>	0.66 <sub>0.03</sub>		0.98 <sub>0.12</sub>	0.99 <sub>0.16</sub>	0.98 <sub>0.24</sub>
	4	0.40 <sub>0.05</sub>	0.52 <sub>0.05</sub>	0.66 <sub>0.03</sub>		1.00 <sub>0.05</sub>	0.99 <sub>0.11</sub>
	5	0.33 <sub>0.06</sub>	0.44 <sub>0.05</sub>	0.52 <sub>0.05</sub>	0.69 <sub>0.03</sub>		1.00 <sub>0.05</sub>
	6	0.30 <sub>0.06</sub>	0.32 <sub>0.06</sub>	0.41 <sub>0.05</sub>	0.57 <sub>0.04</sub>	0.71 <sub>0.03</sub>	

<sup>1</sup>The genetic correlation estimates deviating more than  $1.645 \times SE$  from 1 ( $P < 0.05$ ) are marked with an asterisk (\*).

## DISCUSSION

### *Heritability and Genetic Variances for DMI*

Heritability estimates for DMI in Holstein cows ranged from 0.20 to 0.40 in our study, which is consistent with the estimates of approximately 0.2 to 0.4 reported in previous studies in Holstein cows (Spurlock et al., 2012; Berry et al., 2014; Manzanilla Pech et al., 2016). The mid lactation periods had higher heritability estimates for DMI compared with the beginning of lactation for Holsteins. This was in agreement with recent studies showing a generally increased heritability for DMI from early to mid lactation in Holstein (Hüttmann et al., 2009; Spurlock et al., 2012; Manzanilla Pech et al., 2014a). However, other studies have also reported higher heritability at the beginning of lactation compared with later in lactation in Holstein (Buttchereit et al., 2011; Tetens et al., 2014).

We found that the heritability estimates for Nordic Reds (0.25–0.41) and for Jerseys (0.17–0.42) fell into the same range as that for Holsteins. It was difficult to compare the trajectory of heritability along lactation between breeds due to the standard errors of these estimates. In Nordic Red, Liinamo et al. (2012) estimated the heritability for DMI to be 0.18 to 0.33 within the first 30 lactation weeks, which was in agreement with our results considering the standard errors of estimates. This was expected because the data used by Liinamo et al. (2012) were part of the 663 Nordic Red cows in our study. In our study the data for Nordic Red were the most heterogeneous with respect to data sources, probably because data for Nordic Red were collected in 4 research farms in 3 countries with different recording schemes. In contrast, the Holstein cows in our study were from 2 research farms in 2 countries, and Jersey cows were only from 1 research farm in Denmark. For Holstein cows, whose data were mainly from one research farm with comprehensive data collection, heritability estimates were more consistent across periods. This demonstrated the importance of well-designed data collection to improve reliability of variance component estimates. This could also explain the higher phenotypic variances for DMI in Nordic Red than those in Holstein and Jersey in our study.

Genetic variances estimated for DMI in mid lactation were higher than at the beginning of lactation in Holstein and Jersey, and this tendency was not obvious in Nordic Red. Our result for Holsteins is in agreement with that of Veerkamp and Thompson (1999), who also showed relatively low genetic variances for DMI at the beginning of lactation and within the first 15 lactation weeks in Holstein. Results from our study indicate that the genetic variances for DMI might dif-

fer between breeds, and the breed differences for the genetic variance tended to be more obvious than for heritability. Nordic Red cows tended to have higher genetic variances than the other 2 breeds. The higher genetic variances of Nordic Red might be due to the genetic heterogeneity of the Nordic Red cows, as they are a combination of 9 different breeds with large influences from Finnish Ayrshire, Swedish Red, and Red Danish cattle (Lidauer et al., 2015).

### *Genetic Correlations for DMI Between Lactation Periods*

In Holsteins, the genetic correlations between period 1 and periods 3 to 6 were significantly different from unity, indicating a potentially different genetic basis for DMI between the start of lactation and mid lactation. A possible difference in genetic control of DMI was also found between period 1 and 5 in Jersey. Generally, genetic correlations for DMI tended to be lower between period 1 and mid lactation periods (periods 3 to 6) compared with the correlations within mid lactation periods (periods 3 to 6). This relatively weak genetic correlation between early and mid lactation was also shown in previous studies in Holstein and Nordic Red (e.g., Koenen and Veerkamp, 1998; Liinamo et al., 2012; Manzanilla Pech et al., 2014a). Several studies, including our own, found a low but positive genetic correlation between early and mid lactation (Hüttmann et al., 2009; Liinamo et al., 2012; Tetens et al., 2014), but studies in Holstein have also shown a negative genetic correlation between DMI in early and mid lactation (Karacaören et al., 2006; Buttchereit et al., 2011; Manzanilla Pech et al., 2014a). In general, cows increase feed intake and mobilize body reserves during early lactation to meet the energy demand for milk production (Van Arendonk et al., 1991; Collard et al., 2000; Mao et al., 2003). In mid lactation, body reserves are gradually restored and recovery in energy balance occurs (Mao et al., 2003). The nutritional requirements and metabolic changes from early to mid lactation influence feed intake of dairy cattle and might partly explain the low genetic correlation for feed intake between early and mid lactation.

Because DMI is currently difficult and expensive to measure, it is of interest to know if DMI in certain lactation periods could predict DMI in other periods so as to reduce the number of measurements needed across lactation. As early lactation is potentially genetically different from mid lactation for DMI, measurements of DMI in mid lactation could not be a strong predictor of DMI in early lactation and vice versa. Therefore, to predict DMI of an individual cow across lactation, it could be necessary to record DMI from separate time

points in early, mid, and, perhaps, also in late lactation and consider all the information for the prediction. Our suggestion was in agreement with the previous study by Manzanilla Pech et al. (2014b), who calculated the accuracy of selection for DMI in the entire lactation using different recording schemes. Manzanilla Pech et al. (2014b) reported that when the number of DMI measurements was limited to 15 wk across lactation, spreading those measurements in different lactation periods gave high selection accuracy. In addition, our study suggests a highly genetically correlated period (lactation wk 9–24) as one potential period in which to measure DMI to be representative of mid lactation. If it is not practical to record data over a long period of time, period 5 to 6 (lactation wk 17–24) could be chosen owing to its high heritability and high genetic correlations with other mid lactation periods.

### Considerations on Utilizing DMI Data from Multiple Breeds

Our results were based on data from research stations in different countries to achieve data sets of sufficient size to estimate genetic parameters for feed intake for each breed. One may speculate that this approach could be extended to combine data from different but reasonably similar breeds. However, our results also indicated that variance components for DMI could be different between breeds, although the breed differences were not significant in most of the lactation periods in our study. In that case, any possible breed difference needs to be accounted for properly. However, due to the limited data size of feed intake from research herds, especially for non-Holstein breeds, the potential breed differences or the size of the difference should be further studied by a larger data set of feed intake from multiple breeds. Another problem in using feed intake data from multiple breeds could be that breeds are not well connected (Lund et al., 2014), and in our study the 3 breeds have very few shared ancestors (data not shown).

### CONCLUSIONS

We found moderate heritability (mainly from 0.2 to 0.4) for DMI within the first 24 lactation weeks in primiparous Holstein, Nordic Red, and Jersey cows. The genetic variance for DMI might differ between breeds, but the difference was not significant in most of the periods studied due to large standard errors. Breed differences for genetic variances tended to be more obvious than for heritability. Genetic and phenotypic variances for DMI varied along lactation and tended to be higher in mid lactation than at the beginning of lactation.

Genetic correlations for DMI were high in lactation wk 5 to 24, whereas DMI in the first lactation period (lactation wk 1 to 4) tended to be genetically different from DMI in subsequent lactation periods. The potential breed difference in genetic variation for DMI should be considered when using feed intake information from multiple breeds.

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## Genetic heterogeneity of feed intake, energy-corrected milk, and body weight across lactation in primiparous Holstein, Nordic Red, and Jersey cows

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### ABSTRACT

In this study, we aimed to estimate and compare the genetic parameters of dry matter intake (DMI), energy-corrected milk (ECM), and body weight (BW) as 3 feed efficiency-related traits across lactation in 3 dairy cattle breeds (Holstein, Nordic Red, and Jersey). The analyses were based on weekly records of DMI, ECM, and BW per cow across lactation for 842 primiparous Holstein cows, 746 primiparous Nordic Red cows, and 378 primiparous Jersey cows. A random regression model was applied to estimate variance components and genetic parameters for DMI, ECM, and BW in each lactation week within each breed. Phenotypic means of DMI, ECM, and BW observations across lactation showed to be in very similar patterns between breeds, whereas breed differences lay in the average level of DMI, ECM, and BW. Generally, for all studied breeds, the heritability for DMI ranged from 0.2 to 0.4 across lactation and was in a range similar to the heritability for ECM. The heritability for BW ranged from 0.4 to 0.6 across lactation, higher than the heritability for DMI or ECM. Among the studied breeds, the heritability estimates for DMI shared a very similar range between breeds, whereas the heritability estimates for ECM tended to be different between breeds. For BW, the heritability estimates also tended to follow a similar range between breeds. Among the studied traits, the genetic variance and heritability for DMI varied across lactation, and the genetic correlations between DMI at different lactation stages were less than unity, indicating a genetic heterogeneity of feed intake across lactation in dairy cattle. In contrast, BW was the most genetically consistent trait across lactation, where BW among all lactation weeks was highly correlated. Genetic correlations

between DMI, ECM, and BW changed across lactation, especially in early lactation. Energy-corrected milk had a low genetic correlation with both DMI and BW at the beginning of lactation, whereas ECM was highly correlated with DMI in mid and late lactation. Based on our results, genetic heterogeneity of DMI, ECM, and BW across lactation generally was observed in all studied dairy breeds, especially for DMI, which should be carefully considered for the recording strategy of these traits. The genetic correlations between DMI, ECM, and BW changed across lactation and followed similar patterns between breeds.

**Key words:** feed efficiency, dairy cattle, genetic parameter, genetic heterogeneity, breed difference

### INTRODUCTION

The widely recognized genetic variation in feed efficiency (**FE**) has opened up possibilities for genetically improving the FE of dairy cattle to increase the profitability of dairy production and to reduce the ecological footprint. In the interest of including FE in breeding goals, genetic parameters for FE-related traits, as the important “toolbox” to initiate selection, have recently been studied in several dairy cattle populations worldwide (e.g., Liinamo et al., 2012; Berry et al., 2014; Manzanilla-Pech et al., 2016). Some consensus has been reached among the studies in genetic variation and genetic parameters for FE, whereas potential differences between breeds, parities, and even different lactation stages have also been reported (Spurlock et al., 2012; Manzanilla Pech et al., 2014b; Li et al., 2016).

Two key questions have been widely discussed in previous studies of the genetic parameters of FE-related traits in dairy cattle. The first question focused on the genetic variation and heritability of FE-related traits. From recent studies, the DMI of dairy cows, as the key component of all available FE traits in dairy cattle, was reported with moderate heritability that could vary across lactation (e.g., Koenen and Veerkamp, 1998; Manzanilla Pech et al., 2014b; Li et al., 2016). The

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potential genetic heterogeneity of feed intake across lactation stages has been observed, where feed intake between early and middle lactation was found to be in low or even negative genetic correlation (Buttchereit et al., 2011; Manzanilla Pech et al., 2014b; Tetens et al., 2014). The second question focused on the genetic relationships between feed intake and production or functional traits to draw a picture of the correlated responses and to assess indicator traits for FE. In Holstein cows, the genetic correlation between feed intake and milk production was shown to change across lactation, with a positive correlation at mid and late lactation but a low or even negative correlation in early lactation (Hüttmann et al., 2009; Buttchereit et al., 2011; Liinamo et al., 2012; Manzanilla Pech et al., 2014b). The genetic correlation between feed intake and BW was also shown to vary across lactation in Holstein cows (Veerkamp and Thompson, 1999; Spurlock et al., 2012; Manzanilla Pech et al., 2014b). Findings from recent studies have reached some consensus for the answers to these key questions. However, it remains a challenge to obtain accurate or detailed estimates across lactation, primarily due to the constraint of data sizes or lack of records across the entire lactation.

Another challenge is obtaining sufficient genetic information in non-Holstein populations for FE. Studies of the genetics of FE in the 1980s demonstrated between-breeds or selection-line variation in feed intake as the first impression of genetic differences in feed consumption (Korver, 1988). Over the years, due to considerable genetic progress, the results from old studies may no longer be fully relevant to modern dairy populations of high genetic merit (Liinamo et al., 2012). Recent genetic studies of FE have mostly focused on Holstein cows (e.g., Berry et al., 2014; de Haas et al., 2015). Breeds other than Holstein (e.g., Jersey and Nordic Red; **RDC**) are economically important breeds globally and locally and may have important genetic value with respect to FE. Good knowledge of the genetic parameters for FE-related traits in multiple dairy breeds would benefit diverse selection purposes in dairy production (e.g., genetic evaluation and improvement of different breeds, across-breeds genomic evaluation).

The breeding and feeding systems are similar among research herds in Nordic countries. For this study, we combined FE-related data across lactation from research herds in Denmark, Finland, and Sweden for 3 dairy breeds (Holstein, RDC, and Jersey). The objectives of this study were to estimate and compare the genetic parameters of DMI, ECM, and BW across first lactation in 3 dairy breeds. In addition, genetic correlations between DMI, ECM, and BW were estimated across lactation in these dairy breeds.

## MATERIALS AND METHODS

### *Animals, Feeding, and Data Recording*

Cows in our study were from 6 research herds from Denmark, Finland, and Sweden comprising 3 dairy breeds: Holstein, RDC, and Jersey. The research herds were located at the Danish Cattle Research Center (DCRC, Foulum) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle) in Denmark, at the Natural Resources Institute Finland past research herd (Rehtijärvi, Jokioinen) and current research herd (Minkiö, Jokioinen) in Finland, and at the Swedish University of Agricultural Sciences research herd (Kungsängen, Uppsala) and Öjebyn research herd (Öjebyn) in Sweden. The studied cows calved between 1991 and 2015 for Holstein cows, between 1994 and 2015 for RDC cows, and between 1995 and 2015 for Jersey cows. Pedigree information was extracted from the Nordic Cattle Genetic Evaluation (NAV, Skejby, Denmark) database by tracing back as many generations as possible for cows with records. The cows studied by Li et al. (2016, 2017) were part of the data in this study.

The cows were involved in several nutrition experiments within research herds. The feeding information in the trials has been described in detail in previous studies (Mäntysaari et al., 2003, 2012; Nielsen et al., 2003; Løvendahl et al., 2010; Løvendahl and Chagunda, 2011; Mäntysaari and Mäntysaari, 2015; Byskov et al., 2017). Feed offered to cows and feed refusals were measured individually to calculate the feed intake per cow. The DM contents in TMR and concentrates were analyzed regularly, and the compositions were aligned and merged with feed intake records to obtain daily DMI values per cow. A weekly average DMI per cow was calculated as the average of daily DMI records in each lactation week.

Milking and milk yield recordings were described in previous studies (Mäntysaari et al., 2003, 2012; Nielsen et al., 2003; Løvendahl et al., 2010; Løvendahl and Chagunda, 2011; Mäntysaari and Mäntysaari, 2015; Byskov et al., 2017; Li et al., 2017). A weekly observation of average daily milk yield per cow was obtained from the average of daily milk yield records per cow in each week. Milk samples were taken regularly for analyses of fat, protein, and lactose content (Mäntysaari et al., 2003, 2012; Løvendahl et al., 2010). The average daily ECM (kg) per cow in each lactation week was calculated from average daily milk yield (kg) and milk composition (g/kg) using the formula by Sjaunja et al. (1990):  $ECM (kg) = \text{milk yield (kg)} \times \{[38.30 \times \text{fat content (g/kg)} + 24.20 \times \text{protein content (g/kg)} + 16.54 \times \text{lactose content (g/kg)} + 20.7]/3,140\}$ . Cows were weighed on a

weekly basis in some research herds. In other research herds cows were automatically weighed at each milking so that BW records were averaged to obtain a weekly record of BW per cow in each week (Mäntysaari et al., 2003, 2012; Nielsen et al., 2003; Løvendahl et al., 2010; Mäntysaari and Mäntysaari, 2015; Li et al., 2017).

### Data Editing

The original data set consisted of 160,488 weekly records of DMI, ECM, and BW across lactation for 2,720 dairy cows across breeds and parities. From the original data set, primiparous Holstein, RDC, and Jersey cows were extracted for the current study. For Holsteins and Jerseys, cows' weekly records from lactation wk 1 to 44 were included in the analyses, corresponding to the typical 305-d lactation. For RDC, cows' weekly records from lactation wk 1 to 32 were studied due to sparse records in later lactation weeks in some research herds. Cows with fewer than 4 weekly records of DMI, ECM, and BW during the studied lactation periods were removed from the data set. A few cows with a calving age of more than 38 mo at first calving were also removed from the data set. The age at first calving ranged from 24 to 38 mo, 25 to 38 mo, and 24 to 36 mo for Holstein, RDC, and Jersey cows, respectively. After data editing, a total of 30,717 records of 842 primiparous Holstein cows from 3 research herds in Denmark and Sweden (DCRC, Skovgaard, and Öjebyn herds), 21,279 records of 746 primiparous RDC cows from 5 research herds from all 3 countries (Rehtijärvi, Minkiö, Kungsängen, DCRC, and Skovgaard herds), and 14,021 records of 378 primiparous Jersey cows from 2 research herds in Denmark (DCRC and Skovgaard herds) were included in the statistical analyses. Cows were recorded with weekly records of DMI, ECM, and BW across lactation (Table 1).

### Statistical Analyses

The analyses were carried out separately for each breed. Within each breed, variance components for weekly observations of DMI, ECM, and BW across lactation were estimated using the following random regression model for each trait:

$$y_{jklmp} = u + \text{Herd-Trial}_j + \text{CA}_k + \text{YSC}_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{np} \phi_n + \sum_{n=0}^2 pe_{np} \phi_n + e_{jklmp},$$

where  $y_{jklmp}$  is the weekly observation of DMI, ECM, or BW in lactation week (Lactwk)  $m$  for cow  $p$ , where cow  $p$  is in herd and trial (Herd-Trial)  $j$  at calving age

(CA)  $k$  and in the year-season of calving (YSC)  $l$ ;  $u$  is the intercept for DMI, ECM, or BW; Herd-Trial $_j$  is the fixed effect of herd and trial for the cow; the trials were herd-specific, and some Herd-Trial $_j$  could be shared across breeds ( $j = 1$  to 29 for Holstein cows;  $j = 1$  to 16 for RDC cows;  $j = 1$  to 14 for Jersey cows); CA $_k$  is the fixed effect of calving age in months, where the calving age of Holstein, RDC, and Jersey cows ranged from 24 to 38, 25 to 38, and 24 to 36 mo, respectively; YSC $_l$  is the fixed effect of year-season of calving, where 4 seasons were defined (March to May, June to August, September to November, and December to February;  $l = 1$  to 22 for Holstein cows,  $l = 1$  to 45 for RDC cows, and  $l = 1$  to 39 for Jersey cows); and Lactwk $_m$  accounts for the fixed effect of lactation week ( $m = 1$  to 44 for Holstein and Jersey cows;  $m = 1$  to 32 for RDC cows). Random regression terms were used to describe the cows' additive genetic effect and permanent environmental effect. The  $a_{np}$  and  $pe_{np}$  are the  $n$ th regression coefficients of the Legendre polynomial for the random additive genetic effect and the random permanent environmental effect, respectively, for cow  $p$ ; and  $\phi_n$  is the  $n$ th covariable of the second-order Legendre polynomial for the week of lactation. The analyses failed to converge when higher order polynomials were fitted for animal and permanent environmental effects;  $e_{jklmp}$  is the random residual, which was assumed to have heterogeneous variances across lactation (every 4 consecutive lactation weeks was set as 1 class).

The variance components were estimated by an average information-restricted maximum likelihood algorithm (Jensen et al., 1997) implemented in the software DMU (Madsen and Jensen, 2013). Within each breed, estimates of variance components were used to calculate heritability for DMI, ECM, and BW for each trait in each lactation week. Genetic correlations for each

**Table 1.** Descriptive statistics of DMI, ECM, and BW for 842 primiparous Holstein (HOL) cows in 44 lactation weeks, 746 primiparous Nordic Red cows (RDC) in 32 lactation weeks, and 378 primiparous Jersey (JER) cows in 44 lactation weeks

Item	Mean	SD	Minimum	Maximum
DMI (kg/d)				
HOL	19.4	3.2	3.8	40.9
RDC	18.5	3.3	4.1	39.1
JER	15.8	2.9	5.5	34.5
ECM (kg/d)				
HOL	29.1	6.0	1.2	57.9
RDC	26.9	5.5	1.6	49.0
JER	24.6	5.3	2.8	48.6
BW (kg)				
HOL	601.2	63.8	387.0	869.0
RDC	575.1	61.0	396.0	857.5
JER	433.0	47.9	253.5	630.7

trait between different lactation weeks were calculated for DMI, ECM, and BW across lactation.

In addition, genetic correlations between DMI, ECM, and BW at the same lactation week were estimated in Holstein and RDC cows using bivariate analyses by applying the same random regression model as for single trait analyses. The bivariate analyses between DMI,

ECM, and BW were not performed for Jersey cows due to the small amount of data available.

## RESULTS

### *Phenotypic Means of DMI, ECM, and BW in Holstein, RDC, and Jersey Cows*

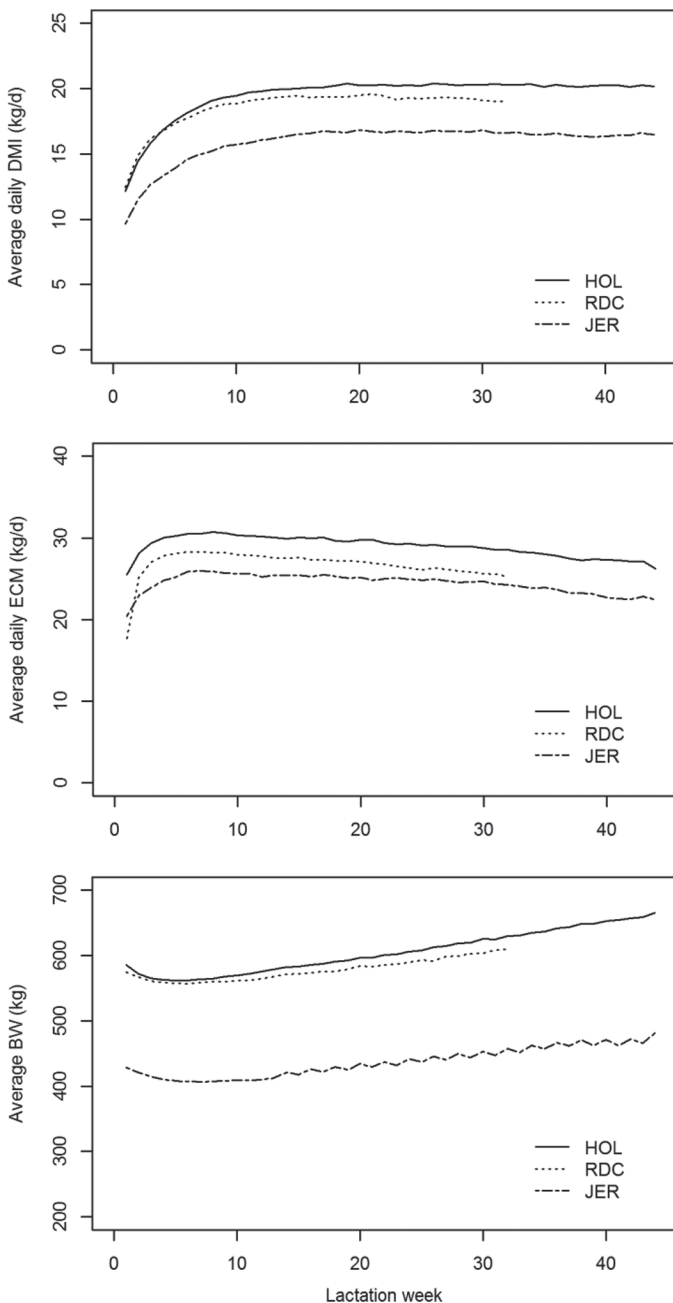
Cows of different breeds followed a similar pattern of phenotypic means of daily DMI over lactation, and the breed difference was in the level of phenotypic means (Figure 1). Generally, the average daily DMI in all 3 breeds increased from the beginning of lactation until reaching a relatively steady level not earlier than lactation wk 11. Holstein cows had the highest level of average daily DMI among the 3 breeds, and Jersey cows had the lowest level of DMI. More specifically, the average daily DMI of Holstein cows increased from 12.1 kg/d (in wk 1) to 20.0 kg/d (in wk 14) and remained quite constant afterward. The RDC cows had an average daily DMI similar to Holstein cows at the beginning of lactation (12.5 kg/d in wk 1) but tended to have lower DMI than Holstein cows afterward.

The pattern of average daily ECM over the course of lactation was similar in 3 breeds (Figure 1). The ECM yield increased in early lactation and peaked in wk 7 (for RDC and Jersey cows) or wk 8 (for Holstein cows), followed by a gradual decrease in yield. Among the 3 breeds, Holsteins and Jerseys had the highest and lowest levels of average daily ECM over lactation, respectively.

As for BW, Holstein and RDC cows had a similar level of average BW compared with Jersey cows, which had a significantly lower level (Figure 1). Loss of BW occurred at the beginning of lactation in all 3 breeds, and the nadir of the BW curve appeared in wk 5 in Holstein cows, in wk 6 in RDC cows, and in wk 7 in Jersey cows. The total loss of BW from wk 1 to the nadir was on average 23.4, 17.1, and 22.1 kg for Holstein, RDC, and Jersey cows, respectively. After the nadir point, the cows' BW were regained gradually to the original level of BW (i.e., BW in wk 1) in wk 16 for all breeds and followed by continuous BW gains. After the nadir, BW increased slightly faster in Holsteins compared with the other 2 breeds.

### *Variance Components and Heritability of DMI, ECM, and BW Across Lactation*

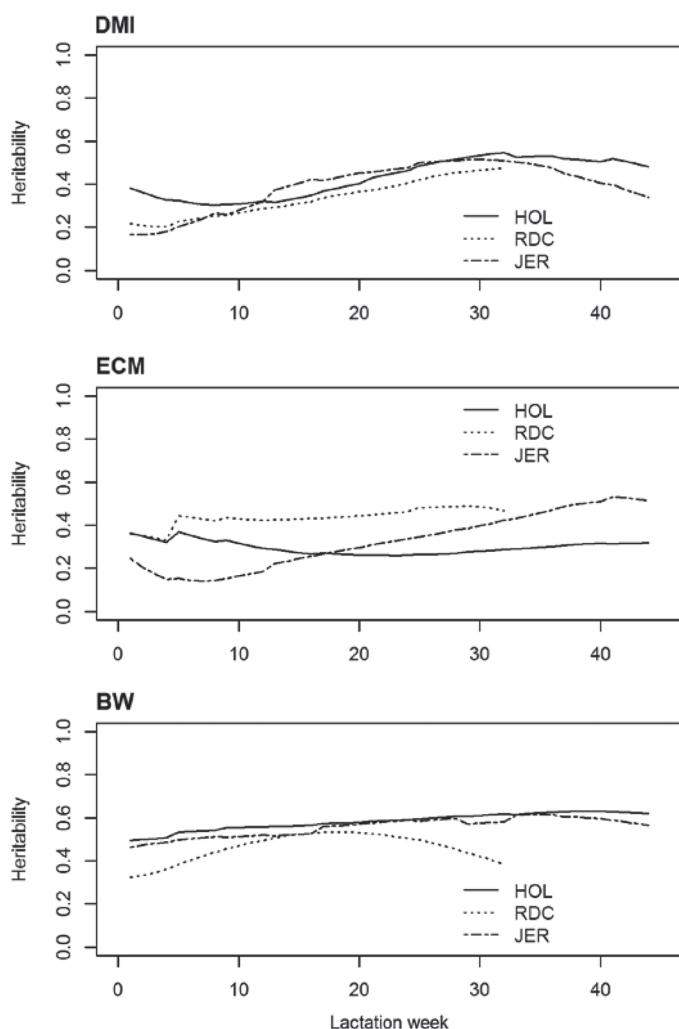
The genetic variances for DMI tended to increase over lactation, whereas the permanent environmental variances were relatively stable over lactation. The residual variance for DMI was slightly higher at the beginning of lactation than later in the lactation. The



**Figure 1.** Phenotypic means of daily DMI, daily ECM, and BW for Holstein cows (HOL) in 44 lactation weeks, Nordic Red cows (RDC) in 32 lactation weeks, and Jersey cows (JER) in 44 lactation weeks.

heritability for DMI followed a similar trajectory over lactation for the 3 breeds and tended to increase from early lactation to later lactation stages (Figure 2). The heritability estimates ranged from 0.30 to 0.55 (mean SE = 0.06) in Holstein cows across 44 wk, 0.20 to 0.48 (mean SE = 0.08) in RDC cows across 32 wk, and 0.17 to 0.52 (mean SE = 0.10) in Jersey cows across 44 wk. There was no significant breed difference in heritability for DMI ( $P > 0.05$ ).

The genetic variance and the residual variance for ECM were higher at the beginning of lactation than at later lactation stages. The permanent environmental variance for ECM tended to increase over lactation.



**Figure 2.** Heritability estimates of average daily DMI (kg/d), average daily ECM (kg/d), and average BW (kg) in Holstein cows (HOL) in 44 lactation weeks, Nordic Red cows (RDC) in 32 lactation weeks, and Jersey cows (JER) in 44 lactation weeks. The mean SE of heritability for DMI was 0.06, 0.08, and 0.10 in HOL, RDC, and JER, respectively. The mean SE of heritability for ECM was 0.06, 0.08, and 0.11 in HOL, RDC, and JER, respectively. The mean SE of heritability for BW was 0.08, 0.10, and 0.12 in HOL, RDC, and JER, respectively.

The heritability for ECM was moderate and tended to differ among breeds (Figure 2). However, differences in heritability estimates between breeds were not statistically significant in this study ( $P > 0.05$ ). In Holstein and RDC cows, the heritability of ECM was relatively stable over lactation, ranging from 0.26 to 0.37 (mean SE = 0.06) in Holstein cows across 44 wk and from 0.33 to 0.49 (SE = 0.08) in RDC cows across 32 wk. The heritability of ECM in Jersey cows showed a tendency of increase over lactation (from 0.14 to 0.53) but with fairly large standard errors (mean SE = 0.11).

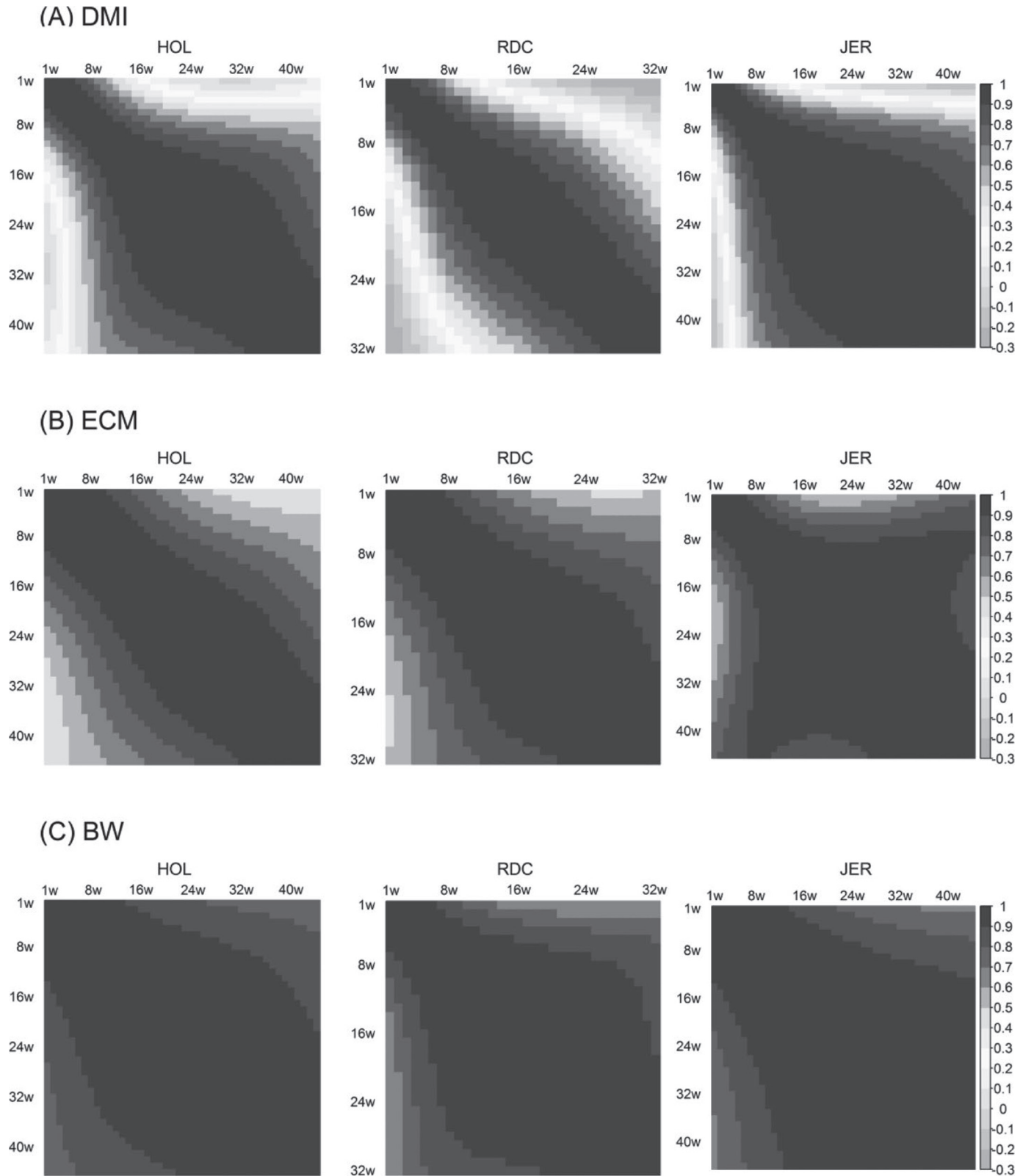
The genetic variances for BW increased over lactation, whereas the permanent environmental variances were relatively stable over lactation. The residual variance for BW was higher at the beginning of lactation than at later lactation. The heritability for BW was higher than the heritability for DMI or ECM in all 3 breeds (Figure 2). Heritability for BW in Holstein and Jersey cows was fairly similar and stable across lactation, ranging from 0.49 to 0.63 in Holsteins (mean SE = 0.08) and 0.46 to 0.61 in Jerseys (mean SE = 0.12). The heritability of BW in RDC was from 0.32 to 0.53 over 32 wk (mean SE = 0.10), which was not significantly different from the heritability for BW in the Holstein or Jersey breeds ( $P > 0.05$ ).

#### Genetic Correlations Within DMI, ECM, and BW Across Lactation in 3 Dairy Breeds

The genetic correlations between DMI at different lactation stages were less than unity (Figure 3A), indicating a genetic heterogeneity of feed intake across lactation. Low or even negative genetic correlations were observed for DMI between early lactation and the mid or late lactation stages, with the lowest values for Holstein, RDC, and Jersey of 0.0,  $-0.27$ , and  $-0.15$ , respectively. However, DMI within mid and late lactation stages generally showed a high genetic correlation. Compared with DMI, ECM showed less genetic heterogeneity across lactation in all breeds, although ECM in early and later lactation stages was still shown to be genetically different, with the lowest genetic correlation at approximately 0.5 (Figure 3B). In contrast, BW was shown to be the most consistent trait across lactation for all breeds, where BW in all weeks was highly correlated (Figure 3C). The genetic correlations for BW across lactation were higher than 0.74, 0.61, and 0.67 in Holstein, RDC, and Jersey cows, respectively.

#### Genetic Correlations Between DMI, ECM, and BW in the Same Week of Lactation

Genetic correlations between DMI, ECM, and BW changed over lactation (Figure 4), and the correlations



**Figure 3.** Genetic correlations for (A) DMI, (B) ECM, and (C) BW across 44 lactation weeks in Holstein cows (HOL), 32 lactation weeks in Nordic Red cows (RDC), and 44 lactation weeks (w) in Jersey cows (JER). The mean SE of genetic correlations for DMI was 0.09, 0.12, and 0.14 in HOL, RDC, and JER, respectively. The mean SE of genetic correlations for ECM was 0.09, 0.12, and 0.15 in HOL, RDC, and JER, respectively. The mean SE of genetic correlations for BW was 0.11, 0.13, and 0.17 in HOL, RDC, and JER, respectively. Color version available online.

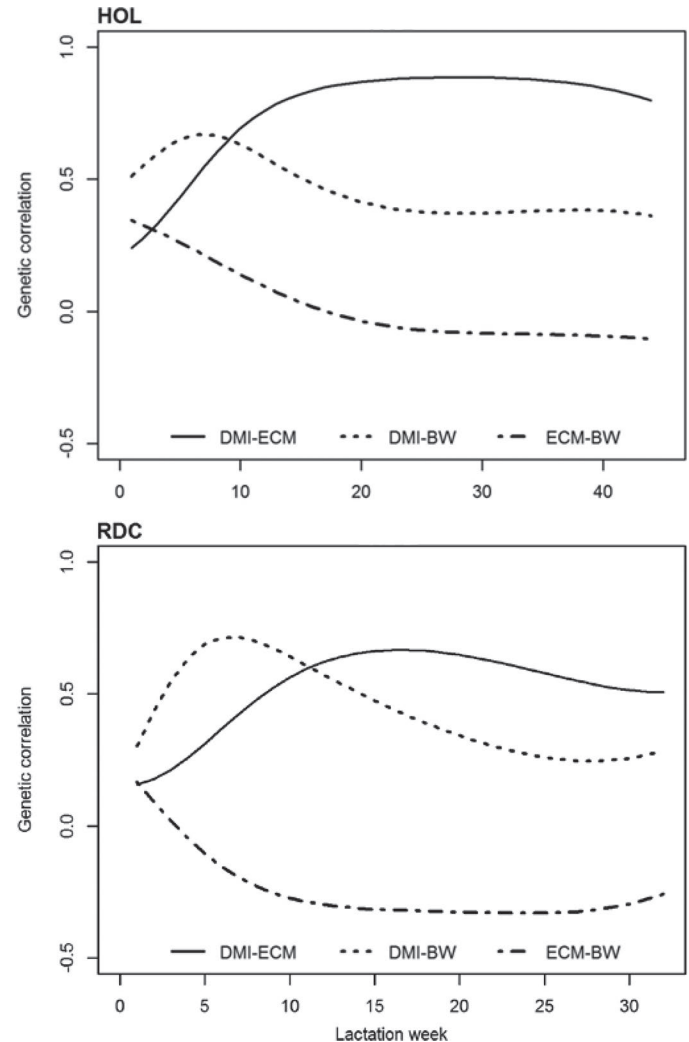
changed considerably more in early lactation compared with mid and late lactation. The trajectories of the correlations over lactation followed similar patterns in Holstein and RDC cows. In both breeds, cows' DMI and ECM were genetically weakly correlated at the beginning of lactation (0.24 for Holstein cows and 0.16 for RDC cows). After the beginning of lactation the correlation between DMI and ECM increased to 0.80 in wk 14 in Holstein cows, and it remained above 0.80 until the end of lactation. Similarly, in RDC cows, the genetic correlation between DMI and ECM continued to increase from early lactation and peaked in wk 16 with a correlation of 0.67; the correlation remained above 0.50 until wk 32. The genetic correlation between cows' BW and ECM was low but positive at the beginning of lactation and decreased to become slightly negative in later lactation stages in both Holstein and RDC cows (Figure 4).

The genetic correlations between DMI and BW in Holstein and RDC cows had a very similar pattern over lactation (Figure 4). In both breeds, the correlation between DMI and BW increased from the beginning of lactation and peaked in wk 7 (with correlation at approximately 0.7), followed by a gradual decrease. The correlations remained positive during the entire lactation.

## DISCUSSION

### *Breed Similarity and Difference in DMI, ECM, and BW Across Lactation*

**Phenotypic Observations.** Cows of different breeds shared very similar patterns of lactation trajectories for phenotypic means of DMI, ECM, and BW. Immediately after calving, cows' average daily DMI and ECM both increased but at different rates. The average daily ECM increased sharply to peak at lactation wk 7 or 8 in all 3 breeds, whereas DMI reached a relatively high stable level no earlier than wk 11 and peaked even later. In dairy cattle, the slower increase in feed intake relative to milk yield in early lactation has been widely recognized, and it explained the deficiency of energy intake for milk production in early lactation as well as the body reserve mobilization of dairy cows (e.g., Berglund and Danell, 1987; Mao et al., 2004; Banos and Coffey, 2010). In our results, the observed BW loss in early lactation also reflected the occurrence of body reserve mobilization in all 3 dairy breeds, where the nadir of the BW curve appeared just before the ECM peaked, which was consistent with Søndergaard et al. (2002). In addition, cows of different breeds differed in the amount of BW loss from the beginning of lactation



**Figure 4.** Genetic correlations among DMI, ECM, and BW in the same week of lactation in Holstein cows (HOL) across 44 lactation weeks and Nordic Red cows (RDC) across 32 lactation weeks. The mean SE of genetic correlations among DMI, ECM, and BW ranged from 0.09 to 0.11 in HOL cows and from 0.12 to 0.13 in RDC cows.

to the nadir of BW. Our study showed that Holstein cows and RDC cows had the highest and lowest BW loss, respectively, which was in agreement with Søndergaard et al. (2002).

**Heritability.** In most studies, including ours, the heritability estimates for feed intake in dairy cattle were moderate and in the same range as the heritability for milk yield, whereas heritability for BW was moderate to high and was higher than the heritability for DMI or yield (Karacaören et al., 2006; Vallimont et al., 2010; Spurlock et al., 2012). The ranges of heritability for DMI and ECM in this study agreed with those found in previous studies in Holstein cows (e.g., Spurlock et al., 2012; Berry et al., 2014; Manzanilla Pech et al., 2014b).

The heritability estimate for ECM in RDC was higher in this study compared with the estimate of RDC by Liinamo et al. (2015). The latter study included only RDC cows from Finland, whereas in this study the RDC cows were from Denmark, Finland, and Sweden; of these, Danish RDC is highly genetically diverse, which might explain our findings. The heritability for DMI in Jerseys across the whole lactation period (44 wk) was to our knowledge first addressed in this study, where our results indicated very similar heritability for DMI in Jerseys and in Holsteins. In this study the data of Jersey cows were only from Danish herds because the Jersey breed is mainly populated in Denmark among Nordic countries. Further studies with larger data sets and from more data sources would be needed to obtain accurate estimates of genetic parameters for Jerseys and the breed similarity or difference between Jerseys and other dairy breeds.

#### **Genetic Heterogeneity of DMI, ECM, and BW Across Lactation**

Feed intake for dairy cows was genetically not the same trait across lactation, where the genetic correlations for DMI between early lactation and later lactation stages were found to be far from unity (e.g., Koenen and Veerkamp, 1998; Berry et al., 2007; Liinamo et al., 2012). Our study confirmed the genetic heterogeneity of DMI across lactation in Holstein and RDC dairy cows and observed the same phenomenon across lactation in Jersey cows. In all 3 breeds, DMI in middle and late lactation was generally highly correlated, in agreement with previous studies on the Holstein breed (Manzanilla Pech et al., 2014b).

In practice, the genetic heterogeneity of DMI across lactation needs to be carefully considered in any recording and selection strategy for FE. Due to the low genetic correlation for DMI between early and later lactation stages, DMI measurements in middle or late lactation cannot be strong predictors of DMI in early lactation and vice versa. To improve FE across lactation, it might be necessary to take DMI records from separate time points across all lactation stages. Apart from recording in middle and late lactation, a few DMI records in early lactation would also be recommended because DMI in early lactation is a different trait from DMI in later lactation. Manzanilla Pech et al. (2014a) estimated the accuracy of DMI breeding values using various recording schemes for DMI and found that higher accuracy was achieved when DMI was recorded at several lactation stages, when the number of measurements was limited across lactation (Manzanilla Pech et al., 2014a).

The genetic heterogeneity of DMI across lactation should also be considered when joining data from dif-

ferent sources. To accumulate sufficient data for genetic and genomic evaluation for FE, feed intake data were usually collected or combined from several herds and experiments within or across countries (e.g., Berry et al., 2014; de Haas et al., 2015). The joint data for FE could be heterogeneous in many aspects—for example, due to the difference in feeding systems, recording periods, or the number of repeated measurements (Hardie et al., 2015; Tempelman et al., 2015; Veerkamp et al., 2015). When joint data come from different lactation periods, the heterogeneity of feed intake across lactation stages may need to be considered before genetic evaluation. Data standardization might be needed in this situation to calibrate data from different lactation periods (Veerkamp et al., 2015). One method of standardization could be based on a random regression prediction of records for a cow using the cow's own repeated records and the covariance structure in the population (Banos et al., 2012; Berry et al., 2014; Veerkamp et al., 2015). Alternatively, feed intake from different lactation stages could also be defined as different traits, where a multiple-trait model could be applied in the genetic analyses.

Compared with feed intake, ECM showed much less genetic heterogeneity across lactation in all 3 breeds, although ECM at the beginning of lactation was still not exactly the same trait as ECM in mid or late lactation. Our findings are consistent with Hüttmann et al. (2009) and Manzanilla Pech et al. (2014b) for Holstein cows and with Liinamo et al. (2012) for RDC cows. The correlations for BW remained high across lactation in our study, in agreement with the findings of previous studies in Holstein cows (Koenen and Veerkamp, 1998; Hüttmann et al., 2009; Manzanilla Pech et al., 2014b) and RDC cows (Liinamo et al., 2012). Considering the high genetic consistency of BW across lactation, the number of repeated measurements of BW per cow across lactation could be reduced when recording BW in practice. However, a certain number of measurements of BW across lactation might still be needed to study cows' BW change.

#### **Dynamics of Genetic Correlations Between DMI, ECM, and BW Across Lactation**

First, it is important to realize that the observed relationships between DMI, ECM, and BW came from a complex metabolic system of lactation and the growth of dairy cattle. The genetic relationships between DMI, ECM, and BW do not stand alone in the system but rather are simultaneously linked to other body functions in the energy metabolic system (e.g., Hüttmann et al., 2009; Vallimont et al., 2010; Manzanilla-Pech et al., 2016). The energy intake and allocation at one



time point affect several correlated responses that may also be expressed later. Therefore, several FE-related traits [e.g., feed intake, yield, BW, BCS, energy balance (EB), fertility] should be considered simultaneously to avoid the perceived gain from improvement of one trait being counteracted by undesirable correlated responses in other traits (Veerkamp, 1998). Additionally, changes in the relationship between FE-related traits over lactation should be considered, factoring in the potential genetic heterogeneity of these traits across lactation (Hüttmann et al., 2009; Liinamo et al., 2012; Manzanilla Pech et al., 2014b). According to our results, the genetic correlations between DMI, ECM, and BW were shown to be very different between early lactation and mid and late lactation, indicating differences in the metabolic mechanism for milk production between early lactation and mid and late lactation.

The feed intake of dairy cows was found to be positively correlated with milk yield when accumulated over the entire lactation period (Veerkamp, 1998; Vallimont et al., 2010; Manzanilla-Pech et al., 2016), indicating that selection for milk yield would concurrently increase DMI. However, recent studies, including ours, showed that the genetic correlation between DMI and ECM in early lactation is low (Hüttmann et al., 2009; Spurlock et al., 2012) or even slightly negative (Karacaören et al., 2006; Manzanilla Pech et al., 2014b). The low correlation between DMI and ECM in early lactation indicated that selection for higher milk yield may lead to only a small genetic change in cows' feed intake in the initial period of lactation and vice versa. This implies an increased negative EB in the case of exclusive breeding for milk yield (Hüttmann et al., 2009). A negative EB has been reported to have an unfavorable genetic correlation with dairy cattle fertility and health (Collard et al., 2000; Veerkamp et al., 2000; Banos and Coffey, 2009). In this case, EB itself or an EB indicator trait (i.e., BCS) for early lactation should be considered in dairy cattle breeding to avoid a more severe negative EB when selecting for higher yield or FE (e.g., Veerkamp, 1998; Coffey et al., 2002; Liinamo et al., 2012).

The genetic correlation between cows' DMI and BW was found to be higher than the correlation between DMI and milk yield at the beginning of lactation (Liinamo et al., 2012; Spurlock et al., 2012; Manzanilla Pech et al., 2014b). However, the genetic correlation between DMI and milk yield increased during early lactation, and DMI became highly correlated with milk yield (above 0.7) in middle and late lactation (Hüttmann et al., 2009; Spurlock et al., 2012; Manzanilla Pech et al., 2014b). The significant increase in the genetic relationship between feed intake and milk yield from

early to middle lactation was also observed in Li et al. (2017), who found a significant increase in the partial efficiency of feed intake on milk yield from the beginning of lactation to approximately lactation wk 12. In contrast, the genetic correlation between DMI and BW was relatively stable and positive throughout the entire lactation period (Liinamo et al., 2012; Manzanilla Pech et al., 2014b), indicating that bigger cows tend to have higher feed intake due to the higher energy required for body maintenance.

The low but positive genetic correlation between ECM and BW at the beginning of lactation—seen in our results and some previous studies (Karacaören et al., 2006; Spurlock et al., 2012; Manzanilla Pech et al., 2014b)—indicated the capacity of larger cows with higher milk yield in the initial part of lactation. However, after the initial lactation weeks, the rapid decrease of the correlation between BW and milk yield was also seen in previous studies (Karacaören et al., 2006; Hüttmann et al., 2009; Liinamo et al., 2012). The change in genetic correlation between milk yield and BW across lactation could be due to the contribution of body tissue mobilization, where milk yield and BW are both closely associated with body tissue mobilization (Veerkamp, 1998). Therefore, traits related to body tissue mobilization (e.g., BCS) could be important for understanding the genetic relationships between FE-related traits, especially for early lactation.

## CONCLUSIONS

The general patterns of genetic parameters for DMI, ECM, and BW across lactation were similar across dairy cattle breeds (Holstein, RDC, and Jersey). Feed intake was genetically not the same trait across lactation stages, especially between the early and later lactation stages. Measurement of feed intake is recommended to be spread over different lactation stages from the entire lactation, or at least from both early and middle lactation. Compared with feed intake, ECM and BW showed much less genetic heterogeneity across lactation in all 3 breeds. The genetic correlations between DMI, ECM, and BW changed across lactation, but the patterns of change in the genetic correlations between DMI, ECM, and BW were very similar between breeds.

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## Neglect of lactation stage leads to naive assessment of residual feed intake in dairy cattle

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### ABSTRACT

Residual feed intake (RFI) is a candidate trait for feed efficiency in dairy cattle. We investigated the influence of lactation stage on the effect of energy sinks in defining RFI and the genetic parameters for RFI across lactation stages for primiparous dairy cattle. Our analysis included 747 primiparous Holstein cows, each with recordings on dry matter intake (DMI), milk yield, milk composition, and body weight (BW) over 44 lactation weeks. For each individual cow, energy-corrected milk (ECM), metabolic BW (MBW), and change in BW ( $\Delta$ BW) were calculated in each week of lactation and were taken as energy sinks when defining RFI. Two RFI models were considered in the analyses; RFI model [1] was a 1-step RFI model with constant partial regression coefficients of DMI on energy sinks (ECM, MBW, and  $\Delta$ BW) over lactation. In RFI model [2], data from 44 lactation weeks were divided into 11 consecutive lactation periods of 4 wk in length. The RFI model [2] was identical to model [1] except that period-specific partial regressions of DMI on ECM, MBW, and  $\Delta$ BW in each lactation period were allowed across lactation. We estimated genetic parameters for RFI across lactation by both models using a random regression method. Using RFI model [2], we estimated the period-specific effects of ECM, MBW, and  $\Delta$ BW on DMI in all lactation periods. Based on results from RFI model [2], the partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW differed across lactation in RFI. Constant partial regression coefficients of DMI on energy sinks over lactation was not always sufficient to account for the effects across lactation and tended to give roughly average information from all period-specific effects. Heritability for RFI over 44 lactation weeks ranged from 0.10 to 0.29 in model [1] and from 0.10 to 0.23 in

model [2]. Genetic variance and heritability estimates for RFI from model [2] tended to be slightly lower and more stable across lactation than those from model [1]. In both models, RFI was genetically different over lactation, especially between early and later lactation stages. Genetic correlation estimates for RFI between early and later lactation tended to be higher when using model [2] compared with model [1]. In conclusion, partial regression coefficients of DMI on energy sinks differed across lactation when modeling RFI. Neglect of lactation stage when defining RFI could affect the assessment of RFI and the estimation of genetic parameters for RFI across lactation.

**Key words:** residual feed intake, dairy cattle, energy sink, lactation stage, genetic parameter

### INTRODUCTION

Alternative feed efficiency (**FE**) traits have been explored recently to select for efficient animals that better use feed energy for production without sacrificing animal health or fertility in the long run. Residual feed intake (**RFI**), as one proposed FE trait, has been widely studied in pig, chicken, beef cattle, and dairy cattle (Berry and Crowley, 2013; Wolc et al., 2013; Patience et al., 2015; Tempelman et al., 2015). Generally, RFI is defined as the difference between an animal's actual feed intake and its expected feed intake based on energy requirements for body maintenance and production (Koch et al., 1963). Individuals with lower RFI are considered to be more efficient. In dairy cattle, milk production, body maintenance, and BW change ( $\Delta$ BW) are usually included as key energy sinks when defining RFI. The expected feed intake of cows is derived from partial regressions of the feed intake on energy sinks (VandeHaar et al., 2016).

Defining RFI in lactating dairy cows is more complicated than defining RFI in growing animals due to the metabolic changes that occur during lactation cycles (Berry and Crowley, 2013). In early lactation, the milk production of dairy cows increases more sharply than feed intake, and body reserves need to be mobilized to

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meet the energy demand (Berglund and Danell, 1987; Roche et al., 2009; Banos and Coffey, 2010). In later lactation, the feed intake of cows is kept at a relatively high level and body reserves are gradually restored (Mao et al., 2004; Vallimont et al., 2010). Generally, the commonly used RFI model employs constant partial regressions of feed intake on energy sinks. Considering the complexity of the metabolic changes of cows across lactation, it is possible that the partial regression coefficients of feed intake on milk production, body maintenance, and  $\Delta$ BW could vary across lactation. Therefore, the general RFI model with constant partial regression coefficients of feed intake on energy sinks might not always hold for the entire lactation period, which might influence the estimation of RFI. Most previous studies corrected for the influence of lactation stages on RFI by using a systematic effect of DIM or lactation week on feed intake, or by including random regression terms in the model for the influence of lactation stage on cow random variances (Mäntysaari et al., 2012; Hardie et al., 2015; Tempelman et al., 2015). However, these commonly used corrections of lactation stages on RFI have ignored the potential influence of lactation stage on the partial regression coefficients of feed intake on energy sinks, and very few studies have been carried out to explore this potential influence when defining RFI. Lu et al. (2017) investigated the influence of management and environmental factors on partial efficiency of converting feed intake to energy sinks for RFI using a Bayesian multivariate modeling method, where the linear and quadratic effects of DIM on the partial efficiency of feed intake on energy sinks tended to be insignificant when 42-d records between 50 and 200 DIM were studied.

Previous studies reported heritability estimates for RFI in dairy cattle that ranged widely from 0.00 to 0.38 (Berry and Crowley, 2013; Tempelman et al., 2015; Manzanilla-Pech et al., 2016) and tended to vary across lactation (Tempelman et al., 2015). In dairy cattle, the genetic correlation for RFI across lactation has rarely been reported. A recent study showed a low genetic correlation for residual energy intake between early lactation and lactation wk 20 in Nordic Red cows (Liinamo et al., 2015).

The objectives of the current study were to investigate the influence of lactation stage on the partial regression coefficients of feed intake on energy sinks when modeling RFI, and also to estimate the genetic parameters for RFI across lactation in dairy cattle. Two RFI models were studied in which partial regression coefficients of feed intake on energy sinks were allowed or not allowed to change across lactation. Genetic parameters for RFI were estimated across lactation and were compared between the 2 RFI models.

## MATERIALS AND METHODS

### *Animals, Feeding, and Data Recording*

Cows in our study were from the Danish Cattle Research Center (DCRC; Foulum, Denmark) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle, Denmark). From the raw data set containing records for 1,749 lactations of 890 Holstein cows, our study included data from 823 primiparous Holstein cows that calved between 1995 and 2015. Cows had been involved in some experiments on the farm (Nielsen et al., 2003; Løvendahl et al., 2010; Løvendahl and Chagunda, 2011). Studied Holstein cows included all Holstein cows from the DCRC studied by Li et al. (2016).

Cows were fed a TMR in weigh bins at DCRC (RIC System, Insentec B.V., Marknesse, the Netherlands). A planned quantity of concentrates was dispensed during each milking in the automatic milking system and leftover quantity was recorded. At Skovgaard, cows were kept and fed in tiestalls, with TMR dispensed manually. Components in the TMR were mainly maize, whole-crop, and grass silage supplied with sugar-beet expellers and protein concentrates. The energy content of feed could be slightly different between trials but was generally constant within each trial. The TMR and concentrates offered to cows and the feed refusals were measured individually to calculate the individual feed intake per cow. The DM contents of the TMR and concentrates were analyzed regularly, and the compositions were aligned and merged with feed intake records to obtain daily DMI per cow. A weekly average DMI per cow was calculated as the average of 7 DMI daily records in each lactation week. Energy intake per cow was not available.

Cows were milked twice daily at Skovgaard and had voluntary access to automatic milking systems at DCRC. The approach of ICAR (2016) was used with a moving average over 3 d to obtain daily milk yield (MY), where the daily MY was obtained from the average milking rate (calculated from the sum of the yield over 3 d divided by the sum of milking intervals in the same period) multiplied by 24 h. Milk composition was measured in all samples from every milking taken over a consecutive 48-h period every week. Milk composition was analyzed by using CombiFoss equipment (Foss, Hillerød, Denmark) operated by Eurofins (Vejen, Denmark). Composition data from each milking were used to calculate yields of fat, protein, and lactose, which were smoothed by the moving average method to obtain daily yields. Calculated daily yields were averaged per week of lactation to get the weekly average yields, similar to the DMI records. At Skovgaard, BW per cow was recorded every week during lactation wk

1 to 12, and every other week during wk 13 to 44. At DCRC, cows were weighted at every milking, and the BW records per cow were averaged per week of lactation to get the weekly BW.

### Data Editing

The data set for our study included weekly records of DMI, MY, milk composition (fat, protein, lactose contents), and BW of the primiparous Holstein cows within the 44 lactation weeks. Cows that were older than 36 mo at first calving and cows with fewer than 5 weekly records of DMI, MY, milk composition, or BW over the 44 lactation weeks were removed from the data set. After data editing, the final data set for the statistical analysis consisted of 747 primiparous Holstein cows with 24,993 weekly records on DMI, MY, milk composition, and BW. Age range at first calving was 24 to 36 mo. Each cow had an average of 33 weekly records (Table 1). Pedigree information was extracted from the Nordic Cattle Genetic Evaluation Database (Skejby, Denmark) by tracing back as many generations as possible for cows with records.

### Statistical Analysis

Energy-corrected milk, metabolic BW (**MBW**), and  $\Delta$ BW were calculated individually in each lactation week. The ECM (kg) was obtained from MY (kg) and milk composition (g/kg) by using  $ECM = MY \times [(38.30 \times \text{fat content} + 24.20 \times \text{protein content} + 16.54 \times \text{lactose content} + 20.7)/3,140]$  (Sjaunja et al., 1990). The weekly BW per cow over 44 lactation weeks was modeled by a third-order Legendre polynomial function of lactation weeks. And the  $\Delta$ BW per cow at each lactation week was obtained from the first derivative (i.e., the slope) of the fitted BW curve of each cow; MBW was computed as  $BW^{0.75}$  (McDonald et al., 2011).

Two RFI models were considered. Model [1] is a 1-step RFI model that combines the energy sink model for estimating RFI and the genetic model (Lu et al., 2015; Tempelman et al., 2015). In model [1], the partial regression coefficient of DMI on each energy

sink (ECM, MBW, and  $\Delta$ BW) was considered to be constant over lactation. Residual feed intake model [2] considered period-specific partial regressions of DMI on ECM, MBW, and  $\Delta$ BW for each lactation period, with the whole lactation (44 lactation weeks) being divided into 11 consecutive 4-wk lactation periods. The 2 models were identical except for the period-specific partial regressions of DMI on energy sinks in the latter model:

$$DMI_{jklmp} = b_1ECM + b_2MBW + b_3\Delta BW + \text{Herd-Trial}_j + CA_k + YS_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{np}\Phi_n + \sum_{n=0}^2 pe_{np}\Phi_n + e_{jklmp}, \quad [1]$$

and

$$DMI_{ijklmp} = b_{1i}ECM + b_{2i}MBW + b_{3i}\Delta BW + \text{Herd-Trial}_j + CA_k + YS_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{np}\Phi_n + \sum_{n=0}^2 pe_{np}\Phi_n + e_{ijklmp}, \quad [2]$$

where  $DMI_{jklmp}$  and  $DMI_{ijklmp}$  are the weekly records of DMI in lactation week (Lactwk)  $m$  for cow  $p$  in model [1] and [2], respectively, where cow  $p$  is in calving age (CA)  $k$  in the year-season of calving (YS)  $l$  and from Herd-Trial  $j$ . In model [1],  $b_1$ ,  $b_2$ , and  $b_3$  are the partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW over lactation, respectively. In model [2],  $b_{1i}$ ,  $b_{2i}$ , and  $b_{3i}$  are the period-specific partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW, respectively, in lactation period  $i$  ( $i = 1$  to  $11$ ). Herd-Trial $_j$  is the fixed effect of herd and trial in which the cows were involved ( $j = 1$  to  $25$ ), where the cows were from 2 research herds and the trials were herd-specific;  $CA_k$  is the fixed effect of calving age in the month of cows' first calving ( $k = 24$  to  $36$ );  $YS_l$  is the fixed effect of year-season of calving, where the year of calving is from 1995 to 2015 and 4 seasons were defined (March to May, June to August, September to November, and December to February;  $l = 1$  to  $64$ );  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week on DMI ( $m = 1$  to  $44$ );  $a_{np}$  and  $pe_{np}$  are

**Table 1.** Descriptive statistics of DMI (kg/d), milk yield (kg/d), milk composition (%), and BW (kg) across 44 lactation weeks in 747 primiparous Holstein cows

Item	Mean	SD	Minimum	Maximum
DMI (kg/d)	19.63	2.97	5.72	40.48
Milk yield (kg/d)	28.55	6.39	2.50	47.00
Milk composition (%)				
Protein	3.51	0.35	2.35	4.70
Fat	4.15	0.65	2.04	6.37
Lactose	4.96	0.26	3.97	5.96
BW (kg)	601.0	62.2	396.5	867.1

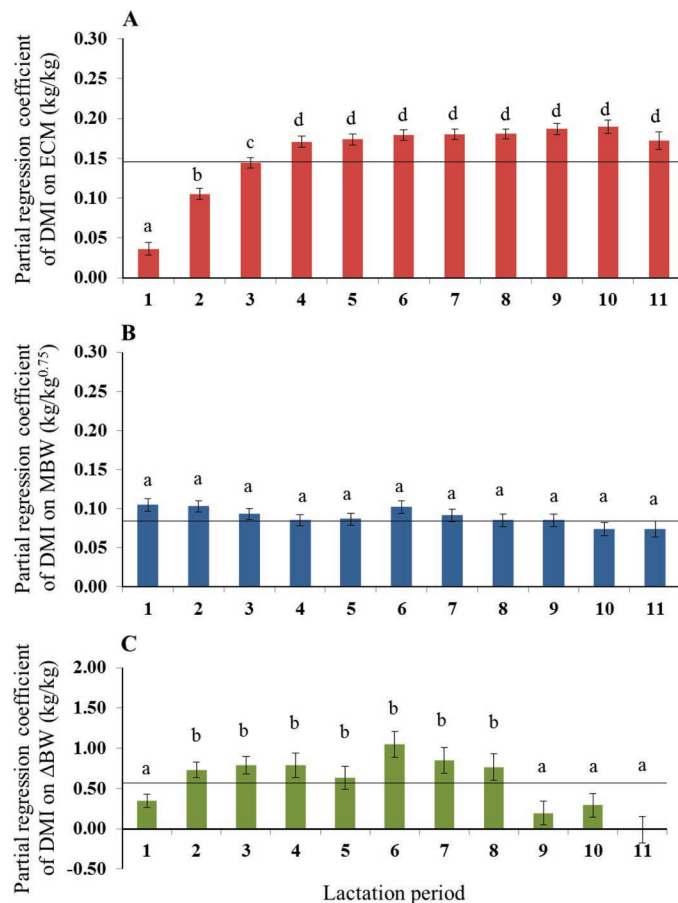
the  $n$ th regression coefficients of the Legendre polynomial for the random additive genetic effect and for the random permanent environmental effect, respectively, of the cow  $p$ ;  $\Phi_n$  is the term of the second-order Legendre polynomial for  $a_{np}$  and  $pe_{np}$ , where the time variable is the week of lactation;  $e_{ijklmp}$  and  $e_{ijklmp}$  are random residuals for model [1] and [2], respectively, which were assumed to be with heterogeneous variances along lactation and were divided into 11 classes of heterogeneous residual variances (every 4 consecutive weeks of the 44 lactation weeks was set as 1 class).

We initially tested the significance of the period-specific partial regressions of DMI on energy sinks (ECM, MBW, and  $\Delta$ BW) by using PROC MIXED in SAS 9.3 (SAS Institute Inc., Cary, NC), where the period-specific partial regressions of DMI on energy sinks (ECM, MBW, and  $\Delta$ BW) were shown to be significant ( $P < 0.05$ ). In this test, we used a mixed model that included the same fixed effects as model [2] and a random cow effect with a third-order Legendre polynomial of lactation weeks, but without using pedigree relationships. Thereafter, we carried out a genetic analysis for RFI with model [1] and [2] with pedigree information, using the restricted maximum likelihood in DMU 5.2 (Madsen and Jensen, 2013). Period-specific partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW were estimated with model [2] and compared with the partial regression coefficients estimated from model [1]. Variance components and genetic parameters for RFI across lactation were estimated from both model [1] and [2] and were compared with each other.

## RESULTS

### Effects of Energy Sinks on DMI in Different Lactation Periods

Period-specific partial regressions of DMI on ECM (Figure 1A), on MBW (Figure 1B), and on  $\Delta$ BW (Figure 1C) from RFI model [2] varied across lactation. From the genetic analysis using model [1], the partial regression coefficient of DMI on ECM over lactation was close to 0.15 (kg of DMI/kg of ECM; SE = 0.004; Figure 1A). When the period-specific effect of ECM on DMI was considered in model [2], the effect of ECM on DMI changed significantly across lactation (Figure 1A). In early lactation (periods 1–2), the estimated regression coefficients of DMI on ECM were significantly lower than 0.15 (kg of DMI/kg of ECM). From period 4 until the end of lactation, partial regression coefficients of DMI on ECM were significantly higher than 0.15 (kg of DMI/kg of ECM). The estimated amount of feed intake for 1 kg of ECM increased from the beginning of lactation until period 4 (Figure 1A).



**Figure 1.** Partial regression coefficients of DMI on (A) ECM, (B) metabolic BW (MBW), and (C) change in BW ( $\Delta$ BW) in each lactation period estimated from residual feed intake (RFI) in model [2]. Error bars are standard errors. Bars not sharing the same letter (a–d) are significantly different ( $P < 0.05$ ). Horizontal lines are the partial regression coefficients of DMI on ECM, MBW, and  $\Delta$ BW across 44 lactation weeks estimated from model [1], respectively. Color version available online.

When model [1] was used, the estimated partial regression coefficient of DMI on MBW over lactation was around 0.08 (kg of DMI/kg of MBW; SE = 0.005; Figure 1B). In model [2], the estimated partial regression coefficients of DMI on MBW tended to be greater than 0.08 (kg of DMI/kg of MBW) in period 1, 2, and 6, but were generally stable across periods (Figure 1B). When model [1] was used, the partial regression coefficient of DMI on  $\Delta$ BW over lactation was 0.57 (kg of DMI/kg of  $\Delta$ BW; SE = 0.06; Figure 1C). In model [2], partial regression coefficients of DMI on  $\Delta$ BW were significantly lower than 0.57 (kg of DMI/kg of  $\Delta$ BW) at the beginning of lactation (period 1) and in the end of lactation (periods 9–11), and tended to be higher than 0.57 (kg of DMI/kg of  $\Delta$ BW) from periods 2 to 8 (Figure 1C).

### Genetic Parameters for RFI Estimated from 2 Models

**Variance Components and Heritability.** Variance components estimated from both RFI models generally followed similar patterns (Figure 2). In RFI model [2], where the partial regression coefficients of DMI on energy sinks were allowed to change over lactation, lower and more stable genetic variances for RFI along lactation were observed compared with the genetic variances estimated from model [1]. The permanent environmental variances estimated from both models were similar. The residual variance from model [2] was slightly lower than model [1] across the whole lactation periods. The total variance from RFI model [2] was lower than the total variance from model [1] in most of the lactation. Additionally, in most of the lactation weeks, the correlations between observed DMI and predicted DMI were higher in model [2] than in model [1], especially in the first 3 lactation weeks when the correlations between predicted and observed DMI were on average 2% higher in model [2] than in model [1].

The heritability for RFI estimated from both models followed a similar trajectory, decreasing from the beginning of lactation to lactation wk 10 from around 0.2 to 0.1 before an increase until around lactation wk 30 (Figure 3). The heritability for RFI estimated from model [1] ranged from 0.10 to 0.29 across lactation (mean SE = 0.05), whereas the heritability from model [2] was slightly lower and more stable over lactation, ranging from 0.10 to 0.23 across lactation (mean SE = 0.05; Figure 3).

**Genetic Correlations for RFI Across Lactation.** Residual feed intake in middle and late lactation were genetically highly correlated, whereas RFI in early lactation was negatively correlated with RFI in later lactation weeks (Figure 4). Genetic correlations for RFI across 44 lactation weeks estimated from model [1] and model [2] ranged from  $-0.51$  to  $1$  and from  $-0.29$  to  $1$ , respectively. Genetic correlations for RFI were shown to be negative between early and middle lactation weeks from both models. However, the most extreme negative genetic correlation for RFI between early and middle lactation was reduced to  $-0.29$  in RFI model [2] (Figure 4B), compared with  $-0.51$  from model [1] (Figure 4A).

## DISCUSSION

### Lactation Stage Influenced the Effects of Energy Sinks in RFI

Our results indicated that the allocation of energy (seen as feed intake) to common energy sinks (ECM, MBW, and  $\Delta$ BW) varied across lactation based on the

current definition of RFI. The assumption of constant partial regressions of feed intake on ECM, MBW, and  $\Delta$ BW over lactation was not always sufficient to explain the feed utilization for energy sinks across lactation and tended to result in roughly average information of all period-specific effects. More specifically, the partial regression coefficients of DMI on ECM were significantly different between early and later lactation stages, with the effect of ECM on DMI being much lower in early lactation compared with later lactation; this result could partly reflect the change of metabolic condition in dairy cows during lactation. A cow's MY increases sharply after calving, and feed intake peaks no earlier than lactation wk 10 to 12 (Gravert, 1985; Mäntysaari et al., 2012; Berry et al., 2014). In early lactation, the energy intake from diet cannot meet the energy demand for rapidly increased MY, and part of the required energy comes from the mobilization of body reserves (Berghlund and Danell, 1987; Mao et al., 2004; Banos and Coffey, 2010). After early lactation, the feed intake of cows remains at a relatively high level to provide energy for milk production, and body reserves are gradually restored (Mao et al., 2004). The potential change in the relationship between feed intake and milk production could also be reflected by a varying genetic correlation between DMI and MY across lactation from previous studies, especially in early lactation when feed intake and MY were weakly genetically correlated (Veerkamp and Thompson, 1999; Hüttmann et al., 2009; Manzanilla Pech et al., 2014). In addition, it should also be noted that the partial regression coefficients of DMI on ECM were relatively constant from period 3 (approximately from DIM 57) until the end of lactation in our study, indicating a fairly weak influence of lactation stage on partial efficiency of DMI on ECM from period 3 onwards. This result is in agreement with Lu et al. (2017), who also reported an insignificant influence of lactation stage on the partial regression of feed intake on milk energy when 42-d records between 50 and 200 DIM were included in the analysis.

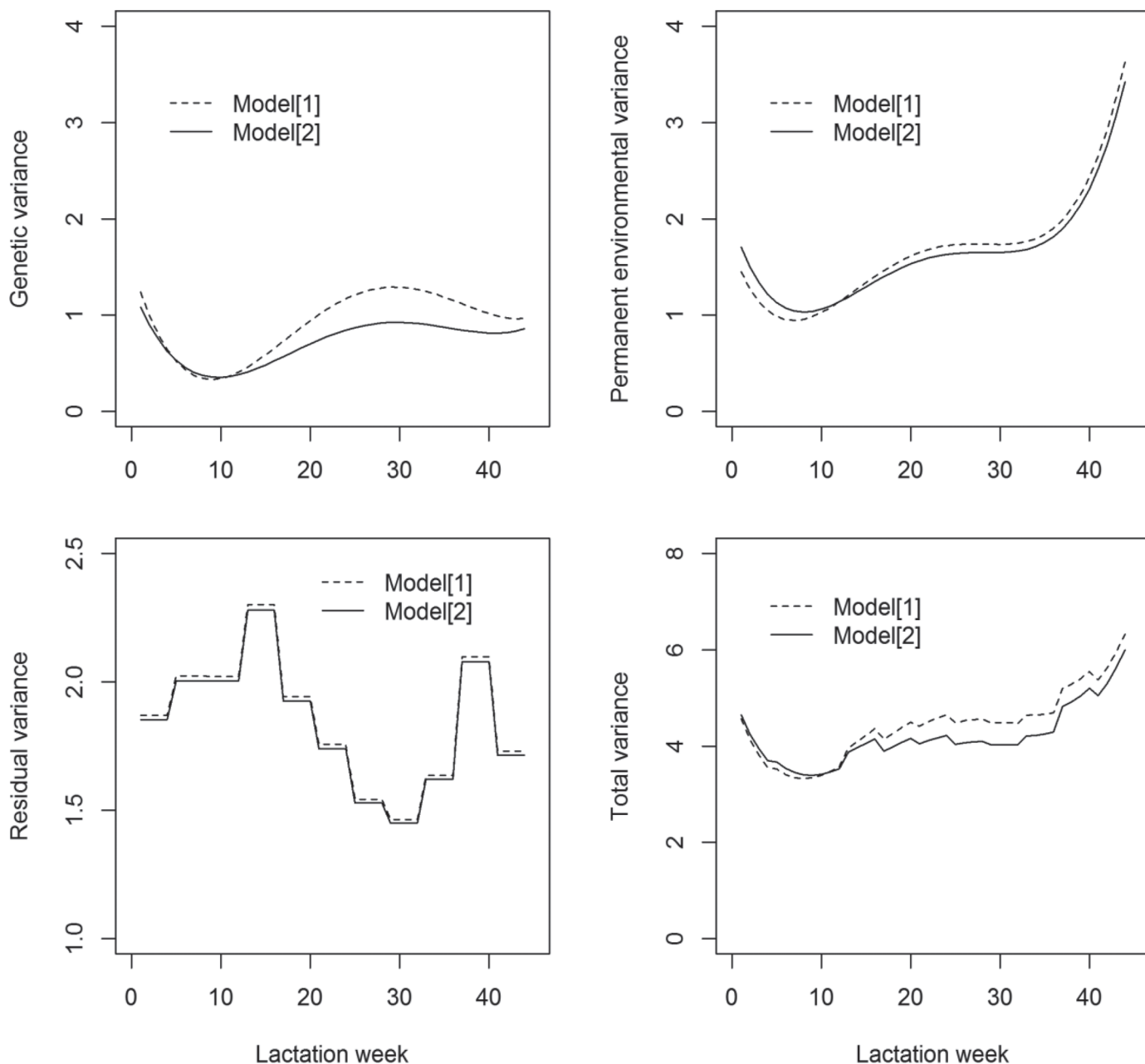
The utilization of feed intake for  $\Delta$ BW was significantly influenced by the lactation period in our study. Generally, lactating cows lose BW at the beginning of lactation and gradually gain BW in later lactation (Valimont et al., 2010). The catabolism and anabolism of body tissues correspond to different energy values, such that the energy generated from a 1-kg loss in BW is less than the energy required for a 1-kg gain (O'Mara, 2000; Coleman et al., 2010). Therefore, the effect of  $\Delta$ BW on feed intake in early lactation (mostly BW loss) would be expected to differ from the effect in middle and late lactation (mostly BW gain). The feed intake of cows could hardly follow a constant partial regression of the cows'  $\Delta$ BW over the whole lactation. In our study, we



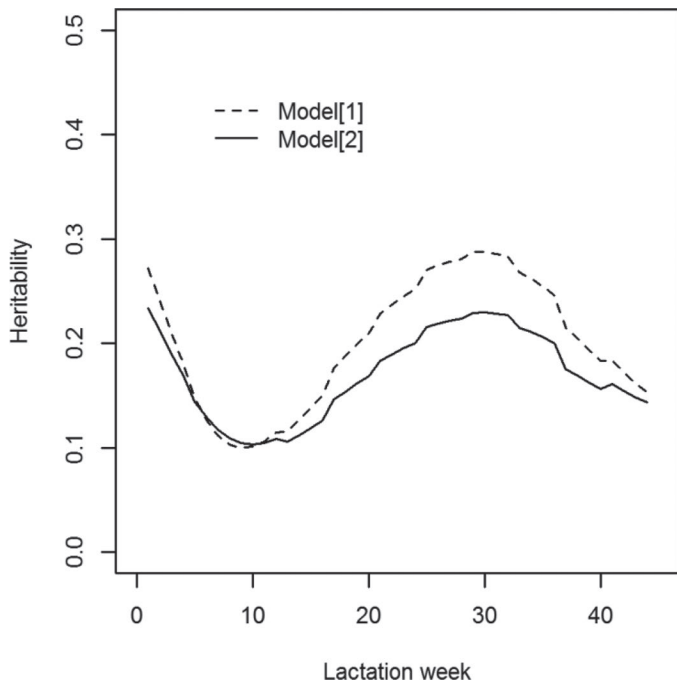
defined a period-specific partial regression of DMI on  $\Delta$ BW, where BW loss was mainly in lactation period 1 and, to some extent, in period 2; after period 2, we mainly observed BW gain. As an alternative, a few studies used partial regressions of DMI on both BW loss and BW gain to explain the associations of feed intake with BW change for estimation of RFI (Coleman et al., 2010; Mäntysaari et al., 2012). We did not specify BW loss and BW gain in the current study because the period-specific partial regressions of DMI

on  $\Delta$ BW were considered and very few cows had BW loss after period 2.

The efficiency of cows would be assessed differently depending on whether lactation stage is considered in calculating RFI, especially for cows' efficiency in early lactation. For example, considering 2 cows from our data set in lactation wk 3; cow 1 had a higher ECM yield and higher feed intake than cow 2 in lactation wk 3, whereas cow 2 was much heavier and mobilized more BW than cow 1. The RFI for both cows in this week



**Figure 2.** Genetic variances, permanent environmental variances, residual variances, and total variances for residual feed intake (RFI) across 44 lactation weeks estimated from RFI in model [1] (dashed lines) and RFI in model [2] (solid lines).



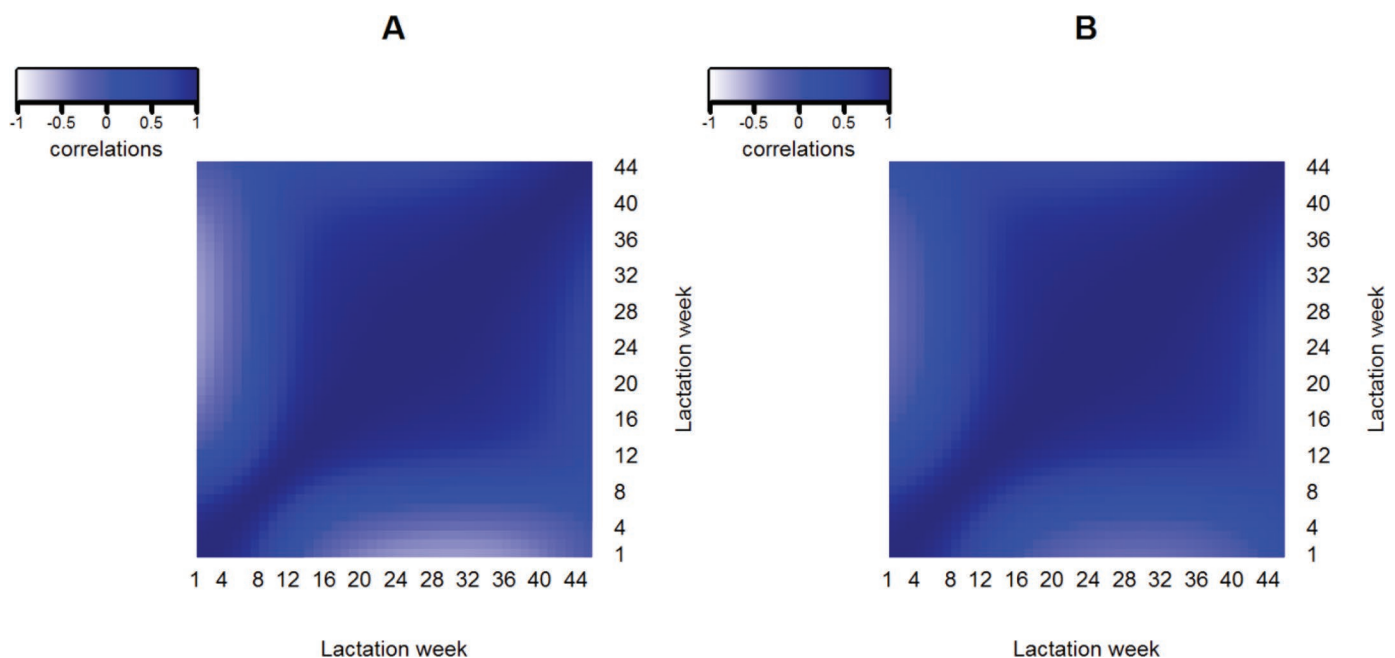
**Figure 3.** Heritability for residual feed intake (RFI) across 44 lactation weeks estimated from RFI in model [1] (dashed line) and RFI in model [2] (solid line).

were estimated as the residuals of DMI after adjusting for ECM yield, MBW, and  $\Delta$ BW. When model [1] was used to estimate RFI, cow 1 and 2 were very

similar in RFI; however, when model [2] was used, cow 2 had a lower RFI and was more efficient than cow 1. Cow 2 met energy requirements in part by mobilizing body reserves, whereas cow 1 met energy requirements solely by intake of feed. The difference was reflected in RFI from model [1] and [2] due to the different partial regression coefficients of DMI on energy sinks for early lactation.

### Genetic Parameters for RFI Across Lactation

The genetic variance for RFI varied along lactation, consistent with the findings of Tempelman et al. (2015), who reported unequal genetic variances for RFI from DIM 50 to 200. In our study, genetic variances for RFI estimated from model [1] and [2] were slightly different. After accounting for the period-specific effects of energy sinks, the genetic variance for RFI was lower and more stable over lactation in model [2] than in model [1]. The higher genetic variance for RFI estimated from model [1] might partly come from the unexplained variance in the period-specific effects of energy sinks. The heritability for RFI estimated from model [2] was slightly lower than model [1] and more stable over the lactation, mainly due to the more stable genetic variance estimated from model [2] compared with model [1] over lactation. The heritability of RFI in dairy cattle ranged from 0.10 to 0.23 across lactation in our study, consistent with the heritability reported by Tempelman et al. (2015; i.e., 0.10–0.25 for DIM 50–200).



**Figure 4.** Genetic correlations for residual feed intake (RFI) across 44 lactation weeks estimated from (A) RFI model [1] and (B) RFI model [2]. Color version available online.

We found that RFI was genetically different across lactation. Liinamo et al. (2015) reported a similar finding of the genetic heterogeneity of residual energy intake during 30 wk of lactation in Nordic Red dairy cattle. The extreme negative genetic correlations between early and middle lactation estimated from model [1] tended to be mitigated when period-specific partial regressions of DMI on energy sinks were included in model [2]. However, this type of correction for the period-specific effects of energy sinks seemed not to influence the conclusion of a genetic heterogeneity of RFI across lactation. In other words, the heterogeneity of RFI across lactation could stem from the basic definition of RFI. Basically, RFI is defined based on the phenotypes of DMI, MY, and BW. Milk yield and DMI have been reported as genetically different traits over lactation, especially between early and later lactation stages (Veerkamp and Thompson, 1999; Manzanilla Pech et al., 2014; Li et al., 2016). Body weight tended to be a more consistent trait across lactation, but the genetic correlation of BW between early and later lactation was still not unity (Veerkamp and Thompson, 1999; Manzanilla Pech et al., 2014). Properties of component traits of RFI (DMI, MY, and BW) across lactation could influence the genetic properties of RFI across lactation.

### **Challenges of Using RFI for FE in Dairy Cattle**

The challenges of using RFI as a measure of FE in dairy cattle have been widely discussed (e.g., Kennedy et al., 1993; Berry and Crowley, 2013; Tempelman et al., 2015). Selecting for RFI has the risk of being mathematically equivalent to selecting for negative energy balance if  $\Delta$ BW is not accounted for properly (Veerkamp, 2002). Another issue is that RFI is genetically correlated with its component energy sink traits (e.g., MY, BW, and  $\Delta$ BW), as RFI was only phenotypically adjusted for the component traits; therefore, selection on RFI would generate correlated responses in production and in BW (Kennedy et al., 1993; Veerkamp and Emmans, 1995). Considering the challenges of using RFI for FE in dairy cattle, we stressed the influence of lactation stages in defining RFI and the potential heterogeneity of RFI across lactation. We focused on the influence of lactation stage on the allocation of DMI to energy sinks when data for modeling RFI cover the entire lactation. Constant partial regressions of DMI on energy sinks were found to be insufficient to account for the effects of energy sinks across lactation, especially during early lactation. Our modeling strategy for RFI in the current study helped us to understand the influence of lactation stages on RFI and could provide useful information for a better

modeling of RFI or FE traits in the future. One limitation of the present study was that we defined RFI based on the phenotypic adjustment of energy sinks for DMI, so that RFI would not be genetically independent from energy sink traits. In contrast, the concept of multiple trait selection or modeling of feed intake itself and the energy sink traits could be alternatives of the current RFI (Kennedy et al., 1993; Veerkamp and Emmans, 1995; Lu et al., 2015). However, as FE-related traits (e.g., DMI, MY, BW) in a multiple-trait selection can be genetically different across lactation, the influence of lactation stage on FE-related traits should be considered in a multiple trait selection for FE in dairy cattle.

### **CONCLUSIONS**

When defining RFI in lactating dairy cows, we found that the partial regression coefficients of cows' feed intake on ECM, MBW, and  $\Delta$ BW varied across lactation, especially in early lactation. Constant partial regressions of feed intake on energy sinks were not always sufficient to explain the effects of ECM, MBW, and  $\Delta$ BW across lactation in defining RFI. Heritability for RFI ranged from 0.10 to 0.23 across lactation; RFI was genetically different across lactation, especially between early and later lactation stages. Considering period-specific partial regressions of DMI on ECM, MBW, and  $\Delta$ BW in RFI could affect the assessment of RFI and the estimated genetic parameters for RFI across lactation.

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1 **Deriving residual feed intake from genetic covariance functions of dry matter intake,**  
2 **energy-corrected milk, and metabolic body weight in Holstein dairy cattle across**  
3 **lactation**

4  
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## **ABSTRACT**

22 Feed efficiency (FE) of dairy cattle has implications for both farm profitability and for  
23 environment. Alternative FE definitions have been recently investigated to properly define FE  
24 in dairy cattle, among which residual feed intake (RFI) is one important FE candidate trait. In  
25 this study, two RFI definitions were studied to investigate the genetic properties of different

26 RFI traits and to assess the possibilities of applying RFI into dairy cattle breeding for FE. A  
27 total of 963 primiparous Holstein dairy cows from Denmark and Sweden were included in the  
28 study, where each cow had weekly records of dry matter intake (DMI), energy-corrected milk  
29 (ECM), and body weight (BW) across 44 lactation weeks. The first RFI definition (denoted as  
30 “genetic RFI”) was based on multivariate modelling, where RFI was derived from genetic  
31 covariance functions of DMI, ECM and Metabolic BW (MBW) in multivariate random  
32 regression analyses across lactation. Genetic RFI is genetically uncorrelated/independent from  
33 milk yield and BW. The second RFI definition (denoted as “phenotypic RFI”) was a  
34 popularly-studied RFI model where RFI was derived from linear regressions of feed intake on  
35 energy sink traits (ECM and MBW). Random regression model was also applied to  
36 phenotypic RFI for the genetic analyses across lactation. Variance components and genetic  
37 parameters across lactation were estimated and compared between genetic RFI and  
38 phenotypic RFI. The estimated breeding values (EBV) were also estimated for cows for  
39 genetic RFI and phenotypic RFI, respectively. As the results, phenotypic RFI had higher  
40 genetic variance and heritability compared with genetic RFI. For both RFI definitions, RFI in  
41 early lactation was not the same trait as RFI in middle and late lactation. Phenotypic RFI  
42 tended to be higher genetically correlated among mid and late lactation stages, compared to  
43 genetic RFI. When it comes to selection, the animals with the lowest (i.e., the most desirable)  
44 breeding values for genetic RFI and for phenotypic RFI were very different from each other.  
45 Selection for FE based on genetic RFI and phenotypic RFI could also lead to different  
46 directions of selection for efficiency.

47 **Key words:** feed efficiency, residual feed intake, dairy cattle, random regression model,  
48 multivariate analyses

49

50

## INTRODUCTION

51 Feed efficiency (FE) of dairy cattle has implications for both farm profitability and for  
52 environment. The topic of feed efficiency is on the tip of every dairy producer's tongue, since  
53 feed accounts for the largest part of operating costs in dairy production (European  
54 Commission, 2013). Also, improving FE in cattle is expected to help lower methane emission  
55 (de Haas et al., 2011), which could have implications for greenhouse gas mitigation (Wall et  
56 al., 2010). Recent studies on FE in dairy cattle have covered several important topics on  
57 alternative FE traits, including genetic parameters, genomic evaluation, and genome-wide  
58 association study for FE (e.g., Berry et al., 2014; de Haas et al., 2015; Lu et al., 2018).  
59 Alternative FE definitions have been investigated in order to properly define FE in dairy cattle  
60 (e.g., Lu et al., 2015; Pryce et al., 2015; Hurley et al., 2016; Li et al., 2017). However, a  
61 controversy remains as to which trait should be used to represent FE in breeding practice.

62 In dairy cattle breeding, dry matter intake (DMI) is the key component of all available  
63 FE traits in dairy cattle, and has been proposed as a FE trait recently to dairy cattle breeding in  
64 the Netherlands (Veerkamp et al., 2014). DMI has been widely recognized to be correlated  
65 with milk yield and some other traits in the selection index (e.g., Buttchereit et al., 2011;  
66 Manzanilla-Pech et al., 2016; Li et al., 2018), so that the correlated responses of selecting for  
67 DMI need to be properly taken into account. Another candidate FE trait in dairy cattle is  
68 residual feed intake (RFI). In general, RFI is defined as the difference between an animal's  
69 actual feed intake and its expected feed intake based on the animal's energy requirements for  
70 production and body maintenance (Koch et al., 1963). In dairy cattle, RFI is defined from an  
71 energy sink model where animals' DMI is linear regressed on their energy sinks (e.g., milk  
72 production, body weight (BW), change of BW ( $\Delta$ BW)) (VandeHaar et al., 2015). The  
73 residuals from the energy sink model are the phenotypes for RFI and have been used in  
74 genetic analyses for RFI. In this way, RFI is phenotypically adjusted by energy sink traits  
75 (e.g., milk production, BW,  $\Delta$ BW). However, RFI is still genetically correlated with energy

76 sink traits, since the adjustment is only on a phenotypic level. The remaining genetic  
77 correlations between RFI and energy sinks would still need to be carefully taken into account  
78 in the selection index.

79 It is of interest to define RFI as genetically uncorrelated with major energy sink traits  
80 (e.g., milk yield, BW). Milk production traits and BW-related traits are usually parts of the  
81 total merit index traits in dairy cattle evaluation. After removing the genetic correlations of  
82 RFI with milk production and BW, RFI becomes a more independent trait representing FE in  
83 the selection index. Defining RFI as genetically independent of production traits leads to  
84 easily interpretable breeding values for FE. To define RFI genetically independent from major  
85 energy sinks (e.g., milk yield, BW), DMI needs to be adjusted genetically for the energy sink  
86 traits. In pig breeding, Strathe et al. (2014) proposed a method of deriving RFI from  
87 covariance functions of DMI, BW, and rate of gain from multivariate random regression  
88 analyses, where they genetically adjusted DMI for BW and rate of gain. Lu et al. (2015)  
89 applied a similar method of multivariate modelling for RFI to dairy cattle, but they didn't  
90 apply random regression analyses to model RFI since they assumed a constant genetic  
91 variance for RFI across lactation.

92 In the current study, we applied the multivariate modelling for RFI (denoted here as  
93 "genetic RFI" in this study) in Nordic Holstein dairy cows in a random regression analysis  
94 across the whole first lactation. RFI derived from phenotypic adjustment of energy sinks  
95 (denoted as "phenotypic RFI" in this study) were also studied in order to compare the two  
96 ways of modelling for RFI. The objective of this study was (1) to derive genetic RFI from  
97 genetic covariance functions of DMI, ECM and MBW by multivariate analyses, (2) to  
98 estimate genetic parameters for genetic RFI across the whole lactation, (3) to compare the  
99 variance components, genetic parameters, and breeding value estimation between the two  
100 definitions of RFI (i.e., genetic RFI and phenotypic RFI).



101

102

## MATERIAL AND METHODS

### 103 **Animals, Feeding, and Data Recording**

104 Holstein dairy cows in our study were from four research herds from Denmark and  
105 Sweden. The research herds were located at the Danish Cattle Research Center (DCRC,  
106 Foulum) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle) in Denmark; and at  
107 the Swedish University of Agricultural Sciences Lövsta research herd (Lövsta, Uppsala) and  
108 Öjebyn research herd (Öjebyn) in Sweden. The studied cows calved between 1991 and 2015.  
109 Pedigree information was extracted from the Nordic Cattle Genetic Evaluation (NAV, Skejby,  
110 Denmark) database, by tracing back as many generations as possible for cows with records.  
111 The cows studied by (Li et al., 2016, 2017, 2018) were part of the data in this study.

112 The studied cows were involved in several nutrition experiments within research herds.  
113 The feeding information in the trials have been described in detail in previous studies (Nielsen  
114 et al., 2003; Løvendahl et al., 2010; Løvendahl and Chagunda, 2011; Byskov et al., 2017;  
115 Andrée O'Hara et al., 2018). Feed offered and feed refusals were measured individually to  
116 calculate the feed intake per cow. The DM contents in forage and concentrates were analysed  
117 regularly, and the compositions were aligned and merged with feed intake records to obtain  
118 daily DMI values per cow. A weekly average DMI per cow was calculated as the average of  
119 daily DMI records in each lactation week.

120 Milking and milk yield recordings were described in previous studies (Nielsen et al.,  
121 2003; Løvendahl et al., 2010; Løvendahl and Chagunda, 2011; Byskov et al., 2017; Li et al.,  
122 2017; Andrée O'Hara et al., 2018). A weekly observation of daily milk yield per cow was  
123 obtained from the average of daily milk yield records per cow in each week. Milk samples  
124 were taken regularly for analyses of fat, protein, and lactose content (Løvendahl et al., 2010).  
125 The average daily ECM (kg) per cow in each lactation week was calculated from average

126 daily milk yield (kg) and milk composition (g/kg) using the formula by (Sjaunja et al., 1990):  
127  $ECM (kg) = \text{milk yield (kg)} \times [(38.30 \times \text{fat content (g/kg)} + 24.20 \times \text{protein content (g/kg)} +$   
128  $16.54 \times \text{lactose content (g/kg)} + 20.7)/3,140]$ . Cows were weighted on a weekly basis in some  
129 research herds. In other research herds cows were automatically weighted at each milking so  
130 that BW records were averaged to obtain a weekly record of BW per cow in each week  
131 (Nielsen et al., 2003; Løvendahl et al., 2010; Li et al., 2017; Andrée O’Hara et al., 2017).

132

### 133 **Data Editing**

134 Primiparous Holstein cows were extracted from the original data set for the current  
135 study. Cows’ weekly records from lactation weeks 1 to 44 were included in the analyses,  
136 corresponding to the typical 305-day lactation. Cows with fewer than 3 weekly records of  
137 DMI, ECM, and BW during the studied 44 lactation weeks were removed from the data set. A  
138 few cows with a calving age of more than 38 months at first calving were also removed from  
139 the data set, resulting in the age at first calving ranging from 24 to 38 months. After data  
140 editing, a total of 34,675 records of 963 primiparous Holstein cows from 4 research herds in  
141 Denmark and Sweden (DCRC, Skovgaard, Lövsta, and Öjebyn herds) were included in the  
142 statistical analyses. Cows had weekly records of DMI, ECM, and BW across lactation (Table  
143 1). Metabolic BW (MBW) was computed as  $BW^{0.75}$  (McDonald et al., 2011).

144

### 145 **Genetic RFI**

146 The first way of modelling RFI, denoted as “genetic RFI” in this study, was to derive  
147 RFI from genetic covariance functions of DMI, ECM and MBW by multivariate random  
148 regression analyses (Strathe et al., 2014). In genetic RFI, DMI was genetically adjusted for  
149 ECM and MBW through decomposition of (co)variances among DMI, ECM, and MBW  
150 (Strathe et al., 2014; Lu et al., 2015).

151 **Multivariate Random Regression Analyses.** Multivariate random regression analyses  
 152 for DMI, ECM, and MBW across lactation were applied to model “genetic RFI”. The random  
 153 regression model, which was the same for each trait in the multivariate analyses, was as  
 154 follows:

155

$$156 \quad y_{ijklm} = u + \text{Herd-Trial}_j + \text{CA}_k + \text{YS\_Country}_l + \text{Lactwk}_m + \sum_{n=0}^2 a_{ni} \Phi_n + \sum_{n=0}^2 pe_{ni} \Phi_n +$$

$$157 \quad e_{ijklm}, [1]$$

158

159 where  $y_{ijklm}$  is the weekly observation of DMI, ECM, or MBW in lactation week (Lactwk)  $m$   
 160 for cow  $i$ , where cow  $i$  is in herd and trial (Herd-Trial)  $j$ , at calving age (CA)  $k$ , and in the  
 161 year-season of recording and country (YS\_Country)  $l$ .  $u$  is the intercept for DMI, ECM, or  
 162 BW;  $\text{Herd-Trial}_j$  is the fixed effect of herd and trial for the cow, where the trials were herd-  
 163 specific ( $j = 1$  to 37);  $\text{CA}_k$  is the fixed effect of calving age in months, where the calving age  
 164 of primiparous Holstein cows ranges from 24 to 38 months;  $\text{YS\_Country}_l$  is the fixed effect of  
 165 year-season of recording for each country, where the year of recording is from 1991 to 2016  
 166 and 4 seasons were defined (March to May, June to August, September to November, and  
 167 December to February, for two countries (Denmark and Sweden) ( $l = 1$  to 117); and  $\text{Lactwk}_m$   
 168 accounts for the fixed effect of lactation week ( $m = 1$  to 44). Random regression terms were  
 169 used to describe the cows’ additive genetic effect and permanent environmental effect. The  
 170  $a_{ni}$  and  $pe_{ni}$  are the  $n^{\text{th}}$  regression coefficients of the second-order Legendre polynomial for  
 171 the random additive genetic effect and the random permanent environmental effect,  
 172 respectively, for cow  $i$ ;  $\Phi_n$  is the  $n^{\text{th}}$  covariable of the second-order Legendre polynomial on  
 173 the weeks of lactation;  $e_{ijklm}$  is the random residual, whose variance was assumed to be  
 174 constant across lactation.

175

176 The variance components were estimated by an average information-restricted  
 177 maximum likelihood algorithm (Jensen et al., 1997) implemented in the software DMU  
 178 (Madsen and Jensen, 2013).

179 The genetic (co)variance matrix among the three traits across 44 lactation weeks ( $G_0$ )  
 180 was derived in the random regression setting as follows:

$$181 \quad G_0 = MK_a M' , \quad [2]$$

182 where  $G_0$  is the genetic (co)variance matrix across traits and weeks. Matrix  $K_a$  contains the  
 183 estimated covariance function describing the genetic variance components for the random  
 184 regression coefficients across three traits, estimated with DMU using Model [1]. Matrix  $M$  is  
 185 a block-diagonal matrix containing the Legendre polynomials for 44 weeks for three traits.

186 Likewise, the permanent environmental (co)variance matrix across traits and week ( $PE_0$ ) was  
 187 calculated by  $PE_0 = MK_{pe} M'$  , where matrix  $K_{pe}$  contains the estimated covariance  
 188 function describing the permanent environmental variance components for the random  
 189 regression coefficients across three traits, estimated with DMU using Model [1]. The residual  
 190 variance matrix across traits ( $E_0$ ) is not with a random regression setting, and is a  $3 \times 3$  matrix  
 191 containing residual (co)variances across three traits.

192

193 ***Derivation of RFI.*** In the next step,  $G_0$  was partitioned into 4 blocks to derive RFI:

$$194 \quad G_0 = \begin{bmatrix} G_{11} & G_{12} \\ G_{21} & G_{22} \end{bmatrix}, \quad [3]$$

195 where  $G_0$  is the genetic (co)variance matrix across weeks and across three traits (DMI, ECM,  
 196 and MBW);  $G_{11}$  corresponds to the (co)variance matrix for DMI across 44 lactation weeks;  
 197  $G_{22}$  corresponds to (co)variance matrix for two energy sink traits (ECM and MBW), which  
 198 contains the (co)variance matrix for ECM across 44 weeks, the (co)variance matrix for MBW  
 199 across 44 weeks, and the covariance matrix between ECM and MBW across 44 lactation

200 weeks;  $G_{12}$  corresponds to the covariance matrix between DMI and energy sink traits (ECM  
 201 and MBW) across 44 weeks; and  $G_{21}$  is the transpose of  $G_{12}$ . Likewise, the same partitioning  
 202 was also applied to the permanent environmental variance matrix ( $PE_0$ ) and the residual  
 203 variance matrix ( $E_0$ ).

204  
 205 The genetic (co)variance matrix for genetic RFI ( $G_{1|2}$ ) was then derived as the genetic  
 206 (co)variances of DMI conditional on energy sink traits (ECM and MBW), as shown in the  
 207 following formula (Strathe et al., 2014):

$$208 \quad G_{1|2} = G_{11} - G_{12} G_{22}^{-1} G_{21}, \quad [4]$$

209 where  $G_{1|2}$  is the genetic (co)variance matrix for genetic RFI across 44 lactation weeks;  $G_{11}$ ,  
 210  $G_{22}$ ,  $G_{12}$ ,  $G_{21}$  are the decomposed genetic (co)variance matrices from  $G_0$  as described before  
 211 in [3]. In this way, the genetic (co)variance matrix for genetic RFI ( $G_{1|2}$ ) was derived as the  
 212 conditional (co)variance of DMI given the energy sink traits (ECM and MBW). The same  
 213 method was applied to obtain the permanent environmental variance for genetic RFI across 44  
 214 weeks ( $PE_{1|2}$ ) and for the residual variance for genetic RFI ( $E_{1|2}$ ).

215 Based on the variance components estimates for genetic RFI across lactation weeks as  
 216 shown above, the heritability for genetic RFI was calculated for each lactation week. The  
 217 proportion of genetic variance of RFI out of DMI was calculated through computing the ratio  
 218 of genetic variance of RFI to genetic variance of DMI. The genetic correlations for genetic  
 219 RFI across 44 lactation weeks were also computed. SE of parameters are mathematically  
 220 intricate to calculate and were thus not available.

221  
 222 **Calculate EBV for genetic RFI.** The EBV for genetic RFI were calculated for all  
 223 animals in each lactation week by the following formula [5] (Strathe et al., 2014). Afterwards,

224 the overall EBV of the entire lactation for animal  $i$  was calculated as the sum of the EBVs of  
 225 each week for animal  $i$ .

$$226 \quad a_{im}^{RFI} = a_{im}^{DMI} - b_{1m} * a_{im}^{ECM} - b_{2m} * a_{im}^{MBW}, \quad [5]$$

227 where  $a_{im}^{RFI}$ ,  $a_{im}^{DMI}$ ,  $a_{im}^{ECM}$ , and  $a_{im}^{MBW}$  are the EBVs for  $i$ th animal for RFI, DMI, ECM, and  
 228 MBW in lactation week  $m$ , respectively;  $a_{im}^{DMI}$ ,  $a_{im}^{ECM}$ , and  $a_{im}^{MBW}$  were calculated as

$$229 \quad \sum_{n=0}^2 a_{ni} \Phi_{nm}$$

for  $i$ th animal in week  $m$ , where  $\hat{a}_{ni}$  are the solutions for the additive genetic

230 effect from the random regression model [1].  $b_{1m}$  is the ratio of genetic covariance between

231 DMI and ECM to the genetic variance of ECM (i.e.,  $b_1 = \text{cov}(\text{DMI}, \text{ECM}) / \text{var}(\text{ECM})$ ) for

232 lactation week  $m$ ;  $b_{2m}$  is the ratio of genetic covariance between DMI and MBW to the

233 genetic variance of MBW (i.e.,  $b_2 = \text{cov}(\text{DMI}, \text{MBW}) / \text{var}(\text{MBW})$ ) for lactation week  $m$ ;  $b_{1m}$

234 and  $b_{2m}$  were derived from the  $G_0$  matrix (i.e., the genetic (co)variance matrix across traits and

235 weeks).

236

### 237 **Phenotypic RFI**

238 The second way of modelling RFI, denoted as “phenotypic RFI” in this study, was

239 based on a one-step RFI model (Lu et al., 2015; Tempelman et al., 2015; Li et al., 2017). In

240 the one-step RFI model, DMI was phenotypically adjusted for energy sink traits by partial

241 linear regressions of DMI on energy sink traits. In order to take account of the potential

242 change in the partial regression coefficients of DMI on energy sinks at different lactation

243 stages, 11 lactation periods were defined during 44 lactation weeks (every 4 consecutive

244 weeks of the 44 lactation weeks was set as one period). Period-specific partial regressions of

245 DMI on ECM and on MBW were considered in the random regression analysis for

246 phenotypic RFI (Li et al., 2017):

247

248

249  $DMI_{ijklms} = u + b_{1s} * ECM + b_{2s} * MBW + Herd-Trial_j + CA_k + YS\_Country_l + Lactwk_m$

250  $+ \sum_{n=0}^2 a_{ni} \Phi_n + \sum_{n=0}^2 pe_{ni} \Phi_n + e_{ijklms}, \quad [6]$

251

252 where  $DMI_{ijklms}$  is the weekly records of DMI in lactation week (Lactwk) m for cow i, where

253 cow i is in calving age (CA) k, in the year-season of recording and country (YS\_Country) l,

254 and from Herd-Trial j.  $b_{1s}$  is the period-specific partial regression coefficient of DMI on ECM

255 in lactation period s (s = 1 to 11);  $b_{2s}$  is the period-specific partial regression coefficient of

256 DMI on MBW in lactation period s (s = 1 to 11). Herd-Trial<sub>j</sub> is the fixed effect of herd and

257 trial in which the cows were involved (j = 1 to 37), where the trials were herd-specific;  $CA_k$  is

258 the fixed effect of calving age in the month of cows' first calving (k = 24 to 38);  $YS\_Country_l$

259 is the fixed effect of year-season of recording for each country, where the year of recording is

260 from 1991 to 2016 and 4 seasons were defined (March to May, June to August, September to

261 November, and December to February, for two countries (Denmark and Sweden) (l = 1 to

262 117); and  $Lactwk_m$  accounts for the fixed effect of lactation week on DMI (m = 1 to 44).

263 Random regression terms were used to describe the cows' additive genetic effect and

264 permanent environmental effect. The  $a_{ni}$  and  $pe_{ni}$  are the n<sup>th</sup> regression coefficients of the

265 Legendre polynomial for the random additive genetic effect and the random permanent

266 environmental effect, respectively, for cow i;  $\Phi_n$  is the n<sup>th</sup> covariable of the second-order

267 Legendre polynomial on weeks of lactation.  $e_{ijklms}$  is the random residual, whose variance was

268 assumed constant across lactation.

269

270 The variance components for phenotypic RFI were estimated by an average

271 information-restricted maximum likelihood algorithm (Jensen et al., 1997) implemented in

272 DMU (Madsen and Jensen, 2013). Variance components and heritability for phenotypic RFI

273 were calculated for each week, and the genetic correlations for RFI across lactation were also

274 computed. EBV for phenotypic RFI for each individual in each lactation week was obtained  
275 from  $\sum_{n=0}^2 \hat{\alpha}_{ni} \Phi_{nm}$  for animal  $i$  in week  $m$ , where  $\hat{\alpha}_{ni}$  are the solutions for the genetic effect  
276 from the random regression model [6]. The overall EBV for animal  $i$  in the entire lactation  
277 was calculated as the sum of the EBVs of each week for animal  $i$ .

278

### 279 **Comparison between genetic RFI and phenotypic RFI**

280 The variance components and genetic parameters were compared between genetic RFI  
281 and phenotypic RFI across lactation. When it comes to comparing EBVs between two RFI  
282 definitions, firstly, animals' overall EBVs (EBV of the entire lactation) from genetic RFI were  
283 correlated with the animals' overall EBVs from phenotypic RFI, among all the animals with  
284 phenotypes. The correlations for EBVs between two RFI definitions were also computed  
285 across EBV of each lactation week. Secondly, among all the animals with phenotypes, the  
286 10% of animals that had the lowest overall EBVs for RFI (i.e., the most desirable animals)  
287 were selected from genetic RFI and phenotypic RFI, respectively. The selected animals from  
288 genetic RFI and phenotypic RFI were compared to see how many animals among the selected  
289 animals were the same between the two RFI definitions. Accordingly, the 10% of animals that  
290 had the highest EBVs for RFI (i.e., inefficient animals) were also selected from genetic RFI  
291 and phenotypic RFI, respectively. The two groups of animals (animals with lowest EBV, and  
292 animals with highest EBV) were compared for their average DMI, ECM, BW, and the ratio of  
293 ECM to DMI (ECM/DMI) across lactation.

294

## 295 **RESULTS AND DISCUSSION**

### 296 **Variance components and heritability for RFI**

297 The genetic variance of phenotypic RFI was higher than that of genetic RFI (Figure 1).  
298 In phenotypic RFI, DMI was only phenotypically corrected for ECM and MBW, and the



299 resulting RFI was still genetically correlated with ECM and MBW. In contrast, in genetic RFI,  
300 RFI was derived as DMI conditional on ECM and MBW, where DMI was genetically  
301 adjusted for the (co)variances of ECM and MBW. The resulting RFI was genetically  
302 uncorrelated with ECM and MBW, making genetic RFI independent from major energy sink  
303 traits (milk energy and MBW). The higher estimate of genetic variance for phenotypic RFI  
304 could be partly attributed to the genetic covariance between DMI and the energy sink traits  
305 (ECM and MBW) that was not removed in phenotypic RFI, but was adjusted for in genetic  
306 RFI.

307         Based on our results, the genetic variance for RFI was higher at the beginning of  
308 lactation compared to later lactation stages in both two RFI definitions, which is probably due  
309 to ignoring the change of BW ( $\Delta$ BW) in both RFI models. In early lactation changes in BW  
310 are common for lactating cows (Li et al., 2017). Cows' changes in BW have genetic  
311 associations with feed intake, so that  $\Delta$ BW could explain part of the variance for feed intake  
312 (Li et al., 2017). Variance components estimates for RFI could be affected by adjusting for  
313  $\Delta$ BW in RFI models. As in Lu et al, we tried but failed to include  $\Delta$ BW in the modelling for  
314 genetic RFI due to the convergence problem in the multivariate analyses for genetic RFI.  
315 Accordingly, we did not apply  $\Delta$ BW to phenotypic RFI in order to compare the two RFI  
316 definitions in the same level. In Li et al. (2017), phenotypic RFI was derived with the  
317 adjustment of ECM, MBW, and also  $\Delta$ BW in the model, positive partial regression  
318 coefficients of DMI on  $\Delta$ BW were seen over lactation. The genetic variance for phenotypic  
319 RFI considering  $\Delta$ BW in Li et al. (2017) was lower than the genetic variance for the  
320 phenotypic RFI in this study where  $\Delta$ BW was not modeled. In future investigation for RFI,  
321  $\Delta$ BW would be recommended to be included in RFI model as one important energy sink for  
322 feed intake and also as a factor to reduce the risk of selecting for negative energy balance of  
323 the animals.

324 The permanent environmental variance for genetic RFI was lower compared to that for  
325 phenotypic RFI, and the residual variance for genetic RFI was higher than that for phenotypic  
326 RFI (Figure 1). Lu et al. (2015) used very similar modelling methods to derive genetic RFI  
327 and phenotypic RFI to what we used in this study but without the random regression setting.  
328 They also found lower genetic variance and lower permanent environmental variance for  
329 genetic RFI compared to those for phenotypic RFI, but they found equal residual variances  
330 between two RFI definitions (Lu et al., 2015).

331 The heritability for genetic RFI and for phenotypic RFI showed different patterns across  
332 lactation (Figure 2). The mean heritability across lactation was 0.11 for genetic RFI, and 0.35  
333 for phenotypic RFI. The lower heritability for genetic RFI compared to that for phenotypic  
334 RFI was due to the lower genetic variance and higher residual variance for genetic RFI. Our  
335 heritability estimate for genetic RFI was close to the estimate of 0.14 found by Lu et al.  
336 (2015). The proportion of genetic variance for DMI explained by the genetic variance of RFI  
337 was 17% on average across 44 lactation weeks (Figure 3). The proportion was highest at the  
338 beginning of lactation (64% in week 1) and was lowest in week 32 (1%). In early lactation,  
339 the high proportion of the genetic variance for DMI explained by RFI was partly due to the  
340 fact that  $\Delta$ BW was not modeled in the multivariate analyses for RFI, in contrast to the  
341 previous work (Li et al., 2017).

342

### 343 **Genetic correlations for RFI across lactation**

344 For genetic RFI, the genetic correlations for RFI ranged from -0.24 to 1 across lactation,  
345 where genetic RFI in early, middle, and late lactation stages were shown to be genetically  
346 different from each other (Figure 4A). The non-unity genetic correlations for genetic RFI  
347 across lactation suggest a changing genetic background of RFI efficiency in dairy cattle. For  
348 phenotypic RFI, the genetic correlation for RFI across lactation ranged from 0.01 to 1, where

349 RFI in early lactation was genetically not the same trait as RFI in middle and late lactation  
350 (Figure 4B), in agreement with Li et al. (2017) where  $\Delta BW$  was considered in the RFI model.  
351 Generally, genetic RFI and phenotypic RFI tended to show different patterns of genetic  
352 correlations across lactation, but in both cases RFI in early lactation is genetically different  
353 from RFI in later lactation stages.

354

### 355 **Correlations between cows' EBVs from genetic RFI and EBVs from phenotypic RFI**

356 For all the animals with phenotype information, summing up every animal's EBVs from  
357 44 weeks to obtain the animal's overall EBV of the entire lactation, the Pearson correlation  
358 between animals' overall EBV from two RFI definitions was 0.47. If we further looked at the  
359 EBV correlations by each lactation week, the EBV correlations between genetic RFI and  
360 phenotypic RFI ranged from -0.18 to 0.80 across 44 lactation weeks (Figure 5). The EBV  
361 correlations between two RFI definitions for the same week were 0.55 on average of 44  
362 weeks. In general, the observed EBVs from two definitions of RFIs were moderately  
363 correlated, indicating different rankings of the efficient animals by using different RFI  
364 definitions for selection.

365

### 366 **Comparison between Animals with Highest and Lowest EBV for RFI**

367 The 10% of the animals with the lowest (i.e., most desirable) EBV for RFI were  
368 selected from genetic RFI and phenotypic RFI, respectively, and 37% of these selected  
369 animals were the same between genetic RFI and phenotypic RFI. From this result, it is quite  
370 interesting to see that two RFI definitions tended to offer somewhat different rankings of RFI  
371 efficient animals. If we further compare the average DMI, ECM, BW, and gross efficiency  
372 (ECM/DMI) between the animals with the lowest EBVs and the animals with the highest  
373 EBVs for RFI, genetic RFI and phenotypic RFI tended to show more differences in the

374 direction of selection for RFI efficiency (Figure 6). Specifically, when phenotypic RFI was  
375 used for selection, animals with the lowest EBVs for RFI had lower DMI, lower ECM, and  
376 higher BW compared to animals with the highest EBVs (Figure 6A, 6B, 6C). When genetic  
377 RFI was used for selection, cows with the lowest EBVs for RFI had similar DMI (or slightly  
378 lower in some weeks), higher BW, and higher ECM compared to cows with the highest EBVs  
379 (Figure 6A, 6B, 6C). Comparing the gross efficiency (i.e., kg ECM per kg DMI), when  
380 genetic RFI was used, cows with low EBVs for RFI had a slightly higher gross efficiency than  
381 cows with high EBVs (Figure 7). However, when the selection was based on phenotypic RFI,  
382 cows with low EBVs tended to have lower gross efficiency than cows with high EBVs for  
383 RFI.

384       There are at least three implications we could get from the comparison of DMI, ECM,  
385 and BW between the two animal groups (high EBV group and low EBV group). Firstly,  
386 selection for FE based on genetic RFI and phenotypic RFI might lead to different directions of  
387 selection for FE. Secondly, the current comparison was based on the difference in the  
388 phenotypic level of DMI, ECM, and BW between the two animal groups. It would be  
389 interesting to see if the difference in phenotypic performances between the two groups could  
390 still be seen among the offspring of these animals. Last but not the least, cows with the lowest  
391 EBVs for RFI (which can be considered as the efficient cows) tended to have higher BW  
392 compared to the inefficient cows, no matter which RFI definition (genetic RFI or phenotypic  
393 RFI) was applied. Higher BW of cows could indicate lower FE due to the high energy  
394 requirement for body maintenance. Therefore, BW could be needed to put together with RFI  
395 in the selection index if RFI is applied to the selection of FE in dairy cattle.

396

397

## CONCLUSIONS

398 RFI derived from multivariate analyses (denoted as genetic RFI in this study) was  
399 genetically uncorrelated with energy sink traits (ECM and MBW). The two RFI definitions,  
400 genetic RFI and phenotypic RFI, showed differences in variance component estimates,  
401 genetic parameters across lactation, and also in the selection for the RFI efficient animals. On  
402 one hand, phenotypic RFI has higher genetic variance and heritability compared with genetic  
403 RFI. On the other hand, genetic RFI is genetically independent from milk production and BW.  
404 Defining RFI as genetically independent of production traits leads to easily interpretable  
405 breeding values for FE in the selection index. For both RFI definitions, RFI in early lactation  
406 was not the same trait as RFI in middle and late lactation. When it comes to selection, the  
407 animals with the lowest (i.e., most desirable) EBVs for genetic RFI and for phenotypic RFI  
408 were different from each other, indicating different rankings of efficient animals when using  
409 genetic RFI and phenotypic RFI. Selection for FE based on genetic RFI and phenotypic RFI  
410 could also lead to different directions of selection for efficient cows.

411

412

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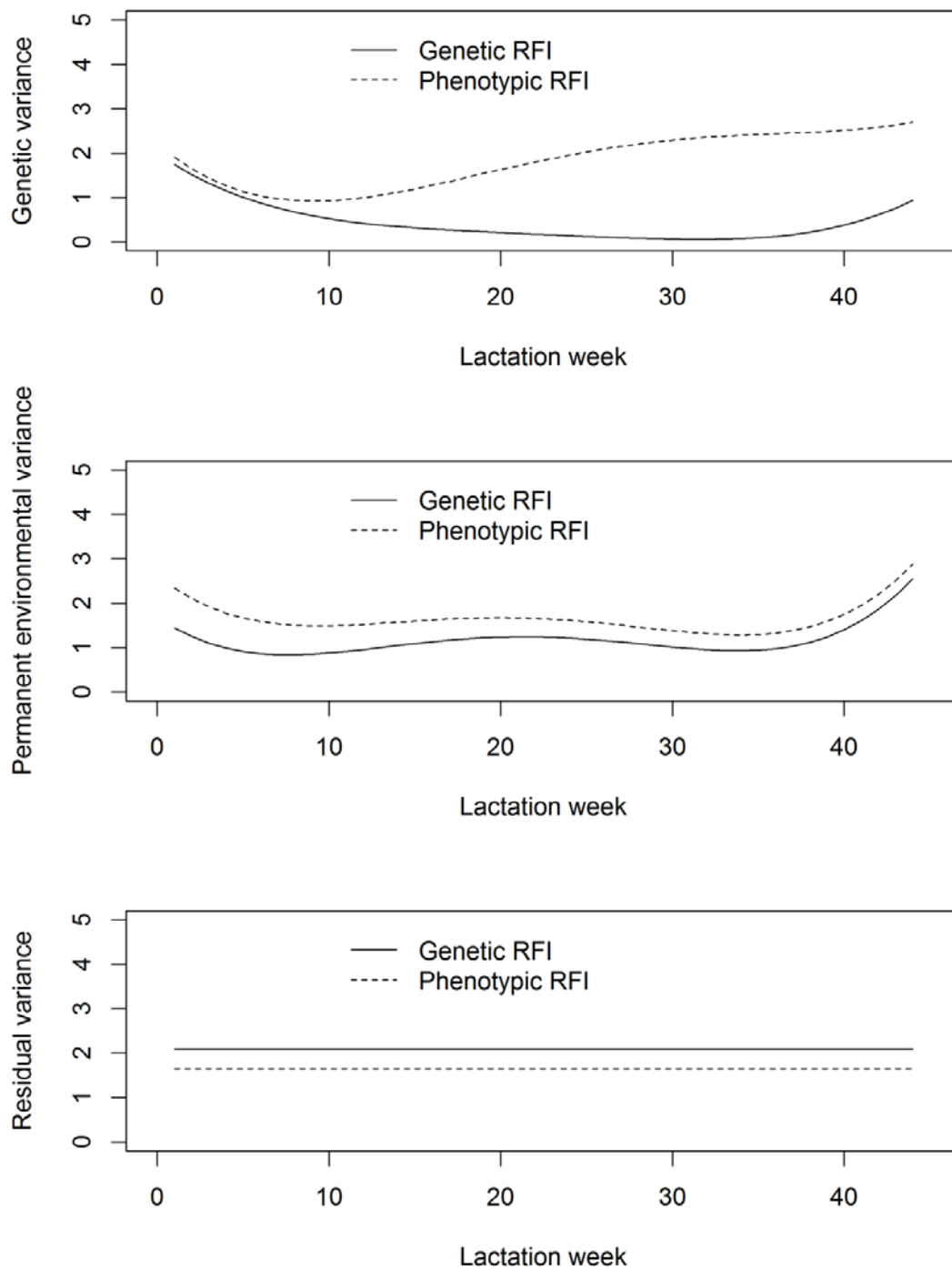
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523

524 Table 1. Descriptive statistics of dry matter intake (DMI, kg/d), energy-corrected milk (ECM,  
525 kg/d), and body weight (BW, kg) for 963 primiparous Holstein cows in 44 lactation weeks

	Mean	SD	Min	Max
DMI (kg/d)	19.5	3.3	1.3	40.9
ECM (kg/d)	29.1	6.1	1.1	57.9
BW (kg)	602.2	63.4	306.0	869.0

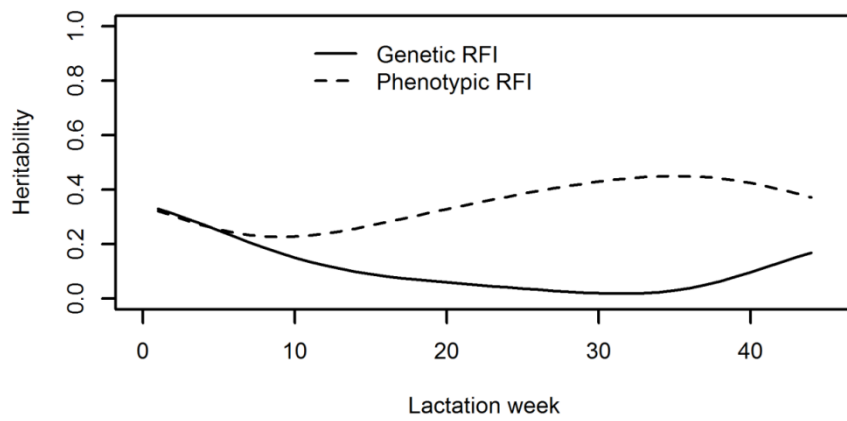
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529 Figure 1. Genetic variances, permanent environmental variances, and residual variances  
 530 across 44 lactation weeks for two definitions of residual feed intake (RFI) in Holstein dairy  
 531 cattle. The estimates for genetic RFI are in solid lines, and the estimates for phenotypic RFI  
 532 are in dashed lines.

533

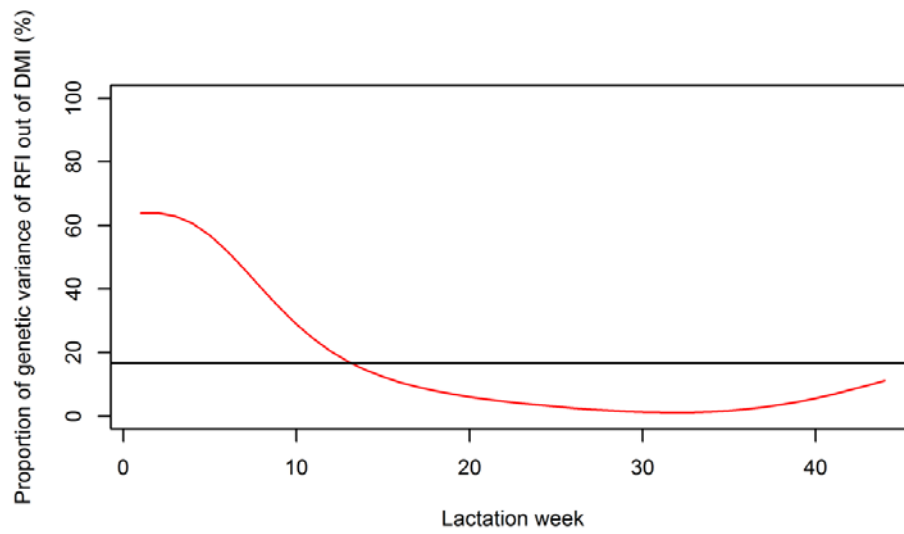


534

535 Figure 2. Heritability estimates across 44 lactation weeks for two definitions of residual feed  
536 intake (RFI) in Holstein dairy cattle. The estimates for genetic RFI are in solid line, and the  
537 estimates for phenotypic RFI are in dashed line.

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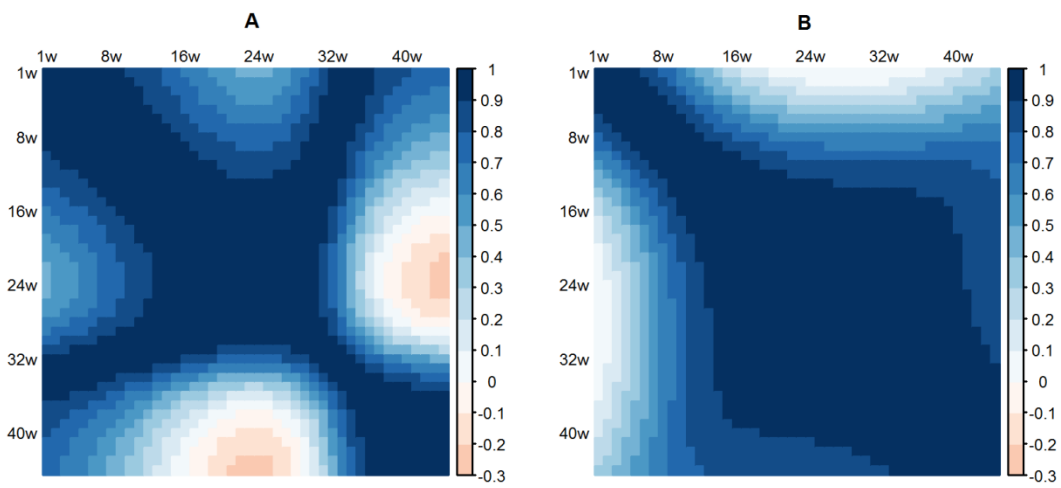
541 Figure 3. Proportion of genetic variance for DMI explained by the genetic variance for RFI in

542 the multivariate analyses for RFI (i.e., genetic RFI) across lactation weeks in Holstein dairy

543 cattle.

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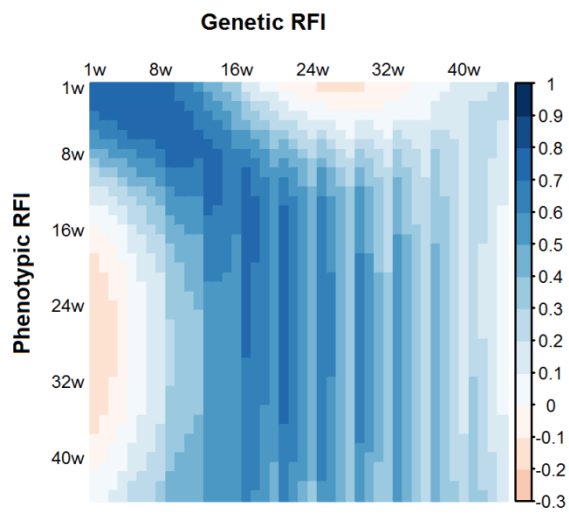


546

547 Figure 4. Genetic correlations across 44 lactation weeks for two definitions of residual feed

548 intake (RFI): (A) genetic RFI, (B) phenotypic RFI.

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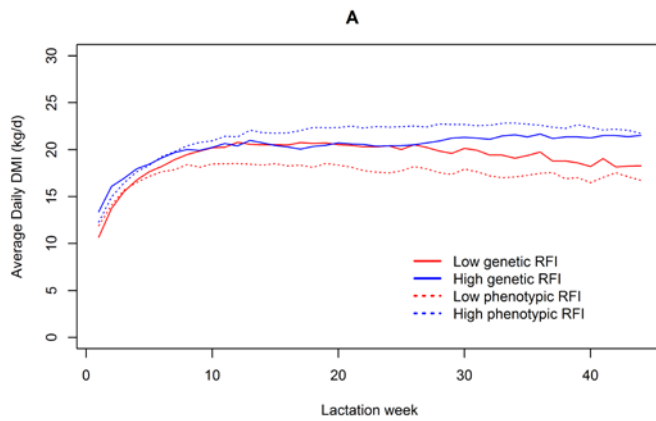


550

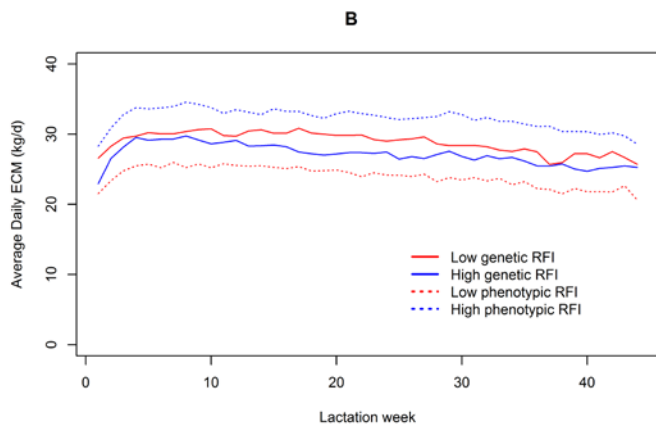
551 Figure 5. The correlations between animals' EBVs calculated from genetic RFI and those  
552 calculated from phenotypic RFI across 44 lactation weeks in Holstein dairy cattle.

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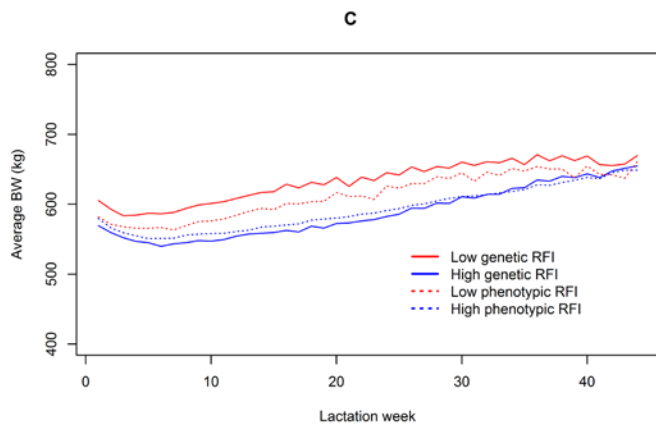




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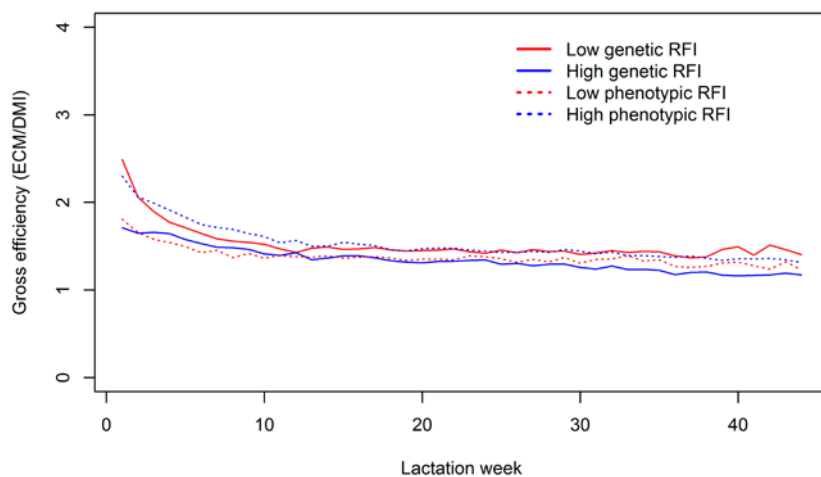


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556

557 Figure 6. (A) Average daily dry matter intake (DMI, kg/d), (B) average daily energy-  
 558 corrected milk (ECM, kg/d), and (C) average body weight (BW, kg) across 44 lactation weeks  
 559 for (1) the 10% of cows with the lowest EBVs for genetic RFI, as “Low genetic RFI”, (2) the  
 560 10% of cows with the highest EBVs for genetic RFI, as “High genetic RFI”, (3) the 10% of  
 561 cows with the lowest EBVs for phenotypic RFI, as “Low phenotypic RFI”, (4) the 10% of  
 562 cows with the highest EBVs for phenotypic RFI, as “High phenotypic RFI”.



563

564 Figure 7. Gross efficiency (kg ECM/kg DMI) across 44 lactation weeks for (1) the 10% of  
 565 cows with the lowest EBVs for genetic RFI, as “Low genetic RFI”, (2) the 10% of cows with  
 566 the highest EBVs for genetic RFI, as “High genetic RFI”, (3) the 10% of cows with the lowest  
 567 EBVs for phenotypic RFI, as “Low phenotypic RFI”, (4) the 10% of cows with the highest  
 568 EBVs for phenotypic RFI, as “High phenotypic RFI”.