

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

**Bingjie Li**

*Faculty of Veterinary Medicine and Animal Science  
Department of Animal Breeding and Genetics  
Uppsala*

*and*

*Centre for Quantitative Genetics and Genomics  
Department of Molecular Biology and Genetics  
Aarhus University, Tjele, Denmark*

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## Abstract

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

In Papers I–IV, we discuss two FE traits, dry matter intake (DMI) and residual feed intake (RFI), to investigate the genetic properties of these traits across lactation. In Papers I and II, we study genetic parameters for DMI, energy-corrected milk (ECM), and body weight (BW) across lactation for Holstein, Nordic Red (RDC), and Jersey cows. Further, in Paper II, we study the genetic heterogeneity of DMI, ECM, and BW across lactation stages and genetic correlations among these traits by random regression models. In Papers III and IV, we focus on alternative modelling methods for RFI. In Paper III, we investigate the influence of lactation stages in modelling RFI, and in Paper IV, we employ multivariate analyses as a novel way to derive RFI of dairy cattle.

We found moderate heritability for DMI in Holstein, RDC, and Jersey cows. The heritability for DMI was in a similar range as that for ECM and was lower than that for BW. Further, we found that DMI has a positive genetic correlation with ECM and BW across lactation stages. 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 yielded different rankings of animals for RFI efficiency. The genetic variance and heritability for RFI were both lower than those for DMI. Genetically, DMI or RFI were not the same across lactation stages. Thus, the genetic heterogeneity for DMI and RFI across lactation stages should be carefully considered in the recording and selection of FE in dairy cattle.

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

*Author's address:* Bingjie Li, SLU, Department of Animal Breeding and Genetics, P.O. Box 7023, 750 07 Uppsala, Sweden

## Genetiska egenskaper för fodereffektivitet och relaterade egenskaper hos mjölkkor

### Sammanfattning

Fodret utgör den största andelen av driftskostnaderna inom mjölkproduktionen. Förbättring av fodereffektiviteten (FE) förväntas öka lönsamheten för mjölkproducenterna och minska klimat- och miljöbelastningen av mjölkproduktionen. Syftet med avhandlingen var att studera de genetiska parametrarna för olika FE-definitioner och FE-relaterade egenskaper hos flera olika mjölkkoraser för att undersöka möjligheten att inkludera FE i nordisk mjölkkoavel.

I artiklarna I-IV undersöktes den genetiska variationen över laktationen och över raser för två viktiga FE-egenskaper, torrfoderintag (DMI) och residualt foderintag (RFI). I artikel I och II blev genetiska parametrar för DMI, energikorrigerad mjölk (ECM) och kroppsvikt (BW) över laktationen undersökt för Holstein, Nordisk Röda (RDC) och Jerseykor. Den genetiska heterogeniteten för DMI, ECM och BW över laktationen och de genetiska korrelationerna mellan dessa egenskaper studerades med hjälp av slumpmässiga regressionsmodeller i artikel II. Artikel III och artikel IV fokuserade på alternativa statistiska modeller för RFI. I artikel III undersöktes inflytandet av olika laktationsstadier på varianskomponenterna för RFI. I artikel IV användes multivariata analyser som ett nytt sätt att ta fram RFI hos mjölkkor.

Vi fann moderat ärftlighet för DMI hos Holstein, RDC och Jerseykor. Arvbarheten för DMI var i liknande storleksordning som för ECM och var lägre än för BW. DMI var positivt genetiskt korrelerad till ECM och BW över laktationsstadiet. Kor av olika raser visade generellt ett liknande mönster av genetiska parametrar för DMI. Olika modelleringsstrategier för RFI påverkade RFI's genetiska egenskaper och gav olika rangordning av korna i förhållande till effektivitet. Den genetiska variansen och arvbarheten för RFI var lägre än för DMI. Genetiskt var DMI eller RFI inte samma egenskap i olika laktationsstadier. Man bör ta hänsyn till den genetiska heterogeniteten för DMI och RFI över laktationen vid avelsvärdering för FE hos mjölkkor.

*Nyckelord: fodereffektivitet, mjölkkor, genetisk heterogenitet, genetiska parametrar, slumpmässig regressionsmodell*

*Author's address: Bingjie Li, SLU, Department of Animal Breeding and Genetics, P.O. Box 7023, 750 07 Uppsala, Sweden*

## 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 II 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 II. Artikel III og artikel IV fokuserede på alternative statistiske modeller for RFI. I artikel III 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 modelleringstrategier 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

*Author's address:* Bingjie Li, SLU, Department of Animal Breeding and Genetics, P.O. Box 7023, 750 07 Uppsala, Sweden

# Dedication

To everyone who has helped me on my way to growing up, particularly 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. *Journal of Dairy Science*, Article in press.
- 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 across lactation in Holstein dairy cattle (manuscript).

Papers I–III have been reproduced with the permission of the publishers.

\* Corresponding author.

Bingjie Li made the following contributions to the papers included in this thesis:

- 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 in 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) in dairy cattle has been of major interest for dairy farmers and researchers for decades. Increasing FE in dairy cattle must be achieved through 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 role in improving FE for the dairy cattle population and also for the subsequent generations of dairy cows. In this thesis, we focus on the genetic aspects of improving FE in 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 Holstein and Jersey cows (Smith and Rice, 1934). After the 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 FE has improved because of the dilution of 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, thereby making it possible to launch genetic analyses of FE with larger data sets. Recent studies on FE in dairy cattle encompass several important topics, including genetic variation, genetic parameter estimation, genomic evaluation, and genome-wide association 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 adequately define FE in dairy cattle (Lu et al., 2015; Pryce et al., 2015; Hurley et al., 2017; Li et al., 2017). However, the question of which trait should be used to adequately represent or measure FE in practice remains a controversial one.

Another challenge is to obtain sufficient genetic information on FE in non-Holstein populations. Recent genetic studies on FE have mostly focused on Holstein cows (Berry et al., 2014; de Haas et al., 2015). Breeds other than Holstein—for example, Jersey and Nordic Red (RDC)—are economically important breeds, both globally and locally, and may offer important genetic information with respect to FE. Studies on 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 entirely relevant to modern high-genetic-merit dairy populations (Liinamo, Mäntysaari, and Mäntysaari, 2012). In-depth knowledge of the genetic variation for FE-related traits in multiple dairy breeds would benefit diverse selection purposes in dairy production, for example, multi-breed genetic evaluation.

With regard to the importance, opportunities, and challenges related to improving FE in dairy cattle breeding, international collaborations have established 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 FE in dairy cattle was established in 2013 with the aim of investigating the genetic variation for FE in dairy cattle and assessing the possibility of including FE in the Nordic genetic evaluation of dairy cattle.

## 1.1 Importance of feed efficiency in dairy breeding

FE has implications for farm profitability and the environment. In recent years, the subject of FE is on the tip of every dairy producer's tongue, since feed accounts for the largest proportion 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 dairy cattle is also expected to help lower methane emissions (de Haas et al., 2011). Methane (CH<sub>4</sub>) contributes to global warming, as it is one of the most important greenhouse gases (GHGs) (Knapp et al., 2014). Thus, improving FE in dairy production could have implications for mitigation of GHGs (Wall, Simm, and Moran, 2010).

## 1.2 Definitions of feed efficiency in dairy cattle

FE 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 increased 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 maintained at a relatively high level and body reserves are gradually restored (Mao et al., 2004; Vallimont et al., 2010). Therefore, during lactation cycles, the complexity of metabolic changes in dairy cows must be considered in defining the FE of dairy cattle.

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

### 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 (DMI), feed energy intake, and possibly a form of feed costs. Feed intake has been proposed as an FE candidate trait in the breeding goal (Veerkamp et al., 2014). Ideally, we would like to select efficient animals that have lower feed intake than inefficient animals, for a certain level of production and a certain cow size as well as without sacrificing the fertility and health of the efficient animals. Currently, only 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 of feed intake.

### 1.2.2 Gross efficiency

In gross efficiency, a cow's efficiency is calculated from the ratio of milk output to feed 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 animals that are able to efficiently convert feed nutrients into milk production. Defining milk outputs and intake inputs has led to the development of several definitions of gross efficiency. Milk outputs can be defined as milk yields, milk energy, and milk fat or protein yields, or can be directly defined as a certain form of milk income. Feed inputs can be defined as the mass of DMI, feed energy intake, and possibly a form of feed costs. There are several limitations of using gross efficiency as an FE trait in dairy cattle breeding; these limitations 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 pigs, chicken, beef cattle, and dairy cattle as a 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 on the basis of the energy intake of the feed instead of DMI.

In dairy cattle, RFI can be defined in several different ways. A popular method of defining RFI in dairy cattle is based on an energy sink model, where the actual feed intake of cows is linearly regressed on their energy sinks (e.g., milk production, BW, change in 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 manner 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 the 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 stages, it is possible that the partial regression coefficients of feed intake on milk production, body maintenance, and  $\Delta$ BW could vary across lactation stages. 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 in turn 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 to account 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. Thus, it is interesting to investigate whether the partial regression coefficients of feed intake on milk production, body maintenance, and  $\Delta$ BW vary across lactation stages, and their 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 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 the genetic evaluation of dairy cattle. After eliminating the genetic correlations of RFI with milk production and BW, RFI becomes a more independent trait for 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 stages.

### 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 to range from 0.04 to 0.54 (Veerkamp and Thompson, 1999; Buttchereit et al., 2011; Berry et al., 2014). Heritability was found to vary with lactation stage, and a low genetic correlation was reported for DMI between early lactation and the remaining lactation stages (Huttmann et al., 2009; Manzanilla Pech et al., 2014; Tetens, Thaller, and Krattenmacher, 2014). Further, feed intake was found to be positively correlated with milk yield (Veerkamp, 1998; Vallimont et al., 2010; Manzanilla-Pech et al., 2016). Apart from Holstein cows, 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). Liinamo, Mäntysaari, and Mäntysaari (2012) studied RDC using 291 primiparous cows, and the heritability for DMI was estimated to range from 0.18 to 0.33 within lactation weeks 2 to 30, with large standard errors (SE) of estimates. However, 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 RFI is under genetic control (Veerkamp, 1998; Coleman et al., 2010). Heritability estimates for RFI in dairy cattle were reported to range 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 RDCs (Liinamo et al., 2015). When RFI was derived from linear regressions of DMI on milk production, metabolic body weight (MBW), and  $\Delta$ BW, RFI was reported to be positively genetically correlated 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 found to be genetically uncorrelated with milk energy and MBW (Lu et al., 2015).

Further, the heritability of gross FE was reported to range 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 was found to be higher than 0.6 (Vallimont et al., 2011; Manafiazar et al., 2015; Lidauer et al., 2018), and negative genetic correlations were reported for gross efficiency with both BW and 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 in dairy cattle breeding is of great interest globally. Due to insufficient FE data in individual countries, international collaborations have been established to conduct FE studies and combine data sets. Combined data sets across countries have 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 for introducing FE in 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 the specific breeding goals of the country.

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

The Netherlands is the second country after Australia to publish EBVs for FE in the genetic evaluation of dairy cattle (Jong et al., 2016). In the

Netherlands and Flanders, a genetic evaluation for DMI was developed using observations of 3,200 cows, of which 1,300 were genotyped (Jong et al., 2016). The EBV for DMI was based on DMI and indicator traits (milk, fat and protein yield, and BW) (Jong et al., 2016). Using information on indicator traits together with DMI, the reliability of EBV for DMI for bulls was reported to be 59% on average (Veerkamp et al., 2014).

In the US, RFI genetically adjusted for milk energy and BW is proposed as an FE candidate trait in selection, where the EBV of milk energy and EBV of BW were used to adjust RFI. The resultant 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). Approximately 4,000 US Holstein cows from research herds with RFI phenotypes were included in the national genomic evaluation for RFI (VanRaden et al., 2018); the average theoretical reliability of genomic EBV was approximately 31% for cows with phenotypes. The EBV for FE in dairy cattle has not been published yet due to low prediction reliability.

In Nordic countries, a joint data set of FE in dairy cattle has been established among Nordic countries since 2013, with the aim of investigating the genetic variation for FE in several dairy breeds in Nordic countries and assessing the possibility of including FE in Nordic dairy cattle breeding. Recently, several genetic studies have been conducted 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 is part of the joint project entitled 'Feed Utilization in Nordic Cattle (FUNC)' among the Nordic countries and the aim is to investigate the genetic properties of alternative FE definitions and the possibility of including FE in Nordic dairy cattle breeding.

## 2 Aims of the thesis

The overall aim of this thesis was to study the genetic properties of alternative FE definitions and FE-related traits in dairy cattle in order to investigate the possibility of including FE in Nordic dairy cattle breeding. More specifically, the specific aims of the thesis were to investigate the following aspects:

- Genetic parameters of DMI in Holstein, RDC, and Jersey cows across lactation stages (Papers I and II).
- Genetic relationships of DMI with milk production and BW in dairy cattle (Paper II).
- Genetic heterogeneity of DMI, energy-corrected milk (ECM), and BW across the entire lactation period in dairy cattle (Paper II).
- Genetic properties of RFI and the influence of lactation stages on estimating RFI (Papers III and IV).
- Alternative modelling strategies for RFI in dairy cattle (Papers III and IV).

### 3 Summary of Investigations

This thesis comprises 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 comprises 199,645 weekly records of DMI, ECM, and BW for 3,258 dairy cows across breeds and lactation stages. The FE data sizes were larger in Papers II and IV than those in Papers I and III, since more FE data were recorded and included over time. The studied cows came from six research herds in Denmark, Finland, and Sweden: the Danish Cattle Research Centre (DCRC, Foulum) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle) in Denmark; the previous research herd (Rehtijärvi, Jokioinen) and current research herd (Minkiö, Jokioinen) in the Natural Resources Institute in Finland; the previous research herd (Kungsängen, Uppsala) in the Swedish University of Agricultural Sciences (SLU), and the current research herds in Lövsta (Lövsta, Uppsala) and in Öjebyn (Öjebyn), SLU, 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. Further, the cows were involved in a few nutrition experiments within research herds. Previous studies provided a detailed feeding and milking information in the trials (Mäntysaari, Nousiainen, and Huhtanen, 2003; Mäntysaari and Mäntysaari, 2015; Nielsen et al., 2003; Løvendahl, Ridder, and Friggens, 2010; Løvendahl and Chagunda, 2011; O'Hara et al., 2018). Feed offered to cows and feed refusals were measured individually to calculate the feed intake per cow. The dry matter (DM) content 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. In addition, 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; O'Hara et al., 2018). Further, 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 given by Sjaunja et al. (1990):  $ECM (kg) = \text{milk yield (kg)} \times [(38.30 \times \text{fat content (g/kg)} + 24.20 \times \text{protein content (g/kg)} + 16.54 \times \text{lactose content (g/kg)} + 20.7)/3140]$ . Cows were weighted on a weekly basis in certain research herds, while 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; O'Hara et al., 2018).

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

Detailed information on the materials and methods as well as 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, RDC, and Jersey cows in different lactation periods within the first 24 lactation weeks.

#### 3.1.1 Data

Data for this study comprised 32,929 weekly DMI records from 1,656 primiparous cows (717 Holstein, 663 RDC, and 276 Jersey). The age of first calving of the cows ranged from 22 to 36 months. The pedigree information included 9,612, 12,762, and 2,810 individuals for Holstein, RDC, and Jersey,

respectively, obtained by tracing back as many generations as possible for cows with DMI records. We included weekly DMI records for the first 24 lactation weeks, and grouped them into six consecutive lactation periods of four weeks each (Table 1). The number of animals and the number of DMI observations in each period are presented in Table 1.

Table 1. *Description of the number of cows and the number of records in six consecutive lactation periods of four weeks each 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

We considered the weekly DMI from the different periods as different traits. 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 includes 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 RDC 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 RDC;  $Trial_m$  is the fixed effect of the trial where the data originated from, to adjust for the feeding difference between trials, where Holstein cows were included in 25 trials, Jersey in 15 trials, and RDC in 16 trials;  $YS\_Rec_n$  is the fixed effect of the 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 RDC);  $LacWk_p$  is the fixed effect of the lactation week within a period ( $p = 1-4$ );  $Trial_m * YS\_Rec_n$  is the fixed effect of the interaction between trial and year-season of recording;  $a_s$  is the random additive genetic effect with  $var(a) \sim N(0, A\sigma_a^2)$ , where  $\sigma_a^2$  is the additive genetic variance and  $A$  is the relationship matrix;  $p_s$  is the random permanent environmental effect with  $var(p) \sim N(0, I\sigma_p^2)$ , where  $\sigma_p^2$  is the permanent environmental variance and  $I$  is the identity matrix; and  $e_{jmm\text{psq}}$  is the random residual with  $var(e) \sim N(0, I\sigma_e^2)$ , where  $\sigma_e^2$  is the residual variance.

The fixed effects included in the repeatability animal model were tested for significance of DMI ( $P < 0.05$ ) using PROC MIXED in SAS 9.3 (SAS Institute Inc., Cary, NC), using a mixed model including these fixed effects and a random animal effect excluding the pedigree relationship. Variance components, heritability, and repeatability of DMI for each breed within each lactation period were estimated using the repeatability animal model through the restricted maximum likelihood (REML) method by ASReml 3.0 (Gilmour et al., 2009). Further, bivariate analyses were conducted 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 found to be similar among breeds (Figure 1). The DMI of cows increased after calving, until around lactation week 12, and then remained at a relatively stable level during lactation weeks 12–24. Holstein and RDC cows had similar levels of DMI at the beginning of lactation; but Holstein cows had a slightly higher DMI than RDC cows after early lactation (Figure 1). In comparison, Jersey cows had a much lower DMI than Holstein and RDC cows within the first 24 lactation weeks (Figure 1).

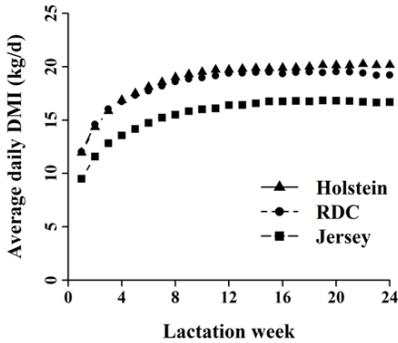


Figure 1. Average daily Dry Matter Intake (DMI, kg/d) within the first 24 lactation weeks in primiparous Holstein (HOL), Nordic Red (RDC), and Jersey (JER) cows.

### *Variance components, heritability, and repeatability of DMI*

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

Further, 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 RDC, 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 increased from approximately 0.68 in the first period of lactation to approximately 0.80 in subsequent periods (Table 3).

Table 2. Genetic variance ( $\sigma_a^2$ ) and phenotypic variance ( $\sigma_p^2$ ) (SE in subscript) for dry matter intake (DMI, kg/d) in six consecutive lactation periods of four weeks each 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 for Jersey cows, 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 ( $h^2$ ) (SE in subscript) and repeatability (SE in subscript) for dry matter intake (DMI, kg/d) in six consecutive lactation periods of four weeks each 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 for Jersey cows, 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, ECM, and BW across the entire first lactation 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. Further, 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. Weekly records of DMI, ECM, and BW were recorded for all three cow breeds 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, weekly records only from lactation weeks 1 to 32 were studied due to sparse records in subsequent lactation weeks in a few 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 conducted 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:

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

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  $j$  (Herd-Trial) $_j$ , at calving age  $k$  ( $\mathbf{CA}_k$ ), and in the year-season of calving  $l$  ( $\mathbf{YSC}_l$ );  $\mathbf{u}$  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 ( $j = 1-29$  for Holstein cows;  $j = 1-16$  for RDC cows;  $j = 1-14$  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) ( $l = 1-22$  for Holstein cows;  $l = 1-45$  for RDC cows;  $l = 1-39$  for Jersey cows); and  $\mathbf{Lactwk}_m$  accounts for the fixed effect of lactation week ( $m = 1-44$  for Holstein and Jersey cows;  $m = 1-32$  for RDC cows). Random regression terms were used to describe the cows' additive genetic effect and permanent environmental effect. Further,  $a_{np}$  and  $pe_{np}$  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  $p$ ; and  $\Phi_n$  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 four 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). For each breed, estimates of variance components were used to calculate heritability for DMI, ECM, and BW for each trait in each lactation week. Further, genetic correlations for each trait among different lactation weeks were calculated for DMI, ECM, and BW across lactation. In addition, genetic correlations among DMI, ECM, and BW in the same lactation week were estimated in Holstein and RDC cows through

bivariate analyses that applied the same random regression model as that for single trait analyses. The bivariate analyses among 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 displayed a similar pattern of phenotypic means of daily DMI over lactation, and breed difference was found 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, which is in accordance with what we found in Paper I.

The three breeds displayed a similar pattern of average daily ECM over the course of lactation (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 and lowest levels of average daily ECM over lactation, respectively.

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

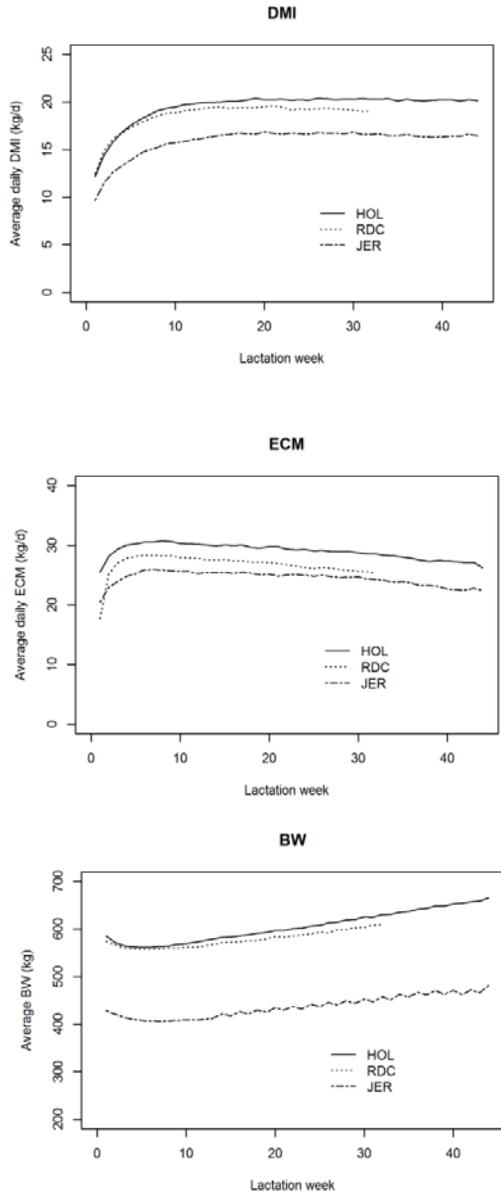


Figure 2. Phenotypic means of daily DMI (kg/d), daily ECM (kg/d), and BW (kg) for Holstein cows (HOL) in 44 lactation weeks, for Nordic Red cows (RDC) in 32 lactation weeks, and for Jersey cows (JER) in 44 lactation weeks.

### *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. In addition, the residual variance for DMI was slightly higher at the beginning of lactation than later in the lactation period. 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 initial lactation stages than at later lactation stages. The permanent environmental variance for ECM tended to increase over the entire lactation period. Further, the heritability for ECM was moderate and tended to differ among breeds (Figure 3). However, differences in heritability estimates among breeds were not statistically significant in this study due to large SE ( $P > 0.05$ ). 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 to increase over lactation (from 0.14 to 0.53), but with fairly large SE (Mean SE = 0.11).

The genetic variances for BW increased over lactation, whereas the permanent environmental variances were relatively stable. The residual variance for BW was higher in the beginning of lactation than at later lactation stages. Further, 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 the lactation period, ranging from 0.49–0.63 in Holstein cows (Mean SE = 0.08) and 0.46–0.61 in Jersey cows (Mean SE = 0.12). The heritability of BW in RDC ranged 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 breeds ( $P > 0.05$ ).

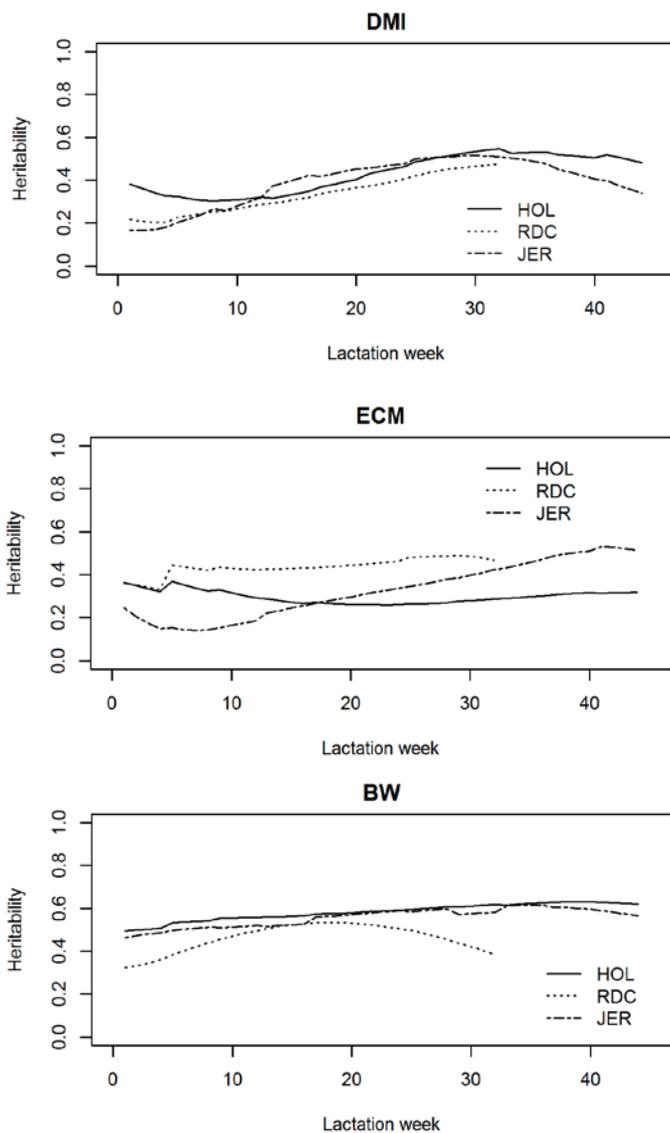


Figure 3. Heritability estimates of average daily DMI (kg/d), average daily ECM (kg/d), and average BW (kg) in Holstein cows (HOL) over 44 lactation weeks, in Nordic Red cows (RDC) over 32 lactation weeks, and in Jersey cows (JER) over 44 lactation weeks. The mean SE of heritability for DMI was 0.06,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

*Genetic correlations within DMI, ECM, and BW across lactation in the three dairy breeds*

The genetic correlations between DMI at different lactation stages were less than unity (Figure 4A), thereby indicating a genetic heterogeneity of feed intake across lactation stages. Low or even negative genetic correlations were observed for DMI between early lactation and middle or late lactation stage, with the lowest values of 0.0, -0.27, and -0.15 for Holstein, RDC, and Jersey, 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 stages 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 stages for all breeds, where BW was highly correlated over all weeks (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.

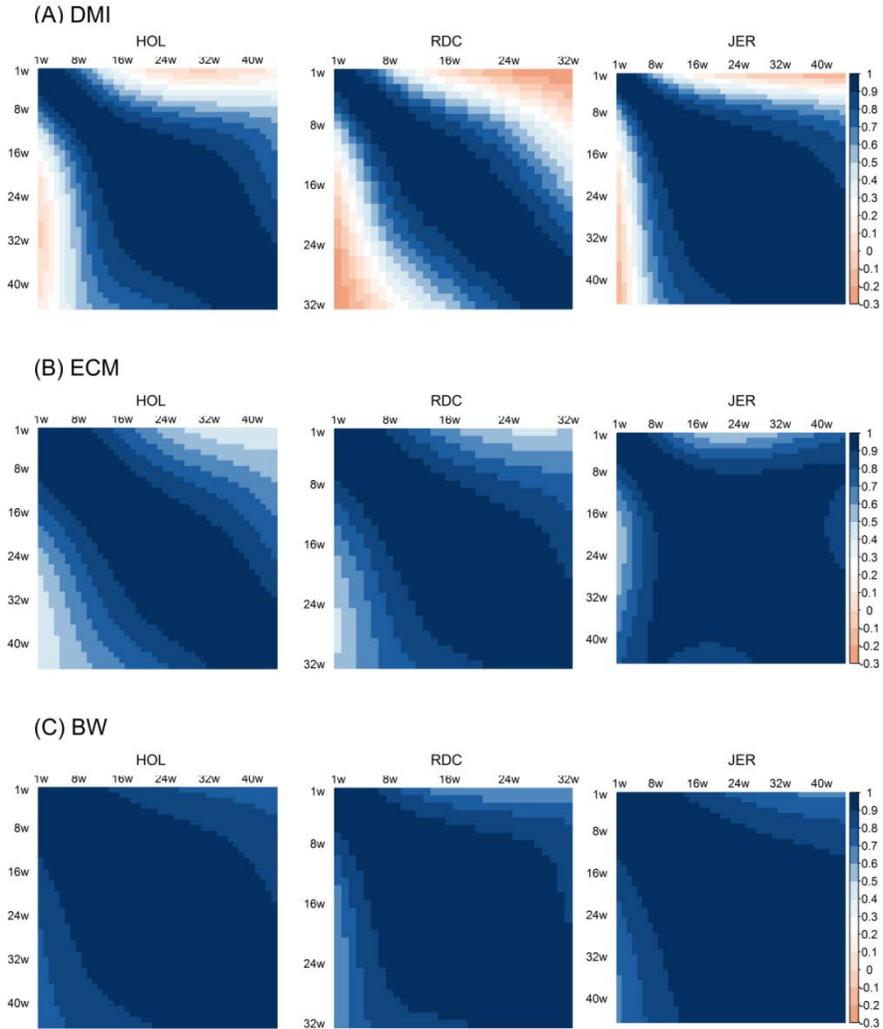


Figure 4. Genetic correlations for (A) DMI, (B) ECM, and (C) BW across 44 lactation weeks in Holstein cows (HOL), across 32 lactation weeks in Nordic Red cows (RDC), and across 44 lactation weeks in Jersey cows (JER). The mean SE of genetic correlations for DMI was 0.09, 0.12, 0.14 in HOL, RDC, and JER,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

*Genetic correlations between DMI, ECM, and BW in the same lactation week*

Genetic correlations between DMI, ECM, and BW changed over lactation (Figure 5), and the correlations changed considerably more in the early

lactation stage compared to the middle and late lactation stages. 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 initial lactation stage, 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 over lactation.

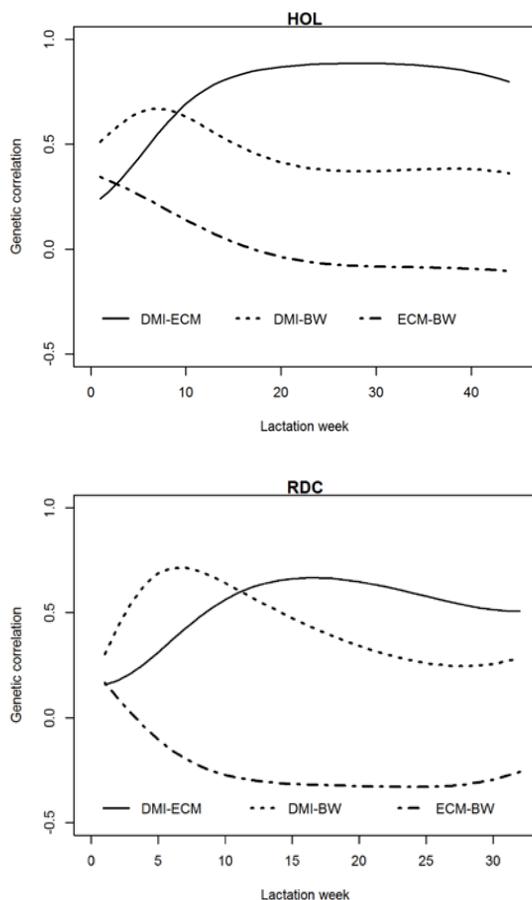


Figure 5. Genetic correlations between DMI, ECM, and BW in the same week of lactation in Holstein cows (HOL) across 44 lactation weeks and in Nordic Red cows (RDC) across 32 lactation weeks. The mean SE of genetic correlations among DMI, ECM, and BW ranged from 0.09 to 0.11 in HOL cows and from 0.12 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 paper 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 statistical analyses (Table 5). The studied cows were from the Danish Cattle Research Centre (Foulum, Denmark) and the Ammitsbøl Skovgaard research herd (Skovgaard, Vejle, Denmark). The weekly records of cows from lactation weeks 1 to 44 were included in the analyses, corresponding to the typical 305-day lactation period. The cows' age at first calving ranged 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 (MY), 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

ECM, MBW, and  $\Delta$ BW were calculated individually for each lactation week. The weekly BW per cow over 44 lactation weeks was modelled using a third-order Legendre polynomial function of lactation weeks. The  $\Delta$ BW per cow in 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 the lactation stages. Model [2] considered period-specific partial regressions of DMI on ECM, MBW, and  $\Delta$ BW for each lactation period, with the entire lactation (44 lactation weeks) divided into 11 consecutive 4-week lactation periods. The two models were identical, with the

only difference being the period-specific partial regressions of DMI on energy sinks in Model [2].

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

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

where  $\text{DMI}_{jklmp}$  and  $\text{DMI}_{ijklmp}$  are the weekly records of DMI in lactation week  $m$  for cow  $p$  in Models [1] and [2], respectively, where cow  $p$  is from Herd-Trial  $j$  (Herd-Trial $_j$ ), in calving age  $k$  ( $\text{CA}_k$ ), and in the year-season of calving  $l$  ( $\text{YS}_l$ ). 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  $i$  ( $i = 1-11$ ). Herd-Trial $_j$  is the fixed effect of the herd and trial in which the cows were involved ( $j = 1-25$ ), 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 ( $k = 24-36$ ).  $\text{YS}_l$  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) ( $l = 1-4$ ).  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week on DMI ( $m = 1-64$ ).  $a_{np}$  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 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 Models [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 one class).

Initially, we 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); 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 those in Model [2] and a random cow effect with a third-order Legendre polynomial of lactation weeks, but without using pedigree relationships. Thereafter, we conducted a genetic analysis for RFI with Models [1] and [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 Models [1] and [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 was found to change significantly across lactation (Figure 6A). In early lactation (Periods 1–2), the estimated regression coefficients of DMI on ECM were significantly lower than subsequent 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 approximately 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 Periods 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 at the end of lactation (Periods 9–11), and tended to be higher than 0.57 kg DMI per kg  $\Delta$ BW from Periods 2–8 (Figure 6C).

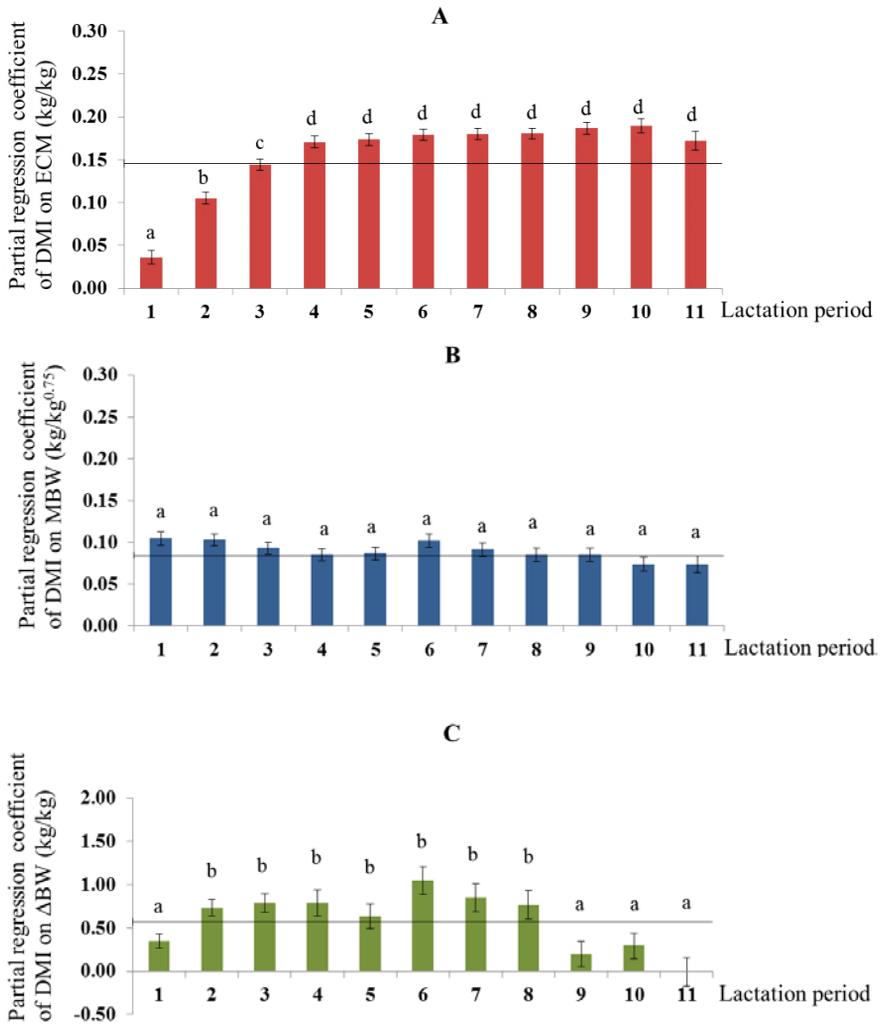


Figure 6. Partial regression coefficients of DMI on (A) Energy-corrected milk (ECM), (B) metabolic BW (MBW), and (C) change in BW ( $\Delta$ BW) in each lactation period estimated from residual feed intake (RFI) Model [2]. Error bars are SE. Bars not sharing the same letter within (A), (B), and (C) are 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 the 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 in Model [1]. The permanent environmental variances estimated in both models were similar. The residual variance in Model [2] was slightly lower than that in Model [1]. The phenotypic variance in RFI Model [2] was lower than the total variance in Model [1] for most part of the lactation. In addition, in a majority of the lactation weeks, the correlations between observed DMI and predicted DMI were higher in Model [2] than in Model [1], particularly in the first three weeks when the correlations between predicted and observed DMI were, on average, 2% higher in Model [2] than in Model [1].

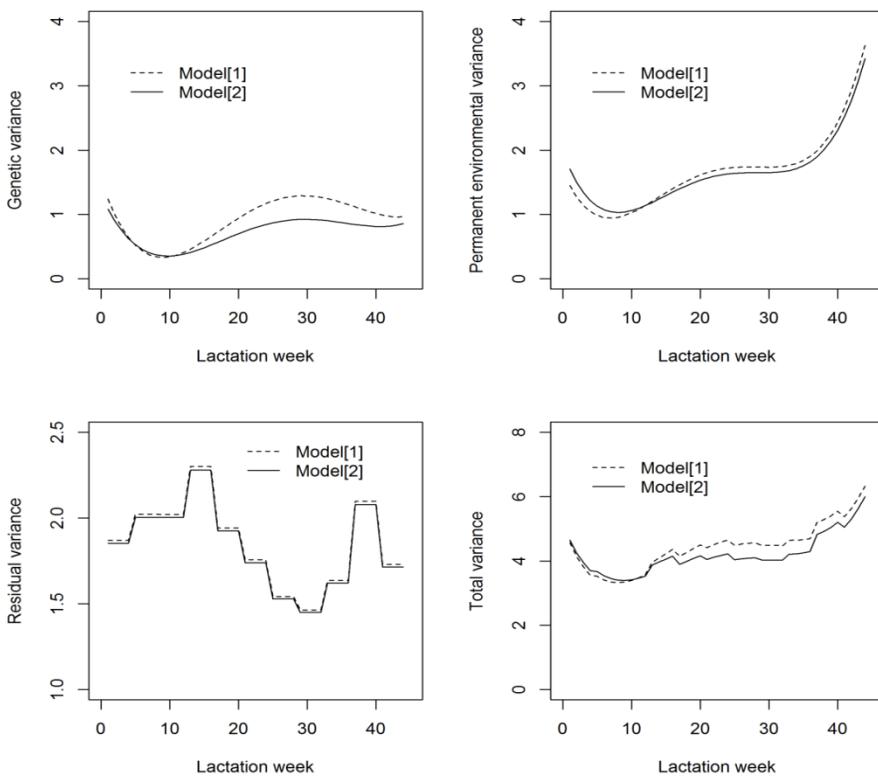


Figure 7. Genetic variances, permanent environmental variances, residual variances, and total variances for residual feed intake (RFI) across 44 lactation weeks estimated from RFI Model [1] (dashed lines) and RFI Model [2] (solid lines).

The heritability for RFI estimated from the 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).

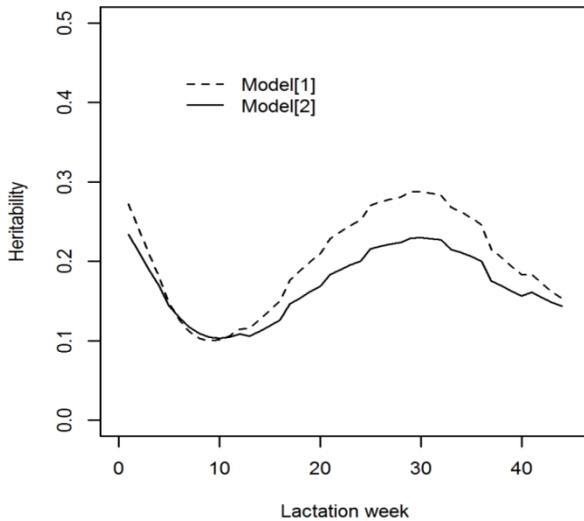
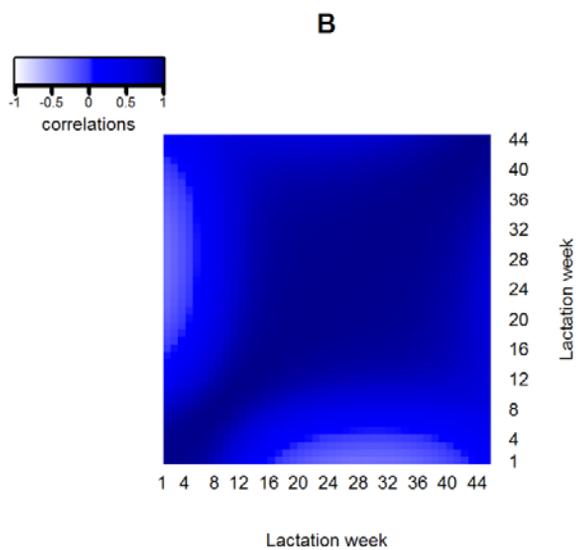
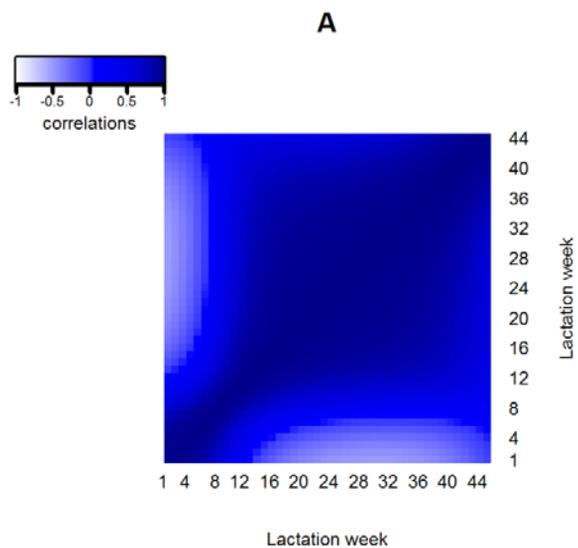


Figure 8. Heritability for residual feed intake (RFI) across 44 lactation weeks estimated from RFI Model [1] (dashed line) and RFI Model [2] (solid line).

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

RFI in middle and late lactation stages 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 Models [1] and [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 reduced to -0.29 in Model [2] (Figure 9B) compared to -0.51 in 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 DMI, ECM and MBW across lactation in Holstein dairy cattle (Paper IV)

In this paper, we applied a multivariate modelling strategy for RFI (denoted as ‘genetic RFI’ here) 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’ here). We compared two ways of defining RFI in this paper. The objective of this study was (1) to derive genetic RFI from genetic covariance functions of DMI, ECM, and MBW across lactation through multivariate analyses, (2) to estimate genetic parameters for genetic RFI across the entire lactation period, and (3) to compare the variance components, genetic parameters, and EBV 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 this study. The studied cows calved between 1991 and 2015. The 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. Further, cows’ weekly records of DMI, ECM, and BW from lactation weeks 1 to 44 were included in the analyses (Table 6). 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 over 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 method of modelling RFI, denoted as ‘genetic RFI’ in this paper, was to derive RFI from genetic covariance functions of DMI, ECM, and MBW through 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 BW across lactation were applied to model ‘genetic RFI’. The random regression model, which was the same for each trait in the multivariate analyses, is expressed below [3]:

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

where  $y_{ijklm}$  is the weekly observation of DMI, ECM, or BW in lactation week (Lactwk)<sub>m</sub> for cow *i*, where cow *i* is in herd and trial *j* (Herd-Trial)<sub>j</sub>, at calving age *k* (CA)<sub>k</sub>, and in the year-season of recording and country *l* (YS\_Country)<sub>l</sub>. *u* is the intercept for DMI, ECM, or BW; Herd-Trial<sub>j</sub> is the fixed effect of herd and trial for the cow, where the trials were herd-specific (*j* = 1–37); CA<sub>k</sub> is the fixed effect of calving age in months, where the calving age of primiparous Holstein cows ranged from 24 to 38 months; YS\_Country<sub>l</sub> is the fixed effect of year-season of recording for each country, where the year of recording was from 1991 to 2016 and four seasons were defined (March to May, June to August, September to November, and December to February, for two countries (Denmark and Sweden) (*l* = 1–117); and Lactwk<sub>m</sub> accounts for the fixed effect of lactation week (*m* = 1–44). Random regression terms were used to describe the additive genetic effect and permanent environmental effect. The  $a_{ni}$  and  $pe_{ni}$  are the *n*<sup>th</sup> 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*<sup>th</sup> covariable of the second-order Legendre polynomial on the weeks of lactation; and  $e_{ijklm}$  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 expressed below 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. Similarly, 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 ( $E_0$ ) does not employ 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 four 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  $G_{12}$ . Similarly, the same partitioning was also applied to the permanent environmental variance matrix ( $PE_0$ ) and the residual variance matrix ( $E_0$ ).

Then, the genetic (co)variance matrix for genetic RFI ( $G_{1|2}$ ) was 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;  $G_{11}$ ,  $G_{22}$ ,  $G_{12}$ , and  $G_{21}$  are the decomposed genetic (co)variance matrices from  $G_0$  as described earlier in [5]. In this manner, 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 of genetic RFI was calculated for each week. The proportion of genetic variance of RFI out of DMI was calculated by computing the ratio of genetic variance of RFI to genetic variance of DMI. In addition, the genetic correlations for genetic RFI across 44 lactation weeks were also computed. The SE of parameters are mathematically intricate to calculate and are, therefore, not available.

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

The EBV for genetic RFI were calculated for all animals in each lactation week by using formula [7] (Strathe et al., 2014), given below. Thereafter, 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  $\hat{a}_{ni}$  is the solution 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 method for modelling RFI, denoted as ‘phenotypic RFI’ in this paper, 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 done in Paper III). The random regression model is expressed below [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  $\text{DMI}_{ijklms}$  represents the weekly records of DMI in lactation week (Lactwk)  $m$  for cow  $i$ , where cow  $i$  is in calving age  $k$  ( $\text{CA}_k$ ), in the year-season of recording and country  $l$  ( $\text{YS\_Country}_l$ ), and from herd and trial  $j$  (Herd-Trial) $_j$ ;  $b_{1s}$  is the period-specific partial regression coefficient of DMI on ECM in lactation period  $s$  ( $s = 1-11$ );  $b_{2s}$  is the period-specific partial regression coefficient of DMI on MBW in lactation period  $s$  ( $s = 1-11$ ). Herd-Trial $_j$  is the fixed effect of herd and trial in which the cows were involved ( $j = 1-37$ ), where the trials were herd-specific;  $\text{CA}_k$  is the fixed effect of calving age in the month of cows’ first calving ( $k = 24-38$ );  $\text{YS\_Country}_l$  is the fixed effect of year-season of recording for each country, where the year of recording is from 1991 to 2016 and four seasons were defined (March to May, June to August, September to November, and December to February) for two countries (Denmark and Sweden) ( $l = 1-117$ ); and  $\text{Lactwk}_m$  accounts for the fixed effect of lactation week on DMI ( $m = 1-44$ ). Random regression terms were used to describe the cows’ additive genetic effect and permanent environmental effect.  $a_{ni}$  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; and  $e_{ijklms}$  is the random residual, whose variance was assumed to be 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. With regard to comparing EBVs between the two RFI definitions, first, the correlation between animals' overall EBVs (EBV of the entire lactation) for genetic RFI and animals' overall EBVs for phenotypic RFI was calculated for all the animals with phenotypes. The correlations for EBVs between the two RFI definitions were also computed across 44 lactation weeks. Second, 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. Then, 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. Thereafter, 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 resultant 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 partially attributed to the genetic covariance between DMI and the

energy sink traits (ECM and MBW), which was not eliminated 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 RFI definitions, which is probably on account of ignoring the change in BW ( $\Delta$ BW) in both RFI models. In early lactation, changes in BW are common for lactating cows (Li et al., 2017).  $\Delta$ BW could explain part of the variance for feed intake (Li et al., 2017). Variance components estimates for RFI could be affected by whether or not  $\Delta$ BW is adjusted for in RFI models. As in Lu et al. (2015), we attempted 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 so that we could compare the two RFI definitions at the same level. In Paper III—where 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 found 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 modelled. In future investigations of RFI, we recommend the inclusion of  $\Delta$ BW in the RFI model as an important energy sink for feed intake and also as a factor for reducing 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 as those used in this study to derive genetic RFI and phenotypic RFI, 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; however, they found equal residual variances between two RFI definitions (Lu et al., 2015).

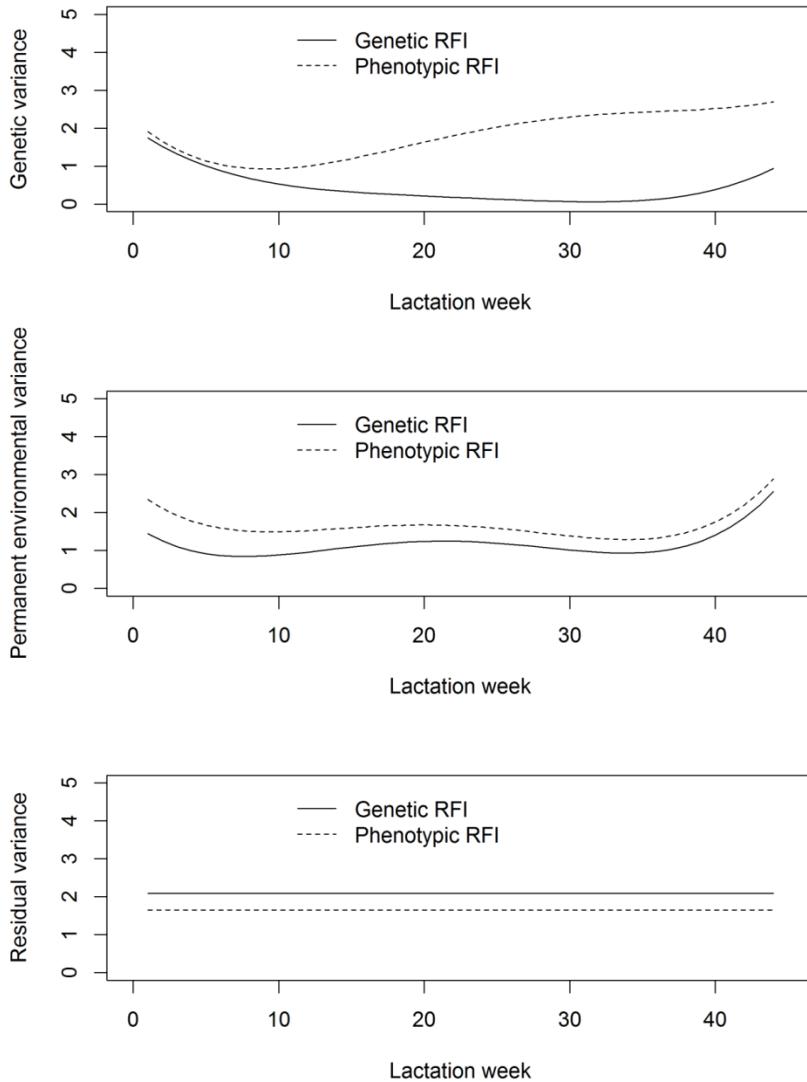


Figure 10. Genetic variances, permanent environmental variances, and residual variances across 44 lactation weeks for two definitions of residual feed intake (RFI) in Holstein dairy cattle. The estimates for genetic RFI are represented by solid lines, and the estimates for phenotypic RFI are represented by 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 lowest in week 32 (1%). In early lactation, the high proportion of the genetic variance for DMI explained by RFI was partially due to the fact that  $\Delta BW$  was not modelled in the multivariate analyses for RFI.

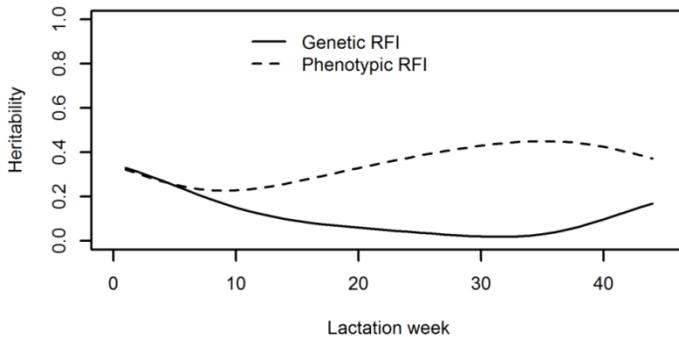


Figure 11. Heritability estimates across 44 lactation weeks for genetic residual feed intake (RFI) and for phenotypic RFI in Holstein dairy cattle. The estimates for genetic RFI are represented by the solid line, and the estimates for phenotypic RFI are represented by the dashed line.

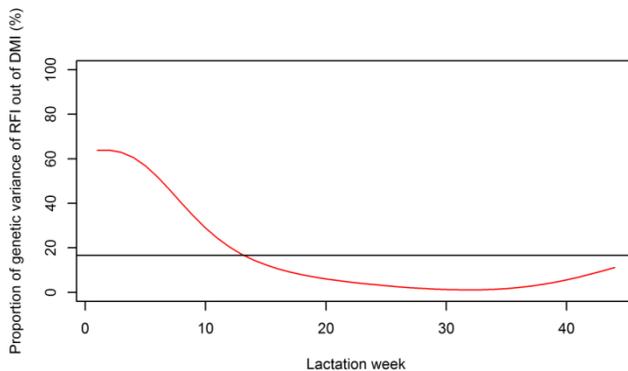
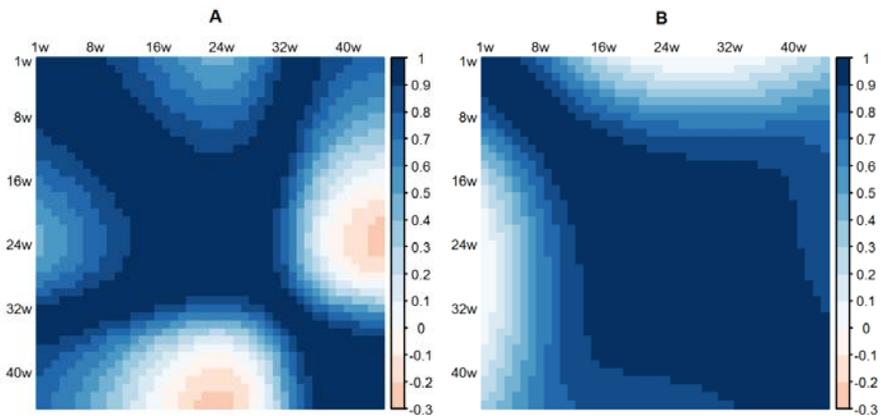


Figure 12. Proportion of genetic variance for dry matter intake (DMI) explained by the genetic variance for RFI in the multivariate analyses for RFI (i.e. genetic RFI) across 44 lactation weeks in Holstein dairy cattle. The horizontal line shows the average of the ratio across lactation.

### *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 the early lactation stage was genetically not the same trait as RFI in middle and late lactation stages (Figure 13B). Generally, genetic RFI and phenotypic RFI tended to show different patterns of genetic correlations across lactation, but in both cases, RFI in the early lactation stage 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 period) for all the cows with phenotypes, the Pearson correlation coefficient between cows' EBVs for genetic RFI and EBVs for phenotypic RFI was only 0.47. Further, if we examine 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 not strongly correlated, thereby indicating different rankings of the animals by using different RFI definitions for selection.

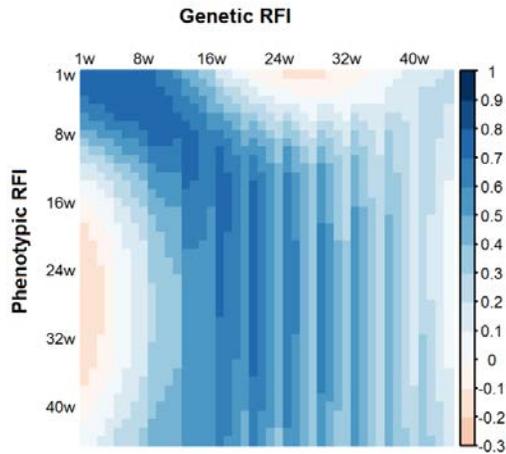


Figure 14. The correlations between cows' EBVs calculated from genetic RFI and those calculated from phenotypic RFI across 44 lactation weeks in all the cows with phenotype.

#### *Comparison between animals with highest and lowest EBVs for RFI*

The 10% of the cows 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 cows were the same between genetic RFI and phenotypic RFI. Further, we compared the average DMI, ECM, BW, and gross efficiency (kg ECM/kg DMI) between the cows with the lowest EBVs and the cows 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, cows with the lowest EBVs (i.e. most desirable) for RFI had lower DMI, lower ECM, and higher BW compared to cows with the highest EBVs (Figures 15A, 15B, and 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 (Figures 15A, 15B, and 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.

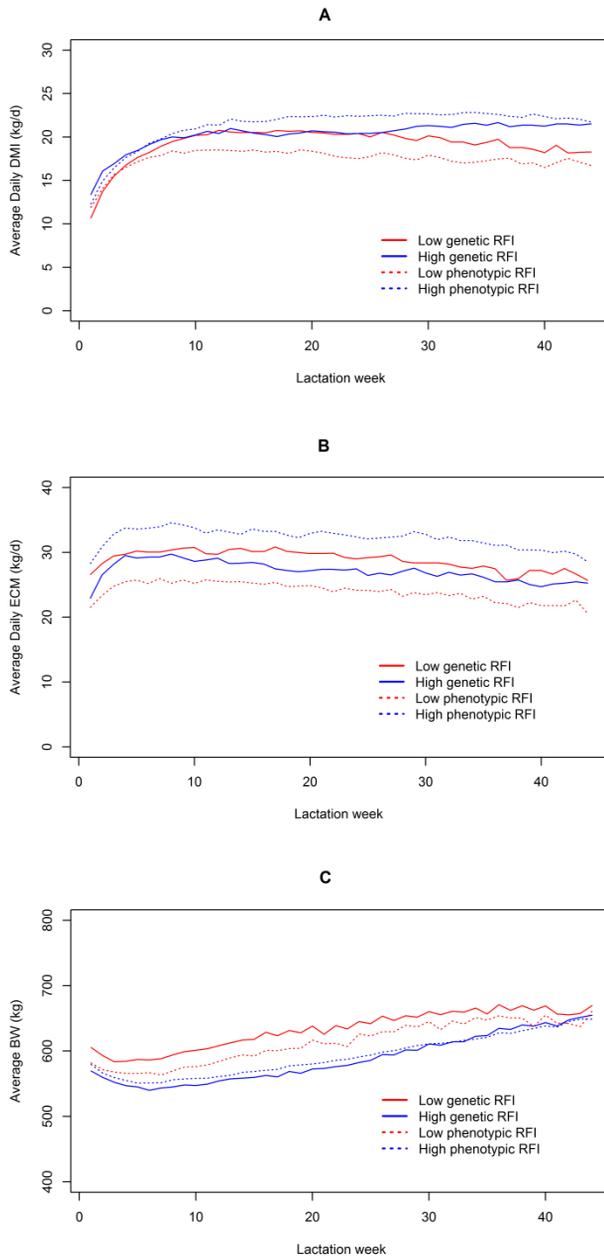
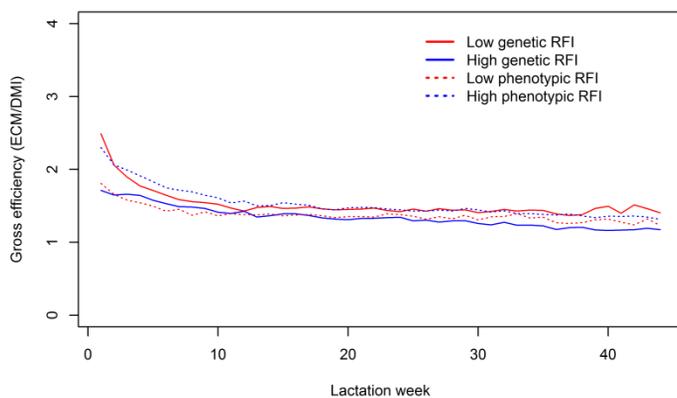


Figure 15. (A) Average daily dry matter intake (DMI, kg/d), (B) average daily energy-corrected milk (ECM, kg/d), and (C) average body weight (BW, kg) across 44 lactation weeks for (1) the 10% of cows with the lowest EBVs for genetic RFI, as ‘Low genetic RFI’, (2) the 10% of cows with the highest EBVs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

## 4 General discussion

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

Defining FE in lactating animals is more complicated than defining FE in growing animals due to the metabolic changes that occur during lactation cycles (Berry and Crowley, 2013). The 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 subsequent 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, it is important that defining FE in dairy cattle adequately takes into account 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 are discussed in detail below. In addition, some other FE definitions (e.g., gross efficiency) are 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 period, 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 (Huttmann 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 (Huttmann et al., 2009). A negative EB has been reported to have an unfavourable genetic correlation with the fertility and health of dairy cattle (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 in order 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 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). MBW is an indicator of energy required by cows 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 have 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). An existing study reports 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 an FE trait, it is important to be aware that DMI is difficult to value on its own, because a higher-producing cow or a heavier cow eats more. Improving FE of cows should not unlimitedly minimize the feed intake of cows due to the risk of decreasing milk production or sacrificing cows' fertility and health. In the Netherlands, DMI has been applied as an 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) (Jong et al., 2016). Using EBVs for feed intake in relation to the EBVs 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. Thus, in one way or another, accurate FE data 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 applied as an FE definition trait in the selection index in a few countries, for example, Australia (Pryce et al., 2015). Compared with feed intake, the general benefit of using RFI is that RFI adjusts for the important energy sinks of feed intake; thus, RFI itself is defined in a manner that is relative to milk production, BW, and  $\Delta$ BW. The challenge is deciding how to adequately model RFI so that RFI can appropriately indicate efficiency physiologically and also be easy to implement. Alternative methods to model RFI have been studied recently, including our studies in Papers III and 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 resultant RFI was genetically independent from ECM and MBW. Defining RFI as genetically independent from production traits makes FE a relatively independent trait in the selection index, which could lead to easily interpretable EBVs for FE in the selection index.

Using genetic RFI or phenotypic RFI tends to yield 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, favoured animals for phenotypic RFI tended to have lower DMI, lower ECM, and higher BW compared to unfavoured animals. In contrast, favoured animals for genetic RFI tended to have similar DMI, higher ECM, and higher BW compared to unfavoured animals. The current comparison was based on differences in the phenotypic level of DMI, ECM, and BW between favoured and unfavoured 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, favoured cows for RFI tended to have higher BW compared to unfavoured cows. Generally, high BW of cows could indicate relatively low FE due to the high energy requirement for body maintenance. Therefore, it may be needed to combine BW 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, there is recent evidence of the application of both phenotypic RFI and genetic RFI to dairy cattle breeding. In Australia, the FE trait of 'feed saved' in the selection index is based on animals' phenotypic RFI and EBVs for BW. In the US, the idea of 'genetic RFI' is planned to be used as an FE trait in dairy cattle breeding, where genetic RFI is genetically uncorrelated with milk production and BW. In the US, the genetic RFI is derived using a slightly different method compared to what we did in Paper IV (VanRaden et al., 2018). In VanRaden et al. (2018), the EBV 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 and 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 based 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). Therefore, if gross efficiency is used in the selection index, the relationship between gross efficiency and production traits would need to be carefully considered.

#### *Herd efficiency*

We can also define the FE of dairy cattle at the level of dairy herds, denoted as 'herd efficiency' here. The feed input to the herd not only includes the feed for lactating cows but also includes feed for 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 not only mainly milk production but also the value of culling cows. This is just a simple example of how the FE of dairy cattle 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, which is 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 of 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 consider 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 combining data from different sources. To accumulate sufficient data for genetic and genomic evaluation for FE, feed intake data are 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 combined 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 combined data come from different lactation periods, the heterogeneity of feed intake across lactation stages may need to be considered before genetic evaluation. Thus, in such a situation, data standardization might be necessary 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 Papers III and 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 genetic heterogeneity of residual energy intake during 30 weeks of lactation in Nordic RDC. 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 remaining lactation stages.

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 on the basis of the phenotypes of DMI, milk yield, and BW. From the findings of Paper II and several previous studies, milk yield and DMI are genetically different traits across lactation stages, particularly 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 stages, 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

Based on the results of Paper III, it can be said that neglecting lactation stages in modelling RFI influences the assessment of RFI and the variance component estimation for RFI. In Paper III, the partial regression coefficients of DMI on energy sinks changed across lactation, when period-specific regressions were allowed in modelling RFI. The assumption of constant partial regressions of feed intake on ECM, MBW, and  $\Delta$ BW over lactation stages was not always

sufficient to explain the feed utilization for energy sinks in the 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 partially reflect the change in metabolic condition in dairy cows during lactation. A cow's MY increases sharply after calving, and feed intake peaks no earlier than lactation weeks 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, based on 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).

Further, based on the results from Paper II, the partial regression coefficients of DMI on  $\Delta$ BW were also found to be significantly influenced by the lactation period. 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 stages (mostly BW gain). The feed intake of cows could hardly follow a constant partial regression of the cows'  $\Delta$ BW over the entire lactation period.

The variance component and genetic parameters for RFI were influenced if period-specific effects of energy sinks were considered. 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 an RFI model without period-specific effects on energy sinks. The higher genetic variance in the RFI model without period-specific effects might partially 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 the 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

We studied FE in three dairy breeds (Holstein, RDC, and Jersey) in Papers I and II. The findings from our papers and previous studies indicate that the phenotypic observations and genetic parameters for DMI and its related traits (ECM and BW) follow similar patterns among 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 in lactation weeks 7 or 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; this explains 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). Our study showed that cows of different breeds differed in terms of the amount of BW loss from the beginning of lactation to the nadir of BW—Holstein cows and RDC cows had the highest and lowest BW loss, respectively, which was in agreement with the results of 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 ranged from 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). Further, feed intake in early lactation was genetically different from that in middle and late lactation stages, irrespective of the breed. The genetic correlations of DMI with ECM and BW in RDC cows followed a similar pattern as the correlations in Holstein cows, as shown in Paper II.

Our studies have certain limitations in understanding breed similarities and differences in the genetic parameters for FE, due to the small data sets of cows in each breed. Feed intake is expensive and difficult to measure, thereby making it very difficult to obtain 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 have affected our variance component estimation for RDC. To the best of our knowledge, our studies are the first to address the genetic parameters for DMI in Jersey cows across the entire lactation period, and 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 sought in future studies, considering the fairly large SE of estimates in Jersey cows in our studies due to the small data sets.

## 5 Conclusions

DMI and RFI are important candidate traits for FE in dairy cattle. The recognized genetic variation in DMI and RFI has opened up possibilities for genetically improving the FE of dairy cattle in order to increase the profitability of dairy production and reduce the ecological footprint. We found moderate heritability for DMI in primiparous Holstein, RDC, and Jersey cows across lactation stages. The heritability for DMI was found to be in a similar range as the heritability for ECM and lower than the heritability for BW in dairy cattle. Further, the heritability for DMI was higher than that for RFI. Cows from different breeds shared a similar pattern of genetic parameters for DMI and RFI across lactation stages, and the breed difference in genetic parameters for DMI and RFI was not significant in our studies.

We found that DMI has a positive genetic correlation with milk production and BW across lactation. The genetic correlation between DMI and ECM was low in early lactation, but keeps higher than 0.8 in the middle and late lactation stages. In practice, when DMI is used as an FE trait, it is important to be aware that DMI is difficult to evaluate on its own, because a higher-producing cow or a heavier cow eats more. Therefore, in selecting for FE based on DMI, it is important to consider the milk yield and maintenance requirement of cows along with DMI.

There are alternative methods to model RFI in dairy cattle. RFI is usually modelled using 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 stages, and also in the ranking of efficient animals. On one hand, phenotypic RFI had higher genetic variance and heritability than genetic RFI. On the other hand, genetic RFI was 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 stages, particularly for ECM in early lactation. Neglecting lactation stages in modelling RFI could lead to a naïve assessment of RFI and affect the genetic parameter estimates of RFI.

DMI is genetically not the same trait across lactation stages, particularly between early and later lactation stages. Genetic heterogeneity across lactation was also found for RFI, thereby 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 stages in all three breeds. In practice, the genetic heterogeneity of DMI across lactation stages needs to be carefully considered in the recording and selection strategies for FE. Due to the low genetic correlation of DMI between early and later lactation stages, DMI measurements in middle or late lactation stages cannot be strong predictors of DMI in early lactation, and vice versa. To improve FE for the entire lactation period, we recommend taking 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 FE in dairy cattle (Pryce et al., 2018). Recently, genomic evaluation for FE in dairy cattle has been initiated in Australia and the Netherlands. Future research on the possibility of using genomic evaluation for FE will be further studied in Nordic dairy cattle breeding. The single-step GBLUP method could be helpful for genomic evaluation for FE, given that certain animals with phenotypes may be not genotyped. The limited data size remains a challenge for the genomic evaluation of FE. International collaboration for combining data to obtain a large reference population and regular refreshment of the reference population could be one efficient solution for obtaining acceptable prediction reliabilities for FE in the genomic evaluation of dairy cattle.

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

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## Popular science summary

Feed efficiency (FE) in dairy cows is an important concept in dairy production. Feed accounts for the largest proportion 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 inefficient cows for a certain amount of milk yield and for a certain cow size. Meanwhile, selecting efficient cows should not imply compromising on their fertility or health.

FE in dairy cattle is influenced by diet, genetic ability, and physiological state of the cow. Selecting cows with better genetic ability for FE plays an important role in improving FE for the entire dairy cattle population and also for subsequent generations of dairy cows. Recent genetic studies on FE in dairy cattle have found evidence of genetic variation for FE in several dairy breeds, thereby making it possible to improve FE in cows through genetics and breeding.

Feed intake and FE are difficult and expensive to measure on a large scale for individual cows. The data are mostly available in research herds with limited data size. International collaborations have been established to combine FE data across countries for genetic studies on FE. A combined data set of FE in dairy cattle has been established among Nordic countries since 2013, thereby aiming to investigate the genetic variation for FE in several Nordic dairy breeds and to assess the possibility of including FE in Nordic dairy cattle breeding. The current thesis is part of a Nordic collaborative project entitled '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 (BW)) in several breeds of dairy cattle, in order to provide an appropriate definition of 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 breeds and lactation stages.

In Papers I–IV, we found genetic variation for DMI for all breeds. Cows of different breeds shared a similar pattern of genetic parameters for DMI. Further, we found moderate heritability for DMI in Holstein, RDC, and Jersey cows. The heritability for DMI was in a similar range as the heritability for ECM and was lower than that for BW. Feed intake was found to have a positive genetic relationship with ECM and BW across lactation, thereby indicating that heavier cows and high-yielding cows eat more feed, genetically. Therefore, defining FE based on the DMI of cows should consider cows' milk production and BW as well. In the Netherlands, the 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 in BW. The heritability for RFI was lower than that for DMI. There are alternative ways of defining RFI using different models. The methods of modelling RFI influence the assessment of RFI and the genetic properties of RFI.

Last but not least, cows' DMI or RFI was found to be genetically different traits across lactation stages, particularly between early and later lactation stages. Cows' feed intake information in early lactation is not a good indicator of feed intake in middle or late lactation, and vice versa. This phenomenon should be considered when recording and selecting for efficiency in dairy cows. In order to improve FE in the entire lactation period, we recommend taking DMI measurements from separate time points across all lactation stages.

## Populärvetenskaplig sammanfattning

Mjölkkornas fodereffektivitet (FE) är en viktig egenskap inom mjölkproduktionen. Fodret svarar för den största andelen av driftskostnaderna inom mjölkproduktionen. En förbättring av FE kan därför förväntas öka lönsamheten för mjölkproducenterna. Fodereffektiva kor förväntas behöva ett lägre foderintag jämfört med mindre effektiva kor vid samma mjölmängd och samma kroppsstorlek på kon. Urval för effektiva kor får dock inte försämra fruktsamheten och hälsan hos korna.

Fodereffektiviteten hos mjölkkor påverkas av foderstat och andra miljöfaktorer, genetisk bakgrund samt den fysiologiska statusen hos kon. Urval av kor för en bättre genetisk förmåga att vara effektiva är viktigt för att förbättra effektiviteten hos hela mjölkkopulationen och också för kommande generationer av mjölkkor. I nyligen genomförda studier av FE hos mjölkkor har man visat att det finns genetisk variation i FE hos ett flertal mjölkkoraser vilket möjliggör en förbättring av FE genom genetik och avel.

Foderintag och FE är svåra och kostsamma att mäta i stor skala för individuella kor. De registreringar som finns är oftast gjorda i försöksbesättningar och har begränsad datastorlek. Internationella samarbeten har etablerats för att skapa gemensamma FE data över länder för genetiska studier av FE. I de nordiska länderna skapades ett gemensamt dataset för fodereffektivitetsrelaterade egenskaper hos mjölkkor år 2013 med syfte att undersöka den genetiska variationen i FE för ett flertal nordiska raser och fastställa möjligheten att inkludera FE i den nordiska avelsvärderingen. Arbetena i den här avhandlingen är en del av projektet "Feed Utilization in Nordic Cattle (FUNC)" mellan Danmark, Finland, Norge och Sverige. Syftet med avhandlingen var att studera de genetiska egenskaperna hos alternativa FE definitioner och FE relaterade egenskaper (mjölkproduktion och kroppsvekt (BW)) i flera mjölkkoraser, för att på ett riktigt sätt definiera FE för användning inom mjölkkoaveln.

Avhandlingen innehåller fyra arbeten. Två viktiga FE egenskaper för mjölkkor, torrfoderintag (DMI) och residualt foderintag (RFI), studerades för att undersöka de genetiska egenskaperna hos dessa två egenskaper över laktationen och över raser.

I arbetena I-IV, påvisades genetisk variation för DMI hos alla studerade mjölkkoraser. Kor av olika raser visade generellt ett liknande mönster av genetiska parametrar för DMI. Vi fann moderat ärftlighet för DMI hos Holstein, Nordisk Röda (RDC) och Jerseykor. Arvbarheten för DMI var i liknande storleksordning som för ECM och var lägre än arvbarheten för BW. DMI var positivt genetiskt korrelerad till ECM och BW över laktationsstadium, vilket genetiskt sett indikerar att tyngre kor respektive högavkastande kor äter mer foder. Av den anledningen ska man när man definierar FE baserat på DMI hos korna samtidigt ta hänsyn till kornas mjölkproduktion och dessutom BW. I Nederländerna används en definition på FE i aveln som baseras på DMI kombinerat med mjölkproduktion och BW.

Som en viktig kandidat till FE egenskap definierades RFI. Detta mått är baserat på kornas DMI med hänsyn taget till deras mjölkproduktion, BW och viktsförändring. Arvbarheten för RFI var lägre än arvbarheten för DMI. Det finns alternativa sätt att definiera RFI på beroende på vilken modell som används. Olika definitioner på RFI påverkar utvärderingen av RFI och har olika genetiska egenskaper i beskrivningen av effektiviteten hos korna. I Australien används RFI som en FE definition i deras avel för effektiva kor.

Sist men inte minst så visades sig kornas DMI respektive RFI genetiskt sett inte vara samma egenskap tvärs över laktationsstadierna, och särskilt inte mellan tidig och sen laktation. Information om kornas foderintag i tidig laktation är därför inte en god indikator för deras foderintag i mellersta delen av laktationen eller i sen laktation, och vice versa. Detta fenomen bör man ta hänsyn till när man registrerar och selekterar för effektiviteten hos mjölkkor. För att förbättra FE under hela laktationen rekommenderas att registrera DMI under olika tidsperioder längs alla laktationsstadier.

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