Genotype by Environment Interaction for Automated and Traditional Fertility Traits in Dairy Cattle

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To my mother who will always be missed.

You are always on my mind & in my heart.

I

PREFACE

This thesis is submitted to the Graduate School of Science and Technology, Aarhus University, as a partial fulfillment of the requirements for the joint Ph.D. degree between Aarhus University, Denmark and the Swedish University of Agriculture Sciences (SLU), Sweden. The research of this work was funded by the AnGR-Nordic NET (NordGen, Nordic Council of Ministers, Ås, Norway). Data were kindly provided by (SEGES, Denmark) and (Växa, Sweden). I am also enrolled in the Erasmus-Mundus joint doctorate European Graduate School in Animal Breeding and Genetics (EGS-ABG).

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List of Publications

This thesis is based on the work contained in the following papers:

1. Ismael, A., E. Strandberg, M. Kargo, A. Fogh, and P. Løvendahl. 2015. Estrus traits derived from activity measurements are heritable and closely related to the time from calving to first insemination. J Dairy Sci 98: 3470-3477.

2. Ismael, A., E. Strandberg, B. Berglund, A. Fogh, and P. Løvendahl. 2016. Seasonality of fertility measured by physical activity traits in Holstein cows. J Dairy Sci 99: In press.

3. Ismael, A., E. Strandberg, B. Berglund, M. Kargo, A. Fogh, and P. Løvendahl. 2016. Genotype by environment interaction for activity based estrus traits regarding to production level for Danish Holstein. (Manuscript in preparation)

4. Ismael, A., E. Strandberg, B. Berglund, M. Kargo, A. Fogh, and P. Løvendahl. 2016. Genotype by environment interaction for the interval from calving to first insemination with regard to calving month and geographic location in Holstein cows in Denmark and Sweden. (Submitted to J Dairy Sci)

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SUMMARY

Genotype by environment interaction (G×E) is one of the issues the dairy farming industry faces due to the globalization of using artificial insemination with genetically superior bulls to improve the performance of their herds. This includes distribution of genetic material to multiple environments within countries and between countries. The major concern is that animal rank may change across the environments which mean that the best animals in one environment are not the best in another environment. In this thesis, the genetic variation and G×E effect on fertility traits was investigated in Nordic cattle. Two types of fertility traits were studied, 1) automatically recorded fertility traits based on the physical activity measuring devices and, 2) traditional fertility traits based on the AI recording.

In **Paper I**, genetic parameters were estimated for interval for calving to first high activity (CFHA); duration of high activity as an indicator of estrus duration (DHA); and strength of high activity as an indicator of estrus strength (SHA), all based on activity measurements from cows in commercial herds. These parameters were compared with parameter estimates for interval from calving to first insemination (CFI). It was found that CFHA shows higher heritability than CFI. Moreover, the two traits were strongly genetically correlated. Consequently, the selection criteria for fertility may be improved by including "time from calving to first high activity", because it reflects the ability of the cow to return to reproductive cycling and heat after calving.

In **Paper II**, Seasonality of estrus activity traits with respect to the month of calving was investigated. It was found that the summer calving season was associated with shorter CFHA than winter, spring, and fall seasons. Moreover, there was evidence for genotype by environment interaction for CFHA with calving season. However, DHA and SHA were less affected by seasonal variation. The results might be useful for the interpretation of seasonal variation in estrus expression traits and fertility traits in Holstein cows kept in the temperate climate zone.

In **Paper III,** the objectives were to estimate genetic parameters of fertility traits derived from activity tags (CFHA, DHA, and SHA), and estimate the genetic correlation between the CFHA and yield of energy corrected milk at 70 days in milk (ECM70). Parameters were

estimated as a function of production level, expressed as herd average yield using reaction norm model in Danish Holstein cows. Heterogeneous genetic variation was found for all traits as a function of production environment, but the genetic correlation estimate of the trait between low and high production environment showed no evidence for G×E effect. The genetic correlation between CFHA and ECM70 decreased with increasing the production level implying that the unfavorable genetic correlation between fertility and milk yield could is reduced in improved production environments.

In **Paper IV,** the G×E interaction effects were studied on CFI in first parity Holstein cows in Denmark and Sweden, with environments defined as calving month and geographic location (in 8 North-South location classes). It was found that that cows calving in September had the shortest CFI. Cows in the northernmost location class had the longest CFI. Furthermore, there was a G×E effect between cold and warm calving months. However, CFI genotypes showed little interaction with geographic location. The obtained results are useful for improving genetic evaluations of Holstein cow fertility using data from a wide range of geographic locations and seasons.

SAMMENDRAG

Genotype-miljø vekselvirkning (G × E) er et af de problemer som mælkeproducenter har i stigende grad på grund af globalisering af anvendelsen af kunstig befrugtning med genetisk overlegne tyre for at forbedre effektiviteten i kvægbesætningerne. Dette indebærer at genetisk materiale flyttes og anvendes i mange forskellige produktionsmiljøer både indenfor lande og i forskellige lande.

Den største bekymring er om avlsdyrenes rangering ændres på tværs miljøer. Det betyder at de bedste dyr i ét miljø ikke er de bedste i et andet miljø. I denne afhandling blev den genetiske variation og G × E effekten på nordiske malkekøers frugtbarhed undersøgt. To typer af frugtbarhedsegenskaber blev undersøgt: 1) automatisk registrerede frugtbarheds-indikatorer baseret på forhøjet fysisk aktivitet, og 2) traditionelle frugtbarhedsegenskaber baseret på resultater fra kunstig befrugtning. Afhandlingens resultater er beskrevet i fire artikler og en sammenfattende diskussion.

I **Artikel I**, beregnes genetiske parametre for interval fra kælvning til første episode af høj aktivitet (CFHA); varighed af høj aktivitet som en indikator for brunstens varighed (DHA); og styrken af høj aktivitet som en indikator for brunststyrke (SHA). Aktivitetsmålingerne var baseret på køer i kommercielle besætninger. Parameterestimaterne for de aktivitetsbaserede mål blev sammenlignet med det traditionelle mål, interval fra kælvning til første inseminering (CFI). Det blev fundet at CFHA viser højere arvelighed end CFI, og at de to egenskaber er stærkt genetisk korreleret. Således kan udvælgelseskriterierne for frugtbarhed forbedres ved at anvende tid fra kælvning til første episode af høj aktivitet, fordi den afspejler koens evne til at vende tilbage til cyklisk brunst efter kælvning.

I **Artikel II** blev sæsonudsving i egenskaben brunstaktivitet undersøgt som effekten af kælvningsmåned. Kælvningssæsonen "sommer" var forbundet med kortere CFHA end vinter, forår og efterårs-sæsonerne. Der blev også fundet G × E effekt for CFHA med kælvning sæson, mens DHA og SHA var mindre påvirket af sæsonvariation. Resultaterne kan være nyttige for fortolkningen af sæsonvariation i brunst og fertilitets-egenskaber hos Holstein køer der holdes i den tempererede klimazone.

I **Artikel III**, var det formålet at beregne genetiske parametre for frugtbarhedsegenskaber afledt af aktivitets-data (CFHA, DHA, og SHA), og beregne den genetiske korrelation mellem CFHA og energi korrigeret mælkeydelse ved 70 dage efter kælvning (ECM70). Parametrene blev beregnet som en funktion af produktionsniveau baseret på besætningsydelse ved hjælp af en reaktionsnorm model. Der blev fundet heterogen genetisk variation for alle egenskaber som funktion af produktionsmiljø, mens den genetiske korrelation mellem lavt og højt produktionsmiljø ikke viste tegn på G × E. Den genetiske korrelation mellem CFHA og ECM70 faldt med stigende produktionsniveau hvilket indebærer, at den ugunstige genetiske korrelation mellem fertilitet og mælkeydelse er svagest i det bedste produktionsmiljø.

I **Artikel IV**, undersøgtes G × E effekter på CFI af hos første kalvs Holstein køer i Danmark og Sverige, med miljø defineret som kælvningsmåned og geografisk placering (nord-syd i 8 sted-klasser). Det blev fundet, at køer som kælver i september havde den korteste CFI. Køer i den nordligste sted-klasse havde den længste CFI. Desuden fandtes tegn på G × E virkning mellem kolde og varme kælvningsmåneder, mens CFI genotype viste meget lidt interaktion med geografisk placering. De opnåede resultater er nyttige til at forbedre avlsværdivurderingen af Holstein køers frugtbarhed ved hjælp af data fra en bred vifte af geografiske steder og årstider.

SAMMANFATTNING

Genotyp-miljösamspel (G×E) har blivit av allt viktigare inom mjölkkoaveln, p g a den ökade globaliseringen med användning av semin från tjurar från en mängd olika länder i svenska och danska mjölkkobesättningar. Fördelen med detta är att världens bästa genetiska material kan användas i olika besättningsmiljöer i flera länder. Det som kan vara ett problem är just G×E, att rangordningen av djuren genetiskt sett inte är densamma i alla miljöer, så att den tjur som är bäst i en miljö inte är bäst i en annan. I denna avhandling har jag studerat genetisk variation och genotyp-miljösamspel i nordiska mjölkkor för fruktsamhetsegenskaper. Två olika slags fruktsamhetsegenskaper har använts, dels egenskaper baserade på automatisk registrering av fysisk aktivitet hos korna, dels de mer traditionella fruktsamhetsegenskaperna baserade på uppgifter om semineringar.

I **artikel I** skattades genetiska parametrar för intervallet från kalvning till första högaktivitetsperiod (KFHA), längden på denna period (LHA) och ett mått på styrkan i aktiviteten (SHA), och alla mått var baserade på aktivitetsmätare från kor i normala mjölkkobesättningar. Dessa skattningar jämfördes med skattningar för den traditionella egenskapen intervallet från kalvning till första insemination (KFI). KFHA hade högre arvbarhet än KFI och egenskaperna var starkt genetiskt korrelerade. Därför kan selektionen för fruktsamhet förbättras genom att också ta hänsyn till KFHA, som är ett mått på hur snabbt kon kommer tillbaka till normala könsfunktioner och visar brunst efter kalvning.

I **artikel II** undersöktes hur kalvningssäsong kan påverka de tre egenskaperna, KFHA, LHA och SHA. Sommarkalvningar var kopplat till kortare KFHA än övriga årstider. Dessutom fanns det ett genotyp-miljösamspel för KFHA kopplat till kalvningssäsong, vilket inte fanns för LHA och SHA. Dessa resultat kan vara till nytta för att förstå hur säsong påverkar brunstvisningsförmågan och andra fruktsamhetsegenskaper för holsteinkor under nordiska (tempererade) förhållanden.

I **artikel III** var syftet att skatta genetiska parametrar för de tre aktivitetsegenskaperna KFHA, LHA och SHA samt att skatta genetiska korrelationer mellan KFHA och mjölkavkastning, här mätt som energikorrigerad mjölk dag 70 i laktationen (ECM70), samt att undersöka om det fanns genotyp-miljösamspel för KFHA med avseende på olika mjölkavkastningsnivåer i danska holsteinbesättningar. Detta gjordes m h a en reaktionsnormsmodell. Den genetiska variationen

för alla fyra egenskaper varierade med besättningens produktionsnivå men den genetiska korrelation mellan en viss egenskaps värde i låg och hög produktionsnivå var nära ett, dvs inga tecken på genotyp-miljösamspel. Den genetiska korrelationen mellan KFHA och ECM70 minskade något med ökad produktionsnivå i besättningen, vilket innebär att en ökad produktionsnivå gav något mindre ogynnsam genetisk korrelation mellan de två egenskaperna.

I **artikel IV** undersöktes om det finns genotyp-miljösamspel för KFI med avseende på kalvningssäsong eller geografiskt läge, för danska och svenska holsteinkor i första laktationen. Kvigor som kalvade in i september hade kortast KFI och kor längst norrut i Sverige hade längst KFI. Det fanns också genotyp-miljösamspel för KFI mellan kalla och varma kalvningsmånader, men inget starkt genotyp-miljösamspel med avseende på geografiskt läge. Dessa resultat kan vara till nytta för att förbättra avelsvärderingen för fruktsamhet när man har uppgifter från besättningar som är geografiskt spridda samt från olika kalvningssäsonger.

GENERAL INTRODUCTION

Dairy cow fertility is becoming increasingly important throughout the world because it has a substantial impact on the overall profitability of dairy cattle production, as declining fertility increases the number of inseminations and veterinary treatments required, increases the calving intervals, and increases the rates of involuntary culling (Sewalem et al., 2008). Selection for improved fertility of dairy cows is hampered by low heritability of traditional fertility traits because of many factors including the nature of traits, missing and censored records, and farmer's interventions. Furthermore, more countries are performing genetic evaluations for female fertility, and in August 2015, 21 countries were included in the international genetic evaluation for female fertility (Interbull, 2015). That provides a wide range of environments which increases the concerns of possible genotype by environment interaction (G×E). This interaction has become critical in dairy cattle because, farmers are using artificial insemination from genetically superior bulls, to increase performance of their herds. This allows genetic material to be distributed across multiple countries and different environments within countries and thereby the possibility to detect G×E.

Possible solution for the low heritability estimate for the traditional fertility trait is by using more precise phenotypes that directly reflect the cow's physiological or behavioral condition such as milk progesterone (P4) and data from activity monitor devices that used widely for estrus detection. Both phenotypes can deliver data free from farmer's interventions and thus higher heritability estimate obtained in compare with the traditional measure based on AI data (Petersson et al., 2007; Løvendahl and Chagunda, 2009, 2010). Possible solution for the raising concerns about the G×E effect is to study the magnitude of that effect then account for it. The major challenge is animal re-ranking which means that the best animals in one environment are not the best in another environment. When re-ranking occurs, selection in one environment may lead to a different response to selection in the other environment (Falconer and Mackay., 1996; Rauw and Gomez Raya, 2015; Sae-Lim et al., 2015). This can cause concerns to the farmers who is selecting animals based upon a predicted performance in another production environment, and therefore does not obtain the expected results. The presence of G×E interaction may also be important for dairy farmers

within a country, because farmers could choose those sires which are best suited to the local production environment (Kolmodin et al., 2002; Strandberg et al., 2009).

1.   Genotype by environment interaction

The phenomenon that different genotypes respond differently to changes in their environments is known as genotype by environment interaction (G×E) (Falconer and Mackay., 1996). The term environmental sensitivity or phenotypic plasticity refers to the ability of living organisms to change their phenotypic expression in response to changing environments, where genotypes with high variation in the phenotypic expression across environments are plastic, while genotypes with low variation in the phenotypic expression are robust (de Jong and Bijma, 2002; Kolmodin et al., 2003).

G×E interaction can cause three possible effects. 1) Scaling effects when the differences between genotypes vary between environments, without changing their ranking. This is also called heterogeneity of genetic variance across environments. The G×E interaction is less important if only a scaling effect occurs, because the superior individuals in one environment would remain superior in the other environments (Hammami et al., 2009b). 2) Re-ranking of individual for expression of a trait may occur due to the varying magnitude of phenotypic change across environments, consequently, selection for best performance in one environment might not lead to improved performance in other environments (Falconer and Mackay., 1996; Lynch and Walsh, 1998). 3) The genetic correlation between different traits across environments might change due to differences in genetic variances across environments (Mulder and Bijma, 2006).

The effect of G×E interactions on a breeding program must be taken into consideration because traits measured in two environments could be considered two different traits and the existence of G×E interaction could be identified by an estimate of genetic correlation between these traits. That means, a genetic correlation not significantly less than unity across environments would suggest that the trait in different environments are controlled by the same set of genes and the effect of G×E is less important. If the genetic correlation is less than unity, it suggests a difference of genetic controls between environments and the effect of G×E interaction is critical because it can result in a re-ranking

genotypes across environments (Falconer and Mackay., 1996). Robertson (1959) suggested that if genetic correlations of the traits in different environments are less than 0.8, this is an indication of a significant G×E. More recently, Mulder and Bijma (2006) investigated G×E interactions in dairy cattle populations and reported that if genetic correlations between environments are greater than 0.8 to 0.9, genetic gain can be increased by selection across environments.

1.1. Methods to estimate G×E interaction

There are two common methods to detect G×E. The type of the environmental descriptors available determines the method to be used to detect the G×E interaction. The first one is the character state model and the second is the reaction norm model. The use of either of them is determined by the type of environmental gradient studied. When the environments are clearly distinct; for instance, geographical regions or seasons, G×E interaction analysis could be performed using character state model, which considers the trait under analysis in each environment as separate traits and estimates the genetic correlations between the different environments. On the other hand, when the environment of interest can be described by a continuous environmental gradient such as temperature, herd size and average herd production G×E interaction can be analyzed using a reaction norm approach, which describes the performance of the genotype as a function of the environmental gradients by regression of the trait on these variables.

1.1.1. Character state model (Multiple-trait approach)

Falconer (1952) suggested that quantitative characters expressed in two environments could be considered being two genetically correlated character states. Therefore, the phenotypic expression of a trait in different environments could be described as different traits, and the genetic correlation between the phenotypes of the same trait expressed in different environments is used to measure the G×E interaction. In this model, the total additive genetic variance of the trait across environments could be classified into the genetic variances of the traits within each environment which indicates whether the genetic variances are constant or heterogeneous across environments and the genetic correlation between different environments which is related to G×E interaction (de Jong and Bijma,

2002). From this perspective, a genetic correlation of unity across environments would suggest that the same set of genes control the variability of the trait in different environments. A genetic correlation less than unity across environments suggests a combination of common and different genetic control in each environment, while a genetic correlation close to zero means unique set of genes regulates the variation of the trait across different environments (Marais et al., 2013).

A clear representation of the application of the character state model is using the Multiple Across Country Evaluation (MACE) introduced by Schaeffer (1994). This is a sire model in which the daughter performances of each sire in different countries are assumed to be different traits. As a result, each sire would have a specific breeding value and ranking for each country. For example, Weigel et al. (2001) estimated variance components and genetic correlations for milk, fat and protein yield for Holstein cows from 17 countries using a multi trait sire model and found heritability estimates ranged between 0.24 and 0.34, while the genetic correlation between countries ranged between 0.77 and 0.96 indicating that there might be slight re-ranking of sires between countries.

The advantage of using a multiple trait model is the consideration of each environment as a distinct trait, and therefore it enable the differences between environments to be accounted for directly. Another important advantage for the multiple trait approach is the direct implementation of the results into a breeding program, with the ability to assign different economic values to each trait (Case et al., 2010). However, the number of environments should be kept limited because the more of environments used, the more of co-variances need to be estimated and consequently more computational resources are needed. Furthermore, when the number of environments is large, problems of convergence of the estimated parameters often occur. Consequently, many separate multi-trait models are required to be performed, increasing the risk of bias of the estimated parameters (Sae-Lim et al., 2015). Moreover, this model is restricted to discrete environments and requires their classification into groups where the accuracy of the estimated parameters depends on the classification of these groups, and number of animals in the experiment and their genetic structure.

1.1.2. Reaction norm model

Reaction norm models are the most recent method introduced to study G×E interaction in animal breeding. This model describes the phenotypic performance of an individual as a function of a continuous measure of the environment (de Jong, 1995; Falconer and Mackay., 1996). The reaction norm model is similar to the random regression test day models used in dairy cattle breeding (Schaeffer, 2004), but the covariate used is the environmental gradients instead of days in milk.

The advantages of the reaction norm model are the continuous representation of the genetic effects over the environmental gradients without the need of grouping the environments such as temperature and humidity. Furthermore, the number of estimated variance components remains limited (Ravagnolo and Misztal, 2000; de Jong and Bijma, 2002). Another advantage of the reaction norm model is that, the genetic parameters for the slope can be used to assess the environmental sensitivity or tolerance such to production level or heat tolerance (Ravagnolo and Misztal, 2000; Kolmodin et al., 2002; Ravagnolo and Misztal, 2002a). On the other hand, some kind of standardization and transformation of the continuous environmental parameters might be needed before inclusion into the model (Schaeffer, 2004). Furthermore, adjustment for the heterogeneity of residual variance should be considered to account for the overestimation of the heritability assuming common residual variance using the random regression models (Schaeffer, 2004; Lillehammer et al., 2009).

1.2. Genotype by environment interaction example in dairy cattle

1.2.1. Milk yield

For milk yield traits, a lot of research has been done on estimating the genetic correlations between different geographical regions (countries) to investigate possible G×E interaction. Many studies reported large heterogeneity of variance between countries that are similar in climate or management conditions. That leads to heterogeneous heritability, but little re-ranking of animals because the genetic correlations for the traits in different environments were close to unity (Carabaño et al., 1989; Stanton et al., 1991; Cienfuegos-Rivas et al., 1999; Costa et al., 2000; Rekaya et al., 2001; Fikse et al., 2003a). On the other hand, weak

genetic correlations were found between the countries that differ strongly in the climatic or management conditions. For instance, a genetic correlation of 0.63 was found between US and Mexico (Cienfuegos-Rivas et al., 1999), 0.49 between Kenya and UK (Ojango and Pollott, 2002), and 0.50 between Luxembourg and Tunisia (Hammami et al., 2009c).

Within the same country, different environmental gradients were used to quantify G×E. For example, production level, herd size and management level (Veerkamp and Goddard, 1998; Kolmodin et al., 2002; Berry et al., 2003b; Fikse et al., 2003b; Hayes et al., 2003; Calus et al., 2005; Haile-Mariam et al., 2008; Hammami et al., 2009a). Hammami et al. (2009a) found a significant G×E interaction with herd management level (low-medium-high) in Tunisia and genetic correlations between these environments ranged from 0.70 to 0.78 suggesting significant sire re-ranking occurred between these environments. When environments were classified based on feeding system, Ramírez-Valverde et al. (2010) found a genetic correlation slightly less than unity (0.76) between grazing and confinement systems in Jersey cattle in Mexico, while higher genetic correlation of 0.88 was reported by Kearney et al. (2004b) between feeding systems in US Holsteins. Genetic correlation for protein yield between organic and conventional production systems in Netherlands was 0.78 indicating that for protein yield, there might be a slight re-ranking of animals between organic and conventional production systems (Nauta et al., 2006).

Weather information was used to describe climatic environment in a study by Ravagnolo and Misztal (2000) who used a random regression on the temperature humidity index (THI) as an indicator for heat stress. THI is a single value that combines air temperature and humidity. They obtained heterogeneous heritabilities for milk, and protein yield in US Holsteins ranged from 0.16 to 0.21 when THI increased from 22.2 to 29.4 °C. Furthermore, the genetic correlation for milk yield traits between the cool environments (THI < 22.2 °C) and any given value for THI (heat tolerance) remained higher than 0.9 till THI exceeded 27.2 °C, while this correlation decreased to 0.83 when THI was 28.3 °C. They also found the genetic correlation between production traits and heat tolerance to be around –0.3 indicating that, a continuous selection for production ignoring the side effect of heat tolerance results in decreased heat tolerance. More recently, Brugemann et al. (2011) studied the effect of THI on test day protein yield for German Holsteins and found an opposite pattern to US Holsteins for the heritability estimate. The lowest heritability was found in

THI=22.2 °C and the highest in THI=-6.1°C. However, genetic correlations for protein yield between different points of THI remained close to unity. Moreover, heritability estimates for test day milk yield in Iranian Holsteins decreased from 0.31 to 0.14 when THI increased from 0 °C to 24.4 °C, while genetic correlations less than unity were obtained between low and high THI values indicating that the trait becomes more different with increasing THI and should be considered as separate traits in different environments (Bohlouli et al., 2014).

1.2.2. Fertility

Contrary to yield traits, relatively little research has been done on G×E in dairy cattle fertility traits. The multiple trait approach was used to estimate the genetic correlation for fertility traits in different countries. The genetic correlation for the interval from calving to first insemination (CFI), days open (DO), and interval from first to last insemination (IFL) were estimated between Canada, Belgium, Switzerland, German Austrian evaluation, and joint Nordic evaluation (Denmark-Sweden- Finland) and didn't differ from unity (Nilforooshan et al., 2010). On the other hand, other studies found genetic correlations less than unity for age at first calving between Brazil and Colombia, for DO between summer and fall calving cows in the United States, and for calving interval (CI), interval from calving to last insemination, and IFL between organic and conventional dairy herds in Sweden (Ceron-Munoz et al., 2004; Oseni et al., 2004; Sundberg et al., 2010).

Although the previous results indicated that expression of fertility is sensitive to environment changes, little research has been done on G×E for female fertility within the same country. Generally, the studies have found very little evidence for G×E and most genetic correlations between environments were close to unity (Kolmodin et al., 2002; Windig et al., 2006; Strandberg et al., 2009). However, Oseni et al. (2004) reported heterogeneity of genetic and residual variances for days open in US Holstein where the genetic variance for winter calvings was 3 times the genetic variance for fall calvings. The largest genetic variance was also associated with largest residual variance for winter calvings, while spring and summer calvings were associated with the smallest residual variance. Consequently, the highest heritability estimate was found for spring calvings and the lowest estimate was found for fall calvings. These authors also reported a slight re-ranking effect due to genetic correlation less than unity (rg = 0.78) between summer and fall

calving seasons. Ravagnolo and Misztal (2002a) presented a random regression model to quantify the effect of THI on non-return rate in Holstein cows and obtained heritability estimates that decreased from 0.055 to 0.006 when THI increased from 21 ºC to 28 ºC. Although, these results showed that the genetic variance of fertility traits is heavily influenced by seasons and climatic factors or both, the studies did not demonstrate a significant G×E effect, because to the genetic correlation between the same traits in different environments remained close to unity.

Fertility traits were found to be sensitive to the herd management level (i.e. herd average yield). For example, Strandberg et al. (2000) used a random regression model to study G×E interactions between populations of Nordic Red and White cattle (Finnish Ayrshire, Norwegian Dairy Cattle, and Swedish Red and White Breed). The production environment was the herd-year average protein production as a deviation from the overall year averages across the three countries (Finland, Norway, and Sweden) the authors found that heritability of DO decreased with increasing production level. Re-ranking of sires was found when herd year averages that were 2 SD units above the average production level indicating a G×E effect for DO with production environment. Kolmodin et al. (2002) reported an increase of heritability estimates for DO with increasing herd-year protein production, and although there was a large heterogeneity of additive genetic variance found for DO, there was a small G×E interaction. When the production environment was classified into grazing or conventional herds in Canada, low genetic correlation of 0.64 was found for CI between environments. However, the heritability estimate for CI in grazing herds was twice the heritability estimate for CI in conventional herds (Boettcher et al., 2003). Furthermore, Kearney et al. (2004a) studied the G×E interaction for the DO, CFI and number of inseminations per conception (NINS) between grazing and confinement herds in US. They found that for DO and NINS the genetic correlations between the two environments was close to unity, although the heritability estimates were higher for the confinement herds. On the other hand, a genetic correlation less than unity was found for DO (0.74 ± 0.12) between the two environments. Haile-Mariam et al. (2008) used average herd lactation milk yield as continuous environmental descriptor for the magnitude of G×E interaction on fertility traits in Holstein cows in Australia. They found that the heritability of CFI decreased with increasing production environment where the heritability of CFI in the low production environment was almost 3 times higher than the heritability in the high

production environment. However, heritability estimates were homogeneous across the production environments for CI, and first service non-return rate. Furthermore, G×E interaction were found between low and high production environments (r_g = 0.47 and 0.58 found for CFI and CI, respectively). That means there is significant re-ranking of bulls across production environments for both traits. Random regression was also used by Strandberg et al. (2009) to model G×E interaction for fertility traits in UK with various environmental descriptors including the average herd production and they found G×E interaction indicated by a genetic correlation less than unity for CFI, between low and high production environments.

Another possible consequence of G×E interaction is a change in the genetic correlations between different traits in different environments. The application of multiple trait reaction norm models allow for genetic correlations between traits to vary across environments. For example, Kolmodin et al. (2002) used a multiple trait random regression model to investigate the heterogeneity of genetic correlation between days open and protein yield using the average herd protein production as environmental descriptor and found a decrease in the genetic correlation between days open and protein yield with increasing protein production. This means that the unfavorable genetic correlation between production and fertility is less important in the high production environment. Furthermore, Haile-Mariam et al. (2008) found heterogeneity of genetic correlation between CFI and milk yield using average milk yield as an environmental trajectory where the genetic correlation increased with increasing the production environment.

2.   Genetic selection for fertility traits in dairy cattle

Fertility in dairy cows is the ability of the animal to conceive and maintain pregnancy if served at the appropriate time in relation to ovulation (Darwash et al., 1997b). Failure to establish pregnancy at the appropriate time is caused by many problems including failure to show and detect estrus, failure to ovulate, inappropriate patterns of ovarian cyclicity (Royal et al., 2000).Therefore, Female fertility is a complex of many traits that reflects many abilities including the ability of cow to return to cycling after calving, estrus expression, conceive following insemination and become pregnant, and maintain pregnancy. For instance, CFI and heat strength (only recorded in Sweden) measures the ability of the cow to

show estrus and return to cycling after calving, while the IFL, NINS, and NRR within 56 d after the first service reflects the ability of the cow to show estrus and conceive (Jorjani, 2007; NAV, 2013).

There is evidence for declining fertility in dairy cows. For example, Washburn et al. (2002) studied the annual averages of estrus detection rates in US and found that estrus detection rates decreased from 1985 to 1999 where estrus detection went from 50.9 to 41.5% in Holsteins, and from 59.6% to 49.5% in Jersey cows. Furthermore, DO for Jersey cows increased by 30 days, and Holsteins increased 44 d of DO for the total period studied. Moreover, NINS increased from 1.91 to 2.94 over the same study period for both breeds. Also, in Sweden, CI increased from 12.6 months in 1974 and 1975 to 13.3 months in 2004 and 2005 (Petersson et al., 2007). Moreover, Fogh et al. (2003) reported a decline of fertility in Nordic countries where CFI and IFL increased by 8 and 12 days, respectively from 1980 to 1996, while NRR decreased by 4% during the same period.

The main obstacle faces the genetic improvement on dairy cattle fertility traits is that the traditional measures of fertility have low heritability estimates of < 0.1 (Roxström et al., 2001a, b; Wall et al., 2003; Averill et al., 2006; Hou et al., 2009; Sun et al., 2009; Sun et al., 2010; Zink et al., 2011). This may be because many fertility traits are categorical in nature (e.g., NRR and NINS), but even those measured on a continuous scale are heavily influenced by management decisions (e.g., voluntary waiting periods), and often include censored records (e.g., missing records for cows that did not cycle or conceive within the observation period) (Sun et al., 2009), which complicates the analysis of the traits and leads to large unexplained variation that can mask genetic effects (Berglund, 2008).

Another important obstacle is the antagonistic relationship between fertility and milk production confirmed in many studies. For example, Roxström et al. (2001a) found genetic correlations ranged from 0.2 to 0.4 between 305 days protein yield and NINS, CFI and IFL in Swedish Red and White dairy cattle. Berry et al. (2003a) used random regression model to estimate the genetic correlation between milk yield and fertility traits as a function of lactation stage and found that the genetic correlation ranged from 0.08 to 0.35 between milk yield and CFI and from 0.28 to 0.58 between milk yield and NINS and from -0.70 to -0.24 between milk and pregnancy rate first service in Holstein cows in Ireland. In Holstein cows

in Germany, König et al. (2008) found genetic correlations of -0.31 and 0.14 between milk yield on one hand and NRR56 and CFI, respectively. These unfavorable correlations mean that selection for increased milk yield will increase the CFI, IFL, NINS and will decrease pregnancy rate first service NRR56. For that reason, selection indices worldwide have changed their previous focus on yield to a more balanced breeding approach that includes longevity, udder health, and fertility (Miglior et al., 2005). However, the genetic progress for fertility traits in Nordic cattle breeds, has been increased by 20% from 2001 till 2013 (SEGES, 2015).

Although cattle are not strictly seen as seasonal breeders, previous studies on fertility traits indicated that a large fraction of the variability in reproduction traits is affected by seasonal changes and climatic factors such as temperature, humidity, and daylight length. For example, at the phenotypic level, DO in September calvings was 50 days longer than for March calvings in US Holstein (Oseni et al., 2004). The same trend for days open was found in Thai Holstein crossbreds where cows calving in March remained open 40 days longer than cows calving in October (Boonkum et al., 2011). Sensitivity to seasonal effects on conception rates was also found by Huang et al. (2008) who reported that cows inseminated in March and April have 10% higher conception rates than cows inseminated in May and June in US Holsteins in New York. Moreover, the effect of seasonal factors such as temperature and humidity expressed as temperature humidity index (THI) as an indicator for heat stress was reported for NRR. NRR decreased by 0.50 - 0.70 percentage units per unit increase of THI > 20 °C on the day of insemination (Ravagnolo and Misztal, 2002b). In the same study, a difference of 10% in NRR was observed between THI < 21 °C and THI=29 °C. Hansen and Hauser (1984) reported that cows calving in the fall and winter that received supplementary light were found to have shorter interval from calving to first estrus and shorter interval from calving to first conception compared with cows receiving only natural lighting hours. Also, Reksen et al. (1999) reported that shorter DO, shorter CI and fewer NINS were required per cow for the herds exposed to supplementary illumination at night compared with herds without light at night in Norwegian Red Cattle. Moreover, estrus occurrences from November till March were less frequent than that from April till October with a positive correlation of 0.39 between the estrus occurrences and the hours of sunshine duration (Bülbül and Ataman, 2009). Similar effect of calving season found for interval from calving to commencement of luteal activity (C-LA) was reported by Royal et al. (2002a) and

Petersson et al. (2006), where C-LA was shorter for cows calved in summer season compared with those calved in the winter season by 8.0 and 10.5 days in UK and Sweden, respectively. It was also shown previously that fertility of dairy cows is sensitive to the heat stress during summer months in North America and that the sensitivity to heat was largest in cows with highest genetic merit for milk production (Ravagnolo and Misztal, 2002a).

2.1. Current traits used to measure the cow fertility

The traits used to measure the cow fertility should reflect the cow's ability to return to cycling status after calving, conceive following insemination and become pregnant, and maintain pregnancy. Therefore, the methods used to measure fertility on indirect measures such as:

The Interval form Calving to First Insemination (CFI): Is an economically important trait in the Nordic Total Merit index (NTM), because it measures the cow's ability to return to cyclic status after calving. The trait is also found to be favorably correlated with the ability of the cow to conceive following inseminations and thus become pregnant. For example, Haile-Mariam et al. (2003) reported that at the phenotypic level, cows with shorter CFI had higher pregnancy rates, shorter calving interval and higher first insemination NRR. Furthermore, the estimated genetic correlations between CFI and pregnancy rate, CI, and first insemination NRR were -0.84, 0.55, and -0.69 respectively. That means selection for shorter CFI is beneficial to the overall fertility. However, the major disadvantage of CFI is that the trait is heavily influenced by the management practices such as inseminating high-yielding cows later than low-yielding cows or the herd's voluntary waiting period (Andersen-Ranberg et al., 2005; Löf et al., 2012).

Days Open (DO): Is defined as the time interval from calving to conception and measure the ability of the cow to conceive following insemination and become pregnant. The disadvantages of DO is that beside the potential bias due to management practices or the herd's voluntary waiting period, the trait is heavily biased from including only the cows that become pregnant, whereas the trait is not defined for the cows that are inseminated and not confirmed pregnant (Ferguson and Galligan, 2000; Leblanc, 2010).

Interval from First to Last Insemination (IFL): Is defined as the number of days between the first insemination and the service of conception (Schneider et al., 2006). The trait is a combination of the cow's ability to show estrus, conceiving following inseminations, and becoming pregnant. The trait is less affected by farmer decisions. However, the trait is heavily affected by the estrus detection rates in the herds (Flores, 1971).

Non-Return Rate (NRR): Is defined as the proportion of cows that are not subsequently re-bred within a specified period of time after an insemination, typically within 56 days. The trait is widely used because it is easy to measure (Leblanc, 2010). However, the trait faces a major drawback because of the unrealistic assumption that all cows not re-bred are pregnant which overestimates the actual proportion of cows becoming pregnant (Weigel, 2004).

Calving interval (CI): Is defined as time between successive calvings. The disadvantage of this trait is that it can only be recorded for cows with more than one calving. Besides, the length of the calving interval may be greatly affected by management decisions because the farmer may intentionally increase or decrease the length of the interval for certain cows (LeBlanc, 2013).

Pregnancy rate (PR): Is defined as the probability that an open cow will become pregnant in a given time frame. The time frame here is 21 days period, which is the length of an estrus cycle. It is considered the best available single measure of the overall reproductive performance (LeBlanc, 2005). The major advantage of PR is that non-pregnant cows are included and contribute time eligible for pregnancy as long as they remain in the herd (LeBlanc, 2013).

2.2. New fertility traits

Detecting a high percentage of cows in estrus is important to maintain high reproductive performance in dairy herds using AI. Accurate estrus detection is important because the false positive detection of estrus will result in missed and untimely inseminations which increase the insemination costs, increase the number of inseminations per pregnancy with consequent losses of income caused by prolonged calving intervals, and expenditure on replacement heifers because of non-successful inseminations (Firk et al., 2002).

New technologies have been developed that allow automated estrus detection that can support or replace visual estrus detection, which is time consuming and labor challenging, with large herd size. Accurate estrus detection by visual observation also requires expertise and well trained manpower (Lucy, 2001; Chanvallon et al., 2014). Furthermore, automated estrus detection allows recording for other fertility traits that have not been included in breeding programs before. Automated estrus detection may also be seen as a more objective method than visual detection. Using objective measures that directly reflect physiological or behavioral changes is not only useful for automated estrus detection, but also has been shown to provide less biased measures. Thereby they could provide better heritability estimates than the traditional measures of fertility and thus, could be helpful in selection for improved female fertility (Petersson et al., 2007; Løvendahl and Chagunda, 2009; Tenghe et al., 2015). Several estrus-related changes have been used for the automated estrus detection includes, mounting events, activity level, lying time, rumination events, and milk progesterone (P4) levels (Petersson et al., 2007; Friggens et al., 2008; Løvendahl and Chagunda, 2010; Saint-Dizier and Chastant-Maillard, 2012; Fricke et al., 2014; Dolecheck et al., 2015).

2.2.1. Milk progesterone measurement

The basic principle behind this technology is that in the non-pregnant cow, the lysis of the corpus luteum 3 days before ovulation leads to a decline in the blood concentration of progesterone (P4) (Saint-Dizier and Chastant-Maillard, 2012). The P4 concentration also decline in milk, because the concentration in milk is closely correlated with that in blood (Roelofs et al., 2006). Thereafter, a set of biological rules are applied to translate the progesterone measurements and classify the cows into 3 different reproductive statuses: post-partum anestrus, estrus cycling and pregnant (Friggens and Chagunda, 2005; Friggens et al., 2008). For estrus cycling cows, an alert is triggered by the software as soon as the P4 value declines below 4 ng⁄ml (Friggens and Chagunda, 2005). Friggens et al. (2008) validated the milk P4 measurements obtained from Herd Navigator system in an experimental herd in Denmark using a subset of cows that had undergone successful AI based on confirmed pregnancy, the estrus detection rate obtained was 99% with a specificity of 94%.

The interval from calving to first commencement of luteal activity (C-LA) occurs 4 to 5 d after first ovulation, and measures the ability of cow to return to cycling after calving (Petersson et al., 2006; Petersson et al., 2007). This trait can be determined by evaluating progesterone profiles, and have heritability estimates between 0.16 to 0.30, which is considerably higher than the heritability estimate of the interval from calving to first insemination. Furthermore, on the genetic level, C-LA was correlated with CFI, NINS, and CI with genetic correlation estimates of 0.53, 0.05, and 0.39, respectively (Royal et al., 2002b; Royal et al., 2003), indicating that selection for a shorter interval from calving to estrus will benefit overall fertility. Furthermore, C-LA showed unfavorable genetic correlation with milk production traits that ranged between 0.04 to 0.18 (Tenghe et al., 2015).The drawback of C-LA is that it is based on frequent measuring of milk P4 (Petersson et al., 2007), which is both costly and logistically challenging: milk samples in the regular milk recording are usually taken infrequently (once a month). However, the progesterone measuring tools have developed allowing the instant measure of milk progesterone by Herd Navigator (HN) (DeLaval International, Tumba, Sweden). In that system, milk is sampled automatically then the progesterone levels in milk are measured immediately and automatically on-farm thus avoiding transport delays and cost (Friggens et al., 2008; Tenghe et al., 2015). However, the HN system is still a major expense for the farmer because of the cost of initial implementation, and the additional cost per cow per year for assay reagents (Saint-Dizier and Chastant-Maillard, 2012).

2.2.2. Activity monitor devices

The basic principle behind this technology is measuring the behavioral changes that occur around estrus in dairy cows. Restlessness is one of the behavioral changes that occur during estrus (Van Eerdenburg et al., 1996; Roelofs et al., 2010). Restlessness behavior has different indicators such as, increased walking activity, following other animals, increased number of position changes, and decrease in the total daily lying time during estrus (Walton and King, 1986; Van Eerdenburg et al., 1996; Diskin and Sreenan, 2000; Kerbrat and Disenhaus, 2004). Restlessness behavior is difficult to detect visually without technical aids (Roelofs et al., 2010). To measure this type of behavior, 3 types of devices are currently available as following: (1) Pedometers attached on one of the legs, which record the number of steps made by the cow per one or two hours bin. (2) Activity tags attached around the

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neck, which measure the cow's activity as the number of electronic impulses per one or 2 hours bin triggered by changes in acceleration due to head and neck movements. (3) Pedometers or activity tags attached to the leg or neck that measure the number of steps or neck movements and quantify lying and standing behaviors using 3d-accelerometer technology (Roelofs et al., 2010; Saint-Dizier and Chastant-Maillard, 2012). Thereafter, the activity data are recorded continuously and transmitted to a receiver at regular time intervals before being forwarded to database in a herd computer. The software supplied with each device triggers an alert for the cow in estrus using estrus detection algorithms that vary between the different manufacturers (Saint-Dizier and Chastant-Maillard, 2012). The efficiency of estrus detection using pedometers or activity tags is generally higher than 80% but varies considerably depending on the devices and the algorithm used by the estrus detection software. That includes the setting of threshold and the reference period of previous activity that are used to define the increase in activity, as well as with the recording intensities (At-Taras and Spahr, 2001; de Mol and Woldt, 2001; Firk et al., 2002; Roelofs et al., 2005; Løvendahl and Chagunda, 2010).

For example, Roelofs et al. (2005) used pedometers for activity measurements recorded in 2 hours interval to describe the estrus characteristics and reported estrus detection rate of 87%. Furthermore, the average estrus duration recorded by pedometers was 10 hours compared to 12 hours by visual observation for 30 minutes every 3 hours. Moreover, the estrus duration recorded by pedometers was positively correlated with the visual estrus duration (r = 0.53), and standing estrus (r = 0.38), while estrus intensity recorded by pedometers (average number of steps) was positively correlated with the individual behavioral signs including sniffing, chin resting, mounting and standing estrus (r: 0.28 to 0.46).

In another study, Løvendahl and Chagunda (2010) used activity data generated from activity tags to develop an algorithm to detect and characterize behavioral estrus from hourly recorded activity data and reported estrus detection rate of 75% with daily error rate of 1.3% using exponentially smoothing algorithm to identify onset, duration, and intensity of estrus. The estrus duration lasted for 8.12 hours, with the average strength of 1.03 ln units (equivalent to a 2.8-fold increase of activity). Furthermore, the authors presented another alternative measure the ability of cow to return to cycling after calving that was the interval

from calving to first high physical activity (**CFHA**) that was found to have moderate heritability estimates of 0.12 to 0.18 (Løvendahl and Chagunda, 2009). The authors also reported the heritability estimates for other estrus-related traits, e.g. strength of high activity as an indicator for estrus strength (**SHA**, h^2 = 0.04 to 0.06) and duration of high activity as an indicator for estrus duration (**DHA**, h^2 = 0.02 to 0.08). Those traits are to our knowledge not measured today in breeding programs, except for Sweden, where a breeding value for a subjectively scored estrus strength has been included in the Swedish total merit index since 1999 (Swedish Dairy Association., 1999), and could be useful for improving the ability to detect cows displaying estrus behavior.

The main advantages of using the physiological or behavioral measures as a fertility indicator trait is that, it is a better reflection of the cow's inherent fertility. Even though these measures are influenced by environmental factors, they are less influenced by farmer's decisions or interventions (Darwash et al., 1997a; Pryce et al., 2004).

3. Objectives of the PhD project

Since the previous studies on G×E interaction for traditional fertility traits using multi trait approaches or reaction norm models found some evidence for G×E effects, it is also important to investigate the G×E interaction for fertility indicator traits derived from activity tags and the interval from calving to first insemination regarding to the environmental gradients such as season or month of calving, geographical position and production environment. Furthermore, the higher heritability estimate reported for CFHA will provide better opportunity to study G×E effects on fertility of dairy cows. Therefore, the overall objective of the project is to investigate the G×E effect in Nordic dairy cattle for fertility traits. Two types of fertility traits will be used. The automated fertility traits based on the physical activity measuring devices and, the traditional fertility traits based on the AI recording. More specifically the objectives are:

1. Estimating genetic parameters for the estrus based fertility traits developed from activity monitoring devices and their relationship with the interval from calving to first insemination seen as the traditional trait (Paper I).

2. Investigate the effect of calving season on the genetic parameters of three fertility traits (the interval from calving to first high activity, and the duration and strength of the first high activity episode) derived from activity tags and investigating possible G×E interaction (Paper II).

3. Investigate the G×E interaction of estrus related traits and its relationship with production traits with regards to the production environment using reaction norm models (Paper III).

4. Investigate the changes of genetic parameters and the possible existence of genotype by environment interaction on the interval from calving to first insemination by calving month and geographical location in Holstein cows in Denmark and Sweden (Paper IV).

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GENERAL DISCUSSION

In this thesis, fertility indicator traits based on activity and AI data were investigated for G×E interaction effect in Holstein cows from Denmark and Sweden. The first type of traits used is the activity-based estrus traits recorded with activity monitoring devices, including the interval from calving to first high activity episode (CFHA) as an indicator of the cow's ability to return to cyclic estrus after calving; duration of high activity episode (DHA) as an indicator for estrus duration, and strength of high activity episode (SHA) as an indicator for estrus strength. Initially, the genetic variation in these traits was studied, and their correlation to AI based fertility traits was validated. For these new traits, the effect of calving month on the phenotypic expression of the traits was studied and the genetic variation and G×E interaction with respect to the calving seasons were investigated using multiple trait approach. Furthermore, genetic parameters, G×E interaction and genetic correlation with production as a function of production level were investigated using reaction norm models. The second type of fertility traits used the interval from calving to first insemination (CFI) based on AI recording. The effects on the phenotypic expression, changes of genetic parameters and the existence of G×E interactions in relationship to calving month and geographical location in Holstein cows in Denmark and Sweden were investigated using a multiple trait approach. The detailed results were reported in 4 papers summarized and discussed jointly in the following.

In the first paper, the aim was to estimate genetic parameters for activity-based estrus traits including CFHA, DHA, and SHA, based on activity measurements from cows in Danish commercial herds, and to compare these with parameter estimates for CFI. In order to develop the activity-based estrus traits, an estrus detection algorithm to replace that used by the commercial manufacturer of the activity tags was developed to detect the high activity episodes. The performance of the new algorithm was similar to previously reported and validated algorithms with respect to detection and error rates (At-Taras and Spahr, 2001; Roelofs et al., 2005; Løvendahl and Chagunda, 2010). CFHA has a higher heritability than CFI (0.16 vs 0.07). Also, CFHA showed a strong genetic correlation with CFI (0.96), which indicates that these traits measure the same aspect of reproductive performance in cows. Moderate genetic correlations of 0.37 and 0.53 between CFI and C-LA were reported by

Tenghe et al. (2015) and Royal et al. (2003), respectively. This strong genetic correlation also implies that including CFHA, in addition to CFI, in the selection criteria might increase the genetic gain for the trait return to cyclicity. For example, if the CFI is the breeding goal trait and all cows had both CFI and CFHA records we expect 13% increase of the accuracy of selection compared with the accuracy obtained from using CFI records only. The study also showed that cows with a delayed first estrus or insemination also have a weak, short estrus, based on the moderate estimates of genetic correlation obtained between CFI or CFHA with estrus duration and estrus strength.

In this paper, heritability of CFI in the herds using activity tags intensively was 0.07 which is slightly higher than the previously reported heritability of 0.04 for CFI in Nordic countries (NAV, 2013).Thereby the AI record based fertility in herds using activity tags becomes more valuable without the need to collect the activity data. This aspect indeed has to be investigated in near future as we will see an increase in heritability coming from those herds since there are about 50% of herds using activity tags in Denmark (Peter Løvendahl, personal communication).

The results of this study have important practical implications. First, incorporating the new traits into the breeding program requires collection and storage of the activity data in a common database. This practice may cause little disruption, because activity tags are currently available in many herds. Second, in addition to measuring CFHA, activity tags can also measure other traits; e.g., estrus strength and estrus duration. These traits are not routinely measured in most current breeding programs, but they could be useful for improving the ability of cows to display estrus behavior.

In the second paper, the objective was to investigate the effect of calving season on the genetic parameters of activity based estrus traits including CFHA, DHA, and SHA derived from activity tags. In order to define the seasonality of the traits, we partitioned the data in three different ways: 1) into 4 subsets based on season of calving as follows: winter , spring , summer , and fall; 2) into a cold season and warm season; 3) into increasing light season (IL), where there is a gradual increase of daylight hours from 7.0 to 17.0 h, and a decreasing light season (DL), where there is a gradual decrease of daylight hours from 17.0 to 7.0 h.

On the phenotypic level, CFHA was more influenced by month of calving than was DHA and SHA. We found positive effect of summer season on CFHA, where cows calving in September had 24 days shorter CFHA than cows calving in December. We speculated that, the decrease of CFHA from May till September was associated with an increase of both daylight length and temperature, while the increase of CFHA from September to December was associated with the decrease of both daylight length and temperature in Denmark. Similar relationships between calving season and the interval from calving to commencement of luteal activity (C-LA) were reported by Royal et al. (2002a) and Petersson et al. (2006), where C-LA was shorter for cows calving during the summer season compared with those calving in the winter season, by 8.0 and 10.5 days in UK and Sweden, respectively. Furthermore, Oseni et al. (2004) reported a similar relationship between days open and season of calving, where spring calvers remained open 27 days longer than summer calvers. However, these studies did not specify the environmental components responsible for the seasonal variations for the interval form calving to first estrus. To our understanding the seasonal components responsible for this variation in the current study were the combined effects of daylight length and temperature.

Heterogeneity of genetic variation and heritability estimates was found for CFHA, DHA, and SHA with respect to all seasons. For example, heritability of CFHA for winter calvings was 3 times higher than the heritability of CFHA for spring calvings. There were clear indications of genotype by environment interaction for CFHA between calving seasons regardless of the seasonal classification.

In the third manuscript, the objectives were to estimate genetic parameters of fertility traits derived from activity tags (CFHA, DHA, and SHA), and estimate the genetic correlation between CFHA and energy corrected milk at 70 days in milk (ECM70) as a function of production level expressed as average herd ECM in Danish Holstein cows. Furthermore, results of random regression models were validated using bivariate model treating low and high production level as distinct traits.

Additive genetic variance and heritability estimates of CFHA decreased with the increase in herd production level. The observed decline in heritability of CFHA over the environmental trajectory was similar to those observed by Haile-Mariam et al. (2008) and

Strandberg et al. (2009) on the interval from calving to first insemination in Holstein cows in Australia and UK, respectively.

The additive genetic variance and heritability estimates of ECM70 decreased with the increase in herd production level. This result was in contrast the previous studies that reported an increase of genetic variance and heritability estimates for milk yield traits using production level as an environmental trajectory. In our study, the results of the univariate random regression model (URRM) for ECM70 do not seem to be an artifact of the random regression model, because the same trend was found in the bivariate model (BM) analysis, albeit with a smaller difference.

Genetic correlations for CFHA, DHA and ECM70 estimated between low and high production level were around 0.80 and were not different from unity indicating that these traits are under the control of the same genes regarding to the production environments and the G×E effect is therefore less important.

The genetic correlation between CFHA and ECM70 was heterogeneous as a function of herd production level and decreased with increasing production level. This suggests that the unfavorable genetic correlation between CFHA and ECM70 could be alleviated by providing better level of the production environment.

In the fourth manuscript, the objectives were to investigate the changes of genetic parameters and the existence of G×E interactions for CFI in relationship to calving month and geographical location for Holstein cows in Denmark and Sweden. AI data from first parity Holstein cows in Denmark and Sweden were used to study the effect of month of calving and geographical location on the genetic parameters of CFI. We found that heritability, genetic variance and residual variance of CFI were heterogeneous across calving months. Generally, cold months were associated with high heritability estimates compared with warm months, with the highest heritability estimate obtained for January calvings. This estimate was three times higher than the estimate for June calvings. These results corroborated the findings of the second paper of the effect of calving season on the CFHA. Our results indicated that seasonal variability in both CFHA and CFI has genetic variation.

Genetic variance and heritability estimates of CFI were heterogeneous across different geographic locations in Denmark and Sweden. Heritability estimates decreased with increasing latitude, from south to north, where the heritability estimate obtained for southern locations was twice the heritability estimate found for the most northern. The main reason for this difference is the genetic variance, which in the south location was twice that in north. Another reason for that is, increasing the residual variance with increasing latitude, where the lowest residual variance was found in south and the highest in north. One explanation for this that the differences between southern and the most northern location regarding to the number of herds and herd sizes, where the southern locations are characterized by less number of herds and much larger sizes than those in most northern. Thus one could speculate that large dairy herds may be better managed in terms of the efficiency of heat detection using activity tags or pedometers to prompt AI services.

Genetic correlations of CFI between months of the winter season on the one hand and months of the spring and summer seasons on the other have the lowest estimates of genetic correlations, where genetic correlations less than 0.80 were found between cold months (December and January) and warm months (June, August and September), indicating there is a significant G×E interaction leading to re-ranking of sires between these months, but the re-ranking is greatest between the January and September calvings. Regarding to geographic location, genetic correlations of CFI between different geographic location classes were very high and most of the estimates were close to unity, indicating that CFI is under the control of the same genes in different locations and the G×E interaction is less important and leads to only a scaling effect. Therefore, sires from different locations in Denmark and Sweden could be used without concerns about the effect of a G×E interaction due to effects of geographic location.

In this thesis, I showed that physical activity data recorded with electronic activity tags were not only useful for heat detection, but also helpful in recording of activity based estrus traits from the field dataset (paper I). This encourages the opportunity to extend the research using the all physical activity data available in Danish herds form different kinds of activity monitoring devices. However, more research is required to investigate whether the same heat detection algorithm we used in the current thesis could be applied to different activity tags from different manufacturers, which may have used different recording

intensities (1-h or 2-h time bins). This step is required before combining the traits developed from different kinds of activity tags into single database.

The major consequence of heterogeneity of genetic variances (paper II, III, and IV) is that selection in the average environment using estimated breeding values leads to different selection responses in different environments (Falconer and Mackay., 1996). For example, if the selection for shorter CFHA was performed in an environment where cows calved in increasing light season (IL), then the response to selection would be different in the environment where cows calved in decreasing light season (DL). This issue was introduced clearly by Calus et al. (2005) and Calus et al. (2006) who found that selection for higher fertility and lower somatic cell score will gain higher selection responses in herds with on average poorer fertility and higher somatic cell score. Moreover, significant heterogeneity of heritability estimates for the traits across environments can cause heterogeneity of accuracies of animals tested in different environments (Hill et al., 1983).

The consequence of the significant G×E interaction found for CFHA and CFI regarding to season or month of calving (paper II and IV) is that selection for shorter CFHA or CFI when this form of G×E is ignored is limiting the rate of genetic progress. Recently, Mulder et al. (2006) reported that for traits with correlations of less than 0.61 between environments it can be more efficient to run two separate breeding programs specific to each environment. However, running two breeding programs is not appropriate, when farmers prefer cows that are fertile year round. Alternatively, this could suggest the use of specific breeding values for each calving seasons, but that approach increases complexity of selection and may not benefit progress in the population. For G×E interaction effects, in case of the scaling effect for the traits in different calving seasons, corrections of the estimated breeding values to an average environment would be sufficient without any consequences on selection decisions (Meuwissen et al., 1996).

In paper IV, the multiple trait approach was used to study the G×E effect for CFI regarding to month of calving. In a preliminary analysis, similar results were obtained using the average monthly daylight length as an environmental descriptor.

In this thesis, activity monitoring devices were used to measure the cow's ability to return to cyclic estrus after calving, while other studies used milk progesterone to measure the same aspect of fertility. The latter are unable to measure the duration and strength of estrus related behavior compared with activity tags. However, the use of both these technologies remains limited by cost and the availability for farmers. Alternatively, visual observations for behavioral estrus signs could be carried out frequently allowing the visual evaluation for estrus duration and estrus strength. However, the use of this method will be hampered by that skillful labor is required for the intensive evaluation of estrus events in large herds. Furthermore, the recording for estrus strength will be heavily influenced by the subjective scoring for estrus behavior.

FUTURE PERSPECTIVES

In this study, heat detection algorithm was built and used to detect the high activity episode before developing 3 activity-based estrus traits. The heat detection algorithm was validated on a subset of cows that had undergone successful AI, based on birth of a calf or a confirmed pregnancy and we found detection rate of 87% and daily error rate of 0.9%. However, studying the relationship between the true estrus behavior duration and strength on one hand and the activity-based estrus duration and strength on the other hand is required before using these traits for recording for activity-based estrus traits.

The activity-based estrus traits reflect the cow's ability to return to cyclic estrus after calving and the ability to show estrus. Investigating the genetic and phenotypic correlation between these traits and traits reflecting ability to become pregnant and maintain pregnancy is required to improve the effectiveness of selection for fertility. For example, the relationship between estrus traits and days open, interval from first to last insemination, calving interval, and pregnancy rate is needed.

In this study, the mechanisms of action underlying the seasonal variations for activity-based estrus traits and CFI are not well known. On the other hand, in real situations light and temperature are confounded. Perhaps more controlled experiments are required to study these factors including temperature, humidity, nutrition, daylight length, supplementary illumination, level of production, but this is not required for the purpose of genetic selection.

CONCLUSIONS

Activity-based traits are heritable, and CFHA is closely correlated to the traditional fertility trait, CFI. The heritability of CFHA is higher than that of CFI, and a strong genetic correlation is found between these two traits. Therefore, including CFHA in the selection criteria, in addition to CFI, would increase the genetic drive for a rapid return to cyclicity, which would also have a positive impact on the overall cow fertility. Furthermore, selection for estrus duration and estrus strength may improve heat detection, due to a longer display period and stronger activity peaks.

CFHA was more influenced by seasonal variation than DHA and SHA. Heterogeneous genetic variation was found for CFHA, DHA, and SHA with respect to all seasons, and there were clear indications of genotype by environment interaction for CFHA between calving seasons regardless of the seasonal classification. This implies that if we want to select sires for shorter CFHA, the feasibility of having separate breeding values for given environments should be considered.

Heterogeneous genetic variation was found for all traits as function of production environment, while the genetic correlation estimates of the trait between low and high production environment showed no evidence of G×E existence because they were not significantly different from unity. Genetic correlations between CFHA and ECM70 decreased with increasing the production level implying that the unfavorable genetic correlation between fertility and milk yield traits could be decreased by improving the production environment.

At the phenotypic level, CFI was affected by calving months, such that the performance improved in warm months compared with cold months. Genetic variances, residual variances and heritability estimates were heterogeneous across calving months but less so between geographic locations. Genetic correlations between different calving months and geographic locations were mostly close to unity, indicating that sires are ranked more or less similarly under a wide range of calving months and geographic locations in Denmark and Sweden.

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INDIVIDUAL TRAINING PLAN (ITP)

TRAINING (30 ECTS minimum)		
Mandatory courses	**Where/when**	**ECTS**
Introduction course for PhD students	28/11/2011 AU	2.00
EGS-ABG Early Fall school 2012 "Animal Breeding and the Society"	24/09/2012 AU	2.00
EGS-ABG Early Fall school 2013 "Food security in developing countries"	27/10/2013 Ethiopia	2.00
Scientific practice	10/10/2012 AU	1.00
Academic English for Non-Danish Speaking PhD students	04/02/2013 AU	3.00
Advanced scientific courses (≥18 ECTS)		
PhD course in Quantitative Genetics	01/02/2012 AU	5.00
Statistical modeling in life and environmental sciences	23/10/2012 AU	4.00
Linkage and association gene mapping	29/01/2013 AU	5.00
Sustainable breeding plans for animal breeding	05/08/2013 AU	5.00
Introduction to Statistical methods in quantitative genetics and breeding	03/03/2014 SLU	4.00
Total credits (≥30 ECTS)		**33**
DISSEMINATION OF KNOWLEDGE		
International conferences and workshops	**Where/when**	
Effects of Climate Change on Primary Industries in the Nordic Countries. (Participant) AnGR-NordicNet Workshop: Effects of Climate Change on Primary Industries in the Nordic Countries.	Uppsala, Sweden, November 2011	
Genetic variation in sensitivity to environmental changes in dairy cattle. (Oral presentation) at the 6th International Cattle Breeders Round Table (ICBRT).	Norway, Hamar, March 2012.	

Managing Small Populations With Pedigree And/or Genomic Information. (Participant) NordGen workshop in animal breeding in the Nordic and Baltic countries. Organized by Nordic Genetic Resource Center (NordGen).	Latvia, Riga, June 2012
Environmental sensitivity in dairy cattle with focus on fertility traits. (Poster presentation) at the workshop of Genotype-by-Environment Interactions and Adaptation of Farm Animals on Phenotypic and Molecular Level.	Finland, Tussula, November 2012
Automated Estrus Traits: Higher Heritability and Well Suited to Study G × E. (Poster presentation) at the International Conference of Genetic Resources for Food and Agriculture in a Changing Climate.	Norway, Lillehammer, January 2014
Estrus Traits Derived from Activity Measurements are Heritable and Closely Related to Conventional Estrus Traits. (Poster presentation) at the 10th World Congress on Genetics Applied to Livestock Production (WCGALP).	Canada, Vancouver, August 2014
Season Affects Expression and Heritability of Automatically Recorded Estrus Traits in Danish Holstein. (Oral presentation) at 66th Annual Meeting of the European Federation of Animal Science (EAAP).	Poland, Warsaw, August 2015