Reaction Norms for the Study of Genotype by Environment Interaction in Animal Breeding

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Abstract

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A reaction norm describes the phenotype of an individual as a function of the environment. A reaction norm model is useful for describing traits that change gradually and continuously over an environmental gradient, for example temperature or feed quality. In this thesis the usefulness of reaction norm models for the study of genotype by environment interaction (GxE) was evaluated. Field data of Nordic red dairy cattle were analysed using reaction norm models, with the purpose of describing the amount and pattern of GxE. Effects of various environmental variables on milk protein yield, days open and length of productive life were studied. The results showed that over the range of environments commonly encountered within Sweden and the Nordic countries, re-ranking of sires due to GxE was negligible.

The slope of a linear reaction norm measures the sensitivity of an individual towards a change in the environment. A simulation study of environmental sensitivity showed that, in the presence of GxE, the average environmental sensitivity is expected to increase in a population selected for high phenotypic value in a continuously improving environment. As genetic variation was found for environmental sensitivity of milk protein yield, days open and length of productive life of dairy cattle it is possible to change environmental sensitivity of these traits with selection. Genetic evaluation of environmental sensitivity is possible using a reaction norm model.

Response to mass selection of a trait affected by GxE was described using a linear reaction norm model combined with selection index theory. Prediction equations were derived for the genetic change in reaction norm coefficients and the average phenotypic value in any environment, depending on the environment in which the animals were evaluated and selected. A breeding program can be optimised by choosing the selection environment that gives the maximum genetic progress for a given breeding objective and environment where the animals are required to live. Equations were derived to predict this optimum selection environment.

Keywords: dairy cattle, days open, environmental sensitivity, genetic correlation, milk protein yield, productive life, random regression model, selection response, simulation, variance component estimation

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Till mormor
Jag önskar du hade varit med

Contents

Appendices

Publications I-V

This thesis is based on the following publications, which will be referred to by their Roman numerals.

I. Kolmodin, R., Strandberg, E., Madsen, P., Jensen, J. & Jorjani, H. 2002. Genotype by environment interaction in Nordic dairy cattle studied by use of reaction norms. *Acta Agric. Scand., Section A, Anim. Sci.*. 52, 11-24.

II. Kolmodin, R., Strandberg, E., Danell, B. & Jorjani, H. 2003. Reaction norms of protein yield and days open in Swedish Red and White dairy cattle in relation to various environmental variables. Submitted.

III. Petersson, K-J., Kolmodin, R. & Strandberg, E. Genotype by environment interaction for productive life in Swedish Red and White dairy cattle. Submitted.

IV. Kolmodin, R., Strandberg, E., Jorjani, H. & Danell, B. 2003. Selection in the presence of a genotype by environment interaction: response in environmental sensitivity. *Anim. Sci.* 76, 375-385.

V. Kolmodin, R. & Bijma, P. Response to mass selection when genotype by environment interaction is modelled as a linear reaction norm. Submitted.

Publications I and IV are reproduced with permission of the journals concerned.

List of abbreviations

ANOVA	analysis of variance
CR	correlated response
DOP	herd-year average of days open
EAST	geographic location in km east of a reference line 1500 km west of the middle of Sweden
ES	population average overall environmental sensitivity
GxE	genotype by environment interaction
Interbull	the International bull evaluation service
MACE	multiple-trait across country evaluation
NORTH	geographic location in km north of the equator
PEAK	herd-year average of peak milk yield
PROT	herd-year average of lactation protein yield
STEMP	average summer temperature
WTEMP	average winter temperature

Introduction

Living organisms respond to changes in their environment; *e.g.* both animals and plants grow fast when nutrients and water are abundant, but slower when water and nutrients are scarce. The ability to alter the phenotype in response to changes in the environment is called phenotypic plasticity (Bradshaw, 1965) or environmental sensitivity, a phrase more often used in animal breeding literature (*e.g.* Falconer & Mackay, 1996). Environmental sensitivity has a genetic basis and can be manifested at the biochemical, physiological, behavioural, and other levels of the organism (Schlichting & Smith, 2002).

Differences in environmental sensitivity between individuals result in genotype by environment interaction (GxE), *i.e.* the difference between the phenotypes of two genotypes is not the same in two environments. If the difference changes sign between environments, the effect of GxE is re-ranking of individuals. If the difference changes in magnitude, but not in sign, there is a scaling effect (Falconer & Mackay, 1996).

The genotype considered when studying GxE is defined *e.g.* by the alleles of a specific locus, by the unique combination of genes of each individual, or by the genes shared by a group of sibs. The environment in the concept of GxE may be described by one of the many factors that influence an individual. Depending on the aim of the study, one may choose to characterise the environment by the temperature, light conditions, availability of nutrients, *etc.* If the interest is not in a specific environmental factor, one may instead use an indicator of a complex of environmental factors influencing a population, such as herd characteristics (production level, management system *etc.*) or the country or region where each individual is living.

Methods for the analysis of GxE

To study GxE, observations are needed on the same or related individuals in two or more environments. Through the common use of artificial insemination in dairy cattle, daughters of the same sire are often spread over many herds in many countries. This offers opportunities to compare the performance of daughters in different kinds of environments. When analysing experimental or field data, the existence of GxE can be detected as a significant interaction term in a two-factor ANOVA, where the genotype and the environment are the two class factors. For further analysis of GxE, there are two classes of models that are commonly used: character state models and reaction norm models. The two models are often, but not always, mathematically interchangeable (de Jong, 1995).

Character state models

In a character state model, phenotypic values in different environments and correlations between these 'character states' are analysed. This approach was first suggested by Falconer (1952). When the genetic correlation between the phenotypic values of the same genotype expressed in different environments is high, the character states are to a large extent controlled by the same set of genes. A low genetic correlation means that the phenotypic expressions in the different environments should be considered as separate traits, determined by partly different sets of genes, and is an indication of GxE (Falconer & Mackay, 1996). Environmental sensitivity is measured as the difference in phenotypic values between environments. Change in environmental sensitivity is described as a correlated response to selection on phenotypic values within environments (Via *et al.*, 1995). If the same individual cannot be measured in more than one environment, information from relatives is needed for the estimation of genetic correlation between environments and environmental sensitivity.

The character state method, as the ANOVA analysis, requires classification of environments into groups, such as herds, countries, or production levels. Clustering methods can be used to group the observations with reference to several environmental factors (*e.g.* Weigel & Rekaya, 2000). The multiple-trait across country evaluation (MACE) used by the International Bull Evaluation Service (Interbull) for routine international genetic evaluation of dairy sires is a character state model: performance in each country is treated as a separate trait, and GxE is accounted for through the genetic correlations between countries (Interbull, 2003).

Reaction norm models

A reaction norm describes the phenotype as a continuous function of the environment (*e.g.* Woltereck, 1909, in: Lynch & Walsh, 1998). Reaction norm models often express the phenotype as a polynomial function of the environmental value, where the polynomial coefficients are assumed to be under genetic influence (*e.g.* Gavrilets & Scheiner, 1993 a, b; de Jong, 1995). The reaction norm approach is useful when phenotypes change gradually and continuously over an environmental gradient (de Jong, 1995). Examples of environmental gradients are temperature, humidity, and feed quality. Complex environments are often quantified by the mean performance of all genotypes in each environment, *e.g.* the herd average production level (*e.g.* Finlay & Wilkinson, 1963; Perkins & Jinks, 1973; Publications I-III).

In a reaction norm model environmental sensitivity is defined as the first derivative of the reaction norm function, *i.e.* the slope of a linear reaction norm (de Jong, 1995). Genetic variation in polynomial coefficients indicates GxE, *i.e.* genetic variation for environmental sensitivity. Change in environmental sensitivity can be the result of selection acting directly on the reaction norm coefficients or a correlated response to selection on phenotypic values within environments (Via *et al.*, 1995).

Within the range of environments normally encountered, it is often reasonable to assume that reaction norms are linear. This has been found *e.g.* for production and functional traits in dairy cattle in relation to the herd-year average of the same trait (Calus & Veerkamp, 2003; Publications I-III). However, a linear increase in phenotypic value would not likely be found, for biological reasons, over very large environmental ranges. Extrapolation of predicted reaction norms outside the environmental range of the data should therefore be done with caution.

Second degree polynomial functions (quadratic reaction norms) can be used to describe situations where there is an optimum environmental value. Quadratic reaction norms have been found for milk yield in relation to the peak calving date of the herd and milk protein yield in relation to milk fat over protein ratio (Calus & Veerkamp, 2003), as well as for milk yield in relation to herd size, within herd SD of milk yield, number of days from calving to peak yield, calving pattern in the herd, ratio of first and second lactation milk yields, and 10 year average rainfall (Fikse, Rekaya & Weigel, 2003a).

A sigmoid shaped reaction norm with a steep slope at the inflection point can be used to describe a categorical trait with two discrete phenotypic values but with an underlying continuous distribution of genetic and environmental effects. The inflection point marks the threshold between the phenotypic values (Scheiner, 1993).

Prediction of reaction norms and covariance functions

A covariance function is a modification of a character state model to describe an infinite number of character states over a continuous gradient of environmental values. In principle, the covariance function interpolates between the values of a covariance matrix to describe the covariances between any pair of character states, and it can be illustrated as a smooth three-dimensional surface (Kirkpatrick & Heckman, 1989; Kirkpatrick & Lofsvold, 1989). Covariance functions are used for modelling traits that change over time, such as growth and lactation, or over an environmental gradient, *i.e.* to model reaction norms (Kirkpatrick & Lofsvold, 1989; Kirkpatrick, Hill & Thompson, 1994), thus combining the character state and the reaction norm model.

Reaction norms are visualised by plotting phenotypic values against environmental values. For large data sets, reaction norms are estimated by regression analysis. A reaction norm for a population is estimated by a fixed regression of mean phenotypic values in each environment on the environmental gradient. Individual reaction norms can be predicted by random regression of phenotypic values of related animals on the environmental gradient, assuming the same individual cannot be measured in many environments. A random regression reaction norm model is equivalent to a covariance function when modelling a longitudinal trait, as both models fit a variance-covariance structure of repeated measurements over a trajectory (Meyer & Hill, 1997; van der Werf, Goddard & Meyer, 1998).

Random regression models

The use of random regression models in animal breeding started with test day models, modelling lactation curves of individual cows (Schaeffer & Dekkers, 1994). Random regression models are, however, useful for the analysis of any longitudinal data; *i.e.* observations that are taken repeatedly over time or space. Typically, random regression models are used to predict, besides lactation curves, reaction norms, growth curves, or egg production curves. The special feature of the random regression model is that it includes a function nested within a random effect and that it allows variance components to change along a trajectory. In animal breeding applications, the function is nested within individuals, thus modelling individual deviations from a fixed regression of the trait on the explanatory variable (Jamrozik, Schaeffer & Dekkers, 1997). The random regression function often describes the additive genetic effect (modelling the genetic deviation from the fixed regression) and sometimes a permanent environmental effect.

The estimates resulting from the random regression analysis are breeding values for the coefficients of the function that describes the lactation curve or reaction norm. In addition, the (co)variances of those coefficients are estimated. The estimated parameters contain information about changes of the measured trait over time or space, the covariance structure between measurements, and the possibilities for change of the shape of the reaction norm or lactation curve in response to selection (Kirkpatrick & Heckman, 1989; Kirkpatrick & Lofsvold, 1989). The coefficients can be used to construct breeding values for performance at a specified time, age or environment, during an interval, and for the stability of performance (Jamrozik, Schaeffer & Dekkers, 1997). Thus, when there is genetic variation for the random regression coefficients, it is possible to change with selection not only the performance at a specified point, but also the pattern of performance (Huisman, 2002).

The random regression model has the following advantages over a traditional multi-trait model, which treat observations at different points in time or space as different traits (character state approach): With observations at many points there is a computational advantage that fewer parameters need to be estimated (*e.g.* Meyer & Hill, 1997; van der Werf, Goddard & Meyer, 1998). The trait is described at all points rather than at a number of fixed points (Kirkpatrick & Heckman, 1989) and measurements at any age or in any environment can be used without adjustment towards a fixed point (*e.g.* Meyer & Hill, 1997; Huisman, 2002). Accounting for the ordering and spacing of observations improves the power of estimation of variance components (Kirkpatrick, Hill & Thompson, 1994). Selection response can be more accurately predicted because variance components are more accurately estimated and because direct and correlated response at all points along the trajectory, not only points with observations, is accounted for (Kirkpatrick & Heckman, 1989). A disadvantage of random regression models is that data points at the extremes of the environmental variable can have a large influence on the predicted coefficients of the function (Meyer, 1998). Reaction norms/covariance functions may have any shape, unless restricted by correlations with other traits or other costs or limits to the environmental sensitivity (DeWitt, Sih & Wilson, 1998), which may be defined in the model.

Occurrence and implications of GxE in dairy cattle

For dairy cattle, GxE has been studied for various environmental factors. Between herd production levels, feeding regimes of management systems within a country, or a group of neighbouring countries, there is seldom re-ranking of genotypes (*e.g.* Cromie, 1999; Boettcher, Fatehi & Schutz, 2003; Calus & Veerkamp, 2003; Publication I). Between countries or regions that differ considerably, *e.g.* in climate or management system, re-ranking of genotypes is more common. For example, the genetic correlation between the same milk production trait evaluated in any country in Western Europe, the USA, or Canada (the northern hemisphere group) is high (0.85-0.9), while the correlation between the northern hemisphere group and New Zealand and Australia is lower (0.75-0.84) (Emanuelsson, Banos & Philipsson, 1999), indicating that re-ranking occurs. Low genetic correlations have also been estimated between milk yield evaluated in Mexico and the USA (0.63)(Cienfuegos-Rivas *et al.*, 1999), milk yield in the UK and Kenya (0.49)(Ojango & Pollott, 2002), and longevity in Canada and New Zealand (-0.07—0.21)(Mwansa & Peterson, 1998).

The phenotypic and genetic variances between animals are often smaller in low yield environments than in high yield environments; *i.e.* there is a scaling effect of GxE. As genetic progress is a function of the genetic variance (Falconer & Mackay, 1996), the expected response to selection is smaller in low than in high yield environments. For example, the expected response in Kenya, a low yield environment, to selection based on UK breeding values is only 44% of the expected response in the UK, a high yield environment (Ojango & Pollott, 2002). Thus, investments in high merit semen from bulls evaluated in high yield environments may not pay off for farmers in low yield environments.

As the ranking of animals or breeds may differ between environments when significant GxE is present, one can argue that the choice of parents for the next generation or breed for a specific farm should be based on evaluations in an environment similar to that in which the offspring or the breed will be kept. For a long time it has been discussed if the highest selection response would always be gained by selecting in the environment where the progeny is required to live or if it would be better to test and select animals in an environment where they have the possibility to express their full potential or in the environment where the heritability of the trait is highest (*e.g.* Hammond, 1947; Falconer, 1952). The problem was partly solved by expressing the genetic progress in one environment as a correlated response to selection in another environment and comparing the genetic progress from selecting in different environments. If selection decisions differ between environments, more genetic diversity can be maintained.

The increasing trade of genetic material has made genetic improvement of livestock a global matter. For dairy sires, Interbull predicts international breeding values aiding farmers and national breeding companies to select sires from the international market (Interbull, 2003). Thus, GxE is an important issue for the maintenance of genetic diversity and trade of genetic material.

Prospects for genetic change of environmental sensitivity

Studies, mostly on insects, plants, or mice, have shown genetic variation and/or heritability of environmental sensitivity (*e.g.* Scheiner & Lyman, 1989; Weis & Gorman, 1990; Holloway & Brakefield 1995) and change in environmental sensitivity in response to selection (Falconer, 1990; Scheiner & Lyman, 1991; Hillesheim & Stearns, 1991). Publications I-III in this thesis present estimates of genetic parameters of environmental sensitivity of milk protein yield, days open, and length of productive life of dairy cattle. Estimates of genetic parameters of environmental sensitivity of other traits in farm animals are scarce and little is known about genetic trends of environmental sensitivity in farm animals. There is reason to believe, however, that in the presence of GxE, environmental sensitivity will increase in populations selected for high phenotypic value in a continuously improving environment (Publication IV). To illustrate the basic principle, assume a population of animals having linear reaction norms with genetic variation in slope. The two sires in Figure 1 have equal phenotypic values in environment 0. Sire A has a steeper reaction norm; *i.e.* higher environmental sensitivity, and thus better ability to take advantage of any improvement of the environment. Therefore, if the environment has improved in a later generation, the progeny of sire A will be favoured over progeny of sire B. With selection for high phenotypic value environmental sensitivity is expected to increase in the population. The described situation is probably relevant for farm animals in an intensive production system where management and the genetic level of the livestock are continuously improved to meet market demands.

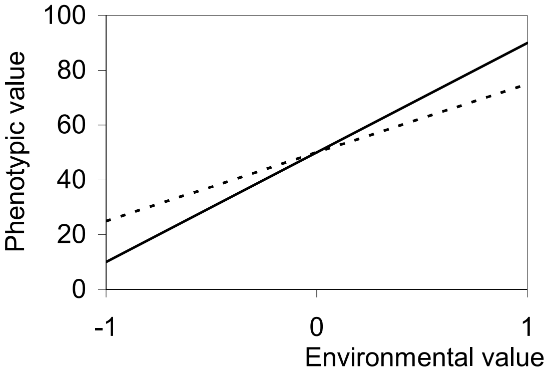

Figure 1. Reaction norms of two sires (sire A —, sire B ---). Arbitrary units of phenotypic and environmental values.

The genetic mechanism resulting in environmental sensitivity is known for some traits and species. Examples, including shade avoidance in plants and the switch between wet and dry season morphs in butterflies, are given by *e.g.* Schlichting & Pigliucci (1995; 1998) and Schlichting & Smith (2002). In principle, there are two main forms of genetic regulation of environmental sensitivity. With regulatory plasticity, receptors detect environmental cues, such as a change in temperature, light conditions, or humidity, and alter the expression of one or several genes - an indirect response. The rate of transcription or translation can be altered, resulting in a gradual change of the phenotype, or genes can be switched on or off, resulting in a sigmoid shaped reaction norm. With allelic sensitivity, the expression of individual genes depends directly on the environment the individual encounters without a receptor mediating the signal (Schlichting & Pigliucci, 1995). It has been suggested (*e.g.* Lerner, 1954) that heterozygotes would have lower plasticity (higher stability) because of a better capacity to buffer against environmental change. Most experimental evidence does not support this hypothesis (see *e.g.* review in Schlichting & Pigliucci, 1998, p. 64-65).

Aim of the thesis

The objectives of this thesis were to contribute to the development of methodology for studying GxE, to use the developed methods for describing the occurrence of GxE in Nordic red dairy cattle, and to predict response to selection in the presence of GxE.

The specific aims of the presented publications were:

- to describe the amount and pattern of GxE in Nordic red dairy cattle and to evaluate the usefulness of reaction norm models for studying GxE (Publications I, II, and III)
- to describe the effects of various environmental variables on protein yield, days open, and productive life of Swedish Red and White dairy cattle (Publications II & III)
- to predict the effect on environmental sensitivity of selection for high phenotypic value in the presence of GxE and in combination with a continuously improving environment (Publication IV)
- to describe selection response of a trait affected by GxE in terms of selection index theory by deriving equations to predict genetic change in reaction norm coefficients (Publication V)
- to find the optimum environment in which to test selection candidates for a given breeding objective (Publication V)

The results of Publications I, II, and III were expected to be of use for dairy cattle breeding organisations in the Nordic countries. The results of Publications IV and V were expected to improve our understanding of the long- and short-term effects of selection in the presence of GxE. The development of methodology in all publications was thought to be of scientific interest.

Overview of the presented publications

Material and methods

Prediction of reaction norms from field data (Publications I, II, and III)

Genotype by environment interaction for production and fertility of dairy cows was studied in Publications I and II and in Publication III GxE for the length of productive life. Data on production, fertility, and pedigree for the Danish Red Dairy Breed, Finnish Ayrshire, Norwegian Dairy Cattle, and Swedish Red and White Breed were analysed in Publication I. In Publications II and III only the Swedish Red and White Breed was included. Data originated from the national milk recording schemes. The measure of production was the 305-days kg milk protein yield. Fertility was measured as the number of days between calving and last insemination (days open), and productive life was measured as the number of days from first calving to culling. First lactation data on cows having their first calving during 1987 to 1995 were used for Publications I and II. The data for Publication III included data from 1988 to 1996 on cows first calving during 1988 to 1991.

In Publication I, the environmental values were defined as the herd-year averages of milk protein yield and days open. These measures have the advantage that they summarise a complex environment and they are easily available. The disadvantage is that the explanatory variables contain, at least partly, the same information as the dependent variable. In Publication II a number of environmental variables were evaluated. In addition to the herd-year averages of protein yield and days open, the herd size, geographic coordinates of the herd, average rainfall during summer, accumulated radiation from the sun during the summer, and average summer and winter temperatures were used. In Publication III, the environmental variables were herd size and the herd-year averages of peak milk yield, first lactation protein yield, and length of productive life.

In Publication II, the effects of the environmental variables were analysed using a fixed regression sire model. The effects of the environmental variables in Publication III were studied by including a fixed linear regression on the environmental variable in a random regression sire model. Genotype by environment interaction was studied by use of reaction norms. Random regression sire models were used for regressing phenotypic values of the daughters of each sire on each of the environmental variables. The number of observations available for the estimation of variance components and reaction norm coefficients were approximately 930 000, 170 000, and 240 000 for Publications I, II, and III, respectively. Variance components were estimated using the average information residual (restricted) maximum likelihood algorithm (Jensen *et al.*, 1997) in the DMU package (Jensen & Madsen, 1994) for Publications I and III and the ASREML software, release 1.0 (Gilmour *et al.*, 2002) for Publication II. Genotype by environment interaction was quantified by the genetic variance for the slope of a linear reaction norm. Different models were compared by their likelihood values (Publications I and II) and/or their residual variances (I, III). In Publication III, multi-trait models were analysed in addition to the reaction norm models. Genotype by environment interaction was then quantified by the genetic correlation between productive life expressed in the highest and lowest quartiles of the environmental variables following a character state approach.

A homogeneous residual variance was assumed in Publications I and III when estimating variance components and reaction norm coefficients. Possible heterogeneity of the residual variance was investigated thereafter. In Publication II, models accounting for heterogeneous residual variance simultaneously with the estimation of variance components and reaction norms coefficients were included. In all three publications, the heterogeneity of the residual variance was evaluated by estimating the residual variance for groups of observations; each group covering a different segment of the environmental range of the data.

Simulation study of environmental sensitivity (Publication IV)

Simulations were performed to study the effect on environmental sensitivity of selection for high phenotypic value of a trait affected by GxE when the environment was continuously changing. A Fortran 90 program was written for the simulation of linear, quadratic, and sigmoid shaped reaction norms for a population of 20 000 animals. The values of the genetic parameters needed for the simulation were chosen to correspond approximately to the parameters estimated in Publication I. Selection for high phenotypic value was practised for 10 (linear reaction norms) or 100 (non-linear reaction norms) non-overlapping generations. For each generation, the average environmental value was increased. The environmental value simulated for each individual was a deviation from the average environment, and it was constant from birth to selection. Mass selection and selection on expected breeding values were studied. Environmental sensitivity was defined as the first derivative of the reaction norm function with respect to the environmental value and evaluated at a specific environmental value. The overall environmental sensitivity of an individual was measured as the weighted average of the absolute value of the derivative over the environmental range of each generation. The population average overall environmental sensitivity (ES) was calculated for each generation to evaluate the effect of selection in combination with environmental change.

Prediction of genetic change of the reaction norm (Publication V)

Prediction equations were derived in Publication V to describe the response to mass selection of a trait affected by GxE. To derive the equations, selection index theory was combined with a reaction norm model and the Bulmer effect. The model was a linear reaction norm model for a single trait. Both the genetic and environmental effects were modelled as linear functions of the environment.

The genetic changes in the reaction norm coefficients level and slope were derived from a regression of the breeding values for level and slope on the selection environment. Knowing the genetic change in reaction norm coefficients, the change in phenotypic value in a specified environment can be derived. This is a function of both the selection environment and the environment where the selection response is to be realised (the response environment). The genetic progress in a given environment, for given population parameters, and a given selection intensity, is maximised by testing the selection candidates in the optimum selection environment. This environment gives the best combination of heritability and accuracy of selection. The optimum selection environment was found by solving $\partial \Delta G_l / \partial x_k = 0$, where ΔG_l is the genetic change in response environment *l*, and x_k is the selection environment *k*.

The relations defined by the prediction equations were illustrated using a Fortran 90 simulation program. Input values were genetic and environmental parameters for the base population. The simulated degree of GxE was determined by the ratio of genetic variances of the slope and level of the reaction norm. Heritability was either kept constant or changing with the environmental value, depending on what was being illustrated. Two levels of heritability in the environment of the intercept of the base population were studied, three levels of GxE and three levels of the correlation between level and slope. The Bulmer effect was accounted for by iterative reduction of the genetic variance until equilibrium was established, applying the results of Cochran (1951) and Bulmer (1971).

Main findings

Prediction of reaction norms from field data (Publications I, II, and III)

Fixed effects of environmental variables (population average reaction norms)

Significant fixed effects of herd level of production and fertility, geographic location of the herd, herd size, radiation from the sun, and summer and winter temperature on protein yield and days open in Swedish Red and White dairy cattle were found in Publication II. The average rainfall during summer did not have a significant effect. The coefficients of the fixed linear regressions on the environmental variables in Publication III predicted the average productive life to decrease 41 days for an increase of herd size with 10 first parity cows, to decrease 44 days for an increase of herd-year average protein yield with 1 SD-unit of 38 kg and to increase 0.5 day for an increase of peak milk yield with 1 SD-unit of 2.5 kg.

Reaction norms, genetic parameters and heritability

The main result of Publication I was that a reaction norm model was successfully applied to the joint Nordic field data. Breeding values and genetic variances for the level and slope of a linear reaction norm could be estimated. As an example, reaction norms for protein yield in relation to herd level of production are shown in Figure 2 for a sample of sires from Publication I. Genetic and residual variances of protein yield and days open, as well as heritability, were heterogeneous over the range of many of the environmental variables. In publication I, it was shown that when genetic (co)variances change over environments, the genetic correlation between two traits, in this case protein yield and days open, can change too.

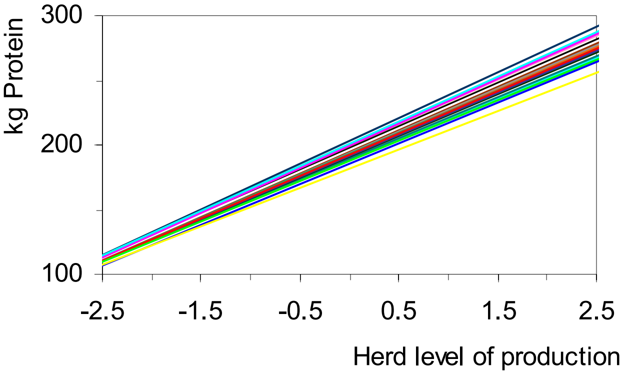

Figure 2. Reaction norms for protein yield in relation to herd level of production for a random sample of 39 bulls. The x-axis shows the environmental value as the deviation from average in SD units of herd-year average protein yield. The figure is reproduced from Publication I.

When heterogeneity of the residual variance was accounted for, heritability of protein yield and days open changed less over the environmental range than when a homogeneous residual variance was assumed. The models accounting for heterogeneous residual variances in Publication II always had a significantly better likelihood than the models assuming homogeneous residual variances. For productive life, the genetic but not the residual variance changed over the range of the environmental variables studied. Thus, heritability changed with the environmental value. The range of estimated heritabilities for the three traits in the range of ± 2 SD units from the average of each environmental variable are summarised in Table 1.

Table 1. *Heritability of protein yield, days open, and productive life in the range of ± 2 SD units from the average of each environmental variable when possible heterogeneity of the residual variance has been accounted for*

Environmental	Trait		
variable[1]	protein yield	days open	productive life
DOP[2]		0.016-0.093	
Herd size	0.25-0.29		0.063-0.074
PEAK[2]			0.064-0.14
PROT[2]	0.09-0.40		0.054-0.17
WTEMP[3]	0.27-0.32	0.030-0.056	
NORTH[4]	0.26-0.29		
EAST[5]	0.27-0.30		

[1] Only variables with which a reaction norm sire model fitted the data better than a corresponding model without a random regression are presented. [2] Herd-year average days open, peak milk yield, and lactation protein yield, respectively. [3] Average winter temperature. [4] Measure of geographic location in km north of the equator. [5] Measure of geographic location in km east of a reference line 1500 km west of the middle of Sweden.

Genotype by environment interaction

Significant genetic variance for the slope of the reaction norm indicated GxE for protein yield in relation to the herd level of production and herd size, for days open in relation to the herd fertility level, and for productive life in relation to herd size and herd-year average peak milk yield and lactation protein yield. High correlations between trait expressions in different environments indicated that re-ranking of sires over the major part of the environmental ranges studied was negligible (Table 2). This means that reaction norms do not often cross within the environmental range studied as can be seen for the sample of sires in Figure 1. The variance in slope is visible as a larger difference between the sires in Figure 1 at higher herd levels of production than in herds with lower production - a scale effect.

Note, however, there was a relatively low rank correlation between predicted productive life in average and low producing herds (Table 2), indicating re-ranking of sires between those environments. In addition some re-ranking was indicated between average and extreme environments; between protein yield in average and extremely unfavourable production environments, days open in average and extremely favourable fertility environments, and productive life at average and extreme herd-year averages of peak milk yield. The correlation between productive life in the highest and lowest quartile of herd-year average productive life was between 0.74 and 0.80.

Table 2. *Correlations between predicted phenotypic value at average and deviating environments (based on estimates from Publications I-III)*

	Environmental	Environmental value in SD units [3]			
Trait	variable	-2	-1	+1	+2
Protein yield	herd size [1]	-	0.998	0.997	0.992
	PROT [1]	0.979	0.997	0.998	0.995
	PROT [2]	0.970	0.997	0.998	0.996
Days open	DOP [2]	-	0.970	0.993	0.995
Productive life	herd size [2]	0.990	0.997	0.997	0.987
	PEAK [2]	0.918	0.976	0.974	0.905
	PROT [2]	0.772	0.943	0.964	0.897

[1] Genetic correlation, orthogonal scale transformed to SD units of the environmental variable, [2] Spearman rank correlation coefficients, [3] SD units of each environmental variable

The scale effect of GxE may affect selection decisions. As genetic progress is a function of the genetic variance, herds having high genetic variance are expected to benefit more from using top ranked sires than herds with lower genetic variance. Hence, when genetic variance is a function of the environment, the economic value of investing in semen from top ranked sires depends on the herd environment.

If environmental effects are not properly accounted for in the genetic evaluation, scaling effects may influence the ranking of animals not evaluated in the same environment. Unless heterogeneity of the variance is accounted for, sires evaluated in an environment where genetic variance is large will be selected more often than sires evaluated in an environment where genetic variance is lower (Wilhelm &

Mao, 1989). One should also be aware that when sires are ranked according to a total merit index including traits that scale differently over the environmental range sires may rank differently in different environments (Namkoong, 1985). With re-ranking of sires between environments, separate ranking lists for each segment of the environment or even for each farm would be beneficial for the cattle breeder. When re-ranking is indicated only between average and extreme environments the usefulness of environment specific sire ranking lists is limited because few data are available for extreme environments, which makes predictions about them unreliable. Therefore, the national sire ranking is recommended as a guide to sire selection by cattle breeders in the whole of Sweden.

Simulation study of environmental sensitivity (Publication IV)

The average overall environmental sensitivity of the population (ES) simulated in Publication IV increased over generations in response to selection for high phenotypic value in combination with a continuously improving environment. Thus, a traditional selection program for farm animals in combination with improvements of animal husbandry can be expected to increase environmental sensitivity of the animals. Environmental sensitivity increased even with small environmental changes such as may be encountered by populations living under natural conditions, in developing countries where the rate of improvement of animal husbandry may be slow, or under standardised conditions such as at test stations, laboratories or specific pathogen free farms. With mass selection, ES increased even without environmental change. This was a result of selecting individuals that have experienced a favourable environment and have the ability to take advantage of that environment, as stated by Falconer (1990). With linear or quadratic reaction norms, ES increased more the larger the environmental change. The development of the population average reaction norms over 10 generations of selection and large environmental change is illustrated in Figure 3.

After many (50-100) generations of selection, the quadratic reaction norms approached linearity, indicating that reaction norms with an optimum environment could not be maintained over a long period of environmental change. However, linear reaction norms are not either, for biological reasons, probable over very large environmental ranges.

For a population having sigmoid reaction norms, ES increased within the environmental range encompassing the threshold. After a large environmental change, the threshold was not within the environmental range encountered by the population and environmental sensitivity was not expressed (Figure 3). However, if the environment deteriorates, the population would again encounter its environmental threshold, and the environmental sensitivity would be expressed and the average performance would be drastically reduced.

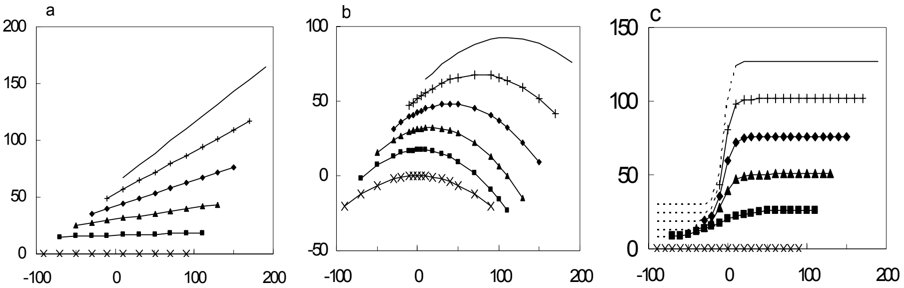

Figure 3. Development of population average a) linear, b) quadratic, and c) sigmoid reaction norms over generations when selection is combined with large environmental change (10 environmental units per generation). Solid lines represent reaction norms in generation 0 (×), 2 (■), 4 (▲), 6 (♦), 8 (+) and 10 (—) in the environment each generation is expected to encounter (± 3 environmental SD units from generation average). Dotted lines in *Figure 3c* represent the reaction norms in environments that generation is not expected to encounter. The x-axes show environmental and y-axes show phenotypic values. The figure is reproduced from Publication IV.

Prediction of genetic change of the reaction norm (Publication V)

The derived equations for prediction of genetic change in reaction norm coefficients, change in genetic merit in a specific environment, and the optimum selection environment for a given breeding objective, were the main results of Publication V. The results show that the optimum selection environment for a given response environment depends on three factors: the degree of GxE (determined by the ratio of genetic variances of slope and level of the reaction norm); the correlation between level and slope; and the heritability of the trait (as a function of the environment). The optimum selection environment was found using the following equation:

$$x_{opt} = \mathbf{x}_l^{'}\mathbf{G}\begin{bmatrix}\sigma_{p_0p_1} \\ -\sigma_{p_0}^2\end{bmatrix} \Bigg/ \mathbf{x}_l^{'}\mathbf{G}\begin{bmatrix}-\sigma_{p_1}^2 \\ \sigma_{p_0p_1}\end{bmatrix} \qquad \text{(Equation 1)}$$

where x_{opt} is the effect of the optimum selection environment, $\mathbf{x}_l^{'}$ is a row vector [1 x_l], x_l is the effect of the response environment, **G** is the genetic (co)variance matrix of the level and slope of the reaction norm, $\sigma_{p_0}^2$ and $\sigma_{p_1}^2$ are the phenotypic variances in level and slope, and $\sigma_{p_0p_1}$ is the corresponding covariance.

The optimum selection environment was neither always equal to the response environment nor to the environment where heritability was highest (Figure 4). The more GxE and/or the flatter the heritability function the closer the optimum selection environment was to the response environment. When heritability was constant over the environmental range, maximum genetic gain was achieved when selection and response environments were equal, which agrees with the classical expression for correlated response, $CR = ih_k r_{g_{k,l}} \sigma_{A_l}$ (Falconer & Mackay, 1996). At constant heritability, the correlated response in environment *l*, *CR*, to selection in environment *k* is maximised when the genetic correlation $r_{g_{k,l}}$ between the two environments is unity; *i.e.*, the two environments are equal.

As expected, the environment had larger effect on the selection response the larger the variance in slope; *i.e.* the higher the degree of GxE. The correlation between level and slope affected the shape of the response curve. Selection response in the level of the reaction norm was highest when selecting in the average environment. Response in slope was highest when selecting in an environment that was better than average.

Theoretically, the optimum selection environment should be calculated from equilibrium genetic parameters. We found, however, that the optimum selection environment calculated using base population genetic parameters was very close to the equilibrium optimum environment. Using base population parameters for calculating the optimum selection environment probably gives sufficient precision for practical applications.

Besides for maximising genetic gain in a specific environment, equations were derived to find the environment where environmental sensitivity (slope of the reaction norm) is kept at a desired level and where the proportion of animals performing below an acceptable level is reduced most efficiently.

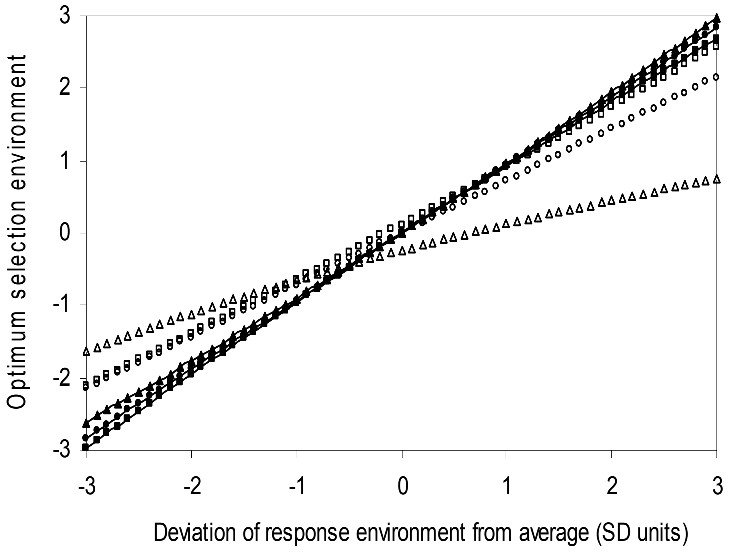

Figure 4. The equilibrium optimum selection environment for a given response environment. Two levels of GxE: Open/filled symbols: little/much GxE; *i.e.* genetic correlation between trait expression at average environment and an environment deviating 1 SD 0.95/0.60 when the correlation between level and slope was 0. Three levels of the correlation between level and slope are shown: -0.4 (■), 0 (●), and 0.4 (▲). Heritability was 0.5 in the average environment and 5% lower at 1 SD from the average. The figure is reproduced from Publication V.

Discussion

The usefulness of the reaction norm model

This thesis shows the usefulness of the reaction norm model for studying GxE in different contexts. The results of Publications I-III suggests that if a relevant measure of the environment can be agreed upon, then the reaction norm model could be used for genetic evaluation within or across countries. Unique breeding values and ranking lists could be presented for each environmental level. Lists of sires especially suited for *e.g.* high- or low-producing herds or herds in a specific region could be of interest for the farmers. The usefulness of the reaction norm model for genetic evaluation to provide a guide to sire selection for commercial purposes is, however, not well investigated. In this thesis, reaction norms have only been predicted for sires having daughters in many environments. Before a reaction norm model can become a realistic alternative to models for genetic evaluation that are used by breeding organisations today, method development is needed so that reaction norms can be predicted for all animals, not only sires. Prediction of reaction norms for all animals could be possible if information from relatives is used. More knowledge is also needed on the shape and genetic variation of reaction norms for important traits of our farm animals.

How to measure the environment?

The environment influences the animal, or any other organism, in many ways. Some aspects of the environment can be summarised by *e.g.* production level, herd size, management system, region, or weather conditions and many other measures can be thought of. A statistical measure of the environment is the fixed effect of herd, herd-year or herd-year-season estimated with a sire or animal model. To measure the environment by the mean performance of a population in that environment is a method that has proved to be useful when a reasonable number of genotypes and environments can be measured (*e.g.* Finlay & Wilkinson, 1963; Perkins & Jinks, 1973; Ceccarelli & Grando, 1991; Publications I-III). The mean performance may, but does not have to, measure the same trait as the trait being analysed. The main advantage of this method is that the environment can easily be scored as more or less favourable, and a continuous gradient is created. The disadvantages are that the measure of the environment depends on the genotypes under study (Ceccarelli & Grando, 1991) and that the correlations between the resulting reaction norm coefficients are often very high (*e.g.* Baker, 1988; Schlichting, 1986; Publication I). This includes the correlation between mean performance/level of the reaction norm and environmental sensitivity/slope of the reaction norm.

Most reaction norms reported in the literature are one-dimensional (Fikse, Rekaya & Weigel, 2003a, b; Calus & Veerkamp, 2003; Publications II & III). Exceptions are the study by Veerkamp & Goddard (1998) and Publication I in this thesis, where also two-dimensional reaction norms are studied. One-dimensional reaction norms are useful for studying GxE from different angles, but they are limited in their ability to describe the complexity of the environment. Using all relevant environmental descriptors; *e.g.* in a multiple regression model, would yield a multi-dimensional reaction norm that would be very difficult to interpret. An option is to construct an environmental index, giving different weights to environmental variables of different importance for the trait. Criteria for choosing the variables to include and how to measure their importance would have to be developed. Important variables to include are probably herd size, herd average of the trait under study, and some indicator of climate zone. When traits are to be combined in a total merit index an indicator of the political/economical system should be considered because regulations on animal production and differences of payment systems could influence the relative importance of different traits.

Genetic correlations between traits

As a consequence of genetic (co)variances changing with the environment, genetic correlations between traits also change (*e.g.* Schlichting & Pigliucci, 1998; Publication I). The character state model explains a correlation less than unity between the same trait expressed in different environments with partly different genes being expressed in the different environments (*e.g.* Falconer & Mackay, 1996). The same explanation applies to a change in correlation between two different traits for a change in the environment (Schlichting, 1986). A change in correlation between two traits over environments can also be explained by the average effects of gene substitution at the loci affecting the trait. In the presence of GxE, the average effect of gene substitution at one or many loci change with the environment and the genetic correlation between traits can change too (de Jong, 1990). If reaction norms or covariance functions for two or more traits are predicted in a bivariate or multivariate analysis, the genetic correlation between the traits can be estimated as a function of the environment (Publication I). Viewing correlations as functions of the environment could add to our understanding of the complex relations between traits.

A negative phenotypic correlation between two traits can be explained by trade-offs in relation to the allocation of resources: if the animal has a fixed total amount of energy to spend, then spending more energy on one trait must mean that less energy is spent on the other trait. Some individuals, however, may be better than others at acquiring energy and hence have more energy to spend on both traits, turning the correlation positive (van Noordwijk & de Jong, 1986). The amount of resources available may depend on the environment of the animal. If, in a favourable environment, more energy can be acquired by the individual, then more energy can be allocated to both traits, and negative correlations may become positive. Therefore, a practical use of reaction norms would be to find environments where the correlation between two traits is the most favourable (or least unfavourable).

Globalisation of genetic improvement of livestock

The globalisation of genetic improvement of livestock has raised concern about genetic diversity and local adaptation. Breeding companies of the industrialised countries market a small number of breeds internationally. These breeds are superior in the climate and production system where they were developed, but they may be less suited for other conditions. International genetic evaluations may show that some breeds are less suited for some countries/ environmental conditions, which may support the use of local breeds and encourage their development. Both broadly adapted generalist breeds and breeds specially suited for producing under marginal conditions or for a specific group of consumers would ideally find their place on the market for genetic material.

The increased cooperation between breeding organisations and the international genetic evaluation of dairy cattle performed by Interbull is probably positive both for improving the future performance of dairy cows and for maintaining genetic diversity. With co-ordinated efforts, even more young bulls could be tested and more proven bulls would be available for farmers to choose among. When the test environments are considered in the international genetic evaluation, sires especially suited for specific environments can be presented. This could increase the number of sires that are used, thereby improving the genetic diversity within breed.

In Interbull's current international evaluation of dairy sires, one country defines one environment. So called borderless genetic evaluations have been suggested, meaning that environmental factors other than countries are used for clustering herds into groups (Weigel & Rekaya, 2000). Then each group is treated as one environment and gets its specific breeding values. The reaction norm model provides an alternative borderless genetic evaluation, but it requires the development of an environmental scale common for all participating countries.

Optimising data recording and selection

The objective of genetic improvement of animals is to improve the performance of future generations in future environments. Therefore, optimisation of a breeding program means maximisation of the response in the expected future environment of the population; *i.e.* the response environment. Unfortunately, the environment of the future cannot be predicted with certainty. Even if the direction of environmental change can be predicted with some certainty, the rate of change might be more difficult to predict. For prediction of the future environment, knowledge of the current frequency distribution of the environment is needed. Thus, observations are needed on the environment of a representative part of the population.

When the expected future environment is defined as a range of environments the population is expected to encounter, a reaction norm model can be used for prediction of breeding values for specific environments. To predict reaction norm coefficients, observations are needed from a broad range of environments. When predicting the environment specific breeding values, observations could be weighed according to the environment where they were recorded, giving higher weights to observations in environments that are similar to the response environment. This idea is similar to Kirkpatrick & Bataillon 's (1999) suggestion to weigh observations by the current environmental frequency distribution.

When the expected future/response environment is defined as one specific environment, the optimum environment for recording of data can be predicted using Equation 1 (Publication V). The value of data recording in a specific environment and the losses due to recording of data in a sub-optimal environment can be quantified. Breeding values that are BLUP using data recorded in the optimum environment will give the maximum genetic progress in the response environment. The theory can be useful *e.g.* for optimising the environment of a nucleus herd of breeding animals. The environment of the nucleus herd is the environment of data recording, *i.e.* the selection environment. The response environment is the environment of the production herds to which the genetic material is distributed. Note that observations from the production herds are needed for the prediction of reaction norm coefficients included in Equation 1 for prediction of the optimum environment.

In the Swedish, Finnish, and Dutch breeding programs for dairy cattle, progeny testing of sires is combined with individual testing of dams in a nucleus herd (Svensk Avel, 2003 a, b; FABA, 2003; Holland Genetics, 2003). The optimum environment for the nucleus herd can be predicted using Equation 1. Several factors related to *e.g.* feeding and management could be used to describe the environment and the optimum value for each could be found.

A problem arises if the environment that would give the maximum selection response is not an ethically or an economically acceptable environment for testing selection candidates. Testing animals in the optimum selection environment for improving *e.g.* disease resistance might be comparable to a challenge test. Few decision-makers would risk the most promising selection candidates in such a test. However, relatives of the selection candidates could be tested if the information is expected to contribute importantly to improvements of animal health and farmer economy.

When the breeding population comprises almost the entire population, as is common for dairy cattle, the selection environment cannot simply be chosen. Furthermore, Equation 1 does not apply to progeny test schemes commonly used for dairy cattle. With progeny testing, the precision of selection is generally high. This means that the optimum environment for recording data will depend more on the genetic correlation with the trait expressed in the response environment than on the heritability function of the trait. Therefore, one can argue that the optimum selection environment is close to the response environment (comparable with the optimum selection environment being equal to the response environment when heritability is equal over the environmental range). A practical approach to optimisation of data recording could then be to record much of the data in environments that are thought to be common in the future or similar to the future environment; *i.e.* mates for the selection candidates should be sought in such environments. Considering the uncertainty about the future environment and the need of data for prediction of reaction norm coefficients and environmental frequency distribution, testing should still be done in a broad range of environments.

Should environmental sensitivity be included as a trait in the breeding objective?

It has been shown that environmental sensitivity can be changed by selection. If considered important enough and if a desired level or direction of change was agreed upon, then environmental sensitivity of a trait could be included in the breeding objective. With mass selection, the selection candidates could be evaluated in the environment giving the desired change in environmental sensitivity (Publication V). With a progeny test program, reaction norms for the sires of the breeding population could be predicted from field data using the methods described in Publications I-III. The first derivative of the reaction norm function for a trait would then give the predicted breeding value for environmental sensitivity of the trait. A more general problem, however, is to determine the desired level of environmental sensitivity. It is a complex problem involving biology, management, economics, and ethics.

Generally, breeding for high environmental sensitivity would be unethical if animals as a result would become restricted to highly controlled environments for their welfare or even survival. On the other hand, breeding for low environmental sensitivity could be of ethical concern if it resulted in animals without the ability to react and respond to stressful treatment. The optimum level of environmental sensitivity depends on the trait and on how predictable and/or adequate the environment is for the animal. In intensive production systems, high environmental sensitivity can be acceptable or even desirable because the herd environment can usually be kept adequate and the risk of disturbances is relatively small. The risk of feed quality problems or disease can be controlled and the risk of feed shortage is minimal. The higher environmental sensitivity of production and functional traits, the more benefit from improvements of management, feeding, and health care.

In agricultural systems where the environment is unpredictable and cannot be controlled, stability of performance is important (Ceccarelli, 1994). Low sensitivity of production traits is needed *e.g.* for livestock kept by subsistence farmers in developing countries. For functional traits, such as disease tolerance and fertility, low environmental sensitivity at an acceptable level would be attractive, not only in problematic environments but in all environments where contagious agents and disease pressure cannot be strictly controlled. Low environmental sensitivity of functional traits and high environmental sensitivity of production traits probably require high environmental sensitivity of resource intake and the many physiological processes involved in coping with a variable environment.

Conclusions

Based on the results presented in this thesis, I have come to the following conclusions:

- The effects of GxE should be considered in animal breeding and in particular in international genetic evaluations and trade of genetic material.
- Re-ranking of dairy sires is negligible over the range of environments commonly encountered in the Nordic countries. Therefore, there is little need to account for GxE in the national genetic evaluations of dairy cattle in the Nordic countries. Furthermore, the results indicate that GxE is not an obstacle for a joint genetic evaluation for dairy cattle in the Nordic countries.
- Genetic and residual variances are heterogeneous over the range of many environmental variables causing heritability to vary with the environment.
- In the presence of GxE, the average environmental sensitivity is expected to increase in a population selected for high phenotypic value in a continuously improving environment.
- Genetic evaluation and selection for environmental sensitivity is possible.
- Breeding programs can be optimised by choosing the selection environment that gives the maximum genetic progress for the given breeding objective and response environment.
- More knowledge is needed about the shape and variation of reaction norms of important traits of farm animals in relation to different environmental variables. The composition of an index summarising important aspects of the environment should be discussed.

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