BEEF IMPROVEMENT FEDERATION

9TH GENETIC PREDICTION WORKSHOP

PREDICTION OF GENETIC MERIT OF ANIMALS FOR SELECTION

December 8-10, 2008
Kansas City, Missouri

National Beef Cattle Evaluation Consortium
Colorado State University-Cornell University-University of Georgia

Genetic Prediction Workshop
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"Prediction of Genetic Merit of Animals for Selection"

Preface

The Beef Improvement Federations publishes Guidelines for use in genetic improvement of beef cattle. These Guidelines have provided for uniformity in methods of measuring traits, recording and analyzing data and estimating breeding value of animals which have provided the basis for significant genetic improvement in beef cattle in the U.S. and Canada for more than forty years. The procedures recommended, developed in committee meetings and workshops and approved by the Beef Improvement Federation Board of Directors, have provided procedures employed in beef cattle genetic improvement programs by member organizations of the Beef Improvement Federation in the United States and Canada. The procedures have also been adopted and used in beef cattle genetic improvement programs in many other countries around the world. Europe, Africa, Australia. This, the 9th Genetic Prediction Workshop was organized and cosponsored by the Beef Cattle Improvement Federation, the Beef Cattle Improvement Consortium and Regional Technical Committee NCR-199 comprised of scientists at land grant Universities, the USDA, breed associations and other organizations that support and conduct beef cattle genetic evaluations in the U.S. and Canada. The primary purpose of this purpose of the workshop was to stimulate discussion and provide manuscripts that could serve as background material for the 9th edition of the Guidelines for Uniform Beef Improvement Procedures to be published by the Beef Improvement Federation.

National Beef Cattle Evaluation Consortium
Colorado State University-Cornell University-University of Georgia

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Kansas City, MO
December 8-10, 2008

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1 pm--Afternoon session--Economically relevant traits—John Pollak (Cornell), Moderator

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2 pm--Genetic prediction of feed efficiency and input components—Denny Crews (Colorado State)

2:45 pm—Break

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A group of people working on updating BIF Guidelines. Anyone is welcome to attend.

Economically relevant traits for genetic improvement

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Introduction

A trait is generally recognized as a characteristic or property of an entity, although some definitions go further to distinguish a trait as something that is genetically determined or involves genes. Selection is the action of carefully choosing something as being the best or most suitable, which requires that it involve informed consideration of relevant traits. Genetic improvement is the outcome of effective selection and our tasks as animal breeders are to invent, research, devise and implement methods to predict the performance of future generations of animals. This provides informed choice of candidates to become parents of the next generation, and facilitates cost-effective improvement of livestock species.

More than a half century ago, a framework for goal-based selection was published, and has been adopted to varying extents in different livestock industries throughout the world. Its application to beef cattle has lagged most other applications, for various reasons. This paper will review the original framework, identify the impediments to its adoption in beef cattle, demonstrate the manner in which the current industry circumstances contribute to sub-optimal improvement, and outline some guidelines for progressing the industry.

Multiple trait selection

The problem of simultaneously taking account of a number of traits that influence the breeding goal has been long recognized. There are at least four approaches to the problem in the context of selecting to improve profit. Three of these (Hazel and Lush, 1942) are communicated in every animal breeding textbook and include tandem selection, independent culling, and selection index. The fourth method is to measure actual income and costs to obtain phenotypic profit on each individual and treat this as a single trait for evaluation and selection. This latter approach is likely to be suboptimal when the non-genetic factors or fixed effects differ for different components of profit, and when heritabilies differ between economically-relevant traits. This is the case because heritabilities determine the degree of emphasis placed on the individual's own records, in relation to its parent average and other relatives.

The Selection Index

The concept of a selection index was researched and communicated by Hazel (1943) and Hazel and Lush (1943). Collectively, these publications demonstrated an approach to combine performance information from various data sources on the individual of interest and/or correlated animals, accounting for genetic and environmental covariances between the data sources. Further, it could take account of information relating to the economic importance of various attributes, leading to a single measure

reflecting the aggregate merit of an animal that could be used as the basis for selection in order to simultaneously change a number of traits contributing to overall merit. The method involves predicting the aggregate economic merit of each selection candidate from a linear function of phenotypic measures on various traits and various animals in the population. It is a one-step method, provided the phenotypes are first adjusted for non-genetic effects such as herd-year, age of dam, and/or birthdate, as appropriate to each trait being used in the selection criteria.

Suppose a is the aggregate merit of one animal, $\hat{a}$ is its estimated aggregate merit, then $\hat{a} = \mathbf{b}'(\mathbf{y} - \mathbf{X}\beta)$ where $\mathbf{y}$ is the vector of observed phenotype on the candidate and its relatives, β is a vector of non-genetic effects used to adjust the phenotypes, $\mathbf{X}$ is an incidence matrix that identifies which particular fixed effects are relevant to each phenotype, and $\mathbf{b}$ is the linear function that will give rise to the most reliable (i.e., best) predictions of a, at least among the class of linear predictors (i.e., BLP). The selection index problem therefore amounts to deriving $\mathbf{b}$, which will likely be different for each animal, and then computing the linear function of adjusted phenotypes as dictated by $\mathbf{b}$.

The well-known solution to this problem involves solving the linear equations $\mathbf{Pb} = \mathbf{Gv}$, where $\mathbf{P}$ is the variance-covariance matrix corresponding to the selection criteria that are the elements in $\mathbf{y}$, $\mathbf{G}$ is the variance-covariance matrix relating the selection criteria to the economically-relevant traits that influence the goal, and $\mathbf{v}$ is a vector of economic or relative economic values that represent the influence of each economically-relevant trait on profit. The equations can be solved as $\mathbf{b} = \mathbf{P}^{-1}\mathbf{Gv}$. These equations were made more tractable in the pre-computer days by limiting the selection criteria to those observations that were most informative, namely observations on the closest relatives or from highly correlated traits. In practice, particularly in the post-computer days, there remains two analytical problems and two acceptance problems with this approach.

Practical problems with selection index

The selection index method assumes that $\mathbf{P, G, X, v}$ and β are known without error. This is never the case, but reasonable approximations of $\mathbf{X}$ are available with careful recording, and $\mathbf{P}$ and β can be estimated from the selection criteria themselves.

The most problematic matrix is $\mathbf{G}$, which is a submatrix of something we will call super-$\mathbf{G}$. In general, super-$\mathbf{G}$ can be considered to include three kinds of components. These are, the selection criteria that are themselves economically-relevant traits (e.g., sale weight), the selection criteria that are indicators but not economically-relevant traits (e.g., scrotal circumference, or ultrasound measures), and the economically-relevant traits that are not observed (e.g., carcass traits). The selection index equations only require direct knowledge of a submatrix of super-$\mathbf{G}$, that part represented by selection criteria as the rows and economically-relevant traits in the columns. Estimating this submatrix is a problem because it includes genetic covariances between selection criteria that we observe and some economically-relevant traits that we do not or cannot easily observe, for example ultrasound traits and fertility, or carcass traits and calving ease. Ideally, a dedicated large-scale experiment would be undertaken to estimate all these parameters, but this has not occurred in beef cattle. There are of course many

estimates of the genetic variances and covariances between traits that are routinely observed, such as birth, weaning and yearling weights.

Estimating the vector $\mathbf{v}$ is also problematic. The elements of this vector are the partial derivatives of the profit function, known as economic values, or scaled versions known as relative economic values. The profit function includes many biological interactions that are not well characterized, and requires considerable knowledge outside animal breeding, such as the nutritional requirements of maintenance and growth according to the body composition of an animal, the prices or products and costs of inputs including the opportunity cost of grazed forage. The profit function likely varies across management and environmental circumstances, as well as changing with time.

The idea of the selection index is to provide livestock managers with a single measure of aggregate economic merit that would be used as the basis for selection. This single measure would take account of all the information available on the animal. Selection on this single measure of profit would account for the compromises between the various traits. This has been shown to work well in selection experiments but is a problem in practice. The livestock manager might reasonably ask "why is this animal ranked more highly than that animal?" The only answer to this question is to communicate the elements of the vector $\mathbf{b}$. Recall that the elements used to weight each source of information are not relative economic values, but weighted linear functions of economic values (i.e., $\mathbf{b} = \left(\mathbf{P}^{-1}\mathbf{G}\right)\mathbf{v}$). That immediately introduces two problems. The first is that the sign of some of the weights in $\mathbf{b}$ may be the opposite of what the manager expects. For example, a favorable attribute might receive negative weight. Second, selection criteria that are not economically relevant will be attributed with a weight, due to their correlated contributions to other economically–relevant traits. Collectively, these two acceptance problems can lead livestock managers to ignore the index values and select in an ad-hoc manner.

Henderson's contributions

Henderson made a number of contributions to advance the situation beyond Hazel and Lush. He showed that the one-step approach of deriving aggregate merit could be undertaken in several steps that gave identical $\hat{a}$ Henderson (1963). First, selection index (or BLUP) can be used to estimate breeding values for the observed traits. This requires $\mathbf{P}$ and $\mathbf{G}$-sub, a component of super-$\mathbf{G}$ that represents the genetic variances and covariances among the selection criteria. Second, estimated breeding values can be derived for the traits that were not observed, using selection index techniques (detailed in Schneeberger et al., 1992). Third, the economically-relevant traits can be multiplied by their relative economic value to obtain index values of aggregate merit. Henderson further showed how to extend BLP to account for simultaneous estimation of fixed effects from the data being used to evaluate merit, generating a translation invariant prediction known as BLUP (Henderson et al., 1959). Compared to BLP, this method ignores some information, but the information that is ignored can only contribute to improved accuracy of evaluations if the fixed effects are known without error. Henderson also showed how to readily account for all relatives in $\mathbf{G}$-sub or $\mathbf{G}$, by directly computing the sparse inverse (Henderson, 1976; Quaas, 1976). Additionally, he extended methods to compute $\mathbf{P}$ and $\mathbf{G}$ from field data (Henderson, 1953; 1984).

An unintended consequence of these developments is that they led to a shift from Hazel's goal-motivated evaluation of animals to a period of data-motivated evaluation (Garrick and Golden, 2008). Whereas the original selection index formulation required the list of economically-relevant traits and their relative emphasis to be determined prior to the evaluation of animals, the data-motivated approach allowed for the immediate evaluation of any new trait that could be collected on a population of animals. Accordingly, as data was collected on new selection criteria, in some cases simply indicator traits such as scrotal circumference or live-animal ultrasound, these data were used to publish EPDs on the indicator trait rather than to improve the prediction of the economically-relevant trait for which they were recorded. The net effect was that there was a proliferation of EPDs that progressively made selection decisions more difficult rather than more straightforward.

Economically-relevant traits

Against this background, Golden et al., (2000) promoted a formal distinction between economically-relevant and indicator traits. Economically-relevant traits (ERTs) directly influence profit through an effect on income or expenses, whereas indicator traits do not directly influence profit but are associated (i.e., correlated) with traits that influence profit.

An economic value describes the impact on profit of a unit change in one trait, all other traits held constant. This is a partial derivative of the profit function. An indicator trait can be distinguished from an ERT because the partial derivative of the profit function with respect to the indicator trait will be zero if the corresponding ERT is included in the profit function. An indicator trait will improve the reliability of predicted aggregate economic merit, through improving the reliability of one or more ERT when used in a multivariate analysis. Heifer pregnancy is an ERT, whereas scrotal circumference can be an indicator of heifer pregnancy. Birthweight is an indicator but not an ERT if calving ease, mature weight and pregnancy feed requirements are in the profit function. A carcass attribute such as marbling is an ERT as it influences carcass returns, whereas an ultrasound measure of IMF is an indicator of the carcass trait and not an ERT in its own right.

Selection decisions can be made simpler by reducing the amount of information that needs to be considered and focusing on the important details. Golden et al., (2000) argued that only the EPDs for ERTs should be published, whereas indicator traits should be collected and used to improve the ERT prediction rather than being published themselves. The American Angus Association recently followed other Breed Associations in adopting this approach by publishing carcass EPDs from a joint carcass and ultrasound analysis (MacNeil and Northcutt, 2008).

Recent interest in feed efficiency has led to consideration of the appropriate EPDs when feed intake measures can be collected. A simple profit function might reward sale weight times sale price and penalize feed intake times feed cost. In that case, neither feed efficiency (gain/feed) or feed conversion ratio (feed/gain) are ERTs, and neither are likely to be good indicators since the numerator and denominator are already both in the profit function. Feed intake can be partitioned into expected feed intake plus residual feed intake, and neither would be ERTs if feed intake is in the profit function. However, if feed intake is not included, both residual and expected feed intake could be used as ERTs. This situation where by the ERTs can be parameterized in

more than one way is not unique to feed intake. It is possible to define ERTs that are themselves indexes of several other components, and either the subindex or the individual components (but not both) could be used as ERTs. For example, yearling weight could be expressed as weaning weight plus post-weaning gain, and in that case both traits would have a non-zero economic value provided yearling weight itself was not included in the profit function.

Considering indicator EPDs along with ERTs reduces response

The term “best” in BLP and BLUP indicates that there is no better predictor among linear unbiased predictors. In this context, best can be interpreted as minimizing the prediction error variance or maximizing the correlation between predicted and true genetic merit. This means that the selection response in aggregate index cannot be improved through knowledge of the individual ERTs. Similarly, the response in selecting for an ERT cannot be improved by taking account of a corresponding indicator trait EPD. Any emphasis on the indicator, whether positive or negative will reduce the response in the ERT as all the useful information in the indicator has bee used in the joint prediction of the EPD for the ERT. This can be demonstrated in an example calculation.

Suppose the range of true birth weight EPD is from -15 to +15 lb. Selection of the 40% lightest birthweight EPDs would produce an average of the selected individuals of -4.7 lbs. Alternatively, truncation selection of the animals with the highest EPDs for calving ease would produce an average of 0.45 on the underlying scale. Assuming a genetic correlation of -0.4 between calving ease and birthweight, there will be correlated responses in calving ease to selection on reduced birthweight and correlated reductions in birthweight to selection on calving ease. Selection could also be undertaken on an index of birthweight and calving ease, and this would produce intermediate responses in the two traits that can be depicted as an ellipse in Figure 1.

In practice, livestock managers do not have the opportunity to select on true merit, but can select on estimated merit such as EPDs. These may be calculated using BLUP, which is a shrinkage estimator, resulting in the variation in EPDs being less than the variation in true merit, with the amount of shrink being defined by the reliability of the EPDs. The reliability is the square of the correlation of true and estimated merit. The shrinkage from true to estimated merit expected for a sire with 50 offspring for each of calving ease and birthweight is also depicted on Figure 1. Selecting to reduce birthweight based on a progeny test with 50 daughters measured for birthweight and calving ease would achieve a selection differential of -4.4 lb, less than the -4.7 lb achievable by selection on true merit. The corresponding values for calving difficulty reduces from 0.45 based on true merit to 0.38 based on 50 offspring. These two values are shown on Figure 1, which can be used to visualize the correlated responses for the two selection strategies.

The selection response on the underlying scale can be backtransformed to derive its impact on reducing the frequency of difficult calvings. Suppose our base herd experiences 20% calving difficulty among bull calves born to first-calving 2 yr old cows. Selection for calving ease could reduce the difficult calvings from 20% to 12% and would result in a correlated reduction of 2.1 lb birthweight. Selection on reduced birthweight to improve calving ease by this same amount would take more than twice as many years of selection and would be associated with a 9 lb reduction in birthweight. Selection on the

ERT alone is more effective at changing the ERT than is selection on the indicator trait, provided the indicator trait is used in a multivariate prediction of the ERT.

Future selection

Selection should ideally focus on future rather than current profit, because of the time delay between today's selection decisions and the realization of income and expenses in the descendant generations. It is the future economic relevance that is therefore critical to selection. Production, economic and management circumstances change with political and legislative factors, the global market and the internalization of externalities. Political and legislative factors such as country of origin labeling (COOL) and the Kyoto protocol on greenhouse gas emissions will alter prices and costs. The global marketplace will influence the supply and demand for oil, feed and labor, altering the nature of beef production costs. Externalities such as variation in human healthfulness of beef, contamination of air and water supplies by excretion of endocrine disrupters and reactive nitrogen will likely in future become internalized, changing the characteristics that are important for selection to improve profit. Collectively, this will result in new traits becoming economically relevant as well as modifying the relative economic emphasis of existing traits.

Many of the traits that are likely to become important in the future could be recognized today as traits that might be of interest, but major obstacles arise in measuring relevant phenotypes. For example, disease traits are difficult to measure because of a lack of quantifiable scale. Animals with bovine respiratory disease might "look sick" or "appear healthy". Inspection of their lungs at slaughter may "show lesions" or be "lesion free". It is not clear which of these scales is more relevant. Further, when most individuals are managed to stay healthy, little information can be collected to rank sires. Feed intake is difficult to measure in a feedlot setting on individual animals, and almost impossible to measure in grazing circumstances. Human healthfulness of individual beef samples is impossible to measure on human feeding studies, but can be approximated on the basis of a few key components such as fatty acid composition. However, those fatty acids are too expensive to routinely measure. In contrast, growth traits have been easy to measure and have therefore received the most attention in research, evaluation and selection. In future, there will be opportunities to predict the straightforward and difficult to measure traits using genomic information and perhaps to routinely and reliably estimate merit of selection candidates without individual phenotypes.

Summary

In these changing times, it will be important to ensure that we distinguish traits according to their classification as ERTs or indicators. Indicators should be measured, recorded and used to predict ERTs. Publication efforts should focus on EPDs for ERTs and not indicators. Focusing sire summaries on ERTs would simplify selection decisions, improve selection responses, and facilitate construction of economic indexes. Collectively, these changes will lead to more cost-effective genetic improvement.

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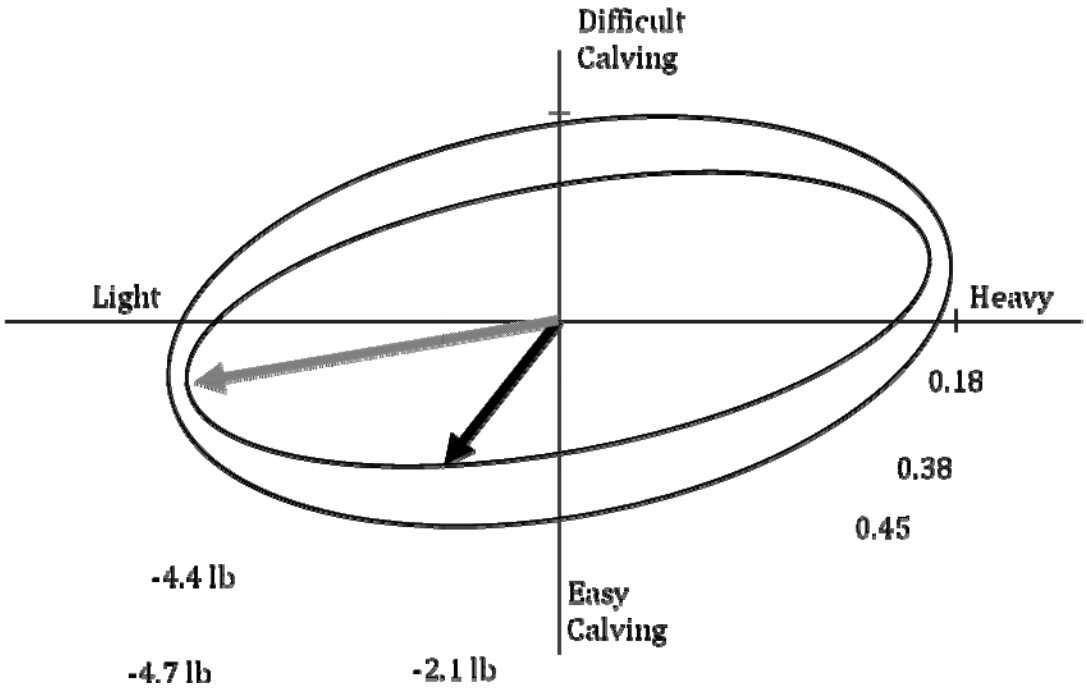
Figure 1. Genetic merit for calving ease on the underlying scale (y-axis) against birthweight in lbs (x-axis) showing the means for index selection with varying economic values of the best 40% (i-bar = 1) on the outer ellipse representing true genetic merit and the inner ellipse representing the shrinkage for sires with 50 daughters measured for calving ease and birthweight. The grey arrow represents selection to reduce birthweight and the black arrow represents selection to improve calving ease.



Genetic Prediction of Feed Efficiency and Input Components[1]

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9th Genetic Prediction Workshop, December, 2008, Kansas City, MO

Introduction

For several decades, genetic evaluation procedures have been developed for traits of economic relevance to beef production. Statistical procedures to accurately predict additive breeding values in the form of expected progeny differences (EPD) have advanced rapidly. Current genetic evaluation models, based on Henderson's mixed model equations (e.g., Henderson, 1984), provide best linear unbiased predictions (BLUP) of genetic merit, and now represent the standard for genetic prediction. Other advances, such as standardization of recording guidelines for performance data (BIF, 2002), increases in computing capabilities, and the development of specialized genetic analysis software (e.g., Boldman et al., 1995; Gilmour, 1997; Crews et al., 2008) have played significant roles in implementation of models for large scale genetic prediction, commonly referred to as national cattle evaluation (NCE).

Nearly all purebred beef cattle associations conduct NCE. Although all breeds compute EPD for basic weight traits (birth, weaning, and yearling), an increasing number of breeds now conduct research and development programs in genetic improvement that include prototype traits with economic importance. Golden et al. (2000) revived the concept of economic relevance as a framework to guide the process of identifying traits for which EPD should be reported and their indicators in the next generation of NCE programs.

The ERT framework centers on the distinction between economically relevant traits (ERT) and their indicators. Much of the recent scientific literature has focused on development of genetic evaluation systems for traits more complex than weight and growth rate. There has been little concentrated effort to standardize the implementation of prototype traits in beef NCE, although most of the more than 60 traits currently evaluated by the numerous breeds worldwide (Golden, 2001) can be characterized as being related to reproductive efficiency, growth performance, and(or) carcass merit (Crews, 2001). Several traits, commonly measured on beef cattle, and used for NCE, do not directly impact revenue or cost and are therefore appropriately termed indicator traits. Because indicator traits are often easier and(or) more cost effective to measure than the ERT, and have high genetic correlation with the ERT, they remain an important component of beef NCE worldwide.

Implementation of genetic prediction systems in the beef industry, including data collection, model development, and routine EPD computation, have resulted in significant and permanent changes in the genetic potential of cattle populations around the world. In most populations, however, selection has been primarily aimed at changing the mean of output (revenue) traits such as weight, fertility, and meat yield (Archer et al., 1999; Crews, 2001). Only recently has there been renewed research interest in the other component of profitability:

1 Taken in parts from: Crews, D. H., Jr. 2005. Genetics of efficient feed utilization and national cattle evaluation: a review. Genetics and Molecular Research 4 (2):152-165.

namely the reduction of inputs (cost). Feed costs and supplementation account for at least 70% of non-fixed beef production costs. Genetic improvement programs aimed at reducing input costs will likely include traits related to feed utilization (Archer et al., 1999; Crews et al., 2003).

Traditional Measures of Efficiency

In the scientific literature, numerous measures of production system efficiency can be found, although efficiency of production in cattle involves a complex of feed inputs and product outputs of animals across several dissimilar industry segments, which likely involve animals evaluated at different ages and stages of production. Most early work described efficiency at the ratio of inputs (e.g., feed) to outputs (e.g., weight gain) within a specific industry segment or stage of animal production, which leads only to limited insight into the efficiency of the entire production system. As such, feed conversion ratio (FCR) is the most common measure of efficiency in the literature, although more than two dozen measures of feed efficiency have been discussed (Archer et al., 1999). Feed intake and FCR are well known to be phenotypically and genetically correlated with measures of growth and therefore mature size. For example, in their meta-analysis of published estimates of genetic parameters for beef production traits, Koots et al. (1994b) found numerous estimates of the genetic correlation of FCR with weights and rates of gain ranging from -0.24 to -0.95, which clearly indicate that increased genetic potential for performance and size is concomitant with improved FCR. Therefore, selection for improved (decreased) FCR would result in increased correlated genetic responses for growth rates, mature size, and presumably, mature maintenance requirement. Koots et al. (1994b) further showed strong evidence that the genetic associations of feed intake with measures of growth rate and weight were positive, with genetic correlation estimates ranging from 0.25 to 0.79. Of particular note among these were estimates of the genetic correlations of mature weight with FCR (-0.14) and feed intake (0.92).

These high estimates of genetic correlation suggest that selection for growth rate would be expected to result in correlated responses in both feed intake and FCR. A drawback of this approach is that favorable correlated decreases in FCR due to selection for increased growth rate are not necessarily correlated to improvement in efficiency. This is strongly supported by Mrode et al. (1990) in which a line of Hereford cattle selected for lean growth rate had a higher correlated response in lean feed conversion ratio than the direct response to selection for lean conversion ratio found in a similar line.

Animals with high genetic potential for growth rate are assumed to have improved (i.e., lower) FCR and also have an increased genetic potential for mature size. In addition to being highly heritable (h^2 = 0.50; Koots et al., 1994a), mature cow weight has high genetic correlations (r_g > 0.60; Koots et al., 1994b) with growth rates measured at younger ages. Therefore, selection to directly increase weight and growth rate in juvenile cattle (e.g., at weaning and(or) yearling) would likely result in strongly positive genetic change in mature size, and presumably, maintenance requirements. Archer et al. (1999) pointed out that although FCR may be a relevant measure of efficiency in industry segments devoted to production of growing animals, if an increase in feed requirements of the breeding herd (e.g., through increased mature cow size) offsets the gains in efficiency of market progeny, little to no progress will be made relative to total system efficiency. These results lead to the conclusion that an alternative measure of efficiency would be desirable, to reduce the antagonisms of correlated responses, and which would reflect more the across-segment differences to enable more effective selection for efficiency.

Feed Intake

Because feeding of harvested forages and concentrates in the feedlot sector, and supplementation of the cow herd, intake is clearly a cost-side ERT, accounting for at least 70% of non-fixed production cost. Among more than two dozen alternative phenotypes described in the literature as measures of efficiency (Archer et al., 1999), one distinction is whether actual intake is measured or predicted. As an ERT, feed intake should be considered in the design of genetic improvement programs, although direct inclusion of feed intake is limited by the costs associated with appropriate data collection. With respect to growing cattle, approximately 70% of the phenotypic variance in dry matter intake can be attributed to live weight, average daily gain, and deposition of major body composition components, leaving approximately 30% essentially unaccounted for. In their meta-analysis, Koots et al. (1994a) summarized 21 studies published up to 1992 wherein the heritability of feed (dry matter) intake was reported and the weighted mean estimate was 0.34. Since that time, seven more recent studies have reported feed intake heritability estimates ranging from 0.19 to 0.62, although adding these estimates to the weighting procedure used by Koots and coworkers only changed the weighted estimate to 0.39. Therefore, given a sufficiency of data and accurate selection decisions, genetic improvement of feed intake should be straightforward.

Koots et al. (1994b) and more recent studies, however, clearly show that feed intake is highly related to growth and production, with genetic correlations often exceeding 0.50. Therefore, decreasing selection for feed intake would have the antagonistic correlated response of decreasing growth rate and other production ERT. Complex, and sometimes antagonistic, inter-correlations among ERT is common in animal breeding which underscores the need to consider feed intake and efficiency within the multiple trait context. Summaries have concluded that alternative measures of feed intake are needed to address the issue of efficient feed utilization in cattle (Archer et al., 1999; Crews, 2005).

Phenotypic Residual Feed Intake

Residual feed intake (RFI), also referred to as net feed intake and net feed efficiency, was first proposed for cattle by Koch et al. (1963), and is defined as the difference between actual feed intake and that predicted on the basis of individual requirements for body weight maintenance and level of production. The concept was first used after study of several measures of efficiency, and development of the hypothesis that feed intake could be adjusted for level of production and maintenance of body weight. Koch et al. (1963) realized that a robust measure of efficiency would allow for adjustment of feed intake for any of the various requirements, or “energy sinks” that differentiate industry segments. For example, whereas hyperplasic and hypertrophic tissue growth may be the major energy requirements for young growing cattle, the requirements for the mature cow herd may be maintenance of body composition for reproductive fitness and lactation. RFI relies simply on partitioning intake into portions required for stage and level of production, and a residual portion that is perhaps more closely related to true metabolic efficiency which would be more comparable across industry segments. Given that identifiable “energy sinks” will differ and lead to different components of expected feed intake across industry segments, residual feed intake is more appropriately characterized as a methodology rather than a static phenotype. Ultimately, RFI is feed intake (with respect to economic relevance) that has simply been rendered independent of measurable correlates such as weight and growth rate.

More recent research (e.g., Basarab et al., 2003; Crews, 2005; Nkrumah et al., 2007) has focused on characterization of RFI in the feeding segment of the beef industry. Therefore,

most of the following discussion will be focused on young, growing cattle although the concept of RFI is not so limited. Calculation of RFI, as reported in several studies (e.g., Arthur et al., 2001a,b; Basarab et al., 2003; Crews et al., 2003), can be generally summarized as:

$$y = \beta_0 + \beta_1(ADG) + \beta_2(MWT) + RFI$$

where y is daily (dry matter) intake, β_0 is the regression intercept, β_1 is the partial regression of intake on average daily gain (ADG), and β_2 is the partial regression of intake on metabolic body size (MWT = $LWT^{0.75}$ where LWT = mid-test live weight). Since Basarab et al. (2004) reported associations and correlations of phenotypic RFI with body and carcass measures of fat and leanness, a North American trend has emerged to further adjust daily intake for ultrasound estimates of subcutaneous fat depth and longissimus muscle area, or their deposition rates (e.g., Crews et al., 2006). The R^2 of these body composition-adjusted RFI regressions only increase by 5-8% compared to the so-called "base RFI" regression model, but the importance of considering body composition in intake and efficiency research seems clear. In fact, any non-zero covariances involving feed intake can be accounted for in RFI estimation, resulting in the same independence from RFI, further illustrating residualization as a methodology of which RFI is an example. Therefore, the above equation can be generally given from multiple linear regression in matrix notation as:

$$\mathbf{y} = \mathbf{X\beta} + \mathbf{e}$$

where **y** (the vector of individual animal intake records) is partitioned into expected intake defined by the matrix **X** (containing an intercept term and observations on live weight, ADG, body composition and potentially other predictors) and regression vector **β**, and **e** = RFI. Simple rearrangement shows that RFI is the difference between actual (**y**) and predicted (**Xβ**) feed intake: **e** = RFI = **y** – **Xβ**.

Using this phenotypic regression approach, the properties of RFI are easily defined using standard statistical procedures. One central feature of these is the distributional property (i.e., RFI ~ $N(0,\sigma^2)$) showing that RFI has zero mean (Searle, 1982). Properties of linear regression can also be used to show that RFI is independent of the partial regression terms in the estimation model including ADG, MWT and any other predictors of intake ($r(\mathbf{X}_i, \mathbf{e}) = 0$). This important result has been verified in recent reports, at least in phenotypic terms. The implication is that for any population, approximately equal halves will have RFI above and below zero, respectively. Efficient animals (i.e., with RFI values below zero) have daily intakes less than would be predicted given their own level of production and body weight, whereas the converse is true for (inefficient) animals with RFI greater than zero.

It is important to note that the above multiple linear regression procedure only forces the independence of RFI from production level and weight at the phenotypic level. With phenotypic regression, important covariances can still exist, resulting in non-zero genetic correlations (Kennedy et al., 1993; Crews, 2005) of RFI with either ADG and(or) MWT. Extension of the above method to genetic regression is straightforward (Crews, 2005), which forces genetic independence of RFI with its components. Some studies (e.g., Arthur et al., 2001b) have estimated near zero genetic correlations of phenotypic RFI with weight and production traits; however, this level of independence is not ensured with phenotypic regression.

Phenotypic and Genetic Variation in RFI

To be a candidate for selection, an ERT must exhibit genetic variability, which is to say that variability in phenotypic expression must be to some extent dependent on additive genetic variance (heritable). All studies that have estimated genetic variance for RFI have reported this parameter to be non-zero. Specific heritability estimates include 0.26 to 0.30 (Crews et al., 2003), 0.28 (Koch et al., 1963), 0.39 (Arthur et al., 2001a) and 0.39 to 0.43 (Arthur et al., 2001b). Selection for RFI would be expected therefore to result in genetic change relatively comparable to that obtained with other moderately heritable traits, given enough phenotypic data and selection intensity.

Heritability alone can be misleading for predicting response to selection for RFI. The variability in the phenotype underlying RFI, feed intake, should be examined. In recent studies, considerable variation has been reported for various measures of daily (dry matter) intake. For example, for four biological types of cattle, Archer and Bergh (2000) reported phenotypic standard deviations (SD) ranging from 1.08 to 1.32 kg/d for dry matter intake. Similarly, Angus bulls and heifers (Arthur et al., 2001a) and Charolais bulls (Arthur et al., 2001b) had daily intakes with phenotypic SD of 1.3 kg/d in Australia and France, respectively. Basarab et al. (2003) reported phenotypic SD of 1.02 kg/d for dry matter intake of composite steers in Alberta, Canada. The partitioning of daily intake into production and residual components dictates that RFI will have lower variance than intake. Basarab et al. (2003) for example, reported RFI regression models with R^2 greater than 0.70 for the phenotypic regression of intake on ADG and metabolic body size of steers. In Australia, phenotypic SD of RFI as a proportion of phenotypic SD of feed intake was reported to be approximately 0.46 (Archer and Bergh, 2000), 0.56 (Arthur et al., 2001a) and 0.59 (Arthur et al., 2001b) among young replacement cattle of various breeds. Among Charolais and Charolais cross steers, Crews et al. (2003) showed that metabolic body size and ADG explained approximately 45 to 50% of the phenotypic variance in daily feed intake. These results confirm that after adjustment for growth rate and proxy measures of maintenance requirements, approximately 30 to 50% of the phenotypic variance in feed intake remains as residual (RFI). Considering that large phenotypic differences exist in intake, moderate heritability would be expected to translate to significant additive genetic change for a more true measure of efficiency and perhaps more importantly, for reduced feed costs.

Genetic (Co)variance and RFI

Because beef production extends over a wide range of environmental conditions and includes a wide range of breeds, crossbreds, and biological types, there are many traits that are economically relevant or are important indicators. As a consequence, it is not recommended that any genetic improvement program focus exclusively on any single trait. An important consideration in comprehensive genetic improvement programs is whether genetic effects among traits and trait-systems are correlated. This consideration is especially important if genetic correlations may be antagonistic.

As noted previously, FCR is a commonly studied measure of feed efficiency and most estimates indicate that a wide array of efficiency measures are at least moderately heritable. Recent studies have reported strongly positive genetic correlations for phenotypic RFI with FCR (0.70, Herd and Bishop, 2000; 0.85, Arthur et al., 2001a; 0.66, Arthur et al., 2001b). Similarly, positive genetic correlations of 0.64 (Herd and Bishop, 2000), 0.69 (Arthur et al., 2001a) and 0.79 (Arthur et al., 2001b) have been reported for RFI with feed intake. These results suggest that selection for improved (decreased) RFI would be associated with a corresponding declining genetic change for feed intake. Arthur et al. (2001a) estimated genetic correlations of RFI with

some measures of body composition in Angus cattle and reported these to be generally small with the exception of ultrasound rib fat (rg = 0.17), which is a small genetic correlation, but does indicate that genetic effects for feed intake may be related to those for subcutaneous fat deposition. Supporting phenotypic evidence for a positive association between improved RFI and reduced carcass fat has been reported by Basarab et al. (2003). Crews et al. (2003) estimated genetic correlations of different RFI measures with carcass traits. In that study, RFI was calculated separately for postweaning growing and finishing periods (i.e., when diets differed in energy density) for Charolais and Charolais-sired crossbred steers in southern Alberta. Improved RFI was in most cases only weakly associated with carcass merit, although standard errors for the estimated parameters were large. Arthur et al. (2001b) pointed out that among the few feed efficiency studies including body composition, estimates of genetic correlations were generally weak in magnitude, implying that no conclusions were yet warranted. Since that time, further adjustment of intake which results in RFI independent of body composition has become standard, at least in North America (Crews et al., 2006; Nkrumah et al., 2007). Without this adjustment, research consistently shows a small and positive correlation of RFI with various measures of carcass fat content (especially subcutaneous fat) and cattle with more efficient RFI phenotypes produced leaner carcasses (Basarab et al., 2003), but do not necessarily differ from less efficient cattle with regard to carcass lean and retail yield (Crews et al. 2003).

Economic Implications of Selection for RFI

Direct selection for RFI would be expected to result in genetic trend similar to that obtained with other traits with similarly moderate heritability (e.g., growth), assuming a sufficiency of data collection. Recent reports have been more variable with respect to the phenotypic range in calculated RFI. Basarab et al. (2003) reported that RFI (mean = 0.00, SD = 0.66 kg/d) ranged from an efficient -1.95 kg/d to an inefficient +1.82 kg/d among composite steers fed for 120 d (i.e., 3.77 kg daily dry matter intake difference between the most and least efficient steers). Archer et al. (1998) identified efficient breeding bulls which consumed 2.5 kg/d less feed over a 120-d test period while maintaining similar live weights and gains compared to less efficient bulls. Crews et al. (2003) reported that during a postweaning growing period, more efficient Charolais-sired steers (group mean RFI = -1.33 kg/d) consumed 2.73 kg less feed daily than less efficient steers (group mean RFI = +1.40 kg/d); similarly during the finishing period, a difference of 1.69 kg/d was reported between more (group mean RFI = -0.84 kg/d) and less (group mean RFI = +0.85 kg/d) efficient steers. In both comparisons, steers had similar live weight gain, metabolic body size, and carcass composition.

Assuming a feed cost of $0.101 per kg (Basarab et al., 2003), a daily intake difference of 2.50 kg translates to a feed cost savings of $0.25 per animal per day, or $37.37 per animal over a typical 150-d finishing period. More than 28.5 million market steers and heifers are produced annually in the United States. Based on industry standard performance, dry matter conversion, and feedlot gain, Herring and Bertrand (2002) pointed out that a 2% reduction in feed consumption (while holding performance traits constant) would provide an increase of $111 million in net return to beef producers. Assuming a standard rate of genetic progress in the range of 0.5 to 2.5% of the mean per year, research suggests the potential to maintain performance (e.g., total postweaning live weight gain) while decreasing daily intake (1% per year) by 0.13 kg per animal (assuming average intake of 13 kg and 1% annual improvement, or total finishing period intake by 19.5 kg per animal per year through selection. In regions where more than 2 million head of market cattle are produced annually, this translates to savings in feed costs of over $5 million. Obviously, these trends and predictions would be considerably impacted by the higher feed costs that have been common in the five years since 2003.

Intake and RFI in Multiple Trait Selection

Even though intake and RFI have been well characterized in recent studies (Archer et al., 1999; Basarab et al., 2003; Crews, 2005), there has been little research on the potential for implementation of multiple trait selection programs including RFI. Crews et al. (2006) developed a multiple trait selection index including RFI with the objective to improve net feedlot revenue in market progeny of performance tested Angus sires. The selection objective defined aggregate genetic merit of fed steers as a function of daily dry matter intake, average daily gain on feed, and final (pre-slaughter) live weight. The selection criteria for bulls was then a linear function of RFI, average daily gain on test, and 365-d live weight. Bull RFI included the usual terms of ADG and MWT, but also ultrasound measures of subcutaneous fat depth and ribeye area such that RFI was independent of both production and body composition. Phenotypic index values on Angus bulls (n = 100) were adjusted to a mean of 100 (SD = 7.81), and ranged from 80.1 to 115.7. The phenotypic correlations of index value with other traits measured on the bull test indicated that bulls with higher index values consumed less daily dry matter, had greater ADG, and were more efficient (i.e., lower RFI), but did not differ from low-indexing bulls with respect to yearling weight. There was a trend for the index to be favorably associated (r = 0.16) with yearling scrotal circumference, suggesting that selection would not be antagonistic with indicators of bull fertility. Although more research should be conducted, this work illustrates the need to consider intake and efficiency within the context of multiple trait selection.

Genetic Evaluation of Efficiency and Future Efficiency Research

ERT related to efficiency of feed utilization have been identified as an example of the next-generation of EPD for the beef industry (E. J. Pollak, personal communication). Important lessons may be learned in terms of selection progress from other species such as poultry and swine, where feed efficiency has been under selection for several generations. Because NCE procedures exist for other relevant traits, the time from the present until actual reported of EPD for efficiency traits can be much shorter than the development required 30 years ago for growth traits. An NCE system requires three essential components: data acquisition, model development, estimation of parameters, and routine genetic evaluation runs.

One factor behind renewed interest in NCE for efficiency is that equipment for measuring individual feed intake is improving. Traditionally, individual feed intake was not measured, and early efficiency research relied on intake at the pen level. Such an approach is inappropriate for an evaluation system with the objective to characterize individual animal differences, because all animals within a pen essentially receive the same phenotypic intake record. When pedigree ties among animals are through sires alone, some of these limitations can be alleviated through removing confounding of sire and pen. Individual feed intake can be recorded when animals are individually housed and fed, but not without serious impacts on feeding behavior and intake. Additionally, technology can be used to house cattle in groups but limit the locations along the feed bunk at which they can feed so that individual intake can be approximated. Technological limitations have always reduced the effectiveness of these approaches. Another concern is that these pseudo-group designs alter feeding behavior such that individual differences are either biased or are not reflective of standard industry practices. Current advances in feed intake measurement equipment have focused on recording individual animal intake in cattle fed in groups while minimally impacting feeding behavior. Such equipment generally couples electronic animal identification or animal-bunk attendance with bunk-based feed disappearance. Results are promising, although the newest technology is also usually the most expensive.

Depending on capacity and useful life, the cost of measuring individual feed intake with state-of-the-art equipment has been estimated to range from $50 to more than $200 per head.

The major limitation to implementing NCE for efficiency is data acquisition. In addition to the added cost of recording individual animal intake, the suitability of data for NCE programs must be considered. In the case of feedlot animals, parentage identity is usually unknown. With the exception of central test station programs and a limited number of progeny testing programs currently in place for evaluation of carcass merit, most calves destined for slaughter are anonymous with regard to parentage and pedigree. This lack of information is even more of a problem with commercial calves from unregistered parents. A minimum of sire identification on animals with intake phenotypes would be required. Pollak and Kirschten (2002) mentioned studies underway to combine DNA-based parentage testing with individual intake recording to maximize the information gained per dollar invested in data acquisition, but the added cost of parentage testing drives the system cost even higher. A further consideration regarding data suitability is standardization of protocols for individual intake data recording. Regardless of the equipment used, standard testing procedures have not been in place for intake data collection, even among scientific studies. In 2007, the Beef Improvement Federation formed a sub-committee of experts from across North America to develop guidelines and recommendations for the recording and reporting of individual feed intake data. Crews et al. (2009) summarized the minimum guidelines for individual intake and efficiency data recording, which will be part of the 9th Beef Improvement Federation Guidelines for Uniform Beef Improvement Programs.

Some procedures exist to compute EPD for efficiency that do not require recording of individual animal intake. The accuracy of these predictions depends on the genetic correlation between traits for which phenotypes are available (e.g., indicator traits) and the trait of interest (e.g., feed intake). Ultimately, there is always a less than 1.0 upper limit on the accuracy of EPD for an unmeasured trait. While animals can be very accurately evaluated for traits for which phenotypic data acquisition is in place, few strongly correlated indicator traits have been identified for efficiency traits such as RFI. This is partially due to the forced independence of RFI with other performance traits.

Improvement in Intake and Efficiency with Genomic Tools

Mapping of the bovine genome and the development of related genomic tools has prompted an interest in augmentation of traditional genetic evaluation systems with gene marker information. Marker assisted evaluation systems would optimally combine genomic and phenotypic data with pedigree to predict EPD with higher accuracy than would be possible from evaluations based solely on phenotypic data alone. Such marker assisted EPD (MAEPD) would be particularly useful for increasing the accuracy of evaluating young animals which have yet to make their own phenotypic record or produce progeny with records for the ERT or indicators. Selection index methodology has been applied to this problem of optimally combining genomic and polygenic breeding values. Polygenic and marker-derived breeding values are combined in a linear index with weighting factors that depend solely on accuracy of the polygenic breeding value or EPD, and the proportion of genetic variance attributable to the marker set. Simulation has confirmed that polygenic EPD accuracy and the gain in accuracy of evaluation due to inclusion of marker information are inversely related (Crews, 2008). Therefore, for traits with high heritability, or that accumulate evaluation accuracy quickly on young animals are less viable candidates for genomic selection. However, traits related to feed intake remain likely candidates for gene assisted evaluation because of the cost and time required for traditional polygenic evaluation (e.g., Moore, 2008). Functional genomics studies which report associations of single nucleotide polymorphisms (SNP) markers and SNP haplotypes with economically

relevant beef traits are now common, but optimal MAEPD systems will require robust estimates of combined marker effects that have yet to be reported. In fact, marker sets or commercial gene marker tests will likely need to account for at least 10-15% of the genetic variance in feed intake and(or) RFI before marker assisted EPD system development and implementation would be cost effective (Crews, 2008). The time then required to build genomic information databases on a critical mass of animals in large field populations will depend on the effectiveness (information density) of the marker panel and commercial genotyping costs. The potential benefits to genetic evaluation of feed intake and efficiency with the influx of genomics tools and marker assisted evaluation remain very large.

Implications

Feed and feed supplementation represent the largest non-fixed costs of beef production. Genetic improvement programs for reducing input costs will likely include traits related to feed utilization. In contrast to traditional ratio-type measures of feed efficiency, residual feed intake is uncorrelated with body weight and growth rate (and body composition), which would at least partially alleviate concerns over the long-term implications of selection and correlated responses in mature size and maintenance requirements. Potential unfavorable correlated responses resulting from selection for residual feed intake should be closely investigated before recommendations are made. Expense associated with individual feed intake data collection limits implementation of efficiency NCE, and dictates the use of optimal data acquisition schemes for computation of EPD. Knowledge gained from functional genomics and tools leading to gene assisted EPD have promise in this area but require more development. In the end, implementation of NCE for efficiency has the potential to significantly increase efficiency of cattle production.

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National Beef Cattle Evaluation Consortium

Genetic Prediction of Animal Health

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Economically Relevant Traits

- Focus on profitability
  - What traits directly influence profitability?
    - Costs versus Revenues
- Where are the weaknesses?
  - Feed requirements
    - Feedlot steer/heifer
    - Cow
  - Animal health
  - Temperament
  - Product Healthfulness
  - Future traits??

What are the issues with genetic evaluation of ERT?

- Data availability
- Accuracy of the EPD for the ERT
  - Find correlated traits that will add accuracy to limited (or nonexistent) data
  - Identify markers/genome to improve accuracy of the prediction for the deficient ERT

Disease

- Caused by environmental factors
  - Viral
  - Bacterial
  - Environmental Toxins
  - Parasites
  - Geographical challenges

From C. Morris, 2007

Hurdles associated with collection of health data

- Variable exposure to challenge
  - Disease vector
- Alternatives:
  - Challenge studies
    - Disease organism
    - Toxin – facial eczema
    - Movement of individuals
      - High altitude
  - Collect large amounts of data on individuals with variable challenge

Our charge is to develop selection tools for health

- Not a new problem
  - "Known individual and species differences in ability to resist infections of certain disease furnish evidence that genetic differences play a part in conditioning resistance to disease"
    - .27 heritability of resistance to mastitis
      - Legates and Grinnells, 1952

Is there evidence for genetic control of health?

- In French outbreaks of FMD (1932 and 1955) evidence of resistant families
- Fecal egg count – 40 fold difference in susceptible versus resistant lines

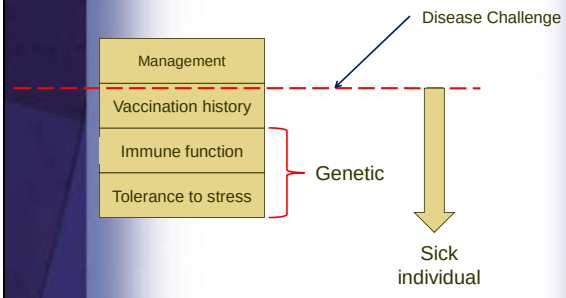
From C. Morris, 2007

Other evidence

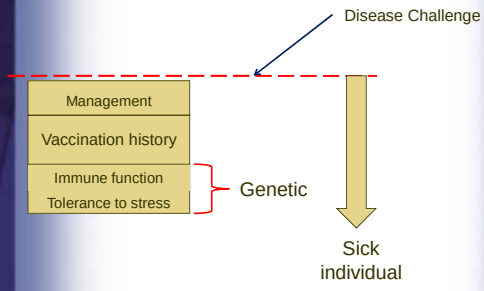
- Toxins – Facial eczema
  - .30 heritability for enzyme indicators
- High altitude disease –
  - .40 heritability
- Tuberculosis resistance in deer
  - .49 heritability

From C. Morris, 2007

Perspective on disease



Perspective on disease



Feedlot Health

The economics behind genetic improvement of cattle health

- The dollars…
  - 1997 estimates put prevention and treatment of disease in the feedlot at >$3 billion (Griffin, 1997)
  - ~1.1 million cattle with an estimated value of over $692 million were lost to respiratory causes in 2005 (USDA, 2006).

The economics behind genetic improvement of cattle health

- Performance!
  - ~16 pounds reduction in hot carcass weight for animals treated in 1st 40 days (Snowder et al., 2007)
  - Lung damage (yes/no) – 34 pounds of carcass weight (Engler, 2007)

Feedlot deaths have increased

- Total feedlot deaths increased 69% in 2003 compared to 1994
- Bovine Respiratory Disease Complex (BRDC) deaths more than doubled (118%) during same time

Guy Loneragan, WTAMU, (2008)
Sentinel Feedlot Monitoring Program (USDA:CEAH)

There is an economic justification but what about genetic variability?

The genetic case for feedlot health

- Snowder et al. (2006)
  - 1987 to 2001 calves with incidence of BRD ranging from 5% to 44%
  - Heritability on observed scale was .04 to .08
    - .18 on the underlying continuous scale
- Muggli-Cockett et al. (1992)
  - Heritability of .10 to .06
  - Incidence ranging from 14% to 38%

Heritability appears to increase with increasing incidence

- Low incidence versus high incidence years (Snowder et al. 2006)
  - True with other binary traits (Comstock, 2008)

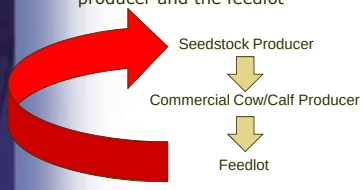
There is genetic variability

- We can make progress with the appropriate tools

- Genetic variability indicates potential for development of selection tools
- Are there any other concerns?

Low accuracy is likely an issue

- Sufficient data is lacking
  - Industry disconnect between the cow/calf producer and the feedlot



  - Few cattle from the "seedstock" sector involved
    - Cull bulls and heifers

What is required for genetic prediction of health?

- Use of genomic tools
- Better mechanisms for "data flow"

Other data issues

- Vaccination background and timing
  - Contemporary group
- On-ranch animal treatments
- Feedlot management decisions
  - "Mass Medicate"
    - Lofgren (1983)
      - 21% to 90% reduction in treatment days/calf

Ongoing study investigating these differences

- Initiated because of the relationships established through the National Beef Cattle Evaluation Consortium

National Beef Cattle Evaluation Consortium

Ongoing study investigating these differences

- Initiated through the relationships established through the National Beef Cattle Evaluation Consortium

National Beef Cattle Evaluation Consortium

- Objectives:
  1. Develop methods to identify animals that are genetically superior for feedlot health characteristics through the use of both molecular and quantitative techniques.
  2. Identify new traits and evaluate their relationships with feedlot cattle health to improve accuracy of selection for disease susceptibility.

Study Background

- Steers (~2900 over 2 years) from a single source, fed at the cooperating Five Rivers Cattle Feeding Lot. Transportation of 340 miles

Background continued

- No vaccination upon arrival
  - Wanted a higher incidence of BRD (higher heritability)
- Cattle were implanted

Sick versus not

- Commercial lot personnel identified "sick" animals
  - What is "sick"? (clinical signs)

Defining "sick"

	Lung Lesions	No Lung Lesions
Treated/Pulled	70%	30%
Not Treated/Pulled	56%	44%

G. Loneragan (Wittum 1996; Thomson 2003)

31% average pull/treatment rate

Phenotypes collected

- Sick (yes/no)
- Time to recovery
- Necropsy results
- Lung lesion scores collected at harvest
- BVD PI information
- Visual scores
  - Nasal discharge, eye, cough, depression, rapid breathing

- Performance traits
  - Weights
  - Carcass traits
    - HCW, MS, QG, REA, BF, YG

Phenotypes continued

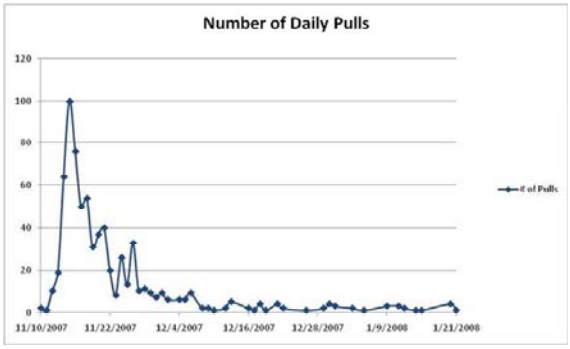
- Baseline stress and behavior characteristics
  - Temperament
    - Flight speed
    - Chute score – 2 evaluators
  - Stress indicators

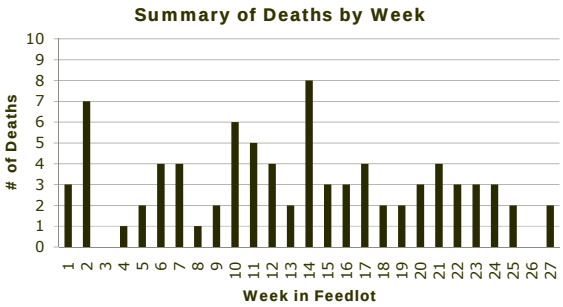
Phenotypes continued

- Baseline disease/immunological status measures
  - Baseline for exposure in the feedlot
    - BVD I & II, PI3, IBR, BRSV
  - Tests for differences in immune response
  - Body temperature profiles

Year 1 Results (1551 steers)

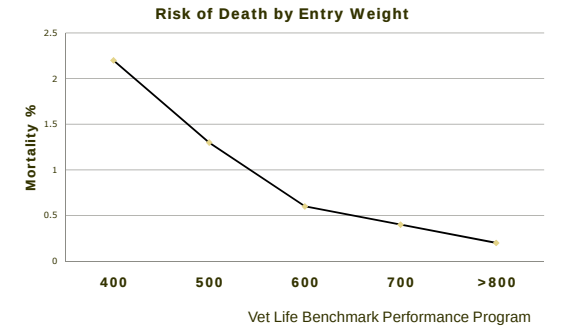
- 692 animals treated
  - 45% treatment rate
  - 20% treated a 2nd time before leaving the hospital pen
- 83 deads
  - 5.4% as percent of total
  - 14% as percent of treated





Preliminary Results

- Higher weights on arrival reduce time to sickness



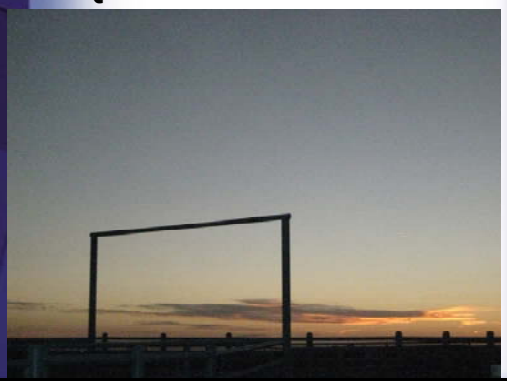
Results

- Higher weights on arrival reduce time to sickness
- Processing time and order influence probability of being "pulled" in the first 35 days of the feedlot phase

Acknowledgements

- Pfizer Animal Genetics
- NBCEC
- Guy Loneragan, West Texas A&M University
- Hana Van Campen, CSU
- Kraig Peel, CSU
- Bob Weaber, University of Missouri
- Christopher Chase, South Dakota State University
- Janeen Salak-Johnson, University of Illinois
- John Pollak, Cornell University
- John Wagner, CSU-Southeast Colorado Research Center
- Tony Bryant, Five Rivers Ranch Cattle Feeding
- Graduate Students!
  - Brian Brigham
  - Chase McAllister
  - Scott Speidel
  - Amanda Pepper
  - Gabriela Marquez
  - Brandon Meiwes
  - Leanne Matthews
  - Jim Latoski
  - Meghan Rohlf

Questions?



Genetic Prediction of Temperament in Beef Cattle

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Introduction:

Interest in the adaptability of ruminant livestock to a variety of production environments is growing quickly. A central theme of adaptability research in domesticated livestock is animal behavior. In ruminant species, routine management protocols can cause stress and fear, which are generally considered to negatively affect animal welfare. Additionally, cattle with poor temperaments can produce dangerous working conditions for employees during handling. Fearfulness in livestock creates additional stress for the animals, which reduces production performance and decreases profitability of livestock enterprises. Both improved animal welfare and increased farm profitability support the motivation to conduct research to investigate the phenotypic and genetic effects of cattle disposition on growth, carcass and feed efficiency traits. Improvements in disposition will reduce the number of employee injuries, equipment damage, animal injuries and associated losses in production due to disposition related stress.

Importance of Temperament Traits in Beef Cattle:

In ruminant species, routine management protocols can cause stress and fear, which are generally considered to negatively affect animal welfare. Procedures like vaccinations, castration, transportation and herding have all been reported as stressful to ruminant species including cattle and sheep (Wohlt et al., 1994; Hargreaves and Hutson, 1990a,b). Additionally, fearfulness has been shown to reduce productivity of cattle. Bouissou et al., 2001, reported that reactions due to fear affects sexual and maternal behavior as well as social dominance behavior in cattle. Increased fear, measured as reduced flight time, is associated with reduced average daily gain and final live weight of fed cattle (Burrow, 2003). Burrow (2003) has also shown that animals with poorer dispositions (faster flight times) produce steaks with higher Warner-Bratzler shear forces, which is indicative of tougher meat. Creason and Weaber (2007) demonstrated that during a post-weaning growing phase, steers with poorer disposition had lower average daily gains. Subsequently, these steers had light placement weights into the feeding phase and had lower average daily gains and lower feed intakes, but now differences in residual feed intake (RFI) during confinement feeding (Creason et al., 2007). Curley and others (2006) demonstrated the ability of Exit Velocity (EV) to effectively categorize animals into groups differing levels of circulating cortisol, a stress related hormone. They also demonstrated that EV is a repeatable measure of temperament and maybe a useful tool to predict stress responsiveness during future handling events.

Researchers at Colorado State University have investigated differences in chute scores between heifers and steers. The researchers demonstrated that steers had a lower (more desirable) average temperament rating than did heifers (Voisinet et al., 1997). Voisinet et al. (1997) also reported that fed cattle with calm temperaments had higher average daily gains than

did cattle with excitable temperaments. In fact, their research demonstrated that cattle with the calmest temperaments, evaluated using chute score, gained 0.19 kg/day more than animals evaluated with most excitable temperaments. They also found that animals with *Bos indicus* influenced cattle had significantly higher mean temperament rating than did those animals without *Bos indicus* influence. Most of the beef cattle temperament research has been conducted using *Bos indicus* influence cattle. A majority of the work to estimate genetic effects associated with temperament has been done in Australian production systems.

Aside from the animal welfare and production issues associated with increased fearfulness in cattle, these animals also pose an increased risk to humans handling them. Reduction of fearfulness through selection should provide improved adaptation to human contact and thereby be of both economic and ethical significance to producers (Boissy et al., 2005).

Phenotypic Record Collection:

A variety of methods have been used to quantify temperament of beef cattle. Three of these methods are: average objective flight speed measured in seconds, visual flight speed and crush (chute) scores (Burrow and Corbet, 2000). Flight speed or Exit Velocity (EV) is the velocity at which an animal leaves restraining device such as a chute or crush. Crush (chute) scores (CS) are categorical scores depicting the animal's behavior during restraint. Visual flight speed and crush scores are both subjective measures, while average flight speed measured electronically is an objective measure. Researchers are investigating the correlation between the objective and subjective measures.

The Beef Improvement Federation (Dolezal et al., 2002) suggests scoring beef cattle temperament during restraint of the animal in a squeeze chute. This system utilizes a categorical system ranging from one to six where: 1=Docile and 6=Very Aggressive. Several organizations have adopted this scoring methodology to collect phenotypic records of cattle disposition including the American Angus Association (AAA) and North American Limousin Foundation (NALF). NALF publishes a Docility EPD and has shown a positive genetic trend for docility EPD with an increase in the mean docility EPD of approximately 15% over the past 20 years (NALF, 2006). This increase means that 15% more progeny sired by a breed average bull born in 2005 should be scored a 1 or 2 on the BIF docility scale than progeny sired by a breed average bull born in 1985.

A fourth method of temperament measurement is pen score, which has been utilized as another subjective measure of disposition (Kunkle et al., 1986; Hammond et al., 1996; Curley et al., 2004). Animals are penned in small groups (n~=5) and approached by observers. The individual animal's response to human approach is scored on a scale from 1 to 5 as described in Table 1 below.

Genetic Evaluation of Temperament Traits:

Like other production measures, the phenotypic manifestation of temperament traits is the combined effects of genetic and environmental effects. Temperament traits have been shown to be moderately heritable, with magnitudes similar to the heritabilities of growth traits. Average objective flight speed measured in seconds, visual flight speed and crush (chute) scores have heritabilities of 0.35, 0.08 and 0.30 respectively (Burrow and Corbet, 2000). Weaber and Creason (2007) found heritabilities of Exit Velocity and Pen Score to be 0.35 and 0.15, respectively. Burrow (2001) found single flight speed scores were moderately heritable

(0.35), but with an average of 2 or 3 flight speed scores, the heritability increased considerably (0.44-0.50). A single generation of selection for improved flight time score resulted in an improvement in temperament by reducing the flight time score in progeny (Burrow, 2001). Several breed associations have implemented temperament or docility genetic evaluations. The American Angus Association, North American Limousin Foundation and the American Salers Association currently have routine genetic evaluation for docility. Beckman and others (2007) have investigated various models for estimation of maternal genetic and permanent environmental effects on calf temperament.

Important genetic relationships between temperament traits and production traits may present additional motivation for selection to improve these traits. Several research groups are investigating these interactions. Genetic correlations between flight time and carcass weight, retail yield, marbling, shear force, and meat color are 0.05, 0.11, -0.05, -0.48 and -0.18 respectively (Burrow, 2003). Curley et al., 2004, reported that increased exit velocity of bulls had a significant negative effect on final body weight (BW) and dry matter intake (DMI). Positive correlations between chute scores, pen scores and exit velocity have been reported (Curley et al., 2004).

Research investigating the relationship between temperament and measures of production performance or genetic sequence has been conducted in a number of species. Momozawa et al. (2005) reported a significant association in equine between a single nucleotide polymorphism (SNP) possibly resulting in an A-G substitution in the dopamine D4 receptor gene and two temperament traits (curiosity and vigilance). A QTL discovery project was undertaken by Schmutz et al. (2001) utilizing the Canadian Beef Cattle Reference Herd. Calves (n=130) from the herd and origination from 17 full-sib families resulting from multiple ovulation embryo transfer (MOET) were evaluated for two measures of behavior: temperament and habituation. Heritability was estimated to be 0.36 for temperament and 0.46 for habituation. QTL for both traits were mapped to bovine chromosomes 1, 5, 9, 11, 14, 15. Behavior and conformation QTL detection studies have been performed (Hiendleder et al., 2003) resulting in the identification of QTL for both udder conformation and behavior traits in dairy cattle.

Current Work:

The National Beef Cattle Evaluation Consortium's Genetics of Feedlot Cattle Health Project has utilized two measures of temperament (CS and EV) of cattle during the finishing phase. Temperament has been included in the phenotypic record collection protocol as a method to possibly describe variation in not only behavior, but also stress, as potential contributor to resistance to disease. The project protocol will also identify associations between temperament and other production and carcass traits. Preliminary results (Weaber et al., 2008) suggest a positive (0.44) correlation between EV at placement into the feed yard and EV measured during re-implant processing approximately 75 d later. EV was also positively correlated with CS at initial and re-implant processing. In preliminary data analysis, which did not include a covariate for treatment count, EV at re-implant had a near zero, negative correlation with ADG and gain.

Work has begun to compute data points for a new phenotype called habituation. In psychology, habituation is the psychological process in humans and animals in which there is a decrease in behavioral response to a stimulus after repeated exposure to that stimulus over a duration of time. It is hypothesized that there is a genetic component to habituation in beef cattle. Habituation is measured by the change in CS between processing events. Animals that 'habituate' have improved (lower numerical) CS at re-implant or a negative deviation of initial and re-implant chute score. CS was transformed to a binary outcome, with acceptable (coded 1) CS of 1, 2, and 3 and unacceptable (coded 0) CS of 4, 5, and 6. Of the 1,505 animals evaluated, 71 head (4.7%) were unacceptable at both processing events, 100 head (6.6%) moved from acceptable to unacceptable categories, and 250 head (16.6%) moved unacceptable to acceptable. Approximately 72% of the animals (1,084) were determined to be acceptable in terms of CS at both processing events.

Future analyses will include the count of number of treatments as a covariate to account for differing numbers of processing events experienced by animals between initial and re-implant processing, as a large number of animals were treated for bovine respiratory disease during the feeding phase. Analyses are also planned to investigate the association between habituation and incidence of disease and other growth and carcass traits. Finally, analyses to provide an estimate of the heritability of habituation are planned.

Table 1: Temperament pen scores and descriptions

Pen Score	Description
1 = Non-aggressive (docile)	Walks slowly, can approach closely, not excited by humans or facilities;
2 = Slightly Aggressive	Runs along fences, will stand in corner if humans stay away, may pace fence;
3 = Moderately Aggressive	Runs along fences, head up and will run if humans move closer, stops before hitting gates and fences, avoids humans;
4 = Aggressive	Runs, stays in back of group, head high and very aware of humans, may run into fences and gates even with some distance, will likely run into fences if alone in pen;
5 = Very Aggressive	Excited, runs into fences, runs over humans and anything else in path, “crazy.”

Adapted from Kunkle et al., 1986.

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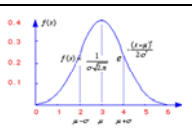


Overview of Healthfulness Project

National Beef Cattle Evaluation Consortium

Go Cyclones!

Overview

- **Goal of Research**
  - Develop the tools to allow breeders to select for enhanced nutrient composition of beef
- **What does this mean to the beef industry?**
  - It will be able to actively address human health concerns with respect to consumption of beef

What are Americans eating?

	Calories from Fat	SFA	MUFA	PUFA
An Average American Diet	34%	16%	11%	7%

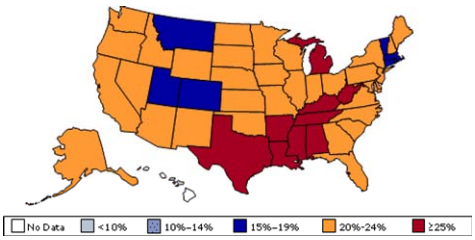
What should Americans be eating?

	Calories from Fat	SFA	MUFA	PUFA
American Heart Association Step I Diet	30%	9%	14%	7%
American Heart Association Step II Diet	25%	7%	12%	6%

Obesity in U.S. in 2004

BMI ≥ 30, or ~ 30 lbs. overweight for 5'4" person

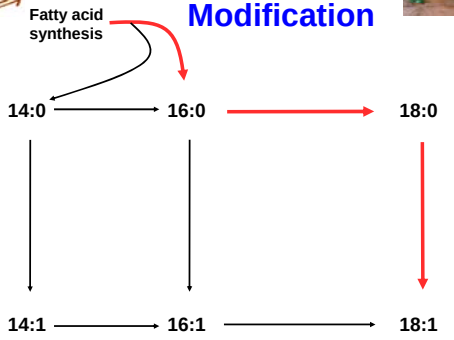
2004



Product Branding

Product Branding

Fatty Acid Synthesis and Modification



Atherogenic index

$$= \frac{12{:}0 + 4*(14{:}0) + 16{:}0}{\Sigma(\text{MUFAs}) + \Sigma(\text{PUFAs})}$$

The atherogenic index as proposed by Ulbricht and Southgate, 1991

Health Promoting Index

$$= \frac{\Sigma(\text{MUFAs}) + \Sigma(\text{PUFAs})}{12{:}0 + 4*(14{:}0) + 16{:}0}$$

Health-promoting index of several foods

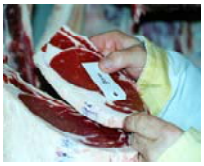
Food	HPI	Food	HPI
Soy oil	7.69	Beef(NLMB)	1.43
Olive oil	7.14	Beef TG(Knight)	1.27
Beef PL(Knight)	3.03	"Extreme" milk fat	1.30
Chicken	2.27	Beef(Beitz)	1.16
Pork	2.13	Tallow	1.12
Lard	1.92	"Greatest" milk	0.94
Beef(Eichhorn)	1.67	"Average" milk fat	0.44
Margarine	1.61	"Low" milk fat	0.30
Beef(Knight)	1.52	Palm kernel oil	0.15
Beef(Garret)	1.49	Coconut oil	0.06

Statistical analysis

- **Steers and bulls slaughtered at normal finishing weight.**
- **Contemporary groups based on year, farm of origin, feedlot, and harvest date.**
- **63 contemporary groups (1-65 cattle per group).**
- **77 sires (1-40 progeny per sire).**

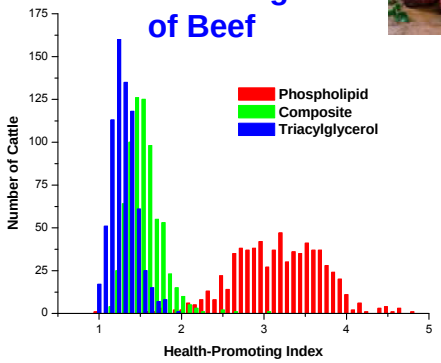
Data Description

- Longissimus dorsi sample



- External connective tissue was removed
- Fatty acids evaluated by gas chromatography

Variation in Health-Promoting Index of Beef



Data Descriptors

Fatty Acid	Mean % of lipid	SD % of lipid	Min % of lipid	Max % of lipid
14:0	2.82	0.49	1.19	4.34
14:1	0.68	0.28	0.00	1.85
16:0	26.48	1.94	16.79	32.38
16:1	3.48	0.67	0.99	5.64
18:0	12.74	1.44	8.28	17.29
18:1	41.34	3.26	23.74	54.06
18:2	7.02	2.99	1.78	29.76

Genetic Analysis

- MTDFREML
  - Sire model
- Contemporary group definition:
  - Herd of origin
  - Sex
  - Feedlot management treatment
  - Harvest date

Genetic Analysis

- Model:

  Y = Xb + Zu + e

  Fixed effects (b):
  - Model I: Contemporary group only
  - Model II: Cont group & lipid covariate

  Random effects (u & e):
  - Sire
  - Error

Heritability Estimates (% of lipid)

Fatty Acid	h^2 Model I	SE Model I
14:0	0.49	0.14
14:1	0.13	0.08
16:0	0.43	0.13
16:1	0.49	0.14
18:0	0.20	0.09
18:1	0.38	0.13
18:2	0.23	0.10

Heritability Estimates (% of lipid)

Fatty Acid	h^2 Model I	SE Model I	h^2 Model II	SE Model II
14:0	0.49	0.14	0.52	0.14
14:1	0.13	0.08	0.14	0.08
16:0	0.43	0.13	0.42	0.13
16:1	0.49	0.14	0.47	0.14
18:0	0.20	0.09	0.21	0.10
18:1	0.38	0.13	0.40	0.14
18:2	0.23	0.10	0.11	0.08

Heritability Estimates (% of lipid)

Fatty Acid	h^2 Model I	SE Model I	h^2 Model II	SE Model II	Δh^2 Model II - I
14:0	0.49	0.14	0.52	0.14	0.022
14:1	0.13	0.08	0.14	0.08	0.010
16:0	0.43	0.13	0.42	0.13	-0.017
16:1	0.49	0.14	0.47	0.14	-0.020
18:0	0.20	0.09	0.21	0.10	0.014
18:1	0.38	0.13	0.40	0.14	0.020
18:2	0.23	0.10	0.11	0.08	-0.119

Discussion

- Generally, little change in h^2 estimates with Model II
- Short-chain, saturated fatty acids are heritable
  - 14:0 (0.49)
  - 16:0 (0.43)
- Monounsaturated fatty acids are heritable
  - 16:1 (0.49)
  - 18:1 (0.38)

Genetic Correlation Estimates

Fatty Acid	HCW	12 Fat	REA	MARB	W-B Shear
14:0	-0.23	0.27	-0.10	0.32	0.31
16:0	-0.24	0.17	-0.25	0.26	-0.04
18:0	0.00	-0.54	-0.50	-0.45	-0.07
18:1	-0.14	0.18	0.01	0.83	0.12
18:2	0.43	-0.17	0.24	-0.93	-0.04

Can we select cattle to have a more healthful fatty acid composition?

YES

Is it possible to decrease palmitic and myristic acid and replace with stearic acid in beef?

YES

Does fatty acid composition of beef vary among different breed types?

Does Breed to Breed Variation Exist in Fatty Acid Composition

- Collaborative project with researchers at Meat Animal Research Center
- 588 animals
  - – Sire Lines
    - Angus — BeefMaster
    - Hereford — Bonsmara
    - Brangus — Romosinuano
  - – Dam Lines
    - Angus — MARC III

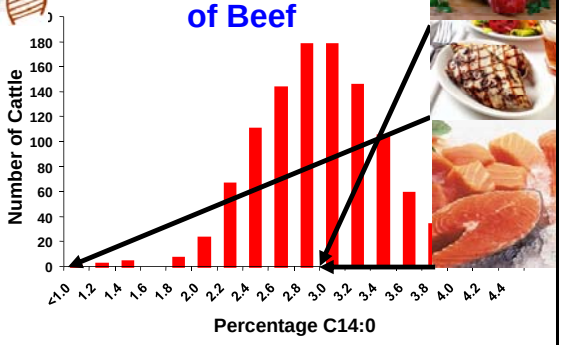
Significant Differences in Fatty Acid Composition Exist Between Breeds

Fatty Acid	Low	High	P-value
14:0	3.40	3.96	<.0001
16:0	27.18	29.38	<.0001
16:1	3.47	3.78	0.0075
18:0	12.51	14.31	<.0001
18:1	33. 90	35.73	<.0001
18:2	1.51	1.87	0.0007

Significant Differences in Fatty Acid Indexes Exist Between Breeds

Index	Low	High	P-value
AI	0.87	1.01	<.0001
16:1/16:0	12.51	13.78	<.0001
18:1/18:0	240.05	274.77	<.0001
x:1/x:0	88.07	96.41	<.0001
16/14	706.97	802.43	<.0001
18/16	43.49	51.34	<.0001

Variation in C14:0 Concentration of Beef

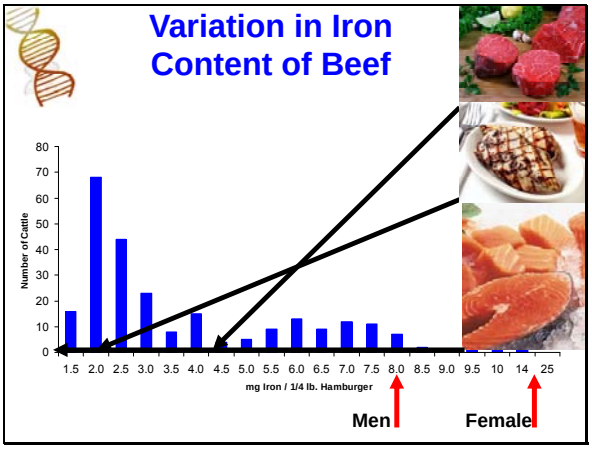


Are there any other nutrients that have been found to be variable among genotypes?

Differences in Other Compounds Between Breeds

Compound	Low	High	P-value
Spingolipids	0.42	0.55	0.644
pCreatine	42.96	51.64	0.974
Creatine	170.41	183.24	0.429
Total Cr	212.46	268.80	0.579
Creatinine	23.03	73.88	0.052
Iron	26.43	43.46	0.320

Variation in Iron Content of Beef



Candidate Genes Associated With Fatty Acid Composition

Thioesterase domain of Fatty Acid Synthase

	g.17924A>G			g.18663T>C			g.18727C>T		
Variable	AA	AG	GG	TT	CT	CC	CC	CT	TT
Number of animals	121	168	42	130	162	39	320	10	1
Genotype frequency	0.36	0.51	0.13	0.39	0.49	0.12	0.97	0.03	0.003

	SNP			
Haplotype	g.17924A>G	g.18663T>C	g.18727C>T	Frequency
1	A	T	C	0.62
2	G	C	C	0.36
3	G	T	T	0.02

Zhang et al. 2008 Animal Genetics

Fatty Acid Synthase

Table 4 Effects of g.17924A>G and g.18663T>C SNPs on phospholipids (PL), triacylglycerols (TAG) and total lipid fatty acid composition.[1]

	g.17924A>G			g.18663T>C		
Traits	AA ($n = 121$)	AG ($n = 168$)	GG ($n = 42$)	TT ($n = 130$)	TC ($n = 162$)	CC ($n = 39$)
PL						
18:1	23.40 ± 0.90[b]	24.01 ± 0.89[a,b]	25.07 ± 1.00[a]	23.46 ± 0.90[B]	24.00 ± 0.88[A,B]	25.16 ± 1.01[A]
20:3 (n-6)	1.94 ± 0.06[a]	1.89 ± 0.06[a,b]	1.75 ± 0.08[b]	1.93 ± 0.06[A]	1.90 ± 0.06[A]	1.74 ± 0.08[B]
22:5 (n-3)	2.44 ± 0.10[b]	2.49 ± 0.10[a,b]	2.61 ± 0.11[a]	2.44 ± 0.10	2.50 ± 0.10	2.59 ± 0.11
MUFA[2]	25.16 ± 0.95[b]	25.83 ± 0.93[a,b]	26.98 ± 1.05[a]	25.23 ± 0.94[B]	25.82 ± 0.93[A,B]	27.09 ± 1.06[A]
PUFA[3]	45.22 ± 0.86	44.89 ± 0.83	43.51 ± 1.02	45.23 ± 0.85[A]	44.91 ± 0.82[A,B]	43.26 ± 1.02[B]
TAG						
14:0	3.46 ± 0.09[a]	3.26 ± 0.09[b]	2.92 ± 0.11[c]	3.41 ± 0.09[A]	3.27 ± 0.09[A]	2.93 ± 0.12[B]
16:0	0.41 ± 0.03[a]	0.39 ± 0.03[a,b]	0.32 ± 0.04[b]	0.40 ± 0.03	0.39 ± 0.03	0.34 ± 0.04
16:0	28.54 ± 0.22[a]	28.09 ± 0.20[a,b]	27.65 ± 0.30[b]	28.41 ± 0.22	28.13 ± 0.21	27.72 ± 0.32
18:1	44.76 ± 0.29[c]	45.62 ± 0.27[b]	46.59 ± 0.40[a]	44.94 ± 0.29[C]	45.58 ± 0.28[B]	46.53 ± 0.42[A]
SFA[4]	46.36 ± 0.40[a]	45.75 ± 0.38[b]	45.11 ± 0.49[b]	46.19 ± 0.40[A]	45.81 ± 0.39[A,B]	45.21 ± 0.50[B]
MUFA	49.99 ± 0.31[b]	50.70 ± 0.29[a]	51.50 ± 0.41[a]	50.15 ± 0.31[B]	50.65 ± 0.29[A,B]	51.42 ± 0.41[A]
16:0/14:0[5]	8.45 ± 1.03[b]	8.76 ± 0.85[b]	14.35 ± 1.73[a]	8.55 ± 1.02[B]	8.71 ± 0.85[B]	14.74 ± 1.73[A]
HI[6]	1.25 ± 0.02[c]	1.30 ± 0.02[b]	1.38 ± 0.03[a]	1.26 ± 0.02[B]	1.30 ± 0.02[B]	1.37 ± 0.03[A]
Total lipids						
14:0	2.85 ± 0.06[a]	2.68 ± 0.05[b]	2.45 ± 0.08[c]	2.81 ± 0.06[A]	2.69 ± 0.05[A]	2.48 ± 0.08[B]
16:0	26.48 ± 0.24[a]	25.91 ± 0.23[b]	25.67 ± 0.31[b]	26.35 ± 0.24[A]	25.93 ± 0.23[B]	25.80 ± 0.32[A,B]
18:1	40.38 ± 0.36[b]	40.98 ± 0.33[b]	42.27 ± 0.48[a]	40.54 ± 0.36[B]	40.90 ± 0.33[B]	42.23 ± 0.48[A]
SFA	43.82 ± 0.21[a]	43.04 ± 0.18[b]	42.82 ± 0.34[b]	43.68 ± 0.21[A]	43.05 ± 0.18[B]	42.99 ± 0.34[A,B]
MUFA	44.96 ± 0.49[b]	45.39 ± 0.47[a,b]	46.49 ± 0.60[a]	45.10 ± 0.49[A]	45.32 ± 0.47[A]	46.53 ± 0.60[A]
16:0/14:0	9.52 ± 0.26[b]	9.87 ± 0.22[b]	11.38 ± 0.41[a]	9.62 ± 0.25[B]	9.84 ± 0.23[B]	11.38 ± 0.43[A]
HI	1.50 ± 0.02[a]	1.57 ± 0.02[a]	1.63 ± 0.03[a]	1.51 ± 0.02[A]	1.57 ± 0.02[A]	1.61 ± 0.03[A]

Fatty Acid Synthase

Table 5 Estimate (±SE) of additive and dominance effects associated with SNP g.17924A>G, estimate (±SE) of the half allele substitution effect (allele g.17924G), and coefficient of determination (R^2) and correlation coefficient (r) from regression and correlation analyses of traits on the number of g.17924G alleles.

Trait	Additive effect	Dominance effect	Allele Effect	R^2	r
PL[2]					
18:1	0.84 ± 0.32**	−0.22 ± 0.40	0.98 ± 0.34**	0.03**	0.17**
20:3 (n-6)	−0.09 ± 0.04**	0.04 ± 0.04	−0.07 ± 0.03*	0.01*	−0.14*
22:5 (n-3)	0.00 ± 0.03*	−0.03 ± 0.04	0.05 ± 0.04	0.01	0.00
MUFA[3]	0.91 ± 0.34**	−0.24 ± 0.43	1.06 ± 0.36**	0.03**	0.17**
PUFA[4]	−0.85 ± 0.41*	0.53 ± 0.52	−1.03 ± 0.40*	0.02*	−0.14*
TAG[5]					
14:0	−0.27 ± 0.05****	0.07 ± 0.06	−0.25 ± 0.05****	0.08****	−0.27****
16:0	−0.04 ± 0.02**	0.02 ± 0.02	−0.06 ± 0.02**	0.03**	−0.17**
16:0	−0.45 ± 0.16**	−0.01 ± 0.19	−0.49 ± 0.14***	0.04***	−0.17**
18:1	0.92 ± 0.20****	−0.05 ± 0.25	1.03 ± 0.19****	0.08****	0.27****
SFA[6]	−0.62 ± 0.20**	0.02 ± 0.26	−0.70 ± 0.20***	0.03***	−0.16**
MUFA	0.75 ± 0.20***	−0.05 ± 0.25	0.86 ± 0.20****	0.05***	0.21****
16:0/14:0[7]	2.95 ± 1.00**	−2.65 ± 1.32*	2.10 ± 0.90*	0.02*	0.13*
HI[8]	0.07 ± 0.01****	−0.01 ± 0.02	0.06 ± 0.01*	0.07****	0.25****
Total lipid					
14:0	−0.20 ± 0.04****	0.02 ± 0.05	−0.19 ± 0.04****	0.06****	−0.24****
16:0	−0.41 ± 0.14**	−0.17 ± 0.17	−0.45 ± 0.14**	0.03**	−0.16**
18:1	0.90 ± 0.24***	−0.29 ± 0.30	0.95 ± 0.27***	0.04***	0.18**
SFA	−0.50 ± 0.20*	−0.28 ± 0.25	−0.61 ± 0.18***	0.04***	−0.17**
MUFA	0.77 ± 0.25**	−0.33 ± 0.33	0.82 ± 0.31**	0.02**	0.13*
16:0/14:0	0.93 ± 0.23****	0.01 ± 0.02	0.73 ± 0.21***	0.04***	0.19***
HI	0.07 ± 0.01****	−0.58 ± 0.30	0.07 ± 0.02****	0.06****	0.22****

Acetyl CoA Carboxylase

	Allele Frequency					
	SNP1		SNP2		SNP3	
Sire Line	T	A	G	T	T	C
Herford	0.33	0.67	0.99	0.01	0.56	0.44
Angus	0.55	0.45	0.99	0.01	0.37	0.63
Brangus	0.32	0.68	0.86	0.14	0.30	0.70
Beefmaster	0.41	0.59	0.97	0.03	0.36	0.64
Bonsmara	0.23	0.77	0.58	0.42	0.36	0.64
Romosinuano	0.37	0.63	0.88	0.12	0.44	0.56
Total	0.36	0.64	0.88	0.12	0.39	0.61

Zhang et al (submitted)

Acetyl CoA Carboxylase

	SNP1			SNP2			SNP3		
	TT	TA	AA	GG	GT	TT	TT	TC	CC
Number of animals	216	290	67	458	93	22	73	312	188
Genotype frequency	0.38	0.50	0.12	0.80	0.16	0.04	0.13	0.45	0.33

Effect of ACC SNP3 on lipid content

	Genotype					
	TT	TC	CC	Allele effect	R^2	r
Lipid Content	5.89 ±0.21	5.72 ±0.12	5.38 ±0.14	-0.27 ±0.11	0.01	0.09

Steroyl CoA Desaturase

Table 1. SNPs in *SCD* cDNA ORF region and the gene frequency of two types of *SCD* defined for 1003 Japanese Black steers. Bold column shows the SNP that is likely to cause amino acid replacement.

	Nucleotide substitutions			*Gene frequency*		
Type	*702*	*762*	*878*	*Group I*	*Group II*	*Total*
A	A	T	C	0.65	0.47	0.59
V	G	C	T	0.35	0.53	0.41

Table 2. Comparison of MUFA content and melting point in fat tissue between two SCD genotypes and sire groups.

Effect	*n*	*MUFA (%)*	*Melting point (°C)*
Genotype			
AA	278	58.8 ± 0.1^a	25.4 ± 0.2^a
VA	635	58.2 ± 0.1^b	26.1 ± 0.1^b
VV	90	57.1 ± 0.3^c	27.6 ± 0.3^c
Sire group			
I	709	58.6 ± 0.1^a	25.7 ± 0.1^a
II	294	57.5 ± 0.1^b	26.8 ± 0.2^b

Mean values with different superscripts in the same column differ significantly ($P < 0.001$).
MUFA indicates the percentage of mono-unsaturated fatty acids including C14:1, C16:1, and C18:1.

Taniguchi et al. 2004 Mammalian Genome

Are Single Nucleotide Polymorphisms Associated with Fatty Acid Composition

- 172 purebred American Angus Bulls and Steers ISU Meat Quality Selection Herd
- Stearoyl-CoA Desaturase SNPs
  - Enzyme responsible for desaturating fatty acids
  - SCD 316, SCD536, SCD1278

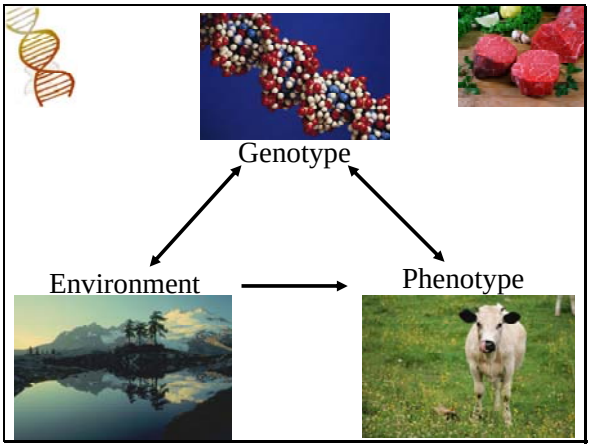
Amino Acid	Genotype	# Animals	Percentage
VV	CC	115	67
VA	CT	57	33

Effect of a Stearoyl-CoA Desaturase DNA polymorphism

Lipid	16:1/16:0		P-Value
	VA	VV	
Phospholipid	**6.3%**	**6.8%**	**0.13**
TAG	**14.5%**	**13.9%**	**0.02**

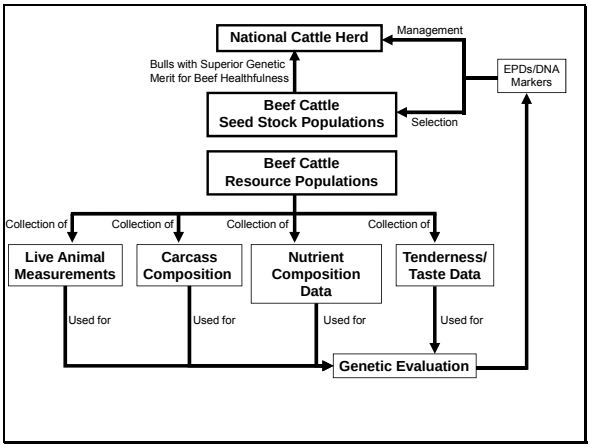
Healthfulness Project Goals

- Develop the tools to allow breeders to select for -
  - –More nutritious beef
  - –Tastier beef
  - –Improved carcass traits
  - –Improved growth traits



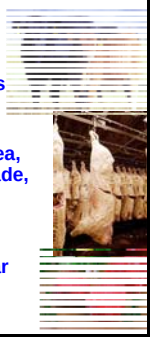
Project Partners

- **Universities**
  - **Iowa State University**
  - **Cornell University**
  - **Oklahoma State University**
  - **University of California – Davis**
- **Producers**
  - **Jack Cowley – California**
  - **DuckSmith Farms – Oklahoma**
- **Pfizer**



Phenotypes

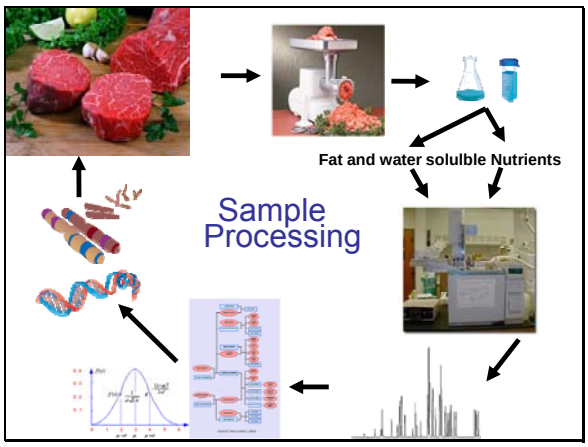
- **Growth**
  - **Birth, weaning, yearling, slaughter weights**
- **Carcass**
  - **Hot carcass weight, dressing %, ribeye area, back fat thickness, yield grade, quality grade, KPH**
- **Meat**
  - **Nutrient composition (extensive list), shear force, taste test panel, ether extract**



Nutrients

1) **Fatty acids**
   - **Triacylgycerol, phospholipid, composite**
2) **Sphingolipids**
3) **Cholesterol**
4) **Minerals**
   - **Iron, sodium, magnesium, zinc, phosphorus, potassium, calcium**
5) **Creatine, creatinine**
6) **Vitamins**
   - **E, B_6, B_{12}, Folate**
7) **Carnitine**

Phenotype collection is the rate limiting step



Genotype Analysis

1) Illumina genechip
2) Parentage/tracking
   - Microsatellites/SNP panel
3) Whole genome association
   - Bayesian
   - Mixed Model

Deliverables

- Industry
  - Ability to calculate genetic merit of an animal based on its genotype
  - Validation of the technology
- National Beef Cattle Evaluation Consortium
  - Resource population for future molecular marker validation

Key personnel

National Beef Cattle Evaluation Consortium

- Iowa State University
  - James Reecy • JR Tait
  - Rohan Fernando • Don Beitz
  - Dorian Garrick • Grace Duan
  - Kadir Kizilkaya • Matt O'Neil
  - Jon Schoonmaker • Travis Knight
  - Mary Sue Mayes • Shu Zhang
- Cornell University
  - John Pollak
- Pfizer
  - Peggy Dillender • Gerard Davis • Mark Allan
  - Nigel Evans • Ronnie Green • Cass Tucker
- Oklahoma State Univ.
  - Raluca Mateescu
  - Deb Van Overbeke
  - Andrea Garmyn
- Univ. California - Davis
  - Alison Van Eenennaam
- Producers
  - Jack Cowley
  - Don Smith

Guidelines for Implementing Breeding Objectives

M. D. MacNeil[1,2]

USDA – Agricultural Research Service, Fort Keogh Livestock and Range Research Laboratory, 243 Fort Keogh Rd., Miles City, MT 59301

The selection problem, choosing which individuals are to become parents, is inherent in all of beef production. This problem almost invariably involves evaluating animals on more than one trait and making compromises among traits to arrive at a final evaluation of each candidate for selection. In addition, that evaluation is always futuristic. Profitability seems a logical unit of expression for that final evaluation. It is certainly the basis of evaluation intended in the original development of selection index in the animal sciences.

One approach for implementing a breeding objective can be seen as the outcome of five integrated steps: 1) develop a bio-economic simulation model that describes a targeted commercial beef production system; 2) manipulate the model to estimate partial derivatives of profit with respect to each biological driving variable, where the economically relevant traits are by definition those driving variables having non-zero partial derivatives (i.e., estimate the economic values); 3) develop a genetic covariance matrix for the economically relevant traits (ERT) and the suite of traits for which genetic evaluations are generated (EPD traits); 4) produce weights (**w**) for the breeding values produced in national cattle evaluation using the economic values (step 2), and genetic variance-covariance matrix for EPD traits (assumed available), and the genetic covariance matrix of ERT and EPD traits (step 3); and 5) application of the relative weights (step 4) to the EPD to evaluate individuals for economic merit as, $I = \sum w_i * EPD_i$ for the i EPD's. This process (Figure 1) has been implemented to produce generic indexes for many breeds, as well as customized indexes.

[1] USDA-ARS is an equal opportunity/affirmative action employer. All agency services are available without discrimination. This research was conducted under cooperative agreements between USDA-ARS and Montana Agric. Exp. Sta. Mention of a proprietary product does not constitute a guarantee or warranty of the product by USDA, Montana Agric. Exp. Sta., or the authors and does not imply its approval to the exclusion of other products that also may be suitable.

[2] Contact: mike.macneil@ars.usda.gov

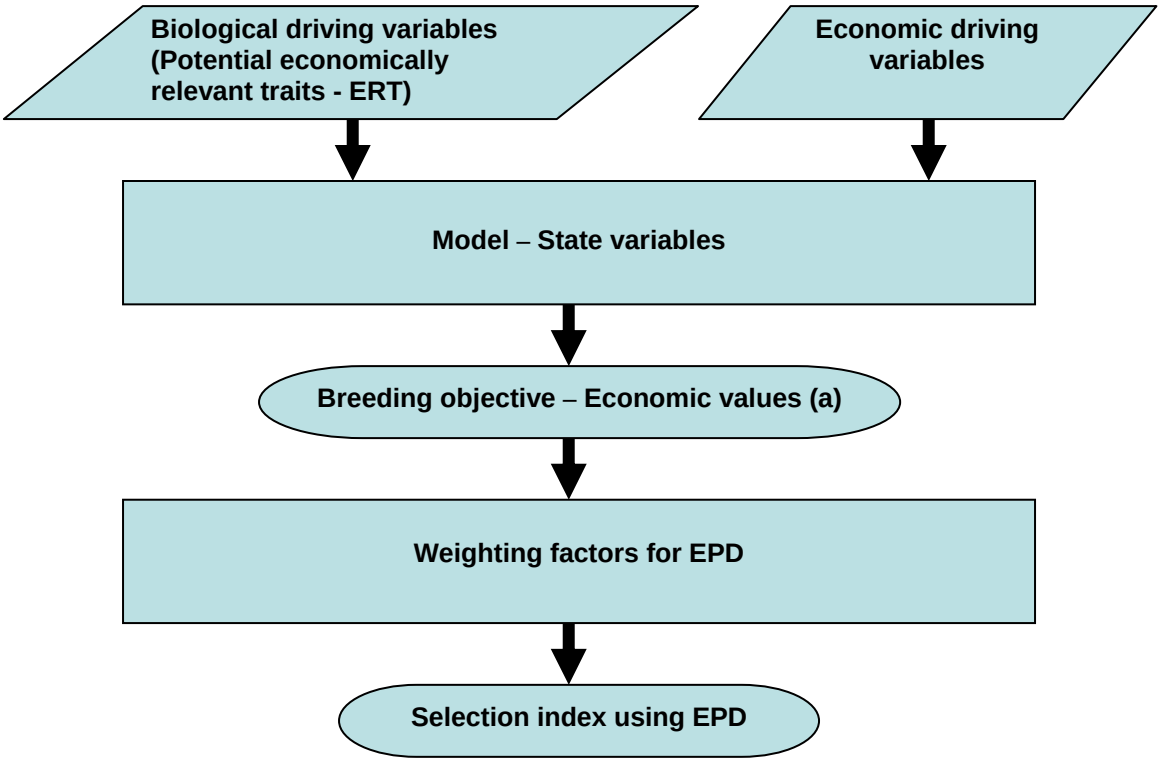


Figure 1. Flowchart for process of implementing selection index technology.

A related alternative approach, referred to as selection by simulation, has also been proposed for economic evaluation of candidates for selection. The need for a model of the production system remains unchanged. The two approaches differ in that before using the model the available EPD are transformed in estimating appropriate values for the driving variables. This transformation replaces the after-the-fact construction of selection indexes based on genetic variances and covariances. One approach to this transformation would be to use the same genetic variances and covariances as would otherwise be used for a selection index. Once appropriate values for the driving variables are obtained, the simulation model is run to predict profitability to be expected from progeny of each candidate for selection. Selection by simulation technology was made available by the American International Charolais Association in 2001 for evaluation of terminal sire candidates.

Model development

The simulation of a commercial beef production system is necessarily an abstraction of any actual system. The simulation should capture virtually all anticipated sources of income and expense associated with the system. Because selection decisions impact future income and expense, it is recommended that the economic parameters reflect long-run, rather than current, costs and returns. If the model used is dynamic with respect to time, then it is recommended that income and expense streams be discounted to a constant point in time. It is also recommended that the biological parameters be data-driven.

Model evaluation

Model evaluation is the subject of a substantial body of literature. After formulating a particular bio-economic model, that model should be subject to some level of verification and validation, before it is put into use to support decision making.

Model verification entails attempting to answer the question; does the model perform as intended? It ensures that the model has been programmed correctly, with the algorithms properly implemented, and that the model does not contain significant errors or oversights. Thus, verification ensures the model is complete and free of mistakes. From a practical perspective, only very simple models can be verified at a level that guarantees an error-free implementation. Model verification proceeds by testing various plausible scenarios, comparing results to expected outcomes, identifying errors, correcting the model, and retesting. Confidence in the model increases as more and different tests are conducted.

Model validation attempts to answer the question; does the model correctly reproduce the behaviors of the real world system? Zeigler (1985) distinguishes between three types of validity:

- *replicative validity*: the model matches data already acquired from the real system;
- *predictive validity*: the model matches data before data are acquired from the real system;
- *structural validity*: the model "not only reproduces the observed real system behavior, but truly reflects the way in which the real system operates to produce the behavior.

Clearly, confidence in the model is improved as validation exercises proceed from replicative, to predictive and ultimately to structural. In all cases, validation entails considerable effort to collect both biological and economic data reflective of the real system and how it operates.

Economic values

At its core, a breeding objective is a formalized statement of economic trade-offs among various traits used in evaluating candidates for selection. Discovering a *complete* set of ERT is somewhat new to our conventional way of thinking about genetic evaluation and improvement. There is a substantial body of literature, stemming from Moav and Hill (1966), in which systems of relatively straightforward "profit equations" have been used as the basis for deriving the economic values necessary to guide genetic improvement (e.g., Ponzoni, 1988; Newman et al., 1992; Wolfová et al., 1995). Systems of profit equations can be thought of as a highly, if informally, aggregated simulation model (MacNeil and Harris, 1988). More explicit and complex bio-economic simulation models can likewise be used to estimate relative economic values using the principles of sensitivity analysis to approximate the required partial derivatives. Alternatively, viewing genetic improvement as technological change using a farm-level model based on neoclassical econometric theory of the firm may provide even more general solutions (Amer and Fox, 1992).

Having modeled the production system and thus identified the ERT, and having quantified their economic importance, and with a genetic evaluation system already in place, the ERT and EPD must be reconciled. As the model of the targeted production system becomes less aggregated and more mechanistic, reconciliation of the ERT and EPD traits becomes more difficult. This difficulty is, at least in part, due the lack of ERT phenotypes and the necessary genetic covariances of ERT with EPD traits.

It is believed that most services providing genetic evaluation services are moving in the general direction of multiple-trait evaluation. Managers of these services could serve their breeders by providing a framework to use in calculating economic values. If desired, the economic values can be customized to account for differences in breeding, production, and marketing systems. This framework would most likely include traits for which data are not recorded. Hence, compiling genetic covariances for the non-recorded economically important traits with recorded traits also becomes an important part of the mission of national cattle evaluation services. Robustness of breeding objectives and the associated selection indices can be evaluated using correlations among the breeding objectives recognizing that very large positive correlations indicate very similar objectives. Breeding objectives should be evaluated using alternative costs for inputs and values for outputs, and different models of production.

In some situations, national cattle evaluation may not develop full multiple trait prediction systems for some time. This may be particularly true for some categorically distributed traits. If the genetic and environmental covariances necessary for multiple-trait BLUP of EDP are assumed known, use of univariate predictions may compromise selection response by up to 15% (Villanueva et al., 1993). However, if the true covariances are unknown, but estimated and subject to error, the loss in efficiency of selection associated with using univariate genetic predictions may be reduced. Wilton (1982) suggested that, in practice, replacement of genetic predictions from multiple-trait evaluations with corresponding predictions from a series of single-trait evaluations may be an adequate approximation. Thus, application of selection index weights to available EPD may be a starting point from which to implement genetic evaluation for profitability.

Bullet points for documenting breeding objectives

- Describe the modeled production system – What are the ERT? What is the targeted production system? What are the main structural equations? How well validated is the model?
- Describe the transformative process by which ERT and EPD are related. – Are genetic variances and covariances used, or some other process?
- Present economic values for the ERT.
- Present relationships between index and EPD traits.

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Estimation of Current Breed Differences in Multibreed Genetic Evaluations using Quantitative and Molecular Approaches

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Introduction

Multibreed genetic evaluation benefits purebred and crossbred producers by providing objective measurements of the genetic potential of all animals in the evaluation regardless of their breed composition. To that end, genetic evaluation centers at Cornell University and the University of Georgia have enabled breeders to take advantage of crossbred data through multibreed evaluations. From these evaluations, genetic predictions are produced for crossbred and composite animals, which allow producers to rank these animals relative to purebreds on their additive genetic merit. However, these systems generally only use crossbred animals from a particular breed database (e.g., Simmental, Gelbvieh) rather than combining breed association databases. Genetic merit of individual animals across breeds is, therefore, relatively unknown.

The ultimate goal of multibreed genetic evaluation is to produce genetic predictions across all US cattle breeds that utilize information from multiple sources, possibly including commercial cattle, and rank animals according to their additive genetic potential. Unfortunately, some barriers currently exist that prevent the realization of a full multibreed genetic analysis. Likely the most important of these barriers is mechanical; data from breed association databases must be combined into a common database and pedigree and phenotypic records from other sources (e.g., commercial herds) must be added. Establishing this 'super' database has several challenges including cooperation between the different entities involved (breed associations, commercial producers) and the establishment of an ID system that prevents and identifies duplications of animals registered in multiple breed association databases.

An additional barrier to full multibreed evaluation is the estimation of population parameters such as additive breed differences and heterosis. Contemporary group structures in industry field data are generally not ideal to simultaneously estimate these parameters because they do not contain the requisite purebred and crossbred progeny required to estimate breed effects independently from heterosis. Methodologies exist to take advantage of published research data and incorporate the results into multibreed prediction models. Standards for designing and utilizing results from these research studies have not been set. Molecular approaches for defining breed composition also may improve the utilization of breed differences in commercial cattle populations.

The objectives of this presentation are to review methods used in current multibreed approaches, suggest guidelines for utilizing information from research estimates of breed differences, describe the new design of the multibreed research program (germplasm evaluation; **GPE**) at the US Meat Animal Research Center (**USMARC**), and demonstrate some results and potential for molecular identification of breeds using high-density marker arrays.

Multibreed Methodology and Implementation

Animal model approaches to multibreed evaluation were first proposed by Arnold et al. (1992). This model is the foundation of current multibreed evaluations in the US (Pollak and Quaas, 2005). The matrix representation of this model is as follows:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{ZQg} + \mathbf{Za} + \mathbf{WSd} + \mathbf{WT}\boldsymbol{\delta} + \mathbf{e}$$

where **y** is a vector of phenotypic observations, **X** is an incidence matrix relating observations to fixed effects, **b** is a vector of fixed effects, **Z** is an incidence matrix relating observations to random additive genetic effects, **Q** is a matrix relating each individual's breed percentages to breed group effects, **g** is a vector of fixed additive breed effects, **a** is a vector of random additive genetic effects, **W** is a square matrix with ones on the diagonals corresponding to crossbred animals and zeros elsewhere, **S** is an incidence matrix relating fixed heterosis effects (vector **d**) to crossbred animals, **T** is matrix relating random heterosis effects (vector **δ**) to crossbred animals, and **e** is a vector of random residual effects. All random effects are assumed to follow a multivariate normal distribution. The variance of the random additive effects and heterosis effects includes correlations due to shared pedigree relationships and breed compositions. Residual variances were heterogeneous to accommodate variable residual structures among breeds.

This model was designed to estimate fixed breed-specific heterosis, random heterosis or animal by breed heterosis (when variance assumptions include nonadditive relationships as described by Elzo (1990)), additive animal effects, and breed differences simultaneously from crossbred data sets. The authors acknowledged that estimating the random heterosis component, **δ,** may be difficult. Additionally, Rodriguez-Almeida et al. (1997) demonstrated that simultaneous estimation of direct and maternal breed effects from unstructured populations produced inconsistent estimates when using a simplified version of the Arnold et al. (1992) model on a data structure similar to field data. Their conclusion was that estimation of these effects in field data sets would be impossible.

These shortcomings illustrate the importance of parameterizing multi-breed models using values from designed experiments. The multibreed model was revised by Klei et al. (1996) to include prior estimates of breed effects or heterosis using Bayesian methodology. Their approach is illustrated by modification of a typical set of equations, $\mathbf{Cb} = \mathbf{y}$, to $(\mathbf{C} + \mathbf{V_p}^{-1})\,\mathbf{b} = \mathbf{y} + \mathbf{V_p}^{-1}\boldsymbol{\mu}_\mathbf{p}$. Prior information is incorporated as mean values in the vector $\boldsymbol{\mu}_\mathbf{p}$ with a prior variance $\mathbf{V_p}$. The values chosen for prior variance reflect confidence in the prior mean. Large values of $\mathbf{V_p}$ reflect little or no confidence in the prior mean relative to the data (the system of equations becomes $\mathbf{Cb} = \mathbf{y}$ as values in $\mathbf{V_p}$ approach ∞), while small values of $\mathbf{V_p}$ reflect high levels of confidence in the prior mean, overwhelming **C**. These methods have been applied to mixed model equations for multibreed evaluations of Simmental and Simbrah for over 11 years (*BEEF* magazine, "Multi-breed Genetic Evaluation"; Feb 2008).

In addition to establishing a framework for incorporating external estimates for breed differences and heterosis into multibreed evaluation, Klei et al. (1996) also detailed several other techniques that are useful in multibreed evaluation. First, they described methods to incorporate heterosis on a breed-type (i.e., British, Continental, Zebu, and other breeds) basis, resulting in 10 levels of heterosis (British x British, British x Continental, etc.). Because heterosis is expected to vary by breed, but breed specific heterosis is difficult to estimate because of the

number of crosses required, this approach allows some variation in heterosis to be exhibited according to broad breed categories. Second, they detailed the incorporation of autoregressive (on year) breed of founder x year effects into the model to allow for non-random sampling of founder animals from other breeds into the Simmental/Simbrah genetic evaluation. This technique is important in current multibreed evaluations such as Simmental and Gelbvieh where genetic merit from founders of other breeds is not known, sampling is unlikely to be random, and the external breeds likely have some genetic trend due to selection. Ideally, this technique would not be necessary in a true 'all breed' multibreed evaluation. Last, Klei et al. (1996) illustrated a method to show genetic changes over time, similar to genetic trends published by most breed associations. These new trends, termed gametic trends, are calculated by within-year least squares regressions of EPD on breed composition. Gametic trends are ideal for multibreed evaluation because all EPD (including crossbreds) contribute to the trend estimate.

The Bayesian framework presented by Klei et al. (1996) was later refined by Quaas and Zhang (2006) to incorporate EPD estimates from other breed evaluation systems into the Simmental/Simbrah multibreed evaluation; the incorporated EPD are termed 'external EPD'. This work was motivated by the fact that high-accuracy EPD in other breed evaluations (e.g., American Angus Association) were substantially reranked in the Simmental/Simbrah multibreed evaluation. The external EPD process incorporates the accuracy of the EPD into the prior variance estimate for that animal's multibreed EPD and the EPD from the external evaluation as the prior mean (adjusted for base differences). External EPD have been incorporated into the Simmental/Simbrah and the Gelbvieh genetic evaluations.

The weight given to prior information can substantially impact the ranking of breeds within multibreed evaluation. Legarra et al. (2007) and Sánchez et al. (2008) both evaluated low, medium, and high confidence levels for prior breed and heterosis estimates in multibreed models. An example from Legarra et al. (2007) is shown in Table 1.

	Low		*Medium*		**High**	
Generation	Gelbvieh	Angus	Gelbvieh	Angus	Gelbvieh	Angus
<1980	90.4	0.0	46.4	0.0	58.3	0.0
1981-1985	79.2	18.9	47.7	7.7	58.3	0.0
1986-1990	99.2	31.9	49.7	14.3	58.3	0.0
1991-1995	91.1	27.5	50.6	15.2	58.3	0.0
>1996	96.1	37.6	51.3	14.1	58.3	0.0

Table 1. Breed of founder effects x generation with low, medium, and high confidence in external prior breed differences for weaning weight (lb).

In the case of low prior confidence, breed of founder effects were essentially completely based on the data whereas with high confidence, breed of founder effects reflected the prior mean. Medium confidence allowed the data to change the prior mean levels. Both studies concluded that the level of confidence placed on the prior mean generally had minor effects on the ranking of bulls within breed types but could substantially change the ranking and even direction of breed and heterosis estimates. Therefore, the choice of prior means and their weighting in multibreed models will affect comparisons of animals across different breeds.

The multibreed models as described have provided breeders a method to utilize data from crossbred/composite animals in national cattle evaluations. Although they do not incorporate all possible stratifications, such as changes in genetic variance due to segregation and recombination loss (see Lo et al., 1993; Cardoso and Templeman, 2004), they do incorporate population parameters (i.e., non-additive effects in the form of breed type heterosis,

additive breed differences) that extend genetic prediction to larger sets of animals. The multibreed models discussed thus far have only been implemented for specific breeds, their crosses/composites, and animals from external breeds that they have been crossed to. As stated in the introduction, a full model combining the databases of all or most breeds would be ideal. A prototype analysis combining records from several breeds has been conducted by the University of Georgia (as presented by Bertrand, 2007 Beef Improvement Federation annual meeting, Fort Collins, CO). If this analysis remains a priority, research estimates of breed differences and heterosis remain important.

Use of Research Data to Estimate Breed Effects

Given the difficulty in predicting breed differences from field data, other sources of these estimates must be used in multibreed models to adjust breeds to a common base. Scientific literature is fraught with breed comparison trials used to estimate direct and maternal breed effects or heterosis or both. These studies generally evaluate only a few select breeds due to resource limitations; therefore, estimates of all possible breed contrasts and breed specific heterosis are not available in a single published study. In fact, for most specific breed crosses experiments required to estimate breed specific heterosis have not been conducted. In order to apply literature estimates to multibreed evaluation, published data must be gathered, coalesced, and analyzed to provide a contrast between all breeds of interest.

Roughsedge et al. (2001) and Williams et al. (2008) both mined the literature to obtain direct and maternal breed differences and heterosis effects. Williams et al. (2008) used least squares means estimates from studies published from 1976 to 1996 and combined data using a fixed linear model with study as a fixed class effect and breed percentage as a covariate. Roughsedge et al. (2001) implemented a similar strategy but added a weighting factor to account for the variable information content of the different sources. In order to weight the published breed cross estimates (*Xc*), approximate standard errors were calculated for each breed cross effect according to Amer et al. (1992):

$$SE(Xc) \cong \sqrt{\frac{\frac{1}{4}h^2CV^2}{n_s} + \frac{\frac{3}{4}h^2CV^2 + (1-h^2)CV^2}{n_o}}$$

where h^2 is the heritability of the traits, *CV* is the coefficient of variation, n_s is the number of sires sampled in the study to produce the estimate *Xc*, and n_o is the number of offspring used in the estimate of *Xc*. Increasing the number of sires used or progeny per sire would decrease *SE(Xc)*; these numbers then serve as a proxy of the extent of breed sampling in each study. The weighting factor used to combine the literature estimates was then 1/*SE(Xc)*. Like Williams et al. (2008), the authors fitted a model with trial as a fixed class effect and covariates for direct and maternal breed effects after preadjusting the data to full heterosis. The direct estimates for birth weight, weaning weight, and yearling weight from the combined analysis of Roughsedge et al. (2001) are summarized later in Table 2.

While useful literature estimates exist, they still are constrained by the sample of bulls used in the study and assumptions about the population of inference. Roughsedge et al. (2001) partially corrected one problem related to bull sampling, that of obtaining a representative sample of bulls, by weighting breed estimates by the number of bulls sampled and the number of progeny contributing to the estimate. However, there was no measure taken to account for

genetic trend within the sample of bulls. The importance of selection cannot be overlooked. Figure 1 shows the changes in breed means for weaning weight of seven prominent breeds since 1970 after adjusting the breed average EPD using across-breed EPD adjustment factors provided by USMARC (Kuehn et al., 2008).

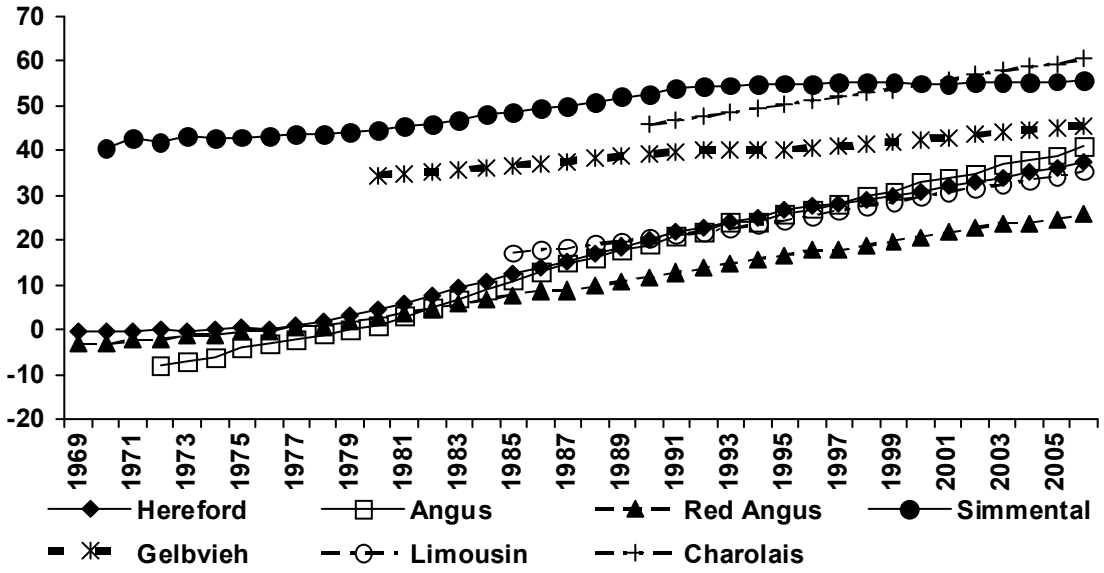

Figure 1. Breed genetic trends for weaning weight adjusted using 2008 across-breed EPD adjustment factors.

In general, the trend for the British breeds is much steeper than for most of the continental breeds. Also, differences between breeds would have been much more different for weaning weight in 1975 than in 2006. Simply estimating breed differences at a given point in time can produce results that do not reflect the current state of the industry. For example, based on Figure 1, we would expect average Angus-sired progeny to weigh 45-50 lb less than average Simmental-sired progeny in the mid 1970s when mated to the same females. By 1990, this difference decreases to about 33 lb. Currently, we would expect Angus-sired progeny to be about 14 lb lighter at weaning. Therefore, the estimated breed difference is highly dependent on the time point at which the breeds were compared and on the level of selection occurring within each breed.

Roughsedge et al. (2001) sampled literature from studies performed from the 1970s and 1980s while the studies cited by Williams et al. (2008) were published from 1976 to 1996. These estimates may help to parameterize a full multibreed model from a certain base year that is approximately equivalent to the period covered by the literature studies. Then genetic/gametic trends, as predicted in the mixed model with relationships, could account for changes in breeds due to selection. While this method is plausible, it depends on the assumptions in the model accurately predicting the genetic trend of each breed. We believe that it is more useful to parameterize a multibreed model using breed means adjusted to current genetic evaluations of the bulls used in the research data. This method provides the best estimate of present additive differences between breeds. Obviously this approach is nearly impossible using literature estimates without knowledge of the bulls used in each study. However, the breed differences,

adjusted for current levels of EPD, are available in the across-breed EPD program released by USMARC each year. These breed differences are obtained using a multi-step process. First, the breed differences are estimated under a mixed sire and dam model (after phenotypes are adjusted to full heterosis), then the breed effect for breed *i* (B_i) is adjusted for EPD and environmental differences at USMARC:

$$B_i = USMARC_i / b + (EPD_{i,YY} - EPD_{i,USMARC})$$

where $USMARC_i$ is the breed solution for breed *i* estimated in the mixed sire and dam model, *b* is a scaling factor estimated during the process that adjusts $USMARC_i$ to the industry scale represented by the EPD, $EPD_{i,YY}$ is the within-breed 2008 EPD for breed *i* for animals born in the base year *YY* which is two years before the across-breed EPD update (2006 for the 2008 update), and $EPD_{i,,USMARC}$ is the weighted (by number of progeny at USMARC) average of 2008 EPD of bulls of breed *i* having progeny with records at USMARC. The breed differences calculated for 2008 are shown as a comparison with those derived from Roughsedge et al. (2001) in Table 2.

	Roughsedge et al.			**ABEPD**		
Breed	BWT	WWT	YWT	BWT	WWT	YWT
Angus	68	361	741	85	524	906
Hereford	67	394	791	97	509	840
Red Angus				85	473	840
Shorthorn	75			103	533	882
S. Devon	75	409	816	94	527	885
Braunvieh	105	513	910	97	503	756
Charolais	85	475	867	109	581	936
Gelbvieh	79	454	848	97	533	831
Limousin	70	443	809	94	506	816
Maine Anjou	86	456	851	103	506	822
Salers	73	494	900	94	539	894
Simmental	82	468	883	97	566	900
Tarentaise	73	419	734	91	506	765
Beefmaster				106	554	849
Brahman				118	551	750
Brangus				100	551	882

Table 2. Breed differences (lb) for birth weight (BWT), weaning weight (WWT), and yearling weight (YWT) from Roughsedge et al. (2001) and from the 2008 across-breed EPD adjustment factor models (ABEPD).

Differences between the two studies are clear, especially relative to growth achieved through selection in the British breeds (Angus, Hereford, and Shorthorn). Based on the methodology applied, we believe the relative differences between the breeds means calculated in the across-breed EPD process provide a more accurate estimate of the current differences between the breeds.

This demonstration was not meant to imply that the across breed EPD methodology is perfect. The process used to estimate breed differences is being modified to accommodate the new structure being implemented for GPE (described later). The breed differences model will change to an animal model with breed percentage regressions, rather than class effects. Sires used via AI will likely remain base animals in the analysis because the results will be adjusted to

their EPD. Another change being considered is to implement a weighting factor to emphasize progeny from more recent matings more heavily than historical records; EPD of bulls sampled recently should be more representative of current sires available in the breed.

The USMARC GPE program will continue to be a resource available to genetic evaluation centers for use in deriving breed differences. However, it is worth contemplating whether this research population alone is sufficient. One location in south central Nebraska is not representative of environmental conditions throughout the U.S. Results from other locations at universities or government research institutions in different environments would complement the GPE program by strengthening the power of the data set and making estimation of genotype by environment (G x E) interactions feasible. It is probably most important to establish a cooperating location in a southern region where tropically adapted breeds have a distinct advantage. It is likely that such a location will be smaller; the power to estimate breed differences and heterosis at these locations can be improved if they sample a portion of the same sires being sampled at USMARC if G x E interactions are not important. The following section describes the methods we suggest implementing to sample representative sires in breed comparison studies; the structure of the new GPE program is highlighted as an example.

Design of New GPE Program

The original GPE consisted of a series of breed comparison studies, referred to as cycles, each producing AI-sired calves over a 2 to 5 year period and sampling approximately 20-30 bulls per breed. Cycle I began in 1971 and the last AI-sired calves in Cycle VIII were born in 2002. During that time, over 30 breeds were evaluated. The original objectives were to evaluate breed differences, especially 'exotic' germplasm, for both direct and maternal effects. In each cycle, AI bulls were mated to base Hereford, Angus, or MARC III (composite) cows to estimate the direct breed effect, assuming a constant level of heterosis. Heifer calves were retained from these crosses and mated for the next several years to evaluate maternal breed differences; the calves from the F_1 females have not been used to estimate direct breed effects. Later the objectives evolved to support the across-breed EPD program and to provide data for the USMARC genomics program (both of these objectives were the primary reasons for resampling the seven largest breeds in Cycle VII). The motivation for changing this structure arises from the need to continue to provide a population structure that supports USMARC genomics efforts while utilizing all animals to estimate direct and maternal breed effects and heterosis.

The structure of the new GPE design relies on establishing herds of purebred females that represent industry populations (through continuous industry sire sampling). Females from these herds will be mated via AI or natural service to purebred bulls of the same or different breeds to produce purebred and F_1 progeny that enable direct breed effects and heterosis estimation (and maternal effects when compared to later generations) and enhance detection of genomic markers through linkage disequilibrium association tests. Later, the F_1 progeny from these matings can be crossed to produce progeny termed F_1^2 progeny (2-way, 3-way, and 4-way crosses). These progeny are the basis for estimation of maternal breed effects and heterosis and enhance marker identification through linkage mapping techniques. Their data also contributes to the estimation of direct breed effects and heterosis. The concurrent recording of data on all of these populations will increase the number of estimable functions in the data analysis. Figure 2 represents a schematic of the new program.

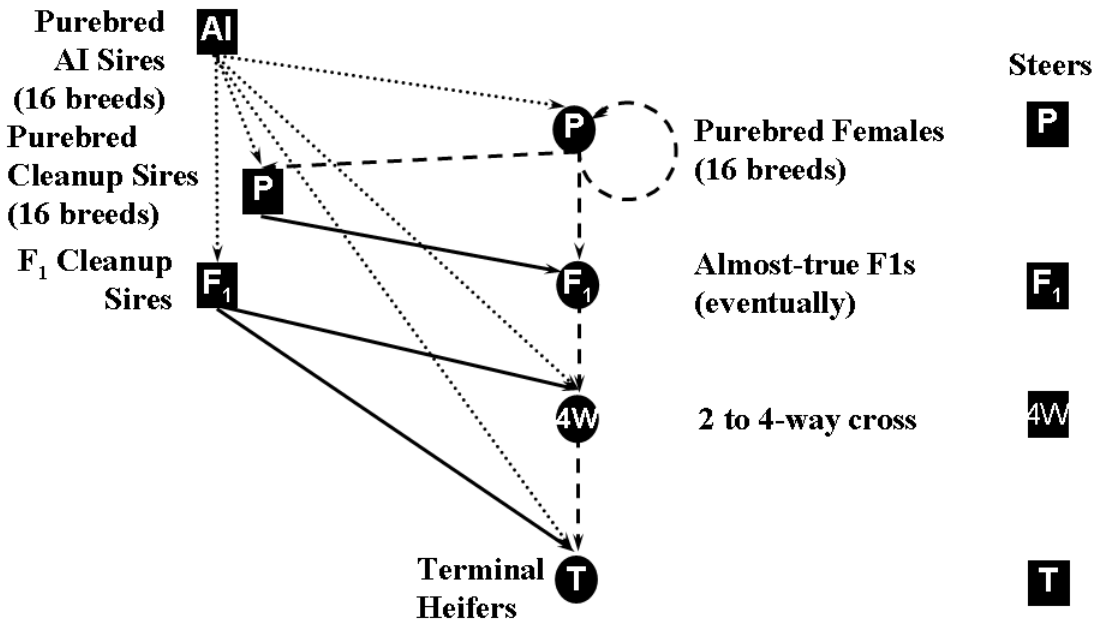

Figure 2. Proposed structure of new GPE program. Boxes represent male populations and circles represent female populations.

Sire sampling for the new program will be roughly continuous. Currently, semen is ordered from producers every two years to supply the needs of the project for that period of time. Sires are sampled through a three step process. First, lists of the top 50 or 100 bulls (depending on breed size) are requested from each of the breed associations represented in the project. Next, a subset of bulls is selected from these lists. Bulls are sampled to represent the average EPD of the whole pool of bulls available and to minimize the relationships among the bulls in the current and previous samples. Bulls with high accuracy EPD for carcass and fertility traits (e.g., stayability) are preferentially chosen as long as other objectives are not compromised. Last, producers are contacted to obtain semen and the list is readjusted depending on the producers' responses. The underlying philosophy is to select bulls that sample influential and accurately evaluated industry germplasm as broadly as possible.

Currently, the 16 largest (in terms of registrations) breeds that have national cattle evaluations for beef production traits are being sampled in GPE. These breeds and the number of animals for each breed after adjusting for whole-herd reporting are shown in Table 3.

Right now, the program is in the process of grading up to purebred herds of each of these breeds (with the exception of Brahman, for which purebred performance would not be representative in the Nebraska environment; a larger herd of F_1 Brahman will be maintained to compensate).

Breed	Adjusted Cow Inventory	%	Breed	Adjusted Cow Inventory	%
Angus	695,144	48.4	Brangus	38,000	2.6
Hereford	139,508	9.7	Beefmaster	37,260	2.6
Simmental	114,816	8.0	Maine Anjou	24,874	1.7
Charolais	74,569	5.2	Brahman	16,270	1.1
Red Angus	73,860	5.1	Santa Gertrudis	15,000	1.0
Limousin	69,380	4.8	Chianina	14,800	1.0
Gelbvieh	63,779	4.4	Salers	13,591	0.9
Shorthorn	41,555	2.9	Braunvieh	5,000	0.3
			TOTAL	1,437,406	100.0

Table 3. Beef cattle breed sizes adjusted to account for whole-herd reporting programs, as well as registrations.

As the population is still being developed and the GPE program is being designed to incorporate changes as needed, any suggestions to improve the program are welcome.

Breed Differences at the Molecular Level

As of now, markers are still being evaluated to determine whether breed composition can be identified. Several studies have been published that identify markers and haplotypic variation across breed (e.g., Wiener et al., 2004; Negrini et al., 2007; McKay et al., 2008). Breed diversity at the molecular level may indicate the expected level of difference in certain phenotypes although it is certainly possible that phenotypic expression can be similar under very different genetic mechanisms. Molecular diversity may also be indicative of the expected heterozygosity expected in crosses; this heterozygosity may imply a greater potential for heterosis.

An assessment of breed diversity was performed at USMARC using approximately 150 bulls representing seven breeds in GPE Cycle VII. These bulls, several of their progeny, and approximately 2,000 grandprogeny (F_1^2) were genotyped for over 52,000 markers using the Illumina Bovine SNP 50 BeadChip[1] (Illumina, San Diego, CA). In order to examine the distance between these breeds, the allelic frequencies for each breed were calculated using the 140 purebred sires. Allelic frequencies were then correlated across each of the 52,000+ markers to develop a correlation matrix. This correlation matrix was then used to estimate the relative genetic distance between each of the seven breeds. A graphic representative of the genetic distance between these breeds is shown in Figure 3.

1 Mention of trade names or commercial products in this article is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture.

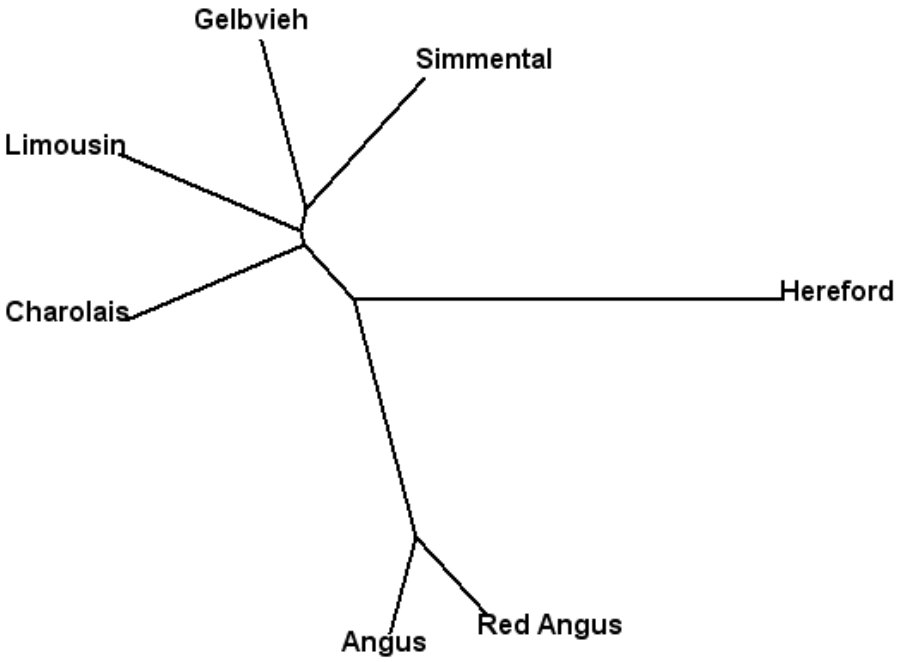

Figure 3. Relative genetic distances between seven beef cattle breeds as determined by correlations of allelic frequencies on 52,000+ markers.

As expected, both Angus and Red Angus were more similar than all of the other breeds in this example. Continental breeds were about twice as far removed from the three British breeds relative to the other continental breeds. Hereford did not seem to be closely related to any other breed; surprisingly, they were as close to Charolais as to Angus and Red Angus. There may be some bias in the markers because they were not sampled randomly across breeds when the chip was created. For example, the distance predicted for Hereford may be biased because several of the SNP used on the chip were discovered using DNA from one purebred Hereford cow. However, this example does show the potential of markers to assess the genomic distance between breeds. This procedure will be repeated on DNA samples from over 2,000 industry bulls that are currently being genotyped on the array at USMARC.

Based on allelic frequencies in the purebred founders, grandprogeny breed composition was predicted under the expectation that half of the alleles arose from two of the seven sire breeds sampled. The likelihood that an allele was representative of the breeds of the four grandparents was calculated for each F_1^2 grandprogeny. This likelihood was compared to the likelihood of all other possible breed configurations to distinguish among possible breed compositions. Breed composition was successfully predicted in 98.9% of genotyped F_1 animals and in 95.3% of the F_1^2 grandprogeny. While breed composition was not directly inferred in these grandprogeny, this exercise demonstrates the utility of high density marker arrays for estimating breed composition. In addition, the genotypes from the 52,000+ SNP markers were used to determine paternity and identify errors in the Cycle VII pedigree.

Summary

In this presentation, we have examined the current extent of multibreed models as used currently by the seedstock industry. Because breeds have placed selection emphasis on different traits and their genetic trends reflect these differences in emphasis, estimates of breed differences must be time-specific in order to be meaningful. Furthermore, such estimates should be adjusted for this trend and for sire sampling by comparing the EPDs of the sires sampled to the average EPDs of calves born in the breed during the reference year.

Industry-wide multibreed genetic evaluation for the U.S. beef industry would be more effective than the current system of across-breed EPD adjustment factors. However, it will be challenging to achieve industry-wide multibreed evaluation given the number of genetic evaluation service providers currently computing national cattle evaluations for U.S. beef breeds. Consequently, it appears likely that the current system of across-breed EPD adjustment factors will need to continue for at least several more years.

There is a need for continued research trials to estimate breed differences relative to current genetic evaluations. Locations participating in breed comparison research in addition to USMARC would enhance the efficacy of the results. It is desirable that any program designed to estimate breed effects would sample bulls that are diverse and relevant to current industry populations. Strategies to achieve this goal have been outlined. Adjusting the breed effects to current industry EPD will result in a better assessment of current breed differences.

Genomic markers may be used to identify breed composition in animals with unknown pedigrees. These characterizations may allow records from those animals to contribute to studies for breed differences and heterosis. Perhaps as more markers are characterized relative to within and between breed genetic variation, marker analyses will allow selection of animals from all breed types or from crossbred populations using whole genome selection strategies.

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Predictive heterosis in multibreed evaluations using quantitative and molecular approaches[1]

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Heterosis is the term used to describe the difference between the average of crossbred progeny and the average of the purebred parent populations. In beef cattle, this difference is often advantageous resulting in faster growth, higher calf survival, and increased reproductive success and longevity of cows. Researchers and others have devised many schemes and strategies to exploit heterosis for more efficient beef production (e.g., Dickerson, 1973; Gregory and Cundiff, 1980; Clarke et al., 1984; Bennett, 1987; MacNeil, 1987; Hayes et al., 2000; Roughsedge et al., 2003).

The biggest genetic source of heterosis likely results from dominance effects expressed at increased frequency by an unknown number of genes due to the increased heterozygosity and decreased homozygosity of crossbred compared to purebred animals. Other genetic causes of heterosis are possible. One that has been studied results from accumulating favorable combinations of genes during the formation and improvement of breeds. Epistatic loss is the term used to describe the break-up of the favorable combinations when crossbreds are used as parents.

Estimates of heterosis are necessary for two important and related tasks. One is to remove sources of genetic differences that are not additive from crossbred data used for calculating EPDs. The other is to add sources of expected non-additive genetic differences to predict crossbred performance for comparing purebred and various crossbreeding systems or mate selection.

The genetic parameters needed for estimation and prediction of heterosis have evolved over time. Dickerson (1969, 1973) summarized how a set of parameters including average direct breed effects, heterosis proportional to expected increases in heterozygosity, and changes in non-allelic interaction effects for individual, maternal, and maternal granddam breeds could be used to predict performance for many of the crossbred mating systems relevant to livestock production. If heterosis parameters are allowed to be different for each combination of breeds, the number of parameters increases much more quickly than the number of breeds (n) and the resources available to estimate them. The number of specific heterosis parameters is equal to $(n^2 - n)/2$.

One parsimonious way of handling many specific heterosis parameters is to consider them as equal. This has been the typical approach used because estimates with small standard errors for many specific combinations are not available. Depending on the source of breed estimates, differences among breed direct effects may be confounded with differences in specific heterosis among breeds. For example, differences between breeds evaluated by crossing sires with a common breed of dam include both differences in additive direct effects of the sire breeds and differences in non-additive effects. Because there is potential for varying levels of specific heterosis, it is worth considering ways to account for specific heterosis.

[1] Mention of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the USDA.

Pollack and Quaas (2005) recommended methodology to estimate EPDs in a multibreed situation including accounting for heterosis effects by assuming they are proportional to the full heterosis between two breeds multiplied by the faction of loci expected to contain one allele from each breed. In addition, they suggested including systematic differences in heterosis by categorizing breeds as British, Continental, Zebu, and other; then multiplying the resulting 10 heterosis categories (British × British; Continental × Zebu; etc.) by fractions of loci expected to contain one allele from a breed in each category. Some breeds (e.g., Angus and Red Angus) are closely related and a decision must be made about whether any heterosis is expected if they are crossed. This could be considered as an 11^{th} category.

These categories are expected to account for some of the most important differences in heterosis between breeds but additional heterosis differences within categories are possible. Estimability is the main issue. One approach to accounting for additional differences in heterosis is to assume random heterosis for specific breed pairs within their broader category. This would limit the influence of poorly estimated specific breed-pair heterosis effects (these effects would regress to the broad category mean; e.g., British × Continental) but allow better estimated specific heterosis effects to differ substantively from their fixed category.

If differences in gene frequencies define genetic diversity, then crossing breeds that are more diverse will increase heterozygosity more than crosses of less diverse breeds. Assuming an infinitesimal dominance model of heterosis (heterosis results from increasing heterozygosity at many genes that have some level of dominant genotypic expression), genomic diversity of breeds should be closely related to specific levels of heterosis. This suggests some approaches to more parsimonious ways of accounting for the many specific heterosis parameters that result from considering many breeds. Note that extreme diversity approaching the level of speciation may decrease performance and fitness (Moll et al., 1965) resulting in a non-linear relationship.

Molecular genetic information has been used to estimate genetic distance (F_{ST}), one measure of diversity at the molecular level. Genetic distance between breeds based on microsatellite genotypes has been used to predict differences in increases of heterozygosity among crossbreds ($F_{ST}/(1 – (F_{ST}/2))$) and then correlate that with differences in heterosis estimates (Goddard and Ahmed, 1982; Roughsedge, et al., 2001). Genetic distances can also be estimated from SNP genotypes and then used to predict differences in heterosis. Figure 1 was derived using SNPs from the Illumina Bovine SNP50 BeadChip. Distances estimated by correlations of frequencies from purebred sires are represented by the linear distance between breeds in the figure.

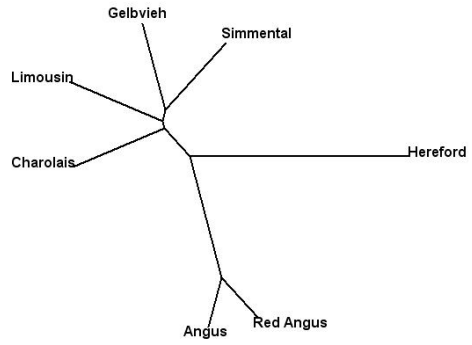

Figure 1. Example of unrooted genetic distance tree.

Eding and Meuwissen (2001) have proposed a kinship measure of diversity that can be easily used with large numbers of genetic markers. Their results indicated that this measure gave a consistent accounting of both within and between genetic diversity. When available, this kinship measure may be a better predictor of the inbreeding-crossbreeding continuum (Figure 2; Dickerson, 1973).

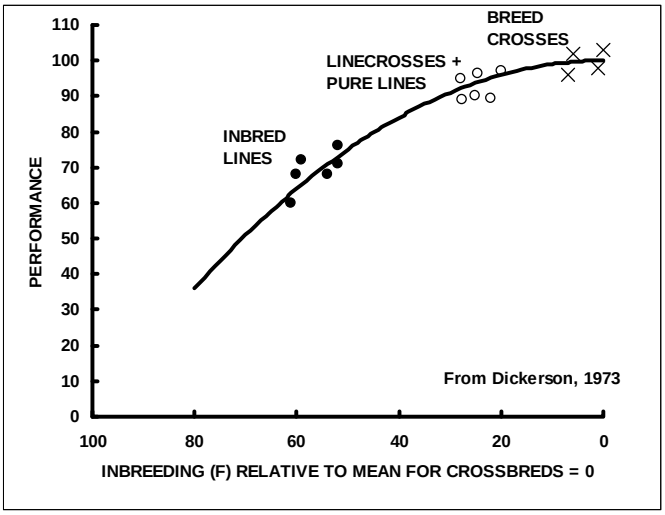

Figure 2. Schematic of relation of performance to level of inbreeding in inbred lines, linecrosses, and breeds relative to that for breed crosses (from Dickerson, 1973).

The recent availability of high-density SNP genotyping platforms presents another approach to estimating relative amounts of heterozygosity in crossbred and purebred cattle. If we assume that heterosis arises from many hundreds or thousands of dominance/recessive genes and that heterozygosity of anonymous SNPs are representative of heterozygosity at all genes, then SNP heterozygosity should predict gene heterozygosity and specific heterosis. However, if heterosis is caused by only a few genes then the ability of random SNPs to predict specific heterosis is greatly decreased.

The USMARC has used the Illumina BovineSNP50 BeadChip to genotype more than 3,000 animals. Results shown below are preliminary, exploratory results from purebred and two-way, four-way, and other crossbred animals used in the GermPlasm Evaluation program. Figure 3 shows the relationship between expected relative difference in heterozgosity and SNP heterozygosity. A technical note is necessary. Very high heterozygosity can be found in the blood of many twin animals due to interchange of hematopoietic stem cells in utero (leukochimerism). Semen and many other tissues from twin cattle do not usually exhibit chimerism. Identified twin animals were removed from the data in the figure and most had high SNP heterozygosity. However, not all calves born as twins are correctly identified. All or most of the extremely high values in the figure are likely twins identified as singles. Most samples from purebred animals were semen. Therefore, undetected twins will not increase SNP heterozygosity estimates for the group with zero predicted relative heterozygosity.

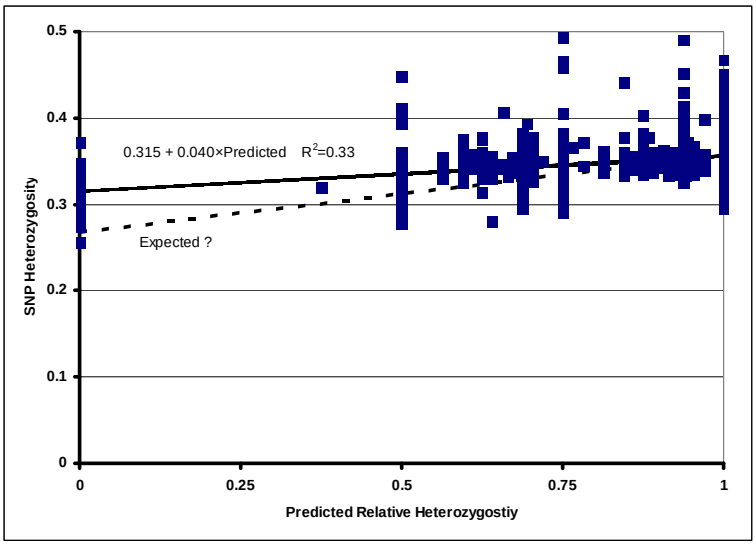

Figure 3. Relationship between predicted relative heterozygosity and SNP heterozygosity. Solid line is regression estimate. Dashed line is based shows a 25% increase in heterozygosity.

Although significant, the slope between predicted relative heterozygosity and SNP heterozygosity seems relatively flat and the variation around the slope is large. Based on comparisons of inbred line crosses to purebreds and comparison of crossbreeds to purebreds suggests that heterosis results in about a 25% increase in heterozygosity (L. V. Cundiff, personal communication). The results for these SNPs are about half this expectation. The reason for this difference could be due to an incorrect expectation of 25%, dominance being a smaller part of heterosis than expected, or bias in SNP heterozygosity.

For many applications (e.g., marker mapping, association analyses, parentage identification), the ideal SNP is one with a frequency of 0.5 for each allele in all populations. However, this ideal SNP shows no increase in heterozygosity when populations are crossed. While the opportunity for effective selection among SNPs for inclusion in the chip was limited, there is always a preference for identifying higher frequency SNPs to increase their informativeness and reduce the chance that they are an error or artifact of sequencing (Van Tassell et al., 2008). Although useful for many applications, selection of highly informative SNPs for various genotyping platforms means that they will overestimate the heterozygosity of purebred animals and, therefore, underestimate increases in heterozygosity for crossbred animals.

There are also differences in the sources of SNPs that could affect heterozygosity and apparent diversity among breeds. A portion of SNPs on the current Illumina BovineSNP50 BeadChip were discovered from sequencing an inbred Hereford cow. For this portion of SNPs, heterozygosity of Herefords is likely overestimated. All SNPs were discovered in some group of breeds and there should be some tendency to overestimate the heterozygosity of those breeds. This will distort estimates of genetic distance and diversity to some degree. Less biased estimates of SNP heterozygosity and genetic distance on a large scale will be facilitated by the advent of low-cost genome sequencing.

Despite possible biases in estimates of breed diversity and increases in heterozygosity of crossbreds, increases in SNP heterozygosity may be nearly proportional to actual increases and a useful way to reduce the number of heterosis parameters estimated. Research is needed

to evaluate this. Operationally, this would require good SNP frequency estimates for different breeds and computing expected heterozygosity of purebreds and crossbreds and their dams based on parental and maternal grandparental breed frequencies. Inbreeding could potentially be used to adjust purebred heterozygosity. Expected heterozygosity of individuals and their dams would then used as covariates in the EPD analyses.

In summary, good estimates of direct and maternal heterosis are important for efficient beef production and as adjustment factors for multibreed EPDs. The large number of heterosis parameters can lead to poor estimates. Some statistical and molecular genetics approaches offer some ways to either reduce the number of heterosis parameters estimated or minimize their impact when poorly estimated.

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Who Will Conduct Genetic Evaluation - Panel

Angus Genetics Inc.SM
Bill Bowman, President

Angus Genetics Inc. (AGI), a subsidiary of the American Angus Association®, was created to assist breed organizations by providing customized genetic evaluation services. In recent years, the seedstock industry has seen a transition where universities have shifted away from genetic evaluation service roles to more fully focus efforts toward research endeavors. AGI was established in 2007 to answer the seedstock industry's need to have a genetic evaluation service provider during this process. AGI is one of four subsidiaries of the American Angus Association. The three additional subsidiaries are Certified Angus Beef, Angus Productions Inc, and the Angus Foundation.

The objectives of AGI include the following:

- To provide services to the beef industry that would assist in the genetic evaluation of cattle traits
- To develop and promote technology for use by the beef industry including DNA technology
- To conduct research, develop and prove new science and technology to benefit all beef producers

AGI fulfills its objectives through three channels: cooperation with existing genetic research specialists/outlets/areas, collaboration with its parent company, the American Angus Association, and by providing specialized services for breed organizations.

AGI maintains a multi-year research agreement with University of Georgia geneticists and utilizes software programs created by the University of Georgia. This cooperative endeavor enhances the University's ability to address genetic evaluation topics, such as random regression, marker assisted selection, and novel trait models, for the betterment of the beef industry. Funding from AGI provides a research scientist position at the University to explore such projects.

Located in Saint Joseph, Missouri, AGI is staffed by full-time and part-time employees with shared responsibilities to the American Angus Association. As of January 2009, the AGI genetic evaluation component provides service to seven breed organizations in the U.S. and Canada. Services are tailored to individual client needs ranging from within breed evaluations, multi-breed evaluations, and development of new evaluation models for requested traits. AGI works cooperatively with scientists at the client breed organizations, as well as university, government and allied industry researchers.

A Brief Synopsis of the Past, Present and Future of Genetic Evaluation at the American Simmental Association

Wade Shafer, American Simmental Association

Darrh Bullock and John Pollak have asked the breed associations that are performing genetic evaluation to provide some insight into what we are currently doing and some sense about what the future holds for us in the area of genetic evaluation. Before addressing those issues, I feel it is beneficial to provide a short synopsis of the history of genetic evaluation at the American Simmental Association (ASA). To do so, I have enlisted the help of our resident historian, Steve McGuire. Given the fact that Steve has been employed by the ASA for over 36 years (nearly encompassing ASA's entire existence), he is eminently qualified to provide an accounting of anything that has transpired at the ASA.

Though there were many individuals involved and several noteworthy events in ASA's genetic evaluation history, this synopsis is quite abbreviated. The ASA's first sire summary was published in 1971. The calculations were performed by Boeing Computer, a division of Boeing Aircraft of Seattle Washington, with Paul Miller of the American Holstein Association as the consulting geneticist. Steve says the evaluation created quite a stir, not so much for the science behind the evaluation, but because each sire was allocated a full-page, color picture in the summary. There were fewer than fifteen bulls in that evaluation.

Another significant advancement occurred in 1984, when Cornell University performed the first Best Linear Unbiased Prediction on ASA's data. This event ushered in a long and extremely fruitful collaboration between Cornell and ASA. For over 20 years, Cornell geneticists Dick Quaas and John Pollak shepherded ASA's genetic evaluation program, which churned out a long list of seminal achievements.

One of the most notable achievements was the industry's first multi-breed genetic evaluation, the results of which were published in 1997. In Steve's opinion, the primary impetus behind the development of multi-breed technology was to allow for a more accurate evaluation of the many crossbred cattle in ASA's database that were produced in the "grading up" process, which took place in the early years of the breed's introduction to the US. The process typically involved mating Simmental sires imported from Europe to domestic cows of various breeds, with the end result being large numbers of crossbred animals born primarily from the late 1960s to the late 1980s, with few crossbreds produced in the 1990s. Over the decade since the implementation of ASA's multi-breed evaluation, however, the considerable increase in demand for composite seedstock has resulted in a dramatic resurgence of crossbred animals in our database—which has underscored and even amplified the value of multi-breed technology.

We recently (2006) moved the genetic evaluation in-house, while continuing to enlist the part-time services of Zhiwu Zhang, formerly a research associate for Quaas and Pollak at Cornell. Our base evaluation is multi-breed for both weight and carcass traits, while calving ease is evaluated in a single-breed analysis. We perform the evaluation twice annually and calculate interim EPDs between evaluations.

Mark Enns along with graduate students Brian Brigham and Scott Speidel from Colorado State University perform our stayability analysis**.** Dorian Garrick, a former Colorado State researcher now at Iowa State University, recently improved our stayability analysis by allowing for the incorporation of outcomes from two- to six-year-old parities.

ASA's database is currently at 6 million animals, with representation from virtually every documented beef and dairy breed. The two most prevalent breeds are Simmental and Angus. Almost half (2.8 million) animals are purebred (7/8 or greater) Simmental, while another 1.6 million are less than 7/8 but at least 1/8 Simmental. There are .25 million purebred Angus and another 1.7 million animals with at least 1/8 Angus that are not considered purebred Angus. The Angus statistics referenced above combine Angus and Red Angus, with Angus representing roughly 90 percent of the whole.

What does the future hold for genetic evaluation at the ASA? Given the substantial changes in the landscape surrounding genetic evaluation in the US, this is a question we have frequently contemplated—and continue to do so. The only thing we can state with absolute certainty is that genetic evaluation is a core function at the ASA.

As a core function, we feel that delivering cutting-edge genetic evaluation technology to our membership is imperative—as is providing this technology in a manner that results in the maximum genetic progress achievable within the beef industry's unique limitations; limitations I will speak to later.

Clearly, carrying out the core function is an ongoing process with various routes to accomplishing the objective—and we are not married to any one of them. At this point, we are primarily focused on examining the tasks involved in genetic evaluation, with the expectation that thorough scrutiny in this area will allow us to make better decisions on which paths to take in the future.

From our experience, we feel the core function of genetic evaluation can be logically and beneficially delineated into what I will reference as its physical and psychological components. The physical aspects of genetic evaluation pertain to those things required to perform an evaluation—from research/development to the production infrastructure necessary to get a national cattle evaluation out the door. By most objective standards, we (the US collectively) have faired quite well in this area. Due to recent changes at the universities that have been performing the bulk of genetic evaluations in the US, however, there is uncertainty as to how it will be provided in the future.

Though sizable among beef cattle breed associations, the ASA is a small company with limited resources. Given that the physical aspects of genetic evaluation are resource intensive, we anticipate the need to seek creative and efficient paths if we are to continue to deliver cutting-edge genetic evaluation technology to our membership. At this point, we envision collaboration with both private and public entities as key to our success in this area.

To dilute evaluation costs, we currently provide genetic evaluation for three other breed associations and are open to similar arrangements with additional breeds. We have already benefited from and hope to continue to harvest the fruits from the efforts of the National Beef Cattle Evaluation Consortium, USDA and commercial genomic companies in advancing evaluation technology. We have also been involved in several collaborative efforts with university researchers around the country. The most notable being a partnership with the University of Illinois and Montana State University in an ongoing feed utilization experiment.

Though a small company, we have consistently allocated a relatively large portion of our budget to genetic improvement endeavors. This commitment has allowed us to tackle several genetic evaluation tasks internally. For example, we are currently in the process of developing

software to perform multi-breed calving-ease evaluations in addition to many other software developments that promise to enhance our evaluation. Also, we have supported and sustained a large-scale structured-sire-testing project for over ten years. Though largely underwritten by ASA, this endeavor is a joint effort between bull owners, AI companies, commercial producers and Montana State University.

As previously mentioned, we consider our genetic-evaluation core function to extend beyond simply delivering cutting-edge evaluation; we are commissioned to do so in a manner that maximizes genetic improvement. We feel the psychological component of genetic evaluation I referred to earlier to be key to accomplishing this task.

The psychological component pertains to the measures taken to encourage seedstock breeders to utilize the technology, and do so effectively. This component is largely unnecessary in the swine or poultry industries, as pigs and chickens are bred by highly trained geneticists; however, very few beef cattle breeders are trained at that level. This fact poses a substantial limitation on the rate of integration of genetic evaluation technology in the beef industry.

When it comes to the psychology of genetic evaluation, the industry's primary focus has been in the area of education. For over 20 years, breed associations, universities and extension services have invested monumental resources teaching beef cattle breeders and commercial producers about the use of EPDs. Unfortunately, in my opinion, the effort has only been marginally effective. Though it colors my assessment, my view is not solely based the anecdotal evidence I have cobbled together over many years in the industry. I also have more definitive support for the claim gathered from a 2006 survey of over 200 producers from Nebraska and South Dakota (Table 1).

Table 1. Primary Source Used in Selection Decisions.

Source	Commercial Producers	Seedstock Producers
Actual Measurements	12%	7%
Adjusted Measurements	8%	8%
Ratios	10%	21%
Visual Appraisal	33%	31%
EPDs	30%	28%
Economic Indexes	7%	5%

As can be seen from Table 1, visual appraisal is the primary source of information used in making selection decisions by both commercial and seedstock producers. Though EPDs are at least second in priority, anyone involved in the massive educational efforts undertaken by the industry has to be disappointed that producers do not put more emphasis on EPDs. Also, given the fact that the same question asked of pig or poultry breeders would yield 100% of the respondents using economic indexes as their primary source, it appears clear that the beef industry is a long ways behind its competitors in the integration of genetic evaluation technology. It should be noted that, when this survey was taken, economic selection indexes had only recently been introduced to the industry and just by a few breed associations.

If considerable educational efforts have not yielded satisfactory results, what can be done to increase the integration of this technology? Possibly due to the lack of industry sophistication in genetic evaluation, beef cattle breeders are often more interested in factors that make their cattle more marketable than factors which actually produce a genetically

superior product. For example, virtually all seedstock breeders prepare their sale bulls by feeding high levels of concentrate so the weight and appearance of their animals give potential customers the impression that their cattle have high growth levels. At the same time, many of the same breeders will eschew the use of growth EPDs as a means of genetically improving growth levels.

Due to the industry's lack of sophistication and focus on marketability, though the notion may be unsavory to those of scientific inclination, our conclusion is that the key to significantly increasing the integration of genetic evaluation technology is making it marketable—and the key to marketability appears to be presenting the technology in a simple and sexy manner.

If we apply the simple and sexy litmus test to EPDs, my opinion is that they fail. Most breeds have upward of 15 EPDs, and assimilating them to pass inference about an animal's net genetic merit is certainly not simple. Furthermore, their abstract nature (expressed as deviations) and numerous units (pounds, percent unassisted births, marbling and yield grade units, etc.) are not particularly appealing from a marketability standpoint.

What can be done to make genetic evaluation technology marketable? From our experience over the last few years, we have come to believe that the economic selection index is the logical vehicle to accomplish the task. If we apply our marketability litmus test, indexes pass with flying colors. Rather than sifting through a myriad of EPDs to render judgment on an animal, a single statistic greatly simplifies the selection process. Furthermore, economic index units (i.e., dollars) are very appealing to producers; ultimately answering the question they ask when making selection decisions: "how much money will I make with this animal compared to that animal?"

Four years ago, working with USDA researcher Mike MacNeil, we developed two, one-size-fits-all indexes; one for selecting animals that will impact the entire production system and the other for terminal sire selection. Though based solely on anecdotal evidence, at this point it appears our breeders have warmed to these indexes comparatively rapidly—much more readily than their acceptance of EPDs.

Competition seems to be a major motivator behind the use of indexes. Having an officially recognized gauge of an animal's overall genetic value yields a "king of the hill" competition—which ultimately yields marketability for the "kings". Indexes are now common currency in most sale catalogs, breeder ads and AI stud books. We have fielded complaints that many breeders are only using the indexes for marketing purposes. We can certainly live with that, given that the indirect result will likely be positive.

Beyond marketability, economic indexes obviously enhance a producer's ability to make selection decisions. Frankly, the industry has been negligent in not providing tools with which to make objective selection decisions long ago. I liken providing EPDs without an objective means of using them to issuing a Porsche to a horse-and-buggy driver without providing direction. Though the upgrade allows the driver to travel much faster—they can quite conceivable end up further away from their destination than they were with their horse and buggy.

We certainly recognize that our one-size-fits-all indexes will not be on the mark in all instances. From a purist's standpoint, there is no question that customized or interactively developed indexes are ideal. Further, we applaud Dorian Garrick in his effort to develop an interactive decision support system and make it available to the entire industry—and we will promote its use. That said, given the industry's modest level of sophistication, we are somewhat

cautious in our expectations that anything beyond one-size-fits-all indexes will be utilized to a significant degree by the industry. Given that an interactive approach requires user input and does not generate an official “king of the hill” claim, it does not fair as well as the one-size-fits-all approach on the marketability scale.

In summary, at the ASA we view genetic evaluation as one of our core functions. The goal of the function is to deliver cutting-edge evaluation technology in a manner resulting in the maximum genetic progress possible. Given the financial constraints that are part and parcel of being a small company and the hurdles to technological integration posed by the beef industry’s structure, efficiency and creativity are necessities if we are to successfully carry out this core function into the future. To keep our genetic evaluation program on the cutting edge, we intend to continue to collaborate with many private and public entities in addition to allocating a relatively large portion of our budget to that end. Though the beef industry’s current rate of technological integration is subpar, we feel the economic selection index holds the key to dramatically ratcheting up the industry’s willingness to incorporate genetic evaluation technology.

Genetics Performance Solutions, LLC
A Breed Association Service Company

Joseph Massey
International Brangus Breeders Association

Genetics Performance Solutions, LLC (GPS) is a breed association registry, database management and genetic performance analysis Service Company whose goal is to provide these services to associations in a cost effective manner on a real-time internet basis. GPS is currently owned by the International Brangus Breeders Association (IBBA) and Red Angus Association of America (RAAA). GPS has been working with the University of Georgia to offer singe breed EPDs and will be publishing multi-breed EPS early in 2009.

GPS currently has contracts with IBBA, RAAA and the Braunvieh Association of America and is in discussions with a number of other breed associations to provide services to them. GPS is currently evaluating its multi-breed EPDs on the Red Angus and Brangus data bases for performance traits and carcass traits. We anticipate that results will become available for publishing in the first quarter to 2009.

I believe that the commercial cattle industry will demand genetic analyses in a comparative format that has predictability of performance across breeds. Breed associations are not in position to address these issues on their own; they have neither the management, the commitment from their boards nor the resources to do so. The role of breed associations is to promote their breeds in the best possible way to the commercial cattlemen and other seedstock producers not to develop software or manage data bases.

For breed associations, genetic analysis represents a potential section tool or sorting tool to make genetic mating decisions and such tools are equally as valuable to the commercial cattlemen. Breed associations forget at times that they are in the business of providing seedstock to the commercial cattlemen with defined and predictable performance. The GPS goal is simple, to provide these tools to both the seed stock producer and the commercial cattlemen. There is little merit in believing that a breed association or a breed of cattle can stand alone and provide much value to the production of beef on a consistent and predictable manner. The tools to evaluate the best genetics for mating become much simpler when a single model is used to evaluate genetic performance across breeds and we get out of the guessing game.

GPS has positioned itself as one of the companies that can service breed association in a cost effective manner and provide the most up to date genetic evaluations, such as multi-breed EPDs.

What Genetic Evaluation System is Best for the Beef Industry?

Darrh Bullock, University of Kentucky

Beef cattle genetic evaluations have a long history in the United States (Garrick and Golden, 2009; Golden et al., 2009). For over 35 years genetic evaluations have been computed and published in the beef industry, however, many changes have taken place. The changes that have occurred have been in methodology, computational capacity and logistics (who does the evaluations). The purpose of this paper is to discuss the changes in logistics and to discuss options for the future.

From the onset in beef cattle genetic evaluations there has been a relationship between breed associations and several universities. The primary universities that have been involved in the computation of genetic evaluations are Colorado State University, Cornell University, Iowa State University and the University of Georgia. Some breeds have changed their affiliation with certain institutions, but these universities have been the primary provider of genetic evaluations in the US. In the early years of genetic evaluation through the heyday period of the 1980's there was fierce competition between the universities for breed association resources. From a positive standpoint this lead to advancements in methodology, to stay competitive, but it also fostered repetition and a lack of collegiality. In the early 1990's the universities involved, along with the Beef Improvement Federation and the National Cattlemen's Beef Association, started a movement to improve the efficiency of genetic evaluations and to investigate removing the service portion from the university systems. Born from this effort was the National Beef Cattle Evaluation Consortium (NBCEC). The NBCEC is currently coordinating and funding research in genetic evaluations and new traits, actively pursuing the incorporation of genetic marker information into genetic evaluations and conducting a nationwide educational program directed at both producers and future scientists.

Since the early formation of the NBCEC the institutions involved have stressed the need to remove the service aspect of genetic evaluation from the universities. This service component is scheduled to end in 2010. The NBCEC will continue to function as the research and educational leaders in beef cattle genetic evaluations, which will include methodological and computational research to facilitate the entities that will compute the genetic evaluations. Several such entities have come into existence in recent years; primarily breed associations, or groups of breed associations that will assume the role of computing genetic evaluations. Additionally, some breed associations are utilizing the services of BREEDPLAN in Australia for their genetic evaluations.

Preceding this presentation was a panel discussion including five breed association executives discussing their breed's efforts to compute genetic evaluations in the absence of direct university computation (Bowman, 2009; Huffhines, 2009; Massey, 2009; Shafer, 2009; Williams, 2009). The purpose of this presentation was to allow audience participation in further discussing what system would best serve the beef industry. Audience response devices were used to record and display the results of poll questions asked of the audience (TurningPoint, 2008). Table 1 represents the primary occupation of the participants in this presentation at the Genetic Prediction Workshop.

The purpose of genetic evaluation is to transform phenotypic and pedigree data into an Expected Progeny Difference (EPD) that can be used as a selection tool. EPDs are best utilized when incorporated in some form of selection index or holistic selection process, typically

based on economic merit (MacNeil, 2009). Keeping in mind the demographics of the participants in the workshop, their assessment of who benefited the greatest from the computation of EPDs were seedstock producers (45.5%), commercial producers (37.9%), consumers (15.1%) and feedlot/packers (1.5%) from greatest to least (Table 2). Some of the benefits of EPDs to seedstock producers are that they allow focused breeding with adequate reliability and they are able to get EPDs with few or no records, not only for purebreds but also for composite and crossbred cattle. One of the major challenges associated with the computation of EPDs are the costs associated with them; seedstock producers, through their respective associations, bear the burden of these costs. Commercial producers also benefit from a reliable selection tool which allows them to target select bulls that fit their environment and production goals. The challenges for commercial producers are low accuracies on young bulls, overwhelming number of EPDs, limited information on the traits of greatest economic importance, reproduction and efficiency, limited selection decision tools and limited means of comparing bulls of different breeds. The benefits to feeders, packers and consumers are more indirect, but ultimately should lead to a more efficiently produced, consumer acceptable product. The main challenge for these groups is the slow pace of change.

This leads to the discussion of what is the best approach to computing genetic evaluations. Prior to discussing what is needed in the industry the audience was polled to determine what they felt was the best approach to computing genetic evaluations (Table 3). No participants felt that we should go back to the method of each breed association computing their own EPDs. However, the largest portion indicated they thought that multiple groups of associations going together to compute EPDs was the best approach (38%), with about a third each choosing a single private entity (29%) and a single government entity similar to the dairy genetic evaluation (33%). When breaking the numbers down further, the greatest supporters of the groups of breed associations computing EPDs was purebred seedstock producers and breed association representatives; the greatest supporters of a single private entity were the composite seedstock producers and Extension personnel; and the biggest supporter of the single government entity was the University/Government researchers.

With several options available and no clear consensus of which direction to take it becomes important to focus on common goals and recognize potential pitfalls. What most people associated with the beef industry can agree would be beneficial in a genetic evaluation system would be, but not limited to:

- Reasonably good accuracy, even on young bulls.
- A mechanism for commercial producers to make selection decisions that are economically based, simple and account for non-additive genetic effects.
- Low cost.
- Researched based decisions with limited political influence.

On the flip side some things we need to avoid are:

- Research community split back into separate camps vying for the good graces of specific breeds/entities.
- Further loss of genetic diversity.
- Multiple EPDs on the same trait for an animal.

In general, it appears that the current direction of the industry is not in the direction that would be most beneficial to the beef industry.

To improve accuracy on young bulls it would be beneficial to utilize commercial data in the evaluation and to incorporate genetic marker information. To improve decision support there needs to be comparable EPDs across breeds, increased support for the development and improvement of decision support systems, along with increased education. Additionally, there needs to be increased efforts in developing EPDs for reproduction and efficiency traits which have the potential to play a large role in any holistic selection decisions. Cost containment in genetic evaluation can only come through increased efficiency, which probably leads to increased consolidation. In weighing many of the factors involved in computing EPDs it appears that the best system for the beef industry would be a single entity computing the EPDs with an independent organized research group focused on supporting this effort, with an educational component.

After this discussion the participants were asked the same question again, "What do you think is the best approach to computing genetic evaluations?", with slightly different results (Table 4). There was a slight shift from multiple breed association groups (29.0%) to a single private entity (40.3%) with little change to a single government entity (30.7%). It appears that initially the multiple groups of association entities will be the system that will be adopted. Depending on what happens with various government projects and the free market system we are likely to see the process evolve even more in the coming years. Hopefully the end product will be what is best for the beef industry.

Table 1: Who are you? (n=63)

Commercial Beef Operation	0.0%
Seedstock/Purebred	12.7%
Seedstock/Composite	9.5%
Feedlot/Packing Industry	0.0%
University/Government Researcher	54.0%
Extension	7.9%
Breed Representative	15.9%

Table 2: Who is the greatest beneficiary of EPD's? (n=66)

Seedstock Producers	45.5%
Commercial Producers	37.9%
Feedlot/Packers	1.5%
Consumers	15.1%

Table 3: What do you think is the best approach to computing genetic evaluations (initial response)? (n=63)

Each Association Generates their own.	0.0%
Groups of Associations forming entities.	38.1%
Single private entity.	28.6%
Single government entity supported by tax $.	33.3%

Table 4: What do you think is the best approach to computing genetic evaluations (after discussing pros and cons)? (n=62)

Each Association Generates their own.	0.0%
Groups of Associations forming entities.	29.0%
Single private entity.	40.3%
Single government entity supported by tax $.	30.7%

Guidelines for Combining Molecular and Quantitative Approaches in Genetic Evaluation[1]

M. W. Tess
Montana State University

Introduction

Research into the molecular basis of inheritance is progressing at a rapid pace. Technologies that permit the identification of molecular genetic differences (i.e., differences in deoxyribonucleic acid (DNA) sequence among animals) are also evolving very rapidly. Several DNA-based tools are being marketed in the beef industry; some as selection tools. These tools are known by a variety of names in the academic community and within the beef industry (e.g., genomic tests, DNA markers, molecular tests or markers).

DNA-based selection tools present opportunities and challenges to the U.S. beef industry. Accurate DNA-based selection tools will give beef cattle breeders opportunity to identify animals with superior breeding value (BV) as soon as a tissue sample can be collected and analyzed, potentially leading to significant savings in time and money associated with performance testing and genetic evaluation. However, as currently marketed, the BV information provided by DNA-based tools is not uniformly reported and the proportion of variation in true BV accounted for by the tools is unknown. Further, the BV information provided by competing DNA-based tools overlaps and is not independent of information provided by current national cattle evaluation (NCE) systems.

Performance testing and genetic evaluation are being conducted on an increasing number of traits. The types of information available (i.e., available from a practical and economical view) varies among traits. Types of information include pedigree relationships, performance measurements (i.e., phenotypes), and DNA test results. Phenotypes may include direct and indirect measurements on the same trait. Table 1 illustrates the various combinations possible. Because most animals marketed in the U.S. as seedstock have known parentage the table assumes that pedigree relationships are known.

Some traits are difficult to measure and there are no DNA tests for these traits available. These traits will likely be the focus of future research. In a second category are traits for which phenotypes are regularly measured in the field, systematically data-based, and for which Expected Progeny Differences (EPD) are computed. The emergence of DNA tests now permits the estimation of BV on animals for which little or no phenotypic information is available (a third category). A current example would be tenderness. Tenderness phenotypes are difficult and expensive to measure, but DNA tests are available. In a fourth category are traits where both phenotypes and DNA tests are available. A current example would be carcass marbling.

[1] Prepared by M. W. Tess and the BIF Commission on DNA Markers. Commission members: Bill Bowman, Ronnie Green, Ronnie Silcox, Darrell Wilkes, and Jim Wilton.

Table 1. Traits categorized according to information available.

DNA Tests	Industry-collected Phenotypes	
	No	Yes
No	---	EPD
Yes	EPD	EPD

Guiding Philosophy

BIF believes that information from DNA tests only has value in selection when incorporated with all other available forms of performance information for economically important traits in NCE, and when communicated in the form of an EPD with a corresponding BIF accuracy. For some economically important traits information other than DNA tests may not be available. Selection tools based on these tests should still be expressed as EPD within the normal parameters of NCE.

Types of Current DNA Technologies

There are a variety of DNA-based tools available to the beef industry today. The number of DNA-based technologies marketed will likely increase rapidly over time. Following is a list of the broad types available based on their applications. All are based on identifying differences in DNA base-pair sequence among animals. The number of base pairs involved, and the lab techniques employed vary greatly.

Parentage Identification/Validation tests are used to identify or validate the sires and dams of calves. They involve testing the calves and at least one parent.

Identification/Traceability tests are used to track animals and tissues through the food production chain as animals and their products change ownership and move from location to location. Variation in DNA is used to identify individual animals. Each animal being tracked must be tested.

Management tests are used to predict the future phenotypes of animals in specific production-marketing systems. They are based on identifying differences in total genetic merit among animals (i.e., additive and non-additive genetic merit).

Selection tests are used to estimate breeding value (i.e., distinguish among animals on the basis of their progeny performance). Traits may be qualitative or quantitative in nature. Qualitative traits are controlled by one or a few loci, and phenotypes generally fall into distinct classes (e.g., presence of horns, coat color, and certain genetic defects). Quantitative traits are

controlled by many loci. Quantitative phenotypes may be measured on a continuous scale (e.g., weights) or in classes (e.g., pregnancy success).

The focus of the guidelines presented here is on DNA tests for quantitative traits used for selection.

Validation

DNA tests are developed based on associations between variations in base-pair sequence at one or more loci with variations in phenotypes. The animal populations used to develop the test may or may not be representative of beef industry populations. Validation generally involves the confirmation or rejection of these associations in populations that are representative of the beef industry and different from those in which the tests were developed. Validation studies are considered to be more reliable if conducted by scientists who have no vested interest in the tests (e.g., development, commercialization, or marketing). To date, components of commercially available DNA tests have been validated by the National Beef Cattle Evaluation Consortium (NBCEC) serving as an independent third party. Validation serves to reduce risk for breeders using DNA tests in selection.

BIF recommends that breeders who use DNA-tests should, whenever possible, choose DNA-tests that have been validated in populations that are representative of the beef cattle industry by scientists independent of the organization that developed or will market the test.

Assessment

Assessment involves determining how specific DNA tests are associated with each other and with non-target phenotypes. Assessment seeks to determine how competing DNA tests overlap and how non-target traits will be influenced by selection based on these tests. For example, it is important to know if selection based on a DNA test for tenderness has any desirable or adverse effects on other economically important traits (growth, feed intake, fertility, etc.). Like validation, assessment studies are considered to be more reliable if conducted by scientists who have no vested interest in the tests.

BIF recommends that assessment studies should be conducted in populations that are representative of the beef cattle industry by scientists independent of the organization that developed or will market the test.

Reference Populations

As used here, reference populations are: 1) pedigreed herds that are representative of and genetically linked to commercial populations in the beef industry, 2) managed in production/marketing systems representative of the beef industry, 3) measured for economically relevant traits and (or) important indicator traits, and 4) from which tissue samples are available. Ownership may be public or private; however, as envisioned here the most useful on-going reference populations are likely to be federally owned and managed.

BIF recognizes the critical importance of pedigreed reference populations for the successful implementation of DNA-based selection tools in the beef industry. BIF considers the partnerships of USDA-ARS and Agriculture Canada in the establishment and maintenance of reference populations to be vital to the successful implementation of DNA-based selection tools in the beef industry.

A Proposed Model

Figure 1 schematically presents a proposed model for national cattle evaluation that incorporates pedigree relationships, performance phenotypes, and DNA test information in the computation of EPD and accuracies. The model will accommodate traits with different amounts and types of information (i.e., pedigree relationships, indirect and direct measures of phenotype, and DNA tests from multiple companies). As envisioned this model would accommodate within-breed NCE as well as multi-breed NCE. The proposed model assumes that breed associations will continue to bear major responsibility for the delivery of EPD to the beef industry.

Statistical procedures for incorporating DNA test information into NCE and the computation of EPD and associated accuracies will be described elsewhere. Briefly, the method utilizes DNA test results in a manner analogous to using correlated traits in more traditional NCE. The method permits incorporation of several competing DNA tests (e.g., tests for the same trait) as well as pedigree and performance information. The method is applicable to any trait for which some information on breeding value is available (i.e., phenotypes and (or) DNA tests; 3 of the 4 cells in Table 1). DNA test scores are assumed to be linear functions of the genotypes measured, and may be based on a few or many loci, including whole-genome scans. The method also accounts for the fact that DNA tests for specific traits are updated from time to time.

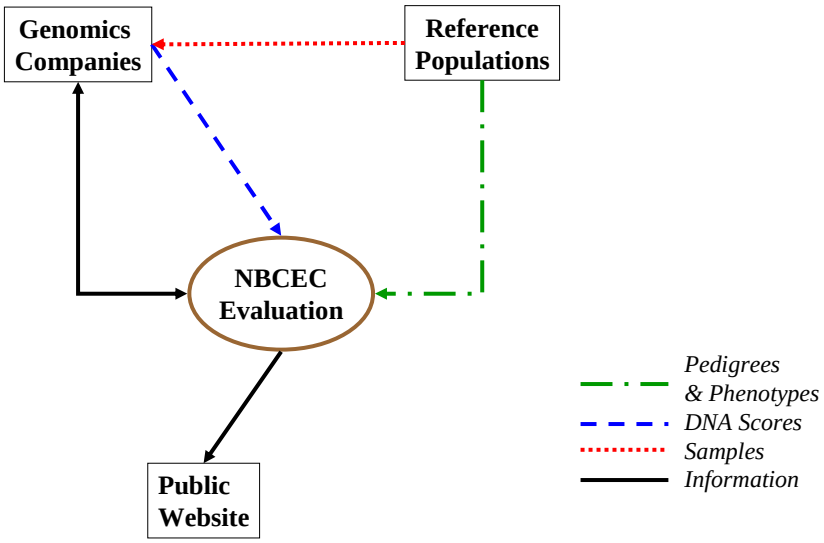
Evaluation of a DNA Test as a Selection Tool

As represented in Figure 1, BIF assumes that the NBCEC will coordinate validation and assessment efforts. At present, the long-term future of NBCEC is uncertain. Nevertheless, the importance of an independent third party in the model is emphasized.

As illustrated in Figure 1, evaluation of a DNA test would include: 1) the delivery of tissue samples from a large number of animals in the reference population to the genomic company that developed the test, 2) the genotyping of the samples and calculation of the relevant test scores for each animal (i.e., completing the DNA test), 3) the communication of the test scores to NBCEC, 4) the statistical evaluation of the test scores using the pedigree relationships and phenotypes collected in the reference population, and 5) the communication of the results to the genomic company and to the public.

Under the proposed model, statistical evaluation of a DNA test as a selection tool includes the concepts of validation and assessment, and also provides information on the accuracy of selection based on the DNA test. Important statistics estimated include: 1) covariances between the DNA test and the target trait (phenotype), 2) covariances among competing DNA tests for the target trait, 3) covariances between the DNA test and non-target traits, and 4) computation of EPD and their associated accuracies. If the DNA test is intended for use in multiple breed types and production/marketing systems, then the reference populations and production systems used should permit the evaluation of the interactions among breed types and production environments.

Figure 1



Inclusion of DNA Test Information in NCE Programs

Results of the evaluation of a DNA test will also provide estimated genetic correlations among competing DNA tests, genetic correlations between DNA tests and non-target traits, and the fraction of the additive genetic variance of the target trait accounted for by the DNA test.

Results of the evaluation phase (described above) will provide all the statistical parameters needed for NCE. The decision to include a DNA test in a NCE system should be made by the organization responsible for computing the EPD. Consideration should be given to the heritability of the trait, the availability of producer-collected phenotypes, and the increase in accuracy provided by the addition of the DNA test information.

BIF recommends that a DNA test should be considered for inclusion in the NCE system when after estimating the covariances and running the NCE system, use of the DNA test results in a more accurate EPD at a young age.

Databases

DNA test scores will need to be stored and accessed in an efficient manner. Figure 2 presents a schematic of how NCE would incorporate DNA test information on an ongoing basis. The proposed model will require the storage and use of potentially large databases of DNA information. Important considerations include: 1) the marketed DNA tests are expected to change frequently over time, 2) multiple companies are likely

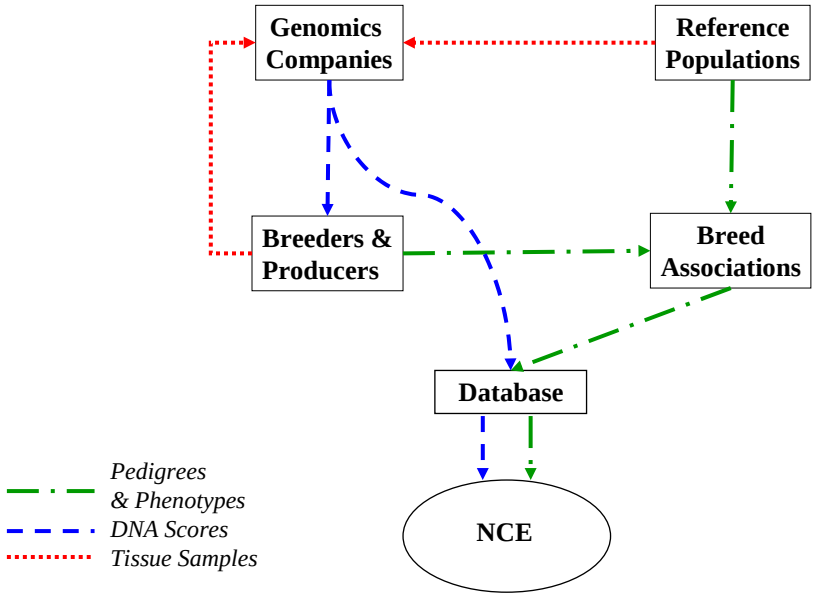
to market DNA tests for the same target trait, and 3) access to the raw data may need to be restricted. Hence, it will be important that the database(s) can accommodate these aspects.

The quality of any EPD is dependent on the quality of the data used to compute the EPD. Much like selective reporting of phenotypic measurements may bias EPD computed from pedigree and phenotypes, selective reporting of DNA tests may bias EPD computed from DNA tests.

BIF recommends that breed associations should establish procedures that encourage the full reporting of all DNA tests.

An important aspect of the proposed model (Figure 2) is that on-going NCE would be based not only on producer-collected measurements (i.e., field data), but also on data from the reference populations. The evaluation of DNA tests (described above) provides the data to essentially "seed" the EPD for the industry – i.e., providing EPD for many animals genetically linked to industry populations as soon as the DNA test is approved.

Figure 2



Interim EPD

To maximize the utility of DNA tests to the beef industry it is critical that the organizations computing EPD be able to provide breeders with EPD (interim EPD) very soon after the DNA tests are completed and the results are added to the database.

BIF recommends that interim EPD be computed and communicated to breeders as soon as possible after DNA tests are completed.

Note that the evaluation of a DNA test as a selection tool (outlined above) will also yield estimates of EPD based on DNA test information alone. Hence, for DNA tests that have been evaluated as described above, genomic companies would be able to provide interim EPD to their customers as soon as the DNA tests are completed.

Reporting of DNA Test Results by Genomic Companies

It is important the DNA test results be reported to beef industry in a consistent, understandable format. Further, the format should be compatible with NCE methods. It's possible that a single DNA test (i.e., genotypes from a single panel of markers) may yield information useful for both management and selection. Predictors based on these tests should be clearly identified with respect to their uses – i.e., future phenotypes versus breeding value.

BIF recommends that DNA test results be reported in the form of an EPD, in the units of the trait, on a continuous scale, and with a corresponding BIF accuracy.

It is likely that research will develop new DNA tests for traits that have no industry-collected phenotypes (see Table 1). If the target trait is measured in the reference populations, evaluation of the DNA test as a selection tool should be as described above.

Novel Traits

It's conceivable that the target traits for some new DNA tests may not be measured in reference populations. In such cases precise definition of the target trait will be important.

An independent organization such as NBCEC should conduct or coordinate the validation studies of novel DNA tests. Validation may be approximated by review and (or) re-analysis of the data used to develop the test. Such data should include the DNA test results, phenotypes, and pedigree relationships. The data used to develop such new tests should be of sufficient quality and quantity as to allow the estimation of the additive genetic variance of the target trait and the covariance between the DNA test score and the target trait.

BIF recommends that, for DNA tests targeting traits that have no industry-collected phenotypes and for which no phenotypes are collected in reference populations, the results from such novel DNA tests should be reported in the form of an EPD, in the units of the trait, on a continuous scale, and with a corresponding BIF accuracy.

Integration of DNA markers into a BREEDPLAN Tenderness EBV

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Introduction

The recently completed SmartGene for Beef project (for full report see www.agbu.une.edu.au/smartgene.php++) identified significant effects of the Catapult Genetics GeneSTAR® tenderness markers on meat tenderness as recorded by the objective measure of shear force. These results have allowed us to further develop the concept of combining EBVs (i.e. phenotypic and pedigree data) and gene marker information into a single marker-assisted EBV. The Brahman breed was chosen to develop the first trial BREEDPLAN EBV for meat tenderness because of its large involvement in the Beef CRC projects and the level of industry uptake of GeneSTAR marker testing. These marker-assisted EBVs will be denoted by **EBV^{M}** to indicate that DNA marker information has been used in the computation of the particular trait EBV. These trial Brahman Tenderness EBV^{M} represent a first for the Australian beef industry, and a significant advancement in genetic evaluation in this country. The methodology, developed at AGBU to incorporate DNA marker information into BREEDPLAN, will be used on other traits and in other breeds in the future.

Data

The computation of the new trial tenderness EBV^{M} used three different sources of data. The first was the phenotypic records of shear force (LDSF) from meat samples from the eye muscle of carcasses measured through the Beef CRC 1 (Johnston *et al.* 2003) and CRC 2 (Wolcott *et al.* 2009) pedigreed breeding programs (N = 1995). Shear force is a mechanical measure of meat tenderness where a blade is pulled up through a piece of cooked meat and the maximum force required to cut through the meat is recorded. The second source of data used was the GeneSTAR tenderness marker results (i.e. 'star' assignment) for each marker. The four markers current commercialized by Catapult Genetics included T1 (SNP = CAST; Barendse 2002), T2 (SNP = *CAPN1*-316; Page *et al.* 2002), T3 (*CAPN1*-4751; White *et al.* 2005) and T4 (anonymous SNP). Marker results were available on the CRC1 and CRC2 Brahmans (genotyped through the SmartGene Project) and also industry tested animals that had their results submitted to the Brahman National Beef Recording Scheme database (N = 4729). The third source of data was flight time records (N = 4737) on animals in the CRC projects and also a small number of recently recorded industry animals. Flight time is an objective measure of an animal's temperament. Results from the Beef CRC showed that flight time (FT) was heritable and also moderately genetically correlated with shear force (Kadel *et al.* 2006), thus representing a potential genetic indicator trait for meat tenderness.

Methods

The three sources of data, along with available pedigree and management group information, were combined into a single EBV for shear force. To include the DNA marker information into an EBV, firstly the effects of each of the markers (i.e. T1, T2, T3, T4) on shear force, specifically for Brahmans were estimated using models (and datasets) developed as part of the SmartGene Project. These estimated partial effects of the markers were combined into a prediction equation and applied to each animal's gene marker genotype to give a predicted marker

* AGBU is a joint venture of NSW DPI and the University of New England

breeding value (MBV). List below in Table 1 are the estimated effects of the four tenderness markers and Figure 1 shows the genotype frequencies in Brahmans.

Table 1. Estimated size of effects (and standard errors) of the 4 tenderness markers on shear force in Brahmans

Marker	Size of effect in kg SF/star
T1	**-0.139** (0.041)
T2	**-0.087** (0.105)
T3	**-0.234** (0.054)
T4	**-0.032** (0.040)

The results showed the additive effects of the four markers differed. Marker T3 had an estimated effect almost as large as the other markers put together, and markers T1 and T2 had intermediate effects. The gene frequencies of the four markers in the Brahman population also differed. The frequency of the desirable form of the T2 marker was extremely low whereas that of T1 exceeded 60%. The different estimated size of the marker effects means that animals with the same total number of stars will have different EBV^M. Given the significance of the T1 and T3 markers, both had to be genotyped for an animal to be included in the analysis.

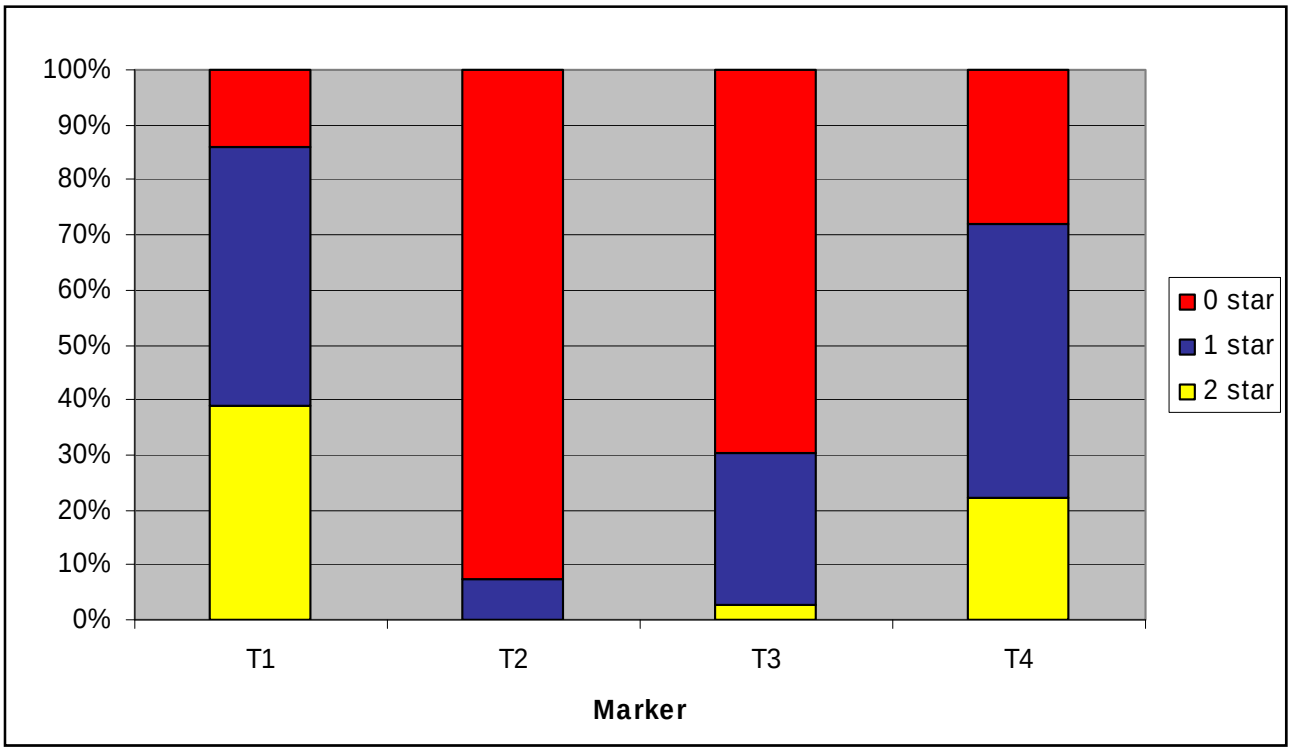

Figure 1: Estimated genotype frequencies for GeneSTAR tenderness markers in Australian Brahman

A multiple trait model was constructed using LDPF and FT phenotypes as two correlated traits and the MBV on animals with GeneSTAR results was included as a third correlated trait with a residual variance close to zero. The heritability of LDPF and FT in Brahmans were 0.30 and 0.20 respectively. The estimated effects of the tenderness markers on FT were small and non significant. The model configuration allowed the information from the markers to contribute to the LDPF EBV through the genetic correlation and the aim is to publish the LDPF EBV now denoted EBV^M and also the FT EBV.

Results

A total of 22052 animals (those with records and their ancestors) had trial shear force EBV^M computed with a mean of 0.02 and a range of -0.98 to +1.36 kg. The units of the tenderness EBV^M are kg of shear force and therefore the lower (i.e. more negative) the EBV^M the lower the shear force and thus the more tender the meat. Listed in Table 2 are sires with tenderness EBV^M accuracies greater than 80%. The spread in the tenderness EBV^M is almost 2 kg SF between the highest (less tender) and the lowest (more tender) EBV^M sires. Sires used in the Beef CRC projects were a random sample of the Brahman breed. However, the large spread generated is mainly the result of the large number of progeny recorded (N=16 to 68) for actual shear force on each of these sires, and the contribution of the other sources of information (i.e. markers and flight time) is minimal. If shear force records are not available the EBV^M have a much lower spread and very much lower accuracies. Figure 2 shows the expected accuracy of an EBV^M from different combinations of data.

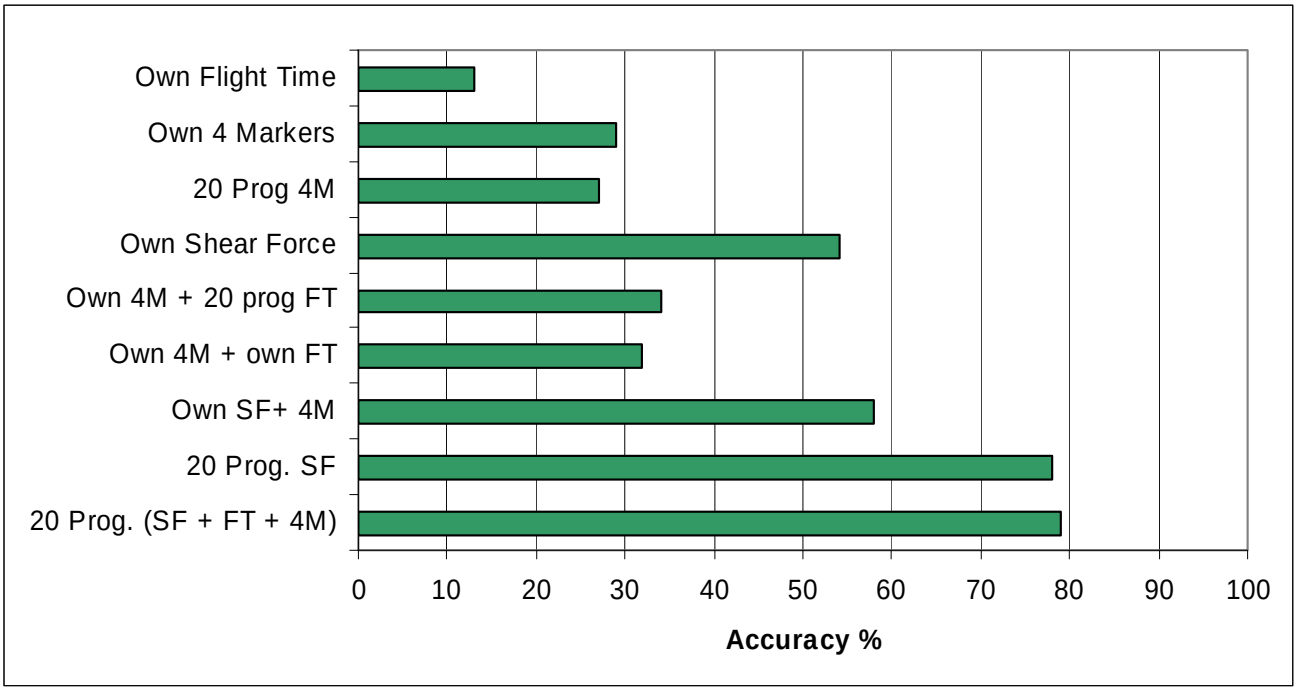

Figure 2. Expected accuracy of tenderness EBV^M from various levels of data recording

The other important output from this analysis is the new Brahman flight time EBV. While the measuring of flight time has some benefits in predicting genetic differences in tenderness it also has a stand-alone role in its ability to predict genetic differences in temperament. The new trial Brahman flight time EBVs are measured in seconds (i.e. time to break two light beams approximately 2 m apart when exiting a crush) and the higher (i.e. longer time) EBVs reflect animals of better temperament compared to lower or negative EBVs representing shorter exiting times and poorer temperament. The sires listed in Table 2 also had progeny recorded for flight time and range of the FT EBV was from -0.49 sec to +0.63 sec.

Table 2. High accuracy trial Brahman BREEDPLAN Tenderness EBVs

	Tenderness			Flight Time		GeneSTAR				
Sire ID	EBV^{M}	Acc.	Nprog SF	EBV	Acc.	T1	T2	T3	T4	Total
LAN4405MM	**-0.77**	81	31	0.18	82	1	0	1	1	3
BEL71/95M	**-0.50**	84	31	0.63	85	1	0	0	.	1
MKR3/840M	**-0.50**	83	25	0.37	79	2	0	0	1	3
CBV96-6822	**-0.34**	82	27	-0.04	83	1	0	0	1	2
JFK1926M	**-0.33**	81	26	-0.13	85	1	0	1	0	2
WAV916263M	**-0.26**	85	33	-0.15	84	2	0	0	1	3
BEL510/97M	**-0.21**	81	28	0.35	81	2	0	1	1	4
LAN3795M	**-0.17**	81	29	-0.32	80	2	0	1	0	3
WAV4866M	**-0.17**	84	36	0.10	80	1	.	.	.	1
BEL79/96M	**-0.13**	86	40	0.08	87	2	0	0	0	2
TTS983511M	**-0.12**	80	16	-0.12	86	1	0	1	2	4
TTS922382M	**-0.08**	86	49	-0.01	86	1	0	0	1	2
TTS973273M	**0.07**	83	41	0.11	81	2	0	0	1	3
JDH818/7M	**0.09**	89	51	0.05	88	2	0	0	2	4
TTS025M	**0.17**	84	35	-0.12	83	2	0	0	0	2
WAV4989M	**0.17**	82	41	0.14	78	2	0	0	2	4
TTS922415M	**0.30**	87	51	-0.01	87	1	0	0	2	3
WAV5576M	**0.39**	85	47	-0.23	85	2	0	0	1	3
HCC91/9M	**0.60**	81	26	0.07	83	1	0	0	2	3
JDH61/9M	**0.79**	83	42	-0.32	82	1	0	0	1	2
LYN1660/7M	**0.84**	82	27	-0.16	82	2	0	0	0	2
LAN6066M	**0.90**	84	32	-0.03	89	2	0	0	0	2
TTS922197M	**0.92**	89	68	-0.13	88	0	0	0	0	0
LAN4461MM	**1.10**	87	75	-0.20	87	1	0	0	0	1
LAN4999MM	**1.23**	83	37	-0.49	86	2	0	0	1	3

Contribution of gene markers to EBV^{M}

As described previously the markers are included in the prediction of the tenderness EBV^{M} by using the estimated effects of the markers and the individual's marker results. The relative contribution of the markers to the EBV^{M} depends on the estimated effect of each marker and its gene frequency in the breed. For example, if a marker has a reasonable size effect but is at high gene frequency (i.e. most animals are 2*) then this marker in this particular breed will be explaining very little of the differences between animals and therefore will have little contribution to differences in EBV^{M} between animals. Therefore to generate EBV^{M} with high accuracies from marker data alone will require finding markers (likely to require several) that explain a large amount of the genetic variation of a trait. In Brahmans, the GeneSTAR tenderness markers cumulatively explained an estimated 8% of the additive genetic variance of shear force.

Note: Once an animal's genotype has been established there is no benefit for that animal in testing relatives. This is different to recording phenotypic information, like flight time, where the records on relatives (i.e. sire, dam, half sibs and progeny) can be of considerable benefit in increasing the accuracy of the EBV.

Using these new EBV^{M}

The methodology developed to compute the new EBV^{M} is such that they can be used just like any other EBV. That is they predicted expected differences between animals for their progenies performance for the trait. And because the computation has optimally used all three

sources of data the tenderness EBV^M is what selection should be based on. It would be incorrect to use the EBV^M as well as the number of stars or flight time records.

The emphasis placed on the tenderness EBV^M when making selection decisions will depend on individual producer's markets (i.e. importance of meat tenderness), and of course all other traits affecting profitability should not be ignored.

Future research

This new trial tenderness EBV^M is only the start to a new chapter in the genetic evaluation of beef cattle in Australia. Important research is underway to determine if tenderness is genetically correlated with other economically important traits. Early indications, using Brahman BREEDPLAN EBVs, are that the tenderness markers are having no substantial effects on any of the published EBVs. CRC2 research has also shown few antagonisms between shear force and other traits, but research is continuing to assess female lifetime reproductive performance and cow survival. Therefore, to include tenderness EBV^M into your breeding program optimally they should be included into a selection index, and this will require the determination of the economic value of tenderness and estimates of genetic correlations with all other traits.

The other important development is the ever-expanding capacity to genotype animals for large numbers of potential markers and therefore the increasing opportunity to explain greater amounts of genetic variation. However, to fully utilize this capacity the Australia beef industry needs to record many more phenotypes on animals with a DNA sample, particularly for traits difficult to record in industry. Efforts to do this are currently underway. Although there are theoretical predictions of completely replacing phenotypic records with large panels of markers in the future, this appears to be some way off for the beef industry. The current experience from the dairy industry, where the phenotypes used are the highly accurate EBVs of well proven sires, is that the accuracies of EBV^M derived from only DNA marker information are likely to be, at best, 70%. This is unlikely to be achieved in beef where, unlike the dairy industry, we must work with relatively few phenotypes of modest heritability and accuracy.

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Current status of whole genome scanning

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This talk will discuss the recent history of genome research in cattle and recent technological advances that are positioning DNA makers to become an integral part of genetic selection. Specifically, looking at the status of whole-genome scanning in beef cattle to enhance selection for output and input traits.

The application of selection based on statistical genetics has provided the framework to respond to the changing marketplace. However, the application of standard estimated breeding values (EBV) for improving production traits that are difficult or expensive to measure is a relatively slow and costly procedure. Fortunately, the development of DNA technologies applied to cattle holds substantial promise to solve this problem, by increasing EBV accuracy, improving selection efficiency, and reducing the cost of altering the genetics of cattle to suit current production goals (Schaeffer, 2006).

Over the last decade many experiments used the half sib design to discover quantitative trait loci (QTL). A large number of the beef cattle experiments used one or a few sires mated to a large number of dams, producing progeny that were phenotyped and genotyped using microsatellite markers to track inheritance of chromosomal regions. The power and resolution of a genome scan is a function of the size of the effect of QTL (larger effect QTL can be more easily detected and more accurately mapped), the number of animals in the population with genotypic information (i.e., the number of animals in each possible genotypic class, and the number of recombination events that can be monitored), and the density of informative markers (to more accurately determine the position of recombinations). Genome scans provide an approximate chromosomal location (confidence intervals of 5-20 cM are common when populations of 500 animals are used) at which the two alleles of the sire have DNA sequence variation causing a statistically distinguishable phenotype in the offspring (Weller, 2001). A QTL mapping study typically identifies a limited number of QTL per sire per trait. These studies have often underestimated the number of QTL contributing to effect and often overestimated the size of the effect for the QTL (Bogdan & Doerge, 2005).

Historically, these deficiencies in QTL mapping in cattle resulted from underpowered studies, mainly because the expense of collecting phenotypic and genotypic information has led to the use of populations too small to detect the many putative QTL with small to moderate effect on phenotype. The low number of recombination events on QTL-carrying chromosomes in these small populations is the principal cause of reduced resolution, and insufficient numbers of animals in each genotypic class in small populations is the principal cause of reduced power to detect QTL (Nadeau & Frankel, 2000). Increased power and resolution can be achieved by increasing population size, although this is an expensive proposition. The majority of published QTL studies suffer from a lack of power that manifests as inability to detect QTL of small effect, a poor estimation of effect size, and low resolution in determining position. Despite their limitations, QTL experiments provide invaluable knowledge about the presence and approximate locations of variation affecting phenotype that segregate in cattle populations.

Implementation of QTL results was pursued by a process of marker development called “fine mapping,” to develop markers reasonably predictive of the genotype at the quantitative trait nucleotide (QTN- causative mution) (for example, Page et al., 2002; White et al., 2005). The

predictive merit of a marker may be expressed as the square of the correlation (denoted r^2) between marker genotype and genotype of the QTN. When $r^2 = 1$, the markers are in a unique haplotype and perfectly predictive of one another, when r^2 approaches 0, they are only randomly correlated (Mckay et al., 2007). Due to the dynamic nature of the genome, the r^2 of a marker and QTN pair can vary between populations, so it is important to select and test markers in a number of independent populations to insure broad applicability among cattle breeds (Van Eenennaam et al., 2007a). The average r^2 for a marker pair among populations is affected by the distance between the two markers, with markers close to the QTN more likely to have high correlation due to a high frequency of coinheritance (called linkage disequilibrium or LD). However, r^2 is also affected by the relative age of the marker—if a nearby marker predates the appearance of the QTN causing a favorable effect, then a proportion of cattle that have the marker genotype predicting the favorable QTN allele may be carrying the unfavorable allele.

There has been substantial effort in the research community to initiate MAS in the beef industry with limited success (Dekkers, 2004). Most economic traits for meat production are influenced by many genes. The tracking of a handful of genes using MAS will only account for a small portion of the genetic variation for a given trait(s). Even this small number of genes requires extremely large numbers of animals with data to accurately estimate their effects (Goddard & Hayes, 2007) and numerous QTL populations and genome scans to reveal their locations. In order to realize the potential for MAS in cattle, a much more comprehensive approach to discovering the sources of variation segregating in commercial populations is needed. Fortunately, recent technological advances provide a framework to achieve a more thorough, efficient approach to discovery of important variation.

The Bovine Genome Sequencing Project (www.hgsc.bcm.tmc.edu), which produced a draft assembly of the complete cattle genome based on the DNA of a Hereford cow, has assisted in the development of much needed technology to move the DNA marker assisted technology forward. The project produced a pool of over 300,000 SNP by sample sequencing animals from other breeds and comparing this sequence to the draft. In addition, a project applying “next generation” sequencing technology identified another 60,000 SNP (Van Tassell et al., 2008). Using these data, a set of ~60,000 SNP were selected for inclusion in a highly parallel SNP genotyping assay (Matukumalli et al., 2008). The Illumina BovineSNP50 BeadChip contains >50,000 SNP spaced with approximately every 60,000-75,000 bp across the genome.

Meuwissen, Hayes, & Goddard (2001), proposed a strategy related to MAS, that they called Whole Genome Selection (WGS). While MAS takes a single QTL and develops a diagnostic test for it, WGS requires a large set of genome-wide markers such as that produced from highly parallel SNP genotyping arrays (Matukumalli et al., 2008), with the aim of capturing all the genetic variance in a single analysis. The analysis assumes the marker set is sufficiently dense that all QTN are in LD with a marker and the number of effects per QTN is small (Goddard & Hayes, 2007). The markers or haplotypes of markers are analyzed as independent random effects using a mixed linear model. An advantage of WGS is that the analysis can predict the additive genetic value of each of the haplotypes for each chromosomal region having effect as well as localizing the effect. Summing across all loci affecting a trait, the genetic merit of an animal is predicted based solely on the multilocus genotype. Simulations showed that EBV could be predicted with an accuracy of 0.85 from marker data alone (Meuwissen et al., 2001), which is a dramatic increase in accuracy for the EBV from the parental averages now estimated for a young animal.

It is important to emphasize that WGS is in its infancy; the research community needs to be careful to not oversell the technology. Meticulously designed experiments need to be

conducted to validate WGS. Steps that will be needed to make WGS possible for the industry include the following (Goddard & Hayes, 2007): First, discovery datasets need to be generated where a large number of SNP have been assayed on a set of animals with extensive industry relevant phenotypes. Second, prediction equations must be developed that use marker data and predict genetic "genome-enabled" EBV (gEBV) from the data set. Third, the process must undergo validation in another large population with phenotypes and the set of markers used in the discovery data set or a subset of markers that could be used by the industry to do WGS. The final step is to use the prediction equations at the industry level with genotypes on industry animals to implement whole genome selection. By using the WGS information in the National Sire Evaluation system, gEBVs will be generated with dramatically increased accuracies for young animals. Additionally, subsets (panels) of DNA markers will be developed from the research done for WGS, for suites of traits custom designed for different segments of the industry. These panels, using low cost genotyping technologies, are presently available or are being developed to make MAM a real possibility for implementation in the beef cattle industry.

The addition of DNA marker technology to the current tools used for genetic selection and management of livestock holds exciting possibilities for enhancing product quality and profitability across the industry. Past efforts to develop DNA markers have been limited by costs and available technology. New advancements in genotyping and sequencing have already led to positional cloning of mutations for single gene birth defects (Charlier et al., 2008). These results show the power of new genomic tools; in time these tools will result in advancements for quantitative traits. As with the implementation of genetic evaluations systems in livestock over 25 years ago, the industry will experience growing pains. However, these growing pains will give way to more accurate genetic selection of young animals, molecular breeding values for traits that can only be measured in a research setting, and decreased numbers of animals needed for progeny testing.

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Incorporation of Marker Scores into National Getentic Evaluations

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Abstract

As genetic tests for production traits become available it becomes important to incorporate them in our genetic evaluations. A model which treats marker scores as correlated traits is presented along with an approximate reduced model approach to make the model computationally feasible.

1 Introduction

Tests based on DNA marker panels have been coming online for a number of traits. The tests offer the potential to increase the reliability of genetic evaluation particularly for animals and traits with limited phenotypic information. To realize this goal it is imperative that information from these tests be incorporated into national genetic evaluations.

The number of markers in a marker panel can range from a single marker, to thousands of markers, to potentially the complete DNA sequence for an animal. Typically the results of a DNA test for a trait will be summarized into a single marker score or molecular breeding value. In most cases, the marker score will be a weighted sum of the number of copies of the different alleles with weights being estimated from a reference population. If the marker scores are on the same scale as a breeding value, then it may be reasonable to refer to the marker score as a molecular breeding value.

The marker scores provide a flexible common denominator between the different types of DNA tests. Using the marker scores as the data has a number of advantages over working with the marker panel data directly. First, it reduces the amount of data that must be processed when conducting the genetic evaluation. Second, it doesn't require that the markers used in the test be identified, Third, and perhaps most importantly, it allows advances in DNA tests and statistical methodology to be taken advantage of in a timely manner.

2 Paradigm

A marker score is a phenotypic trait. That is a marker score is an observable trait. It differs from typical production traits in that environmental influences are expected to be minimal and the heritability is expected to be close to one. Even in the best of circumstances noise is likely to be present due to factors such as missidentification of samples, pedigree errors, and processing errors.

The relationship between a marker score and the phenotype is illustrated in Figure 1. Both the

*I would like to acknowledge the valuable input of Rohan Fernando and Robert Tempelman and the support of the National Beef Cattle Evaluation Consortium.

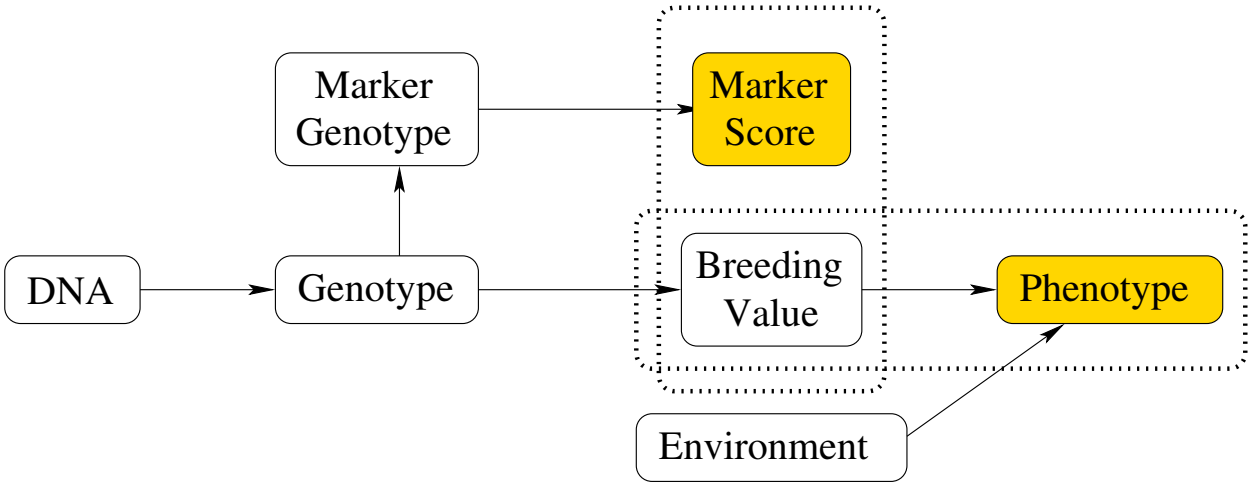

Figure 1: Relationship between a marker score and a phenotypic trait.

genotype associated with the phenotypic trait of interest and marker genotype used to calculate the marker score are based on the same DNA and genotype. Therefore, the marker score and the phenotype are two correlated traits. For a marker score to be highly correlated with the animal's breeding value requires that the marker genotype (i.e. marker panel) include markers highly correlated with that portion of genotype associated with the breeding value and that the translation of the marker genotype into a marker score capture the variability associated with the breeding value.

Since a marker score is a phenotypic trait it can be included as a correlated trait in the genetic evaluation. As with any correlated trait, it will be necessary to estimate the genetic correlation between the marker score and the production traits, heritability, and phenotypic variance of the marker score.

In practice we will need to allow the inclusion of different marker scores in the genetic evaluation. Potentially, one could include each marker score as an additional correlated trait. Therefore, one would also need the genetic correlations between the marker scores. Since including an additional trait for each new marker score is unlikely to be practical, an approximate reduced model will be needed. A reduced model is presented in section 3.1.

3 Statistical Model

The model will be presented for a single production trait and two marker scores. The model with the two marker scores as correlated traits is

$$\begin{pmatrix} \boldsymbol{y} \\ \boldsymbol{m}_1 \\ \boldsymbol{m}_2 \end{pmatrix} = \begin{pmatrix} \boldsymbol{X}_y & 0 & 0 \\ \boldsymbol{0} & \boldsymbol{X}_1 & 0 \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{X}_2 \end{pmatrix} \begin{pmatrix} \boldsymbol{\beta}_y \\ \boldsymbol{\beta}_1 \\ \boldsymbol{\beta}_2 \end{pmatrix} + \begin{pmatrix} \boldsymbol{Z}_y & 0 & 0 \\ \boldsymbol{0} & \boldsymbol{Z}_1 & 0 \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{Z}_2 \end{pmatrix} \begin{pmatrix} \boldsymbol{u}_y \\ \boldsymbol{u}_1 \\ \boldsymbol{u}_2 \end{pmatrix} + \begin{pmatrix} \boldsymbol{e} \\ \boldsymbol{\epsilon}_1 \\ \boldsymbol{\epsilon}_2 \end{pmatrix}$$

where $\boldsymbol{y}$ is the vector of the observed production trait, $\boldsymbol{m}_i$ is the vector of the observed marker score i, $\boldsymbol{\beta}_y$ is the vector of fixed effects for the production trait, $\boldsymbol{\beta}_i$ is the vector of fixed effects for the marker score i, $\boldsymbol{u}_y$ is the vector of production trait breeding values, $\boldsymbol{u}_i$ is the vector of marker

score i breeding values, $\boldsymbol{e}$ is the vector of residuals for the observed production traits, and $\boldsymbol{\epsilon}_i$ is the vector of residuals for marker score i. The vector of breeding values and residual are assumed to be distributed as

$$\begin{pmatrix} \boldsymbol{u}_y \\ \boldsymbol{u}_1 \\ \boldsymbol{u}_2 \end{pmatrix} \sim (\boldsymbol{0}, \boldsymbol{G} \otimes \boldsymbol{A})$$

and

$$\begin{pmatrix} e \\ \epsilon_1 \\ \epsilon_2 \end{pmatrix} \sim (\boldsymbol{0}, \boldsymbol{R} \otimes \boldsymbol{I})$$

where $\boldsymbol{A}$ is the numerator relationship matrix,

$$\boldsymbol{G} = \begin{pmatrix} \sigma^2_{gy} & \sigma_{gy1} & \sigma_{gy2} \\ & \sigma^2_{g1} & \sigma_{g12} \\ \text{sym.} & & \sigma^2_{g2} \end{pmatrix}$$

is the genetic covariance matrix, and

$$\boldsymbol{R} = \begin{pmatrix} \sigma^2_{ey} & 0 & 0 \\ & \sigma^2_{e1} & 0 \\ \text{sym.} & & \sigma^2_{e2} \end{pmatrix}$$

is the residual covariance matrix.

The model does not assume that the random effects are normally distributed. For the marker scores the fixed effect vectors will include an intercept effect to account for baseline effects. Because the marker scores are based on the marker genotype it is expected that their residual variance will be very small relative to their genetic variance.

Given the model and the true variance components the BLUP of the production breeding values can be found by solving the mixed model equations. In practice it will be necessary to estimate the unknown variance components and the resulting predictions will only be approximately BLUP.

A consequence of taking the correlated trait approach is that for a single production trait with two marker scores the dimension of the mixed model equations will be three times larger when compared to single production trait model. Because of the increased number of equations it will become impractical to set up and solve the mixed model equations for this model when their are several different marker scores. Therefore, an approximate reduced model will be presented.

3.1 Full and Reduced Models

The purpose of an approximate reduced model is to have a model which is close to the true model but is computationally feasible. Before presenting the reduced model, a model which is equivalent to the full model will be developed. The motivation behind the equivalent model is to partition the variability associated with the marker score breeding values into one component which is strongly associated with the production trait breeding values and a second component which is independent of the production trait breeding values. Then by restricting any approximations to the independent component it should be possible to have an approximate model which does a good job predicting the production trait breeding values.

In the equivalent model the marker score breeding values are partitioned a component which is a function of the production trait breeding value and an independent residual. The first component is simply the BLUP of the marker score breeding values for an animal given the production trait breeding value for that animal. The resulting parametrization for animal i is

$$\begin{pmatrix} u_{1i} \\ u_{2i} \end{pmatrix} = \begin{pmatrix} \sigma_{g1y} \\ \sigma_{g2y} \end{pmatrix} \left(\sigma^2_{gy}\right)^{-1} u_{yi} + \begin{pmatrix} r_{1i} \\ r_{2i} \end{pmatrix}$$

where u_{mi} is the breeding value of animal i for marker score m, u_{yi} is the production trait breeding value for animal i, and r_{mi} is the residual breeding value of animal i for marker score m. The reparametrized vector of random effects consisting of the vectors of production breeding values and residual breeding values are distributed as

$$\begin{pmatrix} \boldsymbol{u}_y \\ \boldsymbol{r}_1 \\ \boldsymbol{r}_2 \end{pmatrix} \sim \left(\mathbf{0}, \boldsymbol{A} \otimes \begin{pmatrix} \sigma^2_{gy} & 0 & 0 \\ 0 & \sigma^2_{r1} & \sigma_{r12} \\ 0 & \sigma_{r12} & \sigma^2_{r2} \end{pmatrix} \right).$$

The model is now be rewritten in terms of the reparametrized breeding values

$$\begin{pmatrix} \boldsymbol{y} \\ \boldsymbol{m}_1 \\ \boldsymbol{m}_2 \end{pmatrix} = \begin{pmatrix} \boldsymbol{X}_y & 0 & 0 \\ \mathbf{0} & \boldsymbol{X}_1 & 0 \\ \mathbf{0} & \mathbf{0} & \boldsymbol{X}_2 \end{pmatrix} \begin{pmatrix} \boldsymbol{\beta}_y \\ \boldsymbol{\beta}_1 \\ \boldsymbol{\beta}_2 \end{pmatrix} + \begin{pmatrix} \boldsymbol{Z}_y \\ c_1\boldsymbol{Z}_1 \\ c_2\boldsymbol{Z}_2 \end{pmatrix} \boldsymbol{u}_y + \begin{pmatrix} 0 & 0 \\ \boldsymbol{Z}_1 & 0 \\ \mathbf{0} & \boldsymbol{Z}_2 \end{pmatrix} \begin{pmatrix} \boldsymbol{r}_1 \\ \boldsymbol{r}_2 \end{pmatrix} + \begin{pmatrix} \boldsymbol{e} \\ \boldsymbol{\epsilon}_1 \\ \boldsymbol{\epsilon}_2 \end{pmatrix}$$

where

$$\begin{pmatrix} c_1 \\ c_2 \end{pmatrix} = \begin{pmatrix} \frac{\sigma_{g1y}}{\sigma^2_{gy}} \\ \frac{\sigma_{g2y}}{\sigma^2_{gy}} \end{pmatrix}.$$

The residual breeding values are distributed as

$$\begin{pmatrix} \boldsymbol{r}_1 \\ \boldsymbol{r}_2 \end{pmatrix} \sim (\mathbf{0}, \boldsymbol{G}_m \otimes \boldsymbol{A})$$

where

$$\boldsymbol{G}_m = \begin{pmatrix} \sigma^2_{r1} & \sigma_{r12} \\ \sigma_{r12} & \sigma^2_{r2} \end{pmatrix} = \begin{pmatrix} \sigma^2_{g1} - \frac{\sigma^2_{gy1}}{\sigma^2_{gy}} & \sigma_{g12} - \frac{\sigma_{gy1}\sigma_{gy2}}{\sigma^2_{gy}} \\ \sigma_{g12} - \frac{\sigma_{gy1}\sigma_{gy2}}{\sigma^2_{gy}} & \sigma^2_{g2} - \frac{\sigma^2_{gy2}}{\sigma^2_{gy}} \end{pmatrix}.$$

3.2 Approximation

Because interest is in the prediction of the production trait breeding values approximations will focus on the residual breeding component of the model. Because the marker scores share a number of common features a reduced rank approximation (e.g. Kirkpatrick and Meyer, 2004) of $\boldsymbol{G}_m$ will be used. Using the first k components of a singular value decomposition of $\boldsymbol{G}_m$ yields

$$\boldsymbol{G}_m = \sum_{i=1}^{k} \boldsymbol{p}_i \boldsymbol{p}_i' \tau_i^2 + \boldsymbol{R}_m$$

where $\boldsymbol{p}_i$ is eigen vector i, τ_i^2 is eigen value i, and $\boldsymbol{R}_m$ is the unexplained residual marker variance.

The reduced model using the first k components of the singular value decomposition is

$$\begin{pmatrix} \boldsymbol{y} \\ \boldsymbol{m}_1 \\ \boldsymbol{m}_2 \end{pmatrix} = \begin{pmatrix} \boldsymbol{X}_y & 0 & 0 \\ \boldsymbol{0} & \boldsymbol{X}_1 & 0 \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{X}_2 \end{pmatrix} \begin{pmatrix} \boldsymbol{\beta}_y \\ \boldsymbol{\beta}_1 \\ \boldsymbol{\beta}_2 \end{pmatrix} + \begin{pmatrix} \boldsymbol{Z}_y \\ c_1\boldsymbol{Z}_1 \\ c_2\boldsymbol{Z}_2 \end{pmatrix} \boldsymbol{u}_y + \sum_{i=1}^{k} \begin{pmatrix} 0 \\ p_{i1}\boldsymbol{Z}_1 \\ p_{i2}\boldsymbol{Z}_2 \end{pmatrix} \boldsymbol{g}_i + \begin{pmatrix} \boldsymbol{e} \\ \boldsymbol{e}_1 \\ \boldsymbol{e}_2 \end{pmatrix}$$

where $\boldsymbol{g}_i \sim (\boldsymbol{0}, \boldsymbol{A}\tau_i^2)$ and

$$\begin{pmatrix} \boldsymbol{e} \\ \boldsymbol{e}_1 \\ \boldsymbol{e}_2 \end{pmatrix} \dot{\sim} \left(\boldsymbol{0}, \begin{pmatrix} \sigma^2_{ey} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{R}_m + \begin{pmatrix} \sigma^2_{e1} & 0 \\ 0 & \sigma^2_{e2} \end{pmatrix} \end{pmatrix} \otimes \boldsymbol{I} \right).$$

The approximation being that the distribution of the residual is

$$\begin{pmatrix} \boldsymbol{e} \\ \boldsymbol{e}_1 \\ \boldsymbol{e}_2 \end{pmatrix} \sim \left(\boldsymbol{0}, \begin{pmatrix} \boldsymbol{I}\sigma^2_{ey} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{R}_m \otimes \boldsymbol{A} + \begin{pmatrix} \sigma^2_{e1} & 0 \\ 0 & \sigma^2_{e2} \end{pmatrix} \otimes \boldsymbol{I} \end{pmatrix} \right).$$

Using the reduced model for a single production trait with m marker scores the dimension of the mixed model equations will be for a $k+1$ trait model instead of $m+1$ traits in the full model. For example, with 10 marker scores and using the first 2 components of the singular value decomposition the reduced model would be equivalent to a 3 trait model instead of the 11 traits in the full model.

4 Model Parameters

Implementation of this model will require that estimates of the genetic correlations between the marker scores and the production traits be available. As with any set of traits estimates of these parameters will require populations in which production trait and marker scores data are available. Currently, validation of marker scores are carried out in populations with records on approximately 1,000 progeny. Typically, each marker score is evaluated in a different population. Estimation of the required genetic correlations between different marker scores will require that multiple marker scores be evaluated in the same population.

To determine if the current validation populations are adequate for obtaining reasonable estimates of the genetic correlation between a production trait and a marker scores a small set of simulations was conducted.

4.1 Estimation methods

The typical structure of a validation population consists of sets of half-sib progeny with the validation being done using a sire model with the marker breeding value as a covariate. The sire model approach to estimating the genetic correlation would be to use the REML estimate of the sire variance from a reduced sire model without the marker score covariate, $\widehat{\sigma}^2_{SR}$, and the REML estimate from a full sire model with the marker score covariate, $\widehat{\sigma}^2_{SF}$. The estimate of the genetic correlation using the sire model approach being

$$\widehat{r}_{Sg} = \sqrt{\frac{\widehat{\sigma}^2_{SR} - \widehat{\sigma}^2_{SF}}{\widehat{\sigma}^2_{SR}}}.$$

Alternatively the genetic correlation could be estimated using a two trait animal model with the marker score being the second trait.

	Estimated Correlation	
Data Set	Sire Model	Two Trait Model
A	0.40	0.40 ± 0.06
B	0.24	0.43 ± 0.07
C	$\sqrt{-}$	0.37 ± 0.06

Table 1: Estimated genetic correlations with 100 sires, 10 progeny per sire, a genetic correlation of 0.4, and a heritability of 0.4.

	Estimated Correlation	
Data Set	Sire Model	Two Trait Model
A	0.37	0.42 ± 0.02
B	0.47	0.39 ± 0.02
C	0.38	0.39 ± 0.02

Table 2: Estimated genetic correlations with 1,000 sires, 10 progeny per sire, a genetic correlation of 0.4, and a heritability of 0.4.

4.2 Results

A data set with 100 sires, 10 progeny per sire, and data recorded on the progeny, is fairly representative of what is currently being used for validation. Three simulated data sets were generated using a genetic correlation of 0.4 and a heritability of 0.4 for the production trait. The results are presented in Table 1. Even with the three simulated data sets it is clear that the estimates using the sire model approach are not acceptable. In fact, for data set C the estimated sire variance for the full model was actually greater than in the reduced model. The performance using the two trait model was considerably better, through the standard errors were approximately 15% of the true parameter. The better performance of the two trait model may be due to its ability to make use of the genetic variation contained in the sire model's residual.

As expected increasing the number of sires to 1,000 does produce much better results as can be seen in Table 2. The impact of switching from a moderately heritable trait to a lowly heritability trait can be seen in Table 3. In the same way that the accuracy of genetic prediction decreases when the heritability of the trait decreases the standard error of the genetic correlation increase as the heritability of the trait decreases.

Because parameters can vary across breeds and environments, data will be needed for different breeds and environments. Because having a separate large reference population for each possible breed environment combination would be very inefficient, estimators will be needed that will be

	Number of Sires	
Data Set	100	1,000
A	0.39 ± 0.12	0.38 ± 0.05
B	0.30 ± 0.11	0.45 ± 0.05
C	0.08 ± 0.11	0.40 ± 0.05

Table 3: Estimated genetic correlations from a two trait model with 10 progeny per sire, a genetic correlation of 0.4, and a heritability of 0.1.

able make use of both global and subpopulation information. The estimator could possibly be pooling subpopulations appropriately or using a Bayesian estimator.

5 Summary

The reduced multiple trait model offers the promise of being able to make use of the genetic tests that are coming online in national genetic evaluations. Work remains to be done to determine to what degree the full model can be reduced. In addition, alternative reduced models also need to be investigated to determine if an alternative approximation may yield better results. Regardless, the models are linear mixed models which are the methodological backbone of our current genetic evaluations. Using marker scores as the input data for the genetic evaluations will allow advances in DNA tests to be incorporated into the genetic evaluations without the need to develop new software.

One of the big challenges is obtaining production and marker data from appropriate reference populations. It is clear that these populations will need to be representative of the population for which the genetic evaluation is to be conducted. Because the relationship between marker scores and production traits are likely to be different in breed groups, environments, and across time the need for populations containing both phenotypic and marker data will remain.

References

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Marketing the Covariances: Enhancing the Utilization of Genomic Tools in Beef Cattle Improvement[1]

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Genomic selection tools for genetic improvement of beef cattle have been available for nearly a decade, but the utilization of those tools has been limited at best. Independent validation of DNA marker tests for quantitative traits has shown some significance, but modest effects. Because these tools seem to account for a relatively small part of the additive genetic variation for the given trait, there has been little effort made toward incorporating these tools into national cattle evaluation (NCE) programs. However, recent advancements in genomic technology applied to beef cattle populations may potentially increase the proportion of genetic variation accounted for by tests. Kachman et al. (2008) has proposed an elegant method to incorporate DNA test results into NCE. Clearly, the beef industry and those that support it are at a critical juncture, where decisions will soon be made as to whether to pursue marker-assisted expected progeny differences (MA-EPD).

Merging traditional NCE with genomic selection appears to benefit all interested parties. For genomic companies to be successful and profitable, and for them to warrant additional resources for research and development, their sales volume needs to increase. Producers would benefit from increased accuracy that these MA-EPD would provide, but they need more information about the utility of genomic testing, before they spend significant amounts of money on tests. Academia and beef breed associations can help both producers and genomics companies work together, but to make good recommendations, they need more information about the tests themselves, in order to make an accurate, unbiased evaluation of the technology.

In the mid-1980's to early 1990's, live-animal ultrasound was at the same point in it's development and utilization. The technology was largely developed but still being refined, and utilization was significantly less than optimal. Not until ultrasound data was incorporated into NCE did scanning become a regular part of beef seedstock production. Like ultrasound did some years ago, DNA testing is at a point where it would likely become commonplace if incorporated into NCE, but that incorporation requires more test results to parameterize models. Tested populations for research may remain scarce until producers are certain those results will be used in NCE.

While the production and reporting of MA-EPD, which combine phenotypic measurements, pedigree information and DNA test results, is the goal of the academic community, it is important to realize that for some traits, phenotypes may not be available on most animals. Tenderness is a classic example of this type of trait. For these traits, DNA tests may remain the only practical method of genetic evaluation and improvement. To enhance producer understanding and maximize proper use, it seems logical to express DNA test results for these traits on an EPD-like scale, with an associated accuracy value.

[1] The inspiration and assistance of Mark Thallman, US MARC and John Pollak, Cornell University is acknowledged and greatly appreciated.

While validation of DNA tests has rightly focused on the statistical association between test results and phenotypes, potential buyers of DNA tests may have another evaluation criterion in mind. For the most part, animals to be tested will have already been phenotyped for the relevant traits. The potential benefit of DNA testing is the enhanced accuracy of genetic evaluation, and producers might best evaluate the value of tests if the expected increase in accuracy can be conveyed.

In the future, the best metric for evaluating tests may be the proportion of additive genetic variation accounted for by the test. The paper by Thallman at this meeting provides a well-detailed argument for this. In the Kachman model, this value is equal to the squared correlation between the phenotypes and the test results (expressed as molecular breeding values). Starting with that value, a simple table could be contructed that would quantify the increase in (BIF) accuracy from a certain DNA test. The table might provide values with and without a phenotype on the tested animal, and might also consider whether the tested animal's sire has high or low accuracy for the trait. One caveat is that this metric may not adequately reward testing for a very rare allele with a large effect on a trait, until the allele is more widely incorporated into the population.

Once producers have tested animals, they will want to know if additional tests (from other companies) for the same trait would be beneficial. That would depend on the correlations between test results, resulting from the underlying similarity of the tests. The marginal increase in accuracy might be the best way to convey the value of additional testing. As tests evolve and improve, some description of the additional accuracy gained by a newer version of a test will be needed, but to do that, each version of a test will need to be easily identified and tracked.

At some point, beef breed associations will be faced with a difficult decision, whether or not to proceed with incorporation of DNA test results into their NCE program. The challenge is that to make a good decision, large amounts of test results and phenotypes are needed, but the number of animals tested may remain fairly low until the incorporation of the test results into EPD. At that point, breed associations will need to calculate interim EPD and accuracy upon receipt of test results, like they currently do when weights are submitted. Ideally, complete reporting of test results would occur directly from the lab to the breed association database.

While challenges remain, it is clear at this point that there is the potential to develop a system that clearly describes the benefits of testing, provides value to the breeder in the form of enhanced EPD accuracy on young animals, and makes genetic testing a standard operating procedure for many seedstock herds. Developing that system will require unprecedented cooperation among breed associations, genomics companies and the scientific community, but the benefits could favorably impact the beef industry and beef consumers to an unprecedented degree.

Logistics for Working Together to Facilitate Genomic/Quantitative Genetic Prediction

R. Mark Thallman and John Pollak

Introduction:

Substantial progress has been made recently on statistical/computational approaches to incorporate DNA test results into National Cattle Evaluation (**NCE**) and there seems to be general agreement that NCE is the best way to utilize DNA test results for selection. Regardless of the details of the statistical approach eventually adopted, it seems clear that (co)variances among and between DNA test results (sometimes called molecular breeding values (**MBV**)) will be required (Kachman, 2008; Tess, 2008). The current structure for validation of DNA tests does not provide data from which to estimate these (co)variances adequately.

These (co)variance estimates could be readily converted into proportions of genetic variation and correlations among the genetic and residual components of the various MBV. Although some education would be required, these statistics would allow a much more meaningful evaluation of the utility and feasibility of using commercial DNA tests than has ever been possible previously. Furthermore, they would allow an answer to the elusive question "Given that one test has been purchased, what is the marginal benefit from purchasing an additional test from a different company?" Consequently, the use of these statistics in the marketing of DNA tests seems completely appropriate, assuming that the educational challenges can be overcome (Moser, 2008).

Furthermore, the fundamental question of whether a DNA test "works" or not is becoming increasingly irrelevant as we transition from single marker tests. Products based on hundreds of markers can very easily be significant at $P<0.05$, but still account for only a negligible fraction of the variation. The relevant question for potential customers in the future will be: "Does the test increase the accuracy of EPD of young animals sufficiently to justify the expense of running it?"

This approach builds on the suggestion (Curt Van Tassell, personal communication) that we need to move beyond validation of individual DNA tests toward validation that the entire processes of whole genome selection and development of smaller SNP panels work. This approach would be patterned after the validation of EPD themselves; once the concept of EPD was validated experimentally, it was not considered necessary to validate each new breed or trait that was added.

The first step in this transition may be to include estimates of the proportion of variance accounted for by DNA tests into the results of the current National Beef Cattle Evaluation Consortium (**NBCEC**) independent validation process.
It seems obvious that, given the high cost of developing and genotyping resource populations, a collaborative approach to using those populations and genotypes, that protects the investment in developing the populations and promotes competition, would benefit both DNA testing companies and their customers.

The purpose of this presentation is to propose a prototype approach to collaborative estimation of the (co)variances required to incorporate DNA testing into NCE.

Objectives*:*

- Develop a system that will allow estimation of the (co)variances required to incorporate DNA tests into NCE. This would imply that all MBV to be considered for inclusion in NCE would ideally be computed for all of the resource populations included in this approach.
- Collaboratively develop a set of single nucleotide polymorphisms (**SNP**) and associated prediction equations for growth traits that could be developed into a high throughput assay with low cost per animal.
- Attempt to run this assay on a large number of performance recorded animals in seedstock herds distributed throughout the U.S.
- Evaluate alternative approaches to reducing the 50K SNP panel to a subset that is cost effective and accounts for as much genetic variation in the set of target traits as is feasible.

Approach:

We will begin by focusing on the weight traits that are routinely included in NCE: birth weight, weaning weight, yearling weight, and, perhaps, milk (or more properly, the maternal component of weaning weight). The reasons for starting with these traits include:

- There are many more animals with 50K chip data that also have these traits recorded than any other set of traits. Therefore, it is the set of traits for which we are likely to have a success the soonest.
- We can use 50K chip data on high accuracy AI sires as a means to validate the accuracy of any predictions that are developed.
- It will be the best set of traits with which to explore how well DNA tests will work across a variety of breeds, including breeds that were not included in the discovery data sets.
- There has been less private investment in development of commercial DNA tests for these traits.
- Contrary to popular opinion, there is value in DNA tests for these traits:
  - DNA tests may make concurrent selection for genetically antagonistic traits (especially birth weight and growth rate) substantially more effective.
  - DNA tests may provide higher accuracy EPD on young bulls at the time of bull sales (especially relevant for yearling weight and milk).

Pilot Project:

To demonstrate the benefits of a collaborative approach, we propose a pilot project focused on the growth traits, organized in the following stages:

Discovery

- An international collaboration involving the U.S. Meat Animal Research Center (**USMARC)**, the Australian Beef CRC, the University of Guelph, and the University of Alberta will analyze data from animals with genotypes for the Illumina Infinium BovineSNP50 Beadchip[1] (**50K SNP chip**) and phenotypes for growth traits (birth weight, weaning weight, and yearling weight).
- From these analyses, a variety of approaches to identifying sets of SNP that account for the most genetic variance possible for the target traits will be used.
- In identifying these sets of markers, SNP that affect birth weight with minimal or opposite effect on growth and SNP that affect growth with minimal or opposite effect on birth weight will be preferentially included to improve the ability to select for antagonistically correlated traits.
- Subsets of SNP may be derived by individual organizations within the collaboration or from metaanalyses of the combined results.
- Other entities with appropriate populations with 50K SNP chip data may also be included in the discovery process at this point.

1st Stage of Validation

- Identify additional data sets on which 50K SNP chip data exists with which to validate the original subsets of SNP and evaluate the effectiveness of various strategies for identifying SNP and estimating their effects jointly.
- Potential contributors to this stage may include:
  - The USMARC SNP data on approximately 2,000 industry AI sires (excluding sires of the discovery population) of 16 breeds with 50K SNP chip data.
  - DNA testing companies
  - Universities or other research populations with appropriate data
  - The international collaborators may fit into the project at this phase instead of the discovery phase. Provided that the international collaborators contribute to the discovery phase independently, they could validate each others' SNP sets at this stage.
- This stage would be done by providing formulas for MBV to the population owners, with each population owner performing the analysis of their own data.

Panel Selection and Development Stage

- After having examined the results of the 1st validation stage, a subset of the 50K SNP chip will be selected and one or more MBV formulas (restricted to the selected set of SNP) for each trait will be developed.
  - The new formulas will then be checked against the various populations used in 1st stage validation to ensure that the restricted subset of SNP will be sufficiently predictive.
- Assuming the subset is sufficient, a low-cost assay for this subset of SNP will be developed.
- If the subset does not account for sufficient genetic variance, the number of SNP in the subset will be increased.

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1 Mention of trade names or commercial products in this article is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture.

2nd Stage of Validation

- NBCEC is developing plans to collect tissue samples and obtain access to phenotypes on roughly 10,000 purebred cattle from large, influential seedstock producers in a region that is environmentally similar to USMARC. The initial plan was to sample calves born in spring 2009, but there may be substantial advantages to sampling cows in production, or spring 2009 calves and their dams (from a smaller number of herds), instead. The advantages of sampling dams are that the estimation of maternal effects of the SNP would be possible and that a greater number of phenotypes would be leveraged relative to the number of animals genotyped. The advantage of sampling both calves and their dams is that it allows a more efficient partitioning between direct and maternal effects of the SNP. Furthermore, sampling both calves and their dams may provide a pedigree structure that is considerably more efficient for the estimation of the genetic (co)variances required for the inclusion of DNA tests into NCE.
- Contingent on funding, the assay developed in the previous step will be run on these purebred calves.
- The data will be analyzed to provide an independent and stringent validation of the SNP chosen for the assay and the various MBV formulas.

Refinement of Predictions

- At this stage, the SNP effects will be jointly re-estimated considering the 10,000 purebred cattle as well as the discovery and 1st stage validation data sets.
- Assuming that the 2nd validation stage was successful, the refined MBV will also be considered validated. The variance components from this stage will be biased up somewhat due to the re-estimation, but the variance estimates from the 2nd stage validation should provide an underestimate of the true variance. Hopefully, the upward and downward biased estimates will not differ too greatly so that reasonable estimates of the (co)variances can be obtained.
- The re-estimation stage will need to consider how breed-specific the tests are. For example, if the original tests appear to work well in some breeds, but not others, the re-estimated tests may need to become more breed-specific than the original tests were and the 2nd stage validation may provide the additional information required to do that. However, this may cause additional challenges in validation. For example, if the original tests did not work effectively enough in some breeds, the 2nd stage validation data could be used to optimize the prediction formulas for those breeds, but it would then not be sufficient to assume that the tests for those breeds were validated because there would not be a previously validated test from which this test could be considered an improvement.

Commercialization

- It is hoped that one or more DNA testing companies will offer the assay developed in this project (or a subset of it) commercially.
- The results of the project (including SNP included in the assay and MBV formulas) will be published.
- DNA testing companies that participate materially in the project, for example in the 1st validation stage, may be given early access and lead time to the results.

Implementation

- The goal will be to get the MBV generated by the commercial DNA test (and other animals tested in the course of the project) incorporated into the NCE programs of the respective breeds as soon as possible.

- Implementation will also be made much easier if the resource populations used are closely linked to industry herds. Evaluation of the DNA tests (i.e., estimating the covariances) will naturally "seed" the NCE process. If a test is judged good enough to be part of NCE, the resource populations will help greatly in producing the first EPD.
- On the other hand, having the DNA tests included in NCE will inevitably generate additional data that can be used to improve the estimates of (co)variances.

*Expansion of the Project to Study Genotype × Environment (**G** × **E**) Interaction*

- In addition to the large scale, multiple breed validation represented in the 2nd validation stage, we propose to pursue knowledge of the potential for G × E for the molecular breeding values by expanding the regions from which the seedstock herds are selected. Challenging environments that may include fescue regions, hot and humid regions, hot and dry regions, high altitude etc. will be identified.
- As with the 2nd validation phase, collaborating breed associations will identify herds in each geographic region. The target is to collect tissue samples and obtain access to phenotypes on roughly 1,000 purebred cattle from each breed in these regions.
- We will submit a grant to USDA to explore G × E and in that grant we will request funds to run the smaller SNP panel on all cattle in these regions.
- This industry resource will be comprised of approximately 30,000 cattle in the outlying regions in addition to about 10,000 animals used in the 2nd stage validation.

Discussion:

As the MBVs from this project are incorporated into NCE, MBV from whole genome selection (using the entire 50K SNP chip and derived from and validated in some of the same populations used for this pilot project) should also be incorporated into NCE. Therefore, it will be important that the genetic covariances between the MBV from those two different DNA tests be estimated well.

The problem of selecting subsets of SNP that account for as much genetic variance as possible is not trivial; the proposed pilot project presents an important opportunity to explore a variety of approaches to this problem. This will contribute to the immediate problem of maximizing performance for the growth traits, but perhaps more importantly, should provide insight that will be valuable in the more difficult task of selecting optimum subsets of SNP for the traits for which data is much scarcer.

This project additionally represents an important opportunity to evaluate a set of DNA tests in multiple regions of the U.S. and multiple breeds. This is important because many traits, especially growth traits, interact with the environment. Furthermore, it is currently unknown how effective DNA tests developed in one set of breeds will be when applied in a different set of breeds. The proposed project will contribute toward addressing that question.

The potential utility of this approach (and perhaps the potential for significant contributions to it) may be much greater if it encompasses applications of DNA tests that include Marker Assisted Management (**MAM**) as well as Marker Assisted Selection (**MAS**). To do this, it should facilitate estimating non-additive as well as additive components of genetic variation. In this context, the term NCE could be expanded to encompass the estimation of breeding values of seedstock from data on commercial cattle, particularly for traits (e.g., carcass, cow fertility, and disease resistance) that are difficult to measure in sufficient numbers on seedstock animals. It could also be expanded to include the estimation of actual performance of commercial

animals by including factors not typically considered in NCE. However, the expansion into MAM is not necessary to make this approach work; it just might make it more effective and more likely to garner the required participation.

Goal for the Future: A Transition From Validation to Estimation of (Co)variances

The current system of independent validation of DNA tests should be replaced by a system of unbiased collaborative estimation of the (co)variances required for inclusion in NCE.

- The focus will shift from whether the DNA test "works" or not to how much of the genetic variation it accounts for. This should become the primary criteria for determining whether a DNA test is included in NCE or not.

- If the test accounts for too little genetic variation to be of real use to customers, this will be reflected in the (co)variance estimates and in the extent to which it improves the accuracy of the resulting EPD.

Therefore, the primary emphasis of the independent third party (e.g., NBCEC) should become to ensure that the system produces, to the extent possible, unbiased estimates of the genetic variances accounted for by each DNA test and that the increases in accuracies of EPD resulting from DNA testing are as realistic as possible.

Data Challenges

These parameters will be estimated most efficiently if we can obtain MBV for all of the DNA tests that will be considered in NCE on the same population. It would be possible to estimate all of the required covariances by considering each pair of tests on a common population, but this would require that all pairs of tests are available together on some population; it also would be inherently much less efficient than considering all of the DNA tests jointly.

It likely would be possible to estimate these covariances from data structures in which different tests are applied to different individuals within a population, but this approach depends on the different subsets of individuals being sufficiently related to one another and would be inherently less efficient for estimating covariance parameters.

It is, however, possible that the covariances among MBV could be estimated from animals that did not have phenotypes for the traits of interest (or any traits for that matter) and that the covariances between MBV and phenotypes could be estimated on a within-company basis.

It seems clear that the size of populations required for estimation of genetic (co)variances will be much greater than that of the populations we have been using for validation (Kachman, 2008). Furthermore, it will be important to partition additive genetic from residual (and for some traits, maternal) (co)variances. Therefore, the pedigree structure will become much more important. It seems likely that populations with deeper pedigrees and phenotypes in multiple generations may be more effective for (co)variance estimation.

Interpretaion of (Co)variances

In order to determine how much or little overlap exists between different DNA tests that influence the same trait, it will be important to have good estimates of the covariances between those DNA tests. This will be important in NCE when the same animals have been tested for multiple DNA tests, for instance from multiple companies. It could also apply to MBV for a number of different traits from a single panel from a single company or to different versions of the same test from the same company.

An alternative way to look at this that may be easier to interpret is in terms of genetic correlations between the DNA tests. Cattle breeders could use these genetic correlations to help them determine how much additional benefit (increase in accuracy of EPD) they could expect from purchasing a second DNA test, given they have already purchased one test.

Furthermore, we must abandon the antiquated model of one trait per test and instead assume that each commercial panel of markers will be associated with MBV for a number of traits. Subject to availability of appropriate data, the genetic covariances between each of the MBV and each of the other traits in the analysis must be estimated.

The proportion of genetic variation accounted for by a DNA test will not be the only, or necessarily the best, measure of the value of a DNA test for long term improvement of genetic merit. Some rare alleles with large, favorable effects may have substantial economic value while accounting for little current genetic variation. Such tests will be valuable because they will have the potential, given sufficient selection emphasis and time, to account for considerable genetic variation in the future. Therefore, in the future, it will be beneficial to develop methods to estimate potential future genetic variation accounted for by a test. However, this seems unfeasible for the current generation of DNA tests for which the results are presented only as MBV, without the individual genotypes. In this situation, it is impossible to compute allele frequencies and effects of individual SNP, and this is the essence of the information required to estimate potential future genetic variation. Therefore, for the immediate future, it seems most practical to focus on current genetic variation, which will be challenging enough by itself. When that challenge has been substantially met, we can shift the focus to finding feasible approaches to estimating potential future variation.

Statistical Challenges

There are many statistical issues that still need to be addressed. We have recently developed a method for estimating the proportion of genetic variance in the ERT that is accounted for by a DNA test. This proportion is simply the square of the additive genetic correlation between the phenotypic trait and the MBV in a multiple trait model in which the MBVs are fit as additional traits. Further work to verify the statistical properties of this estimator and gain better understanding of the data requirements for estimating it will be required.

Furthermore, we should explore whether there is a way to estimate the genetic parameters from a large data set, assuming that the data set included the discovery data, and correcting the estimates for the bias due to having the discovery data included. This might be done through a simulation approach. It seems possible that this effect would diminish as the total size of the data set exceeded roughly 10,000 animals.

In addition, we need to find ways to objectively measure the quality of data sets so that combined analyses or meta-analyses of them can be weighted based on data quality.

Conclusions

It is becoming increasingly clear is that much larger data sets will be required for estimation of the (co)variances required to move DNA tests into NCE than we have typically used for the third party validation process. Therefore, a collaborative approach toward estimating these parameters by combining many data sets is likely to be the best approach.

The growth traits pilot project could potentially generate genotypes on >50,000 animals with phenotypes. Hopefully, this would be a sufficient resource to answer a number of important questions relatively unambiguously. Assuming that it is, it should provide a very valuable resource for estimating the population requirements for delivering effective DNA tests for more difficult traits. If it is not, then a substantial reallocation of resources currently going into more difficult traits may be appropriate.

We could gain a much clearer picture of what the actual resource requirements for the development of effective DNA tests are by overshooting and then interpolating. However, what we have been doing with genomics population resources up to this point is basically to undershoot and then extrapolate.

The pilot project we described here is intended to demonstrate the advantages and resolve some of the challenges of such a collaborative approach to the estimation of the necessary variances and covariances.

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