Genetics of Beef Cattle: Moving to the genomics era
Matt Spangler, Assistant Professor, Animal Science, University of Nebraska-Lincoln

Several companies offer DNA marker tests for a wide range of traits in beef cattle. Unfortunately the interpretation of the results has caused a great deal of confusion for cattle producers. Testing an animal is simple, but determining exactly what to do after receiving the results can be much more complex. The terminology that accompanies DNA tests only adds to the confusion.

Terminology

Additive Genetic Effects – Average individual gene effects that can be transmitted from parent to progeny.

Allele – Alternate form of a gene. It can also be thought of as variations of DNA sequence. For instance, if an animal has the genotype for a specific gene of Bb then both B and b are alleles.

DNA Marker – A specific DNA variation that can be tested for association with a physical characteristic (Marbling, tenderness, etc.).

Genotype – The genetic makeup of an animal.

Genotyping (DNA marker testing) – The process by which an animal is tested to determine the particular alleles it is carrying for a specific genetic test.

Simple Traits – Traits such as coat color, horned status, or some diseases. These traits are generally controlled by a single gene.

Complex Traits – Traits such as reproduction, growth, and carcass that are controlled by numerous genes. These are also referred to as Economically Relevant Traits (ERTs).

Homozygous – Having two copies of the same allele for a single gene such as BB.

Heterozygous – Having different copies of alleles for a single gene such as Bb.

Locus – Specific location of a marker or a gene.

Marker Assisted Selection (MAS) - The process by which DNA marker information is used along with phenotypic based Expected Progeny Differences (EPDs) to select parents for the next generation.

Marker Assisted Management (MAM) - The process by which DNA marker information is used to assist in making management decisions such as sorting cattle entering the

feedlot based on their propensity to meet certain grid criteria as determined by a genetic test.

Marker Panel- A combination of two or more DNA markers that are associated with a particular trait.

Non-Additive Genetic Effects – Effects such as dominance and epistasis. Dominance is the interaction of alleles at the same locus while epistasis is the interaction of alleles at different loci.

Nucleotide - A structural component of DNA that includes one of four base chemicals: adenine (A), thymine (T), guanine (G), and cytosine (C).

Phenotype – The outward appearance of an animal that can be measured. Phenotypes are influenced by the genetic makeup of an animal and the environment.

Single Nucleotide Polymorphism (SNP) - Pronounced 'Snip'. A SNP is a single nucleotide change in a DNA sequence. For instance, AAGGTTA is changed to ATGGTTA. Here the second 'A' is changed to a 'T'. Not every SNP causes a physical change in an animal. SNPs occur in the hundreds of thousands across the genome.

Parentage Testing

The identification of an animal's parents via DNA marker technology can be advantageous in several situations including multi-sire breeding pastures and ascertaining if a calf is the product of an artificial insemination (AI) mating or a clean-up bull. Genotyping to determine parentage allows for a sire to be correctly linked to a corresponding calf. This promotes knowledgeable culling and breeding decisions by determining which sire(s) are contributing the most (or least) to a particular breeding objective. In the case of correctly identifying if the calf was a result of an AI mating, parentage testing allows for an animal to be registered correctly with the breed association. Parentage testing utilizes several DNA markers to compare two or more animals based on their similarities for the markers tested.

Example
In the following example two bulls are possible sires of a calf given that the calf's dam is known.

Sire 1		Sire 2		Dam	
Marker A		Marker A		Marker A	
A1	A2	A1	A2	A1	A2
C	T	T	T	T	T

Calf	
Marker A	
A1	A2
C	T

In this simple example there is one marker with two alleles (A1 and A2). Using only one marker we can deduce that Sire 1 is the true sire of the calf. The dam had to pass on a T allele to her calf and the only sire that could have provided the C allele is Sire 1. In practice, multiple DNA markers would be used to ascertain parentage.

Popular Tests for Simple Traits

Color, horned status, and carriers for genetic defects are among the genetic tests available for simply inherited traits. Color refers to determining if an animal is homozygous or heterozygous black. Because the allele for red coat color in cattle is recessive, it is possible that an animal will be black hided but still have a red allele to pass to his/her offspring. If an animal is red, then its genotype for color is known with 100% confidence, as they have to be homozygous for the red allele. In some marketing schemes black hided cattle are more desirable because of the association between black hides, Angus cattle, and Certified Angus Beef (CAB). Breeds more commonly tested for color status would be Simmental, Limousin, Gelbvieh, and composite or hybrid animals that may contain a combination of breeds that have both red and black ancestry.

Genetic tests for horned status allow for a producer to determine if a polled animal is homozygous polled or heterozygous polled (carrier of the horned allele). All horned animal are homozygous for the horned allele while animals that have a polled phenotype may be carriers of a horned allele and produce horned offspring if mated to females who are horned or heterozygous polled/horned. Different companies have validated tests for different breeds. Breeds that have tests available include Charolais, Gelbvieh, Hereford, Limousin, Salers, and Simmental.

How are DNA Marker Tests Related to EPDs?

EPDs provide an estimate of the genetic potential of an animal as a parent based upon ancestral information, their own records, and the records of their progeny. With this in mind, an EPD accounts for all the genes that affect a particular trait, regardless of the magnitude of their affect. While an EPD accounts for all the genetic variation, the specific sources of the variation (genes) are unknown. DNA marker tests reveal the genotype of an animal for specific DNA markers for a particular trait but do not account for all of the genetic variation.

It is critical to understand that a desirable genetic test result is not always associated with a desirable EPD. For instance, it would be possible for an animal to be homozygous for the favorable allele for a DNA marker for marbling but still have a marbling EPD that is below breed average. This could occur because although the animal has the favorable form of one gene affecting marbling, it may have unfavorable alleles for numerous other unknown genes that affect marbling as well.

The Value of Improving Accuracy

The uncertainty surrounding early predictions of genetic merit arise as a result of Mendelian sampling. Every animal is passed a random sample of alleles from each

parent, half coming from the dam and half from the sire. We have an estimate of the average effect of what was passed from parent(s) to offspring in the form of pedigree estimates, but the certainty with which we know this estimate is correct (i.e., the accuracy) is low. As more information is collected, such as an individual's own record and data from progeny, accuracy increases. For lowly heritable traits like measures of reproduction, it can take a considerable number of offspring to reach high Beef Improvement Federation (BIF) accuracy levels, given that the BIF scale is more conservative than true accuracy (r) as illustrated in Table 1.

Table 1. Approximate number of progeny needed to reach accuracy levels (true (r) and the BIF standard) for three heritabilities (h^2).

Accuracy		Heritability Levels		
R	BIF	h^2 (0.1)	h^2 (0.3)	h^2 (0.5)
0.1	0.01	1	1	1
0.2	0.02	2	1	1
0.3	0.05	4	2	1
0.4	0.08	8	3	2
0.5	0.13	13	5	3
0.6	0.2	22	7	4
0.7	0.29	38	12	7
0.8	0.4	70	22	13
0.9	0.56	167	53	30
0.999	0.99	3800	1225	700

One primary benefit of molecular information is that it can be garnered much earlier in life (before a phenotypic record can be collected). This knowledge can, in part, reveal a portion of the black box that is Mendelian sampling in young animals. This results in higher accuracy values for young animals, which potentially increases the use of these younger animals in seedstock systems, thus decreasing the generation interval. The equation below predicts the rate of genetic change per year and is dependant on selection intensity, the accuracy of selection, genetic variation, and the length of the generation interval. From this it is apparent that if the generation interval is decreased and /or accuracy is increased this will lead to faster genetic change.

$$\frac{[(\text{Accuracy of Selection})*(\text{Selection Intensity})*(\text{Genetic Standard Deviation})]}{\text{Generation Interval}}$$

However, the magnitude of these benefits will depend on the proportion of variation explained (% GV) by a given marker panel. Without the seamless integration of this technology into EPD calculations, we find ourselves in the current context of being faced with two disjoined pieces of information: traditional EPD and marker panel results. In this scenario, it is impossible to directly compare EPD to marker panel results. This is because the molecular scores only explain a portion of the additive genetic variation. Further, some of the marker panel results have a metric of accuracy associated with them. At the current time, this metric is not directly comparable to the BIF accuracy value associated with EPD simply due to differences in the way they are computed. Table 2

shows the relationship between the genetic correlation (true accuracy), %GV and BIF accuracy.

Table 2. The relationship between true accuracy (r), proportion of genetic variation explained (%GV), and Beef Improvement Federation (BIF) accuracy.

r	%GV	BIF
0.1	1	0.005
0.2	4	0.020
0.3	9	0.046
0.4	16	0.083
0.5	25	0.132
0.6	36	0.200
0.7	49	0.286

In contrast to the thought process of DNA marker panel results being a separate and disjoined piece of information, these test results should be thought of as a potentially useful indicator that is correlated to the trait of interest. As such, the MBV can be included in the National Cattle Evaluation (NCE) as a correlated trait. Other methods have been proposed including using large (50,000+) SNP panels to form a genomic relationship matrix that could allow for known relationships between animals based on genotypes across SNP loci. Combining these sources of information, molecular tools and traditional EPD, has the potential to allow for the benefits of increased accuracy and increased rate of genetic change as discussed earlier.

Figures 1 and 2 illustrate the benefits of including a MBV into EPD (or EBV which is twice the value of an EPD) accuracy (on the BIF scale) when the MBV explains 10, or 40% of the genetic variation (GV), which is synonymous with R^2 values of 0.1, and 0.4. The darker portion of the bars shows the EPD accuracy before the inclusion of genomic information and the lighter colored portion shows the increase in accuracy after the inclusion of the MBV into the EPD calculation. As the %GV increases, the increase in EPD accuracy becomes larger. Additionally, lower accuracy animals benefit more from the inclusion of genomic information and the benefits decline as the EPD accuracy increases. Regardless of the %GV assumed here, the benefits of including genomic information into EPD dissipate when EPD accuracy is between 0.6 and 0.7. On the other hand, when %GV is 40 an animal with 0 accuracy could go to over 0.2 accuracy with genomic information alone. From table 1, this would be the same as having approximately 4 progeny for a highly heritable trait or 7 progeny for a moderately heritable trait.

Figure 1. Increase in accuracy from integrating genomic information that explains 10% of the genetic variation into Estimated Breeding Values (EBV).

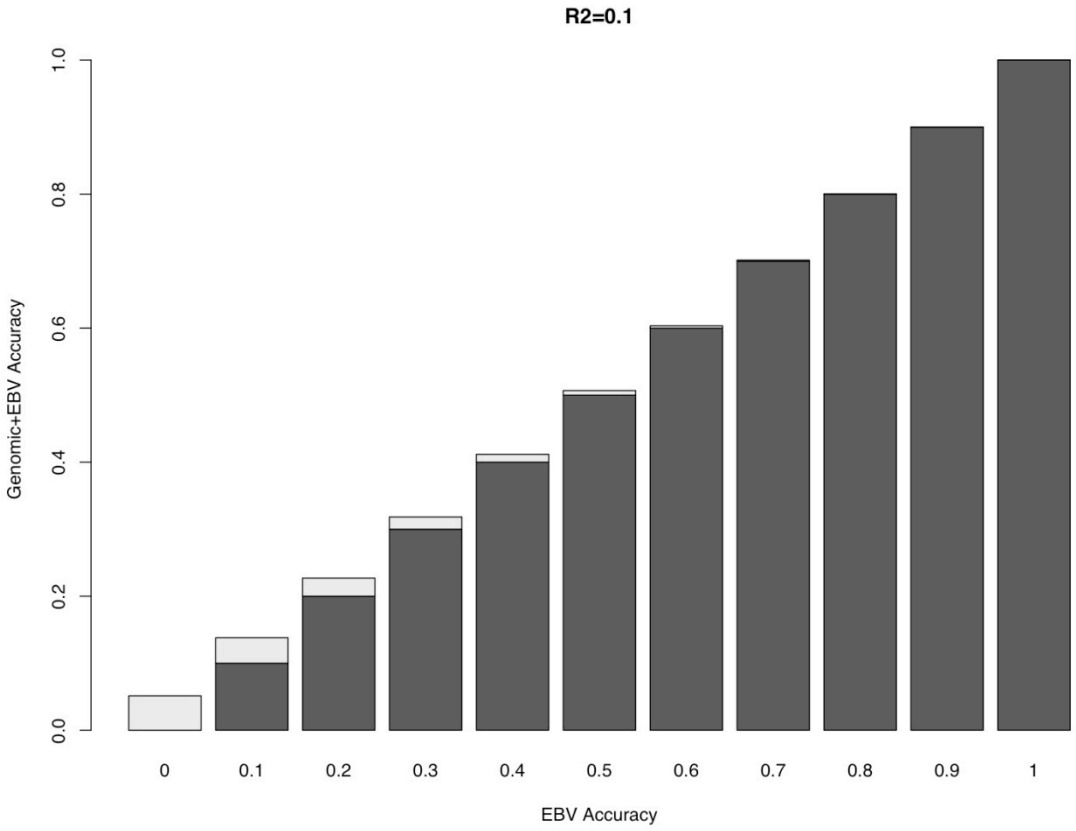
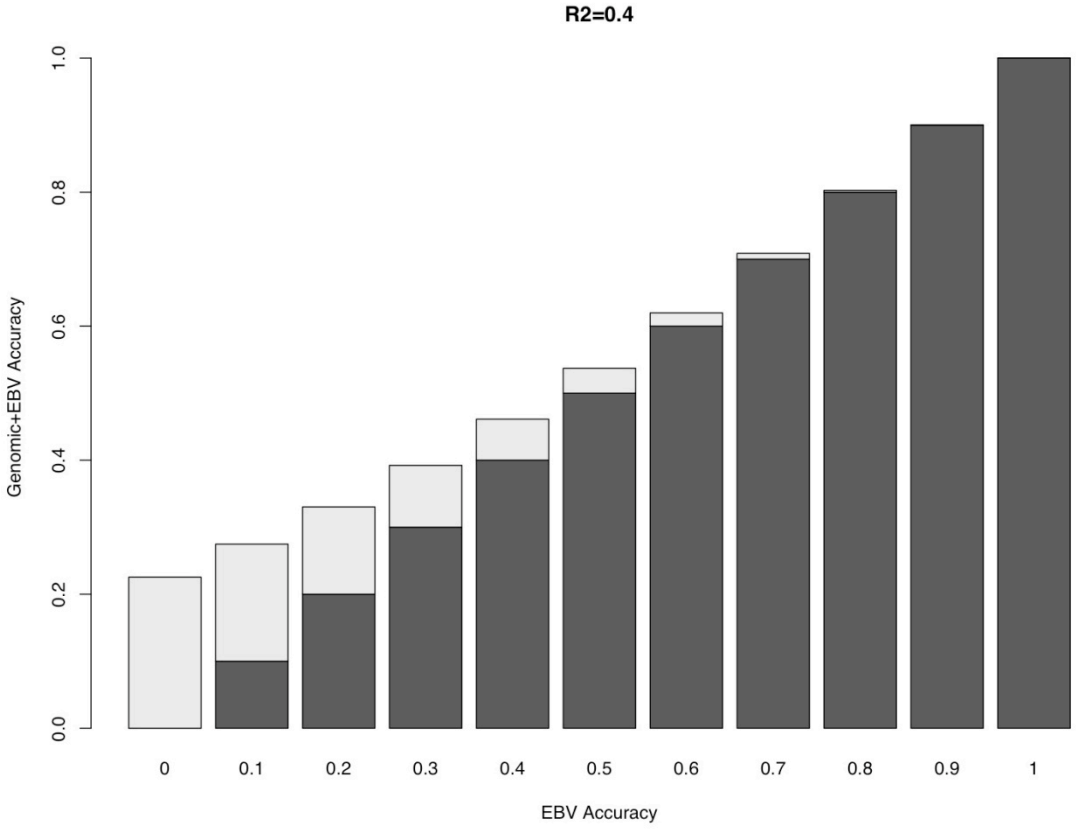


Figure 2. Increase in accuracy from integrating genomic information that explains 40% of the genetic variation into Estimated Breeding Values (EBV).



It is important to understand some limitations in the current application of Marker Assisted Selection. For instance, current marker panels are likely to work best in the populations where discovery occurred, but will potentially decrease in predictive power as the target population becomes more genetically distant from the discovery population (de Roos et al., 2008). The same erosion in accuracy is likely to occur overtime as well (i.e. over generations if panels are not retrained).

Discovery	Target	
Angus	Angus	Closest relationship
Angus	Charolais	↓
Angus	*Bos indicus*	Most distant relationship

Advantages and Disadvantages

The use of DNA marker information can allow for early prediction of the genetic merit of an animal before phenotypic records are collected thus increasing the accuracy of young sires and decreasing the generation interval. In some instances, traits are expensive to measure (tenderness, feed intake) or lowly heritable (stayability, heifer pregnancy) and thus molecular information can be of greater benefit. Benefits of MAS will be increased once this information is validated and combined with traditional EPDs. The use of this technology for MAM requires validation of the DNA marker tests and the ability of the

technology to correctly identify cattle with differences in genetic potential for carcass traits (yield and quality grade) beyond what is possible by simple visual appraisal of breed differences. As with any new technology, the cost of DNA marker tests is decreasing with time. However, careful economic analysis must be performed prior to implementing MAM to determine if the end results justify the cost of the tests.

Summary

Because this technology is rapidly changing it is important to stay abreast of current genetic tools and their application to specific breeding objectives. It is likely that the list of genetic selection tools will continue to expand in the short term as this arena is far from stagnant. Although the goal is the consolidation of information into one of two basic forms, EPD and economic index values, the industry has witnessed several intermediate steps in an effort to quickly commercialize technology that has created confusion. For those who have not yet adopted thirty-year-old technology such as EPD, the inherent selection mistakes that have been made in the past will only be exacerbated in the future when the accuracy of genetic predictions of young animals is increased. And, as molecular-based EPD are developed for phenotypes not usually measured the need to utilize EPD technology will be even greater.

Helpful Websites

These websites contain current information regarding available tests (UC Davis) and validation results (NBCEC). Company websites are also listed below in order to provide information regarding sample collection and costs associated with specific tests. Because this technology is evolving, tests for new traits, additional markers for current tests, and validation results are continually changing.

National Beef Cattle Evaluation Consortium
http://www.nbcec.org

University of California Davis Animal Science
http://animalscience.ucdavis.edu/animalbiotech/Biotechnology/MAS/index.htm.

Pfizer Animal Genetics
http://www.pfizeranimalgenetics.com

Merial IGNENITY®
http://www.igenity.com