Beef Cattle Genomics: Promises from the Past, Looking to the Future

A.D. Herring*, D.G. Riley, J.O. Sanders,
P.K. Riggs and C.A. Gill

Department of Animal Science
Texas A&M University, College Station TX 77843

Improving Life through Science and Technology.

Presentation Layout

- Background on genetic change

- Development of genetic markers

- Research approaches to genetic makers

- Current and future applications in cattle breeding

Basic Principles of Livestock Breeding and Genetics

- Animals tend to resemble their parents and other close relatives for many traits

- Inbred animals tend to breed better than they perform (and conversely that outbred animals tend to perform better than they breed)

- Outbred animals tend to outperform inbred animals for many traits

Concepts of Superior Animals

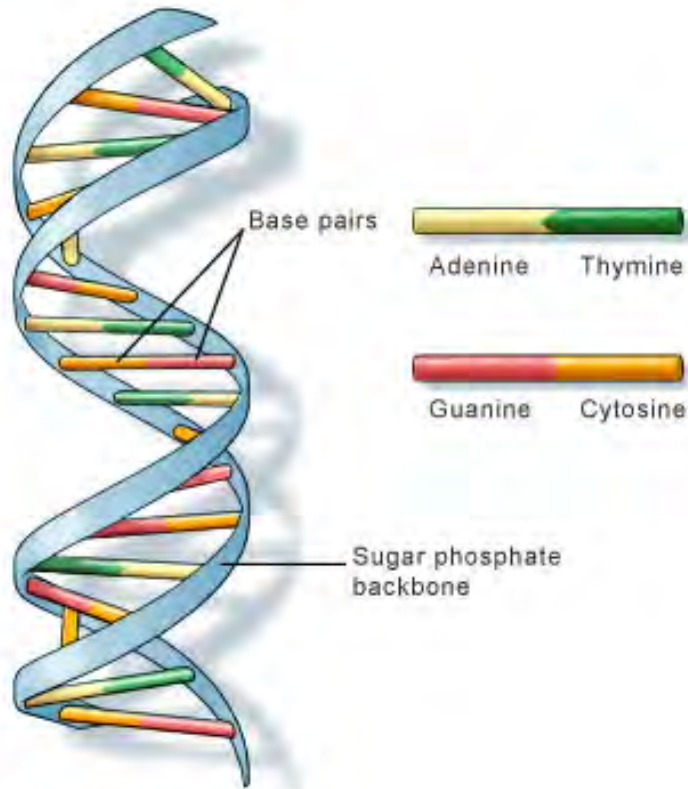Late 1700s
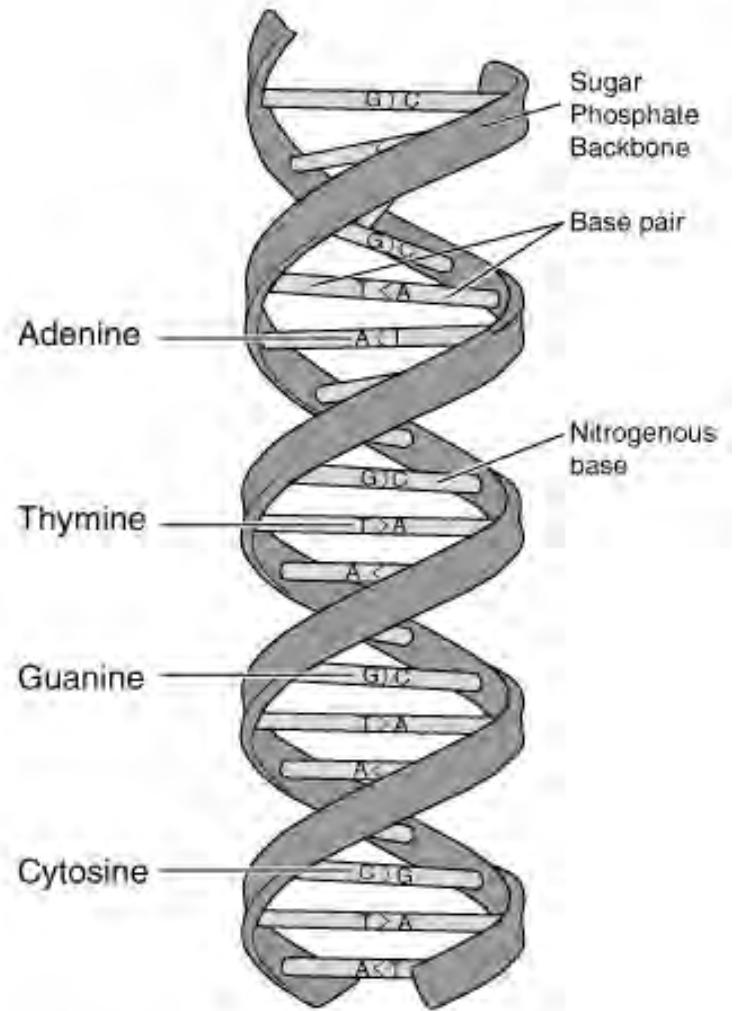

Mid -late 1800s

1903

1951

Fundamentals of Genetic Change

- There are underlying genetic differences among individuals in a population
- These underlying genetic differences influence the phenotypes (performance)

The genetic alphabet has 4 letters (A, C, G, T).

The entire DNA sequence is called the "genome"

ACTGACGATCGATAGCTAGCGAGCTAGCGATGTACTAGTTCAACGCGA

The genomes of mammals contain about 3 billion letters

Sequence 1
ACTGACGATCGATAGCTAGCGAGCTAGCGATGTACTAGTTCAACGCGA

Sequence 2
ACTGACGATCGATAGCTAGTGAGCTAGCGATGTACTAGTTCAACGCGA

This is a SNP

Genetic Markers

- Any DNA sequence that is associated with a particular phenotype or performance level can be a genetic marker.

- An area on a chromosome that influences a quantitatively inherited trait is called a quantitative trait locus (QTL).

TEXAS A&M UNIVERSITY

AgriLIFE RESEARCH
Texas A&M System

Let's assume this SNP is associated with a quantitative trait; there will be different average levels of performance associated with these different marker genotypes.

CC   CT   TT
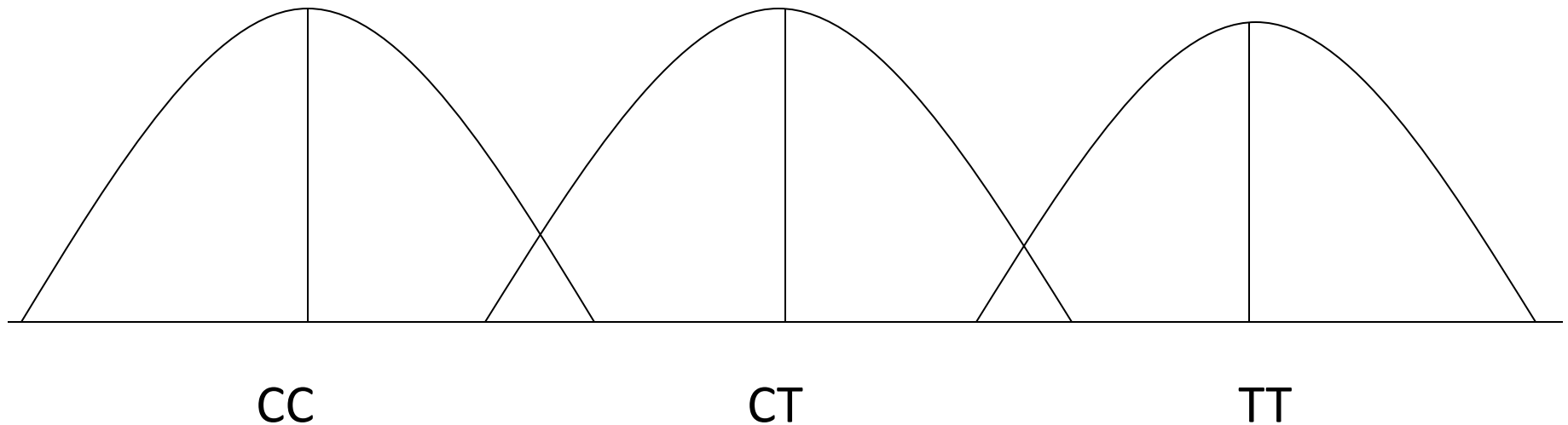
This particular marker acts is an "additive" fashion.

Qualitatively vs. Quantitatively Inherited Traits

Qualitative

Distinct categories
Environment not too influential
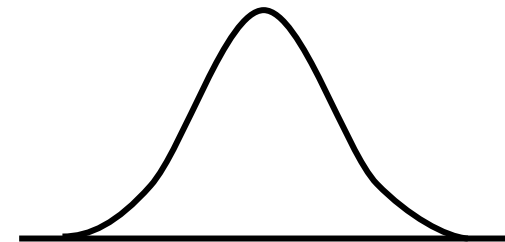One or two gene loci

Examples
Black vs. red
Horned vs. polled
Spotted vs. not

Quantitative

Continuous distribution
Environment important
Many gene loci

Weight, marbling, fertility, feed intake, fat thickness, milk, etc.

This or that

Ability to identify causes of simply-inherited genetic diseases

Short spine syndrome

Curly calf (Arthrogryposis Multiplex)

Highlights from some research projects targeting beef cattle genomics

Search for QTL

- Research designs have relied on having structured families to identify genes segregating within and between families.

- Most of the time this has been based on use of F_1 parents where two genetically different breeds or lines have been crossed.

- Parents pass one allele at each locus.

Texas A&M University Angleton Project (growth and carcass quality traits)

Reciprocal backcross design

Angus

f   m

X

Brahman

f   m

AB

f   m

BA

f   m

80 parents
614 progeny

3/4 A, 1/4 B

3/4 B, 1/4 A

F_2
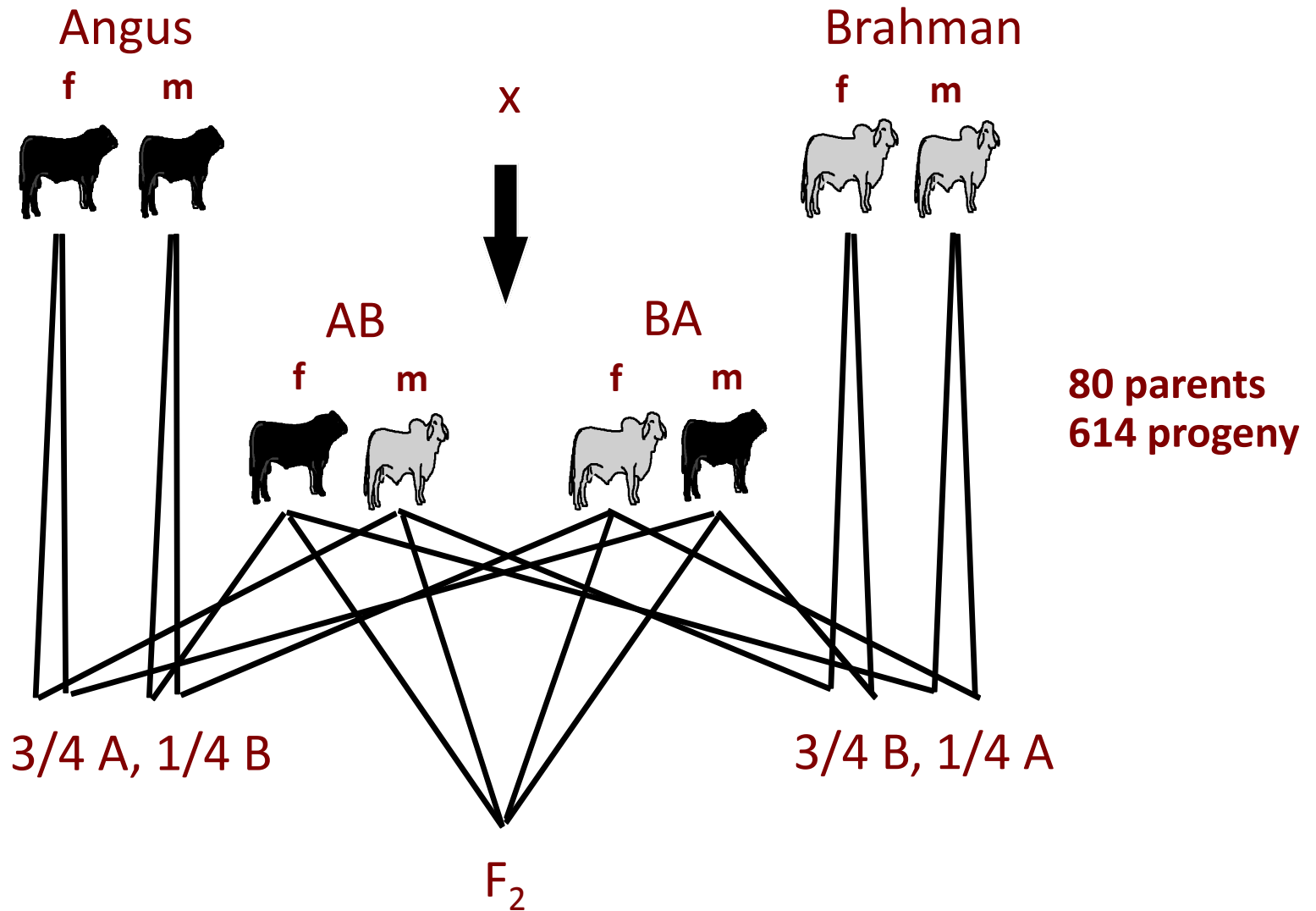
NCBA Carcass Merit Project

Research Objectives:

1. Generate data for tenderness and sensory trait EPDs
2. Further development of carcass EPDs
3. Validate DNA markers from Angleton Project

All breeds were invited to participate. Breeds included:

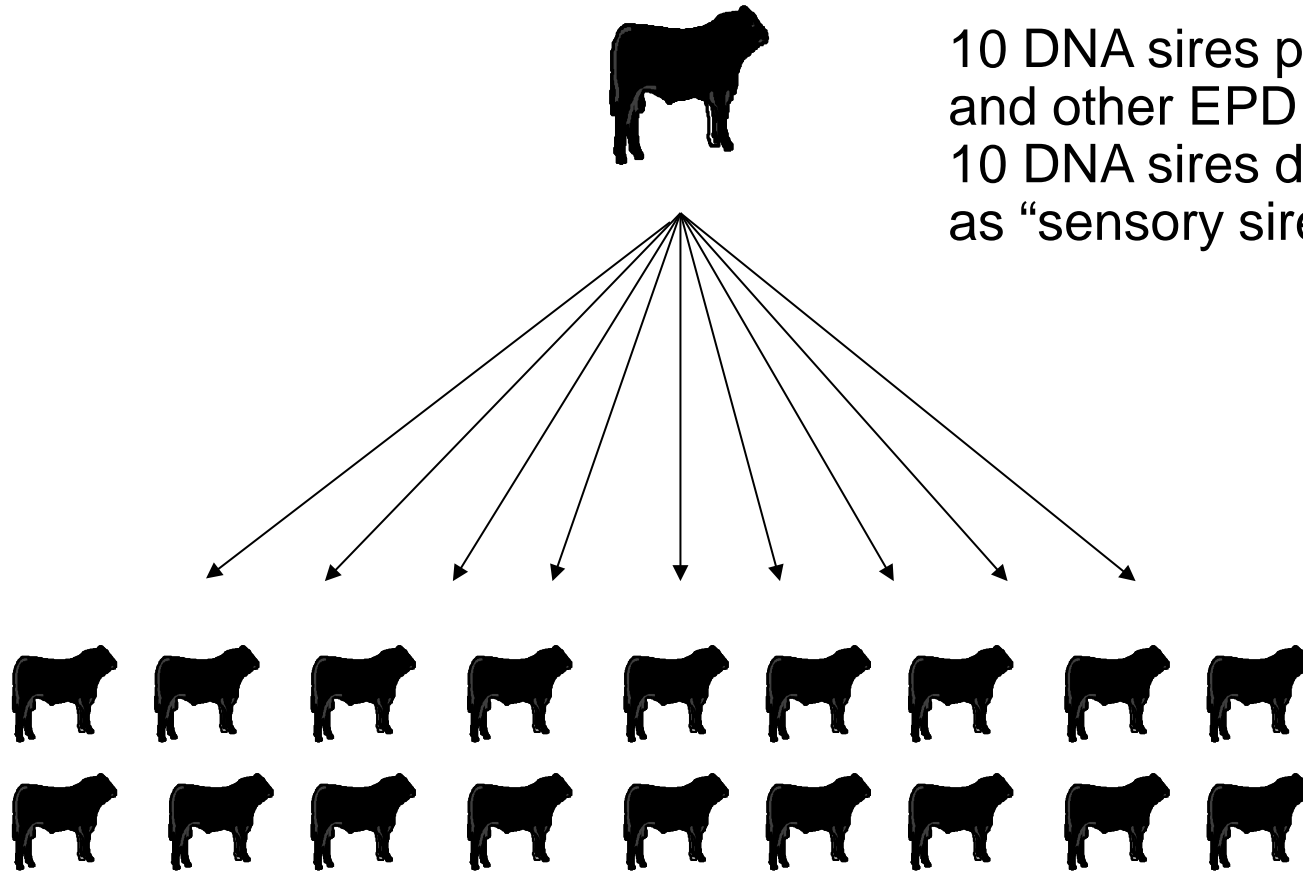|		
Angus	Hereford	Shorthorn
Brahman	Limousin	Simmental
Brangus	Maine-Anjou	Simbrah
Charolais	Red Angus	South Devon
Gelbvieh	Salers	

NCBA Carcass Merit Project - Family Structure

10 DNA sires per breed
and other EPD sires, 5 of
10 DNA sires designated
as "sensory sires."

50 Half-sib progeny per sire

Percentage of Phenotypic Variation Accounted for by Each QTL

QTL # (1 – 11)

Trait	1	2	3	4	5	6	7	8	9	10	11
Shear force	1	0	1	3	3	12	0	6	3	1	0
Overall tend.	0	1	1	1	0	10	2	8	0	4	0
Myofibrilar tend.	1	2	0	1	0	9	2	8	0	4	0
Conn. Tissue tend.	3	1	0	0	0	12	4	8	0	2	0
Juiciness	0	4	1	6	0	6	7	0	0	5	3
Flavor	1	1	0	3	2	1	3	3	2	5	3
Marbling	1	2	2	2	1	4	4	1	4	1	8
Ribeye area	0	0	4	2	3	7	7	3	0	1	1
Fat thickness	3	1	3	5	6	4	3	2	2	2	2
Hot carcass weight	1	0	2	0	0	2	6	10	0	1	3
KPH fat	0	7	0	3	5	2	0	1	2	1	1

McGregor Genomics Project
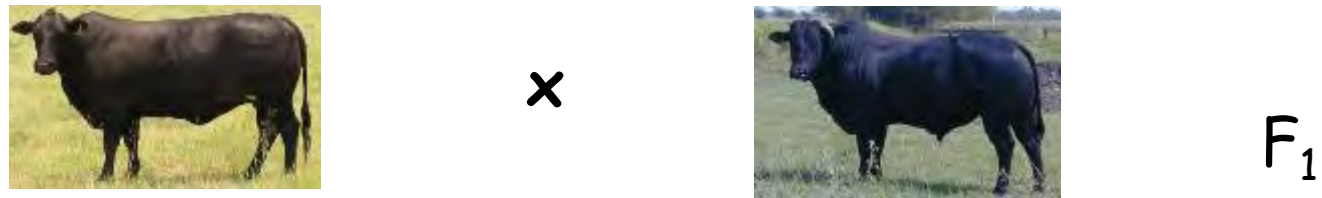
480 F$_2$ progeny266 NS half-sibs

McGregor Genomics Project
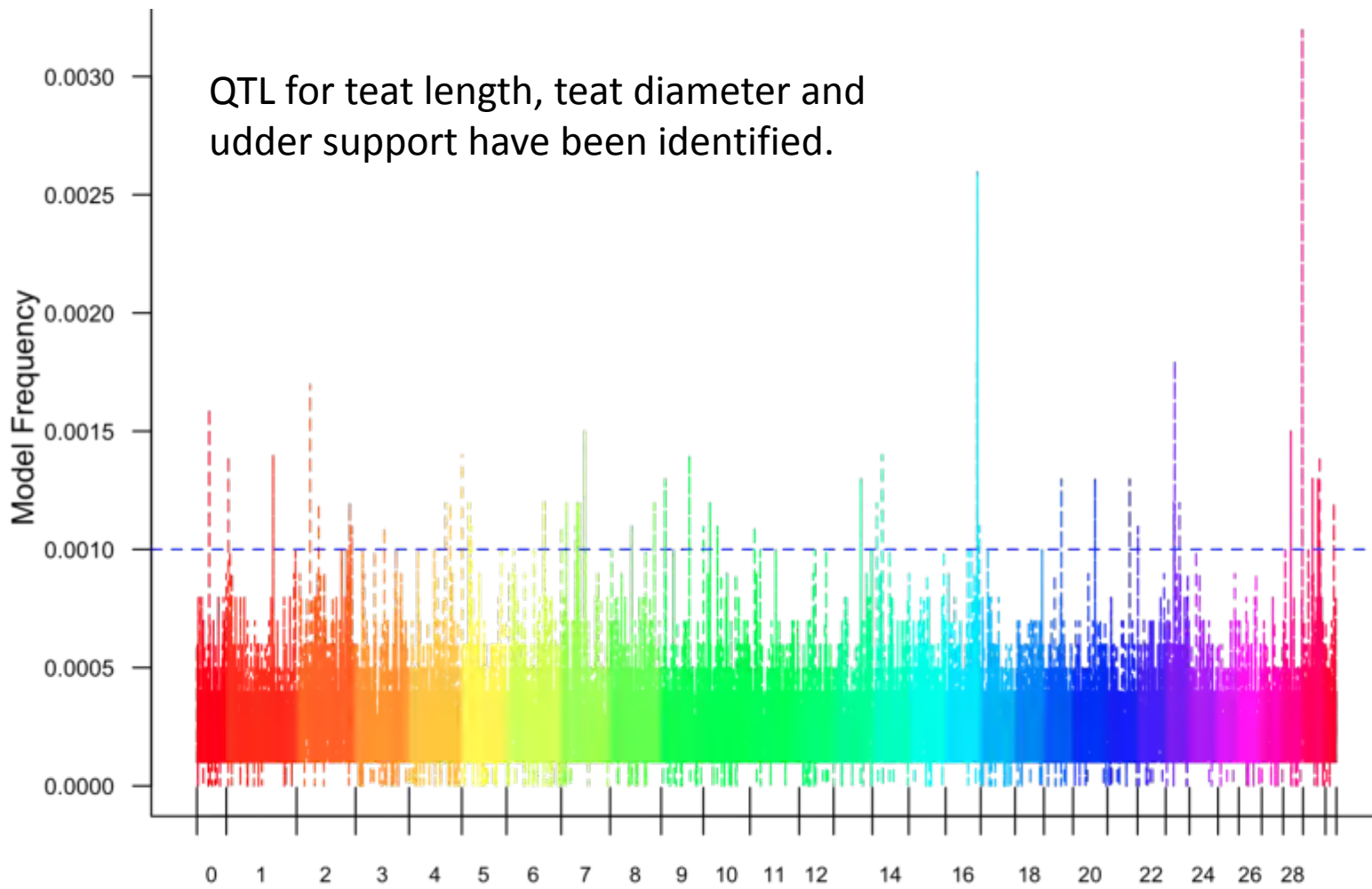
All cattle based on Nelore-Angus crosses

Cycle I	Cycle II	Cycle III
F_2 cattle embryo transfer and natural service cattle born – All F_1 parents Nelore-sired (NA).	Reciprocal F_2 cattle (all 4 types: NANA, NAAN, ANAN, ANNA) produced by natural service.	F_3 cattle produced through natural service breeding F_2 sons of two bulls to F_2 daughters of other two bulls and vice versa.
2003-2007	2009-2012	2009-2012
2013 – about 650 project cows in production.		

AgriLIFE RESEARCH
Texas A&M System

This is whole genome analysis of birth weight incorporating relatedness as defined by all markers on SNP50 that genotyped in Cycle 1 animals.

There is a threshold line for significance for each trait.
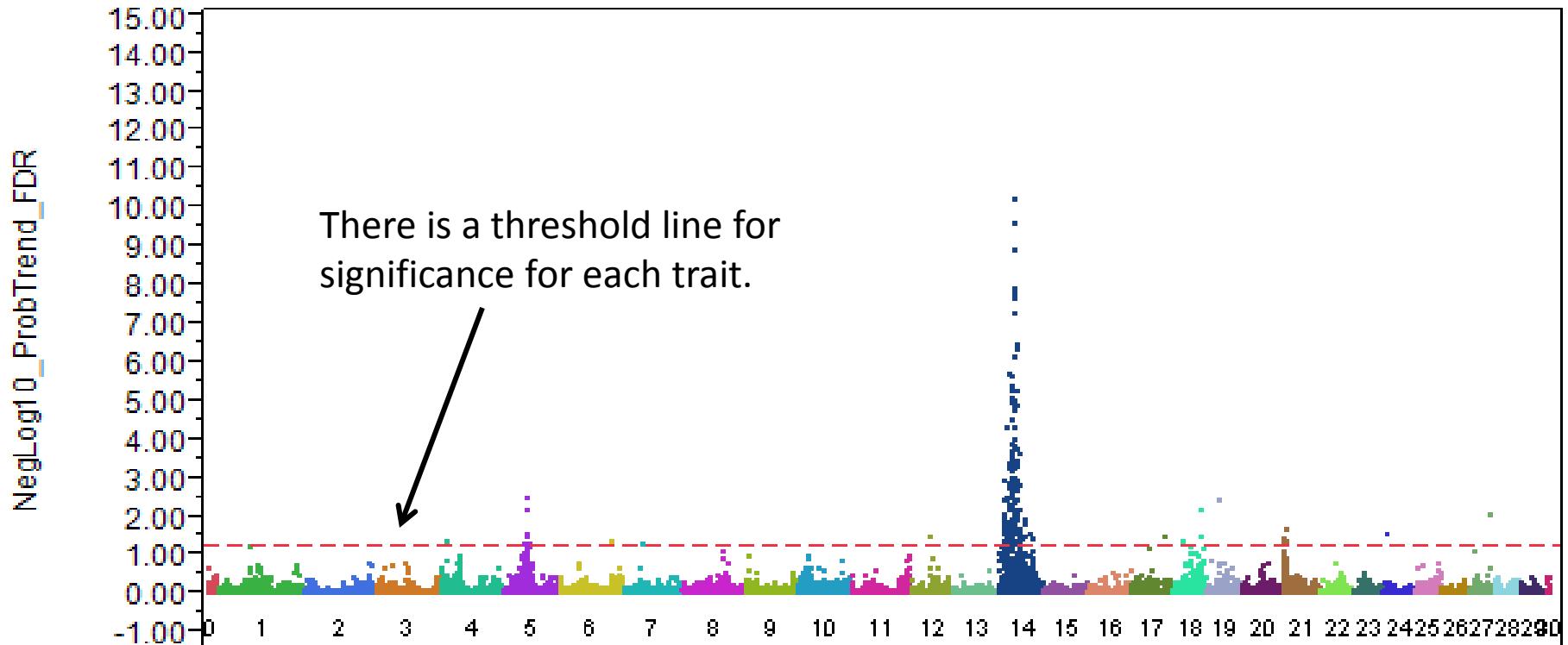
Whole genome scan for teat length at calving

QTL for teat length, teat diameter and udder support have been identified.

Science

Livestock Decoded

The Genome Sequence of Taurine Cattle: A Window to Ruminant Biology and Evolution

The Bovine Genome Sequencing and Analysis Consortium,* Christine G. Elsik,[1] Ross L. Tellam,[2] Kim C. Worley[3]

Genome-Wide Survey of SNP Variation Uncovers the Genetic Structure of Cattle Breeds

The Bovine HapMap Consortium*

Bovine Genome Project

The cattle genome has been sequenced (i.e. the general DNA sequence has been determined).

TraditionalbreedingstrategieshavereliedongatheringpedigreeinformationandperformancedataTheseconceptswillalwaysbeimportanthoweverasnewgeneticmarkersfortraitsofeconomicimportancebecomemoreavailableandassourceverifiedprogramsbecomemorepopularuseofgeneticmarkersofferscattleproducersnewtoolstocomplementtraditionalapproachesThistalkdiscussesthebackgroundofgeneticimprovementandthegeneralconceptsassociatedwithgenetic markers

Genomic Selection

- The past 10 years, much interest and effort has been placed into use of DNA information to enhance traditional genetic evaluations and selection approaches in several species.

- Some U.S. beef breed associations are using or contemplating use of genomically-enhanced EPDs.
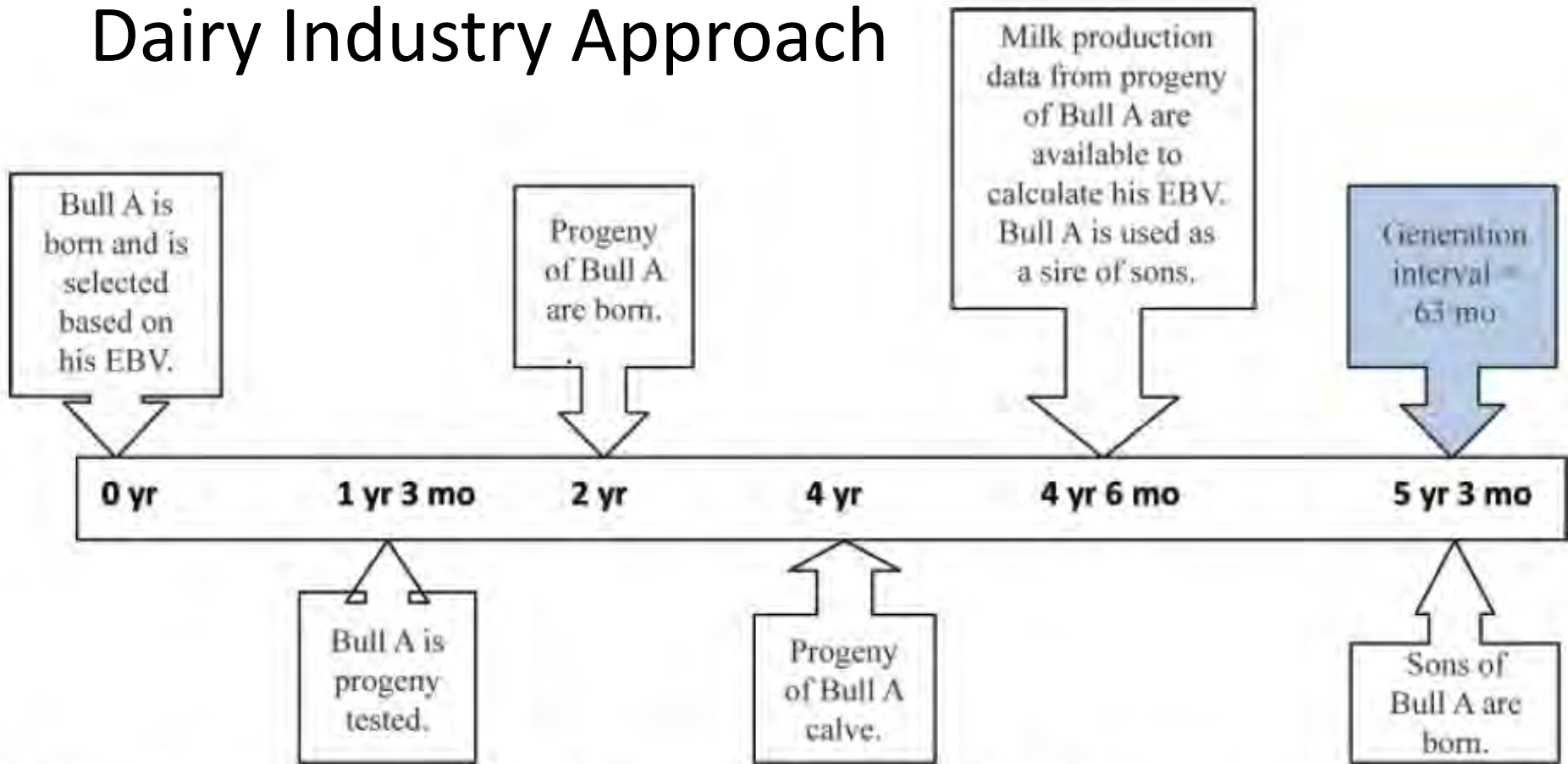
Dairy Industry Approach

Figure 1. Timeline of a traditional artificial insemination breeding program based on progeny testing. EBV = estimated breeding value.

Schefers and Weigel (2012) Animal Frontiers 2: 4-9.

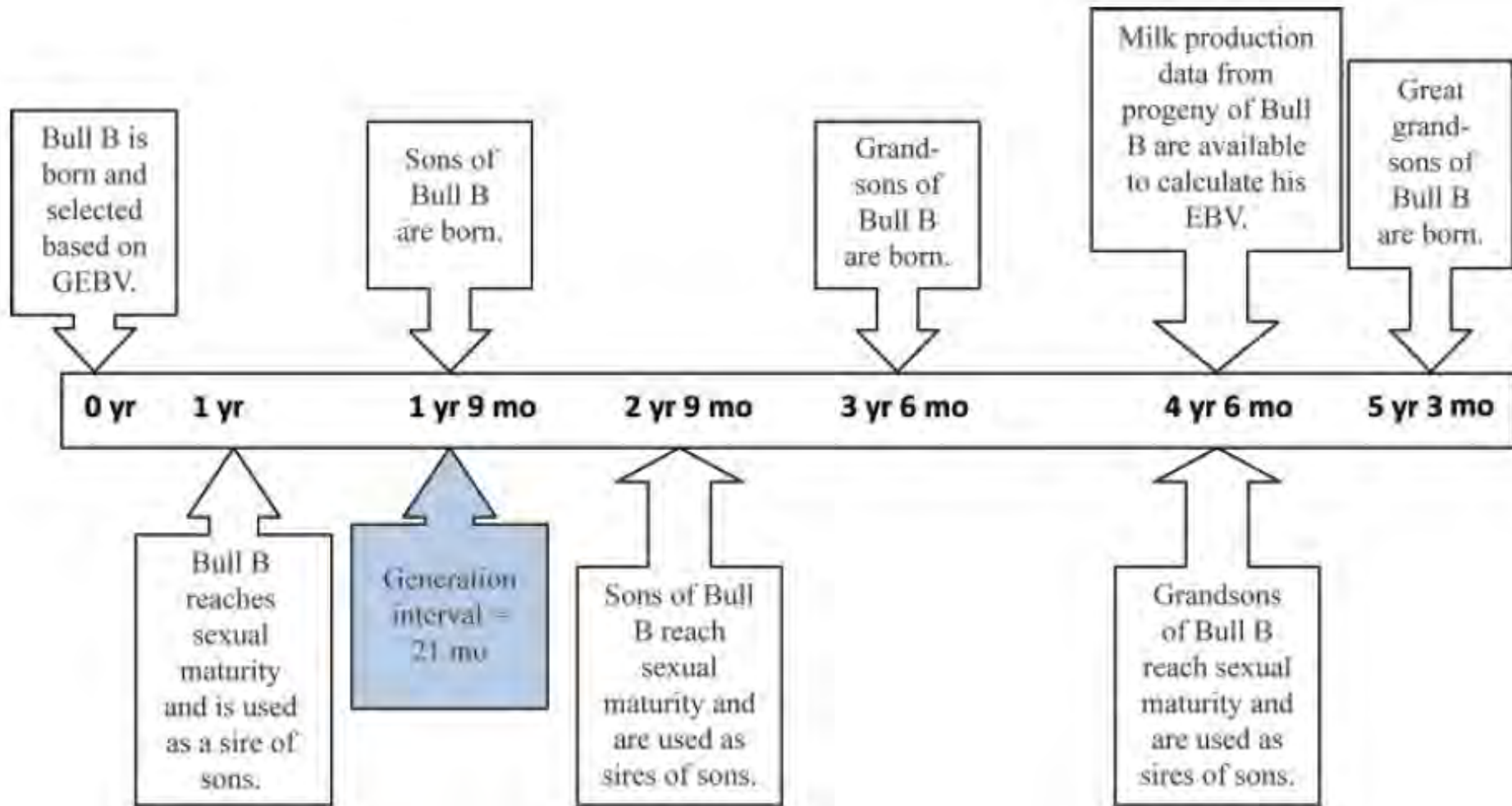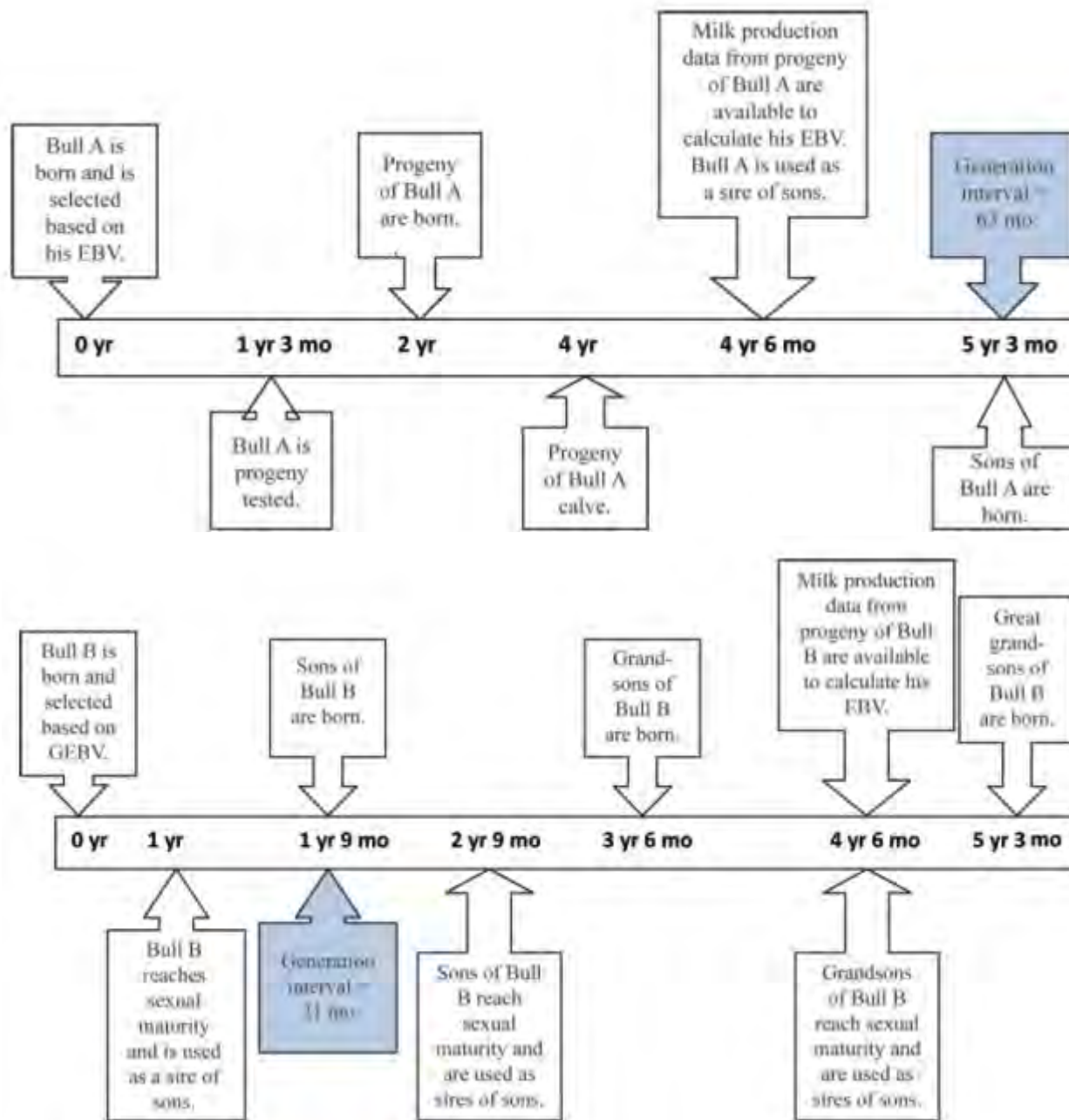# Dairy Industry Model for Genomic Selection and AI

Figure 2. Timeline of an aggressive artificial insemination breeding program based on the use of genomic bulls as sires of sons. GEBV = genomic estimated breeding value; EBV = estimated breeding value.

Bull A is born and is selected based on his EBV.

Progeny of Bull A are born.

Milk production data from progeny of Bull A are available to calculate his EBV. Bull A is used as a sire of sons.

Generation interval = 63 mo

| 0 yr | 1 yr 3 mo | 2 yr | 4 yr | 4 yr 6 mo | 5 yr 3 mo |

Bull A is progeny tested.

Progeny of Bull A calve.

Sons of Bull A are born.

Bull B is born and selected based on GEBV.

Sons of Bull B are born.

Grand-sons of Bull B are born.

Milk production data from progeny of Bull B are available to calculate his EBV.

Great grand-sons of Bull B are born.

| 0 yr | 1 yr | 1 yr 9 mo | 2 yr 9 mo | 3 yr 6 mo | 4 yr 6 mo | 5 yr 3 mo |

Bull B reaches sexual maturity and is used as a sire of sons.

Generation interval = 21 mo

Sons of Bull B reach sexual maturity and are used as sires of sons.

Grandsons of Bull B reach sexual maturity and are used as sires of sons.

Potential of 2 additional generations of selection in the same time frame.

The Decreasing Costs of Obtaining DNA Sequence

Human Genome	Bovine Genome	Early 2012	End of 2013	2014/2015
Took 13 years	Took 4 years	Sequence any genome	Sequence any genome	Sequence any genome
Cost $3.8 Billion	Cost $53 million	Cost $6,000	Cost $1,000	Cost $100
$3,800,000,000	$53,000,000	$6,000	$1,000	$100

The Decreasing Costs of Obtaining DNA Sequence

- *"The cost of obtaining DNA sequence is becoming so inexpensive and could become so prevalent that we have to use it."*

Which traits do we want genomics information on the most?

- Traits that hard to measure on individuals (feed intake/efficiency).

- Traits that are measured after the animal is dead (carcass traits).

- Traits that are evaluated over a long time (cow productivity and longevity).

- Traits where phenotype is hard to accurately measure (sub-clinical illness).

Questions to be asked about genomic tests or profiles

- How much is the performance difference between the genotypes?

- How much variation in the trait is accounted for by the markers?

- Has the test/profile been validated (evaluated in multiple cattle types/groups)?

Commercially Available DNA Services

- Many companies offer various cattle services
- Cost for DNA sire identification - $20 to $30
- Cost for genetic tests/genetic markers - $35 to $75
- Igenity and Zoetis offer a suite of genetic profiles.
- Costs per test will continue to go down
- Number of genetic markers will continue to go up

Cost of DNA Services

For DNA sequence several options are available:

- 50,000 SNP (50K) platform: $80 to $100 per animal
- 777,000 SNP High density (HD) platform: $140 to $160 per animal.

Some questions and considerations regarding use of current genomic selection strategies in beef cattle breeding

Current approaches do not fully account for gene pathways or networks that can affect phenotypes

Shear Force Cellular Components

TERM	ES[1]	NON[1]
Cell Junction	90	127
Cell Projection	115	155
Cell Projection Part	-	90
Cilium Part	14	-
Endomembrane System	-	16
Integral to Membrane	338	-
Intrinsic to Membrane	347	-
Ionotropic Glutamate Receptor Complex	-	13
Membrane	515	-
Membrane Part	404	-
Neuron Projection	58	-
Plasma Membrane	296	-
Plasma Membrane Part	165	-
Postsynaptic Density	26	32
Postsynaptic Membrane	32	44
Synapse	55	78
Synapse Part	63	84
Synaptic Membrane	39	52
Synaptosome	-	25

[1]Number of genes found for unique term by treatment, where "-" indicates no genes identified by that treatment

# Pathways to study shear force based on DNA markers

- ES & NON treatments identified **common** significant terms.

- Pathways showed that common terms were **not always significant in both treatments**, but were present in the pathways.
  - Treatments and corresponding significant enrichment term **identify genes to investigate** expression and characterization related to sensory characteristics.
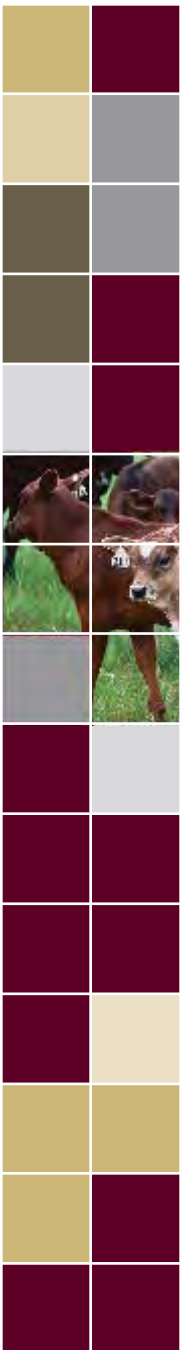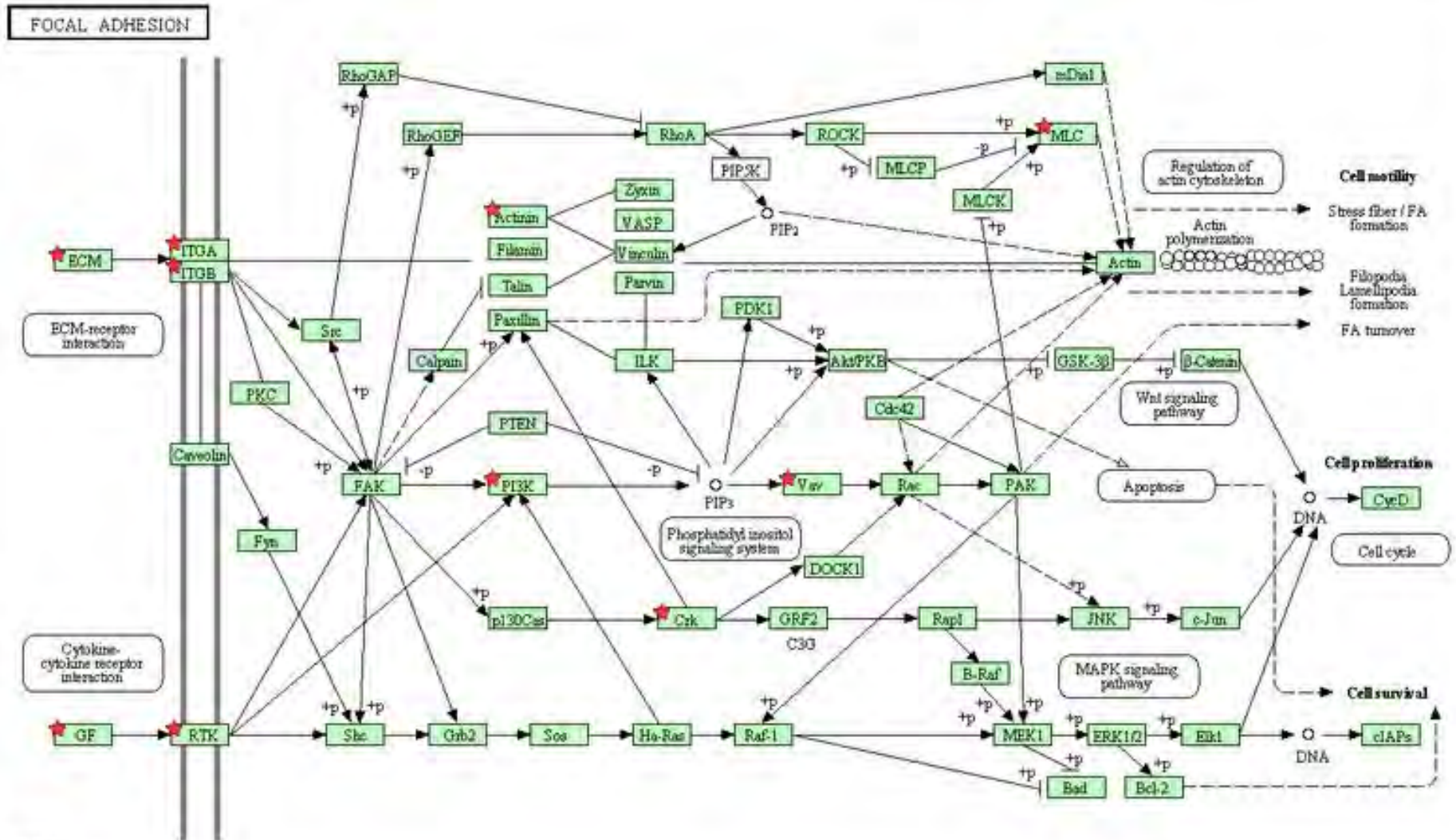
The same DNA sequence may not have the same expression of product
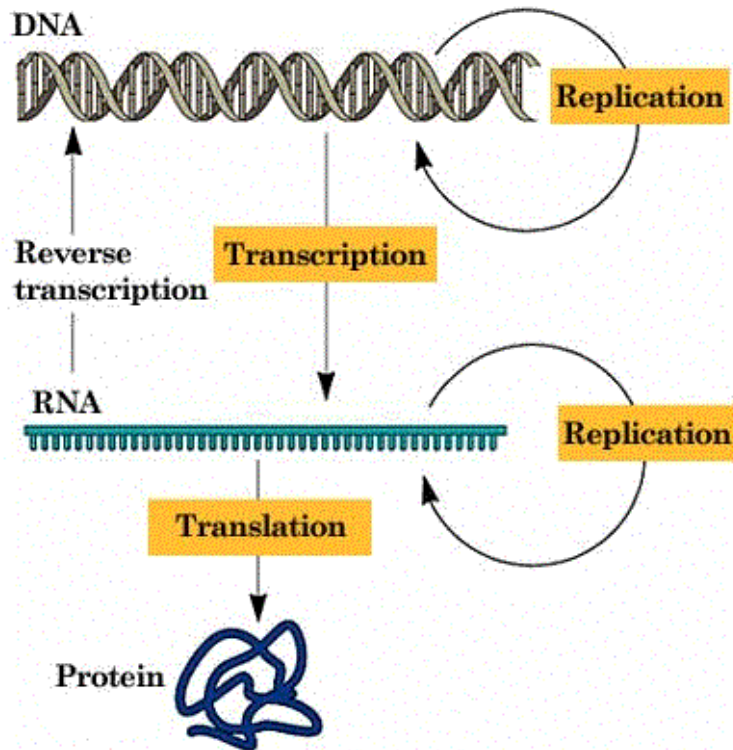
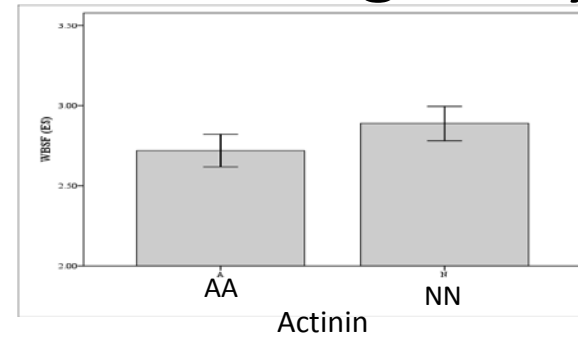mRNA (i.e. gene expression) profile for 15,000 genes for about $200 per animal.
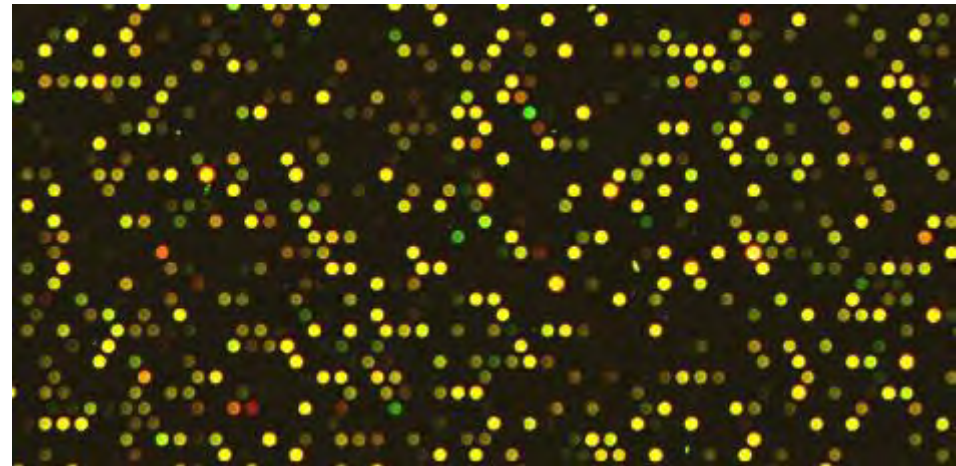
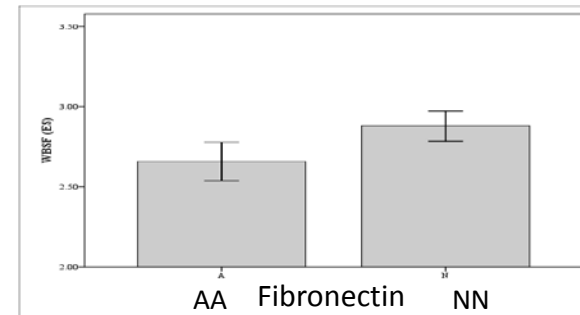# Expression pathway results for shear force

Study of some genes in ECM/Focal Adhesion Pathway combining expression and genotypes
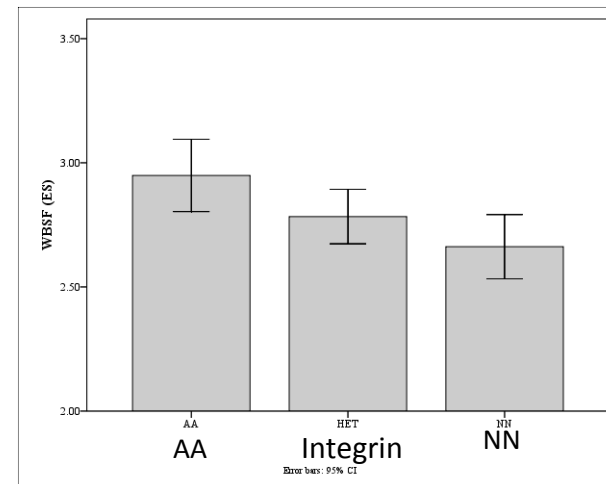
Angus: 5.5% lower WBSF (ES)

Systems-based approach allowed discovery of a pathway of genes that indicates a biological mechanism important for shear force that is different from calpain/calpastatin.

Angus: 7.0% lower WBSF (ES)


Nellore: 5.9% lower WBSF (ES)

Human field is becoming more focused on gene networks and systems as opposed to just DNA sequence analyses.

The role of non-traditional inheritance patterns (i.e. epigenetic influences) is a major effort of study in human health.

We know large non-traditional influences exist in *Bos indicus-Bos taurus* crosses.

Feed Efficiency Candidate Genes
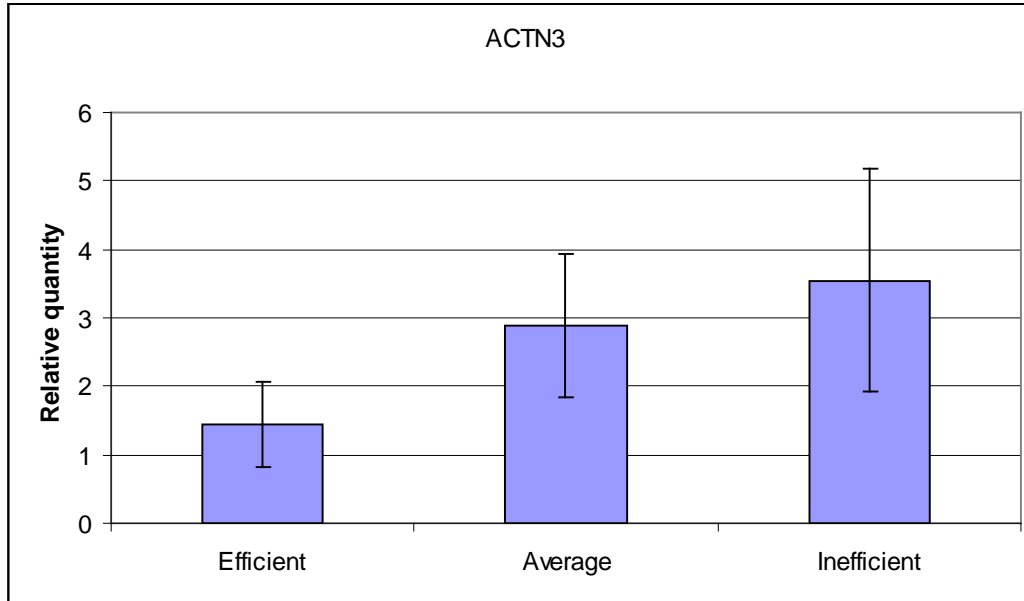
LOCUS	Mean MPRC	ACTN3	Phenotype
AA	1.76	1.99	Inefficient
NA	3.86	4.13	Inefficient
AN	-2.77	2.67	Efficient
NN	-4.09	2.62	Efficient

Big-picture Considerations

There is pressure for increased production per animal due to decreased cattle inventory, but consumers and retailers desire smaller portion sizes.

Big-picture Considerations

Rapid genetic improvement is a desire by many, but increased longevity of beef cows due to fertility is best way for commercial producers to make profit from replacement female investment.

Big-picture Considerations

The concept of local adaptation is important in all cow-calf operations and numerous accounts of genotype x environment interactions exist.

Promises from the past:

"If we were given a map of the chromosomes showing the locations of all important genes as well as convenient marker genes, what could we do with it?"
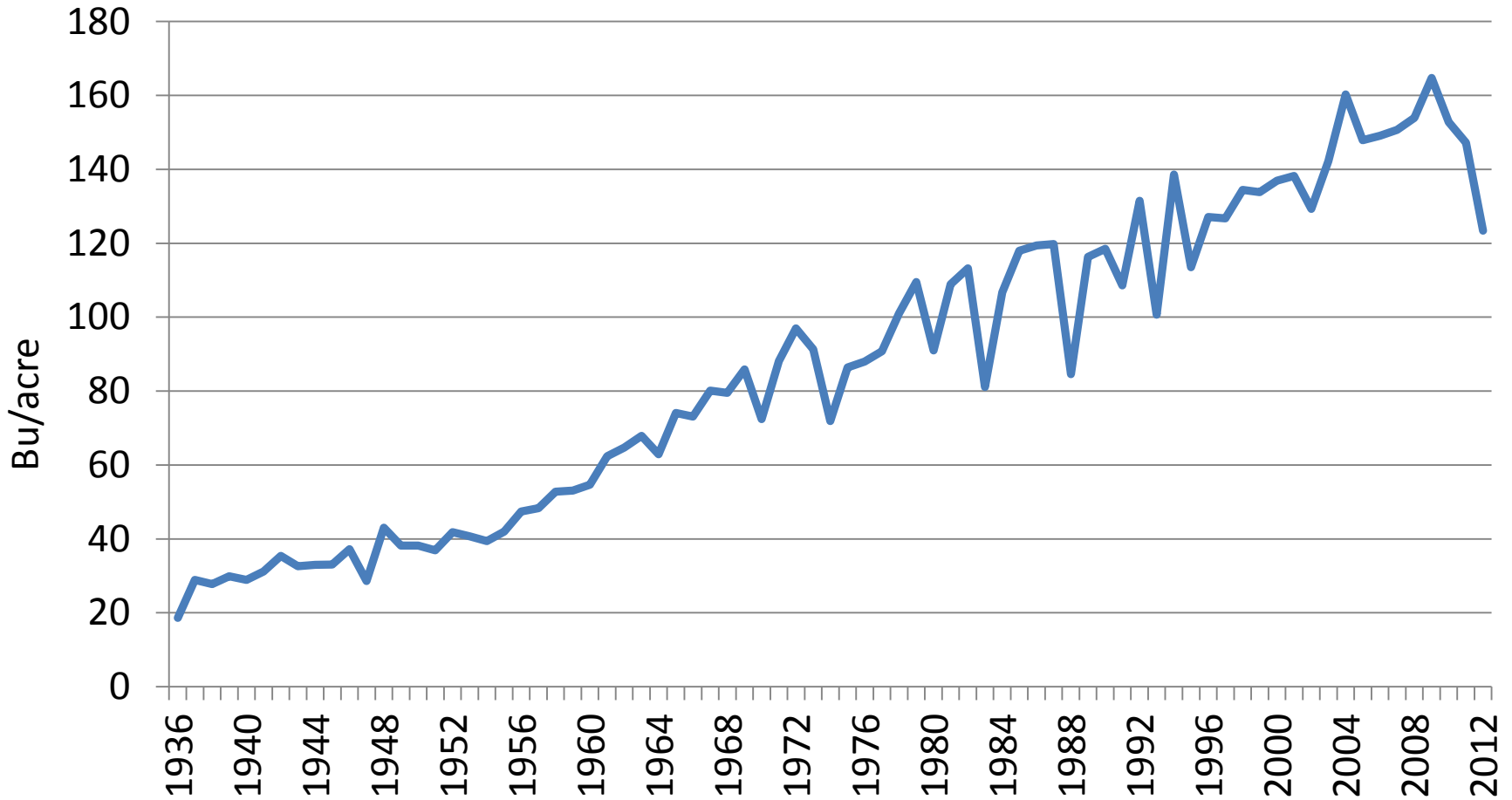
Sewall Wright, 1939

Promises from the past:

There needs to be less emphasis on "breeding better cattle," and more emphasis on "better cattle breeding."
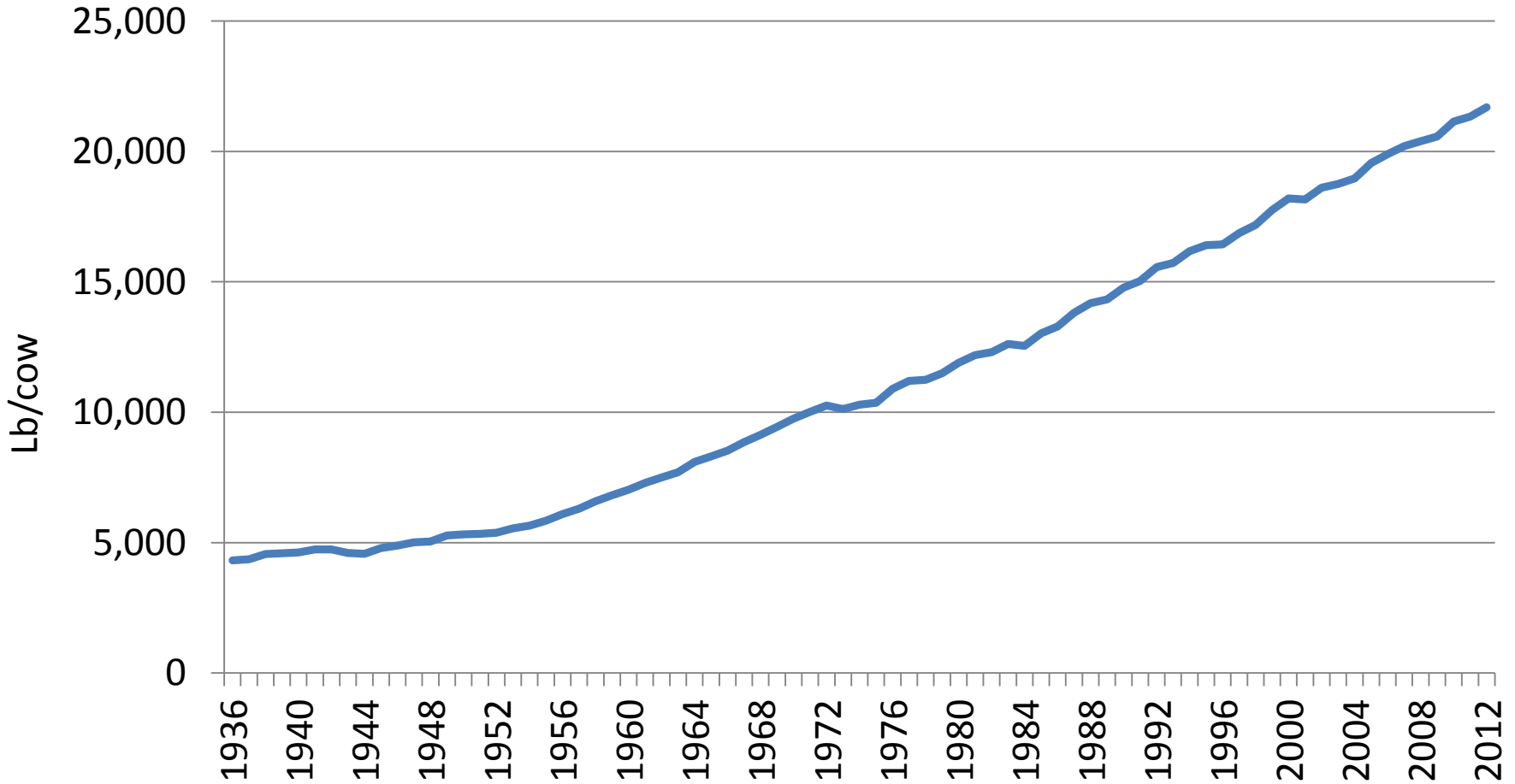
Tom Cartwright, 1970

U.S. Corn Yield 1936-2012

Data from USDA National Agricultural Statistics Service web site

U.S. Milk Production 1936-2012

Data from USDA National Agricultural Statistics Service web site
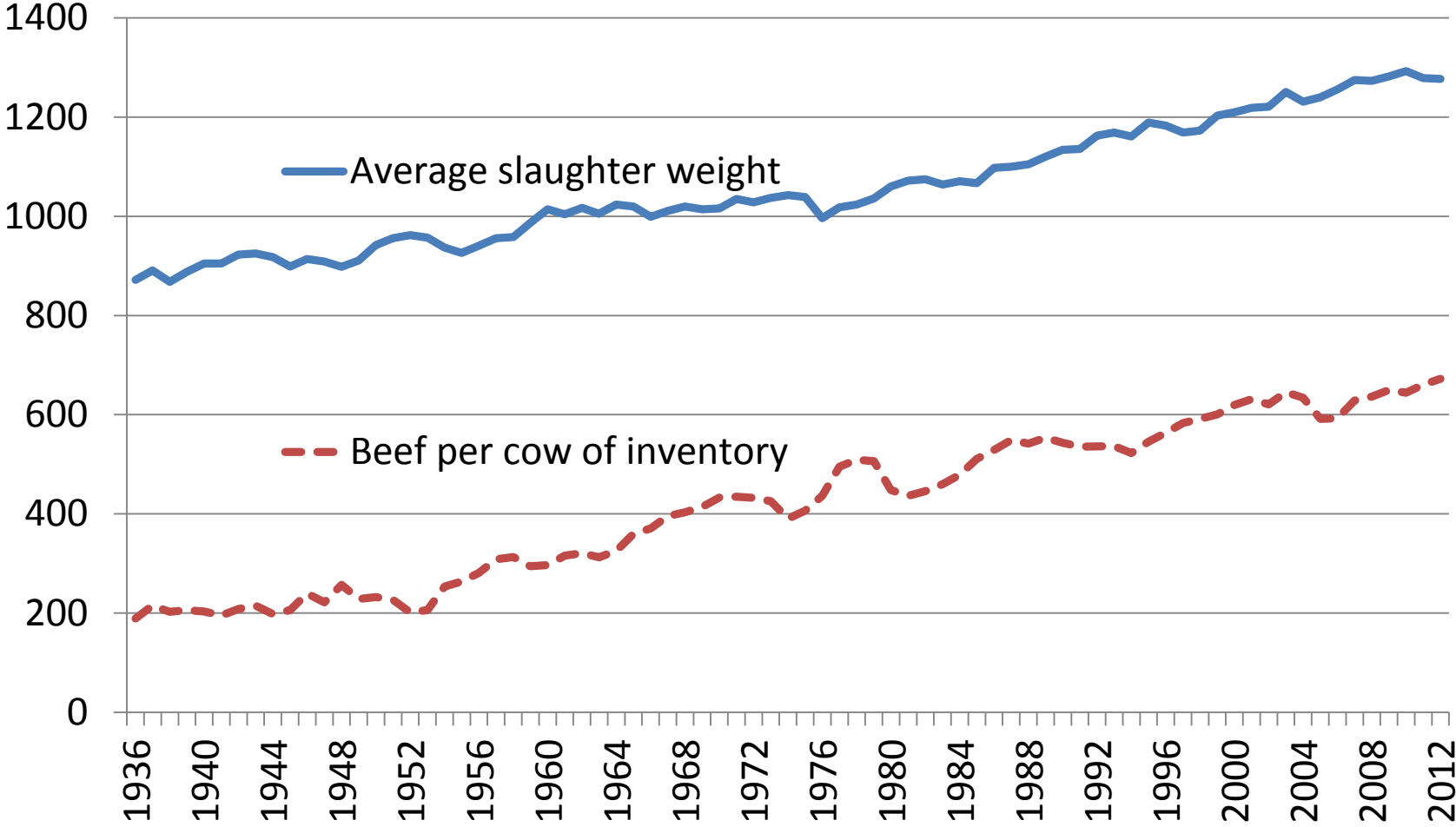
U.S. Beef Produced 1936-2012

Table 1. Comparisons of production levels across time in some agricultural species

Time	Corn (bu/ac)	Milk (lb/cow)	Slaughter weight (lb/animal)	Beef produced (lb) per cow inventory
1940	29	4622	905	195
1960	55	7029	1,004	316
1980	91	11,891	1,072	436
2000	137	18,197	1,219	632
2012	153*	21,697	1,277	672
Current* vs. 1940 (%)	528	469	141	345
Current* vs. 1980 (%)	168	182	119	154

*Current comparisons for corn based on 2010 year.

Looking to the future:

More genomics information will become available and cheaper, but it does not change the fundamental concepts of cattle breeding; it has potential to increase the rate of change dramatically.

Looking to the future:

Producers must maintain balanced approach to selection and know what traits (and what levels of performance) really make them money.
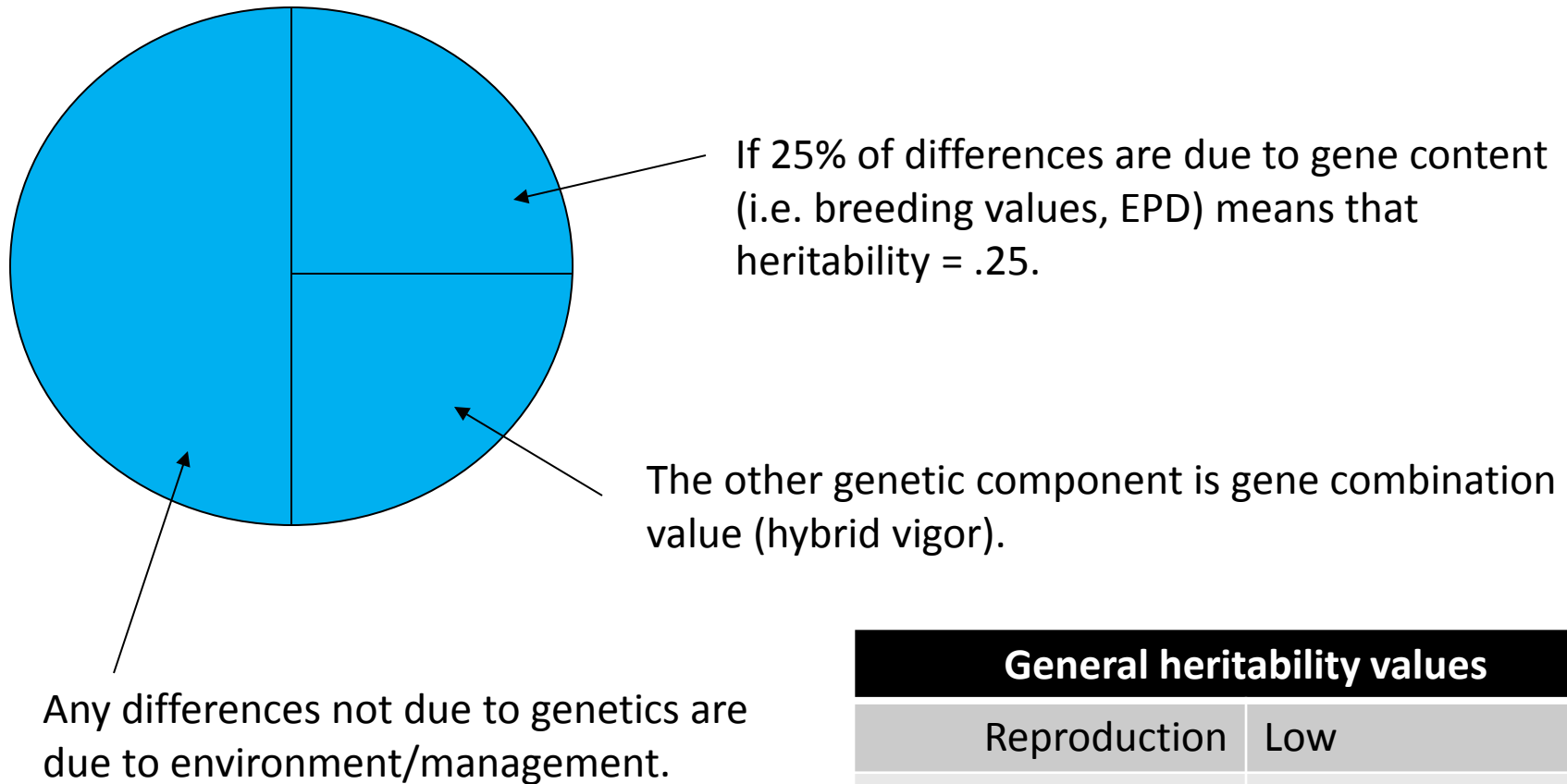
Looking to the future:

- Current genomics-based sire identification is cost-effective in most cases.
- Current genomics procedures are very useful for identification of tests for genetic diseases.

Looking to the future:

- The true potential value of genomics in beef cattle breeding and production is large, but remains to be fully understood.
- It will likely be used as part of a total system of information.

People want simple answers to complex questions.

Differences in performance of quantitative traits are due to different causes

If 25% of differences are due to gene content (i.e. breeding values, EPD) means that heritability = .25.

The other genetic component is gene combination value (hybrid vigor).

Any differences not due to genetics are due to environment/management.

General heritability values	
Reproduction	Low
Production	Moderate
Product	High