



BEEF TRANSLATIONAL GENOMICS: LESSONS FROM THE LITERATURE

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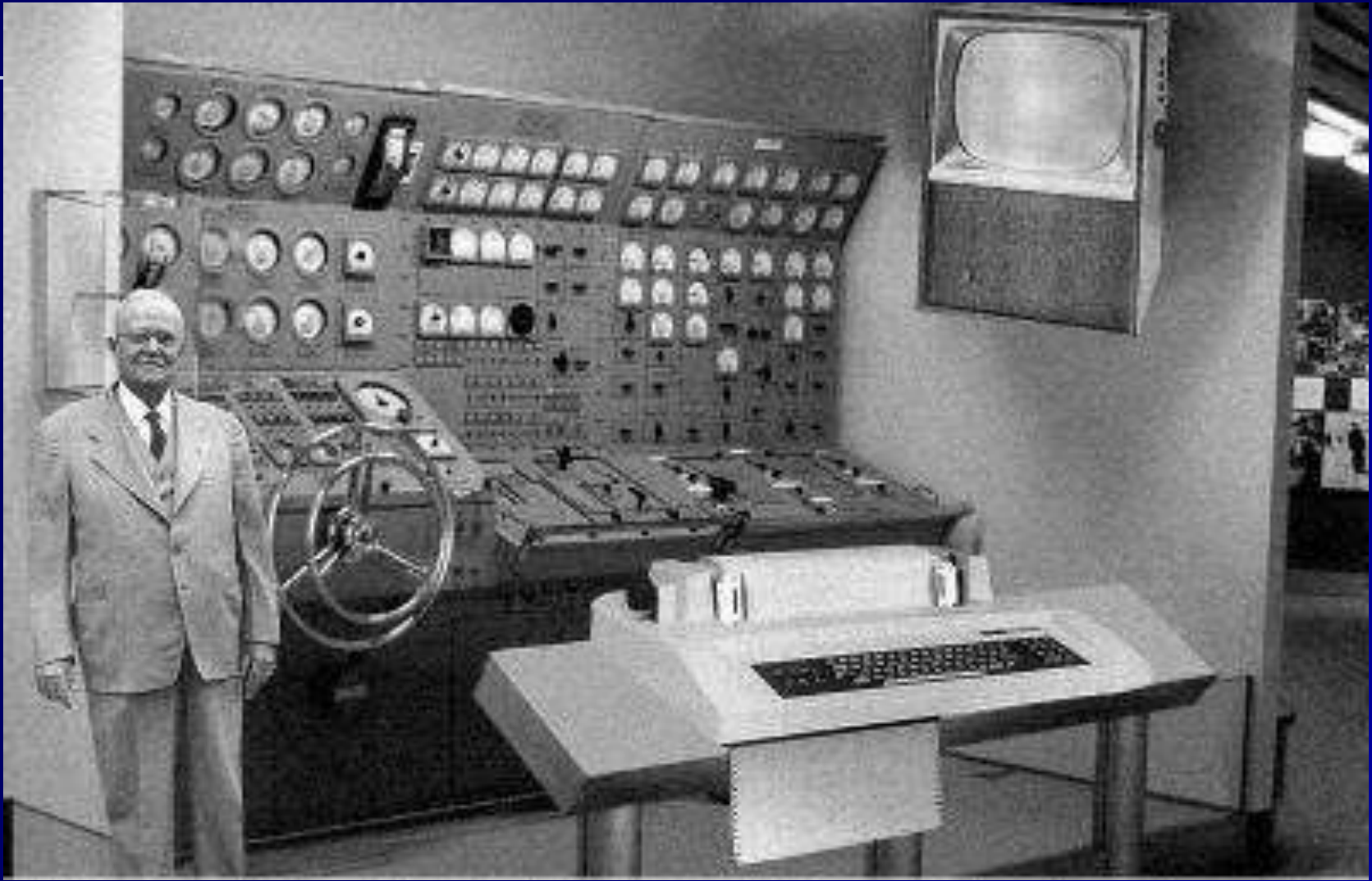
"Translational genomics" is defined as the adaptation of information derived from genome technologies for animal improvement

"We believe DNA marker profiles will become widely used in livestock in the near future as the cost decreases and the benefits increase. In fact, a major research objective may be to make best use of this DNA data in commercial animal production"

Goddard, M. E., and B. J. Hayes. 2007. Genomic selection. *Journal of Animal Breeding and Genetics* 124: 323-330.



“1954 version of what 'home computers' might look like in 50 years time (i.e. 2004)”





Wrong Expert Predictions

I think there's a world market for about five computers.

Thomas J. Watson, chairman of the board of IBM. 1943

There is no reason anyone would want a computer in their home.

Ken Olson, president of Digital Equipment Corp. 1977

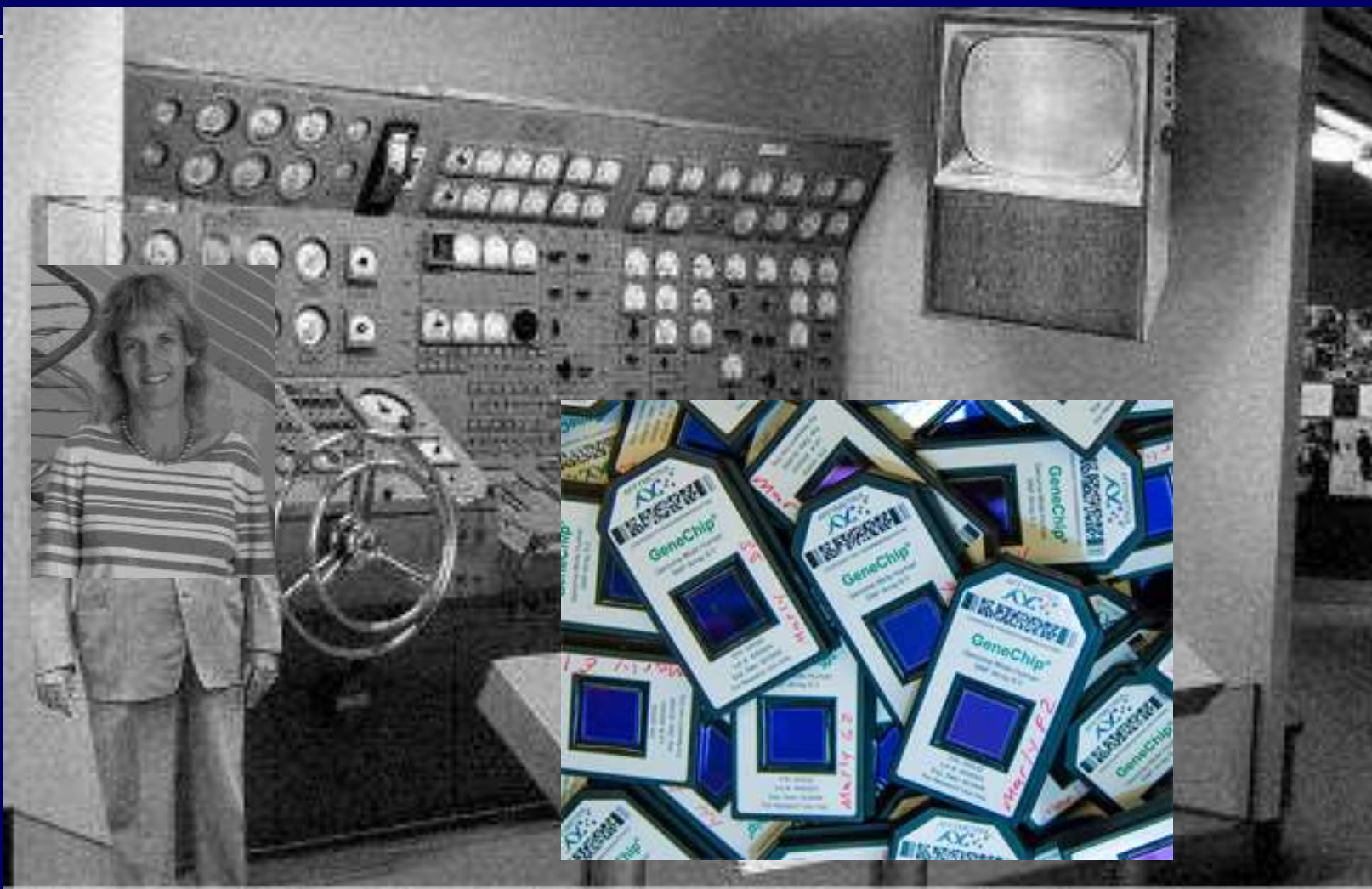
The cost for a genome scan (defined as 18 chromosomes* 7 markers (i.e. 126 markers!) * \$4/marker) = \$504

Ben Hayes and Mike Goddard, 2003. Evaluation of marker assisted selection in pig enterprises. Livestock Production Science 81:197-211.



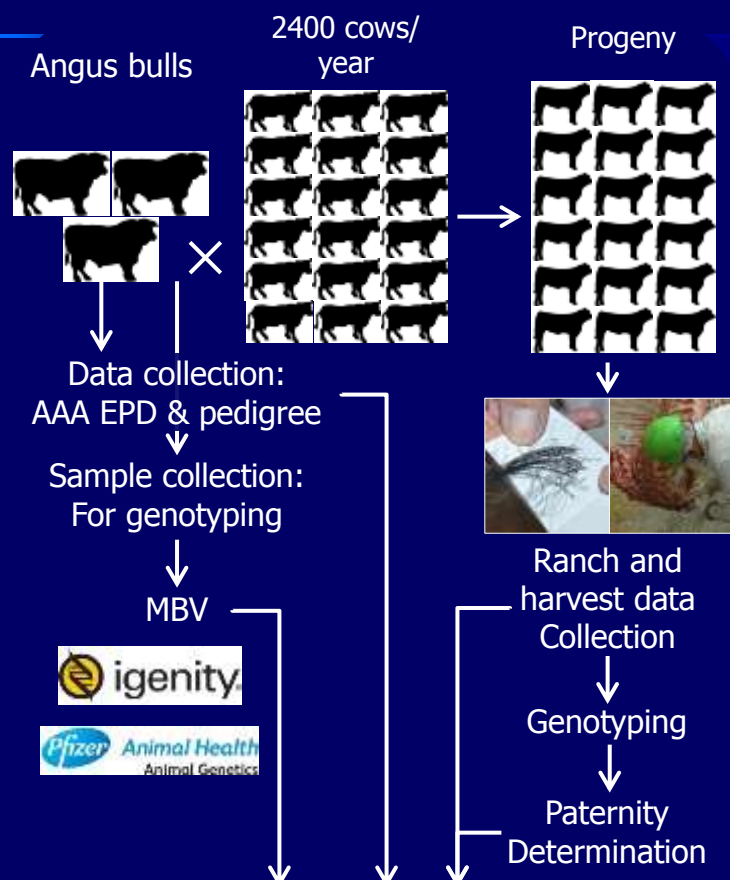


“what escaped their vision was that science might come up with new and different ways of commercializing and using new technologies.”





Ranch resources/collaborators on “Integrating DNA information into beef cattle production systems”



Four ranches:

- Cowley (900 cows)
- Kuck (500 cows)
- Mole-Richardson (700 cows)
- UC Davis (300 cows)

*Approximately 125 Angus
bulls, and 2,400 cows per
year on project*



United States Department of Agriculture
National Institute of Food and Agriculture

**Assessment of DNA-enabled approaches
for predicting the genetic merit of herd
sires on commercial beef ranches**



What does a California Commercial Ranch collaborator look like?



**Photo taken in 1949 at Red Bluff Bull Sale, CA
Generously provided by Cathy Maas from Crowe
Hereford Ranch, Millville, CA.**



Cowley Ranch



Kuck Ranch



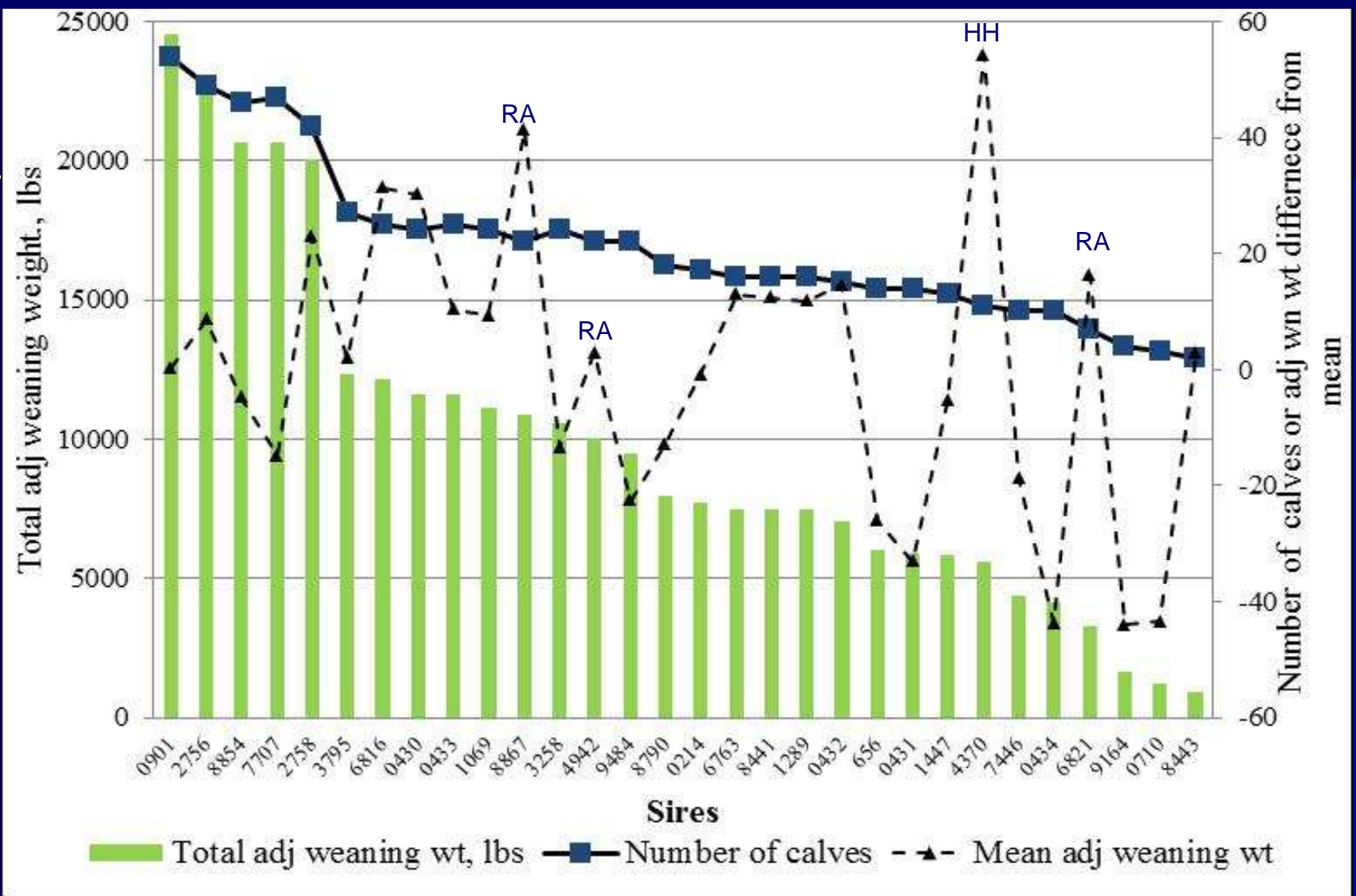


Mole-Richardson Farms





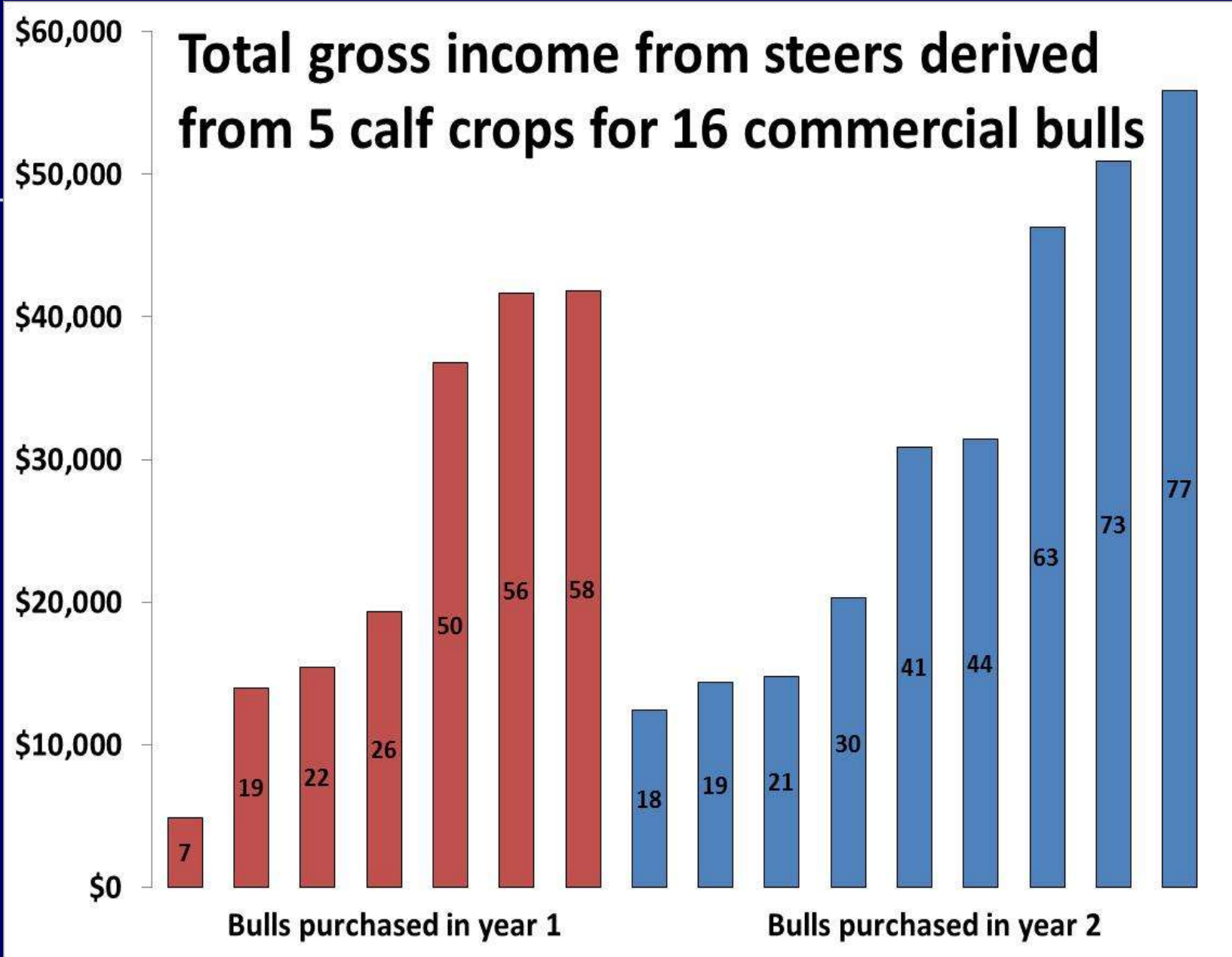
Output of 30 herd bulls total adjusted weaning weight, no. of calves and mean individual calf adjusted weaning weight



D.J. Drake, K.L. Weber, and A.L. Van Eenennaam. 2011. What are herd bulls accomplishing in multiple sire breeding pastures? Proceedings, Applied Reproductive Strategies in Beef Cattle



2004 (red) and 2005 (blue) born-bulls





A key issue in commercial situations is ease of DNA sampling, tracking and quality of resultant DNA





Translational considerations for migrating to SNPs for parentage

It is likely that SNP markers will replace alternatives (i.e. microsatellites) over the next 5 or so years

- How do you switch over from microsatellites to SNPS when a lot of historical information is stored as microsatellites?
- Which SNP genotyping platform should be used and how many and which SNP markers should be included in the panel?
- What should be the number of compared loci cutoff in the case of incomplete genotyping?
- How many exclusions (as a function of number of compared loci) should be allowed to account for genotyping errors – platform dependent?
- Which sample type works best for producers to collect and genotyping entities to run?





Genetic Abnormalities

Images from an article by David S. Buchanan, Department of Animal Sciences, North Dakota State University

<http://www.ag.ndsu.edu/williamscountyextension/livestock/genetic-defects-in-cattle>





Compare dwarfism response in the 50s to the response to curly calf (AM)



An early '50's advertisement that superimposed a measuring stick in the picture of this bull who was nick-named "Short Snorter."

Based upon his height and age, he was less than a frame score 1.

Image from <https://www.msu.edu/~ritchieh/historical/shortsnorter.jpg>



Estimates of US and Australia genetic testing costs (Angus)



	US	AUSTRALIA
AM	113,526	12,021
NH	77,067	9,936
CA	28,837	2,532
TOTAL NUMBER	294,054	34,991
COST (@ \$25/test)	7,351,350	874,775

Numbers kindly shared by Bryce Schumann, American Angus Association;
and Carel Teseling, Angus Australia



Genetic implications of recessive genetic factors

"Carrier animals....their overall breeding value worth may outweigh the economic value of carrier status"

Chalier C. et al. (2008) Highly effective SNP-based association mapping and management of recessive defects in livestock. *Nature Genetics* 40:449-454

Should the market decide or should this choice be directed by industry (e.g. disallowing registration of known carriers)?





The percentage of possible AM, NH, and CA carriers born in Angus Australia, 2004-2010

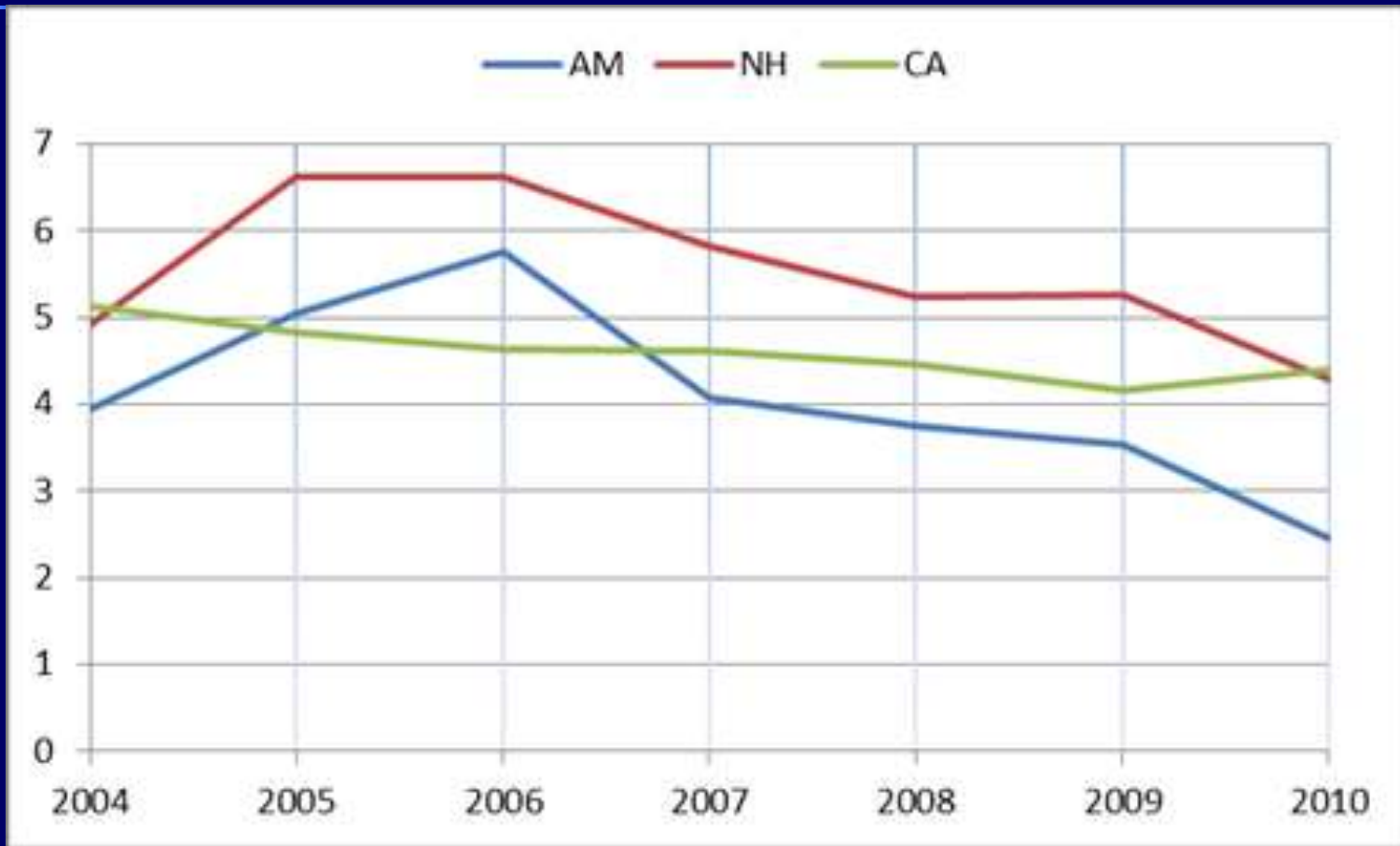


Figure courtesy of Carel Teseling, Angus Australia



Early extension education about dwarfism explaining carriers and inheritance

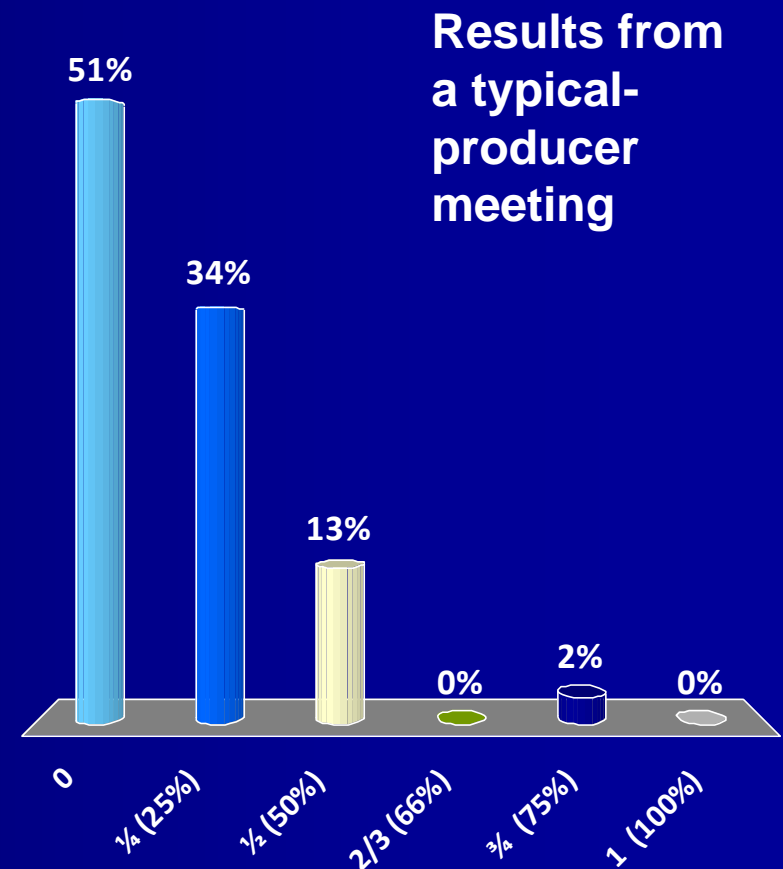


Image from Special Collections University Libraries, Virginia Tech:
<http://spec.lib.vt.edu/imagebase/agextension/boxseven/screen/AGR3618.jpg>



If you breed a curly calf carrier cow (AMC) to an curly calf free bull (AMF), what is the chance that the offspring will be stillborn as a result of being curly calf?

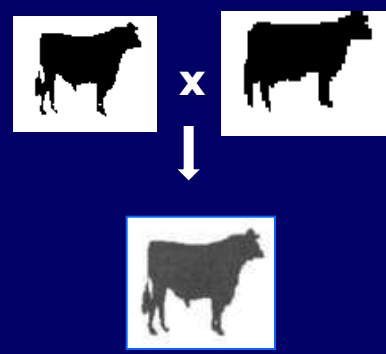
1. 0
2. $\frac{1}{4}$ (25%)
3. $\frac{1}{2}$ (50%)
4. $\frac{2}{3}$ (66%)
5. $\frac{3}{4}$ (75%)
6. 1 (100%)



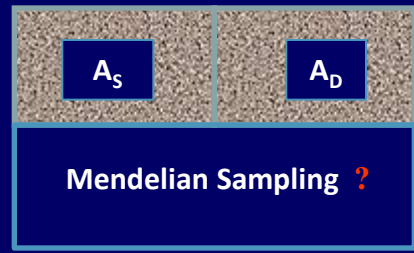


The promise of genomic selection for the dairy industry

Young sire
Parent Average

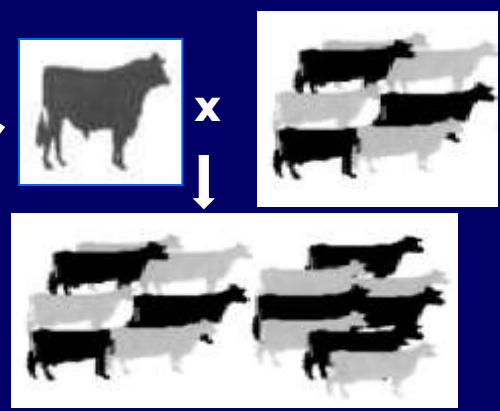


Birth

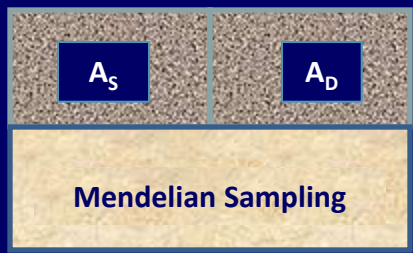


Accuracy **0.20**

Young sire
Progeny Test

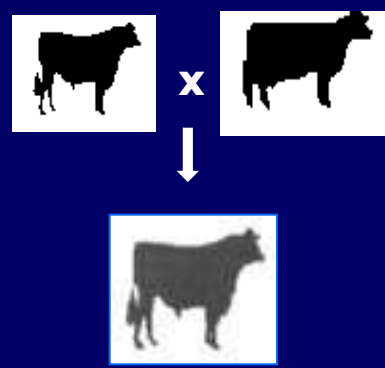


5 years; >>>> cost

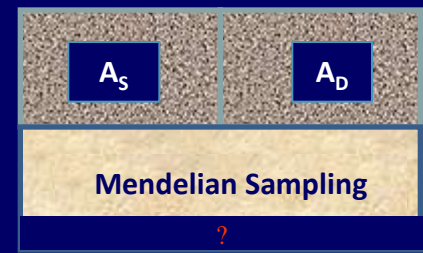


Accuracy **0.80**

Young sire
Genomic
Selection



Birth; <<<< cost



Accuracy **0.65**



Dairy industry suited to WGS

- High use of AI
- Clear selection goal
- One breed used extensively
- Large number of high accuracy A.I. sires for training
- Extensive, uniform collection of data on traits
- Central evaluation (AIPL) receiving genotypes
- Obvious way to increase rate of genetic gain
- AI companies funding the genotyping because they get a clear cost savings in terms of young sire program





Translational Questions for other animal industries

- ? How many phenotypic records are required in the initial experiment estimating the effect of chromosome segments?
- ? How many markers are needed— 50K, 800K, whole genome?
- ? How does the relationship between the training population and the selection candidate affect accuracy?
- ? How often do chromosome segment effects need to be re-estimated?
- ? Do predictions work across breeds?
- ? What is the value generated by the increased accuracy?
- ? Does this technology change optimal breeding program design?



Accuracy of the prediction equation proportional to:

$$\frac{Th^2}{N_eL}$$

T: total number of animals in the training population

h^2 : heritability of the trait

L : length of chromosomes (in Morgans)

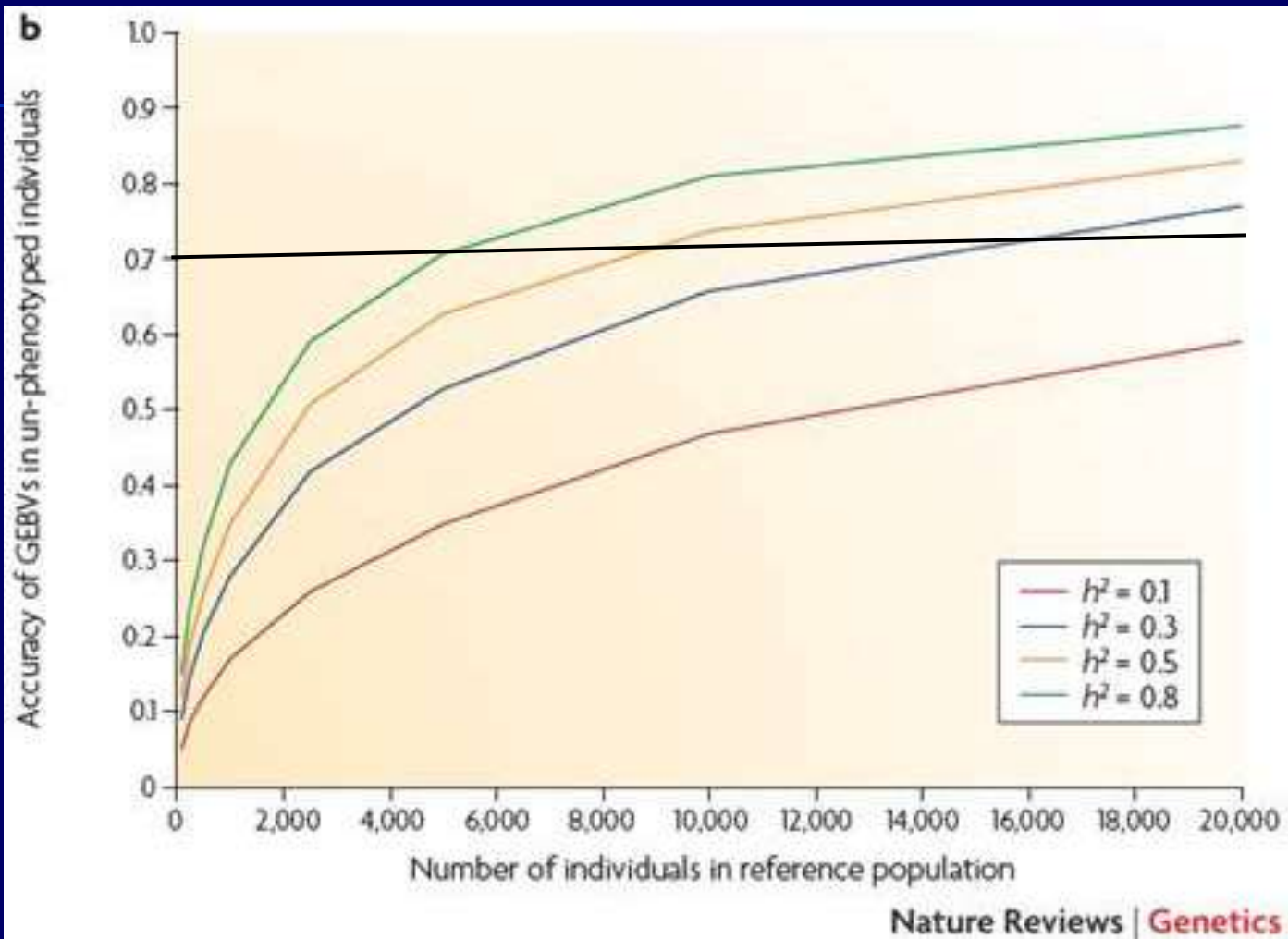
N_e : effective population size

Also influenced by trait architecture, number of markers, availability of economically-relevant phenotypes, and relationship between animals in the training and target population





Effect of number of animals on accuracy of prediction equation (for a N_e of 100)



Goddard, M. E., and B. J. Hayes. 2009. Mapping genes for complex traits in domestic animals and their use in breeding programmes. *Nature Reviews Genetics* 10: 381-391.



Effective population size estimates for cattle

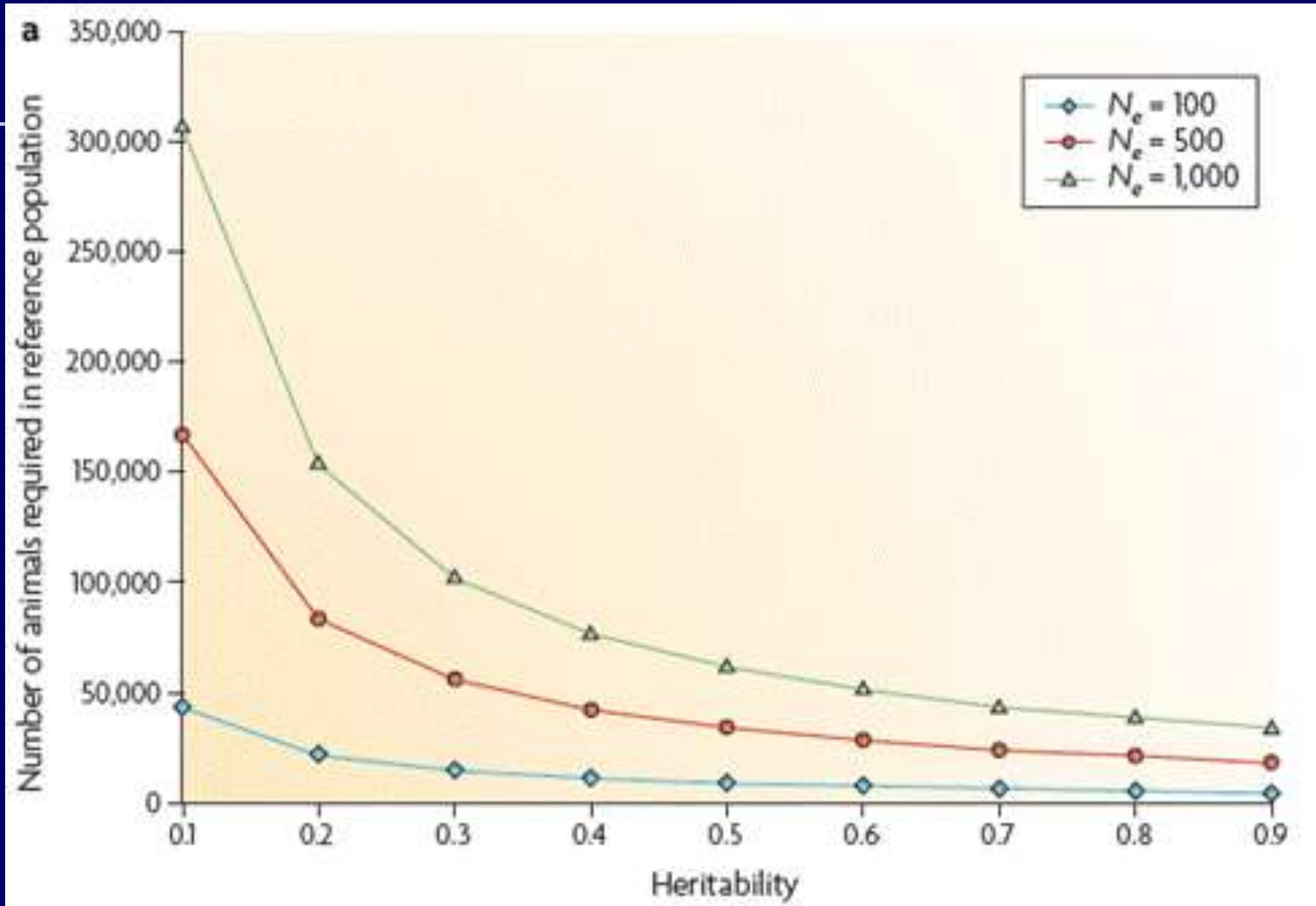


Breed	N _e	Breed	N _e
Angus	136	Brown Swiss	61
Charolais	110	Guernsey	76
Hereford	97	Holstein	99
Limousin	174	Jersey	73
Red Angus	85	Norwegian Red	106
Brahman	115	Gir	133
Nelore	86		
Beef Master	106	Merino (sheep)	~ Big (> 100) Ben Hayes (pers. comm.)
Santa Gertrudis	107		

Genome-Wide Survey of SNP Variation Uncovers the Genetic Structure of Cattle Breeds. 2009 The Bovine HapMap Consortium. Science 3245: 528-532. Supporting Online Material. Table S1. <http://www.sciencemag.org/content/suppl/2009/04/22/324.5926.528.DC1>



Effect of population size and heritability on the number of animals required in the training population (for an accuracy of 0.7)

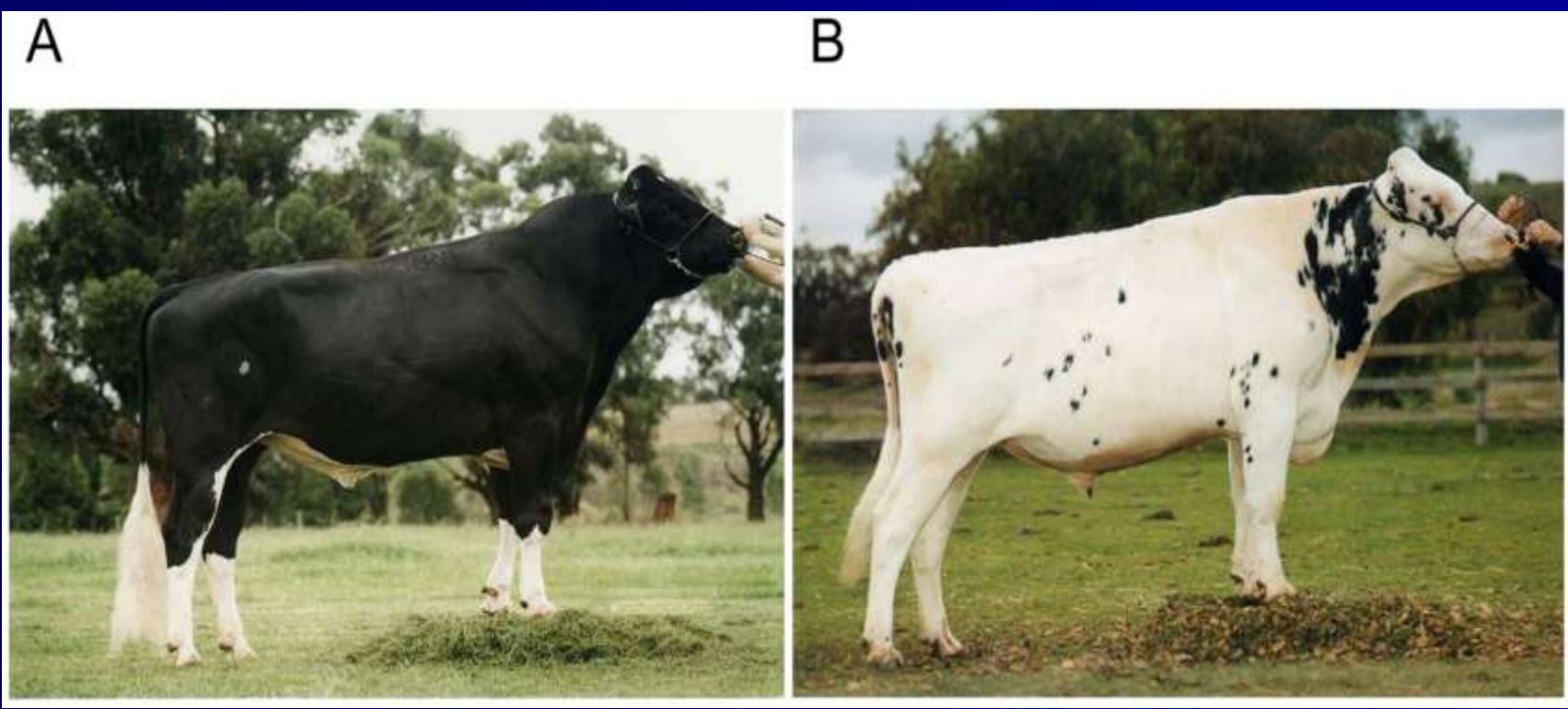


Goddard, M. E., and B. J. Hayes. 2009. Mapping genes for complex traits in domestic animals and their use in breeding programmes. *Nature Reviews Genetics* 10: 381-391.



There is also an effect of trait architecture

The accuracy of predicting genetic values is higher for traits with a proportion of large effects (e.g. proportion black and fat percentage) than for a trait with no loci of large effect (e.g. overall type), provided the method of analysis takes advantage of the distribution of loci effects.



Hayes, B. J., J. Pryce, A. J. Chamberlain, P. J. Bowman, and M. E. Goddard. 2010. Genetic Architecture of Complex Traits and Accuracy of Genomic Prediction: Coat Colour, Milk-Fat Percentage, and Type in Holstein Cattle as Contrasting Model Traits. Plos Genet 6



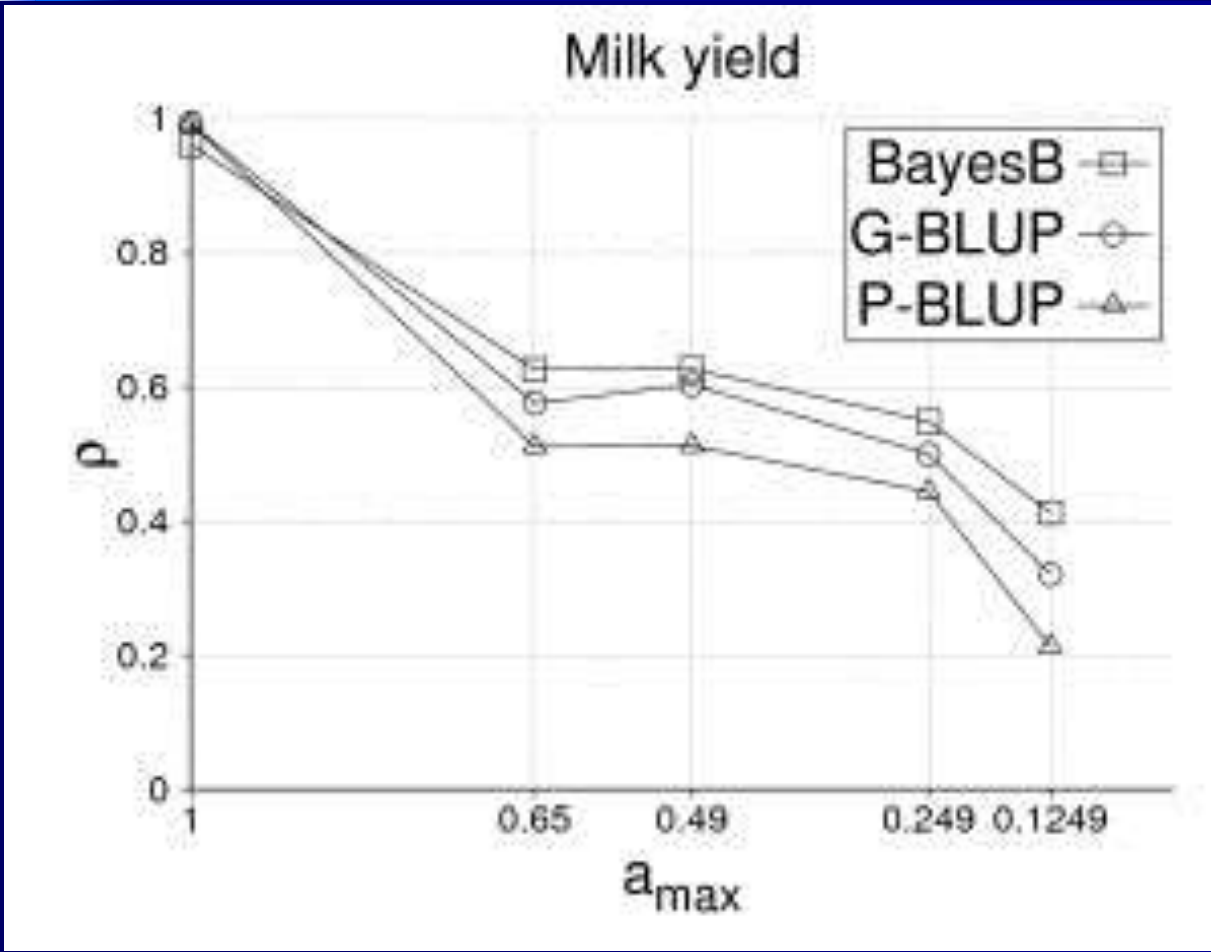
Maybe R.A. Fisher was onto something?



If a nearly infinitesimal model is correct as seems to be the case for most quantitative traits; then large training populations will be needed to achieve high accuracy



Markers can predict family relationships between animals, independently of LD between the markers and QTL (i.e. due to family relationships or linkage)

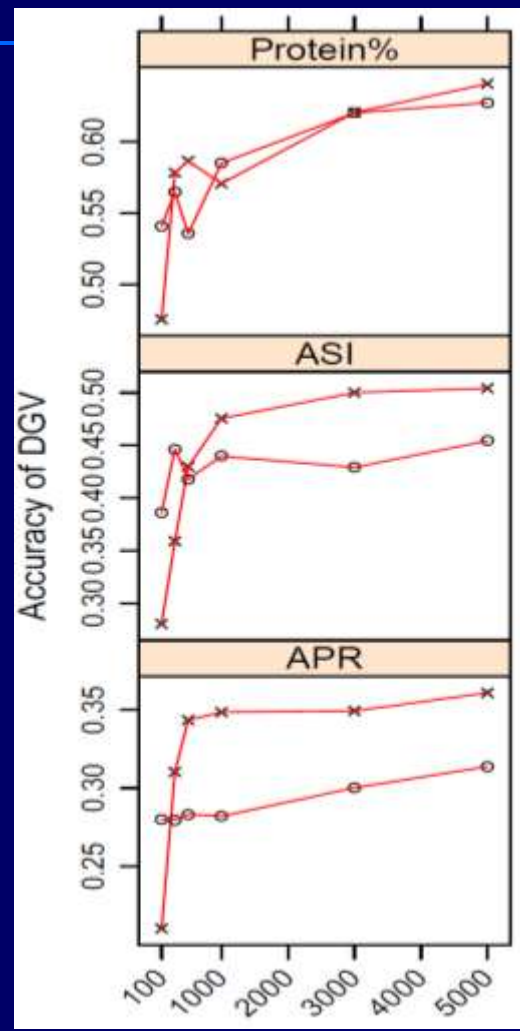


Additive-genetic relationships between training and validation animals was found to be a good indicator of accuracy



Reduced SNP panels: Accuracy of direct genomic value (DGV) of dairy bulls using subsets of 5,000 or less of best SNP for each trait

Accuracy



Number of SNP

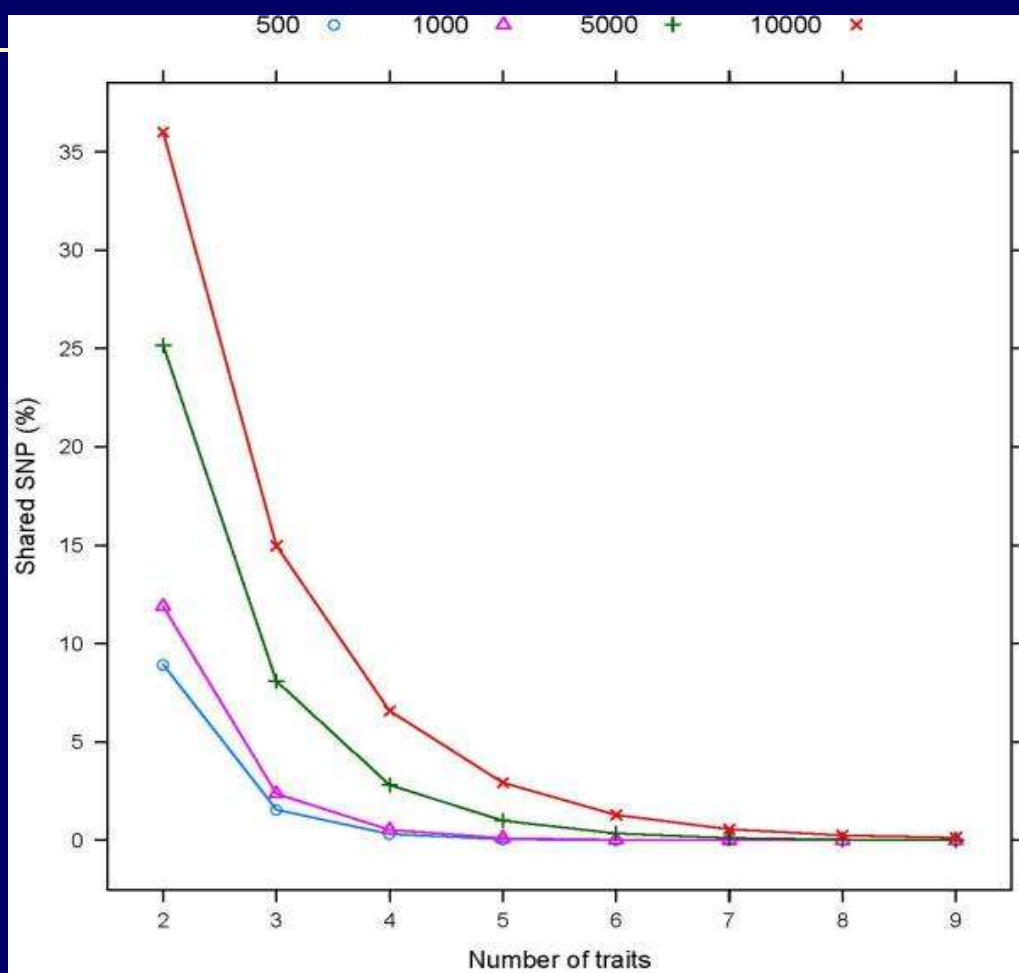
Traits :
Protein %
ASI (Australian Selection Index)
APR (Australian Profit Rank)

Predictions based on <1,000 SNP panels were very sensitive to the selection method and tended to be low accuracy

Moser, G., M. S. Khatkar, B. J. Hayes, and H. W. Raadsma. 2010. Accuracy of direct genomic values in Holstein bulls and cows using subsets of SNP markers. Genetics Selection Evolution 42.



Reduced SNP panels: Percentage of the highest ranked SNP that are shared between sets of traits* for subsets including 500, 1,000, 5,000 or 10,000 SNP



*** Dairy traits included:**

1. Protein
2. Protein %
3. Survival
4. Fat %
5. Milk
6. Overall Type
7. APR (Australian Profit Rank)
8. ASI (Australian Selection Index)
9. Fat

Few SNPs were in common between the trait-specific subsets



The literature tells us that test accuracy will be higher when:

- Small effective population size so small number of chromosome segments to track
- Small number of QTL effecting the trait so there is a marker associated with every QTL
- High density of makers
- Trait is highly heritable
- A large number of animals and high-quality phenotypic records available for training
- There are genetic relationships (linkage) between training and selection candidates





Other relevant interesting findings with practical implications

- If markers are picking up family relationships (linkage), then the accuracy of marker-based selection will decay over generations within breed
- Prediction equations derived in one breed do not predict accurate GEBVs when applied to other breeds
- To find markers that are in LD with QTL across diverged breeds, such as Holstein, Jersey, and Angus, will require high density SNPs (>300,000 markers)
- Combining breeds into one large multi-breed reference population gives reasonable accuracies in purebreds
- Few of the "best" markers for one trait are common to another







The Beef Cattle Industry

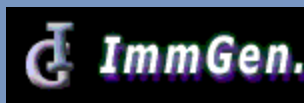


- Little use of AI
- Relatively few high accuracy sires for training
- Multiple competing selection goals – cow/calf, feedlot, processor – little data sharing between sectors
- Few/no records on many economically-relevant traits
- Many breeds, some small with limited resources
- Crossbreeding is important





What commercial products are out there for beef cattle producers?



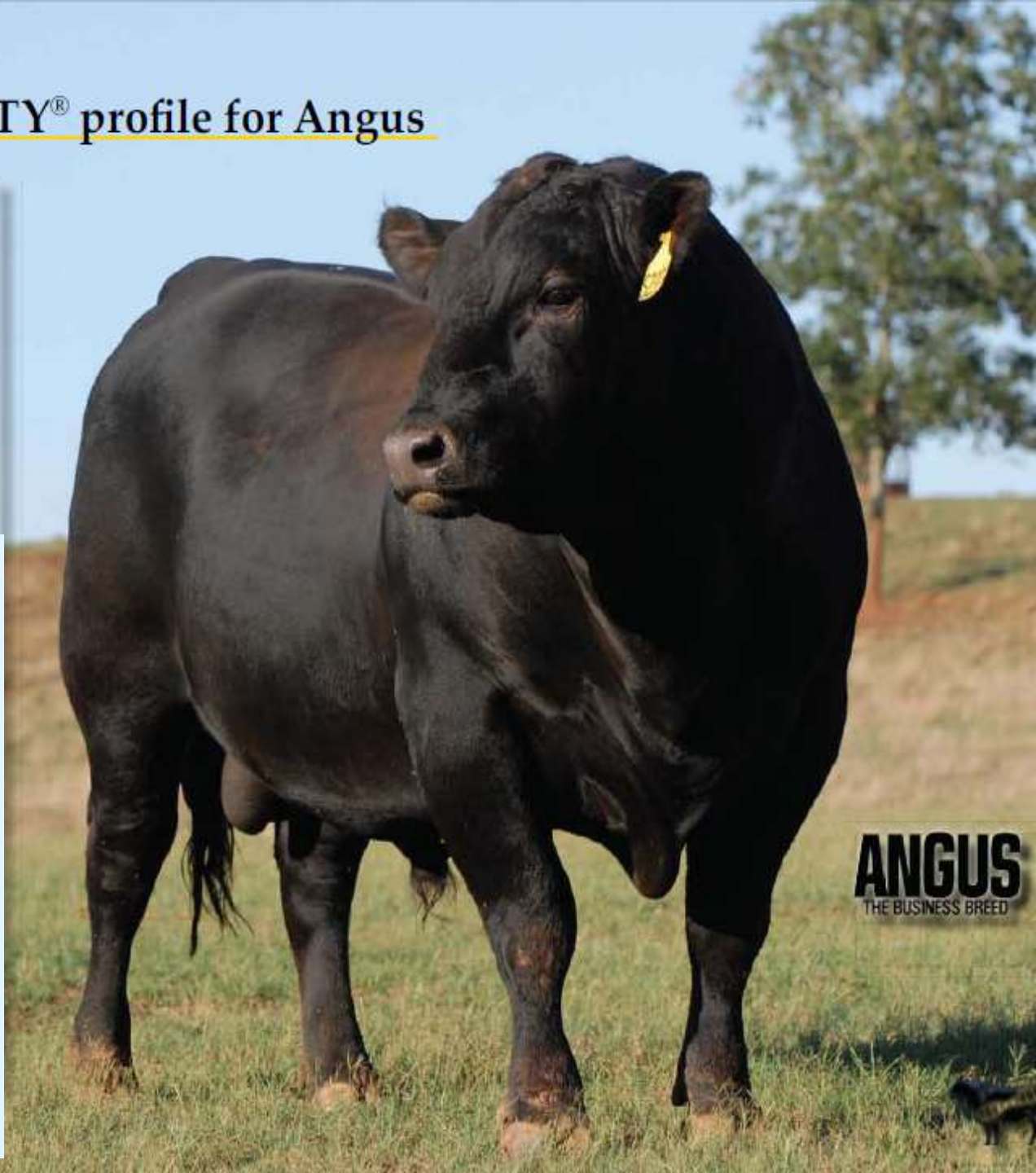
The Power of the IGENITY[®] profile for Angus

The American Angus Association[®] through its subsidiary, Angus Genetics Inc.[®] (AGI), has a vision to provide Angus breeders with the most advanced solutions to their genetic selection and management needs.

Genomic-enhanced Expected Progeny Differences (EPDs) can now be calculated for your animals using the highly predictable American Angus Association database along with IGENITY[®] profile results to provide a more thorough characterization of economically important traits and improved accuracy on young animals.

Using the IGENITY profile for Angus, breeders receive comprehensive genomic results for multiple, economically important traits.

1. Dry Matter Intake
2. Birth Weight
3. Mature Height
4. Mature Weight
5. Milk
6. Scrotal Circumference
7. Weaning Weight
8. Yearling Weight
9. Marbling
10. Ribeye Area
11. Fat Thickness
12. Carcass Weight
13. Tenderness
14. Percent Choice (quality grade)
15. Heifer Pregnancy
16. Maternal Calving Ease
17. Direct Calving Ease
18. Docility
19. Average Daily Gain
20. Feed Efficiency
21. Yearling Height
22. Scrotal Circumference



ANGUS
THE BUSINESS BREED

Lead Today with 50K

1. Birth weight
2. Weaning weight
3. Weaning maternal (milk)
4. Calving ease direct
5. Calving ease maternal
6. Marbling
7. Backfat thickness
8. Ribeye area
9. Carcass weight
10. Tenderness
11. Postweaning average daily gain
12. Daily feed intake
13. Feed efficiency (net feed intake)



Pfizer Animal Health
Animal Genetics

50K SNP chip assays
50,000 SNPs spread
throughout genome





American Angus Association performs weekly evaluations with genomic data



	Igenity	Pfizer
Calving ease (CED)	✓	✓
Growth (BW WW YW Milk)	✓	✓
Residual Average Daily Gain (RADG)	✓	✓
Docility (DOC)	✓	
Carcass (CWT MARB RIB FAT)	✓	✓

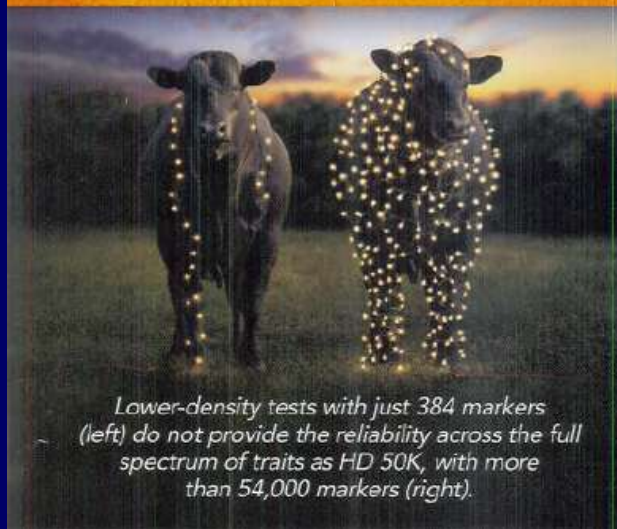
<http://www.angus.org/AGI/GenomicChoice070811.pdf> (updated July 7, 2011)



So the question I get asked a lot is:



Which Genomic Test is Best?



Lower-density tests with just 384 markers (left) do not provide the reliability across the full spectrum of traits as HD 50K, with more than 54,000 markers (right).

Now, thanks to High-Density (HD) 50K genomic technology for Angus, you can more dependably predict the genetic merit of young animals, before progeny information is available. But, what makes this genomic test superior?

High density vs. low density

The HD 50K platform includes more than 54,000 DNA markers, significantly more than IGENITY®, which utilizes only 384 markers. With greater coverage of the genetic makeup of Angus animals, no other DNA test provides more dependable predictions of genetic potential than HD 50K.



Genetic correlations for National Cattle Evaluation traits by company



384 SNP

50K SNP

	Igenity	Pfizer
Calving Ease Direct	.47	.33
Birth Weight	.57	.51
Weaning Weight	.45	.52
Yearling Weight	.34	.64
Milk	.24	.32
Carcass Marbling	.65	.57
Carcass Rib	.58	.60
Carcass Fat	.50	.56
Carcass Weight	.54	.48
Dry Matter Intake (component of RADG)	.45	.65
Docility	.47	n/a



Trait	h ²	Pfizer 50K HD in Angus	
		Number of animals in US training population ¹	% Genetic variation (r ²)
			Predicted from LD
Average Daily Gain	0.28	1254	7%
Net Feed Intake	0.50	1254	10%
Dry matter intake	0.39	1254	10%
Tenderness	0.37	1445	11%
Calving Ease (Direct)	0.2	1188	2%
Birth weight	0.42	1169	7%
Weaning Weight	0.2	1192	5%
Calving ease (maternal)	0.12	1177	2%
Milking Ability	0.14	1187	5%
Carcass weight	0.31	1100	9%
Backfat thickness	0.26	1097	8%
Ribeye area	0.32	1114	10%
Marbling score	0.26	1143	9%

¹ Pfizer Animal Genetics. 2010. Technical Summary.

<http://www.pfizeranimalgenetics.com/sites/PAG/Documents/50K%20Tech%20Summary.pdf>

² Animal Genetics and Breeding Unit (AGBU). 2010. Evaluation of Pfizer Animal Genetics HD 50K MVP Calibration.

http://agbu.une.edu.au/pdf/Pfizer_50K_September%202010.pdf



Trait	h ²	IGENITY® Angus Profile		Pfizer HD 50K for Angus	
		Included in test	AGI Genetic correlation (r) ¹	Included in test	AGI Genetic correlation (r) ^{1,2}
Average Daily Gain	0.28	X		X	.55 ²
Net/residual Feed Intake	0.50	X		X	.35 ²
Dry matter intake	0.31	X	.45	X	.65
Tenderness	0.37	X		X	.51 ²
Calving Ease (Direct)	0.20	X	.47	X	.33
Birth weight	0.42	X	.57	X	.51
Weaning Weight	0.20	X	.45	X	.52
Yearling Weight	0.20	X	.34	X	.64
Yearling Height	0.45	X			
Calving ease (maternal)	0.12	X		X	.63 ²
Milking Ability	0.14	X	.24	X	.32
Heifer Pregnancy	0.20	X			
Docility	0.37	X	.47		
Mature Height	0.82	X			
Mature Weight	0.55	X			
Scrotal Circumference	0.43	male			
Stayability	0.10	female			
Carcass weight	0.31	X	.54	X	.48
Backfat thickness	0.26	X	.50	X	.56
Ribeye area	0.32	X	.58	X	.60
Marbling score	0.26	X	.65	X	.57
Percent choice	--	X			

¹ Northcutt, S.L. (2011) Genomic Choices. American Angus Association®/Angus Genetics Inc. release.

<http://www.angus.org/AGI/GenomicChoice070811.pdf> (Updated 8 July, 2011)

² Pfizer Animal Genetics. 2010. Technical Summary.

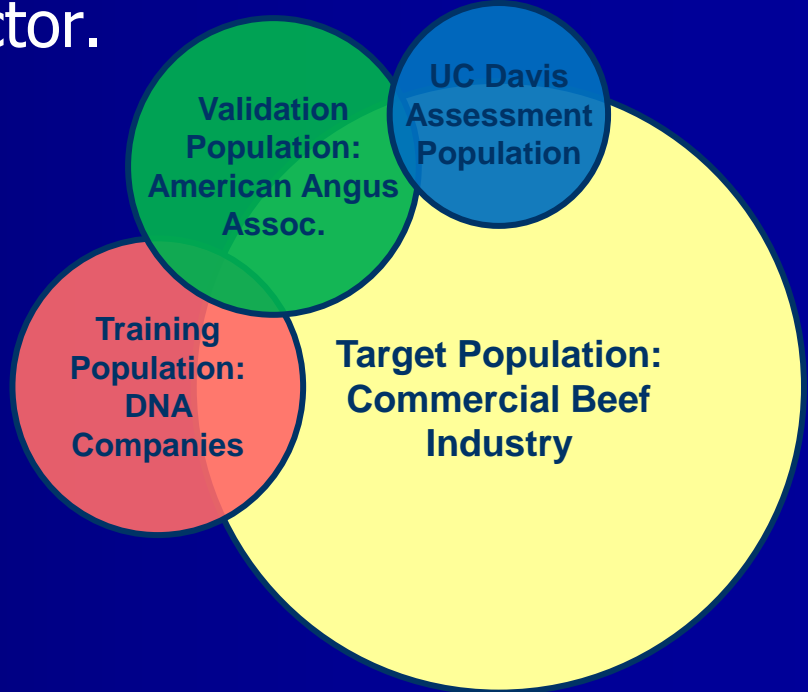
<https://animalhealth.pfizer.com/sites/pahweb/US/EN/PublishingImages/Genetics%20Assets/HD50K/50K%20Tech%20Summary%204-13-10.pdf>



Independent Assessment of Commercial Tests for Beef Cattle Production Traits

The objective of this study was to estimate the genetic correlation between DNA test results and target traits based on ranch genetic evaluations of herd bulls sourced from the Angus seedstock sector.

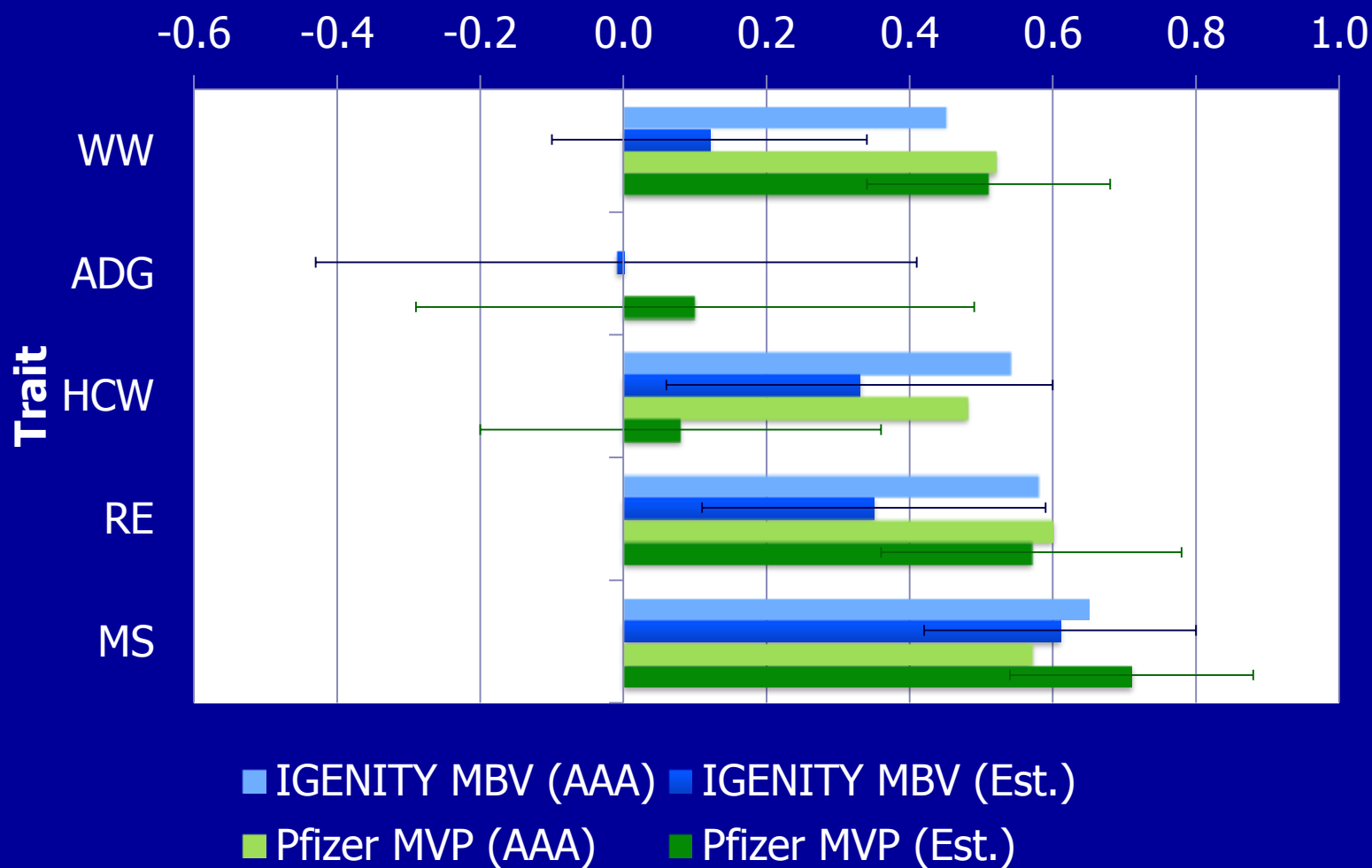
	Trait				
	WW	ADG	HCW	RE	MS
# bulls	29 with ≥ 25 progeny WW or ≥ 10 progeny feedlot in-weight/carcass				
# progeny	1734	341	455	455	455
Avg # progeny per bull	60	12	16	16	16



Weber, KL, and A.L. Van Eenennaam. American Society of Animal Science Late Breaking Abstract, July 11, 2011, New Orleans, LA



The accuracy for herd bulls on these commercial ranches was slightly lower but similar to that observed by AAA, although standard errors were large as N was small





How much do DNA tests help increase accuracy of EBVs?

	AGI Heritability	AGI HD 50K Correlation	Avg. accuracy (<i>r</i>) for animals with only pedigree estimate and DNA test	Approximate Progeny Equivalents
BW	0.42	0.51	0.71	8
WW	0.20	0.52	0.69	16
YW²	0.20	0.64	0.73	20
RADG³	0.31	0.65	0.73	13
Milk	0.14	0.32	0.60	12
CW	0.31	0.48	0.63	7
Marb⁴	0.26	0.57	0.70	12
RE⁴	0.32	0.60	0.69	9
FAT⁴	0.26	0.56	0.69	11

¹These changes are less for higher initial accuracy values

²Post-weaning ADG

³Dry matter intake

⁴Carcass progeny, not scanned progeny

Modified from slide from Kent Anderson, Pfizer Animal Genetics, presented at BIF 2011



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POLLS ARCHIVE

Jul 9, 2010 5:32 PM

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Do you consider genomics (DNA marker data) when buying herd bulls?

- Yes, it is the main consideration: 16%
- Yes, but EPDs are still more important: 39%
- No, I don't consider genomics data. I only look at EPDs.: 32%
- No, I don't consider any genetic information (EPDs, genomics data, ultrasound): 11%



Approx. cost of commercial tests

(estimates only!! - derived from web-sites or personal experience - not official quotes!!)

Test	Species	Cost (\$US)
Parentage	Cattle	\$ 13-25
Genetic Defects	Cattle	\$ 15-150
3K (just the genotypes)	Cattle	\$ 38
50K (just the genotypes)	Cattle	\$150
800K (just the genotypes)	Cattle	\$200-300
384 Angus Profile (Igenity US/AGI)	Beef Cattle	\$ 65
384 SNP Replacement Heifer (Igenity)	Beef Cattle	\$ 20
3K (Pfizer US)	Dairy Cattle	\$ 45
50K (Pfizer US/AGI)	Beef Cattle	\$139
50K (Holstein Ass.)	Dairy Cattle	\$150
800K (Holstein Ass.)	Dairy Cattle	\$365
50K (Pfizer NZ)	Sheep	\$756 (NZ\$990)



“It is perhaps the cumulative value derived from using DNA test information for multiple purposes (traceability, parentage, genetic defects, selection, marker-assisted management, product differentiation), in combination with the rapidly-declining cost of genotyping, that will ultimately push the economics of DNA-based technologies over the tipping point towards more widespread industry adoption”

Industry's most cost-effective DNA product for replacement heifer selection¹

IGENITY®, a division of Merial, announces the introduction of the most cost effective DNA product on the market — the IGENITY profile for replacement heifers. It is designed specifically for cow/calf producers committed to the long-term success of their herd. The IGENITY profile for replacement heifers is available for \$20 per animal.

Through the new cost-effective DNA offering from IGENITY, cow/calf producers can receive analyses on five economically important traits:

- Fertility
- Maternal Calving Ease
- Average Daily Gain
- Percent Choice
- Tenderness

“In the example of percent choice, the IGENITY profile for replacement heifers is the equivalent of having information on up to five progeny from a yearling heifer,” says Dr. DeHaan. “For producers who do not have pedigree documents on their heifers, this information is especially valuable.”

Cow/Calf Producers can Improve Profitability with Genetics Management and Selection Tools



Are you leaving dollars on the table? There is no doubt that in the beef industry, more information equals better decisions. And, better management and selection decisions equal greater profits. Start making better decisions today with world-leading DNA-marker technology from Pfizer Animal Genetics.

With a robust offering of genetic technologies, Pfizer Animal Genetics can help you gain information early in an animal's life that will help you make more precise decisions resulting in faster genetic progress and a healthier bottom line. And, these products come from the animal health company you already know and trust.



High (h^2) and intermediate ($\frac{1}{2} h^2$) accuracy DNA tests explaining genetic variation in all of the economically-relevant traits in the breeding objective and selection criteria

Objective Trait	h^2
Sale liveweight – direct	0.31
Sale liveweight – maternal	0.04
Cow weaning rate	0.05
Cow survival rate	0.03
Cow weight	0.41
Calving ease – direct	0.10
Calving ease – maternal	0.10
Dressing Percentage	0.33
Saleable meat Percentage	0.56
Fat depth (rump)	0.41
Marbling score	0.38

Selection criteria	h^2
Birth weight	0.39
200 d Weight	0.18
400 d Weight	0.25
600 d Weight	0.31
Scrotal Size	0.39
Days to Calving	0.07
Mature Cow Weight	0.41
P8 fat	0.41
RIB fat	0.34
Eye Muscle Area	0.26
Intramuscular Fat	0.25

Van Eenennaam, A. L., J.H. van der Werf, and M.E. Goddard. 2011. The economics of using DNA markers for beef bull selection in the seedstock sector. Journal of Animal Science. 89:307-320.



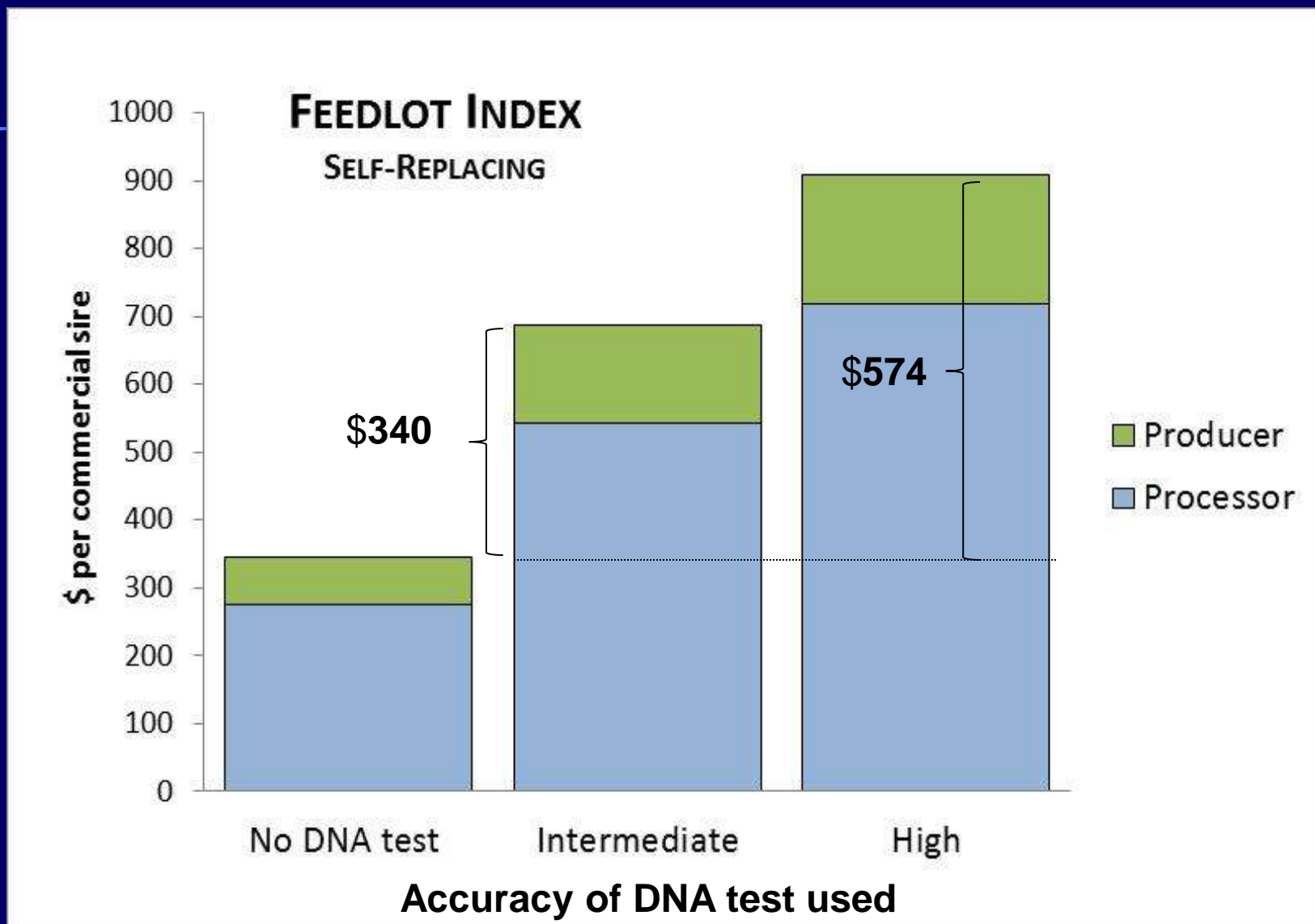
Value of improved selection response for commercial bulls due to DNA-test increase in index accuracy



Variable	Unit	Accuracy of DNA test used	Feedlot
Increased value derived from ΔG in commercial sires	\$/ bull	Intermediate	340
		High	574

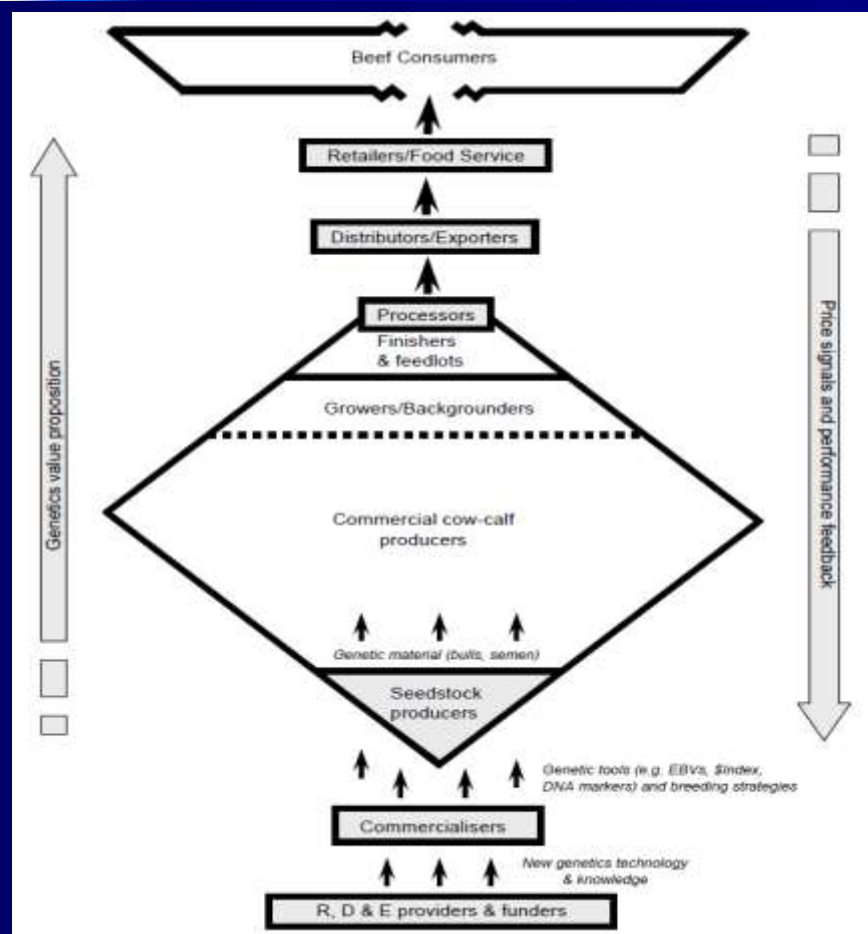


Where are returns from genetic gain (ΔG) realized?





Industry structure may evolve to enable the exchange of information and value between the different sectors



For widespread technology adoption, breeders need to be adequately rewarded for making DNA investments and selection decisions for traits that benefit the different sectors of the beef industry.

Parnell, P.F. 2007. Effective value chain partnerships are essential for rapid adoption of beef genetics technology. Association for the Advancement of Animal Breeding and Genetics. 18. 167-174 .



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Questions?