Users of Technology:

Are there benefits to using these expensive DNA markers?

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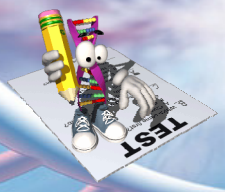
Right now?...No!



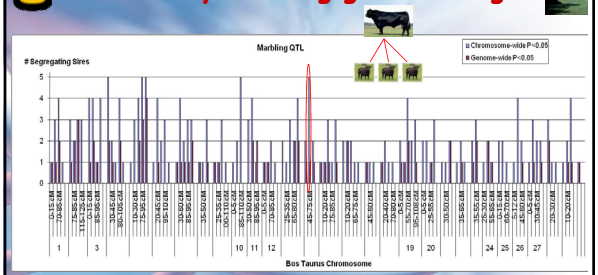
Why not?

- The currently available tests:
  - Explain little of the genetic variation in a trait
    - Think of single marker tests as EPDs with Accuracies ~0.05
    - Van Eenennaam et al. (2007) J. Anim. Sci. 85:891-900
  - Don't exist for many important traits
    - Feed efficiency, fertility, longevity, disease resistance
  - Are not used by Breed Associations for EPD calculations
  - Cost too much!!!

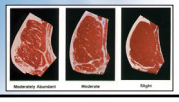
Talk Outline

- What are the impediments?
  - How many genes underlie a trait?
  - Why do we have so few tests?
- How do we solve this?
  - Can we improve the rate at which we identify new tests?
    - New technology!!!!
  - Whole Genome Selection – A brand new approach
  - How do Breed Associations use the data?
  - Can we make it cost effective?

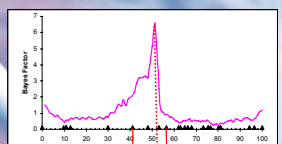
So how many marbling genes in Angus?



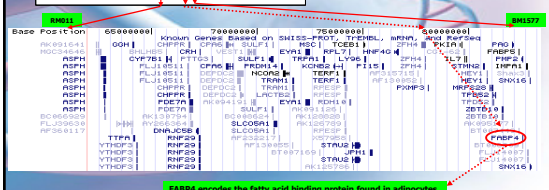
- We genotyped 2,197 progeny from 39 halfsib families for 422 microsatellite markers
- Found evidence for 59 marbling genes



Why is it so hard to develop a genetic test?



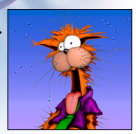
There is a lot of real estate in here and we are only making educated guesses about which genes cause the QTL effect



FABP4 encodes the fatty acid binding protein found in adipocytes

The Impediments?

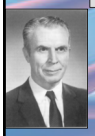
- We haven't genotyped large enough populations to find the locations of all the genes
- There are a LOT of genes to be found!!!!!
  - 60 genes/trait x 20 traits = 1,200 tests
- We have no efficient way of going from a gene location to a test
- We don't have populations to screen for genes that influence longevity, fertility, disease resistance
  - Phenotypes, phenotypes, phenotypes…
- There are a LOT of genes!!!!!



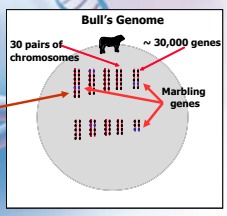
If we had tests for all 59 marbling genes we could produce molecular EPDs

- EPD = ½Breeding Value
  - Sum of the numeric additive values of all alleles at all loci influencing a trait
  - The component of genotype that is transmitted predictably between generations – basis of selection and genetic improvement

$$\begin{bmatrix} X'X & X'Z_1 & X'Z_2 \\ Z_1'X & Z_1'Z_1+A^{-1}\lambda & Z_1'Z_2 \\ Z_2'X & Z_2'Z_1 & Z_2'Z_2+I\lambda \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \\ \hat{p} \end{bmatrix} = \begin{bmatrix} X'y \\ Z_1'y \\ Z_2'y \end{bmatrix}$$

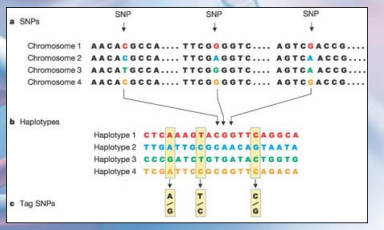


Estimate of the sum of all allelic effects in genome



What are SNPs?

- SNP stands for Single Nucleotide Polymorphism
- SNPs are DNA variants that occur as single base changes



What use are SNPs?

- SNPs can be used for all the same purposes that we previously used microsatellites:
  - Parentage
  - Traceability
  - Genetic testing for trait associations

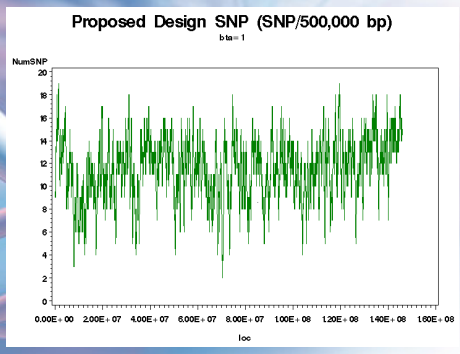
- But SNPs are not as informative as microsatellites
  - For parentage it will take 5-10 times as many SNPs as microsatellites because they only have 2 alleles
- However, they are much easier and cheaper to score than microsatellites
  - This really changes what we can do with DNA typing

New Technologies

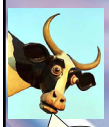
We will soon have high-throughput SNP genotyping

- Illumina iSelect™ Infinium Custom BeadChip
- 12 samples per BeadChip
- 16 chips a day
- 60,800 tags per sample
  - ~50,000 working SNPs
  - ~10M genotypes/day
- SNPs selected from Btau3.1 & a sequencing project
- Collaboration between UMC, MARC, BARC, UA
- Publicly available ~December 2007

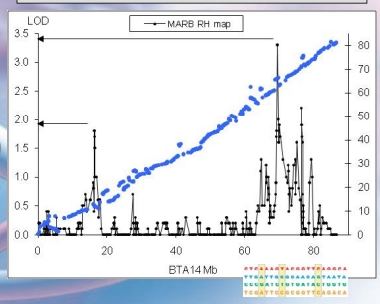
3,350 SNPs on BTA1



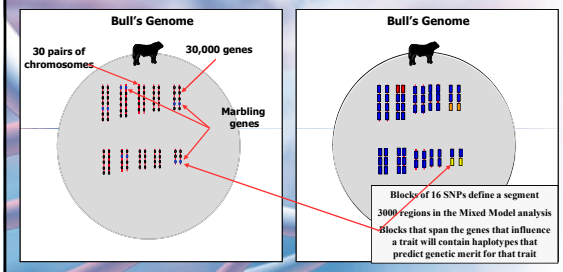
What use are SNPs?



Can those haplotypes predict the bull's marbling genotype?



Whole Genome Selection

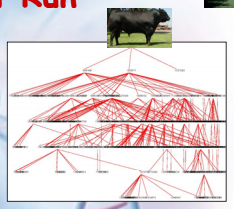


The concept of Whole Genome Selection is that we use a very high resolution map (48K markers) to divide the genome into small segments (fingerprints or haplotypes) and estimate the contribution of each haplotype and chromosomal segment to genetic merit

Whole Genome Selection

- Is a way to use DNA testing to estimate an animal's EPD without needing phenotypic data
  - Not yet proven to work!
  - Preliminary data from Australia suggests that $\rho(EPD_{WGS}, EPD)=81\%$ (milk traits in Holsteins)
- Simultaneously tests for all of the genes that influence a trait – is not a single gene test
- Can predict merit for all traits with phenotypes (including feed efficiency) – not single trait test
- Requires one test to predict EPDs for all traits
- Animals genotyped for prediction of EPD by WGS, are automatically parent verified

WGS Test Run



- 1,768 Angus bulls
- 14 generation pedigree
  - Oldest Bull born 1956
- 50K SNPs
- 88M genotypes – Sept 2007
- EPDs and Accuracies from American Angus Association
- Analysis this Fall

What If WGS Works?

- We are working with the AAA to evaluate impediments to industry adoption of WGS (USDA NRI Integrated)
  - Data pipelines/storage/processing
  - Optimal EPD estimation of animals P^+/G^-, P^+/G^+ and P^-/G^+
- For what traits are phenotypes available?
- WGS will be breed specific
  - QTLs will be the same, haplotypes different
  - WGS analyses need be conducted within breeds for each trait
  - Populations & phenotypes will be critical!!!
- How long will WGS work?
- What IP issues are there?
- What will it cost? ($208/sample?)

Will It Raise Completely New Issues For Animal Breeding?

Chromosome 29 Chromosome 29

Marbling 14 + -

Tenderness 32 + -

Both bulls have the same genotypes, but do they have the same value in a breeding program??

What If WGS Doesn't Work?

- Wouldn't be the first time that the wheels came off a good idea!!!
- But I have others…
- See Emerging Technology talk…

Acknowledgements

Bob Schnabel

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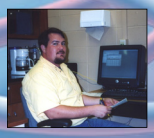
Matt McClure



- Angus DNA
  - Dr. Scott Barao – Semen on 221 Wye Plantation bulls
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Thank You!