

Application of Genome-Wide Selection for Breeding Schemes
John Woolliams (Roslin Institute)



Conference on Genomics for Animal Health
Utrecht, NL 4th-8th June 2007




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Food Quality and Safety

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Plan


1. A Historical Dairy Cattle Perspective
2. Using DNA in Evaluations
3. Important Property of Genome-Wide
4. Potential Benefits
5. SABRE Demonstration
6. Conclusions




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A Historical Dairy Cattle Perspective




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A Historical Dairy Cattle Perspective

- Multiple Ovulation & Embryo Transfer
 - desire to select bulls early
 - based on parental information
 - create full sib families
 - all full sibs have identical EBVs




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A Historical Dairy Cattle Perspective

- How to select among full sibs?
 - physiological predictors
 - Woolliams and Smith
 - DNA markers
 - Meuwissen and van Arendonk
 - bottom up selection, several DNA markers
 - Mackinnon et al




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A Historical Dairy Cattle Perspective

- How to select among full sibs?
 - physiological predictors
 - DNA markers
 - bottom up selection, several DNA markers
- Identify which offspring got the best genes carried by sire & by dam
 - identify MENDELIAN SAMPLING TERM of offspring

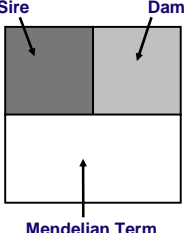


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A Historical Dairy Cattle Perspective

- Decompose BV
- Mendelian term
 - major part of genetic variance
 - > ½ during selection
 - unique to individual
 - independent of parental breeding values



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A Historical Dairy Cattle Perspective

- Multiple Ovulation & Embryo Transfer
 - desire to select bulls early
 - based on parental information
 - create full sib families
 - how to select among full sibs?
 - physiological predictors
 - DNA markers
 - bottom up selection

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A Historical Dairy Cattle Perspective

- Modern technology
 - high throughput SNP chips
 - Dairy: 10k in 2005, 25k in 2006, 60k in 2007
 - Pigs: 8k in 2007
 - Chicken: in use (density?)
 - Sheep: under development
 - change the way we can use the information

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Using DNA in Evaluations

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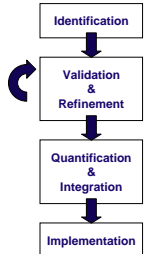
Using DNA in Evaluations

- How might dense SNPs help genetic evaluation?

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Using DNA in Evaluations: Method 1

Classical QTL



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Using DNA in Evaluations: Method 1

Classical QTL

- Strengths
 - Increased accuracy
 - Causative mutation gives
 - IP
 - simpler implementation
 - Delivered in practice

```

graph TD
    A[Identification] --> B[Validation & Refinement]
    B --> C[Quantification & Integration]
    C --> D[Implementation]
    B --> A
    
```

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Using DNA in Evaluations: Method 1

Classical QTL

- Weaknesses
 - Expensive with long lead-in
 - Requires precise quantification
 - each QTL a fraction of variance
 - error reduce accuracy
 - need to remove bias
 - Requires pedigree & performance
 - for unexplained variance

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Using DNA in Evaluations: Method 1

Classical QTL

- Dense SNPs
 - help detection
 - add precision
- Evaluation
 - Pedigree A-matrix
 - IBD matrix at QTL position(s)
 - Extension of current BLUP

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Using DNA in Evaluations: Method 2

Genomic or Genome Wide Selection

- Estimate effect of individual haplotypes
- No attempt to identify QTLs
- Estimate sum of haplotypes as EBV
 - haplotypes poorly estimated
 - negative covariances among estimates
- Meuwissen et al (2001)

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graph TD
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Using DNA in Evaluations: Method 2

Genomic or Genome Wide Selection

- Strengths
 - Does not partition variance explicitly
 - Increases accuracy in simulation
 - May not need to record all animals
 - May not need pedigree

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Using DNA in Evaluations: Method 2

Genomic or Genome Wide Selection

- Strengths
 - Does not partition variance explicitly
 - Increases accuracy in simulation
 - May not need to record all animals
 - May not need pedigree
- Weakness
 - May need to re-write evaluation software
 - Only preliminary results available in practice

```


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Important Property of Genome Wide




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Important Property of Genome Wide

- Meuwissen et al simulate a trait of $h^2 = 0.5$
- Demonstrate accuracy of newborn 0.85





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Important Property of Genome Wide

- Meuwissen et al simulate a trait of $h^2 = 0.5$
- Demonstrate accuracy of newborn 0.85
- Know parent's BVs precisely accuracy = 0.71





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Important Property of Genome Wide

- Meuwissen et al simulate a trait of $h^2 = 0.5$
- Demonstrate accuracy of newborn 0.85
- Know parent's BVs precisely accuracy = 0.71
- Therefore know ~ Mendelian Term
 - accuracy > 0.67




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Important Property of Genome Wide


- Genome Wide Prediction is multi-SNP version of 'who got best genes from parents?'
- Accuracy of Mendelian term determines gain in relation to rate of inbreeding
- Genome-Wide Prediction delivers more gain compared at same rate of inbreeding
 - cf changes in intensity and BLUP truncation
 - both these add to gain but also add to inbreeding rate



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Potential Benefits



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Potential Benefits (1)

- Reduce resources to manage rates of inbreeding
 - c.f. introduction of BLUP
 - resources needed to be enlarged to realise benefit sustainably

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Potential Benefits (2)

- Potential to deliver accuracy with no records in a generation
 - providing sufficient prior recording with genotyping
 - sex-limited traits
 - re-balance indices toward desired gains
 - revise the need for progeny testing
 - destructive traits e.g. carcass
 - expensive to measure traits

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Potential Benefits (3)

- Potential to deliver accuracy with no pedigree
 - e.g. close loop from slaughterhouse to elite

Progress from Elite

Haplotypes for Selection

Dissemination

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Potential Benefits

- Potential benefits
- Application depends on costs
 - in some cases recovered by restructuring
 - time trends on cost?
- To what degree can they be delivered?

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SABRE Demonstration

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SABRE Demonstration

- Genotype ~ 800 progeny tested bulls
 - 2 breeds, Norwegian Red & Holstein
- Obtain dense SNPs > 25k
- Estimated BVs with genome-wide prediction
 - within breed
- Cross validate within breed
- Cross validate between breeds


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Conclusions

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Conclusions

Genome Wide Prediction using dense SNPs

- Distinct philosophy for use of DNA

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Conclusions

Genome Wide Prediction using dense SNPs

- Distinct philosophy for use of DNA
- Increases gain at same rate of inbreeding

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Conclusions

Genome Wide Prediction using dense SNPs

- Distinct philosophy for use of DNA
- Increases gain at same rate of inbreeding
- Driver for innovation and re-structuring

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Conclusions

Genome Wide Prediction using dense SNPs

- Distinct philosophy for use of DNA
- Increases gain at same rate of inbreeding
- Driver for innovation and re-structuring
- The cutting edge of sustainable breeding!

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