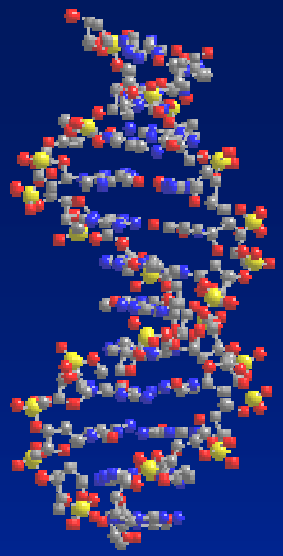
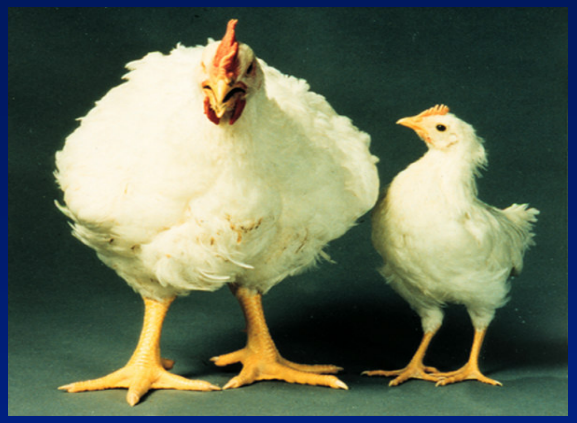
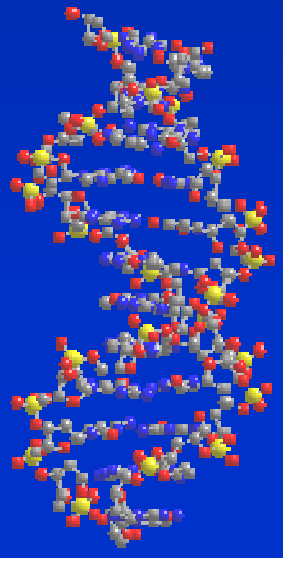




Linkage Disequilbrium to Genomic Selection



Course overview

- Day 1
  - Linkage disequilibrium in animal and plant genomes
- Day 2
  - QTL mapping with LD
- Day 3
  - Marker assisted selection using LD
- Day 4
  - Genomic selection
- Day 5
  - Genomic selection continued

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

IBD approach to genomic selection

- In the methods BayesA, BayesB, the model assumed that haplotypes were in LD with QTL alleles
  - Eg. $\mathbf{g}_i \sim N(0, \mathbf{I}\sigma_{gi}^2)$

IBD approach to genomic selection

- In the methods BayesA, BayesB, the model assumed that haplotypes were in LD with QTL alleles
  - Eg. $\mathbf{g}_i \sim N(0, \mathbf{I}\sigma_{gi}^2)$
- An alternative approach is to assume for two haplotypes sampled from the population, at a putative QTL position, there is a probability that the QTL alleles are identical by descent (IBD matrix)

IBD approach to genomic selection

- Model for single QTL

$$y_j = \mu + u_j + vp_j + vm_j + e_j$$

- $v \sim (0, \mathbf{G}\sigma_v^2)$

IBD approach to genomic selection

- Model for single QTL

$$y_j = \mu + u_j + vp_j + vm_j + e_j$$

- $v \sim (0, \mathbf{G}\sigma_v^2)$
- $u \sim (0, \mathbf{A}\sigma_a^2)$, $e \sim \sim (0, \mathbf{I}\sigma_e^2)$

IBD approach to genomic selection

- **G** is the IBD matrix
  - Elements g_{kl} are the probability that haplotypes *k* and *l* are IBD at the putative QTL position

IBD Approach

IBD Approach single QTL

IBD Approach single QTL

Animal 1 vp1

vm1

Animal 2 vp2

vm2

Animal 3 vp3

vm3

$$\sim N(0, \mathbf{G}\sigma_v^2)$$

IBD Approach single QTL

Animal 1 vp1

vm1

Animal 2 vp2

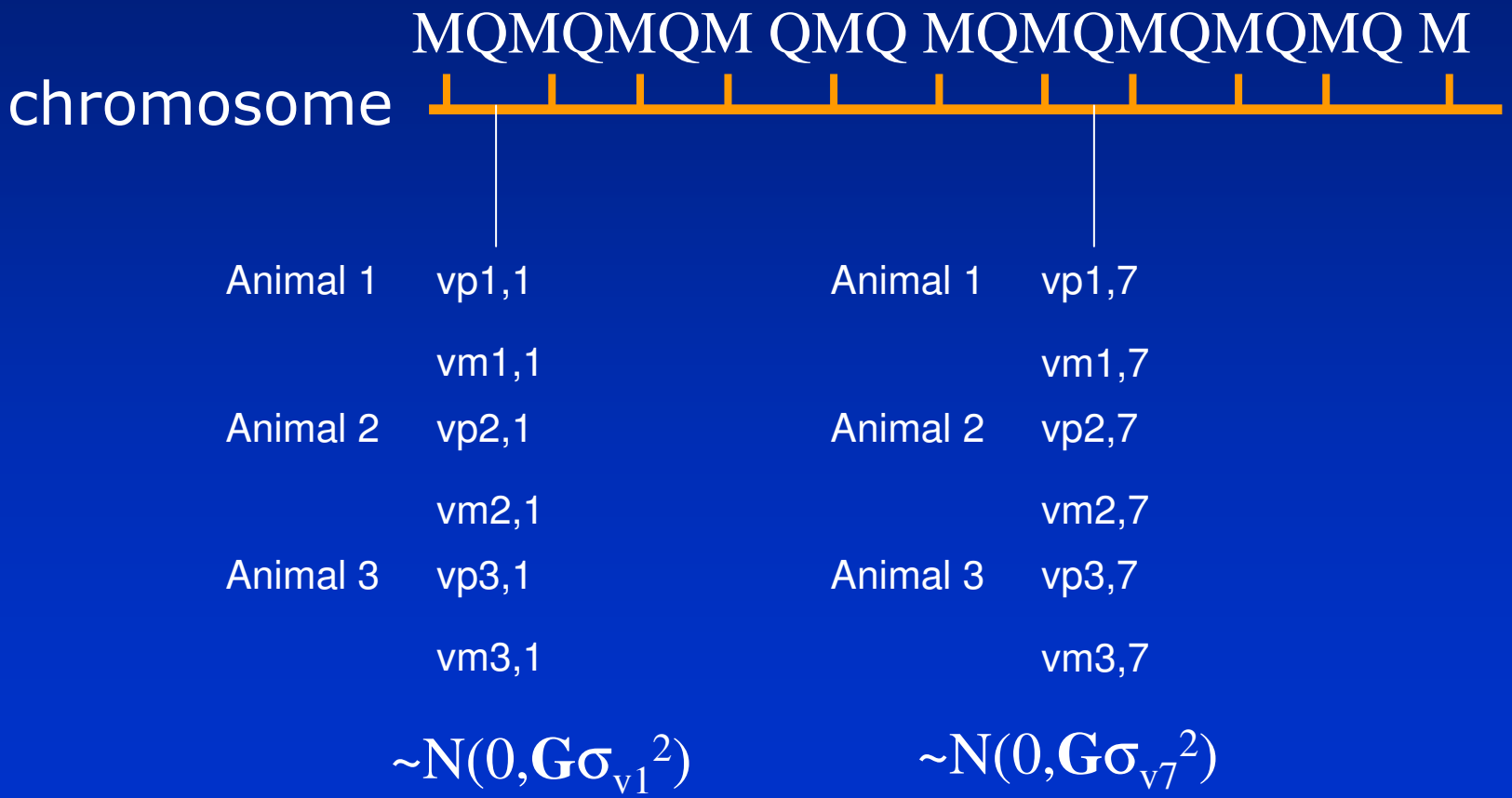
vm2

Animal 3 vp3

vm3

$$\sim N(0, \mathbf{G}\sigma_v^2)$$

IBD Approach Genomic selection



IBD approach to genomic selection

- With genomic selection
- Prior($v_i|\mathbf{G_i},\sigma_{vi}^2$) = N(0,$\mathbf{G_i}\sigma_{vi}^2$)
- Prior($\mathbf{u}|\mathbf{A},\sigma_a^2$)= N(0, $\mathbf{A}\sigma_a^2$)

IBD approach to genomic selection

- Prior($v_i|\mathbf{G_i}\sigma_{vi}^2$) = N(0,$\mathbf{G_i}\sigma_{vi}^2$)
- Prior($u|\mathbf{A}\sigma_a^2$)= N(0, Prior($u|\mathbf{A}\sigma_a^2$)
- Implement by
  - 1. Calculating **G** for all putative QTL positions (mid-marker brackets)
  - 2. Run a Gibbs chain to sample from posterior distributions for v_i, u, e, σ_e^2 , σ_a^2, σ_{vi}^2

IBD approach to genomic selection

- Allows linkage to be included
  - build **G** with LDLA
- More detail in Meuwissen and Goddard (2004)

IBD approach to genomic selection

- Information from multiple traits can increase support for the QTL if the QTL has pleiotropic effects
- How to model this?
- Large sampling space?

IBD approach to genomic selection

- QTL at each position has vector d_i which describes direction of effects on QTL alleles on traits
- eg. d_i = [1 2]'
  - if QTL allele has effect 2 on first trait, will be 4 on second trait
- eg. d_i = [1 -1]'
  - If QTL allele has effect 2 on first trait will be -2 on other trait
- Each QTL allele (2 for each animal) will have own QTL allele, but for a single QTL all effects follow direction vector
- Reduces sampling space substantially
- The d_i are sampled in the Gibbs chain

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

Accuracy of genomic selection

- Factors affecting accuracy of genomic selection r(GEBV,TBV)
  - Linkage disequilibrium between QTL and markers = density of markers
  - Single markers, haplotypes or IBD
  - Number of records used to estimate chromosome segment effects

Accuracy of genomic selection

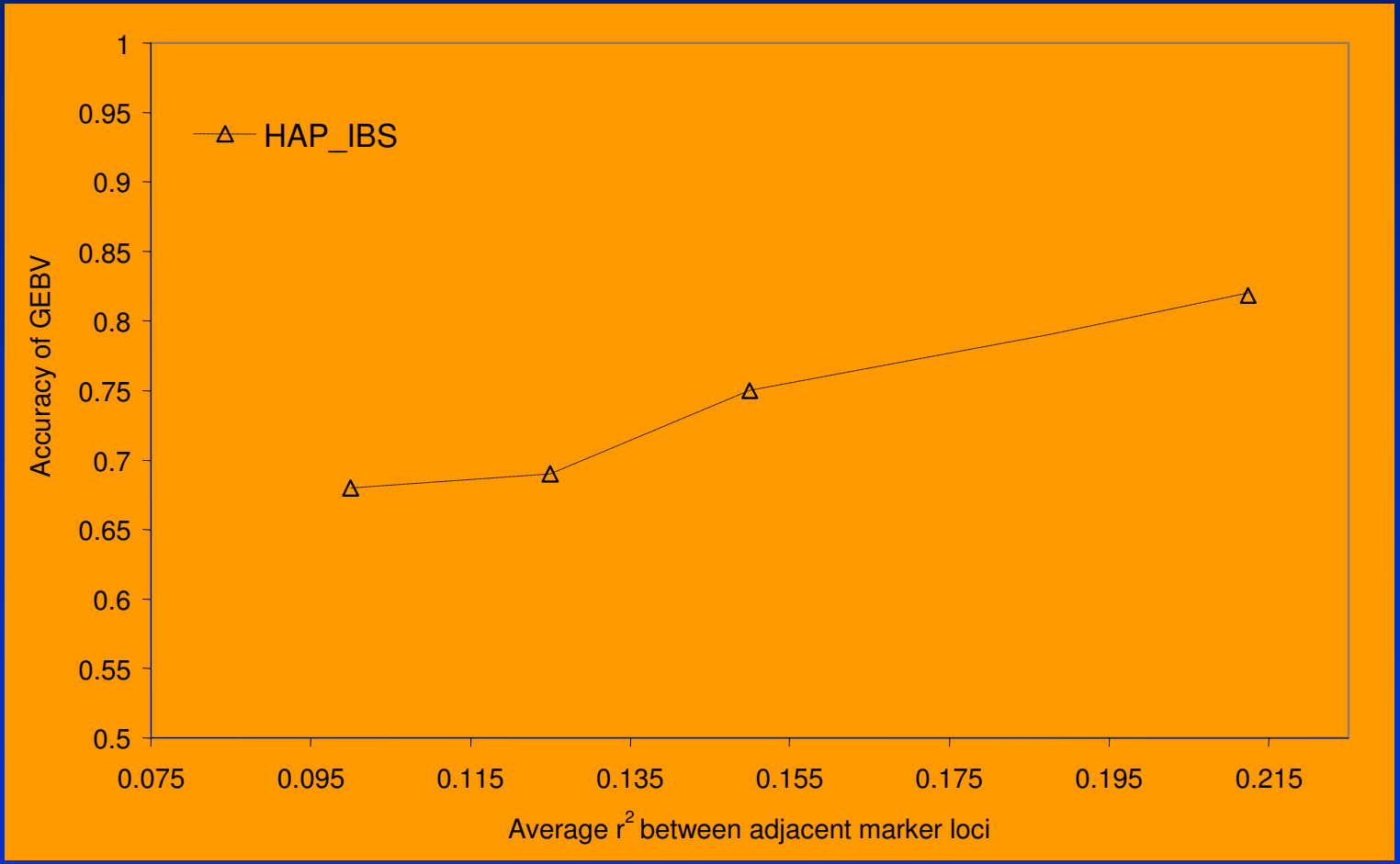
- Factors affecting accuracy of genomic selection r(GEBV,TBV)
  - Linkage disequilibrium between QTL and markers = density of markers
    - Haplotypes or single markers be in sufficient LD with the QTL such that the haplotype or single markers will predict the effects of the QTL across the population.

Accuracy of genomic selection

- Factors affecting accuracy of genomic selection r(GEBV,TBV)
  - Linkage disequilibrium between QTL and markers = density of markers
    - Haplotypes or single markers be in sufficient LD with the QTL such that the haplotype or single markers will predict the effects of the QTL across the population.
    - Calus et al. (2007) used simulation to assess effect of LD between QTL and markers on accuracy of genomic selection

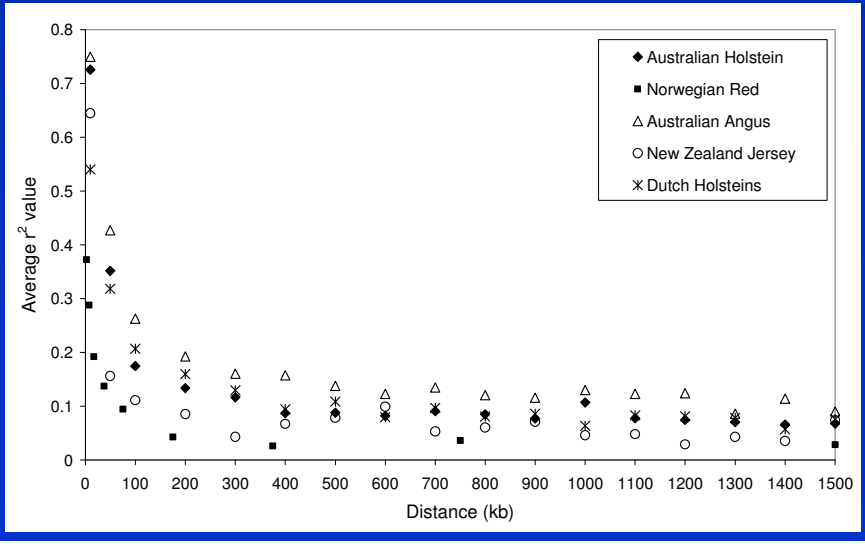
Accuracy of genomic selection

- Effect of LD on accuracy of selection



Accuracy of genomic selection

- Factors affecting accuracy of genomic selection r(GEBV,TBV)
  - Linkage disequilibrium between QTL and markers = density of markers
  - In dairy cattle populations, an average r^2 of 0.2 between adjacent markers is only achieved when markers are spaced every 100kb.



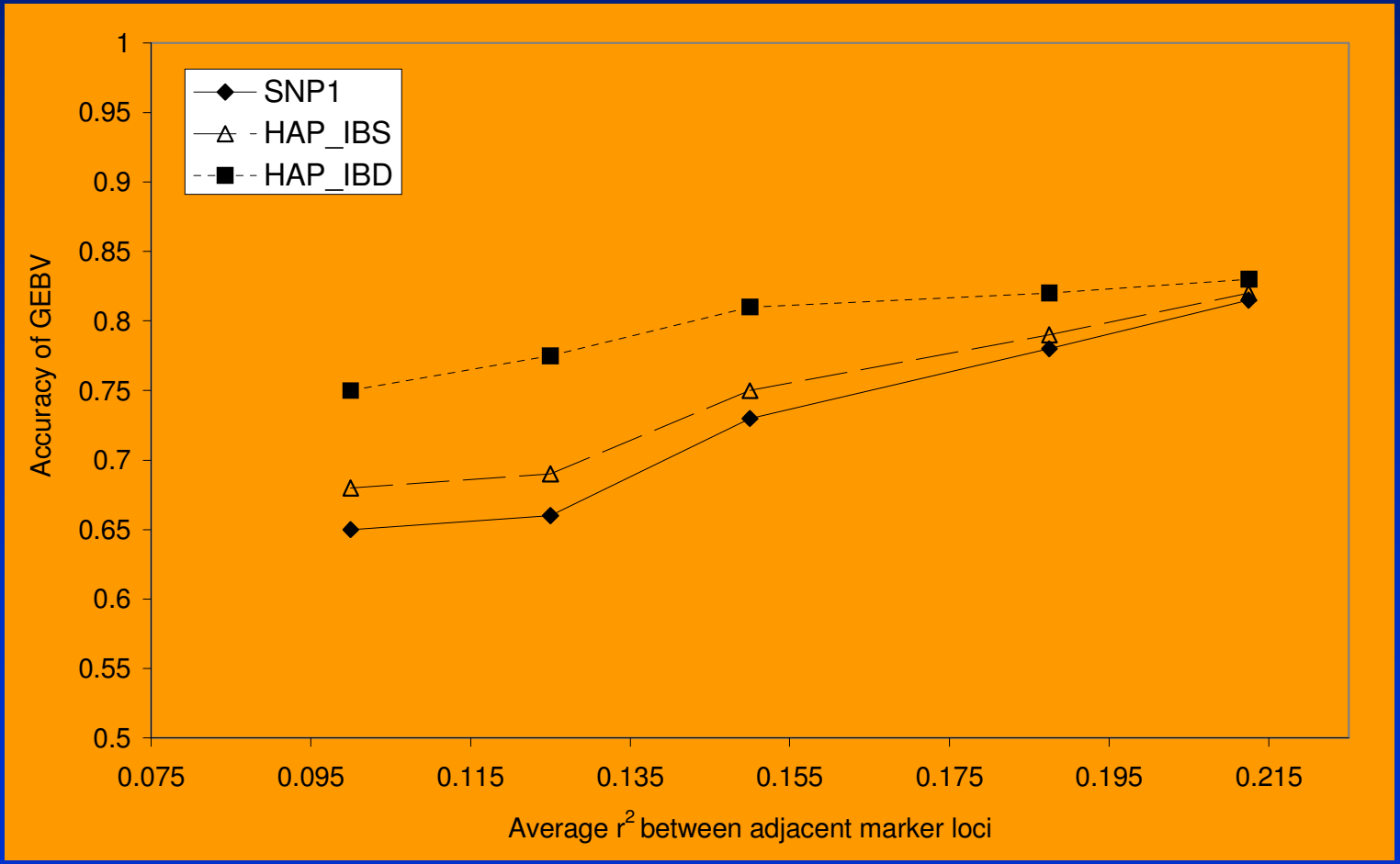
Accuracy of genomic selection

- Factors affecting accuracy of genomic selection r(GEBV,TBV)
  - Linkage disequilibrium between QTL and markers = density of markers
  - In dairy cattle populations, an average r^2 of 0.2 between adjacent markers is only achieved when markers are spaced every 100kb.
  - Bovine genome is approximately 3000000kb
  - Implies that in order of 30 000 markers are required for genomic selection to achieve accuracies of 0.8!!

Accuracy of genomic selection

- Comparing the accuracy of genomic selection with
  - IBD approach
  - haplotypes
  - single markers
  - Calus et al (2007) used simulated data

Accuracy of genomic selection



Accuracy of genomic selection

- Number of records used to estimate chromosome segment effects
  - Chromosome segment effects g_i estimated in a reference population
  - How big does this reference population need to be?
  - Meuwissen et al. (2001) evaluated accuracy using LS, BLUP, BayesB using 500, 1000 or 2000 records in the reference population

Accuracy of genomic selection

- Number of records used to estimate chromosome segment effects

	No. of phenotypic records		
	500	1000	2200
Least squares	0.124	0.204	0.318
Best linear unbiased prediction (BLUP)	0.579	0.659	0.732
BayesB	0.708	0.787	0.848

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

Non-additive effects

- Non additive effects include:
  - Dominance

Non-additive effects

- Non additive effects include:
  - Dominance

  - Epistasis

	aa	*Aa*	*AA*
bb	100	200	300
Bb	200	700	400
BB	300	400	500

- *A* allele of gene 1 gives 100 L extra milk
- *B* allele of gene 1 gives 100 L extra milk
- But *AaBb* genotype gives 400 L extra milk

Non-additive effects

- Why are we interested in non-additive effects?
  - Not important for selection as only additive gene action inherited across generations
    - Breeding values should contain only additive effects

Non-additive effects

- Why are we interested in non-additive effects?
  - Not important for selection as only additive gene action inherited across generations
    - Breeding values should contain only additive effects
  - But can exploit to improve genetic merit of commercial progeny
    - Eg. Set up mating designs so all commercial cows are *AaBb*.

	aa	*Aa*	*AA*	
bb	100	200	300	
Bb	200	700	400	
BB	300	400	500	

Non-additive effects

- Why are we interested in non-additive effects?
  - Not important for selection as only additive gene action inherited across generations
    - Breeding values should contain only additive effects
  - But can exploit to improve genetic merit of commercial progeny
  - We can use genomic selection to estimate *genetic merit* of progeny including dominance and epistasis effects

Non-additive effects

- Why are we interested in non-additive effects?
  - Not important for selection as only additive gene action inherited across generations
    - Breeding values should contain only additive effects
  - But can exploit to improve genetic merit of commercial progeny
  - We can use genomic selection to estimate *genetic merit* of progeny including dominance and epistasis effects
    - Also map genes with these effects

Non-additive effects

- Approach of Xu (2007)
  - Model with additive effects only (single marker)

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \mathbf{X_i} g_i + \mathbf{e}$$

  - Model with epistatic effects

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \mathbf{X_i} g_i + \sum_{i=1}^{p} \sum_{j=1}^{i-1} \mathbf{X_i} \mathbf{X_j} \alpha_{ij} + \mathbf{e}$$

Non-additive effects

- Approach of Xu (2007)
  - Model with additive effects only (single marker)

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \mathbf{X_i} g_i + \mathbf{e}$$

  - Model with epistatic effects

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \mathbf{X_i} g + \sum_{i=1}^{p} \sum_{j=1}^{i-1} \mathbf{X_i X_j} \alpha_{ij} + \mathbf{e}$$

α_{ij} = Epistatic effect between markers i and j

Non-additive effects

- Approach of Xu (2007)
  - Model with additive effects only (single marker)

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \mathbf{X_i} g_i + \mathbf{e}$$

  - Model with epistatic effects

$$\mathbf{y} = \mu \mathbf{1_n} + \sum_{i=1}^{p} \sum_{j=1}^{i} \mathbf{X_i X_j} \alpha_{ij} + \mathbf{e}$$

If $i=j$, $g_i = \alpha_{ii}$

Non-additive effects

- Approach of Xu (2007)
  - Then Prior(α_{ij}) = N(0,$\sigma_{\alpha ij}^2$)
  - Prior($\sigma_{\alpha ij}^2$) = $\chi_{t,u}^{-2}$
  - Model selection step?
  - Set up Gibbs chain to sample from posterior distributions

Non-additive effects

- Approach of Xu (2007)
  - Then Prior(α_{ij}) = N(0,$\sigma_{\alpha ij}^2$)
  - Prior($\sigma_{\alpha ij}^2$) = $\chi_{t,u}^{-2}$
  - Model selection step?
  - Set up Gibbs chain to sample from posterior distributions

  - Xu (2007) showed that epistatic effects could be estimated in simulated data with this approach using 600 records in a back-cross design.
  - They also applied the method to real data from a barley backcross experiment.

Non-additive effects

- Approach of Xu (2007)
  - Then Prior(α_{ij}) = N(0,$\sigma_{\alpha ij}^2$)
  - Prior($\sigma_{\alpha ij}^2$) = $\chi_{t,u}^{-2}$
  - Model selection step?
  - Set up Gibbs chain to sample from posterior distributions
- Gianola et al. (2006) is another method to predict non additive effects

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

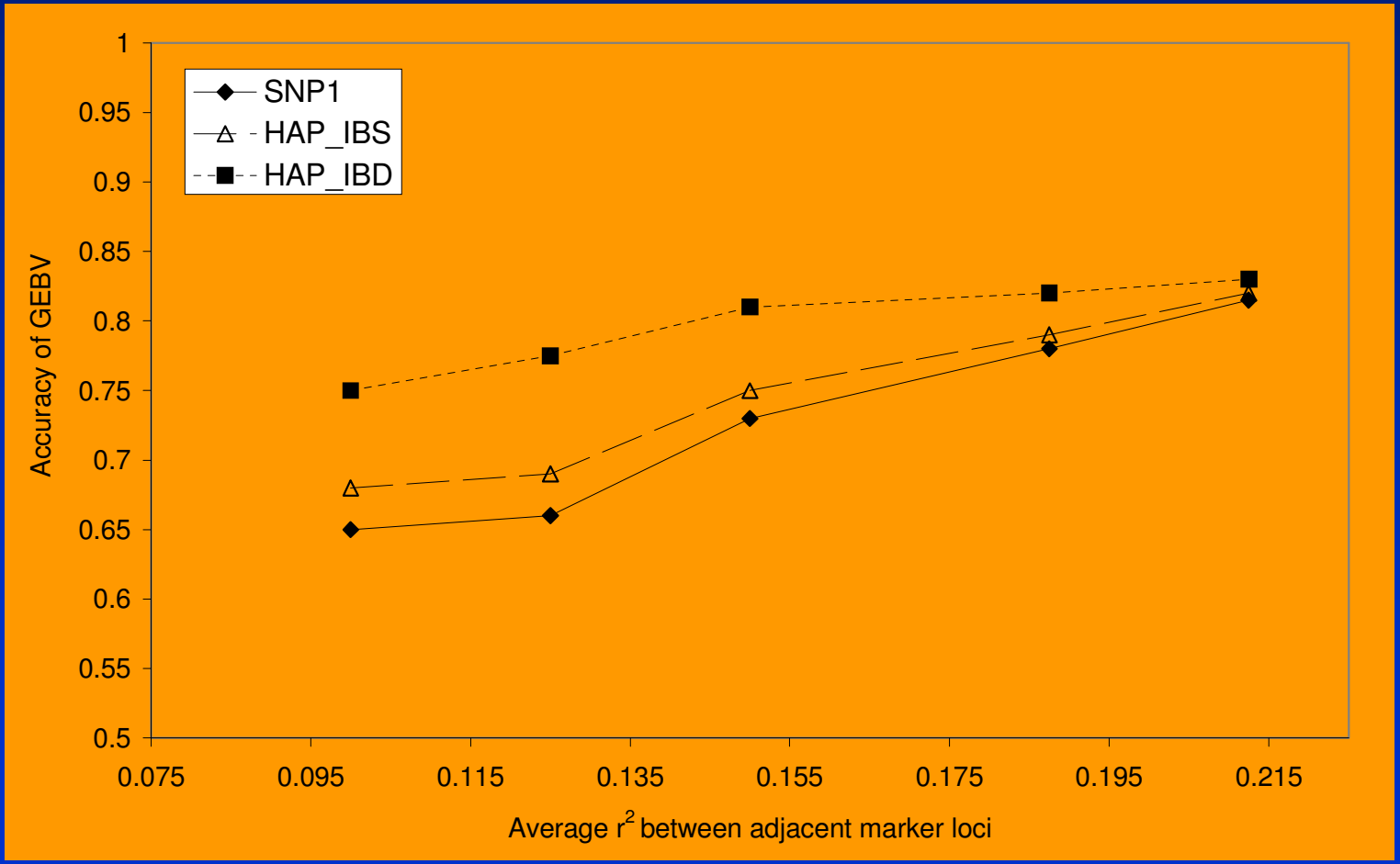
Genomic selection

- Genomic selection with low marker density
  - May not be enough markers across genome to ensure adjacent markers have $r^2>=0.2$.
  - Will not capture all the genetic variance with the markers.

Genomic selection

- Genomic selection with low marker density
  - May not be enough markers across genome to ensure adjacent markers have $r^2 >= 0.2$.
  - Will not capture all the genetic variance with the markers.
  - Two strategies
    - Exploit linkage as well as linkage disequilibrium by using the IBD approach

Accuracy of genomic selection



Genomic selection

- Genomic selection with low marker density
  - May not be enough markers across genome to ensure adjacent markers have $r^2>=0.2$.
  - Will not capture all the genetic variance with the markers.
  - Two strategies
    - Exploit linkage as well as linkage disequilibrium by using the IBD approach
    - Include a polygenic effect to capture some of the genetic variance not captured by the markers (exploit pedigree)

$$\mathbf{GEBV} = \hat{\mathbf{u}} + \sum_{i}^{p} \mathbf{X}_i \hat{\mathbf{g}}_i$$

Genomic selection

- Genomic selection with low marker density
  - An example in dairy cattle
  - De Roos et al. (2007) predicted GEBVs for fat%
    - Reference population of 1300 Holstein-Friesian bulls
    - Genotyped for 32 markers on chromosome 14 (habours DGAT1 gene, large effect on fat%)
    - Predict EBVs with Genomic selection (IBD approach+polygenic effect for a new set of bulls
    - These new bulls actually have progeny test results for fat%, so can correlate GEBV and Progeny test results

Genomic selection

- Genomic selection with low marker density
  - An example in dairy cattle
  - De Roos et al. (2007) predicted GEBVs for fat%
  - Genomic selection accuracy = 0.76
  - EBV only = 0.51
  - Even with low marker density, genomic selection can improve accuracy of breeding value
    - However in this example known mutation on chromosome 14 with very large effect on fat%

Genomic selection

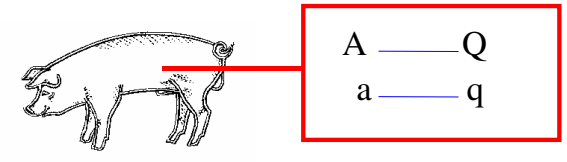
- Genomic selection with low marker density
  - genomic selection can also be used to increase the efficiency of development of ***composite lines*** (Piyasatian et al. 2006).
  - crosses between breeds will exhibit much greater levels of LD than within breed populations.
  - Piyasatian et al. (2006) demonstrated that genetic merit of composite lines can be improved by using genomic selection to capture chromosome segments with largest effects from contributing breeds, even with a sparse marker map

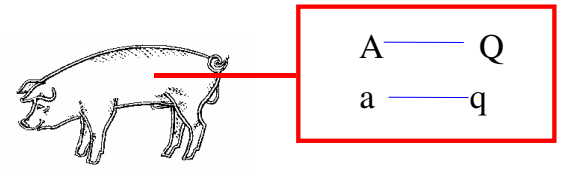
Genomic selection

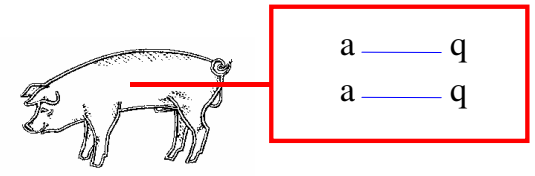
- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

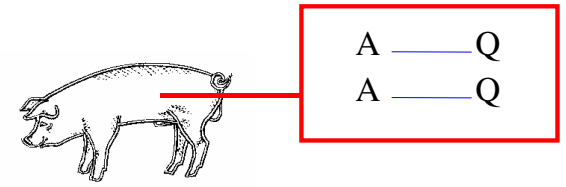
Genomic selection across breeds

- Genomic selection relies on the phase of LD between markers and QTL being the same in the selection candidates as in the reference population.
- However as the two populations diverge, this is less and less likely to be the case
  - especially if the distance between markers and QTL is relatively large.


A Q
a q

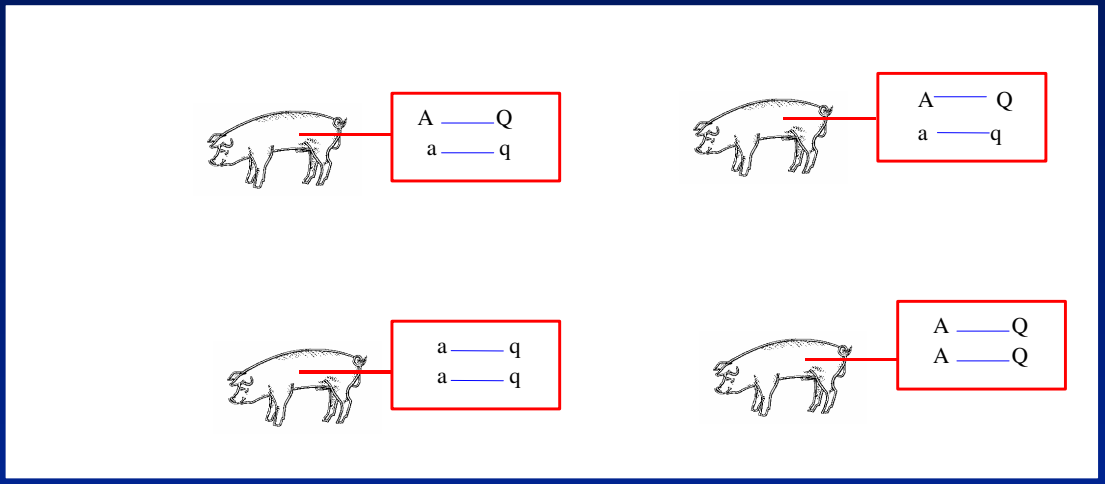

A Q
a q


a q
a q


A Q
A Q

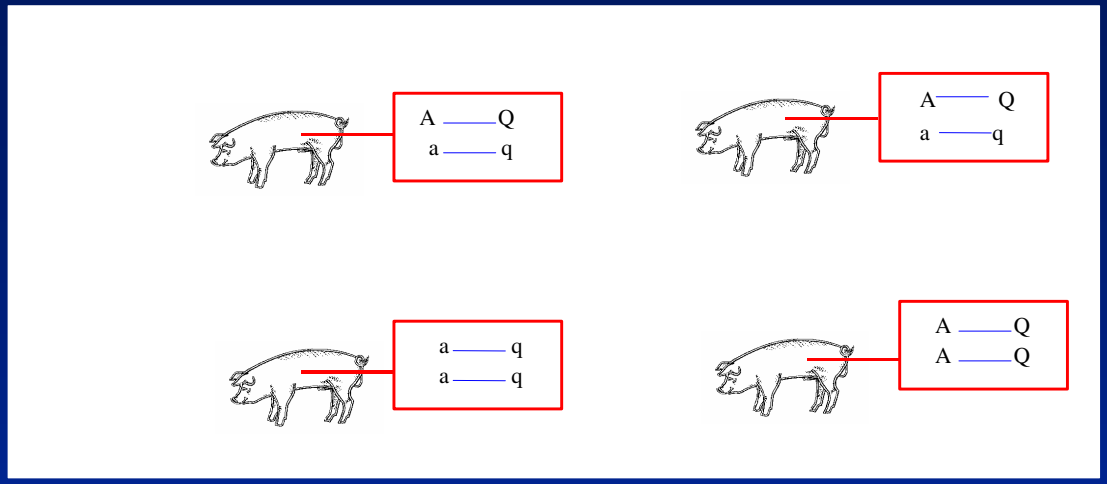
Same Breed

Predict g_i in reference population



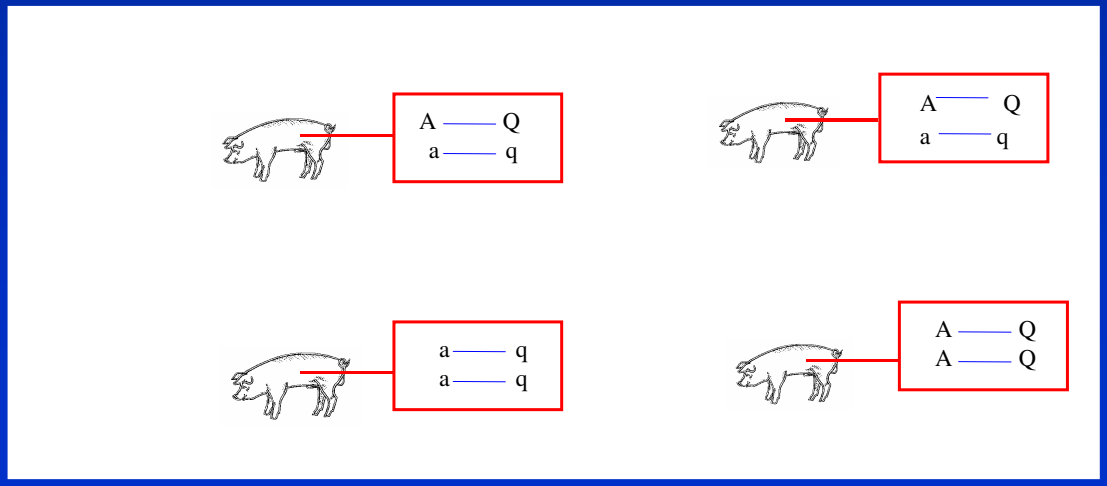
Same Breed

Predict g_i in reference population



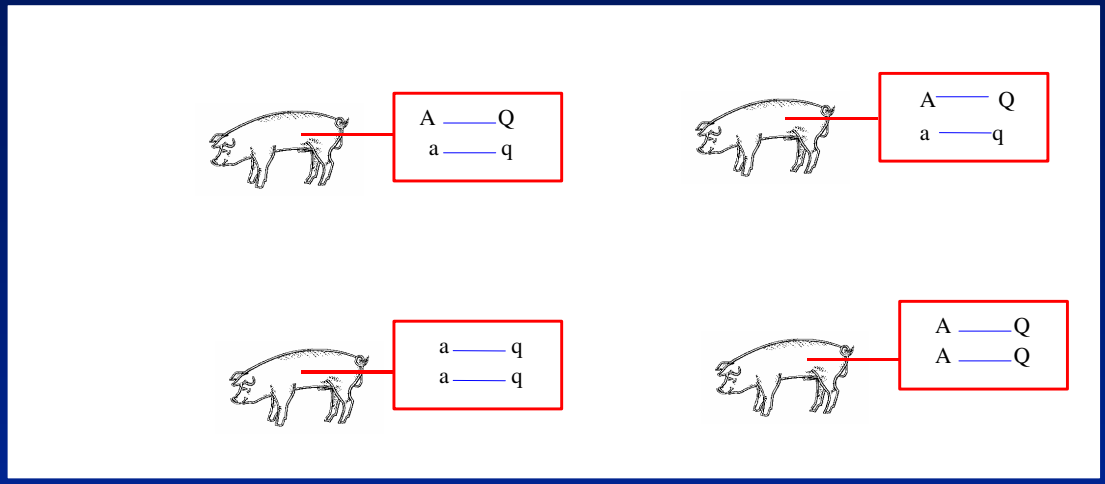
Calculate GEBV in selection candidates

$$\mathbf{GEBV} = \sum_{i}^{p} \mathbf{X}_i \hat{\mathbf{g}}_i$$



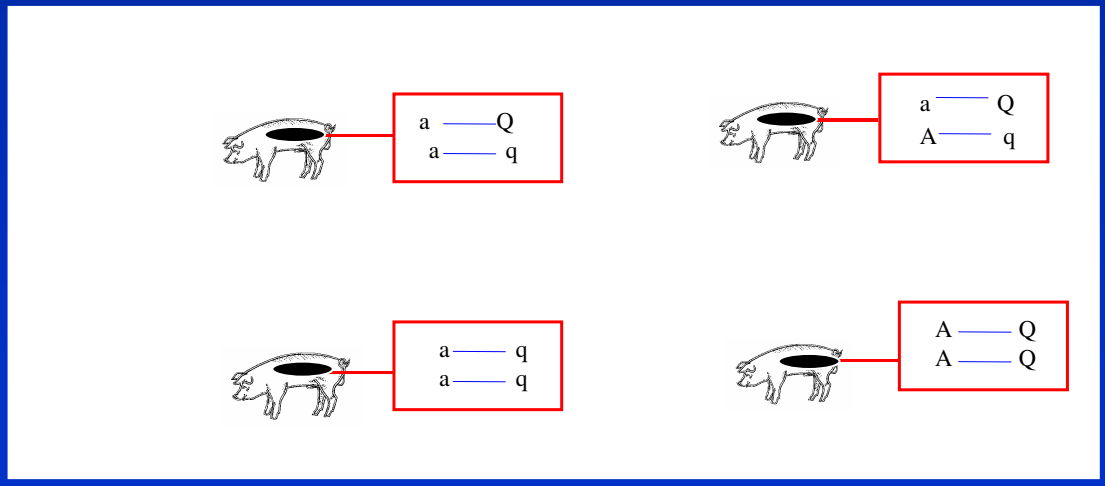
Different Breeds

Predict g_i in reference population



Calculate GEBV in selection candidates

$$\mathbf{GEBV} = \sum_{i}^{p} \mathbf{X}_i \hat{\mathbf{g}}_i$$



Genomic selection across breeds

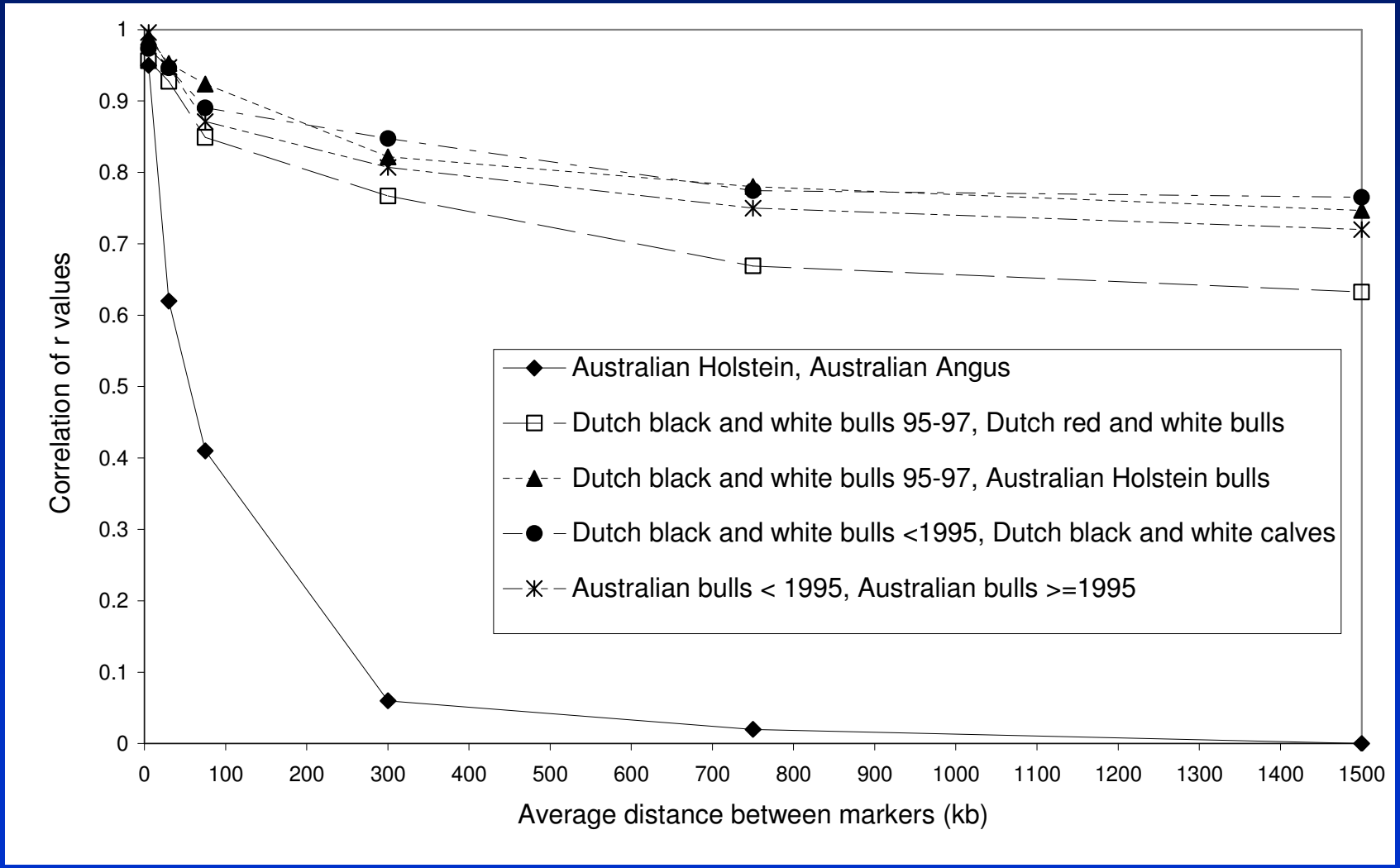
- Use correlation between r in two populations, corr(r1,r2), to assess persistence of LD across populations.
  - Signed r^2 statistic
  - If same sign in different breeds, same marker allele associated with increasing QTL allele

Genomic selection across breeds

- Use correlation between r in two populations, corr(r1,r2), to assess persistence of LD across populations.
  - Signed r^2 statistic
  - If same sign in different breeds, same marker allele associated with increasing QTL allele

- If the chromosome segment effects are estimated in population 1, and GEBVs in that population can be predicted with an accuracy *x1*, then the GEBVs of animals population 2 may be predicted from the chromosome segment effects of population 1 with an accuracy *x2* = *x1**corr(r1,r2)

Genomic selection across breeds



Genomic selection across breeds

- Recently diverged breeds/lines, may be possible to use estimates of SNP effects across lines?
- More distantly related breeds, will need very dense marker maps before implementation?
- Important in multi breed populations
  - eg. beef, sheep, pigs
- Assumes same QTL mutation in both breeds

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

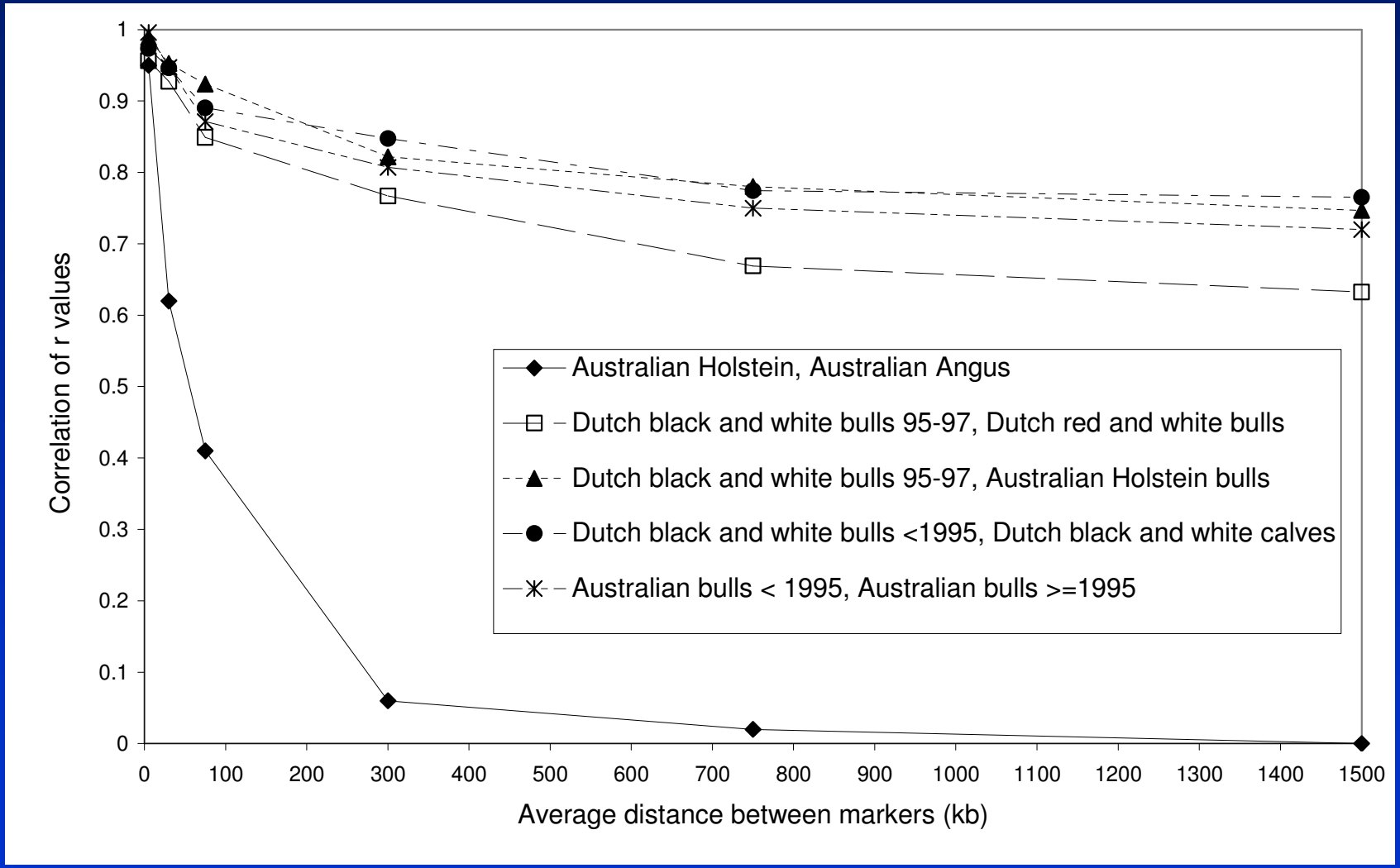
Genomic selection

- How often to re-estimate the chromosome segment effects?
  - If the markers used in genomic selection were actually the underlying mutations causing the QTL effects, the estimation of chromosome segment effects could be performed once in the reference population.
  - GEBVs for all subsequent generations could be predicted using these effects.

Genomic selection

- How often to re-estimate the chromosome segment effects?
  - In practise is that there will be markers with low to moderate levels of r^2 with the underlying mutations causing the QTL effect.
  - Do not capture all of QTL variance
  - Over time, recombination between the markers and QTL will reduce the accuracy of the GEBV using chromosome segment effects predicted from the original reference population.
  - We need to re-estimate chromosome segment effects
  - How often?

Genomic selection across breeds



Genomic selection

- How often to re-estimate the chromosome segment effects?

Table 4.3. The correlation between estimated and true breeding values in generations 1003–1008, where the estimated breeding values are obtained from the BayesB marker estimates in generations 1001 and 1002. From Meuwissen et al. (2001).

Generation	$r_{TBV;EBV}$
1003	0.848
1004	0.804
1005	0.768
1006	0.758
1007	0.734
1008	0.718

The generations 1004–1008 are obtained in the same way as 1003 from their parental generations.

Genomic selection

- How often to re-estimate the chromosome segment effects?

Table 4.3. The correlation between estimated and true breeding values in generations 1003–1008, where the estimated breeding values are obtained from the BayesB marker estimates in generations 1001 and 1002. From Meuwissen et al. (2001).

Generation	$r_{TBV;EBV}$
1003	0.848
1004	0.804
1005	0.768
1006	0.758
1007	0.734
1008	0.718

The generations 1004–1008 are obtained in the same way as 1003 from their parental generations.

  - Denser markers >> generations between re-estimation of effects

Genomic selection

- However decay of accuracy is dependant on genomic selection method…..

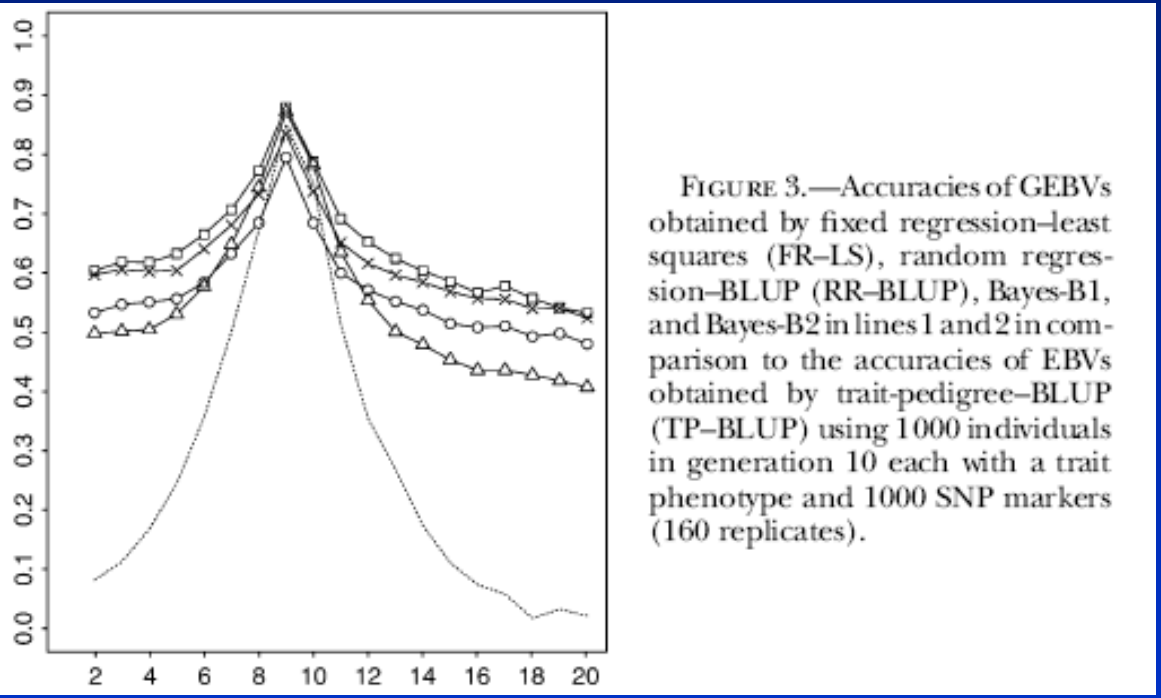


FIGURE 3.—Accuracies of GEBVs obtained by fixed regression–least squares (FR–LS), random regression–BLUP (RR–BLUP), Bayes-B1, and Bayes-B2 in lines 1 and 2 in comparison to the accuracies of EBVs obtained by trait-pedigree–BLUP (TP–BLUP) using 1000 individuals in generation 10 each with a trait phenotype and 1000 SNP markers (160 replicates).

- Habier et al. (Genetics 177:2389)

Genomic selection

- Decay of accuracy actually depends on LD between QTL and SNPs
  - Higher LD slower decay
- ***Genomic selection methods will also pick up pedigree effects if this is not accounted for!!***
  - Eg a rare SNP heterozygous in a sire is a good marker for the family derived from that sire!

Genomic selection

- Decay of accuracy actually depends on LD between QTL and SNPs
  - Higher LD slower decay
- ***Genomic selection methods will also pick up pedigree effects if this is not accounted for!!***
  - Eg a rare SNP heterozygous in a sire is a good marker for the family derived from that sire!
  - BLUP especially bad, as is the same as fitting average relationship matrix derived from markers
    - Eg each segment has same variance

Genomic selection

- Decay of accuracy actually depends on LD between QTL and SNPs
  - Higher LD slower decay
- ***Genomic selection methods will also pick up pedigree effects if this is not accounted for!!***
  - Eg a rare SNP heterozygous in a sire is a good marker for the family derived from that sire!
  - Solutions
    - Fit polygenic effect in model
      - Sample **u** from $N(0,A\sigma^2)$ in Gibbs chain and correct when sampling other effects
      - *Demonstration with R……*

Genomic selection

- Decay of accuracy actually depends on LD between QTL and SNPs
  - Higher LD slower decay
- ***Genomic selection methods will also pick up pedigree effects if this is not accounted for!!***
  - Eg a rare SNP heterozygous in a sire is a good marker for the family derived from that sire!
  - Solutions
    - Fit polygenic effect in model
      - Sample **u** from $N(0,A\sigma^2)$ in gibbs chain and correct when sampling other effects
    - Use multiple breeds?
      - Must be very close to QTL for SNP to have effect across multiple breeds

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

Cost effective genomic selection

- Depending on the genotyping technology used, the cost of genotyping animals for ~ 30 000 SNPs may be $500
- This limits the application of genomic selection to valuable animals
  - Eg. Proven dairy bulls
- Can we reduce the cost of genotyping?

Cost effective genomic selection

- When the method BayesB of Meuwissen et al. (2001) is applied many of the chromosome segment effects will be set to close to zero.
- Only the subset of markers in chromosome segments with a non-zero effect need be genotyped.
  - 100 -150 markers?
- Problem with multiple traits

Genomic selection

- An IBD approach
- Factors affecting accuracy of genomic selection
- Non-additive effects
- Genomic selection with low marker density
- Genomic selection across breeds
- How often to re-estimate the chromosome segment effects?
- Cost effective genomic selection
- Optimal breeding program design with genomic selection

Optimal breeding program design

- With genomic selection, we can predict GEBV with an accuracy of 0.8 for selection candidates at birth
- How does this change the optimal breeding program design?

Optimal breeding program design

- With genomic selection, we can predict GEBV with an accuracy of 0.8 for selection candidates at birth
- How does this change the optimal breeding program design?

- Breed from animals as early as possible

Optimal breeding program design

- In dairy cattle current structure is
  - Each year select a team of calves to form a progeny test team
  - At two years of age these bulls are mated to random cows from the population
  - At four years of age the daughters of the bulls start lactating

Optimal breeding program design

- In dairy cattle current structure is
  - Each year select a team of calves to form a progeny test team
  - At two years of age these bulls are mated to random cows from the population
  - At four years of age the daughters of the bulls start lactating
  - At five years of age the bulls receive a progeny test "proof" based on the performance of their daughters
  - The bulls are then selected on the basis of these proofs to be "breeding bulls"
    - Semen sold to commercial farmers

Optimal breeding program design

- In dairy cattle with genomic selection..
  - Genotype a large number of bull calves from the population
  - Calculate GEBVs for these calves
    - Accuracy = 0.8 = accuracy of progeny test
  - Select team based on GEBV
  - Sell semen from these bulls as soon as they can produce it

Optimal breeding program design

- In dairy cattle with genomic selection..
  - Genotype a large number of bull calves from the population
  - Calculate GEBVs for these calves
    - Accuracy = 0.8 = accuracy of progeny test
  - Select team based on GEBV
  - Sell semen from these bulls as soon as they can produce it
  - Generation interval reduced from ~4 yrs to ~ 2 yrs
    - $\Delta G = ir\sigma_g/L$
  - Double rate of genetic gain

Optimal breeding program design

- In dairy cattle with genomic selection..
  - Genotype a large number of bull calves from the population
  - Calculate GEBVs for these calves
    - Accuracy = 0.8 = accuracy of progeny test
  - Select team based on GEBV
  - Sell semen from these bulls as soon as they can produce it
  - Generation interval reduced from ~4 yrs to ~ 2 yrs
    - $\Delta G = ir\sigma_g/L$
  - Double rate of genetic gain
  - Save the cost of progeny testing!
    - Reduce costs by 92% (Schaeffer et al. 2006)

Optimal breeding program design

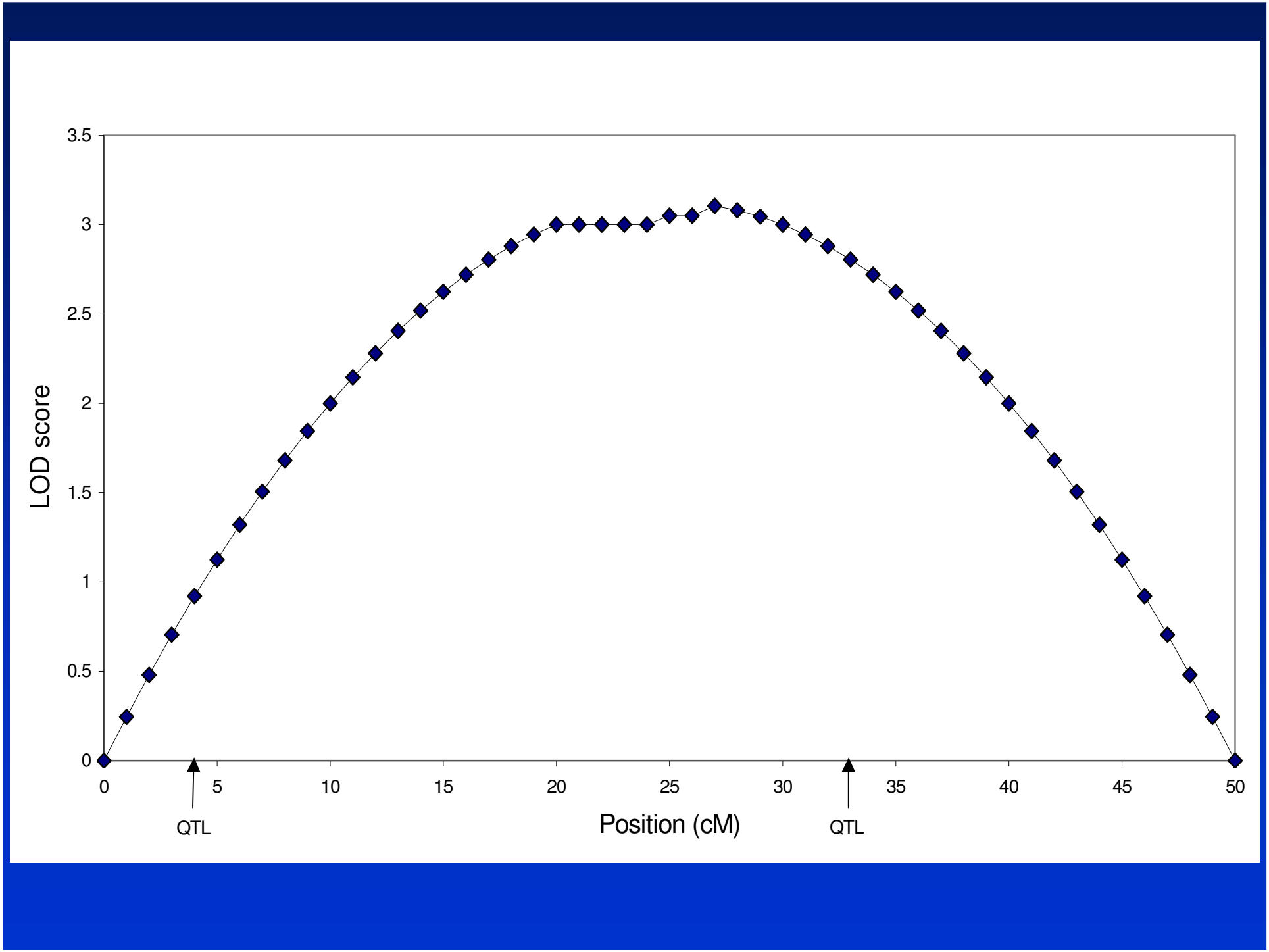
- In pigs
  - Currently EBV for traits like meat quality, sow fertility, disease resistance based on performance of relatives
  - Exploits between family variance, not within
  - Feed conversion efficiency = expensive

Optimal breeding program design

- In pigs with genomic selection
  - Accurate GEBVs for meat quality, sow fertility, disease resistance based on own marker genotype
  - Exploits between and within family variance
  - Feed conversion efficiency GEBV?
  - Will accelerate genetic gain for these traits
  - Reverse declines in meat quality for example

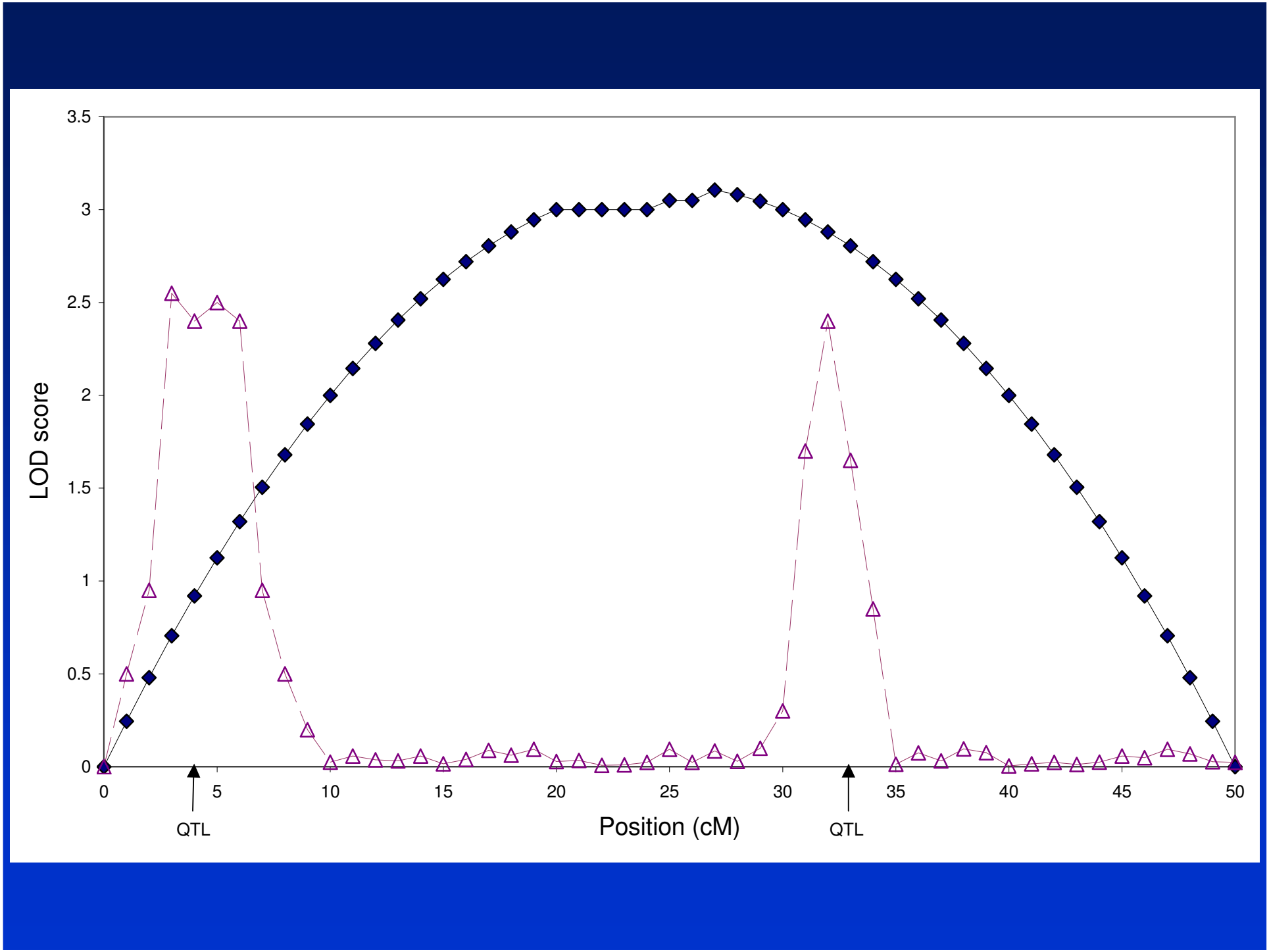
Genomic selection for QTL mapping

- The existence of two or more QTL on a chromosome can bias the estimates of position and effect in QTL mapping
  - "Ghost QTL"


LOD score
3.5
3
2.5
2
1.5
1
0.5
0
0
5
10
15
20
25
30
35
40
45
50
QTL
Position (cM)
QTL

Genomic selection for QTL mapping

- The existence of two or more QTL on a chromosome can bias the estimates of position and effect in QTL mapping
  - "Ghost QTL"
- In genomic selection we fit all QTL simultaneously
- Remove effect of QTL in adjacent marker brackets


3.5
3
2.5
2
1.5
1
0.5
0
LOD score
0
5
10
15
20
25
30
35
40
45
50
Position (cM)
QTL
QTL

Genomic selection for QTL mapping

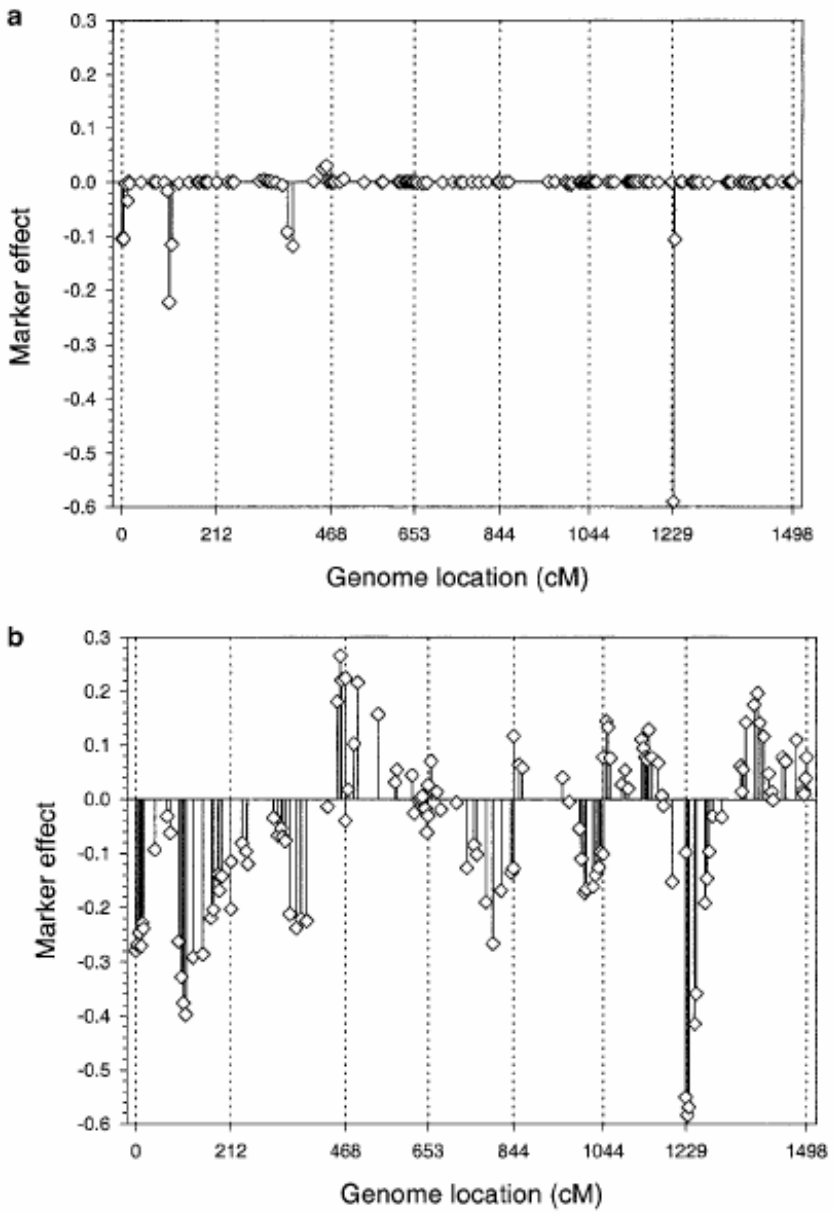


FIGURE 1.—Marker effects of kernel weight in barley plotted against marker locations along the genome. (a) Multiple-marker Bayesian analysis; (b) individual-marker regression analysis. The dotted vertical reference lines separate the seven linkage groups.

Genomic selection

- Accuracy of genomic selection depends on
  - LD between markers and haplotyes
    - r2>=0.2 required to achieve r(GEBV,TBV) = 0.8
  - Number of records used to estimate segment effects
- With low marker density, IBD approach has some advantages
  - Include polygenic effect
  - Capture linkage information

Genomic selection

- Higher marker densities necessary to apply genomic selection across breeds
  - Choose reference populations carefully!
- Number of generations between estimating chromosome segment effects depends on marker density
- Cost effective genomic selection possible?
- May radically alter breeding programs for some species