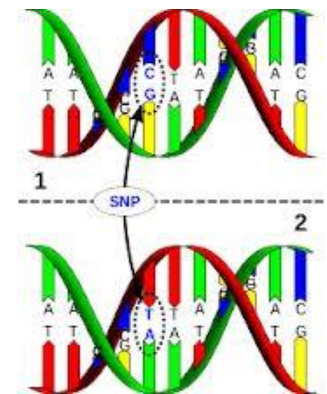
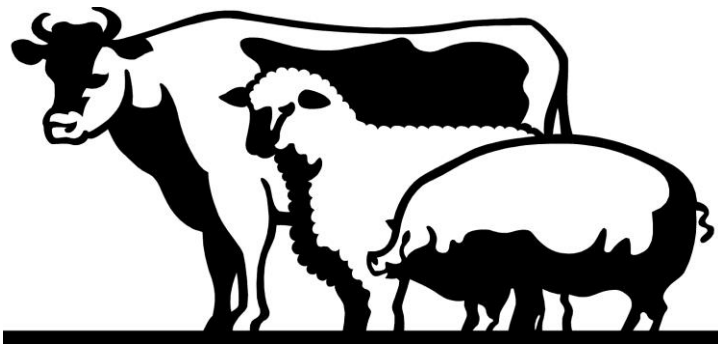


# Genomic information and inbreeding



# Why use information from relatives?

- High degree of similarity between relatives
- More accurately predict breeding value

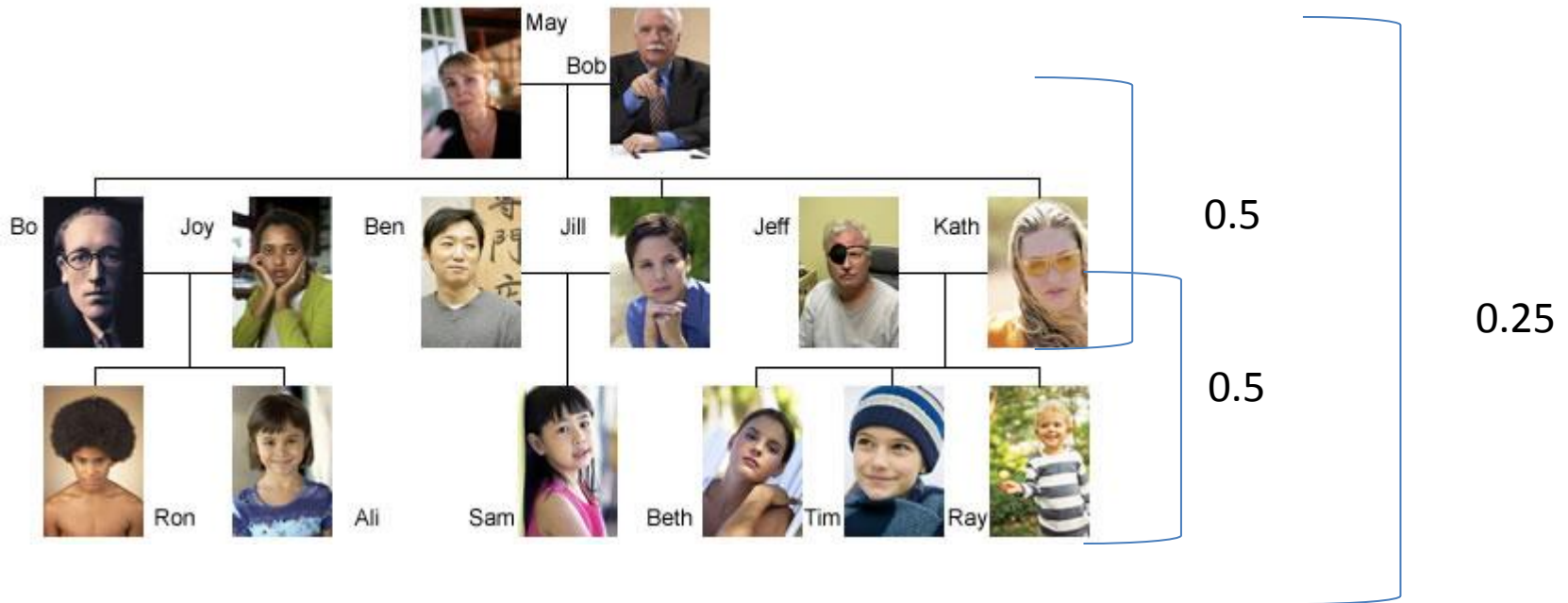


# Relationships between Individuals

- Estimated using:
  - Expected probabilities from PEDIGREE
  - Estimated proportion of genome shared
    - Thousands of genetic markers (SNPs)

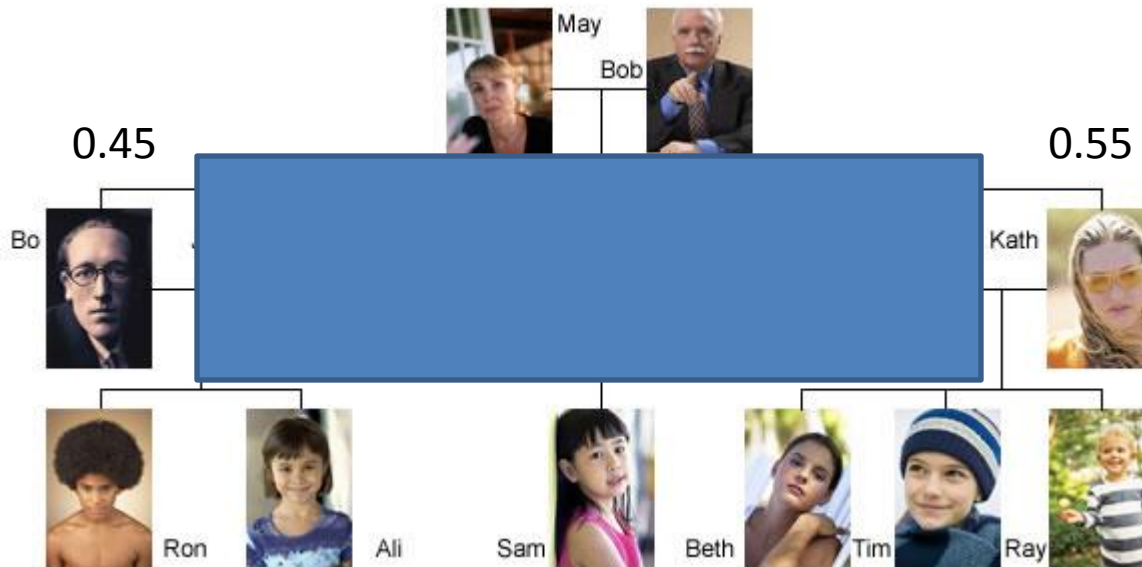
# Genomic vs Pedigree BLUP

## Pedigree



# Genomic vs Pedigree BLUP

## Genomic



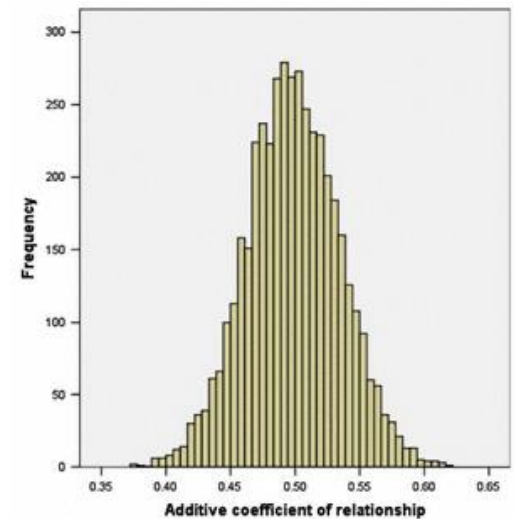
Full siblings

Relationship with Kath

There is variation in actual relationship, e.g.  
0.45-0.55 in FS  
0.20-0.30 in HS  
We can see this with genomic relationships

# Estimates of relationship using genotypes:

- The expectations A
- Replaced by the estimated G
  - Genomic relationship matrix
  
- Still half mum and half dad
  - But which half?
  - Variation around the expectation?



There is variation in actual relationship, e.g. 0.40-0.50 in FS

We can see this with genomic relationships

# Genomic Prediction: GBLUP

## Example:

Data on sire 1, his sons (2 and 3) and an unrelated individual (4)

want to predict 5 (also a son of 1) ← no data

A-matrix (pedigree-based)

1	0.5	0.5	0	0.5
0.5	1	0.25	0	0.25
0.5	0.25	1	0	0.25
0	0	0	1	0
0.5	0.25	0.25	0	1

G-matrix (DNA-based)

1	0.5	0.5	0.02	0.5
0.5	1	0.20	0.015	0.20
0.5	0.20	1	0.025	0.30
0.02	0.015	0.025	1	0.025
0.5	0.20	0.30	0.025	1

Variation in  
relationship  
(animal 5 with 2  
and 3

Also a small  
relationship with  
'unrelated'

# Genomic Prediction: GBLUP

Example:

Data on sire 1, sons 2 and 3, 4  
unrelated, want to predict 5

A-matrix (pedigree-based)

1	0.5	0.5	0	0.5
0.5	1	0.25	0	0.25
0.5	0.25	1	0	0.25
0	0	0	1	0
0.5	0.25	0.25	0	1

G-matrix (DNA-based)

1	0.5	0.5	0.02	0.5
0.5	1	0.20	0.015	0.20
0.5	0.20	1	0.025	0.30
0.02	0.015	0.025	1	0.025
0.5	0.20	0.30	0.025	1

BLUP

$$\hat{u}_5 = 0.1136.y_1 + 0.0455.y_2 + 0.0455.y_3$$

GBLUP

$$\hat{g}_5 = 0.1135.y_1 + 0.0328.y_2 + 0.0591.y_3 + 0.00519.y_4$$



# Genomic Prediction: GBLUP

Example:

Data on sire 1, sons 2 and 3, 4  
unrelated, want to predict 5

A-matrix (pedigree-based)

1	0.5	0.5	0	0.5
0.5	1	0.25	0	0.25
0.5	0.25	1	0	0.25
0	0	0	1	0
0.5	0.25	0.25	0	1

BLUP uses: Family Info

G-matrix (DNA-based)

1	0.5	0.5	0.02	0.5
0.5	1	0.20	0.015	0.20
0.5	0.20	1	0.025	0.30
0.02	0.015	0.025	1	0.025
0.5	0.20	0.30	0.025	1

GBLUP uses: Family Info  
Segregation within family  
Info on 'unrelated'

# Inbreeding- revision

- Mating of relatives
- Consequences
  - Many are bad, but not all.....
- Management – restricting mating of relatives
  - Optimal contribution selection
- How does Genomics change this?
  - *If performing truncation selection....*
  - *If performing optimal contribution selection...*

# Truncation selection

- Pedigree BLUP

Vs

- Genomic breeding value (GBLUP)
- Variation in BV among selection candidates

$$V_a = \frac{1}{4} \text{ sire} + \frac{1}{4} \text{ dam} + \frac{1}{2} \text{ MS}$$

# What information is used in BVs

- $$V_a = \frac{1}{4} \text{ sire} + \frac{1}{4} \text{ dam} + \frac{1}{2} \text{ MS}$$

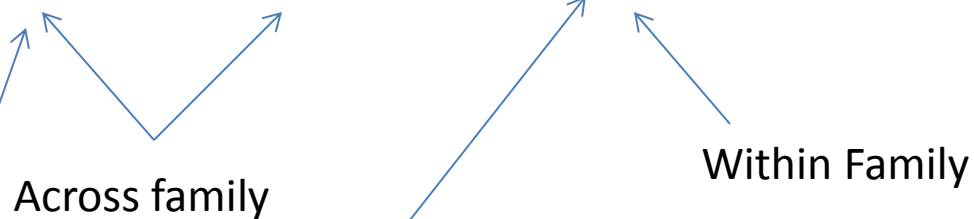


Table 2- The proportion of variation in breeding value explained by between family (Sire and Dam) and within family (MS) information.

<i>LIC</i>					<i>ADHIS</i>				
BV	Sire	Dam	MS+e	Prop. of PT	BV	Sire	Dam	MS+e	Prop. of PT
PA EBV	0.56	0.44	0.001	0.001	PA EBV	0.44	0.52	0.04	0.05
GEBV	0.43	0.26	0.31	0.56	GEBV	0.33	0.37	0.30	0.36
PT	0.21	0.31	0.48	1.0	PT	0.16	0.32	0.52	1.0

# Correlation of breeding values and co-selection of relatives

Breeding value type	Half sib correlation	Full Sib correlation	Accuracy
PA EBV	0.55	1.0	0.45
GEBV	0.50	0.85	0.57
TBV	0.26	0.53	1.0

## Full Sibs

- share the same Parent average BV ( $\frac{1}{2}$  sire  $\frac{1}{2}$  dam)
- no longer the case with genomics

## Half Sibs

- Share different PA breeding values
- Small advantage of using G to restrict inbreeding

# Truncation selection on breeding values estimated using TBLUP or GBLUP

(Sonesson, Woolliams, Meuwissen, 2012)

Genetic gain

Inbreeding

Breeding value estimation

$\Delta G$  (se)

$\Delta F_{ped}$  (se)

$\Delta F_{IBD}$  (se)

TBLUP

2.49 (0.035)

0.0156 (0.0001)

0.0235 (0.0009)

GBLUP

2.77 (0.026)

0.0053 (0.0002)

0.0209 (0.0005)

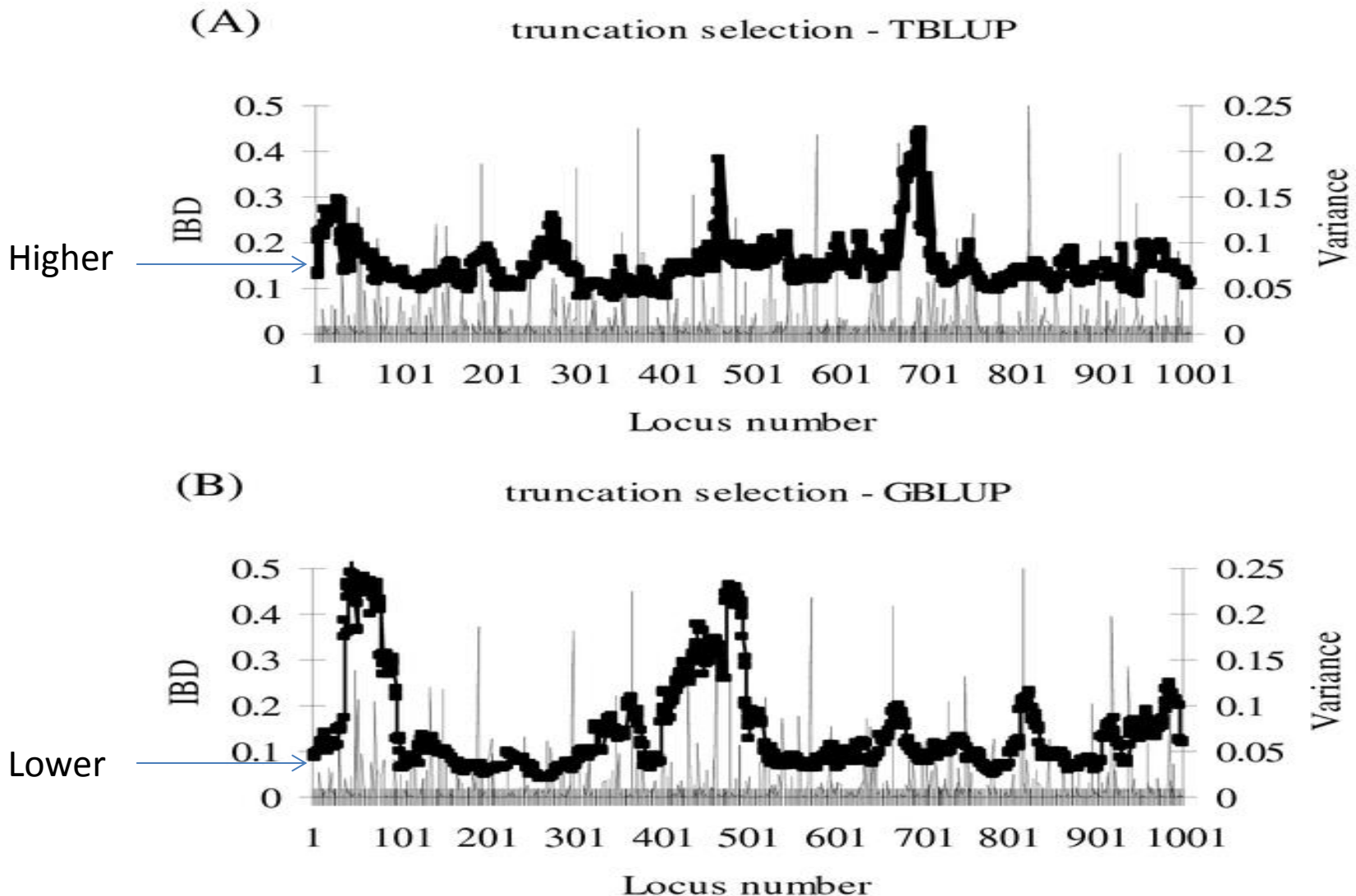
$$\Delta F_{PED} < \Delta F_{IBD}$$

$\Delta F_{PED}$  lower with GBLUP

$\Delta F_{IBD}$  only slightly lower with GBLUP (and even less so if using BayesB)

# Truncation selection on breeding values estimated using TBLUP or GBLUP

(Sonesson, Woolliams, Meuwissen, 2012)



---- Selecting 100 sires and 100 dams from 3000 cand. ---- After 10 generations

# Constraining Inbreeding:

Pedigree or Genomics, Optimal contributions

- Measures of genetic merit ( $\bar{g}$ )
  - Pedigree vs genomic  
*Pedigree based BLUP --- Genomic BLUP*
- Measures of inbreeding
  - Pedigree vs genomic (A or G)  
*NRM (Pedigree) --- GRM (genomic)*

$$\begin{aligned} \text{Max} &= \mathbf{c}_t' \bar{\mathbf{g}}_t - \lambda \mathbf{c}_t' \mathbf{A}_t \mathbf{c}_t \\ \text{or:} &= \mathbf{c}_t' \bar{\mathbf{g}}_t - \lambda \mathbf{c}_t' \mathbf{G}_t \mathbf{c}_t \end{aligned}$$



# Measuring inbreeding

- Pedigree
  - The probability that animals share alleles IBD.
- Genomics
  - GRM (IBS) *or what is actually shared.*
  - others

# Genomic Inbreeding estimates

- Estimates of the number of homozygotes
  - Sharing of markers (IBS)
  - Long runs of homozygotes (more IBD)
- Genomic relationships (IBS)
  - Various methods
  - Choice of allele frequencies

# Example GRM

- $Z = M - 2(\pi - 0.5)$
- $ZZ' / 2 * \sum \pi_i(q_i)$  (more weighting to rare alleles)
- Choice of allele frequencies
  - Forni 2012
  - Sets base population
  - Although this is relative and is more important when combining data (Single step)

# management

- Optimal contribution
- Pedigree or genomic
  - Pedigree – expected based on IBD prob.
  - Genomic observed (although an estimate)

**Table 2 Optimum contribution selection on breeding values estimated using TBLUP or GBLUP**

Ntest	$\Delta F_d$	$\Delta G$ (se)	$\Delta F_{ped}$ (se)	$\Delta F_{IBD}$ (se)
<b><math>\Delta F_A</math> constraint – GBLUP</b>				
3000	0.005	3.08 (0.035)	0.0050 (0.0001)	0.0211 (0.0004)
6000	0.005	3.10 (0.035)	0.0048 (0.0001)	0.0226 (0.0004)
6000	0.010	3.31 (0.037)	0.0098 (0.0003)	0.0422 (0.0008)
<b><math>\Delta F_G</math> constraint – GBLUP</b>				
3000	0.005	1.91 (0.026)	0.0041 (0.0001)	0.0051 (0.0001)
6000	0.005	1.95 (0.024)	0.0039 (0.0001)	0.0053 (0.0001)
6000	0.010	2.41 (0.028)	0.0071 (0.0002)	0.0102 (0.0002)
<b><math>\Delta F_A</math> constraint – TBLUP</b>				
3000	0.005	2.26 (0.003)	0.0050 (0.0001)	0.0068 (0.0001)
6000	0.005	2.50 (0.003)	0.0049 (0.0001)	0.0074 (0.0001)
6000	0.010	2.63 (0.003)	0.0102 (0.0002)	0.0151 (0.0003)
<b><math>\Delta F_G</math> constraint – TBLUP</b>				
3000	0.005	1.41 (0.041)	0.0193 (0.0004)	0.0121 (0.0002)
6000	0.005	1.44 (0.039)	0.0185 (0.0004)	0.0122 (0.0002)
6000	0.010	1.48 (0.046)	0.0300 (0.0008)	0.0183 (0.0003)

Genetic gain ( $\Delta G$ ), rate of inbreeding based on pedigree ( $\Delta F_{ped}$ ) and on genomic IBD ( $\Delta F_{IBD}$ ) relationship matrices at generation  $G_{10}$  when the constraint on relationship was either pedigree-based ( $\Delta F_A$ ) or marker-based ( $\Delta F_G$ ) with TBLUP or GBLUP breeding value estimates<sup>a</sup>.

<sup>a</sup>Ntest = number of test sibs;  $\Delta F_d$  = desired rates of inbreeding; number of selection candidates = 3000.

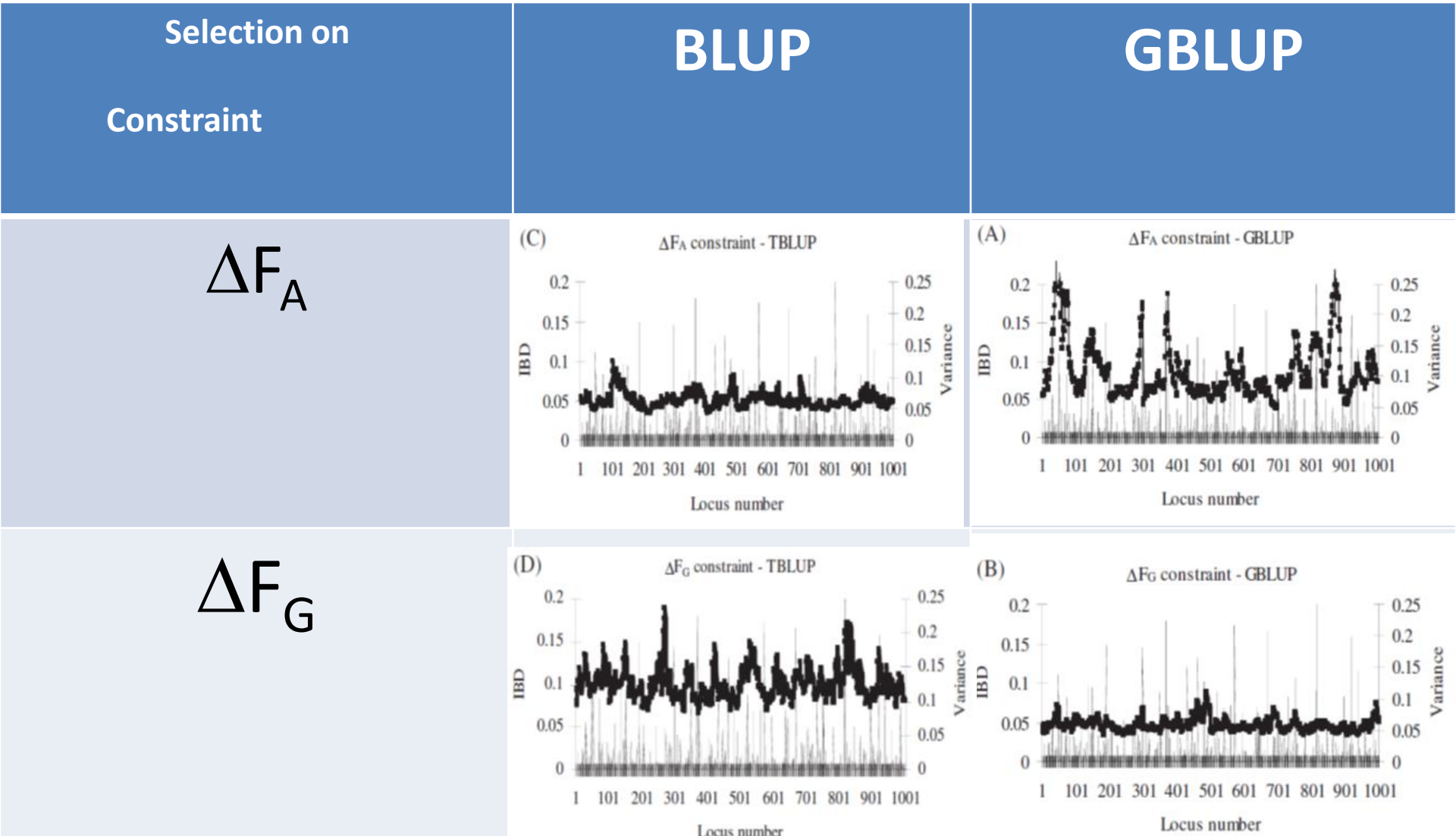
# Constraining Inbreeding:

Pedigree or Genomics, Optimal contributions

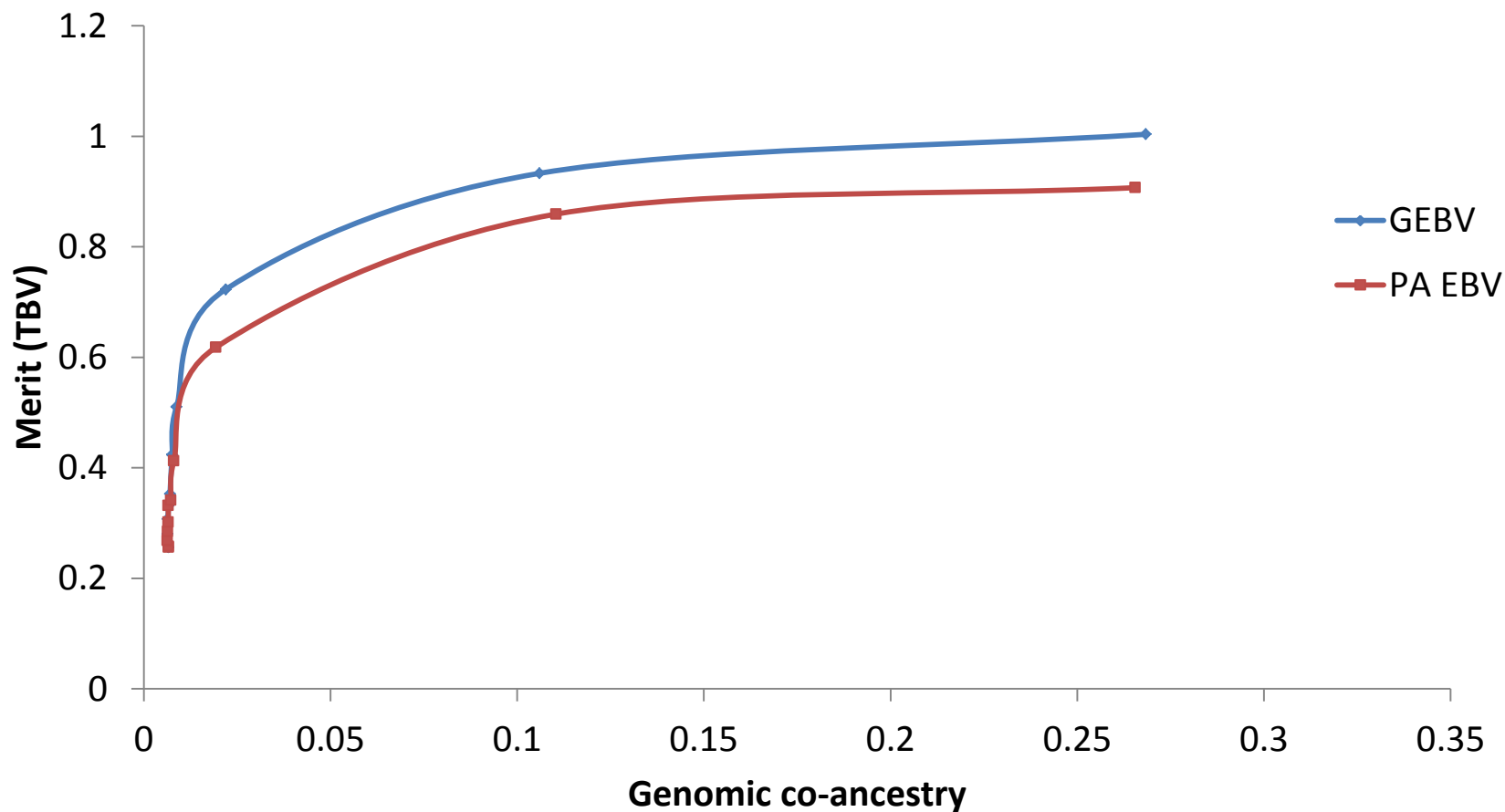
Selection on Constraint	BLUP	GBLUP
$\Delta F_A$	$\Delta F_A$ constrained $\Delta F_G$ not well constrained	$\Delta F_A$ constrained $\Delta F_G$ badly constrained
$\Delta F_G$	$\Delta F_A$ not constrained $\Delta F_G$ not constrained	$\Delta F_A$ constrained $\Delta F_G$ constrained

# Constraining Inbreeding:

Pedigree or Genomics, Optimal contributions

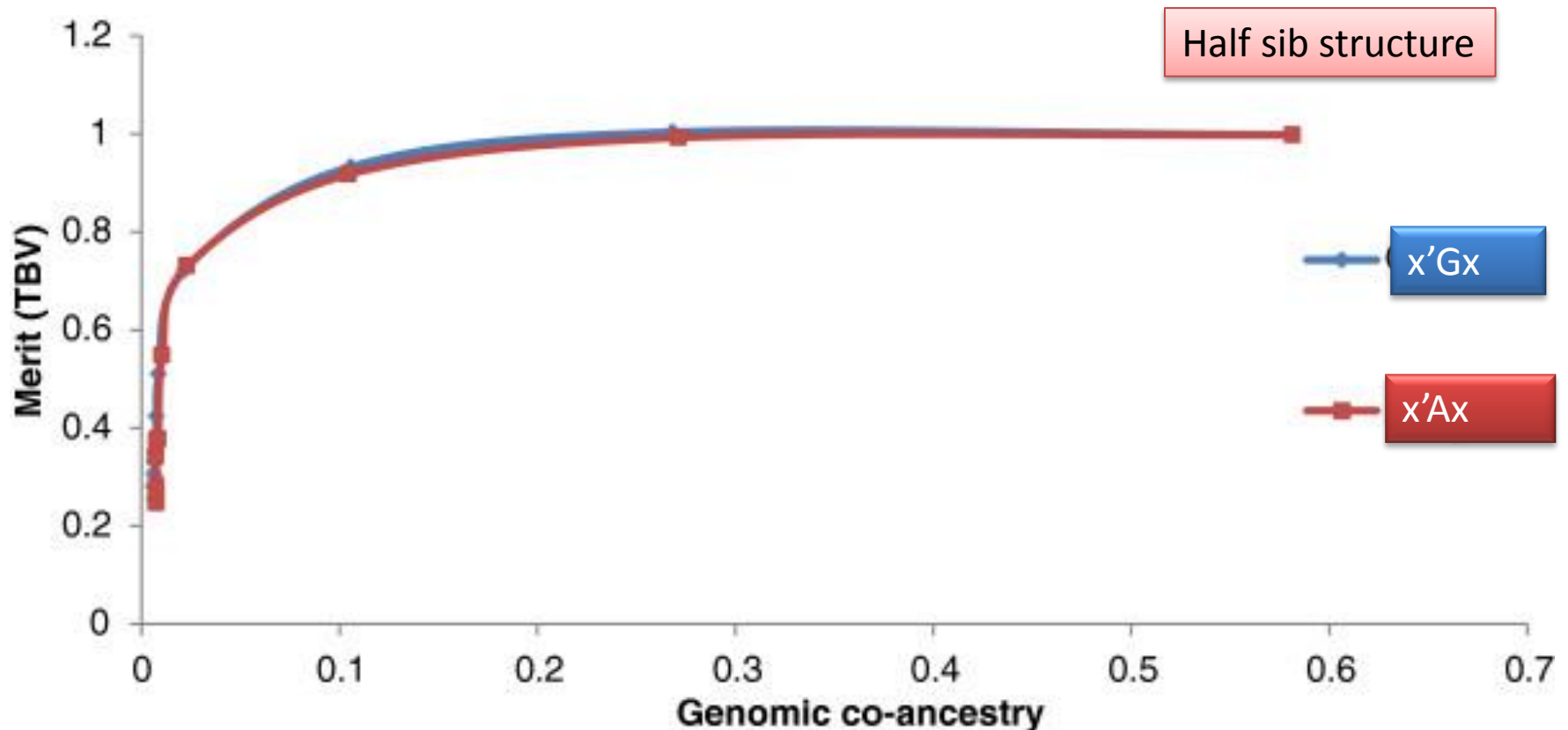


# How much can we utilize additional diversity? selecting on GEBV vs EBV

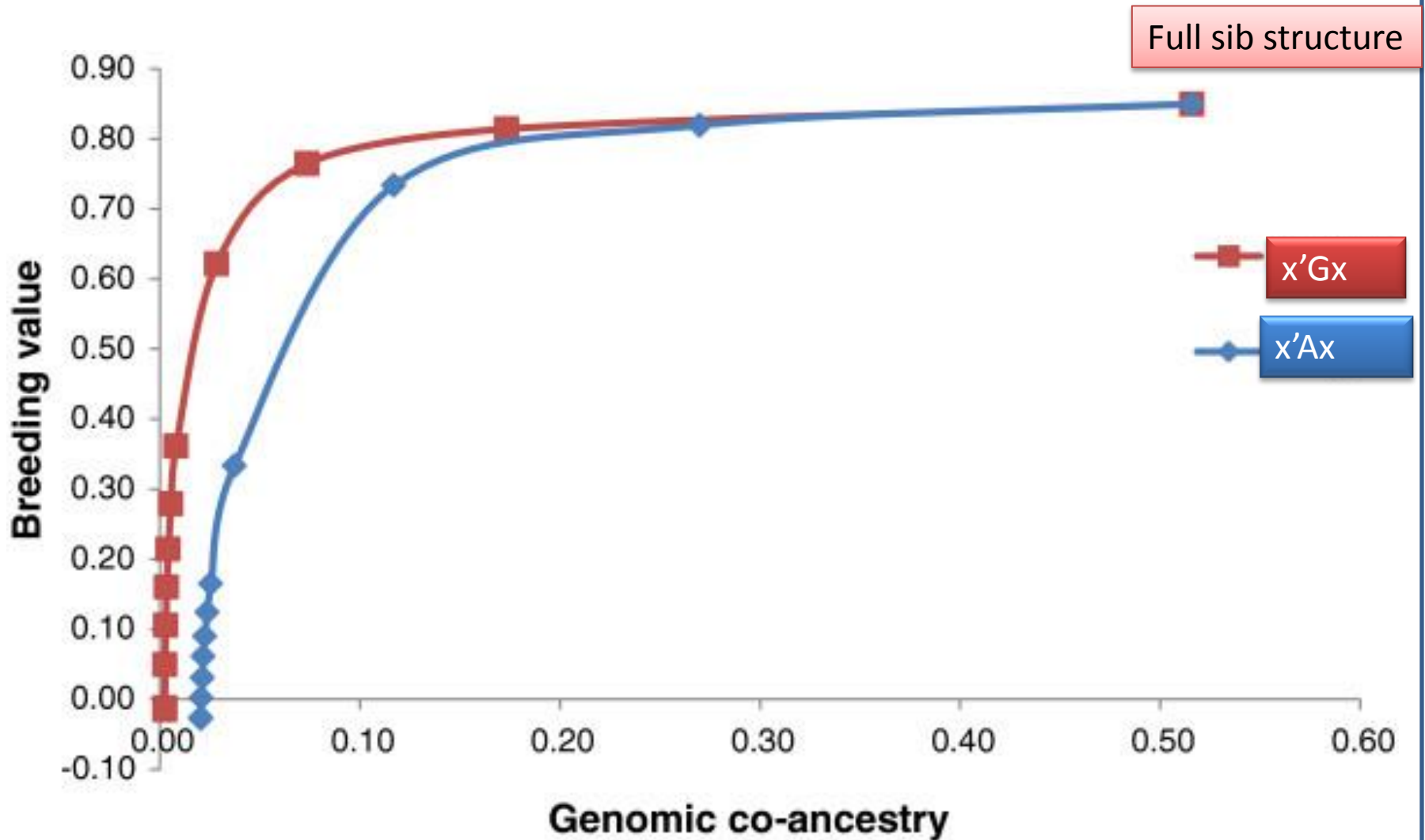




How much can we utilize additional diversity?  
using  $x'Ax$  vs  $x'Gx$ ?



How much can we utilize additional diversity?  
using  $x'Ax$  vs  $x'Gx$ ?



# Genomic information helps to manage inbreeding

1. Uses genomic relationships helps to restrict genomic inbreeding.
2. Utilizes information about Mendelian sampling
  1. More accuracy: more  $\Delta G$  for same  $\Delta F$
  2. More diversity  $\rightarrow$  more selection space giving raise to even more  $\Delta G$  for same  $\Delta F$ 

but mainly useful for large FS families