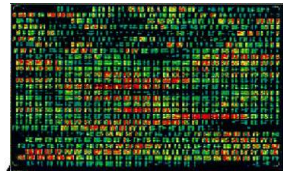
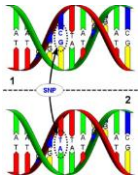


Genomic Selection Impacts

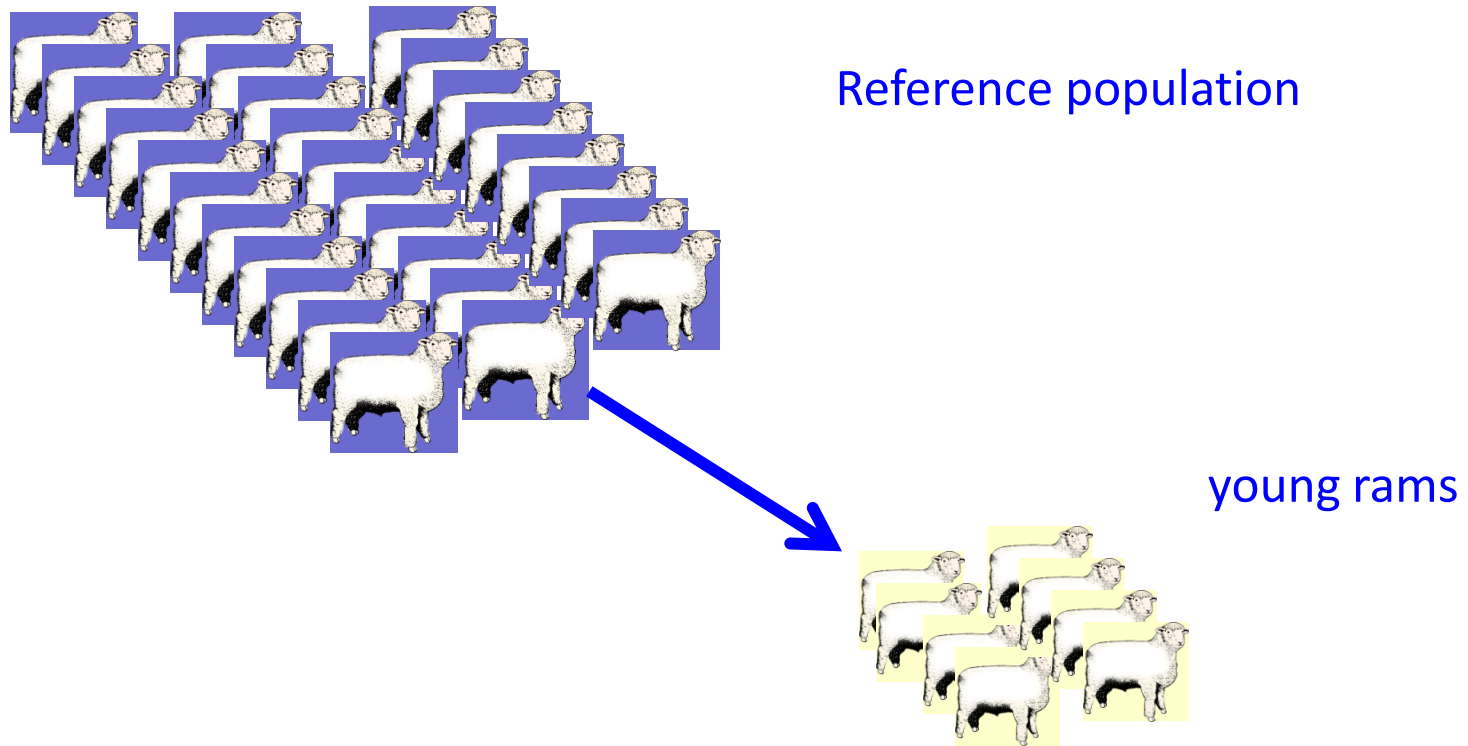
Julius van der Werf

School of Environmental & Rural Science, UNE, Armidale

CRC for Sheep Industry Innovation, Armidale



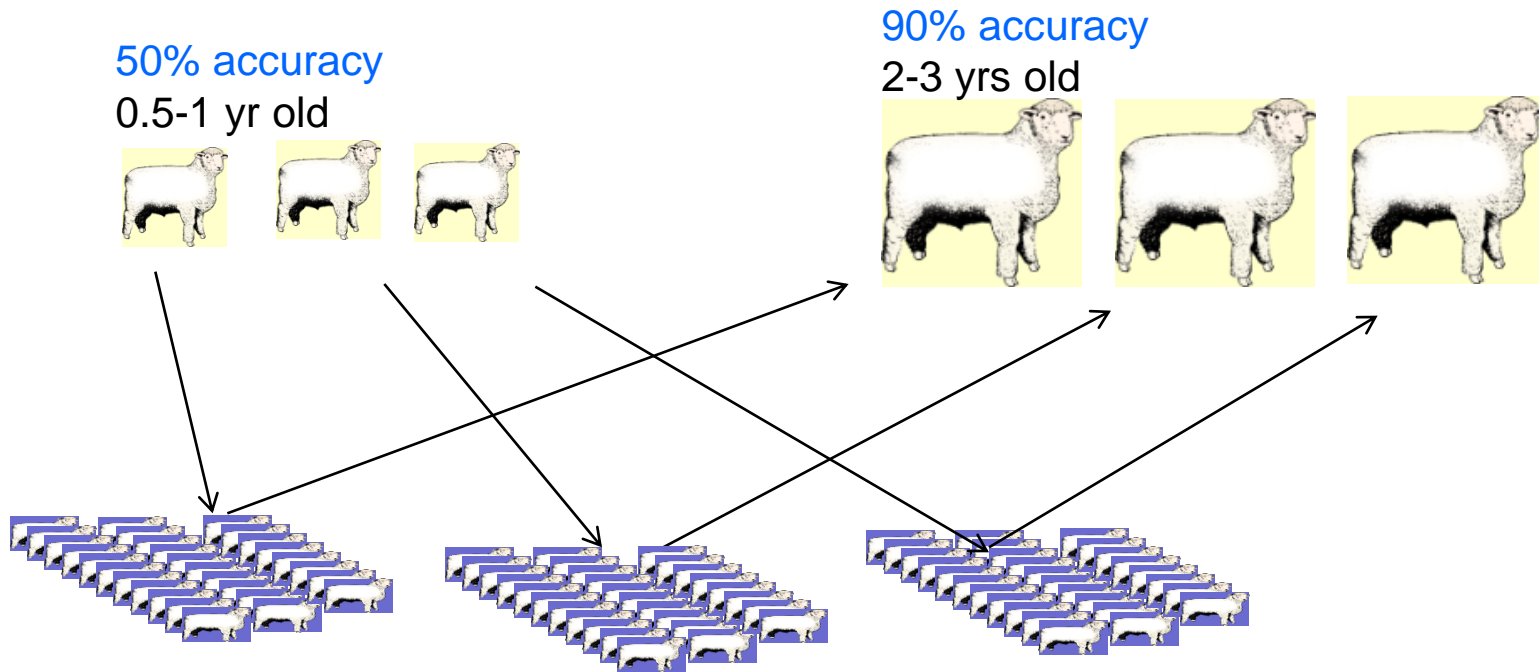
Genomic Prediction: basic idea



- 3) Computer centre can predict breeding value for young rams based on **genomic relationship**, combines it with other info

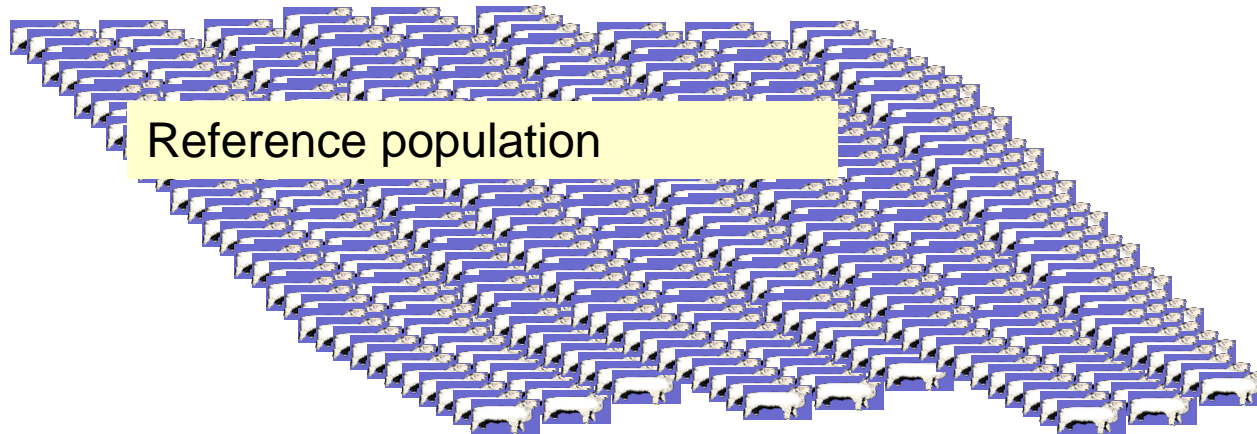
Can predict breeding value of young animals for 'any trait' measured in reference

Compare: Progeny Testing



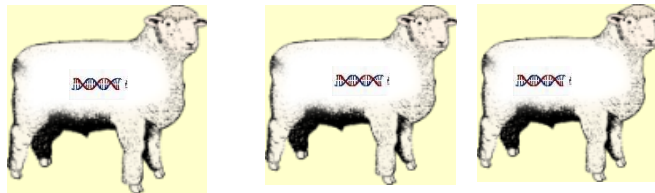
Each progeny group only informs one sire

Genomic Testing



Relationship = 0.02.....0.5

70% accuracy
0.5-1 yrs old



One large reference population informs all young rams

EBV accuracy increased at young age

Genomic Selection: Benefit

Overall:

More accurate prediction of genetic merit for breeding objective

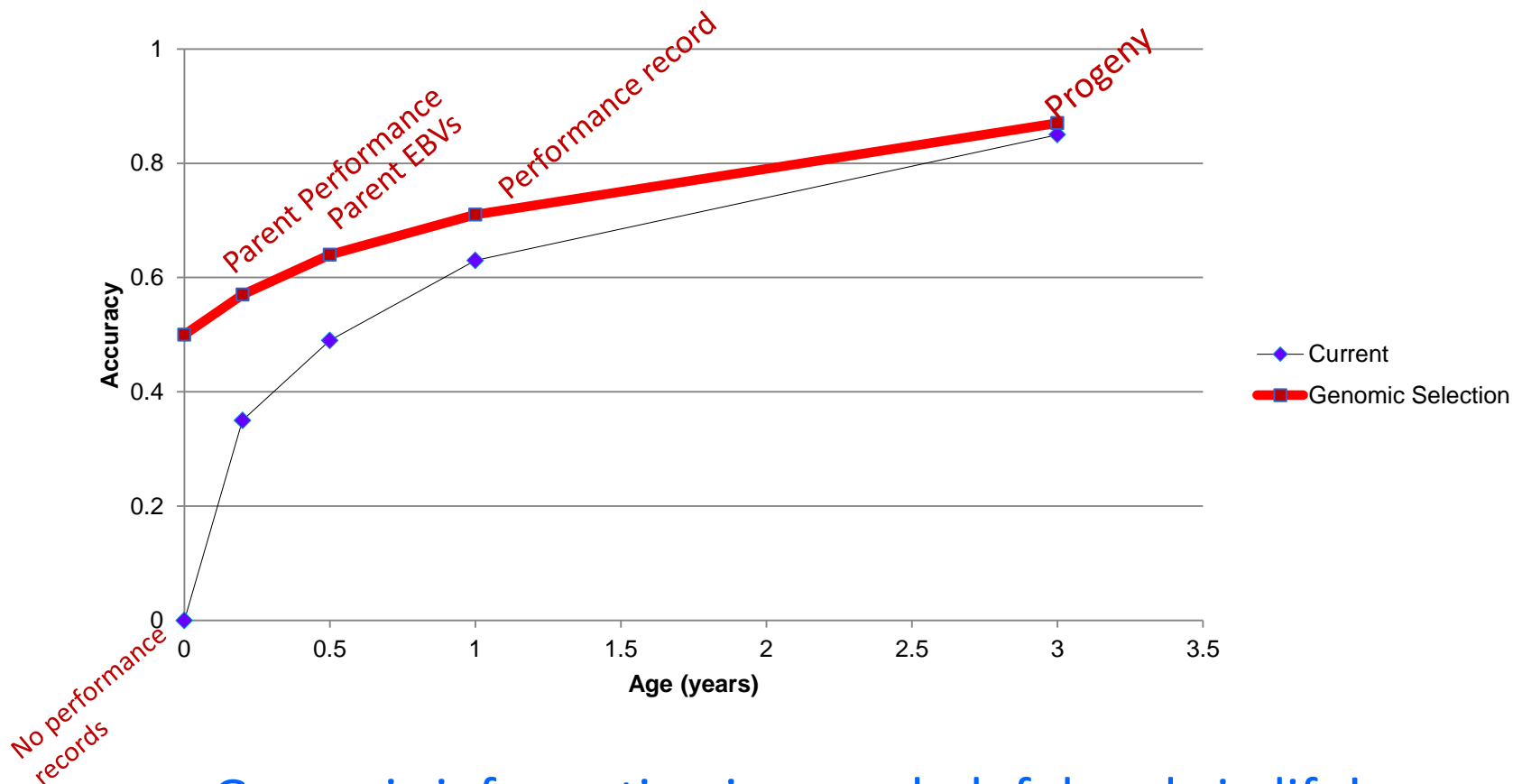
Specific:

Traits that are usually difficult to improve
difficult or expensive to measure
can not be measured early
low heritability

e.g. Carcass traits
Lifetime time wool production
Reproductive rate
Parasite resistance

Accuracy of predicting a breeding value

- increases as an animal gets older -



Genomic information is more helpful early in life!

Potential benefits of GS - some principles

% increase in EBV accuracy (male 1yo) and genetic gain

Trait Measurability	$h^2 = 0.1 = r^2$		$h^2 = 0.3 = r^2$	
	%Δ Acc	%Δ Gain	%Δ Acc	%Δ Gain
< 1 year, both sexes	15	7	7	7
> 1 year, both sexes	68	19	59	37
>1 year, females only	119	27	112	52
on Corr. Trait, $r_g = 0.9$	20	12	20	26
on Corr. Trait, $r_g = 0.5$	67	50	76	86

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These effects underestimated due to not accounting for Bulmer effect

Shifting the *trait* balance with genomic selection

		Current Selection
	Accuracy	Response
Weight kg	0.71	0.79
Dressing %	0.26	0.23
Saleable meat yield %	0.33	0.29
Overall Merit \$Index	0.58	2.03

Benefits across Species

	<u>% extra gain</u>	<u>impact</u>
• Early trait	small	small accuracy/ gen int
• Late Trait	moderate	gen int/acc
• Sex limited trait		
– females only, late	very large	gen int
– Males only early	small to modest	acc/gen int

Benefits - Dairy

- Extra gain ~100%
- Breeding objective dominated by sex-limited trait
- No more progeny testing (save money)
- Very much shorter generation intervals
- More use of reproductive technologies
- Potential to select on hard to measure traits but only if these are being measured!
- Commercial males have more chance to be selected
- AI companies can easily afford testing
- Widely used in the industry

Benefits - Beef

- Extra gain ~25-50%
- Breeding objective has some hard to measure traits
- More emphasis on carcass and meat, less on growth
- More emphasis on females reproductive rate
- Somewhat shorter generation intervals
- More use of reproductive technologies
- Potential to select on hard to measure traits if these are being measured! but only
- Genotyping cost can be high for breeders
- Who pay for the reference population?

Benefits - Sheep

- Extra gain ~25-50%
- Breeding objective has some hard to measure traits
- More emphasis on: carcass and meat, reproductive rate, 'lifetime wool', parasite resistance
- Somewhat shorter generation intervals
- Some more use of reproductive technologies
- Potential to select on hard to measure traits but only if these are being measured!
- Genotyping cost can be high for breeders
- Implemented in Australia, New Zealand
- Who pay for the reference population?

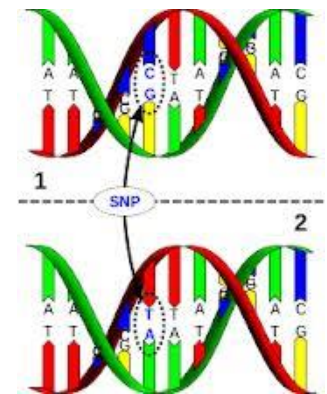
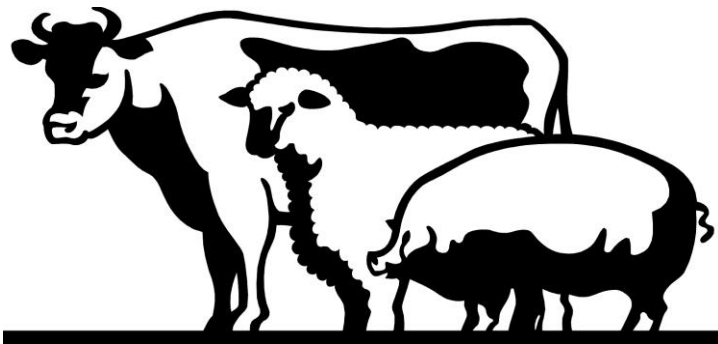
Benefits – Pigs & Poultry

- Extra gain ~50%?
- More emphasis on meat quality, Feed Efficiency?
- Sex limited traits
- shorter generation intervals in layers
- Potential to select on hard to measure traits if these are being measured! but only
- Genotyping cost can be high?

Conclusion

- Genomic selection can benefit breeding programs
- A challenge to implement:
 - cost to breeders
 - Need for phenotypes → reference population / multi breed
- Reference population needs to contain (indirect) relatives of selection candidates – *at this stage*
- Reference population needs to be continuously updated

Genomic information and inbreeding



Why use information from relatives?

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

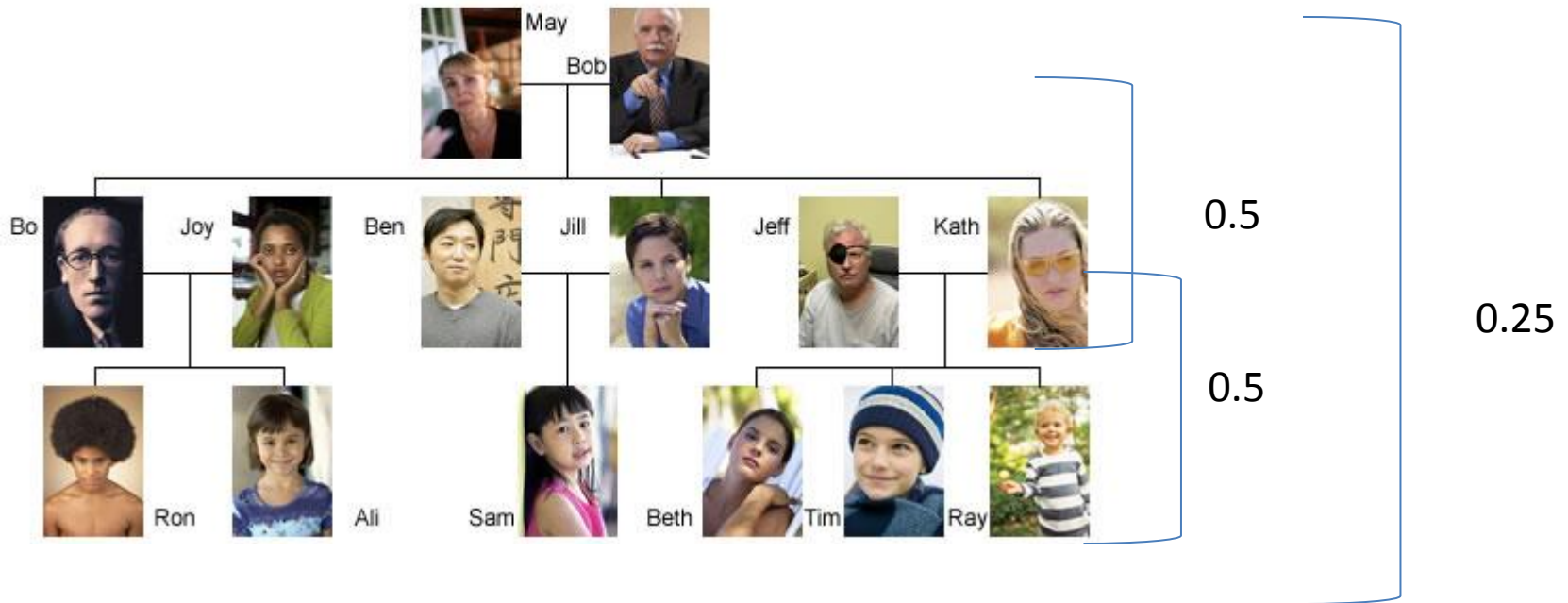


Relationships between Individuals

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

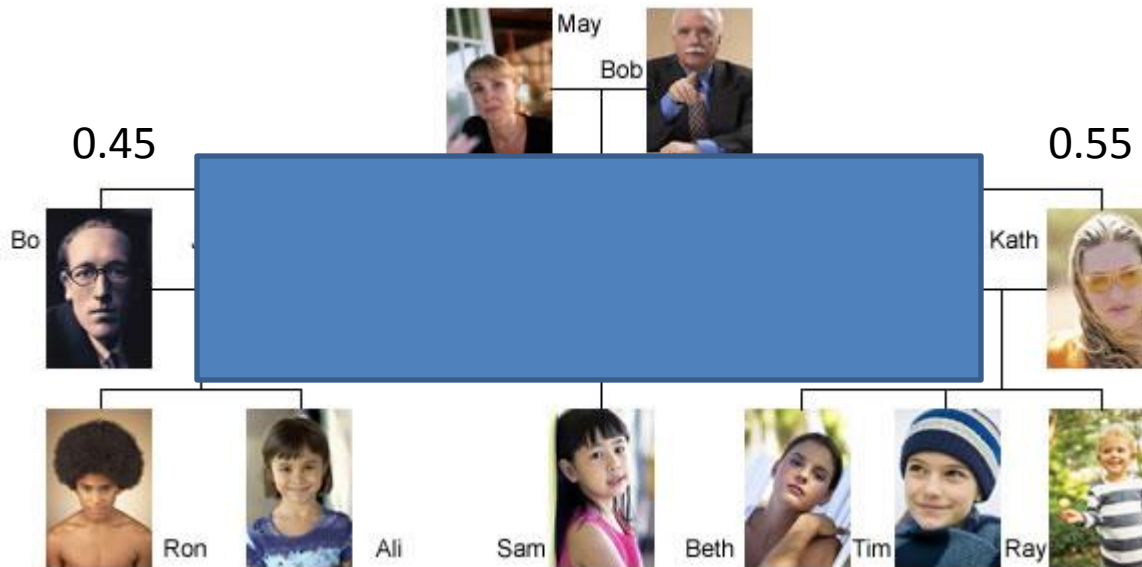
Genomic vs Pedigree BLUP

Pedigree



Genomic vs Pedigree BLUP

Genomic



Full siblings

0.20

0.28

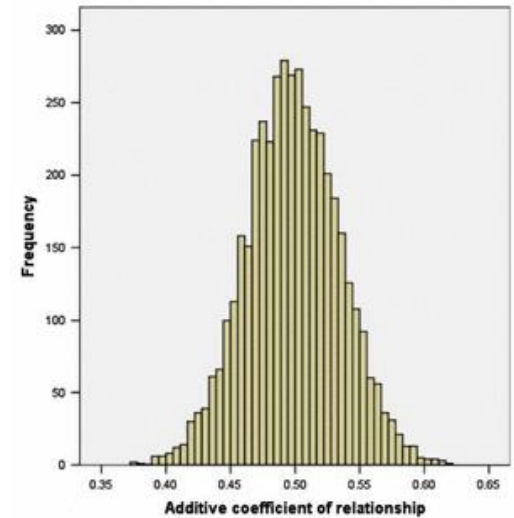
Relationship with Kath

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'

What information is used in BVs?

Clark et al, 2013 GSE

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

Across family

Within Family

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

	NZ dairy bulls					Australian dairy bulls				
	BV	Sire	Dam	MS+e	Prop. of PT	BV	Sire	Dam	MS+e	Prop. of PT
Parent Average		0.56	0.44	0.001	0.001	PA EBV	0.44	0.52	0.04	0.05
Genomic BV		0.43	0.26	0.31	0.56	GEBV	0.33	0.37	0.30	0.36
Progeny Test		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
Parent Average	0.55	1.0	0.45
Genomic BV	0.50	0.85	0.57
Progeny Test	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

ΔG (se)

ΔF_{ped} (se)

ΔF_{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)

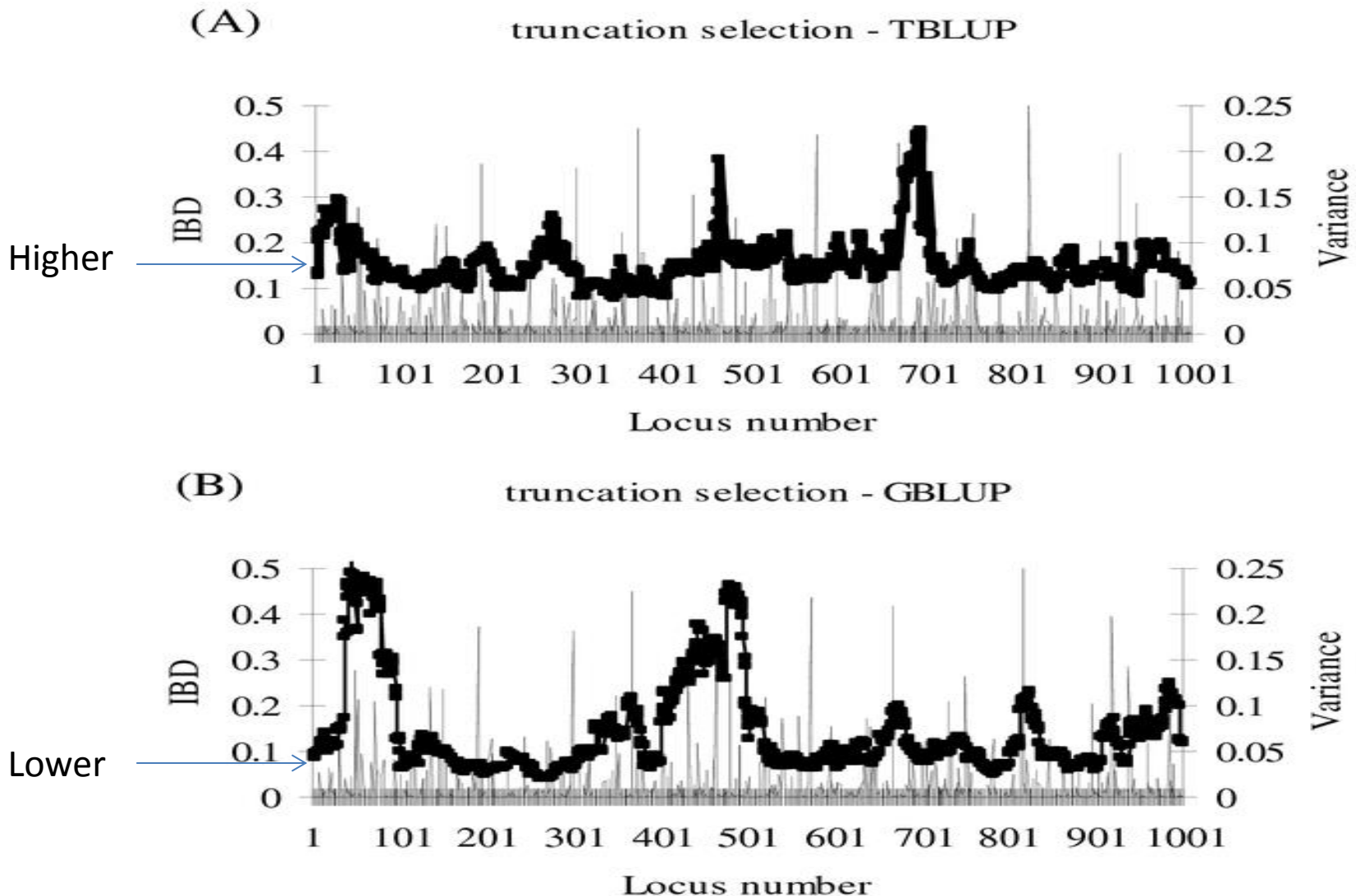
$$\Delta F_{PED} < \Delta F_{IBD}$$

ΔF_{PED} lower with GBLUP

ΔF_{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

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

Ntest	ΔF_d	ΔG (se)	ΔF_{ped} (se)	ΔF_{IBD} (se)
ΔF_A constraint – GBLUP				
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)
ΔF_G constraint – GBLUP				
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)
ΔF_A constraint – TBLUP				
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)
ΔF_G constraint – TBLUP				
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 (ΔG), rate of inbreeding based on pedigree (ΔF_{ped}) and on genomic IBD (ΔF_{IBD}) relationship matrices at generation G_{10} when the constraint on relationship was either pedigree-based (ΔF_A) or marker-based (ΔF_G) with TBLUP or GBLUP breeding value estimates^a.

^aNtest = number of test sibs; ΔF_d = desired rates of inbreeding; number of selection candidates = 3000.

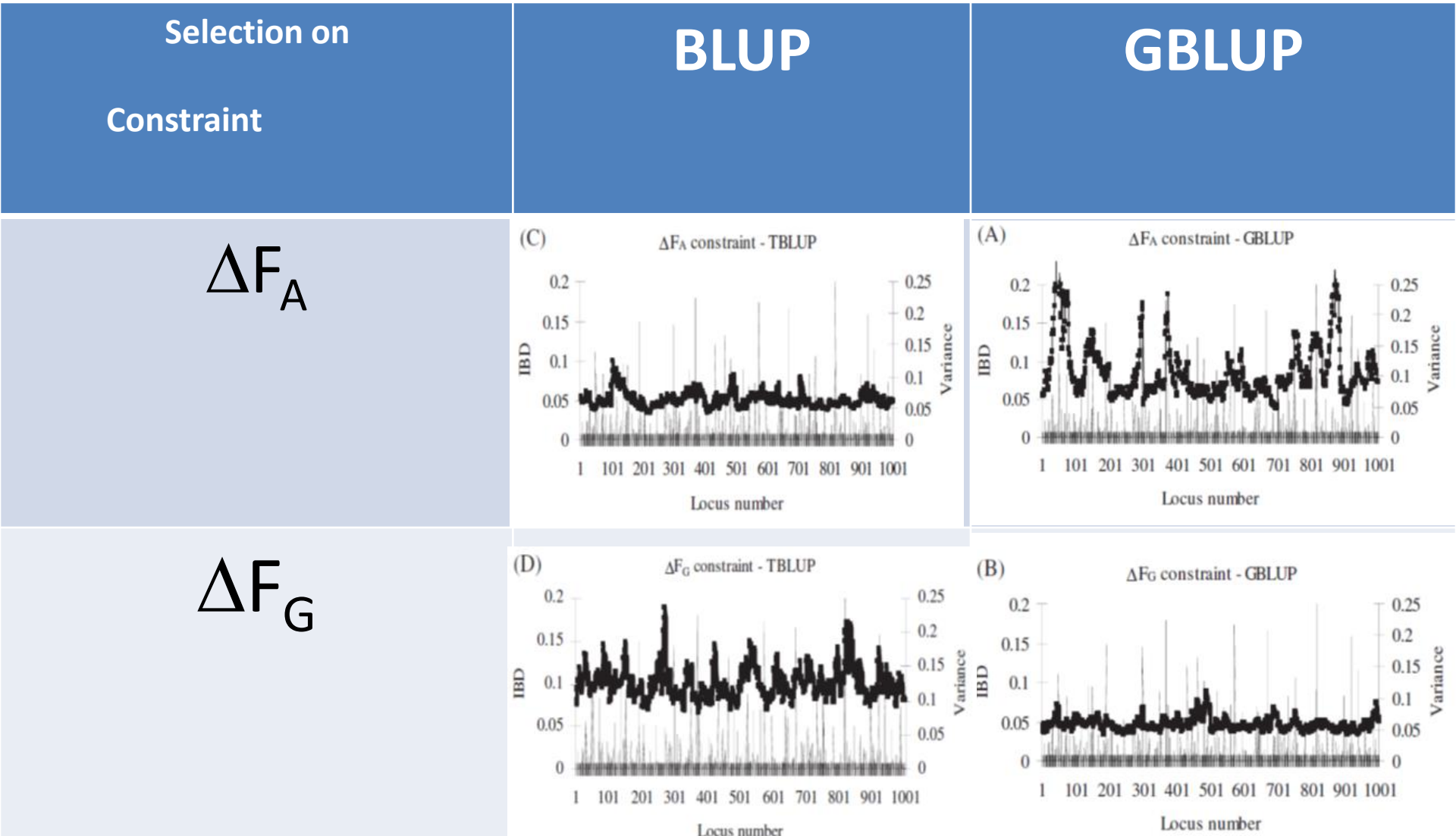
Constraining Inbreeding:

Pedigree or Genomics, Optimal contributions

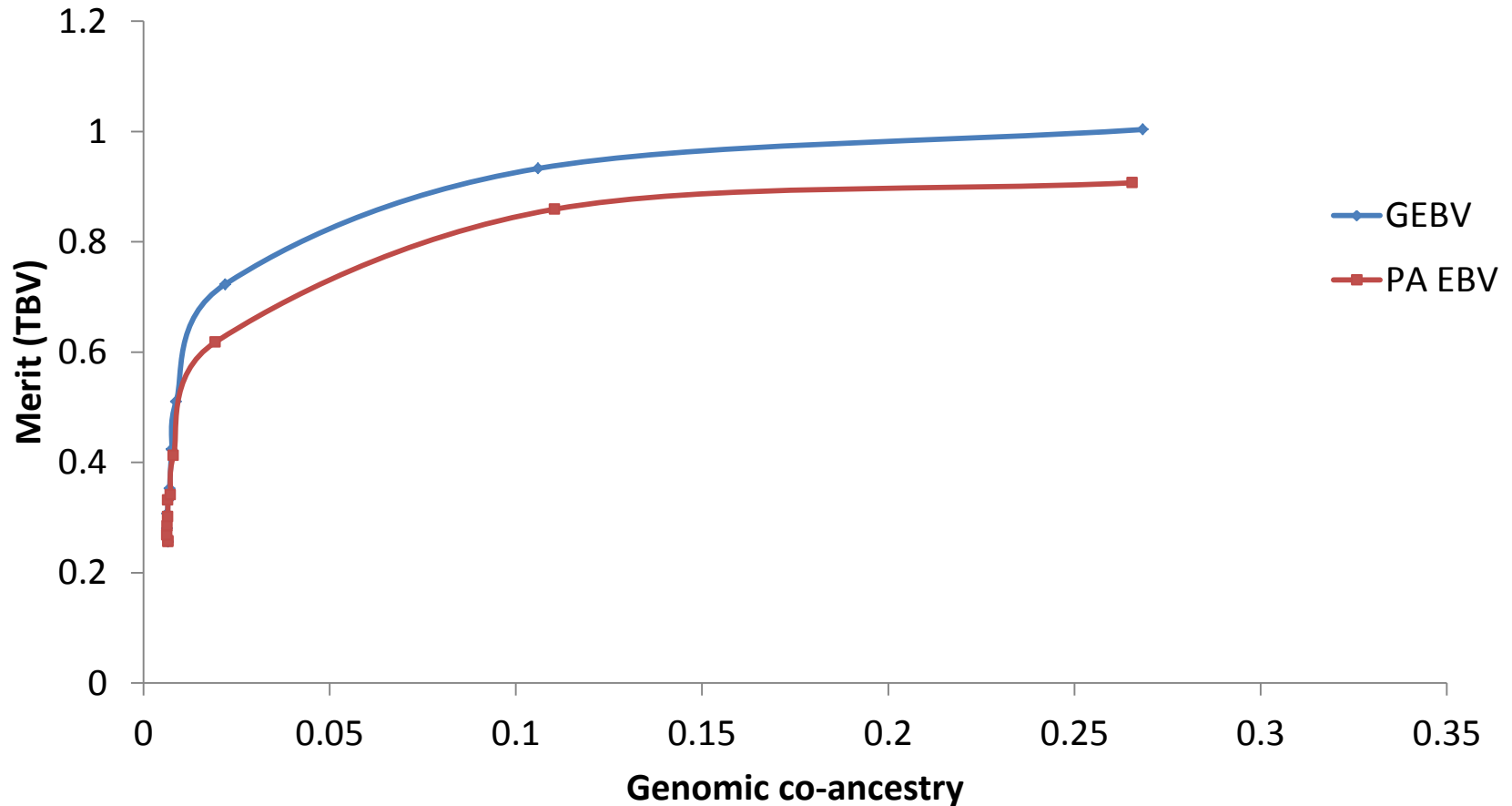
Selection on Constraint	BLUP	GBLUP
ΔF_A	ΔF_A constrained ΔF_G not well constrained	ΔF_A constrained ΔF_G badly constrained
ΔF_G	ΔF_A not constrained ΔF_G not constrained	ΔF_A constrained ΔF_G constrained

Constraining Inbreeding:

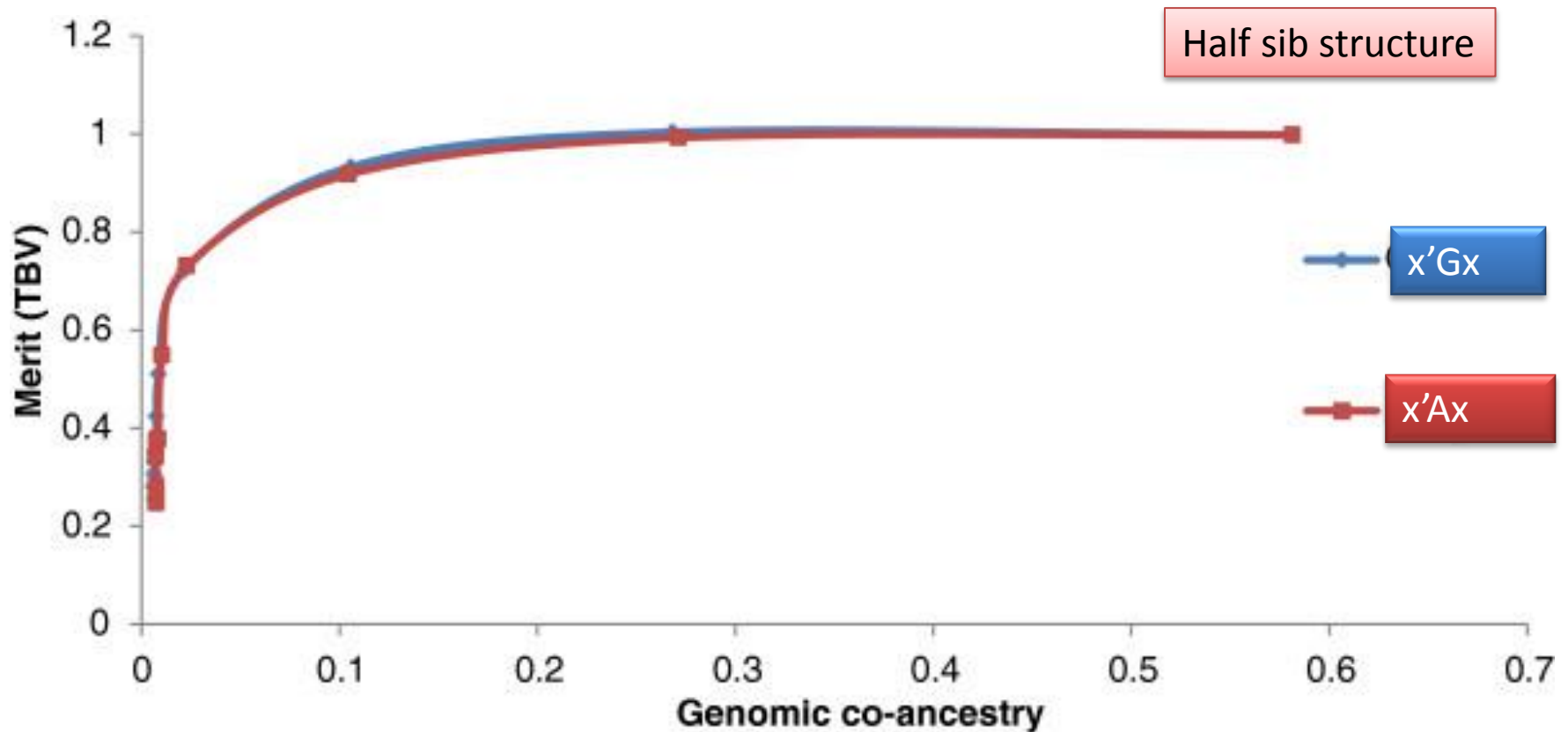
Pedigree or Genomics, Optimal contributions



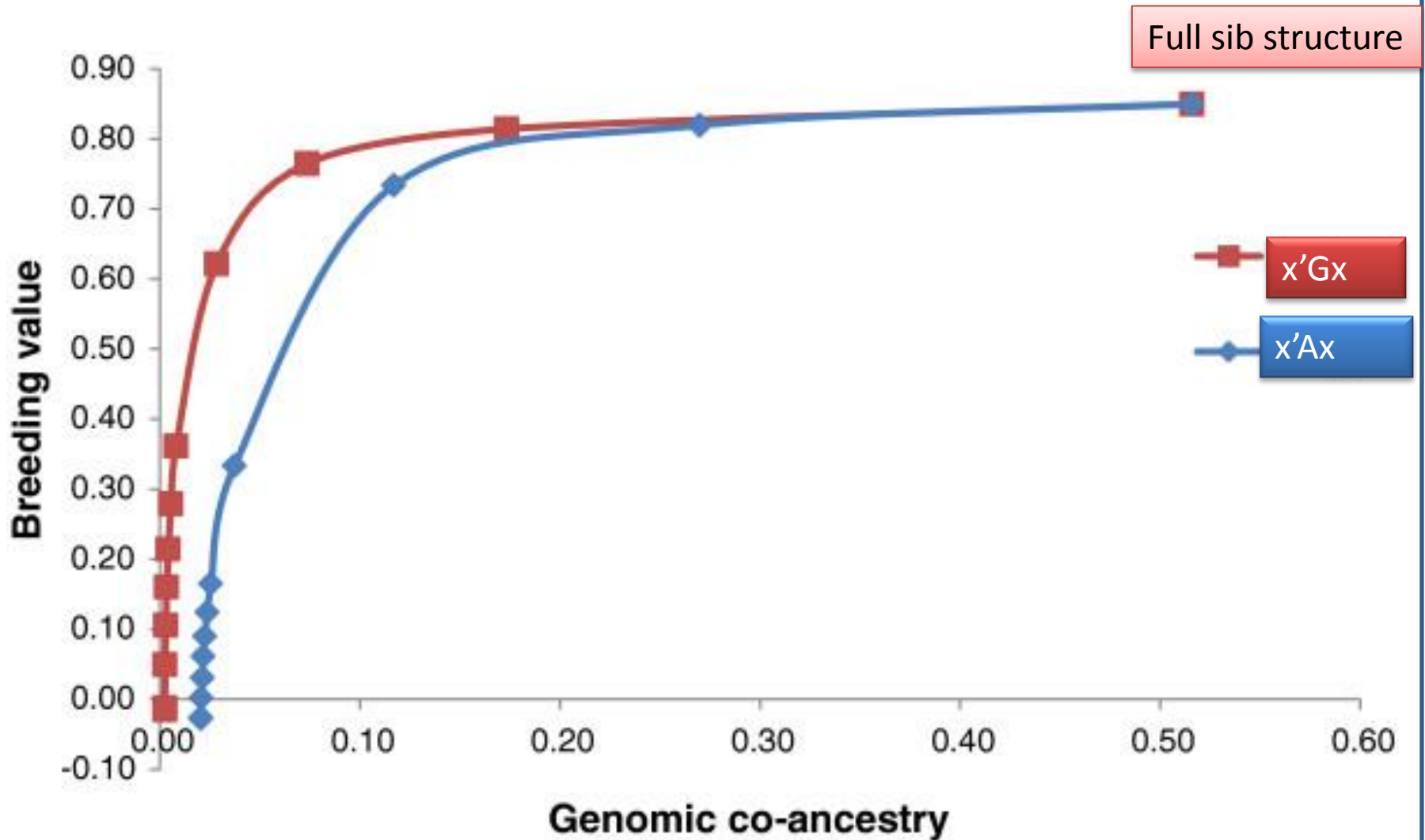
How much can we utilize additional diversity? selecting on GEBV vs EBV (parent average)



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 ΔG for same ΔF
 2. More diversity \rightarrow more selection space giving raise to even more ΔG for same ΔF

but mainly useful for large FS families