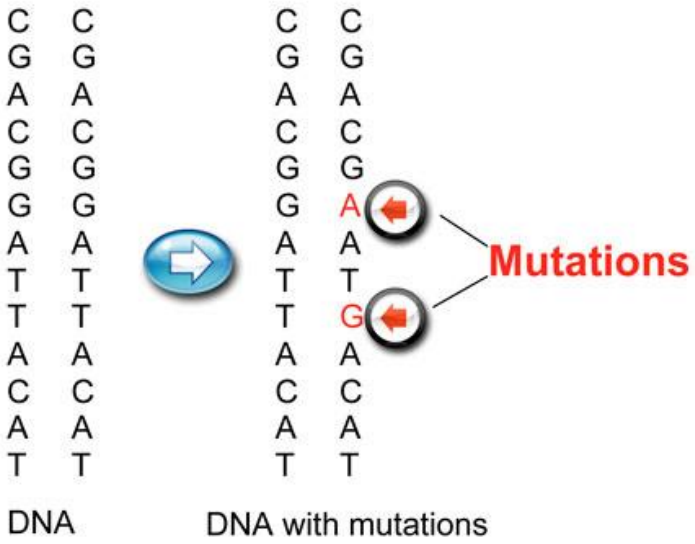
Genomic selection without own phenotypes exploits new mutational variance less than BLUP selection

Han Mulder, Sang Hong Lee, Sam Clark, Ben Hayes and Julius van der Werf



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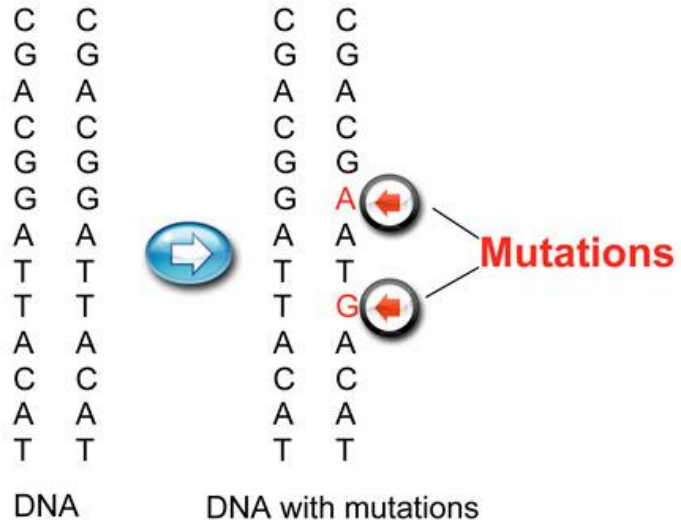
Acknowledgements

- WUR-ABG supporting my sabbatical, February – March 2017

- Prof. Julius van der Werf for hosting me at University of New England

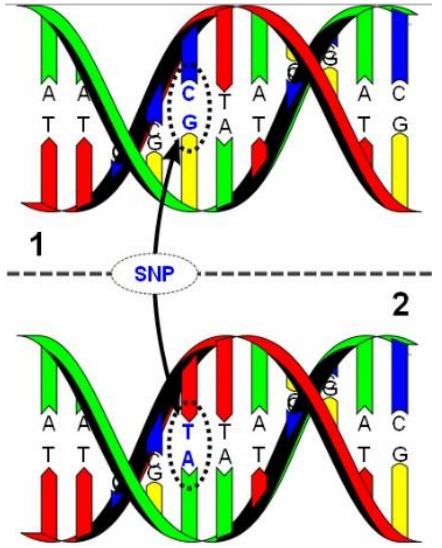
Magnitude of mutational variance

- De novo mutation rate: 1.0 – 1.8 $\times 10^{-8}$ per site per gamete
  - 20-80 per individual in humans
  - 1.1 $\times 10^{-8}$ per site per gamete in cattle
  - 0.5 deleterious mutation per individual in cattle (Charlier et al. 2016)
- Some mutations have favourable effects
- Contribution to genetic variance: 0.001Ve
  - Houle (1996), Hill (1982)



Does genomic selection exploit mutational variance?

- Mutations are not on a SNP-chip
- Young mutations are in no LD with SNP on chip
- Mutations in selection candidate are not yet expressed if selection is at young age on GEBV before the phenotype is expressed
- Hardly any selection pressure on new mutations



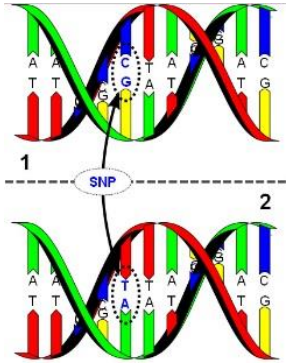
Hypothesis and objectives

- Hypothesis: genomic selection exploits new mutational variance less than traditional selection

- Aims:
  - Investigate long-term selection response for mass, BLUP_OP, BLUP_no_OP, GBLUP_OP, GBLUP_no_OP selection
  - Investigate development of standing genetic variance and mutational genetic variance

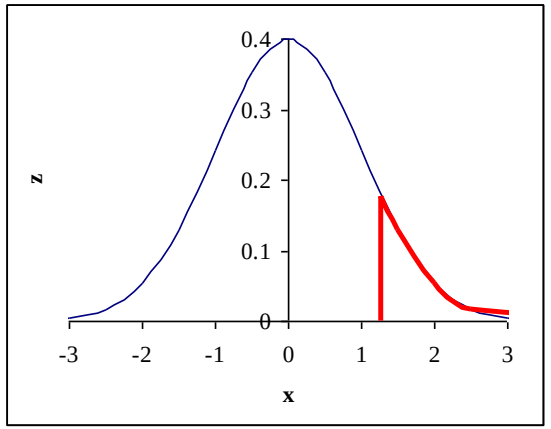
Simulation

- Sequence data Holstein bulls 1000 bull genomes project
  - Chromosomes 1, 2 and 3
  - 300,000 SNV used
  - 5000 QTL
  - 20,000 markers for chip
- 0.5 mutation/animal
- Vm=0.001Ve
- h^2=0.3
- QTL and mutations sampled from normal or gamma distribution

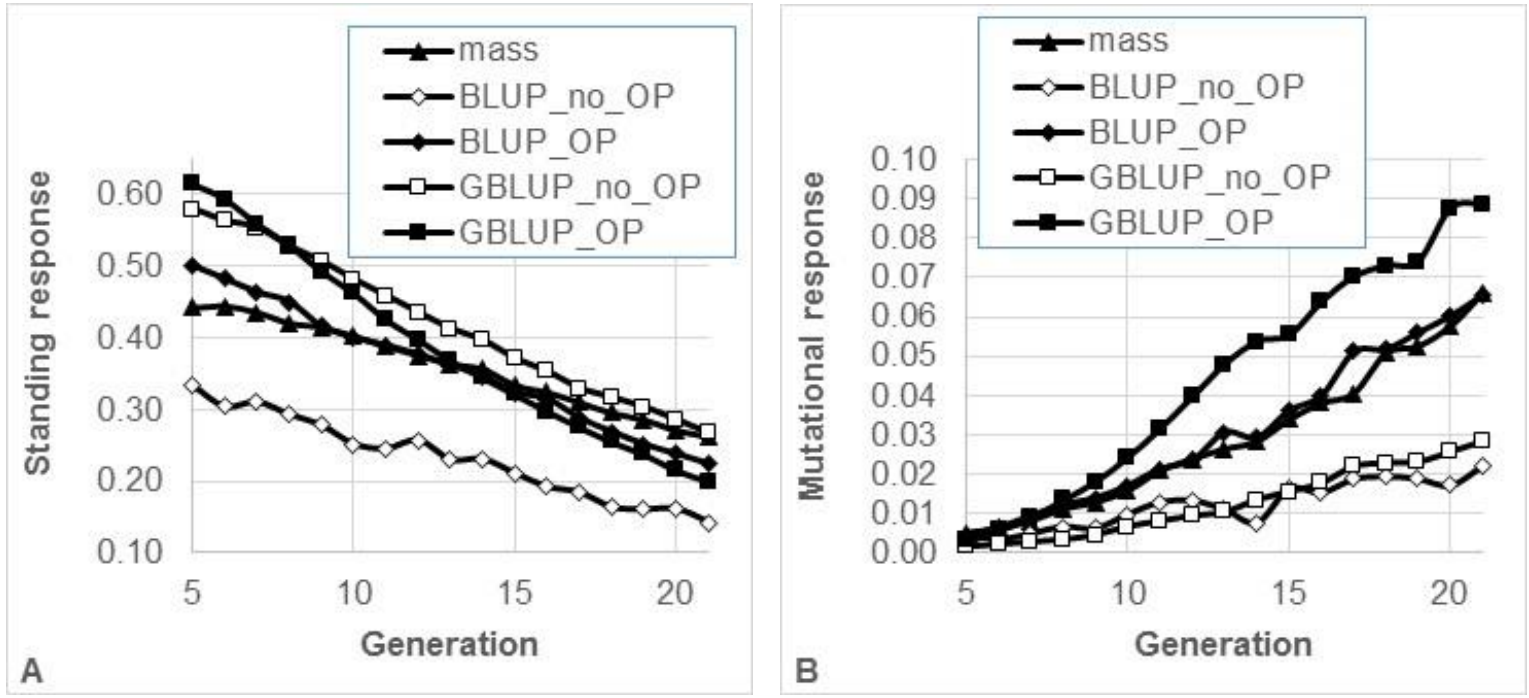


Selection strategies

- Each generation 1000 males and 1000 females
- 50 males to be selected
- 200 females to be selected; 10 offspring/female
- 20 generations of animals
- Parents are selected on
  - Own phenotype (mass selection)
  - Pedigree-BLUP EBV with or without own phenotype
  - GBLUP-EBV, with or without own phenotype



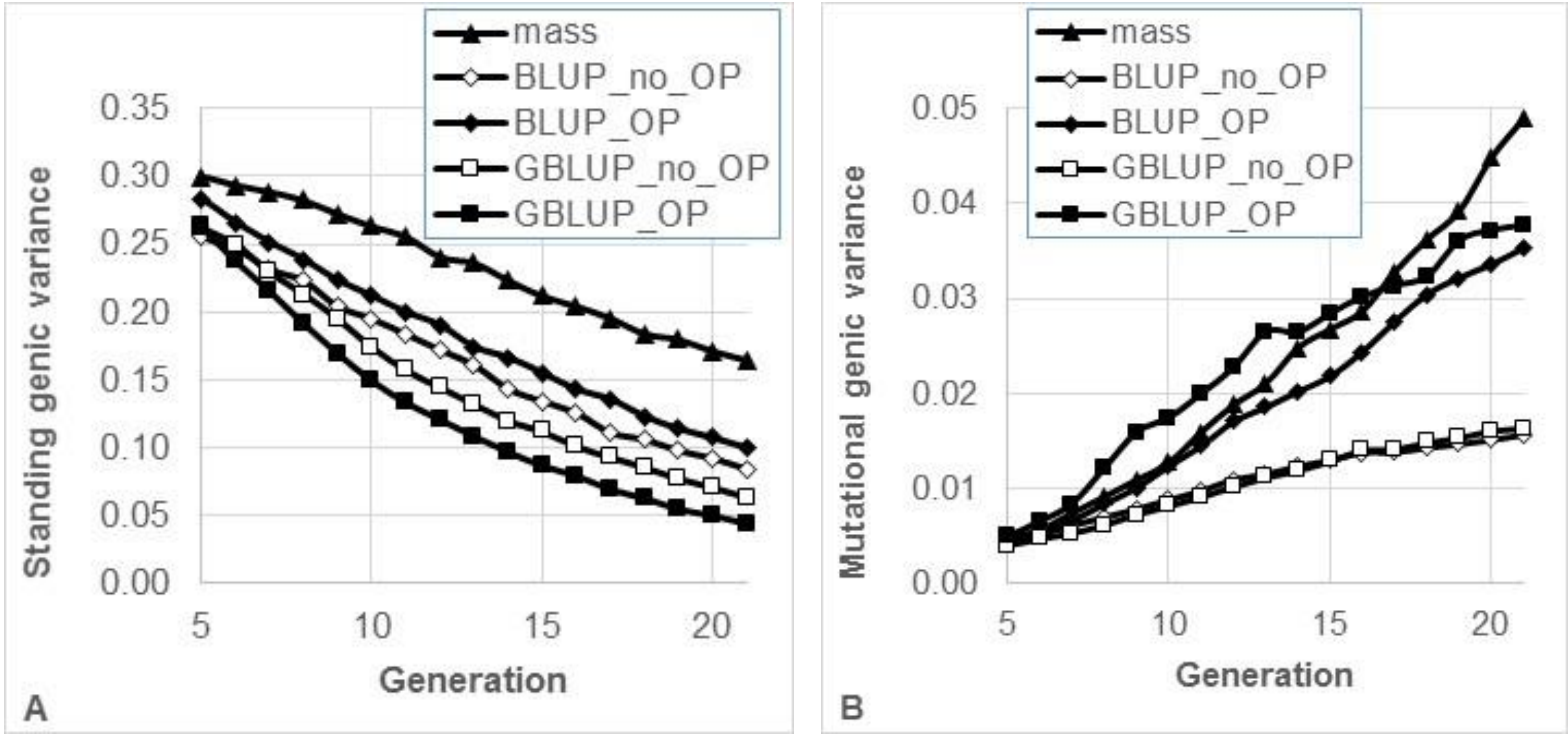
Standing and mutational selection response



Genomic selection without own phenotype (and BLUP_no_OP) has lower mutational response than GBLUP_OP, mass and BLUP_OP selection

Mulder et al. 2019; early online Genetics:
https://doi.org/10.1534/genetics.119.302336

Standing and mutational genic variance



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The fate of DNM:

DNM that segregate for 10 generations after appearance

	NQTL	N mut	N pos	N neg	prop pos
mass	3313	104.6	58.0	46.5	0.56
BLUP_no_OP	1602	55.6	28.6	27.0	0.51
BLUP_OP	2357	67.7	36.8	30.9	0.54
GBLUP_no_OP	2268	82.4	42.7	39.7	0.52
GBLUP_OP	2296	81.4	55.2	26.2	0.68

Very few DNM survive!

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100years 1918 — 2018

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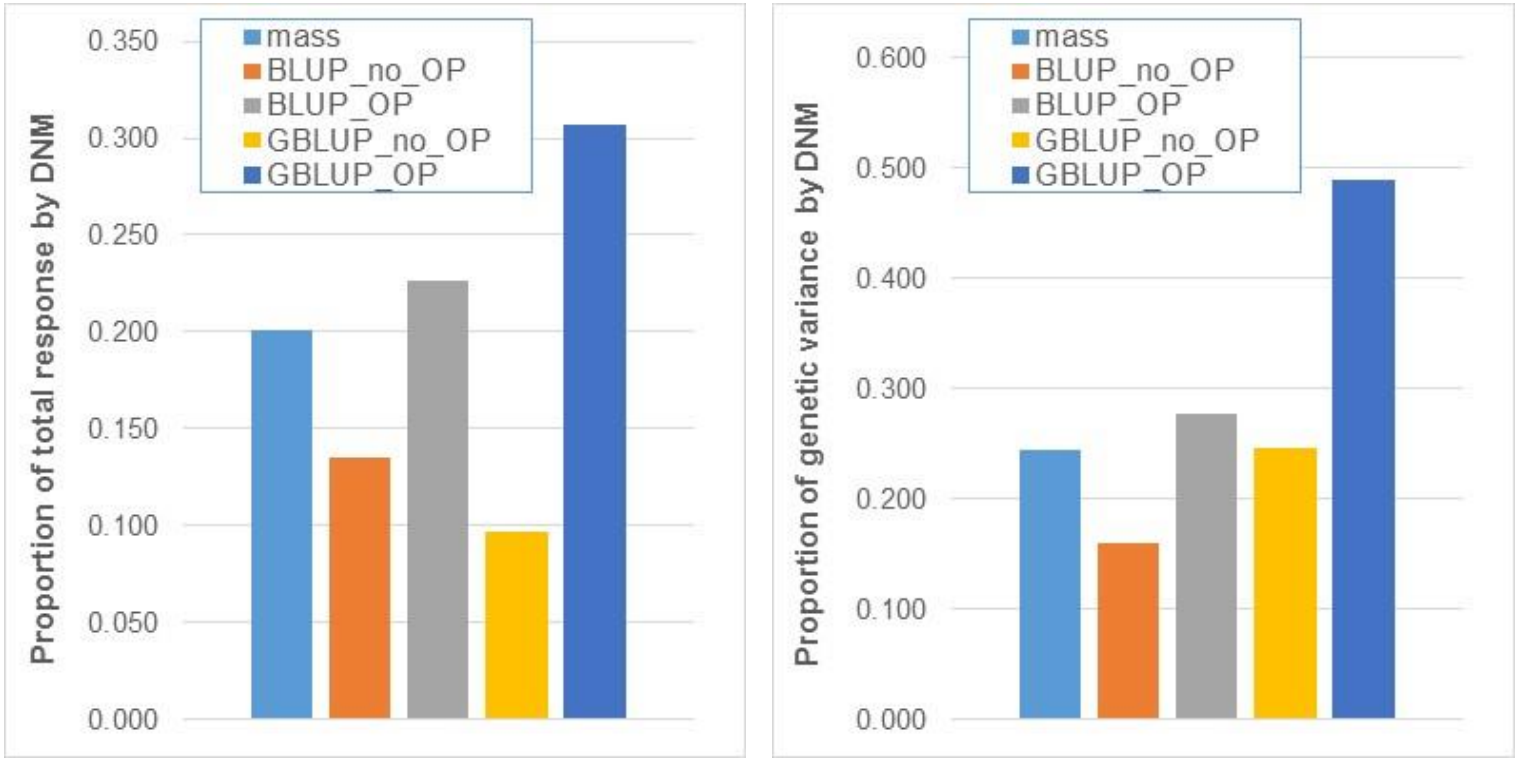
Can the contribution of DNM be ignored?

Proportions in generation 21 after 20 generations of truncation selection



Mutational variation accounts for 10-30% of response and 15-50% of genetic variance!

Take-home message

- GBLUP_OP is best in exploiting mutational variance
- Genomic selection without own phenotype exploits mutational variance less than traditional selection using own phenotype
    - Crucial factor is the role of the own phenotype
- Faster decline in total genetic variance with genomic selection than with BLUP, no mutation-selection-drift equilibrium
- Need for sustainable genomic selection strategies

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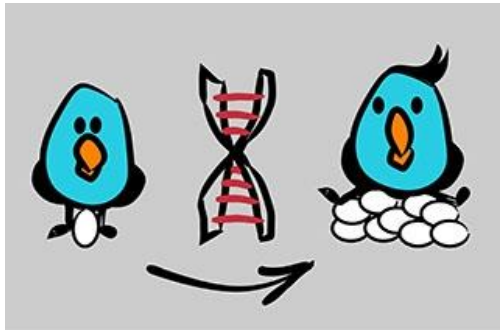
ABG01x:
Genetic Models in
Animal Breeding



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African Chicken Genetic Gains

Koepon Stichting

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Theo Meuwissen - QG theory in livestock and crops


Han Mulder - QG of GxE Interaction


Yaniv Erlich - QG in Crowd-Sourced Data


Daniel Gaffney - QG in Human Induced Pluripotent Stem Cells


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Sensitivity analysis

- Mutational variance per generation has large impact: 0.001 versus 0.004Ve
- Number of DNM per individual has large impact: 0.5 versus 2 DNM
- Distribution of mutational effects has large effect: mutational response/variance smaller with normal distribution
- Epistasis and dominance have minor effects on mutational response/variance

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