Allele frequency changes by hitch-hiking in genomic selection programs

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Outline of this presentation

1. Background
2. Simulation and Methods
3. Results and Discussion
4. Conclusion

Introduction

- Genetic improvement ← increasing the favourable allele frequencies

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- The size of the increase ← allele frequency and accuracy of selection
- Genomic selection (GS) ↗ the accuracy of estimating BV
- GS ↘ pedigree inbreeding compared to BLUP

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Solution: runs of homozygosities (ROH)

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Solution: runs of homozygosities (ROH)

Further question: Is inbreeding reduced by GS?

main purposes

1. allele frequencies
2. reduction of heterozygosity at linked loci due to hitch-hiking
3. inbreeding measured by ROH and pedigree
4. impact of heritability

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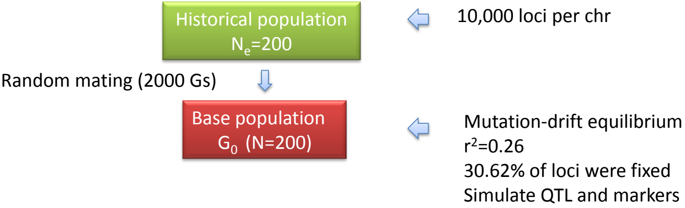
Historical population
N_e=200

100 males and 100 females
mutation 2.5 X 10^{-5}
Simulate loci 10,000 per chr



Historical population
N_e=200

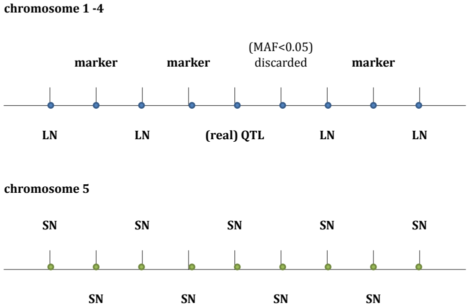
10,000 loci per chr

Random mating (2000 Gs)

Base population
G_0 (N=200)

Mutation-drift equilibrium
r^2=0.26
30.62% of loci were fixed
Simulate QTL and markers

QTL and markers



chromosome 1 -4

marker **marker** (MAF<0.05) discarded **marker**

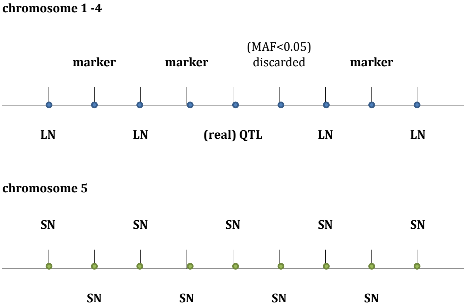
LN **LN** **(real) QTL** **LN** **LN**

chromosome 5

SN **SN** **SN** **SN** **SN**

SN **SN** **SN** **SN**

QTL and markers

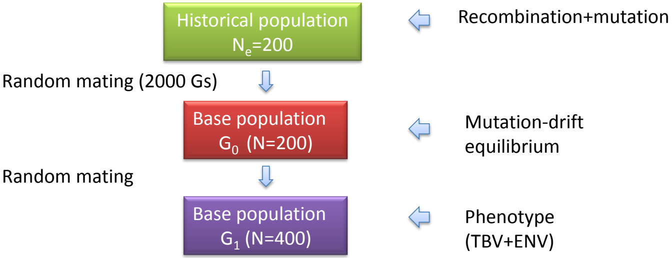


LN=linked neutral locus

SN=selectively neutral locus

QTL favorable allele freq= 0.01-0.3

LN/SN minor allele freq > 0.01



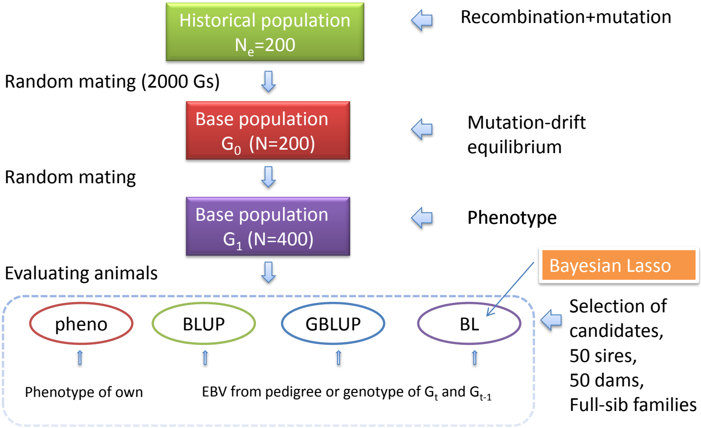
Historical population $N_e=200$ ← Recombination+mutation

Random mating (2000 Gs)

Base population G_0 (N=200) ← Mutation-drift equilibrium

Random mating

Base population G_1 (N=400) ← Phenotype (TBV+ENV)



Historical population N_e=200

Recombination+mutation

Random mating (2000 Gs)

Base population G_0 (N=200)

Mutation-drift equilibrium

Random mating

Base population G_1 (N=400)

Phenotype

Evaluating animals

Bayesian Lasso

pheno

BLUP

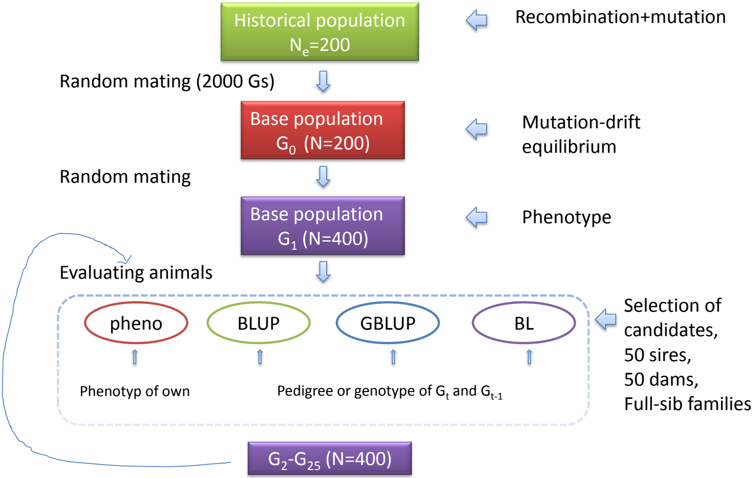
GBLUP

BL

Phenotype of own

EBV from pedigree or genotype of G_t and G_{t-1}

Selection of candidates,
50 sires,
50 dams,
Full-sib families



Historical population
N_e=200

Recombination+mutation

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Base population
G_0 (N=200)

Mutation-drift equilibrium

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Base population
G_1 (N=400)

Phenotype

Evaluating animals

pheno

BLUP

GBLUP

BL

Phenotyp of own

Pedigree or genotype of G_t and G_{t-1}

Selection of candidates,
50 sires,
50 dams,
Full-sib families

G_2-G_{25} (N=400)

Hitch-hiking and inbreeding

- Allele frequency changes $\triangle p_t$ were scaled by $\sqrt{p_{t-1} * (1 - p_{t-1})}$
- level of hitch-hiking $= \dfrac{\sigma^2(\triangle p_{LN})}{\sigma^2(\triangle p_{SN})}$
  - numerator ← indirect selection and random sampling
  - denominator ← random sampling
- F_{ped} and F_{ROH}
- Tukey's HSD ($p < 0.05$)

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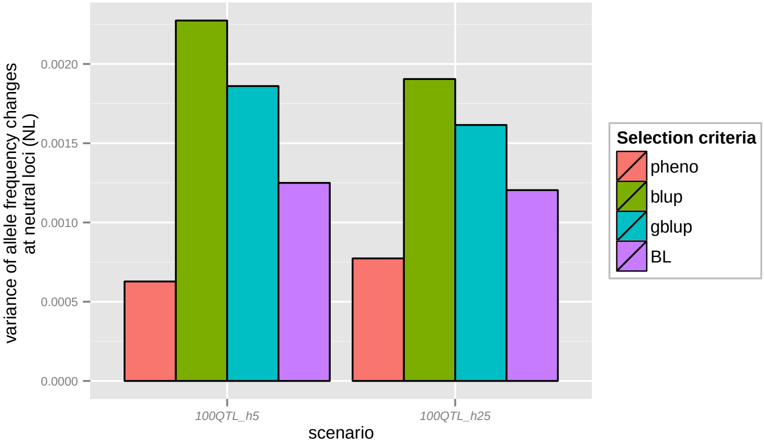
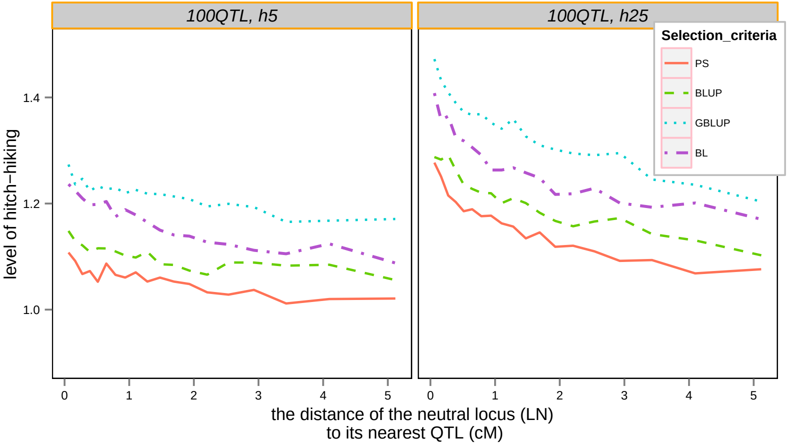
variance of change in allele frequencies of neutral loci on chr 5 (drift)



Level of Hitch-hiking on chr 1-4



rate of inbreeding

Table 2 - The rate of inbreeding based on pedigree (ΔF_{ped},%) and runs of homozygosity (ΔF_{ROH}). (SE<0.05%)

	selection criterion			
Rate of inbreeding	PS	BL	GBLUP	BLUP
ΔF_{ped*}	0.67	1.30	1.88	2.01
	0.88	1.26	1.50	1.65
$\Delta F_{ROH10}^{\dagger}$	0.68	1.43	2.15	2.05
	0.89	1.40	1.74	1.77

*The rate of inbreeding was calculated based on the first 8 generations.

† The number followed by ROH represents the number of markers involved for each window.

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Conclusion

- The neutral variation is substantially shaped by the hitch-hiking effects.
- pedigree inbreeding reduces from BLUP to GBLUP, but not for genomic inbreeding.
- compared to GBLUP, Bayesian lasso:
  1. less pedigree inbreeding ← more accurate estimate of Mendelian sampling term
  2. less hitch-hiking → less genomic inbreeding
- genomic control of inbreeding
  1. optimum contribution selection (Sonesson et al. 2012)
  2. put higher weight on rare favorable alleles (Goddard, 2009)

Acknowledgments

Thank you for your attention!