Efficient computational strategies for multivariate single-step SNPBLUP

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CRV

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HENDRIX GENETICS

Topigs Norsvin
PROGRESS IN PIGS

Single-step genomic evaluations

- Prediction of genomic breeding values
  - Genotyped and non-genotyped animals
  - Potentially high computational costs
- Most software not suitable for single-step SNPBLUP
- Usual iterative solver
  - Preconditioned Conjugate Gradient method
  - Main cost
    - Coefficient matrix * vector

Aim

Investigate the main computational costs and

implement solutions

for efficiently solving

a multivariate single-step SNPBLUP

with the PCG method

ssSNPBLUP – model

- Hybrid model
  - Non-genotyped animals : breeding value model
  - Genotyped animals : SNP model

$$\mathbf{y} = \mathbf{Xb} + \begin{bmatrix} \mathbf{Z}_n & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_g & \mathbf{Z}_g\mathbf{M} \end{bmatrix} \begin{bmatrix} \mathbf{u}_n \\ \mathbf{a}_g \\ \mathbf{g} \end{bmatrix} + \mathbf{e}$$

$$\mathbf{u}_g = \mathbf{a}_g + \mathbf{Mg}$$

$\mathbf{u}_n$, $\mathbf{u}_g$: aggregate GEBVs for (non-)genotyped animals

$\mathbf{a}_g$: residual polygenic effects for genotyped animals

$\mathbf{g}$: SNP effects

$\mathbf{M}$: SNP genotypes

Fernando et al., 2016; Mantysaari and Stranden, 2016

PCG in animal breeding

- Main computational cost for one iteration
  - Coefficient matrix (**C**) * vector (**v**)

- Usually performed in two parts + matrix-free approach

$$\mathbf{C} * \mathbf{v} = \mathbf{L} * \mathbf{v} + \mathbf{R} * \mathbf{v}$$

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \mathbf{G}^{-1} \end{bmatrix} * \mathbf{v} = \begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} \end{bmatrix} * \mathbf{v} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{-1} \end{bmatrix} * \mathbf{v}$$

Least Squares part of **C**

Random part of **C**

ssSNPBLUP – potential costs

- "Traditional" matrix-free approach

$$\mathbf{C} * \mathbf{v} = \mathbf{L} * \mathbf{v} + \mathbf{R} * \mathbf{v}$$

Least Squares part

2 multiplications with M

Random part

2 multiplications with M

➔4 multiplications with **M**

➔High memory/IO requirement for **M**

- 1,000,000 50K genotypes (dp): 373 GB

➔Difficult to parallelize (e.g., inverted pedigree relationship (sub-)matrices $\mathbf{A}^{xx}$)

ssSNPBLUP – solutions

1. Potential cost: 4 multiplications with **M**

➔**Solution: Rearrangement of the equations**

$$\mathbf{C} * \mathbf{v} = \mathbf{L} * \mathbf{v} + \mathbf{R} * \mathbf{v} = \begin{bmatrix} \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{M}' \end{bmatrix} \left(\mathbf{L}_{sub} + \mathbf{R}_{sub_1} \right) \begin{bmatrix} \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{M} \end{bmatrix} * \mathbf{v} + \mathbf{R}_{sub_2} * \mathbf{v}$$

With **M**

Without **M**

➔Computation of $\mathbf{C} * \mathbf{v}$ in 4 steps

➔Only **2** multiplications with **M**

ssSNPBLUP – solutions

2. Potential cost: high memory/IO for **M**

➔**Solution**: **Compressed genotypes** (Plink bed format)

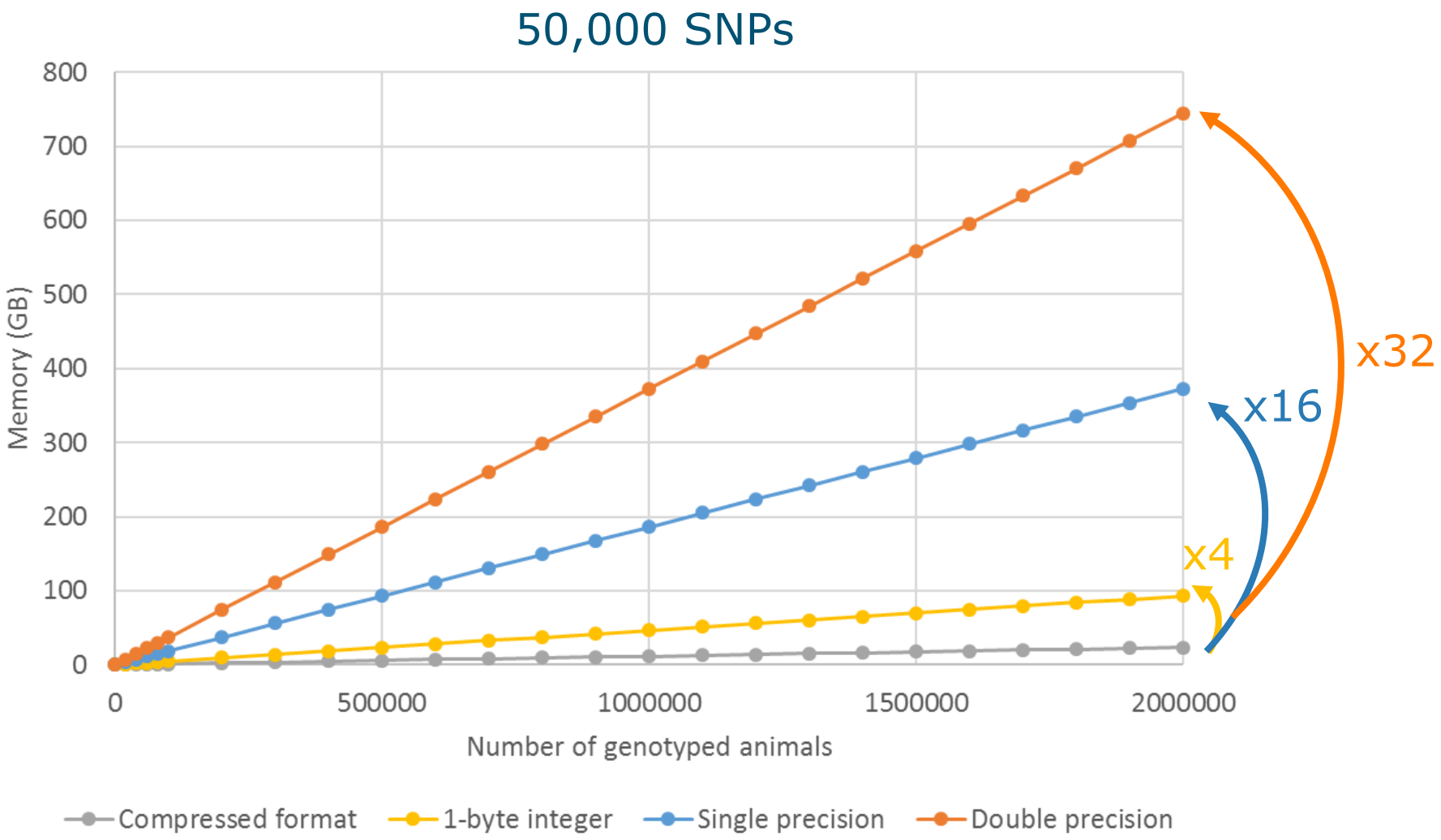
SNP genotype	Homozygous first allele	Heterozygous	Homozygous second allele	Missing
Decimal	0	1	2	3
2-bit	00	01	11	10

3210 ⇔ 00101101 ⇔ 45

4 SNP genotypes
4-32 bytes

1-byte integer

ssSNPBLUP – solutions



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ssSNPBLUP – solutions

3. Potential cost: difficult to parallelize operations with $\mathbf{A}^{xx}$

➔**Solution**: **hold $\mathbf{A}^{xx}$ in memory**

- Optimized and parallelized libraries
  - E.g., Sparse BLAS, Pardiso

ssSNPBLUP – solutions

4. Potential cost: "On-the-fly imputation"

➔**Solution**: **New equation**

$$\mathbf{Qv} = \left(\mathbf{A}^{gg} - \mathbf{A}_{gg}^{-1}\right)\mathbf{v}$$

$$= (\mathbf{A}^{gn}(\mathbf{A}^{nn})^{-1}\mathbf{A}^{ng})\mathbf{v}$$

$$= \left(\mathbf{A}_{anc}^{gn}(\mathbf{A}_{anc}^{nn})^{-1}\mathbf{A}_{anc}^{ng} + \Delta\right)\mathbf{v}$$

Dense $\mathbf{A}_{gg}^{-1}$

Large and sparse $\mathbf{A}^{nn}$ (~size(pedigree))

Small and sparse $\mathbf{A}_{anc}^{nn}$

$\mathbf{A}_{anc}^{nn}$: size(ancestors of genotyped animals)

Δ: sparse + depends only on non-genotyped progeny of genotyped animals

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Fernando et al., 2016; Legarra and Ducrocq, 2012

Example – data & hard/software

- CRV 4-trait evaluation
  - Temperament and milking speed
  - Pedigree 6,130,519
  - Phenotypes 3,882,772
  - Genotypes 90,963
  - SNPs 37,994
- Hardware: 528 GB RAM / 32 CPUs (only 5 CPUs used)
- Fortran + OpenMP program
  - Intel MKL library (BLAS, sparse BLAS, PARDISO)

Example – Time and memory

ssSNPBLUP: limited amount of memory and time / iteration

- Max. RAM 7.7 GB
- Average time / iteration 3.6 s
  - Time / imputation on-the-fly 0.15 s
  - Time / 2 multiplications with **M** 1.48 s
- # iterations 10,000

ssGBLUP + APY (13K core animals)

- Max. RAM 14.2 GB
- Average time / iteration 2.5 s
- # iterations 1258

Conclusions

- Multi-trait ssSNPBLUP
  - Feasible on current hardware
    - With limited amounts of memory and time
    - Even with >1,000,000 genotypes
      - Jan ten Napel, EAAP 2018, session 12
  - Under study
    - More complex models
    - Convergence issues

Thank you!

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