Single-Step genomic evaluation with many more genotyped animals

Esa Mäntysaari   Ismo Strandén

Genetic Research
Green Technology
Natural Resources Institute Finland (Luke)

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ssGBLUP is computational challenge

- Original single-step genomic evaluions were based on $var(\mathbf{u}) = \mathbf{H}$
  that has the size of N_a (animals in evaluation).

- The critical parts in $\mathbf{H}^{-1}$ are dense matrices $\mathbf{G}^{-1}$ and $\mathbf{A}_{22}^{-1}$
  that both have the size of number of genotyped animals N_{gta}.

  ▸ In many current (beef and dairy cattle) genomic evaluations $N_{gta} >> 150\,000$

For $\mathbf{A}_{22}^{-1}$ sparse matrices are solution
(in this session Strandén et al. 2016)

For $\mathbf{G}^{-1}$ APY is one choice (in this session Misztal 2016)

APY has still finetuning

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# Existing approaches have still room for improvement

We present 2 alternative computational solutions for large scale single-step genomic evaluations:

1. single-step SNP-BLUP — revisiting Liu et al. (2014)
   - but now modeling observations with SNPs and polygenic BVs

2. ssTBLUP — using Woodbury matrix identity for $\mathbf{G}^{-1}$ in ssGBLUP
   - i.e., $(\mathbf{G}_0 + k\mathbf{A}_{22})^{-1} - \mathbf{A}_{22}^{-1}$ replaced by $(\frac{1}{k} - 1)\mathbf{A}_{22}^{-1} + \mathbf{TT}'$

A single-step SNP model: Definitions

Definitions adapted from Liu et al. (2014)

- A mixed linear model in a general form
  $\mathbf{y} = \mathbf{Xb} + \mathbf{Wu} + \mathbf{e}$, with $\mathbf{u}' = \begin{bmatrix} \mathbf{u}'_1 & \mathbf{u}'_2 \end{bmatrix}$
- For genotyped animals (group2) $\mathbf{u}_2 = \mathbf{Zg} + \mathbf{a}_2$

- Distribution of SNP marker effects
  - $var(\mathbf{g}) = \mathbf{B}\sigma_g^2$

- Let k be the proportion of residual polygenic effect in $\mathbf{u}_2$
  $var(\mathbf{a}_2) = \mathbf{A}_{22}k\sigma_g^2$ and $var(\mathbf{u}_2) = (\mathbf{ZBZ}' + k\mathbf{A}_{22})\sigma_g^2 = \mathbf{G}_{22}\sigma_g^2$

- It is possible to write $\mathbf{u}_1$ (non-genotyped animals, group 1)
  $\mathbf{u}_1 = \mathbf{Pu}_2 + \mathbf{d}$
  - with projection matrix $\mathbf{P} = \mathbf{A}_{12}\mathbf{A}_{22}^{-1}$ and a deviation effect $\mathbf{d}$, with $var(\mathbf{d}) = \mathbf{D}\sigma_g^2$

  note that $\mathbf{D} = (\mathbf{A}^{11})^{-1}$

$\mathbf{a}_2$ is residual polygenic effect
RPG
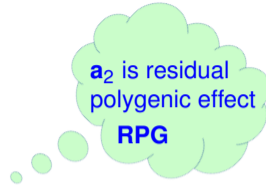
Joint variance of u and g

$$var \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{u}_2 \\ \mathbf{g} \end{bmatrix} = \mathbf{H}\sigma_g^2$$

Following Liu et al. (2014)

$$\mathbf{H}^{-1} = \begin{bmatrix} \mathbf{A}^{11} & \mathbf{A}^{12} & \mathbf{0} \\ \mathbf{A}^{21} & \mathbf{A}^{22} + (\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & -\frac{1}{k}\mathbf{A}_{22}^{-1}\mathbf{Z} \\ \mathbf{0} & -\frac{1}{k}\mathbf{Z}'\mathbf{A}_{22}^{-1} & \mathbf{B}^{-1} + \frac{1}{k}\mathbf{Z}'\mathbf{A}_{22}^{-1}\mathbf{Z} \end{bmatrix} \sigma_g^{-2}$$

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1. Model with SNPs and residual polygenic effects

In Liu et al. the data model only included the aggregate breeding values $\mathbf{u}_2$.
... Not the marker effects!

We can as well model $\mathbf{y}$ using the marker effects and RPG separately

$$\mathbf{y} = \mathbf{Xb} + \begin{bmatrix} \mathbf{W}_1 & 0 & 0 \\ 0 & \mathbf{W}_2 & \mathbf{W}_2\mathbf{Z} \end{bmatrix} \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{a}_2 \\ \mathbf{g} \end{bmatrix} + \mathbf{e}$$

Now we need the variance

$$\mathbf{H}_* \sigma_g^2 = var \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{a}_2 \\ \mathbf{g} \end{bmatrix}$$

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Variance structure $\mathbf{H}_*$

We can write a matrix $\mathbf{S}$ to map the $\mathbf{u}_2$ and $\mathbf{Zg}$ into $\mathbf{a}_2$

$$\mathbf{S} \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{u}_2 \\ \mathbf{g} \end{bmatrix} = \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & -\mathbf{Z} \\ \mathbf{0} & \mathbf{0} & \mathbf{I} \end{bmatrix} \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{u}_2 \\ \mathbf{g} \end{bmatrix} = \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{u}_2 - \mathbf{Zg} \\ \mathbf{g} \end{bmatrix} = \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{a}_2 \\ \mathbf{g} \end{bmatrix}$$

Now we get the variance structure for the mapped function

$$var \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{a}_2 \\ \mathbf{g} \end{bmatrix} = \mathbf{SHS}' = \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & -\mathbf{Z} \\ \mathbf{0} & \mathbf{0} & \mathbf{I} \end{bmatrix} var \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{u}_2 \\ \mathbf{g} \end{bmatrix} \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \mathbf{0} \\ \mathbf{0} & -\mathbf{Z}' & \mathbf{I} \end{bmatrix} = \mathbf{H}_* \sigma_g^2$$

And the inverse

$$\mathbf{H}_*^{-1} = \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}' & \mathbf{I} \end{bmatrix} \mathbf{H}^{-1} \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \mathbf{Z} \\ \mathbf{0} & \mathbf{0} & \mathbf{I} \end{bmatrix}$$

$$= \begin{bmatrix} \mathbf{A}^{11} & \mathbf{A}^{12} & \mathbf{A}^{12}\mathbf{Z} \\ \mathbf{A}^{21} & \mathbf{A}^{22} + (\frac{1}{k} - 1)\mathbf{A}_{22}^{-1} & (\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\ \mathbf{Z}'\mathbf{A}^{21} & \mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \mathbf{B}^{-1} \end{bmatrix} \sigma_g^{-2}$$

$$= \begin{bmatrix} \mathbf{H}_*^{11} & \mathbf{H}_*^{12} & \mathbf{H}_*^{13} \\ \mathbf{H}_*^{21} & \mathbf{H}_*^{22} & \mathbf{H}_*^{23} \\ \mathbf{H}_*^{31} & \mathbf{H}_*^{32} & \mathbf{H}_*^{33} \end{bmatrix} \sigma_g^{-2}$$

MME for ssSNP-BLUP

Model equations for all the observations

$$\begin{bmatrix} \mathbf{y}_1 \\ \mathbf{y}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}_1 \\ \mathbf{X}_2 \end{bmatrix} \begin{bmatrix} \mathbf{b} \end{bmatrix} + \begin{bmatrix} \mathbf{W}_1 & \mathbf{0} \\ \mathbf{0} & \mathbf{W}_2 \end{bmatrix} \begin{bmatrix} \mathbf{u}_1 \\ \mathbf{a}_2 \end{bmatrix} + \begin{bmatrix} \mathbf{0} \\ \mathbf{W}_2\mathbf{Z} \end{bmatrix} \begin{bmatrix} \mathbf{g} \end{bmatrix} + \begin{bmatrix} \mathbf{e}_1 \\ \mathbf{e}_2 \end{bmatrix}$$

The mixed model equations

$$\left[\begin{bmatrix} \mathbf{X'X} & \mathbf{X}_1'\mathbf{W}_1 & \mathbf{X}_2'\mathbf{W}_2 & \mathbf{X}_2'\mathbf{W}_2\mathbf{Z} \\ \mathbf{W}_1'\mathbf{X}_1 & \mathbf{W}_1'\mathbf{W}_1 & \mathbf{0} & \mathbf{0} \\ \mathbf{W}_2'\mathbf{X}_2 & \mathbf{0} & \mathbf{W}_2'\mathbf{W}_2 & \mathbf{W}_2'\mathbf{W}_2\mathbf{Z} \\ \mathbf{Z'W}_2'\mathbf{X}_2 & \mathbf{0} & \mathbf{Z'W}_2'\mathbf{W}_2 & \mathbf{Z'W}_2'\mathbf{W}_2\mathbf{Z} \end{bmatrix} + \lambda \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{H}_*^{11} & \mathbf{H}_*^{12} & \mathbf{H}_*^{13} \\ \mathbf{0} & \mathbf{0} & \mathbf{H}_*^{21} & \mathbf{H}_*^{22} & \mathbf{H}_*^{23} \\ \mathbf{0} & \mathbf{0} & \mathbf{H}_*^{31} & \mathbf{H}_*^{32} & \mathbf{H}_*^{33} \end{bmatrix} \right] \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W}_1'\mathbf{y} \\ \mathbf{W}_2'\mathbf{y} \\ \mathbf{Z'W}_2'\mathbf{y} \end{bmatrix}$$

where $\lambda = \sigma_e^2/\sigma_g^2$

MME

$$
\begin{bmatrix}
\mathbf{X'X} & \mathbf{X'_1 W_1} & \mathbf{X'_2 W_2} & \mathbf{X'_2 W_2 Z} \\
\mathbf{W'_1 X_1} & \mathbf{W'_1 W_1} + \lambda \mathbf{A}^{11} & \lambda \mathbf{A}^{12} & \lambda \mathbf{A}^{12} \mathbf{Z} \\
\mathbf{W'_2 X} & \lambda \mathbf{A}^{21} & \mathbf{W'_2 W_2} + \lambda \mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W'_2 W_2 Z} + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\
\mathbf{Z'W'_2 X_2} & \lambda \mathbf{Z'A}^{21} & \mathbf{Z'W'_2 W_2} + \lambda \mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z'W'_2 W_2 Z} + \lambda \mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda \mathbf{B}^{-1}
\end{bmatrix}
\begin{bmatrix}
\mathbf{\hat{b}} \\
\mathbf{\hat{u}_1} \\
\mathbf{\hat{a}_2} \\
\mathbf{\hat{g}}
\end{bmatrix}
=
\begin{bmatrix}
\mathbf{X'y} \\
\mathbf{W'_1 y} \\
\mathbf{W'_2 y} \\
\mathbf{Z'W'_2 y}
\end{bmatrix}
$$

We can redefine/rename the marker design matrix for phenotypes: $\mathbf{W_2 Z} = \mathbf{Z_2}$

$$
\begin{bmatrix}
\mathbf{X'X} & \mathbf{X'_1 W_1} & \mathbf{X'_2 W_2} & \mathbf{X'_2 Z_2} \\
\mathbf{W'_1 X_1} & \mathbf{W'_1 W_1} + \lambda \mathbf{A}^{11} & \lambda \mathbf{A}^{12} & \lambda \mathbf{A}^{12} \mathbf{Z} \\
\mathbf{W'_2 X} & \lambda \mathbf{A}^{21} & \mathbf{W'_2 W_2} + \lambda \mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W'_2 Z_2} + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\
\mathbf{Z'_2 X_2} & \lambda \mathbf{Z'A}^{21} & \mathbf{Z'_2 W_2} + \lambda \mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z'_2 Z_2} + \lambda \mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda \mathbf{B}^{-1}
\end{bmatrix}
\begin{bmatrix}
\mathbf{\hat{b}} \\
\mathbf{\hat{u}_1} \\
\mathbf{\hat{a}_2} \\
\mathbf{\hat{g}}
\end{bmatrix}
=
\begin{bmatrix}
\mathbf{X'y} \\
\mathbf{W'_1 y} \\
\mathbf{W'_2 y} \\
\mathbf{Z'_2 y}
\end{bmatrix}
$$

MME

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X_1'W_1} & \mathbf{X_2'W_2} & \mathbf{X_2'W_2Z} \\ \mathbf{W_1'X_1} & \mathbf{W_1'W_1} + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\ \mathbf{W_2'}X & \lambda\mathbf{A}^{21} & \mathbf{W_2'W_2} + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W_2'W_2Z} + \lambda(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1})\mathbf{Z} \\ \mathbf{Z'W_2'X_2} & \lambda\mathbf{Z'A}^{21} & \mathbf{Z'W_2'W_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1}) & \mathbf{Z'W_2'W_2Z} + \lambda\mathbf{Z'}(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W_1'y} \\ \mathbf{W_2'y} \\ \mathbf{Z'W_2'y} \end{bmatrix}$$

We can redefine/rename the marker design matrix for phenotypes: $\mathbf{W_2Z} = \mathbf{Z_2}$

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X_1'W_1} & \mathbf{X_2'W_2} & \mathbf{X_2'Z_2} \\ \mathbf{W_1'X_1} & \mathbf{W_1'W_1} + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\ \mathbf{W_2'}X & \lambda\mathbf{A}^{21} & \mathbf{W_2'W_2} + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W_2'Z_2} + \lambda(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1})\mathbf{Z} \\ \mathbf{Z_2'X_2} & \lambda\mathbf{Z'A}^{21} & \mathbf{Z_2'W_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1}) & \mathbf{Z_2'Z_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22}-\mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W_1'y} \\ \mathbf{W_2'y} \\ \mathbf{Z_2'y} \end{bmatrix}$$

MME

$$
\begin{bmatrix}
\mathbf{X}'\mathbf{X} & \mathbf{X}_1'\mathbf{W}_1 & \mathbf{X}_2'\mathbf{W}_2 & \mathbf{X}_2'\mathbf{W}_2\mathbf{Z} \\
\mathbf{W}_1'\mathbf{X}_1 & \mathbf{W}_1'\mathbf{W}_1 + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\
\mathbf{W}_2'\mathit{X} & \lambda\mathbf{A}^{21} & \mathbf{W}_2'\mathbf{W}_2 + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W}_2'\mathbf{W}_2\mathbf{Z} + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\
\mathbf{Z}'\mathbf{W}_2'\mathbf{X}_2 & \lambda\mathbf{Z}'\mathbf{A}^{21} & \mathbf{Z}'\mathbf{W}_2'\mathbf{W}_2 + \lambda\mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z}'\mathbf{W}_2'\mathbf{W}_2\mathbf{Z} + \lambda\mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1}
\end{bmatrix}
\begin{bmatrix}
\hat{\mathbf{b}} \\
\hat{\mathbf{u}}_1 \\
\hat{\mathbf{a}}_2 \\
\hat{\mathbf{g}}
\end{bmatrix}
=
\begin{bmatrix}
\mathbf{X}'\mathbf{y} \\
\mathbf{W}_1'\mathbf{y} \\
\mathbf{W}_2'\mathbf{y} \\
\mathbf{Z}'\mathbf{W}_2'\mathbf{y}
\end{bmatrix}
$$

We can redefine/rename the marker design matrix for phenotypes: $\mathbf{W}_2\mathbf{Z} = \mathbf{Z}_2$

$$
\begin{bmatrix}
\mathbf{X}'\mathbf{X} & \mathbf{X}_1'\mathbf{W}_1 & \mathbf{X}_2'\mathbf{W}_2 & \mathbf{X}_2'\mathbf{Z}_2 \\
\mathbf{W}_1'\mathbf{X}_1 & \mathbf{W}_1'\mathbf{W}_1 + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\
\mathbf{W}_2'\mathit{X} & \lambda\mathbf{A}^{21} & \mathbf{W}_2'\mathbf{W}_2 + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W}_2'\mathbf{Z}_2 + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\
\mathbf{Z}_2'\mathbf{X}_2 & \lambda\mathbf{Z}'\mathbf{A}^{21} & \mathbf{Z}_2'\mathbf{W}_2 + \lambda\mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z}_2'\mathbf{Z}_2 + \lambda\mathbf{Z}'(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1}
\end{bmatrix}
\begin{bmatrix}
\hat{\mathbf{b}} \\
\hat{\mathbf{u}}_1 \\
\hat{\mathbf{a}}_2 \\
\hat{\mathbf{g}}
\end{bmatrix}
=
\begin{bmatrix}
\mathbf{X}'\mathbf{y} \\
\mathbf{W}_1'\mathbf{y} \\
\mathbf{W}_2'\mathbf{y} \\
\mathbf{Z}_2'\mathbf{y}
\end{bmatrix}
$$

The model bounds logically: if k –> 1.0 then we have animal model MME

MME

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'_1W_1} & \mathbf{X'_2W_2} & \mathbf{X'_2W_2Z} \\ \mathbf{W'_1X_1} & \mathbf{W'_1W_1} + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\ \mathbf{W'_2}X & \lambda\mathbf{A}^{21} & \mathbf{W'_2W_2} + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W'_2W_2Z} + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\ \mathbf{Z'W'_2X_2} & \lambda\mathbf{Z'A}^{21} & \mathbf{Z'W'_2W_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z'W'_2W_2Z} + \lambda\mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W'_1y} \\ \mathbf{W'_2y} \\ \mathbf{Z'W'_2y} \end{bmatrix}$$

We can redefine/rename the marker design matrix for phenotypes: $\mathbf{W_2Z} = \mathbf{Z_2}$

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'_1W_1} & \mathbf{X'_2W_2} & \mathbf{X'_2Z_2} \\ \mathbf{W'_1X_1} & \mathbf{W'_1W_1} + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\ \mathbf{W'_2}X & \lambda\mathbf{A}^{21} & \mathbf{W'_2W_2} + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W'_2Z_2} + \lambda(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} \\ \mathbf{Z'_2X_2} & \lambda\mathbf{Z'A}^{21} & \mathbf{Z'_2W_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) & \mathbf{Z'_2Z_2} + \lambda\mathbf{Z'}(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1})\mathbf{Z} + \lambda\mathbf{B}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W'_1y} \\ \mathbf{W'_2y} \\ \mathbf{Z'_2y} \end{bmatrix}$$

The model bounds logically: if k –> 0.0 then we have Legarra & Ducroq (JDS 2012)

MME version with projection matrices

An alternative form can be presented using the projection matrix $\mathbf{P}$:

$$(\mathbf{A}^{22} - \mathbf{A}_{22}^{-1}) = \mathbf{A}^{22} - (\mathbf{A}^{22} - \mathbf{A}^{21}(\mathbf{A}^{11})^{-1}\mathbf{A}^{12}) = \mathbf{A}^{22} - \mathbf{A}^{22} + \mathbf{A}^{21}(\mathbf{A}^{11})^{-1}\mathbf{A}^{12}$$
$$= \mathbf{P}'\mathbf{A}^{11}\mathbf{P}$$

This is because projection matrix can be written either $\mathbf{A}_{12}\mathbf{A}_{22}^{-1}$ or $-(\mathbf{A}^{11})^{-1}\mathbf{A}^{12}$.

With the terms of projection matrix, we can rewrite the MME:

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}_1'\mathbf{W}_1 & \mathbf{X}_2'\mathbf{W}_2 & \mathbf{X}_2'\mathbf{Z}_2 \\ \mathbf{W}_1'\mathbf{X}_1 & \mathbf{W}_1'\mathbf{W}_1 + \lambda\mathbf{A}^{11} & \lambda\mathbf{A}^{12} & \lambda\mathbf{A}^{12}\mathbf{Z} \\ \mathbf{W}_2'\mathbf{X} & \lambda\mathbf{A}^{21} & \mathbf{W}_2'\mathbf{W}_2 + \lambda\mathbf{A}^{22} + \lambda(\frac{1}{k}-1)\mathbf{A}_{22}^{-1} & \mathbf{W}_2'\mathbf{Z}_2 - \lambda\mathbf{A}^{21}\mathbf{P}\mathbf{Z} \\ \mathbf{Z}_2'\mathbf{X}_2 & \lambda\mathbf{Z}'\mathbf{A}^{21} & \mathbf{Z}_2'\mathbf{W}_2 - \lambda\mathbf{Z}'\mathbf{P}'\mathbf{A}^{12} & \mathbf{Z}_2'\mathbf{Z}_2 + \lambda\mathbf{Z}'\mathbf{P}'\mathbf{A}^{11}\mathbf{P}\mathbf{Z} + \lambda\mathbf{B}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{a}}_2 \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{W}_1'\mathbf{y} \\ \mathbf{W}_2'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \end{bmatrix}$$

ssSNP-BLUP Discussion

- It is possible to build a model that adds SNP EFFECTS and RPG EFFECT only for the genotyped animals
  - ► MME are logical: genotyped animals have 2 separate contributions
- Computationally feasible
  - ► "standard ssGBLUP": each PCG iteration round involves one "solve" $A_{22}^{-1} d_{a2}$
  - ► ssSNP-BLUP: each iteration requires 2 solves [$A_{22}^{-1} d_{a2}$ and $A_{22}^{-1} d_{Zg}$]

expected computing time small

- Numerical (iteration) properties better than in augmented GBLUP if the proportion of polygenic variance in model is low
  - ► This in our test runs with small 74000 animals data
    - only 2885 genotyped animals
    - but 38 000 markers

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2. From ss-GBLUP to ssTBLUP

ssGBLUP MME w. residual polygenic effects

Standard single-step GBLUP MME:

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'_1 W_1} & \mathbf{X'_2 W_2} \\ \mathbf{W'_1 X_1} & \mathbf{W'_1 W_1} + \lambda \mathbf{A}^{11} & \lambda \mathbf{A}^{12} \\ \mathbf{W'_2 X} & \lambda \mathbf{A}^{21} & \mathbf{W'_2 W_2} + \lambda \mathbf{A}^{22} + \lambda \mathbf{M} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}}_1 \\ \hat{\mathbf{u}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W'_1 y} \\ \mathbf{W'_2 y} \end{bmatrix}$$

where

$$\mathbf{M} = \mathbf{G}_k^{-1} - \mathbf{A}_{22}^{-1}$$

with

$$\mathbf{G}_k = (k \mathbf{A}_{22} + \mathbf{Z B Z'})$$

Note that inverse of $\mathbf{G}_k$ can be derived from Woodbury matrix identity

$$\mathbf{G}_k^{-1} = (k \mathbf{A}_{22} + \mathbf{Z B Z'})^{-1}$$

$$= \frac{1}{k} \mathbf{A}_{22}^{-1} - \frac{1}{k} \mathbf{A}_{22}^{-1} \mathbf{Z} \left(\frac{1}{k} \mathbf{Z'} \mathbf{A}_{22}^{-1} \mathbf{Z} + \mathbf{B}^{-1} \right)^{-1} \frac{1}{k} \mathbf{Z'} \mathbf{A}_{22}^{-1}$$

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Luke
NATURAL RESOURCES
INSTITUTE FINLAND

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Variance structure for genotyped animals

$$\mathbf{M} = \mathbf{G}_k^{-1} - \mathbf{A}_{22}^{-1}$$
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$$= \mathbf{M}_1 - \mathbf{M}_2$$

where

$$\mathbf{M}_1 = (\frac{1}{k} - 1)\mathbf{A}_{22}^{-1}$$

and

$$\mathbf{M}_2 = \frac{1}{k}\mathbf{A}_{22}^{-1}\mathbf{Z}(\frac{1}{k}\mathbf{Z}'\mathbf{A}_{22}^{-1}\mathbf{Z} + \mathbf{B}^{-1})^{-1}\mathbf{Z}'\mathbf{A}_{22}^{-1}\frac{1}{k}$$

Although $\mathbf{M}_2$-matrix looks cumbersome, it is computationally simple because the inverse is only done for p×p matrix.   Or actually inverse is not needed at all....

Instead of inverting the "coefficent matrix", make a Cholesky decomposition:

$$\mathbf{L}'\mathbf{L} = (\tfrac{1}{k}\mathbf{Z}'\mathbf{A}_{22}^{-1}\mathbf{Z} + \mathbf{B}^{-1})$$

Note that the $\mathbf{A}_{22}^{-1}\mathbf{Z}$ can be calculated using projection matrix formula $\qquad \mathbf{A}_{22}^{-1} = \mathbf{A}^{22} - \mathbf{A}^{21}(\mathbf{A}^{11})^{-1}\mathbf{A}^{12}$,
which can be solved without inverting the $\mathbf{A}^{11}$ (Strandén et al. EAAP 2016)

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Finally

$$\mathbf{M}_2 = \tfrac{1}{k}\mathbf{A}_{22}^{-1}\mathbf{Z}\mathbf{L}^{-1}\,\mathbf{L}^{-T}\mathbf{Z}'\mathbf{A}_{22}^{-1}\tfrac{1}{k}$$

This means that $\mathbf{M}_2$ can be written as outerproduct of two rectangular matrices:

$$\mathbf{M}_2 = [\tfrac{1}{k}\mathbf{A}_{22}^{-1}\mathbf{Z}\mathbf{L}^{-1}]\,[\tfrac{1}{k}\mathbf{A}_{22}^{-1}\mathbf{Z}\mathbf{L}^{-1}]' = \mathbf{T}\mathbf{T}'$$

In which $\mathbf{T}$ has N_{gta} rows (number of animals genotyped) and N_p columns (number of SNPs).

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ssTBLUP Discussion

- In solving the ssGBLUP:
  - PCG iteration requires multiplications $\mathbf{G}^{-1}\mathbf{d}$ and $\mathbf{A}_{22}^{-1}\mathbf{d}$ in each iteration ($\mathbf{d}$ is direction vector)
  - In state of art implementation, $\mathbf{A}_{22}^{-1}\mathbf{d}$ is formed explicitely using pedigree information

  In ssTBLUP program $\mathbf{A}_{22}^{-1}$ is scaled using $\frac{1-k}{k}$, and
  the multiplication $\mathbf{G}_k^{-1}\mathbf{d}$ is replaced by consecutive $\mathbf{T}(\mathbf{T}'\mathbf{d})$

  - Computing <u>increases linearly on the number of genotyped animals</u> (not quadratically)

- In computation of $\mathbf{T}$, no approximations are needed
  –> the solutions are exactly the same as with same $\mathbf{G}_k$ in ssGBLUP

- ssTBLUP has convergence properties of ssGBLUP but avoids making and inverting $\mathbf{G}$ matrix

- computing load in forming $\mathbf{T}$ is essentially the same as in projecting (imputing)
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  - with few animals: flops to make $\mathbf{G}_k^{-1}$ < flops to make $\mathbf{T}$
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Thank you for your attention !

We are grateful for the data and financing