meBLUP: a single step gBLUP combining pedigree and SNP information without genomic inverse

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From Mixed Models (MME) to Model Equations (ME)

Henderson's **mixed model equations**

$$\begin{pmatrix} X^T D^{-1} X & X^T D^{-1} Z \\ Z^T D^{-1} X & Z^T D^{-1} Z + G^{-1} \end{pmatrix} \begin{pmatrix} \beta \\ u \end{pmatrix} = \begin{pmatrix} X^T D^{-1} y \\ Z^T D^{-1} y \end{pmatrix}$$

for estimating β and u, which only involve the inverse G^{-1}. The vector $\widehat{u}$ (containing the estimated breeding values) is usually called the **best linear unbiased predictor (BLUP)** of the random effects.

The model equation formulation of a mixed model

Fellner observed, that Henderson's mixed model equations are just the normal equations of a simple form giving the **ME formulation**:

$$Ax = b,$$

where

$$A = \begin{pmatrix} X & Z \\ 0 & -I \end{pmatrix}, x = \begin{pmatrix} \beta \\ u \end{pmatrix}, b = \begin{pmatrix} y \\ 0 \end{pmatrix},$$

Thus computing this $\widehat{u}$ of the ME formulation will be the same as that of the mixed model.

Note here is no G^{-1}.

Model equations animal model BLUP $Ax = b$

- setting up and solving ME $Ax = b$ equivalent to using MME

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`http://www.wcgalp.org/system/files/proceedings/2018/blup-without-inverse-relationship-matrix.pdf`

Setting up model equations in $Ax = b$

```
snp1-pedi.txt    snp1-data.txt           snp4.txt
 1 6 7         bf    wt   sex Animal       SNPS
 2 1 7         10.5 90.1  1   1          1 0112
 3 1 4         13.2 87.3  1   2          2 2101
 4 2 1         12.6 93.5  2   3          3 1022
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```
ANIMAL  8 13 14            1.4 -0.7 -0.7                     2
ANIMAL  9  8 14            1.4 -0.7 -0.7                     2
ANIMAL 10  8 11            1.4 -0.7 -0.7                     2
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ANIMAL 12 10 11            1.4 -0.7 -0.7                     2
ANIMAL 13  0  0            1.0  0.0  0.0                     2
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```

```
SNP    16                  1.0                                3
SNP    17                  1.0                                3
SNP    18                  1.0                                3
SNP    19                  1.0                                3
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```

```
SNP    16                  1.0                               3
SNP    17                  1.0                               3
SNP    18                  1.0                               3
SNP    19                  1.0                               3
```

```
GENOMIC 16 17 18 19  8 20   0.0  1.0  1.0  2.0 -1.0  1.0     4
GENOMIC 16 17 18 19  9 20   2.0  1.0  0.0  1.0 -1.0  1.0     4
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```

solve $Ax = b$ by PCG

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13  0  0               1.0  0.0  0.0                         2
14 15  0               1.2 -0.6  0.0                         2
15  0  0               1.0  0.0  0.0                         2
16                     1.0                                   3
17                     1.0                                   3
18                     1.0                                   3
19                     1.0                                   3
16 17 18 19  8 20      0.0  1.0  1.0  2.0 -1.0  1.0          4
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- inverses have max. dimension *ntrait* ∗ *ntrait*

Implementation, Scope and Performance

- implemented in Fortran in PEST2 and VCE
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33mio	2	53mio	41K@116000	1	52.7sec

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33mio	2	53mio	41K@116000	1	52.7sec
33mio	2	53mio	41K@135000	1	60.1sec

Validation me_BLUP vs ss_BLUP

Correlations true/estimated breeding value

for the last generation (without phenotypes)

```
 h^2 |    number of SNPs used     | method
     | 40000  | 50000  | 60000  |
-----------------------------------------
0.05 | 0.435+ | 0.446+ | 0.450- | meBLUP
0.05 | 0.426  | 0.445  | 0.455  | ssBLUP
0.10 | 0.425+ | 0.429- | 0.446- | meBLUP
0.10 | 0.418  | 0.436  | 0.459  | ssBLUP
0.20 | 0.591+ | 0.593+ | 0.599+ | meBLUP
0.20 | 0.581  | 0.586  | 0.597  | ssBLUP
0.30 | 0.528- | 0.537- | 0.555- | meBLUP
0.30 | 0.530  | 0.551  | 0.584  | ssBLUP
0.40 | 0.572- | 0.591- | 0.598- | meBLUP
0.40 | 0.577  | 0.615  | 0.635  | ssBLUP
0.50 | 0.617+ | 0.640- | 0.650- | meBLUP
0.50 | 0.616  | 0.655  | 0.679  | ssBLUP
0.60 | 0.717+ | 0.735- | 0.745- | meBLUP
0.60 | 0.704  | 0.745  | 0.767  | ssBLUP
```

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- The resulting linear system is always positive definite and can be solved by conjugate gradients, without slow convergence.
- The ME approach leads to a different way of combining pedigree data and genomic data. It is not equivalent to ssBLUP.

Outlook

- estimate (co)variances SNP, Genomic, scaling vector
- nonlinear optimization as initial part of PCG
- weighing of sources of SNP vs pedigree
- finding ME that inherently do not double count

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Thank you for your attention!