Deflated preconditioned conjugate gradient method for solving single-step single nucleotide polymorphism BLUP

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Breed4Food is dedicated to be the leading research consortium in animal breeding, genetics and genomics enabling the Breed4Food partners to breed better products to benefit society’s needs.
Single-step models

- Prediction of genomic breeding values
  - Genotyped and non-genotyped animals

- Single-step GBLUP
  - Animal-based model
  - Limited?

- Single-step SNPBLUP
  - SNP-based model
  - Several equivalent formulations
  - No limitation?!

Fernando et al., 2016; Legarra et al., 2014; Liu et al., 2014; Taskinen et al., 2017
Single-step SNPBLUP

System of equations has the form \( \mathbf{C} \mathbf{x} = \mathbf{b} \)

- **Iterative solver**: Preconditioned Conjugate Gradient
- **Convergence issues** often reported...

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Liu et al., 2014; Manzanilla Pech et al. 2017; Taskinen et al., 2017
Aim

1. Comparison of properties of coefficient matrices of ssGBLUP and ssSNPBLUP

   ➔ Comprehension of convergence patterns of PCG

2. Implementation of a Deflated PCG method for solving efficiently ssSNPBLUP
Equivalent single-step models

\( \text{asGBLUP:} \quad y = Xb + \begin{bmatrix} 
  \tilde{W}_g & \tilde{u}_g 
\end{bmatrix} + e \)

\( \text{ssSNPBLUP:} \quad y = Xb + \begin{bmatrix}
  W_n & 0 & 0 \\
  0 & W_g & W_g Z
\end{bmatrix} \begin{bmatrix}
  u_n \\
  a_g \\
  g
\end{bmatrix} + e \)

\[ u_g = a_g + Zg \]

- \( b \): fixed effects
- \( u_n, u_g \): aggregate GEBVs for (non-)genotyped animals
- \( a_g \): residual polygenic effects for genotyped animals

Fernando et al., 2016; Mantysaari and Stranden, 2016
Conjugate Gradient (CG)

- Successive approximations to obtain a more accurate solution of $\mathbf{x}$ by solving
  \[ C\mathbf{x} = b \]

- Convergence
  - Function of the effective condition number of $C$
    \[ \kappa(C) = \frac{\text{largest eigenvalue of } C}{\text{(non-zero) smallest eigenvalue of } C} \]

  - Smaller condition number \( \Rightarrow \) faster convergence
Preconditioned CG (PCG)

- Improvement of the condition number from $\kappa(C)$ to $\kappa(M^{-1}C)$ by introducing a preconditioner $M$

  $$M^{-1}C \mathbf{x} = M^{-1} \mathbf{b}$$

- In animal breeding
  - PCG often implemented
  - Usually: $M = \text{diag}(C)$ (or a variant)
Deflated PCG (DPCG)

- Improvement of the condition number from $\kappa(M^{-1}C)$ to $\kappa(M^{-1}PC)$ by introducing a second-level preconditioner $P$

$$M^{-1}PCx = M^{-1}Pb$$

$P$ chosen such that unfavourable eigenvalues are set to 0 (deflated)
Deflated PCG (DPCG)

- \( P = \text{deflation matrix} \)
  
  \[ = I - CZ_d(Z_d' CZ_d)^{-1}Z_d' \]

- \( Z_d \) contains the deflation vectors
  
  • Approximation of the same space of the span of unfavourable eigenvectors

  ➜ Set of deflation vectors \( \approx \) Set of unfavourable eigenvectors
Deflated PCG (DPCG)

- Setting-up of $\mathbf{Z}_d$ following a subdomain deflation approach
  - 1 subdomain per fixed/random effect
  - 1 subdomain per set of $n$ (1, 5, 50, or 200) SNP equations

Vector of solutions $\mathbf{x}$

<table>
<thead>
<tr>
<th>$\mathbf{Z}_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$b_1$</td>
</tr>
<tr>
<td>$b_2$</td>
</tr>
<tr>
<td>$u$</td>
</tr>
<tr>
<td>$g_1$</td>
</tr>
<tr>
<td>...</td>
</tr>
<tr>
<td>$g_y$</td>
</tr>
<tr>
<td>1 0 0 0</td>
</tr>
<tr>
<td>1 0 0 . 0</td>
</tr>
<tr>
<td>0 1 0 . 0</td>
</tr>
<tr>
<td>0 0 1 0</td>
</tr>
<tr>
<td>... ...</td>
</tr>
<tr>
<td>0 0 0 ... 1</td>
</tr>
</tbody>
</table>

Sparse $\mathbf{Z}_d \Rightarrow$ efficient implementation $\Rightarrow$ small extra-costs
Data

- 61,592 Ovum pick-up sessions
- 37,021 animals
  - 4,109 phenotyped animals
  - 6,169 genotyped animals (without phenotype)
- 9,994 segregating SNPs

- Heritability = 0.35
- Residual polygenic variance = 5%

Cornelissen et al. 2017
## Results – Spectra and condition numbers

<table>
<thead>
<tr>
<th>Model</th>
<th>Method</th>
<th>Smallest eigenvalue</th>
<th>Largest eigenvalue</th>
<th>$\kappa$</th>
<th>#iter.</th>
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<tbody>
<tr>
<td>ssG</td>
<td>PCG</td>
<td>$1.1 \times 10^{-4}$</td>
<td>11.9</td>
<td>$1.1 \times 10^5$</td>
<td>273</td>
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<tr>
<td>ssSNP</td>
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**ssSNPBLUP vs ssGBLUP**

- Unchanged smallest eigenvalues
- Increased largest eigenvalues
  - Larger condition number
  - Increased number of iterations
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<td>DPCG (200)</td>
<td>PCG</td>
<td>$1.1 \times 10^{-4}$</td>
<td>99.4</td>
<td>$9.3 \times 10^5$</td>
<td>1195</td>
</tr>
</tbody>
</table>

200 SNPs equations per subdomain

- Unchanged smallest value
- Decreased largest eigenvalue
- Better condition number after deflation
## Results – Spectra and condition numbers

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<td>1195</td>
</tr>
<tr>
<td>DPCG (50)</td>
<td>PCG</td>
<td>1.1*10^{-4}</td>
<td>40.5</td>
<td>3.8*10^5</td>
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</tr>
<tr>
<td><strong>DPCG (5)</strong></td>
<td>PCG</td>
<td>1.1*10^{-4}</td>
<td>6.0</td>
<td>5.6*10^4</td>
<td>338</td>
</tr>
<tr>
<td><strong>DPCG (1)</strong></td>
<td>PCG</td>
<td>1.1*10^{-4}</td>
<td>6.0</td>
<td>5.4*10^4</td>
<td>240</td>
</tr>
</tbody>
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1 and 5 SNPs per subdomain

- Similar (decreased) condition numbers
- #iterations similar as ssGBLUP
- **Reduction** of #iter. by up to a factor 6!
Conclusions

- ssSNPBLUP - **PCG**: larger eigenvalues
  ➡️ Larger condition number

- ssSNPBLUP - **Deflated PCG**
  - Treats the largest unfavourable eigenvalues
  ➡️ Smaller condition number
  ➡️ Faster convergence (similar to ssGBLUP)

- Similar pattern on large and multivariate ssSNPBLUP
Thank you!