IT-Solutions for
Animal Production

A SNP MACE model for international genomic evaluation:

- technical challenges and possible solutions

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Overview

Current status of (inter)national conventional and genomic evaluations

- A SNP MACE model for international evaluation
- Solving algorithms for the SNP MACE model
- Approximation of prediction error (co)variances
- Further development and extension
  - Different SNP sets across countries

    Countries use MACE info as phenotypes

International evaluation based on SNP effects

- Concept of a SNP based international evaluation (Goddard, 2011)
- A SNP-Focus Model replacing the Animal Model (Schaeffer, 2014)
- Interbull estimation of SNP effects (Goddard, 2016)
- A SNP MACE model proposed (Goddard, 2017)
  - Interbull Technical Workshop, Slovenia
- Interbull project on the SNP MACE model

A SNP MACE model

- A SNP genomic model for Multiple Across Country Evaluation

$$\mathbf{g}_i^N \quad ==\gg \quad \mathbf{g}_i \qquad [1]$$

for country i (i = 1, …, c)

- A SNP BLUP model for national genomic evaluation

$$\mathbf{y}_i = \mu_i \mathbf{1} + \mathbf{Z}_i \mathbf{g}_i^N + \mathbf{e}_i \qquad [2]$$

where $\mathbf{y}_i$ is phenotype after absorbing all other effects (including the residual polygenic effect)

$$var(\mathbf{e}_i) = \mathbf{R}_i^{-1} = diag\{n_{ik}\sigma_{e_i}^{-2}\}$$

$$var(\mathbf{g}_i) = \mathbf{B}_i\sigma_i^2 \quad \text{with DGV variance } \sigma_i^2$$

$$\mathbf{B}_i = \frac{1}{\sum_j 2p_{ij}(1-p_{ij})}\mathbf{I} = \theta_i \mathbf{I}$$

SNP genetic (co)variances between countries (I)

- A (co)variance matrix for countries (i = 1, …, c) **for a single SNP marker** $\mathbf{G}_{cou} =$

$$\begin{bmatrix} \sigma_1^2\theta_1 & r_{12}\sigma_1\sigma_2\sqrt{\theta_1\theta_2} & \cdots & r_{1c}\sigma_1\sigma_c\sqrt{\theta_1\theta_c} \\ & \sigma_2^2\theta_2 & \cdots & r_{2c}\sigma_2\sigma_c\sqrt{\theta_2\theta_c} \\ & & \ddots & \vdots \\ & symm. & & \sigma_c^2\theta_c \end{bmatrix} = \begin{bmatrix} g_{11} & g_{12} & \cdots & g_{1c} \\ & g_{22} & \cdots & g_{2c} \\ & & \ddots & \vdots \\ & symm. & & g_{cc} \end{bmatrix}$$

- Its inverse $\mathbf{G}_{cou}^{-1} = \begin{bmatrix} g^{11} & g^{12} & \cdots & g^{1c} \\ & g^{22} & \cdots & g^{2c} \\ & & \ddots & \vdots \\ & symm. & & g^{cc} \end{bmatrix}$

SNP genetic (co)variances between countries (II)

- Genetic (co)variance matrix for **ALL** SNP effects **(ordered by countries)**

$$\text{var}\begin{bmatrix}\mathbf{g_1}\\ \mathbf{g_2}\\ \vdots\\ \mathbf{g_c}\end{bmatrix} = \mathbf{G} = \mathbf{G_{cou}} \otimes \mathbf{I} = \begin{bmatrix} g_{11}\mathbf{I} & g_{12}\mathbf{I} & \cdots & g_{1c}\mathbf{I} \\ & g_{22}\mathbf{I} & \cdots & g_{2c}\mathbf{I} \\ & & \ddots & \vdots \\ symm. & & & g_{cc}\mathbf{I} \end{bmatrix}$$

- Its inverse $\mathbf{G^{-1}} = \mathbf{G_{cou}^{-1}} \otimes \mathbf{I} = \begin{bmatrix} g^{11}\mathbf{I} & g^{12}\mathbf{I} & \cdots & g^{1c}\mathbf{I} \\ & g^{22}\mathbf{I} & \cdots & g^{2c}\mathbf{I} \\ & & \ddots & \vdots \\ symm. & & & g^{cc}\mathbf{I} \end{bmatrix}$

- Inter-SNP genetic correlations: within or between countries are all 0
- Intra-SNP genetic correlations between countries to be estimated
  - Set to country correlations as in current MACE

Mixed model equations of the SNP MACE model

$$\begin{bmatrix} \ddots & \cdots & \cdots & \\ & \left[\begin{bmatrix} 1'Z_i'R_i^{-1}Z_i1 & 1'Z_i'R_i^{-1}Z_i \\ Z_i'R_i^{-1}Z_i1 & Z_i'R_i^{-1}Z_i \end{bmatrix} + \begin{bmatrix} 0 & 0 \\ 0 & g^{ii}I \end{bmatrix}\right] & \left[\Psi_{ii^+} + \begin{bmatrix} 0 & 0 \\ 0 & g^{ii^+}I \end{bmatrix}\right] & \\ \cdots & \left[\Psi_{ii^+} + \begin{bmatrix} 0 & 0 \\ 0 & g^{ii^+}I \end{bmatrix}\right] & \ddots \\ & \ddots & \left[\begin{bmatrix} 1'Z_{i^+}'R_{i^+}^{-1}Z_{i^+}1 & 1'Z_{i^+}'R_{i^+}^{-1}Z_{i^+} \\ Z_{i^+}'R_{i^+}^{-1}Z_{i^+}1 & Z_{i^+}'R_{i^+}^{-1}Z_{i^+} \end{bmatrix} + \begin{bmatrix} 0 & 0 \\ 0 & g^{i^+i^+}I \end{bmatrix}\right] \\ & & \ddots \end{bmatrix}$$

$$x\begin{bmatrix} \vdots \\ \hat{\mu}_i \\ \hat{\mathbf{g}}_i \\ \vdots \\ \hat{\mu}_{i^+} \\ \hat{\mathbf{g}}_{i^+} \\ \vdots \end{bmatrix} = \begin{bmatrix} \vdots \\ 1'Z_i'R_i^{-1}y_i \\ Z_i'R_i^{-1}y_i \\ \vdots \\ 1'Z_{i^+}'R_{i^+}^{-1}y_{i^+} \\ Z_{i^+}'R_{i^+}^{-1}y_{i^+} \\ \vdots \end{bmatrix}$$

Zero residual covariances between countries $\Psi_{i\,i^+} = 0$, if the countries do not use MACE EBV for national genomic evaluation

Solving the mixed model equations

- MME of the SNP MACE model have special structures:
  - Data contribution by country, zero residual covariances (off-diagonals)
  - SNP genetic contribution: only diagonal and sub-diagonals ≠ 0
    - Block-diagonal matrix in the SNP-major order
- Identical processes for every country or every SNP → parallel computing
- PCG algorithm using multiple cores

$$\mathbf{C}\,\mathbf{v} = \left\{\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i\right\}\mathbf{v} + \{\mathbf{G}_{cou}^{-1}\}\mathbf{v}$$

for country i — parallelised by countries

for every SNP marker j — parallelised by SNP markers

- Conditioner may be the inverted diagonal block for country i

$$\mathbf{M}_i = (\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i + \mathbf{G}^{ii})^{-1}$$

the matrix $\mathbf{M}_i$ is also used in reliability calculation.

Calculation of prediction error (co)variances

- Countries need to calculate reliabilities of DGV (sum of all SNP effects)
- Not only reliabilities of MACE SNP effect estimates but also (co)reliabilities between the SNP effect estimates
  - the whole PEC block of 50k x 50k
- Absorbing all the other countries into own SNP effects

$$\mathbf{C}_i = \left(\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i + \mathbf{G}^{ii}\right) - \sum_{j\neq i}\mathbf{G}^{ij}\left(\mathbf{Z}_j'\mathbf{R}_j^{-1}\mathbf{Z}_j + \mathbf{G}^{jj}\right)^{-1}\mathbf{G}^{ji}$$

$$= \left(\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i + \mathrm{g}^{ii}\,\mathbf{I}\right) - \sum_{j\neq i}\mathrm{g}^{ij}\,\mathbf{I}\left(\mathbf{Z}_j'\mathbf{R}_j^{-1}\mathbf{Z}_j + \mathbf{G}^{jj}\right)^{-1}\mathrm{g}^{ji}\,\mathbf{I}$$

$$= \left(\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i + \mathrm{g}^{ii}\,\mathbf{I}\right) - (\mathrm{g}^{ij})^2\sum_{j\neq i}\mathbf{M}_j$$

- Invert the own block matrix $\mathbf{C}_i^{-1}$
- Provide the PEC matrix to countries $\mathbf{C}_i^{-1}$

Three methods for handling different sets of SNP markers

- Method 1: conversion of country SNP effects to a common set
- Method 2: conversion of SNP effects for GBLUP models
- Method 3: direct modelling heterogeneous sets of SNP markers

Method 1: Conversion of country SNP effects to a common set of SNP markers

- SNP effects of national set of SNP markers for *i*-th country: $\mathbf{g}_i^N$
- SNP effects of a common set of SNP markers: $\mathbf{g}_c^N$
- Define DGV of all reference animals with own set of SNP markers:

$$\mathbf{u}_i = \mathbf{Z}_i \mathbf{g}_i^N$$

- A SNP BLUP model is fitted to model the DGV of reference animals:

$$\mathbf{u}_i = \mathbf{Z}_i^c \mathbf{g}_c^N + \xi$$

$$(\mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} \mathbf{Z}_i^c + \sigma_i^{-2} \mathbf{B}_c^{-1}) \mathbf{g}_c^N = \mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} \mathbf{u}_i$$

$$\mathbf{g}_c^N = (\mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} \mathbf{Z}_i^c + \sigma_i^{-2} \mathbf{B}_c^{-1})^{-1} \mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} (\mathbf{Z}_i \mathbf{g}_i^N)$$

- Additional data needed for the conversion

$$\mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} \mathbf{Z}_i \qquad \mathbf{Z}_i^{c\prime} \mathbf{R}_i^{-1} \mathbf{Z}_i^c$$

  in addition to $\mathbf{Z}_i' \mathbf{R}_i^{-1} \mathbf{Z}_i$

- Back conversion of MACE SNP effect estimates to the own SNP set

Method 2: Conversion of country SNP effects for GBLUP models

- Country uses a GBLUP model with its own SNP set
- Assumption: equal GEBV for reference animals with both SNP sets
- For all reference animals: GEBV vector $\mathbf{u}_i^*$
- Genomic relationship matrix for all reference animals is invertible: $\mathbf{G}_{rel}^{-1}$
- Estimate SNP effects of the common set

$$\mathbf{g}_i^c = (1-k)\mathbf{B}_c\mathbf{Z}_i^{c\prime}\mathbf{G}_{rel}^{-1}\mathbf{u}_i^*$$

- Equal genomic relationship matrices

$$(1-k)\mathbf{Z}_i^{c\prime}\mathbf{B}_c\mathbf{Z}_i^c + k\mathbf{A}_i = (1-k)\mathbf{Z}_i{}'\mathbf{B}_i\mathbf{Z}_i + k\mathbf{A}_i$$

Summary

- The SNP MACE model is an efficient tool for utilizing phenotype info of foreign reference animals
  - Particularly useful for new traits with large-scale genotyped cows
- No requirement for direct access to original national genotype and phenotype data
  - Keep the current infra-structure of national evaluation systems
- Parallel computing for efficiently solving the SNP MACE equations
  - No more pedigree relationship matrix, difficult to be parallelized
- Direct modelling different sets of SNP reduces the need for conversion to a common set of SNP markers
- A gain in accuracy of prediction is expected, especially for novel traits

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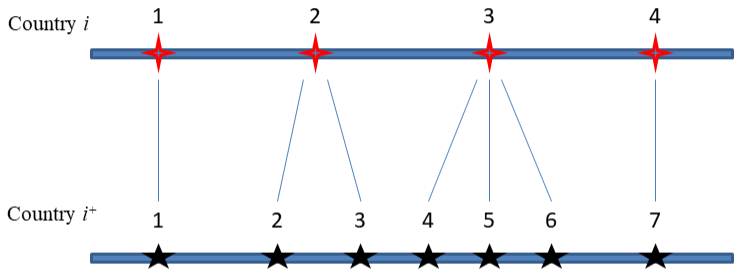
Method 3: Direct modelling of SNP effects of different marker sets

- Cross reference two SNP sets for a country pair (same allele coding)



$$m_i = 4 \quad m_{i^+} = 7$$

- SNP effect covariance matrix

$$\sigma_{i,i^+}\mathbf{B}_{i,i^+} = \sigma_{i,i^+}\sqrt{\theta_i\theta_{i^+}}\mathbf{E}_{i,i^+}$$

$$\mathbf{E}_{i,i^+} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{3} & \frac{1}{3} & \frac{1}{3} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

- Same modelling of **SNP/DGV variances** as in national genomic evaluations
- Correct **covariance of DGV** for any pair of countries
- But **covariances of SNP** are only correct for countries with fewer markers

Considering the SNP array differences

- Modelling SNP effect covariances between countries
  - Country A with more SNPs with unequal SNP covariance: less optimal
  - Country B with fewer SNPs with equal SNP covariance: exact modelling
  - But **DGV covariance** is correct for both countries
- For every one of all country pairs:
  - Set up a SNP cross-reference table
  - Determine the SNP covariances for each country pair
  - In case of a change in SNP arrays in one country, re-do the SNP cross-referencing with all the other countries
- Advantages of the procedure Method 3:
  - Countries do not have to be forced to use the same SNP arrays
  - SNP effects conversion to the common SNP set is not needed
- Disadvantages of Method 3:
  - More work of the SNP MACE, particularly when countries change their SNP sets
  - Approximate inverse of **G** matrix

    Residual covariances to be modelled as the procedure for genetic covariances

Introduction

- Interbull MACE / GMACE evaluation for bulls / genomic bulls
  - Based on national conventional / genomic evaluation
- National genomic evaluation uses MACE EBV of foreign reference bulls
  - Significant increase in accuracy of genomic prediction
  - Fear of domination of foreign reference bulls on own SNP effects
  - Negative impact of genomic pre-selection on conventional EBV of bulls
    - Single-step national evaluation beneficial
- LD info of foreign reference cows NOT used in own SNP effect estimation
  - More countries add cows into national reference population
  - No MACE for cows, exchanging genotype of millions of cows infeasible
- Novel traits have relatively small national reference population
  - MACE bull evaluation perhaps not ready yet
  - Expected to have the largest gain in accuracy of prediction

An example with 2 countries and 3 SNP markers (1)

Data contribution: least squares parts

$$\begin{bmatrix} \varphi_{\mu_1} & \varphi_{\mu_1 s_1} & \varphi_{\mu_1 s_2} & \varphi_{\mu_1 s_3} & 0 & 0 & 0 & 0 \\ \varphi_{\mu_1 s_1} & \varphi_{1\,s_{11}} & \varphi_{1\,s_{12}} & \varphi_{1\,s_{13}} & 0 & & & \\ \varphi_{\mu_1 s_2} & \varphi_{1\,s_{21}} & \varphi_{1\,s_{22}} & \varphi_{1\,s_{23}} & 0 & & & \\ \varphi_{\mu_1 s_3} & \varphi_{1\,s_{31}} & \varphi_{1\,s_{32}} & \varphi_{1\,s_{33}} & 0 & & & \\ 0 & 0 & 0 & 0 & \varphi_{\mu_2} & \varphi_{\mu_2 s_1} & \varphi_{\mu_2 s_2} & \varphi_{\mu_2 s_3} \\ 0 & & & & \varphi_{\mu_2 s_1} & \varphi_{2\,s_{11}} & \varphi_{2\,s_{12}} & \varphi_{2\,s_{13}} \\ 0 & & & & \varphi_{\mu_2 s_2} & \varphi_{2\,s_{21}} & \varphi_{2\,s_{22}} & \varphi_{2\,s_{23}} \\ 0 & & & & \varphi_{\mu_2 s_3} & \varphi_{2\,s_{31}} & \varphi_{2\,s_{32}} & \varphi_{2\,s_{33}} \end{bmatrix} \begin{bmatrix} \hat{\mu}_1 \\ \hat{g}_{1s_1} \\ \hat{g}_{1s_2} \\ \hat{g}_{1s_3} \\ \hat{\mu}_2 \\ \hat{g}_{2s_1} \\ \hat{g}_{2s_2} \\ \hat{g}_{2s_3} \end{bmatrix} = \begin{bmatrix} \Delta_{\mu_1} \\ \Delta_{1s_1} \\ \Delta_{1s_2} \\ \Delta_{1s_3} \\ \Delta_{\mu_2} \\ \Delta_{2s_1} \\ \Delta_{2s_2} \\ \Delta_{2s_3} \end{bmatrix}$$

- Only the products of matrices or vectors are available, not the matrices or vectors themselves

$$\mathbf{Z_i}'\mathbf{R}_i^{-1}\mathbf{Z_i} \rightarrow \{\varphi_{\mathbf{1}\,\boldsymbol{s_{11}}}\}$$

$$\mathbf{Z_i}'\mathbf{R}_i^{-1}\mathbf{y_i} \rightarrow \{\Delta_{\mathbf{2}\,\boldsymbol{s_3}}\}$$

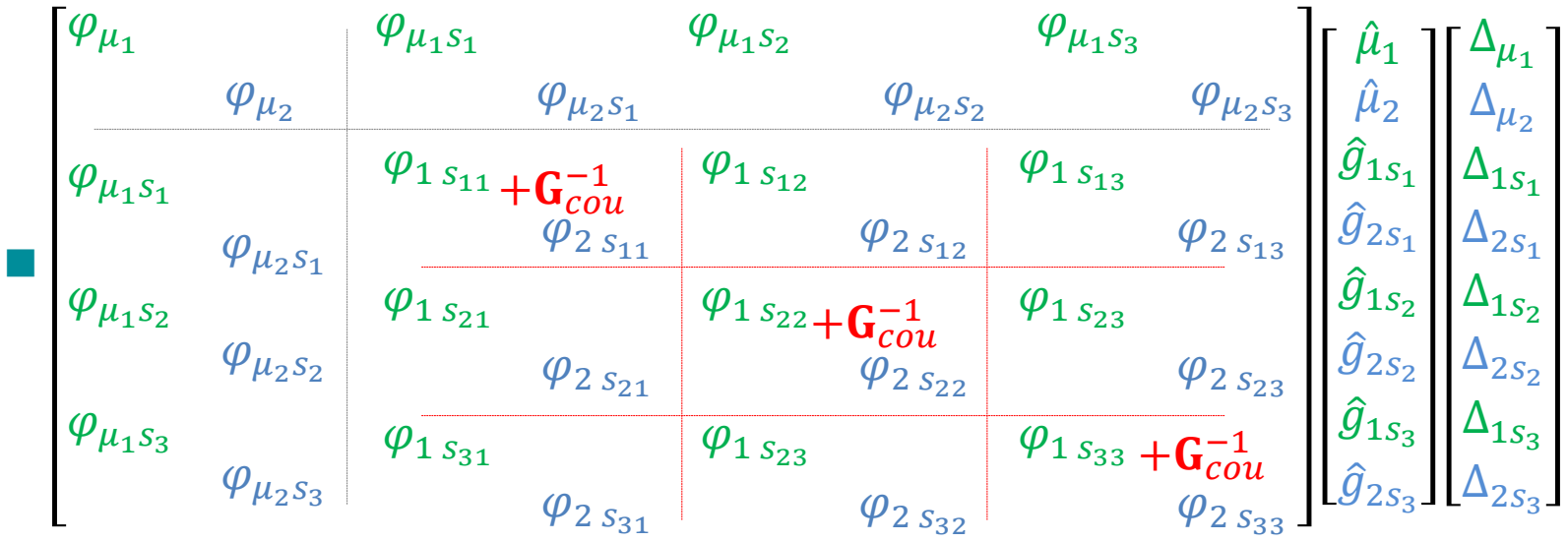
An example with 2 countries and 3 SNP markers (2)

Data contribution: least squares parts + SNP genetic parts

$$\begin{bmatrix} \varphi_{\mu_1} & \varphi_{\mu_1 s_1} & \varphi_{\mu_1 s_2} & \varphi_{\mu_1 s_3} & 0 & 0 & 0 & 0 \\ \varphi_{\mu_1 s_1} & \varphi_{1\,s_{11}} & \varphi_{1\,s_{12}} & \varphi_{1\,s_{13}} & 0 & & & \\ \varphi_{\mu_1 s_2} & \varphi_{1\,s_{21}} & \varphi_{1\,s_{22}} & \varphi_{1\,s_{23}} & 0 & & & \\ \varphi_{\mu_1 s_3} & \varphi_{1\,s_{31}} & \varphi_{1\,s_{32}} & \varphi_{1\,s_{33}} & 0 & & & \\ 0 & 0 & 0 & 0 & \varphi_{\mu_2} & \varphi_{\mu_2 s_1} & \varphi_{\mu_2 s_2} & \varphi_{\mu_2 s_3} \\ 0 & & & & \varphi_{\mu_2 s_1} & \varphi_{2\,s_{11}} & \varphi_{2\,s_{12}} & \varphi_{2\,s_{13}} \\ 0 & & & & \varphi_{\mu_2 s_2} & \varphi_{2\,s_{21}} & \varphi_{2\,s_{22}} & \varphi_{2\,s_{23}} \\ 0 & & & & \varphi_{\mu_2 s_3} & \varphi_{2\,s_{31}} & \varphi_{2\,s_{32}} & \varphi_{2\,s_{33}} \end{bmatrix} + \begin{matrix} g^{11}\mathrm{I} \\ \\ \\ \\ g^{21}\mathrm{I} \\ \\ \\ \\ \end{matrix} + \begin{bmatrix} \hat{\mu}_1 \\ \hat{g}_{1s_1} \\ \hat{g}_{1s_2} \\ \hat{g}_{1s_3} \\ \hat{\mu}_2 \\ \hat{g}_{2s_1} \\ \hat{g}_{2s_2} \\ \hat{g}_{2s_3} \end{bmatrix} \begin{matrix} \\ \\ g^{12}\mathrm{I} \\ \\ \\ \\ g^{22}\mathrm{I} \\ \\ \end{matrix} = \begin{bmatrix} \Delta_{\mu_1} \\ \Delta_{1s_1} \\ \Delta_{1s_2} \\ \Delta_{1s_3} \\ \Delta_{\mu_2} \\ \Delta_{2s_1} \\ \Delta_{2s_2} \\ \Delta_{2s_3} \end{bmatrix}$$

- Order: SNP markers within country (in country-major order)

An example with 2 countries and 3 SNP markers (3)



- Order: countries within SNP marker (in SNP-major order)

$$\mathbf{G}_{cou}^{-1} = \begin{bmatrix} \sigma_1^2\theta_1 & \sigma_{12}\sqrt{\theta_1\theta_2} \\ \sigma_{12}\sqrt{\theta_1\theta_2} & \sigma_2^2\theta_2 \end{bmatrix}^{-1}$$

Why not fitting the residual polygenic effect?

- Needs to know the identifications of reference animals
- Needs to directly access genotypes and phenotypes of reference animals
  - Keep the infra-structure of current national evaluation systems
- In future, millions of cows will be added to ref. pop. worldwide
  - Exchange of genotypes of millions of reference cows may be infeasible
  - Estimating RPG of the millions of cows for all countries is challenging

A SNP MACE model: SNP effect covariances

Country ; SNP marker ; reference animal

- Countries may have different sets of SNP markers

$$\text{var}\begin{bmatrix}\mathbf{g}_1\\ \mathbf{g}_2\\ \vdots\\ \mathbf{g}_c\end{bmatrix} = \begin{bmatrix}\sigma_1^2\mathbf{B}_1 & \sigma_{12}\mathbf{B}_{12} & \cdots & \sigma_{1c}\mathbf{B}_{1c}\\ & \sigma_2^2\mathbf{B}_2 & \cdots & \sigma_{2c}\mathbf{B}_{2c}\\ & & \ddots & \vdots\\ symm. & & & \sigma_c^2\mathbf{B}_c\end{bmatrix} = \mathbf{G}$$

DGV variance of country i, σ_i^2

DGV covariance between countries i and i^+. σ_{ij}

$$\mathbf{B}_{i,i^+} = \frac{1}{\sqrt{\sum_j 2p_{ij}(1-p_{ij})}\sqrt{\sum_j 2p_{i^+j}(1-p_{i^+j})}}\mathbf{I} = \sqrt{\theta_i\theta_{i^+}}\mathbf{I}$$ for same SNP set

$\mathbf{B}_{i,i^+} = \sqrt{\theta_i\theta_{i^+}}\mathbf{E}_{i,i^+}$ is not a squared matrix for two different SNP sets

National data for the SNP MACE evaluation: replacing the deregression step of national bull EBV in MACE

- $$\begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i\mathbf{1} & \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{Z}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{1} & \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i + \sigma_i^{-2}\mathbf{B}_i^{-1} \end{bmatrix} \begin{bmatrix} \hat{\mu}_i \\ \hat{\mathbf{g}}_i^N \end{bmatrix} = \begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \end{bmatrix}$$

- Re-written as:

$$(\boldsymbol{\Psi}_i + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \sigma_i^{-2}\mathbf{B}_i^{-1} \end{bmatrix}) \begin{bmatrix} \hat{\mu}_i \\ \hat{\mathbf{g}}_i^N \end{bmatrix} = \boldsymbol{\Delta}_i$$

- Least-square part of the LHS of MME:

$$\boldsymbol{\Psi}_i = \begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i\mathbf{1} & \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{Z}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{1} & \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i \end{bmatrix}$$

- Right-hand-side of the MME:

$$\boldsymbol{\Delta}_i = \begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \end{bmatrix}$$

Mixed model equations of the SNP MACE model

$$\begin{bmatrix} \ddots & & \cdots & & \cdots \\ & \begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i\mathbf{1} & \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{Z}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{1} & \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{ii} \end{bmatrix} & \cdots & \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{\Psi}_{ii^+} \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{ii^+} \end{bmatrix} & \\ \vdots & \cdots & \ddots & \vdots & \\ & \begin{bmatrix} \mathbf{1}'\mathbf{Z}_{i^+}'\mathbf{R}_{i^+}^{-1}\mathbf{Z}_{i^+}\mathbf{1} & \mathbf{1}'\mathbf{R}_{i^+}^{-1}\mathbf{Z}_{i^+} \\ \mathbf{Z}_{i^+}'\mathbf{R}_{i^+}^{-1}\mathbf{1} & \mathbf{Z}_{i^+}'\mathbf{R}_{i^+}^{-1}\mathbf{Z}_{i^+} \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{i^+i^+} \end{bmatrix} & \cdots & \ddots \end{bmatrix}$$

$$\mathrm{X}\begin{bmatrix} \cdots \\ \begin{bmatrix} \hat{\mu}_i \\ \hat{\mathbf{g}}_i \end{bmatrix} \\ \vdots \\ \begin{bmatrix} \hat{\mu}_{i^+} \\ \hat{\mathbf{g}}_{i^+} \end{bmatrix} \\ \cdots \end{bmatrix} = \begin{bmatrix} \cdots \\ \begin{bmatrix} \mathbf{1}'\mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \end{bmatrix} \\ \vdots \\ \begin{bmatrix} \mathbf{1}'\mathbf{Z}_{i^+}'\mathbf{R}_{i^+}^{-1}\mathbf{y}_{i^+} \\ \mathbf{Z}_{i^+}'\mathbf{R}_{i^+}^{-1}\mathbf{y}_{i^+} \end{bmatrix} \\ \cdots \end{bmatrix}$$

Residual covariance: $\boldsymbol{\Psi}_{ii^+} = (\mathbf{Z}_i'\mathbf{R}_i^{-\frac{1}{2}})(\mathbf{R}_{i^+}^{-\frac{1}{2}}\mathbf{Z}_{i^+})$

$\boldsymbol{\Psi}_{ii^+} = 0$ when countries use only national phenotypes for SNP effect estimation

Mixed model equations of the SNP MACE model (mu)

$$\begin{bmatrix} \ddots & & \cdots & & \cdots & \\ & \begin{bmatrix} \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{1} & \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{Z}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{1} & \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{Z}_i \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{ii} \end{bmatrix} & \cdots & \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{\Psi}_{ii'} \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{ii'} \end{bmatrix} & \cdots \\ \vdots & & \ddots & & \vdots & \\ & & & \begin{bmatrix} \mathbf{1}'\mathbf{R}_{i'}^{-1}\mathbf{1} & \mathbf{1}'\mathbf{R}_{i'}^{-1}\mathbf{Z}_{i'} \\ \mathbf{Z}_{i'}'\mathbf{R}_{i'}^{-1}\mathbf{1} & \mathbf{Z}_{i'}'\mathbf{R}_{i'}^{-1}\mathbf{Z}_{i'} \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{i'i'} \end{bmatrix} & \vdots \\ & & & & & \ddots \end{bmatrix}$$

$$\mathbf{X}\begin{bmatrix} \cdots \\ \begin{bmatrix} \hat{\mu}_i \\ \hat{\mathbf{g}}_i \end{bmatrix} \\ \vdots \\ \begin{bmatrix} \hat{\mu}_{i+} \\ \hat{\mathbf{g}}_{i+} \end{bmatrix} \\ \cdots \end{bmatrix} = \begin{bmatrix} \cdots \\ \begin{bmatrix} \mathbf{1}'\mathbf{R}_i^{-1}\mathbf{y}_i \\ \mathbf{Z}_i'\mathbf{R}_i^{-1}\mathbf{y}_i \end{bmatrix} \\ \vdots \\ \begin{bmatrix} \mathbf{1}'\mathbf{R}_{i+}^{-1}\mathbf{y}_{i+} \\ \mathbf{Z}_{i+}'\mathbf{R}_{i+}^{-1}\mathbf{y}_{i+} \end{bmatrix} \\ \cdots \end{bmatrix}$$

Method 2: Conversion of country SNP effects using the genomic relationship matrix: DGV

- Country uses a SNP BLUP model with its own SNP set
- Assumption: equal DGV for reference animals with both SNP sets
- DGV genomic relationship matrix for all reference animals is invertible:

$$\mathbf{G}^{-1}_{rel\_c} = (\mathbf{Z}_i^{c\prime}\mathbf{B}_c\mathbf{Z}_i^c)^{-1} = (\mathbf{Z}_i'\mathbf{B}_i\mathbf{Z}_i)^{-1} = \mathbf{G}^{-1}_{rel\_i}$$

- SNP marker cross-referencing (7 own SNPs, 4 common SNPs)

$$\mathbf{B}_{c,i} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

- SNP effects converted to the common set:

$$\mathbf{g}_i^c = \mathbf{B}_{c,i}\mathbf{Z}_i'\mathbf{G}^{-1}_{rel\_i}(\mathbf{Z}_i\mathbf{g}_i)$$

- Back conversion of MACE SNP effects to own SNP set:

$$\mathbf{g}_i = \mathbf{B}_{c,i}'\mathbf{Z}_c'\mathbf{G}^{-1}_{rel\_c}(\mathbf{Z}_c\mathbf{g}_i^c)$$