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Alternative single-step type genomic prediction equations

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Partitioning Genetic (Co)variances

⇒ General Model for Genomic Prediction

- **Two sources of genetic (co)variances**
 1. **Explained by genomic differences** between animals
 - Currently SNP based
 - But can also be known QTLs, major gene effects or copy-number variant (CNV) based effects
 2. **Explained by pedigree** ⇒ polygenic “residual”
- **Logical choice**
 - **Random mixed inheritance model**
 - Jointly modelling and estimating:
 - SNP (or similar) effects and
 - residual polygenic effects

General Model

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u}^* + \mathbf{e} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} + \mathbf{Z}\mathbf{Q}\mathbf{g} + \mathbf{e}$$

- Expectation and variances

$$\mathbf{E} \begin{pmatrix} \mathbf{g} \\ \mathbf{u} \\ \mathbf{u}^* \\ \mathbf{e} \end{pmatrix} = \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix} \quad \text{and} \quad \text{Var} \begin{pmatrix} \mathbf{g} \\ \mathbf{u} \\ \mathbf{u}^* \\ \mathbf{e} \end{pmatrix} = \begin{pmatrix} \mathbf{D} & \mathbf{0} & \mathbf{D}\mathbf{Q}' & \mathbf{0} \\ \mathbf{0} & \mathbf{G} & \mathbf{G} & \mathbf{0} \\ \mathbf{Q}\mathbf{D} & \mathbf{G} & \mathbf{G}^* & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{R} \end{pmatrix}$$

$$\text{with } \mathbf{G}^* = \mathbf{G} + \mathbf{Q}\mathbf{D}\mathbf{Q}' = \mathbf{G} + \mathbf{F}$$

- Remarks:

- \mathbf{G} , \mathbf{Q} and \mathbf{D} can have whatever structure needed
- \mathbf{G} always function of \mathbf{A} (pedigree based relationship) and polygenic (co)variances \mathbf{G}_0 (e.g., $\mathbf{G} = \mathbf{A} \otimes \mathbf{G}_0$)
- \mathbf{u}^* , \mathbf{G}^* where “*” indicates linked to polygenic **AND** SNP effects
- \mathbf{F} strictly genomic (co)variance structure

Traditional MME for

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u}^* + \mathbf{e} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} + \mathbf{Z}\mathbf{Q}\mathbf{g} + \mathbf{e}$$

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{*-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix} \quad (1)$$



$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z}\mathbf{Q} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{-1} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z}\mathbf{Q} \\ \mathbf{Q}'\mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Q}'\mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{Q}'\mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z}\mathbf{Q} + \mathbf{D}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}} \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Q}'\mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix} \quad (2)$$

Traditional MME for

$$y = X\beta + Zu^* + e = X\beta + Zu + ZQg + e$$

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{*-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix} \quad (1)$$



$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & X'R^{-1}ZQ \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & Z'R^{-1}ZQ \\ Q'Z'R^{-1}X & Q'Z'R^{-1}Z & Q'Z'R^{-1}ZQ + D^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \\ Q'Z'R^{-1}y \end{bmatrix} \quad (2)$$

Simpler MME?

Traditional MME for

$$y = X\beta + Zu^* + e = X\beta + Zu + ZQg + e$$

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{*-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix} \quad (1)$$



$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & X'R^{-1}ZQ \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & Z'R^{-1}ZQ \\ Q'Z'R^{-1}X & Q'Z'R^{-1}Z & Q'Z'R^{-1}ZQ + D^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \\ Q'Z'R^{-1}y \end{bmatrix} \quad (2)$$

Simpler MME? \Rightarrow Similarity to Genetic Groups!

Alternative MME based on Quaas-Pollack Transformation

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & 0 \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & -G^{-1}Q \\ 0 & -Q'G^{-1} & Q'G^{-1}Q + D^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \\ 0 \end{bmatrix} \quad (3)$$

- Please note **three advantages**:

1. Inverted **G** here based on inverted **A**, no genomic relationships!

⇒ **Major advantage, usual method to set-up A^{-1}**

2. Explicit equations for estimation of SNP effects (**g**)

⇒ **Major advantage of multi-step genomic prediction (MS-GP)**

3. Direct estimation of \hat{u}^*

⇒ **Major advantage of single-step genomic prediction (SS-GP)**

General MME based on Quaas-Pollack Transformation

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{-1} & -\mathbf{G}^{-1}\mathbf{Q} \\ \mathbf{0} & -\mathbf{Q}'\mathbf{G}^{-1} & \mathbf{Q}'\mathbf{G}^{-1}\mathbf{Q} + \mathbf{D}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Identification Of Two Blocks in Transformed MME – 1st Block

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & 0 \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & -G^{-1}Q \\ 0 & -Q'G^{-1} & Q'G^{-1}Q + D^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \\ 0 \end{bmatrix}$$



$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y + G^{-1}Q\hat{g} \end{bmatrix}$$

Identification Of Two Blocks in Transformed MME – 2nd Block

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & 0 \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & -G^{-1}Q \\ 0 & -Q'G^{-1} & Q'G^{-1}Q + D^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \\ 0 \end{bmatrix}$$



$$\left[Q'G^{-1}Q + D^{-1} \right] \hat{g} = Q'G^{-1}\hat{u}^*$$

Practical Considerations

- In practice **not all animals genotyped**
 - Non-genotyped animals = “1”
 - Genotyped animals = “2”
- Definition of **direct SNP contribution to GEBV (dGV)**
 - For genotyped animals:

$$\hat{\mathbf{d}}_2 = \mathbf{Q}_2 \hat{\mathbf{g}}$$

- For non-genotyped animals predicted from dGV of genotyped animals using selection index theory:

$$\hat{\mathbf{d}}_1 = \mathbf{G}_{12} \mathbf{G}_{22}^{-1} \hat{\mathbf{d}}_2 = \mathbf{G}_{12} \mathbf{G}_{22}^{-1} \mathbf{Q}_2 \hat{\mathbf{g}}$$

$$\mathbf{Q}_1 = \mathbf{G}_{12} \mathbf{G}_{22}^{-1} \mathbf{Q}_2$$

Not All Animals Are Genotyped (System II: “SNP” System)

$$\left[\mathbf{Q}' \mathbf{G}^{-1} \mathbf{Q} + \mathbf{D}^{-1} \right] \hat{\mathbf{g}} = \mathbf{Q}' \mathbf{G}^{-1} \hat{\mathbf{u}}^*$$

$$\mathbf{G}^{-1} = \begin{bmatrix} \mathbf{G}^{11} & \mathbf{G}^{12} \\ \mathbf{G}^{21} & \mathbf{G}^{22} \end{bmatrix}$$



$$\mathbf{Q} = \begin{bmatrix} \mathbf{G}_{12} & \mathbf{G}_{22}^{-1} \\ \mathbf{I} & \end{bmatrix} \mathbf{Q}_2 = \begin{bmatrix} -(\mathbf{G}^{11})^{-1} \mathbf{G}^{12} \\ \mathbf{I} \end{bmatrix} \mathbf{Q}_2$$

$$\left[\mathbf{Q}_2' \mathbf{G}_{22}^{-1} \mathbf{Q}_2 + \mathbf{D}^{-1} \right] \hat{\mathbf{g}} = \mathbf{Q}_2' \mathbf{G}_{22}^{-1} \hat{\mathbf{u}}_2^*$$

NB: 1 = non-genotyped, 2 = genotyped animals

Not All Animals Are Genotyped (System I: “BLUP” System)

- First assume only genotyped animals have records

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}_2^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} + \mathbf{G}_{22}^{-1}\mathbf{Q}_2\hat{\mathbf{g}} \end{bmatrix}$$

- Recovering genetic (co)variance not explained by strictly polygenic effect by assuming proportionality between polygenic and total (co)variance:

$$\mathbf{G} = \phi\mathbf{T} \text{ then } \mathbf{G}^{-1} = \frac{1}{\phi}\mathbf{T}^{-1}$$

- Predicting animals without genotypes $\hat{\mathbf{u}}_1^* = \mathbf{T}_{12}\mathbf{T}_{22}^{-1}\hat{\mathbf{u}}_2^*$

Further Modification “BLUP” System

- Introducing T_{22}^{-1}

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + T_{22}^{-1} + G_{22}^{-1} - T_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}_2^* \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y + G_{22}^{-1}Q_2\hat{g} \end{bmatrix}$$

- Predicting animals without genotypes inside MME (Henderson, 1976)
- Lifting restriction on records only for animals 2

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + \begin{bmatrix} T^{11} & T^{12} \\ T^{21} & T^{22} \end{bmatrix} + G_{22}^{-1} - T_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}_1^* \\ \hat{u}_2^* \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y + \begin{bmatrix} 0 \\ G_{22}^{-1}Q_2\hat{g} \end{bmatrix} \end{bmatrix}$$

Further Modification “BLUP” System

- Using again $\mathbf{G}^{-1} = \frac{1}{\phi} \mathbf{T}^{-1}$, following MME are derived

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}_1^* \\ \hat{u}_2^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} + \begin{bmatrix} 0 \\ \frac{1}{\phi} \mathbf{T}_{22}^{-1} \mathbf{Q}_2 \hat{\mathbf{g}} \end{bmatrix} \end{bmatrix}$$

- Please note similarity to **Bayesian procedures to integrate external information into genetic evaluations** (Vandenplas and Gengler, 2012)

Reassembling Systems I and II

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{0} \end{bmatrix} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} \\ -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} & \mathbf{Q}_2'\mathbf{T}_{22}^{-1} \end{bmatrix} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Reassembling Systems I and II

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1}\mathbf{Q}_2 \end{bmatrix} \\ \mathbf{0} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} & \mathbf{Q}_2'\mathbf{T}_{22}^{-1} \end{bmatrix} & \frac{1}{\phi} (\mathbf{Q}_2'\mathbf{T}_{22}^{-1}\mathbf{Q}_2 + \phi\mathbf{D}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Alternative MME using **strictly** genomic (co)variances \mathbf{F}

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \mathbf{0} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} & \mathbf{T}_{22}^{-1} \end{bmatrix} & \frac{1}{\phi} (\mathbf{T}_{22}^{-1} + \phi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Equivalence with Single-Step MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\varphi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} & -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \mathbf{0} & -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} & \mathbf{T}_{22}^{-1} \end{bmatrix} & \frac{1}{\varphi} (\mathbf{T}_{22}^{-1} + \varphi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix} \quad (3)$$



$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + (\varphi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \end{bmatrix} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix} \quad (4)$$

Equivalence derived from:

1. Absorb equations for \mathbf{d} into those for \mathbf{u}^*
2. Apply rules inverse of sum of matrices:

$$(\varphi\mathbf{T}_{22} + \mathbf{F})^{-1} = \frac{1}{\varphi} \mathbf{T}_{22}^{-1} - \frac{1}{\varphi} \mathbf{T}_{22}^{-1} (\mathbf{T}_{22}^{-1} + \varphi\mathbf{F}^{-1})^{-1} \mathbf{T}_{22}^{-1}$$

Polygenic and Genomic (Co)Variances

$$\begin{bmatrix}
 \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & & & \\
 \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} & + \begin{bmatrix} \mathbf{T}^{11} & & \\ & \mathbf{T}^{22} & + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \\ & & \end{bmatrix} & \\
 \mathbf{0} & & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} & \mathbf{T}_{22}^{-1} \end{bmatrix} & \\
 & & & \frac{1}{\phi} (\mathbf{T}_{22}^{-1} + \phi\mathbf{F}^{-1})
 \end{bmatrix}
 \begin{bmatrix}
 \hat{\beta} \\
 \hat{\mathbf{u}}^* \\
 \hat{\mathbf{d}}_2
 \end{bmatrix}
 =
 \begin{bmatrix}
 \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\
 \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\
 \mathbf{0}
 \end{bmatrix}$$



$$\begin{bmatrix}
 \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & & & \\
 \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} & + \begin{bmatrix} \mathbf{T}^{11} & & \\ & \mathbf{T}^{22} & + (\phi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \\ & & \end{bmatrix} & \\
 & & & \\
 & & &
 \end{bmatrix}
 \begin{bmatrix}
 \hat{\beta} \\
 \hat{\mathbf{u}}^*
 \end{bmatrix}
 =
 \begin{bmatrix}
 \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\
 \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y}
 \end{bmatrix}$$

Polygenic and Genomic (Co)Variances

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\varphi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} & -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \mathbf{0} & -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} & \mathbf{T}_{22}^{-1} \end{bmatrix} & \frac{1}{\varphi} (\mathbf{T}_{22}^{-1} + \varphi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Often called genomic (co)variance matrix
(infact combined one with implicit weights)

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + (\varphi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \end{bmatrix} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix}$$

Polygenic and Genomic (Co)Variances

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{0} \end{bmatrix} \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \\ -\frac{1}{\phi}[\mathbf{0} & \mathbf{T}_{22}^{-1}] \end{bmatrix} \begin{bmatrix} \mathbf{0} \\ -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \frac{1}{\phi}(\mathbf{T}_{22}^{-1} + \phi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Definition of polygenic “residual” as part of total genetic (co)variance \mathbf{T}

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} \end{bmatrix} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + (\phi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix}$$

Polygenic and Genomic (Co)Variances

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{0} \end{bmatrix} \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\varphi} - 1\right)\mathbf{T}_{22}^{-1} \\ -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} & \mathbf{T}_{22}^{-1} \end{bmatrix} \end{bmatrix} \begin{bmatrix} \mathbf{0} \\ -\frac{1}{\varphi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \frac{1}{\varphi} (\mathbf{T}_{22}^{-1} + \varphi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

F represents strictly genomic (co)variance matrix

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \end{bmatrix} \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + (\varphi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix}$$

Polygenic and Genomic (Co)Variances

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{0} \end{bmatrix} \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \\ -\frac{1}{\phi}[\mathbf{0} & \mathbf{T}_{22}^{-1}] \end{bmatrix} \begin{bmatrix} \mathbf{0} \\ -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1} \end{bmatrix} \\ \frac{1}{\phi}(\mathbf{T}_{22}^{-1} + \phi\mathbf{F}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{d}}_2 \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

Weight here defined as constant across all traits, however equations can be modified to allow different weights across traits

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} \\ \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \end{bmatrix} \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + (\phi\mathbf{T}_{22} + \mathbf{F})^{-1} - \mathbf{T}_{22}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \end{bmatrix}$$

Most Useful MME \Leftrightarrow No F^{-1} Needed

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \begin{bmatrix} \mathbf{T}^{11} & \mathbf{T}^{12} \\ \mathbf{T}^{21} & \mathbf{T}^{22} + \left(\frac{1}{\phi} - 1\right)\mathbf{T}_{22}^{-1} \end{bmatrix} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} \\ \mathbf{T}_{22}^{-1}\mathbf{Q}_2 \end{bmatrix} \\ \mathbf{0} & -\frac{1}{\phi} \begin{bmatrix} \mathbf{0} & \mathbf{Q}_2' \mathbf{T}_{22}^{-1} \end{bmatrix} & \frac{1}{\phi} (\mathbf{Q}_2' \mathbf{T}_{22}^{-1} \mathbf{Q}_2 + \phi \mathbf{D}^{-1}) \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

- **Alternative Single Step Genomic Prediction (SS-GP)**
 - Allows combining advantages of SS-GP and MS-GP
- **Different implementations, other advantages**
 - Setting-up as one systems (cf. above) \Rightarrow direct solving
 - Setting-up two systems as seen before, some advantages:
 - Solving through parallel systems by updating RHS periodically
 - Alternative “SNP” Systems possible \Rightarrow alternative models, solvers
 - Excluding some u^* (e.g., preferentially treated cows), adding other u^* (e.g., external (G)EBV for external animals)

Conclusions

- **Developed alternative genomic prediction equations have many advantages:**
 - Explicit weighting of genomic (SNP) and polygenic effects
 - Direct estimation of SNP effects
 - Better use of High-Density SNP panels
 - Other genetic effects (e.g. CNV) can be accommodated
 - Direct estimation of GEBV effects
 - Genomic relationship matrix never explicitly formed, stored or inverted
 - Implementation straight-forward
 - Based on use of existing software
 - System I and System II can run in parallel (updating of RHS)
- **But additional research required:**
 - Especially to test and validate proposed method for large data sets

Final Remarks

- **General consensus**

- Single-step methods combine all sources of information into accurate rankings for animals with and without genotypes
- Especially adapted for novel traits (e.g., **milk fat composition**) and more complex models (e.g., **multitrait, random regression model**)
- With increasing number of genotyped animals equivalent models not requiring inverting genomic relationship matrix

- **Therefore currently different research efforts**

- To get these equivalent models

- **This development complementary approach because**

- Not based on (matrix of) relationship differences
- But on partitioning of genetic (co)variances
- However **still inverse of A_{22} needed** \Leftrightarrow **New methods** (Faux et al. 2012)

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