Combination of genotype, pedigree, local and foreign information

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Introduction

- ✓ For genomic prediction
  - To get reliable GEBV use of multiple sources needed
- ✓ Traditional traits (*i.e.*, in dairy cattle)
  - Local genomic evaluations ← MACE
- ✓ Novel traits (e.g., milk quality, feed efficiency, methane)
  - Combining different sources of often locally sparse phenotypic data even more needed

→ Adapting strategies to use multiple sources

Aims

- ✓ To develop strategies to use simultaneously:
  - Genotypes,
  - Pedigree,
  - Local phenotypes and,
  - Foreign phenotypes
- ✓ By combining and adapting:
  - Single-step genomic evaluations (**ssGBLUP**) and,
  - Bayesian procedure to integrate external information*

*Vandenplas, J., & Gengler, N. (2012). *J. Dairy Sci. 95*: 1513-1526

Aims

- ✓ To develop strategies to use simultaneously:
  - Genotypes,
  - Pedigree,
  - Phenotypes from multiple sources

→ **ssGBAYES**

ssGBLUP

- ✓Single-step genomic evaluation (ssGBLUP)
  - Allows direct combination of genomic, pedigree and phenotypic information
- ✓However: current limitation
  - Only available local phenotypic records can be used

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- ✓However: current limitation
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➔ In opposition to multi-step methods
(e.g., use of local-EBV and MACE-EBV in prediction equation step)

ssGBLUP

- ✓Single-step genomic evaluation (ssGBLUP)
  - Allows direct combination of genomic, pedigree and phenotypic information
- ✓However: current limitation
  - Only available local phenotypic records can be used
- ✓Reason for this limitation
  - Local ssGBLUP based on modified system of mixed model equations (**MME**)

Modified MME

- ✓ssGBLUP

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

- $\mathbf{G}^{*-1} = \mathbf{H}^{-1} \otimes \mathbf{G}_0^{-1}$: inverse of combined genomic-pedigree based (co)variances matrix
- $\mathbf{y}_L$: vector of local phenotypes
- $\hat{\boldsymbol{\beta}}_L^*$: vector of estimated local fixed effects
- $\hat{\mathbf{u}}_L^*$: vector of estimated local GEBV
- $\mathbf{p}(\mathbf{u}_L^*) = MVN(\mathbf{0}, \mathbf{G}^{*-1})$

Alternative

- ✓As alternative to introduce phenotypes
  - ❑ Also allowing for foreign information
- ✓However avoiding double counting
  - ❑ E.g. MACE-EBV contain our phenotypes
- ✓Also avoiding deregression
  - ❑ Potential source of trouble
- ✓Be simple and flexible
  - ❑ Allowing to extend to multiple sources

Concept of "Hybrid" ssGBLUP

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

$$\left(G^{*-1} + \Lambda_L\right)\hat{u}_L^* = D_L^{-1}\hat{u}_L$$

➔ More details later

Bayesian priors

- ✓Assumption: *a priori* known information on $\hat{u}_L^*$

  ➔ y_L replaced by $\hat{u}_L$ and D_L

  - ❑ Source of phenotypic information
    - ➢ Vector of local EBV: $\hat{u}_L$ ← "external"* information
    - ➢ Prediction error (co)variances matrix: D_L
- ✓Allows use of simplified models
  - ❑ *E.g.,* Test-day model ➔ lactation EBV

* "external" = outside of original system of MME

"Hybrid" ssGBLUP ⇨ ssGBAYES

- ✓Using only local information as source

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

$$\left(G^{*-1} + \Lambda_L\right)\hat{u}_L^* = D_L^{-1}\hat{u}_L$$

Least square part of LHS of hypothetical BLUP generating local information

RHS of hypothetical BLUP generating local information

Bayesian priors

✓ Assumption: *a priori* known information on $\hat{\mathbf{u}}_L^*$
- Extended to 2 sources of phenotypic information
  - Vector of local EBV: $\hat{\mathbf{u}}_L$ ← 1st "external"* information
    Vector of foreign EBV: $\hat{\mathbf{u}}_F$ ← 2nd "external"* information
  - Prediction error (co)variances matrices: $\mathbf{D}_L$, $\mathbf{D}_F$

- Issue: only available for some animals

➔ $\hat{\mathbf{u}}_L$, $\hat{\mathbf{u}}_F$, $\mathbf{D}_L$ and $\mathbf{D}_F$: (partially) unknown

* "external" = outside of original system of MME

Methods

✓ For both sources: estimation of $\hat{\mathbf{u}}_i$ (i=L,F)
- Available
  - EBV of some animals (so-called "external" $\hat{\mathbf{u}}_{i_E}$)
- "Internal" animals: prediction of EBV ($\hat{\mathbf{u}}_{i_I}$)

$$p\left(\hat{\mathbf{u}}_{i_I} \middle| \hat{\mathbf{u}}_{i_E}\right) = MVN\left(\mathbf{G}_{i_{IE}}\mathbf{G}_{i_{EE}}^{-1}\hat{\mathbf{u}}_{i_E}, \left(\mathbf{G}^{i_{II}}\right)^{-1}\right)$$

$\mathbf{G} = \mathbf{A} \otimes \mathbf{G}_0$: genetic (co)variances matrix

- $\hat{\mathbf{u}}_i = \left[\hat{\mathbf{u}}_{i_E}' \quad \hat{\mathbf{u}}_{i_I}'\right]'$

➔ Correct propagation of information

Methods

✓ For both sources: estimation of $\mathbf{D}_i$ (i=L,F)

$$\mathbf{D}_i = \mathbf{G}^{-1} + \mathbf{\Lambda}_i$$

$$\mathbf{\Lambda}_i = block\ diag\left(\mathbf{\Delta}_j \mathbf{R}_0^{-1} \mathbf{\Delta}_j\right); j = 1,\ldots,n \text{ animals}$$

$$\begin{cases} \text{For external animals}: \mathbf{\Delta}_j = diag\left(\sqrt{RE_k}\right); k = 1,\ldots,t \text{ traits} \\ \text{For internal animals}: \mathbf{\Delta}_j = \mathbf{0} \end{cases}$$

➔ All matrices $\mathbf{\Lambda}_i$ depend only on contributions due to own records

Issue

✓ Non-Independence of information sources
- E.g., Local information included in MACE-EBV

$$\mathbf{D}_{Ff}^{-1}\hat{\mathbf{u}}_{Ff} = \mathbf{D}_F^{-1}\hat{\mathbf{u}}_F - \mathbf{D}_{Lc}^{-1}\hat{\mathbf{u}}_{Lc}$$

Vector of foreign EBV free of local information

Vector of foreign EBV

Vector of local EBV contributing to foreign information

➔ Estimation of external information free from local information

Methods

✓ Combination of genotype, pedigree, local and foreign information (ssGBayes)

$$\left(G^{*-1} + \Lambda_L + \Lambda_F - \Lambda_{Lc}\right)\hat{u}_L^* = D_L^{-1}\hat{u}_L + D_F^{-1}\hat{u}_F - D_{Lc}^{-1}\hat{u}_{Lc}$$

- Λ_L: Least square part of LHS of hypothetical BLUP of local information
- $\Lambda_F - \Lambda_{Lc}$: Least square part of LHS of hypothetical BLUP of foreign information free of local information
- $D_L^{-1}\hat{u}_L$: RHS of hypothetical BLUP of local information
- $D_F^{-1}\hat{u}_F - D_{Lc}^{-1}\hat{u}_{Lc}$: RHS of hypothetical BLUP of foreign information free of local information

➔ No double counting of contributions

Example : Walloon genomic evaluation

✓ ssGBAYES results for milk yield
- But already used for all INTERBULL traits

✓ 1,909 genotyped Holstein bulls and cows

✓ 16,234 animals (genotyped and ancestors)
- 12,046 animals with Walloon EBV (EBV_W)
- 1,981 bulls with MACE EBV (EBV_M)
- 601 bulls with Walloon EBV contributing to MACE (EBV_{Wc})

✓ Reliabilities (REL) for GEBV obtained through inversion of left-hand side

Results

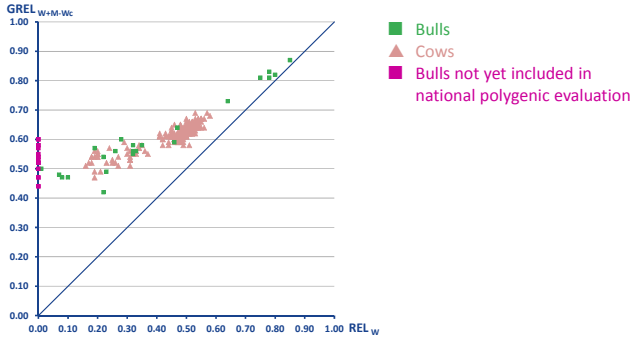
✓ Averaged REL (SD) associated to EBV_W, $GEBV_W$ and $GEBV_{W+M-Wc}$ for genotyped bulls for milk yield

Class of REL_W	N	EBV_W [1]	No. of publishable bulls	$GEBV_W$ [2]	No. of publishable bulls	$GEBV_{W+M-Wc}$ [3]	No. of publishable bulls
< 0.50	647	0.25 (0.12)	0	0.44 (0.09)	194	0.80 (0.09)	628
0.50 – 0.74	173	0.63 (0.07)	173	0.69 (0.06)	173	0.87 (0.05)	173
≥ 0.75	390	0.90 (0.07)	390	0.91 (0.06)	390	0.94 (0.04)	390

[1] REL obtained from Walloon polygenic evaluation
[2] REL obtained from Walloon genomic evaluation using only EBV_W
[3] REL obtained from Walloon genomic evaluation using EBV_W, EBV_M and EBV_{Wc}

Results

✓ Increase of REL for genotyped animals without MACE results and sired by genotyped bulls with MACE results



Conclusions

✓Applied to Walloon dairy genomic evaluations

- Bayesian approach integrates well MACE results into ssGBLUP

➔Recovers large amount of phenotypic information

- More accurate predictions for genotyped animals and their progeny

➔Correct propagation of all available information

General notation

✓Combining "s" sources of information

$$\left(G^{*-1} + \sum_{i=1,s} \Lambda_i\right) \hat{u}_C^* = \sum_{i=1,s} D_i^{-1} \hat{u}_i$$

Least square part of LHS of hypothetical BLUP for information source i

RHS of hypothetical BLUP for information source i

➔ Potential to improve current genomic prediction strategies

Further implications ssGBayes

✓No deregression

- Direct use of EBV from multiple sources

✓Applicable to multi-trait models

- *E.g.,* external information for correlated and/or predictor traits

✓Open general framework, can be modified to accomodate latest genomic models, *e.g.:*

- GWAS models based on ssGBLUP
- SNP based single-step models

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