Genomic predictability of single-step GBLUP for production traits in US Holstein

Y. Masuda[1], P. M. VanRaden[2], H. L. Bradford[2], A. Legarra[3], I. Misztal[1], and T. J. Lawlor[4]

1 University of Georgia, USA; 2 AGIL, USDA, USA;
3 INRA, France; 4 Holstein Association USA, Inc., USA

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Background

- Genomic prediction with single-step GBLUP (ssGBLUP)
  - Genotyped + non-genotyped animals
  - Accountability for pre-selection
  - APY: dimensionality reduction in marker genotypes
- Required: compatibility among relationship matrices

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1} \end{bmatrix}$$

  - Reasonable in complete pedigree
  - Missing pedigree: adjustment of $\mathbf{A}_{22}^{-1}$ by ω
  - How to use unknown parent groups (UPG)?

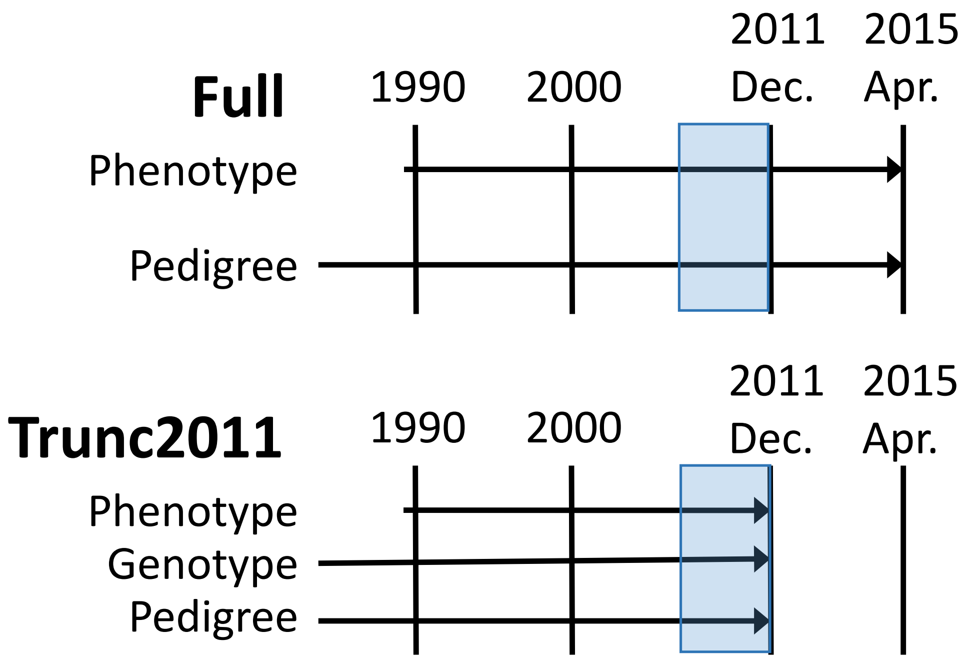
Objectives

- To validate genomic predictions for young bulls by different configurations of UPG in US Holstein
- To discuss possible modifications on $\mathbf{H}^{-1}$ to handle UPG in ssGBLUP: a simulation study

Full data in Holstein

	Description	Number of records/animals
Phenotype	Milk, fat, and protein yield (305-d basis) for US Holstein cows recorded between Jan. 1990 and Apr. 2015	37,259,427
	Cows with phenotype(s)	15,891,366
Pedigree	Animals born in Apr. 2015 or earlier (3-gen. back from phenotyped cows) **185 UPGs**	22,963,255
Genotype	Animals born in Apr. 2015 or earlier (60,671 markers)	764,029

Validation study



For Daughter Yield Deviation (DYD2015)

For GPTA using ssGBLUP (GPTA2011)

Validation Bulls:
Genotyped young bulls with no tested daughters in 2011 but with at least 50 tested daughters in 2015 (N=3,797)

$$DYD2015 = b_1 \times GPTA2011 + b_0$$

- R^2 : validation reliability
- Slope (b_1): Inflation of prediction

Different UPG in $\mathbf{H}^{-1}$

1. Weight (ω) on $\mathbf{A}_{22}^{-1}$: **0.9** or **1.0**
2. UPG: **pedigree + genomic UPG** **(genomic UPG)**, **pedigree UPG only** **(pedigree UPG)**, **or no UPG**

$$\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1} & 0 \\ 0 & 0 & 0 \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -(\mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1})\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'(\mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1}) & \mathbf{Q}_2'(\mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1})\mathbf{Q}_2 \end{bmatrix}$$

DYD2015 vs GPTA2011 (Protein)

Data				R2	b1
Official GPTA 2011				0.51	0.81

Data	UPG	ω=0.9 R2	b1	ω=1.0 R2	b1
GPTA2011	Genomic UPG	0.39	0.74	0.32	0.51

DYD2015 vs GPTA2011 (Protein)

Data				**R2**	**b1**
Official GPTA 2011				0.51	0.81
Data	**UPG**	**ω=0.9 R2**	**b1**	**ω=1.0 R2**	**b1**
GPTA2011	Genomic UPG	0.39	0.74	0.32	0.51
	Pedigree UPG	0.50	0.96	0.52	0.78
	No UPGs			0.50	0.78

Low accuracy with exact UPG

- GPTA for young genotypes
  - Pedigree UPG: $GPTA = w_1 PA + w_2 DGV - w_3 PI \approx DGV$
  - Genomic UPG: $GPTA = w_1 PA + w_2 DGV - w_3 PI + w_4 UPG \approx DGV + UPG$

Larger weights with many genotypes

Too large for young animals

- Possible solutions
  - Just using pedigree UPG
  - Discounting UPG effects
  - Removing double counting between DGV and UPG
  - Scaling $\mathbf{A}$ to $\mathbf{G}$ (“metafounders”)

$$\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} & -(\mathbf{G}^{-1} - \mathbf{A}_{22}^{-1})\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'(\mathbf{G}^{-1} - \mathbf{A}_{22}^{-1}) & \mathbf{Q}_2'(\mathbf{G}^{-1} - \mathbf{A}_{22}^{-1})\mathbf{Q}_2 \end{bmatrix}$$

Missing parents in ssGBLUP

- Genomic UPG
  - $\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} & 0 \\ 0 & 0 & 0 \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{G}^{-1}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{G}^{-1} & \mathbf{Q}_2'\mathbf{G}^{-1}\mathbf{Q}_2 \end{bmatrix} - \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{A}_{22}^{-1}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{A}_{22}^{-1} & \mathbf{Q}_2'\mathbf{A}_{22}^{-1}\mathbf{Q}_2 \end{bmatrix}$
- Genomic UPG without Q'G^{-1}Q
  - $\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} & 0 \\ 0 & 0 & 0 \end{bmatrix} - \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{A}_{22}^{-1}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{A}_{22}^{-1} & \mathbf{Q}_2'\mathbf{A}_{22}^{-1}\mathbf{Q}_2 \end{bmatrix}$
- Pedigree UPG
  - $\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} & 0 \\ 0 & 0 & 0 \end{bmatrix}$

With A_{22}^{*}

- Genomic UPG
  - $$\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{*} & 0 \\ 0 & 0 & 0 \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{G}^{-1}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{G}^{-1} & \mathbf{Q}_2'\mathbf{G}^{-1}\mathbf{Q}_2 \end{bmatrix} - \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{A}_{22}^{*}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{A}_{22}^{*} & \mathbf{Q}_2'\mathbf{A}_{22}^{*}\mathbf{Q}_2 \end{bmatrix}$$
- Genomic UPG without Q'G^{-1}Q
  - $$\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{*} & 0 \\ 0 & 0 & 0 \end{bmatrix} - \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & -\mathbf{A}_{22}^{*}\mathbf{Q}_2 \\ 0 & -\mathbf{Q}_2'\mathbf{A}_{22}^{*} & \mathbf{Q}_2'\mathbf{A}_{22}^{*}\mathbf{Q}_2 \end{bmatrix}$$
- Pedigree UPG
  - $$\mathbf{H}^* = \mathbf{A}^* + \begin{bmatrix} 0 & 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{*} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

A_{22}^{*}: Modification with UPG

- Indirect inversion

$$A_{22}^{-1} = A^{22} - A^{21}(A^{11})^{-1}A^{12}$$

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

- With UPG

$$A_{22}^{*} = A^{22} - \begin{bmatrix} A^{21} & A^{23} \end{bmatrix} \begin{bmatrix} A^{11} & A^{13} \\ A^{31} & A^{33} + I \end{bmatrix} \begin{bmatrix} A^{12} \\ A^{32} \end{bmatrix}$$

where $\mathrm{A}^{*} = \begin{bmatrix} A^{11} & A^{12} & A^{13} \\ A^{21} & A^{22} & A^{23} \\ A^{31} & A^{32} & A^{33} \end{bmatrix} = \begin{bmatrix} A^{11} & A^{12} & -[A^{11} \quad A^{12}]Q \\ A^{21} & A^{22} & -[A^{21} \quad A^{22}]Q \\ -Q'\begin{bmatrix} A^{11} \\ A^{21} \end{bmatrix} & -Q'\begin{bmatrix} A^{12} \\ A^{22} \end{bmatrix} & Q'A^{-1}Q \end{bmatrix}$

Simulation study

- Structure
  - $h^2 = 0.3$
  - Sex-limited trait (n = 90,000)
  - EBV selection
  - 10 generations (n = 164,500)
  - Ne: 200 theoretical; 25 realized
  - Mean F in last generation: 0.11
- Genotypes
  - 18,674 total
  - 5108 in gen. 10 for validation

- Assignment of UPGs
  - UPG1 for generation 0-4
  - UPG2 for generation 5-7
  - UPG3 for generation 8-10

Category	Non genotyped	Genotyped
Top bulls	0	0
Top cows	5% (dam)	0
Bottom bulls	30% (dam)	10% (dam)
Bottom cows	30% (dam)	10% (dam)

Results from simulation

	Standard A_{22}^{-1}		Modified A_{22}^{*}	
	R2	**b1**	**R2**	**b1**
Genomic UPG	0.53	0.86	0.61	1.01

* Genotyped young animals without records

Results from simulation

	Standard A_{22}^{-1}		Modified A_{22}^{*}	
	R2	**b1**	**R2**	**b1**
Genomic UPG	0.53	0.86	0.61	1.01
without $Q'G^{-1}Q$	0.62	1.05	0.63	1.04
Pedigree UPG	0.63	1.06	0.63	1.06

	R2	**b1**
Metafounders	0.63	1.08

* Genotyped young animals without records

Summary

- Missing pedigree may reduce the accuracy of genomic prediction in single-step GBLUP.
  - Specific data structure with many missing parents
- We have several options to discount the possible double-counting of the UPG contribution in $\mathbf{H}^*$.
  - Removal of $\mathbf{G}^{-1}$ from the additional UPG contribution
  - Use of Modified $\mathbf{A}_{22}^{-1}$
  - Metafounders

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