Integration of single step DGV in conventional genetic evaluations using DGV-PBLUP

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Reason for integrating

CRV holding is divided into two parts

1. CRV Company
   - Commercial branch (sale of semen and embryo's, breeding program)
2. CRV Herdbook
   - **National genetic evaluation**

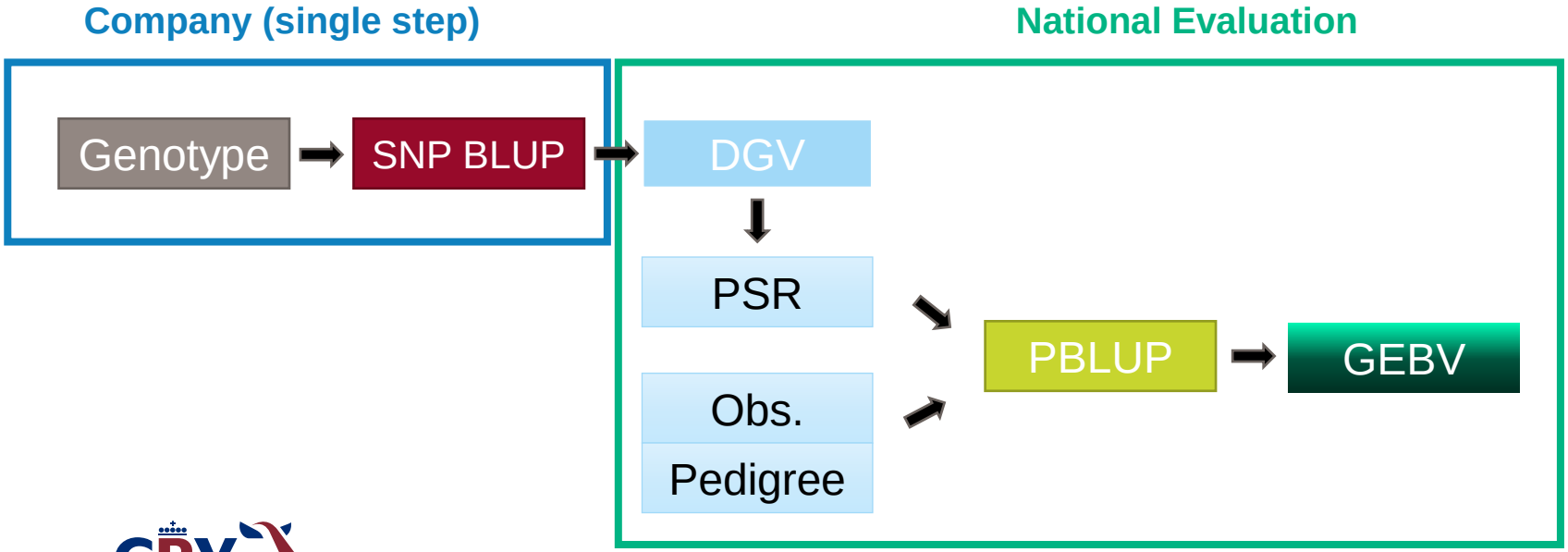
Single step (and earlier genomic evaluations) proprietary to CRV Company

The herdbook cannot use genotypes or SNP effects in the national evaluation.

– Solution: Integrate Direct Genomic Values into national evaluation

Schematic overview of national genetic evaluation

CRV Company supplies DGV for integration into the national genetic evaluations done by the herdbook



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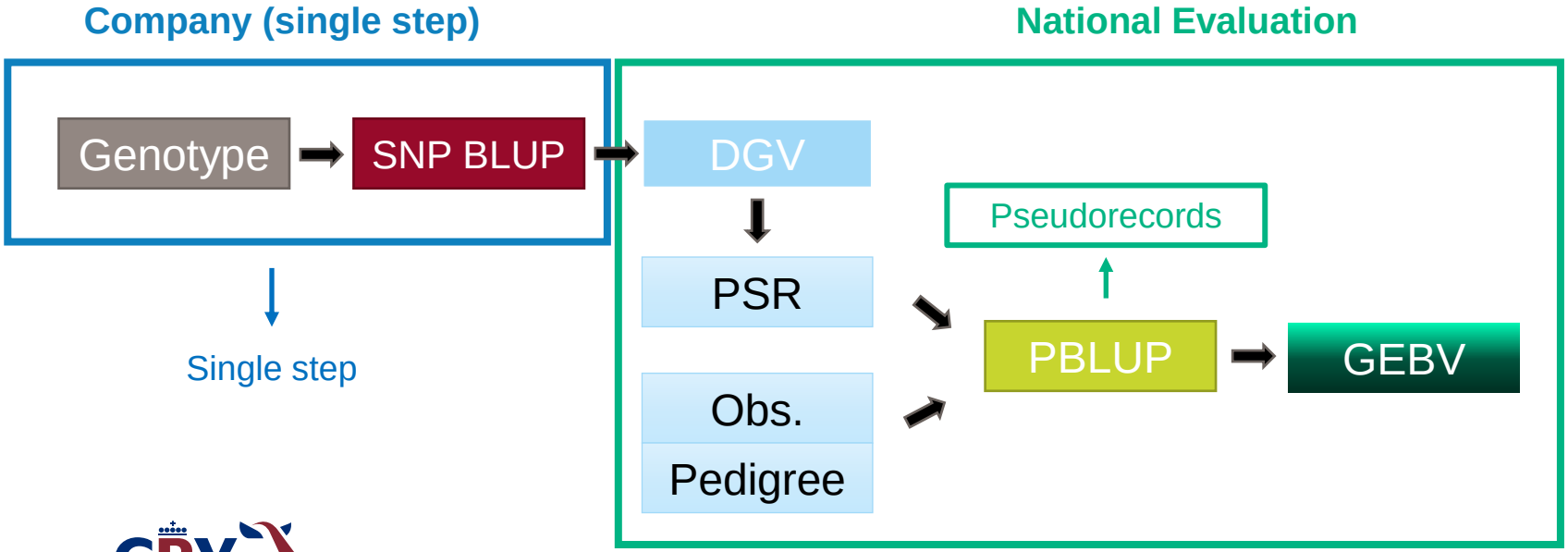

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Adding genomic information to national evaluation

Current national evaluation uses a pseudorecord system
DGV supplied for national evaluations used as observations on a pseudo-trait

$$\begin{bmatrix} y \\ d \end{bmatrix} = \begin{bmatrix} a_y \\ a_d \end{bmatrix} + \begin{bmatrix} e_y \\ a_e \end{bmatrix} \quad \text{and} \quad \text{var}\begin{bmatrix} a_y \\ a_d \end{bmatrix} = \begin{bmatrix} \sigma_g^2 & r_{yd}^2\sigma_g^2 \\ r_{yd}^2\sigma_g^2 & \sigma_g^2 \end{bmatrix}$$

- The correlation to existing trait integrates genomic data into EBV of existing trait

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Adding genomic information to national evaluation

Current national evaluation uses a pseudorecord system
DGV fitted as observations on a pseudo-trait
The correlation to existing trait integrated genomic data in EBV of existing trait

But:
- Many extra traits to fit (runtime and memory requirements)
- Imbalances in variance component matrices cause noise on GEBV/reliability

Ultimate goal: national GEBV == single step GEBV

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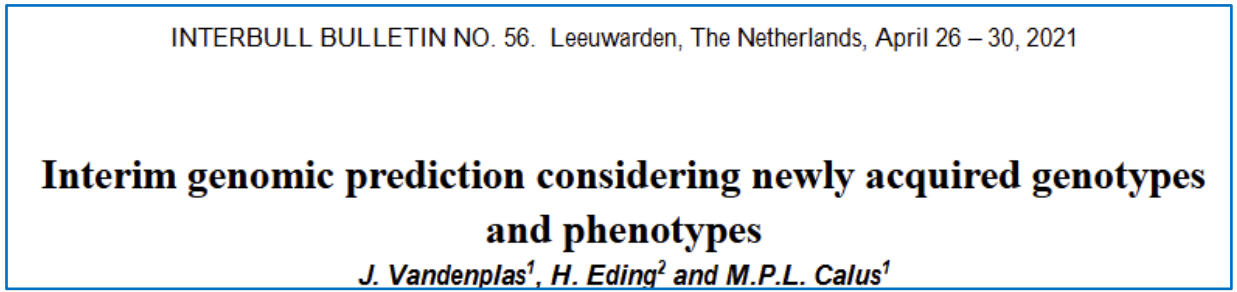
Theory

Single step SNP BLUP allows for interim genomic predictions
Equations derived assuming prior knowledge of SNP effects ($\hat{\mathbf{g}}$)


INTERBULL BULLETIN NO. 56. Leeuwarden, The Netherlands, April 26 – 30, 2021

Interim genomic prediction considering newly acquired genotypes and phenotypes

J. Vandenplas[1], H. Eding[2] and M.P.L. Calus[1]

Allows prediction of GEBV given a genotype using a conventional PBLUP

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Theory

Interim prediction equation

Equivalent to a full single step genomic evaluation

$$\begin{bmatrix} \mathbf{X'RX} & \mathbf{X'RW} \\ \mathbf{W'RX} & \mathbf{W'RW} + \frac{1}{\sigma^2}\mathbf{A}^{*-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X'Ry} \\ \mathbf{W'Ry} + \frac{1}{\sigma^2}\mathbf{A}^{*-1}\boldsymbol{\mu} \end{bmatrix}$$

Where:

$$\boldsymbol{\mu} = \begin{bmatrix} \mathbf{I} \\ \mathbf{A}_{ng}\mathbf{A}_{gg}^{-1} \end{bmatrix} \mathbf{Z}\hat{\mathbf{g}}$$

Theory

Intermediate prediction equation
Equivalent to a full single step genomic evaluation

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Where:

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$\mathbf{Z}\hat{\mathbf{g}}$ → allele substitution effects

$\mathbf{Z}\hat{\mathbf{g}}$ → genotypes

$\mathbf{A}_{ng}\mathbf{A}_{gg}^{-1}$ → ‘imputes’ from genotyped to non-genotyped relatives

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Theory

Intermediate prediction equation
Equivalent to a full single step genomic evaluation

$$\begin{bmatrix} \mathbf{X'RX} & \mathbf{X'RW} \\ \mathbf{W'RX} & \mathbf{W'RW} + \frac{1}{\sigma^2}\mathbf{A}^{*-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X'Ry} \\ \mathbf{W'Ry} + \frac{1}{\sigma^2}\mathbf{A}^{*-1}\boldsymbol{\mu} \end{bmatrix}$$

Where:

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→ genotype x ASE = DGV

Theory

DGV-PBLUP

Replace $\mathbf{Zg}$ with a vector of DGV $\mathbf{d}$:

$$\begin{bmatrix} \mathbf{X'RX} & \mathbf{X'RW} \\ \mathbf{W'RX} & \mathbf{W'RW} + \frac{1}{\sigma^2}\mathbf{A}^{*-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X'Ry} \\ \mathbf{W'Ry} + \frac{1}{\sigma^2}\mathbf{A}^{*-1}\boldsymbol{\mu} \end{bmatrix}$$

Where:

$$\boldsymbol{\mu} = \begin{bmatrix} \mathbf{I} \\ \mathbf{A}_{ng}\mathbf{A}_{gg}^{-1} \end{bmatrix} \mathbf{d}$$

- Possible replacement for pseudorecord system?

Theory

DGV-PBLUP: Conventional pedigree BLUP evaluation, augmented with DGV of genotyped animals.

DGV from genomic prediction fitted as a prior mean.

- Animal effect estimated as a deviation from the mean
  - In regular eval. BV = **0** +/- deviation
  - In DGV-PBLUP BV = **DGV** +/- deviation

Run as conventional pedigree BLUP evaluation
  - No SNP effects, no genotypes

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Proof of concept: Longevity

Routine single-step evaluation:

- #Phenotypes: 472,767,427
- #Pedigree : 16,660,929
- #Genotypes : 803,898

PSR:

- #Phenotypes: 472,767,427
- #Pedigree : 16,660,929
- #DGVs : 773,340

Longevity model is a 5th order random regression model:
6 polynomials (Effect 1…6)

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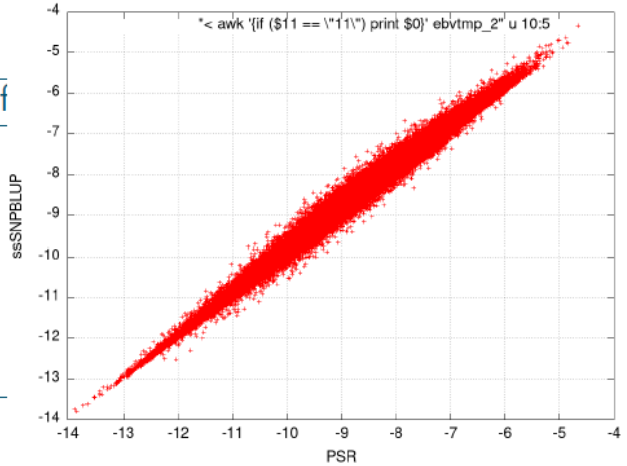
Proof of concept: Longevity

Genotyped animals with DGV in system

Effect	#animals	Correlation	Intercept	Reg. Coef
1	773340	0.9965	0.2771	1.01782
2	773340	0.9975	0.1108	1.01561
3	773340	0.9968	-0.013	1.01229
4	773340	0.9969	-0.006	1.00339
5	773340	0.9970	-0.001	0.98558
6	773340	0.9988	-0.000	0.98822



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Proof of concept: Longevity

DGV-PBLUP seems a promising replacement of our current pseudorecord system

- More accurate integration of DGV with phenotypic data
  - Expectation: Higher correlations and less GEBV changes compared to single step

- No need for extra evaluated pseudo-traits
  - Further simplifies evaluations (same model for all types of flows)
  - Easy to fit all traits with DGV from single step.
  - Less computer resources

Application: Milk production test day model

Five lactation random regression model with 4th order Legendre polynomials

- 5 polynomials per lactation: 25 animal solutions

Traits using this test day model

- Milk, fat, protein and lactose production
- Somatic cell score
- Urea content

Single-step evaluation:

- #Phenotyped: 13,662,463
- #Pedigree : 16,313,781
- #Genotyped : 828,590

PSR:

- #Phenotyped: 13,662,463
- #Pedigree : 16,382,568
- #DGVs : 851,704

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Run time iteration phase evaluation

Trait group	Single step	DGV-PBLUP	Conventional
Milk	51:28	18:17	17:53
Fat	47:26	18:39	17:37
Protein	49:05	19:20	18:08
Somatic Cell	48:47	19:02	19:30
Urea	56:02	18:22	18:31
Lactose	63:00	18:49	19:45

Evaluations were run on a test machine using 5 CPU for parallel computing

Intel(R) Xeon(R) Gold 6448H 64bit X86 4000MHz

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Results: Young bulls with genotype and DGV

Bulls without offspring born after 2020

	corr		< 1/4 s.d.	
Trait	**dgv**	**psr**	**dgv**	**psr**
Milk	0,999	0,928	100,0%	72,2%
Fat	0,999	0,964	100,0%	80,1%
Protein	0,998	0,934	100,0%	74,8%
Somatic Cell	0,995	0,972	99,8%	85,3%
Urea	0,999	0,994	100,0%	98,3%
Lactose	0,999	0,918	100,0%	70,5%

- **corr** **:** correlation GEBV with those from single step
- **< ¼s.d** : fraction of GEBV changes less than 25% genetic s.d.

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Discussion

Relative to current PSR system DGV-BLUP improves integration of genomic data

- Higher correlations
- Smaller differences in GEBV
- Improved agreement between national and single step evaluations

Runtime acceptable for operational use

- Comparable to conventional evaluation, faster than single step

Next steps

1. Implement and test in all other flows
2. Provide stakeholders with test file and await go/no go
3. Roll out as replacement of current pseudorecord system

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