UNIVERSITY OF GEORGIA
College of Agricultural & Environmental Sciences

Big Data Genomic Analysis in Dairy Cattle

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The fact

3.9 million genotyped animals

Why is it important?

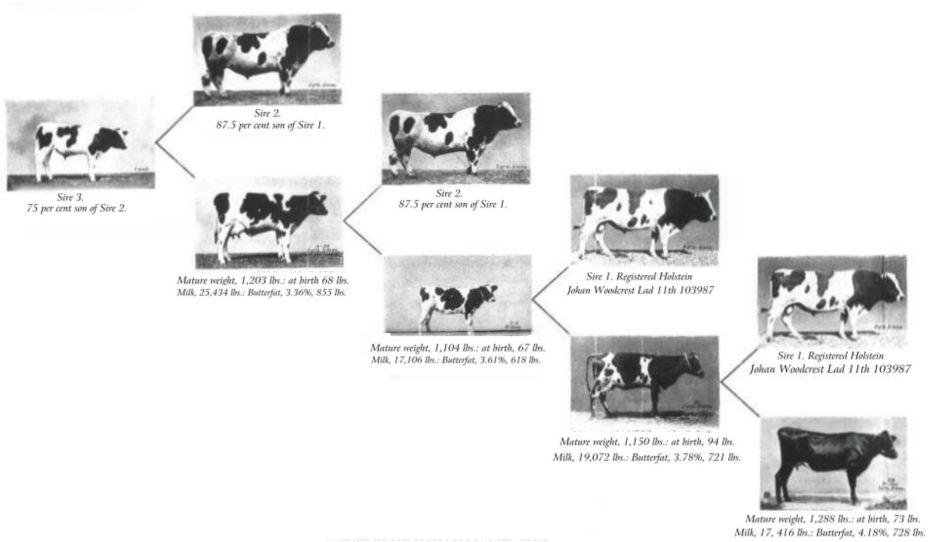
- Impossible in 2015
  - Methods
  - Computing resources vs. algorithms
  - Data availability

- Sends a message
  - Work to accommodate new data
  - Make the most out of available resources

Data

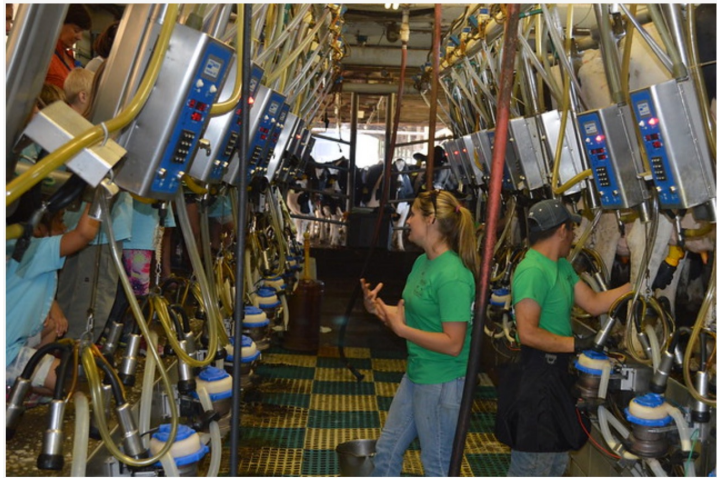
3.9 million

~ 30 million



VanRaden & Miller

45 million



https://www.usda.gov/media/blog/2020/06/18/data-saydairy-has-changed

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Data

	Phenotypes		Animals	
Breed	**N**	**Cows**	**Genotypes**	**Total**
All	**45M**	**19.4M**	**3.9M**	**29.5M**
Ayrshire	116k	47k	9.2k	94k
Brown Swiss	328k	138k	47k	292k
Guernsey	129k	58k	5k	100k
Holstein	40.3M	17.5M	3.4M	26.6M
Jersey	4.1M	1.7M	427k	2.5M

Objectives

Alberto Cesarani

- ssGBLUP multi-breed genomic evaluations for US dairy cattle
- Reliability of GEBV from multi-breed ≈ single-breed
- Improve software efficiency ⟶ BLUPF90

Single-step (ssGBLUP)

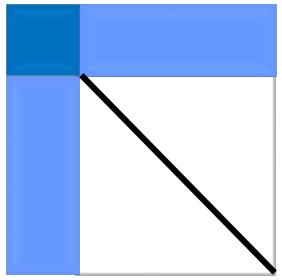
$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'W} \\ \mathbf{W'X} & \mathbf{W'W}+\mathbf{H}^{-1}\frac{\sigma_e^2}{\sigma_u^2} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{W'y} \end{bmatrix}$$

Aguilar et al. (2010)
Christensen and Lund (2010)

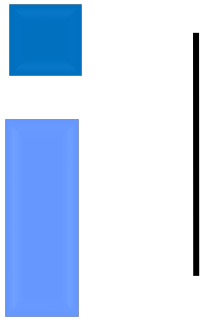
$$\mathbf{H}^{-1}=\mathbf{A}^{-1}+\begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{-1}-\mathbf{A}_{22}^{-1} \end{bmatrix}$$

$\mathbf{G}^{-1}$

$\mathbf{G}_{\mathrm{APY}}^{-1}$



$\mathbf{G}_{\mathrm{APY}}^{-1}$



- $\mathbf{G}_{\mathrm{APY}}^{-1}$ sparse
- Efficient computations

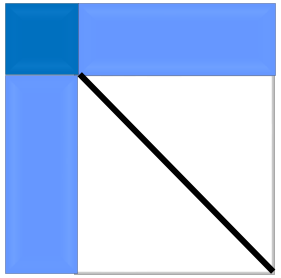
Misztal et al. (2014)

APY

$\mathbf{G}^{-1}$ 

Dense ➔ $u_i|u_1 + u_2 + u_3, \ldots, u_{i-1} = \sum_{j=1}^{n-1} p_{ij}u_j + \varepsilon_i$

Genotyped animals ➔ Core and Noncore

$\mathbf{G}^{-1}_{\text{APY}}$ 

Sparse ➔ $u_i|u_{c1} + u_{c2} + u_{c3}, \ldots, u_{ci} = \sum_{j=1}^{c} p_{ij}u_j + \varepsilon_i$

$$\mathbf{G}^{-1}_{\text{APY}} = \begin{bmatrix} \mathbf{G}^{-1}_{cc} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{bmatrix} + \begin{bmatrix} -\mathbf{G}^{-1}_{cc}\mathbf{G}_{cn} \\ \mathbf{I} \end{bmatrix} \mathbf{M}^{-1}_{nn} \begin{bmatrix} -\mathbf{G}_{nc}\mathbf{G}^{-1}_{cc} & \mathbf{I} \end{bmatrix}$$

Misztal et al. (2014)
Fragomeni et al. (2015)
Lourenco et al. (2015)
Masuda et al. (2016)

core animals = # eigenvalues of **G** explaining ≥ 98% variance

- Cattle 10k to 15k
- Pigs and chicken 4k to 8k

The Dimensionality of Genomic Information and Its Effect on Genomic Prediction

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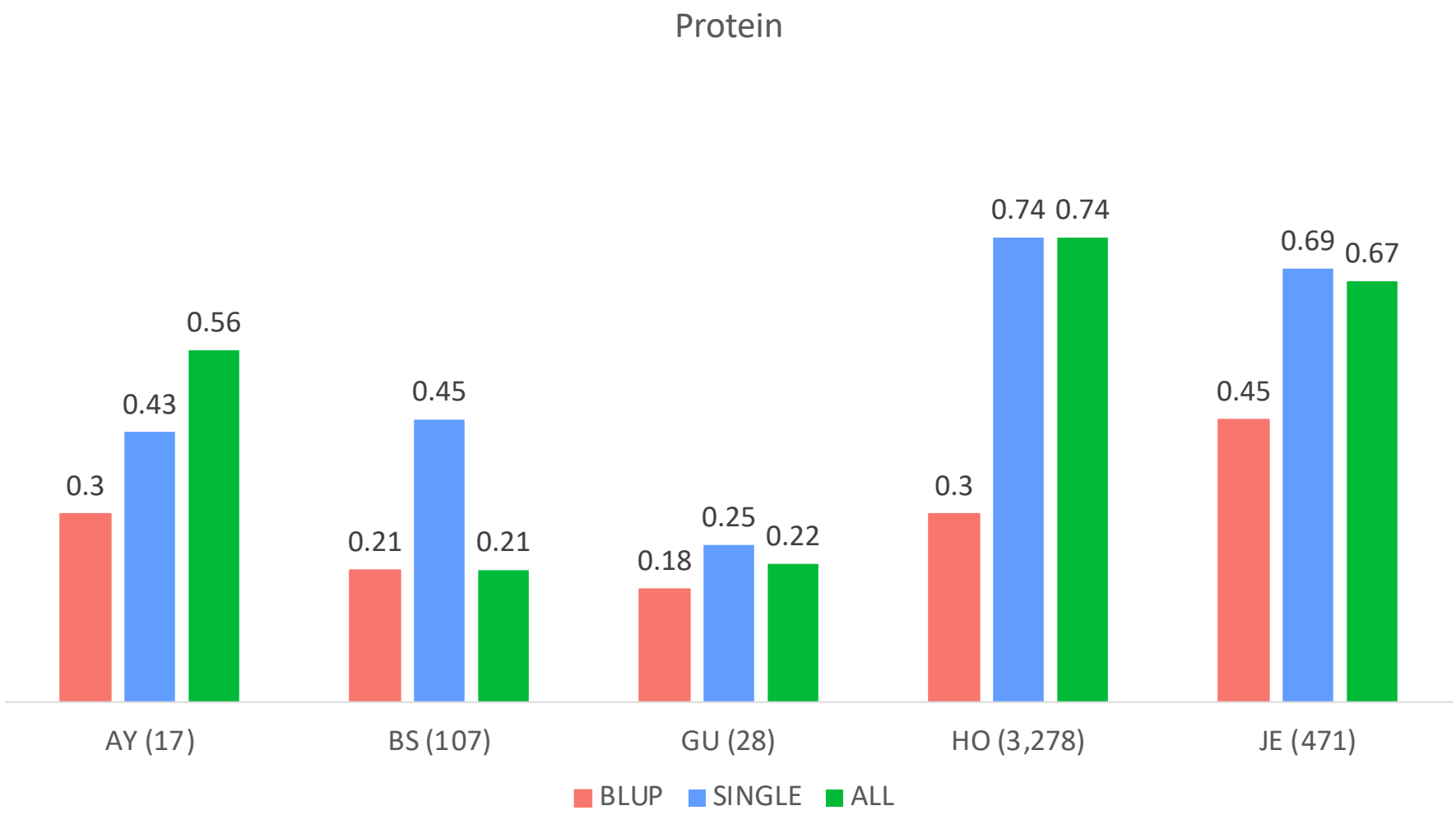
Evaluations

- **SINGLE BREED**
  - each breed separately
  - HO and JE: APY ssGBLUP with 15k random core animals

- **ALL BREEDS**
  - five breeds together
  - breed-specific effects
  - 15k random core animals in APY

Milk (MY), fat (FY), and protein (PY) yields recorded from January 2000 to June 2020

R^2 for bulls



Core animals in ssGBLUP ALL

AY = 32

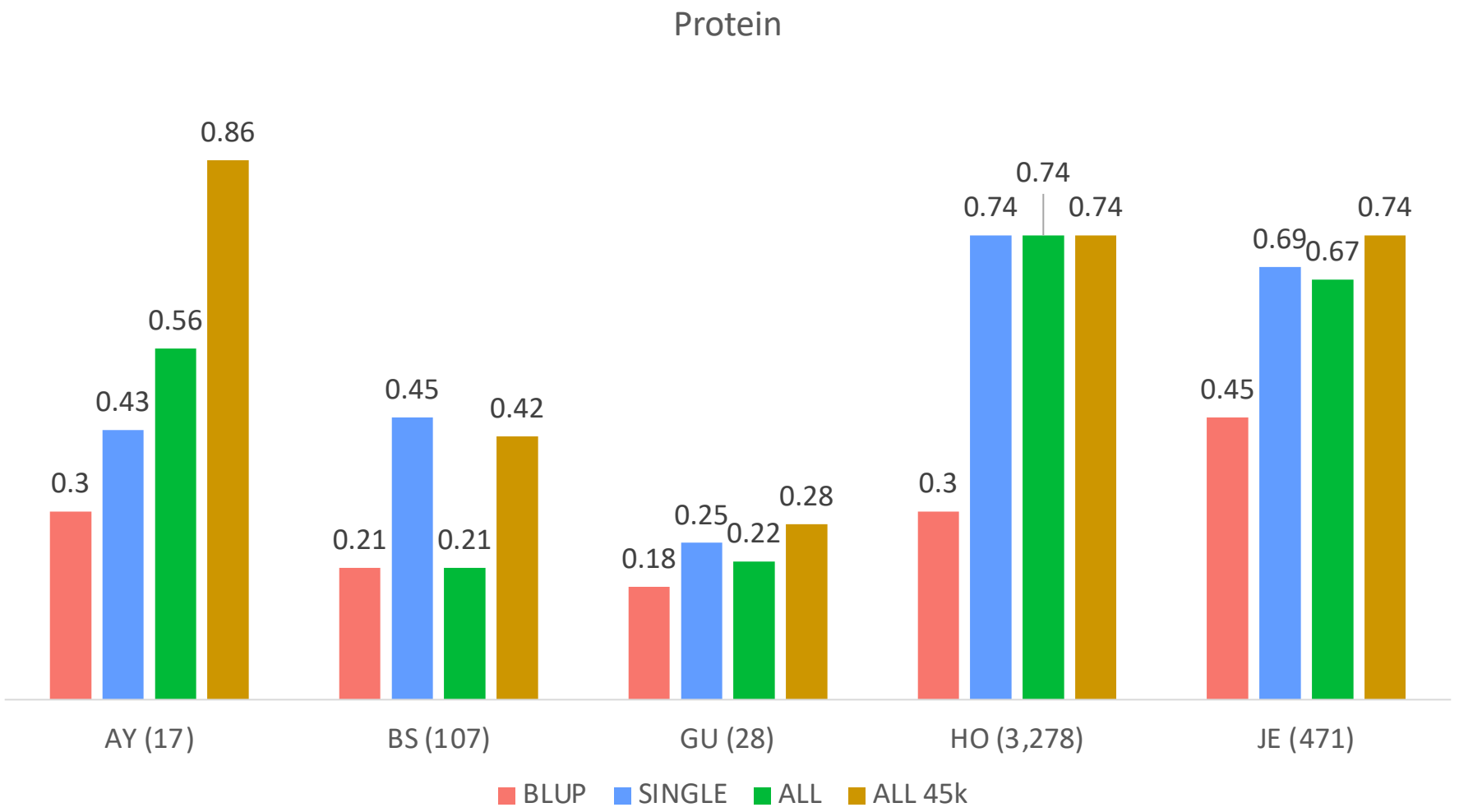
BS = 182

GU = 17

HO = 13k

JE = 1.7k

R^2 for bulls



ALL 45k

AY = 5k

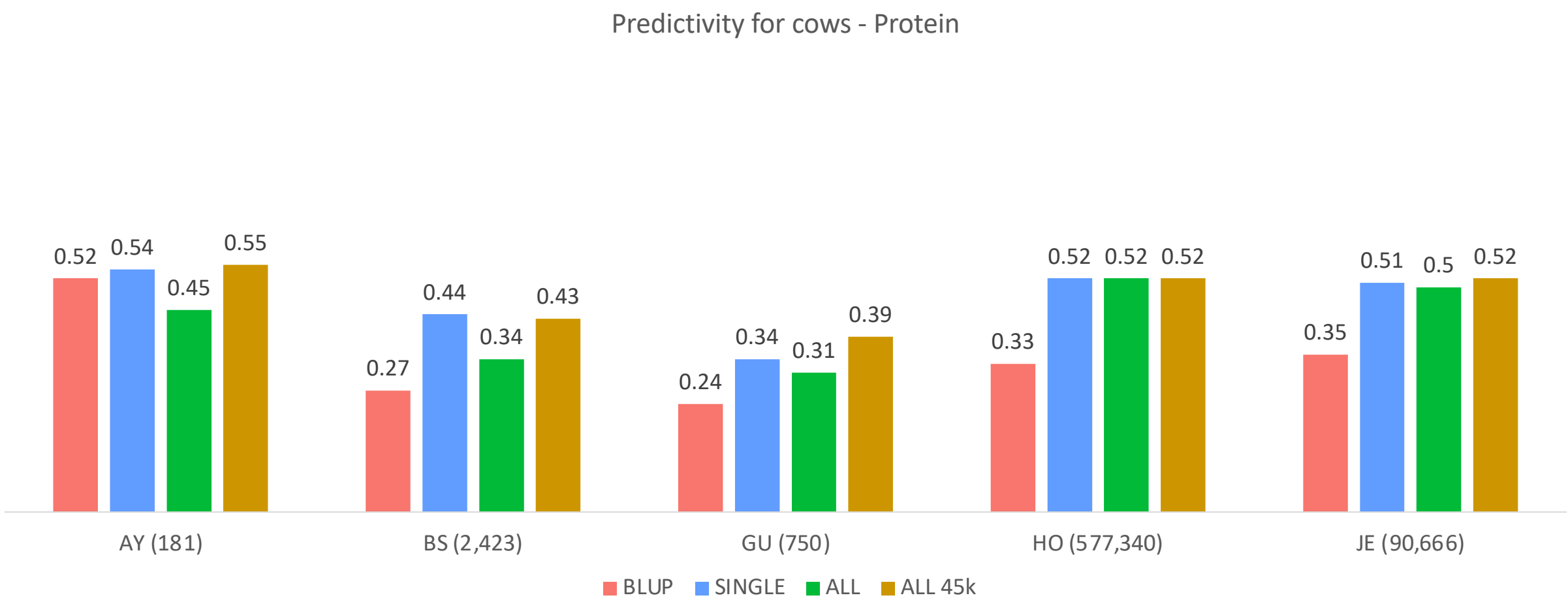
BS = 5k

GU = 5k

HO = 15k

JE = 15k

Predictivity for cows



Computing time

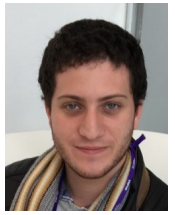
	Rounds		Sec / round		Time	
	BLUP	ssGBLUP	BLUP	ssGBLUP	BLUP	ssGBLUP
AY	504	863	0.08	0.08	< 1 min	~ 1 min
BS	364	867	0.18	0.45	1 min	~ 6 min
GU	345	757	0.07	0.07	< 1 min	< 1 min
HO	457	473	21.25	56.31	2.7 h	7.4 h
JE	586	432	2.00	5.58	~ 20 min	~ 40 min
ALL	643	1,142	27.01	64.84	4.8 h	~ 20 h
ALL_45k		1,763		130.68		~ 64 h

- 2.5 days for solutions
- 5 days for computing $\mathbf{G}_{\text{APY}}^{-1}$ and $\mathbf{A}_{22}^{-1}$ in ALL_45k

Linux server (x86_64) with Intel Xeon E5-2683 2.10 GHz processor with 32 cores

Updates in $\mathbf{A}_{22}$ for blending

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



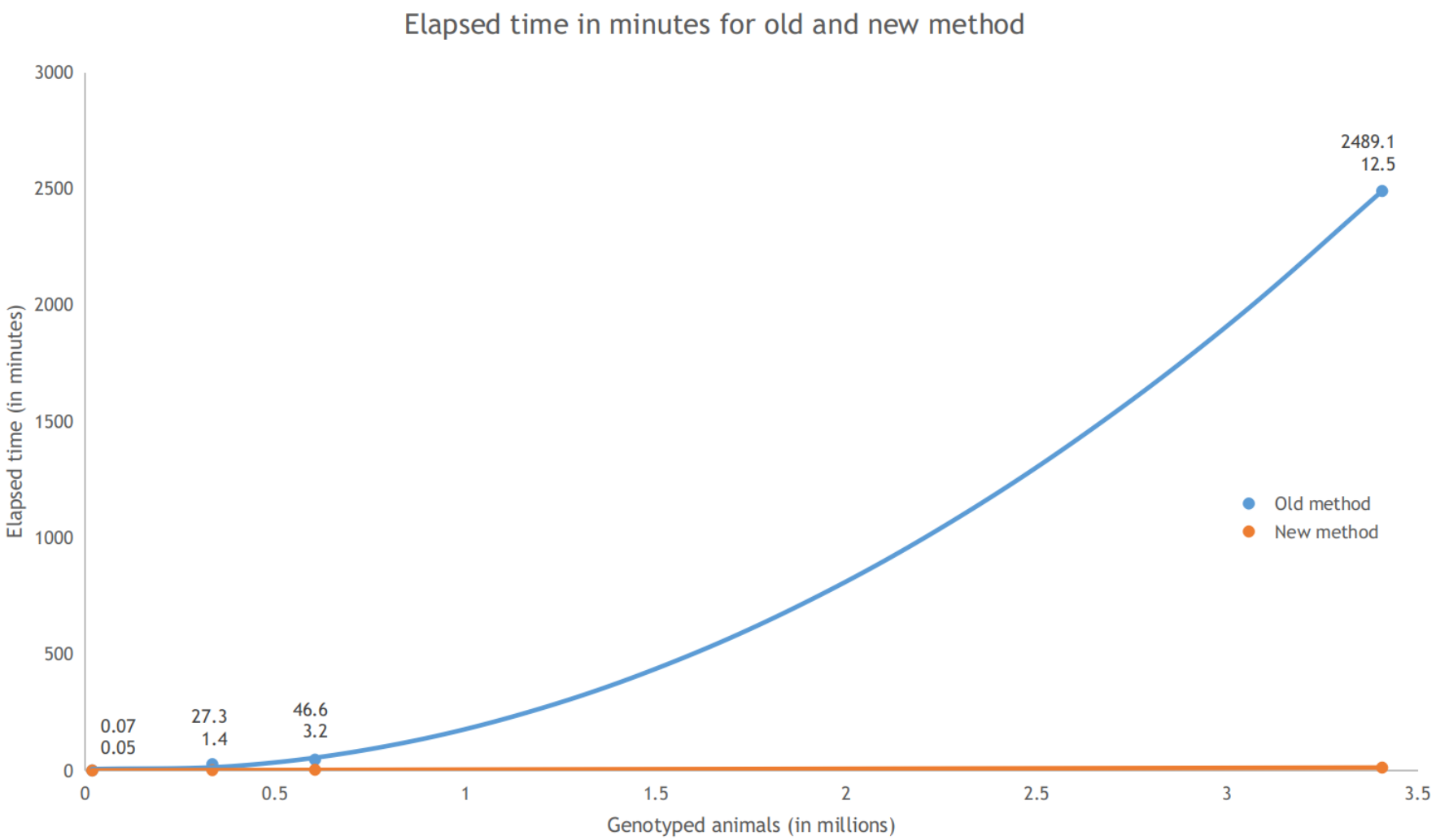
Matias Bermann

$\mathbf{A}_{22}^{-1}$ components: $\mathbf{A}_{22}^{-1}=\mathbf{A}^{22}-\mathbf{A}^{21}(\mathbf{A}^{11})^{-1}\mathbf{A}^{12}$

APY $\mathbf{G}^{-1}$: $\mathbf{G}_{\text{APY}}^{-1}=\begin{bmatrix}\mathbf{G}_{\text{cc}}^{-1} & \mathbf{0}\\ \mathbf{0} & \mathbf{0}\end{bmatrix}+\begin{bmatrix}-\mathbf{G}_{\text{cc}}^{-1}\mathbf{G}_{\text{cn}}\\ \mathbf{I}\end{bmatrix}\mathbf{M}_{\text{nn}}^{-1}\begin{bmatrix}-\mathbf{G}_{\text{nc}}\mathbf{G}_{\text{cc}}^{-1} & \mathbf{I}\end{bmatrix}$

- Blending: $\mathbf{G}$ = 0.95 $\mathbf{G}^{*}$ + 0.05 $\mathbf{A}_{22}$
  - Colleau (2002)
  - 3.4M genotyped Holsteins 15k core: 41 hours
  - Rearranging Colleau for core and noncore: 12.5 minutes

Updates in $\mathbf{A}_{22}$ for blending



Alberto Cesarani

- From 5 days to 8 hours to compute $\mathbf{G}_{\mathrm{APY}}^{-1}$ and $\mathbf{A}_{22}^{-1}$ in ALL_45k

Next challenge

Take home message

Large-scale single-step genomic evaluations are feasible for dairy cattle

- All species
- Reasonable computing time
- Single- or multi-breed populations
    - Respect the dimensionality within each bread

Large-scale genomic evaluations are easier said than done

- Always challenged by the increasing amount of data
- Efficient algorithms and computing power

Acknowledgments

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