Technical options for all-breed Single Step GBLUP for US dairy cattle

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CDCB has

- ~8M genotyped animals imputed at ~79K
- ~100M animals in pedigree
- ~30 “normal” (yield, health, calving ease…) traits + ~20 “type” traits
- 8K to 50M animals in data depending on the trait
- 6 breeds highly unbalanced, crosses, all-breed evaluation
- we receive pedigree and genotypes from all over the world

Here I present choices to test & run ssGBLUP for CDCB

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Trimming pedigree

- In BLUP, we only need animals in data and their ancestors
- a Python program trimming pedigree takes ~10 minutes
- in fertility data: reduction from ~100M to ~60M pedigree

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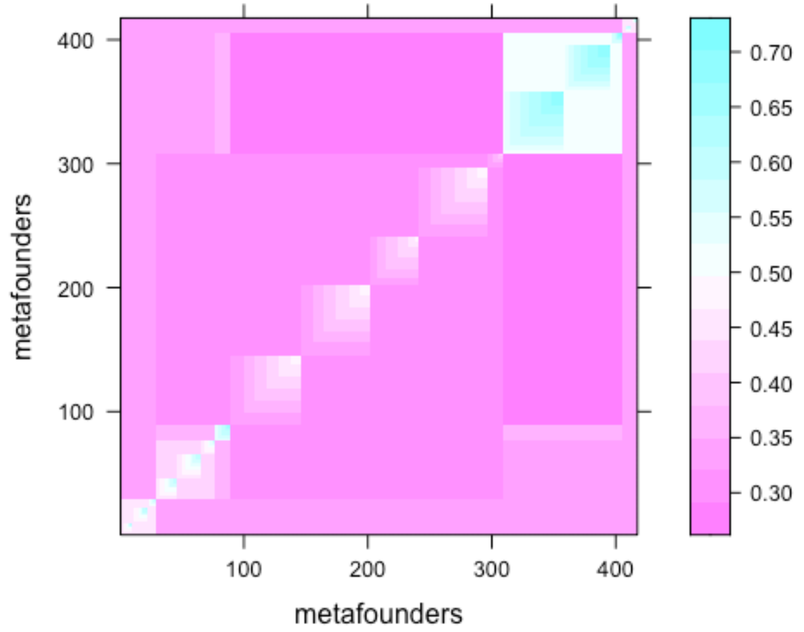
Metafounder covariance for missing pedigree

- 5%-10% missing pedigree
- We used ~400 metafounders based on base allele frequencies (from imputation run) and increase of inbreeding (see recent GSE paper)
- a parallel analysis by Joe Tabet tried J-factors giving slightly more bias and noisier UPG solutions

Sorted by breed and pedigree path



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Trimming genotypes in ssGBLUP

- for sure keep genotypes of animals that either “have records” or “have progeny with records”
- if not the case, do we keep them?
  - if both parents genotyped, the genotype provides Ø information
  - if one (or both) parent(s) is NOT genotyped, the genotype improves a bit the **H**-relationship of parent(s)
  - we consider that this improvement is negligible, so we don’t keep them
- We therefore keep genotypes that either “have records” or “have progeny with records”:
  - reduction from 8M genotypes to 2M “useful” genotypes
- the US reference population now consists in 1.7M cows with records and >30K bulls with phenotyped offspring

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Approaches for Single Step GBLUP

- relationship-based (G_APY, “GT BLUP”, Misztal et al. 2014, Mantysaari et al. 2017)
- SNP-based (Legarra and Ducrocq 2012, Liu et al., 2014, Fernando et al. 2016)
- No free lunch
- They usually involve either approximations, or some kind of blending, or complex programming

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Approaches for Single Step GBLUP

- Why we like APY
- relationship-based
  - incidence matrices of effects are sparse
  - G_APY reduces *enormously* the size of genomic data to handle
  - fast convergence of iterative solvers for MME, good condition number
  - you can use “regular” double precision “multipliers” (Lapack, MKL, etc)
  - flexible: fractional genotypes, MIR readings, -omics …

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Approaches for Single Step GBLUP

- Why we don't like APY
- need to choose an informative, "repeatable" core
  - "random" is not a realistic or practical option for dairy
  - "proven bulls" is not any more a realistic option
  - no realistic way of doing matrix computations (e.g. PCA, Pocrnic et al. 2022) in 2M genotypes

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Choice of Core

- We want a “democratic” core population
- For each breed you have a size of core
- Select “proven” genotyped bulls
  - Holstein: >500 daughters with records
  - other breeds >100 daughters with records
- select a sample of genotyped reference cows
  - tag cows with records
  - select 1 cow every n based on ID until fill in the available spots

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Breed	# of Genotypes
Ayrshire	1,608
Brown Swiss	9,560
Guernsey	3,561
Holstein	1,669,795
Jersey	300,976
Crossbreds	56,528

Breed	# of Sires+ Cows in Core	Core 98%eigenvalues
AY	311 + 1,175	(all animals)
BS	611 + 4,313	5K
GU	219 + 3,258	(all animals)
HO	6,890 + 8,113	15K
JE	3,186 + 11,883	15K
XX	141 + 4,616	5K

- Core: ~45K animals
- Non-core: 2M animals
- Reference population is the sum of core and non-core [and does include crossbreds]

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Preparation of APY

- Once we have the flags core-noncore and the genotypes
- Build by chunks the G_APY matrix (all by MKL Lapack)
  - Biggest chunk: $\boldsymbol{G}_{noncore,core}$ and its reciprocal in $\boldsymbol{G}_{APY}^{-1}$ of size 2M x 45K
  - $\boldsymbol{G}_{APY}^{-1}$ stored double precision: ≈ 720 Gigabytes

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Memory mapping

- use “memory mapping” `mmap()` to handle $\boldsymbol{G}_{APY}^{-1}$
- A **memory-mapped file** is a segment of virtual memory[1] that has been assigned a direct byte-for-byte correlation with some portion of a file [...] this correlation between the file and the memory space permits applications to treat the mapped portion as if it were primary memory.
- 720 Gb RAM become 720 Gb disk
- modern alternative to “read from file and compute” iteration-on-data

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Running of APY

- PreGSf90: Set up $\boldsymbol{G}_{APY}^{-1}$ (with blending of [5% or 10%] $\boldsymbol{A}_{\Gamma 22}$).
  - RAM ≈ 720 Gigabytes [not using mmap()]
- Blup90iod3 (PCG iteration on data)
  - uses "memory mapping" `mmap()` to handle $\boldsymbol{G}_{APY}^{-1}$
  - As a result, only 120 Gb (non-genomic parts, including the 4 x 60M animals GEBVs…) are needed for the iteration
- accf90GS2 for reliabilities (Bermann et al 2022a) also uses `mmap()`
- backsolving SNP solutions only needs "core" animals (Bermann et al. 2022b)

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Rough timings and memory

- Previous editings – perhaps 3h – may be improved
- 4 fertility traits, 50M records, 60M in pedigree, ~2M animals genotyped, ~500M equations

- using 16 threads
- Prep of G_{APY}^{-1}: 16h, 720 Gb RAM
- ssGBLUP itself: 22h , 120 Gb RAM, and 476 rounds of PCG
- Genomic reliabilities (include blending): ~8h per trait, 120 Gb RAM
- Backsolving for SNP solutions: negligible
- similar numbers as Cesarani et al. 2022

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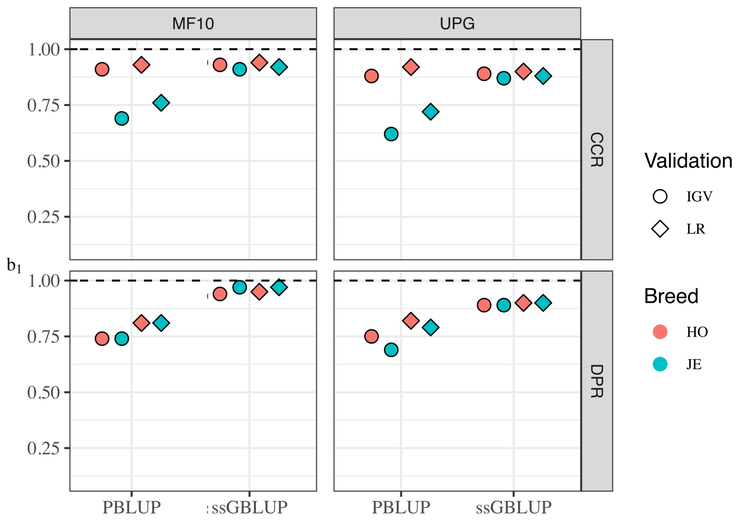
It works (Joe Tabet in prep.)

Slopes b1 within Interbull limits

Bias: ssGBLUP < BLUPMetafounders < (UPG + Jfactors)

LR correlations slightly better than (not shown here) 2-step at CDCB evaluations

Slopes



Correlations

Correlation	ssGBLUP_MF10	ssGBLUP_UPG	PBLUP_MF
[1]HO_CCR	0.87	0.85	0.54
[1]HO_DPR	0.90	0.89	0.49
[2]JE_CCR	0.88	0.81	0.56
[2]JE_DPR	0.86	0.86	0.65

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Improvement?

- Maybe we don't need it
  - we need to benchmark and play with number of threads
  - with some optimization in the pipeline and threads, time: ~2 days
- Anyway, some long-term perspectives just in case
  - $\boldsymbol{G}_{APY}^{-1}$ fully run in mmap()
  - or, $\boldsymbol{G}_{APY}^{-1}$ can be "updated" from previous runs
  - Reliability approaches can be optimized

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