Supplementary Materials: Multitask group Lasso for Genome Wide association Studies in admixed populations

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Appendix A. Data availability

Appendix A.1. *Simulated data*

Code to reproduce our simulations is available on `https://github.com/asmanouira/MuGLasso_GWAS`

Table A1 shows the location of the predefined disease loci, for each population. Table A2 shows the number of predefined disease loci, both common to both population and specific to each population.

Table A1. For simulated data, location of predefined disease loci represented by start/end positions information in each subpopulation through chromosomes: 2, 12, 19, 21 and 22.

Chromosome	Subpopulations	
	CEU	YRI
2	1,000 - 50,000	1,000 - 50,000
12	10 - 37,000	10 - 40,000
19	1,000 - 50,000	1,000 - 50,000
21	10 - 10,000	10 - 7,000
22	-	10 - 2,000

Table A2. For simulated data, number of predefined causal SNPs

Populations	Number of SNPs
Specific-CEU	2,999
Specific-YRI	4,989
Shared (CEU+YRI)	141,982
Total	149,970

Appendix A.2. *DRIVE*

Data access The dataset "General Research Use" in DRIVE Breast Cancer OncoArray Genotypes is available from the dbGaP controlled-access portal, under Study Accession phs001265.v1.p1 (`https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study\_id=phs001265.v1.p1`). Researchers can gain access the data by applying to the data access committee, see `https://dbgap.ncbi.nlm.nih.gov`.

Ethics approval The dataset was obtained from NIH after ethical review of project #17707, titled "Network-guided multi-locus biomarker discovery", and used under approval of this request (#67806-4).

Acknowledgments OncoArray genotyping and phenotype data harmonization for the Discovery, Biology, and Risk of Inherited Variants in Breast Cancer (DRIVE) breast-cancer case control samples was supported by X01 HG007491 andU19 CA148065 and by Cancer Research UK (C1287/A16563). Genotyping was conducted by the Center for Inherited Disease Research (CIDR), Centre for Cancer Genetic Epidemiology, University of Cambridge, and theNational Cancer Institute. The following studies contributed germline DNA from breast cancer cases and controls:the Two Sister Study (2SISTER), Breast Oncology Galicia Network (BREOGAN), Copenhagen GeneralPopulation Study (CGPS), Cancer Prevention Study 2 (CPSII), The European Prospective Investigation intoCancer and Nutrition (EPIC), Melbourne Collaborative Cohort Study (MCCS), Multiethnic Cohort (MEC), NashvilleBreast Health Study (NBHS), Nurses Health Study (NHS), Nurses Health Study 2 (NHS2), Polish Breast CancerStudy (PBCS), Prostate Lung Colorectal and Ovarian Cancer Screening Trial (PLCO), Studies of Epidemiologyand Risk Factors in Cancer Heredity (SEARCH), The Sister Study (SISTER), Swedish Mammographic Cohort(SMC), Women of African Ancestry Breast Cancer Study (WAABCS), Women's Health Initiative (WHI).

Appendix B. Supplementary Methods

Appendix B.1. *LD groups across populations*

Figure B1 illustrates the process by which we obtain LD-groups across populations, from LD-groups obtained on each population separately using adjacency-constrained hierarchical clustering (see Section 2.2.1)

Appendix B.2. *Multitask group lasso*

Figure B2 illustrates the architecture of the multitask group Lasso described in Section 2.3.

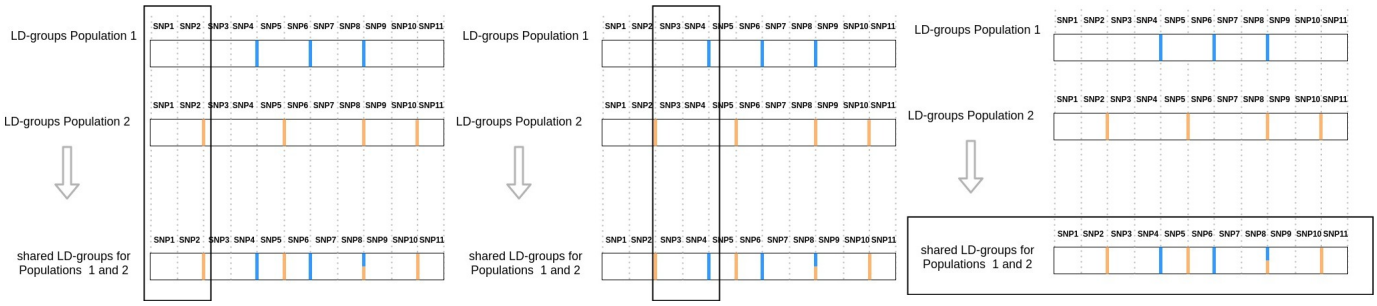


Fig. B1. Choice of shared LD-groups choice after adjacency-constrained hierarchical clustering for each population

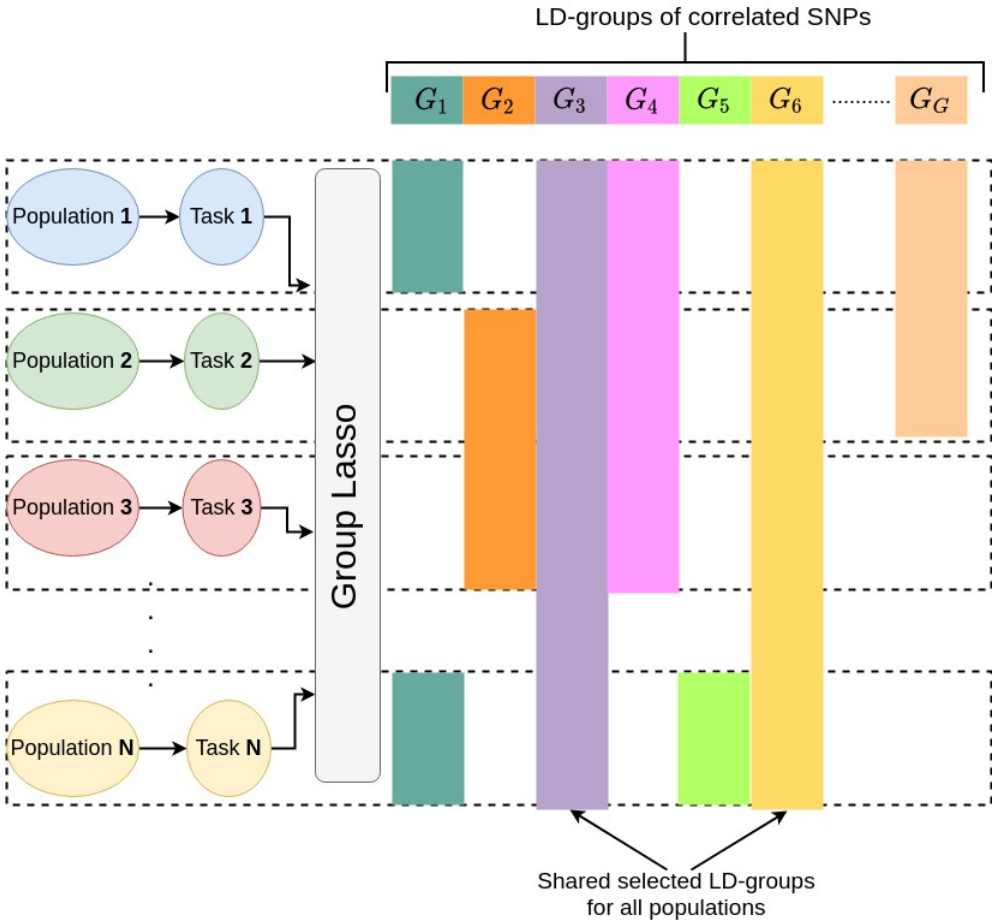


Fig. B2. Multitask group Lasso architecture

Appendix B.3. *Gap safe screening rules*

Let $X \in \mathbb{R}^{n \times d}$ be a design matrix and $\boldsymbol{y} \in \mathbb{R}^n$ the corresponding vector of outcomes, which can be binary or real-valued. We consider the following optimization problem:

$$\widehat{\boldsymbol{\beta}}^{(\lambda)} \in \underset{\boldsymbol{\beta} \in \mathbb{R}^d}{\arg\min}\, P_\lambda(\boldsymbol{\beta}) := \sum_{i=1}^{n} f_i\left(X_{i.}^\top \boldsymbol{\beta}\right) + \lambda\, \Omega(\boldsymbol{\beta}), \tag{B.1}$$

where all $f_i : \mathbb{R} \to \mathbb{R}$ are convex and differentiable functions with $1/\gamma-$Lipschitz gradient, and $\Omega : \mathbb{R}^d \to \mathbb{R}_+$ is a norm that is group-decomposable, i.e., the set of d features is partitioned in G groups of sizes $d_1, d_2, \ldots, d_G$, and

$$\Omega(\boldsymbol{\beta}) = \sum_{g=1}^{G} \Omega_g \left(\boldsymbol{\beta}^{(g)} \right),$$

where each Ω_g is a norm on $\mathbb{R}^{d_g}$ and, as previously, $\boldsymbol{\beta}^{(g)}$ corresponds to the coefficients of $\boldsymbol{\beta}$ restricted to the features in group g. As before, the λ parameter is a non-negative constant controlling the trade-off between the data fitting term and the regularization term.

Equation (2) is a special case of Equation (B.1) because the squared loss and the logistic loss are convex and differentiable.

Safe screening rules make it possible to solve such problems more efficiently by discarding features whose coefficients are guaranteed to be zero at the optimum, prior to using a solver. They usual rely on the dual formulation of Equation (B.1):

$$\widehat{\boldsymbol{\theta}}^{(\lambda)} = \underset{\boldsymbol{\theta} \in \Delta_X}{\arg\max}\, D_\lambda(\boldsymbol{\theta}) := -\sum_{i=1}^{n} f_i^*(-\lambda\theta_i), \tag{B.2}$$

where $f_i^* : \mathbb{R} \to \mathbb{R}$ is the Fenchel-Legendre transform of f_i, defined by $f_i^*(u) = \sup_{z \in \mathbb{R}} \langle z, u \rangle - f_i(z)$ and $\Delta_X \subset \mathbb{R}^n$ is defined by $\Delta_X = \left\{ \boldsymbol{\theta} \in \mathbb{R}^n : \forall g = 1, \ldots, G, \Omega_g^D(X^{(g)\top}\boldsymbol{\theta}) \leq 1 \right\}$, where $\Omega_g^D : \mathbb{R}^{p_g} \to \mathbb{R}$ is the conjugate norm of Ω_g, defined by $\Omega_g^D(\boldsymbol{u}) = \max_{\boldsymbol{z} in \mathbb{R}^{p_g} : \Omega_g(\boldsymbol{z}) \leq 1} \langle \boldsymbol{z}, \boldsymbol{u} \rangle$, and $X^{(g)} \in \mathbb{R}^{n \times p_g}$ is the design matrix X restricted to the features/columns in group g.

In our setting,

- $\Omega_g^D(\boldsymbol{u}) = \left\| \boldsymbol{\beta}^{(g)} \right\|_2$ and $\Omega^D(\boldsymbol{u}) = \max_{g=1,\ldots,G} \frac{1}{w_g} \left\| \boldsymbol{u}^{(g)} \right\|_2$.
- If one uses the squared loss, that is to say, $f_i(z) = \frac{1}{2}(y_i - z)^2$, then $f_i^*(z) = \frac{1}{2}z^2 + y_i z$ and the Lipschitz constant is $\gamma = 1$.
- If one uses the logistic loss, that is to say, $\boldsymbol{y} \in \{0, 1\}^n$ and $f_i(z) = -y_i z + \log(1 + \exp(z))$, then

  $$f_i^*(z) = \begin{cases} (z + y_i)\log(z + y_i) + (1 - (z + y_i))\log(1 - (z + y_i)) & \text{if } 0 \leq (z + y_i) \leq 1 \\ +\infty & \text{otherwise,} \end{cases}$$

  and the Lipschitz constant is $\gamma = 4$.

The general idea of safe-screening rules, introduced by [EGVR10], is to find a region $\mathcal{R} \subset \mathbb{R}^n$ such that if $\widehat{\boldsymbol{\theta}}^{(\lambda)} \in \mathcal{R}$, for any $g \in \{1, \ldots, G\}$,

$$\Omega_g^D \left(X^{(g)\top} \widehat{\boldsymbol{\theta}}^{(\lambda)} \right) < 1 \Rightarrow \widehat{\boldsymbol{\beta}}^{(\lambda)} = 0.$$

Gap safe screening rules [N+17] exploit the duality gap $(P_\lambda(\boldsymbol{\beta}) - D_\lambda(\boldsymbol{\theta}))$ to obtain the radius of the safe region $\mathcal{R}$. More specifically, Ndiaye et al. show that $\forall \boldsymbol{\beta} \in \mathbb{R}^p, \forall \boldsymbol{\theta} \in \Delta_X$,

$$\left\| \widehat{\boldsymbol{\theta}}^{(\lambda)} - \boldsymbol{\theta} \right\|_2 \leq \sqrt{\frac{2(P_\lambda(\boldsymbol{\beta}) - D_\lambda(\boldsymbol{\theta}))}{\gamma\lambda^2}},$$

which leads them to define, for any $\boldsymbol{\beta} \in \mathbb{R}^p$ and $\boldsymbol{\theta} \in \Delta_X$, the ball centered in $\boldsymbol{\theta}$ and of radius $\sqrt{\frac{2P_\lambda(\boldsymbol{\beta}) - D_\lambda(\boldsymbol{\theta})}{\gamma\lambda^2}}$ as a safe region, that is to say a region that is guaranteed to contain $\widehat{\boldsymbol{\theta}}^{(\lambda)}$.

Appendix B.4. *Measuring selection stability*

To measure the stability of a feature selection property, we use the sample's Pearson coefficient [NB16]. This stability index is closely related to that proposed by Kuncheva [Kun08] and is appropriate for the comparison of feature sets of different sizes. This index relies on repeating the feature selection procedure M time (in this work, $M = 10$) and evaluating the overlap if the M resulting feature sets.

Each of the M sets of selected features can be represented by an indicator vector $\boldsymbol{s} \in \{0,1\}^p$, where $s_j = 1$ if feature j is selected and 0 otherwise. The stability index between two feature sets $\mathcal{S}$ and $\mathcal{S}'$, represented by their indicator vectors $\boldsymbol{s}$ and $\boldsymbol{s}'$, is computed as the Pearsons's correlation between these two vectors:

$$\phi(\mathcal{S}, \mathcal{S}') = \frac{\sum_{j=1}^{p}(s_j - \bar{\boldsymbol{s}})(s'_j - \bar{\boldsymbol{s}'})}{\sqrt{\sum_{j=1}^{p}(s_j - \bar{\boldsymbol{s}})^2}\sqrt{\sum_{j=1}^{p}(s'_j - \bar{\boldsymbol{s}'})^2}}, \tag{B.3}$$

where $\bar{\boldsymbol{s}} = \frac{1}{p}\sum_{j=1}^{p} s_j$ and $\bar{\boldsymbol{s}'} = \frac{1}{p}\sum_{j=1}^{p} s'_j$.

Note that, because $\sum_{j=1}^{p} s_j = |\mathcal{S}|$, $\sum_{j=1}^{p} s_j s'_j = |\mathcal{S} \cap \mathcal{S}'|$, and $s_j^2 = s_j$, we can rewrite Equation (B.3) as

$$\phi(\mathcal{S}, \mathcal{S}') = \frac{|\mathcal{S} \cap \mathcal{S}'| - \frac{1}{p}|\mathcal{S}|\,|\mathcal{S}'|}{\sqrt{|\mathcal{S}|\left(1 - \frac{|\mathcal{S}|}{p}\right)}\sqrt{|\mathcal{S}'|\left(1 - \frac{|\mathcal{S}'|}{p}\right)}},$$

hence interpreting this index as the size of the intersection of the two sets, corrected by chance, that is to say, ensuring that the expected value of the index is 0 when the two selections are random.

The stability index between M sets of selected features is computed as the average pairwise stability index between all possible pairs of sets of selected features:

$$\phi(\mathcal{S}_1, \mathcal{S}_2, \ldots, \mathcal{S}_M) = \frac{M(M-1)}{2}\sum_{k=1}^{M}\sum_{l=k+1}^{M}\phi(\mathcal{S}_k, \mathcal{S}_l). \tag{B.4}$$

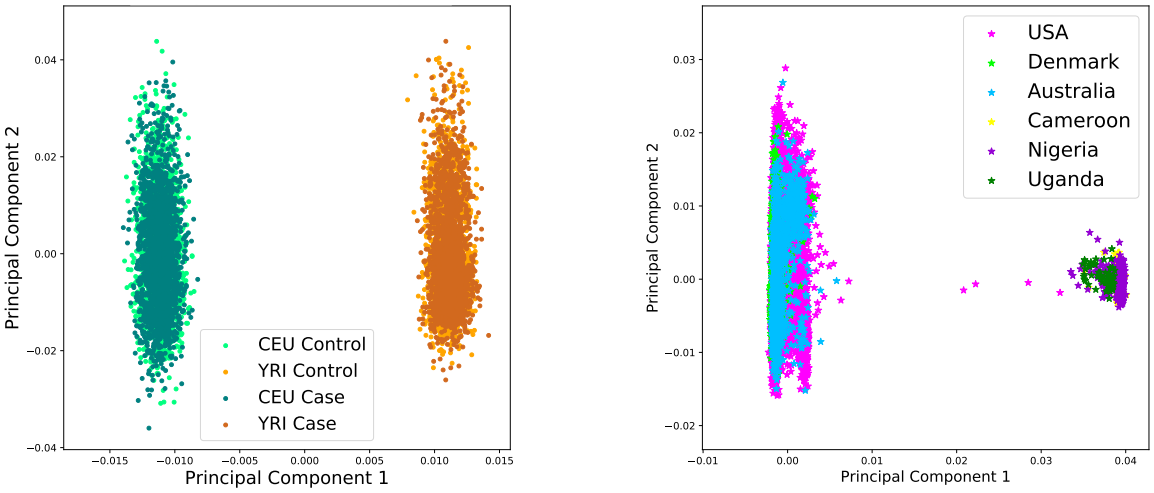
Appendix C. Supplementary Results

Appendix C.1. *PCA of the genotypes*

Figure C1 shows the genotypes of the simulated data (Figure C1a) and the DRIVE data (Figure C1b) projected on the two first principal components of the data.

Appendix C.2. *Runtimes*

Figure C2 shows the runtimes of the different Lasso methods on simulated data.



(a) Population structure in simulated data (b) Population structure in the DRIVE data

Fig. C1. PCA for simulated and real datasets

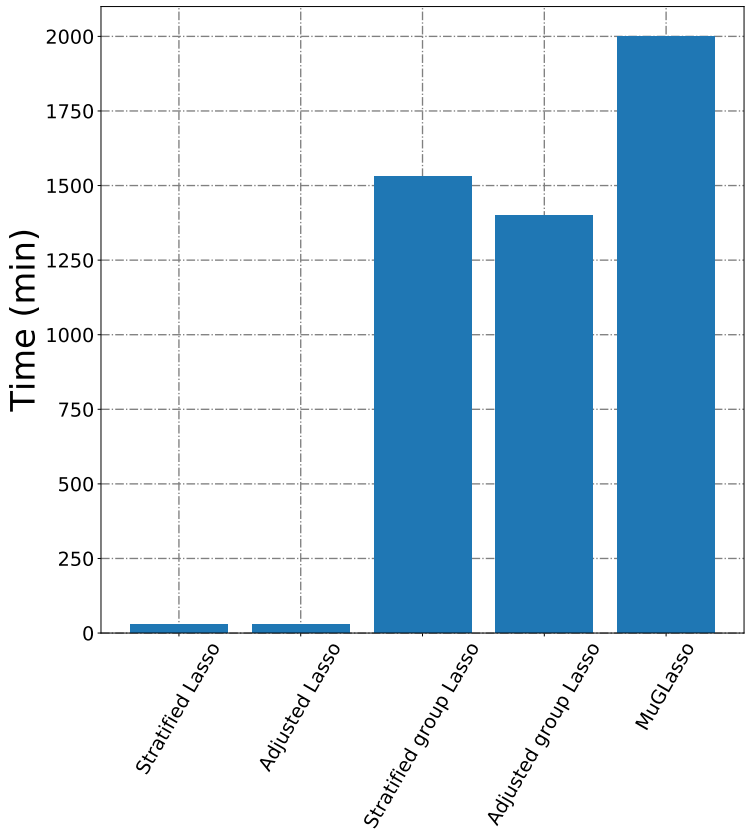


Fig. C2. Runtimes of the different Lasso approaches.

Supplementary References

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