

# The Graph-guided Group Lasso

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# Outline

- 1 Introduction
  - Bioinformatics motivation
  - Penalized regression
  - Incorporating prior knowledge

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- Penalized regression
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## 2 The Graph-guided Group Lasso

- GGGL-1
- GGGL-2
- Estimation algorithms

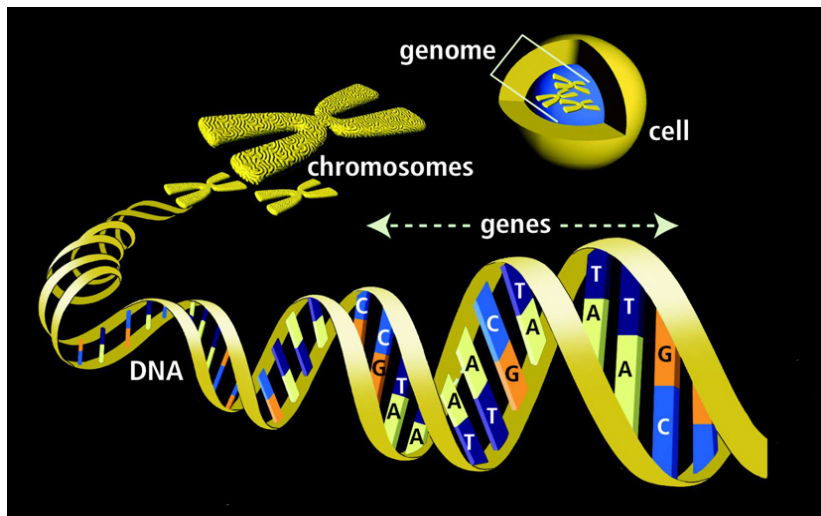
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- 3 Preliminary results

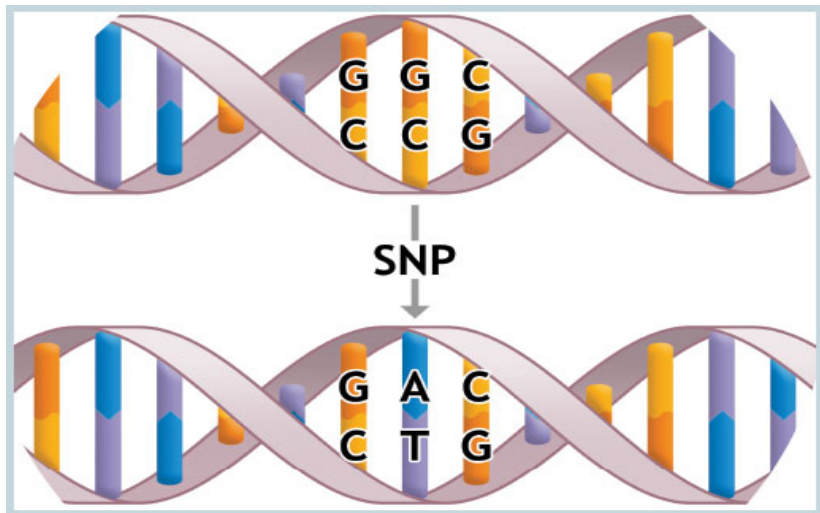
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- 3 Preliminary results
- 4 Future works

# A 30s introduction to the biology



# Single-nucleotide polymorphisms (SNPs)



# Genome-wide association study (GWAs)

<b>Normal</b>	TCTAAGTCCGTATAA AGATTCAAGGCATATT AGATTCAAGGCATATT TCTAAGTCCGTATAA	<b>Green</b>
<b>Carrier</b>	TCTAAGTCCGTATAA AGATTCAAGGCATATT AGATTCAAGCATATT TCTAAGTTCGTATAA	<b>Yellow</b>
<b>Disease</b>	TCTAAGTTCGTATAA AGATTCAAGCATATT AGATTCAAGCATATT TCTAAGTTCGTATAA	<b>Red</b>

Objective: To identify **important** predictors (e.g. SNPs), that account for the variability of a quantitative trait.



# Notation

- $X$ :  $n \times p$  predictor matrix containing  $n$  observations on  $p$  covariates.
- $y$ :  $n$  observations on univariate continuous response.
- $\beta$ :  $p \times 1$  coefficient matrix.
- $\epsilon$ :  $n \times 1$  matrix.  $\mathbb{E}(\epsilon_i) = 0, \forall i$ .

Use linear regression model:

$$y = X\beta + \epsilon$$

where  $X$  and  $y$  are columnwise centered, such that the intercept term can be dropped.

# Sparse solution

Note:

$$\hat{\beta}_i = 0 \Leftrightarrow X_i \text{ is excluded from the model}$$

Thus, if there are only a handful of  $i$  such that:  $\hat{\beta}_i \neq 0$ , then the set:

$$\{X_i : \hat{\beta}_i \neq 0\}$$

corresponds to the set of “important” predictors (causal SNPs).

# Penalized linear regression

An ordinary least square estimate minimizes:

$$\|y - X\beta\|_2^2$$

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A **penalized** linear regression estimate minimizes:

$$\|y - X\beta\|_2^2 + P(\beta)$$

where  $P(\beta)$  is called “the penalty term”.

# Some notable penalties that impose sparsity

Lasso:

$$P(\beta) = \lambda \cdot \|\beta\|_1$$

Elastic-net:

$$P(\beta) = \lambda_1 \cdot \|\beta\|_2 + \lambda_2 \cdot \|\beta\|_1$$

# Incorporating prior biological knowledge - Variable grouping

- Multiple SNPs from one gene often jointly carry out genetic functionalities.

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<sup>1</sup>Association screening of common and rare genetic variants by penalized regression. (*Bioinformatics* 26(19): 2375-2382. 2010.)

<sup>2</sup>Identifying quantitative trait loci via group-sparse multitask regression and feature selection: an imaging genetics study of the ADNI cohort. (*Bioinformatics* 28(2): 229-237. 2012.)

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- Desired sparsity pattern:

$$\hat{\beta} = (\underbrace{[0.2, 0, 0]}_{\text{group 1}}, \underbrace{[0, 0, 0, \dots, 0]}_{\text{group 2}}, \underbrace{[0, 0.5, 0, 0, 0, 0.1]}_{\text{group 3}}, \dots)$$

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- e.g. Zhou *et al.*<sup>1</sup>, H. Wang *et al.*<sup>2</sup>


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- Genes belonging to the same pathway are often expressed similarly in response.


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# Incorporating prior knowledge at multiple levels

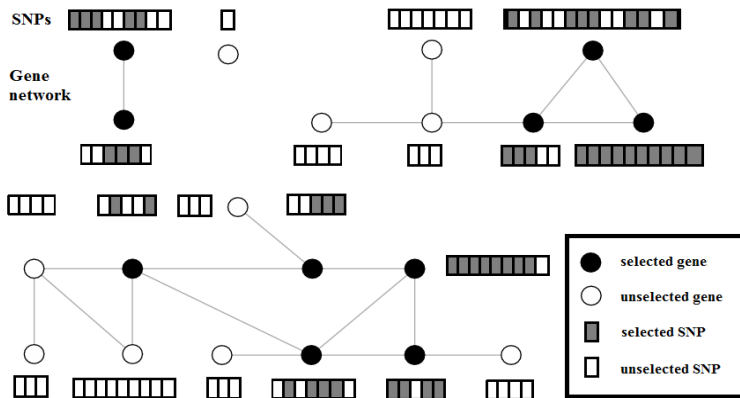

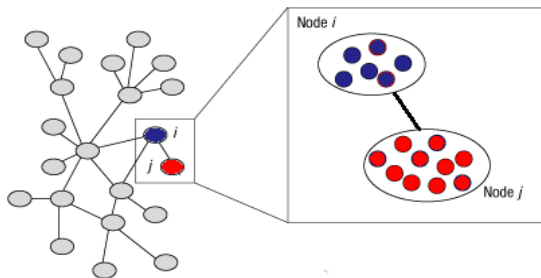


Figure : Sparsity pattern of the proposed “Graph-guided Group Lasso” (GGGL) 



# The between-group relations



**Figure :** The key part of GGGL: How to incorporate information at heterogeneous levels

# Notation

- $X, y, \beta$  as defined before. Further require the columns of  $X$  to have Euclidean norm 1.
- Let  $\mathcal{R} = \{R_1, R_2, \dots\}$  be a **partition** of the predictors. Denote the size of  $R_l$  by  $|R_l|$ , the the  $n \times |R_l|$  sub-matrix of  $X$  by  $X_l$ , and the  $i^{th}$  column of  $X$  by  $X_i$
- Let  $\mathcal{G} = \mathcal{G}(V, E)$  be the given network whose vertex set  $V$  corresponds to the groups in  $\mathcal{R}$ . The weight of the edge  $K - L$  is denoted by  $w_{KL}$  (*w.l.o.g.*  $w_{KL} \geq 0$ ), which can be either binary or continuous.

# GGGL-1: Illustration

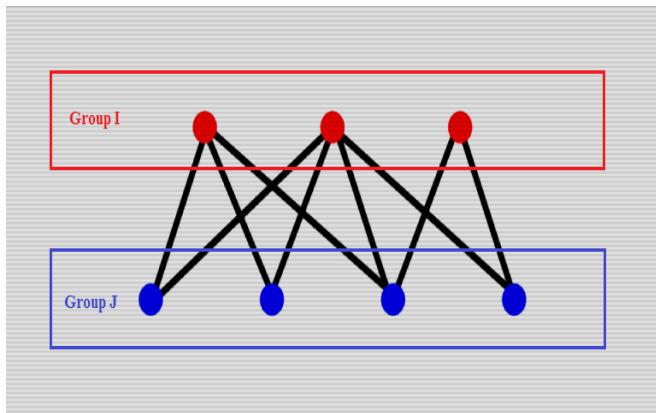


Figure : GGGL-1: If  $R_I \sim R_J$ , then reformulate a complete bipartite graph with vertex sets  $R_I$  and  $R_J$ . Edge weights  $w_{ij} = W_{IJ} \forall i \in R_I, \forall j \in R_J$ .

# GGGL-1: The model

GGGL-1 minimizes the following objective function on  $\beta$ :

$$\frac{1}{2} \|y - X\beta\|_2^2 + P_1(\beta) + P_2(\beta) + P_3(\beta)$$

where:

$$P_1(\beta) = \lambda_1 \sum_{I: R_I \in \mathcal{R}} \sqrt{|R_I|} \cdot \|\beta_I\|_2, \quad P_2(\beta) = \lambda_2 \cdot \|\beta\|_1$$

$$P_3(\beta) = \frac{1}{2} \mu \sum_{i \in R_I, j \in R_J, I \sim J} w_{IJ} (\beta_i - \beta_j)^2$$

## GGGL-1: Smoothing effect

## Proposition (1)

For fixed  $\mu$ , let  $\hat{\beta}$  be the vector that minimizes:

$$\|y - X\beta\|_2^2 + \mu \sum_{k,l: X_k \in R_K, X_l \in R_L} w_{KL} (\beta_k - \beta_l)^2$$

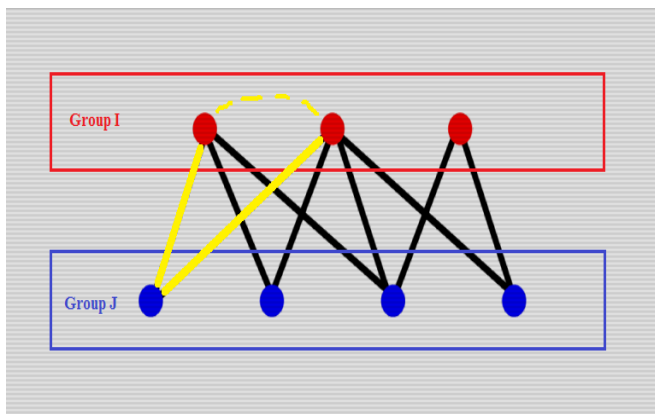
Define the following:

$$\rho_{ij} = X_i' X_j, \quad C_I = \sum_{K \sim I} w_{IK} |R_K|, \quad \Gamma_I = \frac{\sum_{k \in R_K, K \sim I} w_{IK} \hat{\beta}_k}{C_I}$$

Then:

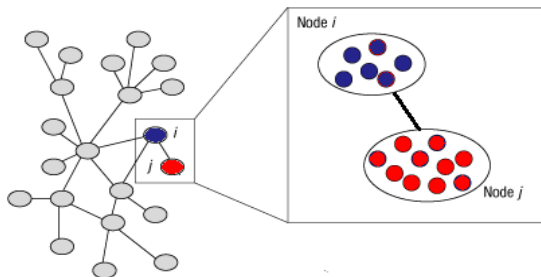
$$|(\hat{\beta}_i - \hat{\beta}_j) - (\Gamma_I - \Gamma_J)| \leq \frac{\|y\|_2}{\mu} \left( \frac{\sqrt{2(1 - \rho_{ij})}}{C_I} + \left| \frac{1}{C_I} - \frac{1}{C_J} \right| \right)$$

# GGGL-1: A potential side effect



**Figure :** GGGL-1: Smoothing the coefficients of variables belonging to the same group may be undesirable.

# GGGL-2: Another interpretation



**Figure :** GGGL-2: encourage connected groups to be selected together  $\neq$  every pair of variables should be encouraged to be selected together

## GGGL-2: The model

In the objective function of GGGL-1,  $P_3(\beta)$  is taken as:

$$P_3(\beta) = \frac{1}{2} \mu \sum_{i \in R_I, j \in R_J, I \sim J} w_{IJ} (\beta_i - \beta_j)^2$$

For GGGL-2, replace it by:

$$P_3(\beta) = \frac{1}{2} \mu \cdot \sum_{I \sim J} w_{IJ} (\bar{\beta}_I - \bar{\beta}_J)^2$$

where  $\bar{\beta}_I = \frac{1}{|R_I|} \sum_{i: i \in R_I} \beta_i$



## GGGL-2: The model

In the objective function of GGGL-1,  $P_3(\beta)$  is taken as:

$$P_3(\beta) = \frac{1}{2} \mu \sum_{i \in R_l, j \in R_J, l \sim J} w_{IJ} (\beta_i - \beta_j)^2$$

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where  $\bar{\beta}_l = \frac{1}{|R_l|} \sum_{i: i \in R_l} \beta_i$

With constraint:  $\beta_i \geq 0, \forall i$ .

## GGGL-2: Smoothing effect

## Proposition (2)

For fixed  $\mu$ , let  $\hat{\beta}$  be the vector that minimises:

$$\|y - X\beta\|_2^2 + \mu \sum_{K \sim L} w_{KL} (\bar{\beta}_K - \bar{\beta}_L)^2$$

Let  $d_I$  be the vertex degree of group  $R_I$  in  $\mathcal{G}$  and define:

$$\Theta_I = \sum_{K \sim I} \frac{w_{IK}}{d_I} \bar{\beta}_K, \quad D_\mu(I, J) = |(\bar{\beta}_I - \bar{\beta}_J) - (\Theta_I - \Theta_J)|$$

Then:

$$D_\mu(I, J) \leq \frac{\|y\|_2}{\mu} \left( \frac{2|R_I|}{d_I} + \left| \frac{|R_I|}{d_I} - \frac{|R_J|}{d_J} \right| \right)$$

# GGGL-2: Within-group effect

## Corollary (3)

Assuming  $X_i$  and  $X_j$  belong to the same group and defining the partial residual  $\hat{r}_{ij} = y - \sum_{k \neq i, j} X_k \hat{\beta}_k$ , the estimated coefficients  $\hat{\beta}$  satisfy:

$$|\hat{\beta}_i - \hat{\beta}_j| = \frac{|(X_i' - X_j')\hat{r}_{ij}|}{1 - \rho_{ij}}$$

# Comparison: GGGL-1 and GGGL-2 smoothing effect

GGGL-1 penalty:

$$P(\beta) = \lambda_1 \sum_{I:R_I \in \mathcal{R}} \sqrt{|R_I|} \cdot \|\beta_I\|_2 + \frac{1}{2} \mu \sum_{i \in R_I, j \in R_J, I \sim J} w_{IJ} (\beta_i - \beta_j)^2$$

GGGL-2 penalty:

$$P(\beta) = \lambda_1 \sum_{I:R_I \in \mathcal{R}} \sqrt{|R_I|} \cdot \|\beta_I\|_2 + \frac{1}{2} \mu \cdot \sum_{I \sim J} w_{IJ} (\bar{\beta}_I - \bar{\beta}_J)^2$$

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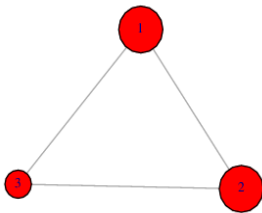
Tune  $\lambda_1$  so that both models select the same number of groups.  
Tune  $\mu$  such that  $\sum_{I \sim J} w_{IJ} (\bar{\beta}_I - \bar{\beta}_J)^2$  are about equal for both models.

# Data generation: key settings

$n = 200$ ,  $p = 60$ , partitioned into 6 equal groups

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$n = 200$ ,  $p = 60$ , partitioned into 6 equal groups  
Specified network:



Groups containing true predictors



Noise groups

# Comparison: small $\mu$ for GGGL-1

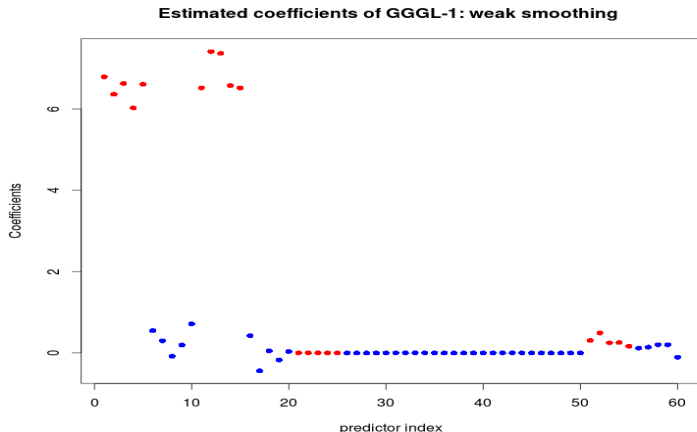


Figure : Red dots represent true variables, blue dots represent noise variables.



# Comparison: large $\mu$ for GGGL-1

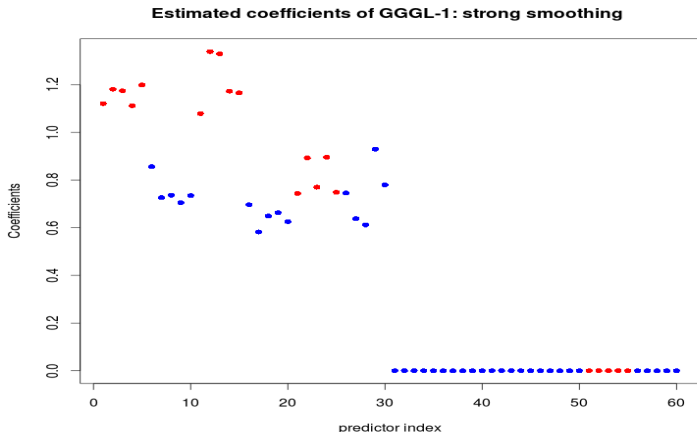


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# Comparison: small $\mu$ for GGGL-2

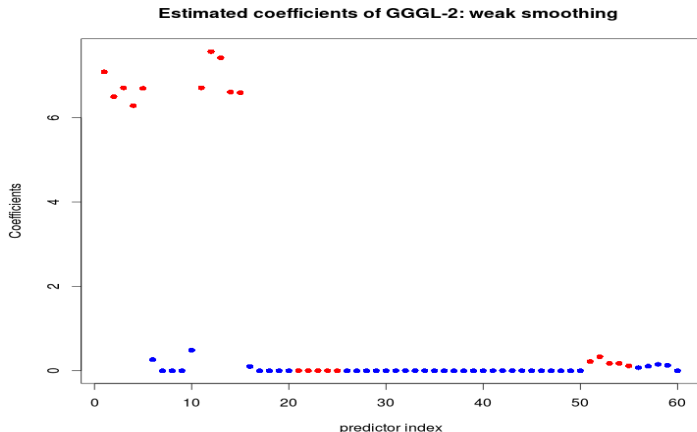


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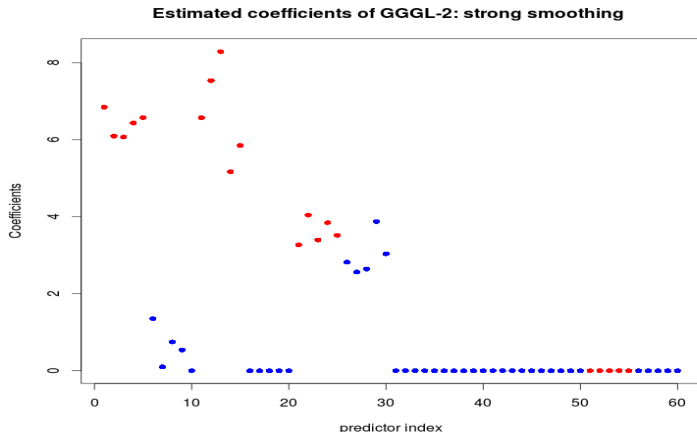


Figure : Red dots represent true variables, blue dots represent noise variables.

# Estimation algorithm: GGGL-1

Note:

$$\sum_{i \in R_l, j \in R_J, l \sim J} w_{lJ} (\beta_i - \beta_j)^2 = \sum_{i \leq j} w_{ij} (\beta_i - \beta_j)^2$$

where  $w_{ij}$  is defined as:

$$w_{ij} = \begin{cases} 0 & \text{if } X_i \text{ and } X_j \text{ belongs to the same group} \\ w_{lJ} & \text{if } X_i \in R_l, X_j \in R_J \neq R_l \end{cases}$$

# Estimation algorithm: GGGL-1

Note:

$$\sum_{i \in R_l, j \in R_j, l \sim j} w_{lj} (\beta_i - \beta_j)^2 = \sum_{i \leq j} w_{ij} (\beta_i - \beta_j)^2$$

where  $w_{ij}$  is defined as:

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Let  $L$  be a  $p \times p$  matrix whose  $(i, j)$ th entry is:

$$(L)_{ij} = \begin{cases} \sum_{j \neq i} w_{ij} & \text{if } i = j \\ -w_{ij} & \text{if } i \neq j \end{cases}$$

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Using  $L$ , the right hand side can be re-formulated into:

$$\sum_{i \leq j} w_{ij} (\beta_i - \beta_j)^2 = \beta' L \beta$$

# Estimation algorithm: GGGL-1

Up to this point, we have:

$$\|y - X\beta\|_2^2 + \mu \sum_{i \in R_l, j \in R_j, l \sim j} w_{lj} (\beta_i - \beta_j)^2 = \|y - X\beta\|_2^2 + \mu \beta' L \beta$$

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Note  $L$  is positive semi-definite, therefore we can find  $p \times p$  matrix  $U$  such that:  $L = UU'$ , using singular value decomposition. We then construct the  $(n + p) \times 1$  matrix  $y^*$  and the  $(n + p) \times p$  matrix  $X^*$  according to:

$$y^* = \begin{pmatrix} y_{n \times 1} \\ 0_{p \times 1} \end{pmatrix}, \quad X^* = \begin{pmatrix} X \\ \sqrt{\mu}U' \end{pmatrix}$$



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$$y^* = \begin{pmatrix} y_{n \times 1} \\ 0_{p \times 1} \end{pmatrix}, \quad X^* = \begin{pmatrix} X \\ \sqrt{\mu} U' \end{pmatrix}$$

Therefore the optimization problem of GGGL-1 is equivalent to:

$$\|y^* - X^* \beta\|_2^2 + 2\lambda_1 \sum_{l: R_l \in \mathcal{R}} \sqrt{|R_l|} \|\beta_l\|_2 + 2\lambda_2 \|\beta\|_1$$

# Estimation algorithm: GGGL-2

Note:

$$\sum_{I \sim J} w_{IJ} (\bar{\beta}_I - \bar{\beta}_J)^2 = \beta' \mathcal{L} \beta$$

where  $\mathcal{L}$  is defined as:

$$(\mathcal{L})_{ij} = \begin{cases} \sum_{\{K: K \sim I\}} \frac{w_{IK}}{|R_I|^2} & \text{if } X_i \in R_I, X_j \in R_I \\ -\frac{w_{IJ}}{|R_I| \cdot |R_J|} & \text{if } X_i \in R_I, X_j \in R_J \end{cases}$$

# Estimation algorithm: GGGL-2

Note:

$$\sum_{I \sim J} w_{IJ} (\bar{\beta}_I - \bar{\beta}_J)^2 = \beta' \mathcal{L} \beta$$

where  $\mathcal{L}$  is defined as:

$$(\mathcal{L})_{ij} = \begin{cases} \sum_{\{K: K \sim I\}} \frac{w_{IK}}{|R_I|^2} & \text{if } X_i \in R_I, X_j \in R_I \\ -\frac{w_{IJ}}{|R_I| \cdot |R_J|} & \text{if } X_i \in R_I, X_j \in R_J \end{cases}$$

Both optimization problems can be solved using standard block coordinate descent algorithm.

# Parallel computation: outline

- For large scale data analysis it is necessary to **parallelize**.
- In each step, update a subset of the groups in parallel.
- An application of Richtarik and Takac <sup>4</sup>
- Code written in CUDA, to run on graphics processing units (GPUs).
- On a data set where  $n = 3000$ ,  $p = 2000$  partitioned into 200 groups, we observed a larger than  $10\times$  speed-up compared with the non-parallel algorithm written in C.

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<sup>4</sup>Parallel coordinate descent methods for big data optimization.

(*arXiv:1212.0873*, 2012.)

# Parallel computation: outline

## Parallel Coordinate Descent Method

Input: Data, parameters,  $m$  groups to update in each step.

Output: column vector  $\hat{\beta}$

- 1 Choose initial estimate  $\hat{\beta}^{(0)}$ .
- 2  $k \leftarrow 1$
- 3 Randomly pick a set of blocks from  $\mathcal{R}$ :  $k_1, k_2, \dots, k_m$ .
- 4 In parallel do:  $\hat{\beta}_{R_{k_m}}^{(k+1)} \leftarrow \phi(\hat{\beta}^{(k)}, k_m)$ , for  $m = 1, 2, \dots$
- 5 Collect estimates from the processors to obtain  $\hat{\beta}^{(k+1)}$ .
- 6 Set  $k \leftarrow k + 1$  and go back to 3 until convergence.

$\phi$  is defined so that at each step:  $\mathbb{E}[F(\hat{\beta}^{(k+1)}) | \hat{\beta}^{(k)}] \leq \mathbb{E}[F(\hat{\beta}^{(k)})]$ ,  
where  $F$  is the objective function.

# Preliminary results

Data generation:

- $n = 200$ ,  $p = 800$ , fixed grouping of  $X$ 's into 80 groups.  
 $X \sim \mathcal{N}(0, \Sigma)$ .
- All predictors in  $R_1, \dots, R_{40}$  are true variables, all predictors in the other groups are noise variables.
- Compute  $y = X\beta + \delta \cdot \epsilon$ , where  $\beta_i$ 's are independently generated from  $\text{uniform}(0.5, 1)$  distribution for true variables.  $\epsilon_i$ 's are *i.i.d.* standard normal *RVs*,  $\delta$  controls signal-to-noise level to 1.
- $X$  is columnwise normalized and  $y$  is centered.

# Networks for GGGL

We categorize the networks into 3 types, according to their relevance to the study:

- **informative**: true variables are connected (not necessarily in one component though) whereas there are very few links between true variables and noise variables.
- **uninformative**: all pairs of variables are connected with roughly equal probabilities.
- **noisy**: true variables and noise variables form an almost bipartite graph and the true variables are rarely linked.

# Illustration of networks

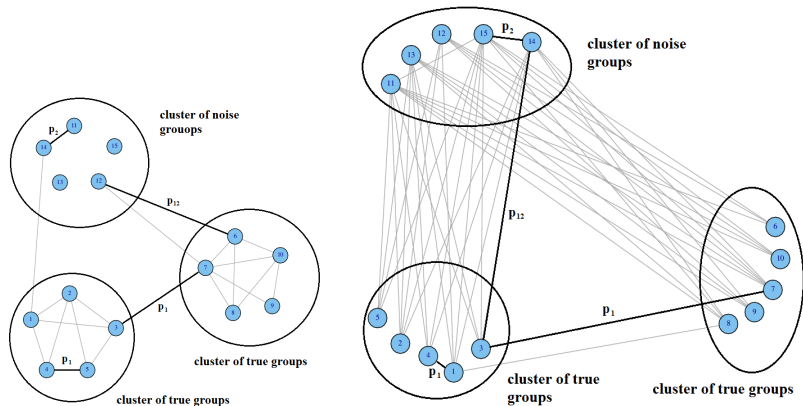


Figure : Left: informative network; Right: noisy network.



## Experiment design: GGGL-1 vs Group lasso

Repeat for 200 data sets:

- Generate random network with probabilities of connection:  $p_1 = 0.7$  (between true groups),  $p_{12} = 0.01$  (between a true group and a noise group),  $p_2 = 0.1$  (between noise groups).
- Fix  $\mu = 50$  and  $\lambda_2 = 0$  in GGGL-1. So the GGGL-1 penalty becomes:

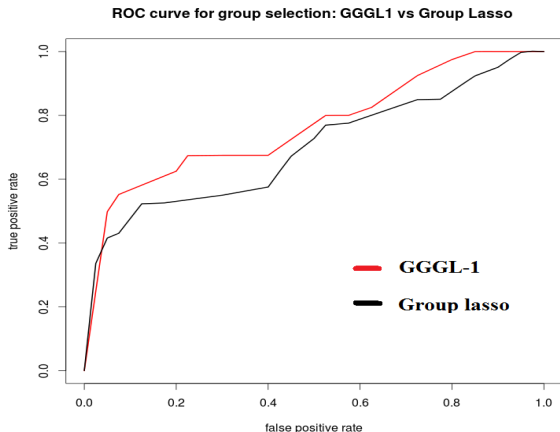
$$P(\beta) = \lambda_1 \sum_{l:R_l \in \mathcal{R}} \sqrt{|R_l|} \cdot \|\beta_l\|_2 + \frac{1}{2} \mu \sum_{i \in R_l, j \in R_{l'}, l \sim l'} w_{ll'} (\beta_i - \beta_j)^2$$

with  $\mu = 10$ , and the group lasso penalty is simply when  $\mu = 0$ .

- Tune  $\lambda_1$  so that both models select exactly 40 groups.

Rank the groups according to selection frequencies for each model, and compare using the receiver operating characteristic (ROC) curves.

# GGGL-1 vs Group lasso



**Figure :** Comparison of GGGL-1 and Group lasso on group selection using ROC curves, where GGGL-1 shows superior power.

# Future works

- Complete simulation study on GGGL-2
- Study the performance of GGGL models on the three types of networks.
- Application to tumor data set.

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