Inferring multiple graph structures

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jointly with Christophe Ambroise, Camille Charbonnier,
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Inferring multiple graphical structures.

Chiquet, Grasseau, Charbonnier and Ambroise,
New release of R-package SIMoNe.

http://stat.genopole.cnrs.fr/softwares/simone
Problem

few arrays ⇔ few examples
lots of genes ⇔ high dimension
interactions ⇔ very high dimension

Inference

Which interactions?

The main trouble is the **low sample size and high dimensional setting**

Our main hope is to benefit from **sparsity**: few genes interact
Handling the scarcity of data

Merge several experimental conditions
experiment 1  experiment 2  experiment 3

Inferring multiple graph structures
Handling the scarcity of data

Inferring each graph **independently** does not help

experiment 1

\[
(X_1^{(1)}, \ldots, X_{n_1}^{(1)})
\]

inference

\[
(X_1^{(2)}, \ldots, X_{n_2}^{(2)})
\]

inference

\[
(X_1^{(3)}, \ldots, X_{n_3}^{(3)})
\]

inference

Inferring multiple graph structures
Handling the scarcity of data

By pooling all the available data

experiment 1

experiment 2

experiment 3

\((X_1, \ldots, X_n), n = n_1 + n_2 + n_3.\)

inference

Inferring multiple graph structures
Handling the scarcity of data

experiment 1

\[(X_1^{(1)}, \ldots, X_{n_1}^{(1)})\]

↓

inference

experiment 2

\[(X_1^{(2)}, \ldots, X_{n_2}^{(2)})\]

↓

inference

experiment 3

\[(X_1^{(3)}, \ldots, X_{n_3}^{(3)})\]

↓

inference

Inferring multiple graph structures
Handling the scarcity of data

By breaking the separability

experiment 1

\[ (X_1^{(1)}, \ldots, X_{n_1}^{(1)}) \]

experiment 2

\[ (X_1^{(2)}, \ldots, X_{n_2}^{(2)}) \]

experiment 3

\[ (X_1^{(3)}, \ldots, X_{n_3}^{(3)}) \]

Inferring multiple graph structures
Handling the scarcity of data

By breaking the separability

experiment 1

\[
\begin{align*}
(X_1^{(1)}, & \ldots, X_{n_1}^{(1)}) \\
\downarrow & \\
\text{inference} & \\
\end{align*}
\]

experiment 2

\[
\begin{align*}
(X_1^{(2)}, & \ldots, X_{n_2}^{(2)}) \\
\downarrow & \\
\text{inference} & \\
\end{align*}
\]

experiment 3

\[
\begin{align*}
(X_1^{(3)}, & \ldots, X_{n_3}^{(3)}) \\
\downarrow & \\
\text{inference} & \\
\end{align*}
\]

Inferring multiple graph structures
Outline

Statistical model

Multi-task learning

Geometrical insights

Optimization strategy

Theoretical results

Experiments
Outline

Statistical model

Multi-task learning

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Theoretical results

Experiments
Gaussian graphical modeling

Let

- \( X = (X_1, \ldots, X_p) \sim \mathcal{N}(0_p, \Sigma) \) and assume \( n \) i.i.d. copies of \( X \),
- \( X \) be the \( n \times p \) matrix whose \( k \)th row is \( X_k \),
- \( \Theta = (\theta_{ij})_{i,j \in \mathcal{P}} \triangleq \Sigma^{-1} \) be the concentration matrix.

Graphical interpretation

Since \( \text{cor}_{ij|\mathcal{P}\backslash\{i,j\}} = -\frac{\theta_{ij}}{\sqrt{\theta_{ii}\theta_{jj}}} \) for \( i \neq j \),

\[
X_i \perp \perp X_j|X_{\mathcal{P}\backslash\{i,j\}} \iff \begin{cases} 
\theta_{ij} = 0 \\
\text{or} \\
\text{edge } (i, j) \notin \text{ network.}
\end{cases}
\]

\( \Rightarrow \) non zeroes in \( \Theta \) describes the graph structure.
The model likelihood

Let $S = n^{-1}X^\top X$ be the empirical variance-covariance matrix: $S$ is a sufficient statistic for $X$ $\Rightarrow \mathcal{L}(\Theta; X) = \mathcal{L}(\Theta; S)$

The log-likelihood

$$\mathcal{L}(\Theta; S) = \frac{n}{2} \log \det(\Theta) - \frac{n}{2} \text{trace}(S\Theta) - \frac{n}{2} \log(2\pi).$$

The MLE of $\Theta$ is $S^{-1}$

- not defined for $n < p$
- not sparse $\Rightarrow$ fully connected graph
Penalized Approaches

Penalized Likelihood (Banerjee et al., 2008)

\[
\maximize_{\Theta \in S_+} \mathcal{L}(\Theta; S) - \lambda \|\Theta\|_1
\]

- well defined for \( n < p \)
- sparse \( \Rightarrow \) sensible graph
- SDP of size \( \mathcal{O}(p^2) \) (solved by Friedman et al., 2007)

Neighborhood Selection (Meinshausen & Bühlman, 2006)

\[
\hat{\beta} = \arg\min_{\beta \in \mathbb{R}^{p-1}} \frac{1}{n} \| X_j - X_{\setminus j} \beta \|_2^2 + \lambda \|\beta\|_1
\]

where \( X_j \) is the \( j \)th column of \( X \) and \( X_{\setminus j} \) is \( X \) deprived of \( X_j \)

- not symmetric, not positive-definite
- \( p \) independent LASSO problems of size \( (p - 1) \)
Penalized Approaches

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Neighborhood vs. Likelihood

Pseudo-likelihood (Besag, 1975)

\[
\mathbb{P}(X_1, \ldots, X_p) \sim \prod_{j=1}^{p} \mathbb{P}(X_j|\{X_k\}_{k \neq j})
\]

\[
\tilde{L}(\Theta; S) = \frac{n}{2} \log \det(D) - \frac{n}{2} \text{trace} \left( SD^{-1} \Theta^2 \right) - \frac{n}{2} \log(2\pi)
\]

\[
L(\Theta; S) = \frac{n}{2} \log \det(\Theta) - \frac{n}{2} \text{trace}(S\Theta) - \frac{n}{2} \log(2\pi)
\]

with \( D = \text{diag}(\Theta) \).

Proposition (Ambroise, Chiquet, Matias, 2008)

Neighborhood selection leads to the graph maximizing the penalized pseudo-log-likelihood

Proof: \( \hat{\beta}_i = -\frac{\hat{\theta}_{ij}}{\hat{\theta}_{jj}} \), where \( \hat{\Theta} = \arg \max_{\Theta} \tilde{L}(\Theta; S) - \lambda \|\Theta\|_1 \)
Neighborhood vs. Likelihood

Pseudo-likelihood (Besag, 1975)

\[ \mathbb{P}(X_1, \ldots, X_p) \approx \prod_{j=1}^{p} \mathbb{P}(X_j | \{X_k\}_{k \neq j}) \]

\[ \tilde{L}(\Theta; S) = \frac{n}{2} \log \det(D) - \frac{n}{2} \text{trace} (SD^{-1} \Theta^2) - \frac{n}{2} \log(2\pi) \]

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Outline

Statistical model

Multi-task learning

Geometrical insights

Optimization strategy

Theoretical results

Experiments
We have \( T \) samples (experimental cond.) of the same variables

- \( X^{(t)} \) is the \( t^{th} \) data matrix, \( S^{(t)} \) is the empirical covariance
- examples are assumed to be drawn from \( \mathcal{N}(0, \Sigma^{(t)}) \)

Ignoring the relationships between the tasks leads to separable objectives

\[
\max_{\Theta^{(t)} \in \mathbb{R}^{p \times p}, t=1..., T} \tilde{\mathcal{L}}(\Theta^{(t)}; S^{(t)}) - \lambda \| \Theta^{(t)} \|_1
\]

Multi-task learning = solving the \( T \) tasks jointly

We may couple the objectives

- through the fitting term term,
- through the penalty term.

Inferring multiple graph structures
Multi-task learning

We have $T$ samples (experimental cond.) of the same variables

- $X^{(t)}$ is the $t^{th}$ data matrix, $S^{(t)}$ is the empirical covariance
- examples are assumed to be drawn from $\mathcal{N}(0, \Sigma^{(t)})$

Ignoring the relationships between the tasks leads to separable objectives

\[
\begin{align*}
\text{maximize} & \quad \hat{L}(\Theta^{(t)}; S^{(t)}) - \lambda \| \Theta^{(t)} \|_1 \\
\Theta^{(t)} & \in \mathbb{R}^{p \times p}, t=1\ldots,T
\end{align*}
\]

Multi-task learning = solving the $T$ tasks jointly

We may **couple** the objectives

- through the **fitting term** term,
- through the **penalty term** term.
Coupling through the fitting term

Intertwined LASSO

\[
\text{maximize} \sum_{t=1}^{T} \tilde{\mathcal{L}}(\Theta^{(t)}; \tilde{S}^{(t)}) - \lambda \|\Theta^{(t)}\|_1
\]

- \(\bar{S} = \frac{1}{n} \sum_{t=1}^{T} n_t S^{(t)}\) is the “pooled-tasks” covariance matrix.
- \(\tilde{S}^{(t)} = \alpha S^{(t)} + (1 - \alpha) \bar{S}\) is a mixture between specific and pooled covariance matrices.

- \(\alpha = 0\) pools the data sets and infers a single graph
- \(\alpha = 1\) separates the data sets and infers \(T\) graphs independently
- \(\alpha = 1/2\) in all our experiments
We group parameters by sets of corresponding edges across graphs:

Graphical group-LASSO

$$\max_{\Theta(t),t,...,T} \sum_{t=1}^{T} \tilde{L} \left( \Theta^{(t)}; S^{(t)} \right) - \lambda \sum_{i \neq j} \left( \sum_{t=1}^{T} \left( \theta_{ij}^{(t)} \right)^2 \right)^{1/2}$$

- Sparsity pattern shared between graphs
- Identical graphs across tasks
We group parameters by sets of corresponding edges across graphs:

**Graphical group-LASSO**

\[
\max_{\Theta(t), t, \ldots, T} \sum_{t=1}^{T} \tilde{L} \left( \Theta^{(t)} ; S^{(t)} \right) - \lambda \sum_{i \neq j} \left( \sum_{t=1}^{T} \left( \theta_{ij}^{(t)} \right)^2 \right)^{1/2}
\]

- Sparsity pattern shared between graphs
- Identical graphs across tasks
Coupling through penalties: group-LASSO

We group parameters by sets of corresponding edges across graphs:

Graphical group-LASSO

\[
\max_{\Theta(t), \ldots, T} \sum_{t=1}^{T} \tilde{L}(\Theta(t); S(t)) - \lambda \sum_{i \neq j} \left( \sum_{t=1}^{T} (\theta_{ij}^{(t)})^2 \right)^{1/2}
\]

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- Sparsity pattern shared between graphs
- Identical graphs across tasks
Coupling through penalties: cooperative-LASSO

- Same grouping, and bet that correlations are likely to be sign consistent
- Gene interactions are either inhibitory or activating across assays

**Graphical cooperative-LASSO**

\[
\max_{\Theta^{(t)}} \sum_{t=1}^{T} \tilde{\mathcal{L}}(S^{(t)}; \Theta^{(t)}) - \lambda \sum_{i \neq j} \left\{ \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]^{2} \right)^{1/2} + \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]^{-} \right)^{1/2} \right\}
\]

where \([u]_{+} = \max(0, u)\) and \([u]_{-} = \min(0, u)\).

- Plausible in many other situations
- Sparsity pattern shared between graphs, which may differ
Efficient coupling through penalties: cooperative-LASSO

- Same grouping, and bet that correlations are likely to be sign consistent
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**Graphical cooperative-LASSO**

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\max_{\Theta(t)} \sum_{t=1}^{T} \tilde{\mathcal{L}}(S(t); \Theta(t)) - \lambda \sum_{i \neq j} \left\{ \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]^2 \right)^{\frac{1}{2}} + \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]_-^2 \right)^{\frac{1}{2}} \right\}
\]

where \([u]_+ = \max(0, u)\) and \([u]_- = \min(0, u)\).

- Plausible in many other situations
- Sparsity pattern shared between graphs, which may differ
Same grouping, and bet that correlations are likely to be **sign** consistent

Gene interactions are either **inhibitory** or **activating** across assays

Graphical cooperative-LASSO

\[
\max_{\Theta^{(t)}} \sum_{t=1}^{T} \tilde{\mathcal{L}}(S^{(t)}; \Theta^{(t)}) - \lambda \sum_{i \neq j} \left\{ \left( \sum_{t=1}^{T} \theta_{ij}^{(t)} \right)^2 + \left( \sum_{t=1}^{T} \theta_{ij}^{(t)} \right)^2 \right\}^{\frac{1}{2}}
\]

where \([u]_+ = \max(0, u)\) and \([u]_- = \min(0, u)\).

- Plausible in many other situations
- Sparsity pattern shared between graphs, which may differ
Coupling through penalties: cooperative-LASSO

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Graphical cooperative-LASSO

$$\max_{\Theta^{(t)}} \sum_{t=1}^{T} \tilde{L}(S^{(t)}; \Theta^{(t)}) - \lambda \sum_{i \neq j} \left\{ \left( \sum_{t=1}^{T} [\theta_{ij}^{(t)}]^2 \right)^{\frac{1}{2}} + \left( \sum_{t=1}^{T} [\theta_{ij}^{(t)}]^2 \right)^{\frac{1}{2}} \right\}$$

where $[u]^+ = \max(0, u)$ and $[u]^− = \min(0, u)$.

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Inferring multiple graph structures
Coupling through penalties: cooperative-LASSO

- Same grouping, and bet that correlations are likely to be sign consistent
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Graphical cooperative-LASSO

\[
\text{maximize } \sum_{t=1}^{T} \tilde{L}(S^{(t)}; \Theta^{(t)}) - \lambda \sum_{i \neq j} \left\{ \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]^{2} \right)^{\frac{1}{2}} + \left( \sum_{t=1}^{T} \left[ \theta_{ij}^{(t)} \right]^{2} \right)^{\frac{1}{2}} \right\}
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where \([u]_+ = \max(0, u)\) and \([u]_- = \min(0, u)\).

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where \( [u]_+ = \max(0, u) \) and \( [u]_- = \min(0, u) \).

- Plausible in many other situations
- Sparsity pattern shared between graphs, which may differ
Outline

Statistical model

Multi-task learning

Geometrical insights

Optimization strategy

Theoretical results

Experiments
A Geometric View of Sparsity
Constrained Optimization

\[
\mathcal{L}(\beta_1, \beta_2) = \max_{\beta_1, \beta_2} \mathcal{L}(\beta_1, \beta_2) - \lambda \Omega(\beta_1, \beta_2)
\]

Inferring multiple graph structures
A Geometric View of Sparsity
Constrained Optimization

\[ \max_{\beta_1, \beta_2} \mathcal{L}(\beta_1, \beta_2) - \lambda \Omega(\beta_1, \beta_2) \]

\[ \iff \begin{cases} 
    \max_{\beta_1, \beta_2} \mathcal{L}(\beta_1, \beta_2) \\
    \text{s.t. } \Omega(\beta_1, \beta_2) \leq c 
\end{cases} \]
A Geometric View of Sparsity
Constrained Optimization

\[
\max_{\beta_1, \beta_2} \mathcal{L}(\beta_1, \beta_2) - \lambda \Omega(\beta_1, \beta_2) \quad \Leftrightarrow \quad \begin{cases} 
\max_{\beta_1, \beta_2} \mathcal{L}(\beta_1, \beta_2) \\
\text{s.t.} \quad \Omega(\beta_1, \beta_2) \leq c
\end{cases}
\]
An hyperplane supports a set iff

- the set is contained in one half-space
- the set has at least one point on the hyperplane
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There are Supporting Hyperplane at all points of convex sets:

Generalize tangents
A Geometric View of Sparsity

Dual Cone

Generalizes normals

Inferring multiple graph structures
A Geometric View of Sparsity
Dual Cone

Generalizes normals

β₂

β₁

β₂

β₁

β₂

β₁

Inferring multiple graph structures
A Geometric View of Sparsity
Dual Cone

Generalizes normals

Inferring multiple graph structures
A Geometric View of Sparsity

Dual Cone

Generalizes normals

Shape of dual cones $\Rightarrow$ sparsity pattern
Group-Lasso balls

Admissible set

- 2 tasks ($T = 2$)
- 2 coefficients ($p = 2$)

Unit ball

$$\sum_{i=1}^{2} \left( \sum_{t=1}^{2} \beta_i^t \right)^{1/2} \leq 1$$
Admissible set
- 2 tasks ($T = 2$)
- 2 coefficients ($p = 2$)

Unit ball
\[
\sum_{i=1}^{2} \left( \sum_{t=1}^{2} \beta_{i}^{(t)} \right)^{1/2} \leq 1
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Group-LASSO balls

Admissible set
- 2 tasks \((T = 2)\)
- 2 coefficients \((p = 2)\)

Unit ball

\[
\sum_{i=1}^{2} \left( \sum_{t=1}^{2} \beta_i(t)^2 \right)^{1/2} \leq 1
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Unit ball

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\sum_{i=1}^{2} \left( \sum_{t=1}^{2} \beta_i(t)^2 \right)^{1/2} \leq 1
\]
Cooperative-LASSO balls

Admissible set
- 2 tasks ($T = 2$)
- 2 coefficients ($p = 2$)

Unit ball

$$\sum_{j=1}^{2} \left( \sum_{t=1}^{2} (\beta_{j}^{(t)})^2 \right)^{1/2} + \sum_{j=1}^{2} \left( \sum_{t=1}^{2} (-\beta_{j}^{(t)})^2 \right)^{1/2} \leq 1$$

$
\beta_1^{(2)} = 0
$

$
\beta_1^{(1)} = 0
$

$
\beta_2^{(2)} = 0.3
$

$
\beta_2^{(1)} = 0
$

$
\beta_2^{(1)} = 0
$
Cooperative-LASSO balls

Admissible set
- 2 tasks \((T = 2)\)
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Unit ball

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\sum_{j=1}^{2} \left( \sum_{t=1}^{2} (\beta_j^{(t)})^2 \right)^{1/2} + \sum_{j=1}^{2} \left( \sum_{t=1}^{2} (-\beta_j^{(t)})^2 \right)^{1/2} \leq 1
\]
Cooperative-LASSO balls

Admissible set
- 2 tasks \((T = 2)\)
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Unit ball
\[
\begin{align*}
\sum_{j=1}^{2} \left( \sum_{t=1}^{2} \left( \beta_j^{(t)} \right)^2 \right)^{1/2} + \\
\sum_{j=1}^{2} \left( \sum_{t=1}^{2} \left( -\beta_j^{(t)} \right)^2 \right)^{1/2} \leq 1
\end{align*}
\]
Cooperative-LASSO balls

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Cooperative-LASSO balls

Admissible set

- 2 tasks ($T = 2$)
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Unit ball

$$\sum_{j=1}^{2} \left( \sum_{t=1}^{2} (\beta_j(t))^2 \right)^{1/2} + \sum_{j=1}^{2} \left( \sum_{t=1}^{2} (-\beta_j(t))^2 \right)^{1/2} \leq 1$$

$\beta_2^{(2)} = 0$

$\beta_2^{(2)} = 0.3$

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Theoretical results

Experiments
Estimate the $j^{th}$ neighborhood of the $T$ graphs

\[
\max_{\Theta^{(t)}, t=1,...,T} \sum_{t=1}^{T} \tilde{\mathcal{L}}(\Theta^{(t)}; S^{(t)}) - \lambda \Omega(K^{(t)})
\]

decomposes into $p$ convex optimization problems of size

\[
\hat{\beta}_j = \arg\min_{\beta \in \mathbb{R}^{T \times (p-1)}} f_j(\beta) + \lambda \Omega(\beta)
\]

where $\hat{\beta}_j$ is a minimizer iff $0 \in \nabla_\beta f_j(\beta) + \lambda \partial_\beta \Omega(\beta)$
Decomposition strategy
Estimate the $j^{\text{th}}$ neighborhood of the $T$ graphs

$$\maximize_{\Theta(t), t=1\ldots,T} \sum_{t=1}^{T} \tilde{\mathcal{L}}(\Theta(t); S(t)) - \lambda \Omega(K^{(t)})$$

decomposes into $p$ convex optimization problems of size

$$\hat{\beta}_j = \argmin_{\beta \in \mathbb{R}^{T \times (p-1)}} f_j(\beta) + \lambda \Omega(\beta)$$

where $\hat{\beta}_j$ is a minimizer iff $0 \in \nabla_{\beta} f_j(\beta) + \lambda \partial_{\beta} \Omega(\beta)$

**Intertwined LASSO:**

$$\Omega(\beta) = \sum_{t=1}^{T} \left\| \beta^{(t)} \right\|_1,$$

where $\beta = (\beta^{(1)}, \ldots, \beta^{(T)})^T, \beta^{(t)} \in \mathbb{R}^{p-1}$
Decomposition strategy
Estimate the $j^{th}$ neighborhood of the $T$ graphs

$$\begin{align*}
\text{maximize} \quad & \sum_{t=1}^{T} \tilde{\mathcal{L}}(\Theta^{(t)}; S^{(t)}) - \lambda \Omega(K^{(t)}) \\
\text{subject to} \quad & \Theta^{(t)}, t=1,\ldots,T
\end{align*}$$

decomposes into $p$ convex optimization problems of size

$$\hat{\beta}_{j} = \arg\min_{\beta \in \mathbb{R}^{T \times (p-1)}} f_{j}(\beta) + \lambda \Omega(\beta)$$

where $\hat{\beta}_{j}$ is a minimizer iff $0 \in \nabla_{\beta} f_{j}(\beta) + \lambda \partial_{\beta} \Omega(\beta)$

**Group-LASSO:**

$$\Omega(\beta) = \sum_{i=1}^{p-1} \left\| \beta_{i}^{[1:T]} \right\|_{2}$$

where $\beta_{i}^{[1:T]}$ is the vector corresponding to the edges $(i, j)$ across graphs

Inferring multiple graph structures
Decomposition strategy

Estimate the \( j \)th neighborhood of the \( T \) graphs

\[
\text{maximize} \sum_{t=1}^{T} \tilde{\mathcal{L}}(\Theta^{(t)}; S^{(t)}) - \lambda \Omega(K^{(t)})
\]

decomposes into \( p \) convex optimization problems of size

\[
\hat{\beta}_j = \arg\min_{\beta \in \mathbb{R}^{T \times (p-1)}} f_j(\beta) + \lambda \Omega(\beta)
\]

where \( \hat{\beta}_j \) is a minimizer iff

\[
0 \in \nabla_{\beta} f_j(\beta) + \lambda \partial_{\beta} \Omega(\beta)
\]

Coop-LASSO:

\[
\Omega(\beta) = \sum_{i=1}^{p-1} \left( \left\| \begin{bmatrix} \beta_i^{[1:T]} \\ -\beta_i^{[1:T]} \end{bmatrix} \right\|_2 + \left\| \begin{bmatrix} \beta_i^{[1:T]} \\ -\beta_i^{[1:T]} \end{bmatrix} \right\|_2 \right)
\]

where \( \beta_i^{[1:T]} \) is the vector corresponding to the edges \((i, j)\) across graphs
Active set algorithm: 👍 yellow belt

// 0. INITIALIZATION $\beta \leftarrow 0, A \leftarrow \emptyset$
while $0 \notin \partial_\beta L(\beta)$ do

// 1. MASTER PROBLEM: OPTIMIZATION WITH RESPECT TO $\beta_A$
Find a solution $h$ to the smooth problem

$$\nabla_h f(\beta_A + h) + \lambda \partial_h \Omega(\beta_A + h) = 0,$$

where $\partial_h \Omega = \{\nabla_h \Omega\}$.

$\beta_A \leftarrow \beta_A + h$

// 2. IDENTIFY NEWLY ZEROED VARIABLES;

$A \leftarrow A \setminus \{i\}$

// 3. IDENTIFY NEW NON-ZERO VARIABLES;
// Select a candidate $i \in A^c$

$$i \leftarrow \arg \max_{j \in A^c} v_j, \text{ where } v_j = \min_{\nu \in \partial_{\beta_j} \Omega} \left| \frac{\partial f(\beta)}{\partial \beta_j} + \lambda \nu \right|$$

Inferring multiple graph structures
Active set algorithm:

// 0. INITIALIZATION $\beta \leftarrow 0$, $A \leftarrow \emptyset$

while $0 \notin \partial_\beta L(\beta)$ do

// 1. MASTER PROBLEM: OPTIMIZATION WITH RESPECT TO $\beta_A$

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where $\partial_h \Omega = \{\nabla_h \Omega\}$.

$\beta_A \leftarrow \beta_A + h$

// 2. IDENTIFY NEWLY ZEROED VARIABLES;

$A \leftarrow A \backslash \{i\}$

// 3. IDENTIFY NEW NON-ZERO VARIABLES;

// Select a candidate $i \in A^c$ which violates the more the optimality conditions

$i \leftarrow \text{arg max}_{j \in A^c} v_j$, where $v_j = \min_{\nu \in \partial_\beta \Omega} \left| \frac{\partial f(\beta)}{\partial \beta_j} + \lambda \nu \right|$

if it exists such an $i$ then

$A \leftarrow A \cup \{i\}$

else

Stop and return $\beta$, which is optimal

end

end
Active set algorithm: 🌿 green belt

// 0. INITIALIZATION $\beta \leftarrow 0, \mathcal{A} \leftarrow \emptyset$

while $0 \notin \partial_\beta L(\beta)$ do

// 1. MASTER PROBLEM: OPTIMIZATION WITH RESPECT TO $\beta_A$

Find a solution $h$ to the smooth problem

$$\nabla_h f(\beta_A + h) + \lambda \partial_h \Omega(\beta_A + h) = 0,$$

where $\partial_h \Omega = \{\nabla_h \Omega\}$.

$\beta_A \leftarrow \beta_A + h$

// 2. IDENTIFY NEWLY ZEROED VARIABLES;

while $\exists i \in \mathcal{A} : \beta_i = 0$ and $\min_{\nu \in \partial_{\beta_i} \Omega} \left| \frac{\partial f(\beta)}{\partial \beta_i} + \lambda \nu \right| = 0$ do

$\mathcal{A} \leftarrow \mathcal{A} \setminus \{i\}$

end

// 3. IDENTIFY NEW NON-ZERO VARIABLES;

// Select a candidate $i \in \mathcal{A}^c$ such that an infinitesimal change of $\beta_i$

provides the highest reduction of $L$

$i \leftarrow \arg \max_{j \in \mathcal{A}^c} v_j$, where $v_j = \min_{\nu \in \partial_{\beta_j} \Omega} \left| \frac{\partial f(\beta)}{\partial \beta_j} + \lambda \nu \right|$

if $v_i \neq 0$ then

$\mathcal{A} \leftarrow \mathcal{A} \cup \{i\}$

else

Stop and return $\beta$, which is optimal

end
Outline

Statistical model

Multi-task learning

Geometrical insights

Optimization strategy

Theoretical results

Experiments
(Sparse) linear regression setup

Let $Y$ be a response variable, $X = (X_1, \ldots, X_p)$ a vector of $p$ features,

$$Y = X\beta^* + \varepsilon = \sum_{j=1}^{p} X_j \beta^*_j + \varepsilon, \quad \varepsilon \sim \mathcal{N}(0, \sigma^2 I),$$

- $S = \{j, \beta^*_j \neq 0\}$ is the true support,
- $\beta^*$ has a group structure $\{G_k\}_{k=1,\ldots,K}$.

Cooperative-Lasso estimate of $\beta^*$

Given the training vector $y = (y_1, \ldots, y_n)^T$ and the $n \times p$ design matrix $X$ whose $j$th column $x_j = (x^1_j, \ldots, x^n_j)^T$,

$$\hat{\beta}^{\text{coop}} = \arg \min_{\beta \in \mathbb{R}^p} \frac{1}{2} \|y - X\beta\|_n^2 + \lambda_n \sum_{k=1}^{K} \|\beta_{G_k}^+\| + \|\beta_{G_k}^-\|.$$
(Sparse) linear regression setup

Let $Y$ be a response variable, $X = (X_1, \ldots, X_p)$ a vector of $p$ features,

$$Y = X\beta^* + \varepsilon = \sum_{j=1}^{p} X_j \beta_j^* + \varepsilon, \quad \varepsilon \sim \mathcal{N}(0, \sigma^2 I),$$

- $S = \{j, \beta_j^* \neq 0\}$ is the true support,
- $\beta^*$ has a group structure $\{G_k\}_{k=1,\ldots,K}$.

Cooperative-Lasso estimate of $\beta^*$

Given the training vector $y = (y_1, \ldots, y_n)^\top$ and the $n \times p$ design matrix $X$ whose $j\text{th}$ column $x_j = (x_j^1, \ldots, x_j^n)^\top$,

$$\hat{\beta}^{\text{coop}} = \arg \min_{\beta \in \mathbb{R}^p} \frac{1}{2} \| y - X\beta \|_n^2 + \lambda_n \sum_{k=1}^{K} \| [\beta_{G_k}]_+ \| + \| [\beta_{G_k}]_- \|. $$
Let $\Psi = \mathbb{E}XX^\top$ be the covariance matrix of $X$.

(A1) $X$ and $Y$ have finite fourth order moments $\mathbb{E}\|X\|^4 < \infty$, $\mathbb{E}\|Y\|^4 < \infty$.

(A2) the covariance matrix $\Psi = \mathbb{E}XX^\top \in \mathbb{R}^{p\times p}$ is invertible.

(A3) for every $k = 1, \ldots, K$, if $\|[\beta^*]_+\| > 0$ and $\|[\beta^*]_-\| > 0$ then for every $j \in G_k$, $\beta^*_j \neq 0$. (There should not be any zero in a group with positive and negative coefficients).
Define $S_k = S \cap G_k$ the support within a group and

$$D(\beta)_{jj} = \|[\text{sign}(\beta_j)\beta_{G_k}]_+\|^{-1}.$$ 

Assume there exists $\eta > 0$ such that

- for every group $k$ to switch off (where $S^c_k = G_k$),

  $$\max(\|[\Psi S^c_k S \Psi^{-1}_S D(\beta^*_S)\beta^*_S]_+\|, \|[\Psi S^c_k S \Psi^{-1}_S D(\beta^*_S)\beta^*_S]_-\|) \leq 1 - \eta,$$

- for every group $k$ with zero coefficients and either positive or negative coefficients, define $\nu_k = 1$ if positive coefficients are activated, $\nu_k = -1$ otherwise, and require

  $$\begin{cases}
  \nu_k \Psi S^c_k S \Psi^{-1}_S D(\beta^*_S)\beta^*_S \leq 0 \text{ component-wise} \\
  \|\Psi S^c_k S \Psi^{-1}_S D(\beta^*_S)\beta^*_S\| \leq 1 - \eta.
  \end{cases}$$
Consistency results

Theorem (Chiquet, Grandvalet, Charbonnier, in progress!)

If assumptions (A1-3) are satisfied and if there exists $\eta > 0$, then for every sequence $\lambda_n$ such that $\lambda_n = \lambda_0 n^{-\gamma}$, $\gamma \in ]0, 1/2[$,

$$
\hat{\beta}^{\text{coop}} \xrightarrow{P} \beta^* \quad \text{and} \quad \mathbb{P}(S(\hat{\beta}^{\text{coop}}) = S) \to 1.
$$

Asymptotically, the cooperative-Lasso is unbiased and enjoys exact support recovery (even when there are irrelevant variables within a group $G_k$).
Outline

Statistical model

Multi-task learning

Geometrical insights

Optimization strategy

Theoretical results

Experiments
Data Generation

We set

- the number of nodes $p$
- the number of edges $K$
- the number of examples $n$

Process

1. Generate a random adjacency matrix with $2K$ off-diagonal terms
2. Compute the normalized Laplacian $L$
3. Generate a symmetric matrix of random signs $R$
4. Compute the concentration matrix $\Theta^*_ij = L_{ij} R_{ij}$
5. Compute $\Sigma^*$ by pseudo-inversion of $\Theta^*$
6. Generate correlated Gaussian data $\sim \mathcal{N}(0, \Sigma^*)$
Simulating Related Tasks

Generate

1. an “ancestor” with $p = 20$ nodes and $K = 20$ edges
2. $T = 4$ children by adding and deleting $\delta$ edges
3. $T = 4$ Gaussian samples

Figure: ancestor and children with $\delta = 2$ perturbations
Simulating Related Tasks

Generate

1. an “ancestor” with $p = 20$ nodes and $K = 20$ edges
2. $T = 4$ children by adding and deleting $\delta$ edges
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Figure: ancestor and children with $\delta = 2$ perturbations
Simulating Related Tasks

Generate
1. an “ancestor” with \( p = 20 \) nodes and \( K = 20 \) edges
2. \( T = 4 \) children by adding and deleting \( \delta \) edges
3. \( T = 4 \) Gaussian samples

Figure: ancestor and children with \( \delta = 2 \) perturbations
Precision/Recall curve

precision = TP/(TP+FP)
recall = TP/P (power)
Simulation results
large sample size

penalty: $\lambda_{\text{max}} \rightarrow 0$

**Figure:** $n_t = 100$, $\delta = 1$
Simulation results

large sample size

penalty: $\lambda_{\text{max}} \rightarrow 0$

Figure: $n_t = 100, \delta = 3$
Simulation results
large sample size

Figure: $n_t = 100, \delta = 5$
Simulation results

medium sample size

Figure: $n_t = 50, \delta = 1$
Simulation results
medium sample size

penalty: $\lambda_{\text{max}} \rightarrow 0$

Figure: $n_t = 50, \delta = 3$
Simulation results
medium sample size

Figure: \( n_t = 50, \delta = 5 \)
Simulation results
small sample size

Figure: $n_t = 25$, $\delta = 1$
Simulation results for small sample size

Figure: $n_t = 25, \delta = 3$
Simulation results

small sample size

Figure: $n_t = 25, \delta = 5$
Two types of patients
Patient response can be classified either as
1. pathologic complete response (PCR)
2. residual disease (not PCR)

Gene expression data
- 133 patients (99 not PCR, 34 PCR)
- 26 identified genes (differential analysis)
Inferring multiple graph structures
Defining a robust biological prior from Pathway Analysis to drive Network Inference

Marine will speak at SMPGD ’11 😊

“Due to the vast space of possible networks and the relatively small amount of data available, inferring genetic networks from gene expression data is one of the most challenging work in the post-genomic era. (...) We propose an original approach for inferring gene regulation network using a robust biological prior on structure in order to limit the set of candidate networks.”
To sum-up

- Clarified links between neighborhood selection and graphical LASSO
- Identified the relevance of Multi-Task Learning in network inference
- First methods for inferring multiple Gaussian Graphical Models
- Consistent improvements upon the available baseline solutions
- Available in the R package SIMoNe
Issues

1. How can we choose for a unique network? (should we?)
   - Explore model-selection capabilities,
   - Network comparison.

2. Robustness
   - Test the validity of an edge? Of a whole motif?
   - Bootstrap greatly improves the inference but is computationally intensive,
   - Introduce more biological prior (semi-supervised learning).

3. Biological studies
   - Breast cancer (Marine),
   - Parkinson (with J.-C. Corvol, Pitié Salpétrière and Camille),
   - Bacillus subtilis and Staphylococcus aureus (ANR NOUGA déposée: heterogeneous data, RNAseq, new, prior etc.).

Coop-Lasso
Theoretical analysis and other applications in genetics with penalized linear / logistic regression.
Model selection

More details on optimisation
Theory based penalty choices

1. Optimal order of penalty in the $p \gg n$ framework: $\sqrt{n \log p}$
   
   *Bunea et al. 2007, Bickel et al. 2009*

2. Control on the probability of connecting two distinct connectivity sets


   $\Rightarrow$ practically much too conservative

Cross-validation

- Optimal in terms of *prediction*, not in terms of selection
- Problematic with small samples: changes the sparsity constraint due to sample size
Theorem (Zou et al. 2008)

\[ \text{df}(\hat{\beta}_\lambda^{\text{lasso}}) = \left\| \hat{\beta}_\lambda^{\text{lasso}} \right\|_0 \]

Straightforward extensions to the graphical framework

\[ \text{BIC}(\lambda) = \mathcal{L}(\hat{\Theta}_\lambda; X) - \text{df}(\hat{\Theta}_\lambda) \frac{\log n}{2} \]

\[ \text{AIC}(\lambda) = \mathcal{L}(\hat{\Theta}_\lambda; X) - \text{df}(\hat{\Theta}_\lambda) \]

Rely on asymptotic approximations, but still relevant for small data set
Outline

Model selection

More details on optimisation
Decomposition strategy (1)

Consider the \((p T) \times (p T)\) block-diagonal matrix \(C\) composed by the empirical covariance matrices of each tasks

\[
C = \begin{pmatrix}
S^{(1)} & 0 \\
\vdots & \ddots \\
0 & S^{(T)}
\end{pmatrix},
\]

and define

\[
C_{\setminus i} = \begin{pmatrix}
S^{(1)}_{\setminus i} & 0 \\
\vdots & \ddots \\
0 & S^{(T)}_{\setminus i}
\end{pmatrix}, \quad C_{i \setminus i} = \begin{pmatrix}
S^{(1)}_{i \setminus i} \\
\vdots \\
S^{(T)}_{i \setminus i}
\end{pmatrix}.
\]

The \((p - 1) T \times (p - 1) T\) matrix \(C_{\setminus i}\) is the matrix \(C\) where we removed each line and each column pertaining to variable \(i\).
Decomposition strategy (2)

Estimate the \(i^{th}\) neighborhood of the \(T\) tasks bind together

\[
\arg\max_{\Theta(t), t=1\ldots,T} \sum_{t=1}^{T} \tilde{L}(\Theta(t); S(t)) - \lambda \Omega(\Theta(t))
\]

decomposes into \(p\) convex optimization problems

\[
\arg\min_{\beta \in \mathbb{R}^{T \times (p-1)}} f(\beta; C) + \lambda \Omega(\beta),
\]

where we set \(\beta(t) = \Theta_{i \setminus i}^{(t)}\) and

\[
\beta = \begin{pmatrix}
\beta^{(1)} \\
\vdots \\
\beta^{(T)}
\end{pmatrix} \in \mathbb{R}^{T \times (p-1)}.
\]
Subdifferential approach

\[
\min_{\beta \in \mathbb{R}^{T \times (p-1)}} L(\beta) = f(\beta) + \Omega(\beta),
\]

\(\beta\) is a minimizer iif \(0_p \in \partial_\beta L(\beta)\), with

\[
\partial_\beta L(\beta) = \nabla_\beta f(\beta) + \lambda \partial_\beta \Omega(\beta).
\]
Solving the sub-problem

Subdifferential approach

\[
\min_{\beta \in \mathbb{R}^{T \times (p-1)}} L(\beta) = f(\beta) + \Omega(\beta),
\]

\(\beta\) is a minimizer iif \(0_p \in \partial_\beta L(\beta)\), with

\[
\partial_\beta L(\beta) = \nabla_\beta f(\beta) + \lambda \partial_\beta \Omega(\beta).
\]

For the graphical Intertwined LASSO

\[
\Omega(\beta) = \sum_{t=1}^{T} \| \beta^{(t)} \|_1,
\]

where the grouping effect is managed by the function \(f\).
Solving the sub-problem

Subdifferential approach

\[
\min_{\beta \in \mathbb{R}^{T \times (p-1)}} L(\beta) = f(\beta) + \Omega(\beta),
\]

\(\beta\) is a minimizer iif \(0_p \in \partial_\beta L(\beta)\), with

\[
\partial_\beta L(\beta) = \nabla_\beta f(\beta) + \lambda \partial_\beta \Omega(\beta).
\]

For the graphical Group-LASSO

\[
\Omega(\beta) = \sum_{i=1}^{p-1} \left\| \beta_{i[1:T]} \right\|_2,
\]

where \(\beta_{i[1:T]} = (\beta_{i(1)}, \ldots, \beta_{i(T)})^T \in \mathbb{R}^T\) is the vector of the \(i\)th component across tasks.
Solving the sub-problem

Subdifferential approach

\[
\min_{\beta \in \mathbb{R}^{T \times (p-1)}} L(\beta) = f(\beta) + \Omega(\beta),
\]

\(\beta\) is a minimizer iff \(0_p \in \partial_\beta L(\beta)\), with

\[
\partial_\beta L(\beta) = \nabla_\beta f(\beta) + \lambda \partial_\beta \Omega(\beta).
\]

For the graphical Coop-LASSO

\[
\Omega(\beta) = \sum_{i=1}^{p-1} \left( \| [\beta_i^{[1:T]}]_+ \|_2 + \| [\beta_i^{[1:T]}]_- \|_2 \right),
\]

where \(\beta_i^{[1:T]} = (\beta_i^{(1)}, \ldots, \beta_i^{(T)})^T \in \mathbb{R}^T\) is the vector of the \(i\)th component across tasks.