Statistical Inference in Gaussian Graphical Models

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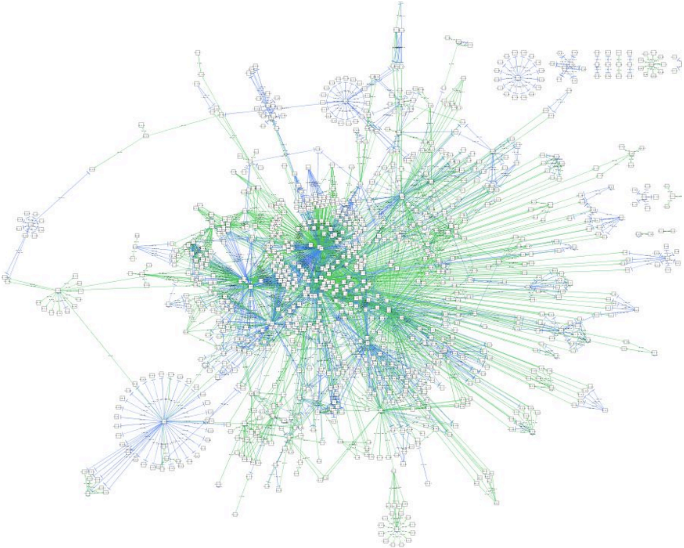
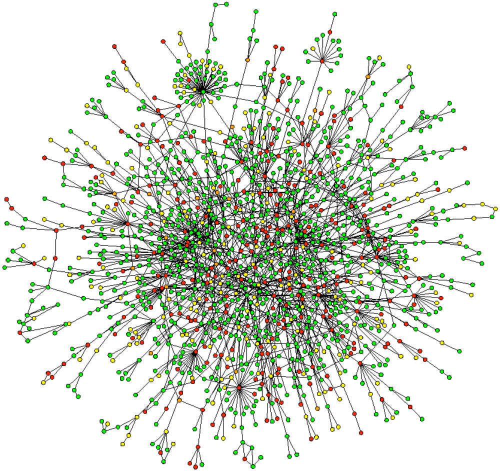
Gene - gene regulation network of *E. coli*



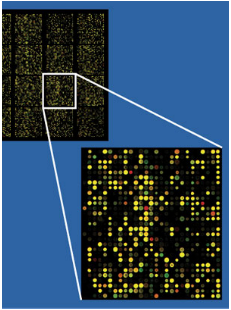
Protein - protein network of *S. cerevisiae*

1458 proteins (vertices) and their 1948 known interactions (edges)



Inferring gene regulation networks

Data: massive transcriptomic data sets produced by microarrays.



- **Differential analysis** of data obtained in different conditions: with or without deletion of a gene, with or without stress, etc.
- **Analysis of the conditional dependences** in the data (exploits the whole data set).

A few statistical tools

Descriptive tools:

- Kernel methods (supervised learning)

Model based tools:

- Bayesian Networks
- Gaussian Graphical Models

Gaussian Graphical Models

Gaussian Graphical Models

Statistical model: The transcription levels $(X^{(1)}, \dots, X^{(p)})$ of the p genes are modeled by a Gaussian law in $\mathbb{R}^p$.

Graph of the conditional dependences: graph $\mathbf{g}$ with

$$\boxed{\begin{array}{c}\text{an edge } i \overset{\mathbf{g}}{\sim} j \text{ between the genes } i \text{ and } j \\ \underline{\text{iff}} \\ X^{(i)} \text{ and } X^{(j)} \text{ are not independent given } \left\{X^{(k)},\ k \neq i,j\right\}\end{array}}$$

$$\text{regulation network} \quad \longleftrightarrow \quad \text{graph } \mathbf{g}$$

The task of the statistician

Goal: estimate $\mathbf{g}$ from a sample $X_1, \ldots, X_n$.

Main difficulty: $n \ll p$

- $p \approx$ a few 100 to a few 1000 genes
- $n \approx$ a few tens

New algorithms: based on thresholding or regularization

$\longrightarrow$ many of them have quite disappointing numerical performances (Villers *et al.* 2008)

$\longrightarrow$ no theoretical results or in an asymptotic framework (with strong hypotheses on the covariance)

Estimation by model selection

Partial correlations

Hypothesis: $(X^{(1)}, \ldots, X^{(p)}) \sim \mathcal{N}(0, C)$ in $\mathbb{R}^p$, with $C \succ 0$.

Notation: We write $\theta = \left(\theta_k^{(j)}\right)$ for the $p \times p$ matrix such that $\theta_j^{(j)} = 0$ and $\mathbb{E}\left(X^{(j)} \mid X^{(k)}, k \neq j\right) = \sum_{k \neq j} \theta_k^{(j)} X^{(k)}$.

Skeleton of θ: we have $\theta_i^{(j)} = \frac{\mathbf{Cov}\left(X^{(i)}, X^{(j)} | X^{(k)},\ k \neq i,j\right)}{\mathbf{Var}\left(X^{(j)} | X^{(k)},\ k \neq j\right)}$ so

$$\boxed{\theta_i^{(j)} \neq 0 \iff i \stackrel{\mathrm{g}}{\sim} j}$$

Goal: Estimate θ from a sample $X_1, \ldots, X_n$ with quality criterion

$$\mathrm{MSEP}(\hat{\theta}) = \mathbb{E}\left[\|C^{1/2}(\hat{\theta} - \theta)\|^2_{p \times p}\right] = \mathbb{E}\left[\|X_{new}^T(\hat{\theta} - \theta)\|^2_{1 \times p}\right]$$

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Estimation procedure

1. **Choose a collection $\mathcal{G}$ of candidate graphs**

   e.g. all the graphs with p vertices and degree $\leq D$,

2. **Associate to each graph $g \in \mathcal{G}$ an estimator $\hat{\theta}_g$**

   $$\hat{\theta}_g = \underset{A \sim g}{\operatorname{argmin}} \|X(I - A)\|^2_{n \times p} \quad \text{(empirical MSEP)}$$

3. **Select one $\hat{\theta}_{\hat{g}}$ by minimizing a penalized empirical risk**

   with a criterion inspired by that in Baraud *et al.*

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Theorem: risk bound.

When $\deg(\mathcal{G}) = \max\{\deg(g),\ g \in \mathcal{G}\}$ fulfills

$$\boxed{\deg(\mathcal{G}) \leq \rho\, \frac{n}{2\left(1.1 + \sqrt{\log p}\right)^2}, \quad \text{for some} \quad \rho < 1,}$$

then the MSEP of $\hat{\theta}$ is bounded by

$$\mathrm{MSEP}(\hat{\theta}) \ \leq \ c_\rho \log(p) \inf_{g \in \mathcal{G}} \left\{ \mathrm{MSEP}(\hat{\theta}_g) \vee \frac{\|C^{1/2}(I-\theta)\|^2}{n} \right\} \ + \ R_n$$

where $R_n = O\left(\mathrm{Tr}(C) e^{-\kappa_\rho n}\right)$.

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Theory

Condition on the degree

Prediction error:

$$\mathrm{MSEP}(\hat\theta) = \mathbb{E}(\|C^{1/2}(\theta-\hat\theta)\|^2) = \mathbb{E}(\|C^{1/2}(I-\hat\theta)\|^2) - \|C^{1/2}(I-\theta)\|^2$$

Proposition: From empirical to population MSEP

Under the previous condition on the degree, we have with large probability

$$(1-\delta)\|C^{1/2}(I-\hat\theta)\|_{p\times p} \le \frac{1}{\sqrt{n}}\|X(I-\hat\theta)\|_{n\times p} \le (1+\delta)\|C^{1/2}(I-\hat\theta)\|_{p\times p}$$

for all matrices $\hat\theta \in \bigcup_{g\in\mathcal{G}} \Theta_g$.

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Lemma: Restricted Inf / Sup of Random Matrices

Consider a $n \times p$ matrix Z with $n < p$ and i.i.d. $Z_{i,j} \sim \mathcal{N}(0,1)$. Consider also a collection $V_1, \ldots, V_N$ of subspaces of $\mathbb{R}^p$ with dimension $d < n$.

Then for any $x > 0$

$$\mathbb{P}\left[\inf_{v \in V_1 \cup \ldots \cup V_N} \frac{\frac{1}{\sqrt{n}}\|Zv\|}{\|v\|} \leq 1 - \frac{\sqrt{d} + \sqrt{2\log N} + \delta_N + x}{\sqrt{n}}\right] \leq e^{-x^2/2}$$

where $\delta_N = \frac{1}{N\sqrt{8\log N}}$.

A geometrical constraint

When $C = I$, there exists some constant $c(\delta) > 0$ such that for any $n, p, \mathcal{G}$ fulfilling

$$\deg(\mathcal{G}) \geq c(\delta) \frac{n}{1 + \log(p/n)},$$

there exists no $n \times p$ matrix X fulfilling

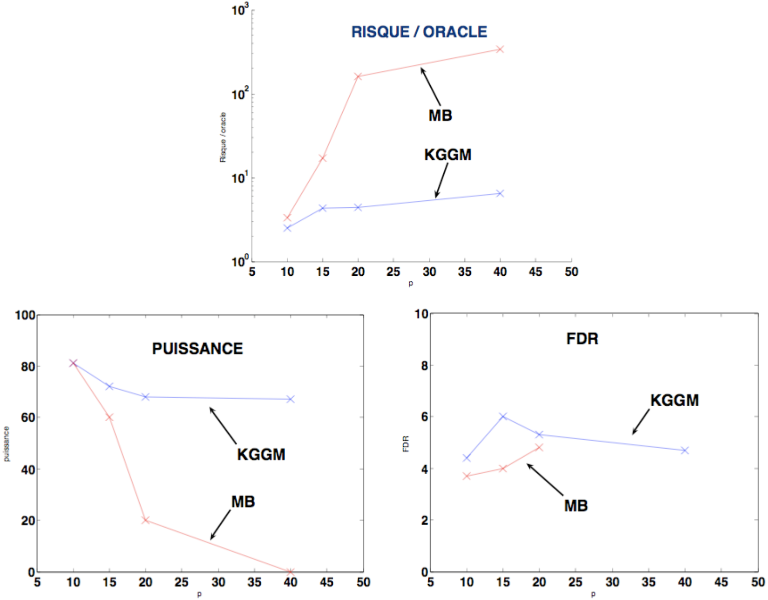
$$(1-\delta)\|C^{1/2}(I - \hat{\theta})\| \leq \frac{1}{\sqrt{n}} \|X(I - \hat{\theta})\| \leq (1+\delta)\|C^{1/2}(I - \hat{\theta})\|$$

for all $\hat{\theta} \in \bigcup_{g \in \mathcal{G}} \Theta_g$.

In practice

Numerical performance

Random graphs, $n = 15$ and p increases



Conclusion

Some nice features:

- **good theoretical properties:** non-asymptotic control of the MSEP with no condition on the covariance matrix C
- **good numerical performances:** even when $n \ll p$

BUT

- **very high numerical complexity:**
  typically $n \times p^{\deg(\mathcal{G})+1}$

  $\boxed{\Longrightarrow \text{ cannot be used in practice when } p > 50 \ldots}$

Ongoing work: with S. Huet and N. Verzelen

Reduction of the size of the collection of graph, using data-driven collections.

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References

Main reference of the talk

C. Giraud. *Estimation of Gaussian graphs by model selection.* Electronic Journal of Statistics. Vol. 2 (2008) pp. 542–563

Related references

- Y. Baraud, C. Giraud, S. Huet. *Gaussian model selection with unknown variance.*
  To appear in the Annals of Statistics (2008).
- N. Verzelen. *High-dimensional Gaussian model selection on a Gaussian design.*
  Personal communication