Sparse Graphs
(from noisy data, obviously)

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God is the answer. But what was the question?

A common design:

Many items are screened across few units

- possibly: redundant items
- sometimes: automatically
- possibly: through time.

Possible question

Sparse dependency structure among the items,
... possibly with longitudinal structure.

Sparsity:

- Identifiability
- Computational efficiency
- Ontological plausibility
- Epistemic expediency?

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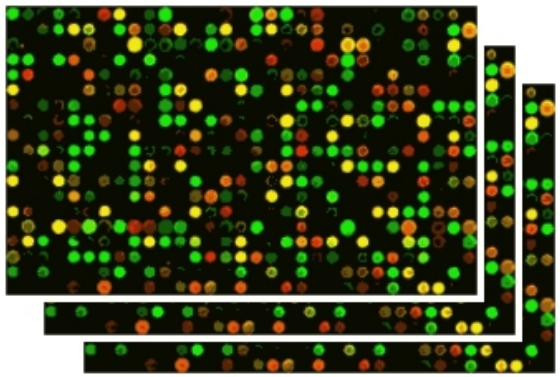
Motivation: Dynamic Genomic Networks

- Transcription: snap-shot of gene activity in time and space (tissue).
- High-throughput microarray and RNA-seq data measure gene activity.



Running example: T-cell time-series dataset.

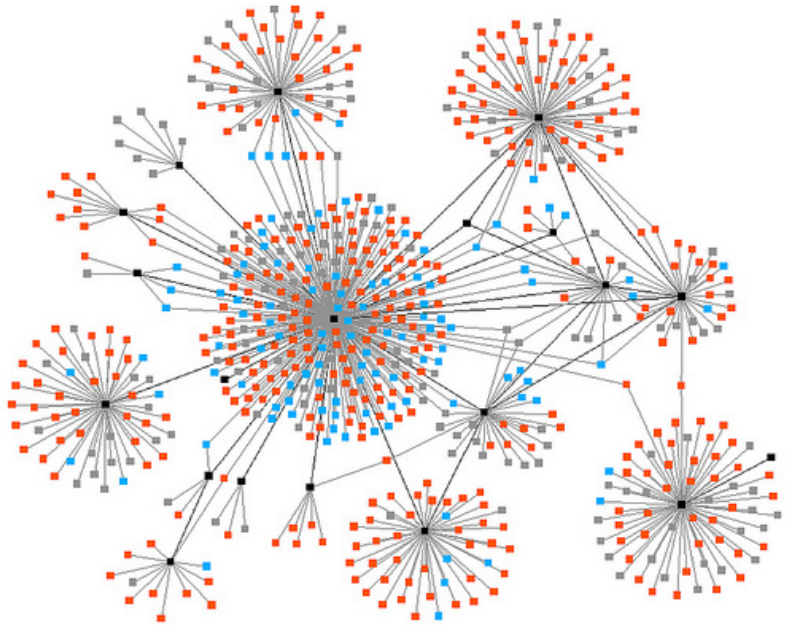
- Temporal expression of 58 genes for 10 unequally spaced time points.
- At each time point there are 44 separate measurements.

Definition (Aim)

Determine dynamic genomic graph G on basis of $\{Y_{gt}^{(i)}\}_{gti}$.

Motivation: Features of a Dynamic Genomic Process

- "**p** >> **n**":
  - Number of observations smaller than number of variables.
  - Thousands of variables and hundreds of observations.
- **Structure:**
  - Highly complex and structured phenomenon.
  - Possibly with additional topographical structure (small world).
- **Sparsity:** only small number of links between nodes.



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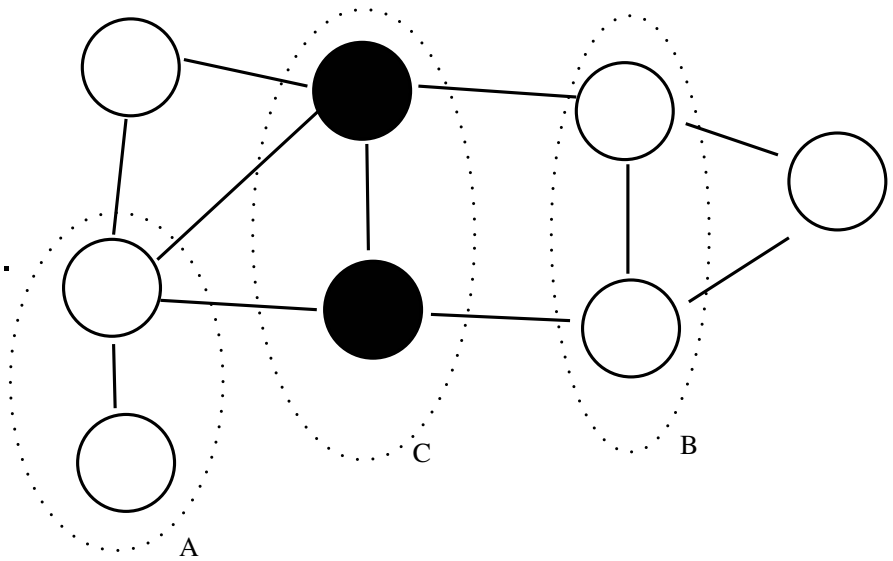
Undirected Graphical Models

- **Graph**: $G = (V, E)$, $V = \{v_1, \ldots, v_p\}$ and $E \subseteq V \times V$.
- Can be interpreted as a **conditional independence graph**.

Markov Properties:

- Global: $Y_A \perp Y_B | Y_C$.
- Local: $Y_i \perp Y_{V \setminus \{ne(i) \cup i\}} | Y_{ne(i)}$.
- Pairwise $Y_i \perp Y_j | Y_{V \setminus \{i,j\}}$.



Definition (Graphical model)

A couple $M = (G, P)$, where G a graph and P a *probability measure* that satisfies a *Markov property*.

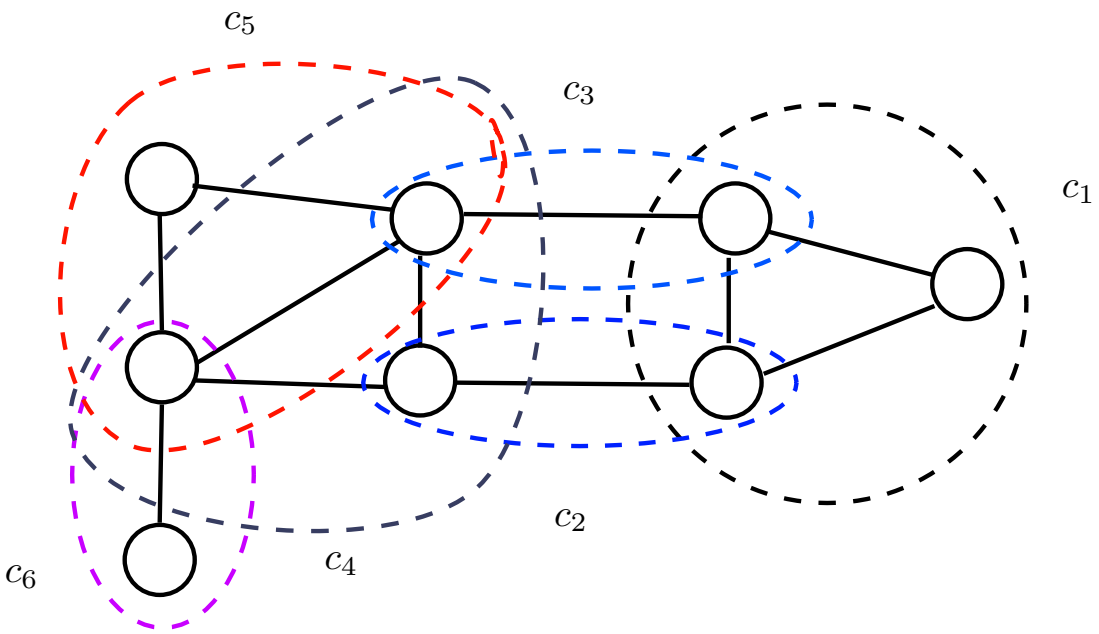
Factorization and Markov properties

Theorem (Hammersley-Clifford)

If the density p=dP is positive and continuous then

$$\textit{Factorization} \iff \textit{Markov}(\textit{Global}/\textit{Local}/\textit{Pairwise})$$

Factorization: $f(\mathbf{y}) = \frac{1}{z}\prod_{c\in C} h_c(\mathbf{y}_c)$, where c are cliques of G.



Example:
Graph (left) contains 6 cliques (complete subgraphs), and so

$$p(\mathbf{y}) = \prod_{i=1}^{6} h_i(y_{c_i}).$$

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Gaussian graphical models

Definition (Gaussian graphical model)

GGM is a graphical model (G, P), where P is determined by:

$$\mathbf{Y} \sim N(\boldsymbol{\mu}, \boldsymbol{\Theta}^{-1}).$$

Note:

$$\begin{aligned} p(\mathbf{y}) &\propto \exp\left(-\frac{1}{2}(\mathbf{y}-\boldsymbol{\mu})'\Theta(\mathbf{y}-\boldsymbol{\mu})\right) \\ &= \prod_{i=1}^{p}\prod_{j=1}^{p} e^{-(y_i-\mu_i)(y_j-\mu_j)\theta_{ij}/2} \\ &= \prod_{c\in C} h_c(\mathbf{y}_c) \end{aligned}$$

So, if $\theta_{ij} = 0$, then certainly nodes i and j are not in **same** clique:

$$\theta_{ij} = 0 \Leftrightarrow Y_i \perp Y_j | \mathbf{Y}_{V\setminus\{i,j\}}.$$

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Traditional: Hypothesis Test

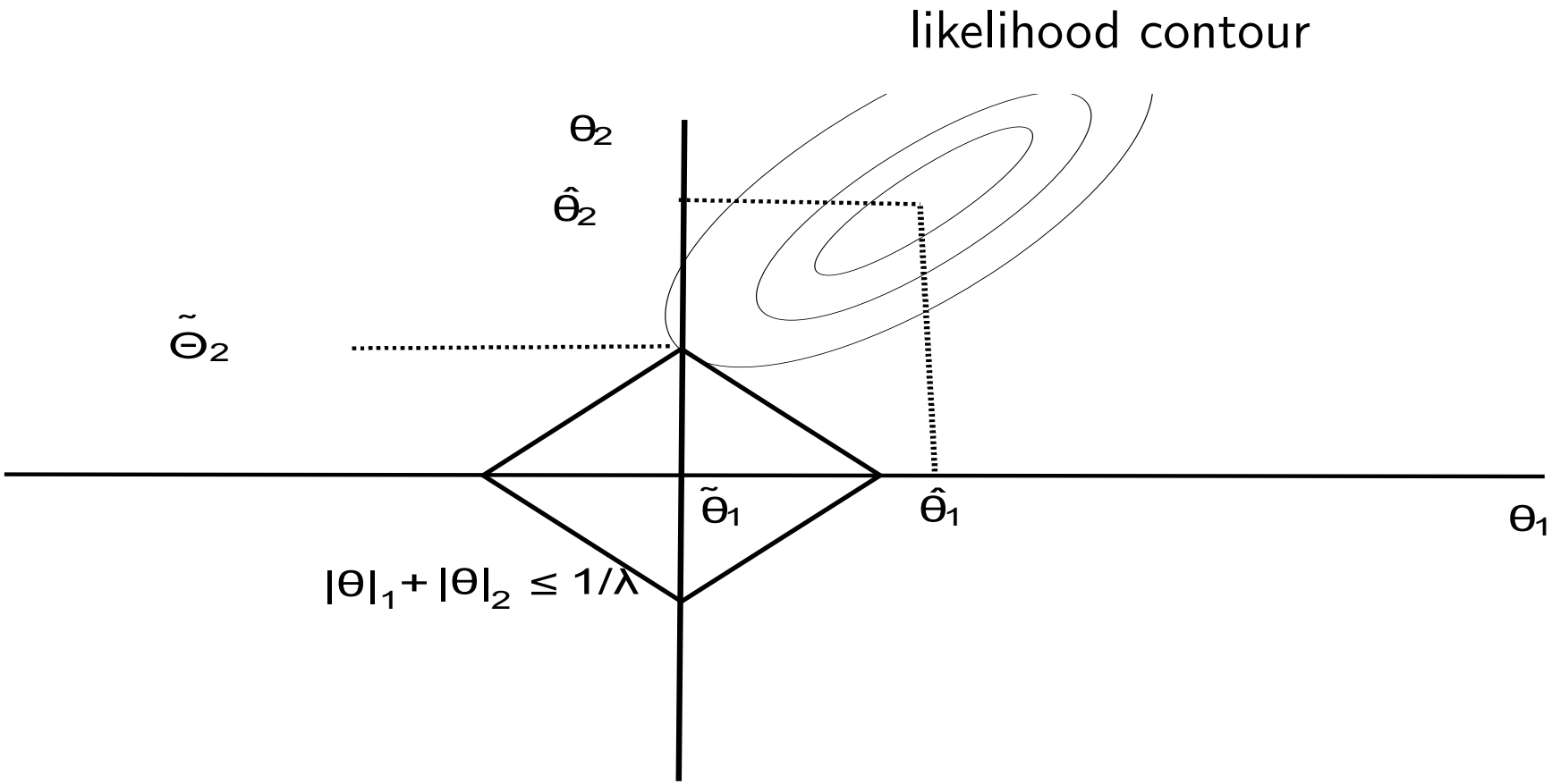
$$H_0 : \theta_{ij} = 0 \iff \text{Edge } (i,j) \text{ is absent}$$
$$H_1 : \theta_{ij} \neq 0 \iff \text{Edge } (i,j) \text{ is present}$$

- Hypothesis tests have poor model selection properties.
- Where do we start to test?
- Multiple testing problem.
- Space of models is of size $2^{\binom{p}{2}}$.
- If $p > n$, then $\mathbf{S}$ is singular.

Penalized Inference

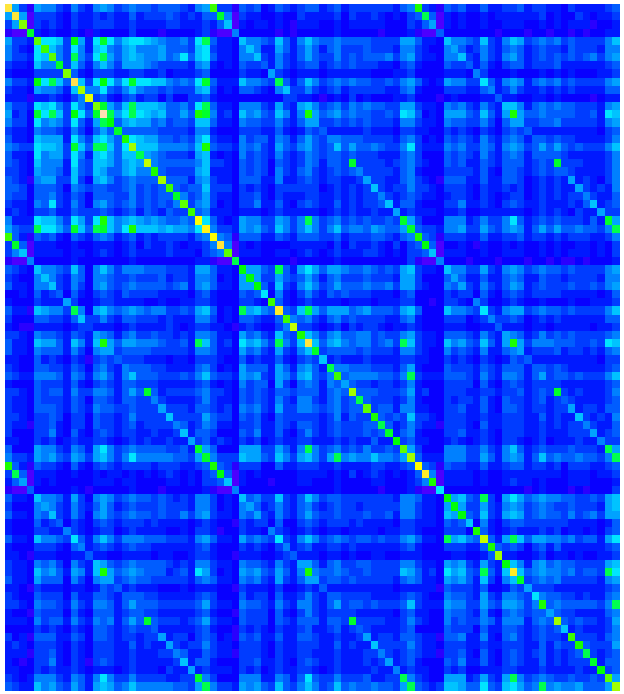
Idea: Maximize the likelihood $l(\mu, \Theta|y)$ **subject to constraint**

$$||\mathbf{\Theta}||_1 = \sum_{i<j} |\theta_{i,j}| \leq 1/\lambda$$



Netherlands Study on Depression and Anxiety (NESDA)

In 3 "waves" 1708 depression patients were scored on 28 items in an IDS questionnaire.

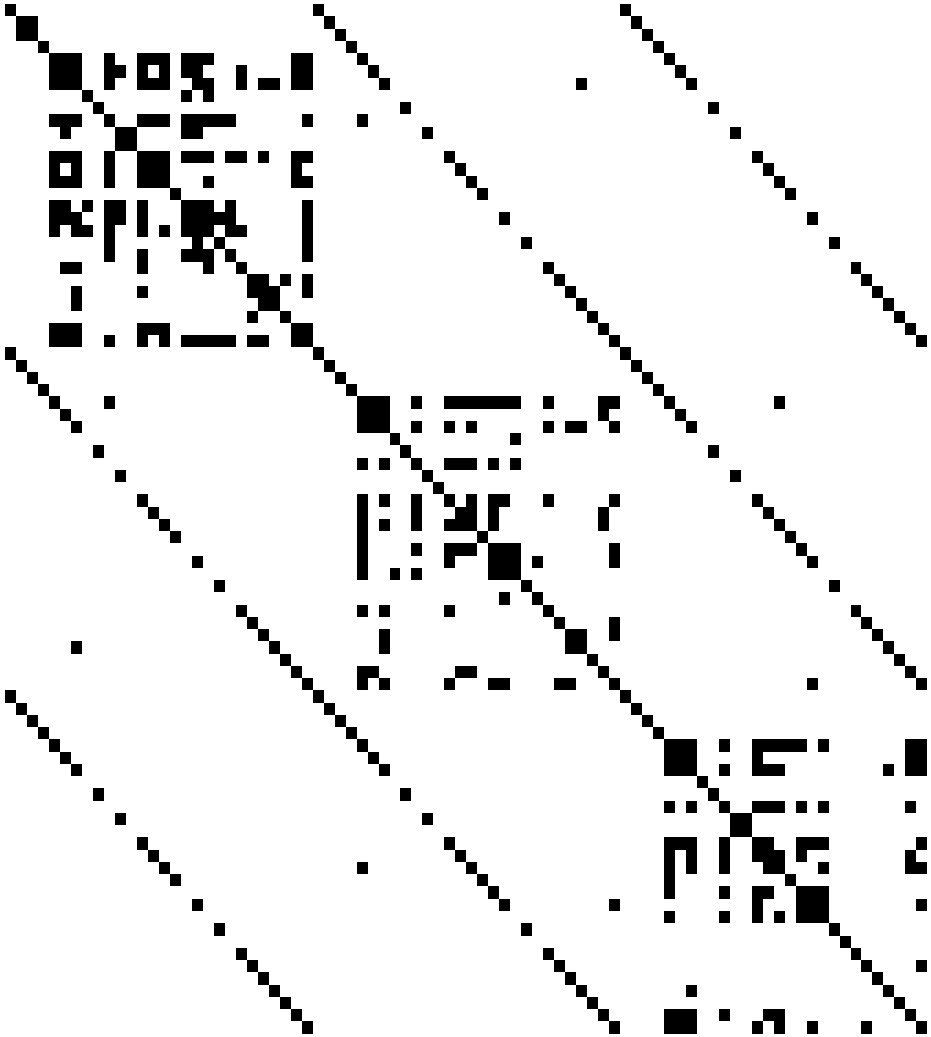


84 $\times$ 84 empirical covariance matrix: notice 3 waves of 28 items

Psychiatrists want to know:

- What is a typical depression "signature"? Are there more than one?
- What is the relationship between the items?

Standard Graphical Lasso: NESDA depression study



Inferred graph for the NESDA study, represented via adjacency matrix

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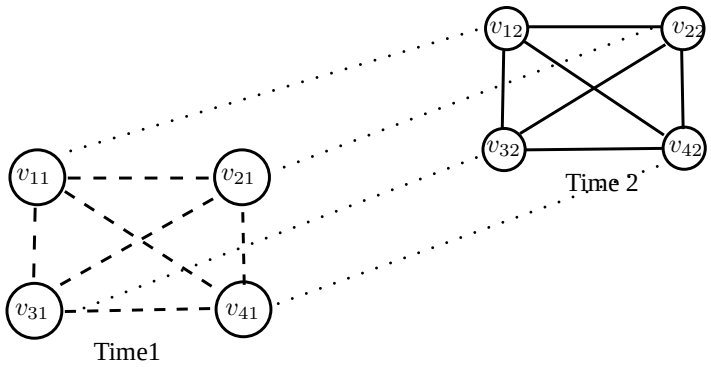
Dynamic Genomic Graphs

- Γ be a set of "genes".
- T be a set of ordered "time points".

Definition (Dynamic genomic graph)

A dynamic genomic graph is a pair $G = (V, E)$.

- Vertices: $V = \{v_{ij}\}_{i \in \Gamma, j \in T}$, where Γ and T are finite sets.
- Links: ordered pair of elements $E \subseteq V \times V$.



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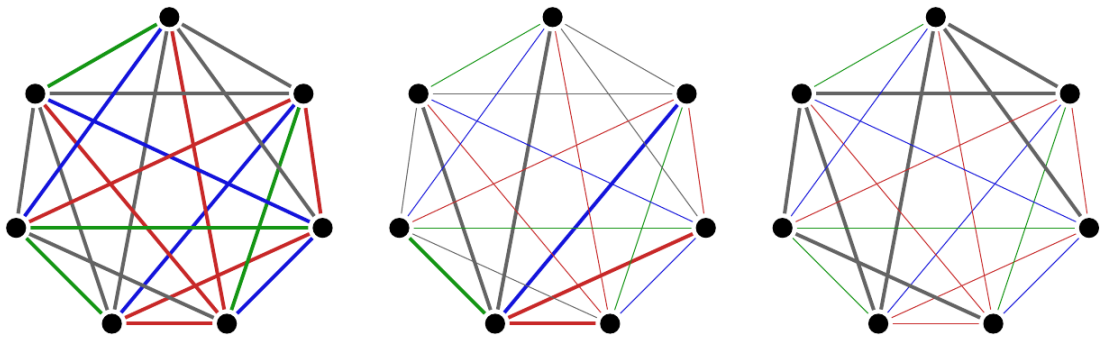
Coloured graphs

Definition (Coloured graph)

A coloured graph is a triplet $G_F = (V, E, F)$, where $G = (V, E)$ is a graph and F is a mapping on the links, i.e.:

$$F : E \to C,$$

where C is a finite set of colours.

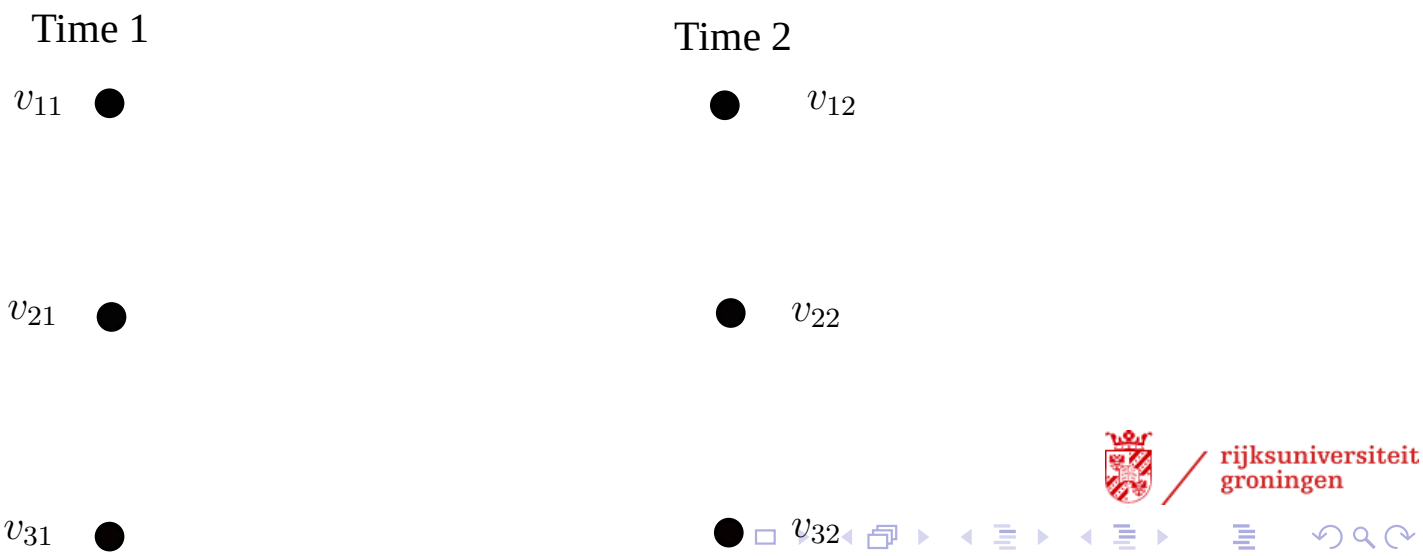


Special kind of coloured graphs: Factorial Graphs

Denote mapping $F : E \to C$ by $E \prec F$.

In analogy with ANOVA, we define the following colouring:

- $\boxed{E \prec 0 \Rightarrow \text{an empty graph.}}$
- $E \prec F_1$.
- $E \prec F_T$.
- $E \prec F_\Gamma$.
- $E \prec F_{\Gamma T}$.



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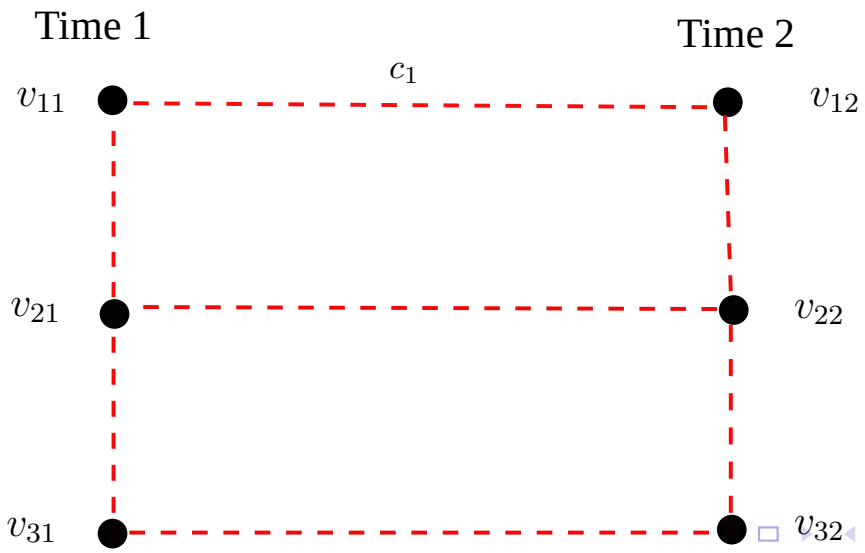

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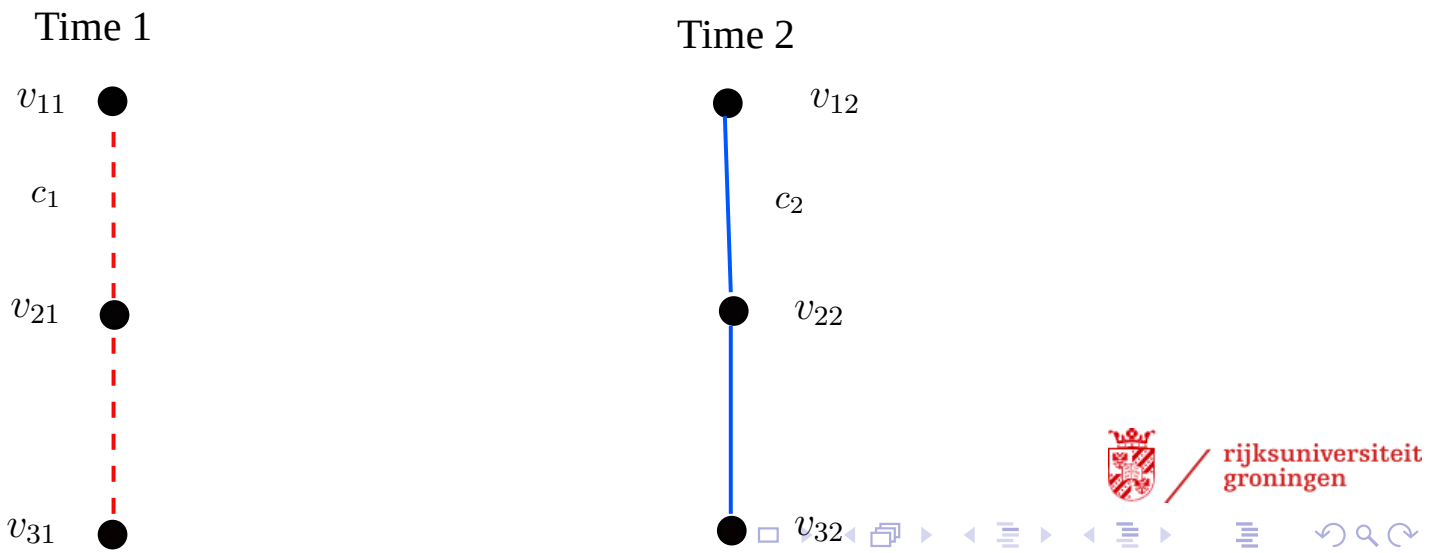

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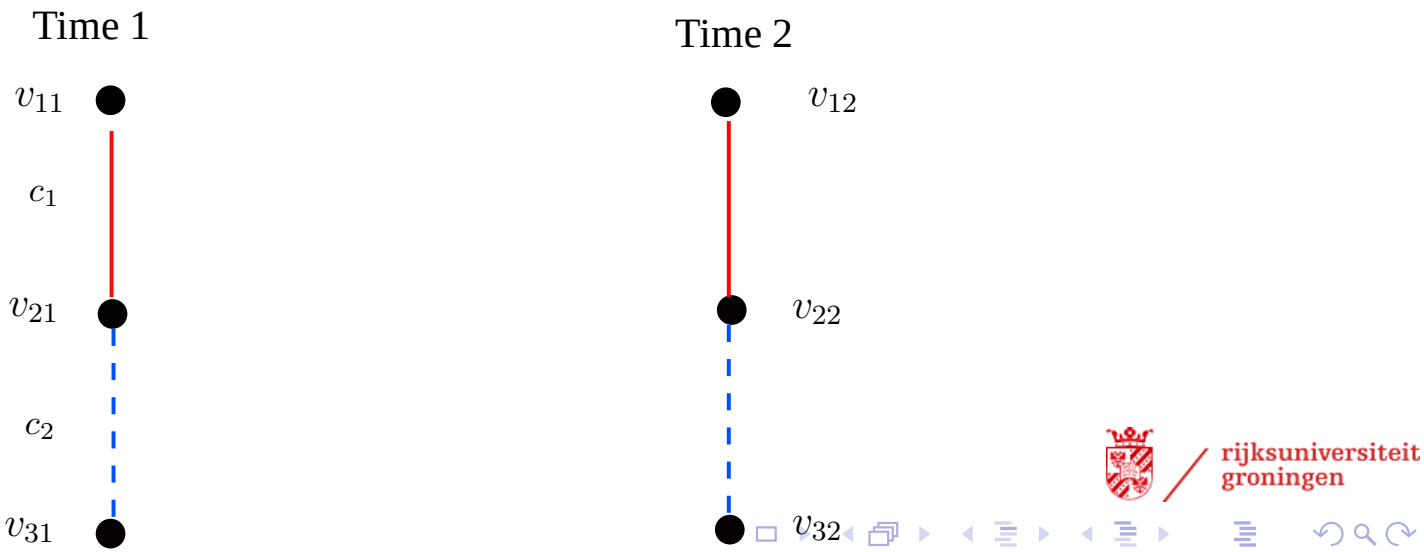

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- $E \prec F_T$.
- $E \prec F_\Gamma$.
- $\boxed{E \prec F_{\Gamma T}\text{: all different colours}}$

Natural Partitions

Definition (Natural partition)

Let $E = \{S_i, N_i\}_{i=0}^{n_T-1}$ be subsets of links where S_i, N_i are defined as follows:

$$S_i = \{\{(v_{jt}, v_{j,t+i}), (v_{j,t+i}, v_{jt})\} | j \in \Gamma, t = 1, \ldots, n_T - i\},$$

and

$$N_i = \{\{(v_{jt}, v_{k,t+i}), (v_{k,t+i}, v_{jt})\} | \forall j \neq k \in \Gamma, t = 1, \ldots, n_T - i\}.$$

The natural partitions imply subgraphs of G and imply partions of $\mathbf{\Theta}$ for GGMs:

$$\mathbf{\Theta} = \left[\begin{array}{cc|cc|cc|cc} S_0 & N_0 & S_1 & N_1 & S_2 & N_2 & \ldots & \ldots \\ & S_0 & N_1 & S_1 & N_2 & S_2 & \ldots & \ldots \\ \hline & & S_0 & N_0 & S_1 & N_1 & S_2 & N_2 \\ & & & S_0 & N_1 & S_1 & N_2 & S_2 \\ \hline & & & & S_0 & N_0 & S_1 & N_1 \\ & & & & & S_0 & N_1 & S_1 \end{array}\right]$$

Factorial Graphical Models

Definition (Gaussian graphical models for factorially coloured graphs)

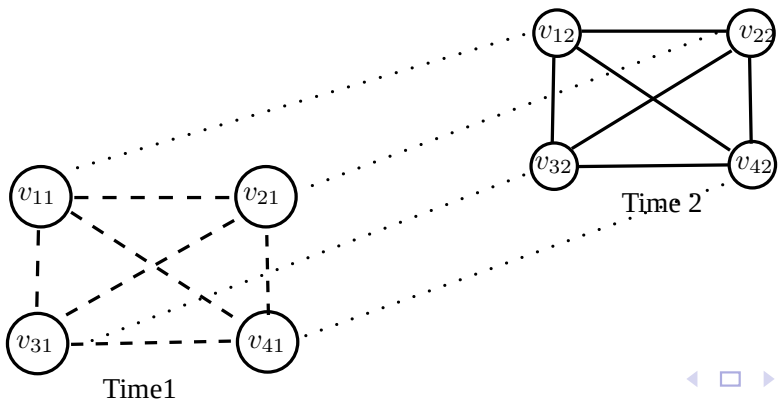
A factorial Gaussian graphical model is a graphical model defined on:

- a dynamic factorial graph $G = (V, E, F)$, where
- a factorial colouring F is applied *separately* to natural partitions

$$S_i \prec F_{S_i}, \quad N_i \prec F_{N_i}, \quad i = 0, \ldots, n_T - 1$$

- which determines Θ in

$$\mathbf{Y} \sim N(\boldsymbol{\mu}, \boldsymbol{\Theta}^{-1}).$$



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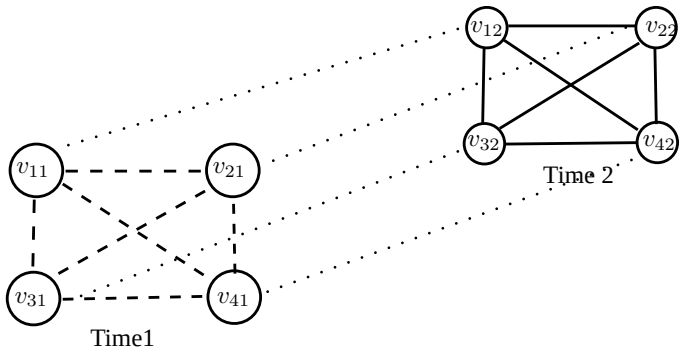
Example: Factorial Gaussian Graphical Model

Model:

$$(S_0 \prec 1), \quad N_0 \prec F_T, \quad S_1 \prec 1, \quad N_1 \prec 0.$$

Factorial coloured graph:



Precision Matrix:

$$\boldsymbol{\Theta} = \left[\begin{array}{cccc|cccc} \theta_1 & \theta_2 & \theta_2 & \theta_2 & \theta_4 & 0 & 0 & 0 \\ & \theta_1 & \theta_2 & \theta_2 & 0 & \theta_4 & 0 & 0 \\ & & \theta_1 & \theta_2 & 0 & 0 & \theta_4 & 0 \\ & & & \theta_1 & 0 & 0 & 0 & \theta_4 \\ \hline & & & & \theta_1 & \theta_3 & \theta_3 & \theta_3 \\ & & & & & \theta_1 & \theta_3 & \theta_3 \\ & & & & & & \theta_1 & \theta_3 \\ & & & & & & & \theta_1 \end{array}\right]$$

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Penalized likelihood for GGMs

- Consider an experiment: $|\Gamma|$ genes measured across $|T|$ time points.
- Assume n iid samples $\mathbf{y}^{(1)}, \ldots, \mathbf{y}^{(n)}$, where $\mathbf{y}^{(i)} = (y_1^{(i)}, \ldots, y_{\Gamma T}^{(i)})$.
- Assume $\mathbf{Y}^{(i)} \sim N(\mathbf{0}, \boldsymbol{\Theta}^{-1})$, then

Likelihood:

$$l(\boldsymbol{\Theta}|\mathbf{y}) \propto \log(\boldsymbol{\Theta}) - \mathrm{tr}(\mathbf{S}\boldsymbol{\Theta}).$$

AIM: Optimization of penalized likelihood:

$$\hat{\boldsymbol{\Theta}} := \mathrm{argmax}_{\boldsymbol{\Theta}}\{l(\boldsymbol{\Theta}|\mathbf{y})\}$$

subject to

- $\boldsymbol{\Theta} \succeq 0$;
- $||\boldsymbol{\Theta}||_1 \leq 1/\lambda$;
- some factorial colouring F.

Inferring penalized factorial Gaussian graphical models

LogdetPPA. Newton-CG primal proximal point algorithm (*Wang et al., 2010*, including Kim Toh and Defeng Sun) is used to solve optimization:

$$\hat{\boldsymbol{\Theta}} := \underset{\boldsymbol{\Theta}}{\operatorname{argmin}} -\{\log|\boldsymbol{\Theta}| - \operatorname{tr}(\boldsymbol{\Theta}\mathbf{S}) + \boldsymbol{\lambda}'\boldsymbol{\theta}^{+} + \boldsymbol{\lambda}'\boldsymbol{\theta}^{-} : A(\boldsymbol{\Theta}) = \mathbf{0},$$

$$B(\boldsymbol{\Theta}) - \boldsymbol{\theta}^{+} + \boldsymbol{\theta}^{-} = \mathbf{0}, \boldsymbol{\Theta} \succeq 0, \boldsymbol{\theta}^{+}, \boldsymbol{\theta}^{-} \geq 0\}$$

- $A(\boldsymbol{\Theta})$: linear constraints which depend on coloured graph.
- $B(\boldsymbol{\Theta})$: ℓ_1-norm penalty on elements of precision matrix.
- $\boldsymbol{\theta}^{+}$ and $\boldsymbol{\theta}^{-}$ are additional variables (slack variables).
- $\boldsymbol{\Theta} \succeq 0$: semi-positive definite constraint.

Solves $\hat{\Theta}$ up to 2000×2000 .

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T-cell data

Aim. Use large time-course experiment to characterize response of human T-cell line (Jurkat) to PMA and ionomycin treatment.

T-cell time-series dataset

- Temporal expression of 58 genes for 10 unequally spaced time points.
- At each time point there are 44 separate measurements.
- See Rangel et al. (2004) for more details.

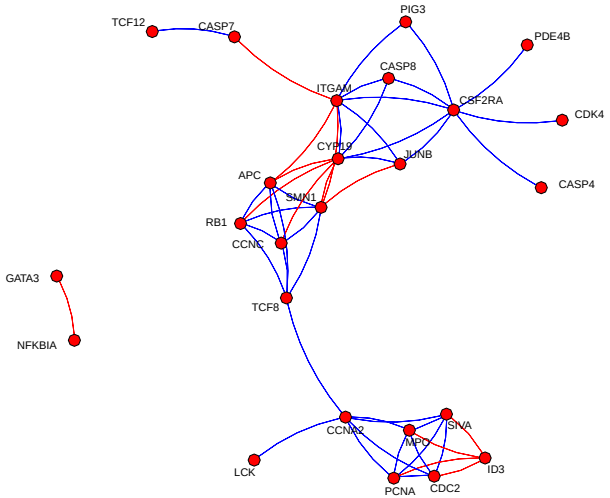
Application to T-cell data

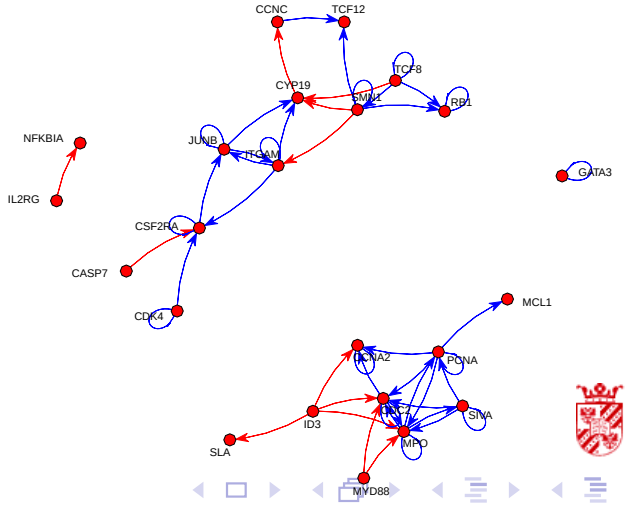
$$S_0 \prec F_1, \mathbf{N_0} \prec \mathbf{F_\Gamma}, S_1 \prec F_T, \mathbf{N_1} \prec \mathbf{F_\Gamma}$$

$$\mathbf{\Theta} = \left[\begin{array}{cc|cc|cc|cc} S_0^1 & N_0^1 & S_1^1 & N_1^1 & 0 & 0 & \dots & \dots \\ & S_0^1 & N_1^1 & S_1^1 & 0 & 0 & \dots & \dots \\ \hline & & S_0^2 & N_0^2 & S_1^2 & N_1^2 & 0 & 0 \\ & & & S_0^2 & N_1^2 & S_1^2 & 0 & 0 \\ \hline & & & & S_0^3 & N_0^3 & S_1^3 & N_1^3 \\ & & & & & S_0^3 & N_1^3 & S_1^3 \end{array}\right]$$

$N_0^1 = N_0^2 = \ldots = N_0^{10}$

$N_1^1 = N_1^2 = \ldots = N_1^{10}$





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What have we achieved so far? And problems!

Summary:

- Penalized Gaussian graphical models
- Coloured graphs
- Natural partitions
- Factorially coloured Gaussian graphical models

Problems:

1. Factorial colouring not particularly flexible in modeling time dynamics.
2. Gaussian assumption may be too restrictive for realistic genomic data.
3. How to choose the appropriate level of penalization?

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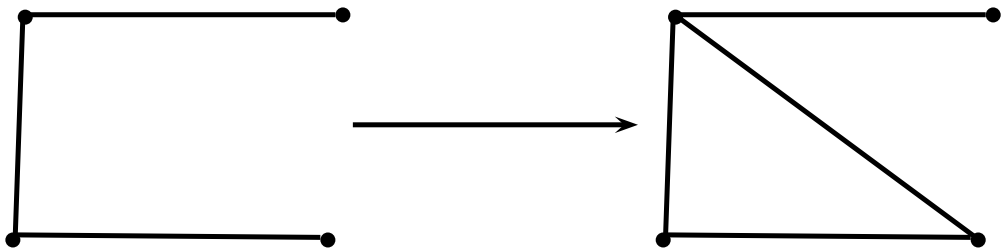
1. Extension: Slowly changing graphical models

- Problem: Estimate changes in the dynamic of the network.

Main Idea: Penalize changes between graphs at different time points

$$||\Delta\Theta||_1 = \sum_{s=0}^{t-1}\sum_{k=0}^{t-1} ||N_s^k - N_s^{k+1}||_1.$$



- Solution: Penalized maximum likelihood subject to constraints.

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Implement Slowly Changing via logdetPPA

$$\hat{\boldsymbol{\Theta}} := \underset{\boldsymbol{\Theta}}{\operatorname{argmin}} \{ -\log |\boldsymbol{\Theta}| + \operatorname{tr}(\mathbf{S}\boldsymbol{\Theta}) + \lambda_1 \mathbf{x}^+ + \lambda_1 \mathbf{x}^- + \lambda_2 \mathbf{y}^+ + \lambda_2 \mathbf{y}^- \}$$

$$\begin{aligned} \text{subject to} \quad & \mathbf{A}(\boldsymbol{\Theta}) - \mathbf{y}^+ + \mathbf{y}^- = \mathbf{0} \\ & \mathbf{B}(\boldsymbol{\Theta}) - \mathbf{x}^+ + \mathbf{x}^- = \mathbf{0} \\ & \mathbf{C}(\boldsymbol{\Theta}) = \mathbf{0} \\ & \boldsymbol{\Theta} \succeq 0, \mathbf{x}^+, \mathbf{x}^-, \mathbf{y}^+, \mathbf{y}^- \geq \mathbf{0}. \end{aligned}$$

- $A(\boldsymbol{\Theta})$: set of linear constraints which depends on the $||\Delta\boldsymbol{\Theta}||_1$.
- $B(\boldsymbol{\Theta})$ ℓ_1-norm penalty on element of precision matrix.
- $C(\boldsymbol{\Theta})$ zero elements a priori.
- $\mathbf{x}^+$, $\mathbf{x}^-$, $\mathbf{y}^-$ and $\mathbf{y}^+$ are slack variables.

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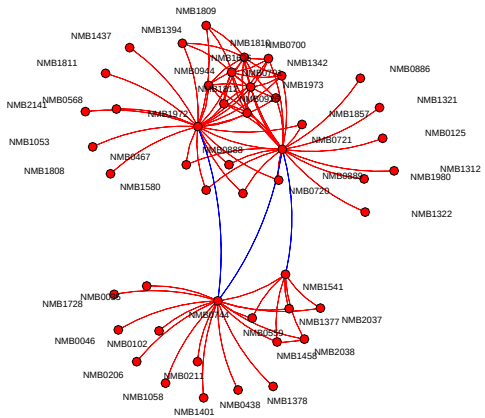
Application to a time-course dataset

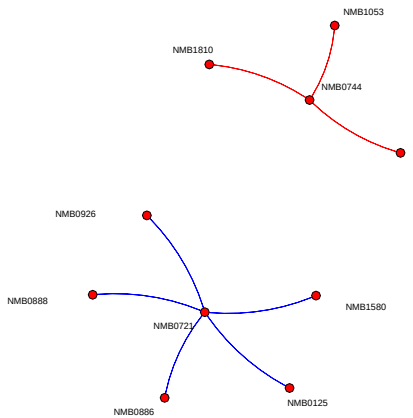
$$\mathbf{S_0} \prec F_{\Gamma T}, \mathbf{N_0} \prec 1, \mathbf{N_1} \prec 1, \mathbf{N_2} \prec 0$$

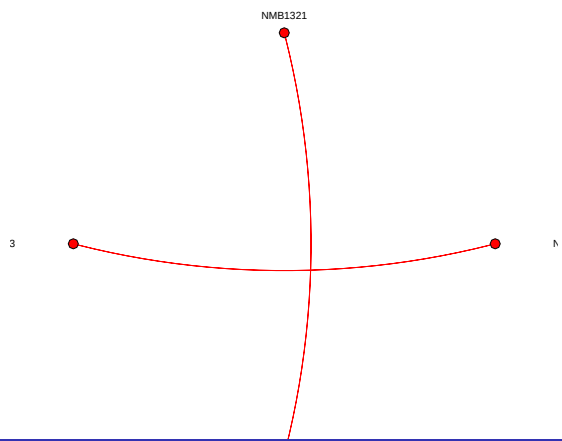
$$\Theta = \left[\begin{array}{cc|cc|cc|cc} S_0^1 & N_0^1 & S_1^1 & N_1^1 & 0 & 0 & \cdots & \cdots \\ & S_0^1 & N_1^1 & S_1^1 & 0 & 0 & \cdots & \cdots \\ \hline & & S_0^2 & N_0^2 & S_1^2 & N_1^2 & 0 & 0 \\ & & & S_0^2 & N_1^2 & S_1^2 & 0 & 0 \\ \hline & & & & S_0^3 & N_0^3 & S_1^3 & N_1^3 \\ & & & & & S_0^3 & N_1^3 & S_1^3 \end{array}\right]$$

N_0^1 $\qquad$ $|N_0^1| - |N_0^2|$ $\qquad$ $|N_0^2| - |N_0^3|$

N0 at time 1 $\qquad$ 1 $\qquad$ 7

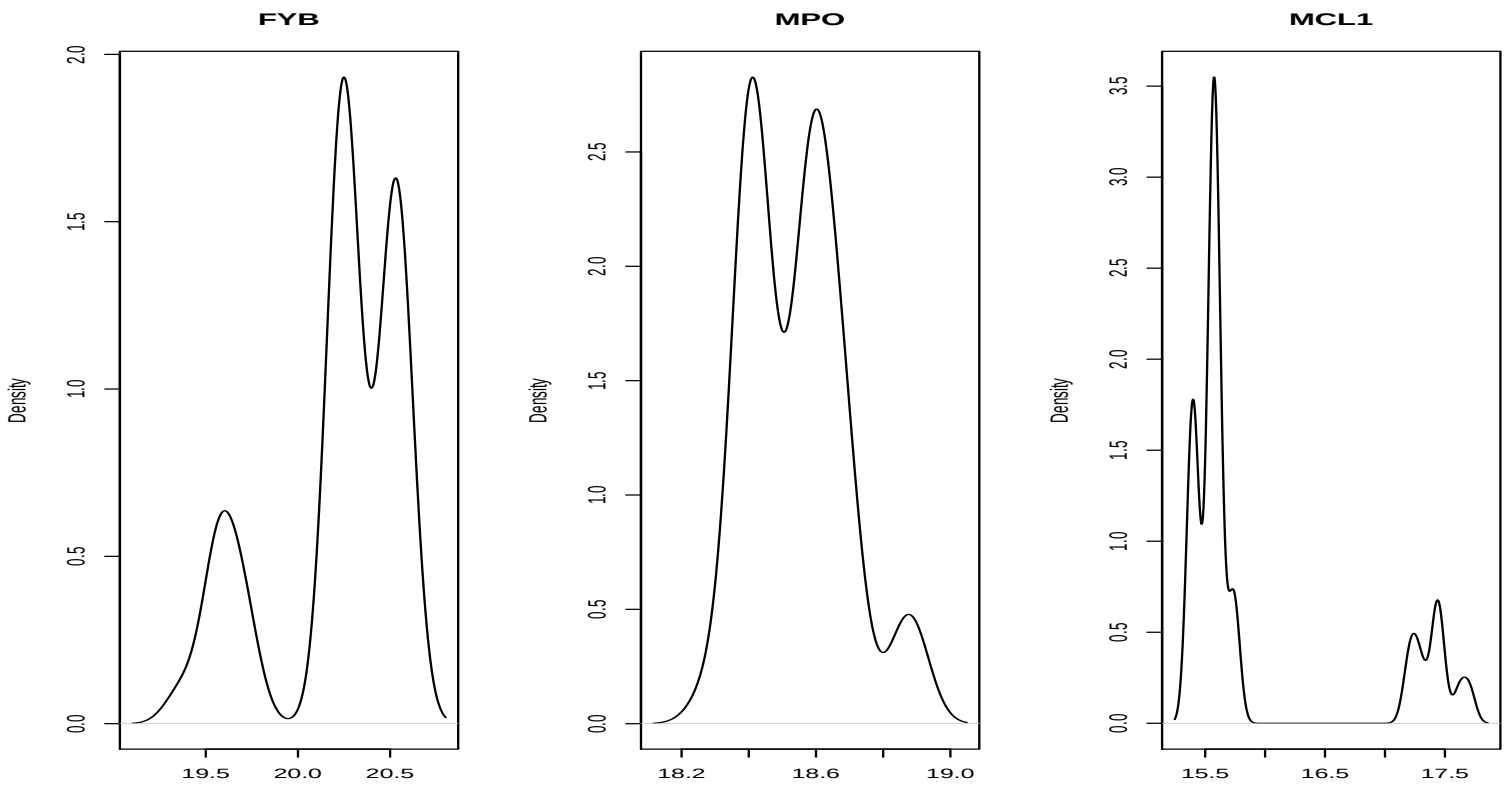






2. Extension: Non-Normality

- Problem: Non-Normality of the data (e.g. T-cell).



- Solution: Copula Gaussian graphical models

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Non-canonical Gaussian copula

- **Sklar's theorem.** Every joint multivariate distribution can be represented by a copula and its marginals.
- We introduced a non-canonical Gaussian copula.

Definition (Non-canonical Gaussian copula)

A non-canonical Gaussian copula with matrix $\mathbf{\Theta}$ and vector $\boldsymbol{\sigma}$ is:

$$C_{\mathbf{\Theta}}(u_1, \ldots, u_p) = \mathbf{\Phi}_{\mathbf{\Theta}}(\Phi_1^{-1}(u_1), \ldots, \Phi_p^{-1}(u_p)),$$

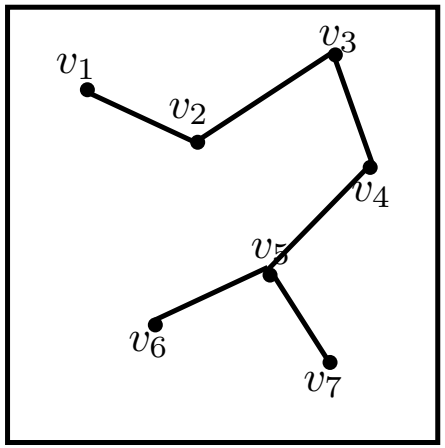
where,

- $\Phi_i(\cdot)$ represents cdf of univariate $N(0, \sigma_i^2)$ distribution,
- $\mathbf{\Phi}_{\mathbf{\Theta}}(\cdot)$ is cdf of multivariate $N(\mathbf{0}, \mathbf{\Theta}^{-1})$ with $\forall i : \theta_{ii} = 1$.

Copula Gaussian graphical models

IDEA:

- Graph exists on a hidden Gaussian variable $\mathbf{Z} \sim N(0, \Theta^{-1})$,
- $\mathbf{Z}$ gives rise to observed non-Gaussian data $\mathbf{Y}$.



Latent Variable: $\mathbf{Z} \sim N(\mu, \mathbf{\Theta^{-1}})$

$$F_1, F_2, \vdots, F_7$$

Marginal Distribution: $\mathbf{F}$

$$Y_1 = F_1^{-1}(\phi(Z_1))$$
$$Y_2 = F_2^{-1}(\phi(Z_2))$$
$$\vdots$$
$$Y_7 = F_p^{-1}(\phi(Z_7))$$

Observed: $\mathbf{Y}$

- We consider the F_i as nuisance parameters.
- For continuous variables: 1-to-1 relationship between Z and Y.
  For discrete variables, relationship is more complicated!

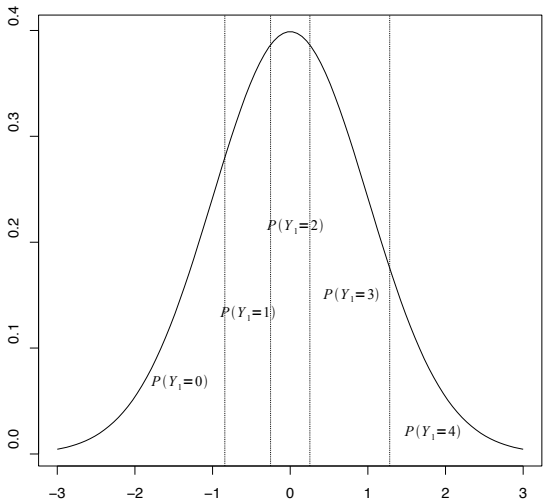
Gaussian Copula for Ordinal Variables

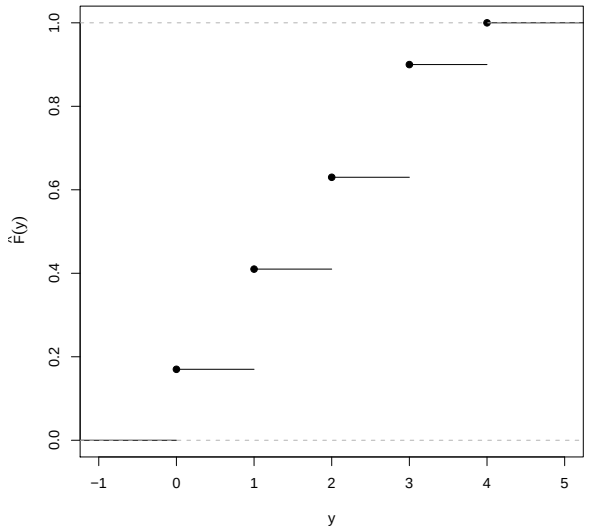
In NESDA depression example $Y = (Y_1, \ldots, Y_p)$ consist of ordinal variables:

$$Y_i \in \{1, 2, 3, 4\}, \quad \text{severity score for item } i$$

Assume existence latent variable $\mathbf{Z} = (Z_1, \ldots, Z_p) \sim N(\mathbf{0}, \mathbf{\Theta}^{-1})$, such that

$$Y_i^{(k)} < Y_i^{(l)} \iff Z_i^{(k)} < Z_i^{(l)}.$$





Values of z_i that correspond to y_i,

$$\mathbf{D}(y_i) = \{\mathbf{z} \in \mathbb{R} \mid F_i^{-1}(\Phi_i(z)) = y_i\}$$

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Maximum Likelihood Estimation

- Gaussian copula density function is:

$$\phi_{\mathbf{\Theta}}(\mathbf{u}) = |\mathbf{\Theta}|^{1/2} exp(-\frac{1}{2}\mathbf{\Phi}^{-1}(\mathbf{u})'(\mathbf{\Theta} - \mathbf{I})\mathbf{\Phi}^{-1}(\mathbf{u})),$$

$$\mathbf{u} = \mathbf{F}(\mathbf{z}) = (F_1(z_1), \ldots, F_p(z_p))$$

- The profile marginal likelihood is:

$$L(\mathbf{\Theta}|\mathbf{D}, \hat{F}_1, \ldots, \hat{F}_p) = \int_{\mathbf{z}\in\mathbf{D}} \phi_{\mathbf{\Theta}}(\mathbf{z}) d\mathbf{z}$$

Problem: Marginal likelihood is hard.

Solution: The iterative EM Algorithm

- **E-Step**:
  Compute the quantity $Q(\mathbf{\Theta}|\mathbf{\Theta}^{(m)}) = \mathbb{E}_{\mathbf{Z}}[l(\mathbf{\Theta})|\mathbf{Y}, \mathbf{\Theta}^{(m)}]$

$$Q(\mathbf{\Theta} \mid \mathbf{\Theta}^{(m)}) \quad = \quad \frac{n}{2}\left\{\log|\mathbf{\Theta}| - \mathrm{tr}\left(\mathbf{\Theta}\bar{\mathbf{R}}\right) + \mathrm{tr}\left(\bar{\mathbf{R}}\right)\right\},$$

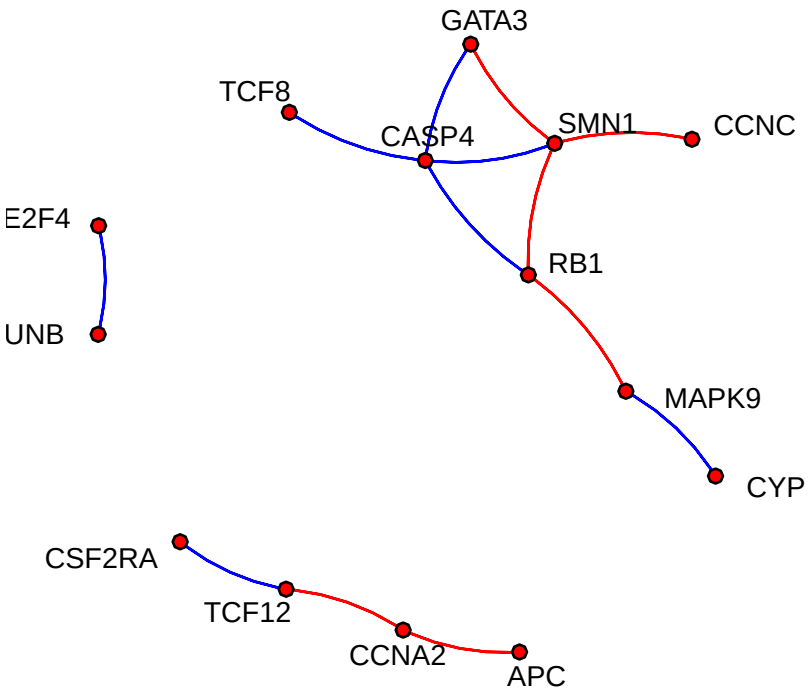
  where

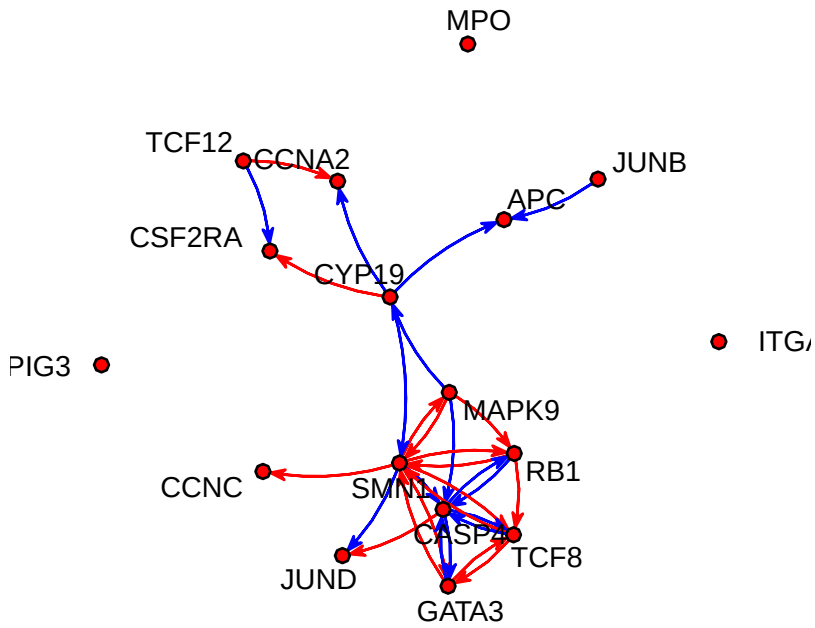
$$\bar{\mathbf{R}} = \mathbb{E}\left[\mathbf{Z}_i\mathbf{Z}_i' \mid \mathbf{Z}_i \in \mathbf{D}(Y_i), \mathbf{\Theta}^{(m)}\right]$$

  can be found explicitly via result in Wilhem. and Manjunath (2010).
- **M-Step**:
  Maximize $Q(\mathbf{\Theta}|\mathbf{\Theta}^{(m)})$ subject to $||\mathbf{\Theta}||_1 \leq 1/\lambda$ and colouring F.

Application of Gaussian copula graphical models to T-cell

$$S_0 \prec F_1, \mathbf{N_0} \prec \mathbf{F_\Gamma}, S_1 \prec F_T, \mathbf{N_1} \prec \mathbf{F_\Gamma}$$





$N_0^1 = N_0^2 = \ldots = N_0^{10}$

$N_1^1 = N_1^2 = \ldots N_1^{10}$

3. Appropriate level of penalization

Model selection

The penalty parameter λ determines the amount of sparsity in the model.

- Consistency for $\lambda = O(\sqrt{log(p)/n})$, but what for small n?
- AIC or BIC are not appropriate for *penalized* likelihoods, because

$$i(\hat{\Theta}_\lambda) \neq 0.$$

Steps for finding the appropriate level of sparsity?

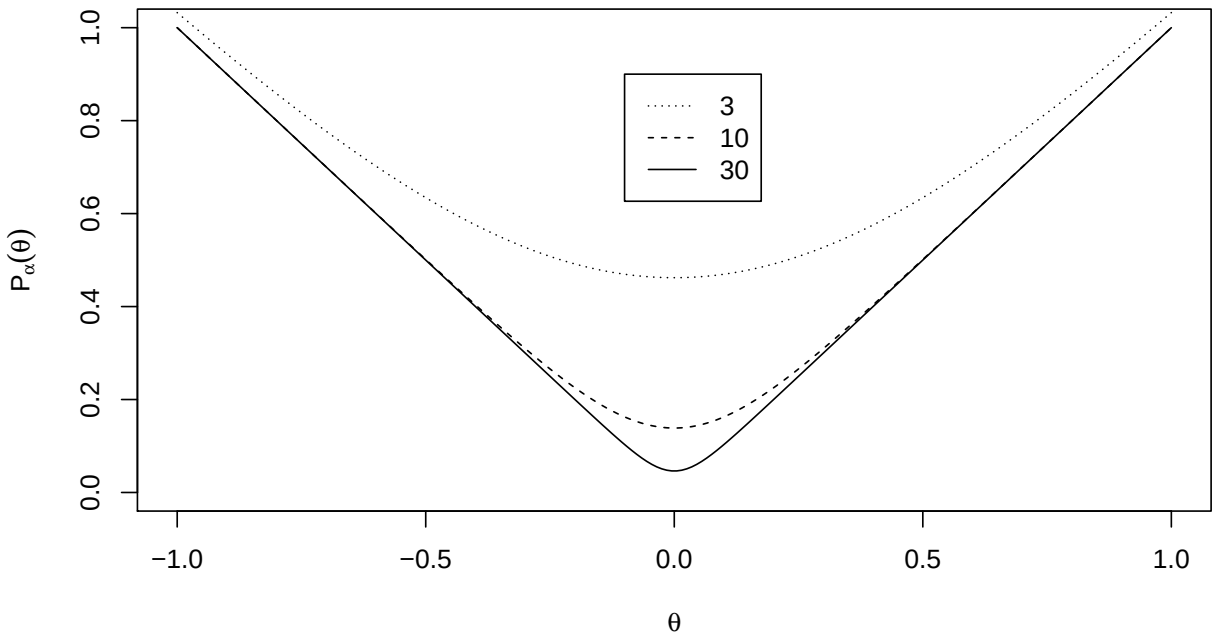
1. We define an approximate problem (AP);
2. We define an information criterion of the AP;
3. We show that limit of solution of AP is meaningful for our problem

Approximated problem: M-estimation

Let $\hat{\Theta}_{\lambda,\alpha}$ be the maximizer of the penalized likelihood

$$l_{\lambda,\alpha}(\Theta) = \sum_{k=1}^{n} l_k(\Theta) - n\lambda P_\alpha(\Theta),$$

where $P_\alpha(\Theta) = \sum_{ij}[\log\{1+\exp(-\alpha\theta_{ij})\} + \log\{1+\exp(\alpha\theta_{ij})\}]/\alpha$.



$\hat{\Theta}_{\lambda,\alpha}$ is an M-estimator of ψ-type: $\sum_{k=1}^{n} l'_{y_k}(\Theta) - \lambda P'_\alpha(\Theta) = 0$.

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GIC for Approximated Problem

Konishi and Kitagawa (2008) defined the GIC for M-estimators:

$$GIC(\hat{\Theta}_{\lambda,\alpha}) = -n\{\log|\hat{\Theta}_{\lambda,\alpha}| - \mathrm{Tr}(\hat{\Theta}_{\lambda,\alpha}S)\} + 2\mathrm{Tr}\{R^{-1}(\alpha)Q\},$$

where $R(\alpha)$ is square matrix of order p^2

$$R(\alpha) = \frac{1}{2}\hat{\Theta}^{-1}_{\lambda,\alpha} \otimes \hat{\Theta}^{-1}_{\lambda,\alpha} + \lambda P''_{\alpha}(\hat{\Theta}_{\lambda,\alpha}), \tag{1}$$

and $P''_{\alpha}(\hat{q}_{\lambda,\alpha})$ diagonal matrix with p^2 elements $(|\hat{\theta}_{11}|''_{\alpha}, \hat{\theta}_{12}|''_{\alpha}, \ldots, |\hat{\theta}_{pp}|''_{\alpha})$ and

$$\begin{aligned} Q(\alpha) &= \frac{1}{4}\mathrm{vect}S\mathrm{vect}S^T - \frac{1}{4n}\sum_{k=1}^{n}\mathrm{vect}_k\mathrm{vect}_k^T \\ &= Q \end{aligned}$$

"GIC" = Limit of AP GIC

L_1 penalized estmimators are no M-estimators, so GIC is not defined.

We define the GIC as α-limit of approximated one.

Definition ("GIC" for L_1 penalized graphical models.)

$$\mathrm{GIC}(\lambda) = -n\{\log|\hat{\Theta}_\lambda| - \mathrm{Tr}(\hat{\Theta}_\lambda S)\} + 2\mathrm{Tr}(R^{-1}Q),$$

Matrix Q is square matrix of order p^2 (as above) and

$$R[I, I] = \hat{\Theta}_\lambda \otimes \hat{\Theta}_\lambda[I, I]^{-1},$$

where I are the non-zero elements in $\mathrm{vect}\hat{\Theta}_\lambda$.

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Performance of the GIC: simulation study

		TP	Sens.	TN	Spec.
N = 8	GIC	13.0	0.531	51.0	0.543
	AIC	0.0	0.000	94.0	1.000
	BIC	0.0	0.000	94.0	1.000
N = 12	GIC	16.0	0.667	45.0	0.479
	AIC	2.0	0.077	93.0	0.989
	BIC	0.5	0.019	94.0	1.000

Results p = 16; Present Links = 26; Absent Links=102

However,

$$\lim_{N\to\infty} GIC = \lim_{N\to\infty} AIC,$$

so GIC is not edge-selection consistent.

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Conclusion and Discussion

Summary:

- Factorial graphical models based on coloured graphs.
- Slowly changing graphical models.
- Extension: Copula Gaussian graphical models.
- How do we evaluate model complexity?

Questions:

- How would we adapt model with other factors?
- Could we combine Copulas with slowly changing networks?
- How to introduce latent structures?