Estimating Graphical Models Combinations

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Outline

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1. Meta-analysis vs structural meta-analysis

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2. Motivating examples

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3. Statistical models combination
    - Combination of distributions
    - Combination of families

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    - Combination of distributions
    - Combination of families
4. Graphical models combination
    - Examples
    - Graphical and non-graphical combinations
    - Estimation

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- **Meta-analysis** is combining evidence about **important parameters** from experiments or studies performed independently under partially comparable circumstances;
- **Structural meta-analysis** (Massa and Lauritzen, 2010), is the combination of evidence about **relationships** between variables from studies or experiments carried out independently under partially comparable conditions.
- By relationships between variables we mean **conditional independence relations**, as defined by Dawid (1979).

Example: Two surveys

Gilula and McCullogh (2011)

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For example:

- Survey A investigates: age, income, gender, smoking habits, . . .;
- Survey B investigates: age, income, opinion about banning smoking in public, ...

Example: Cancer Studies

DuMouchel and Harris (1983)

Rows: 5 studies.

Columns: 10 variables investigated.

A filled circle means data available.

	ROOF TAR	COKE OVEN	GAS ENGINE	BaP	CIG.	DIESEL A	DIESEL B	DIESEL C	DIESEL D	DIESEL E
LUNG CANCER	●	●			●					●
SKIN TUMOR INIT.	●	●	●	●	●	●	●		●	
VIRAL TRANSFORM.	●	●	●	●	●	●	●	●	●	
MUTAGENESIS −MA	●	●	●		●	●	●	●	●	
MUTAGENESIS +MA	●	●	●		●	●	●	●	●	
	1	2	3	4	5	6	7	8	9	10

Example: Teen Drinking

Dee and Evans (2003)

- Data on teen drinking;
- Data on educational attainment;
- No dataset that contains both information on teen drinking and educational attainment.
- Study the effect of teen drinking on educational attainment.

Example: Diseasome

Goh et al. (2007)

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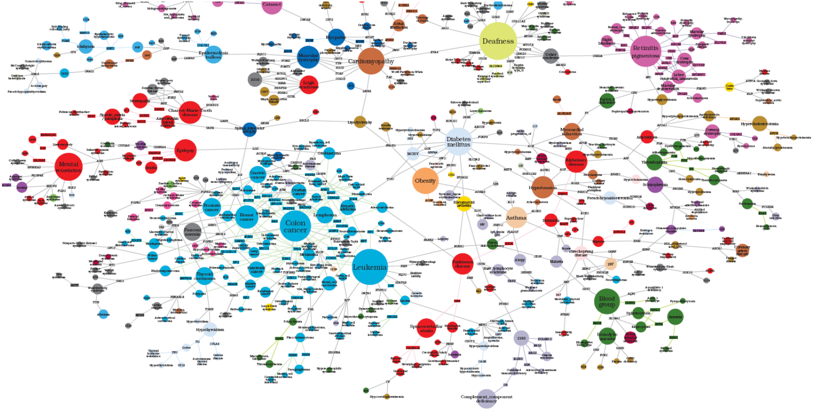
- Example of a **graphical models meta-analysis**.
- A large set of diseases and relevant genes is combined to form "the human diseasome" bipartite network.
- The authors also generate two biologically relevant networks, the human disease network projection and the disease gene network projection.

Diseasome

Goh et al. (2007)

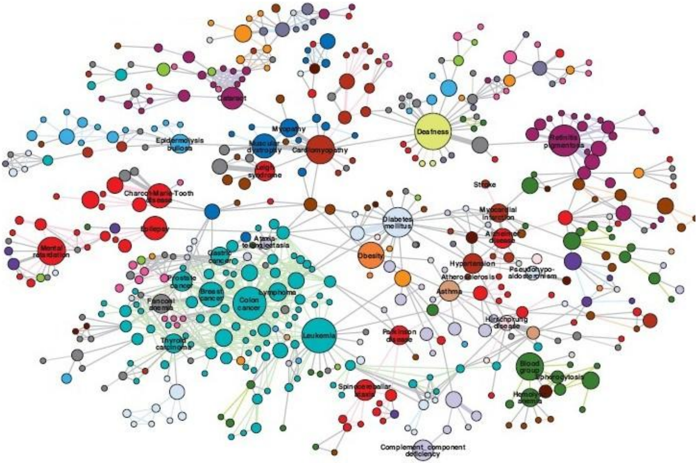
A subset of the diseasome bipartite network. Circles are **disorders**, rectangles are **disease genes**.



The Human Disease Network

Goh et al. (2007)

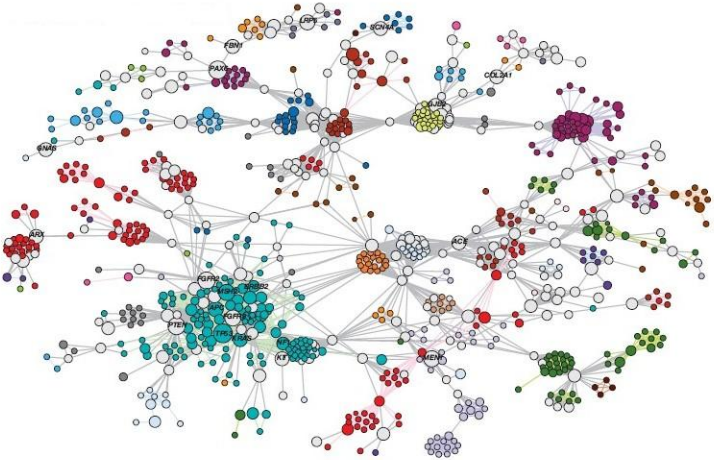
A subset of the **human disease network projection** of the bipartite graph. Each node corresponds to a distinct **disorder**.



The Disease Gene Network

Goh et al. (2007)

A subset of the **disease gene network projection** of the bipartite graph.
Each node is a **gene**.



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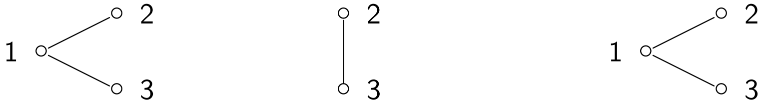

Figure: The rightmost graph represents the combination since both models imply the same constraints for the joint distribution of (Y_2, Y_3).

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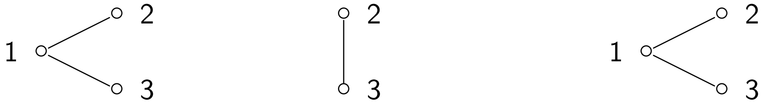

Figure: The rightmost graph represents the combination since both models imply the same constraints for the joint distribution of (Y_2, Y_3).

Figure: Here it is less obvious to define the combination and to represent the combination graphically.

Example

Figure: There are no conditional independence relationships expressed by the two graphs on the left. The graph on the right represents their combination.

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- Different types of graphs: for example DAGs.
- In this talk, for simplicity the focus is only on **Gaussian variables**.

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- $\mathcal{F} = \{f\}$ is the family of distributions over $A \subseteq V$.
- $\mathcal{F}^{\downarrow C}$ are the induced marginal distributions over $C \subseteq A$.

Set-up

Consider two sets of variables A and B, and two families $\mathcal{F}$ and $\mathcal{G}$ of distributions for Y_A and Y_B, where A and $B \subseteq V$.

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Ideally search for a joint family of distributions, $\mathcal{H}$ for $Y_{A \cup B}$, such that

$$\mathcal{H}^{\downarrow A} = \mathcal{F}, \quad \mathcal{H}^{\downarrow B} = \mathcal{G}.$$

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If f and g are **not consistent**, but $f_{A \cap B} << g_{A \cap B}$, their **right composition** (Jiroušek and Vejnarová, 2003) is

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$$f \triangleleft g = \frac{f}{f_{A \cap B}} \cdot g.$$

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If $\mathcal{F}$ and $\mathcal{G}$ are **meta-consistent**, i.e., $\mathcal{F}^{\downarrow A \cap B} = \mathcal{G}^{\downarrow A \cap B}$, this is the **meta-Markov combination** $\mathcal{F} \star \mathcal{G}$ of Dawid and Lauritzen (1993).

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All marginal distributions of the two families are represented also in the combined family.
Here we have

$$(\mathcal{F} \,\bar{\star}\, \mathcal{G})^{\downarrow A} \supseteq \mathcal{F}^{\mathcal{G}}, \quad (\mathcal{F} \,\bar{\star}\, \mathcal{G})^{\downarrow B} \supseteq \mathcal{G}^{\mathcal{F}},$$

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It holds that $\mathcal{F} \,\underline{\star}\, \mathcal{G} \subseteq \mathcal{F} \,\overline{\star}\, \mathcal{G}$.

Cuts and Equivalence of Combinations

Let $\mathcal{F}$ and $\mathcal{G}$ be two families of distributions for random variables Y_A and Y_B. The following are equivalent:

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(iii) $\mathcal{F}$ and $\mathcal{G}$ are meta-consistent and $Y_{A \cap B}$ is a cut for $\mathcal{F}$ and $\mathcal{G}$.

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Recall that $Y_{A\cap B}$ is a cut in $\mathcal{F}$ if $\mathcal{F} \sim \mathcal{F}^{\downarrow A|(A\cap B)} \times \mathcal{F}^{\downarrow A\cap B}$, (Barndorff-Nielsen, 1978).

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$$\mathcal{F} \otimes \mathcal{G} = \mathcal{F}^{\star\star} \star \mathcal{G}^{\star\star}.$$

Summarising

- **Lower** Markov combination (restrictive case)

$$\mathcal{F} \underline{\star} \mathcal{G} = \left\{ \frac{f \cdot g}{f_{A \cap B}}, f \in \mathcal{F}, g \in \mathcal{G}, f \text{ and } g \text{ consistent} \right\}.$$

Summarising

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- **Upper** Markov combination (less restrictive case)

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- **Super** Markov combination (maximal extension of the families)
$\mathcal{F} \otimes \mathcal{G} = \mathcal{F}^{\star\star} \star \mathcal{G}^{\star\star}$ also written as

$$\mathcal{F} \otimes \mathcal{G} = \left\{ f_{A|A \cap B} \cdot h_{A \cap B} \cdot g_{B|A \cap B}, \; f \in \mathcal{F}, h \in \mathcal{F} \cup \mathcal{G}, g \in \mathcal{G} \right\}.$$

Conditional Independence Assumption

- All combinations use the conditional independence assumption $A \perp\!\!\!\perp B | (A \cap B)$.
- If $A \perp\!\!\!\perp B | (A \cap B)$ does not hold, then the separate analyses of A and B can potentially be very misleading as the missing data in each case typically will induce spurious correlations.
- It may make sense to use this assumption and then consider the distortions that this may induce.

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- Is there any context when the problem becomes very simple?
- Difference between **graphical** and **non-graphical** combinations.

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- Meta-consistency is related to but different from **collapsibility** of the two dependence graphs onto $A \cap B$.

- In general, all constraints on the common variables must be investigated.

Examples

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Figure: Two meta-consistent graphical Gaussian models (the two graphs are isomorphic and therefore induce the same restrictions on the common variables).

Conditions for Equivalence of Combinations

If the graphs are collapsible onto $A \cap B$ and the induced subgraphs on the common variables are the same, then

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Here the combination is **graphical** and its dependence graph is given by

$$G(\mathcal{F} * \mathcal{G}) = G(\mathcal{F}) \cup G(\mathcal{G}).$$

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- The **upper Markov combination** combines all the marginal distributions from one family with all the conditional distributions from the other family.

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- We need to distinguish between **graphical** and **non-graphical** combinations.

Example - Graphical Combination

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The **lower Markov combination** is
$\mathcal{F} \underline{\star} \mathcal{G} = \mathcal{F} \star \mathcal{G} = \{ Y \sim N_3(0, \Sigma), \Sigma^{-1} \in S^+(G_A), \Sigma_{\{2,3\}} = \Phi_{\{2,3\}} \}$.

The **upper** and **super Markov** combination are identical and the corresponding graph is a complete graph.

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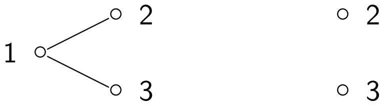
$$\mathcal{F} \underline{\star} \mathcal{G} = \{ Y \sim N_3(0, \Omega), \, \omega_{23}\omega_{11} = \omega_{12}\omega_{13}, \, \omega_{23} = 0 \},$$

where $\Omega = \{\omega_{ij}\}$.

Example - Non-Graphical Combination



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It is the union of the graphical model with vertex set $\{1, 2, 3\}$ and edge $(1, 2)$ and the graphical model with vertex set $\{1, 2, 3\}$ and edge $(1, 3)$.

Example (cont.)

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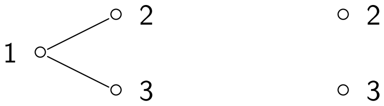

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The **super Markov combination** is

$$\mathcal{F} \otimes \mathcal{G} = \left\{ \frac{f_{123} \cdot g_{23}}{f_{23}}, f_{123} \right\},$$

and they are both **graphical** combinations.

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- Consider an approach that exploits all the available information and converts the problem in a missing data one.
- The available initial data define the complexity of the estimation process (**raw data** vs **derived quantities**).

Missing Data Approach

An example

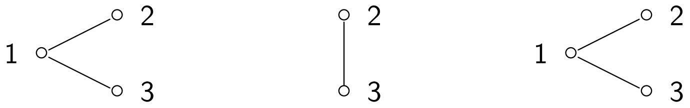

Figure 1: From left to right, families $\mathcal{F}$, $\mathcal{G}$, and $\mathcal{F} \star \mathcal{G}$.

- $y_A = (y_j^i)$ with $j = 1, 2, 3$ and $i = 1, \cdots, n_A$ observations from $\mathcal{F}$.

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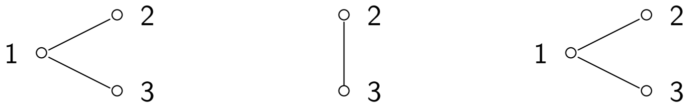

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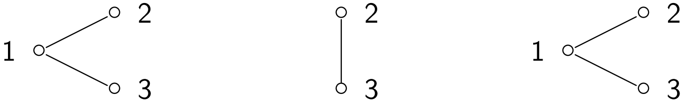

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	1	2	3
$\mathcal{F}$	n_A	n_A	n_A
$\mathcal{G}$		n_B	n_B

Table: Missing pattern for the problem considered.

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Apply standard EM algorithm as detailed for mixed graphical models by Didelez and Pigeot (1998).

The partial imputation EM algorithm (Geng et al., 2000) would be more efficient when dealing with **high dimensional graphs** and **multiple combinations**.

EM Algorithm

- The sufficient statistics are given by

$$w_{jj} = \sum_{i=1}^{n} (y_j^i)^2, \; j = 1, 2, 3 \quad w_{1j} = \sum_{i=1}^{n} y_1^i y_j^i, \; j = 2, 3.$$

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- The maximum likelihood estimate for the complete data case is

$$\hat{K} = n \begin{pmatrix} w_{[1,2]}^{11} & w_{[1,2]}^{12} & 0 \\ w_{[1,2]}^{21} & w_{[1,2]}^{22} & 0 \\ 0 & 0 & 0 \end{pmatrix} + n \begin{pmatrix} w_{[1,3]}^{11} & 0 & w_{[1,3]}^{13} \\ 0 & 0 & 0 \\ w_{[1,3]}^{31} & 0 & w_{[1,3]}^{33} \end{pmatrix} - \begin{pmatrix} \frac{n}{w_{11}} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

$w_{[A]}^{ij}$ is the ijth element in $\hat{W}_{[A]}^{-1}$, where $W = \sum_{i=1}^{n} y^i (y^i)^T$.

E-Step

Compute the expected values of the complete data sufficient statistics, conditional on the observed data, using the current estimate of the parameter.

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Compute the expected values of the complete data sufficient statistics, conditional on the observed data, using the current estimate of the parameter.
At iteration (t), denote the current estimate of the parameter as $\theta^{(t)} = K^{(t)}$. The E-step computes

$$
\begin{aligned}
w_{1j}^{(t)} &= E\left(\sum_{i=1}^{n} Y_1^i Y_j^i \middle| Y_{obs}, \theta^{(t)}\right), \\
w_{11}^{(t)} &= E\left(\sum_{i=1}^{n} (Y_1^i)^2 \middle| Y_{obs}, \theta^{(t)}\right), \\
w_{jj} &= w_{jj}^{(t)} = E\left(\sum_{i=1}^{n} (Y_j^i)^2 | Y_{obs}, \theta^{(t)}\right).
\end{aligned}
$$

M-Step

The M-step computes $\hat{K}^{(t+1)}$, by updating the relevant quantities with the values obtained in the E-step:

$$\hat{K}^{(t+1)} = n \begin{pmatrix} {w^{11}_{[1,2]}}^{(t)} & {w^{12}_{[1,2]}}^{(t)} & 0 \\ {w^{21}_{[1,2]}}^{(t)} & w^{22}_{[1,2]} & 0 \\ 0 & 0 & 0 \end{pmatrix} + n \begin{pmatrix} {w^{11}_{[1,3]}}^{(t)} & 0 & {w^{13}_{[1,3]}}^{(t)} \\ 0 & 0 & 0 \\ {w^{31}_{[1,3]}}^{(t)} & 0 & w^{33}_{[1,3]} \end{pmatrix} - \begin{pmatrix} \frac{n}{{w_{11}}^{(t)}} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

The algorithm performs the two steps until convergence, after having specified an initial value K_0 for K.

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Direct Estimation

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- It would make no difference whether we have the **maximum likelihood estimates** from each of the experiments or the **raw data**.
- We can directly combine the estimates of the single models and a missing data approach is **not** required.

Direct Estimation

Figure: All combinations are identical to the combination on the right.

All the combinations are equivalent to

$$\mathcal{F} \star \mathcal{G} = \{f \star g, f \in \mathcal{F}, g \in \mathcal{G}\}.$$

The estimation of the combination is given by the combination of the separate estimates, i.e., $\hat{f}$ and $\hat{g}$.

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- A comparative evaluation of the two approaches is also interesting.

Some References

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