Causal Discovery for Linear Cyclic Models with Latent Variables

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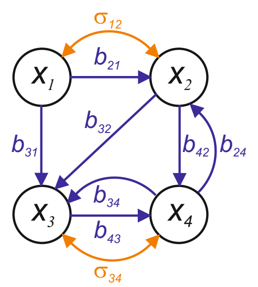
Linear Cyclic Model with Latent Variables



$$\mathbf{B} = \begin{pmatrix} 0 & 0 & 0 & 0 \\ b_{21} & 0 & 0 & b_{24} \\ b_{31} & b_{32} & 0 & b_{34} \\ 0 & b_{42} & b_{43} & 0 \end{pmatrix} \qquad \mathbf{\Sigma_e} = \begin{pmatrix} \sigma_1^2 & \sigma_{12} & 0 & 0 \\ \sigma_{12} & \sigma_2^2 & 0 & 0 \\ 0 & 0 & \sigma_3^2 & \sigma_{34} \\ 0 & 0 & \sigma_{34} & \sigma_4^2 \end{pmatrix}$$

$$\mathbf{x} := \mathbf{Bx} + \mathbf{e} \quad \Leftrightarrow \quad \begin{array}{lll} x_1 & := & e_1 \\ x_2 & := & b_{21}x_1 + b_{24}x_4 + e_2 \\ x_3 & := & b_{31}x_1 + b_{32}x_2 + b_{34}x_4 + e_3 \\ x_4 & := & b_{42}x_2 + b_{43}x_3 + e_4 \end{array}$$

★ The model is parametrized by $\mathbf{B}$ and $\text{cov}(\mathbf{e}) = \mathbf{\Sigma_e}$.

★ Behaviour at equilibrium:

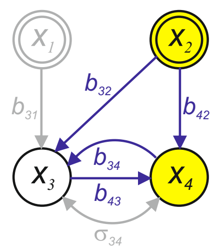
$$\begin{array}{lll} \mathbf{x}_t & := & \mathbf{Bx}_{t-1} + \mathbf{e} \quad \leftarrow \text{background conditions invariant} \\ \mathbf{x}_\infty & := & \mathbf{B}^\infty \mathbf{x}_0 + (\mathbf{I} + \mathbf{B} + \mathbf{B}^2 + \cdots)\mathbf{e} \\ \mathbf{x}_\infty & := & (\mathbf{I} - \mathbf{B})^{-1}\mathbf{e} \end{array}$$

$$\mathbf{e} \sim \mathrm{N}(\mathbf{0}, \mathbf{\Sigma_e}) \Rightarrow \mathbf{x}_\infty \sim \mathrm{N}(\mathbf{0}, (\mathbf{I}-\mathbf{B})^{-1}\mathbf{\Sigma_e}(\mathbf{I}-\mathbf{B})^{-T})$$

A1 Self cycles are not identifiable from equilibrium data, so assuming $\forall i: b_{ii} = 0$.

A2 The model and all possible manipulated models are assumed stable: absolute of the eigenvalues of $\mathbf{B}$ and $\mathbf{B}^m$:s must all be less than 1.

Interventions & Experimental Effects



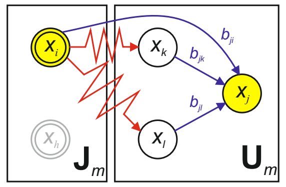
$$\mathbf{B}^m = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ b_{31} & b_{32} & 0 & b_{34} \\ 0 & b_{42} & b_{43} & 0 \end{pmatrix} \qquad \mathbf{\Sigma}^m_\mathbf{e} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & \sigma_3^2 & \sigma_{34} \\ 0 & 0 & \sigma_{34} & \sigma_4^2 \end{pmatrix}$$

$$\mathbf{C}^k_x = (\mathbf{I}-\mathbf{B}^m)^{-1}\mathbf{\Sigma}^m_\mathbf{e}(\mathbf{I}-\mathbf{B}^m)^{-T} = \left(\begin{array}{cc|cc} 1 & \cdot & \cdot & \cdot \\ 0 & 1 & \cdot & \cdot \\ \hline t(x_1 \rightsquigarrow x_3 || \{x_1,x_2\}) & t(x_2 \rightsquigarrow x_3 || \{x_1,x_2\}) & v_3^2 & \cdot \\ t(x_1 \rightsquigarrow x_4 || \{x_1,x_2\}) & t(x_2 \rightsquigarrow x_4 || \{x_1,x_2\}) & v_{34} & v_4^2 \end{array}\right)$$

independent randomizations ↓ ; ↑ experimental effects ; ↑ between observed

$$\begin{array}{lll} \mathbf{t}(\mathbf{x_2} \rightsquigarrow \mathbf{x_4} || \{\mathbf{x_1}, \mathbf{x_2}\}) & = & \text{Regression coefficient of } x_2 \text{ on } x_4 \\ & = & \text{Sum of all open paths from } x_2 \text{ to } x_4 \\ & = & b_{42} + b_{43}b_{32} + b_{43}b_{34}b_{42} + \cdots \\ & = & (b_{42} + b_{43}b_{32})(1 + b_{43}b_{34} + \cdots) \\ \text{nonlinear} \rightarrow & = & \dfrac{b_{42} + b_{43}b_{32}}{1 - b_{43}b_{34}} \\ & = & b_{42} + \dfrac{b_{32} + b_{34}b_{42}}{1 - b_{43}b_{34}} b_{43} \\ \text{linear} \rightarrow & = & \mathbf{b_{42}} + \mathbf{t}(\mathbf{x_2} \rightsquigarrow \mathbf{x_3} || \{\mathbf{x_1}, \mathbf{x_2}\})\mathbf{b_{43}} \end{array}$$

Linear Equations



$$t(x_i \rightsquigarrow x_j || \mathbf{J}_m) = b_{ji} + \sum_{x_k \in \mathbf{U}_m \setminus x_j} t(x_i \rightsquigarrow x_k || \mathbf{J}_m)\, b_{jk}$$

Method

1. Input covariance matrices $\mathbf{C}^1_x, \cdots \mathbf{C}^k_x$.
2. Form linear equations

$$\begin{pmatrix} \mathbf{K}_1 & & \\ & \mathbf{K}_2 & \\ & & \ddots \end{pmatrix} \begin{pmatrix} b_{12} \\ \vdots \\ b_{1n} \\ \hline b_{21} \\ \vdots \end{pmatrix} = \begin{pmatrix} t(x_2 \rightsquigarrow x_1 || \bullet) \\ \vdots \\ t(x_n \rightsquigarrow x_1 || \bullet) \\ \hline t(x_1 \rightsquigarrow x_2 || \bullet) \\ \vdots \end{pmatrix}$$

3. Solve for direct effects b_{ij}.
4. Get the covariances of the error terms σ_{ij} from an experiment where both x_i and x_j are observed with the formula

$$\sigma_{ij} = [(\mathbf{I} - \mathbf{B}^m)\mathbf{C}^k_x(\mathbf{I} - \mathbf{B}^m)^T][i,j]$$

Identifiability & Underdetermination

Identifiability theorem

Given a sequence of experiments the model $(\mathbf{B}, \mathbf{\Sigma_e})$ is fully identified by the method **if and only if** for each **ordered** pair of variables (x_i, x_j) there is

★ an experiment where x_i is **intervened on** and x_j is **observed** (Pair Condition), and

★ another experiment where both x_i and x_j are **observed** (Covariance Condition).

1. Say we have done experiments intervening on variables $\{x_1\}$, $\{x_1, x_2\}$, $\{x_3\}$.

$$\text{PC}: \begin{pmatrix} \cdot & \times & \checkmark & \times \\ \checkmark & \cdot & \checkmark & \times \\ \checkmark & \checkmark & \cdot & \times \\ \checkmark & \checkmark & \checkmark & \cdot \end{pmatrix}, \quad \text{COV}: \begin{pmatrix} \cdot & \cdot & \cdot & \cdot \\ \checkmark & \cdot & \cdot & \cdot \\ \checkmark & \checkmark & \cdot & \cdot \\ \checkmark & \checkmark & \checkmark & \cdot \end{pmatrix}$$

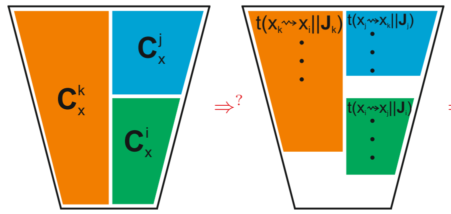
2. Which parameters are identified in the general case?

$$\mathbf{B}: \begin{pmatrix} \cdot & \times & \times & \times \\ \times & \cdot & \times & \times \\ \times & \times & \cdot & \times \\ \checkmark & \checkmark & \checkmark & \cdot \end{pmatrix}, \quad \mathbf{\Sigma_e}: \begin{pmatrix} \times & \cdot & \cdot & \cdot \\ \times & \times & \cdot & \cdot \\ \times & \times & \times & \cdot \\ \times & \times & \times & \checkmark \end{pmatrix}$$

★ Generally, for identifying b_{ji}, pair condition must be satisfied for all pairs $(\bullet, j)$.

★ If pair condition for (i,j) is not satisfied, then b_{ji} is never identified.

Completeness



$\Rightarrow^?$ $\mathbf{Kb} = \mathbf{k} \Rightarrow \mathbf{b} = \mathbf{K}^\dagger \mathbf{k}$

Completeness theorem

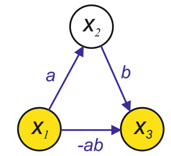
Given the data covariance matrices from a set of experiments, for determining the direct effects b_{ji}, the identifiability condition (Pair Condition) of the approach is **necessary** for any method.

This hinges on the fact that if two different direct effects matrices $\mathbf{B}$ and $\widehat{\mathbf{B}}$ produce the same experimental effects in a given set of experiments, the models $(\mathbf{B}, \mathbf{\Sigma_e})$ and $(\widehat{\mathbf{B}}, (\mathbf{I} - \widehat{\mathbf{B}})(\mathbf{I} - \mathbf{B})^{-1}\mathbf{\Sigma_e}(\mathbf{I}-\mathbf{B})^{-T}(\mathbf{I}-\widehat{\mathbf{B}})^T)$ can be shown to produce the same covariance matrices for those experiments as well.

Assuming Faithfulness

Faithfulness in linear models

Any independence relation between variables is not the result of several exactly cancelling pathways.

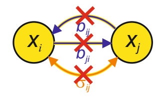


For every experimental dataset

1. Run a search for finding independencies. Add constraint equations from skeleton rule:

Skeleton rule

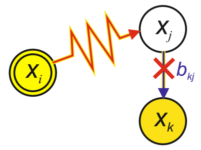
$$\begin{array}{c} x_i \perp\!\!\!\perp x_j \,|\, S \\ x_j \notin \mathbf{J}_m \\ \hline b_{ji} = 0 \end{array}$$



2. Add more constraint equations from orientation rules:

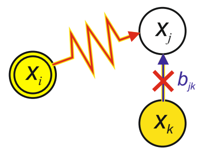
Orientation rule 1

$$\begin{array}{c} t(x_i \rightsquigarrow x_k || \mathbf{J}_m) = 0 \\ t(x_i \rightsquigarrow x_j || \mathbf{J}_m) \neq 0 \\ \hline b_{kj} = 0 \end{array}$$



Orientation rule 2

$$\begin{array}{c} x_i \perp\!\!\!\perp x_k \,|\, x_j \\ t(x_i \rightsquigarrow x_j || \mathbf{J}_m) \neq 0 \\ \hline b_{jk} = 0 \end{array}$$



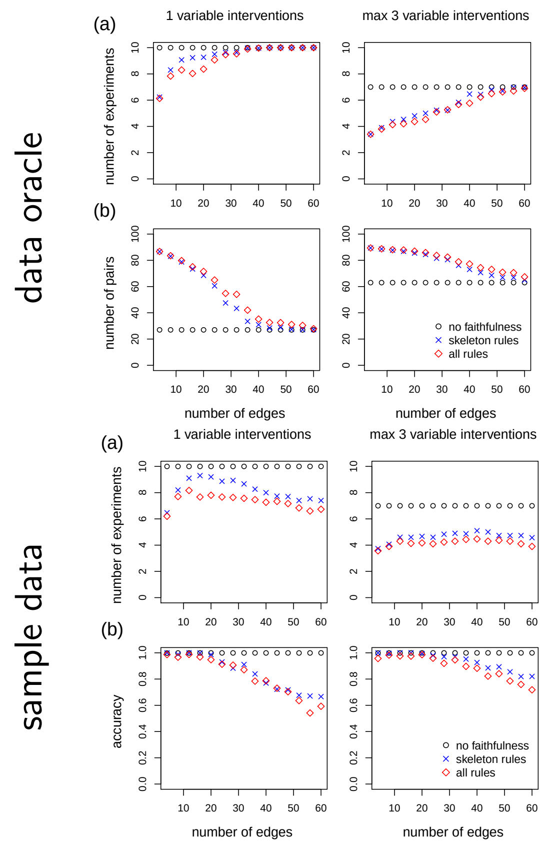
3. Take into account the additional structure found when selecting the next experiment.

Experiment Selection

1. Select the experiment that satisfies the pair condition for most new pairs.
2. If any parameters are identified, consider the pair condition for the corresponding pairs as satisfied.

Test Results

Selecting the experiment in such a way that the model is learned accurately with the fewest number of experiments.



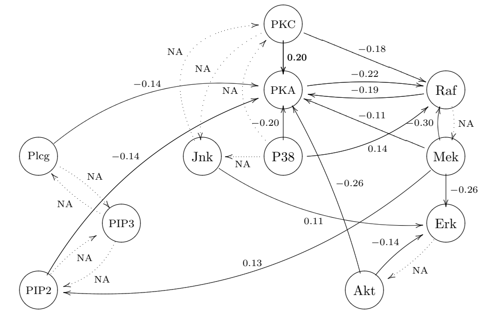
★ Fewer experiments are needed with sparse graphs.

★ More structure is discovered earlier on with sparse graphs.

★ With denser graphs the accuracy gets worse.

Sachs et al Flow Cytometry Data

Learning as much of the structure as possible given only 5 experiments, intervening on {},{Mek},{PIP2},{Akt} and {PKC}.



★ Pair condition was satisfied for only 40/110 of the pairs, yet when assuming faithfulness most of parameters have been identified.

Summary

★ Method for learning linear cyclic models with latent variables using randomized experiments.
★ Complete with regard to search space and assumptions.
★ Necessary and sufficient identifiability condition.
★ Underdetermination characterized.
★ Faithfulness incorporated.
★ R-code available.