# MLSS 2019: Causality

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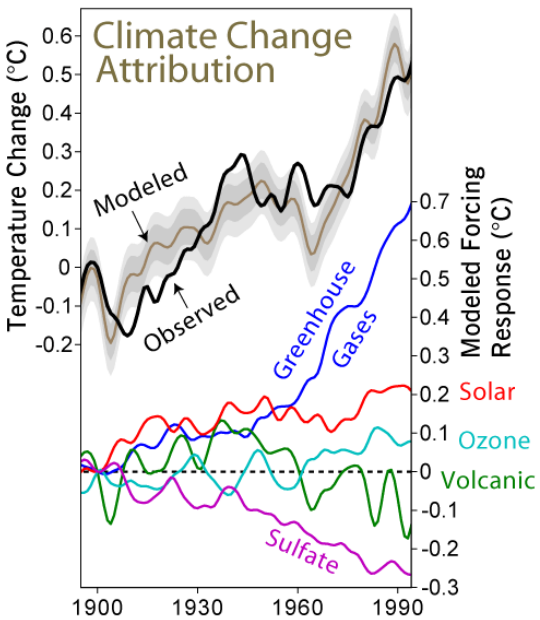
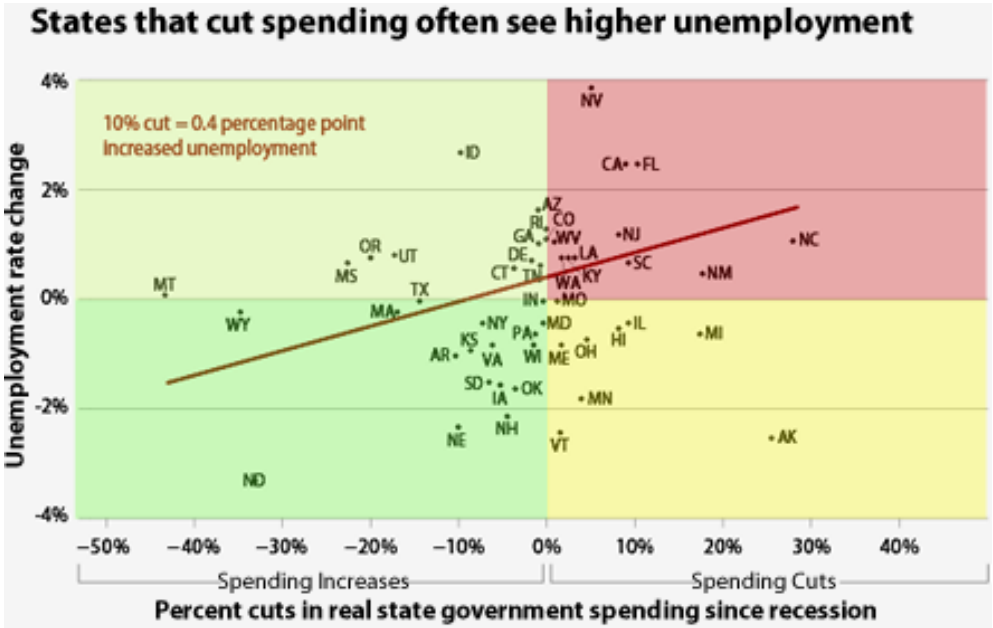
# Many questions in science are *causal*

## **Climatology**:

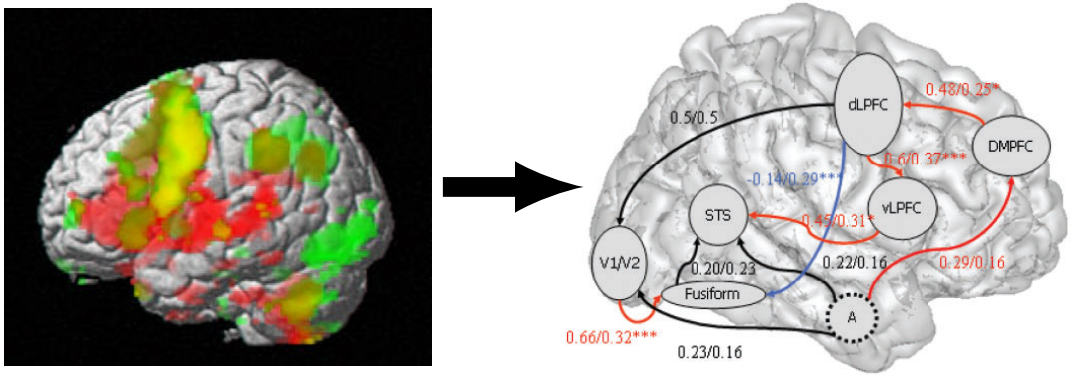



## **Economy**:




## **Medicine**:

## **Neuroscience**:



# Contents of this tutorial

Causality is clearly an important notion in daily life and in science.

- But how should we formalize the notion of causality?
- How to reason about causality?
- How can we discover causal relations from data?
- How to obtain causal predictions?
- How do they differ from ordinary predictions in ML?

That is what you will learn in this tutorial!

# Probabilistic Inference vs. Causal Inference

**Probabilistic Inference (traditional statistics / machine learning)**

- Models the distribution of the data
- Focuses on predicting consequences of observations
- Useful e.g. in medical diagnosis: *given the symptoms of the patient, what is the most likely disease?*

**Causal Inference**

- Models the mechanism that generates the data
- Also allows to predict results of interventions
- Useful e.g. in medical treatment: *if we treat the patient with a drug, will it cure the disease?*

Causal reasoning is essential to answer questions of the type: *given the circumstances, what action should we take to achieve a certain goal?*

# Contents

# Causation $\neq$ Correlation

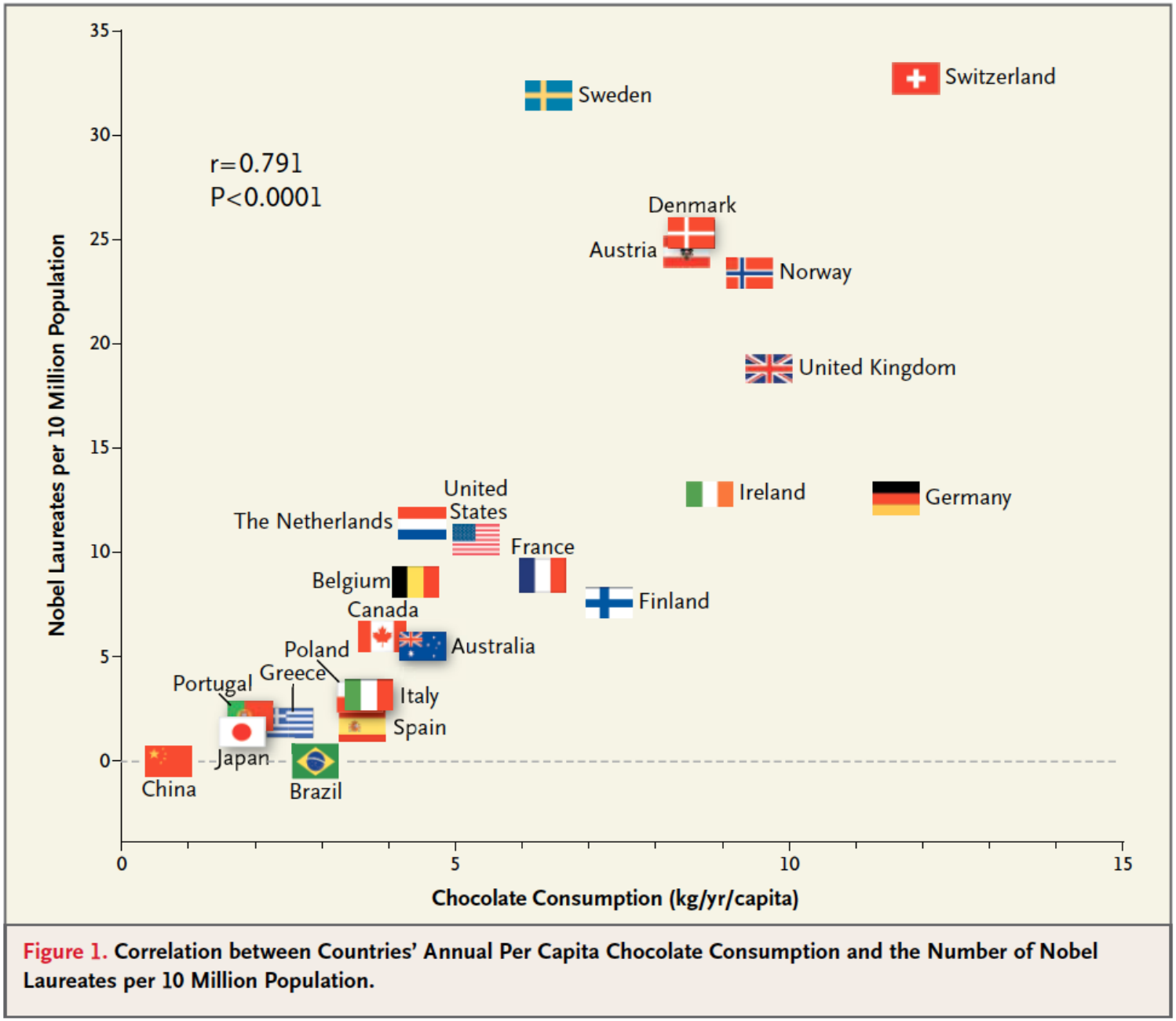



**Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.**

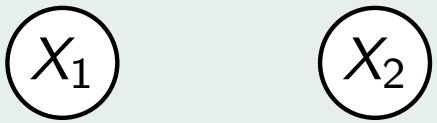
# Causal relations

## Definition (Informal)

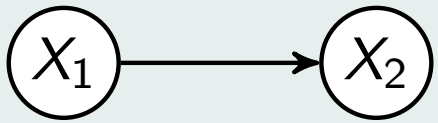
Let $X$ and $Y$ be two distinct variables of system. $X$ causes $Y$ if changing $X$ (*intervening on* $X$) leads to a change of $Y$.

Causal graph represents causal relationships between variables graphically.

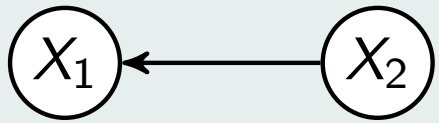
## Example



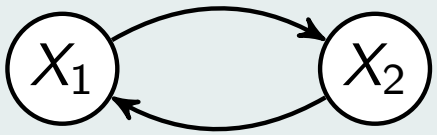

$X_1$ and $X_2$ are causally unrelated



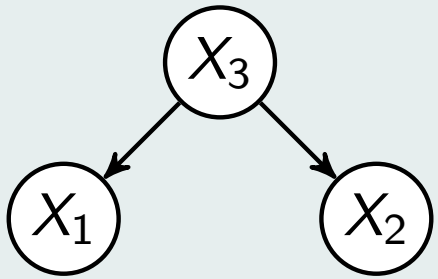

$X_1$ causes $X_2$



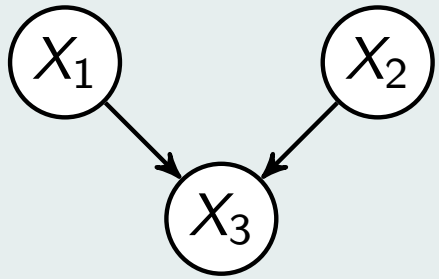

$X_2$ causes $X_1$




$X_1$ and $X_2$ cause each other




$X_1$ and $X_2$ have a common cause $X_3$




$X_1$ and $X_2$ have a common effect $X_3$

# Direct causation

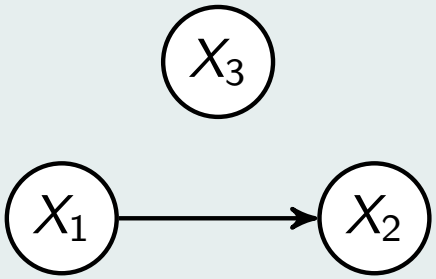
Let $\boldsymbol{V} = \{X_1, \ldots, X_N\}$ be a set of variables.

## Definition (Informal)

If $X_i$ causes $X_j$ even if all other variables $\boldsymbol{V} \setminus \{X_i, X_j\}$ are hold fixed at some values, then

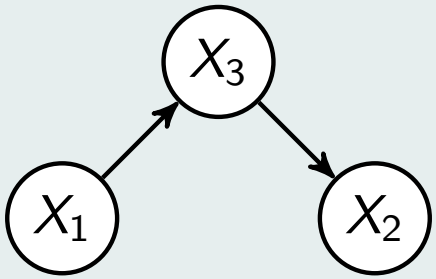
- we say that $X_i$ causes $X_j$ directly with respect to $\boldsymbol{V}$
- we indicate this in the causal graph on $\boldsymbol{V}$ by a directed edge $X_i \to X_j$

## Example



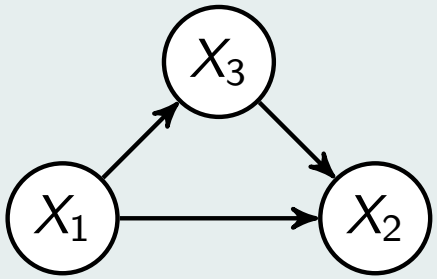

$X_1$ causes $X_2$;

$X_1$ causes $X_2$ directly w.r.t. $\{X_1, X_2, X_3\}$




$X_1$ causes $X_2$;

$X_1$ does not cause $X_2$ directly w.r.t. $\{X_1, X_2, X_3\}$

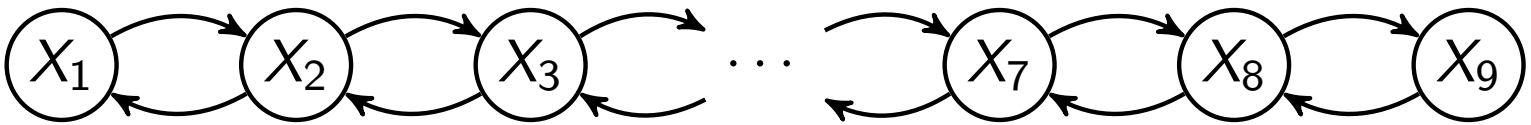



$X_1$ causes $X_2$;

$X_1$ causes $X_2$ directly w.r.t. $\{X_1, X_2, X_3\}$

# Direct vs. indirect causation: Example

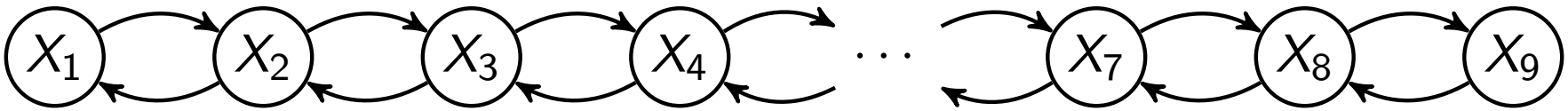
- Each stone causes *all* subsequent stones to topple.
- Each stone only directly causes the next neighboring stone to topple.
- Causal graph:



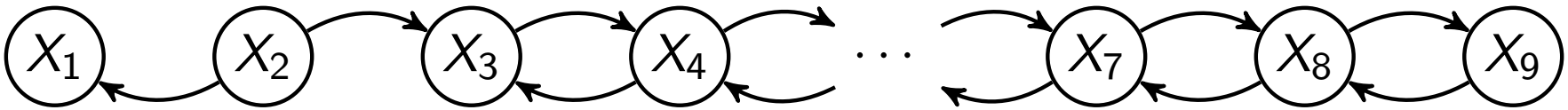
# Perfect interventions: Example

Suppose we intervene by keeping the second stone fixed in an "upright" position (e.g. by glueing it to the floor), an operation that we denote by $\mathrm{do}(X_2 = \mathrm{upright})$.

Before the intervention, the causal graph is:




After the intervention $\mathrm{do}(X_2 = \mathrm{upright})$, the causal graph is:




If we keep the second stone fixed, it is no longer affected by the other stones.

# Perfect interventions

**Definition (Informal)**

A perfect ("surgical") intervention on a set of variables $\boldsymbol{X} \subseteq \boldsymbol{V}$, denoted $\mathrm{do}(\boldsymbol{X} = \boldsymbol{\xi})$, is an externally enforced change of the system that ensures that $\boldsymbol{X}$ takes on value $\boldsymbol{\xi}$ and leaves the rest of the system untouched.

The concept of perfect intervention assumes **modularity**: the causal system can be divided into two parts, $\boldsymbol{X}$ and $\boldsymbol{V} \setminus \boldsymbol{X}$, and we can make changes to one part while keeping the other part **invariant**.

**Note**

The intervention changes the causal graph by removing all edges that point towards variables in $\boldsymbol{X}$ (because none of the variables can now cause $\boldsymbol{X}$).

# Confounders: Definition

Informally: a confounder is a latent common cause.

## Definition

Consider three variables $X, Y, H$. $H$ confounds $X$ and $Y$ if:

1. $H$ causes $X$ directly w.r.t. $\{X, Y, H\}$
2. $H$ causes $Y$ directly w.r.t. $\{X, Y, H\}$

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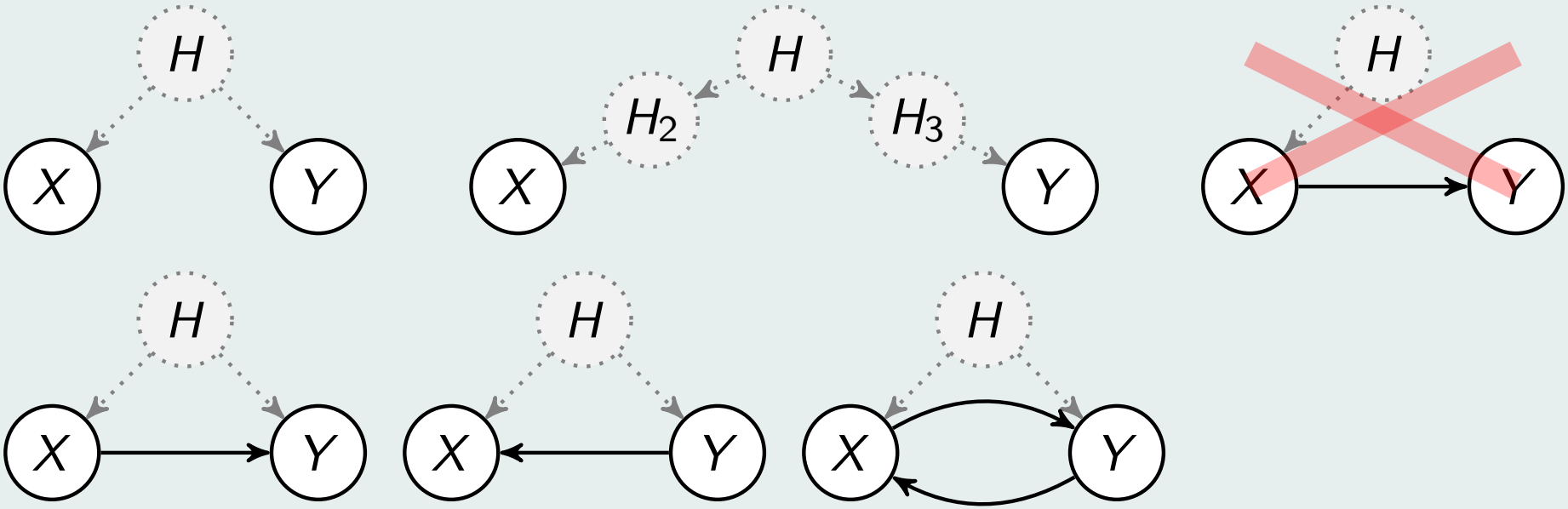
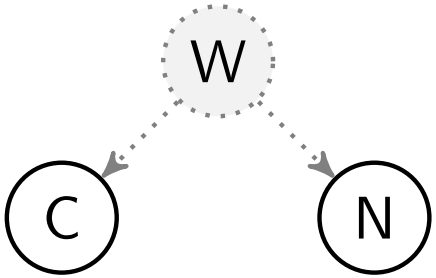
## Example



# Confounders: Example

Wealth might confound chocolate consumption and Nobel prize winners.



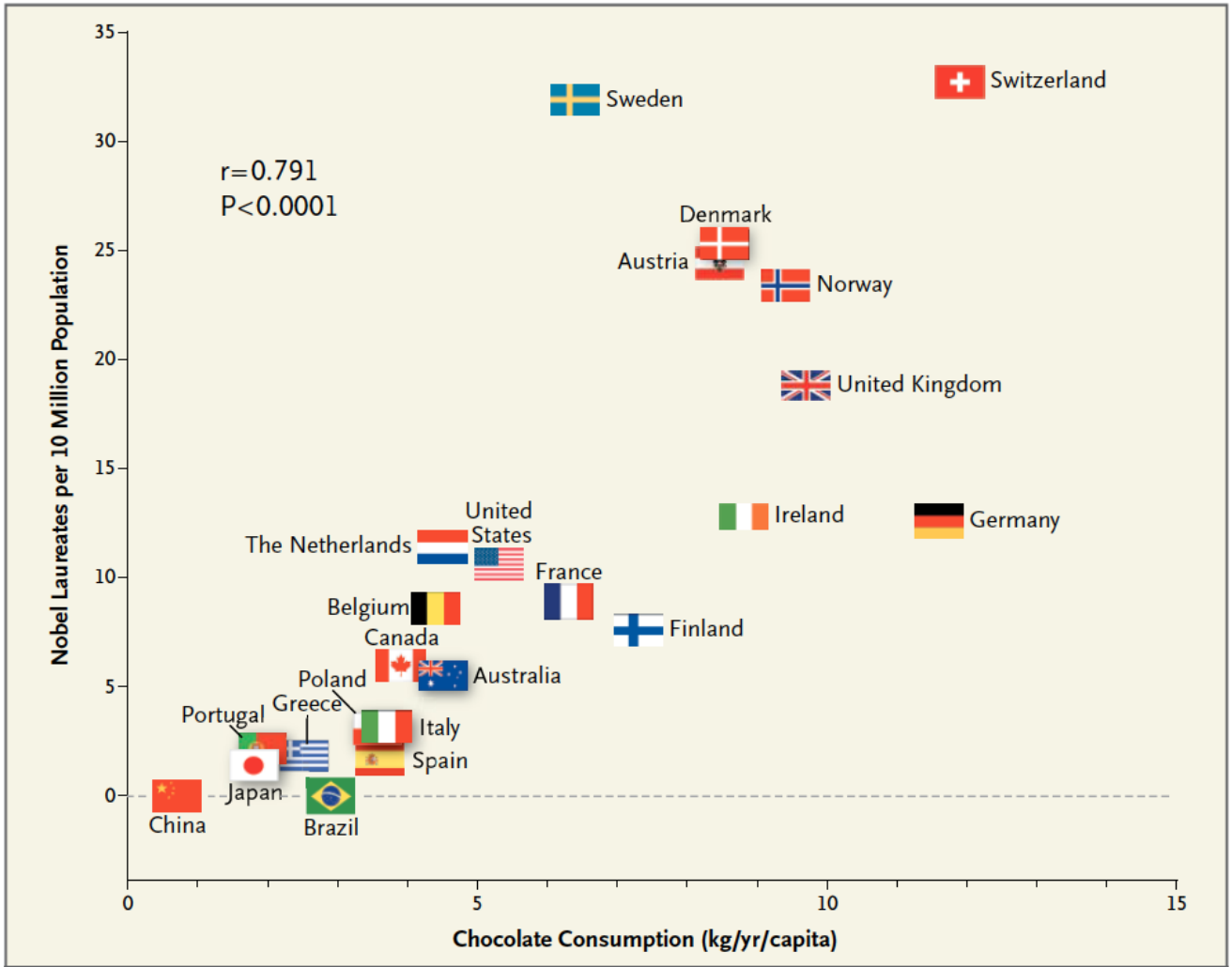
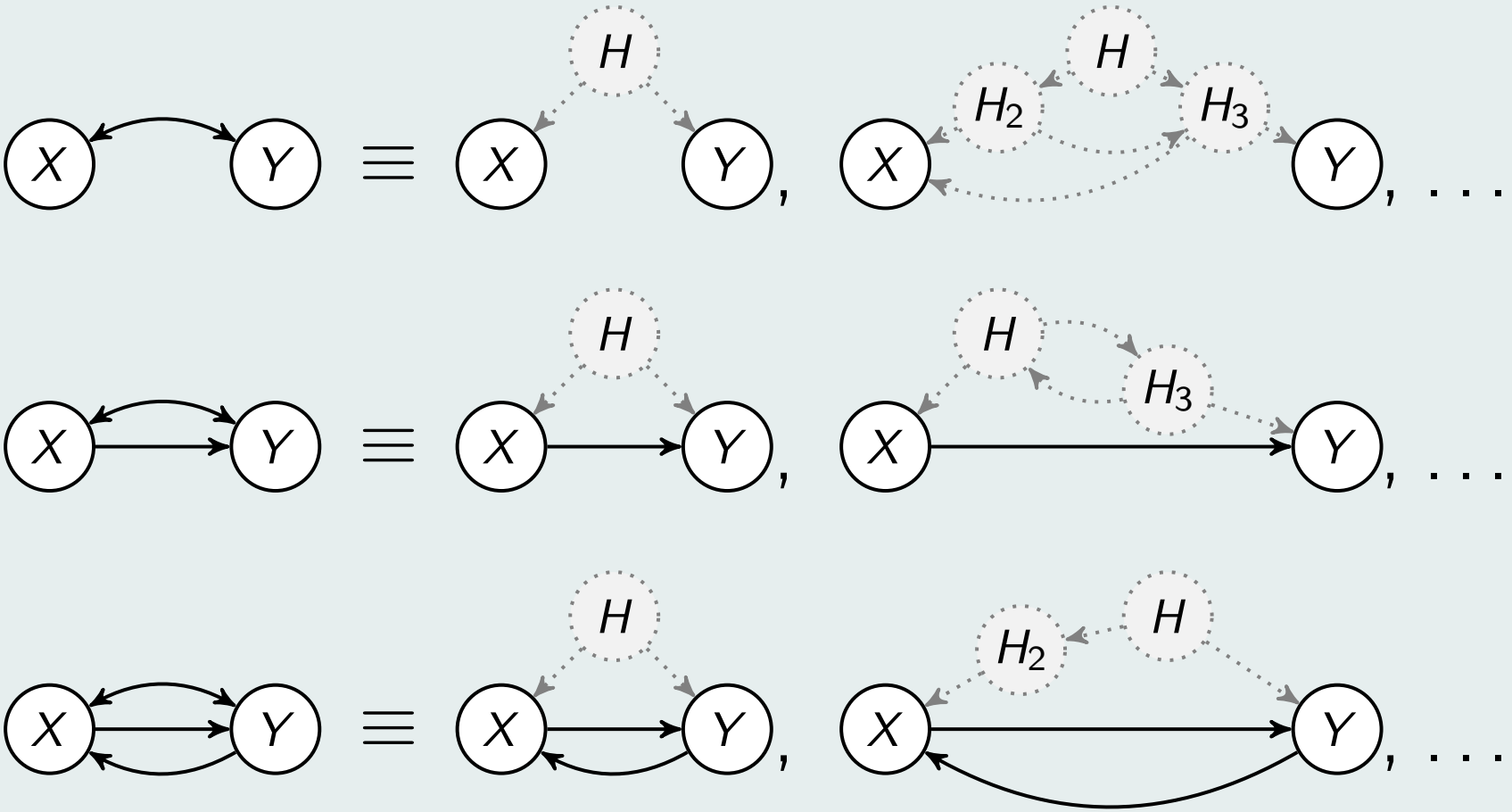




**Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.**

# Confounders: Graphical notation

We denote latent confounders by bidirected edges in the causal graph:

## Example



# Causal Cycles: Definition and Example

Let $X, Y$ be two variables in a system.

**Definition**

If $X$ causes $Y$ *and* $X$ causes $Y$, then $X$ and $Y$ form a causal cycle.

# Causal Cycles: Definition and Example

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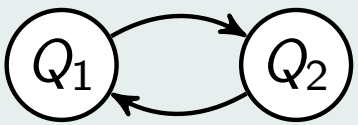
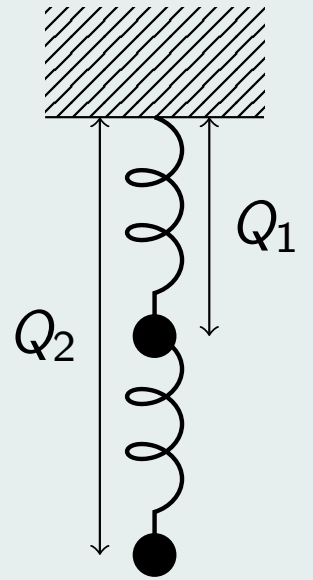
If $X$ causes $Y$ *and* $X$ causes $Y$, then $X$ and $Y$ form a causal cycle.

## Example (Damped Coupled Harmonic Oscillators)

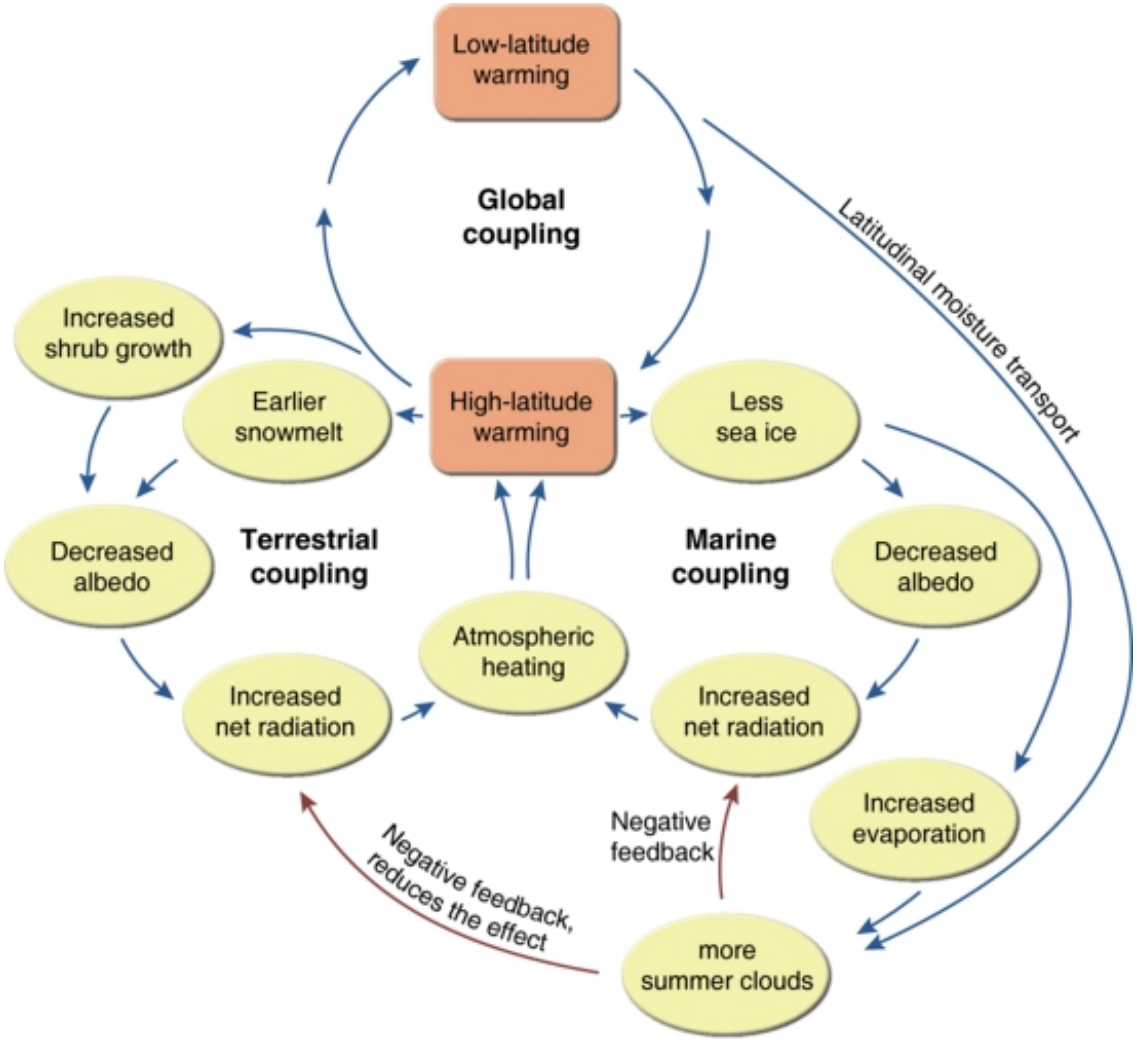
- Two masses, connected by a spring, suspended from the ceiling by another spring.
- Variables: vertical **equilibrium** positions $Q_1$ and $Q_2$.
- $Q_1$ causes $Q_2$.
- $Q_2$ causes $Q_1$.
- Causal graph:




- Cannot be modeled with acyclic causal model!

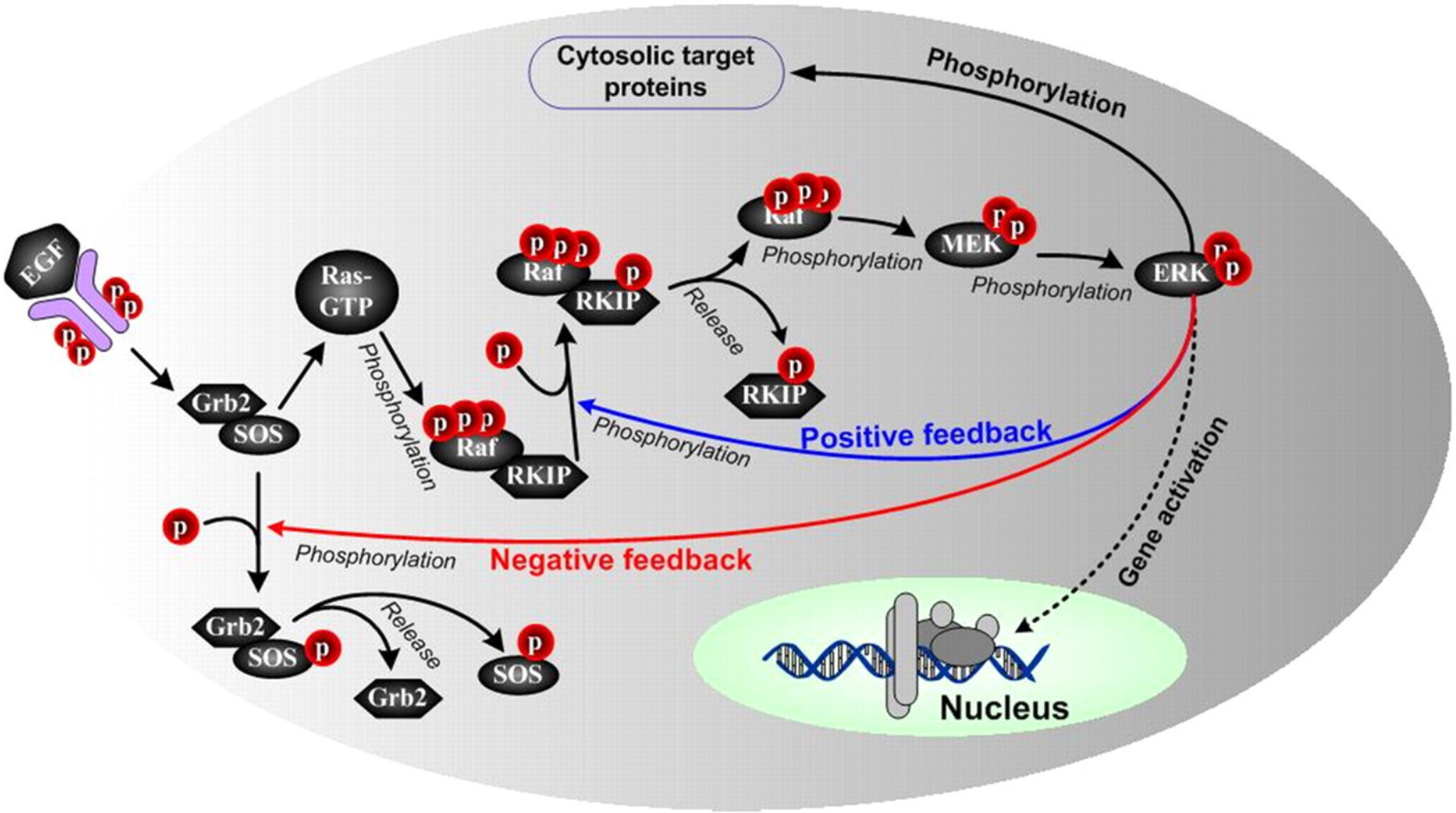


# Cycles: Relevance in Climatology




"Part of the uncertainty around future climates relates to important feedbacks between different parts of the climate system: air temperatures, ice and snow albedo (reflection of the sun's rays), and clouds." [Ahlenius, 2007]

# Cycles: Relevance in Biology

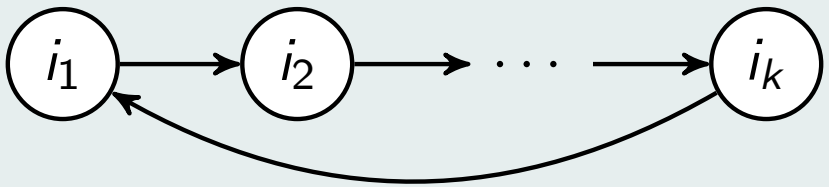



"Feedback mechanisms may be critical to allow cells to achieve the fine balance between dysregulated signaling and uncontrolled cell proliferation (a hallmark of cancer) as well as the capacity to switch pathways on or off when needed for physiologic purposes." [McArthur, 2014]

# Graph Terminology

## Definition

- A graph $\mathcal{G}$ that consists of directed and bidirected edges is called Directed Mixed Graph (DMG).
- If $i_1 \to i_2 \to \cdots \to i_k$ in $\mathcal{G}$ then $i_1$ is ancestor of $i_k$: $i_1 \in \mathrm{an}_{\mathcal{G}}(i_k)$.
- $\mathcal{G}$ is called cyclic if it contains a directed cycle:




- The strongly-connected component of a node $i \in \mathcal{G}$ is the set of nodes $j \in \mathcal{G}$ such that $i$ and $j$ are each other's ancestors.
- If $\mathcal{G}$ does not contain such a directed cycle, it is called acyclic, and known as an Acyclic Directed Mixed Graph (ADMG).
- If, in addition, $\mathcal{G}$ does not contain any bidirected edges, it is called a Directed Acyclic Graph (DAG).

# Contents

# Defining Causality in terms of Probabilities?

When looking for a more quantitative treatment of causality, it is a natural idea to try to *define* causality in terms of probabilities.

A naïve example of such an attempt could be:

**Attempt at a definition**

Given two binary random variables $A, B$. If

- $A$ precedes $B$ in time, and
- $p(B = 1 \,|\, A = 1) > p(B = 1 \,|\, A = 0)$

then $A$ causes $B$.

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then $A$ causes $B$.

This does not work, as exemplified by *Simpson's paradox*.

**Exercise**

Please make Exercise 1.1.

# Simpson's Paradox

## Example (Simpson's paradox)

We collect electronic patient records to investigate the effectiveness of a new drug against a certain disease. We find that:

1. The probability of recovery is higher for patients that took the drug:

$$p(\text{recovery} \mid \text{drug}) > p(\text{recovery} \mid \text{no drug})$$

2. For **both male and female** patients, the relation is **opposite**:

$$p(\text{recovery} \mid \text{drug}, \text{male}) < p(\text{recovery} \mid \text{no drug}, \text{male})$$

$$p(\text{recovery} \mid \text{drug}, \text{female}) < p(\text{recovery} \mid \text{no drug}, \text{female})$$

Does the drug cause recovery? I.e., would *you* use this drug if you are ill?

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Does the drug cause recovery? I.e., would *you* use this drug if you are ill?

*Note: Big data and deep learning* **do not help** *us here!*

# Quantitative Models of Causality

Problems like these have historically prevented statisticians from considering causality.

Nonetheless, different approaches have been proposed to model causality in a quantitative way:

- Potential outcome framework
- Causal Bayesian Networks
- **Structural Causal Models** (SCMs)

We will use SCMs, as they are arguably the most general of the three:

- SCMs can model cycles naturally (close connections to ODE models from physics, chemistry, biology, engineering, . . . )
- Acyclic SCMs are closed under marginalization (can efficiently handle latent variables)
- SCMs can model counterfactuals (provides alternative to potential outcome framework)
- SCMs generalize Causal Bayesian Networks

# Structural Causal Models: Concepts

*SCMs turn things upside down: rather than defining causality in terms of probabilities, probability distributions are defined by a causal model, thereby avoiding traps like Simpson's paradox.*

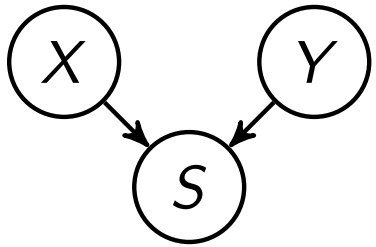
- The *system* we are modeling is described by endogenous variables; endogenous variables are:
  - observed,
  - modeled by structural equations.
- The *environment* of the system is described by exogenous variables; exogenous variables are:
  - latent (unobserved),
  - modeled by probability distributions,
  - *not caused* by endogenous variables,
  - provide the "source" of randomness.
- *Each endogenous variable has its own structural equation, which describes how this variable depends on its direct causes.*
- SCMs are equipped with a notion of perfect intervention, which gives them a *causal* semantics.

# Structural Causal Models: Example

Endogenous variables (binary):

$X$: the battery is charged
$Y$: the start engine is operational
$S$: the car starts

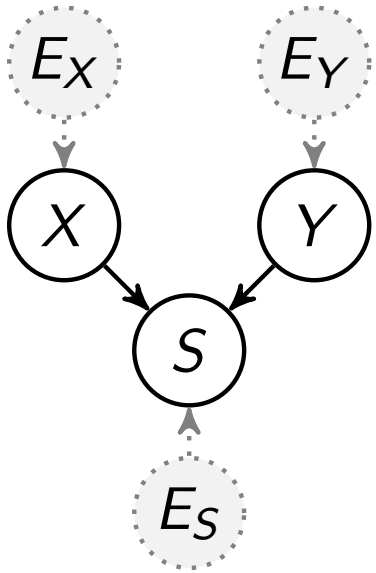
Causal graph:




Exogenous variables (latent, independent, binary):

$$E_X \sim \mathrm{Ber}(0.95)$$
$$E_Y \sim \mathrm{Ber}(0.99)$$
$$E_S \sim \mathrm{Ber}(0.999)$$

Augmented graph:




Structural equations (one per endogenous variable):

$$X = f_X(E_X) = E_X$$
$$Y = f_Y(E_Y) = E_Y$$
$$S = f_S(X, Y, E_S) = X \wedge Y \wedge E_S$$

# Structural Causal Models: Formal Definition

## Definition ([Wright, 1921, Pearl, 2000, Bongers et al., 2018])

A Structural Causal Model (SCM), also known as Structural Equation Model (SEM), is a tuple $\mathcal{M} = \langle \boldsymbol{\mathcal{X}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$ with:

1. a product of standard measurable spaces $\boldsymbol{\mathcal{X}} = \prod_{i \in \mathcal{I}} \mathcal{X}_i$ (domains of the endogenous variables)
2. a product of standard measurable spaces $\boldsymbol{\mathcal{E}} = \prod_{j \in \mathcal{J}} \mathcal{E}_j$ (domains of the exogenous variables)
3. a measurable mapping $\boldsymbol{f} : \boldsymbol{\mathcal{X}} \times \boldsymbol{\mathcal{E}} \to \boldsymbol{\mathcal{X}}$ (the causal mechanism)
4. a product probability measure $\mathbb{P}_{\boldsymbol{\mathcal{E}}} = \prod_{j \in \mathcal{J}} \mathbb{P}_{\mathcal{E}_j}$ on $\boldsymbol{\mathcal{E}}$ (the exogenous distribution)

## Definition

A pair of random variables $(\boldsymbol{X}, \boldsymbol{E})$ is a solution of SCM $\mathcal{M}$ if $\mathbb{P}^{\boldsymbol{E}} = \mathbb{P}_{\boldsymbol{\mathcal{E}}}$ and the structural equations $\boldsymbol{X} = \boldsymbol{f}(\boldsymbol{X}, \boldsymbol{E})$ hold a.s..

# Structural Causal Models: Example

## Example

Structural Causal Model $\mathcal{M}$:

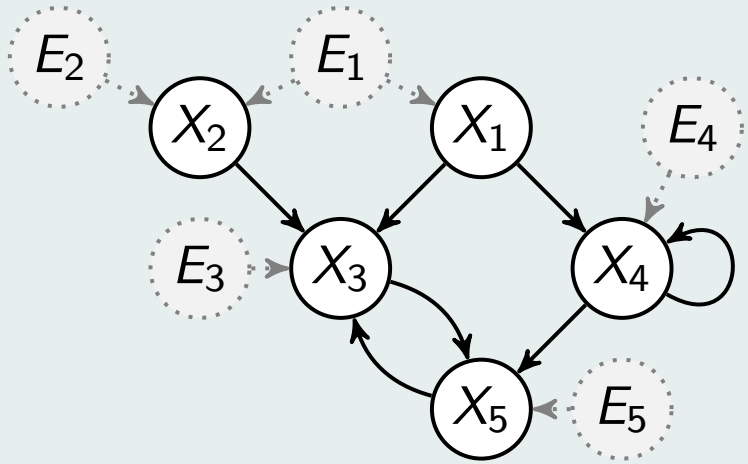
Formally:

$$(\boldsymbol{\mathcal{X}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}, \mathbb{P}_{\boldsymbol{\mathcal{E}}}) = \\ (\prod_{i=1}^{5} \mathbb{R}, \prod_{j=1}^{5} \mathbb{R}, (f_1, \ldots, f_5), \prod_{j=1}^{5} \mathbb{P}_{\mathcal{E}_j})$$

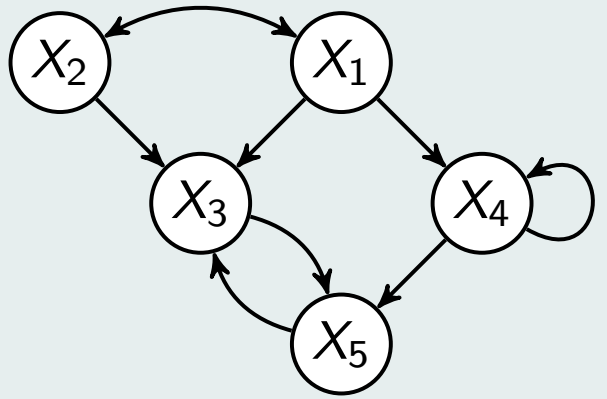
Informally:

$$\begin{array}{ll} X_1 = f_1(E_1) & E_1 \sim \mathbb{P}_{\mathcal{E}_1} \\ X_2 = f_2(E_1, E_2) & E_2 \sim \mathbb{P}_{\mathcal{E}_2} \\ X_3 = f_3(X_1, X_2, X_5, E_3) & E_3 \sim \mathbb{P}_{\mathcal{E}_3} \\ X_4 = f_4(X_1, X_4, E_4) & E_4 \sim \mathbb{P}_{\mathcal{E}_4} \\ X_5 = f_5(X_3, X_4, E_5) & E_5 \sim \mathbb{P}_{\mathcal{E}_5} \end{array}$$

Augmented graph $\mathcal{G}^a(\mathcal{M})$:




Graph $\mathcal{G}(\mathcal{M})$:



# (Augmented) Graphs

## Definition

The components of the causal mechanism usually do not depend on *all* variables: for $i \in \mathcal{I}$,

$$X_i = f_i(\boldsymbol{x}_{\mathrm{pa}_i^{\mathcal{I}}}, \boldsymbol{e}_{\mathrm{pa}_i^{\mathcal{J}}})$$

where $f_i$ only depends on $\mathrm{pa}_i^{\mathcal{I}} \subseteq \mathcal{I}$ (the endogenous parents of $i$) and $\mathrm{pa}_i^{\mathcal{J}} \subseteq \mathcal{J}$ (the exogenous parents of $i$).

## Definition

The augmented graph $\mathcal{G}^a(\mathcal{M})$ of SCM $\mathcal{M}$ is a directed graph with nodes $\mathcal{I} \dot{\cup} \mathcal{J}$ and an edge $k \to i$ iff $k \in \mathrm{pa}_i^{\mathcal{I}} \dot{\cup} \mathrm{pa}_i^{\mathcal{J}}$ is a parent of $i \in \mathcal{I}$.

## Definition

The graph $\mathcal{G}(\mathcal{M})$ of SCM $\mathcal{M}$ is a DMG with nodes $\mathcal{I}$, directed edges $k \to i$ iff $k \in \mathrm{pa}_i^{\mathcal{I}}$, and bidirected edges $k \leftrightarrow i$ iff $\mathrm{pa}_i^{\mathcal{J}} \cap \mathrm{pa}_k^{\mathcal{J}} \neq \emptyset$.

# Unique Solvability

## Definition

An SCM $\mathcal{M}$ is said to be uniquely solvable w.r.t. $\mathcal{O} \subseteq \mathcal{I}$ if there exists a measurable mapping $\boldsymbol{g}_{\mathcal{O}} : \boldsymbol{\mathcal{X}}_{(\mathrm{pa}_{\mathcal{H}}(\mathcal{O})\setminus\mathcal{O})\cap\mathcal{I}} \times \boldsymbol{\mathcal{E}}_{\mathrm{pa}_{\mathcal{H}}(\mathcal{O})\cap\mathcal{J}} \to \boldsymbol{\mathcal{X}}_{\mathcal{O}}$ such that for $\mathbb{P}_{\boldsymbol{\mathcal{E}}}$-almost every $\boldsymbol{e}$ for all $\boldsymbol{x} \in \boldsymbol{\mathcal{X}}$:

$$\boldsymbol{x}_{\mathcal{O}} = \boldsymbol{g}_{\mathcal{O}}(\boldsymbol{x}_{(\mathrm{pa}_{\mathcal{H}}(\mathcal{O})\setminus\mathcal{O})\cap\mathcal{I}}, \boldsymbol{e}_{\mathrm{pa}_{\mathcal{H}}(\mathcal{O})\cap\mathcal{J}}) \quad \Longleftrightarrow \quad \boldsymbol{x}_{\mathcal{O}} = \boldsymbol{f}_{\mathcal{O}}(\boldsymbol{x}, \boldsymbol{e}).$$

(Loosely speaking: if the structural equations for $\mathcal{O}$ provide a unique solution for $\boldsymbol{x}_{\mathcal{O}}$ in terms of the other variables).

## Example

An SCM with structural equations:

$$\begin{cases} X_1 = X_1 \\ X_2 = X_1 + X_3 \\ X_3 = X_3 + 1 \end{cases}$$

is uniquely solvable w.r.t. $\{X_2\}$ but not w.r.t. any other subset.

# Simple SCMs

For simplicity we will here assume only a special subclass of SCMs:

**Definition**

We call an SCM $\mathcal{M}$ simple if it is uniquely solvable with respect to any subset $\mathcal{O} \subseteq \mathcal{I}$.

**Lemma**

*If $\mathcal{G}(\mathcal{M})$ is acyclic, $\mathcal{M}$ is simple.*

- The class of simple SCMs extends the class of acyclic SCMs by allowing for (weak) cyclic causal relations, while preserving most of the simplicity and convenience of acyclic SCMs.
- The theory for non-simple SCMs is considerably more involved [Bongers et al., 2018].
- Simple SCMs induce modular SCMs (mSCMs) [Forré and Mooij, 2017].

# Perfect Interventions

To interpret an SCM as a *causal* model, we also need to define its semantics under interventions.

## Definition (Perfect Interventions, [Pearl, 2000])

- The perfect intervention $\text{do}(\boldsymbol{X}_I = \boldsymbol{\xi}_I)$ enforces $\boldsymbol{X}_I$ to attain value $\boldsymbol{\xi}_I$.
- This changes the SCM $\mathcal{M} = \langle \boldsymbol{\mathcal{X}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$ into the intervened SCM $\mathcal{M}_{\text{do}(\boldsymbol{X}_I = \boldsymbol{\xi}_I)} = \langle \boldsymbol{\mathcal{X}}, \boldsymbol{\mathcal{E}}, \tilde{\boldsymbol{f}}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$ where

$$\tilde{f}_i(\boldsymbol{x}, \boldsymbol{e}) = \begin{cases} \xi_i & i \in I \\ f_i(\boldsymbol{x}_{\text{pa}_i^{\mathcal{I}}}, \boldsymbol{e}_{\text{pa}_i^{\mathcal{J}}}) & i \notin I. \end{cases}$$

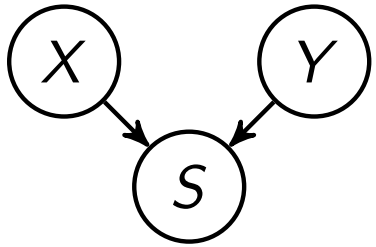
- Interpretation: overrides default causal mechanisms that normally would determine the values of the intervened variables.
- In the (augmented) graph, the intervention removes all incoming edges with an arrowhead at any intervened variable $i \in I$.

# Interventions: Example

Endogenous variables (binary):

$X$: the battery is charged
$Y$: the start engine is operational
$S$: the car starts

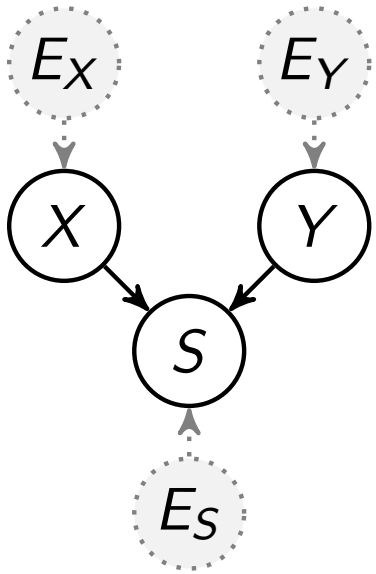
Causal graph:




Exogenous variables (latent, independent, binary):

$E_X \sim \mathrm{Ber}(0.95)$
$E_Y \sim \mathrm{Ber}(0.99)$
$E_Z \sim \mathrm{Ber}(0.999)$

Augmented graph:




Structural equations (one per endogenous variable):

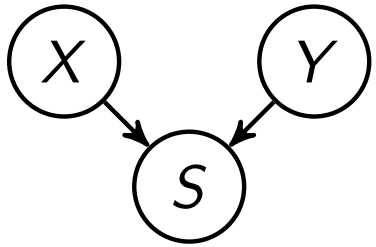
$X = E_X$
$Y = E_Y$
$S = X \wedge Y \wedge E_S$

# Interventions: Example

Endogenous variables (binary):

$X$: the battery is charged
$Y$: the start engine is operational
$S$: the car starts

Causal graph:




Exogenous variables (latent, independent, binary):

$E_X \sim \mathrm{Ber}(0.95)$
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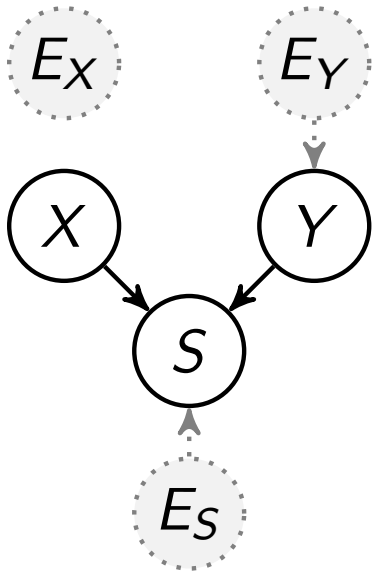
$E_Z \sim \mathrm{Ber}(0.999)$

Augmented graph:




Structural equations (one per endogenous variable):
after charging the battery $\mathrm{do}(X = 1)$:

$X = 1$
$Y = E_Y$
$S = X \wedge Y \wedge E_S$

# Interventions: Example

Endogenous variables (binary):

$X$: the battery is charged
$Y$: the start engine is operational
$S$: the car starts

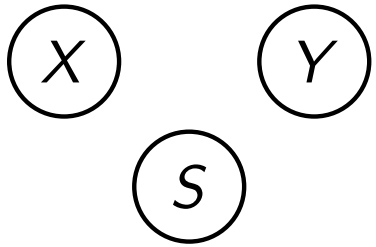
Exogenous variables (latent, independent, binary):

$E_X \sim \mathrm{Ber}(0.95)$
$E_Y \sim \mathrm{Ber}(0.99)$
$E_Z \sim \mathrm{Ber}(0.999)$

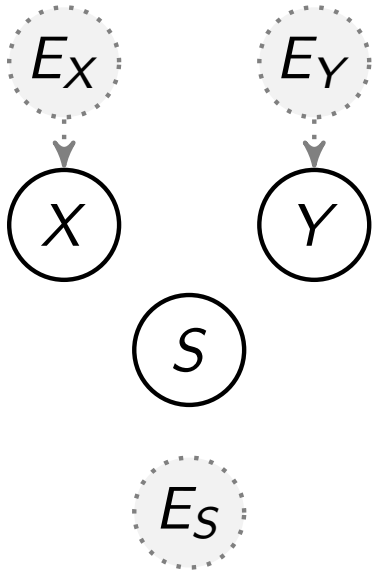
Structural equations (one per endogenous variable):
after loosing the key do($S = 0$):

$X = E_X$
$Y = E_Y$
$S = 0$

Causal graph:




Augmented graph:



# Interventions: Example

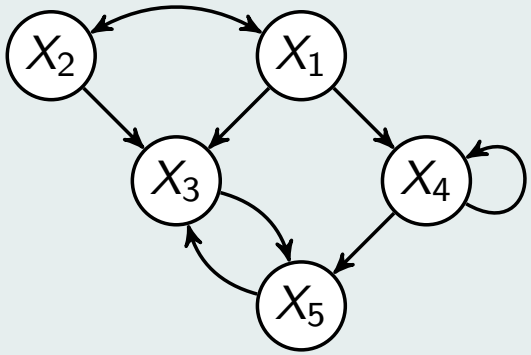
## Example

Observational (no intervention):

SCM $\mathcal{M}$:

$$
\begin{aligned}
X_1 &= f_1(E_1) & E_1 &\sim \mathbb{P}_{\mathcal{E}_1} \\
X_2 &= f_2(E_1, E_2) & E_2 &\sim \mathbb{P}_{\mathcal{E}_2} \\
X_3 &= f_3(X_1, X_2, X_5, E_3) & E_3 &\sim \mathbb{P}_{\mathcal{E}_3} \\
X_4 &= f_4(X_1, X_4, E_4) & E_4 &\sim \mathbb{P}_{\mathcal{E}_4} \\
X_5 &= f_5(X_3, X_4, E_5) & E_5 &\sim \mathbb{P}_{\mathcal{E}_5}
\end{aligned}
$$

Graph $\mathcal{G}(\mathcal{M})$:

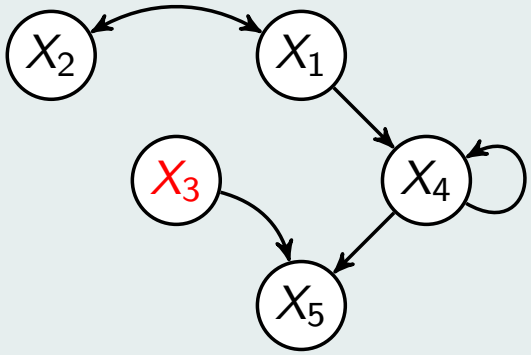



Intervention $\mathrm{do}(X_3 = \xi_3)$:

Intervened SCM $\mathcal{M}_{\mathrm{do}(X_3=\xi_3)}$:

$$
\begin{aligned}
X_1 &= f_1(E_1) & E_1 &\sim \mathbb{P}_{\mathcal{E}_1} \\
X_2 &= f_2(E_1, E_2) & E_2 &\sim \mathbb{P}_{\mathcal{E}_2} \\
X_3 &= \xi_3 & E_3 &\sim \mathbb{P}_{\mathcal{E}_3} \\
X_4 &= f_4(X_1, X_4, E_4) & E_4 &\sim \mathbb{P}_{\mathcal{E}_4} \\
X_5 &= f_5(X_3, X_4, E_5) & E_5 &\sim \mathbb{P}_{\mathcal{E}_5}
\end{aligned}
$$

Intervened Graph $\mathcal{G}(\mathcal{M}_{\mathrm{do}(X_3=\xi_3)})$:



# Observational Distribution(s)

**Definition (Reminder)**

A pair of random variables $(\boldsymbol{X}, \boldsymbol{E})$ is a solution of SCM $\mathcal{M}$ if $\mathbb{P}^{\boldsymbol{E}} = \mathbb{P}_{\boldsymbol{\mathcal{E}}}$ and the structural equations $\boldsymbol{X} = \boldsymbol{f}(\boldsymbol{X}, \boldsymbol{E})$ hold a.s..

**Definition**

For $(\boldsymbol{X}, \boldsymbol{E})$ a solution of SCM $\mathcal{M}$, we call $\mathbb{P}^{\boldsymbol{X}}$ an observational distribution of $\mathcal{M}$.

An important special case:

**Proposition**

*If $\mathcal{M}$ is simple, then its observational distribution exists and is unique.*

**Definition**

Given a simple SCM $\mathcal{M}$ and a fixed background measure on $\boldsymbol{X}$, we denote the density of the observational distribution as $p_{\mathcal{M}}(\boldsymbol{x})$.

# Interventional Distribution(s)

A perfect intervention on $\mathcal{M}$ may change the distributions.

**Definition**

We call the family of sets of observational distributions of $\mathcal{M}_{\text{do}(X_I=\xi_I)}$ (for $I \subseteq \mathcal{I}$, $\xi_I \subseteq \mathcal{X}_I$) the interventional distributions of $\mathcal{M}$.

**Proposition**

*If $\mathcal{M}$ is simple, then all intervened SCMs $\mathcal{M}_{\text{do}(X_I=\xi_I)}$ are simple, and hence all interventional distributions of a simple SCM exist and are unique.*

**Definition ([Pearl, 2000])**

Given a simple SCM $\mathcal{M}$ and a fixed background measure on $\boldsymbol{X}$, we denote the density of the interventional distributions as $p_{\mathcal{M}}\big(\boldsymbol{x} \mid \text{do}(\boldsymbol{X}_I = \boldsymbol{\xi}_I)\big)$

*Crucial difference with traditional probabilistic models: SCMs simultaneously model all distributions that are obtained under all perfect interventions on a system.*

# Self-cycles

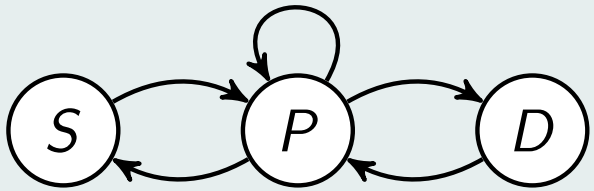
## Definition

We say $\mathcal{M}$ has a self-cycle at $i \in \mathcal{I}$ if $i \in \mathrm{pa}^{\mathcal{I}}_{\mathcal{M}}(i)$.

## Example (Price-supply-demand)

Consider an SCM with three endogenous variables (Price, Supply and Demand) modeling a free market:

$$S = \alpha P + E_S$$
$$D = \beta P + E_D$$
$$P = P + (S - D)$$




The structural equation for $P$ has a self-cycle that cannot be removed without changing the observational and interventional distributions.

Self-cycles complicate matters considerably [Bongers et al., 2018].

## Proposition

*Simple SCMs are equivalent to SCMs without self-cycles.*

# Causal Interpretation of Direct Edges

**Definition**

Let $\mathcal{M}$ be a simple SCM. If $i \to j \in \mathcal{G}(\mathcal{M})$ we call $i$ a direct cause of $j$ according to $\mathcal{M}$.

We can now formalize our earlier informal definition of direct cause as a sufficient condition:

**Proposition**

*Let $\mathcal{M}$ be a simple SCM. If there exist interventions $\mathrm{do}(\boldsymbol{X}_{\mathcal{I}\setminus\{j\}} = \boldsymbol{\xi})$ and $\mathrm{do}(\boldsymbol{X}_{\mathcal{I}\setminus\{j\}} = \boldsymbol{\xi}')$ such that $\boldsymbol{\xi}_{\mathcal{I}\setminus\{i,j\}} = \boldsymbol{\xi}'_{\mathcal{I}\setminus\{i,j\}}$ and $\xi_i \neq \xi'_i$ such that*

$$\mathbb{P}_{\mathcal{M}}(X_j \mid \mathrm{do}(\boldsymbol{X}_{\mathcal{I}\setminus\{j\}} = \boldsymbol{\xi})) \neq \mathbb{P}_{\mathcal{M}}(X_j \mid \mathrm{do}(\boldsymbol{X}_{\mathcal{I}\setminus\{j\}} = \boldsymbol{\xi}'))$$

*then $i$ is a direct cause of $j$ according to $\mathcal{M}$, i.e., $i \to j \in \mathcal{G}(\mathcal{M})$.*

(Interestingly, a necessary condition is not known)

# Causal Interpretation of Directed Paths

## Definition

Let $\mathcal{M}$ be a simple SCM. If there exists a directed path $i \to \cdots \to j \in \mathcal{G}(\mathcal{M})$, i.e., if $i \in \mathrm{an}_{\mathcal{G}(\mathcal{M})}(j)$, then we call $i$ a cause of $j$ according to $\mathcal{M}$.

We can now formalize our earlier informal definition of cause as a sufficient condition:

## Proposition

*Let $\mathcal{M}$ be a simple SCM. If there exist interventions $\mathrm{do}(X_i = \xi)$ and $\mathrm{do}(X_i = \xi')$ with $\xi \neq \xi'$ such that*

$$\mathbb{P}_{\mathcal{M}}(X_j \mid \mathrm{do}(X_i = \xi)) \neq \mathbb{P}_{\mathcal{M}}(X_j \mid \mathrm{do}(X_i = \xi'))$$

*then $i$ is a cause of $j$ according to $\mathcal{M}$, i.e., $i \in \mathrm{an}_{\mathcal{G}(\mathcal{M})}(j)$.*

(Interestingly, a necessary condition is not known)

# Causal Interpretation of Bidirected Edges

**Definition**

Let $\mathcal{M}$ be a simple SCM. If there exists a bidirected edge $i \leftrightarrow j \in \mathcal{G}(\mathcal{M})$, then we call $i$ and $j$ confounded according to $\mathcal{M}$.

We can formulate a sufficient condition for confoundedness:

**Proposition**

*Let $\mathcal{M}$ be a simple SCM. If $j \to i \notin \mathcal{G}(\mathcal{M})$ and there exist an intervention $\mathrm{do}(\boldsymbol{X}_{\mathcal{I}\setminus\{i,j\}} = \boldsymbol{\xi})$ such that*

$$\mathbb{P}_{\mathcal{M}}(X_j \mid \mathrm{do}(i, x_i), \mathrm{do}(\mathcal{I} \setminus \{i,j\}, \boldsymbol{\xi})) \neq \mathbb{P}_{\mathcal{M}}(X_j \mid X_i = x_i, \mathrm{do}(\mathcal{I} \setminus \{i,j\}, \boldsymbol{\xi}))$$

*then $i$ and $j$ are confounded according to $\mathcal{M}$.*

(Again, a necessary condition is not known)

# Marginalization: "Integrating out" a subsystem (Example)

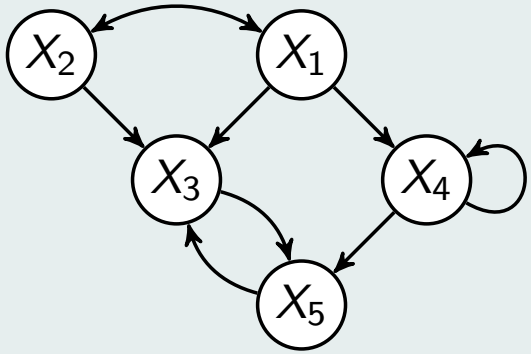
## Example

SCM for complete system:

Structural Causal Model $\mathcal{M}$:

$$
\begin{aligned}
X_1 &= f_1(E_1) & E_1 &\sim \mathbb{P}_{\mathcal{E}_1} \\
X_2 &= f_2(E_1, E_2) & E_2 &\sim \mathbb{P}_{\mathcal{E}_2} \\
X_3 &= f_3(X_1, X_2, X_5, E_3) & E_3 &\sim \mathbb{P}_{\mathcal{E}_3} \\
X_4 &= f_4(X_1, X_4, E_4) & E_4 &\sim \mathbb{P}_{\mathcal{E}_4} \\
X_5 &= f_5(X_3, X_4, E_5) & E_5 &\sim \mathbb{P}_{\mathcal{E}_5}
\end{aligned}
$$

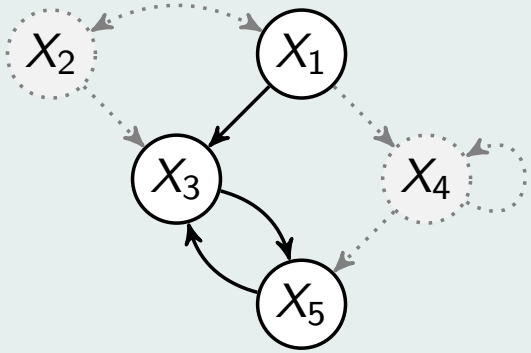
Graph $\mathcal{G}(\mathcal{M})$:



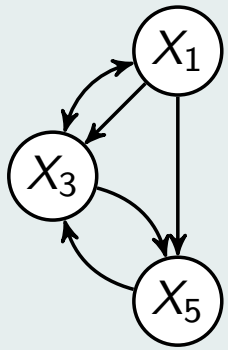

Marginalizing out $\{X_2, X_4\}$:

Marginalization $\mathcal{M}^{\setminus\{2,4\}}$:

$$
\begin{aligned}
X_1 &= f_1(E_1) & E_1 &\sim \mathbb{P}_{\mathcal{E}_1} \\
 & & E_2 &\sim \mathbb{P}_{\mathcal{E}_2} \\
X_3 &= f_3(X_1, g_2(E_1, E_2), X_5, E_3) & E_3 &\sim \mathbb{P}_{\mathcal{E}_3} \\
 & & E_4 &\sim \mathbb{P}_{\mathcal{E}_4} \\
X_5 &= f_5(X_3, g_4(X_1, E_4), E_5) & E_5 &\sim \mathbb{P}_{\mathcal{E}_5}
\end{aligned}
$$




Graph $\mathcal{G}(\mathcal{M}^{\setminus\{2,4\}})$:



# Marginalization: Substituting equations

Given a simple SCM $\mathcal{M}$ and a subset of its endogenous variables $\mathcal{L} \subseteq \mathcal{I}$, with complement $\mathcal{O} := \mathcal{I} \setminus \mathcal{L}$, we can always "substitute out" the structural equations for $\mathcal{L}$:

$$\boldsymbol{X} = \boldsymbol{f}(\boldsymbol{X}, \boldsymbol{E})$$

$$\iff \begin{cases} \boldsymbol{X}_{\mathcal{L}} &= \boldsymbol{f}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{L}}, \boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \\ \boldsymbol{X}_{\mathcal{O}} &= \boldsymbol{f}_{\mathcal{O}}(\boldsymbol{X}_{\mathcal{L}}, \boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \end{cases}$$

$$\iff \begin{cases} \boldsymbol{X}_{\mathcal{L}} &= \boldsymbol{g}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \\ \boldsymbol{X}_{\mathcal{O}} &= \boldsymbol{f}_{\mathcal{O}}(\boldsymbol{X}_{\mathcal{L}}, \boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \end{cases}$$

$$\iff \begin{cases} \boldsymbol{X}_{\mathcal{L}} &= \boldsymbol{g}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \\ \boldsymbol{X}_{\mathcal{O}} &= \boldsymbol{f}_{\mathcal{O}}(\boldsymbol{g}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}), \boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \end{cases}$$

all hold a.s., where $\boldsymbol{g}_{\mathcal{L}} : \boldsymbol{\mathcal{X}}_{\mathcal{O}} \times \boldsymbol{\mathcal{E}} \to \boldsymbol{\mathcal{X}}_{\mathcal{L}}$ is the explicit solution of the structural equations for $\boldsymbol{X}_{\mathcal{L}}$, i.e.,

$$\boldsymbol{X}_{\mathcal{L}} = \boldsymbol{g}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \quad \iff \quad \boldsymbol{X}_{\mathcal{L}} = \boldsymbol{f}_{\mathcal{L}}(\boldsymbol{X}_{\mathcal{L}}, \boldsymbol{X}_{\mathcal{O}}, \boldsymbol{E}) \quad \text{a.s..}$$

# Marginalization of an SCM

## Definition ([Bongers et al., 2018])

Let $\mathcal{M} = \langle \boldsymbol{\mathcal{X}}_{\mathcal{I}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$ be a simple SCM, $\mathcal{L} \subseteq \mathcal{I}$ a subset of endogenous variables and $\mathcal{O} = \mathcal{I} \setminus \mathcal{L}$. Then the marginalization of $\mathcal{M}$ on $\mathcal{I} \setminus \mathcal{L}$ is defined as the SCM $\mathcal{M}^{\setminus \mathcal{L}} := \langle \boldsymbol{\mathcal{X}}_{\mathcal{I} \setminus \mathcal{L}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}^{\setminus \mathcal{L}}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$, where the marginal causal mechanism $\boldsymbol{f}^{\setminus \mathcal{L}}$ is obtained by substitution:
$\boldsymbol{f}^{\setminus \mathcal{L}}(\boldsymbol{x}_{\mathcal{O}}, \boldsymbol{e}) := \boldsymbol{f}_{\mathcal{O}}\big(\boldsymbol{g}_{\mathcal{L}}(\boldsymbol{x}_{\mathcal{O}}, \boldsymbol{e}), \boldsymbol{x}_{\mathcal{O}}, \boldsymbol{e}\big)$.

## Definition

For a DMG $\mathcal{G}$ and a subset $\mathcal{L} \subseteq \mathcal{I}$ of nodes, the latent projection $\mathcal{G}^{\setminus \mathcal{L}}$ is defined as the DMG with nodes $\mathcal{I} \setminus \mathcal{L}$ and edges

- $i \to j$ iff there is a directed path $i \to \ell_1 \to \cdots \to \ell_k \to j$ in $\mathcal{G}$ with $\ell_1, \ldots, \ell_k \in \mathcal{L}$
- $i \leftrightarrow j$ iff there is a path $i \leftarrow \ell_1 \leftarrow \cdots \leftarrow \ell_{k_1} \leftrightarrow \ell_{k_1+1} \to \cdots \to \ell_{k_2} \to j$ in $\mathcal{G}$ with $\ell_1, \ldots, \ell_{k_1}, \ldots, \ell_{k_2} \in \mathcal{L}$

# Marginalization of an SCM: Properties

The marginalization preserves the causal semantics (restricted to the remaining part of the system, $\mathcal{I} \setminus \mathcal{L}$):

**Theorem ([Bongers et al., 2018])**

*Let $\mathcal{M} = \langle \boldsymbol{\mathcal{X}}_{\mathcal{I}}, \boldsymbol{\mathcal{E}}, \boldsymbol{f}, \mathbb{P}_{\boldsymbol{\mathcal{E}}} \rangle$ be a simple SCM and $\mathcal{L} \subseteq \mathcal{I}$ a subset of endogenous variables.*

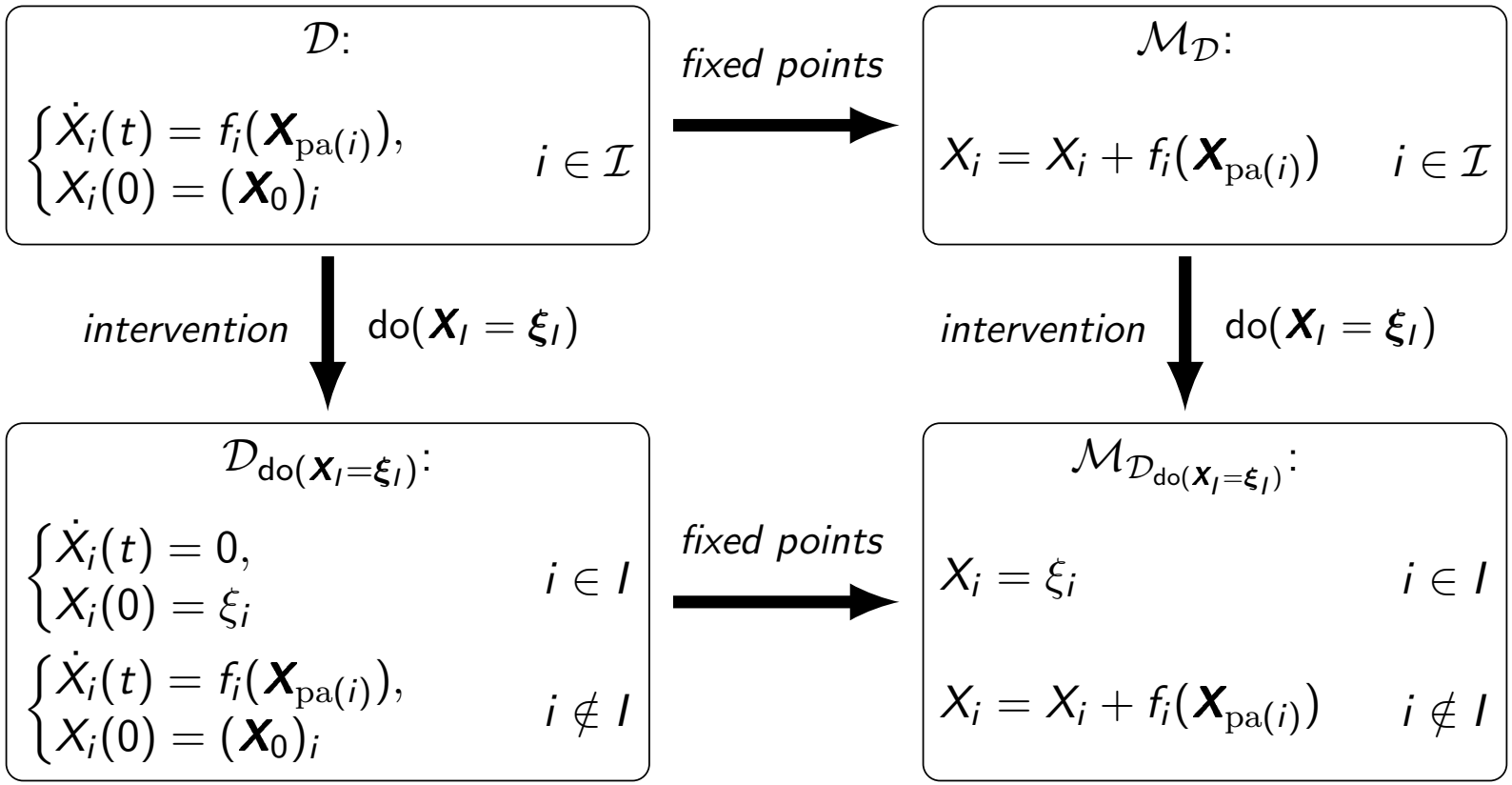
- *The marginalization $\mathcal{M}^{\setminus \mathcal{L}}$ is interventionally equivalent to $\mathcal{M}$ w.r.t. $\mathcal{I} \setminus \mathcal{L}$. I.e., the observational distribution and all interventional distributions of $\mathcal{M}$, marginalized onto $\boldsymbol{\mathcal{X}}_{\mathcal{I} \setminus \mathcal{L}}$, coincide with the corresponding ones of $\mathcal{M}^{\setminus \mathcal{L}}$.*
- *The graph $\mathcal{G}(\mathcal{M}^{\setminus \mathcal{L}})$ of the marginalization of $\mathcal{M}$ on $\mathcal{I} \setminus \mathcal{L}$ is always a subgraph of the latent projection of $\mathcal{G}(\mathcal{M})$ on $\mathcal{I} \setminus \mathcal{L}$ (some edges may cancel out).*
- *The marginal SCM $\mathcal{M}^{\setminus \mathcal{L}}$ is simple.*

# Modeling ODE fixed points with an SCM

Strong motivation for (cyclic) SCMs:

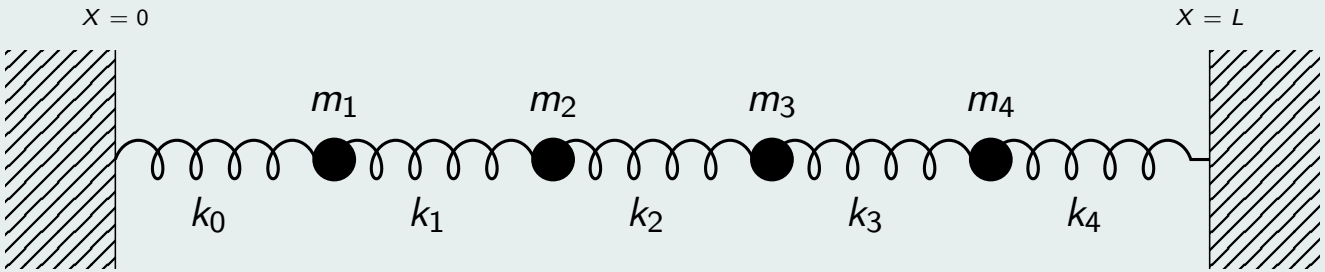
**Theorem ([Mooij et al., 2013, Bongers and Mooij, 2018])**

*An ODE describing a dynamical system induces an SCM that models its equilibrium states, and how these change under perfect interventions.*



# From ODE to SCM: Example 1

## Example (Damped coupled harmonic oscillators)



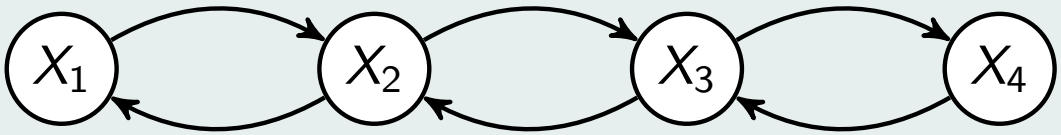

- ODE $\mathcal{D}$:

$$\ddot{X}_i = \frac{k_i}{m_i}(X_{i+1} - X_i - l_i) - \frac{k_{i-1}}{m_i}(X_i - X_{i-1} - l_{i-1}) - b_i\dot{X}_i$$

- Structural Equations of induced SCM $\mathcal{M}_{\mathcal{D}}$:

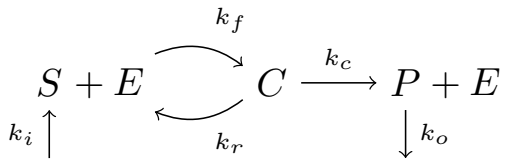
$$X_i = \frac{k_i(X_{i+1} - l_i) + k_{i-1}(X_{i-1} + l_{i-1})}{k_i + k_{i+1}}$$

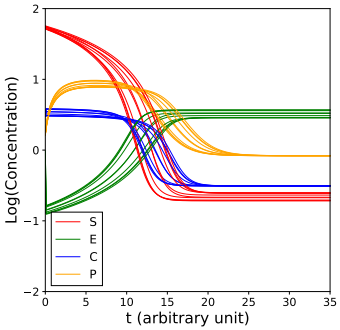
- Graph of induced SCM $\mathcal{G}(\mathcal{M}_{\mathcal{D}})$:



# From ODE to SCM: Example 2

Enzyme reaction:



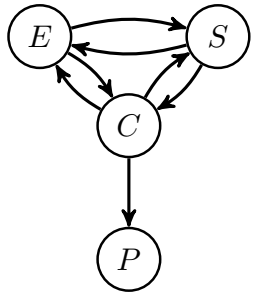

Random differential equations:

$$\frac{d}{dt}S = k_i - k_f ES + k_r C$$
$$\frac{d}{dt}E = -k_f ES + (k_r + k_c)C$$
$$\frac{d}{dt}C = k_f ES - (k_r + k_c)C$$
$$\frac{d}{dt}P = k_c C - k_o P$$

$\xrightarrow{t \to \infty}$

Structural causal model:

$$S = k_i k_f^{-1} E^{-1} - k_r k_f^{-1} E^{-1} C$$
$$E = k_f^{-1}(k_r + k_c) S^{-1} C$$
$$C = k_f (k_r + k_c)^{-1} ES$$
$$P = k_c k_o^{-1} C$$




$\downarrow \mathrm{do}(E = \eta)$

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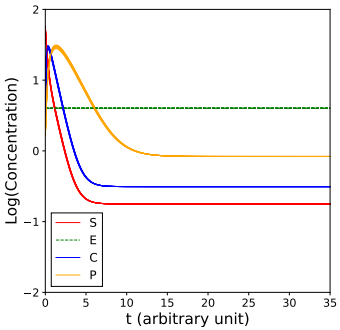


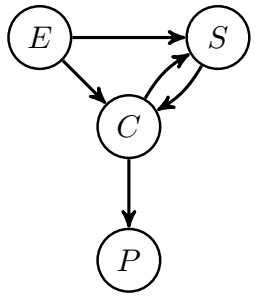

Intervened RDE:

$$\frac{d}{dt}S = k_i - k_f ES + k_r C$$
$$\frac{d}{dt}E = \eta$$
$$\frac{d}{dt}C = k_f ES - (k_r + k_c)C$$
$$\frac{d}{dt}P = k_c C - k_o P$$

$\xrightarrow{t \to \infty}$

Intervened SCM:

$$S = k_i k_f^{-1} E^{-1} - k_r k_f^{-1} E^{-1} C$$
$$E = \eta$$
$$C = k_f (k_r + k_c)^{-1} ES$$
$$P = k_c k_o^{-1} C$$




More generally, any chemical reaction can be modeled as an SCM at equilibrium. (Note: the SCM is in general *underspecified*, i.e., it does not retain all information about the equilibrium states of the dynamical system [Blom & Mooij, 2018]).

# SCMs and other Causal Modeling Frameworks

We can connect SCMs to the potential outcome framework (popular in the statistical literature):

**Definition**

Given a simple SCM $\mathcal{M}$ and let $\boldsymbol{E} \sim \mathbb{P}_{\mathcal{E}}$. For any subset $I \subseteq \mathcal{I}$ and value $\boldsymbol{\xi}_I$, define the potential outcome $\boldsymbol{X}_{\boldsymbol{\xi}_I} := \boldsymbol{g}_{\mathcal{M}_{\text{do}(\boldsymbol{X}_I = \boldsymbol{\xi}_I)}}(\boldsymbol{E})$.

Also, we can connect SCMs to causal Bayesian networks:

**Proposition**

*Given a simple SCM $\mathcal{M}$ with a graph $\mathcal{G}(\mathcal{M})$ that is*

- *acyclic (i.e., has no directed cycles), and*
- *causally sufficient (i.e., it has no bidirected edges).*

*Then $\mathcal{M}$ induces a Causal Bayesian Network $\langle \mathcal{G}(\mathcal{M}), p_{\mathcal{M}} \rangle$. Vice versa, for every Causal Bayesian Network there exists an SCM that induces it.*

# Seeing is not doing; but is doing necessary?

We can now express "correlation does not imply causation" (or, as Pearl says, "seeing is not doing") more precisely:

$$p\big(\boldsymbol{y} \mid \mathrm{do}(\boldsymbol{X} = \boldsymbol{x})\big) \neq p(\boldsymbol{y} \mid \boldsymbol{X} = \boldsymbol{x}) \qquad \text{in general}$$

Do we *really* need to introduce this additional interventional semantics ("the do-operator") on top of the notion of conditioning that we already are so familiar with in probability theory?

Not necessarily: we can introduce additional variables to get a purely **probabilistic** model that can mimic the SCM.

# Extending an SCM with Intervention Variables

## Definition

Given a simple SCM $\mathcal{M}$ with discrete endogenous domains $\mathcal{X}_i$. Define an extended SCM $\hat{\mathcal{M}}$ by (i) for each endogenous variable $X_i$ with $i \in I$, add an endogenous intervention variable $C_i$, taking values in the space $\mathcal{X}_i \cup \{\emptyset\}$; (ii) replace the causal mechanism $\boldsymbol{f}$ by $\hat{\boldsymbol{f}}$ with:

$$\hat{f}_{X_i}(\boldsymbol{x}, \boldsymbol{c}, \boldsymbol{e}) = \begin{cases} c_i & c_i \in \mathcal{X}_i \quad (\text{“set by perfect intervention”}) \\ f_i(\boldsymbol{x}, \boldsymbol{e}) & c_i = \emptyset \quad (\text{“observational default”}) \end{cases}$$

and $\hat{f}_{C_i}(\epsilon_i) = \epsilon_i$ where $\epsilon_i \sim \mathbb{P}_{C_i}$ with strictly positive density.

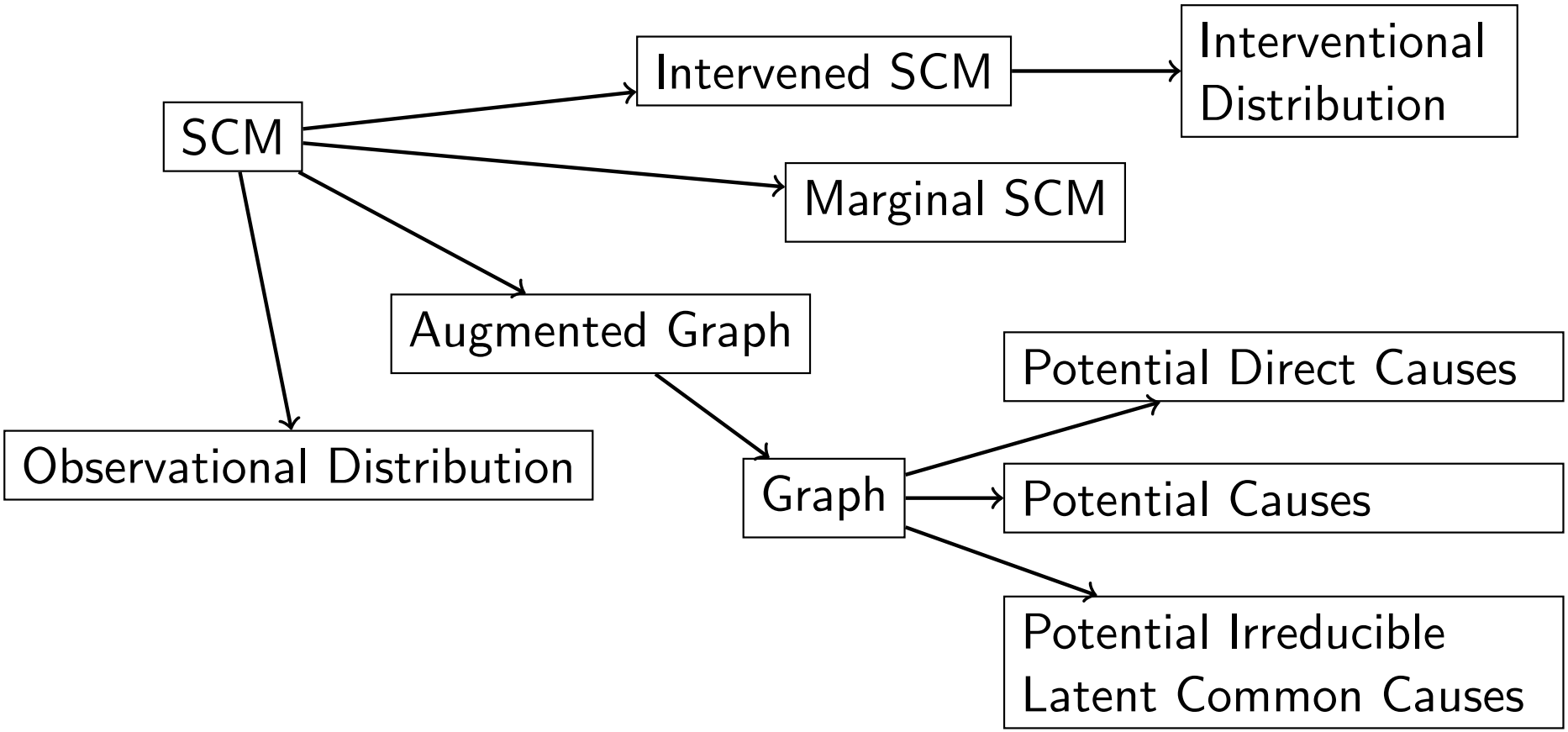
## Proposition

*For any intervention target $I \subseteq \mathcal{I}$ and intervention value $\boldsymbol{\xi}_I \in \mathcal{X}_I$:*

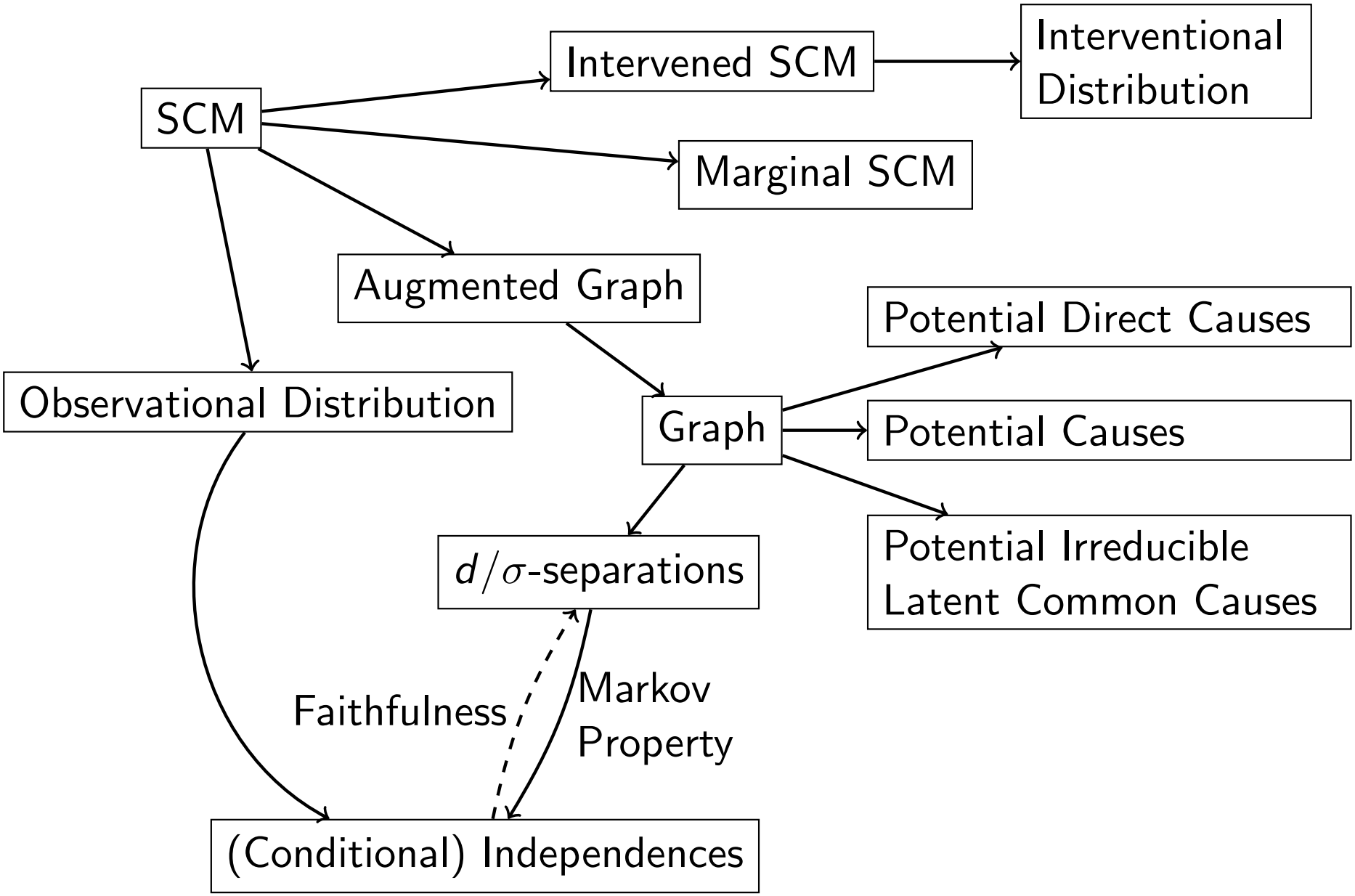
$$p_{\mathcal{M}}(\boldsymbol{x} \mid \text{do}(\boldsymbol{X}_I = \boldsymbol{\xi}_I)) = p_{\hat{\mathcal{M}}}(\boldsymbol{x} \mid C_I = \boldsymbol{\xi}_I, C_{\mathcal{I} \setminus I} = \emptyset)$$

All interventional distributions of $\mathcal{M}$ can be obtained by conditioning $p_{\hat{\mathcal{M}}}$.

# Simple SCMs: Overview



# Simple SCMs: Overview



# Contents

# (Conditional) independences

## Definition (Independence)

Given two random variables $X, Y$, we write $X \perp\!\!\!\perp Y$ and say that $X$ is independent of $Y$ if

$$p(x, y) = p(x)p(y).$$

Intuitively, $X$ is independent of $Y$ if we do not learn anything about $X$ when told the value of $Y$ (or vice versa).

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## Definition (Conditional Independence)

Given a third random variable $Z$, we write $X \perp\!\!\!\perp Y \,|\, Z$ and say that $X$ is (conditionally) independent from $Y$, given $Z$, if

$$p(x, y \,|\, Z = z) = p(x \,|\, Z = z)p(y \,|\, Z = z).$$

Intuitively, $X$ is independent of $Y$ if, given the value of $Z$, we do not learn anything new about $X$ when told the value of $Y$.

# (Directed) Paths

## Definition (Paths, Ancestors)

Let $\mathcal{G}$ be a directed mixed graph.

- A path $q$ is a sequence of adjacent edges in which no node occurs more than once.
- A directed path is of the form $i_1 \to i_2 \to \cdots \to i_k$.
- If there is a directed path from $X$ to $Y$, $X$ is called an ancestor of $Y$.
- The ancestors of $Y$ are denoted $\mathrm{an}_{\mathcal{G}}(Y)$, and include $Y$.

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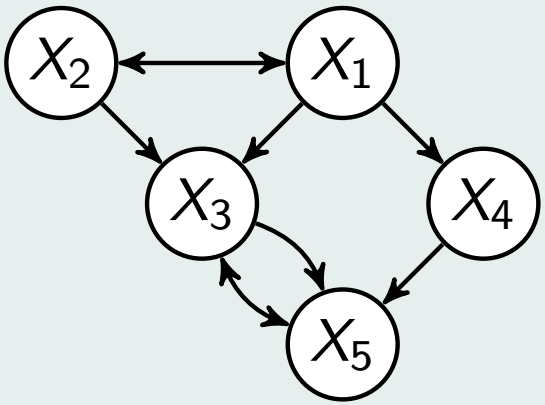
## Example




$X_1 \to X_3 \leftarrow X_1$ is not a path.
$X_1 \leftrightarrow X_2 \to X_3$ is a path.

$X_1 \to X_4 \to X_5$ is a directed path.
$X_4 \to X_5 \leftarrow X_3$ is not a directed path.

The ancestors of $X_3$ are $\{X_1, X_2, X_3\}$.

# Colliders and non-colliders

## Definition (Colliders)

Let $\mathcal{G}$ be a directed mixed graph, and $q$ a path on $\mathcal{G}$.

- A collider on $q$ is a (non-endpoint) node $X$ on $q$ with precisely two arrowheads pointing towards $X$ on the adjacent edges:

$$\rightarrow X \leftarrow, \quad \rightarrow X \leftrightarrow, \quad \leftrightarrow X \leftarrow, \quad \leftrightarrow X \leftrightarrow$$

- A non-collider on $q$ is any node on the path which is not a collider.

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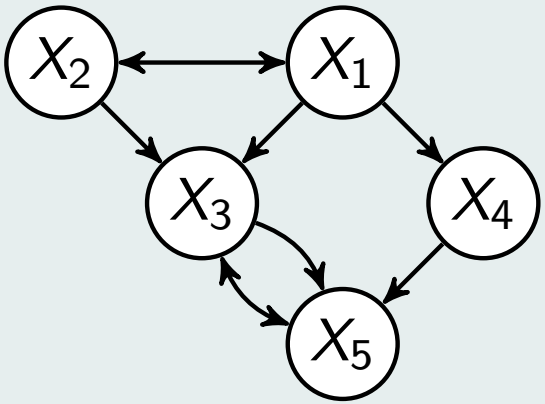


The path $X_3 \rightarrow X_5 \leftarrow X_4$ contains a collider $X_5$.
The path $X_1 \leftrightarrow X_2 \rightarrow X_3$ contains no collider.
$X_5$ is a non-collider on $X_5 \leftrightarrow X_3 \leftarrow X_1$.

# $d$-Blocked paths

**Definition**

Let $\mathcal{G}$ be a directed mixed graph. Given a path $q$ on $\mathcal{G}$, and a set of nodes $\boldsymbol{S}$, we say that $\boldsymbol{S}$ $d$-blocks $q$ if $q$ contains

- a non-collider which is in $\boldsymbol{S}$, or
- a collider which is *not* an ancestor of $\boldsymbol{S}$.

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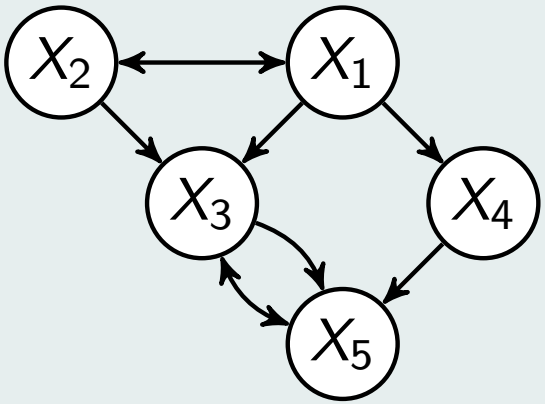


$X_3 \to X_5 \leftarrow X_4$ is $d$-blocked by $\emptyset$.
$X_3 \to X_5 \leftarrow X_4$ is $d$-blocked by $\{X_1\}$.
$X_3 \to X_5 \leftarrow X_4$ is not $d$-blocked by $\{X_5\}$.

$X_3 \leftarrow X_2 \leftrightarrow X_1 \to X_4$ is $d$-blocked by $\{X_1\}$.
$X_3 \leftarrow X_2 \leftrightarrow X_1 \to X_4$ is not $d$-blocked by $\{X_5\}$.

# $d$-separation

**Definition ($d$-separation)**

Let $\mathcal{G}$ be a directed mixed graph. For three sets $\boldsymbol{X}, \boldsymbol{Y}, \boldsymbol{Z}$ of nodes in $\mathcal{G}$, we say that $\boldsymbol{X}$ and $\boldsymbol{Y}$ are $d$-separated by $\boldsymbol{Z}$ iff all paths between a node in $\boldsymbol{X}$ and a node in $\boldsymbol{Y}$ are $d$-blocked by $\boldsymbol{Z}$, and write $\boldsymbol{X} \perp_{\mathcal{G}} \boldsymbol{Y} \mid \boldsymbol{Z}$.

# $d$-separation

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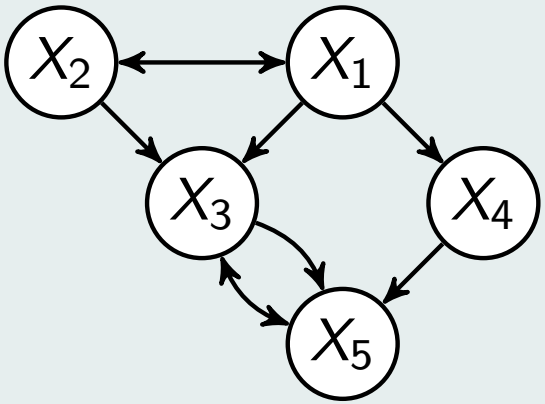
## Example




$X_3$ and $X_4$ are $d$-separated by $\{X_1\}$.
$X_3$ and $X_4$ are $d$-separated by $\{X_1, X_2\}$.
$X_3$ and $X_4$ are not $d$-separated by $\emptyset$.
$X_3$ and $X_4$ are not $d$-separated by $\{X_1, X_5\}$.

# Exercise

Please make Exercise 1.2

# Acyclic Global Markov Property

**Theorem**

*For an acyclic SCM, the Global Markov Property holds:*

$$\boldsymbol{X}, \boldsymbol{Y} \underset{\mathcal{G}(\mathcal{M})}{\perp} \boldsymbol{Z} \qquad \Longrightarrow \qquad \boldsymbol{X} \underset{p_{\mathcal{M}}}{\perp\!\!\!\perp} \boldsymbol{Y} \,|\, \boldsymbol{Z}$$

*for all subsets* $\boldsymbol{X}, \boldsymbol{Y}, \boldsymbol{Z}$ *of nodes.*

In words: every d-separation in the graph $\mathcal{G}(\mathcal{M})$ of $\mathcal{M}$ implies a (conditional) independence in the (unique) observational distribution associated to $\mathcal{M}$.

For *cyclic* SCMs, the notion of d-separation is too strong in general. A weaker notion called $\sigma$-separation has to be used instead [Forré and Mooij, 2017]. For simple SCMs, a global Markov condition using $\sigma$-separation can then be shown to hold.

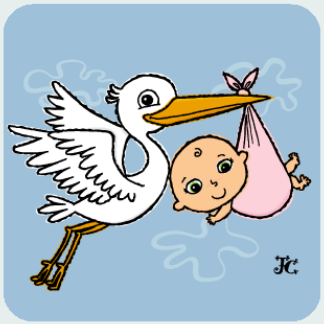
# Reichenbach's Principle

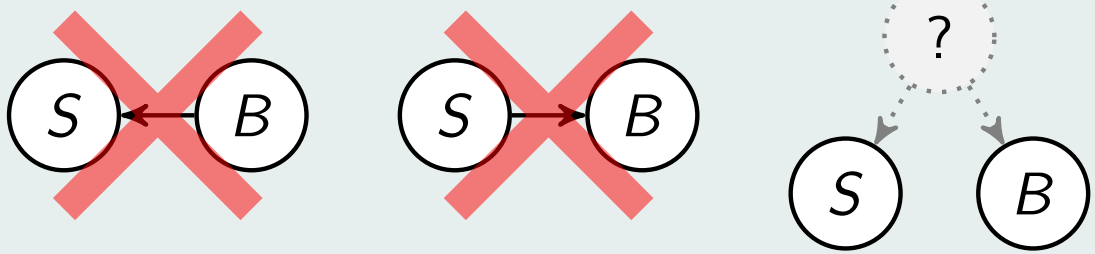
## Reichenbach's Principle of Common Cause

The dependence $X \not\perp\!\!\!\perp Y$ implies that $X \to Y$, $Y \to X$, or $X \leftrightarrow Y$ (or any combination of these three).

## Example

- Significant correlation ($p = 0.008$) between human birth rate and number of stork populations in European countries [Matthews, 2000]
- Most people nowadays do not believe that storks deliver babies (nor that babies deliver storks)
- There must be some confounder explaining the correlation

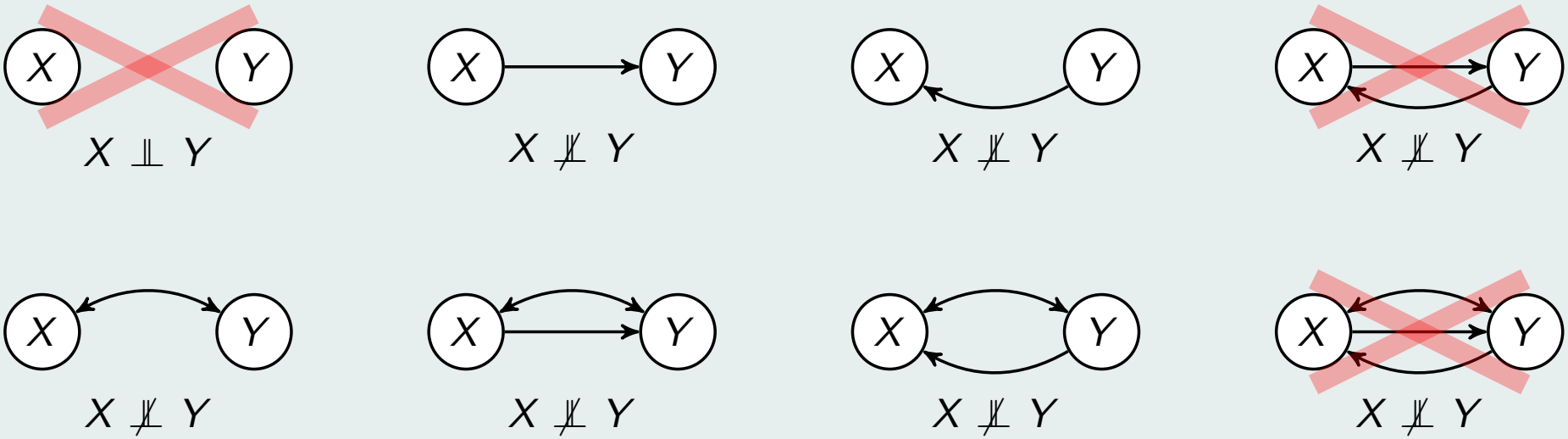




# Proof of Reichenbach's Principle

Assuming that $p(X, Y)$ is generated by an acyclic SCM, we can easily prove Reichenbach's Principle by applying the Global Markov property:

## Proof




(The proof can be extended to include the cyclic case)

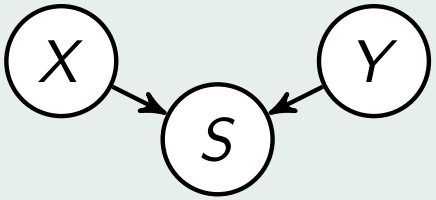
# Selection Bias

Reichenbach's Principle may fail in case of *selection bias*.

## Definition

If a data set is obtained by only including samples conditional on some event, selection bias may be introduced.

## Example




$X$: the battery is charged
$Y$: the start engine is operational
$S$: the car starts

- A car mechanic (who only observes cars for which $S = 0$) will observe a dependence between $X$ and $Y$: $X \not\perp\!\!\!\perp Y \mid S$.
- When the car mechanic invokes Reichenbach's Principle without realizing that he is selecting on the value of $S$ (maybe $S$ is a latent variable), a wrong conclusion will be drawn.

# Faithfulness Assumption

Let $\mathcal{M}$ be an acyclic SCM.

We have seen that the *Global Markov Property* holds:

$$\boldsymbol{X}, \boldsymbol{Y} \underset{\mathcal{G}(\mathcal{M})}{\perp} \boldsymbol{Z} \qquad \Longrightarrow \qquad \boldsymbol{X} \underset{p_{\mathcal{M}}}{\perp\!\!\!\perp} \boldsymbol{Y} \,|\, \boldsymbol{Z}$$

for all subsets $\boldsymbol{X}, \boldsymbol{Y}, \boldsymbol{Z}$ of nodes.

**Definition (Faithfulness Assumption)**

For all subsets $\boldsymbol{X}, \boldsymbol{Y}, \boldsymbol{Z}$ of nodes,

$$\boldsymbol{X}, \boldsymbol{Y} \underset{\mathcal{G}(\mathcal{M})}{\perp} \boldsymbol{Z} \qquad \Longleftarrow \qquad \boldsymbol{X} \underset{p_{\mathcal{M}}}{\perp\!\!\!\perp} \boldsymbol{Y} \,|\, \boldsymbol{Z}$$

**Note**: Faithfulness holds generically, i.e., up to measure-zero sets of parameters [Meek, 1995]. In other words, SCM parameters need to be *carefully tuned* in order to violate the faithfulness assumption.

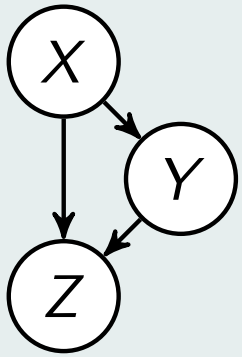
# Faithfulness Violations

Faithfulness violations may occur e.g. in case of parameter cancellations or deterministic relations.

## Example (Parameter cancellation)

Consider an SCM $\mathcal{M}$:

$$X = E_X$$
$$Y = X + E_Y$$
$$Z = X - Y + E_Z$$

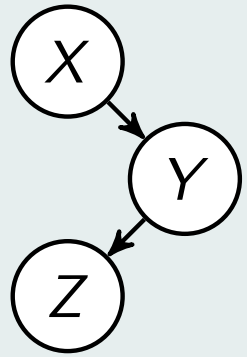



Then:
$Z \perp\!\!\!\perp_{p_{\mathcal{M}}} X$ but $Z \not\perp\!\!\!\perp_{\mathcal{G}(\mathcal{M})} X$.

## Example (Deterministic relation)

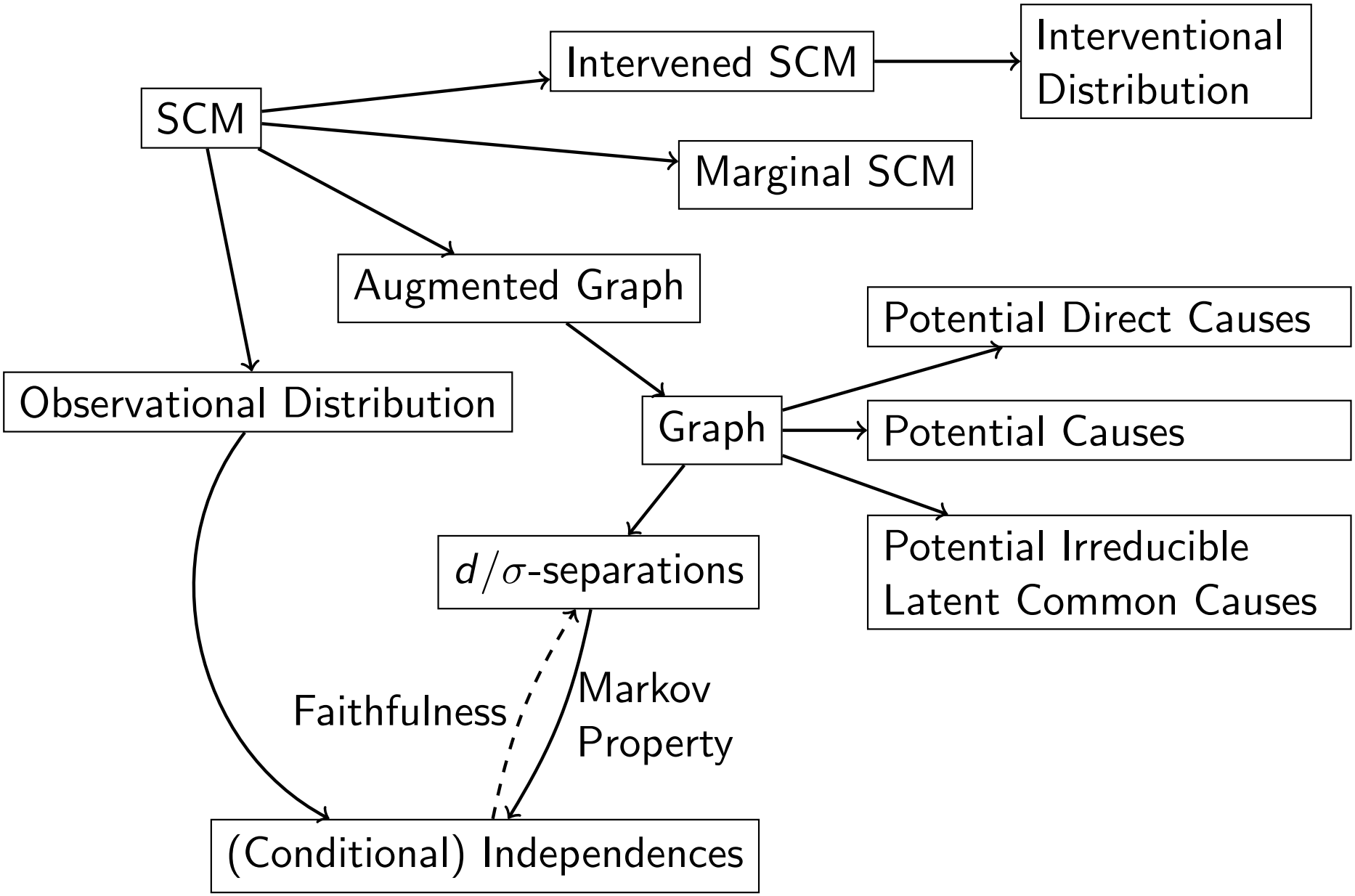
Consider an SCM $\mathcal{M}$:

$$X = E_X$$
$$Y = X$$
$$Z = Y + E_Z$$




Then:
$Z \perp\!\!\!\perp_{p_{\mathcal{M}}} Y \,|\, X$ but $Z \not\perp\!\!\!\perp_{\mathcal{G}(\mathcal{M})} Y \,|\, X$.

# Simple SCMs: Overview



# Contents

# Causal Inference: Predicting Causal Effects

One important task ("*causal inference*") is the prediction of causal effects.

**Definition**

The causal effect of $X$ on $Y$ is defined as $p\big(y \mid \mathrm{do}(X = x)\big)$.

Special cases:

- $X$ binary: $\mathbb{E}\big(Y \mid \mathrm{do}(X = 1)\big) - \mathbb{E}\big(Y \mid \mathrm{do}(X = 0)\big)$
- $X, Y$ linearly related: $\frac{\partial}{\partial x}\mathbb{E}\big(Y \mid \mathrm{do}(X = x)\big)$

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- $X, Y$ linearly related: $\frac{\partial}{\partial x}\mathbb{E}\big(Y \mid \mathrm{do}(X = x)\big)$

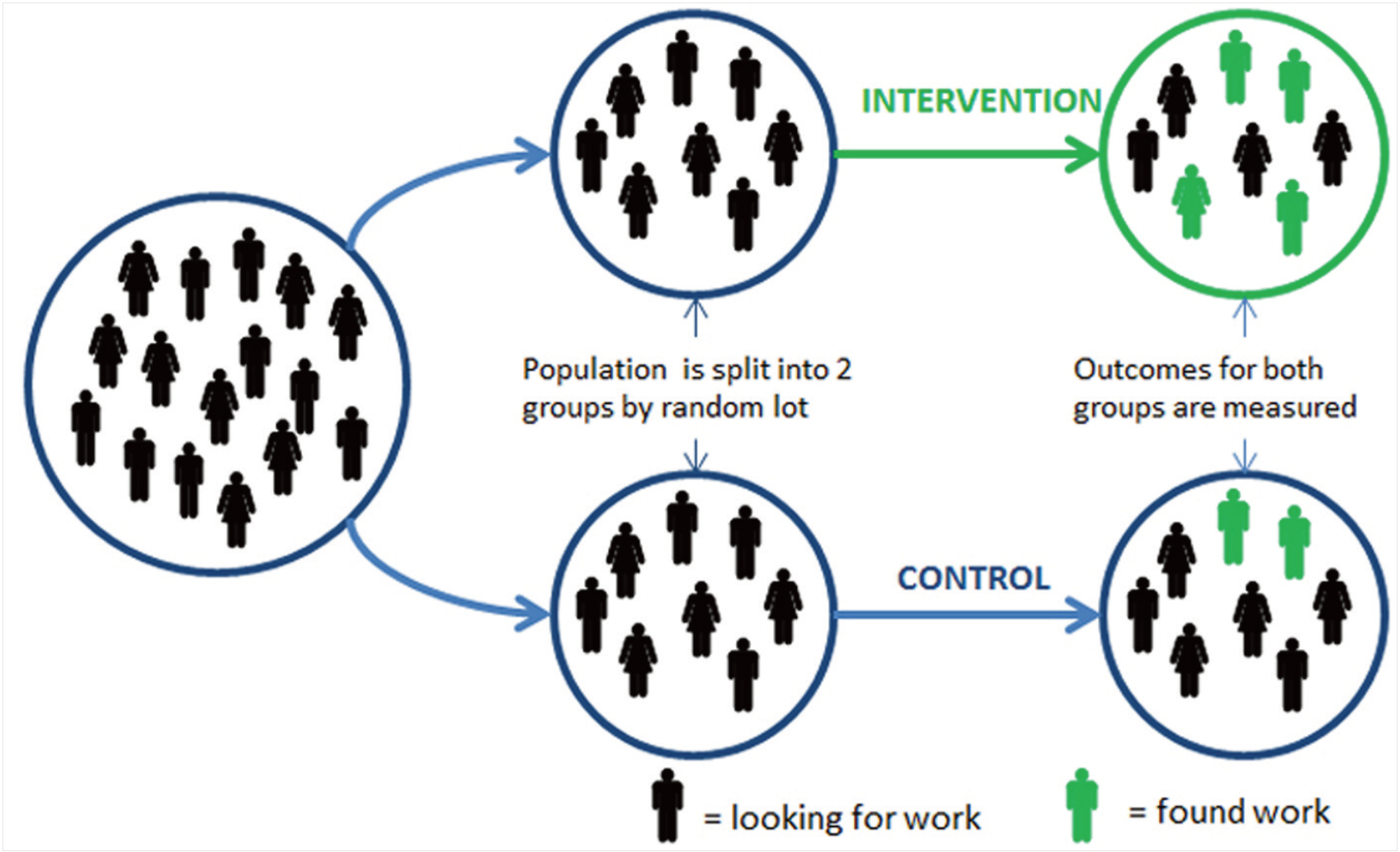
**Note**: In general, since $p\big(y \mid \mathrm{do}(X = x)\big) \neq p(y \mid X = x)$, we cannot use standard supervised learning (regression, classification) for this task.

Two approaches can be used:

- Experimentation (Randomized Controlled Trials, A/B-testing)
- Apply the Back-door Criterion (if causal graph is known)

# Causal discovery by experimentation

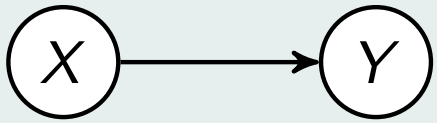
Experimentation (e.g., Randomized Controlled Trials, A/B-testing, . . . ) provides the gold standard for causal effect estimation.



# Identifiability: Example

If we cannot do experiments... Can we express $p\big(y \mid \mathrm{do}(X = x)\big)$ in terms of the observational distribution?

## Example




$$p\big(y \mid \mathrm{do}(X = x)\big)$$

$$=$$

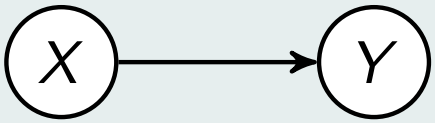
$$p(y \mid X = x)$$

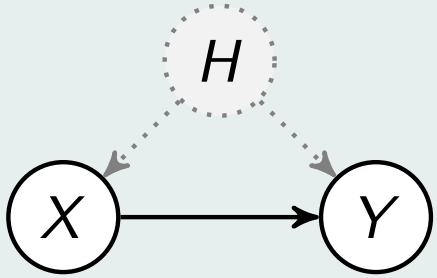
Yes!

# Identifiability: Example

If we cannot do experiments... Can we express $p\big(y \mid \mathrm{do}(X = x)\big)$ in terms of the observational distribution?

## Example




$$p\big(y \mid \mathrm{do}(X = x)\big) = p(y \mid X = x)$$

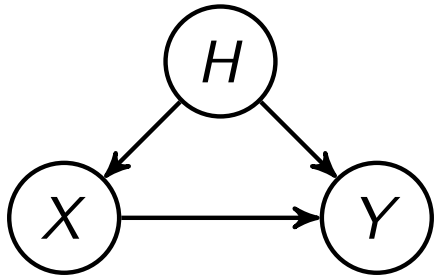
Yes!

$$p\big(y \mid \mathrm{do}(X = x)\big) = \int p(h)p(y \mid x, h)\, dh \neq p(y \mid X = x) = \int p(h \mid x)p(y \mid x, h)\, dh$$

No!

# Adjustment for covariates

We have seen that for the following causal graph,




adjusting for the confounder $H$, yields the causal effect of $X$ on $Y$:

$$\int p(h)p(y \mid x, h)\, dh = p\big(y \mid \mathrm{do}(X = x)\big)$$

More generally, given a causal graph: which variables $\boldsymbol{H}$ could we adjust for in order to express the causal effect of $X$ on $Y$ in terms of the observational distribution?

A sufficient condition is given by the Back-door Criterion.

# The Back-door Criterion

**Theorem (Back-door Criterion (Pearl, 2000))**

*Let $\mathcal{M}$ be an acyclic SCM $\mathcal{M}$ with disjoint subsets of endogenous variables $\{X\}$, $\{Y\}$, $\boldsymbol{H}$. Let $\hat{\mathcal{G}}$ be $\mathcal{G}(\mathcal{M})$ extended with an intervention node $I_X \to X$. If*

1. $H \perp_{\hat{\mathcal{G}}} I_X$;
2. $Y \perp_{\hat{\mathcal{G}}} I_X \,|\, \{X\} \cup H$,

*then $\boldsymbol{H}$ is called admissible for adjustment to find the causal effect of $X$ on $Y$, i.e., this causal effect is given by:*

$$p_{\mathcal{M}}\big(y \,|\, \mathrm{do}(X = x)\big) = \int p_{\mathcal{M}}(y \,|\, x, \boldsymbol{h}) p_{\mathcal{M}}(\boldsymbol{h})\, d\boldsymbol{h}.$$

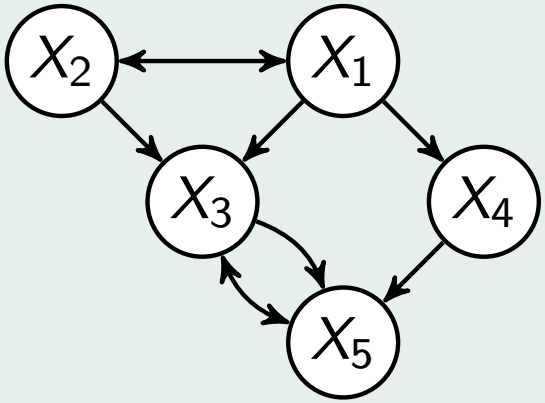
*For the special case $\boldsymbol{H} = \emptyset$, this should be read as:*

$$p_{\mathcal{M}}\big(y \,|\, \mathrm{do}(X = x)\big) = p_{\mathcal{M}}(y \,|\, x).$$

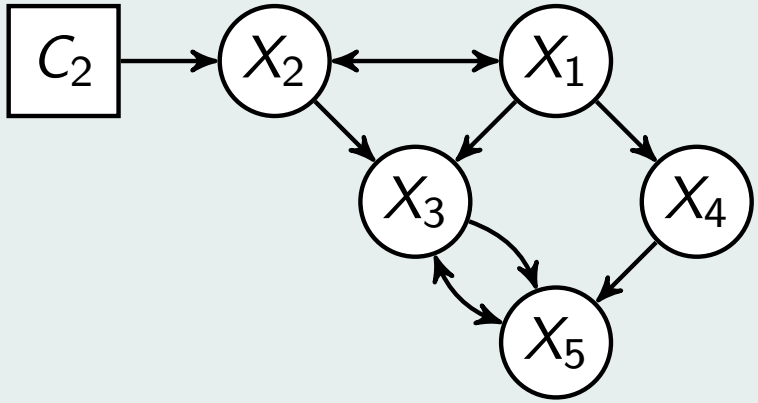
# The Back-door Criterion: Example

## Example

$\mathcal{G}(\mathcal{M})$:




$\hat{\mathcal{G}}$:




The sets of variables that are admissible for adjustment to get the causal effect of $X_2$ on $X_5$ are: $\{X_1\}$, $\{X_1, X_4\}$. Therefore:

$$p(x_5 \mid \mathrm{do}(X_2 = x_2)) = \int p(x_5 \mid x_1, x_2) p(x_1)\, dx_1$$

$$= \int p(x_5 \mid x_1, x_2, x_4) p(x_1, x_4)\, dx_1\, dx_4$$

Some sets of variables that are *not* admissible for adjustment to get the causal effect of $X_2$ on $X_5$ are: $\{X_3\}$, $\{X_1, X_3\}$.

# Exercise

Please make Exercise 2.2

# Simpson's Paradox

Remember Simpson's paradox:

## Example (Simpson's paradox)

We collect electronic patient records to investigate the effectiveness of a new drug against a certain disease. We find that:

1. The probability of recovery is higher for patients that took the drug:

$$p(\text{recovery} \mid \text{drug}) > p(\text{recovery} \mid \text{no drug})$$

2. For **both male and female** patients, the relation is **opposite**:

$$p(\text{recovery} \mid \text{drug}, \text{male}) < p(\text{recovery} \mid \text{no drug}, \text{male})$$

$$p(\text{recovery} \mid \text{drug}, \text{female}) < p(\text{recovery} \mid \text{no drug}, \text{female})$$

Does the drug cause recovery? I.e., would *you* use this drug if you are ill?

The answer depends on the causal relationships between the variables!

# Resolving Simpson's paradox

The crux to resolving Simpson's paradox is to realize:

**Seeing $\neq$ doing**

- $p(R = 1 \mid D = 1)$: the probability that somebody recovers, given the observation that the person took the drug.
- $p\big(R = 1 \mid \text{do}(D = 1)\big)$: the probability that somebody recovers, if we *force* the person to take the drug.

Simpson's paradox only manifests itself if we misinterpret correlation as causation by identifying $p(r \mid D = d)$ with $p\big(r \mid \text{do}(D = d)\big)$.

We should prescribe the drug if

$$p\big(R = 1 \mid \text{do}(D = 1)\big) > p\big(R = 1 \mid \text{do(D=0)}\big).$$

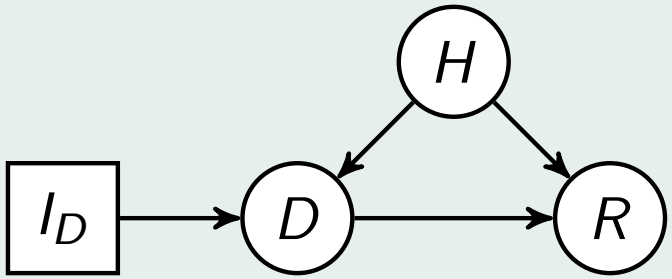
How to find the causal effect of the drug on recovery?

1. Randomized Controlled Trials
2. Back-door Criterion (requires knowledge of causal graph)

# Exercise

Please make Exercise 2.3

## Example (Scenario 1)




$R$: Recovery
$D$: Took drug
$H$: Gender

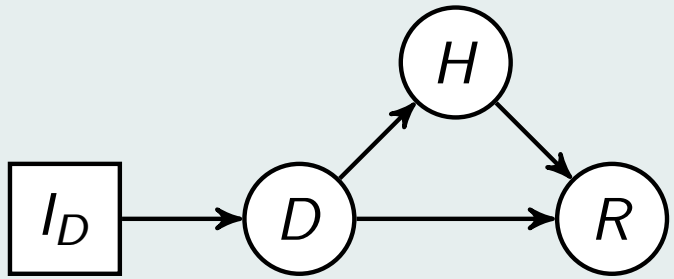
- $I_D \perp H$;
- $I_D \perp R | D, H$;
- Therefore, adjust for $\{H\}$ to obtain causal effect of drug on recovery:

$$p\big(r \mid \text{do}(D = d)\big) = \sum_h p(r \mid D = d, H = h) p(h)$$

- So in scenario 1, you should **not** take the drug: for both males and females, taking the drug lowers the probability of recovery.

# Back-door Criterion for Simpson's paradox

## Example (Scenario 2)




$R$: Recovery
$D$: Took drug
$H$: Gender

- $I_D \not\perp H$ ($H$ is not admissible for adjustment);
- $I_D \perp R|D$;
- Do **not** adjust for $\{H\}$ to obtain causal effect of drug on recovery:

$$p\big(r \mid \mathrm{do}(D = d)\big) = p(r \mid D = d)$$

- So in scenario 2, you **should** take the drug: in the general population, taking the drug increases the probability of recovery.

(If you think gender-changing drugs are unlikely, replace "gender" by "high/low blood pressure", for example).

# Causal Reasoning: Do-calculus [Pearl, 2000]

Pearl formulated three rules (the "**do-calculus**") that can be used in addition to the usual rules for probabilistic reasoning. For acyclic SCMs:

1. **Inserting/deleting observations**:

$$p\big(\boldsymbol{y} \mid \boldsymbol{x}, \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) = p\big(\boldsymbol{y} \mid \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) \qquad \text{if } \boldsymbol{Y} \underset{\hat{\mathcal{G}}_{\mathrm{do}(W)}}{\perp} \boldsymbol{X} \mid \boldsymbol{Z}$$

2. **Inserting/deleting actions**:

$$p\big(\boldsymbol{y} \mid \mathrm{do}(\boldsymbol{x}), \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) = p\big(\boldsymbol{y} \mid \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) \qquad \text{if } \boldsymbol{Y} \underset{\hat{\mathcal{G}}_{\mathrm{do}(W)}}{\perp} \boldsymbol{I}_{\boldsymbol{X}} \mid \boldsymbol{Z}.$$

3. **Action/observation exchange**:

$$p\big(\boldsymbol{y} \mid \mathrm{do}(\boldsymbol{x}), \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) = p\big(\boldsymbol{y} \mid \boldsymbol{x}, \boldsymbol{z}, \mathrm{do}(\boldsymbol{w})\big) \qquad \text{if } \boldsymbol{Y} \underset{\hat{\mathcal{G}}_{\mathrm{do}(W)}}{\perp} \boldsymbol{I}_{\boldsymbol{X}} \mid \boldsymbol{X}, \boldsymbol{Z}$$

The do-calculus allows us to reason with (probabilistic) causal statements, given (partial) knowledge of the causal structure. These rules are more powerful than the Back-door Criterion for causal prediction purposes.

# Contents

# Causal Discovery

We have seen how to perform causal reasoning, given the causal model. But how do we get the causal model in the first place?

Establishing causal relations from data ("causal discovery") is one of the fundamental tasks in science.

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More recently, causal discovery methods from purely observational data have been developed, starting with the work of Spirtes, Gleimour, Scheines, Pearl and others.

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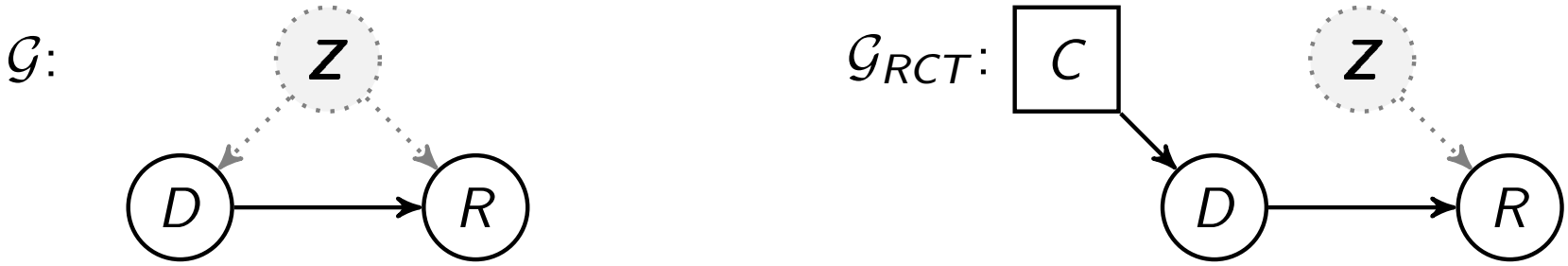
More recently, causal discovery methods from purely observational data have been developed, starting with the work of Spirtes, Gleimour, Scheines, Pearl and others.

These ideas have inspired causal discovery methods that combine observational and interventional data in various ways.

# Contents

# Randomized Controlled Trials [Fisher, 1935]




$R$: Recovery, $D$: Drug, $\boldsymbol{Z}$: latent confounders (e.g., genetics), $C$: coin flip.

- Divide patients into two groups: treatment and control randomly (e.g., by a coin flip).
- Patients in the treatment group are forced to take a drug, and patients in the control group are forced to not take the drug (but to take a placebo instead): $D = C$.
- Estimating the causal effect of the drug now becomes a standard statistical exercise, as $p(R \mid D = C) = p(R \mid \text{do}(D = C))$.
- Gold-standard for causal discovery.

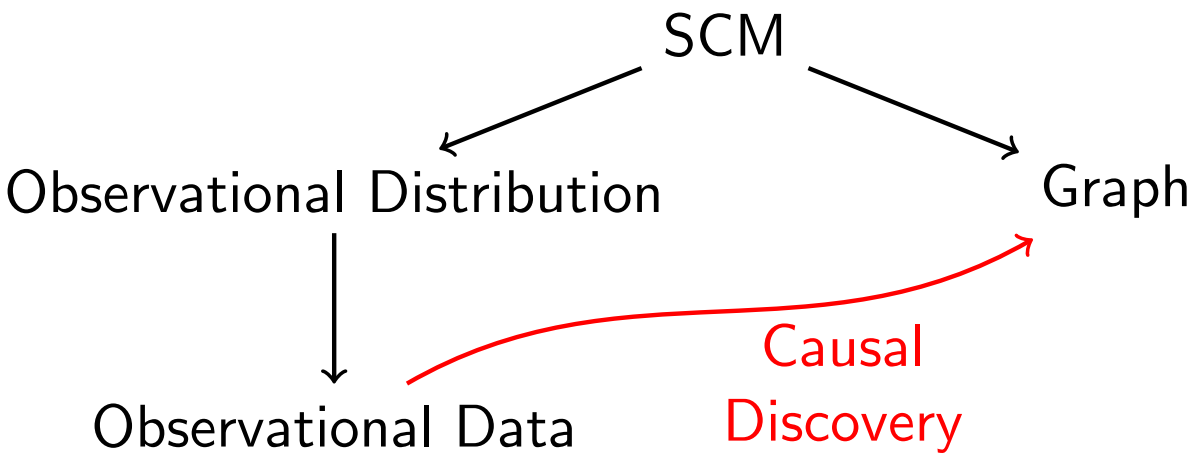
All *evidence-based* medicine is based on this idea.

# Contents

# Causal Discovery from Observational Data

Controlled experiments can be expensive, time-consuming, unethical, impractical or even infeasible.

Intriguing alternative: causal discovery from purely observational data [Spirtes et al., 2000, Pearl, 2000]!




**Disclaimer**: Works only under strong assumptions and with (possibly very) large sample sizes.

# Approaches to Causal Discovery from Observational Data I

## Conditional-independence constraint-based

*Independence patterns in the data constrain the possible causal graphs.*

- **LCD (Cooper, 1997)**
- **Y-Structures (Mani & Cooper, 2004)**
- PC (Spirtes & Gleimour & Scheines, 2000), IC (Pearl, 2000)
- FCI (Spirtes & Meek & Richardson, 1995; Zhang, 2008)
- ...

## General constraint-based

*Similar, but exploiting more general types of constraints in the data.*

- Verma constraints (Robins (1986), Verma & Pearl (1990), Tian & Pearl (2002))
- Nested Markov Models (Richardson, Evans, Robins, Shpitser (2017))
- Algebraic Constraints (Van Ommen & Mooij (2017))
- ...

# Approaches to Causal Discovery from Observational Data II

## Likelihood-based approaches

*Score penalized likelihoods of possible causal graphs and select the best one(s).*

- Bayesian Network Learning (Heckerman, Geiger, Chickering, 1995)
- Greedy Equivalence Search (Chickering, 2002)
- ...

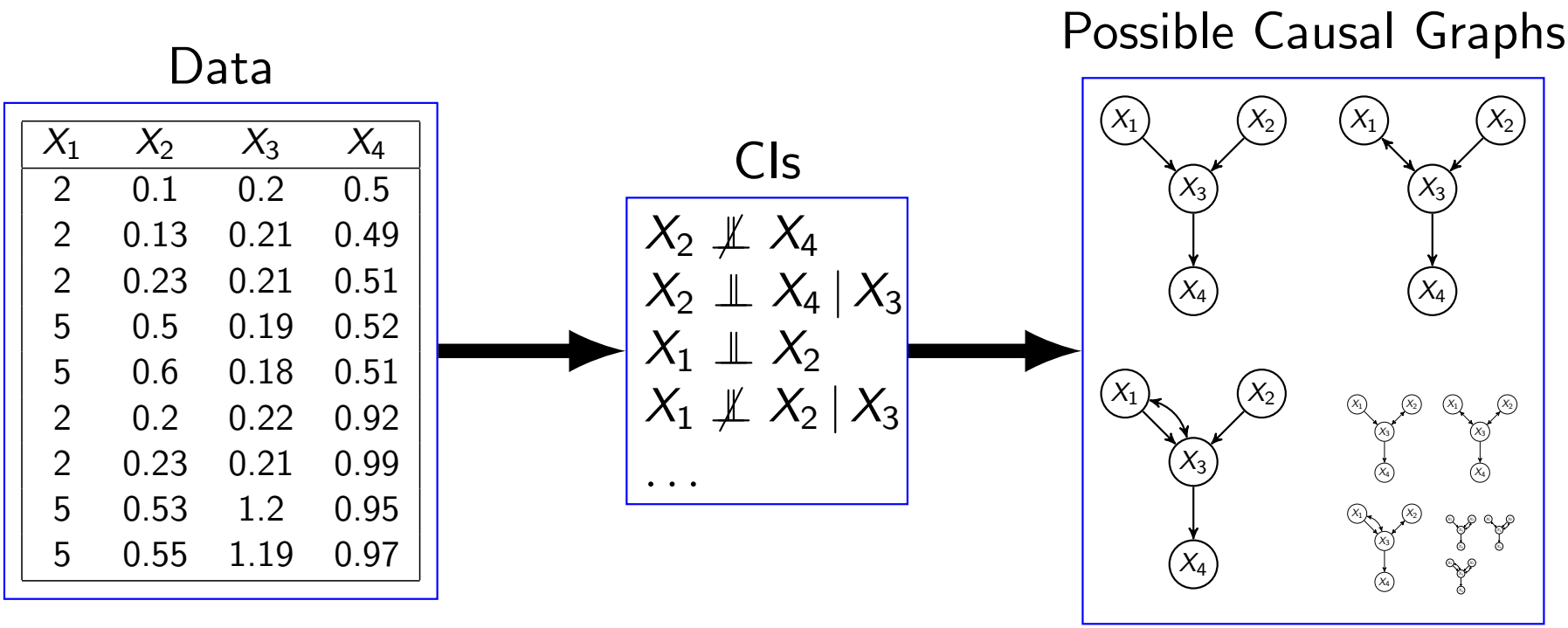
## Restrictions on functional causal relations and noise distributions

*Minimize the "complexity" of causal models.*

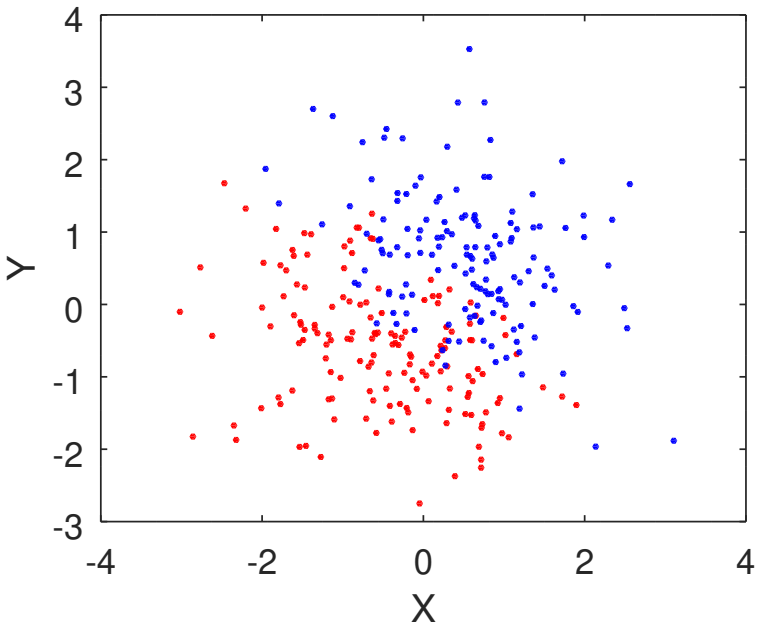
- LINGAM (Kano, Shimizu, 2003; Shimizu *et al.*, 2006)
- Additive Noise Models (Hoyer *et al.*, 2006)
- Post-Nonlinear Model (Zhang & Hyvärinen, 2009)
- ...

# Constraint-based Causal Discovery

From the pattern of conditional independences in the data we can reconstruct a set of possible underlying causal graphs, even when allowing for latent confounders [Spirtes et al., 2000].



# Causal Discovery from Observational Data: V-Structure

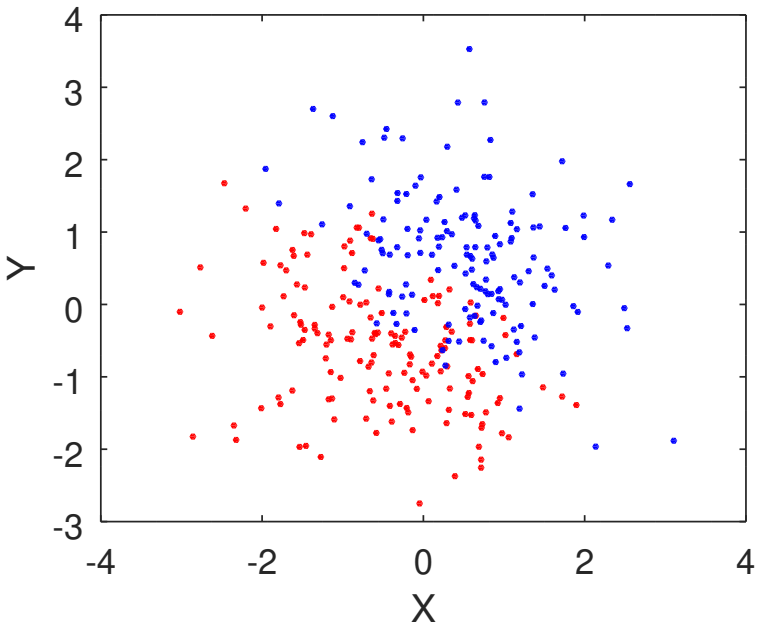



blue: $Z = 0$, red: $Z = 1$

$$X \perp\!\!\!\perp Y,\ X \not\perp\!\!\!\perp Y \mid Z,$$
$$X \not\perp\!\!\!\perp Z,\ X \not\perp\!\!\!\perp Z \mid Y,$$
$$Y \not\perp\!\!\!\perp Z,\ Y \not\perp\!\!\!\perp Z \mid X.$$

**Question: What is the causal relation between $X$, $Y$ and $Z$?**

# Causal Discovery from Observational Data: V-Structure



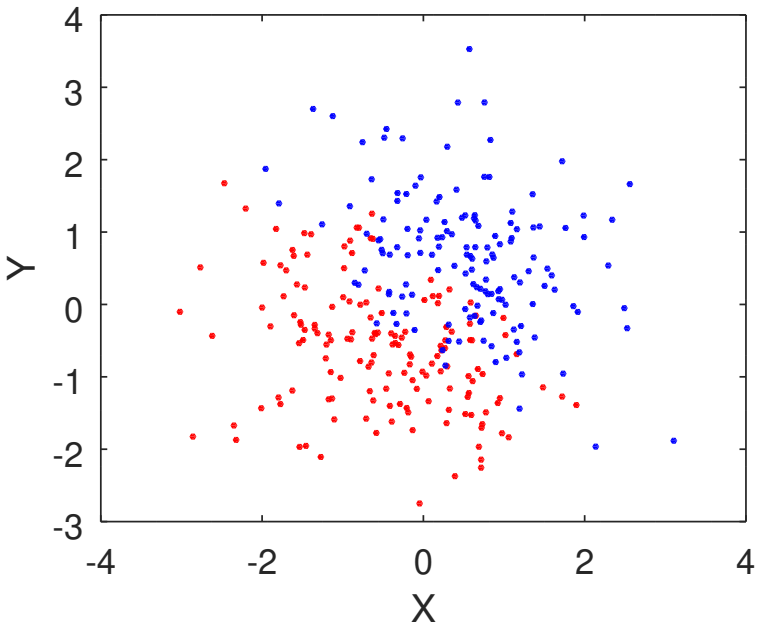

blue: $Z = 0$, red: $Z = 1$

$$X \perp\!\!\!\perp Y,\ X \not\perp\!\!\!\perp Y \mid Z,$$
$$X \not\perp\!\!\!\perp Z,\ X \not\perp\!\!\!\perp Z \mid Y,$$
$$Y \not\perp\!\!\!\perp Z,\ Y \not\perp\!\!\!\perp Z \mid X.$$

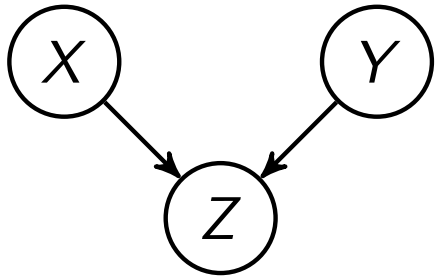
**Question: What is the causal relation between $X$, $Y$ and $Z$?**

*Hint: Assume an acyclic, faithful SCM without latent confounders generated the data, and assume no selection bias or measurement error*

# Causal Discovery from Observational Data: V-Structure




blue: $Z = 0$, red: $Z = 1$




$$X \perp\!\!\!\perp Y,\ X \not\perp\!\!\!\perp Y \mid Z,$$
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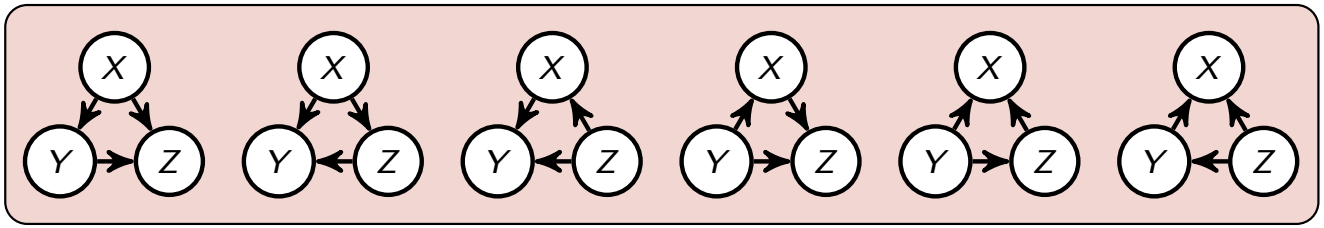
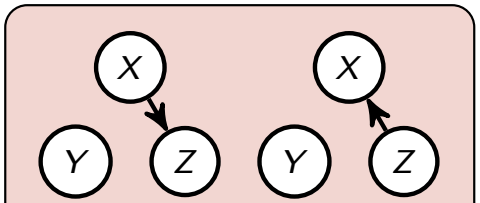
**Question: What is the causal relation between $X$, $Y$ and $Z$?**
*Hint: Assume an acyclic, faithful SCM without latent confounders generated the data, and assume no selection bias or measurement error*

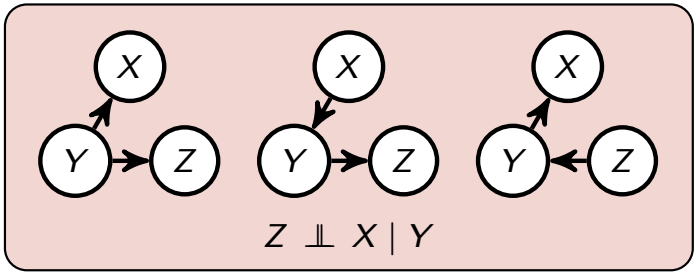
**Answer: $X$ causes $Z$; $Y$ causes $Z$; $X$ and $Y$ causally unrelated**

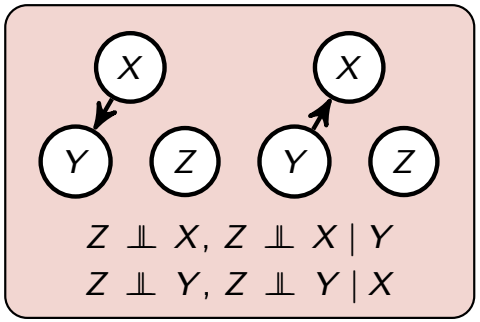
**Note:** Strong assumptions, but no experiments needed!

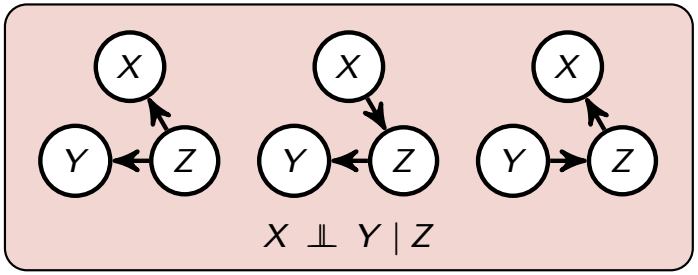
# Markov equivalence classes for three variables

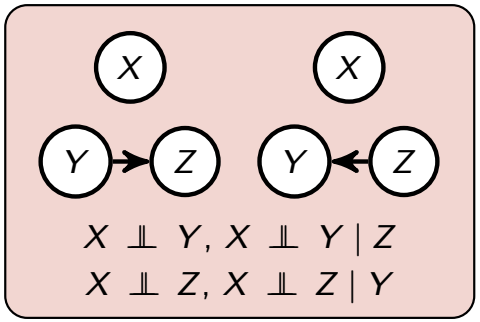


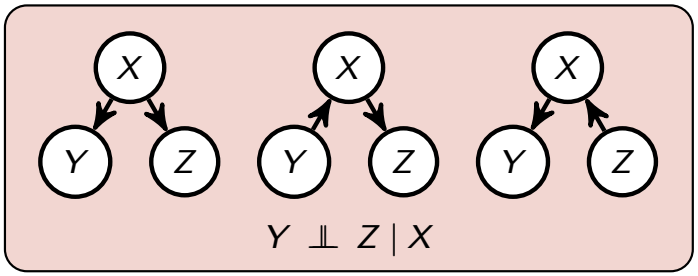



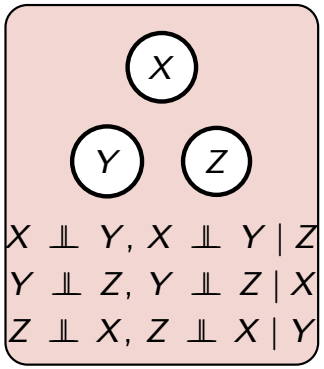



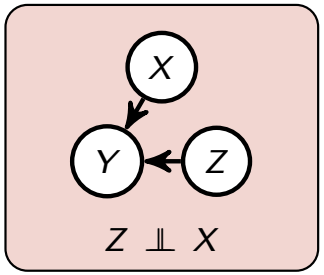



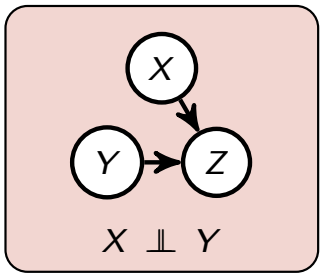



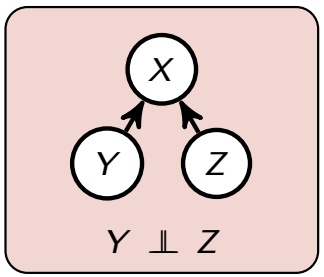



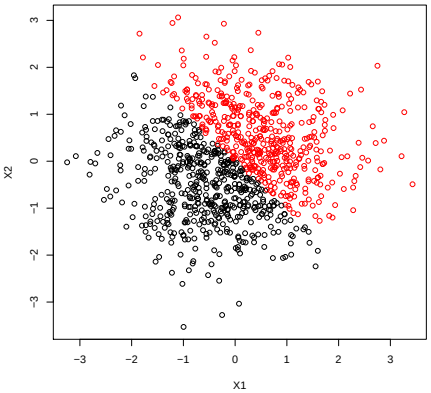



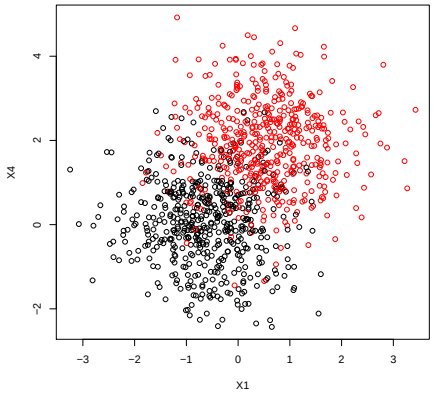



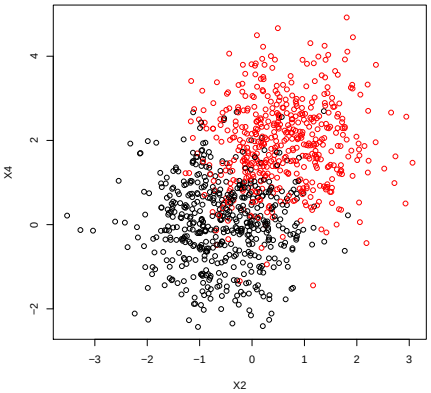
# Exercise

Please make Exercise 2.4

# Causal Discovery from Observational Data: Y-Structure




$X_1 \perp\!\!\!\perp X_2$
$X_1 \not\perp\!\!\!\perp X_2 \,|\, X_3$

$X_1 \not\perp\!\!\!\perp X_4$
$X_1 \perp\!\!\!\perp X_4 \,|\, X_3$

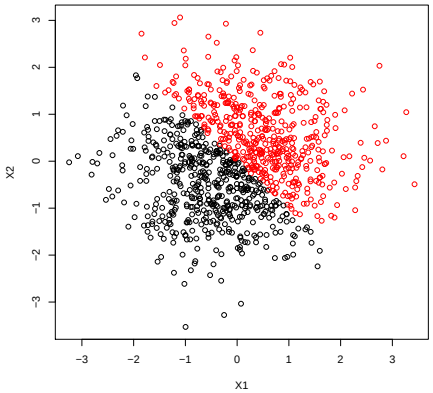
$X_2 \not\perp\!\!\!\perp X_4$
$X_2 \perp\!\!\!\perp X_4 \,|\, X_3$

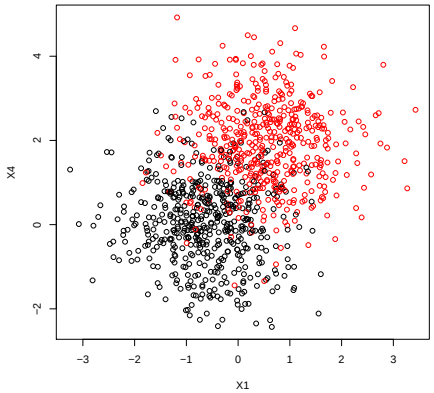
black: $X_3 = 0$, red: $X_3 = 1$

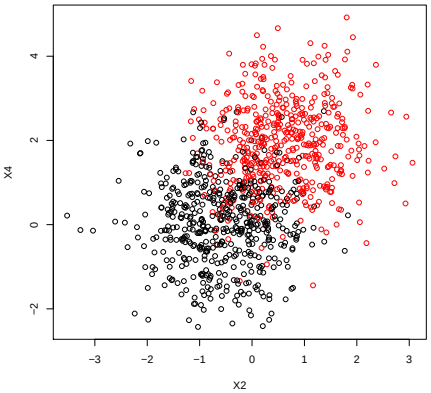
**Question: What is the causal relation between $X_3$ and $X_4$?**

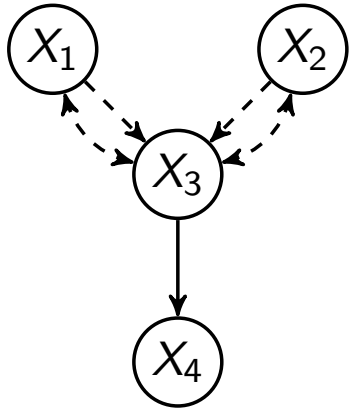
*Hint: Assume an acyclic, faithful SCM generated the data, and assume no selection bias or measurement error.*

# Causal Discovery from Observational Data: Y-Structure




$X_1 \perp\!\!\!\perp X_2$
$X_1 \not\perp\!\!\!\perp X_2 \,|\, X_3$

$X_1 \not\perp\!\!\!\perp X_4$
$X_1 \perp\!\!\!\perp X_4 \,|\, X_3$

$X_2 \not\perp\!\!\!\perp X_4$
$X_2 \perp\!\!\!\perp X_4 \,|\, X_3$

black: $X_3 = 0$, red: $X_3 = 1$

**Question: What is the causal relation between $X_3$ and $X_4$?**
*Hint: Assume an acyclic, faithful SCM generated the data, and assume no selection bias or measurement error.*

**Answer:** $X_3$ causes $X_4$ and they are not confounded. The causal effect of $X_3$ on $X_4$ satisfies $p(x_4 \mid \mathrm{do}(X_3 = x_3)) = p(x_4 \mid x_3)$.

| $d$ | Number of DAGs with $d$ nodes |
|---|---|
| 1 | 1 |
| 2 | 3 |
| 3 | 25 |
| 4 | 543 |
| 5 | 29281 |
| 6 | 3781503 |
| 7 | 1138779265 |
| 8 | 783702329343 |
| 9 | 1213442454842881 |
| 10 | 4175098976430598143 |
| 11 | 31603459396418917607425 |
| 12 | 521939651343829405020504063 |
| 13 | 18676600744432035186664816926721 |
| 14 | 1439428141044398334941790719839535103 |
| 15 | 237725265553410354992180218286376719253505 |
| 16 | 83756670773733320287699303047996412235223138303 |
| 17 | 62707921196923889899446452602494921906963551482675201 |
| 18 | 9942119532215951589522891459235452451655502687858830501478 3 |
| 19 | 3327719012271075917361775733112611258835830762584219025835467735 05 |

Table B.1: The number of DAGs depending on the number $d$ of nodes, taken from `http://oeis.org/A003024` [OEIS Foundation Inc., 2017]. The length of the numbers grows faster than any linear term.

Source: [Peters et al., 2017]

# State-of-the-art Causal Discovery: (Augmented) FCI

[Spirtes *et al.*, 2000, Spirtes *et al.*, 1999, Ali *et al.*, 2005, Zhang, 2008]

$\mathcal{R}0a$ If $X \perp\!\!\!\perp Y \,|\, \mathbf{Z}$, then $X \not\perp\!\!\!\perp Y$, $Sep(X,Y) \leftarrow \mathbf{Z}$.

$\mathcal{R}0b$ If $X *\!\!-\!\!* Z \circ\!\!-\!\!* Y$ and $X \not\perp\!\!\!\perp Y$, then if $Z \notin Sep(X,Y)$, then $X *\!\!\rightarrow Z \leftarrow\!\!* Y$.

$\mathcal{R}1$ If $X *\!\!\rightarrow Z \circ\!\!-\!\!* Y$, and $X \not\perp\!\!\!\perp Y$, then $Z \longrightarrow Y$.

$\mathcal{R}2a$ If $Z \longrightarrow X *\!\!\rightarrow Y$ and $Z *\!\!-\!\!\circ Y$, then $Z *\!\!\rightarrow Y$.

$\mathcal{R}2b$ If $Z *\!\!\rightarrow X \longrightarrow Y$ and $Z *\!\!-\!\!\circ Y$, then $Z *\!\!\rightarrow Y$.

$\mathcal{R}3$ If $X *\!\!\rightarrow Z \leftarrow\!\!* Y$, $X *\!\!-\!\!\circ W \circ\!\!-\!\!* Y$, $X \not\perp\!\!\!\perp Y$, and $W *\!\!-\!\!\circ Z$, then $W *\!\!\rightarrow Z$.

$\mathcal{R}4a$ If $u = \langle X, .., Z_k, Z, Y \rangle$ is a discriminating path between $X$ and $Y$ for $Z$, and $Z \circ\!\!-\!\!* Y$, then if $Z \in Sep(X,Y)$, then $Z \longrightarrow Y$.

$\mathcal{R}4b$ Idem, if $Z \notin Sep(X,Y)$ then $Z_k \longleftrightarrow Z \longleftrightarrow Y$.

$\mathcal{R}5$ If $u = \langle Z, X, .., W, Y, Z, X \rangle$ is an uncov. circle path, then $Z \,\text{—}\, Y$ (idem for all edges on $u$).

$\mathcal{R}6$ If $X \,\text{—}\, Z \circ\!\!-\!\!* Y$, then orient as $Z \,\text{—}\!\!* Y$.

$\mathcal{R}7$ If $X \,\text{—}\!\!\circ Z \circ\!\!-\!\!* Y$, and $X \not\perp\!\!\!\perp Y$, then $Z \,\text{—}\!\!* Y$.

$\mathcal{R}8a$ If $Z \longrightarrow X \longrightarrow Y$ and $Z \circ\!\!\rightarrow Y$, then $Z \longrightarrow Y$.

$\mathcal{R}8b$ If $Z \,\text{—}\!\!\circ X \longrightarrow Y$ and $Z \circ\!\!\rightarrow Y$, then $Z \longrightarrow Y$.

$\mathcal{R}9$ If $Z \circ\!\!\rightarrow Y$, $u = \langle Z, X, W, .., Y \rangle$ is an uncov. p.d. path, and $X \not\perp\!\!\!\perp Y$, then $Z \longrightarrow Y$.

$\mathcal{R}10$ If $Z \circ\!\!\rightarrow Y$, $X \longrightarrow Y \longleftarrow W$, $u_1 = \langle Z, S, .., X \rangle$ and $u_2 = \langle Z, V, .., W \rangle$ are uncov. p.d. paths, (possibly with $S = X$ and/or $V = W$), then if $S \not\perp\!\!\!\perp V$, then $Z \longrightarrow Y$.

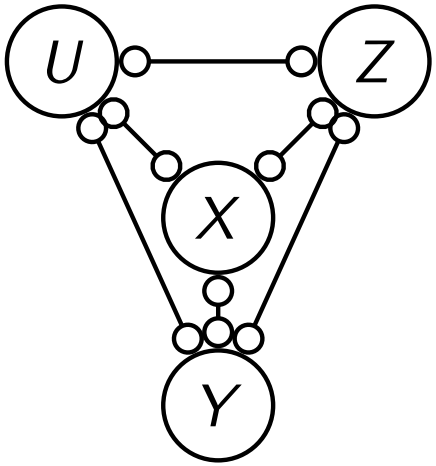
**Input** : independence oracle for $\mathbf{V}$
**Output** : complete PAG $\mathcal{P}$ over $\mathbf{V}$
1: $\mathcal{P} \leftarrow$ fully $\circ\!\!-\!\!\circ$ connected graph over $\mathbf{V}$
2: **for all** $\{X, Y\} \in \mathbf{V}$ **do**
3: search *in some clever way* for a $X \perp\!\!\!\perp Y \,|\, \mathbf{Z}$
4: $\mathcal{P} \leftarrow \mathcal{R}0a$ (eliminate $X \not\perp\!\!\!\perp Y$)
5: record $Sep(X,Y) \leftarrow \mathbf{Z}$
6: **end for**
7: $\mathcal{P} \leftarrow \mathcal{R}0b$ (unshielded colliders)
8: **repeat** $\mathcal{P} \leftarrow \mathcal{R}1 - \mathcal{R}4b$ **until** finished
9: $\mathcal{P} \leftarrow \mathcal{R}5$ (uncovered circle paths)
10: **repeat** $\mathcal{P} \leftarrow \mathcal{R}6 - \mathcal{R}7$ **until** finished
11: **repeat** $\mathcal{P} \leftarrow \mathcal{R}8a - \mathcal{R}10$ **until** finished

**Algorithm 1:** Augmented FCI algorithm

Source: [Claassen & Heskes, 2011]

# FCI: Example ("Extended Y-structure")

Independences: $Z \perp\!\!\!\perp U$, $Z \perp\!\!\!\perp Y \mid X$



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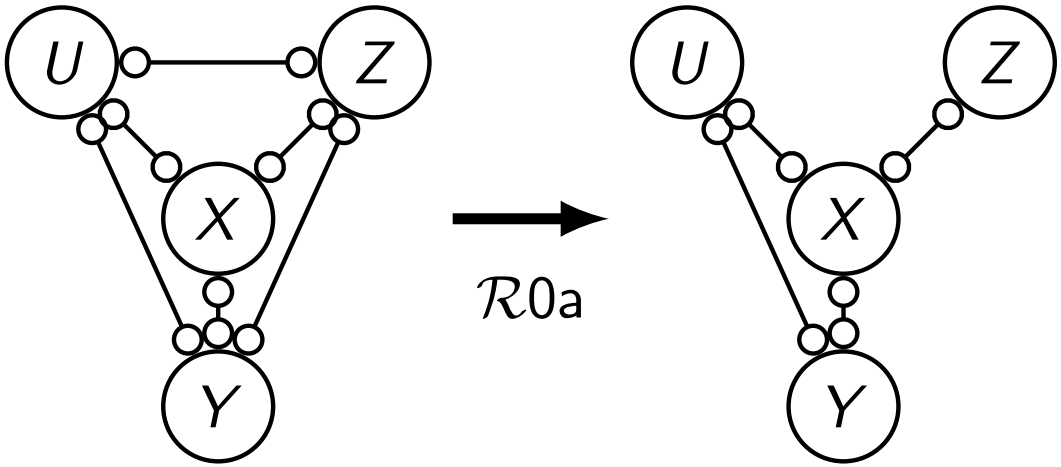

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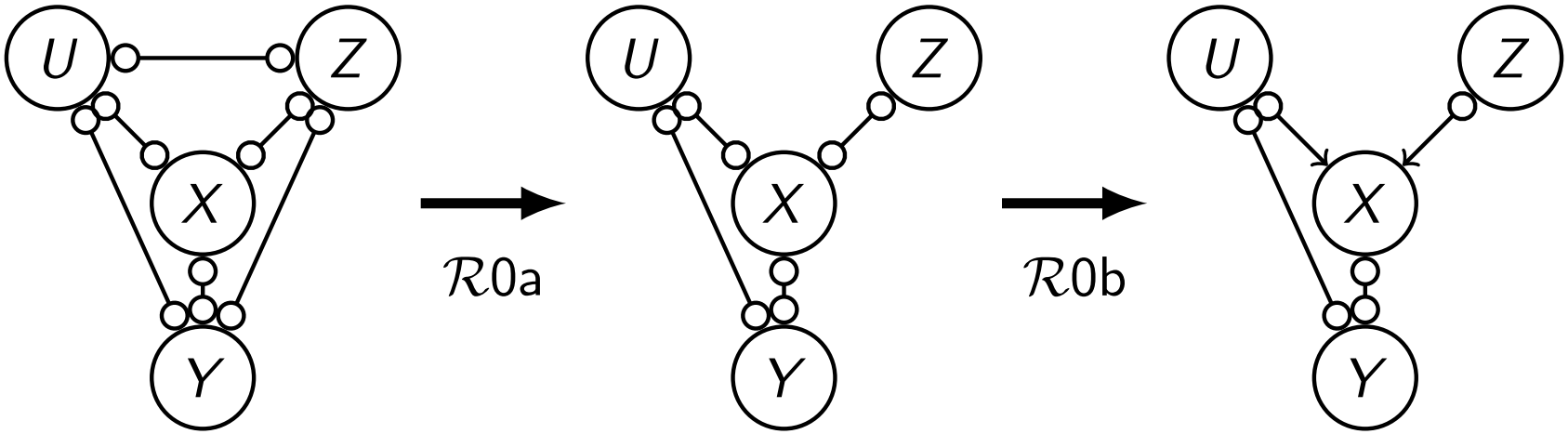

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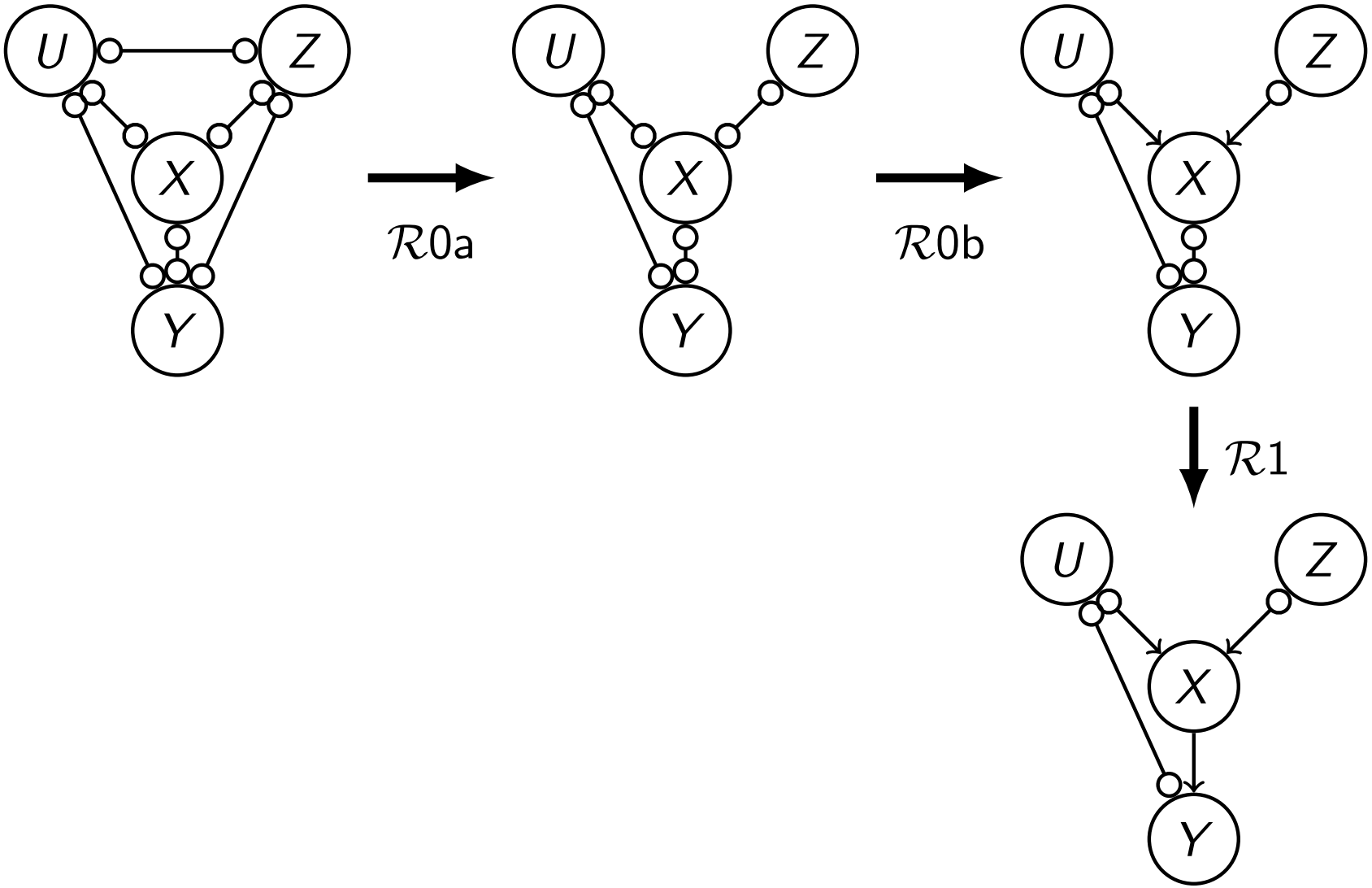

# FCI: Example ("Extended Y-structure")

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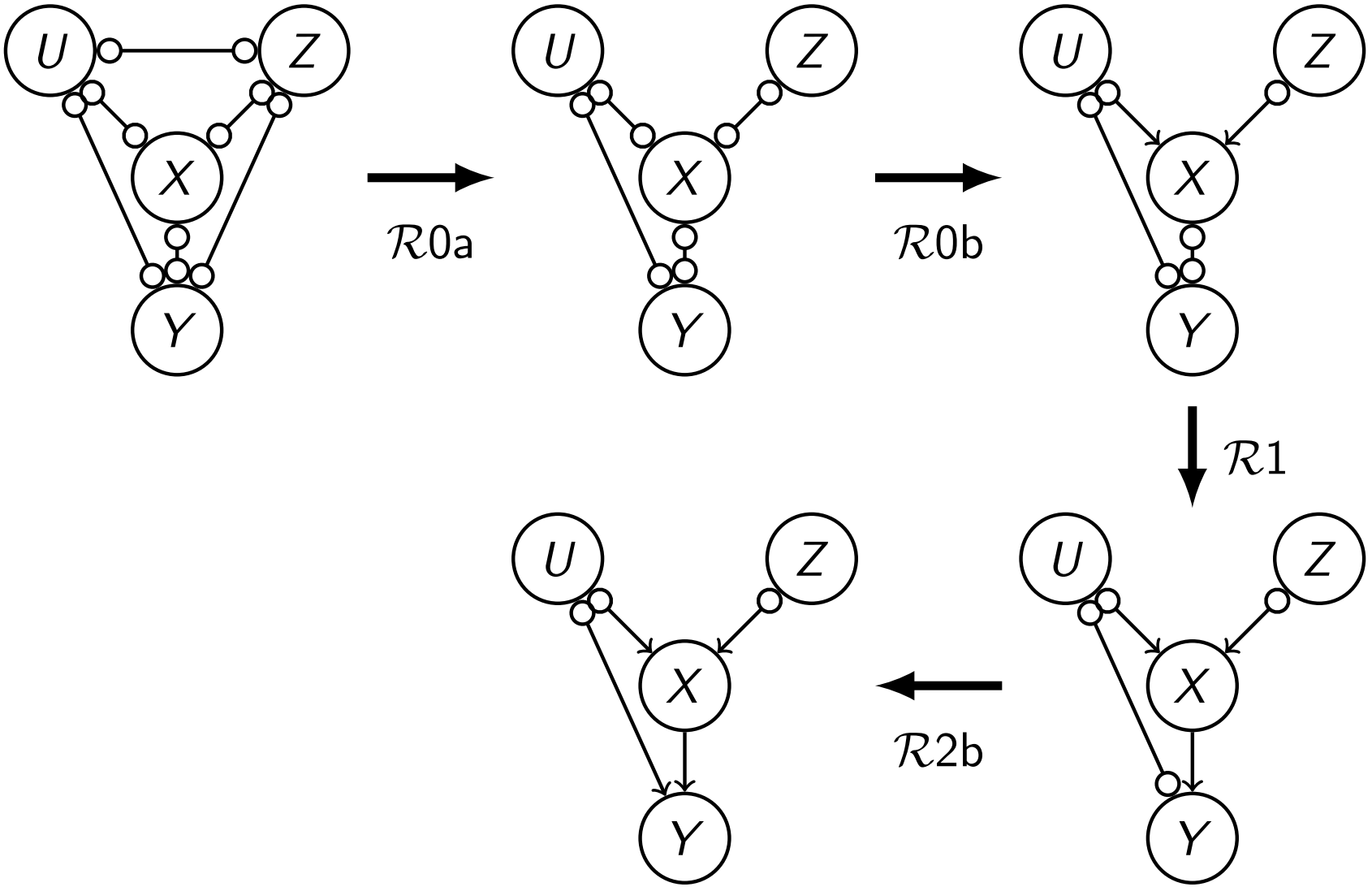

# FCI: Example ("Extended Y-structure")

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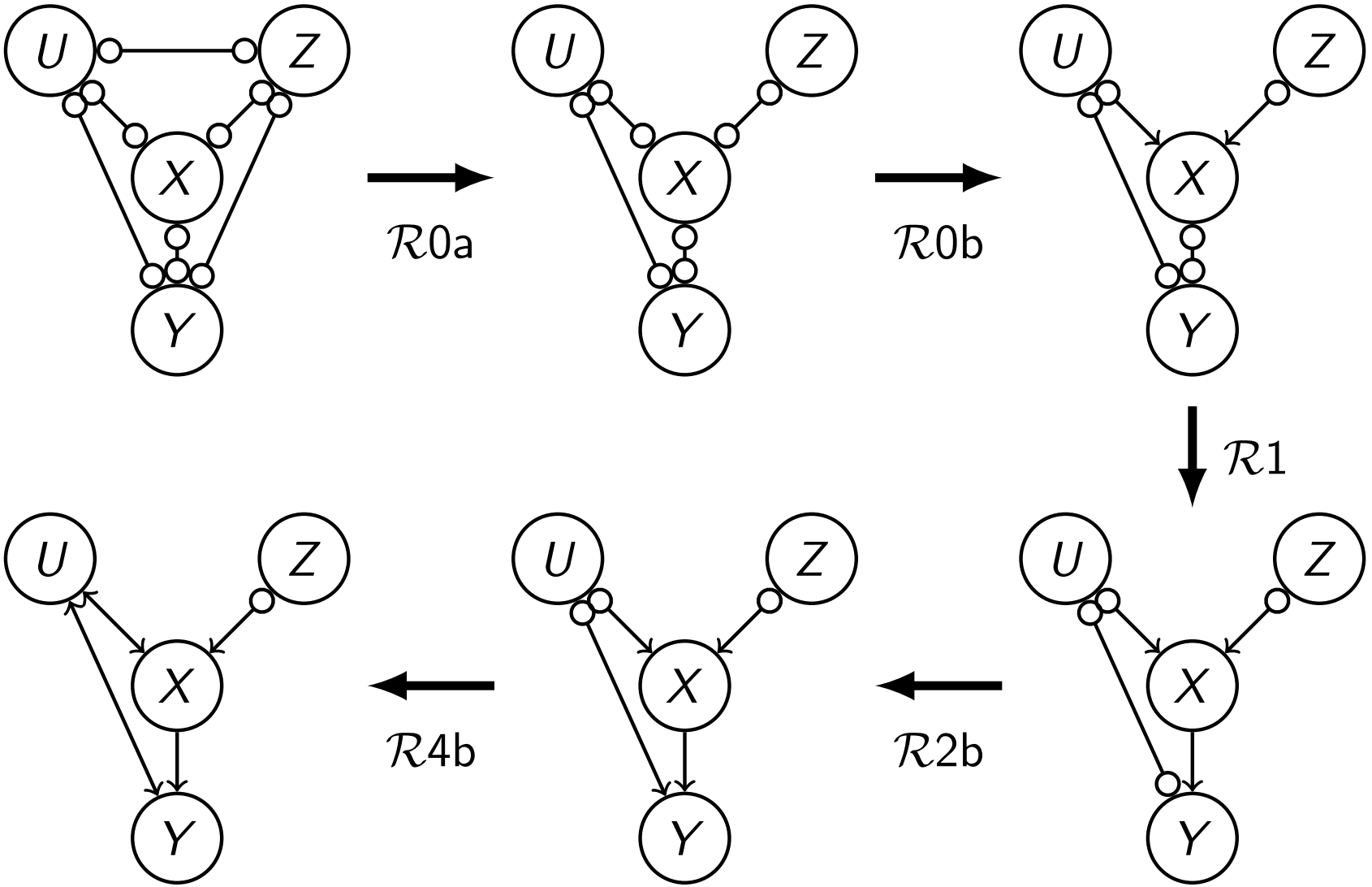


# Local Causal Discovery (LCD)

Local Causal Discovery: simple causal discovery algorithm (Cooper, 1997).

## Definition

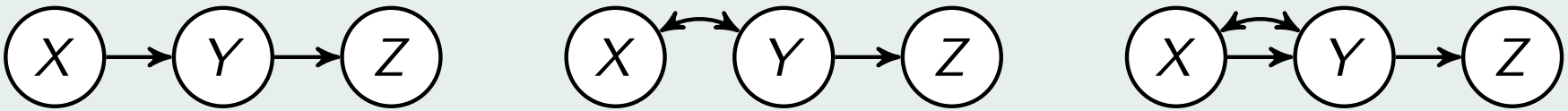
If for three variables $X, Y, Z$:

$$Y \notin \mathrm{an}(X) \;\wedge\; Z \notin \mathrm{an}(X) \;\wedge\; X \not\perp\!\!\!\perp Y \;\wedge\; Y \not\perp\!\!\!\perp Z \;\wedge\; X \perp\!\!\!\perp Z \,|\, Y,$$

then $(X, Y, Z)$ is an LCD triplet.

## Theorem

*If an acyclic, faithful SCM generated the data without selection bias or measurement error, the only causal graphs that yield an LCD triplet are:*




*Therefore,* $Y \in \mathrm{an}(Z)$ *and* $p(Z \mid \mathrm{do}(Y = y)) = p(Z \mid Y = y)$.

# Exercise

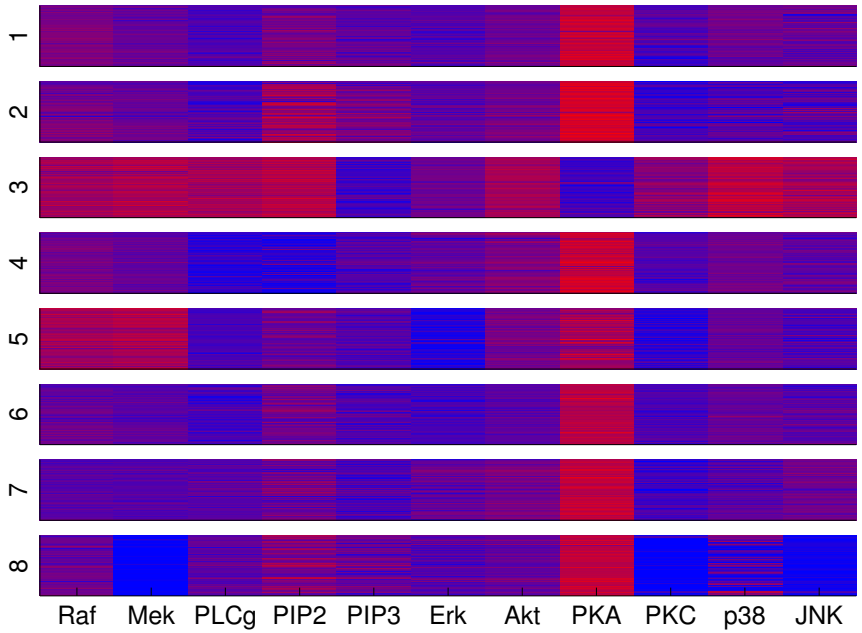
Please make Exercise 2.5

# Contents

# Causal Discovery: Example Application

## Protein Abundance Data:

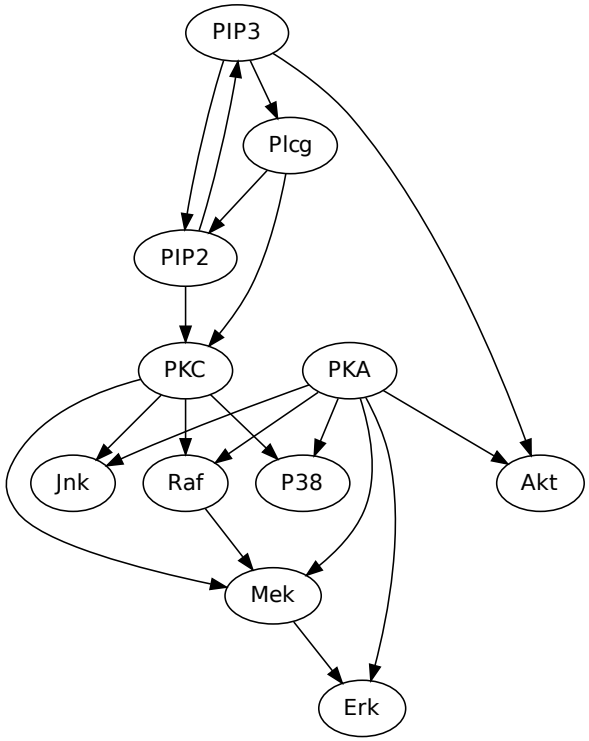
(Sachs *et al*, 2005)




| Condition | Reagent | Intervention |
|---|---|---|
| 1 | - | observational |
| 2 | Akt-inhibitor | inhibits AKT activity |
| 3 | G0076 | inhibits PKC activity |
| 4 | Psitectorigenin | inhibits PIP2 abundance |
| 5 | U0126 | inhibits MEK activity |
| 6 | LY294002 | inhibits PIP2/PIP3 activity |
| 7 | PMA | activates PKC + global |
| 8 | $\beta$2CAMP | activates PKA + global |

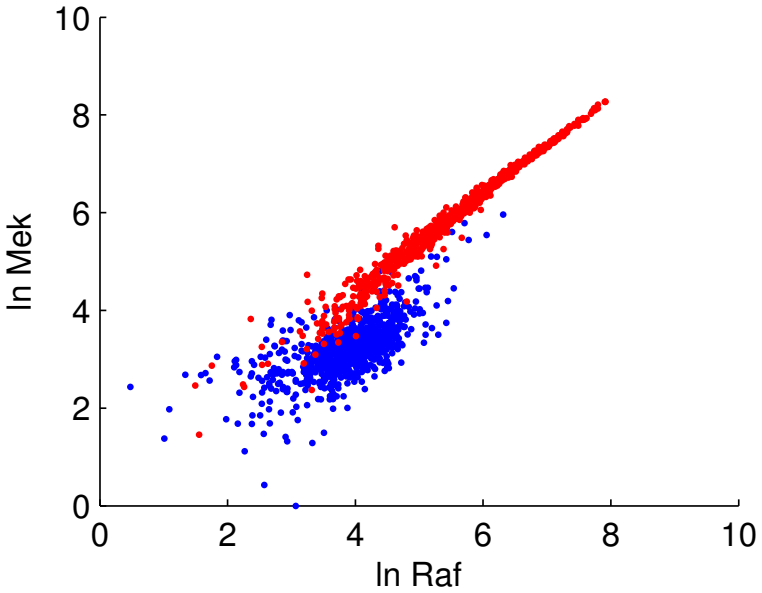
## Causal Graph:

("Signalling network")




(depicted here: "consensus" network)

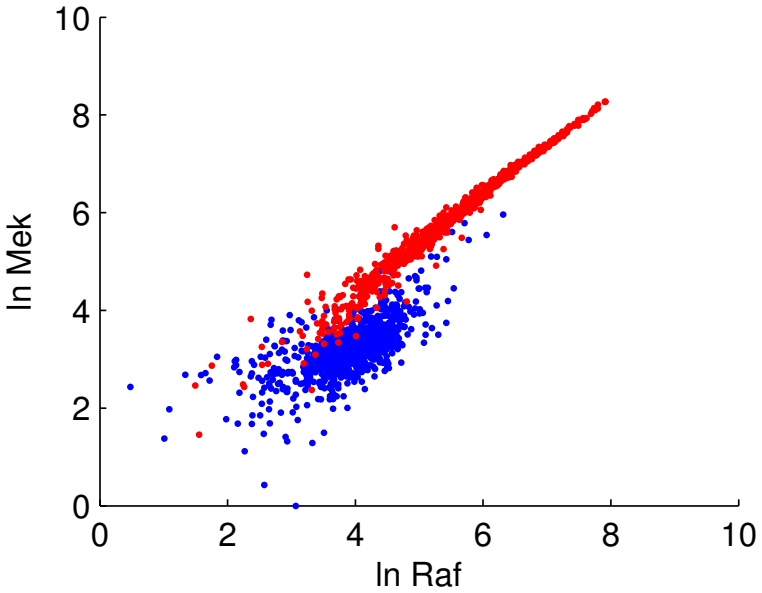
# Causal Discovery by Experimentation: Example




- Each dot is a measurement in a single human immune system cell
- Raf: abundance of phosphorylized Raf
- Mek: abundance of phosphorylized Mek
- blue = baseline,
  red = reagent U0126 added

**Question: What is the causal relation between Raf and Mek?**

# Causal Discovery by Experimentation: Example

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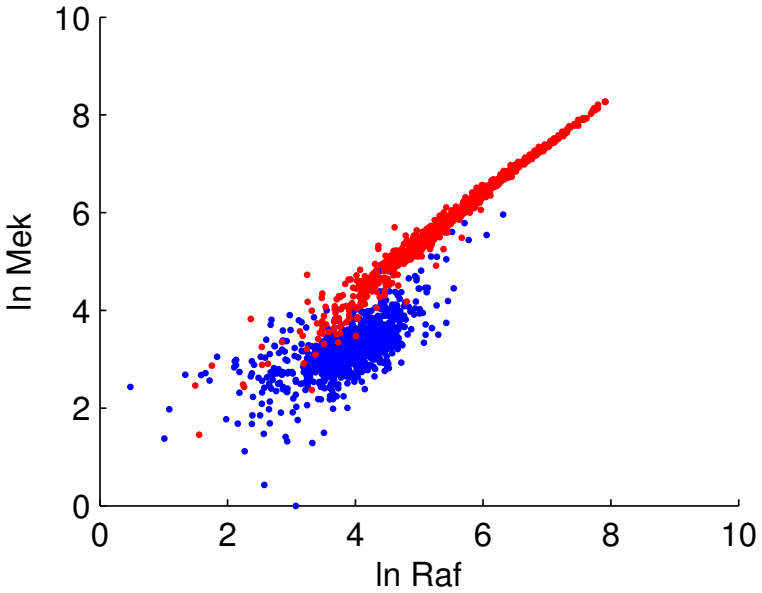
*Hint: U0126 inhibits Mek.*

# Causal Discovery by Experimentation: Example

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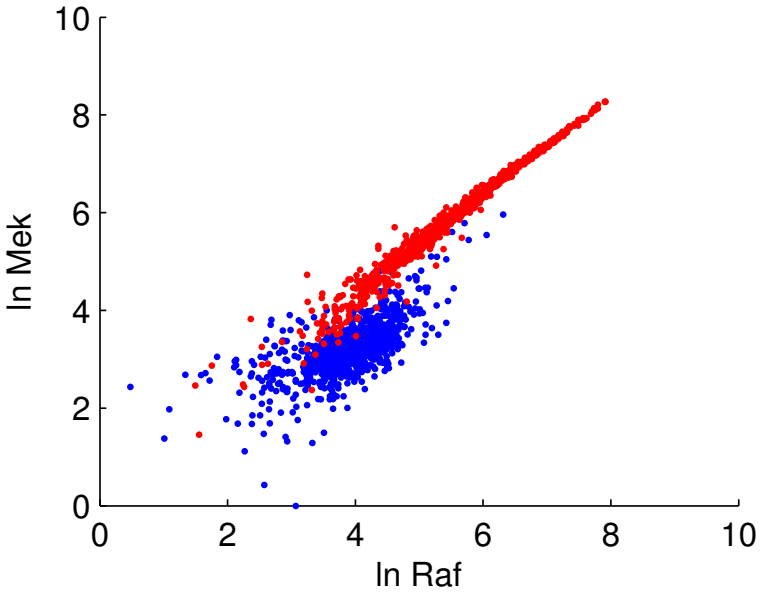
**Question: What is the causal relation between Raf and Mek?**
*Hint: U0126 inhibits Mek.*

**Answer: Mek causes Raf**
*(Changing activity of Mek changes abundance of Raf.)*

# Causal Discovery by Experimentation: Example

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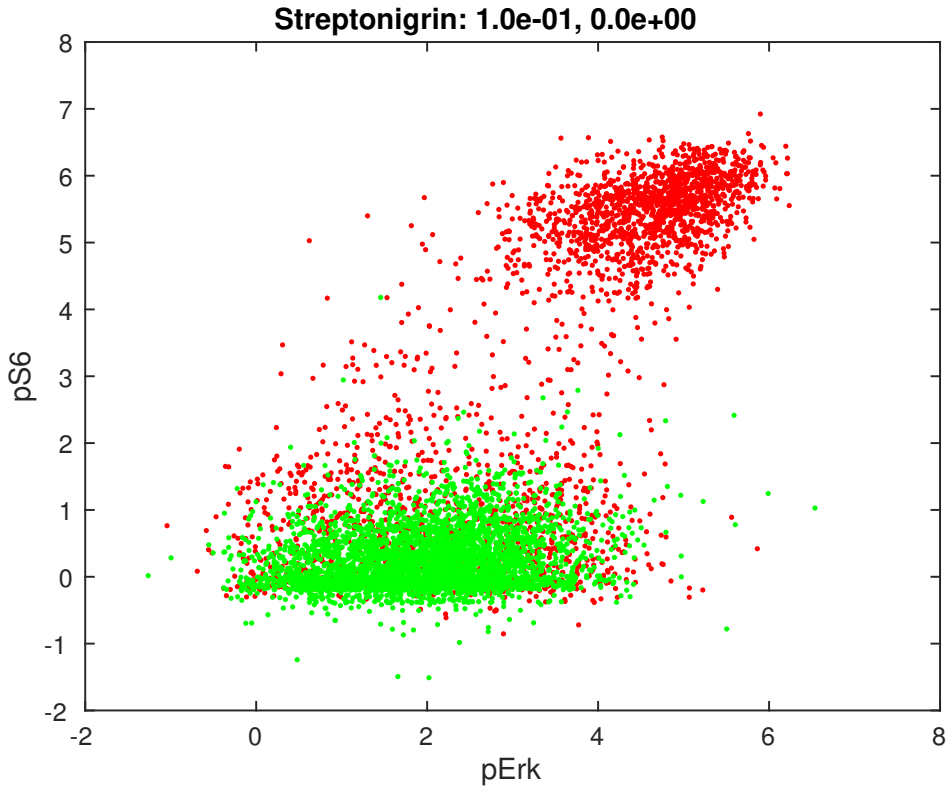
**Question: What is the causal relation between Raf and Mek?**
*Hint: U0126 inhibits Mek.*

**Answer: Mek causes Raf**
*(Changing activity of Mek changes abundance of Raf.)*

**Note:** How did we know that "U0126 inhibits Mek" in the first place?

# LCD: Example

- *pErk*: abundance of phosphorylized Erk in each cell
- *pS6*: abundance of phosphorylized S6 in cell
- $I$: green = baseline, red = PMA-IONO activator added




$(X, Y, Z)$ is LCD triplet iff:

$$Y \notin \mathrm{an}(X)$$
$$Z \notin \mathrm{an}(X)$$
$$X \not\perp\!\!\!\perp Y$$
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*What is the causal relation?*

# LCD: Example

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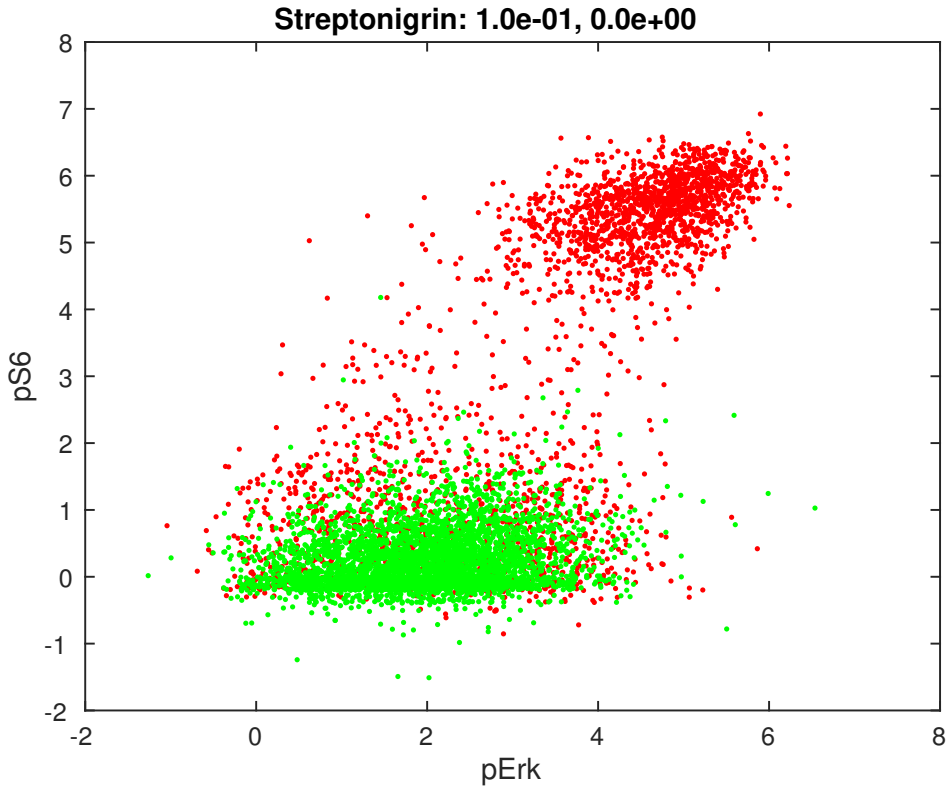


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$$X \perp\!\!\!\perp Z \mid Y$$

*What is the causal relation?* LCD triplet $(I, pS6, pErk)$, so $pS6 \to pErk$.

**Note**: no prior knowledge on the effects of PMA-IONO needed!

# Causal Discovery from Multiple Contexts

| | Latent confounders | Nonlinear mechanisms | Cycles | Perfect interventions | Mechanism changes | Activity interventions | Side effects | Other context changes | Unknown intervention/context targets | Learns intervention/context targets | Multiple system variables | Different variables per context | Combination strategy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (Fisher, 1935) | + | + | + | + | + | + | + | + | + | + | - | - | b |
| (Cooper and Yoo, 1999) | - | + | - | + | - | - | - | - | - | - | + | - | b |
| (Tian and Pearl, 2001) | - | + | - | - | + | - | - | + | - | - | + | - | b |
| (Sachs et al., 2005) | - | + | - | + | - | - | - | - | - | - | + | - | b |
| (Eaton and Murphy, 2007) | - | + | - | + | + | + | + | + | + | + | + | - | b |
| (Chen et al., 2007) | + | + | + | + | + | + | + | + | + | + | + | - | b |
| (Claassen and Heskes, 2010) | + | + | - | - | + | + | + | + | + | - | + | + | a |
| (Tillman and Spirtes, 2011) | + | + | - | - | + | + | + | + | + | - | + | + | a |
| (Hauser and Bühlmann, 2012) | - | + | - | + | - | - | - | - | - | - | + | - | b |
| (Hyttinen et al., 2012) | + | - | + | + | - | - | - | - | - | - | + | - | a |
| (Mooij and Heskes, 2013) | - | ± | ± | + | + | + | - | + | - | - | + | - | b |
| (Hyttinen et al., 2014) | + | + | ± | + | - | - | - | - | - | - | + | + | a |
| (Triantafillou and Tsamardinos, 2015) | + | + | - | + | - | - | - | - | - | - | + | + | a |
| (Rothenhäusler et al., 2015) | + | - | ± | - | - | - | - | + | + | + | + | - | a |
| (Peters et al., 2016) | ± | ± | ± | + | + | + | + | + | + | - | + | - | b |
| (Oates et al., 2016a) | - | - | - | - | - | - | - | + | - | - | + | - | b |
| (Zhang et al., 2017) | - | + | - | + | + | + | + | + | + | + | + | - | b |
| JCI | + | + | + | + | + | + | + | + | + | + | + | ± | b |
| JCI-LCD (Cooper, 1997) | + | + | + | + | + | + | + | + | + | + | + | - | b |
| JCI-HEJ | + | + | ± | + | + | + | + | + | + | + | + | - | b |
| JCI-FCI | + | + | - | + | + | + | + | + | + | + | + | - | b |

# JCI: Combining the best of two worlds

## Question

Can we combine the ideas of the "classical" approach to causal discovery based on experimentation with the "modern" approach based on conditional independences in observational data in observational dataa?

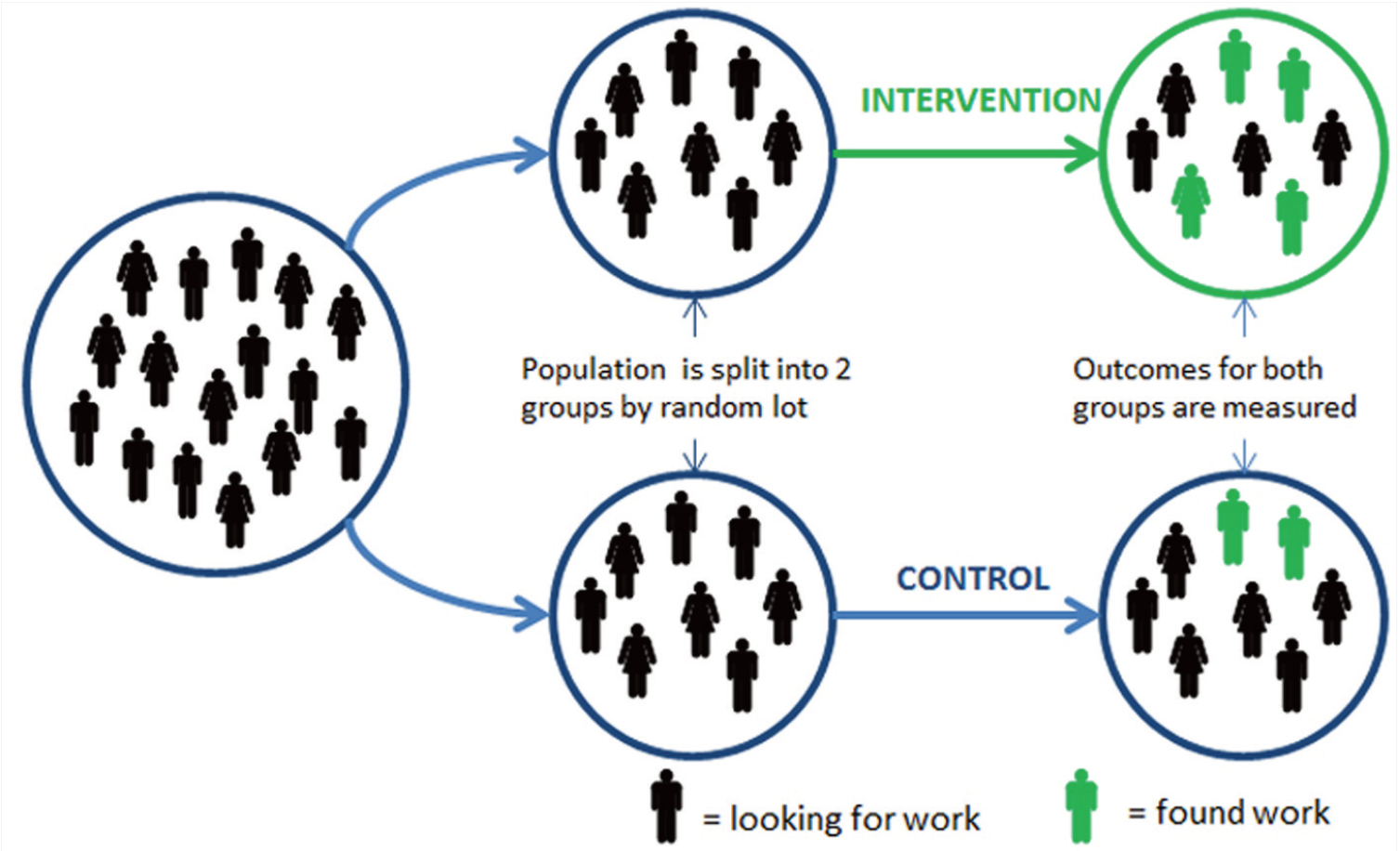
We hope to:

- obtain reliability of "classical" approach
- exploit conditional independences in the data to reduce the number of experiments necessary

## Answer

We propose Joint Causal Inference [Mooij et al., 2019], a framework for causal discovery, that achieves this.

# Randomized Controlled Trials, or A/B-testing




| $C_1$ | $X_1$ |
|---|---|
| 0 | 1 |
| 0 | 0 |
| 0 | 1 |
| 0 | 0 |
| 0 | 0 |
| 0 | 0 |
| 0 | 0 |
| 0 | 0 |
| 1 | 0 |
| 1 | 0 |
| 1 | 1 |
| 1 | 1 |
| 1 | 0 |
| 1 | 1 |
| 1 | 0 |
| 1 | 1 |

Two variables: context variable $C_1$, system variable $X_1$

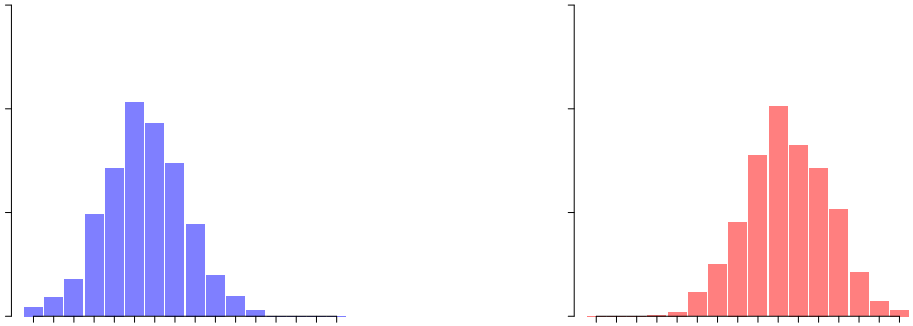
$C_1$: 0=control, 1=intervention
$X_1$: 0=looking for work, 1=found work

# Two equivalent points of view

(a) Separate data sets

| Placebo ($C = 0$): |
|---|
| $X$ |
| -0.2 |
| 0.6 |
| -1.7 |
| ... |

| Drug ($C = 1$): |
|---|
| $X$ |
| -0.3 |
| 1.8 |
| -0.1 |
| ... |

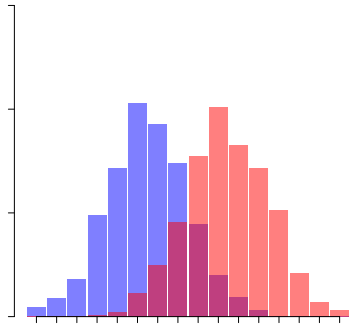


Two-sample test:

Is $p\big(x \mid \mathrm{do}(C = 0)\big) = p\big(x \mid \mathrm{do}(C = 1)\big)$?

(b) Pooled data

| $C$ | $X$ |
|---|---|
| 0 | -0.2 |
| 0 | 0.6 |
| 0 | -1.7 |
| 0 | ... |
| 1 | -0.3 |
| 1 | 1.8 |
| 1 | -0.1 |
| 1 | ... |



Independence test:

Is $X \perp\!\!\!\perp C$?

# Causal Inference for Randomized Controlled Trial

## Proposition

Suppose $C$ (treatment) and $X$ (outcome) can be modeled with a Structural Causal Model. The Randomized Controlled Trial assumptions

- $X$ does not cause $C$ (*because $X$ happens after $C$*)
- $X$ and $C$ are unconfounded (*because of the randomization*)
- no selection bias (*measure and analyze all samples*)

imply that if $C \not\perp\!\!\!\perp X$, then $C$ causes $X$ (*correlation implies causation*).

# Causal Inference for Randomized Controlled Trial

## Proposition

Suppose $C$ (treatment) and $X$ (outcome) can be modeled with a Structural Causal Model. The Randomized Controlled Trial assumptions

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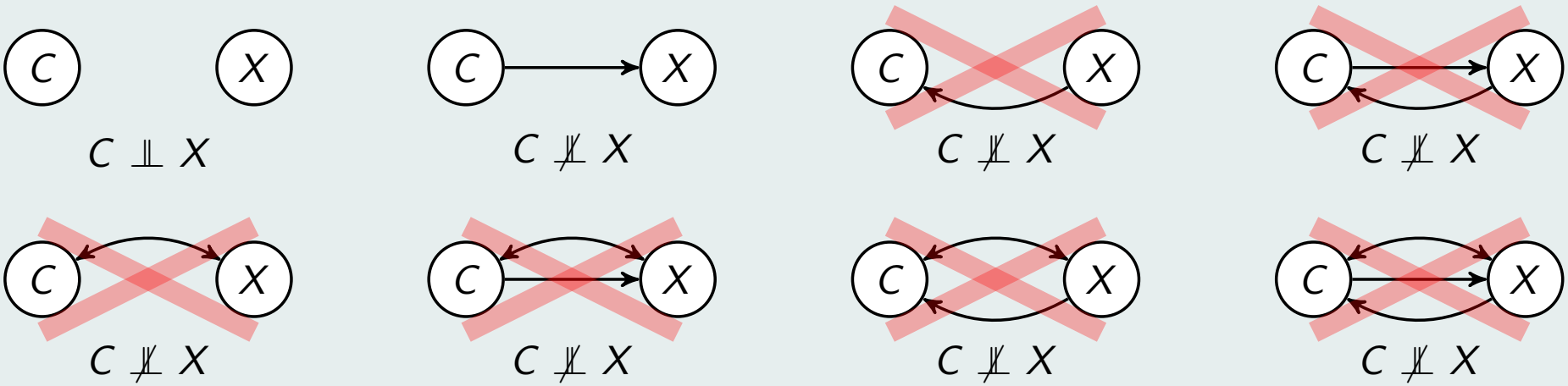
## Proof



# JCI: Two types of variables

## Definition

JCI generalizes the idea of RCTs to multiple context and system variables.
Distinguish:

- **Context variables** $\{C_i\}_{i \in \mathcal{I}}$ that model the context of the system,
- **System** variables $\{X_j\}_{j \in \mathcal{J}}$ that model the system of interest.

## Example

Data for 3 observed system variables in 4 experimental conditions:

**System variables:**
$X_1$: salary
$X_2$: drug abuse
$X_3$: depression

**Context variables:**
$C_1$: back-to-work program
$C_2$: psychotherapy

*no interventions*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.1 | 0.2 | 0.5 |
| 0.13 | 0.21 | 0.49 |
| 0.23 | 0.21 | 0.51 |

*only psychotherapy*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.5 | 0.19 | 0.52 |
| 0.6 | 0.18 | 0.51 |

*only back-to-work program*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.2 | 0.22 | 0.92 |
| 0.23 | 0.21 | 0.99 |

*both interventions*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.53 | 1.2 | 0.95 |
| 0.61 | 1.21 | 0.90 |
| 0.55 | 1.19 | 0.97 |

# JCI: Pooling the data

After explicitly adding the context variables, we pool the data:

## Example

*no interventions*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.1 | 0.2 | 0.5 |
| 0.13 | 0.21 | 0.49 |
| 0.23 | 0.21 | 0.51 |

*only psychotherapy*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.5 | 0.19 | 0.52 |
| 0.6 | 0.18 | 0.51 |

*only back-to-work program*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.2 | 0.22 | 0.92 |
| 0.23 | 0.21 | 0.99 |

*both interventions*:

| $X_1$ | $X_2$ | $X_3$ |
|---|---|---|
| 0.53 | 1.2 | 0.95 |
| 0.61 | 1.21 | 0.90 |
| 0.55 | 1.19 | 0.97 |

| $C_1$ | $C_2$ | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|
| 0 | 0 | 0.1 | 0.2 | 0.5 |
| 0 | 0 | 0.13 | 0.21 | 0.49 |
| 0 | 0 | 0.23 | 0.21 | 0.51 |
| 0 | 1 | 0.5 | 0.19 | 0.52 |
| 0 | 1 | 0.6 | 0.18 | 0.51 |
| 1 | 0 | 0.2 | 0.22 | 0.92 |
| 1 | 0 | 0.23 | 0.21 | 0.99 |
| 1 | 1 | 0.53 | 1.2 | 0.95 |
| 1 | 1 | 0.61 | 1.21 | 0.90 |
| 1 | 1 | 0.55 | 1.19 | 0.97 |

**System variables:**
$X_1$: salary
$X_2$: drug abuse
$X_3$: depression

**Context variables:**
$C_1$: back-to-work program
$C_2$: psychotherapy

# JCI: Assumptions

## JCI Assumptions (Intuitive formulation)

We are modelling a generic setting in which the experimenter decides on the performed interventions *before* the measurements are performed, and this decision does not depend on anything else that might affect the system of interest.

## Formal JCI Assumptions

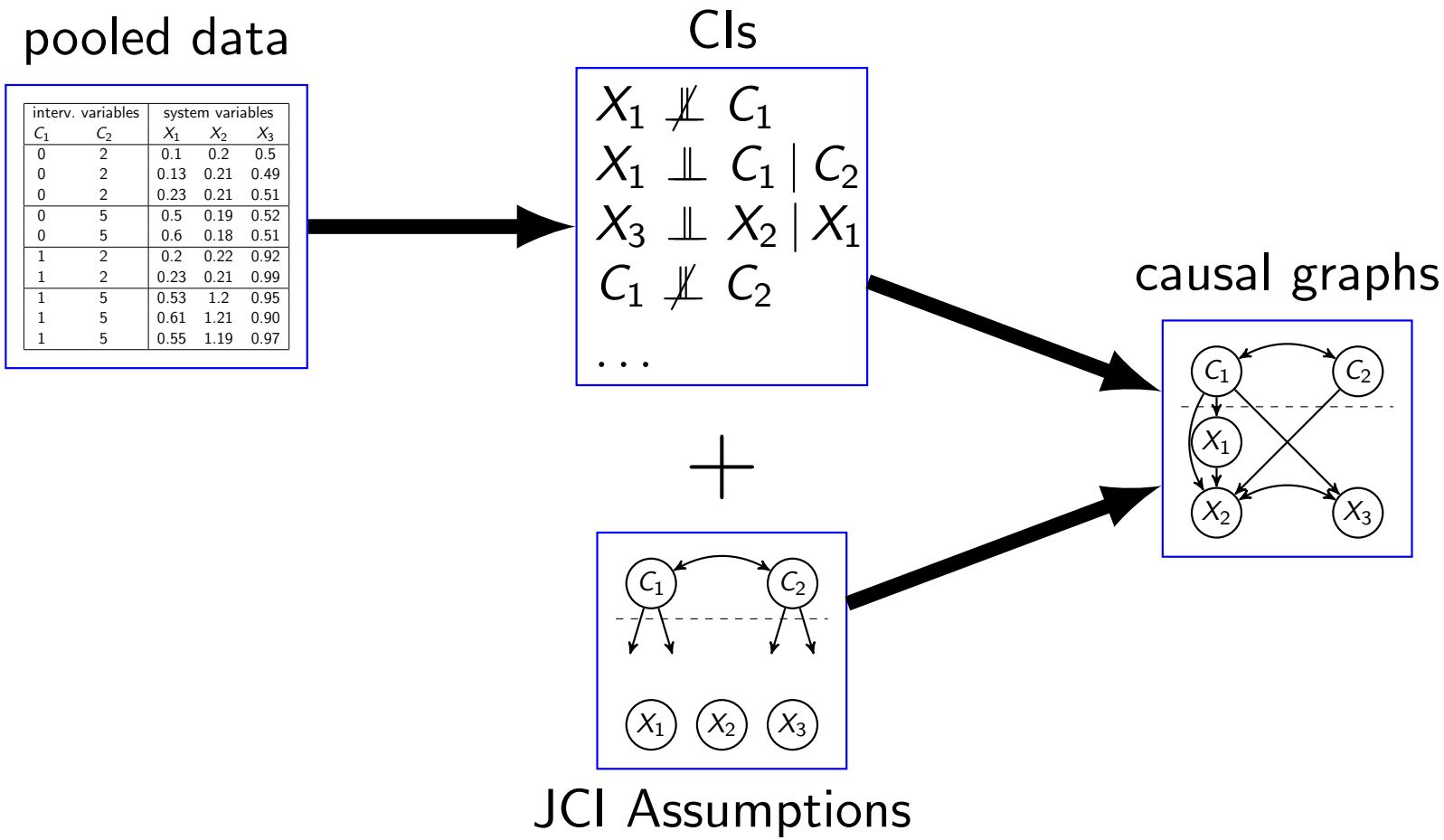
The causal graph $\mathcal{G}$ that includes both system variables $\{X_1, \ldots, X_p\}$ and context variables $\{C_1, \ldots, C_d\}$, which jointly models the experimental design and the system in *all* experimental conditions, satisfies:

- no variable directly causes any context variable $C_i$, and
- none of the pairs $\{X_k, C_i\}$ of system and context variables is confounded, and
- each pair of context variables $\{C_i, C_j\}$ is confounded.

Furthermore, we assume the absence of selection bias.

# Joint Causal Inference

**Question**: How can we now reconstruct the causal graph from the data?




| interv. variables | | system variables | | |
|---|---|---|---|---|
| $C_1$ | $C_2$ | $X_1$ | $X_2$ | $X_3$ |
| 0 | 2 | 0.1 | 0.2 | 0.5 |
| 0 | 2 | 0.13 | 0.21 | 0.49 |
| 0 | 2 | 0.23 | 0.21 | 0.51 |
| 0 | 5 | 0.5 | 0.19 | 0.52 |
| 0 | 5 | 0.6 | 0.18 | 0.51 |
| 1 | 2 | 0.2 | 0.22 | 0.92 |
| 1 | 2 | 0.23 | 0.21 | 0.99 |
| 1 | 5 | 0.53 | 1.2 | 0.95 |
| 1 | 5 | 0.61 | 1.21 | 0.90 |
| 1 | 5 | 0.55 | 1.19 | 0.97 |

$X_1 \not\perp\!\!\!\perp C_1$

$X_1 \perp\!\!\!\perp C_1 \mid C_2$

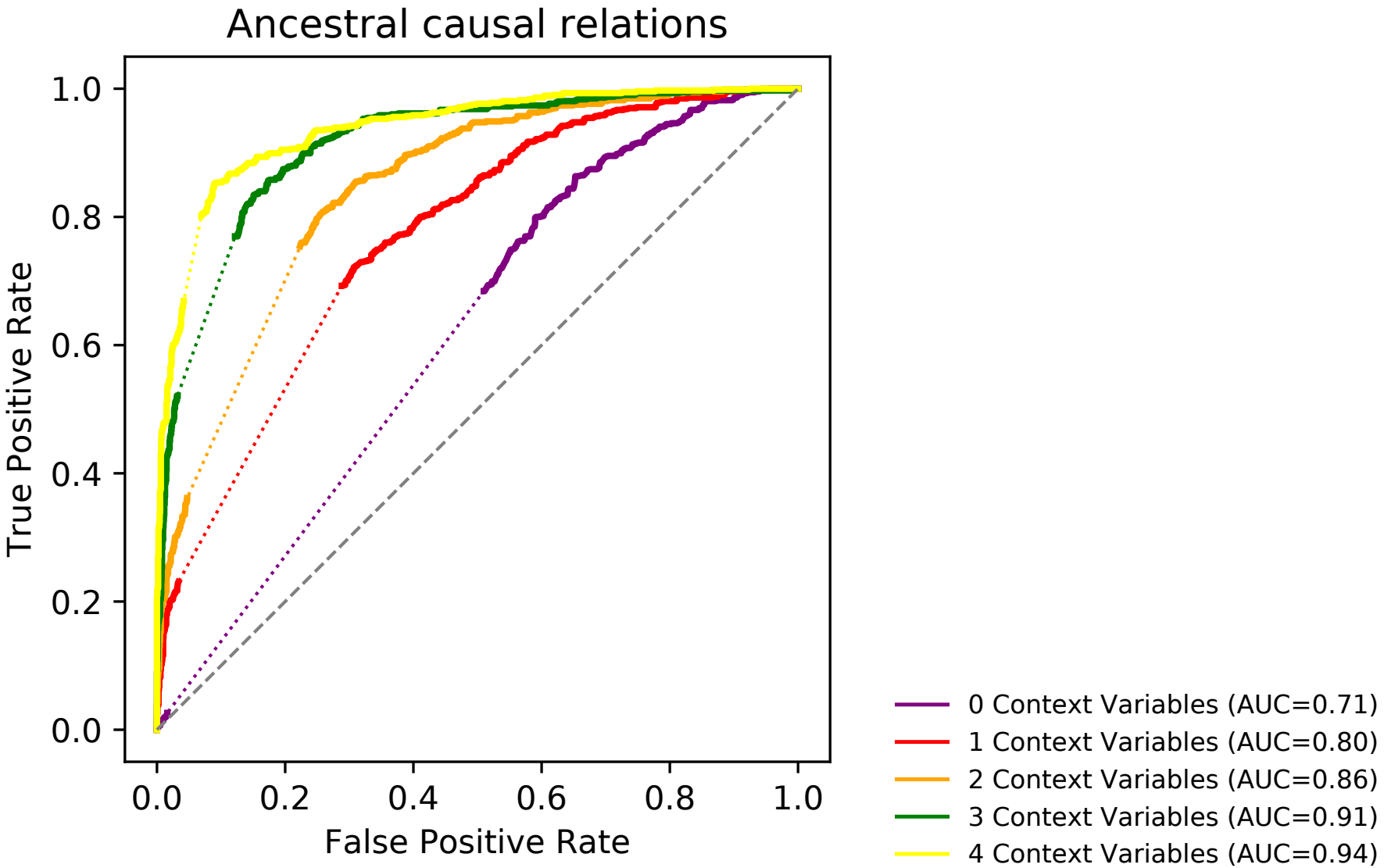
$X_3 \perp\!\!\!\perp X_2 \mid X_1$

$C_1 \not\perp\!\!\!\perp C_2$

$\ldots$

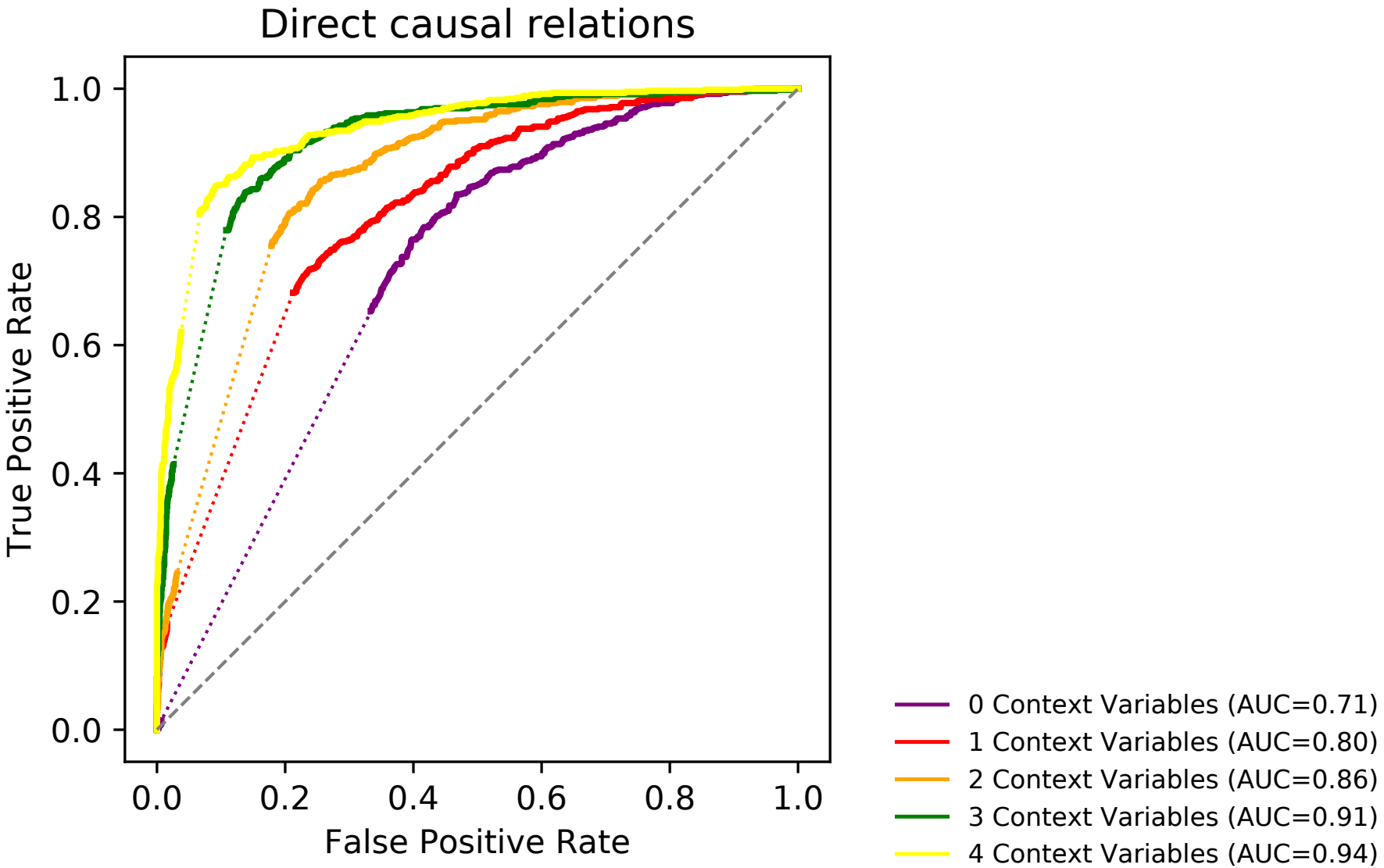
**Answer**: Simply apply a standard constraint-based causal discovery method (designed for purely observational data) on the *pooled* data, and incorporate the JCI assumptions as background knowledge.

# Evaluation on simulated data I



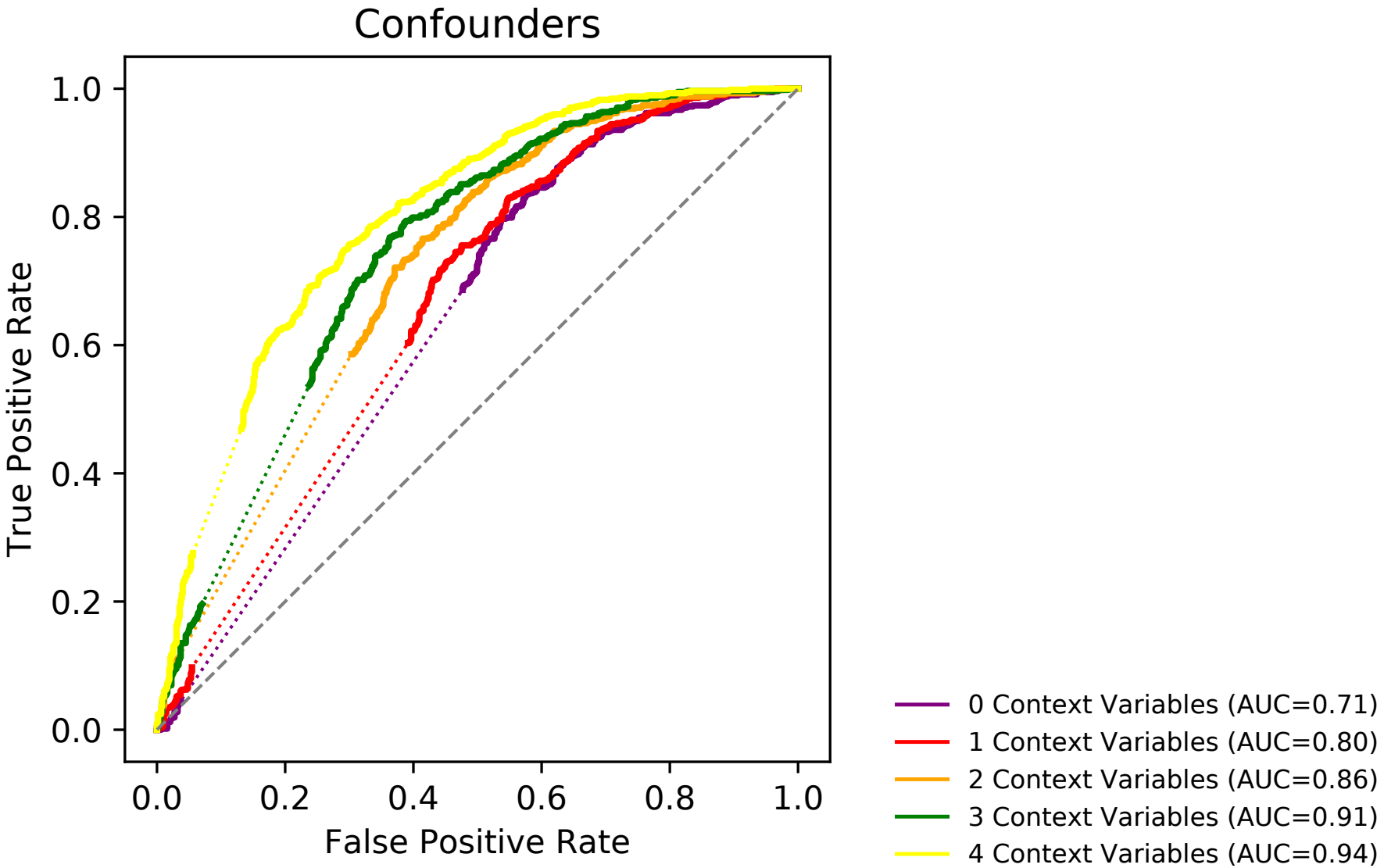

(4 system variables, 500 samples in each data set)

# Evaluation on simulated data II




(4 system variables, 500 samples in each data set)

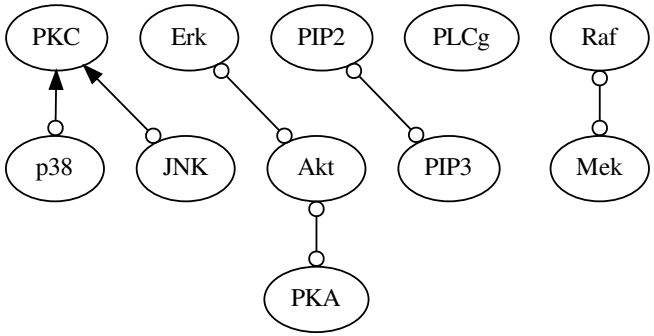
# Evaluation on simulated data III



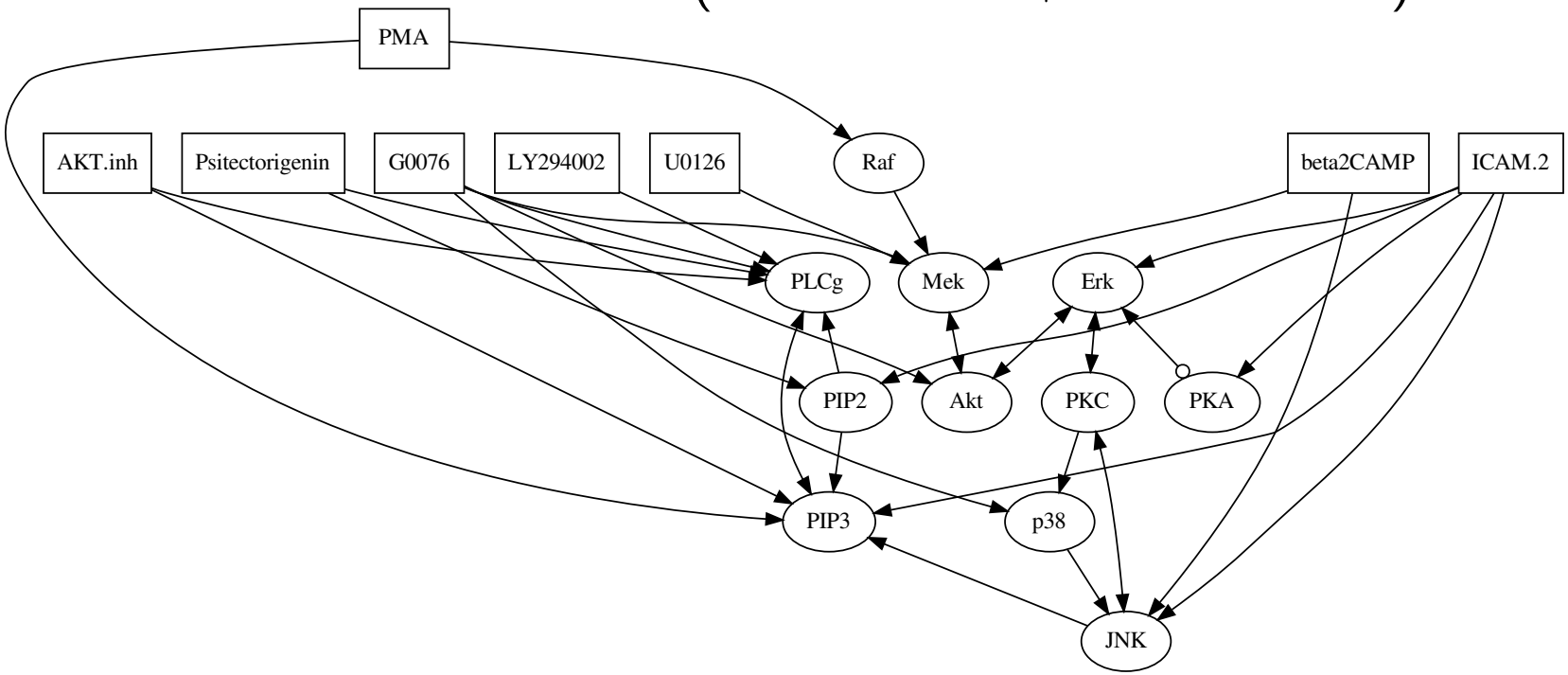

(4 system variables, 500 samples in each data set)

# Evaluation on real-world flow cytometry data

Only observational data:




All (observational+interventional) data:



# Contents

# The generalized directed global Markov property

Given the importance of the Markov property, the first thing we need is a Markov property for cyclic SCMs. We introduced a notion $\sigma$-separation that generalizes d-separation [Forré and Mooij, 2017]:

- $\sigma$-separation implies d-separation.
- For acyclic graph, $\sigma$-separation is equivalent to d-separation.

Inspired by ideas by [Spirtes, 1996], we showed:

**Theorem ([Forré and Mooij, 2017])**

*For a simple SCM $\mathcal{M}$, the generalized directed global Markov property holds for its observational distribution $\mathbb{P}_{\mathcal{M}}(\boldsymbol{X})$:*

$$A \overset{\sigma}{\underset{\mathcal{G}(\mathcal{M})}{\perp}} B \,|\, Z \implies \boldsymbol{X}_A \underset{\mathbb{P}_{\mathcal{M}}}{\perp\!\!\!\perp} \boldsymbol{X}_B \,|\, \boldsymbol{X}_Z \qquad A, B, Z \subseteq \mathcal{I}.$$

# Markov properties: $\sigma$-separation

## Definition ($\sigma$-separation, [Forré and Mooij, 2017])

In a DMG $\mathcal{G}$, a path

$$i_1 \; \begin{matrix} \leftarrow \\ \rightarrow \\ \leftrightarrow \end{matrix} \; \cdots \; \begin{matrix} \leftarrow \\ \rightarrow \\ \leftrightarrow \end{matrix} \; i_n$$

is called $\sigma$-blocked by a set of nodes $Z$ iff

- one or both end nodes $i_1, i_n$ are in $Z$, or
- it contains a collider $i_{k-1} \; \begin{matrix} \rightarrow \\ \leftrightarrow \end{matrix} \; i_k \; \begin{matrix} \leftarrow \\ \leftrightarrow \end{matrix} \; i_{k+1}$ with $i_k \notin \mathrm{an}_{\mathcal{G}}(Z)$, or
- it contains a non-collider with $i_k \in Z$:

$$i_{k-1} \; \begin{matrix} \rightarrow \\ \leftarrow \\ \leftrightarrow \end{matrix} \; i_k \rightarrow i_{k+1}, \quad i_{k-1} \leftarrow i_k \; \begin{matrix} \rightarrow \\ \leftarrow \\ \leftrightarrow \end{matrix} \; i_{k+1},$$

**where the child $i_{k+1}$ (resp. $i_{k-1}$) is not in $\mathrm{sc}_{\mathcal{G}}(i_k)$.**

We say that $A$ is $\sigma$-separated from $B$ by $Z$, denoted $A \perp^{\sigma}_{\mathcal{G}} B \mid Z$, if every path with one end node in $A$ and one end node in $B$ is $\sigma$-blocked by $Z$.

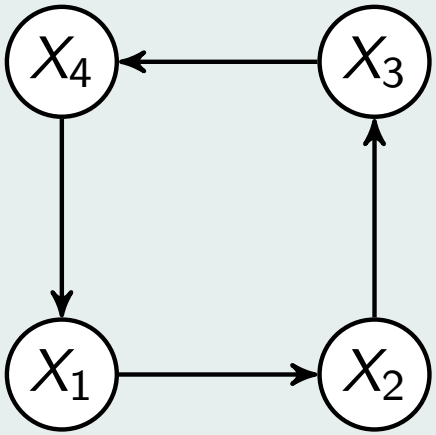
# Markov properties: Example

## Example

SCM $\mathcal{M}$:

$$
\begin{aligned}
X_1 &= f_1(X_4, E_1) = X_4 + E_1 \\
X_2 &= f_2(X_1, E_2) = X_1 \cdot E_2 \\
X_3 &= f_3(X_2, E_3) = X_2 + E_3 \\
X_4 &= f_4(X_3, E_4) = X_3 \cdot E_4
\end{aligned}
$$

Graph $\mathcal{G}(\mathcal{M})$:




$$X_1 \perp^d X_3 \,|\, X_2, X_4$$

but

$$X_1 \not\perp^\sigma X_3 \,|\, X_2, X_4$$

Indeed, as one can check explicitly, $X_1 \not\perp\!\!\!\perp_{p_{\mathcal{M}}} X_3 \,|\, X_2, X_4$.

In general: No $\sigma$-separations between nodes within the same strongly connected component.

# Directed global Markov property

Stronger statements can be derived for special cases:

**Theorem ([Forré and Mooij, 2017])**

*If a simple SCM $\mathcal{M}$ satisfies at least one of the following three conditions:*

1. *$\mathcal{M}$ is linear and its exogenous variables have a density with respect to Lebesgue measure, or*
2. *all endogenous variables are discrete-valued, or*
3. *$\mathcal{M}$ is acyclic;*

*then the directed global Markov property holds for any solution $\boldsymbol{X}$ of $\mathcal{M}$ with respect to the graph $\mathcal{G}(\mathcal{M})$:*

$$A \overset{d}{\underset{\mathcal{G}(\mathcal{M})}{\perp}} B \,|\, Z \implies \boldsymbol{X}_A \underset{\mathbb{P}_{\mathcal{M}}}{\perp\!\!\!\perp} \boldsymbol{X}_B \,|\, \boldsymbol{X}_Z \qquad A, B, Z \subseteq \mathcal{I}.$$

# Extensions: Acyclic SCMs to Simple SCMs by s/d/$\sigma$/

By simply replacing d-separation with $\sigma$-separation, it turns out that one can directly extend the applicability from acyclic SCMs to (possibly cyclic) simple SCMs of:

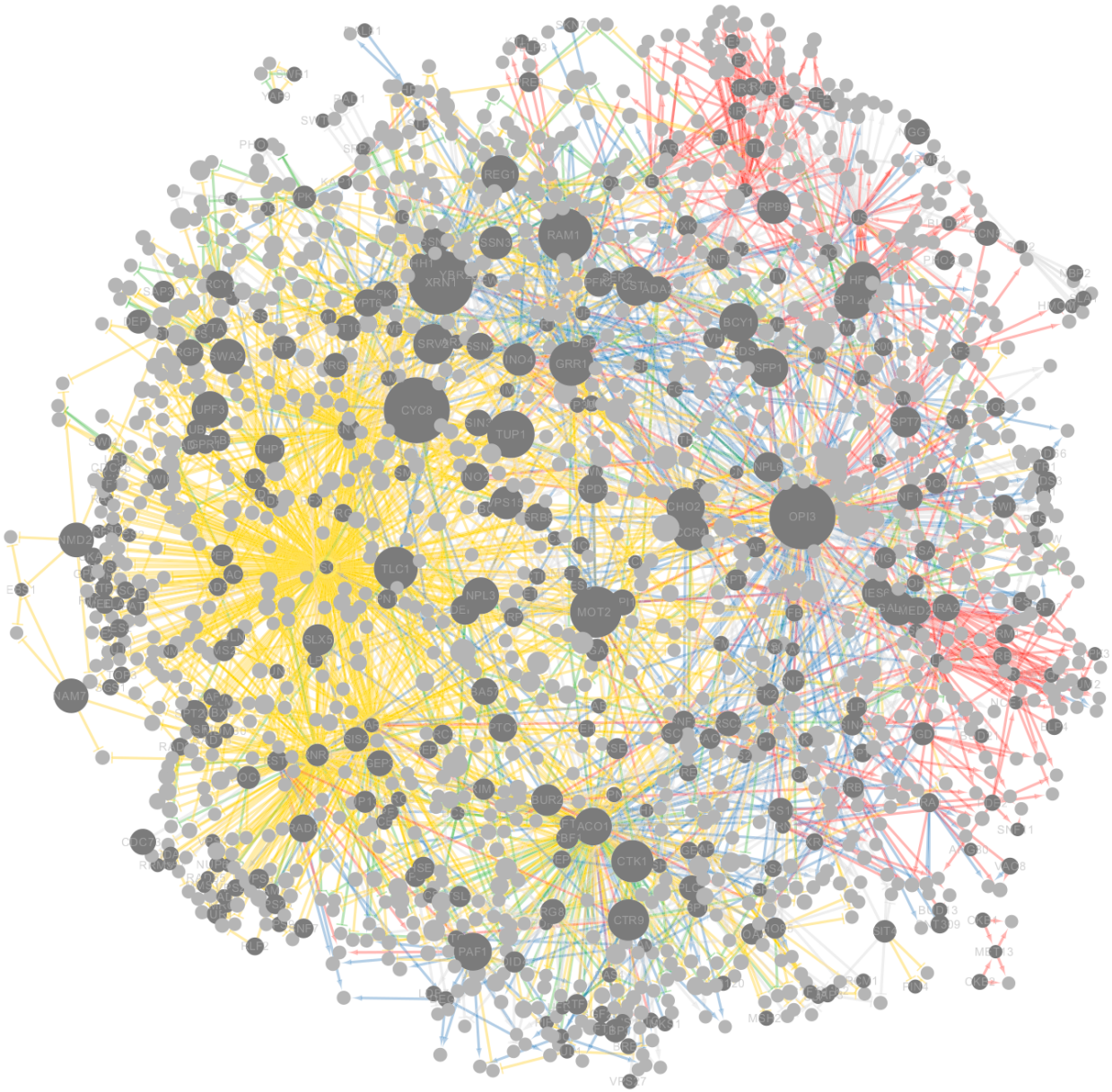
- The Back-door Criterion [Forré and Mooij, 2019];
- The do-Calculus [Forré and Mooij, 2019];

Causal Discovery algorithms can be adapted, or turn out to need no modification:

- [Forré and Mooij, 2018]: the first causal discovery algorithm that can handle cycles, nonlinear relationships, latent confounding variables and data from different (interventional) contexts.
- LCD, Y-structures, FCI and JCI all work out-of-the-box on simple SCMs [Mooij et al., 2019]

# Contents

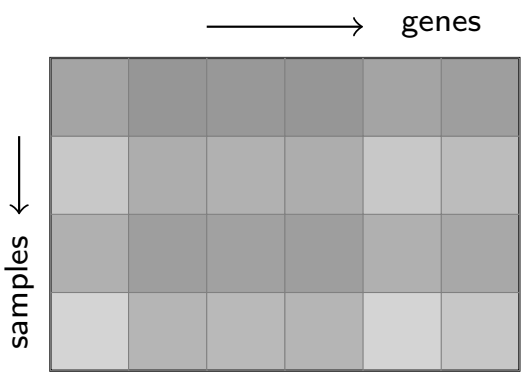
# Gene Regulatory Network = Causal Graph



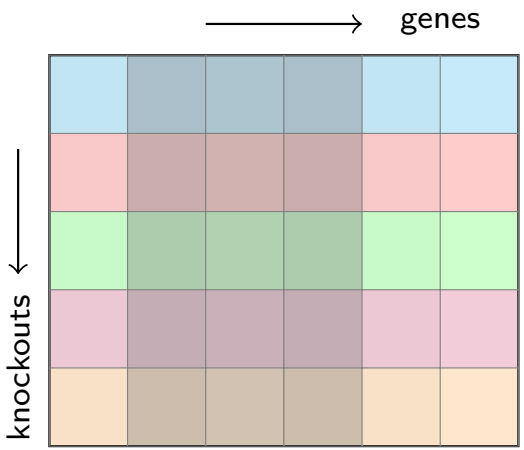

Source: [Kemmeren et al., 2014]

# Causal Discovery of Gene Regulatory Networks

observational:
(wild-type vs. wild-type):




interventional:
(mutant vs. wild-type):

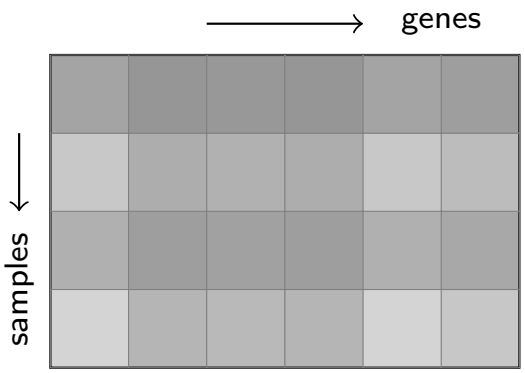



Large-scale Single Gene Knockout Micro-Array Data [Kemmeren et al., 2014]:

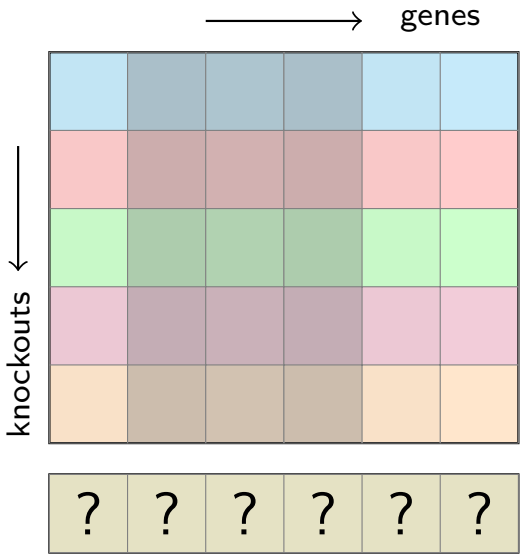
- ∼6,500 variables (gene expression)
- ∼260 observational samples (wild-type vs. wild-type)
- ∼1,500 interventional samples (single-gene knockouts/knockdowns)

# Causal Discovery of Gene Regulatory Networks

observational:
(wild-type vs. wild-type):




interventional:
(mutant vs. wild-type):




Large-scale Single Gene Knockout Micro-Array Data [Kemmeren et al., 2014]:

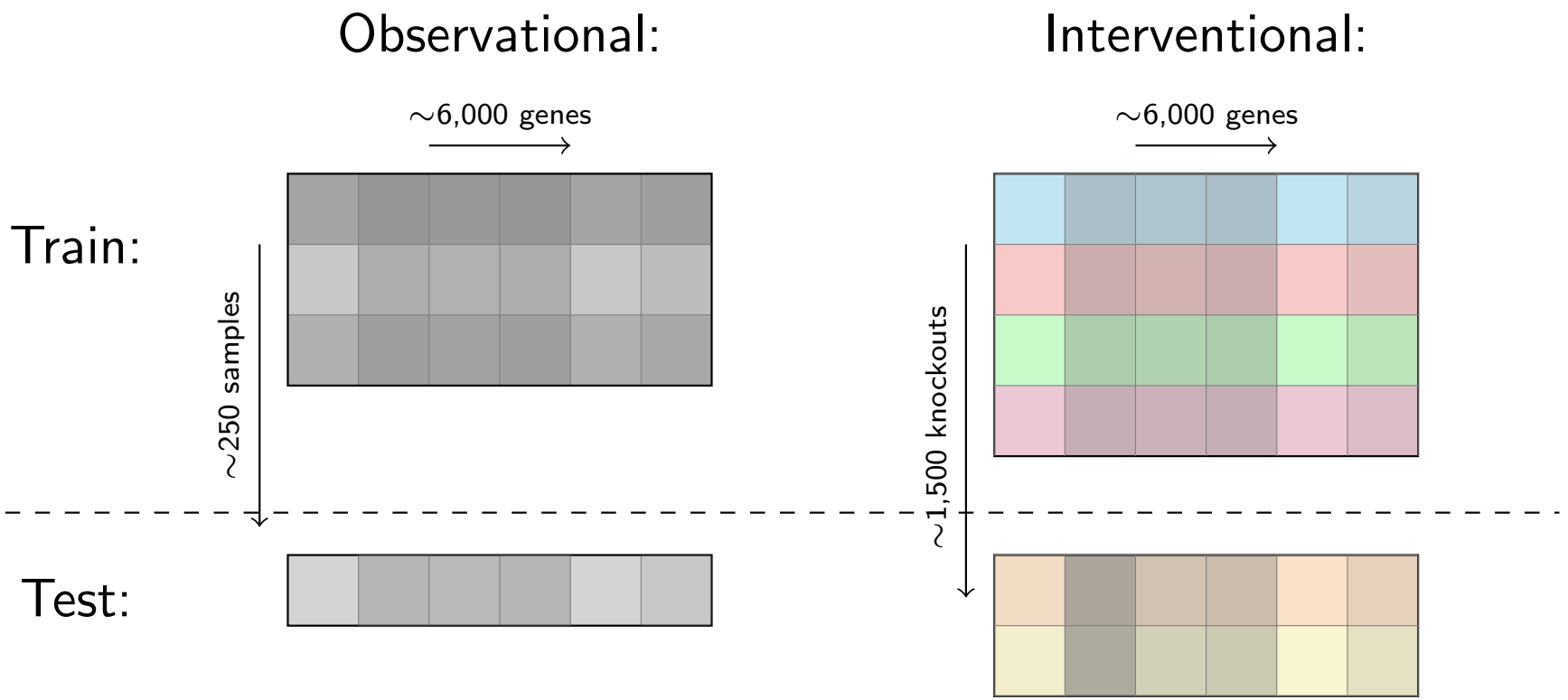
- ∼6,500 variables (gene expression)
- ∼260 observational samples (wild-type vs. wild-type)
- ∼1,500 interventional samples (single-gene knockouts/knockdowns)

**Challenge**

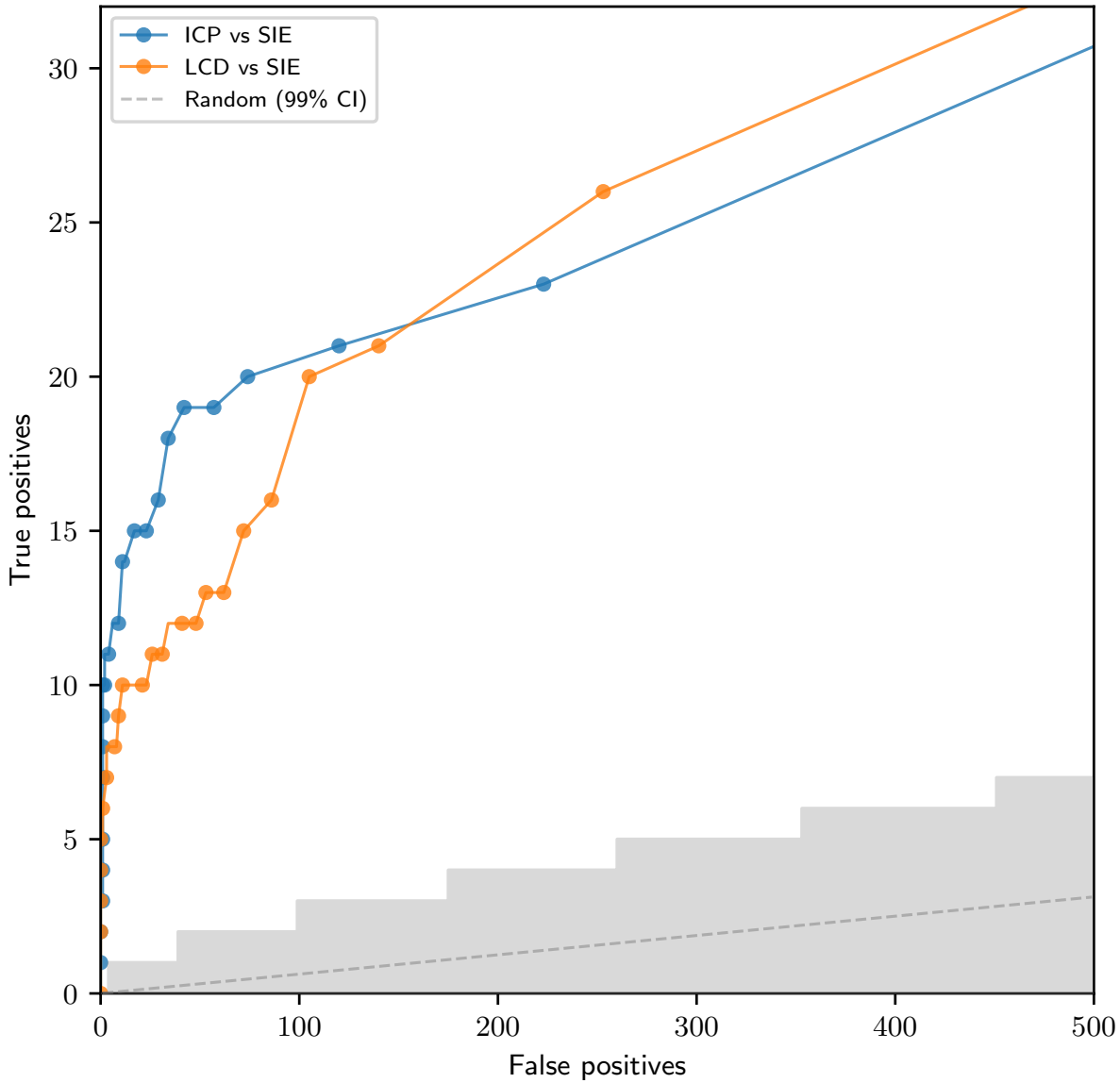
Can we, in a purely data-driven way (without using biological knowledge), predict which genes strongly change their expression when we knock-out a given gene (without using any data corresponding to that particular knock-out experiment)?

# $k$-fold Cross-validation

Using 5-fold cross-validation, we split the data into a training set used to make predictions, and a test set used to define a ground truth for validating the predictions.



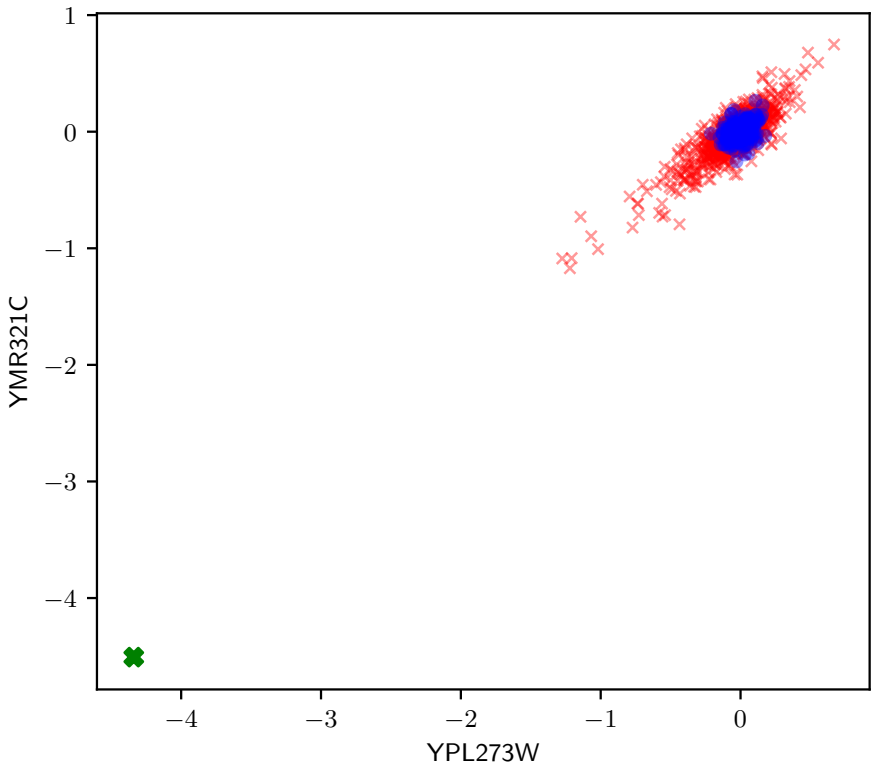
# First successful validation of causal discovery



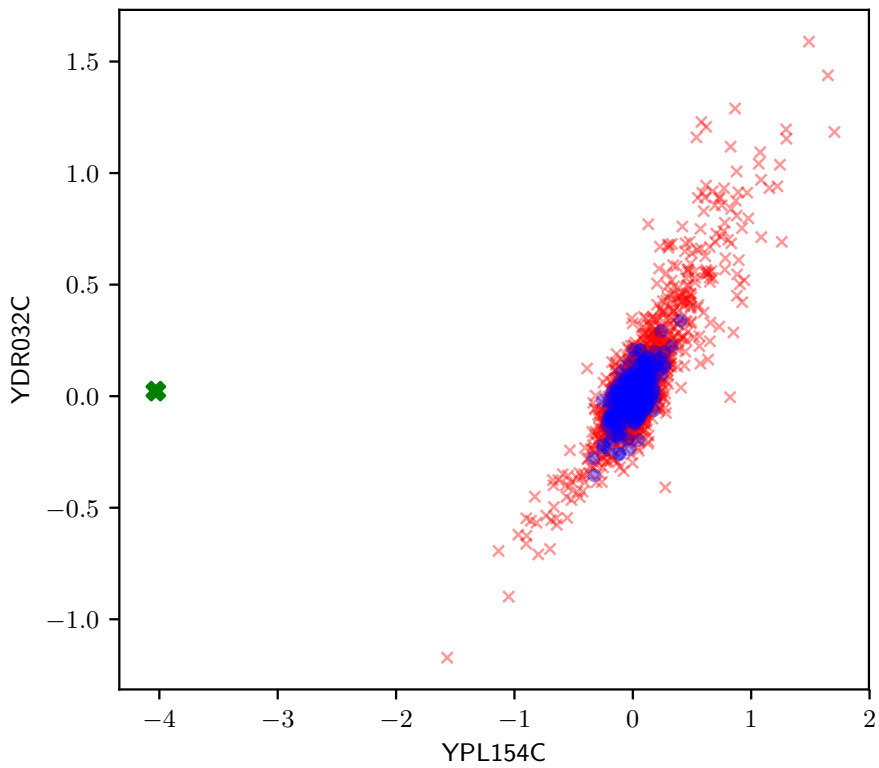

ICP: [Meinshausen et al., 2016]; LCD: high-dimensional version of LCD

# Correlation: Causation or Confounding?

True positive:




False positive:




(Training data: Observational and Interventional. Test data: single intervention.)

# Conclusion

Causality is clearly an important notion in daily life and in science, and yet underexplored in statistics and machine learning.

In this tutorial, you have learned how to:

- formalize the notion of causality;
- reason about causality;
- discover causal relations from data;
- make causal predictions;
- that *seeing* is not the same as *doing*.

This was just a sample of topics in an exciting research field. There is still much more to learn and to discover!

# Further reading I


Bongers, S. and Mooij, J. M. (2018).

From random differential equations to structural causal models: the stochastic case.

*arXiv.org preprint*, arXiv:1803.08784v2 [cs.AI].

Bongers, S., Peters, J., Schölkopf, B., and Mooij, J. M. (2018).

Theoretical aspects of cyclic structural causal models.

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Forré, P. and Mooij, J. M. (2017).

Markov properties for graphical models with cycles and latent variables.

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Forré, P. and Mooij, J. M. (2018).

Constraint-based causal discovery for non-linear structural causal models with cycles and latent confounders.

In *Proceedings of the 34th Annual Conference on Uncertainty in Artificial Intelligence (UAI-18)*.

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Causal calculus in the presence of cycles, latent confounders and selection bias.

In *Proceedings of the 35th Annual Conference on Uncertainty in Artificial Intelligence (UAI-19)*.

# Further reading III


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Large-scale genetic perturbations reveal regulatory networks and an abundance of gene-specific repressors.

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# Further reading IV


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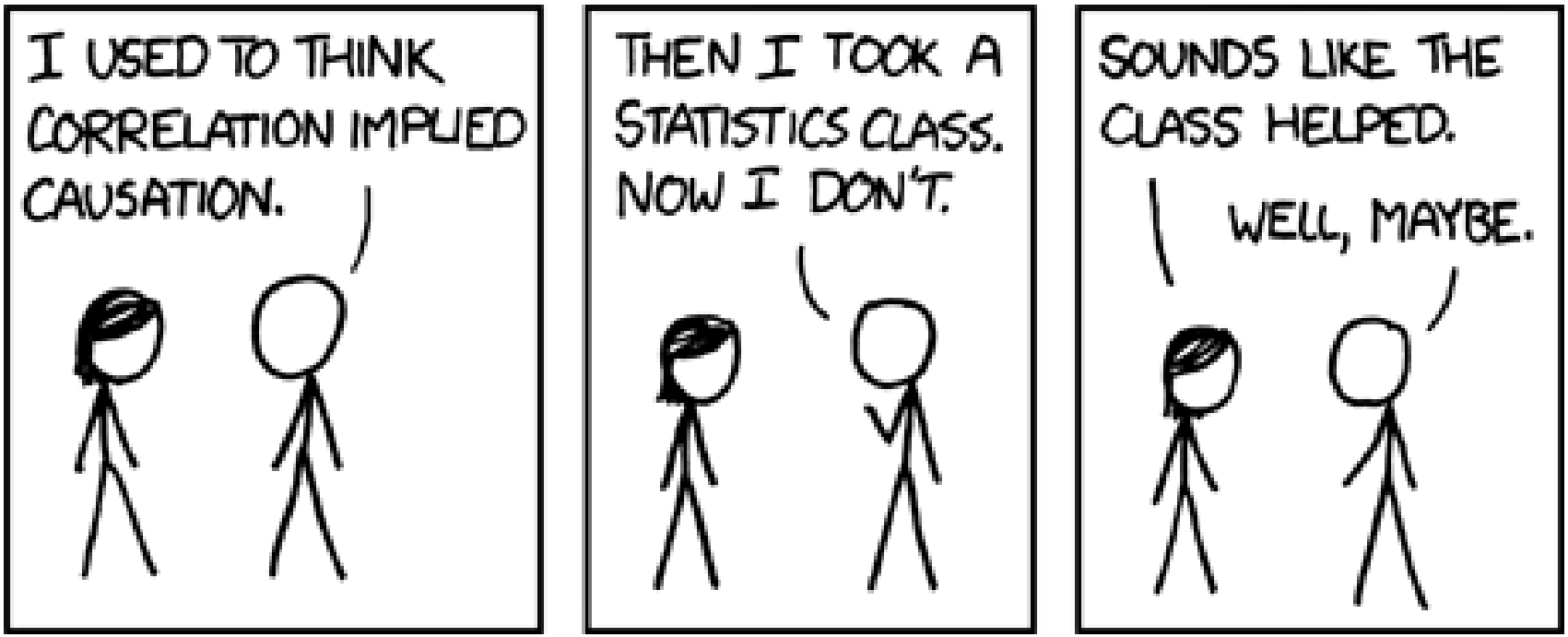
*Journal of Agricultural Research*, 20:557–585.

# Thank you for your attention!

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