Causal Inference and Invariance

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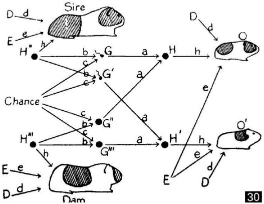
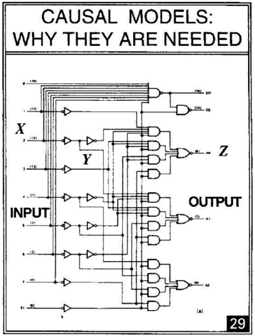
(Part 1/2)

Understanding = cause and effect




CAUSAL MODELS:
WHY THEY ARE NEEDED

X
Y
Z
INPUT
OUTPUT
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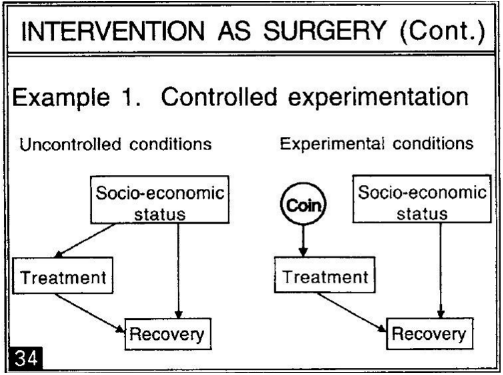

INTERVENTION AS SURGERY (Cont.)

Example 1. Controlled experimentation

Uncontrolled conditions

Socio-economic status

Treatment

Recovery

Experimental conditions

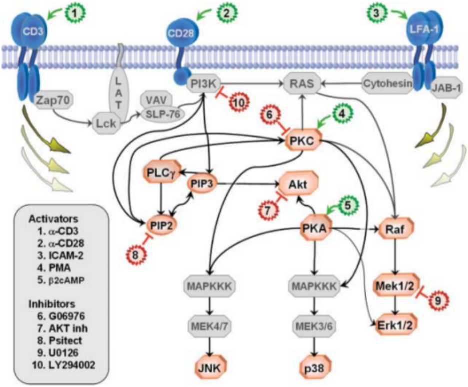
Coin

Socio-economic status

Treatment

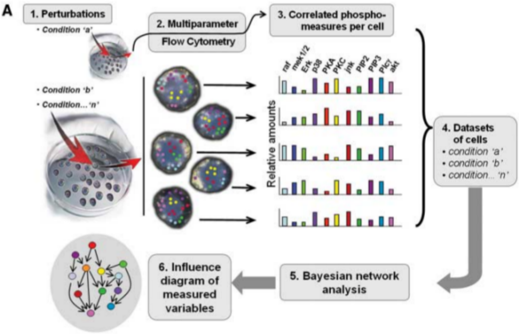
Recovery

A hot application: systems biology



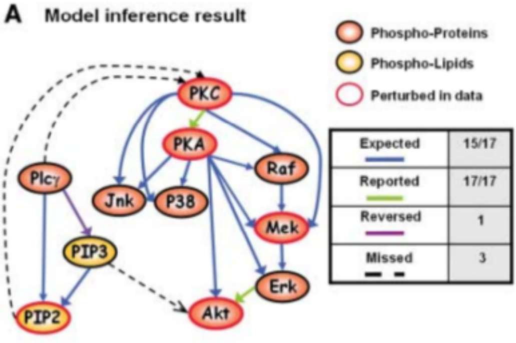
- Causal relationships = *chemical interactions*.
- Experimenters *intervene* by injecting *activators* and *inhibitors*.

Protein signalling data



- Flow cytometry data from Sachs et al.*Science*, 2005.
- 1 observational data set + 9 interventions.

Putative causal model



Expected	15/17
Reported	17/17
Reversed	1
Missed	3

- Causal inference applied to observational + interventional data.
- Recovered most of the known interactions.

The many facets of causality

- *Philosophy.* What is causality? How do we learn about cause and effect? *Aristotle, Hume.*
- *Computer science.* Can we build an artificial intelligence which reasons like humans? *Judea Pearl.*
- *Social science.*
- *Biology.*
- *Policy.* How will increasing interest rates influence unemployment?
- *Law.* Whose "fault" is it??
- *Statistics.* Answering the above questions using data!

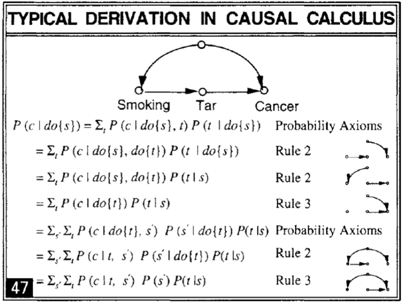
Statistics and causality

- *Estimating causal effects from data.* Can we predict a causal effect based on observational or experimental data? E.g. effect of a medical treatment based on clinical trial data? Motivation for potential outcomes approach developed by Rubin, etc.
- *Bayesian networks/structure learning from data.* Can we model multivariate relationships using a network structure? Networks *can be* given causal interpretation, but causal inference is not the only motivation. Motivation for graphical lasso.

Section 1

Introduction

Graphical approach pioneered by Judea Pearl.



TYPICAL DERIVATION IN CAUSAL CALCULUS

$P(c \mid do\{s\}) = \Sigma_t P(c \mid do\{s\}, t)\, P(t \mid do\{s\})$	Probability Axioms
$= \Sigma_t P(c \mid do\{s\}, do\{t\})\, P(t \mid do\{s\})$	Rule 2
$= \Sigma_t P(c \mid do\{s\}, do\{t\})\, P(t \mid s)$	Rule 2
$= \Sigma_t P(c \mid do\{t\})\, P(t \mid s)$	Rule 3
$= \Sigma_{s'} \Sigma_t P(c \mid do\{t\}, s')\; P(s' \mid do\{t\})\, P(t \mid s)$	Probability Axioms
$= \Sigma_{s'} \Sigma_t P(c \mid t,\; s')\; P(s' \mid do\{t\})\, P(t \mid s)$	Rule 2
$= \Sigma_{s'} \Sigma_t P(c \mid t,\; s')\; P(s')\, P(t \mid s)$	Rule 3

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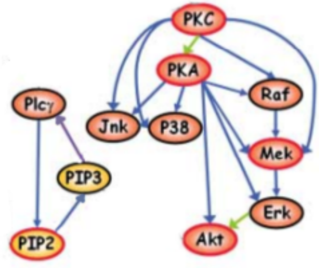
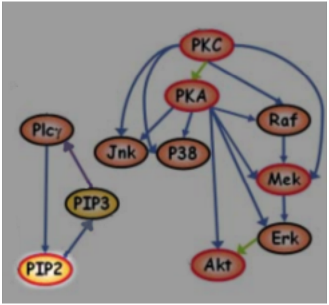
Graphs: nodes and vertices



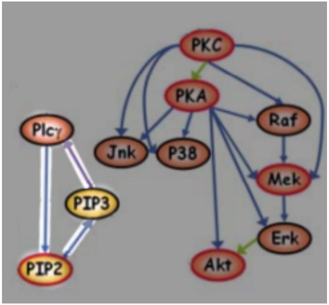
- Each variable in the dataset is given a *node*.
- Arrows indicate which variables *cause* which other variables. (Parents → children).

Causality and experiments



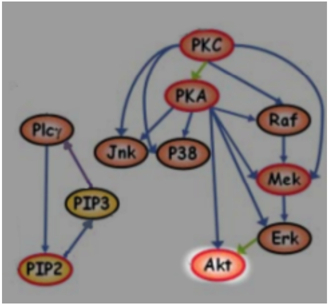
Intervening on variables in the system causes the distribution to change.

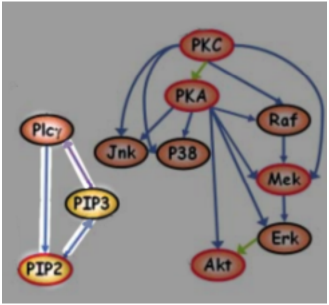
Causality and experiments



- Not every variable will be affected by the intervention!
- Following the arrows tells you *which* variables which are affected.

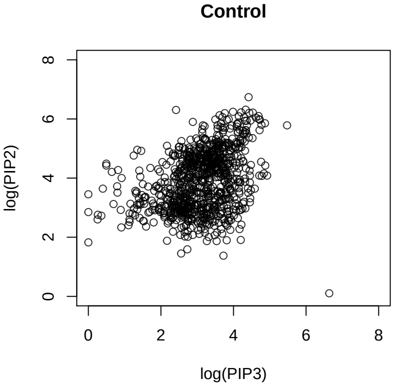
Principle I: Which variables are affected.





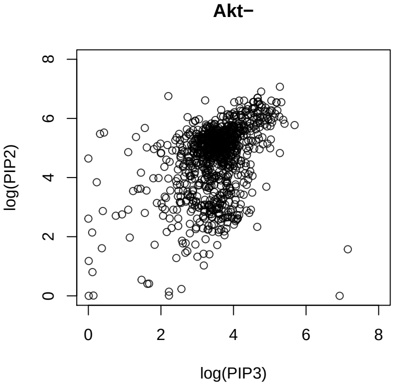
- If we *inhibit* Akt, no other variables should be affected.
- If we *inhibit* PIP2, then we may not only change the distribution of PIP2, but also PIP3.

Principle I: Which variables are affected.



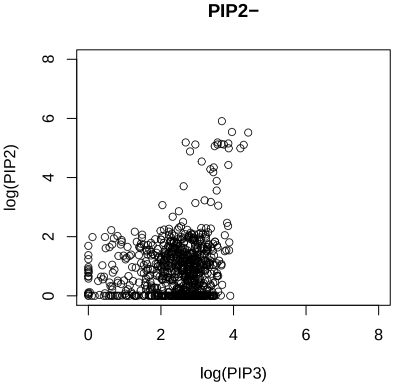
Looking at Sachs data.
Joint distribution of PIP2 and PIP3 in the "control" case.

Principle I: Which variables are affected.



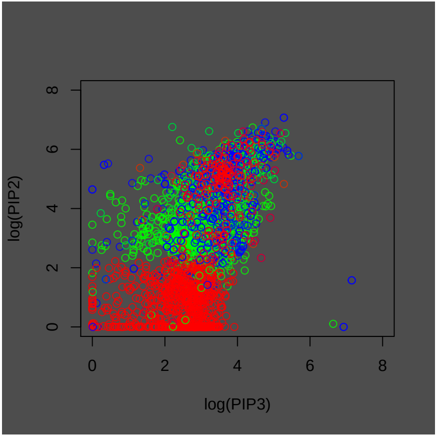
Joint distribution of PIP2 and PIP3 when we intervene on Akt.

Principle I: Which variables are affected.



Joint distribution of PIP2 and PIP3 when we intervene on PIP2.

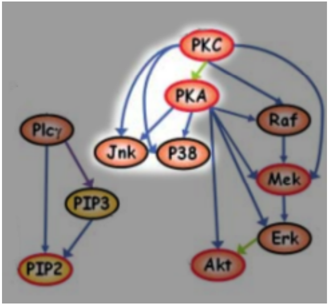
Principle I: Which variables are affected.



Control, **PIP2-**, **Akt-**

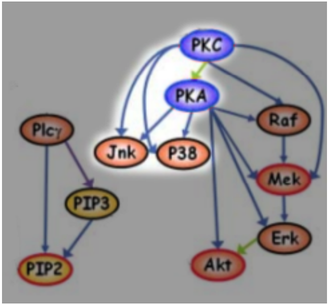
Intervening on PIP2 also affects the distribution of PIP3, while intervening on Akt does not (drastically) change the distribution.

Principle II: Conditional independence.



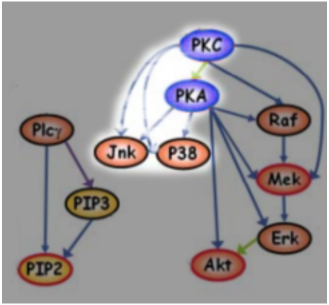
- Surprisingly, the structure of the causal graph implies certain *conditional independence* relationships.
- This allows the potential to infer causal relationships from observational data.

Principle II: Conditional independence.



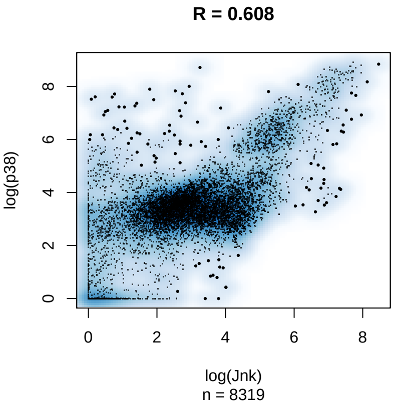
- Two variables are independent conditional on their common parents.
- Conditioning on PKC and PKA, Jnk and p38 should be independent.

Principle II: Conditional independence.



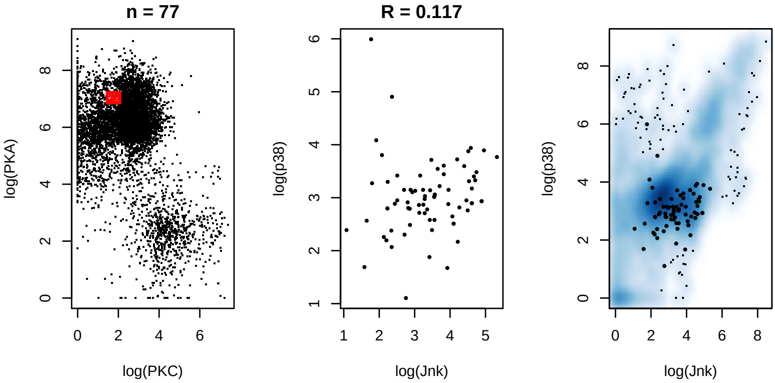
- “Once you and I condition on common factors, we are left with nothing in common.”

Principle II: Conditional independence.



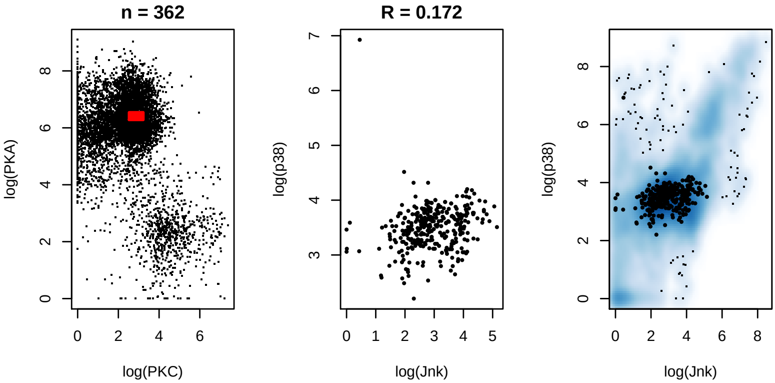
Marginally, p38 and Jnk are correlated.

Principle II: Conditional independence.



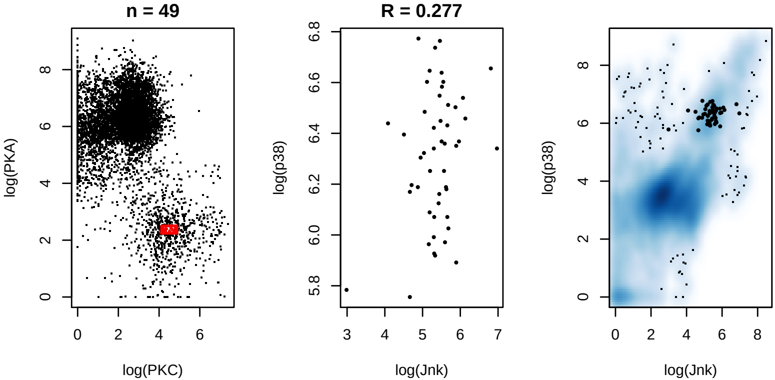
We can't condition on PKA and PKC since the data is continuous. But, conditioning on small windows seems to reduce association.

Principle II: Conditional independence.



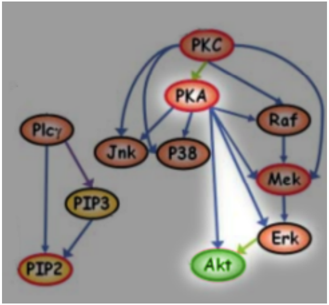
Left: We condition on (PKA, PKC) to lie within the indicated window. *Center:* Conditional joint distribution of (Jnk, p38). *Right:* Conditional join distribution, overlaid on marginal distribution.

Principle II: Conditional independence.



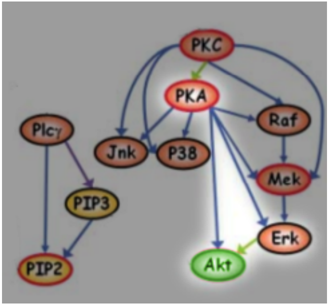
PKA and PKC *explain away* some (if not all) of the association between Jnk and p38. (Recall that R = 0.608 marginally.)

Principle III: Predictive invariance



- The conditional distribution $\Pr[Akt|PKA, Erk]$ is invariant to interventions applied to other variables.
- Therefore, the optimal rule for predicting $\hat{Akt}(PKA, Erk)$ is invariant as well.

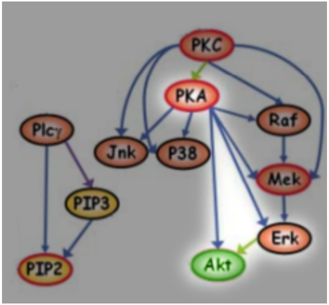
Principle III: Predictive invariance

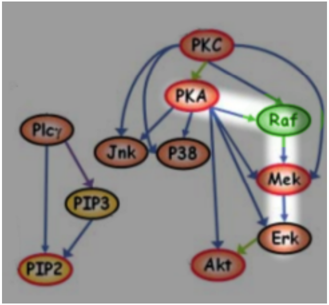


$\{PKA, Erk\}$ is an "invariant set" for Akt since:

- It includes all of the "direct" causes of Akt in the graph.
- It doesn't include any variables caused by Akt.

Principle III: Predictive invariance

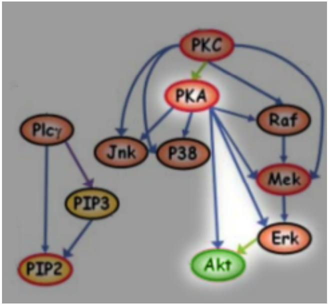


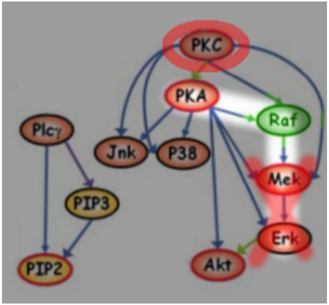


In contrast, $\{PKA, Mek, Erf\}$ is *not* an invariant set for *Raf* since:

- .
- .

Principle III: Predictive invariance

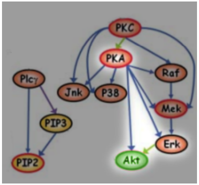


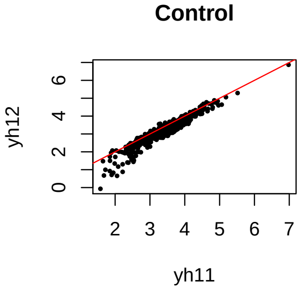


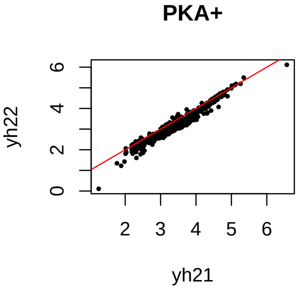
In contrast, $\{PKA, Mek, Erf\}$ is *not* an invariant set for *Raf* since:

- It is missing a direct cause of *Raf*.
- It contains variables which are caused by *Raf*.

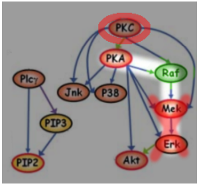
$\{PKA, Erk\}$ is an invariant set for Akt.

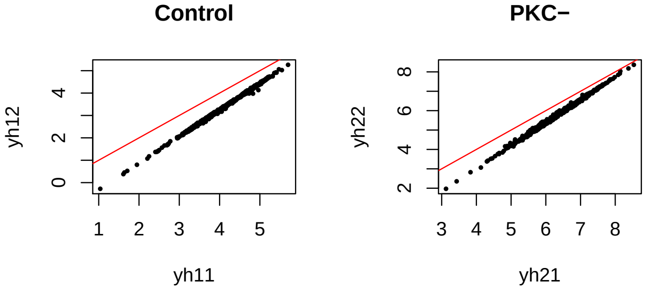




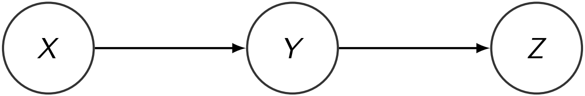


$\{PKA, Mek, Erf\}$ is *not* an invariant set for *Raf*.



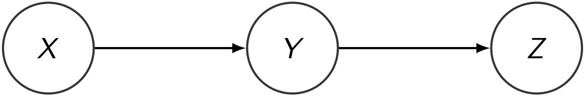


Predictive Invariance: Example



- Suppose we are trying to predict Y.
- $X \sim N(0, a)$.
- $Y|X \sim N(X, b)$.
- $Z|Y \sim N(Y, c)$.

Predictive Invariance: Example



$$X \sim N(0, a), \;\; Y|X \sim N(X, b), \;\; Z|Y \sim N(Y, c).$$

- We can intervene by adding noise to X = changing $a \to a'$.
- Intervene by injecting noise to Z = changing $c \to c'$.
- Consider a linear model which predicts Y given X and Z.
- *Is the optimal prediction rule invariant under intervention?*

Predictive Invariance: Example

$$X \to Y \to Z$$

$$X \sim N(0, a), \;\; Y|X \sim N(X, b), \;\; Z|Y \sim N(Y, c).$$

The joint distribution is

$$\begin{bmatrix} X \\ Y \\ Z \end{bmatrix} \sim N\left(\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} a & a & a \\ a & a+b & a+b \\ a & a+b & a+b+c \end{bmatrix} \right)$$

The optimal prediction rule is given by

$$\mathbf{E}[Y|X, Z] = \mu_Y + \Sigma_{Y,XZ}\Sigma_{XZ}^{-1}(X - \mu_X, Z - \mu_Z) = \frac{c}{b+c}X + \frac{b}{b+c}Z.$$

Predictive Invariance: Example

$$X \sim N(0, a), \;\; Y|X \sim N(X, b), \;\; Z|Y \sim N(Y, c).$$

Optimal prediction rule:

$$\mathbf{E}[Y|X, Z] = \underbrace{\frac{c}{b+c}}_{\beta_X} X + \underbrace{\frac{b}{b+c}}_{\beta_Z} Z.$$

i.e. Y is a weighted average of X and Z ($\beta_X + \beta_Z = 1$).

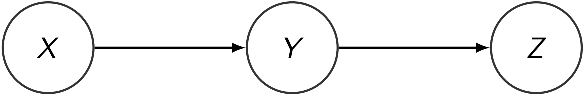
- Imagine c is very small, i.e. $Z = Y +$ tiny noise. Then Z is a great predictor of Y! $\beta_Z \approx 1$.
- Conversely, if b is small, that means $Y = X +$ tiny noise. $\beta_X \approx 1$.
- If $b = c$, then $\beta_X = \beta_Z = 1/2$.

Predictive Invariance: Example

But is the OLS predictive rule invariant?

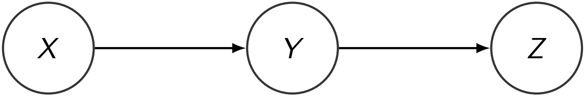
$$\mathbf{E}[Y|X,Z] = \frac{c}{b+c}X + \frac{b}{b+c}Z.$$

If we intervene on Z, changing c to c', the OLS coefficients change too. The model is not invariant.



"Real-life" example. $X =$ lifetime total number of bagels eaten, $Y =$ Body Mass Index (BMI), $Z =$ how many pull-ups you can do?
Z is a good predictor of Y, unless you "intervene" by offering a $100 prize for doing 10 pull-ups.

Predictive Invariance: Example

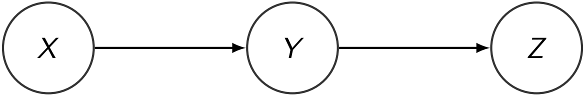


- In contrast, consider predicting Y using *only* X.
- $\{X\}$ is an invariant set for Y because it contains all direct parents and no children of Y.
- Indeed,

$$\mathbf{E}[Y|X] = \frac{\mathrm{Cov}(Y,X)}{\mathrm{Cov}(X)}X = \frac{a}{a}X = X.$$

  The OLS coefficient, 1, does not depend on a or c, and hence is *invariant* under interventions.
- *Exercise.* Is $\{Z\}$ an invariant set for Y?

Predictive Invariance: General case



$$p(x, y, z) = p(x)p(y|x)p(z|y)$$

Interventions:

$$p(x) \to \tilde{p}(x) \text{ or } p(z|y) \to \tilde{p}(z|y)$$

Non-invariant rule:

$$p(y|x, z) = \frac{p(x, y, z)}{p(x, z)} = \frac{p(x)p(y|x)p(z|y)}{p(x)p(z|x)} = \frac{p(y|x)p(z|y)}{p(z|x)}$$

affected by intervention $p(z|y) \to \tilde{p}(z|y)$.

Overview: Principles of Causal Inference

Causal relationships in a system represented by a graph. The graph tells you:

I. which variables are affected by an intervention.

II. what conditional independence relationships exist in the joint distribution (*d-separation*.)

III. which sets of predictors and responses will have “invariant” optimal predictive rules.

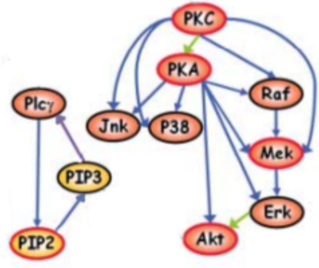
These three intuitive principles are equivalent to *factorization* definition of graphical model:

$$p(x_1, \ldots, x_k) = \prod_{i=1}^{k} p(x_i | \text{Parents}(x_i)).$$

Section 2

Methods Overview

Estimating Causal Effects



- Suppose we want to reduce the expression level of PKC in the cell. We have an enzyme that activates PIP2 and another enzyme that inhibits PIP2. Which one should we use, if at all?

Three Languages

First, we need to define *causal effect*. Three essentially equivalent ways:

- The graphical approach via Bayesian network.

$$\mathrm{E}[PKC|do(PIP2)]$$

  - Thomas Bayes (1763), Sewell Wright (1920s), Judea Pearl (1980s–1990s).

- The functional approach: Structural Equation Models.

$$Y = f(\mathrm{parents}(Y); \epsilon_Y)$$

  - Sewell Wright's path analysis (1920s), Karl Jöreskog and Dag Sörbom's LISREL (1970s), confirmatory factor analysis, "invariance principle".

- The potential outcome appraoch:

$$\mathrm{E}[PKC_{PIP2+} - PKC_{PIP2-}]$$

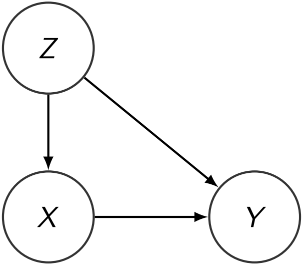
  - Neyman (1923), Rubin (1970s).

Three *Causal* Questions

- Given a number of variables, which pairs are causally related?
  - Infer the *graph*.
- Given a number of variables and a fixed Y, which variables causally affect Y?
  - Infer the *invariance set*.
- Given a fixed X and a fixed Y, what is the causal effect of X on Y?
  - Infer the *causal effect*.

Why different languages? Convenience!

Example: observational study



- $X = \{0, 1\}$ treatment variable, Y outcome of interest, Z confounders.
- Want to estimate average treatment effect.
- No confounders?? Use $\mathbf{E}[Y|X = 1] - \mathbf{E}[Y|X = 0]$, done!
- *Unobserved* confounders?! We'll discuss next time..
- For now, assume all confounders are observed.

Adjusting for confounders: the graphical approach

It suffices to estimate $\mathrm{P}(y|do(x))$.

- Factorization: $\mathrm{P}(x, y, z) = \mathrm{P}(y|x, z)\mathrm{P}(x|z)\mathrm{P}(z)$.
- Step one: convert between 'do' notation and probability

$$\mathrm{P}(y|x, z) = \mathrm{P}(y|do(x), z).$$

- Step two: applying law of total probability gives the *backdoor formula*

$$\begin{aligned}\mathrm{P}(y|do(x)) &= \sum_z \mathrm{P}(y, z|do(x)) = \sum_z \mathrm{P}(y|do(x), z)\mathrm{P}(z|do(x)) \\ &= \sum_z \mathrm{P}(y|x, z)\mathrm{P}(z).\end{aligned}$$

- Step three: plug in the empirical $\hat{\mathrm{P}}(y|x, z)$ and $\hat{\mathrm{P}}(z)$.

Adjusting for confounders: the potential outcome approach

It suffices to estimate $\mathrm{P}(x|z)$, because

$$\begin{aligned}\mathrm{P}(y|do(x)) &= \sum_z \mathrm{P}(y|x,z)\mathrm{P}(z) = \sum_z \frac{\mathrm{P}(x,y,z)}{\mathrm{P}(x,z)}\mathrm{P}(z) \\ &= \sum_z \frac{\mathrm{P}(x,y,z)}{\mathrm{P}(x|z)}.\end{aligned}$$

- $\mathrm{P}(x|z)$ is called the *propensity score* (Rosenbaum and Rubin, 1983).
- $\mathrm{P}(x|z)^{-1}$ is called the *inverse probability weight*.
- Coarsened version: matching, subclassification.
- This approach is more appealing to statisticians and was derived before Judea Pearl's *do* calculus.

Adjusting for confounders: the functional approach

It “sufficies” to estimate $\mathrm{P}(y|x,z)$, because $\mathrm{P}(y|x,z) = \mathrm{P}(y|do(x),z)$.

- The quantity of interest is changed from $\mathrm{P}(y|do(x))$ to $\mathrm{P}(y|do(x),z)$, but that’s perhaps even better!
- In practice, we just run an *outcome regression*.
- The same idea appears in
  - Covariance adjustment in randomized experiment (Fisher, 1935).
  - Doubly robust estimation (Robins, 1990s).
  - The invariance principle (Peters, Bühlmann and Meinshausen, 2015).

Conclusions

- Causal models imply statements about which variables get affected by interventions, which conditional independencies exist, and which sets of variables lead to invariant prediction rules.
- Real data may reveal a causal model to be more of a useful approximation than a literal description.
- Estimation of causal effects from experiments with imperfect randomization or observational data is a common goal in causal inference, and can be addressed using the graphical approach or potential outcomes framework.

Next time...

In part II of the talk, we'll go into more detail about inference with finite sample, limitations and criticism, with a focus on the invariance approach by Peters, Bühlmann and Meinshausen. Could this new approach extend the applicability of causal inference?

References

- Sachs, Karen, et al. “Causal protein-signaling networks derived from multiparameter single-cell data.” *Science* 308.5721 (2005): 523-529.
- Nagarajan, Radhakrishnan, Marco Scutari, and Sophie Lèbre. ”Bayesian networks in R.” Springer 122 (2013): 125-127.
- Pearl, Judea. *Causality.* Cambridge university press, 2009.
- Morgan, Stephen L., and Christopher Winship. *Counterfactuals and causal inference.* Cambridge University Press, 2014.
- Peters, Jonas, Peter Bühlmann, and Nicolai Meinshausen. “Causal inference using invariant prediction: identification and confidence intervals.” arXiv preprint arXiv:1501.01332 (2015).