GitHub repo with materials!

Causality for Neuroscientists

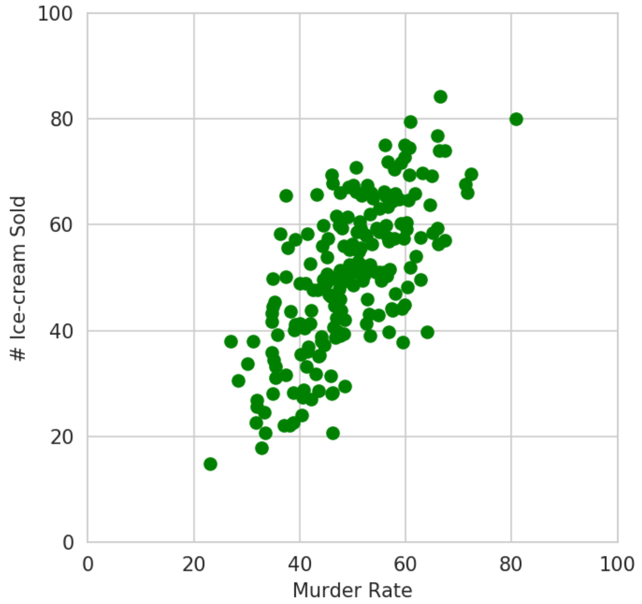
Ole Jonas Wenzel, Hongbiao Chen and Akshay Kumar Jagadish

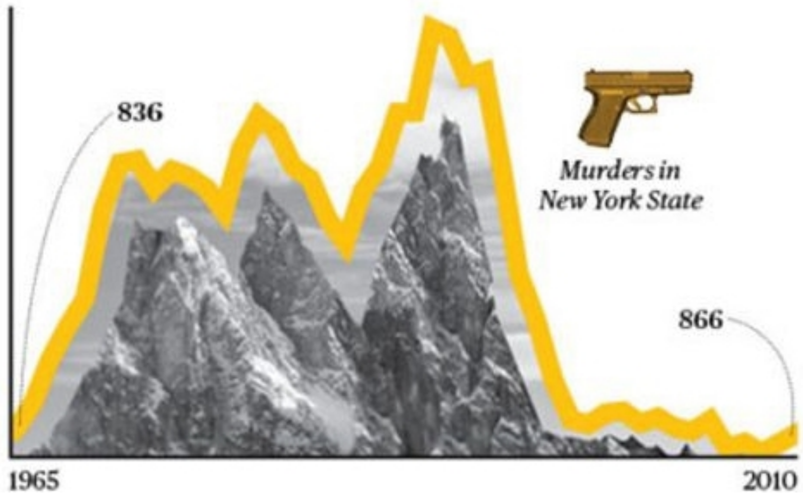
5th November 2019
Neurowissenschaftliche Nachwuchskonferenz (NeNa) 2019

Promise

- Spurious correlation is everywhere around us
- Causality - if you are honest - is what we all of us want!
- Confounders: the arch nemesis of causality
- Fundamental Math concepts
- Formal approach to adjust for confounders and find causal effect
- Extend the formal approach to deal with complex systems
- Incorporate causal principles to understand the brain

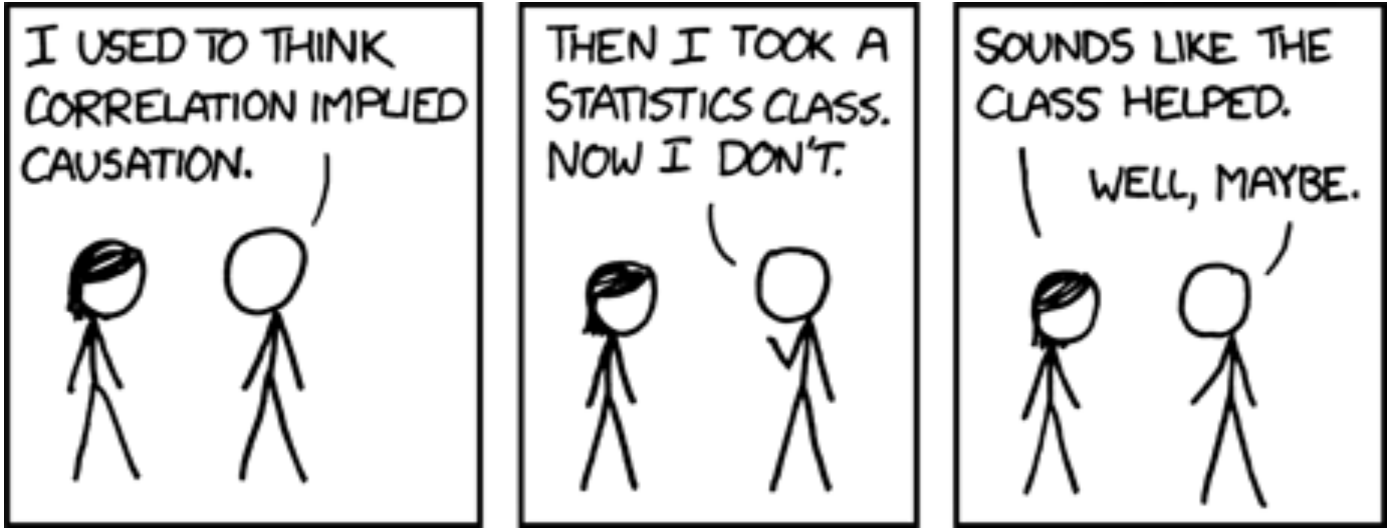
World is full of correlations





Ice Cream Sales “Lead” to Homicide: Why? - Lifehack
Correlation or Causation? - Bloomberg

Correlation doesn't imply Causation



correlation - xkcd 552

What is Causality?

cau·sal·i·ty
/kôˈzalədē/

noun

1. the relationship between cause and effect.

"We think we do not have knowledge of a thing until we have grasped its why, that is to say, its cause"

- Aristotle

Above description gives way to deterministic causality but philosophers ***like Hume, Kant and Russell*** that came later defined a probabilistic notion of causality.

Phys. 194 b 17–20

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Neuronal Causes and Behavioural Effects:

a Review on Logical, Methodological, and Technical Issues With Respect to Causal Explanations of Behaviour in Neuroscience

A Preprint

Kayson Fakhar*[1] and Lisa Schmors,[2] Dominic Gonschorek,[2] Natalia Z. Bielczyk[3]

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August 19, 2019

Phys. 194 b 17–20

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1. the relationship between cause and effect.

According to the philosopher ***John Stuart Mill***, there are three criteria for inferring a cause:

1. Cause and effect have to be related;
2. Cause had to precede the effect in time;
3. No other plausible alternative explanation for the effect.

Shadish, Cook, Campbell 2002

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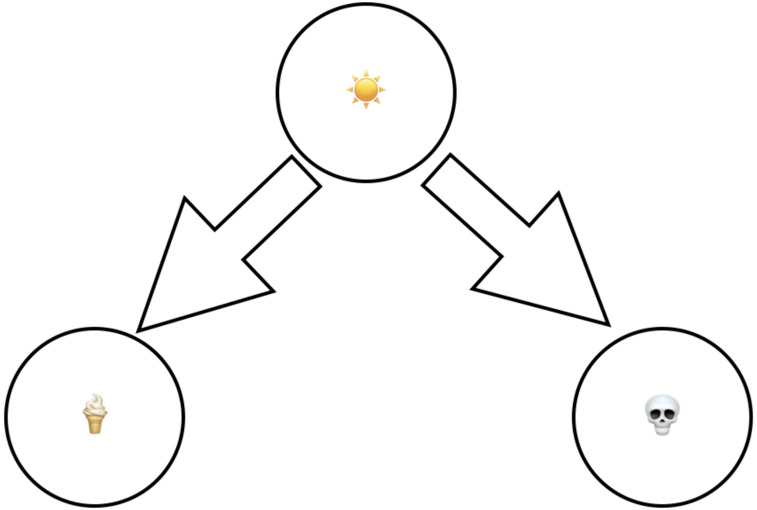
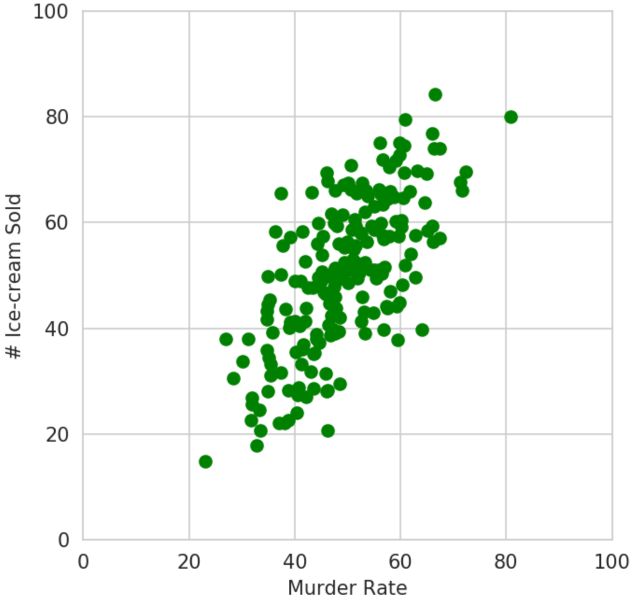
Confounders: The arch nemesis of Causality





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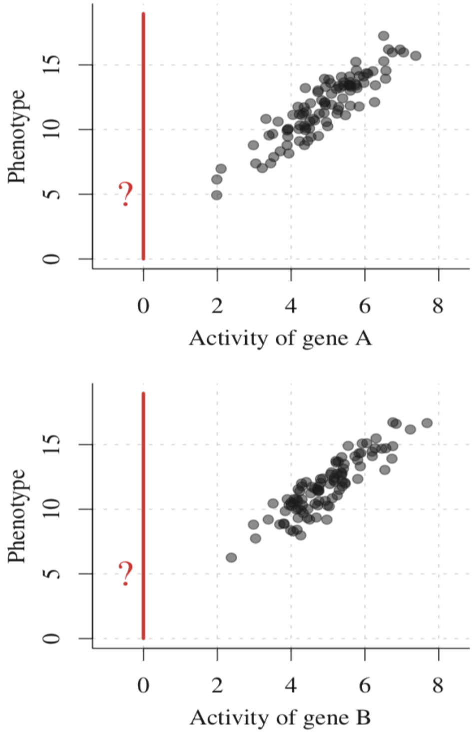
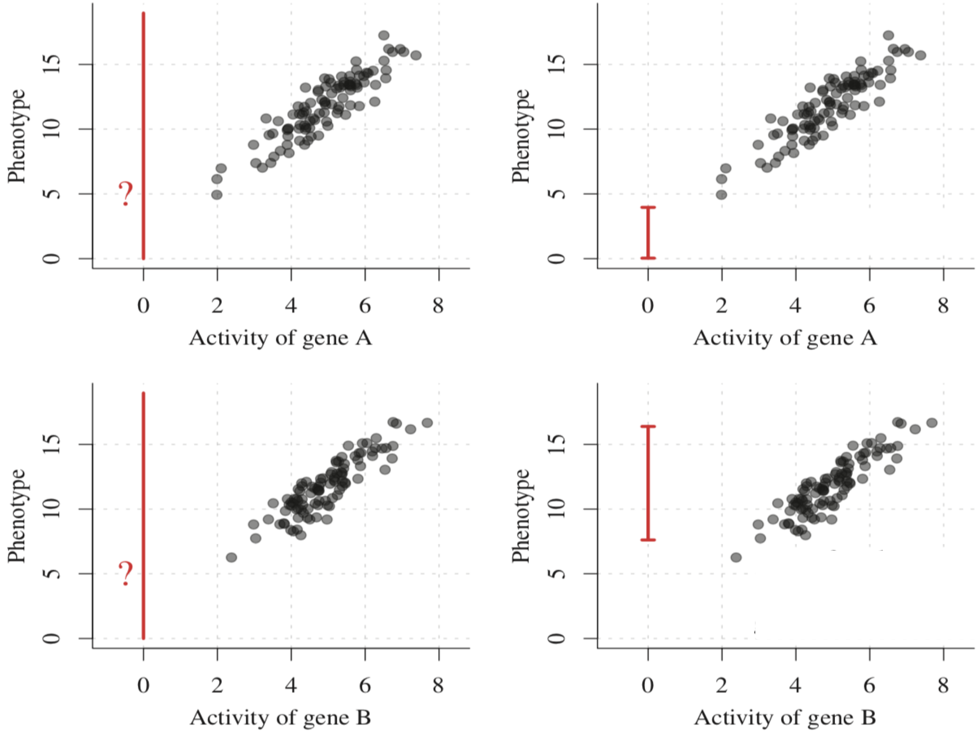


Peters et al 2017

Confounders: The arch nemesis of Causality



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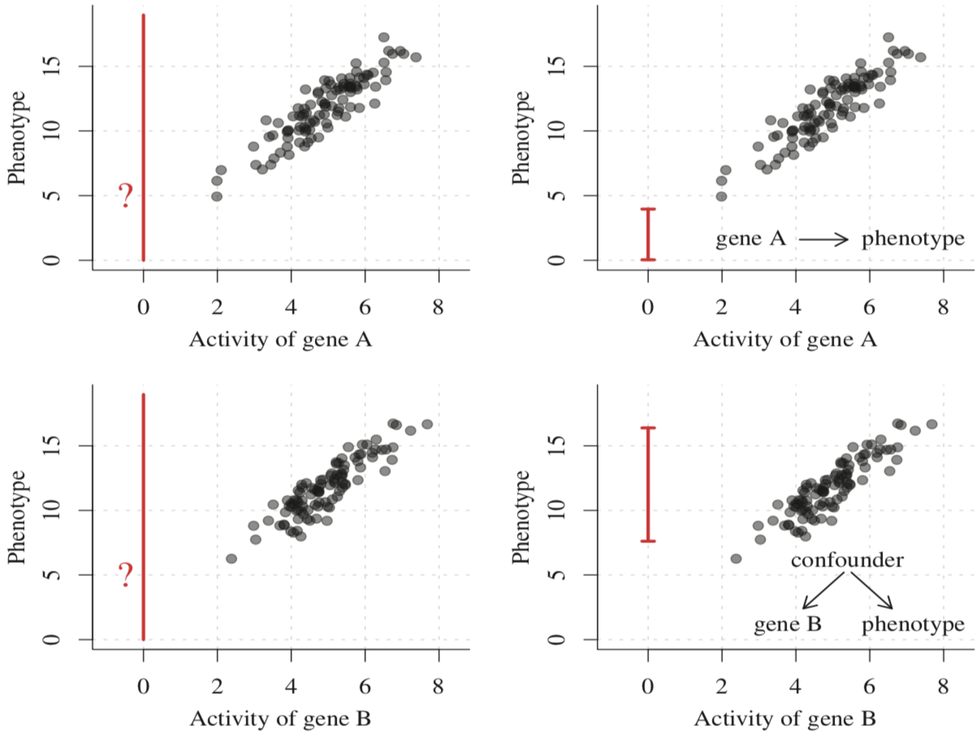

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Kidney Stones 🤢

	Overall
Treatment *a*: Open surgery	78% (273/350)
Treatment *b*: Percutaneous nephrolithotomy	**83%** (289/350)

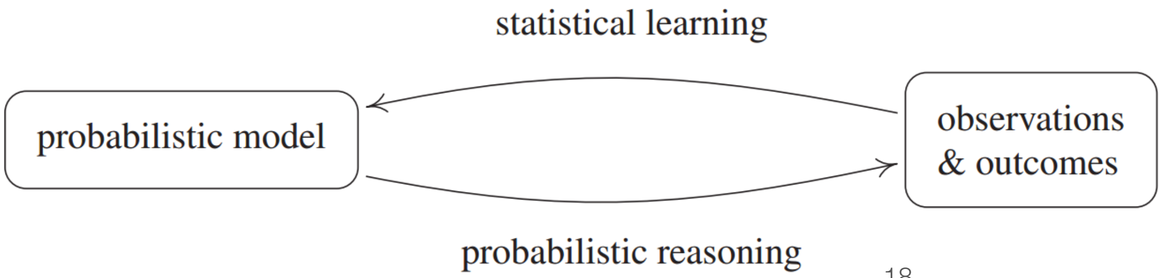
Charig et al., 1986

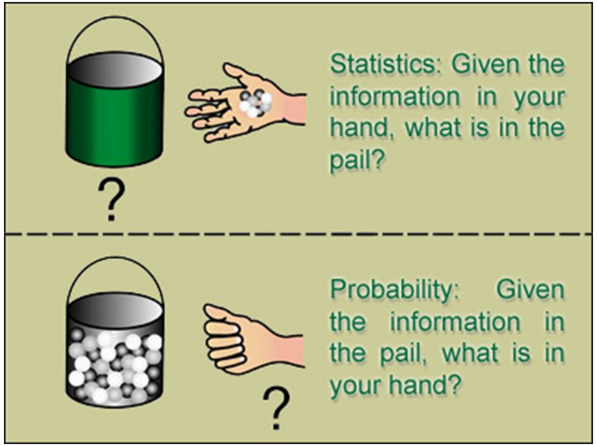
Kidney Stones

	Overall	Patients with small stones	Patients with large stones
Treatment *a*: Open surgery	78% (273/350)	**93%** (81/87)	**73%** (192/263)
Treatment *b*: Percutaneous nephrolithotomy	**83%** (289/350)	87% (234/270)	69% (55/80)

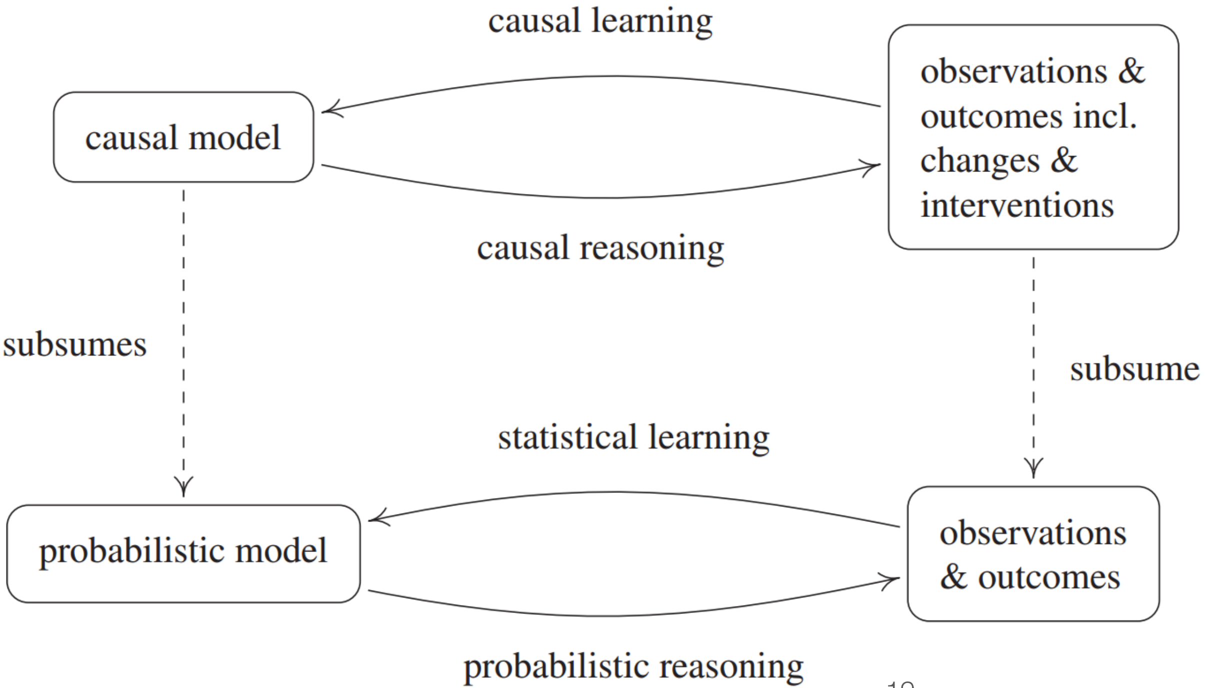
Charig et al., 1986

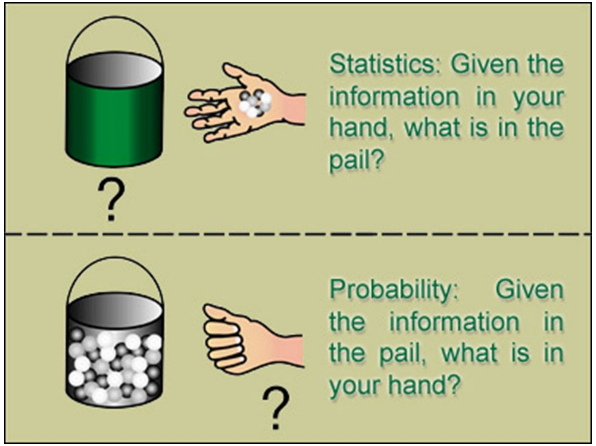
From probabilistic to causal model





From probabilistic to causal model

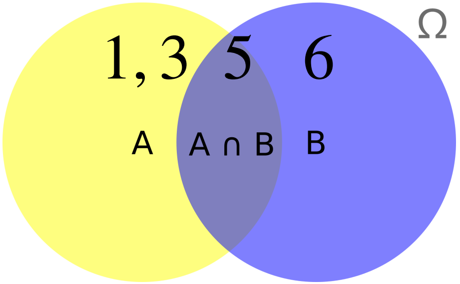




Probabilistic Model

Probabilistic model:

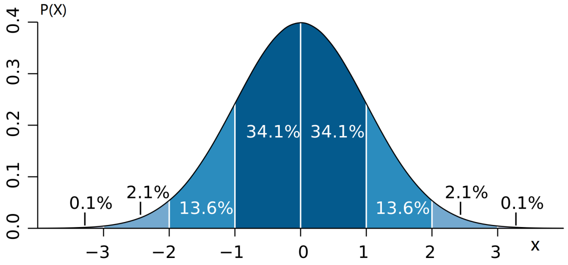
- Event: A, B, A∩B
- Probability of an event: P(A), P(B), P(A,B)
- Conditional Probability: P(A|B) = P(A,B) / P(B)
- Independent events: $P(A) = P(A \mid B)$

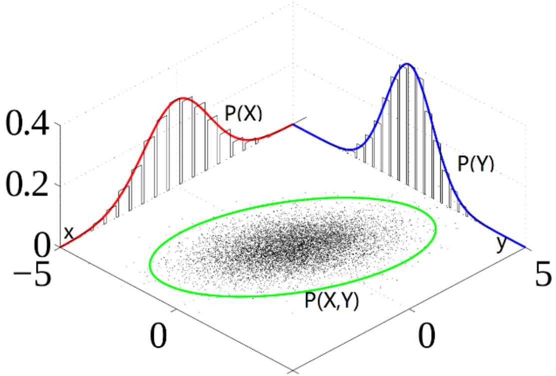


Probabilistic Model

Probabilistic model:

- Random variable: X, Y
- Probability distribution: P(X), P(Y), P(X,Y)
- Joint, Conditional Probability and Independency for ***random variables***
- Marginalization: $P(X = x) = \sum_{Y} P(X = x, Y)$





Causal model

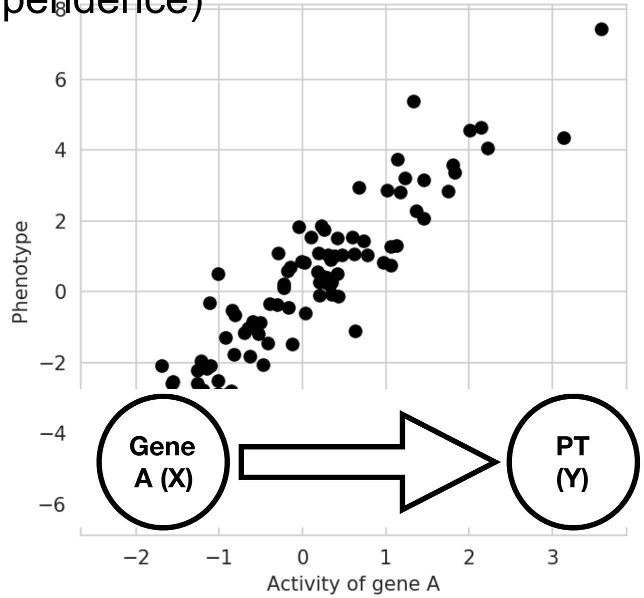
Structural Causal model (SCM):

- structural equation (assignment vs. equal operator)
- causal graph (node: random variable; arrow: dependence)

$$X := N_X$$
$$Y := 2X + N_Y$$

$$N_X, N_Y \sim \mathcal{N}(0, 1)$$

P(X,Y) ~ Bivariate normal joint distribution
- Mean = [0; 0]
- Covariate matrix = [1, 2;
  2, 5]



do-intervention

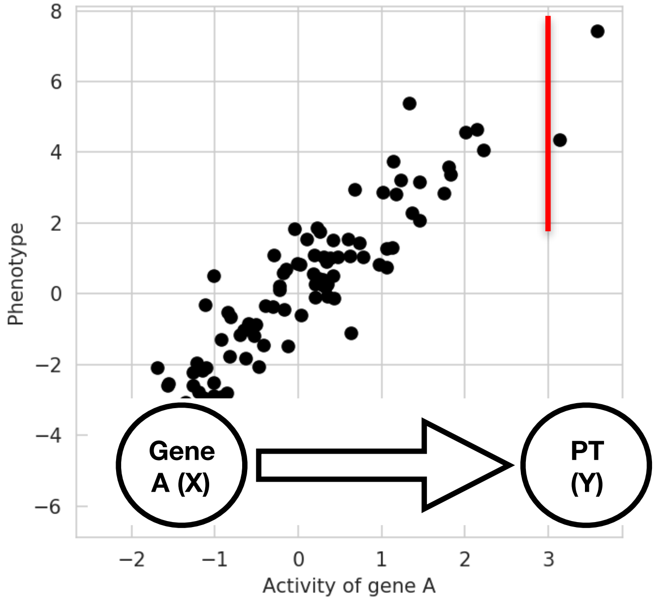
On the cause variable

$$X := N_X \quad \boldsymbol{X := 3}$$

$$Y := 2X + N_Y$$

$$N_Y \sim \mathcal{N}(0, 1)$$

$$\boldsymbol{P\Big(X, Y \Big| do\big(X := 3\big)\Big)} = \mathrm{P}(\mathrm{X}, \mathrm{Y} \mid \mathrm{X}{=}3)$$



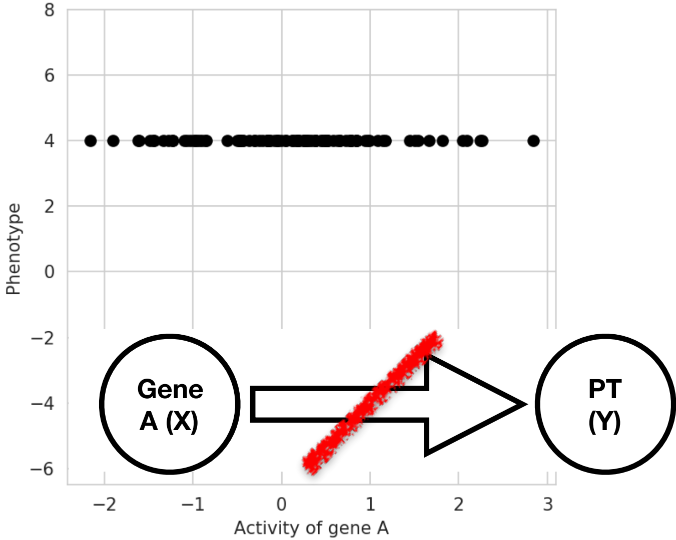
do-intervention

On the effect variable

$$X := N_X$$

$$Y := 2X + N_Y \quad \boldsymbol{Y := 4}$$

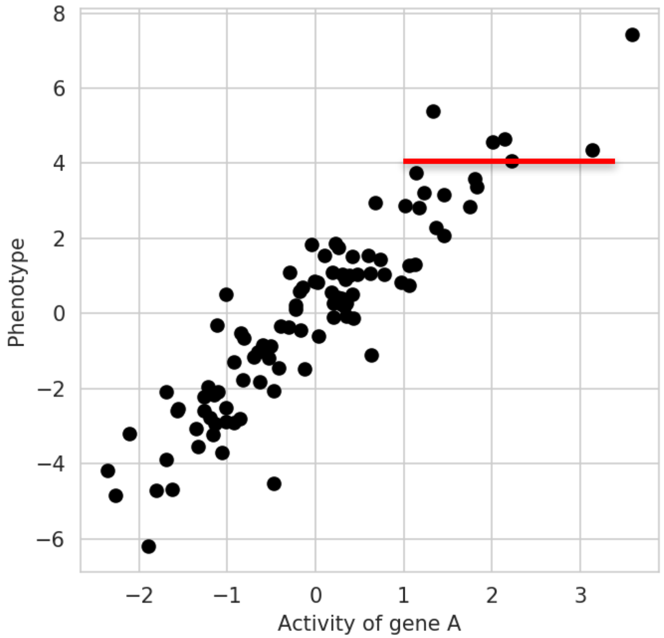
$$N_X \sim \mathcal{N}(0, 1)$$



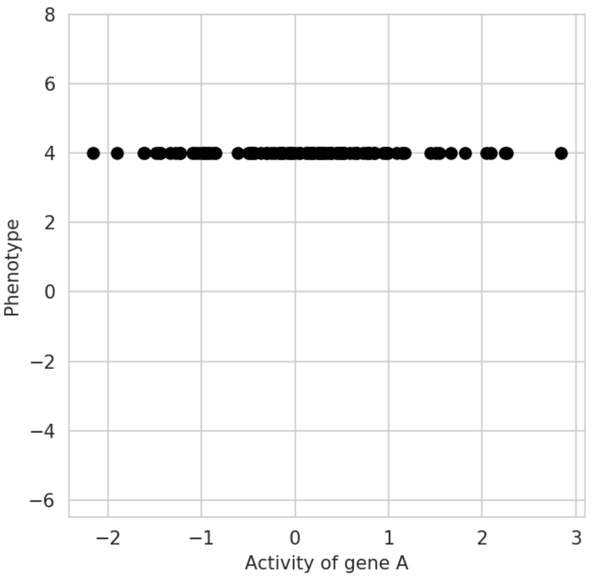
$$\boldsymbol{P\left(X, Y \middle| do(Y := 4)\right)} \neq \mathrm{P(X, Y \mid Y{=}4)}$$

do-intervention v/s conditional probability

On the effect variable



$$\boldsymbol{P\left(X, Y \middle| do(Y := 4)\right)}$$
$$\neq P(X, Y \mid Y = 4)$$



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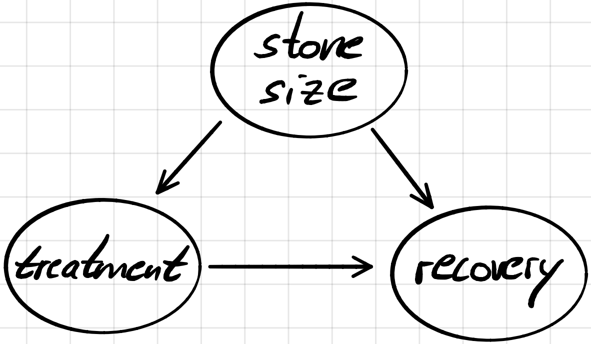


$$S \sim \mathcal{D}_S$$
$$T := f_T(S)$$
$$R := f_R(S, T)$$

S : stone size

R : recovery

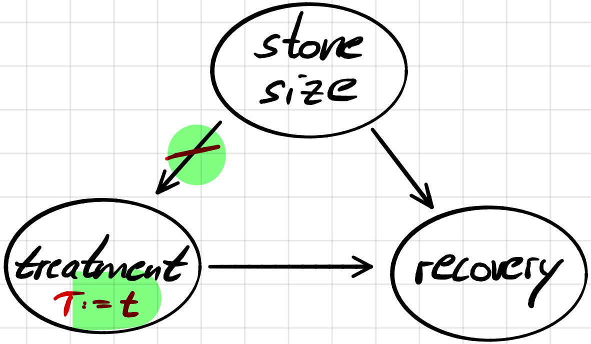
T : treatment

We are interested in $P(R=1 \mid do(T:=t))$, $\quad r, t \in \{0,1\}$

where $t=1$ means „the patients receives the treatment"

$r=1$ means „the patient recovered"

$s=1$ means „the patient's kidney stones are large"



$S \sim \mathcal{D}_S$

$T := t$

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is the ...

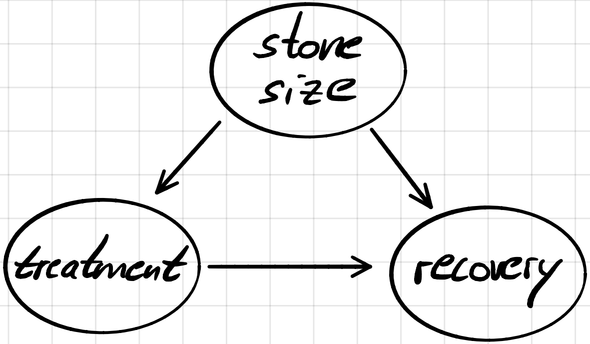
...graphical and ...assignment

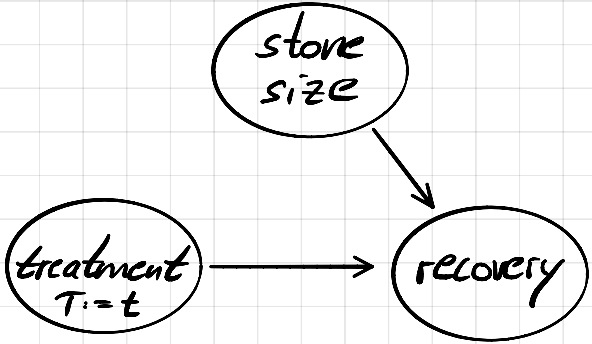
interpretation of

$$P(R = r \mid do(T := t))$$

Overview: we distinguish two structural causal models (SCMs)

graph





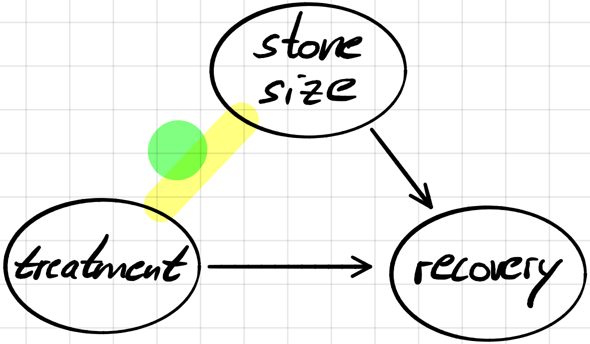
assignments

$$S \sim \mathcal{D}_S \qquad T := f_T(S) \qquad R := f_R(S, T)$$

$$S \sim \mathcal{D}_S \qquad T := t \qquad R := f_R(S, T)$$

we define as $=: \mathcal{M}$ $\qquad$ $= \mathcal{M}^{do(T:=t)} =: \mathcal{M}^T$

$$\Longrightarrow \quad P^{\mathcal{M}}(R=r \mid do(T:=t)) = P^{\mathcal{M}^T}(R=r)$$



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$$P^{\mathcal{M}^T}(R=r) = P^{\mathcal{M}^T}(R=r, T=t)$$

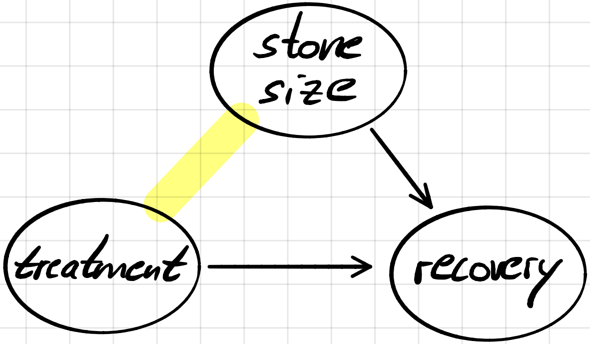
$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r, S=s, T=t)$$

„marginalization"

$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r \mid S=s, T=t)\, P^{\mathcal{M}^T}(S=s, T=t)$$

„def. cond. probab."

$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r \mid S=s, T=t)\, P^{\mathcal{M}^T}(S=s)$$



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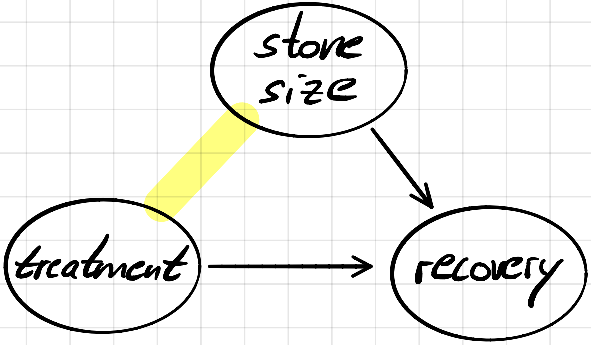
$$= \dots$$

$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r \mid S=s, T=t)\, P^{\mathcal{M}^T}(S=s)$$

$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r \mid S=s, T=t)\, P(S=s)$$

„d-separation"



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$$= \ldots$$

$$= \sum_{s=0}^{1} P^{\mathcal{M}^T}(R=r \mid S=s, T=t)\, P(S=s)$$

„d-separation"

$$= \sum_{s=0}^{1} P(R=r \mid S=s, T=t)\, P(S=s)$$

Replacing letters with numbers

$$P^{\mathcal{M}_T}(R=r) = \sum_{s=0}^{1} P(R=r \mid S=s, T=t)\, P(S=s)$$

Recovery Rates

	Overall	Patients with small stones	Patients with large stones
Treatment a: Open surgery	78% (273/350)	**93%** (81/87)	**73%** (192/263)
Treatment b: Percutaneous nephrolithotomy	**83%** (289/350)	87% (234/270)	69% (55/80)
$P(R=1 \mid T=t)$ / $P(R=1 \mid S=s)$		$88\% \left(\frac{314}{357}\right)$	$72\% \left(\frac{247}{343}\right)$

Charig et al., 1986

$$P(R=1 \mid S=s) = \sum_{t \in \{a,b\}} P(R=1 \mid T=t, S=s)\, P(T=t \mid S=s)$$

$$P(R=1 \mid T=t) = \sum_{\substack{s \in \{small,\\ large\}}} P(R=1 \mid T=t, S=s)\, P(S=s \mid T=t)$$

for $t = A$ $\Rightarrow 0.93 \cdot \frac{87}{350} + 0.73 \cdot \frac{263}{350} \approx 78\%$

$$P(R=1 \mid S=small) = 0.93 \cdot \frac{87}{\underbrace{270+87}_{=357}} + 0.87 \cdot \frac{270}{270+87}$$

$$\approx 0.88$$

$$P(R=1 \mid S=large) = 0.73 \cdot \frac{263}{343} + 0.69 \cdot \frac{80}{343} \approx 0.72$$

$$P^{\mathcal{M}^T}(R=r) = \sum_{s=0}^{1} P(R=r \mid S=s, T=A)\, P(S=s)$$

We need:

$$P(S=\text{small}) = \frac{357}{700} = 0.51$$

$$P(S=\text{large}) = \frac{343}{700} = 0.49$$

We want to compute

$$P^{\mathcal{M}^{T:=A}}(R=1)$$

$$= 0.93 \cdot 0.51 + 0.73 \cdot 0.49 \approx 83\%$$

$$P^{\mathcal{M}^{T:=B}}(R=1)$$

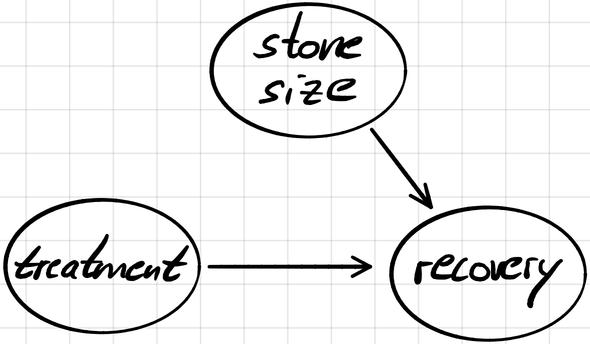
$$= 0.87 \cdot 0.51 + 0.69 \cdot 0.49 \approx 78\%$$

It follows:

$$P^{\mathcal{M}^{T:=A}}(R=1) \approx 83\% > 78\% \approx P(R=1 \mid T=A)$$

$$P^{\mathcal{M}^{T:=B}}(R=1) \approx 73\% < 83\% \approx P(R=1 \mid T=B)$$

$\Rightarrow$ in general, treatment A is better indeed!



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$$P^{\mathcal{M}^T}(R = r)$$

$$= \dots =$$

$$= \sum_{s=0}^{1} P(R = r \mid T = t, S = s)\, P(S = s)$$

$$\neq \sum_{s=0}^{1} P(R = r \mid T = t, S = s)\, P(S = s \mid T = t) = P(R = r \mid T = t)$$

„marginalization"

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JUDEA PEARL

WINNER OF THE TURING AWARD

AND DANA MACKENZIE

THE BOOK OF WHY

α  β

THE NEW SCIENCE OF CAUSE AND EFFECT

The two different schools

Pearl's work is interesting, and many researchers find his arguments that path diagrams are a natural and convenient way to express assumptions about causal structures appealing. In our own work, perhaps influenced by the type of examples arising in social and medical sciences, we have not found this approach to aid drawing of causal inferences.

- Imben and Rubins 2015

Quasi-experiments

Observations **Quasi-experiments** **Interventions**

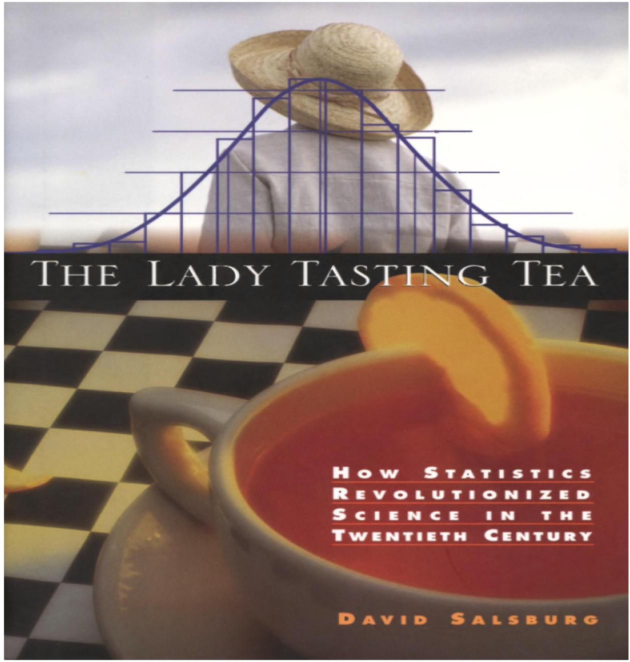
Causal validity

Idea: find something that is locally kinda random

Marinescu, Lawlor, Kording, Nature Human Behavior

Randomised experiments

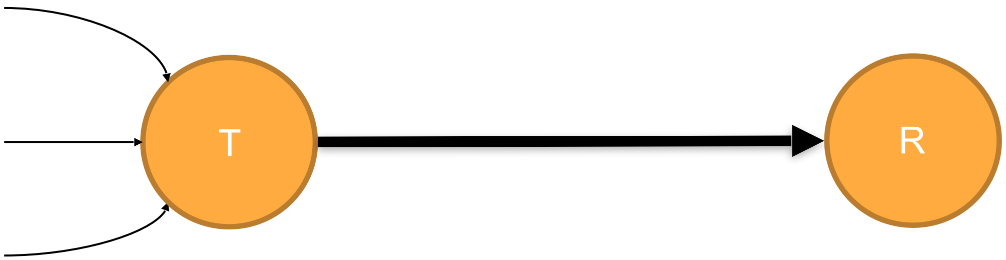
- **Sir Ronald Fisher** was first to propose randomisation in experiments.
- Mystery? A lady asserts that she can taste whether the milk or the tea was added first to a cup.
- Experimental Design:
  - Randomly assign eight cups to 2 conditions:
    - Tea first (control)
    - Milk first (treatment)
  - Ask the lady to discriminate between tea first and milk first



Randomised experiments

Randomised the Teas
(0: add milk first; 1: add tea first)

Lady’s discrimination Result
(0: fail to tell the order; 1: correct)



$$P_{do(T:=0)}(R) = P(R \mid T = 0)$$

Marinescu, Lawlor, Kording, Nature Human Behavior

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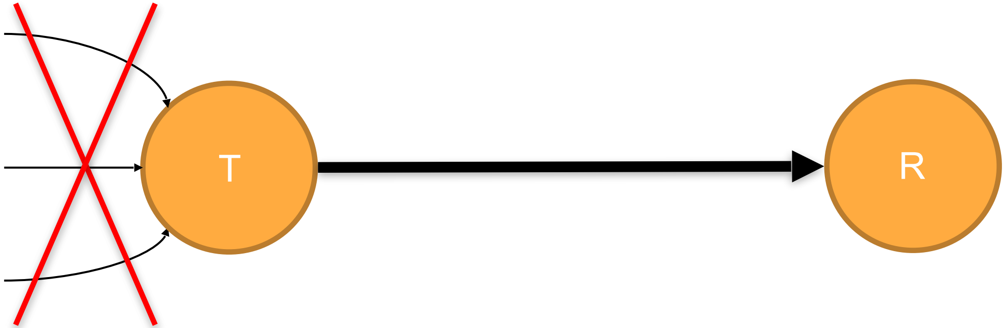

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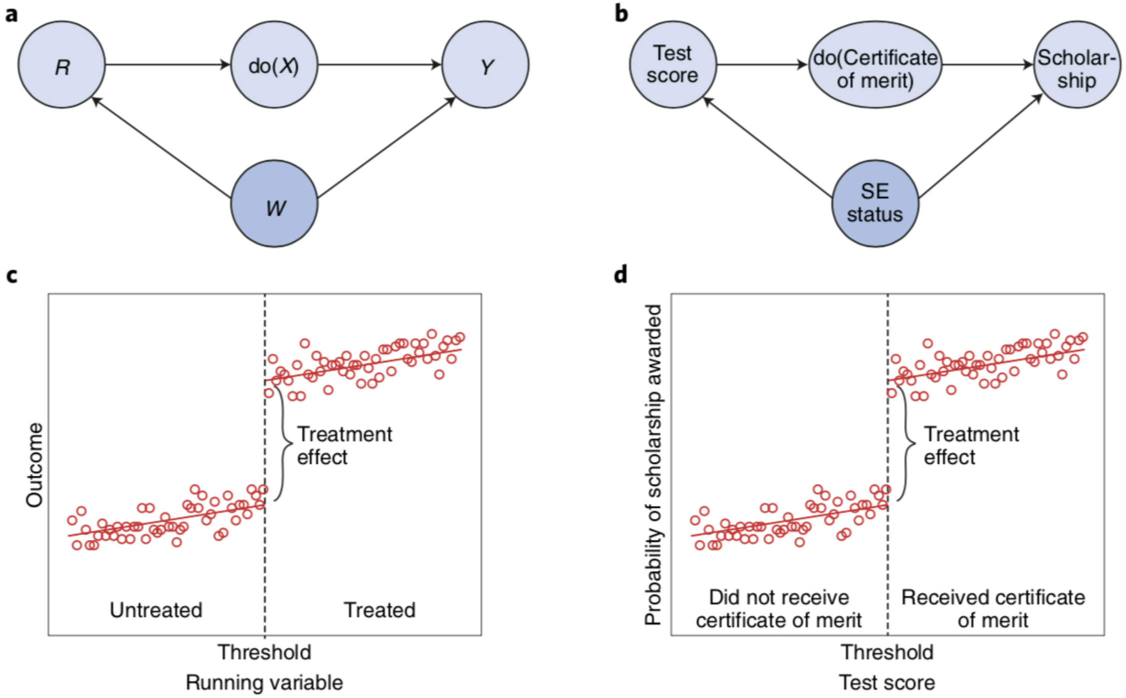
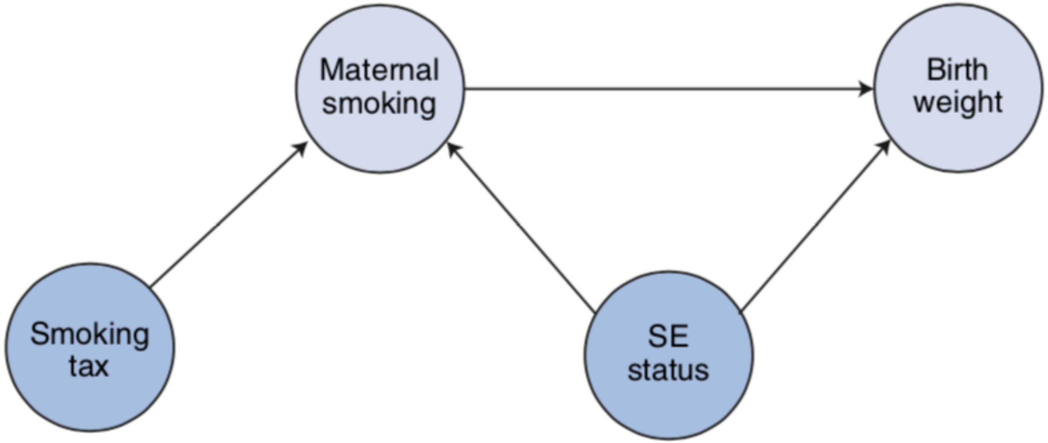
Marinescu, Lawlor, Kording, Nature Human Behavior

Regression Discontinuity Design (RDD)

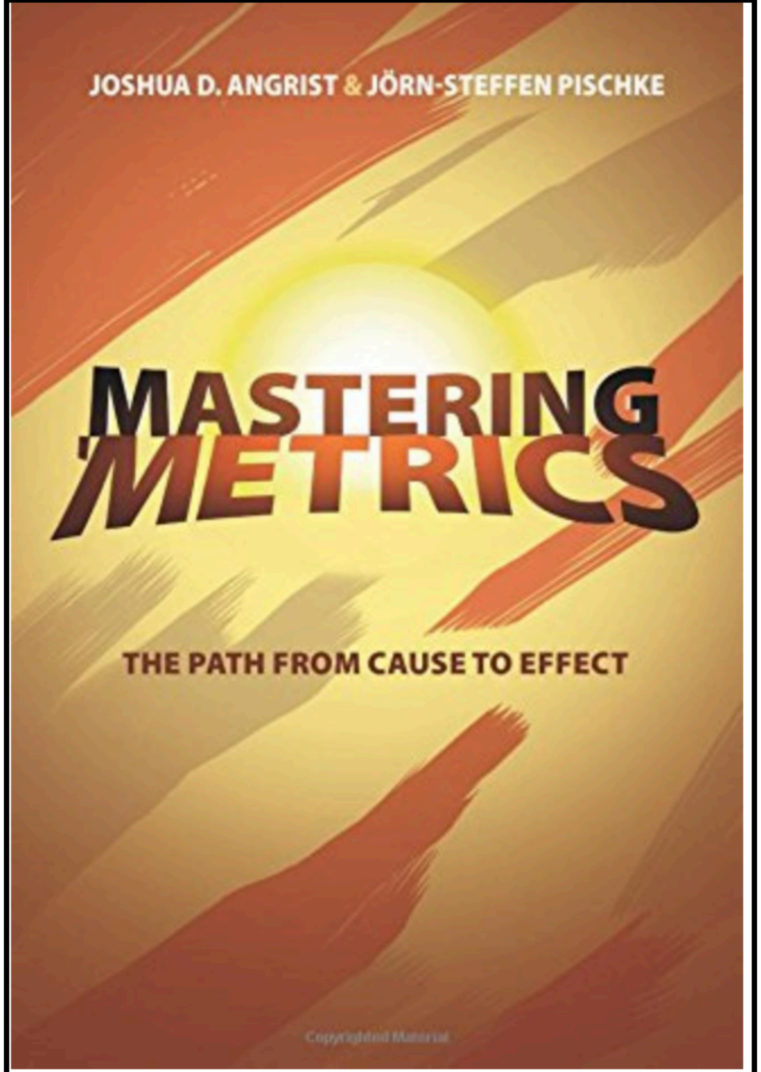


Marinescu, Lawlor, Kording, Nature Human Behavior

Instrumental variable



Marinescu, Lawlor, Kording, Nature Human Behavior


JOSHUA D. ANGRIST & JÖRN-STEFFEN PISCHKE
MASTERING 'METRICS
THE PATH FROM CAUSE TO EFFECT

Promise

- ~~Spurious correlation is everywhere around us~~
- ~~Causality - if you are honest - is what we all of us want!~~
- ~~Confounders: the arch nemesis of causality~~
- ~~Fundamental Math concepts~~
- ~~Formal approach to adjust for confounders and find causal effect~~
- ~~Extend the formal approach to deal with complex systems~~
- Incorporate causal principles to understand the brain

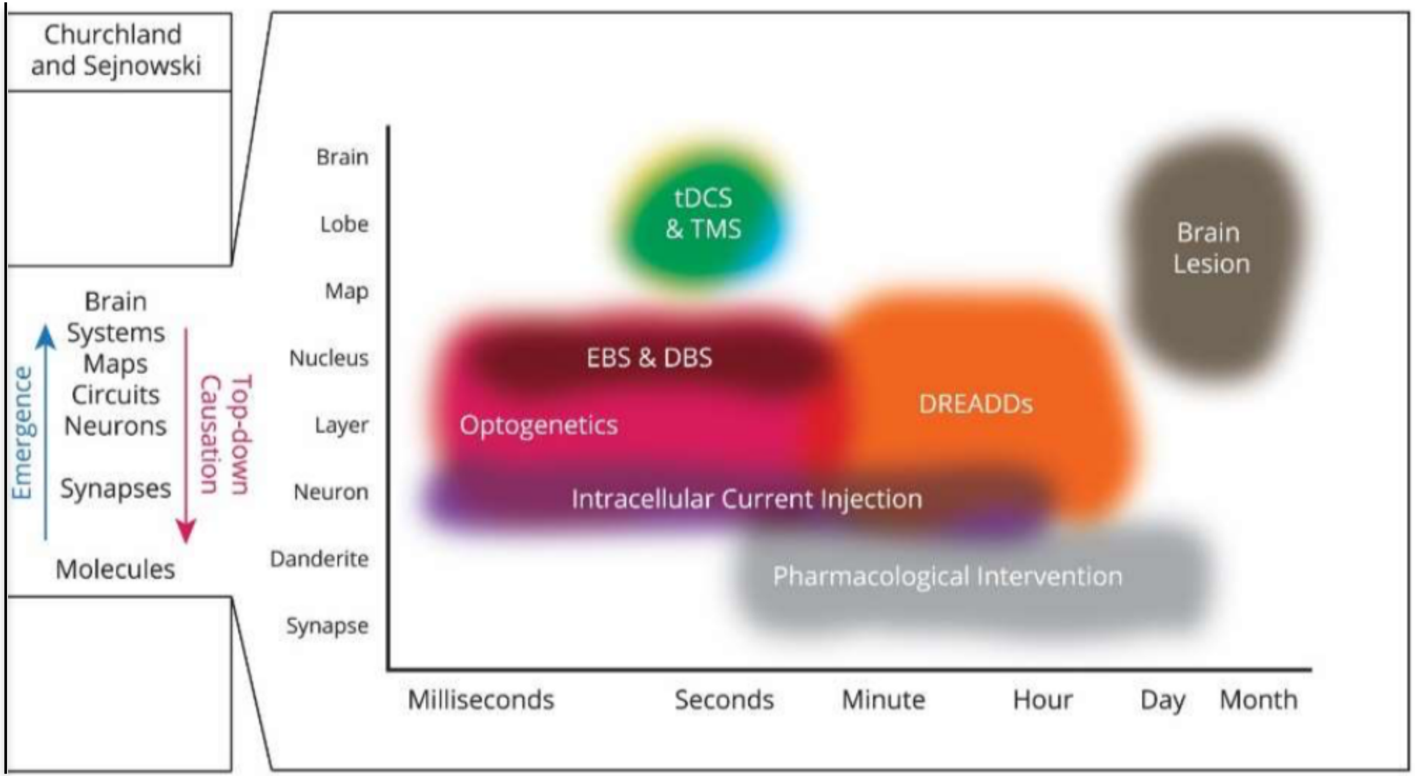
Brain: a complex system

(1) A ton of **reciprocal connections** — mutual causality!

(2) the causal influence from one component to the other may be **only one of many** causal agents;

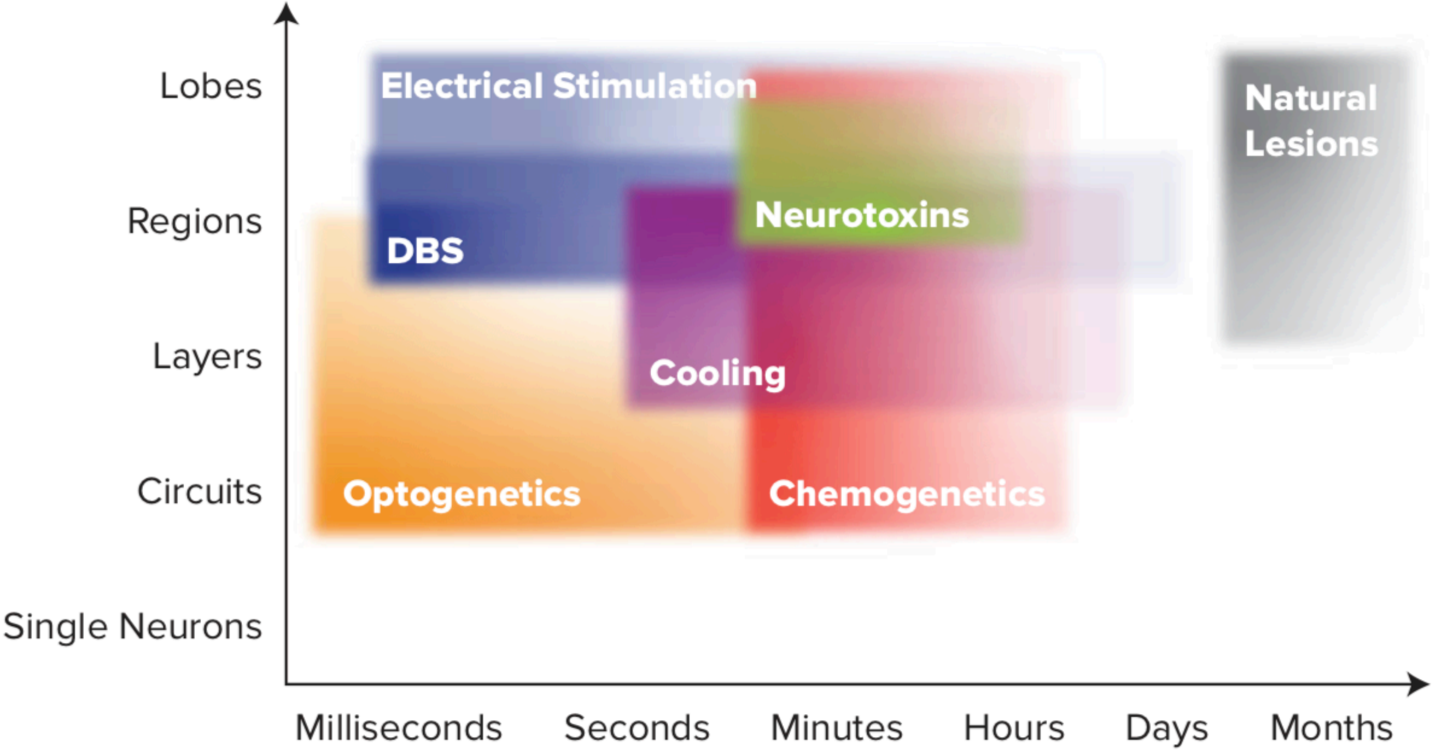
(3) causal influences **do not always** result in observable effects

Need for Interventions



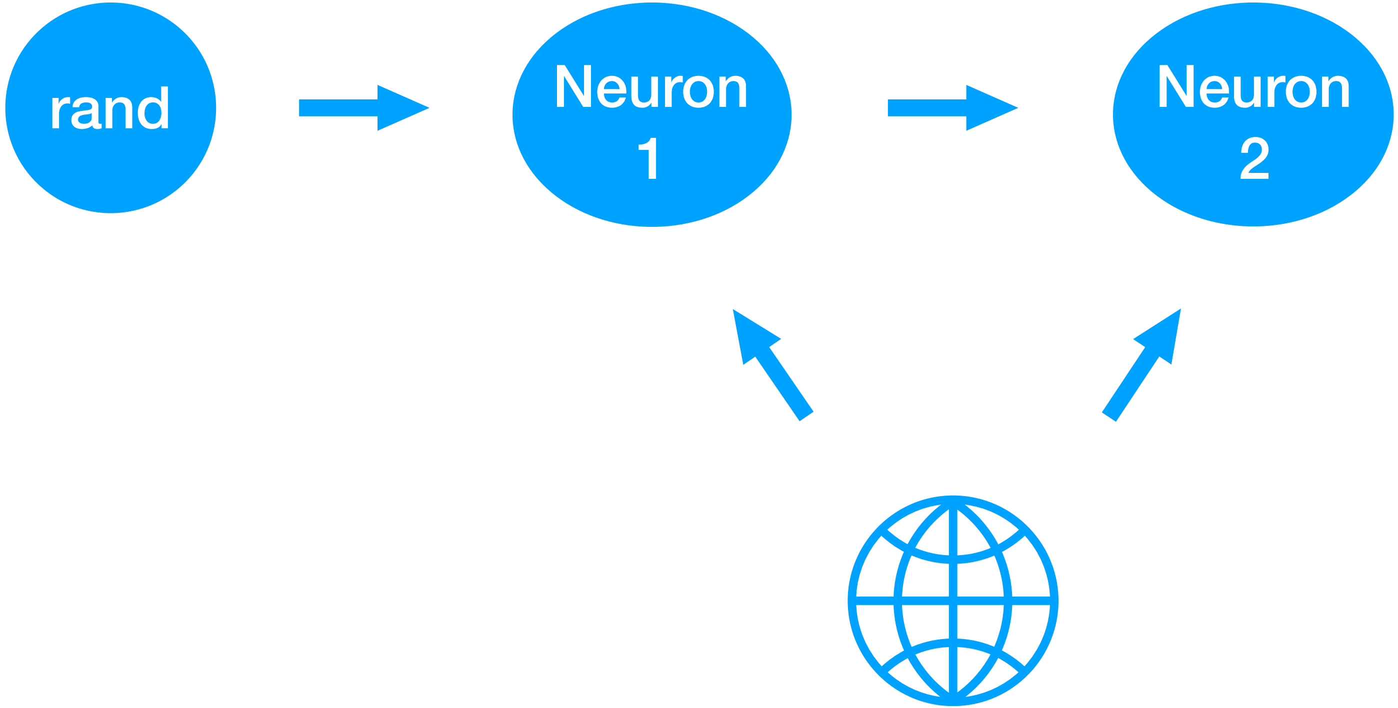
Kayson Fakhar, 2018

Interventions for causal discovery



Kayson Fakhar, et al 2019

Instrumental variable



Konrad and Mikkel Lepperod

Other notions of causality

1. Shannon Entropy

2. Transfer Entropy

3. Granger Causality

4. Dynamic Causal Modelling

4. Difference in Differences

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Take home message

- Be critical and careful with correlations, confounders are everywhere!
- Pearl's do-calculus provides a formal framework but doesn't scale
- Quasi-experiments allow causal estimation in practice
- Brain is a complex system and interventions serves as gold standard for causal discovery.