Identifying Direct and Indirect effects

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Outline

- Basics
- Why DAGs are useful!
- Examples
- Causal?
- Regimes
  - Heuristic
  - Formal
- Definition of effects
- Identification of effects
- Extensions
- Conclusions

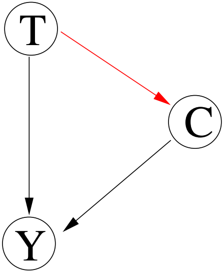
Basics

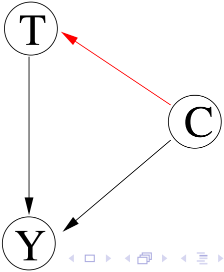
Conditional Independence

$$p(A, C|B) = p(A|B) \times p(B|C) \Rightarrow A \perp\!\!\!\perp B|C$$

DAGs

- Directed Acyclic Graphs
- Encode conditional independence
- More than one can encode same CI - like intuitve DAG for direct and indirect effects.





Basics continued

Notation

- T treatment: 0,1
- F_T treatment assignment: 0,1,$\emptyset$
- C intermediate variable: 0,1
- Y outcome/response variable: y

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F_T: the intervention

- F_T is such that
- $p(T = t|X, F_T = t) = 1$ when $t \neq \emptyset$ and
- $p(T = t|X, F_T = \emptyset) = p(T = t|X)$
  i.e. T is drawn from its "natural" distribution
- F_T is an intervention variable, treatment assignment indicator, regime indicator.
- DAGs with intervention variables = Augmented DAGs

Causality and ADs

Causes=interventions

- In the framework proposed here, causes are equated to intervention
- i.e when $F_T \neq \emptyset$ then we are talking cause!

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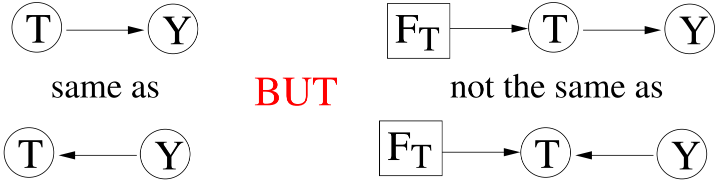

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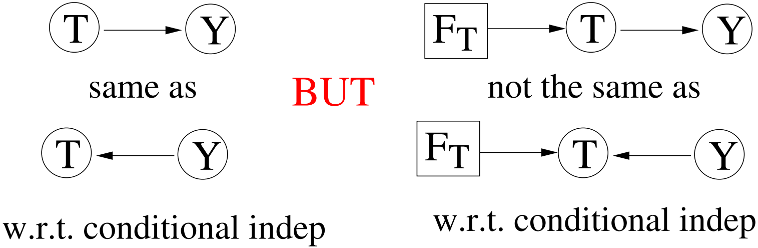

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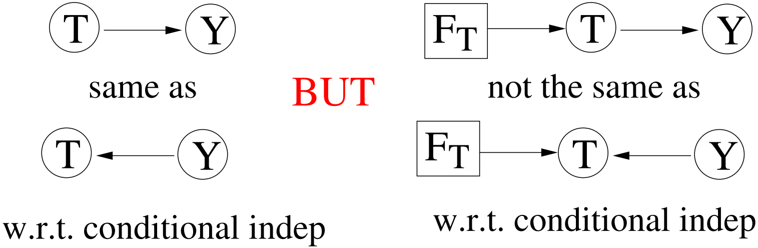
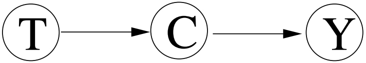


- LHS - T and Y are dependent
- RHS - top says $Y \perp\!\!\!\perp F_T | T$ so T causes Y
- RHS - bottom says $Y \perp\!\!\!\perp F_T$ so T does not cause Y

DAGs are useful for direct and indirect effects

(i)



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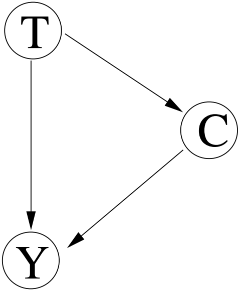
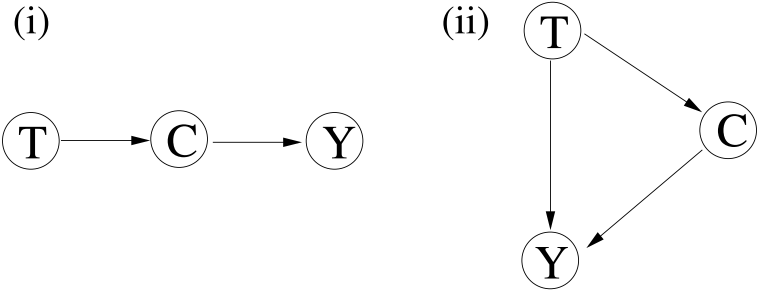


The DAGs mean something!

(i) says $T \perp\!\!\!\perp Y | C$ i.e. if we know C, T cannot tell us anything more about Y

DAGs are useful for direct and indirect effects



The DAGs mean something!

(i) says $T \perp\!\!\!\perp Y | C$ i.e. if we know C, T cannot tell us anything more about Y

(ii) says nothing ... but that silence speaks volumes! We can extract more out of it if we add more variables - see how later

Rubin's data are dodgy

Fraction of Population	Potential Outcomes $C(1)$	$C(0)$	$Y(1)$	$Y(0)$	Observed Data T	C_{obs}	Y_{obs}
1/4	3	2	10	9	0	2	9
1/4	3	2	10	10	1	3	10
1/4	4	3	12	11	0	3	11
1/4	4	3	12	12	1	4	12

- Our response to every possible treatment is set in stone (like e.g. sex,genetic make-up)
- Everything is determined - only random aspect is which responses we get to see
- BUT do red values really exist? I think not!

Rubin's data are dodgy continued

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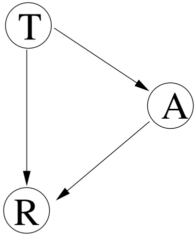
of Population	$C(1)$	$C(0)$	$Y(1)$	$Y(0)$	T	C_{obs}	Y_{obs}
1/4	3	2	10	[illegible]	0	2	9
1/4	3	[illegible]	[illegible]	10	1	3	10
1/4	4	[illegible]	[illegible]	11	0	3	11
1/4	[illegible]	3	12	[illegible]	1	4	12

- What we know is what we see!
- What we see seems to say treatment worse than control.
- This could be wrong of course by bad luck or because we need to account for biases etc.

Example 1: side-effects

Story

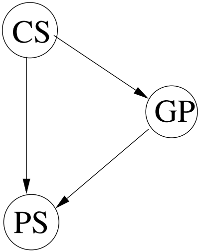
- A drug has strong head-aches as a side-effect
- Patients take aspirin to alleviate this
- It is thought that the aspirin might affect the outcome
- Drug company wants to know what are direct/indirect effects?



Example 2: cost sharing

Story

- Many health insurance companies (HIC) have cost-sharing (CS) schemes
- HIC pay some of treatment, patient pays rest
- Does this discourages people from
  - directly seeking preventive services for say cancer
  - visiting GP and getting referred to preventive services?



Causal?

Remember Causes=interventions

- i.e. sex, genes, age, race are not causes!!
- ....except perhaps with fruit flies
- instead treatment, information, education are potential causes

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C can be intervened upon

- For there to be a direct/indirect effect, it must be possible to intervene on C
- Ex 1: aspirin intake of patients can in principle be controlled
- Ex 2: GP visits can be encouraged or even set-up

Identifiable?

Problem

- OK C can be intervened upon in principle....
- but in practice often not possible:
- cannot deny a patient with head-ache pain relief
- even if set up appointments with GP people might not want to go!

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- It all depends on the conditional independences!
- Using these and some cunning, we can identify the direct and indirect effects

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Solution

- It all depends on the conditional independences!
- Using these and some cunning, we can identify the direct and indirect effects
- and often estimate them using data that are purely observational!

Direct & indirect effects: a heuristic overview

The type of direct and indirect effect you get depends on what you do to C

Ways of manipulating C

- Fix C

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Ways of manipulating C

- Fix C
- Draw C from $p(C|T)$
- Draw C from an appropriate distribution

Each one of these manipulations can be described by a regime.

Fixing regime: heuristic

Ex 1: imaginary experiment

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- then can estimate the direct effect of treatment for 2 levels of aspirin and some kind of indirect effect by comparing the two direct effects.

Problems

- Not ethical!
- Not realistic – people “out there” in the population do not behave like this.

Drawing C from $p(C|T)$ regime: heuristic

Ex 1: imaginary experiment

- One random group of patients are given the control $F_T = 0$ and we record their “natural” aspirin intake $p(C|F_T = 0)$

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- This way we can compare direct effects fixing not the aspirin intake, rather its distribution to that of the control treatment

Problem

- Not ethical!

Drawing C from $p(C^*)$ regime: heuristic

Ex 1: imaginary experiment

- We cannot estimate $p(C|T)$ - lack of funds!
- So we pick a suitable distribution $p(D)$ such that domain of C is same as D.
  - If a patient gets $F_T = 1$, they are administered aspirin according to $p(D)$
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- In this case, the comparison is not as easily interpretable, but we can still get a handle on the direct and indirect effects.

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Standardisation

- The 2^{nd} and 3^{rd} regimes are forms of direct standardisation.

Formal definition of Regimes

Manipulating C

- Define M_C the variable of manipulations of C
- M_C has 4 regimes:
  1. $\mathbf{M_C} = \mathbf{c}$: C is left alone and comes from $p(C|T=t, F_T=\emptyset, M_C=\emptyset) = P_t$

Formal definition of Regimes

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  3. $\mathbf{M_C} = \mathbf{t}^*$: C is drawn from $p(C|F_T = \emptyset, M_C = t^*) = P_t$

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  2. $\mathbf{M_C} = \mathbf{c}$: C is set to c with no uncertainty, distribution of C is δ_c
  3. $\mathbf{M_C} = \mathbf{t}^*$: C is drawn from $p(C|F_T = \emptyset, M_C = t^*) = P_t$
  4. $\mathbf{M_C} = \mathbf{D}$: C is drawn from $p(D) = P_D$
- Note that Regime 2 is a special case of regime 3 which in turn is a special case of regime 4.

Formal definition of Regimes continued

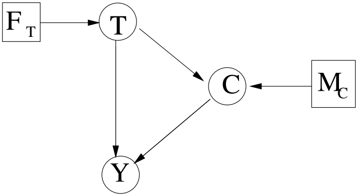
Conditional independences

$$(Y, C) \perp\!\!\!\perp F_T | T; \quad (1)$$

$$Y \perp\!\!\!\perp M_C | (C, T); \quad (2)$$

$$C \perp\!\!\!\perp (F_T, T) | M_C \neq \emptyset. \quad (3)$$

Equation 3 only for regimes 2-4



Now the DAG speaks!

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- The framework of these regimes is determined by M_C as defined
- Adding other variables might require a redefinition of M_C
- As there are only 3 variables we consider here, we call this the 3DI framework
- Extensions are quite straightforward, might show some later

Definition of direct & indirect effects

DE for C set at c - Set effect (SE_c)

The direct effect of $F_T = t$ with respect to baseline $F_T = t^*$ on response Y for C set at c is given by

$$E(Y|F_T = t, M_C = c) - E(\quad |F_T = t^*, M_C = c). \tag{4}$$

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DE for C drawn from P_{t^*}: Generated effect (GDE_{t^*})

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$$\equiv E(Y|F_T = t, M_C = t^*) - E(Y|F_T = t^*, M_C = \emptyset). (5)$$

Definition of direct & indirect effects cont

DE for C drawn from P_D: Generated effect (GDE_D)

The direct effect of $F_T = t$ with respect to the baseline $F_T = t^*$ on response for C drawn from a specified distribution over D is given by:

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Total effect: TE

The total effect of $F_T = t$ with respect to the baseline $F_T = t^*$ on response is given by

$$E(Y|F_T = t) - E(Y|F_T = t^*). \tag{7}$$

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IDE for C drawn from P ($P \in \{\delta_c, P_{t^*}, P_D\}$)

$$IDE = DE - TE$$

Identifying effects in 3DI

- The TE is always identifiable, even when $F_T = \emptyset$ if there are no confounders
- If we can identify the DE then it follows we can identify the IDE, so focus is on DE
- We look first at scenario where there are no confounders and $F_T \neq \emptyset$
- Then consider what happens if there are confounders i.e. when

$$Y \perp\!\!\!\perp M_C | (C, T)$$

  does not hold
- AND $F_T = \emptyset$.

Identifying SE_c

The set effect is easy:

$$\begin{aligned} &E(Y|F_T = t, M_C = c) \\ &\quad = E(Y|F_T = t, C = c, M_C = c) \end{aligned} \tag{8}$$

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& \quad = E(Y|F_T = t, C = c, M_C = \emptyset) && (9)
\end{aligned}
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& \quad = E(Y|T = t, F_T = \emptyset, C = c, M_C = \emptyset) && (10)
\end{aligned}
$$

- from (8)-(9) by (4)
- from (9)-(10) by (3)

Identifying GDE_{t^*}

$$GDE_{t^*} = \underbrace{E(Y|F_T = t, M_C = t^*)}_{(a)} - \overbrace{E(Y|F_T = t^*, M_C = \emptyset)}^{(b)}$$

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(b) is easy $= E(Y|T = t^*, F_T = \emptyset, M_C = \emptyset)$ by (3)

$(a) =$

$$= \sum_c E(Y|F_T = t, C = c, M_C = t^*)p(C = c|F_T = t, M_C = t^*) \quad (11)$$

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$$= \sum_c E(Y|F_T = t, C = c, M_C = \emptyset)p(C = c|M_C = t^*) \quad (12)$$

$$= \sum_c E(Y|T = t, F_T = \emptyset, C = c, M_C = \emptyset) \times p(C = c|T = t^*, M_C = \emptyset) \quad (13)$$

- from (11)-(12) by (4)
- from (12)-(13) by (3)

Identifying continued

GDE_D is identified in same way as GDE_{t*} with P_D replacing P_{t*}

Pros

- So it is possible to identify and hence estimate the 3DI effects from data that are purely observational for both T and C as F_T and M_C are both $\emptyset$.

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Cons

- No counfounder assumption is unlikely to hold in practice

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Confounder between T and C or T and Y

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- In this situation it is necessary to observe the confounders - if the are unobserved, we're in trouble

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- In this situation it is necessary to observe the confounders - if the are unobserved, we're in trouble
- If observed, we treat them as usual - condition and sum over

Identifying with confounders

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Confounder between C and Y

- This requires a redefiniton of M_C as the distribution of C now depends on this confounder - call it W as well as T.

W confounder between C and Y

W is a niusance

- Ex 1: Two doctors administer the treatment.

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- Ex 2: W is information about breast cancer. Women with a family history of cancer are more likely to seek preventive services and see the GP
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W as sex

Just consider this - the other case in the paper

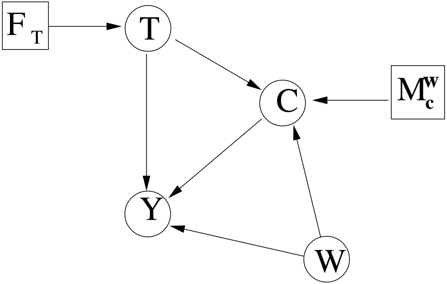
New variable and conditional independence - 4DI

Define M_C^W as a manipulation variable on C s.t.

$$(Y, C, W) \perp\!\!\!\perp F_T | T \quad (14)$$

$$W \perp\!\!\!\perp (F_T, M_C^W) \quad (15)$$

$$Y \perp\!\!\!\perp M_C^W | (T, C, W). \quad (16)$$



W as sex continued

Regimes of M_c^w

1. $M_c^w = \emptyset$: C is left alone
2. $M_c^w = t^*$: C is drawn from $p(C | T = t^*, W = w, F_T = \emptyset)$ where w corresponds to the realised value of W.

W as sex continued

Regimes of M_C^W

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2. $M_C^W = t^*$: C is drawn from $p(C|T = t^*, W = w, F_T = \emptyset)$ where w corresponds to the realised value of W.

- No need for other regimes as they sever relationship between C and W and are equivalent to 3DI
- that means that there is only 1 extra DE
- Regime 2 induces

$$C \perp\!\!\!\perp (F_T, T) | M_C^W = t^* \tag{17}$$

Identifying DE's

We want the woman ($W = 1$) specific GDE_{t^*}

$$E(R|F_T = t, M_C^W = t^*, W = 1) - E(R|F_T = t^*, M_C^W = t^*, W = 1)$$
$$= \sum_c [E(R|F_T = t, M_C^W = \emptyset, W = 1, C = c)$$

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$$
\begin{aligned}
& E(R|F_T = t, M_C^W = t^*, W = 1) - E(R|F_T = t^*, M_C^W = t^*, W = 1) \\
& \quad = \sum_c [E(R|F_T = t, M_C^W = \emptyset, W = 1, C = c) \\
& \qquad \times p(C = c|F_T = t^*, M_C^W = \emptyset, W = 1)]
\end{aligned}
$$

Identifying DE's

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\begin{aligned}
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= \sum_c [E(R|F_T = t, M_C^W = \emptyset, W = 1, C = c) \\
\times p(C = c|F_T = t^*, M_C^W = \emptyset, W = 1)] \\
- E(R|F_T = t^*, M_C^W = \emptyset, W = 1).
\end{aligned}
$$

This can be further expressed with $F_T = \emptyset$ and can thus also be estimated from purely observational data.

Conclusions

- DAGs and conditional independences are useful
- It does make sense to talk about direct and indirect effects
- We need to be clear about what is going on though - what CI's hold?
- Provided we do this, we have a wealth of DEs we can estimate
- The reason that the idea can be confusing is because of the different types of DEs
- Also remember that the concepts don't make much sense if we cannot intervene on the intermediate.
- The 3DI and 4DI are tools that can be used to clarify what we mean.
- The framework can be extended further.

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