An Interventionist Approach to Mediation Analysis

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基础信息

- 该论文的基础信息
  - 论文作者：James Robins
  - 提出了FFRCISTG，G-formula等工作，在因果推断领域有很大贡献。

James M. Robins

FOLLOW

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Verified email at hsph.harvard.edu

TITLE	CITED BY	YEAR
Marginal structural models and causal inference in epidemiology JM Robins, MA Hernan, B Brumback Epidemiology 11 (5), 550-560	3824	2000
Causal diagrams for epidemiologic research S Greenland, J Pearl, JM Robins Epidemiology, 37-48	2714	1999
Estimation of regression coefficients when some regressors are not always observed JM Robins, A Rotnitzky, LP Zhao Journal of the American statistical Association 89 (427), 846-866	2210	1994
Causal diagrams for empirical research J Pearl Biometrika 82 (4), 669-688	1848	1995
A structural approach to selection bias MA Hernán, S Hernández-Díaz, JM Robins Epidemiology, 615-625	1813	2004
A new approach to causal inference in mortality studies with a sustained exposure period—application to control of the healthy worker survivor effect J Robins Mathematical modelling 7 (9-12), 1393-1512	1748	1986
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论文背景

- Robins认为Pearl的NPSEM-IE(nonparametric structure equation model with independent errors)的模型对于counterfactual因果模型的描述不够精确。该文章主要详细阐述了中介分析的一种新视角。

- Robins认为自己在该论文中提出的interventionist方法在实际中更能被各个领域的专家所接受。同时也能更好的看出中介分析识别性的一些假设。

以往的进展

- 该文章主要基于Robins的FFRCISTG(finest fully randomized causal interpreted structural tree model)/SWIG(Single World Intervention Graph)以及Pearl的NPSEM-IE。关于中介分析，之前往往关心下面一些参数。

- 如果将处理A和中介变量都看成处理，则可定义CDE(controlled direct effect):

- $CDE_{a,a'}(m) = E[Y(a',m) - Y(a,m)]$

- 另一个则是PDE(pure direct effect)或NDE(natural direct effect)

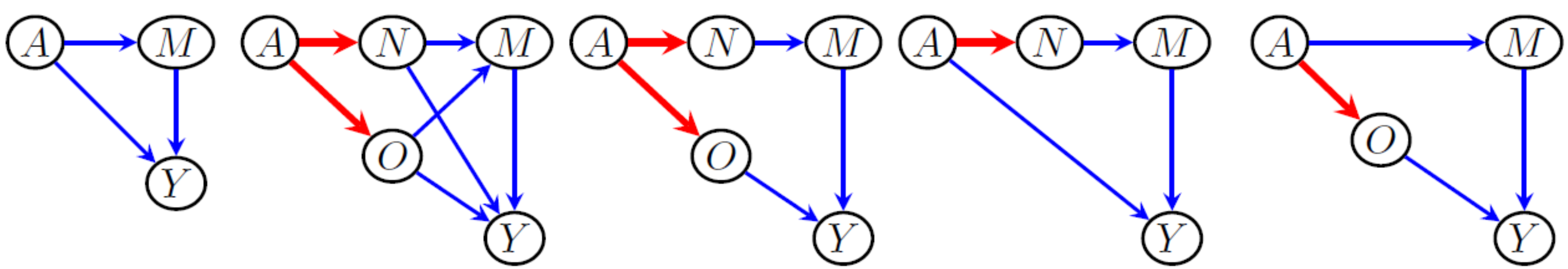
- $PDE_{a,a'} = E[Y\left(a',M(a)\right) - Y\left(a,M(a)\right)]$

解决的科学问题

- 先分析了CDE和PDE的识别性问题。
- 然后提出了基于干预的中介分析新框架。
- 并给出了识别性的一些定理。

解决问题的思路

- Robins在该文章中的想法是：将处理A分解成两部分N和O，其中N对中介变量M有作用，而O对结局变量Y有作用。



(a) (b) (c) (d) (e)

背景知识

- Pearl的图模型与Robins 的FFRCISTG模型

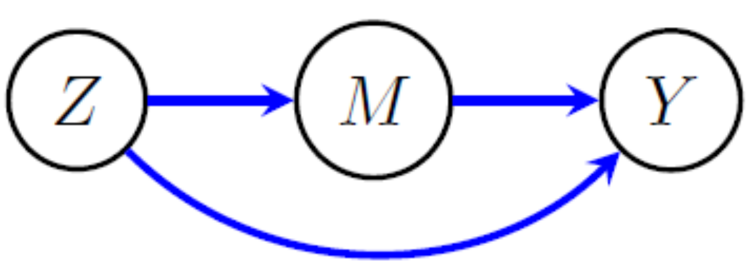
Definition 1 (NPSEM Counterfactual Existence Assumption)**.**

(i) *For each variable* $V \in \mathbf{V}$ *and assignment* $\widetilde{\mathbf{pa}}$ *to* $\mathrm{pa}_{\mathcal{G}}(V)$*, the parents of* V *in* $\mathcal{G}$*, we assume the existence of a counterfactual variable* $V(\widetilde{\mathbf{pa}})$*.*

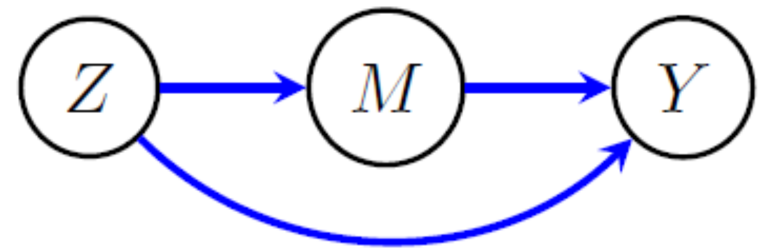
(ii) *For any set* $\mathbf{R}$*, with* $\mathbf{R} \neq \mathrm{pa}_{\mathcal{G}}(V)$*,* $V(\tilde{\mathbf{r}})$ *is defined recursively via:*

$$V(\tilde{\mathbf{r}}) = V\left(\tilde{\mathbf{r}}_{(\mathrm{pa}_{\mathcal{G}}(V)\cap\mathbf{R})}, (\mathbf{PA}_V \setminus \mathbf{R})(\tilde{\mathbf{r}})\right), \tag{14}$$

where $(\mathbf{PA}_V \setminus \mathbf{R})(\tilde{\mathbf{r}}) \equiv \{V^*(\tilde{\mathbf{r}}) \mid V^* \in \mathrm{pa}_{\mathcal{G}}(V), V^* \notin \mathbf{R}\}$.



背景知识



- Pearl的图模型与Robins 的FFRCISTG模型

Definition 2 (FFRCISTG Independence Assumption[27]).

For every $\mathbf{v}^\dagger$, *the variables* $\left\{ V(\mathbf{pa}_V^\dagger) \;\middle|\; V \in \mathbf{V},\ \mathbf{pa}_V^\dagger = \mathbf{v}^\dagger_{\mathrm{pa}_{\mathcal{G}}(V)} \right\}$ (17)

are mutually independent.

The NPSEM-IE model is the submodel of the FFRCISTG obeying the stronger independence assumption:[28]

Definition 3 (NPSEM-IE Independence Assumption).
The variables $\{\epsilon_V \mid V \in \mathbf{V}\}$ *are mutually independent.*
This is equivalent to:

The sets of variables $\left\{ \{V(\mathbf{pa}_V^\dagger) \mid \textit{for all } \mathbf{pa}_V^\dagger\} \;\middle|\; V \in \mathbf{V} \right\}$ (18)

are mutually independent.

背景知识

- 例子

- 在FFRCISTG模型下，我们假设

$$Z \perp M(z) \perp Y(z,m)$$

- 而在NPSEM-IE模型下，我们假设

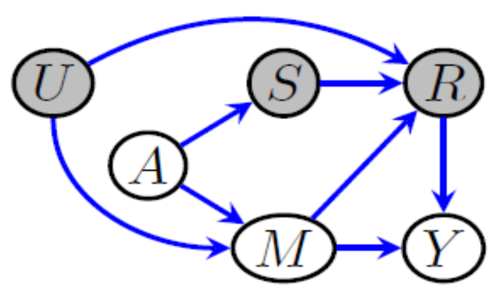
$$Z \perp \{M(z=0), M(z=1)\} \perp \{Y(z,m)\ for\ all\ z,m\}$$

- 例如在NPSEM-IE模型假设中，有$M(1) \perp Y(0,m)$，而该条件在FFRCISTG模型中并不一定成立。

- 例子
- 在FFRCISTG模型下，我们假设 $Z \perp M(z) \perp Y(z,m)$
- 而在NPSEM-IE模型下，我们假设 $Z \perp \{M(z=0), M(z=1)\} \perp \{Y(z,m)\ for\ all\ z,m\}$
- 例如在NPSEM-IE模型假设中，有$M(1) \perp Y(0,m)$，而该条件在FFRCISTG模型中并不一定成立。

背景知识

- Robins and Richardson的SWIG图模型，是一种表示方式，能够更直观的看出变量之间的相关关系。



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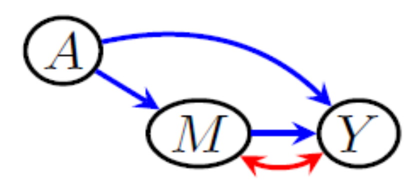

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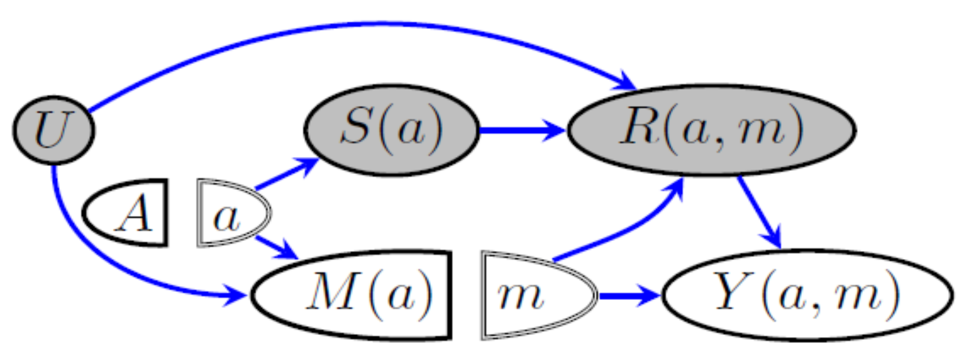

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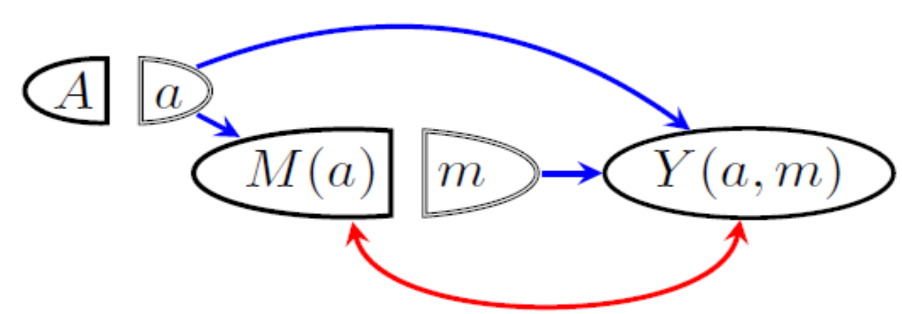


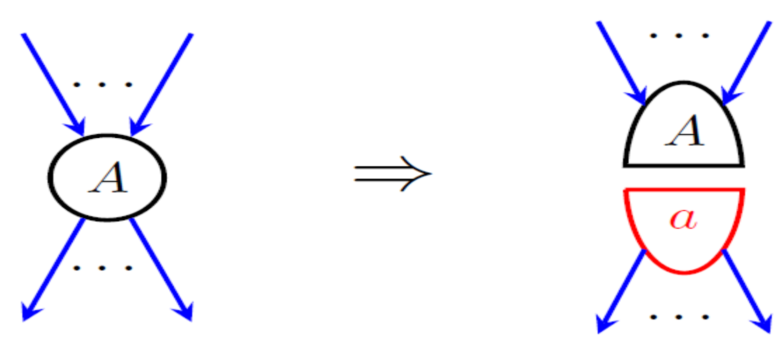
(b^*)

背景知识

- 构造SWIG的方法。

The SWIT $\mathcal{G}(\mathbf{a})$ resulting from intervening to set the variables in $\mathbf{A}$ to $\mathbf{a}$ in a directed acyclic graph $\mathcal{G}$ with vertex set $\mathbf{V}$ is constructed in two steps as follows:

(1) *Split Nodes*: For every $A \in \mathbf{A}$ split the node into a random and fixed component, labelled A and a respectively, as follows:



Splitting: Schematic Illustrating the Splitting of Node A

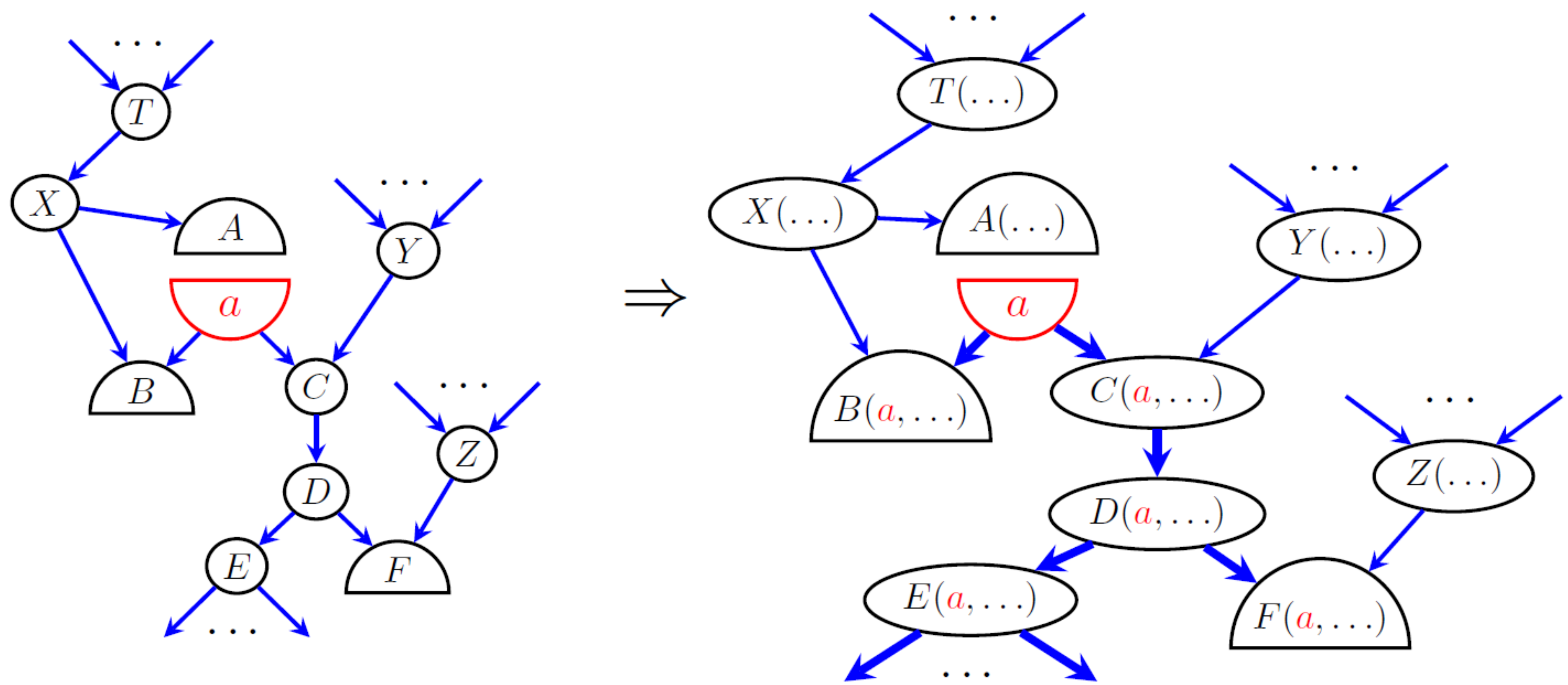
Thus the random half inherits all edges directed into A in $\mathcal{G}$; the fixed half inherits all edges directed out of A.

Let the resulting graph be $\mathcal{G}^*$. For each random vertex V in $\mathcal{G}^*$, let $\mathbf{a}_V$ denote the subset of fixed vertices that are ancestors of V in $\mathcal{G}^*$.

背景知识

(2) *Labeling:* For every random node V in $\mathcal{G}^*$, label it with $V(\mathbf{a}_V)$ (see the schematic below).

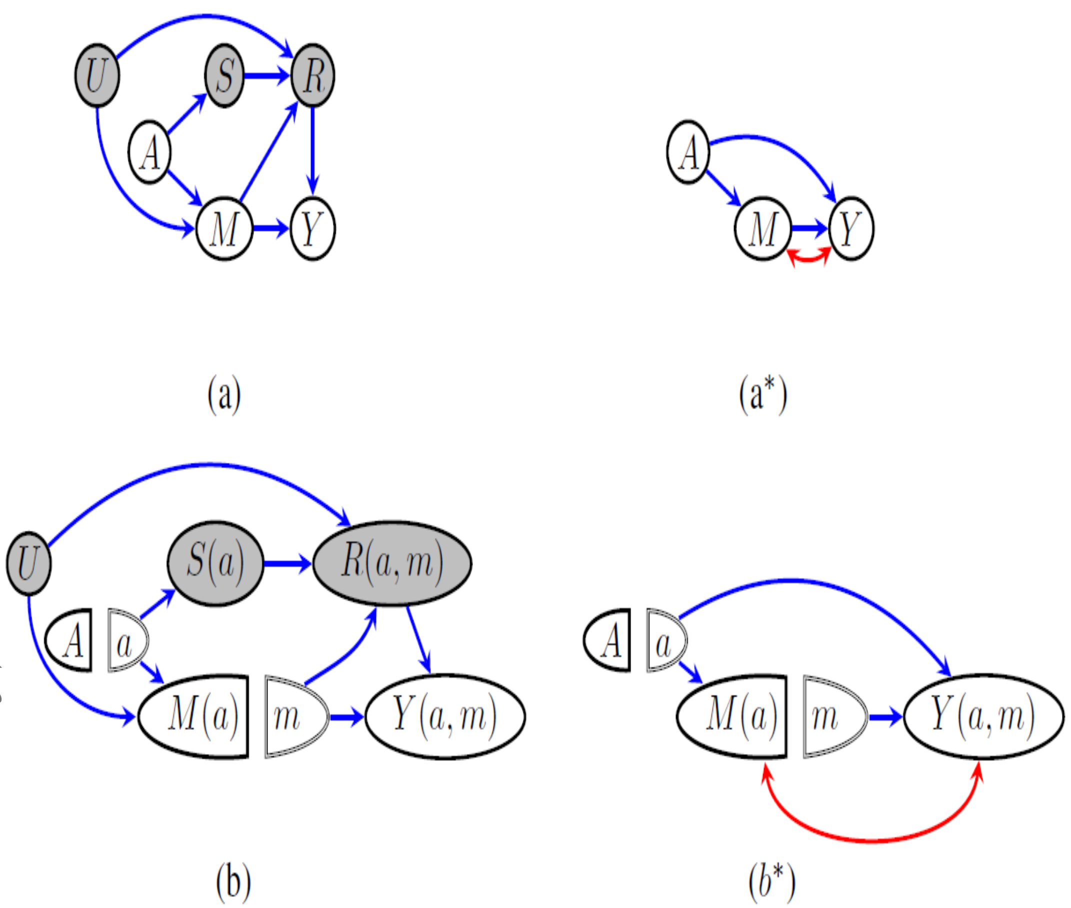
It is implicit here that if $\mathbf{a}_V = \emptyset$ then $V(\mathbf{a}_V) = V$. The resulting graph is the SWIT $\mathcal{G}(\mathbf{a})$. Let $\mathbb{V}(\mathbf{a}) \equiv \{V(\mathbf{a}_V) \mid V \in \mathbf{V}\}$ be the set of random vertices in $\mathcal{G}(\mathbf{a})$.



labeling: Schematic showing the nodes $V(\mathbf{a}_V)$ in $\mathcal{G}(\mathbf{a})$ for which $a \in \mathbf{a}_V$.

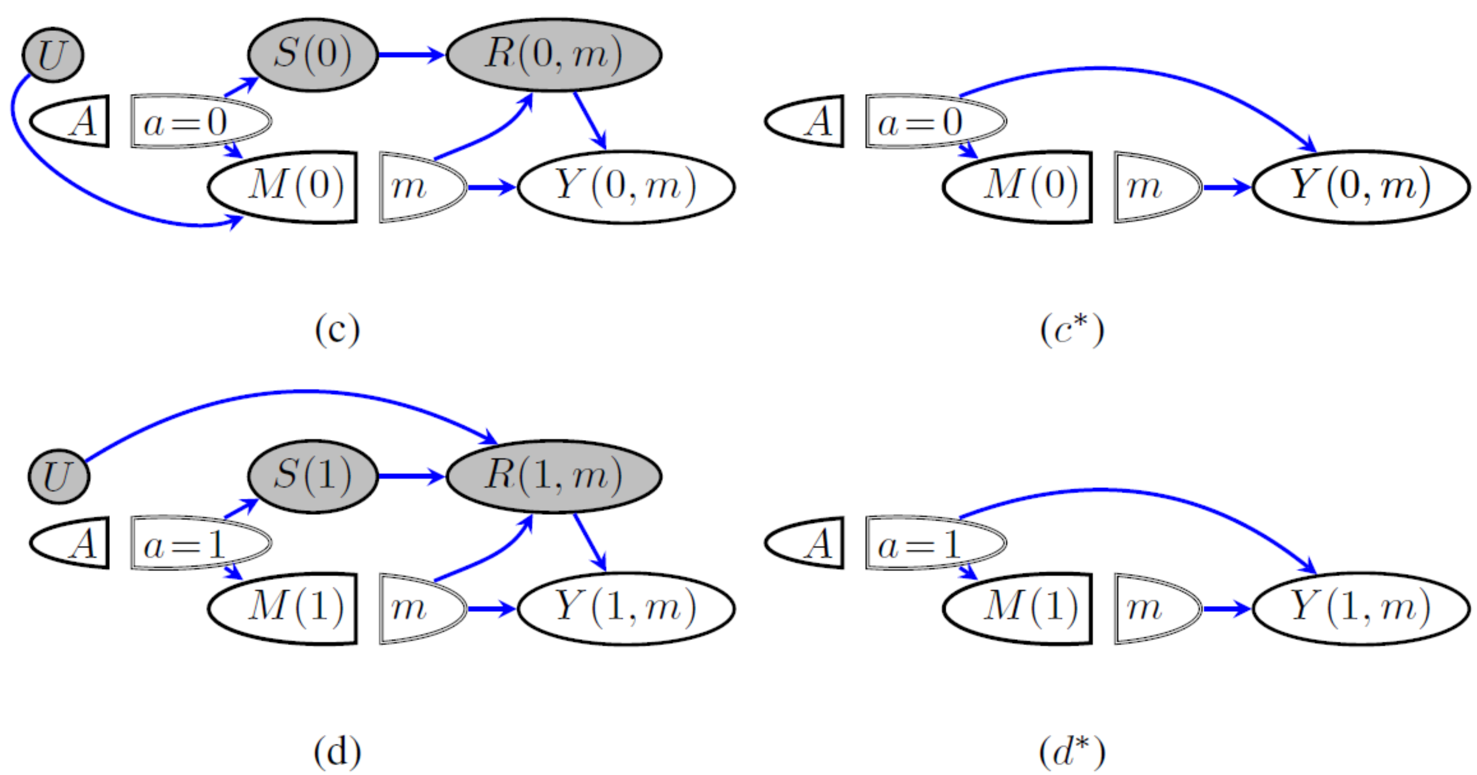
实例

- River Blindness Treatment Study
- A表示是否进入随机化实验，M表示是否接受药物，结局变量Y表示视力是否下降。S表示是否有机会得到抗过敏药，R表示是否接受抗过敏药。U为未观测混杂变量(是否接受药物治疗的倾向)。
- 由于某些原因，我们只有(A, M, Y)的数据。



CDE的识别性

- 在上述例子中，对A = 0的群体, U与M正相关. 而在A=1的群体中，由于M随机给定，所以U和M独立.
- $p(Y|A=a, M=m) = p(Y(a,m))$，从而CDE(m)可识别。

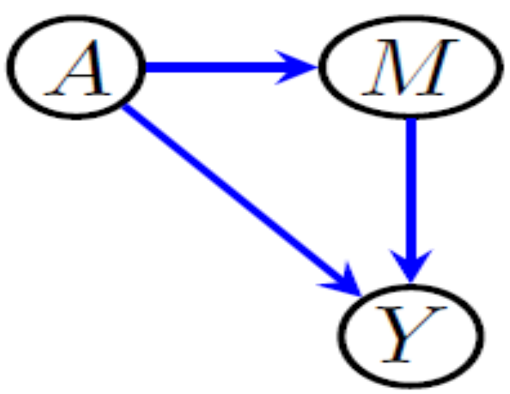


(c) (c*)

(d) (d*)

PDE的识别性

- 在上述例子中的PDE都是不识别的。
- 然后Robins讨论了更简单情形下的识别性。在该情形下，在NPSEM-IE(nonparametric structure equation model with independent error)模型中是可识别的
- 在FFRCISTG模型中不可识别，但可以做到部分识别(得到PDE的上下界)。



(a)

WHY?

$$\text{med}_{a,a'} \equiv \sum_m \left(\mathbb{E}[Y \mid m, a] - \mathbb{E}[Y \mid m, a']\right) p(m \mid a')$$
$$= \left(\sum_m \mathbb{E}[Y \mid m, a] p(m \mid a')\right) - \mathbb{E}[Y \mid a']$$

The proof of this result, under the NPSEM-IE is as follows:

$$\begin{aligned}
&p(Y(a, M(a') = m) = y) \\
&\quad = \sum_m p(Y(a, M(a') = m) = y \mid M(a') = m) p(M(a') = m) \\
&\quad = \sum_m p(Y(a, m) = y) p(M(a') = m) \\
&\quad = \sum_m p(Y = y \mid A = a, M = m) p(M = m \mid A = a')
\end{aligned}$$

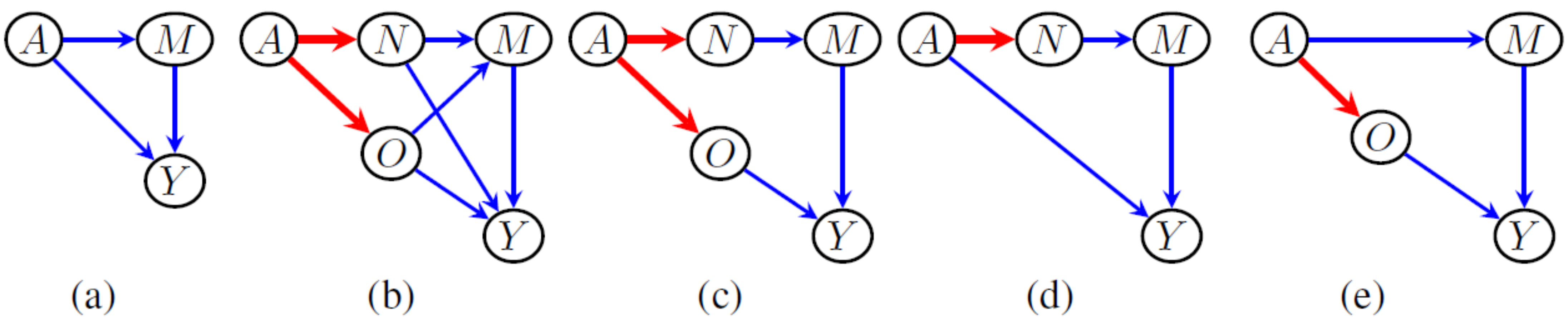
- This follows from the fact that the proof relies on the cross-world independence $Y(a, m) \perp M(a')$.

实例：Nicotine-Free Cigarette

- 有随机戒烟实验数据。吸烟状态A， 6个月后的高血压状态M，以及一年后的结局变量Y。
- 文章假设尼古丁对Y的作用都是通过M造成的，其他毒素对M没有作用。同时M到Y没有未观测的混杂变量。
- $PDE = E\left[Y\left(a = 1, M(a = 0)\right)\right] - E[Y(a = 0, M(a = 0))]$
- 而$\mathrm{E}[\mathrm{Y}(\mathrm{a} = 1, \mathrm{M}(\mathrm{a} = 0))] = \sum_m E[Y|A = 1, M = m]p(m|A = 0)$，从而PDE可识别。

Expanded DAG

Given a DAG $\mathcal{G}$ with a single treatment variable A, an *expanded graph* $\mathcal{G}^{ex}$ *for* A is a DAG constructed by first adding a set of new variables $\{A^{(1)}, \ldots, A^{(p)}\}$ corresponding to a decomposition of the treatment A into p separate components (proposed by the investigator); every variable $A^{(i)}$ is a child of A with the same state space and $A^{(i)}(a) = a$, but A has no other children in $\mathcal{G}^{ex}$; each child C_j of A in $\mathcal{G}$ has in $\mathcal{G}^{ex}$ a subset of $\{A^{(1)}, \ldots, A^{(p)}\}$ as its set of parents.



Expanded DAG

- $PDE = E[Y(n = 0, o = 1)] - E[Y(n = 0, o = 0)]$
- $PDE = \sum_m E[Y|O = 1, M = m]p(m|N = 0)$
- $\{O = 1, M = m\} = \{A = 1, M = m\}$
- $\{N = 0, M = m\} = \{A = 0, M = m\}$
- $PDE = \sum_m E[Y|A = 1, M = m]p(m|A = 0)$

Identification of four arms from two

- 文章给出了三种类型的数据
- 第一种：从实验中得到的原始数据(A,M,Y)，其中A是随机化的。
- 第二种：随机化(N,O)的得到的四组的数据，在每一组中(n,o)属于{0,1}^2。
- 第三种：第二种数据中n=o的这一部分数据。

Identification of four arms from two

- $p(M=m,Y=y|A=a)=$
  $p(M(n=a,o=a)=m,Y(n=a,o=a)=y|A=a)=$
  $p(M(n=a,o=a)=m,Y(n=a,o=a)=y)$
- 由上式可以看出第三种数据的分布可以由第一种数据识别。
- 从而我们的目标就是当$n\neq o$时去识别$E[Y(n,o)]$。

Identification of four arms from two

Proposition 1 *If for some $x \in \{0,1\}$ the following two conditions hold:*

$$p(M(n{=}x, o{=}0) = m) = p(M(n{=}x, o{=}1) = m), \tag{14}$$

$$\begin{aligned} &p(Y(n{=}1, o{=}x^*) = y \mid M(n{=}1, o{=}x^*) = m) \\ &\qquad = p(Y(n{=}0, o{=}x^*) = y \mid M(n{=}0, o{=}x^*) = m), \end{aligned} \tag{15}$$

where $x^* = 1 - x$, then:

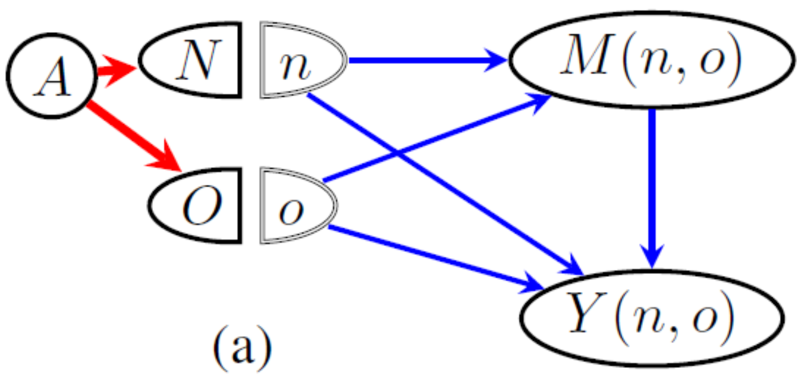
$$\begin{aligned} &p(M(n{=}x, o{=}x^*) = m, Y(n{=}x, o{=}x^*) = y) \\ &\quad = p(Y(n{=}x^*, o{=}x^*) = y \mid M(n{=}x^*, o{=}x^*) = m) p(M(n{=}x, o{=}x) = m). \end{aligned} \tag{16}$$

Proof:

$$\begin{aligned} &p(M(n{=}x, o{=}x^*), Y(n{=}x, o{=}x^*)) \\ &\qquad = p(Y(n{=}x, o{=}x^*) \mid M(n{=}x, o{=}x^*)) p(M(n{=}x, o{=}x^*)) \\ &\qquad = p(Y(n{=}x^*, o{=}x^*) \mid M(n{=}x^*, o{=}x^*)) p(M(n{=}x, o{=}x)). \end{aligned}$$

Identification of four arms from two

Proposition 2 *Assume the distribution of the variables on an unexpanded DAG $\mathcal{G}$ is positive. Under an FFRCISTG corresponding to the population SWIG $\mathcal{G}^{ex}(n, o)$ there is no vertex that has both n and o as parents if and only if the joint distributions $p(V(n = x, o = x^*))$ for $x \neq x^*$ are identified from the counterfactual distributions $p(V(n=x, o=x))$. Further, since $P(V(n=x, o=x)) = P(V(a=x))$, also from the distribution of the variables in $\mathcal{G}$.*[30]



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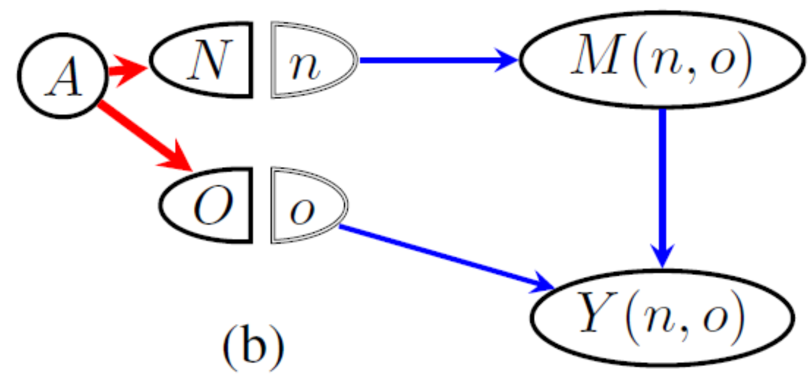
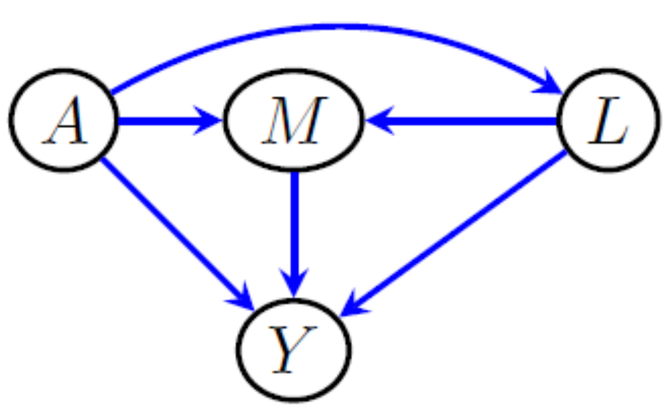


(b)

对于单个处理的识别性条件

Lemma 1 *Assume the distribution of the variables on an unexpanded DAG $\mathcal{G}$ is positive. Under an FFRCISTG corresponding to an expanded (population) graph $\mathcal{G}^{ex}$ for treatment A, the intervention distribution $p(V(a^{(1)} = x^{(1)}, \ldots, a^{(p)} = x^{(p)}))$ is identified by the g-formula applied to $\mathcal{G}^{ex}$ from the data on $\mathcal{G}$ if for every child C_j of A in $\mathcal{G}$, the set of parents of C_j in $\mathcal{G}^{ex}$ that are components of A take the same value.*[32]



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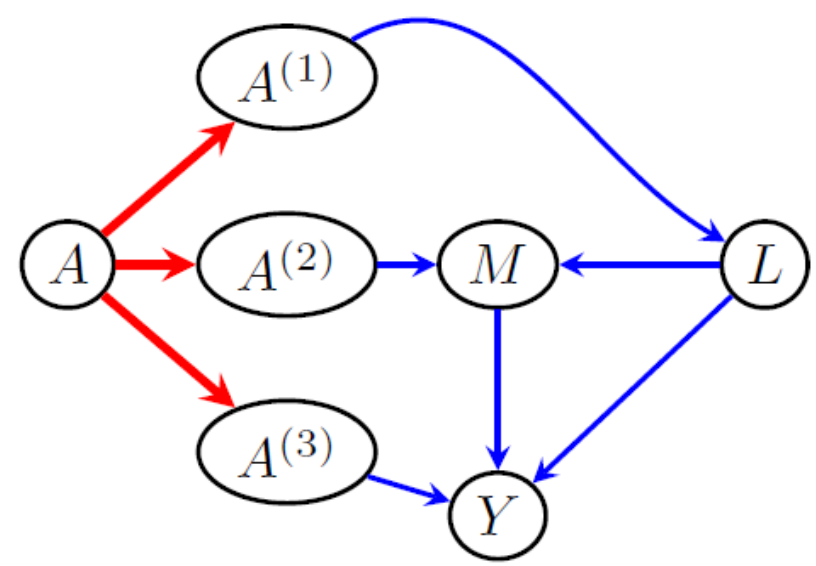

Generalizations

Theorem 1 *If $V(\pi, a, a')$ is edge consistent, then under the NPSEM-IE for the DAG $\mathcal{G}$,*

$$p(V(\pi, a, a')) = \prod_{i=1}^{K} p(V_i \mid a \cap \mathrm{pa}_i^{\pi}, a' \cap \mathrm{pa}_i^{\overline{\pi}}, \mathrm{pa}_i^{\mathcal{G}} \setminus A). \tag{26}$$

Theorem 2 *Under the FFRCISTG model associated with the edge expanded DAG $\mathcal{G}^e$, for any edge consistent π, a, a':*

$$p^e(V(a^{\pi})) = \prod_{i=1}^{K} p^e(V_i \mid a^{\pi} \cap \mathrm{pa}_i^{\mathcal{G}^e}, \mathrm{pa}_i^{\mathcal{G}^e} \setminus A). \tag{27}$$

讨论

- 这篇文章将处理A分成了几个成分，然后去利用这成分来进行中介分析，并研究其识别性条件。
- 但是在实际应用时，A应该如何分解往往很困难。
- 同时FFRCISTG的相关论文很少，研究的人不多。

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