

Towards graphical rules for efficient estimation in causal graphical models

Andrea Rotnitzky .

Universidad Di Tella and Harvard T.H. Chan School of Public Health

Based on

Rotnitzky and Smucler, 2020, Journal of Machine Learning Research, 21 188: 1-86,

Smucler, Sapienza and Rotnitzky, 2021, Biometrika, 109, 1, 49-65.

Guo, Perkovic and Rotnitzky, 2022, <https://arxiv.org/abs/2202.11994>

BIRS, Kelowna, May 23, 2022

Causality in the 21st century

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- ▶ 1/2 a century ago different disciplines had their own opinions about causal inference.
- ▶ Today there is nearly unanimous acceptance.
- ▶ "Causal revolution" in great part due to the emergence and adoption of two formalisms:
 - ▶ Counterfactual Models
 - ▶ Graphical Models

Graphical Models

- ▶ **In epidemiology and medical research:** graphical models are responsible for the acceptance and adoption of modern causal analytic techniques because they **facilitate encoding complex causal assumptions** and reasoning in an intuitive way

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- ▶ *Simple graphical rules* exist to explain the **potential biases** of one's preferred estimation procedure and the possible remedial approaches.

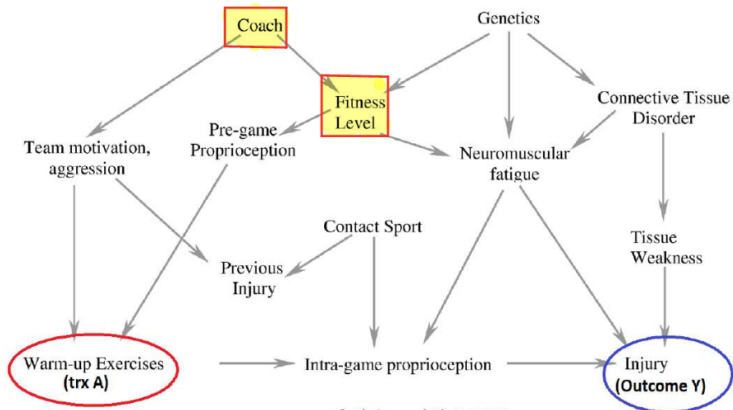
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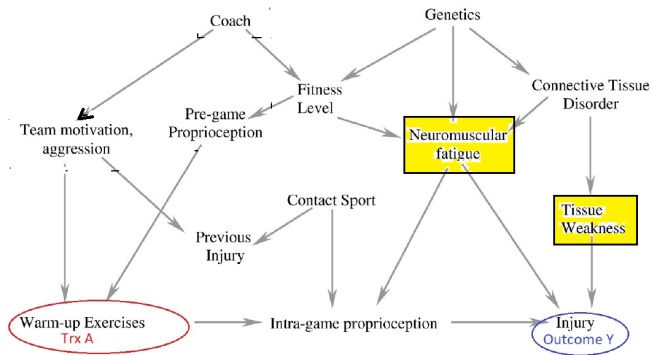
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- ▶ **In this talk: some work towards filling this gap**

An adjustment set



Another adjustment set

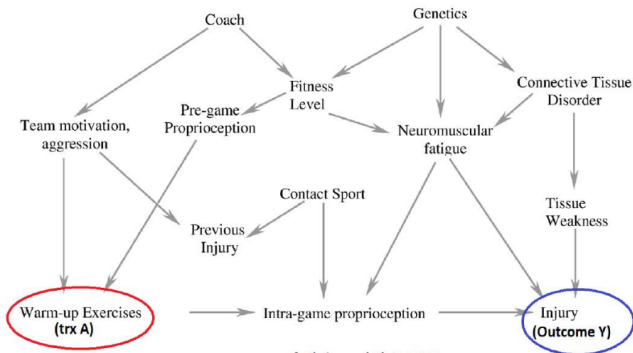


Graph taken from Shrier and Platt, 2008.

Road map of the talk

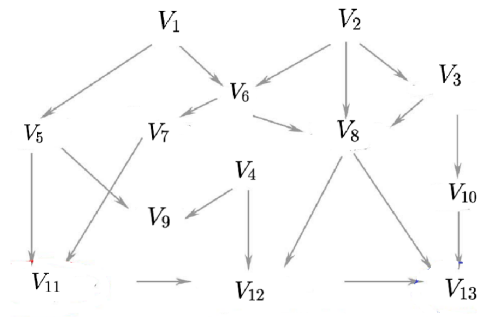
- ▶ **Gentle introduction to causal graphical models.**
- ▶ Some results with Smucler and Sapienza on optimal adjustment sets
 - ▶ Rules for comparing adjustment sets for point exposure studies
 - ▶ Time dependent adjustment sets for time dependent exposures
- ▶ Some results with Guo and Perkovic on uninformative variables and graph reduction
- ▶ Final remarks

Causal Graphical Models in a nutshell



ref: Shrier and Platt, 2008

Causal Graphical Models in a nutshell



$$V_1 = f_1(\varepsilon_1)$$

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$$V_5 = f_5(V_1, \varepsilon_5)$$

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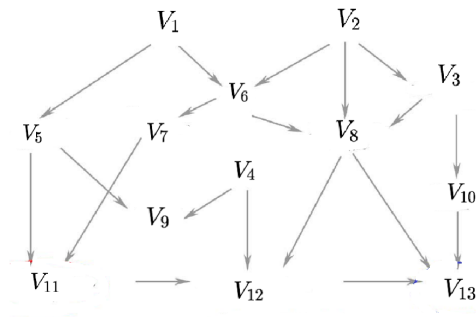
$$V_{11} = f_{11}(V_5, V_7, \varepsilon_{11})$$

$$V_{12} = f_{12}(V_{11}, V_4, \varepsilon_{12})$$

$$V_{13} = f_{13}(V_8, V_{10}, V_{12}, \varepsilon_{13})$$

$\varepsilon_1, \dots, \varepsilon_{13}$ omitted
non-common causes

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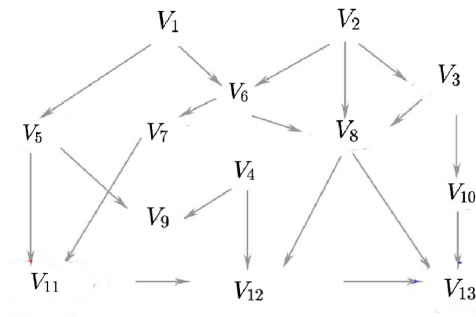
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No omitted common cause assumption formalized as: the ε_j 's are mutually independent (Pearl, 1995)

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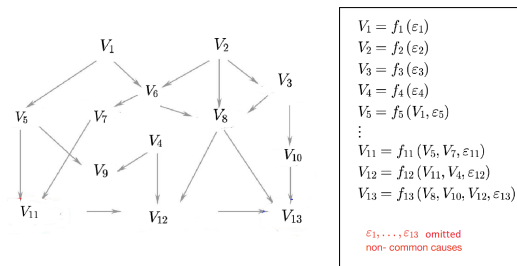
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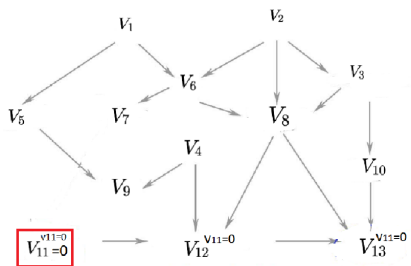


- ▶ Graphical model with independent ε'_j 's is tantamount to:

$$p(\mathbf{v}) = \prod_j p(v_j | \text{pa}_{\mathcal{G}}(v_j))$$

- ▶ The collection of laws for V that factor like this is called a **Bayesian Network** $\mathcal{B}(\mathcal{G})$.

Causal Graphical Models in a nutshell: counterfactual world static intervention



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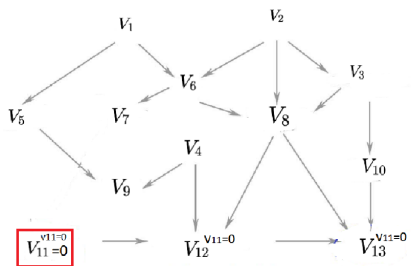
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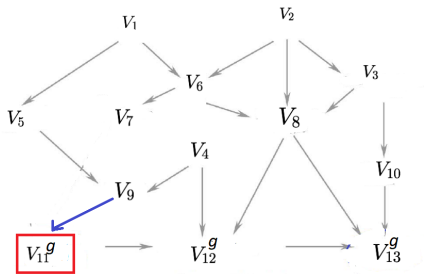
$$V_{13}^{v_{11}=0} = f_{13}(V_8, V_{10}, V_{12}^{v_{11}=0}, \varepsilon_{13})$$

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Corollary: counterfactual law is **identified** and given by

$$p_{(v_{11}=0)}(\mathbf{v}) = \prod_{j \neq 11} p(v_j | \text{pa}_G(v_j)) \times I_{\{0\}}(v_{11})$$

Causal Graphical Models in a nutshell: counterfactual world, deterministic dynamic intervention



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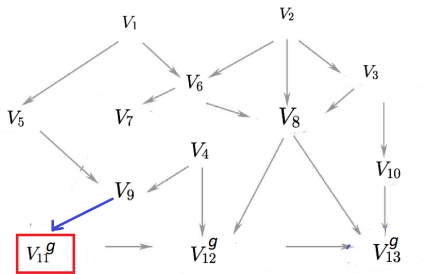
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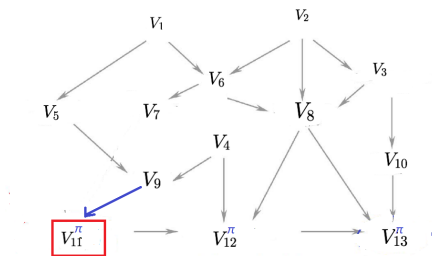
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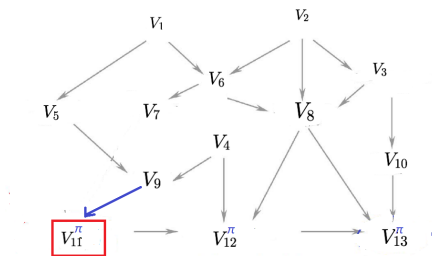
$$V_{11}^\pi = g(V_9, U_{11})$$

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$$p_\pi(\mathbf{v}) = \prod_{j \neq 11} p(v_j | \text{pa}_G(v_j)) \times \pi(v_{11} | v_9)$$

Causal graphical models

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- a. **Factual world.** The law p of $\mathbf{V} = (V_1, \dots, V_J)$ belongs to *Bayesian Network* $\mathcal{B}(\mathcal{G})$, i.e. it factorizes as

$$p(\mathbf{v}) = \prod_{j=1}^J p(v_j | pa_{\mathcal{G}}(v_j))$$

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- b. **Counterfactual world.** For any $\mathbf{A} = (A_1, \dots, A_s) \subset \mathbf{V}$, the distrib. of the data when a regime that assigns a_t to A_t with prob. $\pi_t(a_t | \mathbf{z}_t)$ is implemented in the population (where \mathbf{z}_t are non-descendants of A_t), is

$$p_{\pi}(\mathbf{v}) = \prod_{V_j \in \mathbf{V} \setminus \mathbf{A}} p(v_j | pa_{\mathcal{G}}(v_j)) \times \prod_{t=1}^s \pi_t(a_t | \mathbf{z}_t)$$

So, p_{π} is **identified** from p

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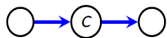
- ▶ **Theorem** (Geiger, Verma & Pearl, 1990) :

$$A \perp\!\!\!\perp_{\mathcal{G}} B \mid C \Leftrightarrow$$

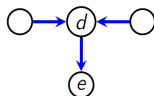
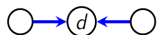
A is cond. indep. of B given C under any $p \in \mathcal{B}(\mathcal{G})$

d-separation

- ▶ A, B single vertices, $C \subset V \setminus \{A, B\}$
- ▶ a path from A to B is **blocked** by C if either
 - (1) at least one non-collider is in C

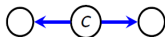


- (2) \exists at least one collider, such that neither itself nor its descendants is in C

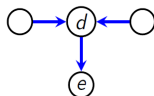
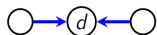


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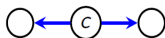
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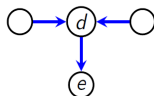
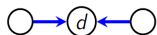
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- ▶ A and B are **d-separated** by C if all paths bw A and B are blocked by C
- ▶ A set A is d-separated from another set B by $C \subset V \setminus \{A, B\}$ if all $A_j \in A$ and $B_k \in B$ are d-separated by C , in which case we write

$$A \perp\!\!\!\perp B \mid C$$

Counterfactual law under a point exposure intervention

- ▶ **Counterfactual law.**

$$p_{\pi}(\mathbf{v}) = \prod_{j: V_j \in \mathbf{V} \setminus A} p(v_j | pa_G(v_j)) \times \pi(a | \mathbf{z})$$

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- ▶ Then for $Y = V_J$,

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Adjustment formula and adjustment sets

► **Adjustment formula:**

$$\underbrace{E_{\pi}[Y]}_{\text{intervention mean}} = \underbrace{\sum_{a=0}^1 \int E[Y|A=a, \mathbf{L}=\mathbf{l}] \pi(a|\mathbf{z}) p_{\mathbf{L}}(\mathbf{l}) d\mathbf{l}}_{\text{g-functional}}$$
$$= E_p \left[\frac{\pi(A|\mathbf{Z})}{p(A|\mathbf{L})} Y \right]$$

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- ▶ **Definition:** A **Z**-adjustment set for a single trx A and outcome Y is any \mathbf{L} disjoint with A and Y such that
 - ▶ $\mathbf{Z} \subset \mathbf{L}$ and,
 - ▶ Under the causal graphical model, for any regime $\pi(A|\mathbf{Z})$, $E_{\pi}[Y]$ is equal to the corresponding adjustment formula.

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 - ▶ Under the causal graphical model, for any regime $\pi(A|\mathbf{Z})$, $E_{\pi}[Y]$ is equal to the corresponding adjustment formula.
- ▶ If $\mathbf{Z} = \emptyset$, then we say \mathbf{L} is a *static adjustment set*.

Characterization of Z-adjustment sets

- ▶ **Generalized adj. criterion for static (i.e. $Z = \emptyset$) treatments** (Shpitser. et. al., 2010, Perkovic et. al., 2015, 2018): **L** is static adj. set iff

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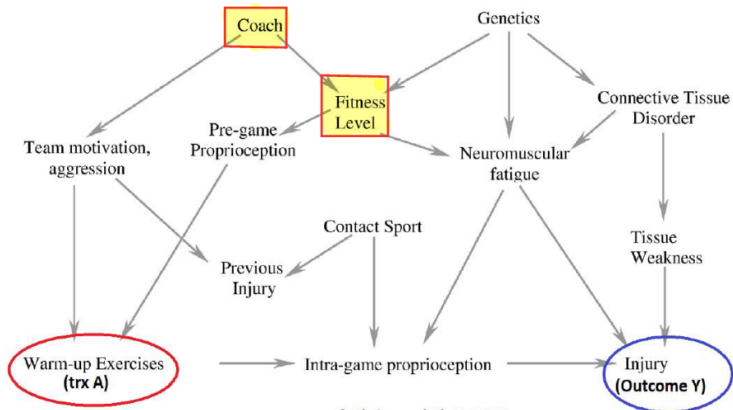
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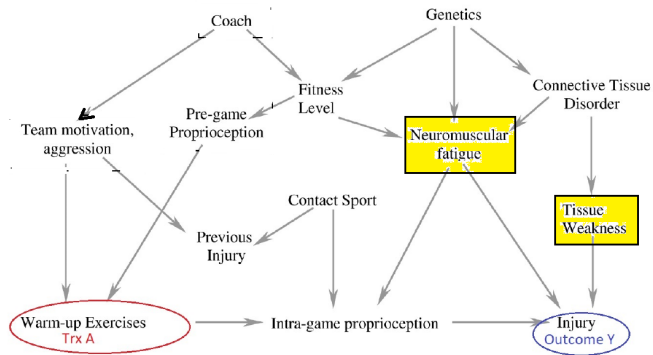
- ▶ **Result (Smucler and Rotnitzky, 2020):**

Class of all Z – adj sets = $\{L : L \text{ is a static adj. set and } Z \subset L\}$

Static adjustment set

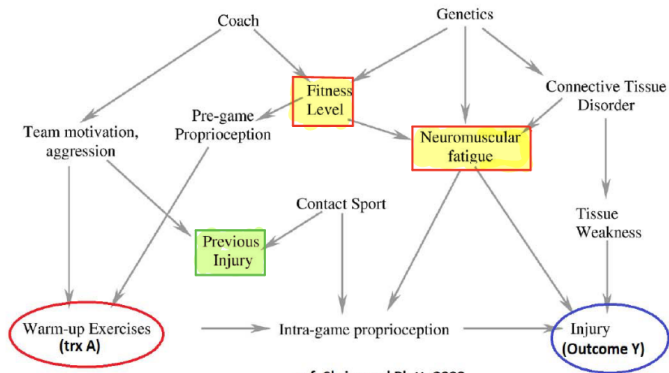


Another static adjustment set

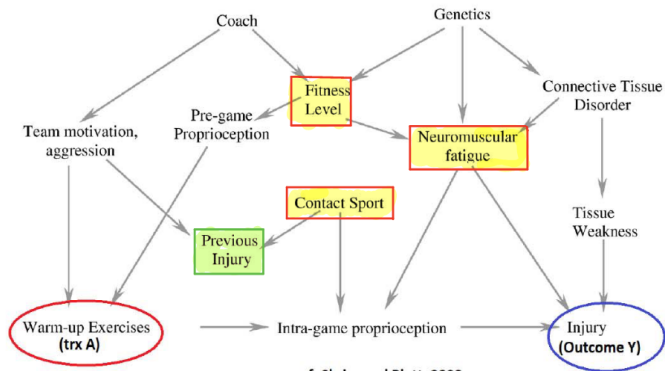


Graph taken from Shrier and Platt, 2008.

An invalid Z-adjustment , Z= previous injury



A valid Z-adjustment set, $Z = \text{previous injury}$



Road map of the talk

- ▶ Gentle introduction to causal graphical models.
- ▶ **Some results with Smucler and Sapienza on optimal adjustment sets**
 - ▶ **Rules for comparing adjustment sets for point exposure studies**
 - ▶ Time dependent adjustment sets for time dependent exposures
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- ▶ Final remarks

L-NPA estimators of a counterfactual mean

- ▶ **Recall:** a \mathbf{Z} -adj. set \mathbf{L} satisfies that for any regime $\pi(A|\mathbf{Z})$, the counterfactual mean $E_\pi(Y)$ is equal to

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Related literature

- ▶ Henckel, Perkovic and Maathuis (2019) provided graphical rules
 - ▶ for comparing certain pairs of static adjustment sets
 - ▶ for determining the globally optimal static adjustment set
- ▶ Also, Kuroki and Miyakawa, 2003 and Kuroki and Cai 2004.
- ▶ These works assume:
 - ▶ causal graphical **linear** model, i.e. $V_j = \beta_j^T \text{pa}_G(V_j) + \varepsilon_j, \{\varepsilon_j : j\}$ indep.
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Our work with Smucler and Sapienza on adjustment sets

- ▶ **Proved** that Henckel et. al. rules also apply when **causal graphical model is agnostic** and **trx effect estimated via non-parametric L-covariate adjustment** .
- ▶ **Derived graphical rules and efficient algorithms for finding:**
 - ▶ globally optimal adj. sets for personalized **Z**– dependent regimes
 - ▶ optimal static and personalized adj. sets among **observable adj. sets**
- ▶ **Extended** rules for comparing adjustment sets to **time dependent treatments and confounding**
- ▶ **Proved** that **optimal time dependent** adj. sets do not always exist
- ▶ **Characterized** graphs under which the semip. efficient estimator of the counterfactual mean is asym. equivalent to the optimally adjusted estimator

Supplementing adjustment sets with precision variables.

- ▶ **Lemma 1.** Suppose \mathbf{B} is a \mathbf{Z} -adj. set and \mathbf{G} , disjoint with \mathbf{B} , satisfies

$$A \perp\!\!\!\perp_{\mathcal{G}} \mathbf{G} \mid \mathbf{B}$$

then, $\mathbf{G} \cup \mathbf{B}$ is also a \mathbf{Z} -adj. set and for all $p \in \mathcal{B}(\mathcal{G})$ and all regimes $\pi(A|\mathbf{Z})$

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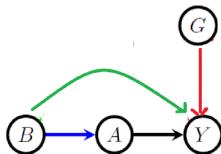
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- ▶ In particular, for the *static regime* π that sets A to a ,

$$\sigma_{\pi, \mathbf{B}}^2(p) - \sigma_{\pi, \mathbf{G} \cup \mathbf{B}}^2(p) = E \left[\left\{ \frac{1}{P(A=a|\mathbf{B})} - 1 \right\} \text{var} \{ E(Y|A=a, \mathbf{G}, \mathbf{B}) | A=a, \mathbf{B} \} \right]$$



Deleting overadjustment variables

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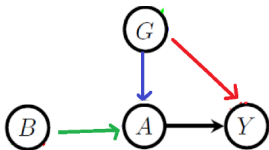
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Comparing two arbitrary adjustment sets

- ▶ **Corollary:** Suppose that \mathbf{G} and \mathbf{B} are two \mathbf{Z} -adj. sets such that

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Then, for all $p \in \mathcal{B}(\mathcal{G})$ and all regimes $\pi(A|\mathbf{Z})$

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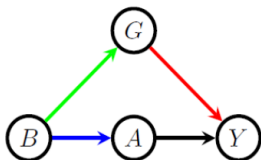
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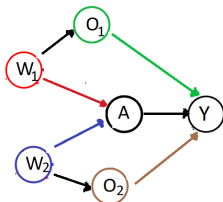
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- **Proof:**

$$\sigma_{\pi, \mathbf{B}}^2 - \sigma_{\pi, \mathbf{G}}^2 = \underbrace{\sigma_{\pi, \mathbf{B}}^2 - \sigma_{\pi, \mathbf{B} \cup (\mathbf{G} \setminus \mathbf{B})}^2}_{\text{gain due to supplementation with precision component } \mathbf{G} \setminus \mathbf{B}} + \underbrace{\sigma_{\pi, \mathbf{G} \cup (\mathbf{B} \setminus \mathbf{G})}^2 - \sigma_{\pi, \mathbf{G}}^2}_{\text{gain due to deletion of noisy component } \mathbf{B} \setminus \mathbf{G}}$$



Not all adjustment sets are comparable



- ▶ (O_1, W_2) is preferable to (O_2, W_1) if green association stronger than brown, and blue association weaker than red
- ▶ (O_2, W_1) is preferable to (O_1, W_2) if brown association stronger than green, and red association weaker than blue
- ▶ but... (O_1, O_2) is more efficient than both

Optimal adjustment set

► **Theorem:** (Henckel, et. al. (2019)). The set

\mathbf{O} = non-descendants of A that are parents of Y or
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is a *static* adjustment set. Furthermore, for any other static adjustment set \mathbf{L} ,

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- ▶ **Corollary** (Rotnitzky and Smucler, 2020): \mathbf{O} is the **globally optimal static** adjustment set.

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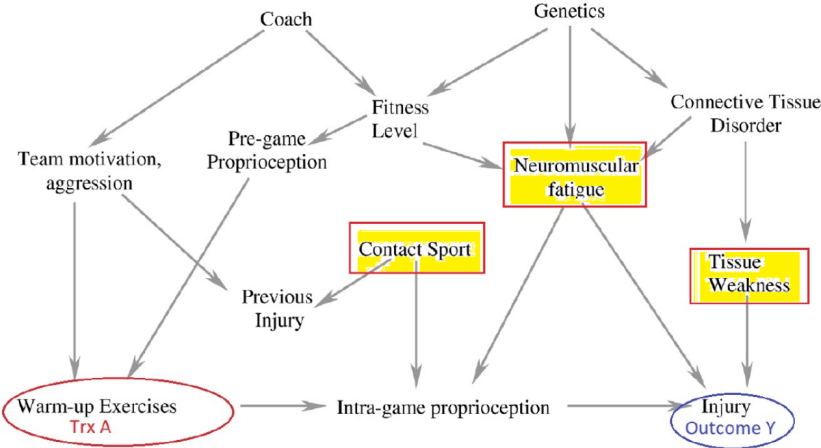
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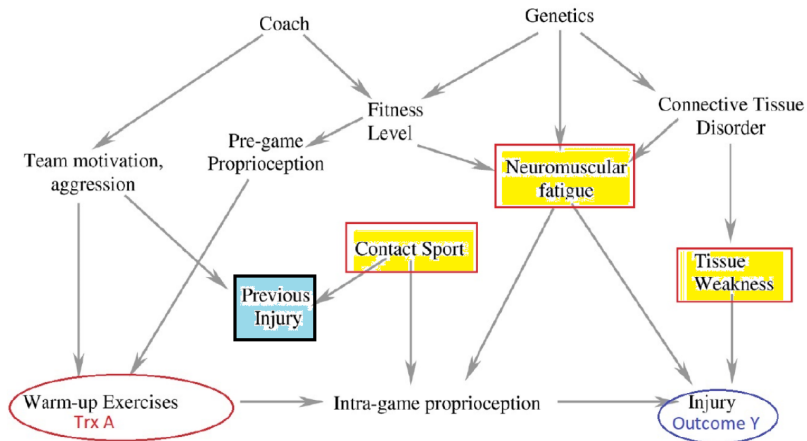
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- ▶ **Lemma** (Smucler, Sapienza and Rotnitzky, 2021): $\mathbf{O} \cup \mathbf{Z}$ is the **globally optimal \mathbf{Z} - adjustment set**

Globally optimal static adjustment set



Optimal personalized adjustment set



DAGs with hidden variables

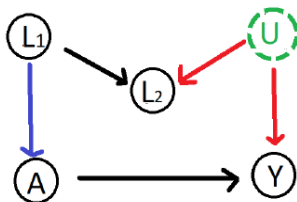
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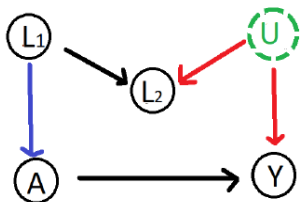
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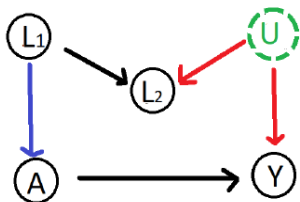
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- ▶ If U is unobserved, then $\mathbf{L} = \{L_1, L_2\}$ and $\mathbf{L} = \emptyset$ are two valid static adjustment sets which do not dominate each other
 - ▶ $\mathbf{L} = \{L_1\}$ is another adj. set but is dominated by $\mathbf{L} = \emptyset$

Optimal adjustment sets in DAGs with hidden variables

- ▶ $An_{\mathcal{G}}(A, Y, \mathbf{Z})$ = set of nodes that are ancestors of at least one of A , Y or a component of \mathbf{Z}
- ▶ **Result:** (van der Zander, Liskiewicz and Textor, 2019): if an observable \mathbf{Z} -adj. set exists then

$$\mathcal{S} = \{\mathbf{L} : \mathbf{L} \text{ is observable } \mathbf{Z} - \text{adj.set and } \mathbf{L} \subset An_{\mathcal{G}}(A, Y, \mathbf{Z})\}$$

is not empty.

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- ▶ **Result** (Smucler et al, 2021): If $\mathcal{S} \neq \emptyset$ then an optimal \mathbf{Z} -adj. set exists in the class \mathcal{S} .
- ▶ In Smucler et al, 2021, we derived a graphical algorithm, *based on a particular latent projected undirected moralized graph*, that finds the optimal \mathbf{Z} -adj. set in \mathcal{S} .

Road map of the talk

- ▶ Gentle introduction to causal graphical models.
- ▶ **Some results with Smucler and Sapienza on optimal adjustment sets**
 - ▶ Rules for comparing adjustment sets for point exposure studies
 - ▶ **Time dependent adjustment sets for time dependent exposures**
- ▶ Some results with Guo and Perkovic on uninformative variables and graph reduction
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Time dependent treatments

Suppose A_1 and A_2 are two treatments, $A_1 \in \text{nd}_{\mathcal{G}}(A_2)$. Under a causal graphical model represented by DAG G , the mean of Y_{a_0, a_1} when the static regime that sets A_0 to a_0 and A_1 to a_1 is

$$\begin{aligned} E(Y_{a_0, a_1}) &= E \left\{ \frac{I_{a_0}(A_0)}{p(a_0 | \text{pa}_{\mathcal{G}}(A_0))} \frac{I_{a_1}(A_1)}{p(a_1 | \text{pa}_{\mathcal{G}}(A_1))} Y \right\} \\ &= E \{ E [E [Y | a_0, a_1, \text{pa}_{\mathcal{G}}(A_0), \text{pa}_{\mathcal{G}}(A_1)] | a_0, \text{pa}_{\mathcal{G}}(A_0)] \} \end{aligned}$$

Definition: $\mathbf{L} = (\mathbf{L}_0, \mathbf{L}_1) \subset \mathbf{V}$ is a **static time dependent adjustment set** relative to $\text{trxs}(A_0, A_1)$ and outcome Y in G iff for all $P \in \mathcal{B}(\mathcal{G})$,

$$E(Y_{a_0, a_1}) = E \{ E [E [Y | a_0, a_1, \mathbf{L}_0, \mathbf{L}_1] | a_0, \mathbf{L}_0] \}$$

The right hand side is the so-called the **g-functional with respect to $(\mathbf{L}_0, \mathbf{L}_1)$** .

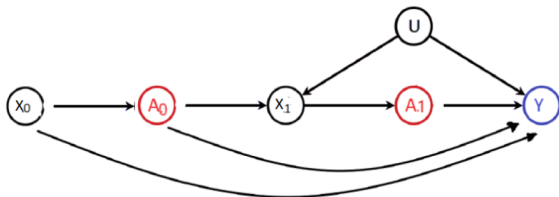
Time dependent treatments

Lemma (Robins, 1986) $(\mathbf{L}_0, \mathbf{L}_1)$ is a time-dependent adjustment set if :

- (i) \mathbf{L}_j non-descendant of $A_j, j = 0, 1$, and
- (ii) Sequential randomization:

$$Y_{a_0, a_1} \perp\!\!\!\perp A_1 \mid (A_0, \mathbf{L}_0, \mathbf{L}_1) \text{ and } Y_{a_0, a_1} \perp\!\!\!\perp A_0 \mid \mathbf{L}_0$$

Example:



- ▶ X_0 is a time 0 adjustment set ($= \mathbf{L}_0$)
- ▶ X_1, U and (X_1, U) are time 1 adjustment sets ($= \mathbf{L}_1$)

Time dependent treatments

Lemma: Suppose that $(\mathbf{B}_0, \mathbf{B}_1)$ and $(\mathbf{G}_0, \mathbf{G}_1)$ are time dependent adjustment sets. If

(1)

$$\begin{aligned} A_0 &\perp\!\!\!\perp_{\mathcal{G}} [\mathbf{G}_0 \setminus \mathbf{B}_0] \mid \mathbf{B}_0 \\ A_1 &\perp\!\!\!\perp_{\mathcal{G}} [(\mathbf{G}_0, \mathbf{G}_1) \setminus (\mathbf{B}_0, \mathbf{B}_1)] \mid (\mathbf{B}_0, \mathbf{B}_1, A_0) \end{aligned}$$

(2)

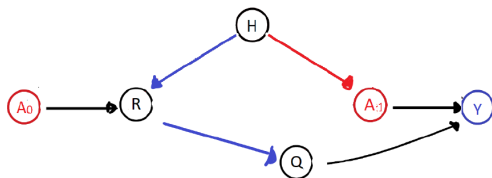
$$\begin{aligned} \mathbf{G}_1 &\perp\!\!\!\perp_{\mathcal{G}} [\mathbf{B}_0 \setminus \mathbf{G}_0] \mid (\mathbf{G}_0, A_0) \\ Y &\perp\!\!\!\perp_{\mathcal{G}} [(\mathbf{B}_0, \mathbf{B}_1) \setminus (\mathbf{G}_0, \mathbf{G}_1)] \mid (\mathbf{G}_0, \mathbf{G}_1, A_0, A_1) \end{aligned}$$

then, for all $P \in \mathcal{B}(\mathcal{G})$

$$\sigma_{\mathbf{G}_0, \mathbf{G}_1}^2 \leq \sigma_{\mathbf{B}_0, \mathbf{B}_1}^2$$

where for any adj. set $(\mathbf{L}_0, \mathbf{L}_1)$, $\sigma_{\mathbf{L}}^2$ is the variance of the NP inf. fcn of the g-functional adjusted for $(\mathbf{L}_0, \mathbf{L}_1)$.

Time dependent treatments



The following adjustment sets dominate all other adjustment sets but they don't dominate each other

Time 0 adj. set (= L_0)

\emptyset

H

Time 1 adj. set (= L_1)

Q

Q

Better when

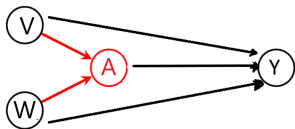
red assoc. strong, blue assoc weak

red assoc. weak, blue assoc strong

In Rotnitzky and Smucler we exhibited two laws P_1 and P_2 in $\mathcal{B}(\mathcal{G})$ for binary data such that:

- (i) under P_1 , (H, Q) is 8% more efficient than (\emptyset, Q) , and
- (ii) under P_2 , (\emptyset, Q) is 47% more efficient than (H, Q)

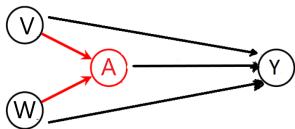
Semip. efficient estimation vs optimal non-parametric adjusted estimation



- ▶ The interventional mean $E(Y^a)$ is

$$E[E(Y|A = a, V, W)] = \int E(Y|A = a, V = v, W = w) \underbrace{p(v) p(w)}_{=p(v,w)} dv dw$$

Semip. efficient estimation vs optimal non-parametric adjusted estimation

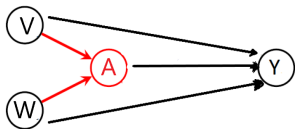


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- ▶ Optimal non-parametric adjusted estimator *ignores* restrictions on the marginal law of covariates, i.e. that V and W are marginally independent.

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- ▶ **Optimal non-parametric adjusted estimator** *ignores* restrictions on the marginal law of covariates, i.e. that V and W are marginally independent.
- ▶ **Semiparametric efficient (SE)** *exploits* these restrictions and can be much much more efficient than optimally adjusted NP estimator.

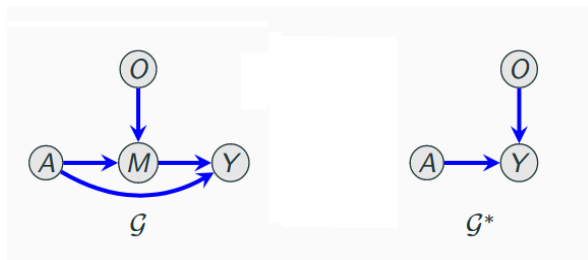
There is also information in the mediators structure



$$\begin{aligned} E(Y^a) &= E(Y|A = a) \\ &= \int \int y \underbrace{p(y|m) p(m|a)}_{=p(y,m|a)} dm dy \end{aligned}$$

- ▶ Markov chain structure carries information about $E(Y|A = a)$.

However ... in some graphs the optimally adjusted estimator is efficient



- ▶ With discrete data the MLE of $p_a(y)$ under \mathcal{G} is

$$\hat{p}_{a,MLE}(y) = \sum_{m,o} \mathbb{P}_n(y|m,a) \mathbb{P}_n(m|a,o) \mathbb{P}_n(o)$$

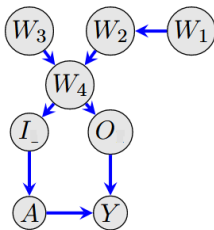
- ▶ Surprisingly, $\hat{p}_{a,MLE}(y)$ is asym. equivalent to the MLE of $p_a(y)$ under \mathcal{G}^* is

$$\tilde{p}_{a,MLE}(y) = \sum_o \mathbb{P}_n(y|o,a) \mathbb{P}_n(o)$$

Road map of the talk

- ▶ Gentle introduction to causal graphical models.
- ▶ **Some results with Smucler and Sapienza on optimal adjustment sets**
 - ▶ Rules for comparing adjustment sets for point exposure studies
 - ▶ Time dependent adjustment sets for time dependent exposures
- ▶ **Some results with Guo and Perkovic on uninformative variables and graph reduction**
- ▶ Final remarks

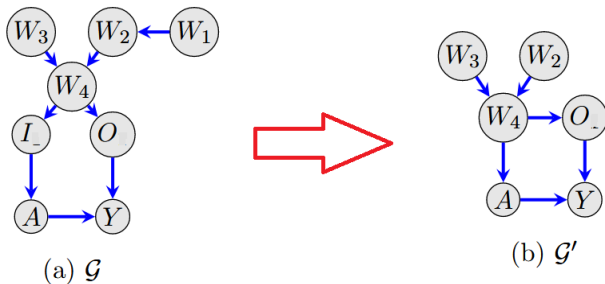
Graph reduction for semiparametric efficient estimation (joint work with Richard Guo and Ema Perkovic)



(a) \mathcal{G}

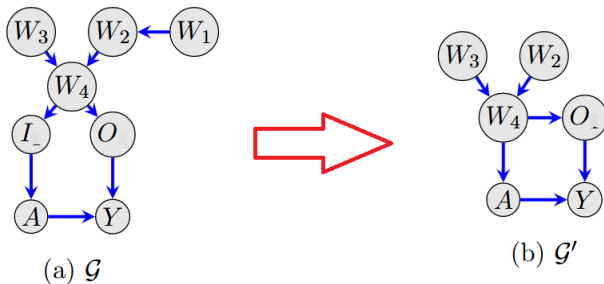
$$p_a(y) = \sum_{i, w_1, w_2, w_3, w_4, o} p(y|o, a) p(i|w_4) p(o|w_4) p(w_4|w_2, w_3) p(w_3) p(w_2|w_1) p(w_1)$$

Graph reduction for semiparametric efficient estimation (joint work with Richard Guo and Ema Perkovic)



$$p_a(y) = \underbrace{\sum_{w_2, w_3, w_4, o} p(y|o, a) p(o|w_4) p(w_4|w_2, w_3) p(w_3) p(w_2)}_{\text{g-formula in } \mathcal{G}'}$$

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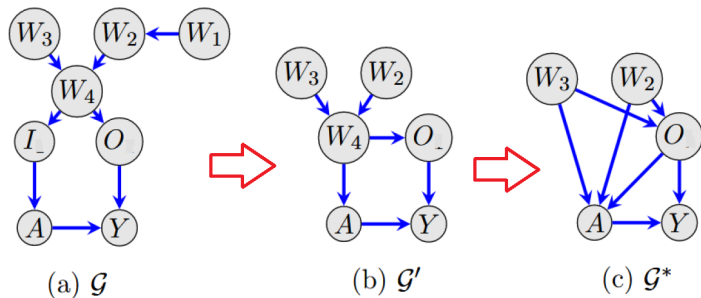


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- ▶ With discrete data, MLE under \mathcal{G}' is

$$\hat{p}_{a,MLE}(y) = \sum_{w_2, w_3, w_4, o} \mathbb{P}_n(y|o, a) \mathbb{P}_n(o|w_4) \mathbb{P}_n(w_4|w_2, w_3) \mathbb{P}_n(w_3) \mathbb{P}_n(w_2)$$

Graph reduction for semiparametric efficient estimation (joint work with Richard Guo and Ema Perkovic)



- ▶ Surprisingly, MLE under \mathcal{G}^* is asymptotically equivalent to MLE under \mathcal{G}'

$$\tilde{p}_{a,MLE}(y) = \sum_{w_2, w_3, o} \mathbb{P}_n(y|o, a) \mathbb{P}_n(o|w_2, w_3) \mathbb{P}_n(w_3) \mathbb{P}_n(w_2)$$

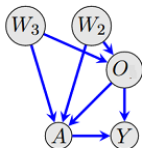
Graph reduction for semiparametric efficient estimation of a counterfactual mean

- ▶ Given a graph \mathcal{G} we derived an algorithm that outputs another graph \mathcal{G}^* over a subset of the variables in \mathcal{G} such that
 - ▶ the g -formula in \mathcal{G}^* is an identifying formula in \mathcal{G} ,
 - ▶ the semiparametric variance bound for estimation of $E(Y^a)$ in model $\mathcal{B}(\mathcal{G})$ and in model $\mathcal{B}(\mathcal{G}^*)$ agree
 - ▶ \mathcal{G}^* is the smallest such possible graph in the sense that all variables in \mathcal{G}^* are informative. More precisely, the efficient influence function for $E(Y^a)$ is a function of every variable in \mathcal{G}^* for at least one P in $\mathcal{B}(\mathcal{G}^*)$

Final remarks

► Estimation via adjustment vs semip. efficient estimation:

- Usual variance/bias trade-off: adjustment relies on less model assumptions
- Equally or perhaps even more importantly: efficient estimation requires estimation of each cond. density $p(V_j | pa_G(V_j))$. Even debiased, influence-function based, i.e. one-step estimation or TMLE, will hardly control the estimation bias of these densities.

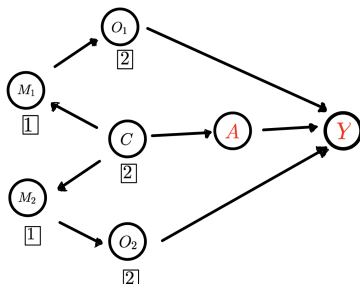


$$\hat{E}(Y^a)_{MLE} = \sum_{w_2, w_3, o} \mathbb{E}_n(Y|o, a) \mathbb{P}_n(o|w_2, w_3) \mathbb{P}_n(w_3) \mathbb{P}_n(w_2)$$

$$\hat{E}(Y^a)_{adj} = \sum_o \mathbb{E}_n(Y|o, a) \mathbb{P}_n(o)$$

Final remarks

- ▶ **Study design:** assign cost to each graph variable and find the adjustment set leading to smallest estimation variance:
 - ▶ subject to a cost constraint \rightarrow a universal solution does not exist



- ▶ among adjustment sets of minimum cost \rightarrow for point exposure we provide the universal solution in Smucler and Rotnitzky, 2022, and graphical rules for finding it

Open problems

- ▶ Inference about the functional returned by the ID algorithm when no observable adj. set exists
 - ▶ Some special cases have been studied, e.g. the generalized front door formula, (Fulcher, et. al. 2019). General theory for an arbitrary functional not yet available.
- ▶ Optimal adj. sets and efficient estimation for other parameters e.g., τ_{tr} effect on the treated, and natural direct and indirect effects

THANKS!

Cuts and moralized graphs.

- ▶ **Separation and cuts in undirected graphs:** In an undirected graph \mathcal{H} , **A** is separated from **B** by **C**, denoted as

$$\mathbf{A} \perp_{\mathcal{H}} \mathbf{B} | \mathbf{C}$$

iff all paths between **A** and **B** have a vertex in **C**. In such case **C** is called a **cut between A and B**.

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Cuts and moralized graphs.

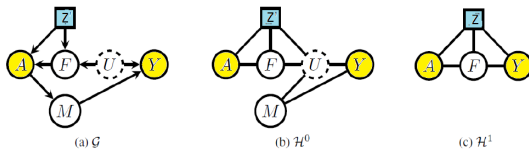
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Construction of the latent projected moralized graph



1. $\mathcal{H}^0 \leftarrow (\mathcal{G}_A[\text{An}_{\mathcal{G}}(A, Y, \mathbf{Z})])^m$ (Textor and Liskiewicz, 2011 and van der Zander et al, 2019)
 - 1.1 compute ancestral subgraph $\mathcal{G}[\text{An}_{\mathcal{G}}(A, Y, \mathbf{Z})]$
 - 1.2 delete edges pointing out of A
 - 1.3 moralize the resulting subgraph
2. \mathcal{H}^1 constructed from \mathcal{H}^0 by
 - 2.1 Latent project out the hidden nodes and the nodes in $\text{forb}(A, Y, \mathcal{G})$
 - 2.2 Add to latent projected graph edges bw \mathbf{Z} and A and bw \mathbf{Z} and Y