A theoretical treatment of conditional independence testing under Model-X

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Joint work with Aaditya Ramdas (CMU)

Conditional independence testing under Model-X

For random variables \((X, Y, Z) \in \mathbb{R}^{1+1+p}\), would like to test

\[ H_0 : X \perp \perp Y \mid Z \]

based on a sample \((X, Y, Z) = \{(X_i, Y_i, Z_i) : i = 1, \ldots, n\}\).
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Model-X assumption (Candès et al., 2018)

\[ f_{X \mid Z} = f_{X \mid Z}^* \text{ for known } f^* \]
Model-X methodologies

MX knockoffs and the conditional randomization test (CRT) proposed by Candès et al., 2018.

**Algorithm: Conditional Randomization Test**

**Data:** Samples \((X_i, Y_i, Z_i)\), test statistic \(T(X, Y, Z)\), MX \(f_{X|Z}^*\)

Compute \(T(X, Y, Z)\);

for \(b = 1, \ldots, B\) do

| Resample \(\tilde{X}_i^b\) from \(f_{X|Z=Z_i}^*\) and recompute \(T(\tilde{X}_i^b, Y, Z)\);

end

**Return:** \(p_{CRT} = \frac{1}{1+B} \left( 1 + \sum_{b=1}^{B} \mathbb{1}(T(\tilde{X}_b, Y, Z) \geq T(X, Y, Z)) \right)\)

A variety of knockoffs and CRT extensions are now available.
Common themes in MX methodology

• $T$ usually based on a statistical machine learning method
• Performance of the ML method impacts the power of the test
• Randomness in $X$ used for inference, conditioning on $Y$ and $Z$
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Goal of this talk:
Develop a quantitative understanding of these themes.
Most powerful CRT against a point alternative

Given alternative distributions $\bar{f}_Z$ and $\bar{f}_{Y|X,Z}$, consider testing

$$H_0 : (X, Y, Z) \sim f_Z f^*_{X|Z} f_{Y|Z} \text{ for some } f_Z, f_{Y|Z}$$

$$H_1 : (X, Y, Z) \sim \bar{f}_Z f^*_{X|Z} \bar{f}_{Y|X,Z}.$$ 

Composite null prevents directly deducing the most powerful test.
Most powerful CRT against a point alternative

Given alternative distributions \( f_Z \) and \( f_{Y|X,Z} \), consider testing

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H_1 : (X, Y, Z) \sim f_Z f_{X|Z} f_{Y|X,Z}.
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Composite null prevents directly deducing the most powerful test.

But the CRT \( \phi_T \) is also a \textit{conditionally valid} test:

\[
\sup_{H_0} \mathbb{E}[\phi_T(X, Y, Z)|Y = y, Z = z] \leq \alpha \quad \text{for all } y, z.
\]

What is the most powerful \textit{conditionally valid} test?
Conditioning reduces a composite null to a point null

Fix realizations $Y_i$ and $Z_i$ for each $i$. Then,

$$
\text{Under } H_0, \quad X_i | Y_i, Z_i \overset{\text{ind}}{\sim} f^*_X|Z_i ;
$$

$$
\text{Under } H_1, \quad X_i | Y_i, Z_i \overset{\text{ind}}{\sim} f^*_X|Z_i \frac{\bar{f}_{Y_i | X_i, Z_i}}{f_{Y_i | Z_i}} .
$$

So, conditioning on $Y, Z$ gives a simple hypothesis testing problem.
Neyman-Pearson gives the most powerful CRT

By NP, most powerful conditionally valid test rejects for large

\[ T^{\text{opt}}(X, Y, Z) = \prod_{i=1}^{n} \frac{\bar{f}_{Y_i|X_i,Z_i}}{f_{Y_i|Z_i}} \propto \prod_{i=1}^{n} \bar{f}_{Y_i|X_i,Z_i}. \]
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**Theorem**

CRT based on \( T^{\text{opt}} \) is the most powerful conditionally valid test against \((X, Y, Z) \sim \bar{f}_Z f^*_X|Z \bar{f}_Y|X,Z.\)

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\(^1\text{All results stated informally}\)
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**Theorem**

CRT based on \( T_{\text{opt}} \) is the most powerful conditionally valid test against \((X, Y, Z) \sim \bar{f}_Z f^*_X f_Y |X, Z\).

The knockoff statistic \( T_{\text{opt}}([X, \tilde{X}], Y) = \prod_{i=1}^{n} \bar{f}_{Y_i|X_i} \) maximizes the probability \( \mathbb{P}[T([X, \tilde{X}], Y) > T([X, \tilde{X}]_{\text{swap}(j)}, Y)]. \)

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ML methods \( T \) used in practice learn approximations to \( \bar{f}_Y|X,Z. \)

\(^1\)All results stated informally
Connections

• **Least squares:** If $\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}\gamma + \epsilon$, the optimal CRT statistic is $\| \mathbf{Y} - \mathbf{X}\beta - \mathbf{Z}\gamma \|^2 - \| \mathbf{Y} - \mathbf{Z}\gamma \|^2$, akin to the OLS $F$-statistic.
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- **Unbiased testing:** In parametric families with nuisance params, MP unbiased test is MP test conditional on nuisance sufficient statistic.
Connections

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- **Unbiased testing**: In parametric families with nuisance params, MP unbiased test is MP test conditional on nuisance sufficient statistic.

- **Holdout randomization test$^2$**: $\hat{f}_{\mathbf{Y}|\mathbf{X},\mathbf{Z}}$ learned on a training set and CRT based on loss $\sum_i \log \hat{f}_{\mathbf{Y}_i|\mathbf{X}_i,\mathbf{Z}_i}$ run on a test set.

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$^2$Tansey et al., 2018, Bates et al., 2020
Impact of ML prediction error on CRT power

Suppose that $Y = X\beta + g(Z) + \epsilon$, $\epsilon \sim N(0, \sigma^2)$, and we estimate $\hat{g}$ based on a separate training set (like HRT). How does test error in $\hat{g}$ impact the power of the CRT based on $\hat{g}$?

In particular, consider the CRT based on $3_T(X, Y, Z) = 1/\sqrt{n} \sum_{i=1}^{n} (X_i - \mu_i)(Y_i - \hat{g}(Z_i))$, where $\mu_i = E[X_i | Z_i]$. 

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How does test error in $\hat{g}$ impact the power of the CRT based on $\hat{g}$?

In particular, consider the CRT based on

$$T(X, Y, Z) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} (X_i - \mu_i)(Y_i - \hat{g}(Z_i)),$$

where $\mu_i = \mathbb{E}[X_i|Z_i]$.

\footnote{Related to the \textit{generalized covariance measure} of Shah and Peters (2020); studied in the double robustness literature, e.g. Chernozhukov et al. (2018).}
Prediction error impacts asymptotic efficiency of the CRT

For simplicity, suppose \( \text{Var}[X|Z] = s^2 \) a.s. for some \( s^2 > 0 \).

Define the test error \( \mathcal{E} = \mathbb{E}[(\hat{g}(Z) - g(Z))^2] \).

Fixing dimension and training set, let \( n \to \infty \) and \( \beta_n = \frac{h}{\sqrt{n}} \).
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Fixing dimension and training set, let \( n \to \infty \) and \( \beta_n = \frac{h}{\sqrt{n}} \).

**Theorem**

*Under the MX assumption and bounded fourth moments,*

\[
\mathbb{E} [\phi_T(X, Y, Z)|Y, Z] \to \Phi \left( z_{\alpha} + \frac{hs}{\sqrt{\sigma^2 + \mathcal{E}}} \right),
\]

*almost surely in \( Y, Z \).*
More connections to linear regression

Note that

\[ Y - \hat{g}(Z) = X \beta + (g(Z) - \hat{g}(Z) + \epsilon) = X \beta + \epsilon'; \quad \epsilon' \sim (0, \sigma^2 + \mathcal{E}). \]

Estimation error in \( \hat{g} \) inflates the noise level by \( \mathcal{E} \).
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\[ T(X, Y, Z) = \frac{1}{\sqrt{n}} (X - \mu)^T (Y - \hat{g}(Z)) \] is unnormalized OLS \( t \)-stat.
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\[ T(\tilde{X}, Y, Z)|Y, Z \to N(0, s^2(\sigma^2 + \mathcal{E})) \]
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If the semiparametric model is true, CRT resampling distribution asymptotically equivalent to OLS null distribution.
Asymptotic validity under a weaker assumption than MX
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Under the null,

\[ \text{Var} \left[ T_n \mid Y, Z \right] = \frac{1}{n} \sum_{i=1}^{n} \text{Var}[X_i \mid Z_i](Y_i - \hat{g}(Z_i))^2 = S_n^2, \]

with \( S_n^2 \) known. We can show that, almost surely in \((Y, Z)\),

\[ \mathcal{L} \left( S_n^{-1} T_n \mid Y, Z \right) \to N(0, 1). \]

\((S_n, T_n)\) only involves first and second moments \( \mathbb{E}[X \mid Z], \text{Var}[X \mid Z] \).
Asymptotic validity under a weaker assumption than MX

This observation motivates the following:

Definition (MX(2) assumption)

\((X, Y, Z)\) is such that \(\mathbb{E}[X|Z] = \mu(Z)\) and \(\text{Var}[X|Z] = s^2(Z)\), for known functions \(\mu(\cdot)\) and \(s^2(\cdot)\).
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There is an asymptotically valid conditional independence test that does not require the MX assumption or resampling:

**Theorem**

*Under MX(2), \(\phi = 1(S_n^{-1}T_n > z_{1-\alpha})\) has uniform asympt. level \(\alpha\).*
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\((X, Y, Z)\) is such that \(E[X|Z] = \mu(Z)\) and \(Var[X|Z] = s^2(Z)\), for known functions \(\mu(\cdot)\) and \(s^2(\cdot)\).

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**Theorem**

*Under MX(2), \(\phi = 1(S_n^{-1}T_n > z_{1-\alpha})\) has uniform asympt. level \(\alpha\).*

Related to the double robustness literature, but the latter focuses on approximating the first moments \(E[X|Z]\) and \(E[Y|Z]\).*
Connections to causal inference

The MX setting is like that of a randomized experiment: 
\( X \) is the treatment; \( Y \) is the response; \( Z \) are the covariates.

Instead of complete randomization, the treatment \( X \) is assigned to units based on the covariates \( Z \) using a known mechanism \( f^*_{X|Z} \).

Even in the absence of confounding, adjusting for covariates known to reduce variance in estimates of causal effect.
Connections to causal inference

Non-asymptotic tests based on resampling $X$ go back to Fisher (1935) and Rosenbaum (1984). Both treat $Y, Z$ as fixed.

Asymptotic “superpopulation” approach (e.g. Robins et al., 1992) treats $Y$ as random, focused on semiparametric models.

Current work reinforces close links between the two approaches; see also discussion in Rosenbaum (2002).
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Summary

In this talk, we

- Identified the CRT most powerful against point alternatives;
- Expressed CRT’s asymptotic power in terms of ML test error;
- Weakened the MX assumption, retaining asymptotic validity;
- Drew some connections between MX and causal inference.
Future work

Many questions still remain open:

- Are all valid tests under MX also conditionally valid? If not, are all optimal tests conditionally valid?
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These lines of inquiry can improve our understanding of MX methodologies and help guide their development in the future.

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