

# ADVANCES IN INTEGRATIVE CAUSAL ANALYSIS

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# CREDIT AND ACKNOWLEDGEMENTS

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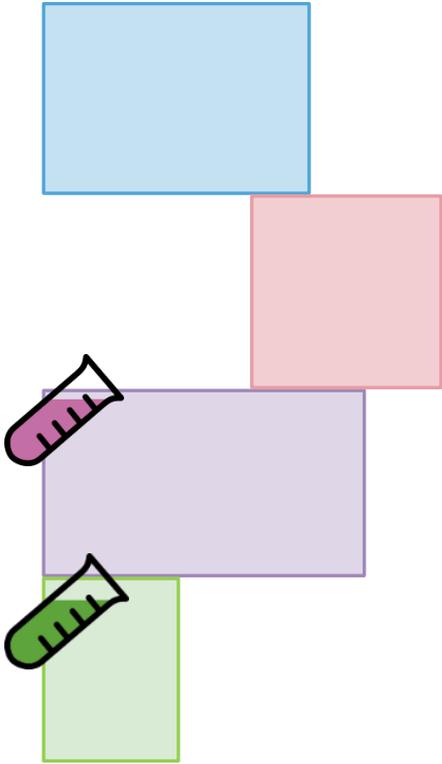
Computer Science Department,  
University of Crete

EU STATegra, EU ERC Causalpath, GSRT  
ARISTEIA II Epilogeas

# HETEROGENEOUS DATA SETS MEASURING THE SAME SYSTEM UNDER STUDY

Study \ Variables	Thrombosis 	Contraceptives 	Protein C 	Breast Cancer 	Protein Y 	Protein Z 
1 observational data	Yes	No	10.5	Yes	-	-
	No	Yes	5.3	No	-	-
					-	-
	No	Yes	0.01	No	-	-
2 observational data	-	-	-	Yes	0.03	9.3
	-	-	-			
	-	-	-	No	3.4	22.2
3 experimental data	No	No	0 (Control)	No	3.4	-
	Yes	No	0 (Control)	Yes	2.2	-
					-	-
	Yes	Yes	5.0 (Treat.)	Yes	7.1	-
	No	Yes	5.0 (Treat.)	No	8.9	-
4 experimental data	No	No (Ctrl)	-	-	-	-
	No	No (Ctrl)	-	-	-	-
			-	-	-	-
	Yes	Yes(Treat)	-	-	-	-

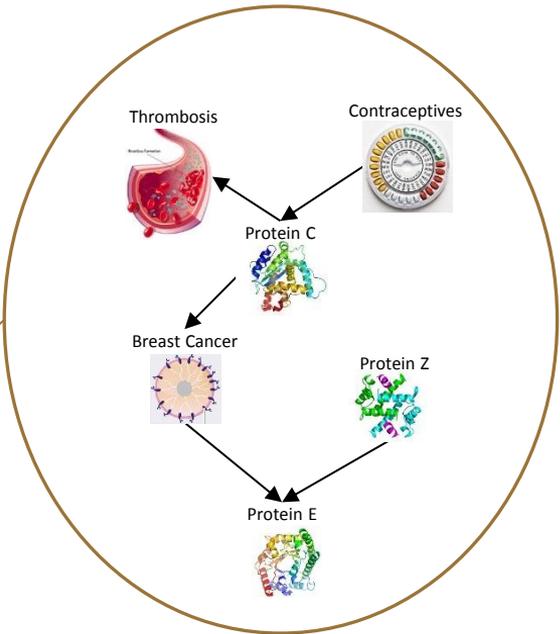
# INTEGRATIVE CAUSAL ANALYSIS



Data can not be pulled together:

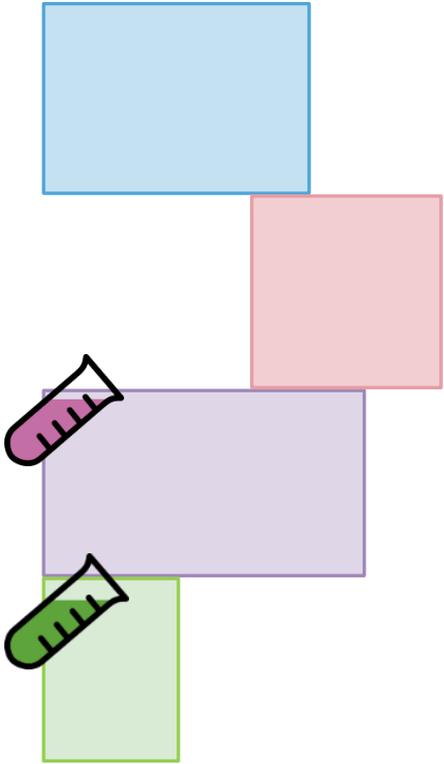
**Missing variables** cannot be treated as missing values.

They come from **different experimental conditions (different distributions)**.

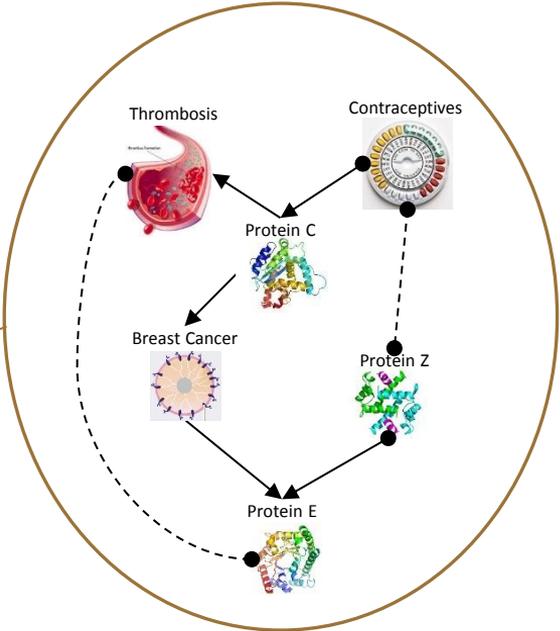


Data come from the **same causal mechanism**.

# INTEGRATIVE CAUSAL ANALYSIS

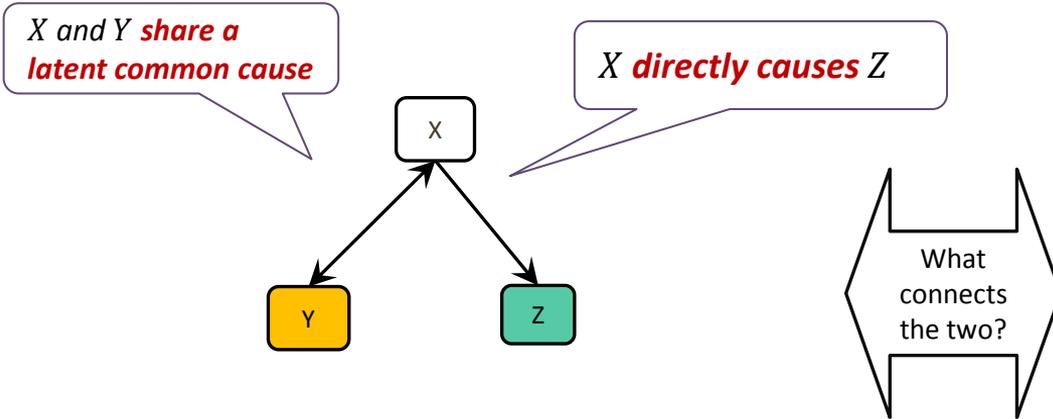


Identify the causal graphs that simultaneously fit all data.



# CAUSAL MODELS

Semi Markov Causal Graph  $\mathcal{G}$



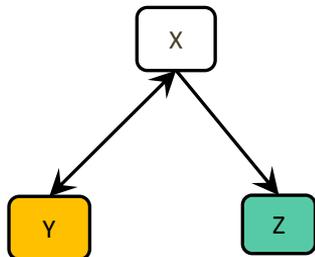
- Edges represent direct causal relations.
- Both edges allowed for a single pair of variables.
- No directed cycles (no causal feedback).

JPD  $\mathcal{P}$

		Z	
X	Y	Yes	No
Yes	Yes	0,01	0,04
Yes	No	0,01	0,04
No	Yes	0,000045	0,044955
No	No	0,000855	0,854145

- $P(Y|V, Z) = P(Y|V)$  or  $Y$  is **independent** of  $Z$  given  $V$  : **Ind**( $Y, Z | V$ )
- Otherwise : **Dep**( $Y, Z | V$ )
- The set of conditional independencies entailed by the JPD is called the **independence model J**

# CAUSAL ASSUMPTIONS



$$Ind(Y, Z | X)$$

$$Dep(Y, Z | \emptyset)$$

$$Dep(X, Z | \emptyset)$$

$$Dep(X, Z | Y)$$

$$Dep(Y, X | \emptyset)$$

$$Dep(Y, X | Z)$$

## Causal Markov Assumption:

Every variable is independent of its **non-effects** (non-descendants in the graph) given its **direct causes** (parents).

## Causal Faithfulness Assumption:

Independences stem **only** from the causal structure, **not the parameterization** of the distribution.

All independencies in  $\mathcal{J}$  can be identified in  $\mathcal{G}$  using the graphical criterion of **m-separation**.

# $m$ -SEPARATION

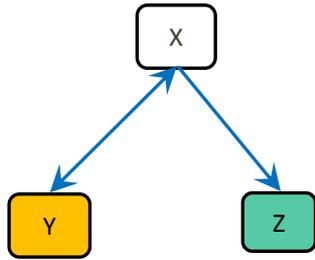
A path  $X_1, \dots, X_n$  between  $X_1$  and  $X_n$  is  **$m$ -connecting given  $V$**  if for every triple  $\langle X_{i-1}, X_i, X_{i+1} \rangle$  on the path:

- If  $X_{i-1} * \rightarrow X_i \leftarrow * X_{i+1}$ ,  
     $X_i$  or one of its descendants  $\in V$
- Otherwise,  $X_i \notin V$

**$m$ -connecting** path  $\Rightarrow$  information flow  $\Rightarrow$  **dependence**

**No  $m$ -connecting** path  $\Rightarrow$  no information flow  $\Rightarrow$  **independence** ( $m$ -separation)

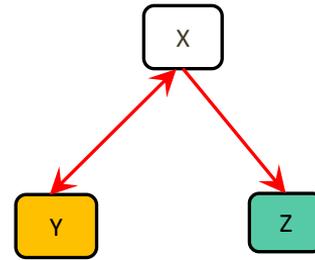
# *m*-SEPARATION



$$Y \leftrightarrow X \longrightarrow Z$$

is *m*-connecting given  $\emptyset$

$$\Leftrightarrow Dep(Y, Z | \emptyset)$$



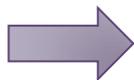
$$Y \leftrightarrow X \longrightarrow Z$$

is **NOT** *m*-connecting given  $X$

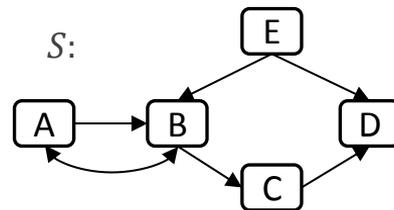
$$\Leftrightarrow Ind(Y, Z | X)$$

# REVERSE ENGINEERING CAUSAL MODELS

A	B	C	D	E
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—
—	—	—	—	—



$Dep(A, D|\emptyset)_{D_2}$   
 $Dep(A, D|B)_{D_2}$   
 $Dep(A, D|E)_{D_2}$   
 $Dep(A, D|C)_{D_2}$   
 ...  
 $Ind(A, E|\emptyset)_{D_2}$



$\exists$   $m$ -connecting path from A to D given  $\emptyset$  in S  
 $\exists$   $m$ -connecting path from A to D given B in S  
 $\vdots$   
 $\exists$   $m$ -connecting path from A to B given  $\emptyset$  in S  
 $\vdots$   
 $\nexists$   $m$ -connecting path from A to E given  $\emptyset$  in S

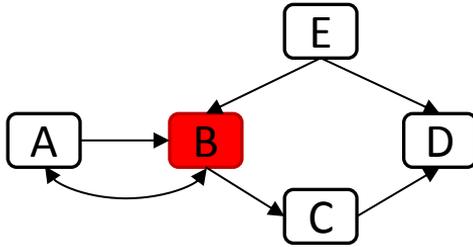
Dataset  $D_i$  measuring a set of variables

Independence model  $J_i$

Path constraints on the underlying causal graph

# INTERVENTIONS / MANIPULATIONS IN CAUSAL MODELS

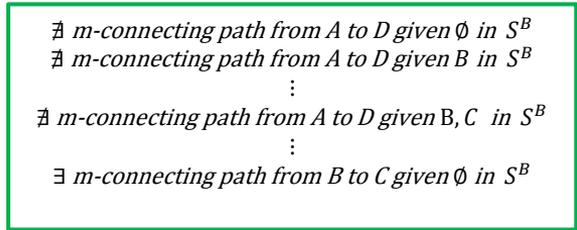
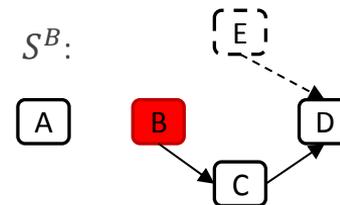
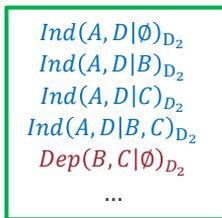
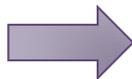
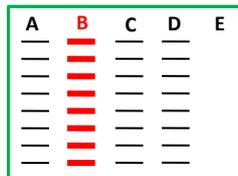
Graph (SMCG)  $S$



Values of B are **set solely by the manipulation procedure.**

If you know direct causal relations, **remove all edges into the manipulated variable.**

# INCA: OVERLAPPING VARIABLES, INTERVENTIONS

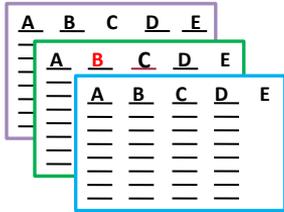


Dataset  $D_i$  measuring a subset of variables, some of which are manipulated

Manipulated independence model  $J_i$

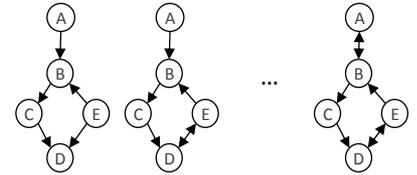
Path constraints on the **manipulated** underlying causal graph

# PROBLEM DEFINITION



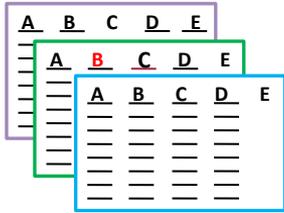
Data sets  $D_1, \dots, D_n$  measuring overlapping variables under different manipulations

Causal Markov Assumption  
Causal Faithfulness Assumption

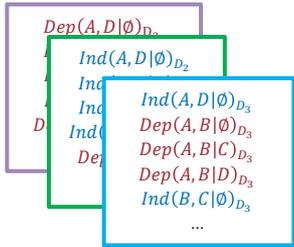


Graphs  $S$  that simultaneously fit all data

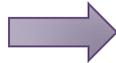
# PROPOSED APPROACH



Data sets  $D_1, \dots, D_n$

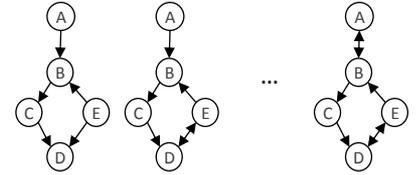
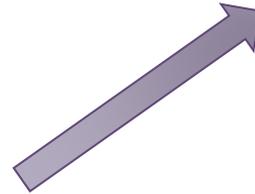


Independence models  $J_1, \dots, J_n$



$\exists$   $m$ -connecting path from  $A$  to  $D$  given  $\emptyset$  in  $S^{I_1}$   
 $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $B$  in  $S^{I_1}$   
 $\vdots$   
 $\exists$   $m$ -connecting path from  $A$  to  $B$  given  $\emptyset$  in  $S^{I_2}$   
 $\vdots$   
 $\nexists$   $m$ -connecting path from  $B$  to  $C$  given  $\emptyset$  in  $S^{I_n}$

path constraints in  $S_1, \dots, S_n$



Graphs  $S$  that simultaneously fit all data

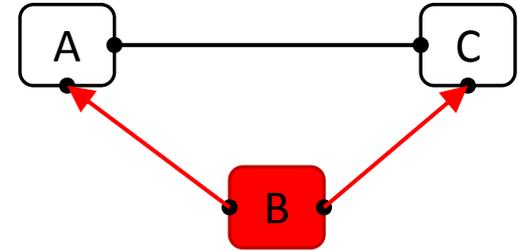
# CONSTRAINTS AS BOOLEAN FORMULAE

- Suppose you know nothing about the structure  $S$  of the three variables.

- In a data set where  $B$  is manipulated,  $\text{Ind}(A, C|\emptyset)$

- In path terms:

$\nexists$  m-connecting path between  $A$  and  $C$  given  $\emptyset$  in  $S^B$



**A-C does not exist**

$\neg \text{edge}(A, C)$

**AND**

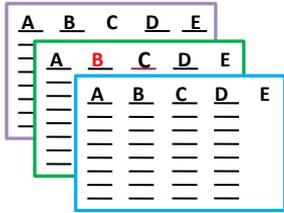
**A  $\leftarrow$  B  $\rightarrow$  C does not exist**

$[\neg \text{edge}(A, B)$   
 $\vee \neg \text{tail}(A, B)$   
 $\vee \neg \text{edge}(B, C)$   
 $\vee \neg \text{tail}(C, B)]$

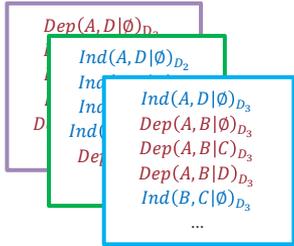
In SATisfiability terms:

$\neg \text{edge}(A, C) \wedge$   
 $[\neg \text{edge}(A, B) \vee \neg \text{tail}(A, B) \vee \neg \text{edge}(B, C) \vee \neg \text{tail}(C, B)]$

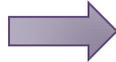
# PROPOSED APPROACH



Data sets  $D_1, \dots, D_n$

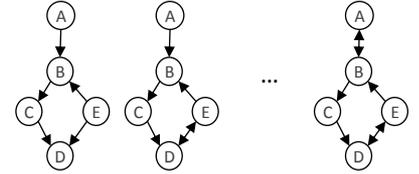


Independence models  $J_1, \dots, J_n$



$\exists$   $m$ -connecting path from  $A$  to  $D$  given  $\emptyset$  in  $S^{I_1}$   
 $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $B$  in  $S^{I_1}$   
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 $\vdots$   
 $\nexists$   $m$ -connecting path from  $B$  to  $C$  given  $\emptyset$  in  $S^{I_n}$

path constraints in  $S_1, \dots, S_n$



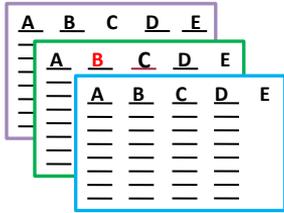
Graphs  $S$  that simultaneously fit all data



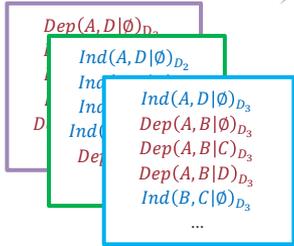
$[edge(A-D) \vee (edge(A-C)$   
 $\wedge edge(C-D) \wedge tail(C, A) \dots] \wedge$   
 $\vdots$   
 $[edge(A-D) \vee (edge(A-C) \dots] \wedge$   
 $\vdots$   
 $[\neg edge(A-D) \wedge (\neg edge(A-C) \dots)]$

Formula  $\Phi$  encoding path constraints in  $S$

# SCALING UP

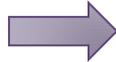


Data sets  $D_1, \dots, D_n$



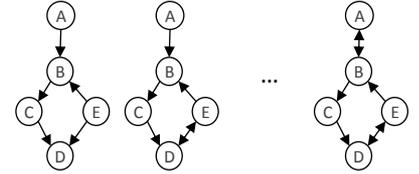
Independence models  $J_1, \dots, J_n$

How many constraints?



$\exists$   $m$ -connecting path from  $A$  to  $D$  given  $\emptyset$  in  $S^{I_1}$   
 $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $B$  in  $S^{I_1}$   
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 $\nexists$   $m$ -connecting path from  $B$  to  $C$  given  $\emptyset$  in  $S^{I_n}$

path constraints in  $S_1, \dots, S_n$



Graphs  $S$  that simultaneously fit all data



$[edge(A-D) \vee (edge(A-C)$   
 $\wedge edge(C-D) \wedge tail(C, A) \dots] \wedge$   
 $\vdots$   
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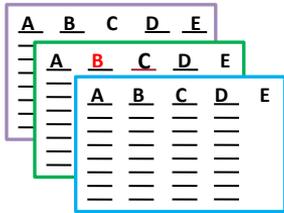
Formula  $\Phi$  encoding path constraints in  $S$

# SCALING UP

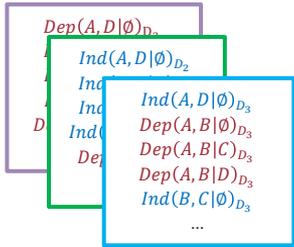
How many constraints?

- Independence model:  $2^n$  conditional (in)dependencies.
  - You only need a subset that entail all others ( $\binom{n}{2}$ ).
  - FCI (Spirtes, Glymour, Scheines 2000, Zhang 2008) finds this subset of conditional (in)dependencies
    - also outputs a graph that summarizes the characteristics of every possible causal structure that entails them.
  - Use FCI and only convert
    - (non) adjacencies to  $(\not\exists)\exists$  inducing path.
    - Colliders with order to  $(\not\exists)\exists$  inducing and directed paths.

# SCALING UP



Data sets  $D_1, \dots, D_n$

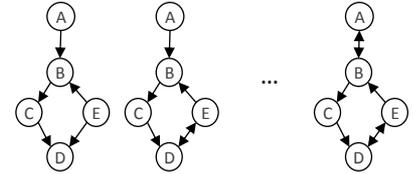


Independence models  $J_1, \dots, J_n$

How many paths?

- $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $\emptyset$  in  $S^{I_1}$
- $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $B$  in  $S^{I_1}$
- $\vdots$
- $\exists$   $m$ -connecting path from  $A$  to  $B$  given  $\emptyset$  in  $S^{I_2}$
- $\vdots$
- $\nexists$   $m$ -connecting path from  $B$  to  $C$  given  $\emptyset$  in  $S^{I^n}$

path constraints in  $S_1, \dots, S_n$



Graphs  $S$  that simultaneously fit all data



$$\begin{aligned}
 & [edge(A-D) \vee (edge(A-C) \\
 & \wedge edge(C-D) \wedge tail(C, A) \dots] \wedge \\
 & \vdots \\
 & [edge(A-D) \vee (edge(A-C) \dots] \wedge \\
 & \vdots \\
 & [\neg edge(A-D) \wedge (\neg edge(A-C) \dots)]
 \end{aligned}$$

Formula  $\Phi$  encoding path constraints in  $S$

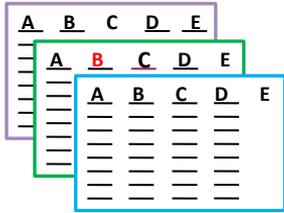
# SCALING UP

Reduce the number of paths.

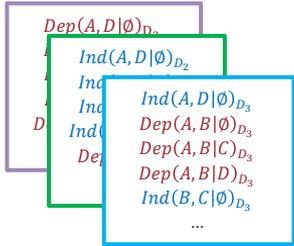
- Remove edges based on preprocessing.
- Restrict the path length.

How many paths?

# SCALING UP

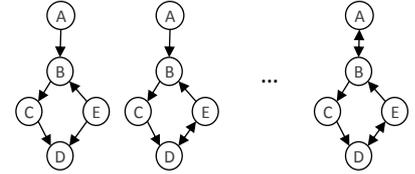


Data sets  $D_1, \dots, D_n$



Independence models  $J_1, \dots, J_n$

How many solutions?



Graphs  $S$  that simultaneously fit all data



$\exists$   $m$ -connecting path from  $A$  to  $D$  given  $\emptyset$  in  $S^{I_1}$   
 $\exists$   $m$ -connecting path from  $A$  to  $D$  given  $B$  in  $S^{I_1}$   
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path constraints in  $S_1, \dots, S_n$



$[edge(A-D) \vee (edge(A-C)$   
 $\wedge edge(C-D) \wedge tail(C, A) \dots] \wedge$   
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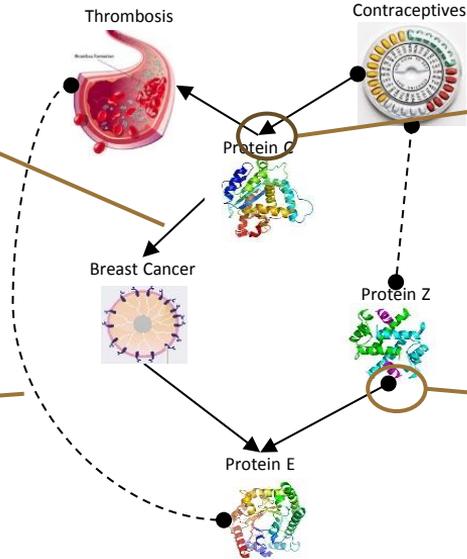
Formula  $\Phi$  encoding path constraints in  $S$

# SCALING UP – QUERY-BASED LEARNING

How many solutions?

solid edges:  
present in **all**  
solutions

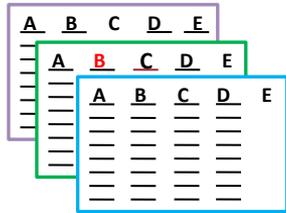
dashed edges:  
present in **some**  
solutions



solid endpoints:  
same orientation in  
**all** solutions

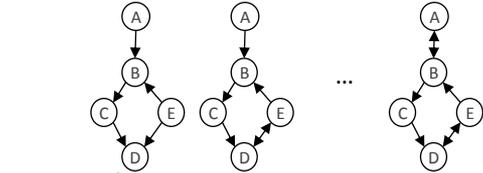
dashed endpoints:  
different  
orientation in  
**different** solutions

# STATISTICAL ERRORS

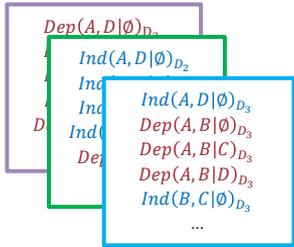


Data sets  $D_1, \dots, D_n$

Statistical Errors



paths  $S$  that simultaneously fit all data



Independence models  $J_1, \dots, J_n$

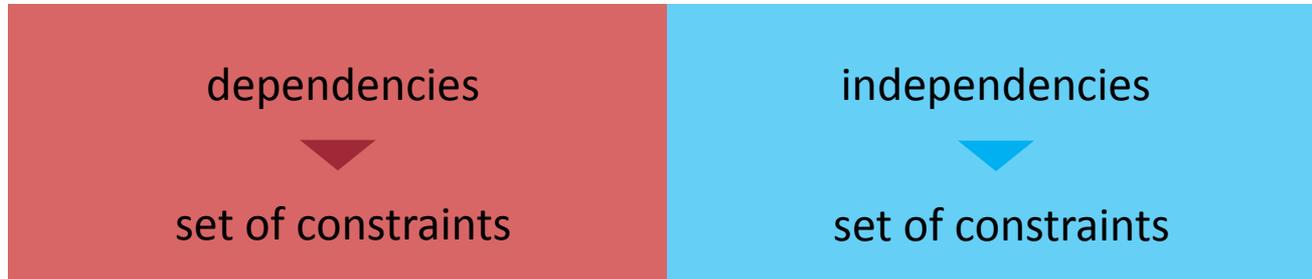
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 $\vdots$   
 $\nexists$   $m$ -connecting path from  $B$  to  $C$  given  $\emptyset$  in  $S^{I_n}$

path constraints in  $S_1, \dots, S_n$

$[edge(A-D) \vee (edge(A-C) \wedge edge(C-D) \wedge tail(C, A) \dots)] \wedge$   
 $\vdots$   
 $[edge(A-D) \vee (edge(A-C) \dots)] \wedge$   
 $\vdots$   
 $[\neg edge(A-D) \wedge (\neg edge(A-C) \dots)]$

Formula  $\Phi$  encoding path constraints in  $S$

# STATISTICAL ERRORS



Select non conflicting constraints!

- How?
- Assign confidence to every constraint.

What happens with statistical errors?

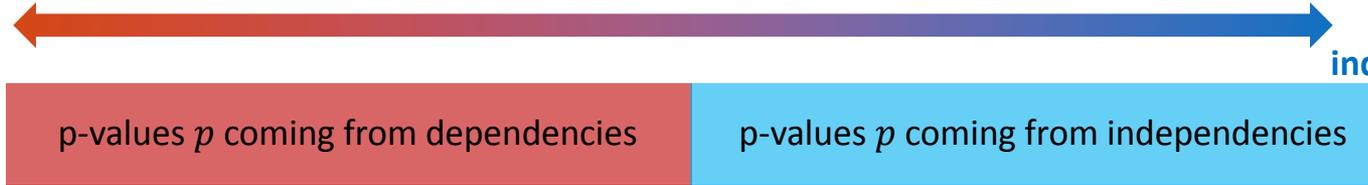
Conflicts make SAT instance unsatisfiable!



# p-VALUES TO PROBABILITIES

low p-values suggest dependence

high p-values suggest independence



$$H_1: p \sim \text{Beta}(\xi, 1), \quad \xi \in (0, 1)$$

$$H_0: p \sim \text{Beta}(1, 1)$$

$$f(p|\pi_0, \xi) = \pi_0 + (1 - \pi_0)\xi p^{\xi-1}$$

The proportion of p-values coming from  $H_0$

If you know  $\hat{\pi}_0, \hat{\xi}$  you can find posterior probabilities

$$P(H_0|p) = \frac{\frac{\hat{\pi}_0}{(1 - \hat{\pi}_0)\hat{\xi}p^{(1-\hat{\xi})}}}{1 + \frac{\hat{\pi}_0}{(1 - \hat{\pi}_0)\hat{\xi}p^{(1-\hat{\xi})}}}$$
$$P(H_1|p) = 1 - P(H_0|p)$$

# ALGORITHM PROPeR

## PROPeR

identify  $\widehat{\pi}_0$ :  
(Storey and Tibshirani,  
2003)



Identify  $\widehat{\xi}$ :  
Minimize negative log  
likelihood of

$$f(p|\widehat{\pi}_0, \xi) = \widehat{\pi}_0 + (1 - \widehat{\pi}_0)\xi p^{\xi-1}$$



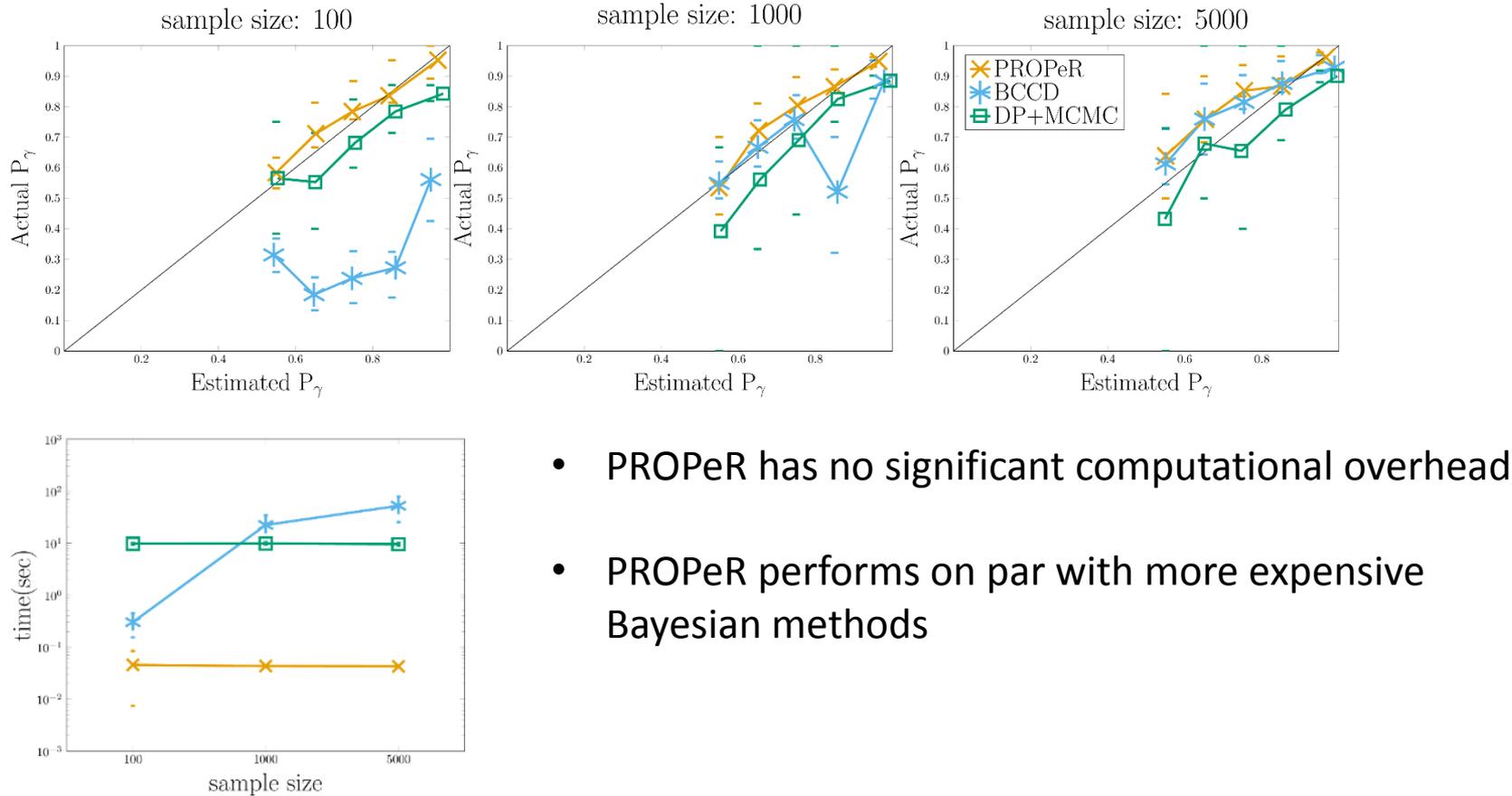
Estimate  
 $P(H_0|p), P(H_1|p)$

- Constraints correspond to adjacencies (or absence thereof), not (in) dependencies
  - adjacent(X, Y): The maximum p-value for X, Y was  $< \alpha$
  - $\neg$  adjacent(X, Y): The maximum p-value for X, Y was  $> \alpha$
- Maximum p-values may not follow a uniform distribution
- Samples (p-values) are not i.i.d.
- Did we cut too many corners?

### Calibration of probability estimates compared to

- BCCD: Posterior probability of a feature is obtained by the weighted sum of the likelihoods of all networks with  $< 6$  variables [Claassen and Heskes, 2012]
- DP+MCMC: Exact method, scales up to  $\sim 20$  variables, MCMC priors [Eaton and Murphy, 2007]

## Discrete variables



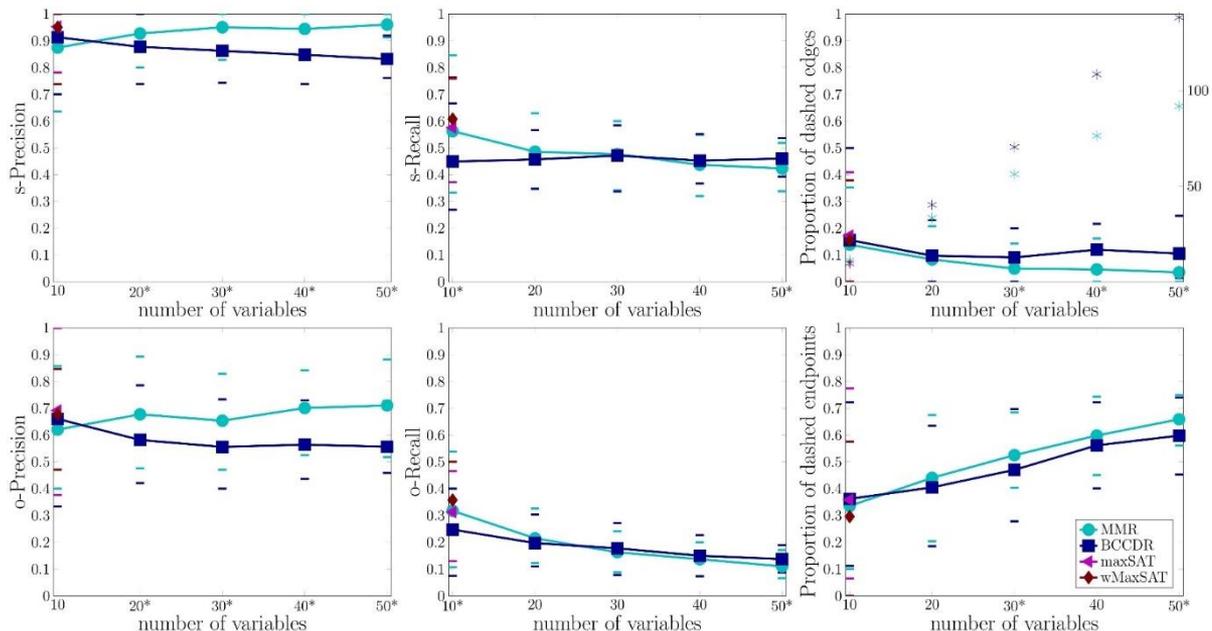
# CONFLICT RESOLUTION STRATEGIES

P(constraint)	constraint
0.999	$\exists$ m-connecting path from A to D given $\emptyset$ in $S^{I_n}$
0.998	$\nexists$ m-connecting path from A to D given $\emptyset$ in $S^{I_1}$
$\vdots$	$\vdots$
0.510	$\exists$ m-connecting path from A to B given $\emptyset$ in $S^{I_1}$

- MMR: Estimate confidence using PROPeR, satisfy constraints in decreasing order of confidence.
- BCCDR: Estimate confidence using BCCD, satisfy constraints in decreasing order of confidence.
- maxSAT: satisfy maximum number of constraints.
- wMaxSAT: satisfy constraints with maximum sum of weights, where weights are PROPeR estimates.

# CONFLICT RESOLUTION STRATEGIES

20 variables, 5 overlapping data sets, 100 samples each

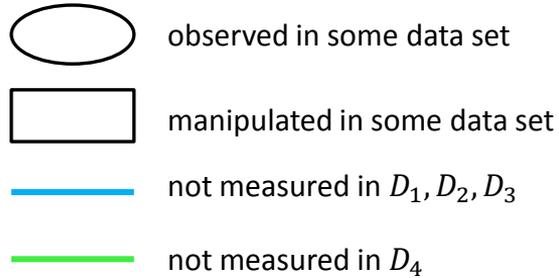


- Greedy strategies perform similarly
- Max/ weighted max strategies do not scale up.
- All strategies are equally conservative.

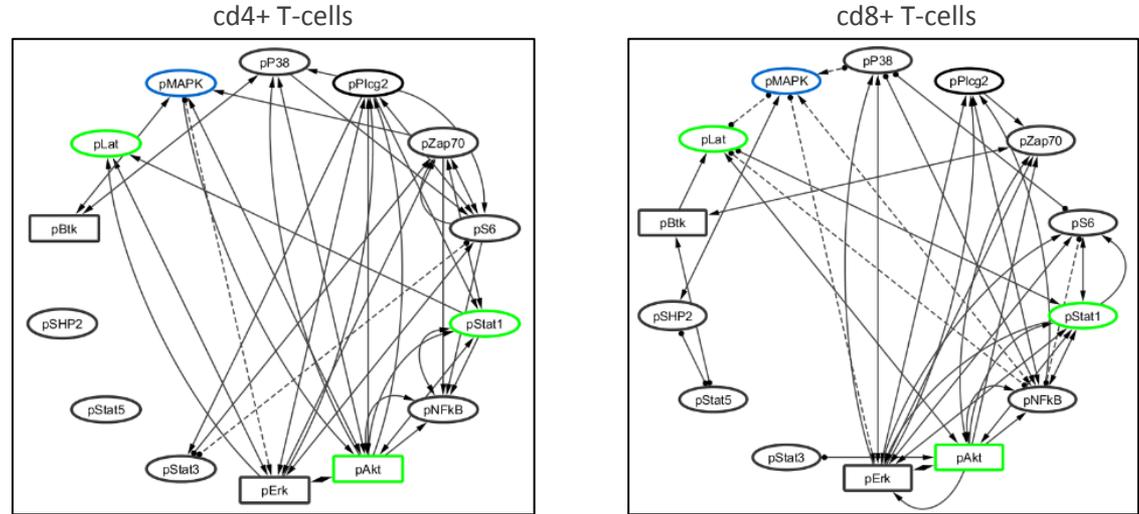
# PERFORMANCE EVALUATION

- ~2000 runs in simulated networks
- vs maximum path length, number of variables, sparseness of the ground truth networks, sample size, number of input data sets, proportion of non-overlapping variables.
  
- Performance improves with more data sets.
- Performance improves with more samples.
- Performance is better for sparser networks.
- COmbINE scales up to 100 variables.
- Maximum path length and number of non-overlapping variables do not influence COmbINE's performance.

# APPLICATION ON MASS CYTOMETRY DATA

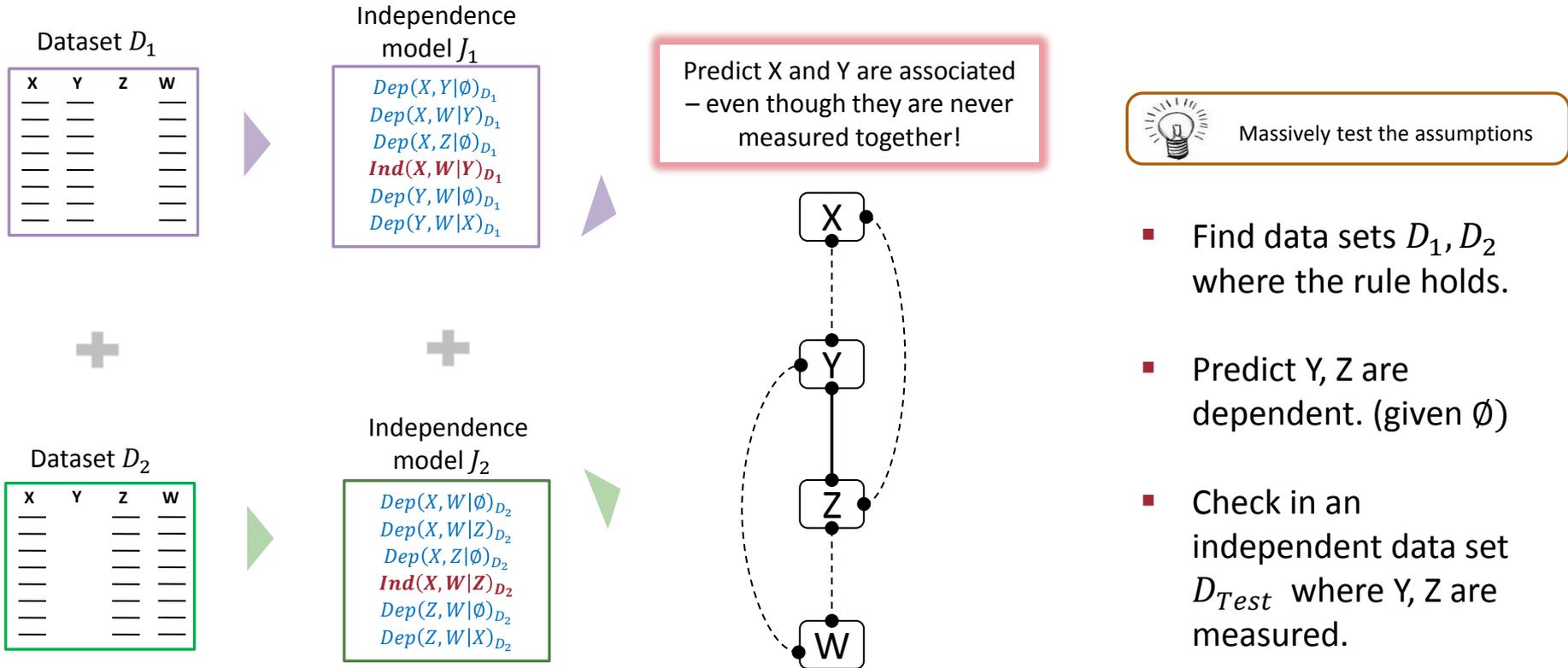


- 4 data sets.
- 3 different manipulations.
- 14 variables (phosphorylated proteins).
- 2 different cell populations.

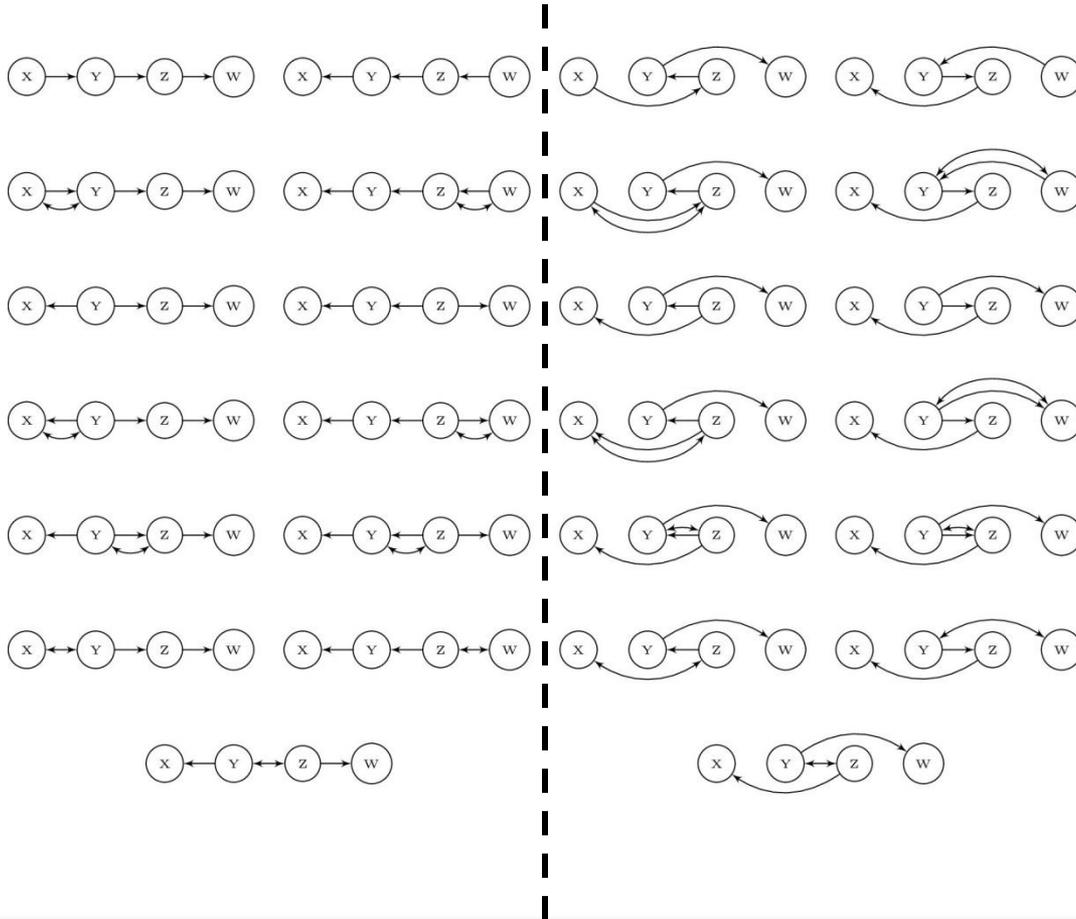


Data set	Source	latent ( $L_i$ ):	manipulated ( $I_i$ )
$D_1$	Bodenmiller et al. (2012)	pMAPK	pAkt
$D_2$	Bodenmiller et al. (2012)	pMAPK	pBtk
$D_3$	Bodenmiller et al. (2012)	pMAPK	pErk
$D_4$	Bendall et al. (2011)	pAkt, pLat, pStat1	pErk

# INCA RULE



# FURTHER INFERENCE: PREDICT CORRELATION STRENGTH



# MAKING IT WORK ON REAL DATA

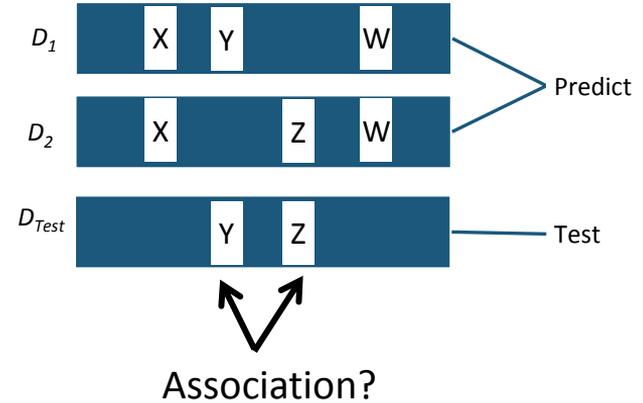
1. Original Dataset



2. Split to  $D_1$ ,  $D_2$  and  $D_{test}$  containing different samples



3. Find  $X, Y, W$  in  $D_1$  and  $X, Z, W$ , in  $D_2$  such that the INCA rule applies



- Restrict inferences only to cases where the probability of errors is small, i.e.  $p$ -values are extreme

$p_{XY.Z} < 0.05$  accept  $Dep(X, Y|Z)$

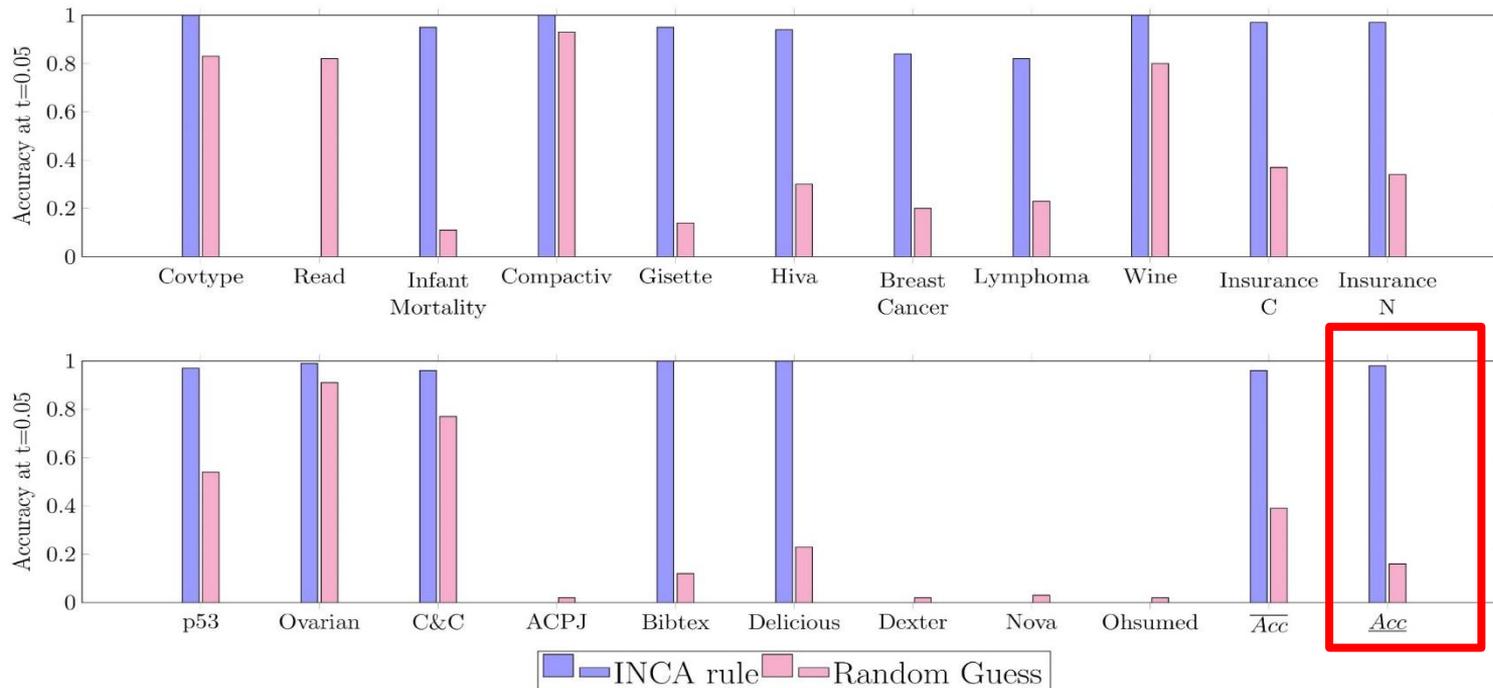
$p_{XY.Z} > 0.3$  accept  $Ind(X, Y|Z)$

Else, undecided (forgo making any inferences)

# DATASETS

Name	# instances	# variables	Group Size	Variables type	Scientific domain	# predictions
<b>Covtype</b>	581012	55	55	Nominal/Ordinal	Agricultural	222
<b>Read</b>	681	26	26	Nominal/Continuous/Ordinal	Business	0
<b>Infant-mortality</b>	5337	83	83	Nominal	Clinical study	22
<b>Compactiv</b>	8192	22	22	Continuous	Computer science	135
<b>Gisette</b>	7000	5000	50	Continuous	Digit recognition	423
<b>Hiva</b>	4229	1617	50	Nominal	Drug discovering	554
<b>Breast-Cancer</b>	286	17816	50	Continuous	Gene expression	1833
<b>Lymphoma</b>	237	7399	50	Continuous	Gene expression	7712
<b>Wine</b>	4898	12	12	Continuous	Industrial	4
<b>Insurance-C</b>	9000	84	84	Nominal/Ordinal	Insurance	1839
<b>Insurance-N</b>	9000	86	86	Nominal/Ordinal	Insurance	226
<b>p53</b>	16772	5408	50	Continuous	Protein activity	46647
<b>Ovarian</b>	216	2190	50	Continuous	Proteomics	539165
<b>C&amp;C</b>	1994	128	128	Continuous	Social science	99241
<b>ACPJ</b>	15779	28228	50	Continuous	Text mining	0
<b>Bibtex</b>	7395	1995	50	Nominal	Text mining	1
<b>Delicious</b>	16105	1483	50	Nominal	Text mining	856
<b>Dexter</b>	600	11035	50	Nominal	Text mining	0
<b>Nova</b>	1929	12709	50	Nominal	Text mining	0
<b>Ohsumed</b>	5000	14373	50	Nominal	Text mining	0

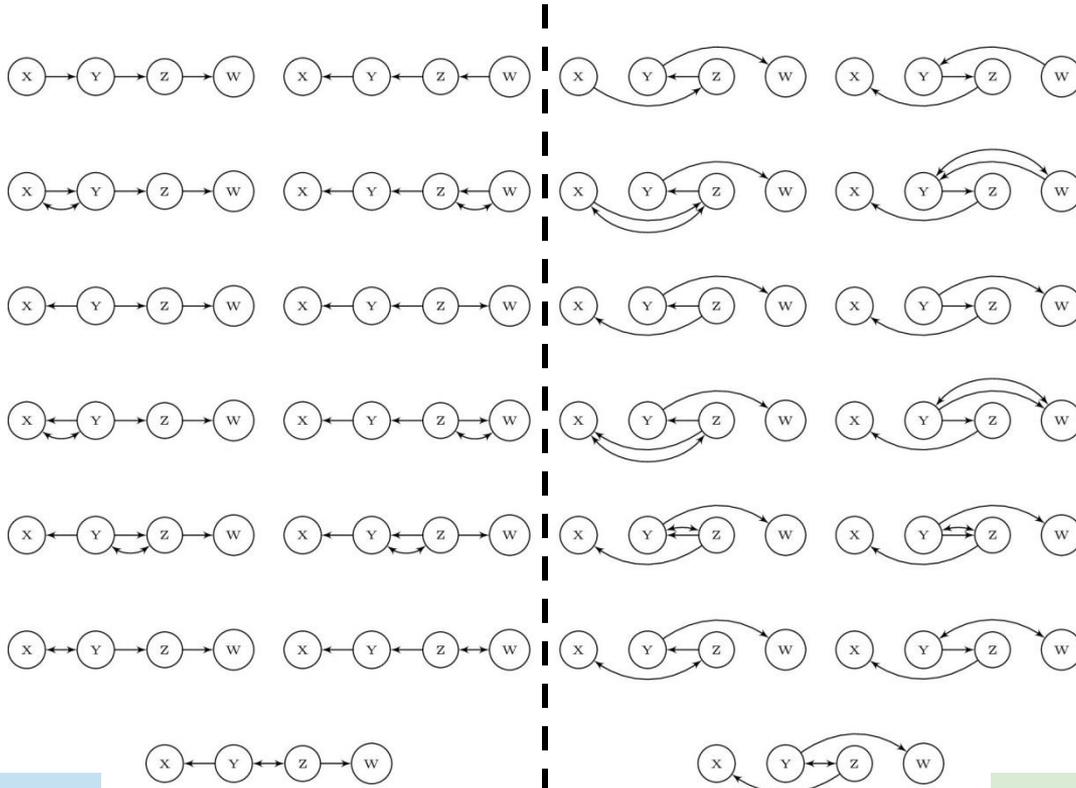
# HOW DID WE DO?



- About 700000 predictions in 20 datasets.
- Accuracy: The percentage of p-values  $< 0.05$ .
  - May include false positives and exclude false negatives.

98% accuracy vs.  
16% of random guessing

# FURTHER INFERENCE: PREDICT CORRELATION STRENGTH



$$\rho_{XZ} = \rho_{XY} \times \rho_{YZ}$$

$$\rho_{YW} = \rho_{YZ} \times \rho_{ZW}$$

$$\rho_{XY} = \rho_{XZ} \times \rho_{YZ}$$

$$\rho_{ZW} = \rho_{YZ} \times \rho_{YW}$$

$$\text{Predict } \widehat{r}_{YZ}^1 \approx \frac{1}{2} \left( \frac{r_{XZ}}{r_{XY}} + \frac{r_{YW}}{r_{ZW}} \right)$$

Only one of  $|\widehat{r}_{YZ}^1|, |\widehat{r}_{YZ}^2|$  is  $< 1$

$$\text{Predict } \widehat{r}_{YZ}^2 \approx \frac{1}{2} \left( \frac{r_{XY}}{r_{XZ}} + \frac{r_{ZW}}{r_{YW}} \right)$$

# VS STATISTICAL MATCHING



Conditional Independence Assumption (CIA)

**Non common** variables are **independent** given the **common variables**

+ Multivariate Normality

VS.



1. (Causal) Markov
2. (Causal) Faithfulness
3. Acyclicity
4. Multivariate normality

Data Sets	SMR	INCA rule
ACPJ	0.00 [0.00;0.01]	-
Breast-Cancer	0.25 [0.24;0.25]	0.88 [0.87;0.90]
C&C	0.68 [0.65;0.71]	0.91 [0.91;0.91]
Compactiv	0.49 [0.44;0.54]	0.88 [0.83;0.92]
Insurance-C	0.47 [0.42;0.51]	0.90 [0.89;0.91]
Lymphoma	0.32 [0.31;0.32]	0.50 [0.47;0.52]
Ohsumed	0.01 [0.00;0.01]	-
Ovarian	0.50 [0.50;0.51]	0.14 [0.14;0.14]
Wine	0.58 [0.52;0.64]	0.99 [0.47;1.00]
p53	0.45 [0.44;0.45]	0.87 [0.87;0.87]
Mean over data sets	0.38 [0.35;0.40]	0.76 [0.68;0.77]
<b>On all predictions</b>	<b>0.58 [0.57;0.58]</b>	<b>0.89 [0.89;0.89]</b>

- When predictions are based on only 2 common variables, statistical matching is unreliable.
- INCA rule's predictions are highly correlated with sample estimates (0.89 correlation).

# CONTRIBUTIONS

- Comparison of causal models under causal insufficiency.
  - Introduction of SAT-based causal analysis: exploit 40 years of SAT-solving technology.
  - Query-based approach to avoid explosion of possible solutions.
  - Method for estimating posterior probabilities from p-values.
  - Scalable INCA algorithm.
  - A proof of concept that causal assumptions can make testable qualitative and quantitative predictions.
  - Being local and conservative improves applicability of causal methods.
-

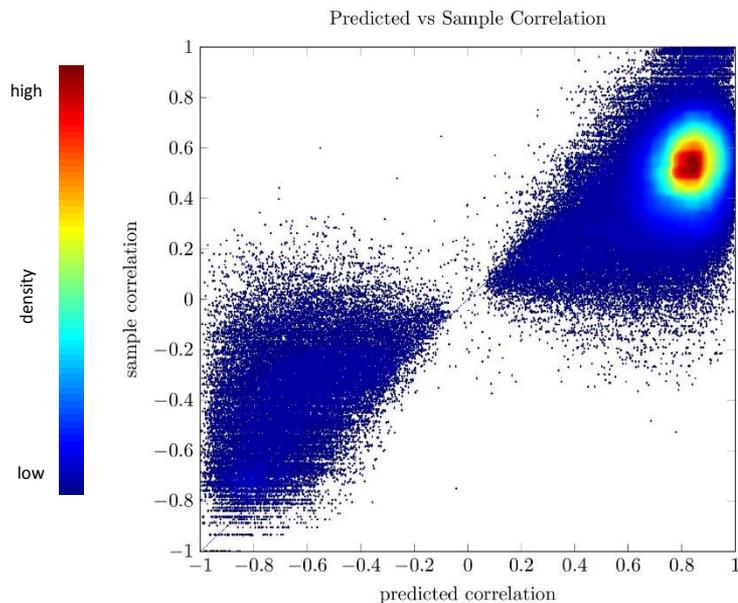
# CONCLUSIONS AND FUTURE WORK

- Beyond one dataset at a time
  - Vision of automatically analyzing a large portion of available datasets in a domain
- Inclusion of Prior Causal Knowledge [ICML 2012, UAI 2013]
- Handling Case-Control Data [UAI 2015]
- Handling batch effects [upcoming]
- Handling temporal data and temporal information
- Improve reliability
- Ability to work with semantically similar data
- Quantitative Algorithms?

# PUBLICATIONS

- S. Triantafillou and I. Tsamardinos, Causal Discovery from Multiple Interventions, *JMLR*, to appear.
  - Giorgos Borboudakis, Ioannis Tsamardinos (2015). **Bayesian Network Learning with Discrete Case-Control Data**. *Uncertainty in Artificial Intelligence (UAI)*, 2015.
  - S. Triantafillou, I. Tsamardinos and A. Roupelaki ,Finding Neighborhoods of High Confidence in Constraint-based Causal Discovery, *PGM 2014*.
  - Borboudakis G., & Tsamardinos, I. (2013). Scoring and Searching over Bayesian Networks with Informative, Causal and Associative Priors. *Uncertainty in Artificial Intelligence (UAI) 2013*
  - Borboudakis, G., & Tsamardinos, I. (2012). Incorporating Causal Prior Knowledge as Path-Constraints in Bayesian Networks and Maximal Ancestral Graphs. *Proceedings of the 29th International Conference on Machine Learning, ICML 2012*
  - I. Tsamardinos, S. Triantafillou and V. Lagani ,Towards Integrative Causal Analysis of Heterogeneous Datasets and Studies. *JMLR.*, 13:1097-1157, 2012.
  - S. Triantafillou, I. Tsamardinos, and I. G. Tollis. Learning causal structure from overlapping variable sets. In *Artificial Intelligence and Statistics*, pages 860-867, 2010.
  - S. Triantafillou and I. Tsamardinos, Predicting associations from multiple “omics” data sets, HSCBB12, Best Poster Award Recipient.
  - V. Lagani, S. Triantafillou, G. Ball, I. Tsamardinos and J. Tegner, Probabilistic Computational Causal Discovery for Systems Biology, In *Uncertainty in Biology: a computational modeling approach*, Amit Gefen (Editor), to appear.
  - G. Borboudakis, S. Triantafillou and I. Tsamardinos Tools and Algorithms for Causally Interpreting Directed Edges in Maximal Ancestral Graphs, *PGM 2012*.
  - V. Lagani, I. Tsamardinos and S. Triantafillou Learning from mixture of experimental data: a constraint-based approach In *Hellenic Conference on Artificial Intelligence (SETN 2012)*.
  - G. Borboudakis, S. Triantafillou, V. Lagani, I. Tsamardinos, A constraint-based approach to incorporate prior knowledge in causal model, *ESANN 2011*.
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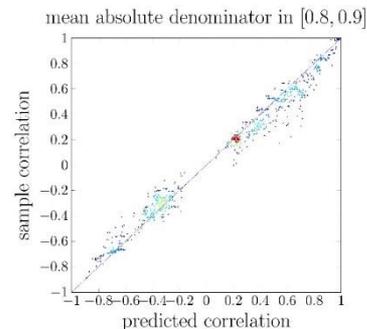
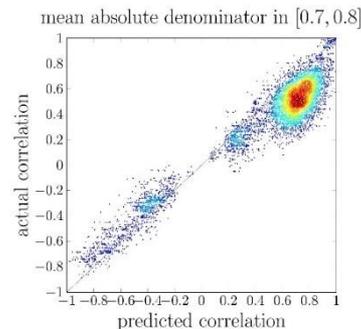
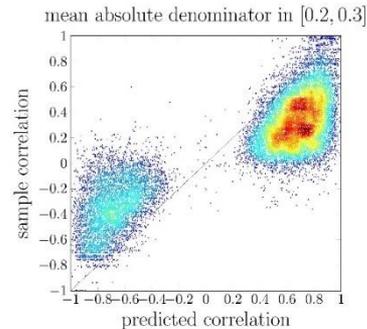
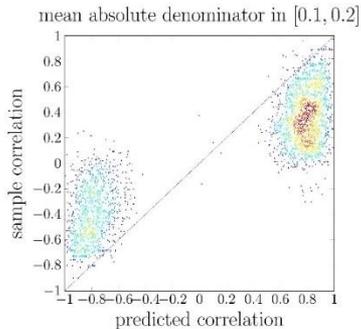
# BIAS OF PREDICTIONS



why?

When actual correlation is low, only overestimated sample correlations pass the independence test

Predicted vs sample correlations over all data sets, grouped by mean absolute value of the denominators used in their computations



- Correlation of predicted vs sample correlations is 0.89
- Predictions based on large correlations have reduced bias

# VS STATISTICAL MATCHING



Conditional Independence Assumption (CIA)

**Non common** variables are **independent** given the **common variables**

+ Multivariate Normality

VS.



1. (Causal) Markov
2. (Causal) Faithfulness
3. Acyclicity
4. Multivariate normality

Data Sets	$SMR_{all}$	$SMR_{xw}$	INCA rule
ACPJ	0.05 [0.04;0.05]	0.00 [0.00;0.01]	-
Breast-Cancer	0.55 [0.55;0.55]	0.25 [0.24;0.25]	0.88 [0.87;0.90]
C&C	0.99 [0.99;0.99]	0.68 [0.65;0.71]	0.91 [0.91;0.91]
Compactiv	0.97 [0.96;0.98]	0.49 [0.44;0.54]	0.88 [0.83;0.92]
Insurance-C	0.83 [0.82;0.84]	0.47 [0.42;0.51]	0.90 [0.89;0.91]
Lymphoma	0.60 [0.60;0.60]	0.32 [0.31;0.32]	0.50 [0.47;0.52]
Ohsumed	0.02 [0.01;0.03]	0.01 [0.00;0.01]	-
Ovarian	0.62 [0.62;0.63]	0.50 [0.50;0.51]	0.14 [0.14;0.14]
Wine	0.83 [0.74;0.90]	0.58 [0.52;0.64]	0.99 [0.47;1.00]
p53	0.91 [0.91;0.91]	0.45 [0.44;0.45]	0.87 [0.87;0.87]
Mean over data sets	0.64 [0.62;0.65]	0.38 [0.35;0.40]	0.76 [0.68;0.77]
<b>On all predictions</b>	<b>0.73 [0.73;0.73]</b>	<b>0.58 [0.57;0.58]</b>	<b>0.89 [0.89;0.89]</b>

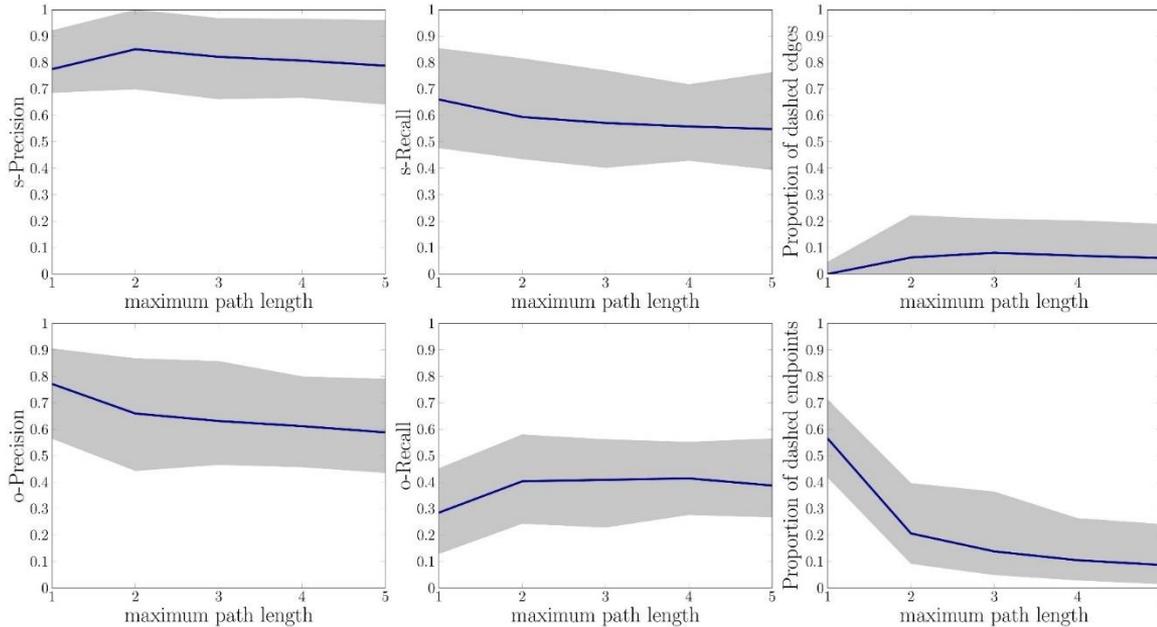
• When predictions are based on only 2 common variables, statistical matching is unreliable

• SM is more successful when the predictions are based on larger sets of common variables.

• INCA rules's predictions are highly correlated with sample estimates (0.89 correlation)

# MAXIMUM PATH LENGTH

20 variables, 5 overlapping data sets, 100 samples each



- MPL controls path length.
- Unconstrained MPL corresponds to soundness and completeness.
- $MPL > 1$  does not affect performance, allows more orientations.