

# Comment on “Causal inference using invariant prediction”

Charles Zheng and Qingyuan Zhao

May 4, 2016

We congratulate the authors on this thought-provoking paper. Statistical inference of causation has been thoughtfully studied in randomized experiments or observational studies, but is seldomly considered when data from both *observational* and *interventional* settings are available. Peters et al. made an important contribution by tackling this problem with their notion of invariant causal prediction (ICP).

At first look, the ICP is just a corollary of structural equation models, but we think its value might be much more substantial. Given a response variable, ICP can discover its invariant prediction sets, in some sense its “causes”. Holland [1986], Dawid [2000], Pearl [2000], among many others, suggest that we should distinguish between the problem of “effects of causes” and “causes of effects”. As argued by Robins and Greenland [2000] and Pearl [2000], a counterfactual language is usually required to study the latter problem. Does ICP enable us to study “causes of effects” without counterfactuals? Although ICP is motivated by structural models which naturally encodes counterfactuals, ICP seems not to involve any counterfactual term. We hope the authors can answer this question in the rejoinder.

We think the concept of invariant prediction is quite general and goes beyond a specific modeling assumption. Unfortunately, the bulk of the paper is devoted to linear model with Gaussian noise. Generalizations of ICP to more flexible models (GLMs, nonparametric models, non-additive models) would be extremely useful in practice.

We evaluated ICP on a protein signaling network dataset of Sachs et al. [2005] using the software provided by the authors. Sachs et al. [2005] collected a combination of observational and interventional data to infer the causal structure of a network consisting of 11 proteins. Using their own method, Sachs et al. [2005] reportedly recovered 15 of the known directed arcs (colored black in Figure 1) and discovered two new putative links (not shown), and missed 3 of the interactions which were known in the literature (dashed lines). We tried to use ICP to recover part of the graph structure: ICP discovered one arrow correctly and two incorrent arrows. No other discoveries were reported.

The overly-restrictive linear model could be the reason for the poor performance of ICP on this dataset. The authors take this as a robustness property,

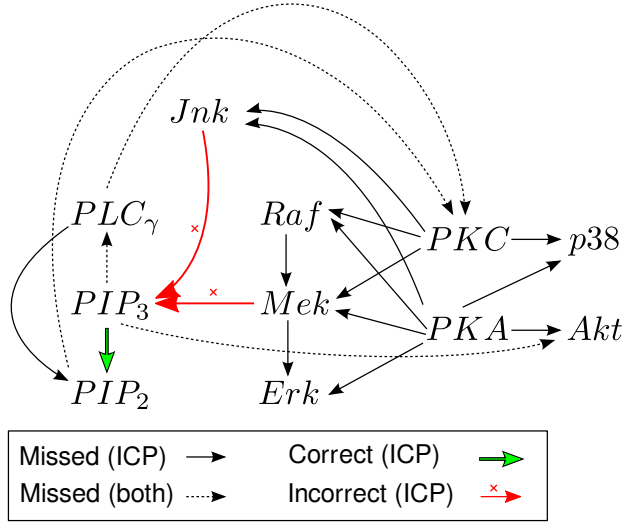


Figure 1: Application of ICP procedure to recover protein signaling network, taking in turn each of the 11 variables as the response of interest and selecting the subset of environments in which the response was not perturbed. The invariant set for each variable can be identified as the parents of that variable in the graph. For 9 of the 11 proteins, ICP rejected the model and reported no discoveries. For the protein  $PIP_2$ , ICP correctly identified one parent,  $PIP_3$ . For the protein  $PIP_3$ , ICP reported  $Mek$  and  $Jnk$  as part of the invariant set, but these do not match any interactions known in the literature.

but it also means ICP is very sensitive to modeling assumption. A small departure from the linear model can result in no causal discovery. We did not find in the paper a summary of the robustness of ICP, so we tried our best to outline in Table 1 the behavior of linear ICP when some of its assumptions are not met. [[Charles, can you explain the behaviors in the table?]] The authors are welcomed to comment on the table and point out any inconsistency.

## References

- A Philip Dawid. Causal inference without counterfactuals. *Journal of the American Statistical Association*, 95(450):407–424, 2000.
- Paul W. Holland. Statistics and causal inference. *Journal of the American Statistical Association*, 81:945–960, 1986.
- Judea Pearl. *Causality*. Cambridge university press, 2000.
- James M Robins and Sander Greenland. Comment on “causal inference without counterfactuals”. *Journal of the American Statistical Association*, 95(450): 431–435, 2000.

	Issues	ICP's behavior
a)	Intervene on $Y$ (or a missing cause)	$\bigcap_{\emptyset}$
b)	Non-linear, non-additive, and/or heteroskedastic	$\bigcap_{\emptyset}$
c)	Not enough interventions	False causal positives
d)	Small sample size	$\emptyset$
e)	Left out a confounder	$\bigcap_{\emptyset}$
f)	Left out an unconfounding predictor	okay
g)	Misspecified noise model <sup>2</sup>	False positives

Table 1: Robustness properties of ICP procedure. Under certain types of model misspecification, ICP will return a “model reject”, denoted by  $\bigcap_{\emptyset}$  (i.e. all subsets including the empty set are not invariant), rather than produce false positives. (a) when interventions are performed on  $Y$ , no predictor set can be invariant; (b) when the homoskedastic linear model is misspecified, the prediction rule will vary depending on the range of the predictors; (c) without enough interventions, the set of causal parents is unidentifiable, and non-causal invariant sets exist; (d) when the sample size is small, the hypothesis test for invariance has insufficient power to reject the invariance null, hence many sets are accepted as invariant; (e) if a confounder is left out, this is equivalent to intervening on  $Y$ ; (f) when an unconfounding predictor is left out, its effect is equivalent to i.i.d. noise; (g) under a misspecified noise model, the hypothesis test may not be sensitive to differences in the noise distribution, leading to low power.

Karen Sachs, Omar Perez, Dana Pe’er, Douglas A Lauffenburger, and Garry P Nolan. Causal protein-signaling networks derived from multiparameter single-cell data. *Science*, 308(5721):523–529, 2005.