

Comment on Jonas et. al paper

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Causal inference using data from both *observational* and *interventional* settings is a promising idea. Jonas et al. define *invariant prediction sets* which can be detected using such data, which can therefore be used to identify part of the causal structure. The concept of invariant prediction is quite general, going beyond a specific modeling assumption. However, the bulk of the paper is devoted linear structural models; furthermore, the specific hypothesis testing approach cannot be easily generalized beyond the linear case. We evaluated their approach using a dataset which is well-known in the graphical models literature: the Sachs et. al. protein signaling network data. Sachs et al. collected a combination of observational and interventional data in order to infer the causal structure of a network consisting of 11 proteins. Using their own method, Sachs et. al. reported recovering 15 of the known directed arcs (colored black in Figure 2.) Sachs et al. also discovered two new putative links (not shown), and missed 3 of the interactions which were known in the literature (dashed lines.) We used ICP to recover part of the graph structure, 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. However, for 9 of the 11 proteins, ICP rejected the model and reported no discoveries. For the protein PIP2, ICP correctly identified one parent, PIP3. For the protein PIP3, ICP reported Mek and Jnk as part of the invariant set, but these do not match any interactions known in the literature.

While the linear model may be overly restrictive, it is worth further considering the general idea of combining causal and statistical modeling assumptions in order to draw conclusions. [[for Qingyuan to write.]]

References

Sachs, Karen, et al. "Causal protein-signaling networks derived from multi-parameter single-cell data." *Science* 308.5721 (2005): 523-529.

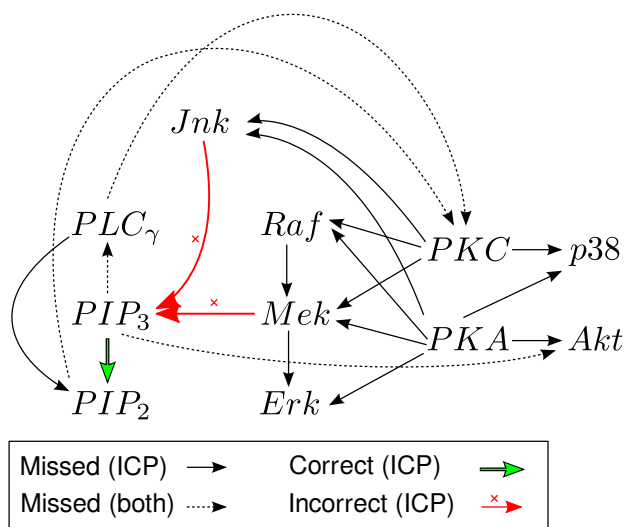


Figure 1: Application of ICP procedure to recover protein signaling network. ICP recovered one arrow correctly and two incorrent arrows: no other discoveries were reported.

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

Figure 2: Robustness properties of ICP procedure. Under certain types of model misspecification, ICP will return a “model reject”, denoted by \cup_{\emptyset} , rather than produce false positives.