



# Nonparametric-efficient Causal Mediation Analysis for Stochastic Interventions

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## OVERVIEW & MOTIVATIONS

- Using stochastic interventions, we present a decomposition of the *population intervention effect* into direct and indirect effects.
  - Define causal contrasts of effects of continuous and categorical exposures.
  - Identify a parameter required to construct both direct and indirect effects.
- We propose estimators for constructing these direct and indirect effects:
  - Classical*: substitution and IPW estimators using parametric methods.
  - Nonparametric-efficient*: one-step and TMLE leveraging machine learning.
- Our efficient estimators are asymptotically linear under  $n^{1/4}$ -consistency of nuisance functions (may use highly adaptive lasso).

## SOFTWARE IMPLEMENTATION

- The `medshift` R package [3] implements these estimators and leverages state-of-the-art machine learning in the procedure.
  - Construction of all estimators via the eponymous `medshift()` function.
  - Uses the `sl3` R package to incorporate machine learning facilities.
  - Relies on the framework of the `tmle3` R package for TMLE implementation.
  - Flexible cross-fitting implementation via the `origami` R package.
- `sl3`, `tmle3`, and `origami` are core engines of the new **tlverse** software ecosystem.
  - Check out <https://tlverse.org>
  - Our handbook: <https://tlverse.org/tlverse-handbook>

## CONSTRUCTION OF NONPARAMETRIC-EFFICIENT ESTIMATORS

- To avoid entropy conditions on initial estimators, we rely on cross-validation [6, 1], letting  $\hat{\eta}_j$  be the estimator of  $\eta = (g, e, m, \phi)$  and  $j(i)$  the index of the validation set containing observation  $i$ .
- A one-step estimator [4] may be constructed by augmenting the substitution estimator with the auxiliary scores ( $D^A$  and  $D^Y$ ) in the efficient influence function (EIF), yielding

$$\hat{\theta}_{OS}(\delta) = \frac{1}{n} \sum_{i=1}^n D_{\hat{\eta}_{j(i)}, \delta}(O_i) = \frac{1}{n} \sum_{i=1}^n \left\{ D_{\hat{\eta}_{j(i)}, \delta}^Y(O_i) + D_{\hat{\eta}_{j(i)}, \delta}^A(O_i) + D_{\hat{\eta}_{j(i)}, \delta}^{Z,W}(O_i) \right\}.$$

- A targeted minimum loss estimator (TMLE) may be constructed by using the efficient influence function to update components of the substitution estimator via a targeting procedure:

$$\hat{\theta}_{TMLE}(\delta) = \int m_n^*(z, a, w) g_{\delta, n}^*(a | w) d\kappa(a),$$

where  $g_{\delta, n}^*(a | w)$  and  $m_n^*(z, a, w)$  are generated via parametric *targeting* processes, respectively,  $\text{logit}(g_{\delta, n, k\epsilon}) = \text{logit}(g_{\delta, n, (k-1)\epsilon}) + \epsilon_{\Delta}^{\text{lfm}} \mathbf{H}_{(\mathbf{k}-1)\epsilon}^A$  and  $\text{logit}(m_{n, k\epsilon}) = \text{logit}(m_{n, (k-1)\epsilon}) + \epsilon_{\Delta}^{\text{lfm}} \mathbf{H}_{(\mathbf{k}-1)\epsilon}^Y$ .

- Unlike the one-step estimator, TMLE constructs a substitution estimator, respecting bounds.
- Targeting step uses the method of universal least favorable one-dimensional submodels [5].
- Both are multiply robust and allow confidence intervals and hypothesis tests to be constructed from an EIF-based variance estimator  $\mathbb{V}(\hat{\theta}(\delta)) = D_{\hat{\eta}, \delta}^2(O)$ , valid even when using machine learning.

## STOCHASTIC POPULATION INTERVENTION (IN)DIRECT EFFECTS

- Consider  $O = (W, A, Z, Y) \sim P_0 \in \mathcal{M}$ , for  $W$  a set of baseline covariates,  $A$  an intervention,  $Y$  the outcome, and  $Z$  a mediator between  $A$  and  $Y$ , with no assumptions on nonparametric model  $\mathcal{M}$ .
- We decompose the total population intervention effect (PIE) in terms of a *population intervention direct effect (PIDE)* and a *population intervention indirect effect (PIIE)*:

$$\psi(\delta) = \overbrace{\mathbb{E}\{Y(g, q) - Y(g_{\delta}, q)\}}^{\text{PIDE}} + \overbrace{\mathbb{E}\{Y(g_{\delta}, q) - Y(g_{\delta}, q_{\delta})\}}^{\text{PIIE}}.$$

- We show the causal parameter  $\mathbb{E}\{Y(g_{\delta}, q)\}$  is identified by the observed data parameter [2]:

$$\theta(\delta) = \int m(z, a, w) g_{\delta}(a | w) p(z, w) d\nu(a, z, w),$$

for outcome mechanism  $m(z, a, w)$  and post-intervention treatment mechanism  $g_{\delta}(a | w)$  — a stochastic intervention on  $A$  while drawing  $Z$  as though  $A$  came from its natural distribution.

- Letting  $\eta = (g, e, m, \phi)$ , the efficient influence function for  $\theta(\delta)$  in the nonparametric model  $\mathcal{M}$  is  $D_{\eta, \delta}^Y(o) + D_{\eta, \delta}^A(o) + D_{\eta, \delta}^{Z,W}(o) - \theta(\delta)$  for

$$D_{\eta, \delta}^{Z,W}(o) = \int m(z, a, w) g_{\delta}(a | w) d\kappa(a), \quad D_{\eta, \delta}^Y(o) = \frac{\mathbf{g}_{\delta}(\mathbf{a} | \mathbf{w})}{\mathbf{e}(\mathbf{a} | \mathbf{z}, \mathbf{w})} \{y - m(z, a, w)\},$$

$$D_{\eta, \delta}^A(o) = \frac{\delta \phi(\mathbf{w}) \{a - g(1 | w)\}}{\{\delta \mathbf{g}(\mathbf{1} | \mathbf{w}) + 1 - \mathbf{g}(\mathbf{1} | \mathbf{w})\}^2}, \quad \phi(w) = \mathbb{E}\{m(1, Z, W) - m(0, Z, W) | W = w\},$$

where, for simplicity, we present the case  $A \in \{0, 1\}$ . For an unabridged treatment, see [2].

## RESULTS & DISCUSSION

- All estimators approximately unbiased in large samples; TMLE outperforms one-step uniformly in smaller-sample settings.
- Inference is only valid for the one-step and TMLE when using machine learning (here, HAL) for estimating nuisance regressions.

## REFERENCES

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## BUT WAIT, THERE’S MORE!

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- <https://arxiv.org/abs/1901.02776>
- Check out Iván’s talk Friday morning!