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.
  - Introduce a parameter necessary to construct direct and indirect effects.
- We propose estimators for constructing these direct and indirect effects:
  - *Classical*: G-computation and IPW based on parametric models.
  - *Nonparamtric-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`

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)*:

$$\psi(\delta) = \overbrace{\mathbb{E}\{Y(A_\delta, Z(A_\delta)) - Y(A_\delta, Z)\}}^{\text{PIIE}} + \overbrace{\mathbb{E}\{Y(A_\delta, Z) - Y(A, Z)\}}^{\text{PIDE}}.$$

- We show causal parameter $\mathbb{E}\{Y(A_\delta, Z)\}$ is identified by a functional of the distribution of O [2]:

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

  for outcome mechanism $m(z, a, w)$ and post-intervention treatment mechanism $g_\delta(a \mid w)$ — a stochastic intervention drawing $A_\delta \sim g_\delta(a \mid w)$ while drawing $Z \sim q(z \mid a, w)$, where $A \sim g(a \mid w)$.
- Letting $\eta = (g, e, m, \phi)$, the efficient influence function for $\theta(\delta)$ in the nonparametric model $\mathcal{M}$ is $D^Y_{\eta,\delta}(o) + D^A_{\eta,\delta}(o) + D^{Z,W}_{\eta,\delta}(o) - \theta(\delta)$ for

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

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

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

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

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

- 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:

$$\hat{\theta}_{\text{TMLE}}(\delta) = \int m^\star_n(z, a, w) g^\star_{\delta,n}(a \mid w) d\kappa(a),$$

  where $g^\star_{\delta,n}(a \mid w)$ and $m^\star_n(z, a, w)$ are generated via *targeted* fluctuation processes, respectively, $\text{logit}(g_{\delta,n,k\xi}) = \text{logit}(g_{\delta,n,(k-1)\xi}) + \xi^{\text{lfm}}_\Delta \mathbf{H}^{\mathbf{A}}_{\mathbf{(k-1)\xi}}$ and $\text{logit}(m_{n,k\xi}) = \text{logit}(m_{n,(k-1)\xi}) + \xi^{\text{lfm}}_\Delta \mathbf{H}^{\mathbf{Y}}_{\mathbf{(k-1)\xi}}$.
  - 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, efficient, and allow construction of confidence intervals and hypothesis tests based on the EIF — i.e., $\mathbb{V}\hat{\theta}(\delta) := \mathbb{V}D_{\hat{\eta},\delta}(O)$ — valid even when leveraging machine learning.

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!