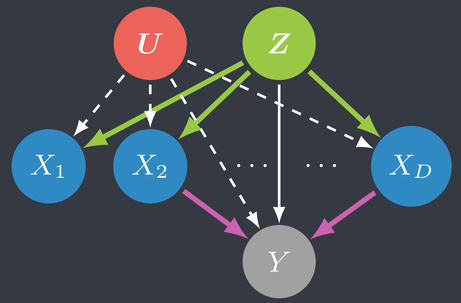
Unobserved confounders render causal effects of neuroanatomy on cognition non-identifiable.

Identifiability can be achieved by leveraging the dependencies among multiple causes via a probabilistic latent factor model.



Estimation of Causal Effects in the Presence of Unobserved Confounding in the Alzheimer's Continuum

Sebastian Pölsterl and Christian Wachinger

Background

- *Goal*: **Infer cause-effect relationships** of neuroanatomy on cognition.
- The **gold-standard** to answer this question is performing a **randomized trial** (Pearl, 2000).
- Randomizing neuroanatomy is impossible ⇒ resort to **observational data**.
- Making untestable assumptions is required, including that there is **no unmeasured confounder** affecting both the neuroanatomy and cognition.
- **Sources of confounding are plentiful** in neuroimaging, most of which we do not have data on (Alfaro-Almagro et al., 2021).

Methods

- *Research Question*: What is the **average causal effect** of changes in volume/thickness of a subset of neuroanatomical structures on the ADAS13 score in patients with an Alzheimer's pathologic change?

$$\mathbb{E}\left[\text{ADAS} \mid do(X_{\mathcal{S}} = x'_{\mathcal{S}})\right] = \int \text{adas} \cdot P(\text{adas} \mid do(x'_{\mathcal{S}}))\, d\text{adas}$$

- *Identifiability*: Can the **post-intervention distribution** be estimated from the observed joint distribution over volume/thickness and ADAS?

  Answer: **No, due to unobserved confounding**.

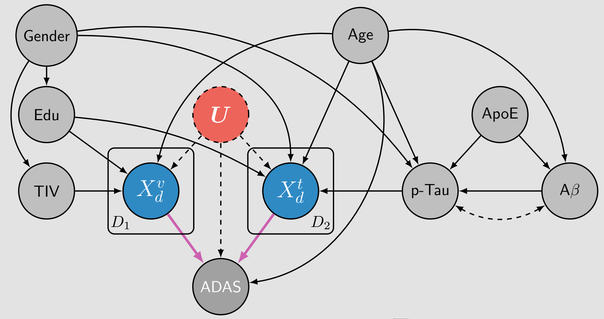
- *Probabilistic Latent Factor Model*: Note that all neuroanatomical measures X become conditionally independent, given their parents:

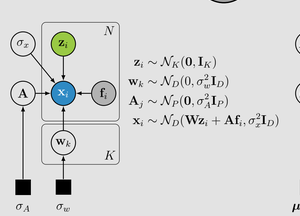
$$P(x_1, \ldots x_D \mid PA_{X_1,\ldots,X_D}) = \prod_{d=1}^{D} P(x_d \mid PA_{X_1,\ldots,X_D}).$$

- Wang and Blei showed that, under *certain assumptions*, it is possible to estimate a **substitute confounder $\mathbf{z}_i$**, and treat it as observed.

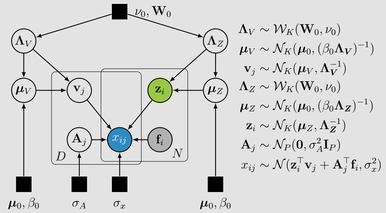
$$\mathbf{x}_i \sim \mathcal{N}_D(\mathbf{W}\mathbf{z}_i + \mathbf{A}\mathbf{f}_i, \sigma_x^2 \mathbf{I}_D), \quad \forall i = 1, \ldots, N.$$

- We extend the approach to account for observed confounders too.





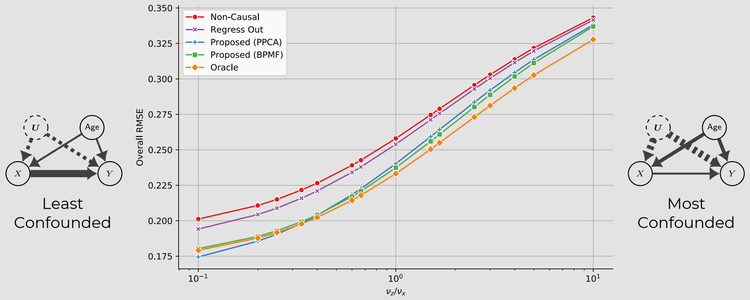
Probabilistic PCA



Probabilistic Matrix Factorization

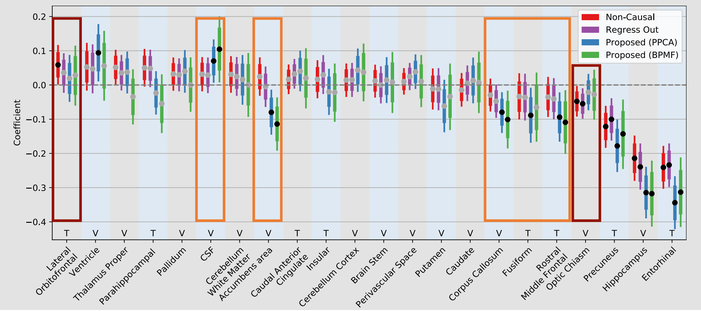
Experiment: Semi-Synthetic Data

- 19 regional brain volumes of 11,800 subjects from UK Biobank.
- Measure error w.r.t. the true effect.



Experiment: Real Data from ADNI

- 14 volume and 8 thickness measures of 711 subjects.
- True effect is *unknown*.



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