

Causal Discovery on Gut Microbial Data for Disease Risk Prediction

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Background

- **Association vs. Causation**
- **Causal Discovery Algorithms in Gut Microbiome Studies** Previous research has explored causal discovery in gut microbiome studies, notably using algorithms like PC-stable to construct causal networks and implement do-calculus for estimating microbe-microbe and microbe-outcome causal effects. More recent advancements include CD-NOD, specifically designed for heterogeneous data, which is particularly valuable for gut microbiome research where samples often come from different studies. These algorithms aim to identify true causal relationships by performing conditional independence tests and orienting edges using established rules, while accounting for the unique challenges of microbiome data analysis.

Research Questions

1. **Microbe-Microbe:** How do the microbe-microbe interaction networks between the healthy and diseased participants differ?
2. **Microbe-Disease:** What microbes have a causal relationship to disease status?
3. **Prediction:** Is it possible to predict disease status with the current composition of the dataset given causal representation learning techniques? How do they differ with the microbes learned in question 2?

Data

To answer the questions above, we apply our framework to gut microbial data that investigated T2D and an individual participant data meta-analysis dataset that investigated PCOS.

- **T2D:** For T2D, we use the NIH Human Microbiome Project (HMP2) dataset, filtered on healthy samples and individuals with a known insulin resistance or insulin sensitivity status.
- **PCOS:** For PCOS, we use a dataset aggregated from 14 different clinical studies. (elaborate)

Causal Discovery

Causal discovery is all about recovering the true causal structure of system given observed data. One way to model this causal structure is through a graph One of the oldest and most widely-used general-purpose causal discovery algorithms is PC.

Methods

In this study, we use causal discovery algorithms and compare them with predictive modeling to explore the causal relationships between the gut microbiome and two diseases: T2D and PCOS. Due to the high-dimensionality of the data and small sample sizes, we first select features through sparse estimation methods and sure-screening to reduce the number of microbes.

1. **Filter out rare OTUs.** Remove microbes where all samples have less than 1% relative abundance.
2. **Feature selection and sure screening.** For the microbe-microbe network, we use two methods, SparCC and graphical lasso to reduce the number of edges between pairs of microbes. For the microbe-disease network, we use logistic lasso regression to reduce the number of features that are not helpful in predicting disease.
3. **Causal discovery algorithms.** For the microbe-microbe network, we implement PC-stable with a max depth of 2. For the microbe-outcome network, we implement CD-NOD where the covariates correspond to the heterogeneity index.
4. **Variational autoencoder.** xxx.

T2D

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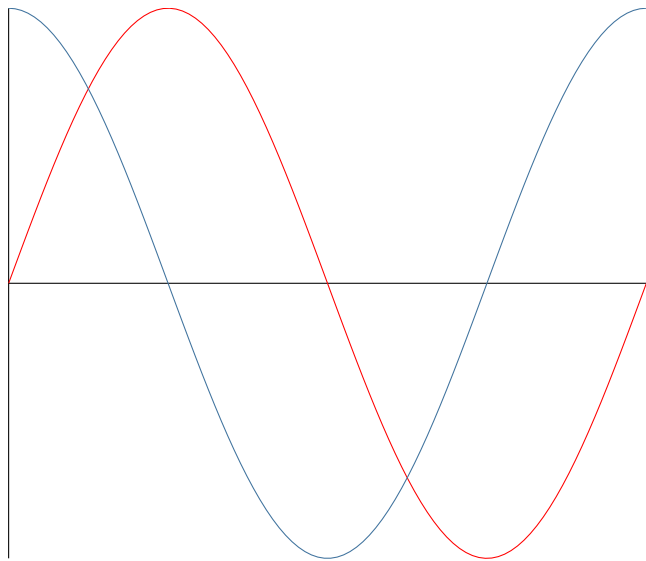


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PCOS

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Results

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Conclusion/Future Work

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Baz	3.14	83,742	δ
Qux	7.59	974	γ

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References