Scale Uncertainty in ALDEx2

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Overview

- These slides are by no means polished.
- Idea: Use a simulation and Vandputte to introduce SRI + SSRVs + modifications to ALDEx2

Recap: Sequencing Depth is Unrelated to Scale

- Example: Either picture with two conditions highlighting scale and system of each or a table.

Recap: This can mislead analyses.

- Highlight the differences in LFC estimation on the observed data and the true system.

Recap: . . . and lead to unacknowledged bias.

- Plot of FDR versus sample sizes from one of our examples.

Motivating Example: Antibiotic Study

Consider a simple study of the microbiome pre/post antibiotic administration.

- Research question: Which taxa change in absolute abundance after taking an antibiotic?
- How do we analyze this data to answer the question?

Motivating Example: Antibiotic Study

- Simulation details + code

Scale Reliant Inference (Informal)

Scale Reliant Inference: The Basics

A middle ground approach:

- Y is a measurement of the underlying system W.
- Desired quantity depends on W (i.e., $\theta = f(W)$). However, W depends on both the composition and system scale:

$$W_{dn} = W_{dn}^{\parallel} W_n^{\perp}$$

$$W_n^{\perp} = \sum_{d=1}^{D} W_{dn}$$

Scale Simulation Random Variables

Goal: Estimate $\theta = f(W^{\|}, W^{\perp})$.

1. Draw samples of $W^{\|}$ from a measurement model (can depend on Y).
2. Draw samples of $W^{\perp}$ from a scale model (can depend on $W^{\|}$).
3. Estimate samples of $\theta = f(W^{\|}, W^{\perp})$.

Scale Reliant Inference (Formal)

Scale Reliant Inference: Formal Definition

The Updated ALDEx2 Software

The Original ALDEx2 model

Unacknowledged bias in ALDEx2

Moving Past Normalizations to Scale

ALDEx2 as an SSRV

Coding Changes to ALDEx2

Including scale

Option 1: Default Scale Model

Option 2: More Complex Scale Models

Real Data Examples

Real Example: SELEX

Real Example: Vandputte