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M.Sc. Thesis Proposal: *Alpha diversity measures for microbiome data*

Objective: Complex microbiome samples can be summarized into a single measure by alpha diversity indices, characterizing the structure of a community in (microbial) ecology. Alpha diversity can be measured by two contrasting components, Richness and Evenness, or a mixture of both (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6819366/). To date, a wide variety of alpha diversity measures has been developed, ranging from traditional diversity estimates from macro-ecology to recently developed microbiome-specific measures. However, clinical microbiome research typically applies one of the two most widely used standard measures for alpha diversity: the Shannon or the Simpson diversity index. We would like to review the appropriateness of traditional and new alpha diversity measures for microbiome data from a statistical point of view, and to compare these diversity measures on mock and clinical microbiome data.

Plan and deliverables: The M.Sc. thesis should cover the following aspects:

- A theoretical/methodological analysis of alpha diversity measures regarding their appropriateness for microbiome data,
- An application-oriented analysis of alpha diversity measures for real mock or clinical microbiome data,
- Additional aspects could be: an analysis of the indices' components of Richness and Evenness, the effect of unobserved species and sequencing depth, the effect of different taxonomic levels at which diversity analyses are performed, and appropriate corresponding data normalization methods.

A desirable outcome would a recommendation on which measure(s) to use to detect differences in community structures for microbiome data. We are looking for a student with a strong interest in comparing methodologies and practical biological applications. A write-up in thesis form and commented code on GitHub are mandatory deliverables at the end of the thesis. Working on this project as a thesis is possible from October 2021 on.