

246 A workflow for metabolomics using CRAN packages to demonstrate association between a covariate and multiple analytes (some with detection limit)

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In metabolomics, to demonstrate an association between one clinical covariate of interest and multiple analytes from diverse metabolomics platforms is a recent problem. (e.g. Bassi et al.).

For this problem, we present a workflow using the CRAN packages `multcomp` (for `mmm`), `tukeytrend` and `mlt`, share its code and demonstrate it using the KarMeN cross-sectional data (Rist et al.). Specifically, the association between the clinical covariate age for the KarMeN sample and two selected analytes (without and with detection limit) is presented.

Generally, the relationship between a continuous covariate (also grouped in a randomized design) and multiple, differently distributed analytes (including those with observations under a detection limit) can be demonstrated by a Tukey trend test (Tukey et al.) based on previously transformed analytes by means of the most likely transformation concept (Hothorn et al.). The Tukey trend test is sensitive to different forms of association, allows both a global claim (by the smallest adjusted p-value), and also a local claim, i.e. at each individual analyte. It takes into account the correlation between the analytes and the models through the multiple marginal models concept (Pipper et al.). Using the most likely transformation approach, differently distributed analytes, including those with ties and/or censorship, are analyzed on a uniform, comparable scale.

A particularly interesting modification is the interpretation of an optimal odds ratio using continuous outcome logistic regression (Lohse et al.). By this modification, it is possible to consider the association between a continuous covariate and an arbitrarily distributed analyte, independently of certain cut-off for categorization of the covariate. These odds ratios can be evaluated for all potential values or cut-off of the covariate function, which allows the associations for different categorization types.

References:

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