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Nonparametric multiple comparisons and simultaneous confidence intervals for multivariate designs

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Over the last half-century, the use of multivariate designs has grown rapidly in many scientific disciplines. Such designs can have more than two possibly correlated response variables (endpoints) observed on each experimental unit and should allow comparisons across different treatment groups. Existing parametric tests in multivariate data analysis are based on the assumption that the observations follow multivariate normal distributions with equal covariance matrices across the groups. Such assumptions, however, are impossible to justify in real observations, e.g., for skewed data or ordered categorical data. In fact, existing parametric methods that rely on the assumption of equal covariance matrices tend to be highly liberal or conservative when the covariance matrices of the different groups are actually different. Therefore, a nonparametric approach is desirable that is valid even when covariance matrices are different – even under the null hypothesis of no treatment effect. In this study, purely nonparametric methods that overcome the existing gaps have been introduced. The procedures are robust in the sense that they assume neither any specific data distribution nor identical covariance matrices across the treatment groups, flexible in the sense that the inference method can be adjusted to specific research questions and in particular, the methods are consonant, coherent and compatible. To test hypotheses formulated in terms of purely nonparametric treatment effects, pseudo-rank based multiple tests are derived. The results are achieved by computing the distribution of normalized rank-means under general but fixed alternatives. Instead of using quadratic forms as test statistics, the *t*-test type statistics are used and the joint distribution of them has been computed in a closed form, asymptotically. Small sample size approximations using methods-of-moments by multivariate *t*-approximation achieve accurate control of the multiple type-I error rate of the methods and comparable power to existing global testing procedures. To illustrate the application of the proposed tests, a part of an immunotoxicity study on the effects of silicone on the immune system is considered. There were three treatment groups of mice involved in the study and five clinical chemistry endpoints were measured on each mouse after the treatment. To answer the main question, that is, quantifying (significant) differences between the treatment groups under each endpoint for making biological conclusions on the effects of silicone, the multiple hypotheses are tested using many-to-one comparisons.

Keywords: Multivariate data, Nonparametric treatment effects, Rank statistics, Multiple comparisons, Simultaneous confidence intervals.