Multiple testing under structural assumptions

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A multiple test problem is characterized by $m > 1$ hypotheses that shall be tested simultaneously under the scope of one statistical experiment. First theoretical investigations of multiple test problems reach back to the 1950s and were primarily concerned with biometrical and agricultural applications. Aim was the development of test procedures controlling the family-wise error rate (FWER), meaning that the probability for rejecting at least one true hypothesis is bounded by a pre-defined significance level α. Since the 1990s, driven by large-scale applications like, for instance, genomics (microarray analyses), proteomics or cosmology, the field of multiple testing has emerged as one of the "hot topics" in statistics, contributing approximately 8% of all articles in the four leading methodological statistics journals (data from [1]), and a variety of new concepts for error control have been developed, the most popular of which, the false discovery rate (FDR), having become a quasi-standard analysis tool for exploratory screening studies with large numbers of hypotheses.

We are considered with three scenarios in which structural properties of the system of hypotheses to be tested can be exploited in order to exhaust the pre-defined multiple type I error bound (for FWER or FDR, respectively) accurately and thereby optimizing power of the test procedure. First, we discuss classical closed testing and partitioning principles (cf. [2]) allowing to test each partition hypothesis at full level α and using the hypotheses structure to deduce the final decision rule. Second, we are concerned with genetic association studies and linkage disequilibrium structure among genetic markers. This will lead to the concept of "effective number of tests" (cf., e.g., [3] and references therein). Third, projection methods under asymptotic normality (see [4]) will be examined. Here, the known (asymptotic) correlation structure helps to deduce marginal rejection thresholds by utilizing joint statistical properties among the individual tests. As an outline, we will discuss the case in which presence of a correlation structure is assumed, but it is only partially known or unknown in advance.

References:

[1] Benjamini, Y. (2010). Simultaneous and selective inference: Current successes and future challenges. Biometrical Journal 52, 6, 708–721.

[2] Finner, H., and Strassburger, K. (2002). The partitioning principle: a powerful tool in multiple decision theory. The Annals of Statistics 30, 4, 1194–1213.

[3] Dickhaus, T., Straßburger, K., Schunk, D., Morcillo, C., and Navarro, A. (2011). Refined statistical inference methods for contingency table analyses in genetic association studies. In revision.

[4] Hothorn, T., Bretz, F., Westfall, P. (2008). Simultaneous inference in general parametric models. Biometrical Journal, 50, 3, 346–363.