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Randomization Deduction with General Impedance Editing

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Description

Motivated by the analysis of complex dependent functional data such as Event-Related Brain Potentials (ERP), this paper considers a time-varying coefficient multivariate regression model with fixed-time covariates for testing global hypotheses about population mean curves. Based on a reduced-rank modeling of the time correlation of the stochastic process of point wise test statistics, a functional generalized F-test is proposed and its asymptotic null distribution is derived. Our analytical results show that the proposed test is more powerful than functional analysis of variance testing methods and competing signal detection procedures for dependent data. Simulation studies confirm such power gain for data with patterns of dependence similar to those observed in ERPs. The new testing procedure is illustrated with an analysis of the ERP data from a study of neural correlates of impulse control. The field of neuroimaging dedicated to mapping connections in the brain is increasingly being recognized as key for understanding neurodevelopment and pathology. Networks of these connections are quantitatively represented using complex structures, including matrices, functions, and graphs, which require specialized statistical techniques for estimation and inference about developmental and disorder-related changes. Unfortunately, classical statistical testing procedures are not well suited to high-dimensional testing problems. In the context of global or regional tests for differences in neuroimaging data, traditional Analysis Of Variance (ANOVA) is not directly applicable without first summarizing the data into univariate or low-dimensional features, a process that might mask the salient features of high-dimensional distributions. In this work, we consider a general framework for two-sample testing of complex structures by studying generalized within-group and between-group variances based on distances between complex and potentially high-dimensional observations. We derive an asymptotic approximation to the null distribution of the ANOVA test statistic, and conduct simulation studies with scalar and graph outcomes to study finite sample properties of the test. Finally, we apply our test to our motivating study of structural connectivity in autism spectrum disorder.

For regression with covariates missing not at random where the missingness depends on the missing covariate values, Complete-Case (CC) analysis leads to consistent estimation when the missingness is independent of the response given all covariates, but it may not have the desired level of efficiency. We propose a general empirical likelihood framework to improve estimation efficiency over the CC analysis. Improve efficiency by modeling the missingness probability conditional on the response and fully observed covariates by allowing the possibility of modeling other data distribution-related quantities. We also give guidelines on what quantities to model and demonstrate that our proposal has the potential to yield smaller biases than existing methods when the missingness probability model is incorrect. Simulation studies are presented, as well as an application to data collected from the US National Health and Nutrition Examination Survey.

Dose-Schedule Regimes

This paper proposes a two-stage phase I-II clinical trial design to optimize dose-schedule regimes of an experimental agent within ordered disease subgroups in terms of the toxicity-efficacy trade-off. The design is motivated by settings where prior biological information indicates it is certain that efficacy will improve with ordinal subgroup level. We formulate a flexible Bayesian hierarchical model to account for associations among subgroups and regimes, and to characterize ordered subgroup effects. Sequentially adaptive decision-making is complicated by the problem, arising from the motivating application, that efficacy is scored on day 90 and toxicity is evaluated within 30 days from the start of therapy, while the patient accrual rate is fast relative to these outcome evaluation intervals. To deal with this in a practical manner, we take a likelihood-based approach that treats unobserved toxicity and efficacy outcomes as missing values, and use elicited utilities that quantify the efficacy-toxicity trade-off as a decision criterion. Adaptive randomization is used to assign patients to regimes while accounting for subgroups, with randomization probabilities depending on the posterior predictive distributions of utilities. A simulation study is presented to evaluate the design's performance under a variety of scenarios, and to assess its sensitivity to the amount of missing data, the prior, and model misspecification.

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