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# Pan-Malignant Growth Endurance Expectation Utilizing Protein Articulation Information

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## Description

Accurate prognostic prediction using molecular information is a challenging area of research, which is essential to develop precision medicine. In this paper, we develop translational models to identify major actionable proteins that are associated with clinical outcomes, like the survival time of patients. There are considerable statistical and computational challenges due to the large dimension of the problems. Furthermore, data are available for different tumor types; hence data integration for various tumors is desirable. Having censored survival outcomes escalates one more level of complexity in the inferential procedure. We develop Bayesian hierarchical survival models, which accommodate all the challenges mentioned here. We use the hierarchical Bayesian accelerated failure time model for survival regression. Furthermore, we assume sparse horseshoe prior distribution for the regression coefficients to identify the major proteomic drivers. We borrow strength across tumor groups by introducing a correlation structure among the prior distributions. The proposed methods have been used to analyze data from the recently curated "The Cancer Proteome Atlas" (TCPA), which contains reverse-phase protein arrays-based high-quality protein expression data as well as detailed clinical annotation, including survival times. Our simulation and the TCPA data analysis illustrate the efficacy of the proposed integrative model, which links different tumors with the correlated prior structures. Bayesian methods allow borrowing of historical information through prior distributions. The concept of prior Effective Sample Size (prior ESS) facilitates quantification and communication of such prior information by equating it to a sample size. Prior information can arise from historical observations; thus, the traditional approach identifies the ESS with such a historical sample size. However, this measure is independent of newly observed data, and thus would not capture an actual "loss of information" induced by the prior in case of prior-data conflict. We build on a recent work to relate prior impact to the number of (virtual) samples from the current data model and introduce the Effective Current Sample Size (ECSS) of a prior, tailored to the application in Bayesian clinical trial designs. Special emphasis is put on robust mixture, power and commensurate priors.

We apply the approach to an adaptive design in which the number of recruited patients is adjusted depending on the effective sample size at an interim analysis. We argue that the ECSS is the appropriate measure in this case, as the aim is to save current (as opposed to historical) patients from recruitment. Furthermore, the ECSS can help overcome lack of consensus in the ESS assessment of mixture priors and can, more broadly, provide further insights into the impact of priors. An R package accompanies the paper. Bayesian methods allow borrowing of historical information through prior distributions. The concept of prior Effective Sample Size (prior ESS) facilitates quantification and communication of such prior information by equating it to a sample size. Prior information can arise from historical observations; thus, the traditional approach identifies the ESS with such a historical sample size.

## Multivariate Meta-Analysis

Multivariate meta-analysis is gaining prominence in evidence synthesis research because it enables simultaneous synthesis of multiple correlated outcome data, and random-effects models have generally been used for addressing between-studies heterogeneities. However, coverage probabilities of confidence regions or intervals for standard inference methods for random-effects models (e.g., restricted maximum likelihood estimation) cannot retain their nominal confidence levels in general, especially when the number of synthesized studies is small because their validities depend on large sample approximations. In this article, we provide permutation-based inference methods that enable exact joint inferences for average outcome measures without large sample approximations. We also provide accurate marginal inference methods under general settings of multivariate meta-analyses. We propose effective approaches for permutation inferences using optimal weighting based on the efficient score statistic. The effectiveness of the proposed methods is illustrated via applications to bivariate meta-analyses of diagnostic accuracy studies for airway eosinophilia in asthma and a network meta-analysis for antihypertensive drugs on incident diabetes, as well as through simulation experiments.

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