Robust Confidence Intervals for Generalized Linear Models with an application to RNA-Sequencing Data

Andrea Panarotto*†[1], Riccardo De Santis[1], and Livio Finos[1]

[1]Università degli Studi di Padova = University of Padua – Italy

Abstract

Confidence sets provide essential inferential summaries beyond point estimates in generalized linear models (GLMs). However, parametric interval construction critically depends on correct model specification. In high-throughput genomic data-such as RNA sequencing and other omics assays-model assumptions are often violated due to overdispersion, heteroskedasticity, and unobserved sources of variability. These factors can lead to serious undercoverage of nominal confidence levels. We propose a robust approach for constructing confidence intervals for regression parameters in GLMs. Our method is based on the inversion of hypothesis tests derived from sign-flipping of individual score contributions, combined with a bisection search algorithm for interval determination. We introduce two implementations of the procedure: an equitailed interval, which, given a level 1-α, balances one-sided p-values at level $\alpha/2$, and a symmetric interval, centered around the point estimate and defined by a joint condition on both tails. These frameworks inherit the properties of the flip-score test, guaranteeing asymptotic nominal coverage while remaining valid under variance misspecification. Simulation studies demonstrate the robustness and finite-sample accuracy of the proposed intervals across a range of model misspecifications. We further illustrate the method with an application to differential expression analysis in RNA-seq data. The proposed intervals provide a practical, distributionally robust alternative to conventional quasi-likelihood or Wald-based methods, particularly suited to the complex error structures of modern post-genomic datasets.

Keywords: Confidence sets, Generalized linear models, RNA seq, Semiparametric test, Sign flip, Variance misspecification

*Speaker

†Corresponding author: andrea.panarotto@unipd.it