Empirical simulation study for differential structure estimation of graphical models

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Abstract

Network inference is widely used to study direct associations between biomarkers, and differential network analysis aims to identify how these associations differ between conditions. Here, we focus on the 2 graphs setting, comparing networks estimated under two conditions (e.g., disease vs control). Although many methods have been proposed to jointly estimate multiple graphs or directly infer differential edges, existing evaluations typically rely on a limited set of simulation scenarios and do not systematically compare the major methodological families under realistic high-dimensional conditions.
To address this gap, we develop a comprehensive simulation framework to evaluate differential support estimation between 2 graphs. Our comparison includes neighborhood selection, graphical lasso, and a partial-correlation based method, fitted with either independent penalties on each graph or with an additional joint regularization, including fused, group, node-based, and data-shared lasso penalties. We also evaluate a direct differential network estimator, D-trace. For each condition, we generate networks from 2 biologically relevant topologies, scale-free graphs and random networks with hubs, across a large range of dimensionalities (p = 30, 100, 200, 500 nodes). We focus on high dimensional settings where sample sizes considered are n = 50 or 100 per condition. Differential structure is introduced through hub-based disruptions or random edge perturbations across a large range of differential edge proportions. We also evaluate hyperparameter calibration using the Sharp (Stability-enHanced Approaches using Resampling Procedures) stability selection framework, considering both differential edge stability and individual graph stability.

Joint estimation with sparse group penalties consistently outperforms models with independent or sparse fused penalty especially when networks share moderate to strong similarity, improving both differential-structure discovery and overall graph inference. Sparse group penalties also offer favorable computational efficiency relative to fused penalties, while direct estimators such as D-trace exhibit prohibitive runtimes.

Finally, we demonstrate the practical relevance of these findings using proteomic data from cancer patients and controls, revealing disease-related rewiring of protein networks.
All simulation code and implementations will be made publicly available in an R package.

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