CPH Seminar in Precision Medicine

"Biomarker selection for personalized medicine: Prediction-Oriented Marker Selection (PROMISE)"

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In personalized medicine, biomarkers are used to select therapies with the highest likelihood of success based on an individual patient's biomarker/genomic profile. Two goals are to choose important biomarkers that accurately predict treatment outcomes and to cull unimportant biomarkers to reduce the cost of biological and clinical verifications. These goals are challenging due to the high dimensionality of genomic data. Variable selection methods based on penalized regression (e.g., the lasso and elastic net) have yielded promising results. However, selecting the right amount of penalization is critical to simultaneously achieving these two goals. Standard approaches based on cross-validation (CV) typically provide high prediction accuracy with high true positive rates but at the cost of too many false positives. Alternatively, stability selection (SS) controls the number of false positives, but at the cost of yielding too few true positives. To circumvent these issues, I propose prediction-oriented marker selection (PROMISE), which combines SS with CV to conflate the advantages of both methods. My application of PROMISE with the lasso and elastic net in data analysis shows that, compared to CV, PROMISE produces sparse solutions, few false positives, and small type I + type II error, and maintains good prediction accuracy, with a marginal decrease in the true positive rates. Compared to SS, PROMISE offers better prediction accuracy and true positive rates. In summary, PROMISE can be applied in many fields to select regularization parameters when the goals are to minimize false positives and maximize prediction accuracy.

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