

**Biomarker cutoff estimation and inferences around the associated
true and false class rates for the three-class problem.
A misclassification cost-based framework**

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Abstract

The ROC surface is often used as a statistical tool for the evaluation of continuous biomarkers in trichotomous settings. Recent literature has focused on cutoff estimation in such settings and involves the extensions of the popular Youden index and the distance from the perfection corner among other previously used criteria. Under a trichotomous setting, the ROC does not visualize all the true and false classification rates (tradeoffs), as opposed to the usual ROC curve in the common 2-class problem. As a partial consequence, under a 3-class setting, the corresponding false class rates have not received sufficient attention in terms of estimation and inferences. In addition, most of the presented cutoff estimation approaches operate under the assumption that miss-classification costs are equal. In this work, we present the recent literature, and then provide an inferential framework for inferences around the cutoffs, the true class rates, and the false class rates in trichotomous settings. We illustrate how mis-classification costs can be accounted for along with the underlying prevalences. We demonstrate parametric and a non-parametric approaches as well as a newly developed comprehensive R package that accommodates several options involving, apart from our approaches, other known methods. For illustration purposes, we will also discuss an application involving pancreatic ductal adenocarcinoma patients.