The Hong Kong University of Science and Technology

Department of Mathematics

MPhil THESIS EXAMINATION

Nonregular Inference in Precision Medicine

By

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ABSTRACT

The increasing importance of precision medicine stems from its ability to leverage individual variability to improve treatment effectiveness. However, such pursuit of personalized healthcare is often challenged by nonregularity, particularly when evaluating treatment effects for specific subgroups or estimating the effectiveness of Optimal Treatment Regimes (OTR). This thesis tackles these challenges by developing novel methods and theory that address nonregularity in two fundamental areas of precision medicine. First, we focus on inference for potentially identified subgroups which represent the underlying truth of subgroups identified post-hoc. To overcome the severe bias issues caused by nonregularity, we propose a model-free, asymptotically efficient inference procedure based on a shift-based method combined with cross-fitting and subsampling. This approach can be viewed as an asymmetric smoothing technique that effectively mitigates bias. Second, we focus on evaluating the effect of the OTR under nonregularity. We address the bias issue induced by nonregularity via adaptive smoothing over the estimated OTR and develop a valid inference procedure on its mean outcome. We also establish the optimality of the proposed method by deriving a lower bound of the asymptotic variance for the robust asymptotically linear unbiased estimator to the mean outcome of the OTR and showing that our proposed estimator achieves the lower bound. The considered class of the estimator is general and includes the efficient regular estimator and the current state-of-the-art approach, and the derived lower bound of the asymptotic variance can be viewed as an extension of the classical semiparametric theory to a more general scenario allowing nonregularity. The effectiveness of our proposed methods is demonstrated through simulations and a re-analysis of the ACTG 175 clinical trial.

Date : 31 July 2024, Wednesday

Time : 4:00 p.m.

Venue : Room 2463 (Lifts 25/26)

Thesis Examination Committee

Chairman	**:**	**Prof. Zhigang BAO, MATH /HKUST**
Thesis Supervisor	**:**	**Prof. Xinzhou GUO, MATH/HKUST**
Member	**:**	**Prof. Can YANG, MATH/HKUST**

(Open to all faculty and students)

The student's thesis is now being displayed on the reception counter in the General Administration Office (Room 3461).