A Parsimonious Personalized Dose Finding Model via Dimension Reduction

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Abstract: Learning an individualized dose rule in personalized medicine is a challenging statistical problem. Existing methods for estimating the optimal individualized dose rule often suffer from the curse of dimensionality, especially when the dose rule is learned nonparametrically using machine learning approaches. To tackle this problem, we propose a dimension reduction framework that effectively reduces the estimation of dose rule in a lower-dimensional subspace of the covariates, leading to a more parsimonious model. To achieve this, the proposed methods exploit that the subspace is spanned by a few linear combinations of the original covariates, which can be solved efficiently using an orthogonality constrained optimization approach. Based on this framework, we propose two approaches: a direct learning approach that yields the dose rule as commonly desired in personalized medicine, and a pseudo-direct learning approach that focuses more on learning the dimension reduction subspace. Under mild regularity assumptions, we show that the estimators of the proposed methods are asymptotically normal. For both approaches, we formulate the numerical optimization problem as solving solutions on the Stiefel manifold. The performances of the proposed methods are evaluated through simulation studies and a warfarin pharmacogenetic dataset.