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HIGH-DIMENSIONAL *A*-LEARNING FOR OPTIMAL DYNAMIC TREATMENT REGIMES

BY CHENGCHUN SHI[1], AILIN FAN, RUI SONG[1] AND WENBIN LU[2]

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Precision medicine is a medical paradigm that focuses on finding the most effective treatment decision based on individual patient information. For many complex diseases, such as cancer, treatment decisions need to be tailored over time according to patients' responses to previous treatments. Such an adaptive strategy is referred as a dynamic treatment regime. A major challenge in deriving an optimal dynamic treatment regime arises when an extraordinary large number of prognostic factors, such as patient's genetic information, demographic characteristics, medical history and clinical measurements over time are available, but not all of them are necessary for making treatment decision. This makes variable selection an emerging need in precision medicine.

In this paper, we propose a penalized multi-stage *A*-learning for deriving the optimal dynamic treatment regime when the number of covariates is of the nonpolynomial (NP) order of the sample size. To preserve the double robustness property of the *A*-learning method, we adopt the Dantzig selector, which directly penalizes the A-leaning estimating equations. Oracle inequalities of the proposed estimators for the parameters in the optimal dynamic treatment regime and error bounds on the difference between the value functions of the estimated optimal dynamic treatment regime and the true optimal dynamic treatment regime are established. Empirical performance of the proposed approach is evaluated by simulations and illustrated with an application to data from the STAR*D study.

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Key words and phrases. A-learning, Dantzig selector, NP-dimensionality, model misspecification, optimal dynamic treatment regime, oracle inequality.

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TEST FOR HIGH-DIMENSIONAL REGRESSION COEFFICIENTS USING REFITTED CROSS-VALIDATION VARIANCE ESTIMATION

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Testing a hypothesis for high-dimensional regression coefficients is of fundamental importance in the statistical theory and applications. In this paper, we develop a new test for the overall significance of coefficients in high-dimensional linear regression models based on an estimated U-statistics of order two. With the aid of the martingale central limit theorem, we prove that the asymptotic distributions of the proposed test are normal under two different distribution assumptions. Refitted cross-validation (RCV) variance estimation is utilized to avoid the overestimation of the variance and enhance the empirical power. We examine the finite-sample performances of the proposed test via Monte Carlo simulations, which show that the new test based on the RCV estimator achieves higher powers, especially for the sparse cases. We also demonstrate an application by an empirical analysis of a microarray data set on Yorkshire gilts.

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MSC2010 subject classifications. 62F03, 62H15.

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ARE DISCOVERIES SPURIOUS? DISTRIBUTIONS OF MAXIMUM SPURIOUS CORRELATIONS AND THEIR APPLICATIONS

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Over the last two decades, many exciting variable selection methods have been developed for finding a small group of covariates that are associated with the response from a large pool. Can the discoveries from these data mining approaches be spurious due to high dimensionality and limited sample size? Can our fundamental assumptions about the exogeneity of the covariates needed for such variable selection be validated with the data? To answer these questions, we need to derive the distributions of the maximum spurious correlations given a certain number of predictors, namely, the distribution of the correlation of a response variable Y with the best s linear combinations of p covariates $\mathbf{X}$, even when $\mathbf{X}$ and Y are independent. When the covariance matrix of $\mathbf{X}$ possesses the restricted eigenvalue property, we derive such distributions for both a finite s and a diverging s, using Gaussian approximation and empirical process techniques. However, such a distribution depends on the unknown covariance matrix of $\mathbf{X}$. Hence, we use the multiplier bootstrap procedure to approximate the unknown distributions and establish the consistency of such a simple bootstrap approach. The results are further extended to the situation where the residuals are from regularized fits. Our approach is then used to construct the upper confidence limit for the maximum spurious correlation and to test the exogeneity of the covariates. The former provides a baseline for guarding against false discoveries and the latter tests whether our fundamental assumptions for high-dimensional model selection are statistically valid. Our techniques and results are illustrated with both numerical examples and real data analysis.

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ADAPTIVE ESTIMATION OF PLANAR CONVEX SETS

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In this paper, we consider adaptive estimation of an unknown planar compact, convex set from noisy measurements of its support function. Both the problem of estimating the support function at a point and that of estimating the whole convex set are studied. For pointwise estimation, we consider the problem in a general nonasymptotic framework, which evaluates the performance of a procedure at each individual set, instead of the worst case performance over a large parameter space as in conventional minimax theory. A data-driven adaptive estimator is proposed and is shown to be optimally adaptive to every compact, convex set. For estimating the whole convex set, we propose estimators that are shown to adaptively achieve the optimal rate of convergence. In both of these problems, our analysis makes no smoothness assumptions on the boundary of the unknown convex set.

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CONSISTENCY OF AIC AND BIC IN ESTIMATING THE NUMBER OF SIGNIFICANT COMPONENTS IN HIGH-DIMENSIONAL PRINCIPAL COMPONENT ANALYSIS

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In this paper, we study the problem of estimating the number of significant components in principal component analysis (PCA), which corresponds to the number of dominant eigenvalues of the covariance matrix of p variables. Our purpose is to examine the consistency of the estimation criteria AIC and BIC based on the model selection criteria by Akaike [In *2nd International Symposium on Information Theory* (1973) 267–281, Akadémia Kiado] and Schwarz [*Estimating the dimension of a model* **6** (1978) 461–464] under a high-dimensional asymptotic framework. Using random matrix theory techniques, we derive sufficient conditions for the criterion to be strongly consistent for the case when the dominant population eigenvalues are bounded, and when the dominant eigenvalues tend to infinity. Moreover, the asymptotic results are obtained without normality assumption on the population distribution. Simulation studies are also conducted, and results show that the sufficient conditions in our theorems are essential.

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ON THE SYSTEMATIC AND IDIOSYNCRATIC VOLATILITY WITH LARGE PANEL HIGH-FREQUENCY DATA[1]

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In this paper, we separate the integrated (spot) volatility of an individual Itô process into integrated (spot) systematic and idiosyncratic volatilities, and estimate them by aggregation of local factor analysis (localization) with large-dimensional high-frequency data. We show that, when both the sampling frequency n and the dimensionality p go to infinity and $p \geq C\sqrt{n}$ for some constant C, our estimators of High dimensional Itô process; common driving process; specific driving process, integrated High dimensional Itô process, common driving process, specific driving process, systematic and idiosyncratic volatilities are $\sqrt{n}$ ($n^{1/4}$ for spot estimates) consistent, the best rate achieved in estimating the integrated (spot) volatility which is readily identified even with univariate high-frequency data. However, when $Cn^{1/4} \leq p < C\sqrt{n}$, aggregation of $n^{1/4}$-consistent local estimates of systematic and idiosyncratic volatilities results in p-consistent (not $\sqrt{n}$-consistent) estimates of integrated systematic and idiosyncratic volatilities. Even more interesting, when $p < Cn^{1/4}$, the integrated estimate has the same convergence rate as the spot estimate, both being p-consistent. This reveals a distinctive feature from aggregating local estimates in the low-dimensional high-frequency data setting. We also present estimators of the integrated (spot) idiosyncratic volatility matrices as well as their inverse matrices under some sparsity assumption. We finally present a factor-based estimator of the inverse of the spot volatility matrix. Numerical studies including the Monte Carlo experiments and real data analysis justify the performance of our estimators.

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BALL DIVERGENCE: NONPARAMETRIC TWO SAMPLE TEST

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In this paper, we first introduce Ball Divergence, a novel measure of the difference between two probability measures in separable Banach spaces, and show that the Ball Divergence of two probability measures is zero if and only if these two probability measures are identical without any moment assumption. Using Ball Divergence, we present a metric rank test procedure to detect the equality of distribution measures underlying independent samples. It is therefore robust to outliers or heavy-tail data. We show that this multivariate two sample test statistic is consistent with the Ball Divergence, and it converges to a mixture of χ^2 distributions under the null hypothesis and a normal distribution under the alternative hypothesis. Importantly, we prove its consistency against a general alternative hypothesis. Moreover, this result does not depend on the ratio of the two imbalanced sample sizes, ensuring that can be applied to imbalanced data. Numerical studies confirm that our test is superior to several existing tests in terms of Type I error and power. We conclude our paper with two applications of our method: one is for virtual screening in drug development process and the other is for genome wide expression analysis in hormone replacement therapy.

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A SMOOTH BLOCK BOOTSTRAP FOR QUANTILE REGRESSION WITH TIME SERIES

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Quantile regression allows for broad (conditional) characterizations of a response distribution beyond conditional means and is of increasing interest in economic and financial applications. Because quantile regression estimators have complex limiting distributions, several bootstrap methods for the independent data setting have been proposed, many of which involve smoothing steps to improve bootstrap approximations. Currently, no similar advances in smoothed bootstraps exist for quantile regression with dependent data. To this end, we establish a smooth tapered block bootstrap procedure for approximating the distribution of quantile regression estimators for time series. This bootstrap involves two rounds of smoothing in resampling: individual observations are resampled via kernel smoothing techniques and resampled data blocks are smoothed by tapering. The smooth bootstrap results in performance improvements over previous unsmoothed versions of the block bootstrap as well as normal approximations based on Powell's kernel variance estimator, which are common in application. Our theoretical results correct errors in proofs for earlier and simpler versions of the (unsmoothed) moving blocks bootstrap for quantile regression and broaden the validity of block bootstraps for this problem under weak conditions. We illustrate the smooth bootstrap through numerical studies and examples.

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ASYMPTOTIC DISTRIBUTION-FREE TESTS FOR SEMIPARAMETRIC REGRESSIONS WITH DEPENDENT DATA

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This article proposes a new general methodology for constructing nonparametric and semiparametric Asymptotically Distribution-Free (ADF) tests for semiparametric hypotheses in regression models for possibly dependent data coming from a strictly stationary process. Classical tests based on the difference between the estimated distributions of the restricted and unrestricted regression errors are not ADF. In this article, we introduce a novel transformation of this difference that leads to ADF tests with well-known critical values. The general methodology is illustrated with applications to testing for parametric models against nonparametric or semiparametric alternatives, and semiparametric constrained mean–variance models. Several Monte Carlo studies and an empirical application show that the finite sample performance of the proposed tests is satisfactory in moderate sample sizes.

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GRADIENT-BASED STRUCTURAL CHANGE DETECTION FOR NONSTATIONARY TIME SERIES M-ESTIMATION

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We consider structural change testing for a wide class of time series M-estimation with nonstationary predictors and errors. Flexible predictor-error relationships, including exogenous, state-heteroscedastic and autoregressive regressions and their mixtures, are allowed. New uniform Bahadur representations are established with nearly optimal approximation rates. A CUSUM-type test statistic based on the gradient vectors of the regression is considered. In this paper, a simple bootstrap method is proposed and is proved to be consistent for M-estimation structural change detection under both abrupt and smooth nonstationarity and temporal dependence. Our bootstrap procedure is shown to have certain asymptotically optimal properties in terms of accuracy and power. A public health time series dataset is used to illustrate our methodology, and asymmetry of structural changes in high and low quantiles is found.

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MODERATE DEVIATIONS AND NONPARAMETRIC INFERENCE FOR MONOTONE FUNCTIONS

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This paper considers self-normalized limits and moderate deviations of nonparametric maximum likelihood estimators for monotone functions. We obtain their self-normalized Cramér-type moderate deviations and limit distribution theorems for the nonparametric maximum likelihood estimator in the current status model and the Grenander-type estimator. As applications of the results, we present a new procedure to construct asymptotical confidence intervals and asymptotical rejection regions of hypothesis testing for monotone functions. The theoretical results can guarantee that the new test has the probability of type II error tending to 0 exponentially. Simulation studies also show that the new nonparametric test works well for the most commonly used parametric survival functions such as exponential and Weibull survival distributions.

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UNIFORM ASYMPTOTIC INFERENCE AND THE BOOTSTRAP AFTER MODEL SELECTION

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Recently, Tibshirani et al. [*J. Amer. Statist. Assoc.* **111** (2016) 600–620] proposed a method for making inferences about parameters defined by model selection, in a typical regression setting with normally distributed errors. Here, we study the large sample properties of this method, without assuming normality. We prove that the test statistic of Tibshirani et al. (2016) is asymptotically valid, as the number of samples n grows and the dimension d of the regression problem stays fixed. Our asymptotic result holds uniformly over a wide class of nonnormal error distributions. We also propose an efficient bootstrap version of this test that is provably (asymptotically) conservative, and in practice, often delivers shorter intervals than those from the original normality-based approach. Finally, we prove that the test statistic of Tibshirani et al. (2016) does not enjoy uniform validity in a high-dimensional setting, when the dimension d is allowed grow.

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DETECTION THRESHOLDS FOR THE β-MODEL ON SPARSE GRAPHS

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In this paper, we study sharp thresholds for detecting sparse signals in β-models for potentially sparse random graphs. The results demonstrate interesting interplay between graph sparsity, signal sparsity and signal strength. In regimes of moderately dense signals, irrespective of graph sparsity, the detection thresholds mirror corresponding results in independent Gaussian sequence problems. For sparser signals, extreme graph sparsity implies that all tests are asymptotically powerless, irrespective of the signal strength. On the other hand, sharp detection thresholds are obtained, up to matching constants, on denser graphs. The phase transitions mentioned above are sharp. As a crucial ingredient, we study a version of the higher criticism test which is provably sharp up to optimal constants in the regime of sparse signals. The theoretical results are further verified by numerical simulations.

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ADAPTIVE SUP-NORM ESTIMATION OF THE WIGNER FUNCTION IN NOISY QUANTUM HOMODYNE TOMOGRAPHY

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In quantum optics, the quantum state of a light beam is represented through the Wigner function, a density on $\mathbb{R}^2$, which may take negative values but must respect intrinsic positivity constraints imposed by quantum physics. In the framework of noisy quantum homodyne tomography with efficiency parameter $1/2 < \eta \leq 1$, we study the theoretical performance of a kernel estimator of the Wigner function. We prove that it is minimax efficient, up to a logarithmic factor in the sample size, for the $\mathbb{L}_\infty$-risk over a class of infinitely differentiable functions. We also compute the lower bound for the $\mathbb{L}_2$-risk. We construct an adaptive estimator, that is, which does not depend on the smoothness parameters, and prove that it attains the minimax rates for the corresponding smoothness of the class of functions up to a logarithmic factor in the sample size. Finite sample behaviour of our adaptive procedure is explored through numerical experiments.

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DISTRIBUTED TESTING AND ESTIMATION UNDER SPARSE HIGH DIMENSIONAL MODELS

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This paper studies hypothesis testing and parameter estimation in the context of the divide-and-conquer algorithm. In a unified likelihood-based framework, we propose new test statistics and point estimators obtained by aggregating various statistics from k subsamples of size n/k, where n is the sample size. In both low dimensional and sparse high dimensional settings, we address the important question of how large k can be, as n grows large, such that the loss of efficiency due to the divide-and-conquer algorithm is negligible. In other words, the resulting estimators have the same inferential efficiencies and estimation rates as an oracle with access to the full sample. Thorough numerical results are provided to back up the theory.

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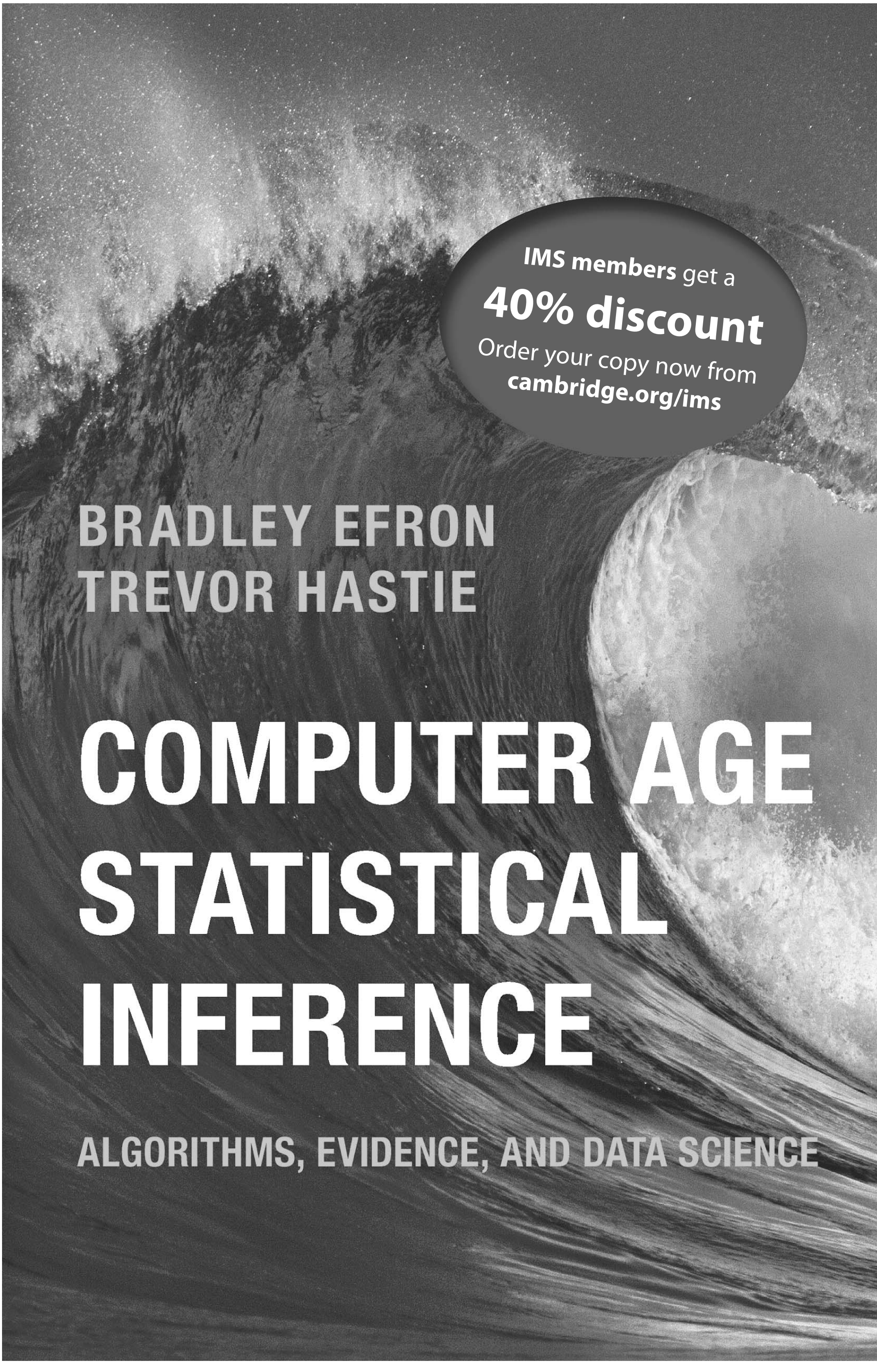
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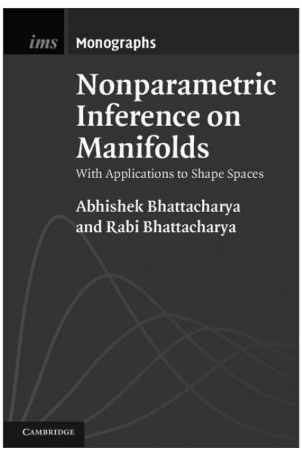

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