

Local false discovery rate based methods for multiple testing of one-way classified hypotheses*

Sanat K. Sarkar[†], and Zhigen Zhao[‡]

Department of Statistics, Operations, and Data Science, Temple University, Philadelphia, PA, 19122, USA
e-mail: sanat@temple.edu; zhaozhg@temple.edu

Abstract: This paper continues the line of research initiated in Liu, Sarkar and Zhao (2016) on developing a novel framework for multiple testing of hypotheses grouped in a one-way classified form using hypothesis-specific local false discovery rates (Lfdr’s). It is built on an extension of the standard two-class mixture model from single to multiple groups, defining hypothesis-specific Lfdr as a function of the conditional Lfdr for the hypothesis given that it is within an important group and the Lfdr for the group itself and involving a new parameter that measures grouping effect. This definition captures the underlying group structure for the hypotheses belonging to a group more effectively than the standard two-class mixture model. Two new Lfdr based methods, possessing meaningful optimalities, are produced in their oracle forms. One, designed to control false discoveries across the entire collection of hypotheses, is proposed as a powerful alternative to simply pooling all the hypotheses into a single group and using commonly used Lfdr based method under the standard single-group two-class mixture model. The other is proposed as an Lfdr analog of the method of Benjamini and Bogomolov (2014) for selective inference. It controls Lfdr based measure of false discoveries associated with selecting groups concurrently with controlling the average of within-group false discovery proportions across the selected groups. Simulation studies and real-data application show that our proposed methods are often more powerful than their relevant competitors.

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[†]Sanat K. Sarkar is Professor of Department of Statistics, Operations, and Data Science, Temple University.

[‡]Zhigen Zhao is Associate Professor of Department of Statistics, Operations, and Data Science.

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1. Introduction

Modern scientific studies aided by high-throughput technologies, such as those related to brain imaging, microarray analysis, astronomy, atmospheric science, drug discovery, and many others, are increasingly relying on large-scale multiple testing as an integral part of statistical investigations focused on high-dimensional inference. With many of these investigations, notably in genome-wide association and neuroimaging studies, giving rise to testing of hypotheses that appear in groups, the multiple testing paradigm seems to be shifting from testing single to multiple groups of hypotheses. These groups, forming at single or multiple levels creating respectively one- or multiway classified hypotheses, can occur naturally due to the underlying biological or experimental process or be created using internal or external information capturing certain specific features of the data. Several newer questions arise with this paradigm shift. We will focus in this paper on the following two questions related to one-way classified hypotheses that seem relevant in light of what is available in the literature:

- Q1. For multiple testing of hypotheses grouped into a one-way classified form, how to effectively capture the underlying group/classification structure, instead of simply pooling all the hypotheses into a single group, while controlling overall false discoveries across all individual hypotheses?

Q2. For hypotheses grouped into a one-way classified form in the context of post-selective inference where groups are selected before testing the hypotheses in the selected groups, how to effectively capture the underlying group/classification structure to control the expected average of false discovery proportions across the selected groups?

Progress has been made toward answering Q1 (Hu, Zhao and Zhou (2010), Nandi, Sarkar and Chen (2021)) and Q2 (Benjamini and Bogomolov (2014)) for one-way classified hypotheses in the framework of Benjamini-Hochberg (BH, Benjamini and Hochberg (1995)) type false discovery rate (FDR) control. However, research addressing these questions based on local false discovery rate (Lfd) (Efron et al. (2001)) based methodologies are largely absent, excepting the work of Cai and Sun (2009) and a recent work of Liu, Sarkar and Zhao (2016) where a method has been proposed in its oracle form to answer the following question slightly different from Q1: When making important discoveries within each group is as important as making those discoveries across all hypotheses, how to maintain a control over falsely discovered hypotheses within each group while controlling it across all hypotheses?

The fact that an Lfd based approach with its Bayesian/empirical Bayesian and decision theoretic foundation can yield powerful multiple testing method controlling false discoveries effectively capturing dependence as well as other structures of the data in single- and multiple-group settings has been demonstrated before (Sun et al. (2006), Sun and Cai (2007), Efron (2008), Ferkingstad et al. (2008), Sarkar, Zhou and Ghosh (2008), Sun and Cai (2009), Cai and Sun (2009), Zhao (2010), Hu, Zhao and Zhou (2010), Zhao and Hwang (2012), Zablocki et al. (2014), Zhao and Sarkar (2015), Ignatiadis et al. (2016), Kwon and Zhao (2022)). However, the work of Liu, Sarkar and Zhao (2016) is fundamentally different from these works in that it takes into account the sparsity of signals both across groups and within each active group. Consequently, the effect of a group's importance in terms of its Lfd can be explicitly factored into an Lfd based importance measure of each hypothesis within that group.

In this article, we continue the line of research initiated in Liu, Sarkar and Zhao (2016) to answer Q1 in an Lfd framework. More specifically, we borrow ideas from Liu, Sarkar and Zhao (2016) in developing methodological steps to present a unified group-adjusted multiple testing framework for one-way classified hypotheses that introduces a grouping effect into overall false discoveries across all individual hypotheses. This new insight clearly demonstrates how the group effect influences the existing testing method. We also provide an answer to Q2 from the Bayes/empirical Bayes perspective. To the best of our knowledge, this is the first result to study the FDR control for the selection from the Bayesian/empirical Bayesian perspective.

The paper is organized as follows. In Section 2, we present the current state of knowledge closely related to the present work, before presenting our Lfd based methods answering Q1 and Q2 in Section 3. In Section 4, we introduce a Gibbs sampler using a hierarchical Bayes approach to estimate the model parameters, and demonstrate the performances of the proposed methods based on these

estimates and compare them to many existing methods. We further applied the proposed method answering Q1 to the Adequate Year Progress (AYP) data set [Liu, Sarkar and Zhao (2016)]. We conclude the paper with a few remarks in Section 5.

2. Literature review

Suppose there are N hypotheses that appear in m non-overlapping families/groups, with H_{ij} being the j th hypothesis in the i th group ($i = 1, \dots, m; j = 1, \dots, n_i$). We refer to such a layout of hypotheses as one-way classified hypotheses.

Let X_{ij} be the test statistic/ p -value associated with H_{ij} , and θ_{ij} be the binary parameter indicating the truth ($\theta_{ij} = 0$) or falsity ($\theta_{ij} = 1$) of H_{ij} . The Lfdr corresponding to H_{ij} , defined by the posterior probability $P(\theta_{ij} = 0 | \mathbf{X})$, where $\mathbf{X} = \{X_{ij}, i = 1, \dots, m; j = 1, \dots, n_i\}$, is the basic ingredient for constructing Lfdr based approaches controlling false discoveries. The single-group case (or the case ignoring the group structure) has been considered extensively in the literature, notably by Sun and Cai (2007), Cai and Sun (2009) and He, Sarkar and Zhao (2015) who focused on constructing methods that are optimal, at least in their oracle forms. These oracle methods correspond to Bayes multiple decision rules under a single-group two-class mixture model (Efron et al. (2001), Newton et al. (2004), Storey (2002), Zhao (2022)) that minimize marginal false non-discovery rate (mFNR), a measure of false non-discoveries closely related to the notion of false non-discoveries (FNR) introduced in Genovese and Wasserman (2002) and Sarkar (2004), subject to controlling marginal false discovery rate (mFDR), a measure of false discoveries closely related to the BH FDR and the positive FDR (pFDR) of Storey (2002). Multiple-group versions of single-group Lfdr based approaches to multiple testing have started getting attention recently, among them the following seem more relevant to our work.

Cai and Sun (2009) extended their work from single to multiple groups (one-way classified hypotheses) under the following model: with i taking the value k with some prior probability π_k , (X_{ij}, θ_{ij}) , $j = 1, \dots, n_i$, given $i = k$, are assumed to be iid random pairs with

$$X_{kj} | \theta_{kj} \sim (1 - \theta_{kj})f_{k0} + \theta_{kj}f_{k1},$$

for some given densities f_{k0} and f_{k1} , and $\theta_{kj} \sim \text{Bernoulli}(p_k)$. They developed a method, which in its oracle form minimizes mFNR subject to controlling mFDR and is defined in terms of thresholding the conditional Lfdr's: $\text{CLfdr}^i(X_{ij}) = (1 - p_i)f_{i0}(X_{ij})/f_i(X_{ij})$, where $f_i(X_{ij}) = (1 - p_i)f_{i0}(X_{ij}) + p_if_{i1}(X_{ij})$, for $j = 1, \dots, n_i$, $i = 1, \dots, m$, before proposing a data-driven version of the oracle method that asymptotically maintains the original oracle properties. It should be noted that the probability p_k relates to the size of group k and provides little information about the importance of the group itself. Ferkingstad et al. (2008) brought the grouped hypotheses setting into testing a single family of hypotheses

in an attempt to empower typical Lfdr based thresholding approach by leveraging an external covariate. They partitioned the p -values into a number of small bins (groups) according to ordered values of the covariate. With the underlying two-class mixture model defined separately for each bin depending on the corresponding value of the covariate, they defined the so called covariate-modulated Lfdr as the posterior probability of a null hypothesis given the value of the covariate for the corresponding bin. They estimated the covariate-modulated Lfdr in each bin using a Bayesian approach before proposing their thresholding method, not necessarily controlling an overall measure of false discoveries such as the mFDR or the posterior FDR. An extension of this work from single to multiple covariates can be seen in Zablocki et al. (2014), Scott et al. (2015). Recently, Cai, Sun and Wang (2019) developed a novel grouped hypotheses testing framework for two-sample multiple testing of the differences between two highly sparsified mean vectors, having constructed the groups to extract sparsity information in the data by using a carefully constructed auxiliary covariate. They proposed an Lfdr based optimal multiple testing procedure controlling FDR as a powerful alternative to standard procedures based on the sample mean differences.

A sudden upsurge of research has taken place recently in selective/post-selection inference due to its importance in light of the realization by the scientific community that the lack of reproducibility of a scientist's work is often caused by his/her failure to account for selection bias. When multiple hypotheses are simultaneously tested in a selective inference setting, it gives rise to a grouped hypotheses testing framework with the tested groups being selected from a given set of groups of hypotheses. Benjamini and Bogomolov (2014) introduced the notion of the expected average of false discovery proportion across the selected groups as an appropriate error rate to control in this setting and proposed a method that controls it. Since then, a few papers have been written in this area (Peterson et al. (2016) and Heller et al. (2018)); however, no research has been produced yet in Lfdr framework.

Remark 2.1. When grouping of hypotheses occurs, an assumption can be made that the importance of a hypothesis is influenced by that of the group it belongs to. The Lfdr under the standard two-class mixture model, however, does not help in assessing a group's influence on *true* importance of its hypotheses. This has been the main motivation behind the work of Liu, Sarkar and Zhao (2016), who considered a group-adjusted two-class mixture model that yields an explicit representation of each hypothesis-specific Lfdr as a composition of its group-adjusted form and the Lfdr for the group it is associated with. It allowed them to produce a method that provides a separate control over within-group false discoveries for truly important groups in addition to having a control of false discoveries across all individual hypotheses. This paper motivates us to proceed further with the development of newer Lfdr based multiple testing methods for one-way classified hypotheses as described in the following section.

3. Proposed methods

This section presents the two Lfdr based methods we propose in this article to answer Q1 and Q2. The development of the methods takes place under the model introduced in Liu, Sarkar and Zhao (2016), which extends the standard two-class mixture model (Efron et al., 2001) from single to multiple groups. For completeness, we will recall this model here, with a different name, along with the formulas for different types of Lfdr associated with it before developing the methods.

3.1. Model and Lfdr formulas

Following are the two basic ingredients in building the aforementioned model in Liu, Sarkar and Zhao (2016): (i) expressing each θ_{ij} as $\theta_{ij} = \theta_{i\cdot} \cdot \theta_{j|i}$, with $\theta_{i\cdot} = I(\sum_{j=1}^{n_i} \theta_{ij} > 0)$ indicating the truth ($\theta_{i\cdot} = 0$) or falsity ($\theta_{i\cdot} = 1$) of $H_{i\cdot} = \cap_{j=1}^{n_i} H_{ij}$, and $\theta_{j|i} = \theta_{ij}$, if $\theta_{i\cdot} = 1$ and $= 0$ if $\theta_{i\cdot} = 0$ which reflects the underlying group structure of the hypotheses; and (ii) use of the following distribution for the $\theta_{j|i}$'s as an adjustment of the product Bernoulli distribution for the binary states of a set of hypotheses given that the group they belong to is important:

Definition 3.1 (Truncated Product Bernoulli (TPBern (π, n))). *A set of n binary variables Z_1, \dots, Z_n with the following joint probability distribution is said to have a TPBern (π, n) distribution:*

$$\begin{aligned} P(Z_1 = z_1, \dots, Z_n = z_n) &= \frac{1}{1 - (1 - \pi)^n} \prod_{i=1}^n \{ \pi^{z_i} (1 - \pi)^{1 - z_i} \} I \left(\sum_{i=1}^n z_i > 0 \right) \\ &= \frac{(1 - \pi)^n}{1 - (1 - \pi)^n} \left(\frac{\pi}{1 - \pi} \right)^{\sum_{i=1}^n z_i} I \left(\sum_{i=1}^n z_i > 0 \right). \end{aligned}$$

The model is stated in the following:

Definition 3.2 (Group-Adjusted Two-Class Mixture Model for One-Way Classified Hypotheses (One-Way GAMM)). *For each $i = 1, \dots, m$,*

$$\left\{ \begin{array}{l} X_{ij} \mid \theta_{i\cdot}, \theta_{j|i} \stackrel{\text{ind}}{\sim} (1 - \theta_{i\cdot} \cdot \theta_{j|i}) f_0(x_{ij}) + \theta_{i\cdot} \cdot \theta_{j|i} f_1(x_{ij}), \\ \text{for some densities } f_0 \text{ and } f_1, \\ P(\theta_{j|i} = 0 \mid \theta_{i\cdot} = 0) = 1, \text{ for } j = 1, \dots, n_i; \\ (\theta_{1|i}, \dots, \theta_{n_i|i}) \mid \theta_{i\cdot} = 1 \sim \text{TPBern}(\pi_{2i}, n_i), \\ \theta_{i\cdot} \sim \text{Bern}(\pi_1). \end{array} \right.$$

The sets $(X_{ij}, \theta_{i\cdot}, \theta_{j|i}, j = 1, \dots, n_i)$, for $i = 1, \dots, m$, are mutually independent.

Let

$$\text{Lfdr}_{ij}(\pi_1, \pi_{2i}) \equiv \text{Lfdr}_{ij}(\mathbf{x}; \pi_1, \pi_{2i}) = \Pr(\theta_{ij} = 0 \mid \mathbf{X} = \mathbf{x}),$$

$$\text{Lfdr}_{i\cdot}(\pi_1, \pi_{2i}) \equiv \text{Lfdr}_{i\cdot}(\mathbf{x}; \pi_1, \pi_{2i}) = \Pr(\theta_{i\cdot} = 0 \mid \mathbf{X} = \mathbf{x}),$$

and

$$\text{Lfdr}_{j|i}(\pi_1, \pi_{2i}) \equiv \text{Lfdr}_{j|i}(\mathbf{x}; \pi_1, \pi_{2i}) = \Pr(\theta_{j|i} = 0 \mid \theta_{i\cdot} = 1, \mathbf{X} = \mathbf{x}),$$

respectively, be the local FDRs under One-Way GAMM corresponding to H_{ij} , $H_{i\cdot}$, and H_{ij} conditional on $H_{i\cdot}$ being false. It is easy to see that

$$\text{Lfdr}_{ij}(\pi_1, \pi_{2i}) = 1 - [1 - \text{Lfdr}_{i\cdot}(\pi_1, \pi_{2i})][1 - \text{Lfdr}_{j|i}(\pi_1, \pi_{2i})], \quad (3.1)$$

showing how a hypothesis specific local FDR factors into the local FDR for the group and that for the hypothesis conditional on the group being important.

Let $\text{Lfdr}_{ij}^*(\pi_{2i}) = [(1 - \pi_{2i})f_0(x_{ij})]/m_i(x_{ij})$, with $m_i(x) = (1 - \pi_{2i})f_0(x) + \pi_{2i}f_1(x)$, be the local FDR corresponding to H_{ij} under the standard two-class mixture model. Then, as noted in Liu, Sarkar and Zhao (2016), and also shown in Appendix of this article using alternative and simpler arguments, $\text{Lfdr}_{j|i}(\pi_1, \pi_{2i})$ and $\text{Lfdr}_{i\cdot}(\pi_1; \pi_{2i})$ can be written explicitly in terms of the $\text{Lfdr}_{ij}^*(\pi_{2i})$'s as follows:

$$\text{Lfdr}_{j|i}(\pi_1, \pi_{2i}) \equiv \text{Lfdr}_{j|i}(\pi_{2i}) = \frac{\text{Lfdr}_{ij}^*(\pi_{2i}) - \text{Lfdr}_{i\cdot}^*(\pi_{2i})}{1 - \text{Lfdr}_{i\cdot}^*(\pi_{2i})}, \quad (3.2)$$

and

$$\text{Lfdr}_{i\cdot}(\pi_1; \pi_{2i}) \equiv \text{Lfdr}_{i\cdot}(\lambda_i; \pi_{2i}) = \frac{\text{Lfdr}_{i\cdot}^*(\pi_{2i})}{\text{Lfdr}_{i\cdot}^*(\pi_{2i}) + \lambda_i[1 - \text{Lfdr}_{i\cdot}^*(\pi_{2i})]}, \quad (3.3)$$

where $\text{Lfdr}_{i\cdot}^*(\pi_{2i}) = \prod_{j=1}^{n_i} \text{Lfdr}_{ij}^*(\pi_{2i})$, and

$$\lambda_i = \frac{\pi_1}{1 - \pi_1} \div \frac{1 - (1 - \pi_{2i})^{n_i}}{(1 - \pi_{2i})^{n_i}}. \quad (3.4)$$

Remark 3.1. The parameter λ_i plays a key role in One-Way GAMM. As noted from (3.3),

$$\frac{\Pr(\theta_{i\cdot} = 1 \mid \mathbf{X})}{\Pr(\theta_{i\cdot} = 0 \mid \mathbf{X})} = \lambda_i \times \frac{\Pr^*(\theta_{i\cdot} = 1 \mid \mathbf{X})}{\Pr^*(\theta_{i\cdot} = 0 \mid \mathbf{X})},$$

with \Pr^* denoting the probability under the standard two-class mixture model. That is,

$$\text{Posterior odds of significance of group } i \text{ under one-way GAMM} = \lambda_i \times \text{Posterior odds of significance of group } i \text{ under no group structure}$$

In other words, λ_i can be seen to act as a ‘group effect’ in One-Way GAMM. When $\lambda_i = 1$, $\text{Lfdr}_{ij}(\pi_1, \pi_{2i})$ reduces to $\text{Lfdr}_{ij}^*(\pi_{2i})$, and so One-Way GAMM with $\lambda_i = 1$ for all i represents the case of ‘no group effect’. As λ_i increases from 1, the posterior odds of the i th group being important increases under one-way grouping, which is likely to make our proposed procedures developed under One-Way GAMM more powerful in the sense of making more discoveries than those developed under the standard two-class mixture model.

We are now ready to develop our methods under One-Way GAMM.

3.2. Methods answering Q1 and Q2

Let $\delta_{ij}(\mathbf{X}) \in \{0, 1\}$ be the decision rule associated with θ_{ij} . Similar to θ_{ij} , we express $\delta_{ij}(\mathbf{X})$ as follows: $\delta_{ij}(\mathbf{X}) = \delta_{i\cdot}(\mathbf{X}) \cdot \delta_{j|i}(\mathbf{X})$, with $\delta_{i\cdot}(\mathbf{X}) = I(\sum_{j=1}^{n_i} \delta_{ij}(\mathbf{X}) > 0) \in \{0, 1\}$ and $\delta_{j|i}(\mathbf{X}) = \delta_{ij}(\mathbf{X})$ if $\delta_{i\cdot}(\mathbf{X}) = 1$, and $= 0$ if $\delta_{i\cdot}(\mathbf{X}) = 0$.

This article focuses on developing $\delta_{ij}(\mathbf{X})$ for $i = 1, \dots, m$, $j = 1, \dots, n_i$, controlling the following error rates at a given level α under One-Way GAMM: (i) The posterior expected proportion of false discoveries across all hypotheses, referred to as the total posterior FDR (PFDR_T), defined below

$$\text{PFDR}_T = E \left[\frac{\sum_{i=1}^m \sum_{j=1}^{n_i} (1 - \theta_{ij}) \delta_{ij}(\mathbf{X})}{\max \left\{ \sum_{i=1}^m \sum_{j=1}^{n_i} \delta_{ij}(\mathbf{X}), 1 \right\}} \middle| \mathbf{X} \right], \quad (3.5)$$

to answer Q1; and (ii) the posterior expected average false discovery proportion across selected groups, referred to as the selective posterior FDR (PFDR_S), defined below

$$\text{PFDR}_S = E \left[\frac{1}{|\mathcal{S}|} \sum_{i \in \mathcal{S}} \frac{\sum_{j=1}^{n_i} (1 - \theta_{ij}) \delta_{ij}(\mathbf{X})}{\max \left\{ \sum_{j=1}^{n_i} \delta_{ij}(\mathbf{X}), 1 \right\}} \middle| \mathbf{X} \right], \quad (3.6)$$

with \mathcal{S} being the set of indices for the selected groups, to answer Q2. The expectations in (3.5) and (3.6) are taken with respect to the θ_{ij} 's given \mathbf{X} .

Remark 3.2. Some remarks regarding the methods to be developed in the next subsection are worth making at this point. Hiding the symbol \mathbf{X} in the δ 's for notational convenience, we first note that $E \left[\sum_{j=1}^{n_i} (1 - \theta_{ij}) \delta_{ij} | \mathbf{X} \right] = \sum_{j=1}^{n_i} \text{Lfd}_{ij}(\lambda_i, \pi_{2i}) \delta_{ij}$ can be expressed as either

$$\sum_{j=1}^{n_i} \left[1 - \frac{\lambda_i [1 - \text{Lfd}_{ij}^*(\pi_{2i})]}{\lambda_i + (1 - \lambda_i) \text{Lfd}_{i\cdot}^*(\pi_{2i})} \right] \delta_{ij}, \quad (3.7)$$

as noted by using (3.2) and (3.3) in (3.1), or as

$$R_i \delta_{i\cdot} \{1 - [1 - \text{Lfd}_{i\cdot}(\lambda_i, \pi_{2i})] [1 - \text{PFDR}_{W_i}]\}, \quad (3.8)$$

where $\text{PFDR}_{W_i} = \sum_{j=1}^{n_i} \delta_{j|i} \text{Lfd}_{j|i}(\pi_{2i}) / \max(R_i, 1)$, with $R_i = \sum_{j=1}^{n_i} \delta_{j|i}$, is the within-group posterior FDR for group i , as noted from (3.1). However, we'll be using (3.7) in the expression for PFDR_T and determine δ_{ij} 's that will provide a single-stage approach to controlling this error rate, as opposed to Liu, Sarkar and Zhao (2016) where they use (3.8) to develop a two-stage Lfd based approach to controlling not only PFDR_T but also PFDR_{W_i} , for each i . While determining δ_{ij} 's controlling PFDR_S , which, as said in Introduction, will produce for the first time an Lfd analog of Benjamini and Bogomolov (2014), we will consider controlling it along with controlling a measure of false selection of groups. In other words, our approach to controlling PFDR_S will be a two-stage one relying on its expression in terms of (3.8).

The above discussions provide a **Group Adjusted TEesting** (GATE) framework for one-way classified hypotheses allowing us to produce Lfdr based algorithms (in their oracle forms) answering Q1 and Q2. We commonly refer to these algorithms as One-Way GATE algorithms.

3.2.1. Answering Q1

Before we present an algorithm in its oracle form answering Q1, it is important to note the following theorem that drives the development of it with some optimality property.

Theorem 3.1. *Let*

$$PFNR_T(\delta) = E \left[\frac{\sum_{i=1}^m \sum_{j=1}^{n_i} \theta_{ij} (1 - \delta_{ij}(\mathbf{X}))}{\max\{\sum_{i=1}^m \sum_{j=1}^{n_i} (1 - \delta_{ij}(\mathbf{X})), 1\}} \middle| \mathbf{X} \right] \tag{3.9}$$

denote the total posterior FNR (PFNR_T) of a decision rule

$$\delta(\mathbf{X}) = \{\delta_{ij}(\mathbf{X}), i = 1, \dots, m, j = 1, \dots, n_i\}.$$

The PFNR_T(δ) of the decision rule δ(X) with δ_{ij}(X) = I(Lfdr_{ij}(λ_i, π_{2i}) ≤ c), for c ∈ (0, 1) satisfying PFDR_T(δ) = α, is always less than or equal to that of any other δ'_{ij}(X) with PFDR_T(δ') ≤ α.

A proof of this theorem can be seen in Appendix.

Algorithm 1 One-Way GATE 1 (Oracle).

1: Calculate

$$Lfdr_{ij}(\lambda_i, \pi_{2i}) = 1 - \frac{\lambda_i [1 - Lfdr_{ij}^*(\pi_{2i})]}{\lambda_i + (1 - \lambda_i) Lfdr_i^*(\pi_{2i})},$$

the hypothesis specific local FDR under One-Way GAMM, for each $i = 1, \dots, m, j = 1, \dots, n_i$;

2: Pool all these Lfdr_{ij}(λ_i, π_{2i})'s together and sort them as Lfdr₍₁₎ ≤ ... ≤ Lfdr_(N);

3: Reject the hypotheses associated with Lfdr_(k), $k = 1, \dots, R$, where $R = \max \left\{ l : \sum_{k=1}^l Lfdr_{(k)} \leq l\alpha \right\}$.

Theorem 3.2. *The oracle One-Way GATE 1 controls PFDR_T at α.*

This theorem can be proved using standard arguments used for Lfdr based approaches to testing single group of hypotheses (see, e.g., Sun and Cai (2007), Sarkar and Zhou (2008)). It is important to note that PFDR_T may not equal a pre-specified value of α, and so Algorithm 1 is generally sub-optimal in the sense that it is the closest to one that is optimal as stated in Theorem 1.

Remark 3.3. When λ_i = 1 for all i, i.e., when the underlying grouping of hypotheses has no effect in the sense that a group's own chance of being important is no different from when it is formed by combining a set of independent

hypotheses, One-Way GATE 1 reduces to the standard Lfdr based approach (like that in Sun and Cai (2007), He, Sarkar and Zhao (2015); and in many others). As we will see from simulation studies in Section 4, with λ_i increasing (or decreasing) from 1, i.e., when a group's chance of being important gets larger (or smaller) than what it is if the group consists of independent hypotheses, the standard Lfdr based approach becomes less powerful (or fails to control the error rate).

3.2.2. Answering Q2

To introduce the algorithm, consider the following notations: for $0 < \alpha' < 1$, $R_i(\alpha') = \max\{1 \leq k \leq n_i : \sum_{j=1}^k \text{Lfdr}_{(j)|i}(\pi_{2i}) \leq k\alpha'\}$, with $\text{Lfdr}_{(j)|i}(\pi_{2i})$, $j = 1, \dots, n_i$, being the sorted values of the $\text{Lfdr}_{j|i}(\pi_{2i})$'s in group i . When assuming all the Lfdr scores are available, we derive an algorithm for Q2 as an alternative to the hierarchical testing method of Peterson et al. (2016). It allows a control over

$$\text{PFDR}_B = \frac{\sum_{i=1}^m \delta_i \text{Lfdr}_{i.}(\lambda_i, \pi_{2i})}{\max(\sum_{i=1}^m \delta_i, 1)},$$

an Lfdr analog of the aforementioned between-group FDR for the selected groups, while controlling PFDR_S .

Algorithm 2 One-Way GATE 2 (Oracle).

- 1: Given an $\eta \in (0, \alpha)$, select the largest subset of group indices \mathcal{S} such that $\frac{1}{|\mathcal{S}|} \sum_{i \in \mathcal{S}} \text{Lfdr}_{i.}(\lambda_i, \pi_{2i}) \leq \eta$;
- 2: For each $i \in \mathcal{S}$, and any given $\alpha' \leq \alpha$, find $R_i(\alpha')$ to calculate

$$\text{PFDR}_S(\alpha') = 1 - \frac{1}{|\mathcal{S}|} \sum_{i \in \mathcal{S}} (1 - \text{Lfdr}_{i.}(\lambda_i, \pi_{2i})) \left(1 - \frac{1}{R_i(\alpha')} \sum_{j=1}^{R_i(\alpha')} \text{Lfdr}_{(j)|i}(\pi_{2i}) \right) \quad (3.10)$$

- 3: Find $\alpha^*(\mathcal{S}) = \sup\{\alpha' : \text{PFDR}_S(\alpha') \leq \alpha\}$;
 - 4: Reject the hypotheses associated with $\text{PFDR}_S(\alpha^*(\mathcal{S}))$.
-

Theorem 3.3. *The oracle One-Way GATE 2 controls PFDR_S at α subject to a control over PFDR_B at $\eta < \alpha$.*

This theorem can be proved by noting that the left-hand side of (3.10) is the PFDR_S of the procedure produced by Algorithm 2.

Let

$$\text{PFNR}_B = E \left[\frac{\sum_{i=1}^m \theta_i (1 - \delta_{i.}(\mathbf{X}))}{\max\{\sum_{i=1}^m (1 - \delta_{i.}(\mathbf{X})), 1\}} \middle| \mathbf{X} \right],$$

and

$$\text{PFNR}_{W_i} = E \left[\frac{\sum_{j=1}^{n_i} \theta_{j|i} (1 - \delta_{j|i}(\mathbf{X}))}{\max\{\sum_{j=1}^{n_i} (1 - \delta_{j|i}(\mathbf{X})), 1\}} \middle| \mathbf{X} \right]$$

denote between-group posterior FNR and within-group posterior FNR for group i , respectively, for a decision rule of the form $\delta_{ij}(\mathbf{X}) = \delta_{i.}(\mathbf{X})\delta_{j|i}(\mathbf{X})$, with

$\delta_{i\cdot}(\mathbf{X}) = I(Lfdr_{i\cdot}(\lambda_i, \pi_{2i}) \leq c)$ and $\delta_{j|i}(\mathbf{X}) = I(Lfdr_{j|i}(\pi_{2i}) \leq c')$, for some $0 < c, c' < 1, i = 1, \dots, m$.

Remark 3.4. From Theorem 3.1, we have the following optimality result regarding One-Way GATE 2: Given any $0 < \eta < \alpha < 1$,

(i) the $PFNR_B$ of the decision rule of the form $\delta_{i\cdot}(\mathbf{X}) = I(Lfdr_{i\cdot}(\lambda_i, \pi_{2i}) \leq c)$ with $0 < c < 1$ satisfying $PFDR_B = \eta$ is less than or equal to that of any other $\delta'_{i\cdot}(\mathbf{X})$ with $PFDR_B \leq \eta$.

(ii) Given $\delta_{i\cdot}(\mathbf{X}), i = 1, \dots, m$, with $PFDR_B \leq \eta$, there exists an $\alpha'(\eta) \leq \alpha$, subject to $PFDR_S = \alpha$, such that, for each i , $PFNR_{W_i}$ of the decision rule of the form $\delta_{j|i}(\mathbf{X}) = I(Lfdr_{j|i}(\pi_{2i}) \leq c')$ with $0 < c' < 1$ satisfying $PFDR_{W_i} = \alpha(\eta)$ is less than or equal to that of any other decision rule in that group for which $PFDR_{W_i} \leq \alpha'(\eta)$.

Remark 3.5. It is important to note that One-Way GATE 2 without Step 1 can be used in situations where the focus is on controlling $PFDR_S$ given a selection rule (or \mathcal{S}).

4. Numerical studies

In this section we propose data-driven versions of One-Way GATE 1 and One-Way GATE 2, assuming that $\pi_{2i} = \pi_2$ for all i , and present results of numerical studies we conducted to examine their performances against other relevant methods.

4.1. Data-driven methods

The development of our methods are based on One-Way GAMM model where π_1, π_2 and $f_1(x)$ are assumed to be known. In practice when these parameters are unknown, one can develop data-driven versions of these methods using various estimation techniques, such as the EM algorithm (Liu, Sarkar and Zhao (2016)) and others (Cai, Sun and Wang (2019)). In this paper, however, we take a Bayesian approach by considering a hierarchical structure for modeling these unknown parameters and deriving a Gibbs sampler to estimate the parameters using the corresponding posterior distributions. To make it more clear, we re-state the One-Way GAMM by adding to it this hierarchical structure for the unknown parameters in the following:

$$\left\{ \begin{array}{l} X_{ij} \mid \theta_{i\cdot}, \theta_{j|i} \stackrel{ind}{\sim} (1 - \theta_{i\cdot} \cdot \theta_{j|i})f_0(x_{ij}) + \theta_{i\cdot} \cdot \theta_{j|i}f_1(x_{ij}), \\ \text{for some densities } f_0 \text{ and } f_1, \\ P(\theta_{j|i} = 0 \mid \theta_{i\cdot} = 0) = 1, \text{ for each } j = 1, \dots, n_i; \\ (\theta_{1|i}, \dots, \theta_{n_i|i}) \mid \theta_{i\cdot} = 1 \sim TP\text{Bern}(\pi_2, n_i), \\ \theta_{i\cdot} \sim \text{Bern}(\pi_1); \\ f_1(x_{ij}) \sim \sum_{k=1}^K Z_{ij}^k N(\mu_k, \sigma_k^2), \text{ where } \mathbf{Z}_{ij} \sim \text{Multinomial}(1, \boldsymbol{\eta}_K), \\ \boldsymbol{\eta}_K \sim \text{Dirichlet}(d_1, d_2, \dots, d_K), \\ \mu_k \sim N(0, \sigma_\mu^2), \sigma_k^2 \sim \text{InGamma}(r, \nu), \pi_1 \sim \text{Beta}(\alpha_1, \beta_1), \pi_2 \sim \text{Beta}(\alpha_2, \beta_2). \end{array} \right.$$

The following is the Gibbs sampler given by the above hierarchical structure of the model parameters:

Algorithm 3 Gibbs Sampler.

- 1: $P(\theta_i = 0 | \mathbf{X}, \text{the rest}) = Lfdr_i(\pi_1, \pi_2)$, provided in (3.3);
- 2: Given $\theta_i = 1$, generate $\theta_{j|i} \stackrel{\text{ind}}{\sim} \text{Bernoulli}(1 - Lfdr_{j|i}(\pi_1, \pi_2))$. Keep $\theta_{j|i}$ if $\sum_j \theta_{j|i} > 0$; otherwise set $\theta_{k|i} = 1$ where $Lfdr_{k|i}(\pi_1, \pi_2) = \min_j Lfdr_{j|i}(\pi_1, \pi_2)$;
- 3:

$$\pi_1 | \mathbf{X}, \text{the rest} \sim \text{Beta}(\alpha_1 + \sum_i \theta_i, \beta_1 + G - \sum_i \theta_i),$$

and

$$\pi_2 | \mathbf{X}, \text{the rest} \sim \text{Beta}(\alpha_2 + \sum_i \theta_i \sum_j \theta_{j|i}, \beta_2 + \sum_i \theta_i \sum_j (1 - \theta_{j|i}));$$

- 4: $\mathbf{Z}_{ij} | \mathbf{X}, \text{the rest} \sim \text{Multinomial}(1, \mathbf{p})$ where

$$\mathbf{p} = \frac{1}{\sum_k \eta_k \frac{1}{\sigma} \phi\left(\frac{x_{ij} - \mu_k}{\sigma}\right)} \left(\eta_1 \frac{1}{\sigma} \phi\left(\frac{x_{ij} - \mu_1}{\sigma}\right), \eta_2 \frac{1}{\sigma} \phi\left(\frac{x_{ij} - \mu_2}{\sigma}\right), \dots, \eta_K \frac{1}{\sigma} \phi\left(\frac{x_{ij} - \mu_K}{\sigma}\right) \right);$$

- 5:

$$\mu_k | \mathbf{X}, \text{the rest} \sim N\left(\frac{\sum_{ij} \theta_i \theta_{j|i} z_{ij}^k x_{ij}}{\sum_{ij} \theta_i \theta_{j|i} z_{ij}^k}, \frac{\sigma_k^2}{\sum_{ij} \theta_i \theta_{j|i} z_{ij}^k}\right),$$

and

$$\sigma_k^2 \sim \text{InGamma}\left(r + \frac{\sum_i \theta_i \sum_j \theta_{j|i} (x_{ij} - \mu_k)^2 z_{ij}^k}{2}, \left(\frac{1}{\nu} + \sum_i \theta_i \sum_j \theta_{j|i} z_{ij}^k\right)^{-1}\right).$$

- 6: $(\eta_1, \dots, \eta_k) | \mathbf{X}$,

$$\text{the rest} \sim \text{Dirichlet}\left(d_1 + \sum_{ij} \theta_i \theta_{j|i} z_{ij}^1, d_2 + \sum_{ij} \theta_i \theta_{j|i} z_{ij}^2, \dots, d_K + \sum_{ij} \theta_i \theta_{j|i} z_{ij}^K\right).$$

In Step 2 we have used an approximation, which is necessitated by the computational difficulty, especially for large n_i , in finding the exact posterior distribution of the $\theta_{j|i}$'s as it requires enumeration for all the elements in $\{0, 1\}^{n_i}$.

The parameters π_1, π_2, η_k 's, μ_k 's and σ_k^2 's are estimated by the medians based on samples drawn from the corresponding posterior distributions. These estimates are then used in place of the corresponding parameters appearing in the formulas for $Lfdr_{ij}(\pi_1, \pi_{2i})$ and $Lfdr_{j|i}(\pi_1, \pi_{2i})$ (with $\pi_{2i} = \pi_2$) in Algorithms 1 and 2, yielding our proposed data-driven GATE methods. These data-driven methods will be referred to as simply One-Way GATE 1 or One-Way GATE 2 in what follows.

4.2. One-Way GATE 1

We considered various simulation settings involving 2,000/5,000 hypotheses grouped into equal-sized groups to investigate how One-Way GATE 1 performs against its relevant competitors. These competitors are the Naive Method, SC Method (Sun and Cai (2009)) and GBH (Hu, Zhao and Zhou (2010)) Method, operating as follows under our model:

Naive Method: The single-group Lfdr based method of Sun and Cai (2007) is applied to the mn hypotheses pooled together into a single group under a two-class mixture model $X_{ij} \sim (1 - p)f_0(x_{ij}) + pf_1(x_{ij})$, with $p = p_{ij} = \pi_1\pi_2/[1 - (1 - \pi_2)^n]$, where the parameter π_2 and the density function $f_1(x)$ are estimated using Algorithm 3.

SC Method: The single-group Lfdr based method of Sun and Cai (2007) is applied to the mn hypotheses pooled together into a single group assuming a two-class mixture model $X_{ij} \sim (1 - \pi_2)f_0(x_{ij}) + \pi_2f_1(x_{ij})$, where the parameters π_2 and the density function $f_1(x)$ are estimated using Algorithm 3.

GBH Method: X_{ij} is converted to its p -value P_{ij} . We considered both the LSL-GBH (Least-Slope Group BH) method and the TST-GBH (Two-Stage Group BH) method proposed in Hu, Zhao and Zhou (2010).

The simulations involved generated triplets of observations $(X_{ij}, \theta_i, \theta_j|i)$ independently, $i = 1, \dots, m (= 100 \text{ or } 1,000)$; $j = 1, \dots, n (= 50 \text{ or } 5)$, with (i) $\theta_j|i$'s jointly following TPBern(π_2, n); (ii) $\theta_i \sim \text{Bern}(\pi_1)$; and (iii) $X_{ij}|\theta_{ij} \sim N(0, 1)$ if $\theta_{ij} = 0$, and $\sim \sum_{k=1}^K c_k N(\mu_k, \sigma_k^2)$ if $\theta_{ij} = 1$. Different cases for choosing (π_1, π_2) were considered. When $m = 1,000, n = 5$, we fixed π_2 and computed π_1 according to Equation (3.4), with λ being allowed to vary between 0.02 and 1.65. We wanted to observe the pattern of the aforementioned methods when λ increases. When $m = 100, n = 50$, we fixed π_2 and let π_1 vary between 0.1 and 0.9 with increment of 0.1. The value of π_2 was chosen among 0.1, 0.3, 0.5, and 0.7. We considered $K = 1$ and 2 and

$$(\mathbf{c}, \mu, \sigma^2) = \begin{cases} (1, 2, 1) & \text{when } K = 1, \\ ((0.4, 0.6), (-2, 2.5), (1.2, 0.8)) & \text{when } K = 2. \end{cases}$$

The One-Way GATE 1 in its oracle form, SC, TST-GBH, LSL-GBH, the One-Way GATE 1 using EM algorithm and the One-Way GATE 1 using Gibbs sampler were applied to the data for testing $\theta_{ij} = 0$ against $\theta_{ij} = 1$ simultaneously for all (i, j) at $\alpha = 0.05$. When running the Gibbs sampler, the hyperparameters are chosen as: $\alpha_1 = \alpha_2 = \beta_1 = \beta_2 = 1$, $d_1 = \dots = d_K = 1$, $\sigma_\mu^2 = 1000$, $r = 0.0001$ and $\nu = 1000$. The simulated values of Bayes FDR (defined as the expectation of PFDR_T over \mathbf{X}) and expected number of rejections were obtained for each of them based on 1000 replications.

Figures 1 and 2 display how these methods compare across different values of π_1 . Our proposed One-Way GATE 1 (labeled GATE) is clearly seen to control the false discovery rate at the desired level 0.05. The SC, TST-GBH and One-Way GATE 1 using EM algorithm (labeled GATE-EM) fail to control the FDR at the desired level. The Naive Method and GBH-LSL control the FDR at the desired level; however, they are much less powerful than the One-Way GATE 1 in terms of the total number of rejections. The One-Way GATE 1 performs similar to its oracle version.

The results for the case of $m = 1,000$ and $n = 5$ are displayed in Figures 3 and 4. We plot the simulated values of FDR and expected number of rejections for all the methods against $\lambda = \frac{\pi_1}{1 - \pi_1} \frac{(1 - \pi_2)^n}{1 - (1 - \pi_2)^n}$. As noted from these figures, the SC method fails to control the FDR when π_1 is small, i.e. when λ is small.

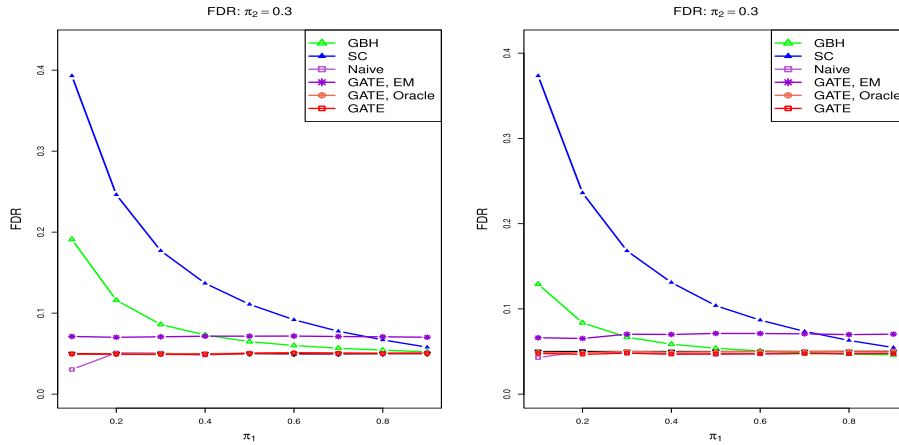


FIG 1. Performance in terms of FDR of One-Way GATE 1 across different values of π_1 when $m = 100, n = 50$. The left and right panels correspond to $K = 1$ and 2 , respectively.

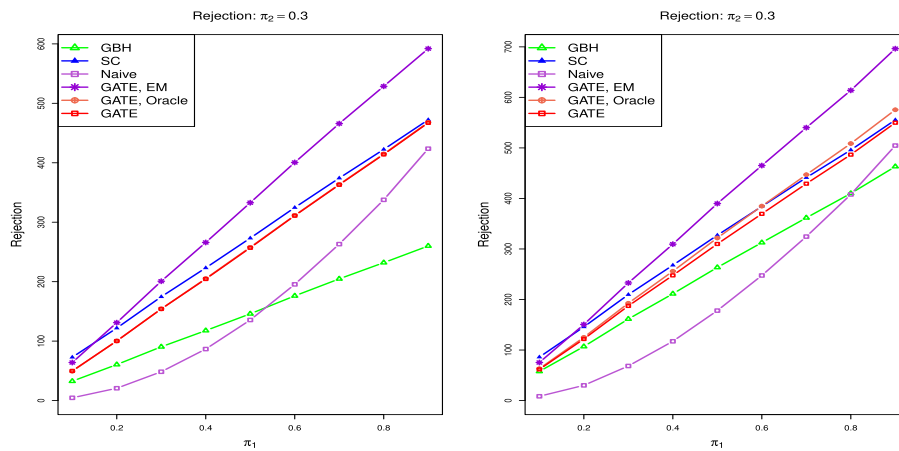


FIG 2. Performance in terms of expected number of rejections of One-Way GATE 1 across different values of π_1 when $m = 100, n = 50$. The left and right panels correspond to $K = 1$ and 2 , respectively.

This happens because it uses a larger value of π_1 when λ is small, inflating the FDR by an amount related to the value of λ . When λ is larger, it uses a smaller value of π_1 , resulting in a method which is conservative. The FDR level of the GBH-TST is inflated and GBH-LSL is too conservative. Interestingly, the oracle and two data-adaptive versions of One-Way GATE 1 work similarly under this setting.

As suggested by a referee, we investigated how well the estimated Lfdr score using our proposed One-Way GATE 1, denoted by $\widehat{\text{Lfdr}}$, approximates the true

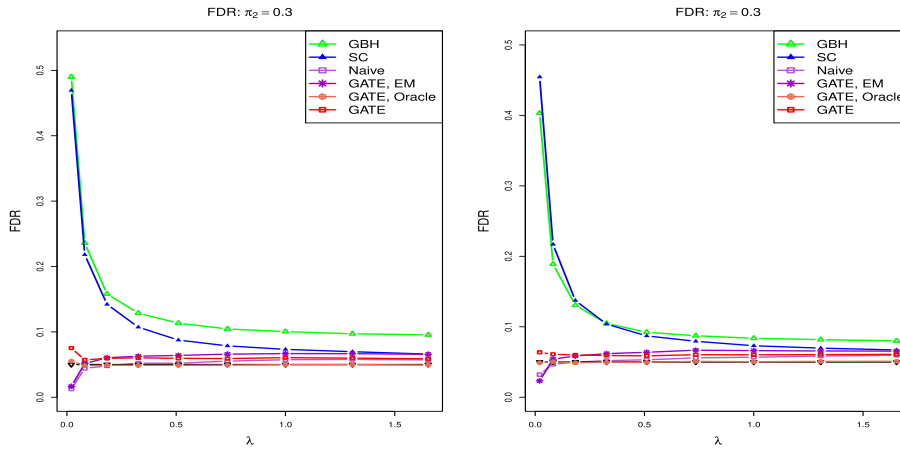


FIG 3. Performance in terms of FDR of One-Way GATE 1 across different values of λ when $m = 1000, n = 5$.

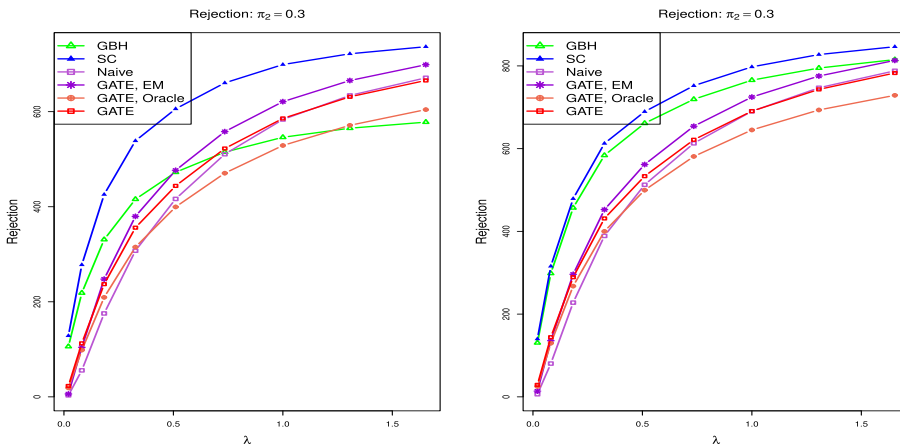


FIG 4. Performance in terms of expected number of rejections of One-Way GATE 1 across different values of λ when $m = 1000, n = 5$.

Lfdr. For that, we considered the following quantity:

$$EL(\widehat{\text{Lfdr}}, \text{Lfdr}) = \frac{\sum_{ij} \mathbf{1}(\text{Lfdr}_{ij} < 0.1) (\widehat{\text{Lfdr}}_{ij} - \text{Lfdr}_{ij})^2}{\sum_{ij} \mathbf{1}(\text{Lfdr}_{ij} < 0.1)},$$

the mean squared error of $\widehat{\text{Lfdr}}$ given that the true scores are low. It is an efficiency measure for our estimate when there are few strong signals. We simulated this measure under different parameter settings based on 1000 replications and reported them in Figure 5. As seen from this figure, the estimated local fdr using

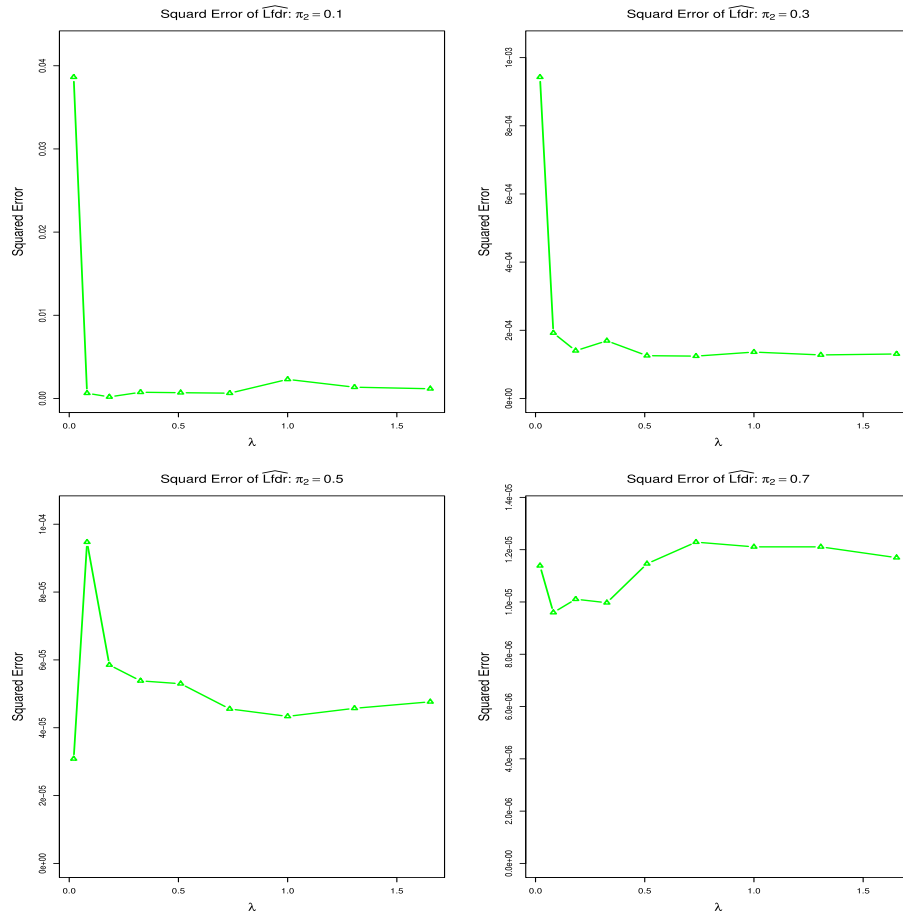


FIG 5. The mean squared error for the estimation of the local fdr scores using the proposed method: $m = 1000, n = 5, L = 1, \pi_2 = 0.1, 0.3, 0.5$ and 0.7 respectively.

our method gets more efficient as π_2 and λ increase.

Additional numerical results obtained through extensive numerical calculations are put in Appendix. It is clearly seen that One-Way GATE 1 performs similarly to its oracle form, and, more importantly, it beats the performances of others which ignore the underlying group structure.

4.3. One-Way GATE 2

Simulation studies were conducted to compare One-Way GATE 2 to its competitors: the BB method (Benjamini and Bogomolov (2014)), One-Way GATE 2 where the parameters are estimated according to the EM algorithm.

BB method: Convert X_{ij} to its p -value P_{ij} . With $P_{i(1)} \leq \dots \leq P_{i(n_i)}$ denoting

the sorted p -values in group i . Let \mathcal{G} be the set of indices of the group that are rejected according to Step 1 in Algorithm 2. Reject the hypotheses corresponding to $P_{i(j)}$ for all $i \in \mathcal{G}$ and $j \leq R_i$ where $R_i = \max\{j : P_{i(j)} \leq \frac{j}{n_i} \frac{\#\mathcal{G}}{G}\}$.

One-Way GATE 2 (EM): the hyper-parameters are estimated according to the EM algorithm before applying it in One-Way GATE 2.

The comparison was made in terms of Bayes selective FDR (defined as the expectation of PFDR_S over \mathbf{X}), expected number of total rejections, and average number of true rejections calculated under same simulation setting as in One-Way GATE 1. Figures 6 and 7 present the comparison for the setting where $m = 500$, $n = 20$, $\pi_1 = 0.14, 0.95$, and $\pi_2 = 0.30$. Additional numerical results are put in the appendix.

One-Way GATE 2 is seen to control the selective FDR, like the BB Method, quite well. However, the One-Way GATE 2 is seen to be more powerful in terms of yielding a large number of true rejections. The EM version of One-Way GATE 2, however, fails to control the overall FDR and selective FDR.

4.4. Real data analysis

In this section, we revisit the Adequate Yearly Progress (AYP) study of California elementary schools in 2013. This data set has been analyzed in Liu, Sarkar and Zhao (2016). The processed data can be loaded from the R package *GroupTest* and the reader can read Liu, Sarkar and Zhao (2016) for a complete description of how the data is prepared. In the final data set, we have 4118 elementary schools and 701 qualified school districts. For each school, there is an associated z -statistics, a quantity to compare the success rates in math exams of socioeconomically advantaged students and socioeconomically disadvantaged students.

We fit the Bayesian hierarchical model with $K = 2$ and $\sigma^2 = 1$. We ran the Gibbs sampling 20,000 times and chose the first 10,000 as burn-in and select 1 out of every 20 in the remaining sequence. We ran the MCMC algorithm three times with different initial points. Eventually, the estimated parameters are

$$\hat{\pi}_1 = 0.53, \hat{\pi}_2 = 0.59, (\hat{\eta}_1, \hat{\eta}_2) = (0.22, 0.78), (\hat{\mu}_1, \hat{\mu}_2) = (2.64, -1.88).$$

Figure 8, which compares the kernel density estimate based on the available z -values for all the schools with the same based on the z -values produced by the data generated using the Bayes hierarchical model, seems to indicate that this model fits the AYP data quite well.

Based on these estimated values, we applied One-Way GATE 1 with $\alpha = 0.05$. It rejected 773 schools, located in 209 school districts. The GATE 1 (EM) yielded 687 schools being rejected. The GBH (TST) Method rejected 588 schools. The data-driven version of SC Method yielded 929 rejections. It should be pointed out that λ_i ranges from 0 to 0.78, depending on the number of schools in district i , which varies between 1 and 277.

The GATE 1 has the following two features: (i) incorporating the groups can help to allocate errors among the groups appropriately; (ii) group structure can

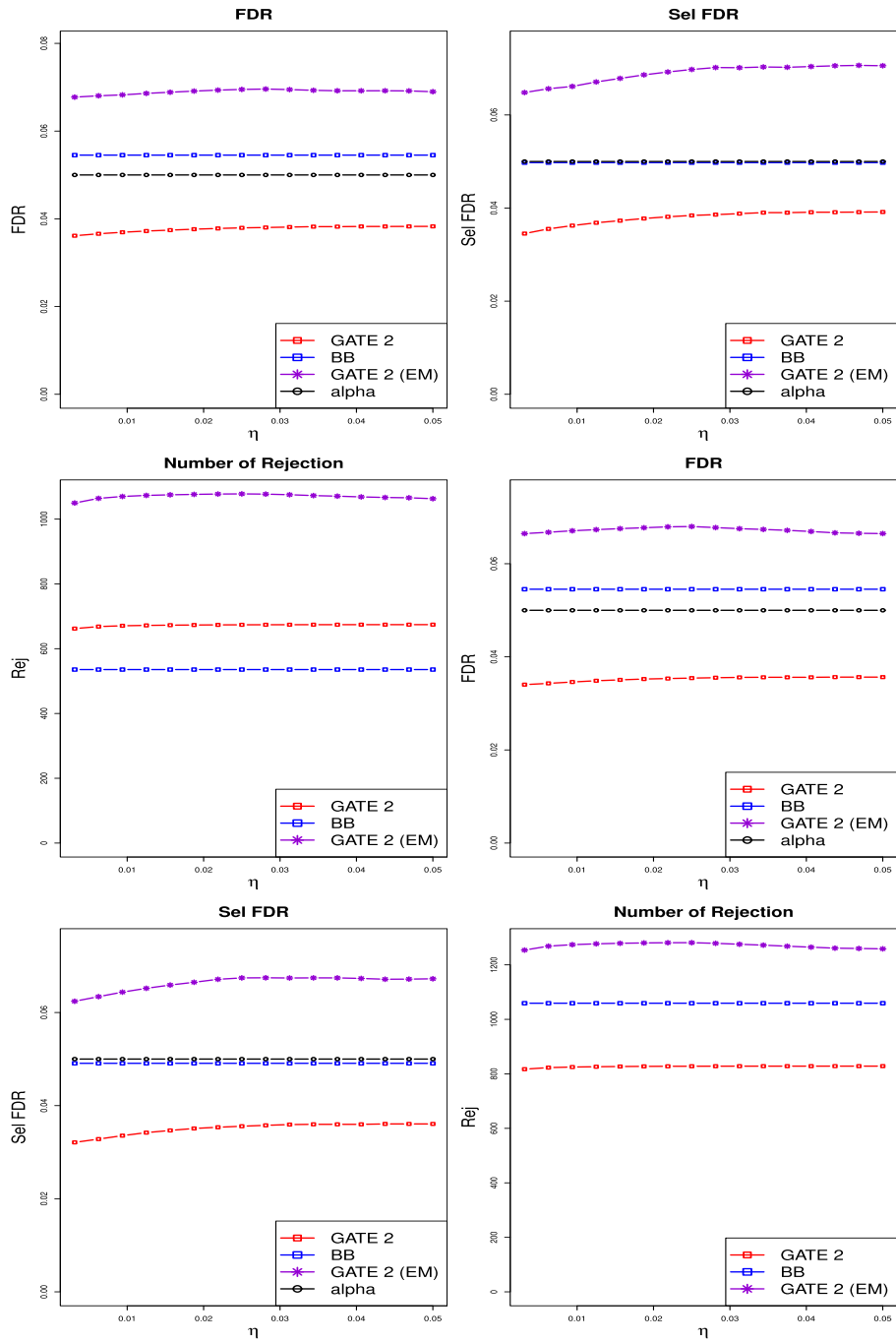


FIG 6. Performance of One-Way GATE 2 when $m = 500, n = 20, \pi_1 = 0.143$. The top panels correspond to cases when $K = 1$ and the bottom ones correspond to $K = 2$.

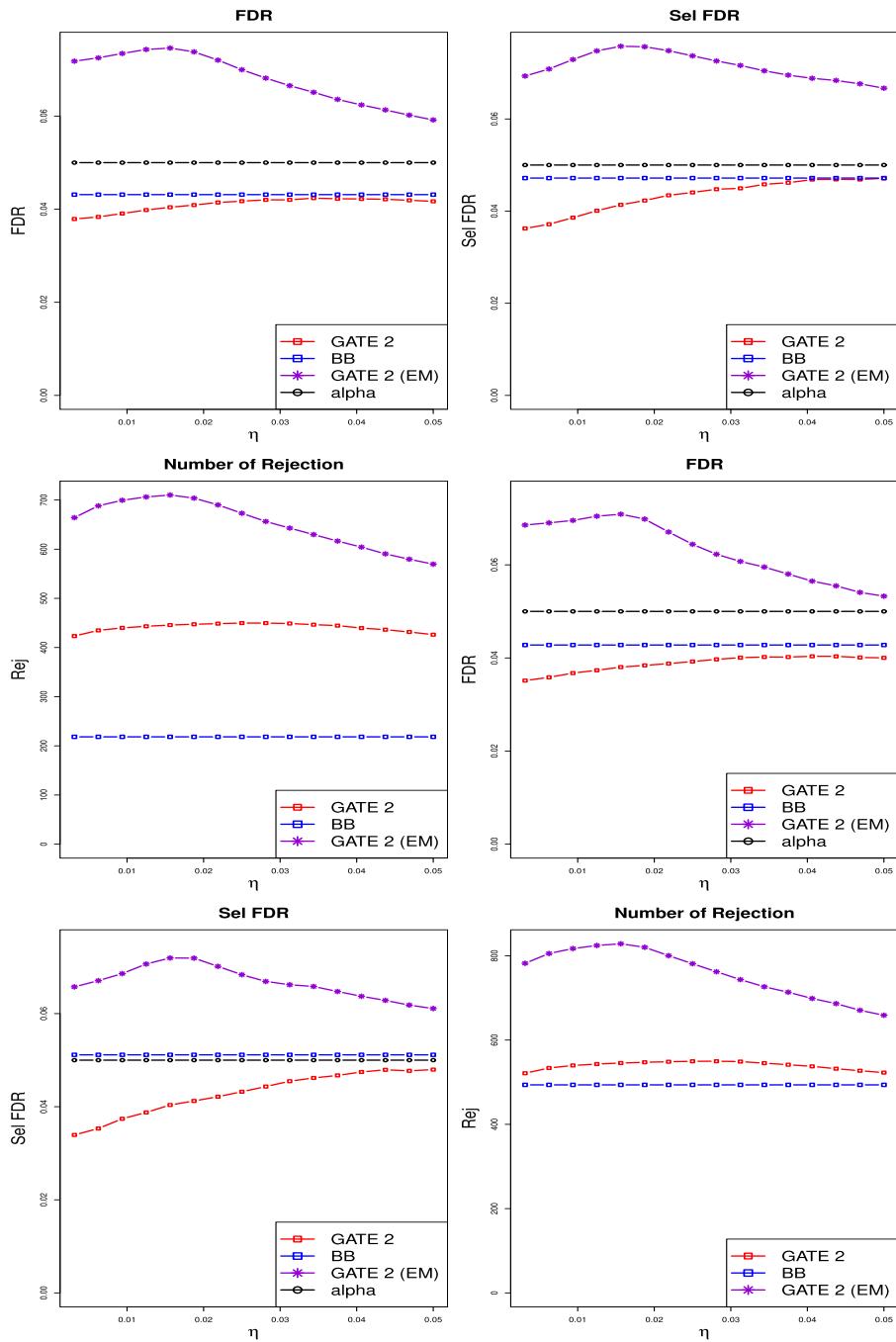


FIG 7. Performance of One-Way GATE 2 when $m = 500, n = 20, \pi_1 = 0.95$. The top panels correspond to cases when $K = 1$ and the bottom ones correspond to $K = 2$.

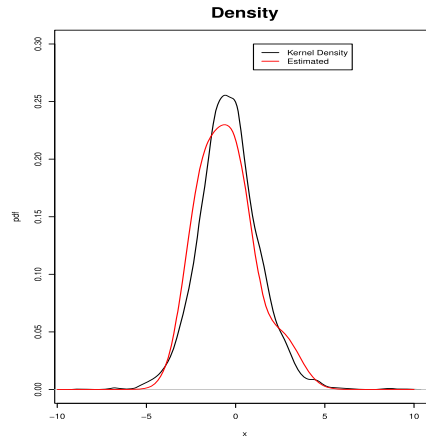


FIG 8. Comparison of the kernel density estimation of the pdf based on the z-statistics of all the data and the density function based on the estimated parameters.

alter the relative importance of different schools and thus change the ranking of the schools. These two features are playing important roles in the analysis of AYP data, which can be seen from the results for the following two districts:

New Haven Unified, Guy Jr. Emanuele Elementary: $z=3.05$
 $-0.45, -0.38, -0.28, 0.83, 0.92, 3.05, 0.27$

Berkeley Unified, Oxford Elementary: $z=2.65$.
 $1.77, 3.60, 4.40, -0.14, 1.83, 2.52, 2.65, 1.18, 3.25, 1.41, 0.86$

The Emanuele Elementary school is not rejected, while the Oxford Elementary school is rejected, though the corresponding z-values are 3.05 and 2.65 respectively. The New Haven Unified school district is not rejected because most of the schools has a moderate statistic except for the Guy Jr. Emanuele Elementary. On the other hand, the Berkeley Unified school district is rejected due to the fact that many schools within this district have relatively large z-values.

To cross-validate this conclusion, we downloaded the AYP data for the year of 2015 and look into these two school districts. We get the following information:

New Haven Unified, Guy Jr. Emanuele Elementary: $z=-1.45$
 $-1.27, 0.67, -1.51, 0.89, 3.05, -1.45, 1.18$

Berkeley Unified, Oxford Elementary: $z=3.95$
 $1.49, 3.90, 3.69, 4.50, 2.35, 5.63, 3.95, 4.71, 7.64, 3.27, 2.98$

It is seen that our conclusion made based on the data of 2013 agrees with the data in 2015. In Figure 9, we plot the z-values for the AYP data in 2015 against that for the data in 2013. We excluded those schools with the absolute z-values in 2013 being less than or equal to 2 because all the methods fail to reject them. We also exclude the schools with the absolute z-values being greater than 5 for

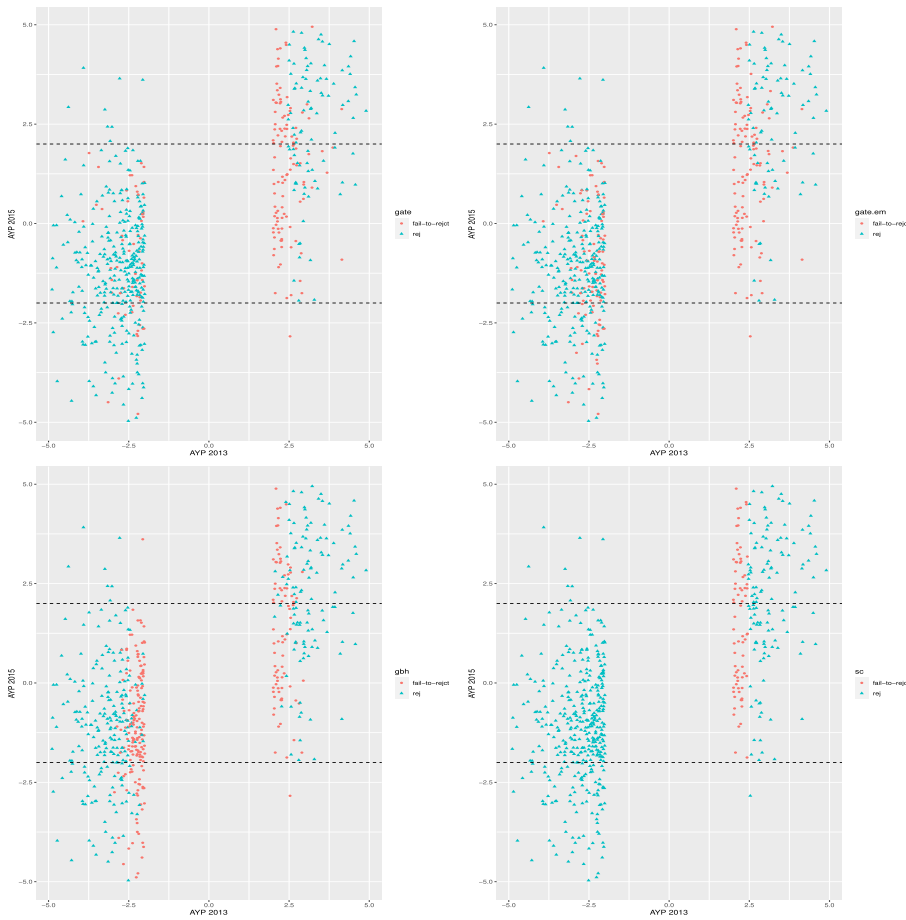


FIG 9. AYP data analysis result. Four panels, from top-left to the bottom-right, correspond to: One-Way GATE 1, One-Way GATE 1 (EM), GBH (TST) Method and SC Method.

clear rejection. The four panels in this figure correspond to One-Way GATE 1, One-Way GATE 1 (EM), GBH (TST) and SC from the top-left to the bottom-right. In each panel, the red dots represent the schools which are not rejected based on the data in 2013 and the blue triangles represent the schools which are rejected.

Note that the rejection region of GBH’s method is roughly symmetric around zero while the rejection regions of SC and GATE methods are not. Due to the effect of the group structure, whether to reject a hypothesis depends on the magnitude of z-statistic and the z-statistic of all the schools within the same school district. This is a unique feature of GATE which could provide some new insights for the local government.

The code used in performing our numerical investigations is made available

via github. The link is <https://github.com/zhaozhg81/GATE>.

5. Concluding remarks

The primary focus of this article has been to continue the line of research in Liu, Sarkar and Zhao (2016) to answer Q1 and Q2 for one-way classified hypotheses. It can provide the ground work for our broader goal of answering these questions in the setting of two-way classified hypotheses. Two-way classified setting is seen to occur in many applications. For instance, in time-course microarray experiment (see, e.g., Storey et al. (2005), Yuan and Kendziorski (2006), Sun and Wei (2011)), the hypotheses of interest can be laid out in a two-way classified form with ‘gene’ and ‘time-point’ representing the two categories of classification. In multi-phenotype GWAS (Peterson et al. (2016), Segura et al. (2012)), the families of the hypotheses related to different phenotypes form one level of grouping, while the other level of grouping is formed by the families of hypotheses corresponding to different SNPs. Two-way classified structure of hypotheses occurs also in brain imaging studies (Liu et al. (2009), Stein et al. (2010), Lin, Calhoun and Wang (2014), Barber and Ramdas (2015)). Now that we know the theoretical framework that can successfully capture the underlying group effect and yield powerful approaches to multiple testing in one-way classified setting, proceeding further towards extending it to produce newer and powerful Lfdr based approaches answering Q1 and Q2 in two-way classified setting would be a worthwhile goal. Some initial progress towards this goal has been made in Nandi, Sarkar and Chen (2021), Sarkar and Nandi (2021). We intend to expand upon it in our future research.

We strongly recommend using the One-Way GATE 1 we have proposed in this article for answering Q1, motivated by its desirable theoretical properties (as stated in Theorems 1 and 2) and strong numerical findings in comparison with its natural competitors (discussed in Sections 4.2 and 4.4). For answering Q2, the proposed One-Way GATE 2 is a better alternative to the BB method when only a few of the selected groups are likely to be important, which happens in many applications.

Appendix A: Appendix

A.1. Proofs of (3.2) and (3.3)

These results, although appeared before in Liu, Sarkar and Zhao (2016), will be proved here using different and simpler arguments. They are re-stated, without any loss of generality, for a single group with slightly different notations in the following lemma.

Lemma A.1. *Conditionally given $\theta_{\cdot} \sim \text{Bern}(\pi_1)$, let (X_j, θ_j) , $j = 1, \dots, n$, be distributed as follows: (i) $X_1, \dots, X_n \mid \theta_1, \dots, \theta_n \stackrel{\text{ind}}{\sim} (1 - \theta_{\cdot} \cdot \theta_j) f_0(x_j) + \theta_{\cdot} \cdot \theta_j f_1(x_j)$, and (ii) $\theta_1, \dots, \theta_n \sim \text{TPBern}(\pi_2, n)$. Let $\text{Lfdr}_j(\pi_2) \equiv \text{Lfdr}(x_j; \pi_2) = (1 -$*

$\pi_2)f_0(x_j)/m(x_j)$, with $m(x) = (1 - \pi_2)f_0(x) + \pi_2f_1(x)$, for $j = 1, \dots, n$, and $Lfdr.(\pi_2) = \prod_{j=1}^n Lfdr_j(\pi_2)$. Then,

$$\Pr(\theta_j = 0 | \theta. = 1, X_1 = x_1, \dots, X_n = x_n) = \frac{Lfdr_j(\pi_2) - Lfdr.(\pi_2)}{1 - Lfdr.(\pi_2)} \tag{A.1}$$

and

$$\Pr(\theta. = 0 | X_1 = x_1, \dots, X_n = x_n) = \frac{Lfdr.(\pi_2)}{Lfdr.(\pi_2) + \lambda[1 - Lfdr.(\pi_2)]}, \tag{A.2}$$

where $\lambda = \frac{\pi_1}{1 - \pi_1} \div \frac{1 - (1 - \pi_2)^n}{(1 - \pi_2)^n}$.

Proof. First, note that

$$(X_1, \dots, X_n) | \theta. = 0 \sim \prod_{j=1}^n f_0(x_j) = \frac{\prod_{j=1}^n m(x_j)}{(1 - \pi_2)^n} Lfdr.(\pi_2), \tag{A.3}$$

and

$$\begin{aligned} & (X_1, \dots, X_n) | \theta. = 1 \\ & \sim \frac{1}{1 - (1 - \pi_2)^n} \sum_{\sum_{j=1}^n \theta_j > 0} \left[\prod_{j=1}^n \{(1 - \theta_j)f_0(x_j) + \theta_j f_1(x_j)\} \prod_{j=1}^n \{\pi_2^{\theta_j} (1 - \pi_2)^{1 - \theta_j}\} \right] \\ & = \frac{1}{1 - (1 - \pi_2)^n} \left[\prod_{j=1}^n m(x_j) - (1 - \pi_2)^n \prod_{j=1}^n f_0(x_j) \right] \\ & = \frac{\prod_{j=1}^n m(x_j)}{1 - (1 - \pi_2)^n} [1 - Lfdr.(\pi_2)], \end{aligned} \tag{A.4}$$

from which we get

$$(X_1, \dots, X_n) \sim \left\{ \frac{(1 - \pi_1)Lfdr.(\pi_2)}{(1 - \pi_2)^n} + \frac{\pi_1[1 - Lfdr.(\pi_2)]}{1 - (1 - \pi_2)^n} \right\} \prod_{j=1}^n m(x_j). \tag{A.5}$$

Formula (A.2) follows upon dividing $(1 - \pi_1)$ times (A.3) by (A.5).

When $\theta_j = 0$, the conditional distribution of X_1, \dots, X_n given $\theta. = 1$ can be obtained similar to that in (A.4) as follows:

$$\begin{aligned} & \frac{(1 - \pi_2)f_0(x_j)}{1 - (1 - \pi_2)^n} \sum_{\sum_{k(\neq j)=1}^n \theta_k > 0} \left[\prod_{k(\neq j)=1}^n \{(1 - \theta_k)f_0(x_k) + \theta_k f_1(x_k)\} \right] \\ & \times \prod_{k(\neq j)=1}^n \{\pi_2^{\theta_k} (1 - \pi_2)^{1 - \theta_k}\} \end{aligned} \tag{A.6}$$

$$\begin{aligned}
&= \frac{(1-\pi_2)f_0(x_j)}{1-(1-\pi_2)^n} \left[\prod_{k(\neq j)=1}^n m(x_k) - (1-\pi_2)^{n-1} \prod_{k(\neq j)=1}^n f_0(x_k) \right] \\
&= \frac{\prod_{j=1}^n m(x_j)}{1-(1-\pi_2)^n} [\text{Lfd}r_j(\pi_2) - \text{Lfd}r_j(\pi_2)]. \tag{A.7}
\end{aligned}$$

Formula (A.1) then follows upon dividing (A.6) by (A.4). \square

Proof of Theorem 3.1. For notational simplicity, we will hide \mathbf{X} in $\delta_{ij}(\mathbf{X})$, $\delta'_{ij}(\mathbf{X})$, $Lfdr_{ij}(\mathbf{X})$.

First, we note the following inequalities:

$$\alpha \sum_{ij} (\delta_{ij} - \delta'_{ij}) \leq \sum_{ij} (\delta_{ij} - \delta'_{ij}) Lfdr_{ij} \leq c \sum_{ij} (\delta_{ij} - \delta'_{ij}), \tag{A.8}$$

the first of which follows from the fact that the $\text{PFDR}_T(\delta') \leq \alpha = \text{PFDR}_T(\delta)$, while the second one follows from $\sum_{ij} (\delta_{ij} - \delta'_{ij}) (c - Lfdr_{ij}) \geq 0$, because of the definition of δ_{ij} .

Since $\alpha = \sum_{ij} \delta_{ij} Lfdr_{ij} / \max\{\sum_{ij} \delta_{ij}, 1\} \leq c$, we have from (A.8) that $\sum_{ij} (\delta_{ij} - \delta'_{ij}) Lfdr_{ij} \geq 0$, that is,

$$\sum_{ij} (1 - \delta_{ij}) Lfdr_{ij} \leq \sum_{ij} (1 - \delta'_{ij}) Lfdr_{ij}. \tag{A.9}$$

With $\text{PFNR}_T(\delta)$ and $\text{PFNR}_T(\delta')$ denoting the PFNR_T of δ and δ' , respectively, we now note that

$$\begin{aligned}
&c \left[\frac{\text{PFNR}_T(\delta)}{1 - \text{PFNR}_T(\delta)} - \frac{\text{PFNR}_T(\delta')}{1 - \text{PFNR}_T(\delta')} \right] \\
&= c \sum_{ij} \left[\frac{(1 - \delta_{ij})(1 - Lfdr_{ij})}{\sum_{ij} (1 - \delta_{ij}) Lfdr_{ij}} - \frac{(1 - \delta'_{ij})(1 - Lfdr_{ij})}{\sum_{ij} (1 - \delta'_{ij}) Lfdr_{ij}} \right] \\
&= \sum_{ij} \left[\frac{1 - \delta_{ij}}{\sum_{ij} (1 - \delta_{ij}) Lfdr_{ij}} - \frac{1 - \delta'_{ij}}{\sum_{ij} (1 - \delta'_{ij}) Lfdr_{ij}} \right] [c(1 - Lfdr_{ij}) - (1 - c)Lfdr_{ij}] \\
&\leq 0,
\end{aligned}$$

with the inequality holding due to the definition of δ_{ij} and the inequality in (A.9). Thus, we have

$$\text{PFNR}_T(\delta) \leq \text{PFNR}_T(\delta'),$$

which proves the theorem. \square

A.2. EM algorithm

In this section, we provide steps of the EM algorithm. To better present the result, define $\pi_1^1 = \pi_1$, $\pi_1^0 = 1 - \pi_1$, $\pi_2^1 = \pi_2$ and $\pi_2^0 = 1 - \pi_2$. Let $A_i = \frac{1}{1 - (\pi_2^0)^{n_i}}$.

Consider $(\mathbf{x}, \boldsymbol{\theta})$ as the complete data. Then the complete log-likelihood function can be written as:

$$\begin{aligned}
 l(\mathbf{x}, \boldsymbol{\theta}) &= \sum_i \sum_{l=0}^1 I(\theta_i = l)(\log \pi_1^l + \log f(\mathbf{x}_i | \theta_i = l)) \\
 &= \sum_i \left\{ I(\theta_i = 0) \left[\log \pi_1^0 + \sum_{j=1}^{n_i} \log f(x_{ij} | \theta_i = 0) \right] + I(\theta_i = 1) \left[\log \pi_1^1 + \log f(\mathbf{x}_i | \theta_i = 1) \right] \right\} \\
 &= \sum_i \sum_{l=0}^1 I(\theta_i = l) \log \pi_1^l \\
 &+ \sum_i \sum_{j=1}^{n_i} \sum_{k=1}^K [I(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k) \log(c_k \pi_2^1 / A_i) + I(\theta_i = 1, \theta_{j|i} = 0) \log(\pi_2^0 / A_i)] \\
 &+ \sum_i \left[I(\theta_i = 0) \sum_{j=1}^{n_i} \log f_0(x_{ij}) + I(\theta_i = 1) \sum_{j=1}^{n_i} I(\theta_{j|i} = 0) \log f_0(x_{ij}) \right] \\
 &+ \sum_i I(\theta_i = 1) \sum_{j=1}^{n_i} \sum_{k=1}^K I(\theta_{j|i} = 1, m_{j|i} = k) \log f_k(x_{ij} | \theta_{j|i} = 1),
 \end{aligned}$$

where $m_{j|i} = k$ implies that x_{ij} is generated from $N(\mu_k, \sigma_k^2)$.

The expected value of the complete-data log-likelihood $l(\mathbf{x}, \boldsymbol{\theta})$ with respect to the unknown $\theta_i, \theta_{j|i}$, given the observed data \mathbf{x} and the current value $\boldsymbol{\beta}'$ of the parameter is:

$$\begin{aligned}
 Q(\boldsymbol{\beta}, \boldsymbol{\beta}') &= E [l(\mathbf{x}, \boldsymbol{\theta}) | \mathbf{x}, \boldsymbol{\beta}'] \\
 &= \sum_i \sum_{l=0}^1 \log \pi_1^l P(\theta_i = l | \mathbf{x}, \boldsymbol{\beta}') \\
 &+ \sum_i \sum_{j=1}^{n_i} \sum_{l=0}^1 \log(\pi_2^l / A_i) P(\theta_i = 1, \theta_{j|i} = l | \mathbf{x}, \boldsymbol{\beta}') \\
 &+ \sum_i \sum_{j=1}^{n_i} \sum_{k=1}^K \log c_k P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}') \\
 &+ \sum_i \sum_{j=1}^{n_i} \log f_0(x_{ij}) P(\theta_i = 0 | \mathbf{x}, \boldsymbol{\beta}') + \sum_g \sum_{j=1}^{n_i} \log f_0(x_{ij}) P(\theta_i = 1 | \mathbf{x}, \boldsymbol{\beta}') \\
 &+ \sum_i \sum_{j=1}^{n_i} \sum_{k=1}^K \log f_k(x_{ij}) P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}').
 \end{aligned}$$

Note that

$$P(\theta_i = 1, \theta_{j|i} = 1 | \mathbf{x}, \boldsymbol{\beta}') = (1 - f_{dr_{j|i}}(\boldsymbol{\beta}'))(1 - f_{dr_i}(\boldsymbol{\beta}')),$$

and

$$P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}') = P(\theta_i = 1, \theta_{j|i} = 1 | \mathbf{x}, \boldsymbol{\beta}') * \frac{c_k \frac{1}{\sigma_k} \phi\left(\frac{x_{ij} - \mu_k}{\sigma_k}\right)}{\sum_{k=1}^K c_k \frac{1}{\sigma_k} \phi\left(\frac{x_{ij} - \mu_k}{\sigma_k}\right)}.$$

We want to maximize the Q function which can be realized by maximizing each of these parts to get the estimates of π_1, π_2, c_k and μ_k, σ_k^2 , since these parts are not related. To maximize the first part with the restriction that $\pi_1^0 + \pi_1^1 = 1$, using the Lagrange multipliers, we can find the maximizer for π_1^1 as

$$\pi_1^{new} = 1 - \frac{\sum_i P(\theta_i = 0 | \mathbf{x}, \boldsymbol{\beta}')}{m} = 1 - \frac{\sum_i f d r_i(\boldsymbol{\beta}')}{m},$$

The parameter π_2^0 is updated as

$$\pi_2^{new} = \operatorname{argmax} \left\{ \pi_2^0 : \sum_i \sum_{j=1}^{n_i} \sum_{l=0}^1 \log(\pi_2^l / A_i) P(\theta_i = 1, \theta_{j|i} = l | \mathbf{x}, \boldsymbol{\beta}') \right\}.$$

The parameter c_k is updated as

$$c_k^{new} = \frac{\sum_i \sum_{j=1}^{n_i} P(\theta_{j|i} = 1, \theta_i = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}')}{\sum_i \sum_{j=1}^{n_i} P(\theta_i = 1, \theta_{j|i} = 1 | \mathbf{x}, \boldsymbol{\beta}')}$$

For the last part of Q function, we know that $f_0(x) \sim N(0, 1)$, $f_k(x) \sim N(\mu_k, \sigma_k^2)$ with probability c_k . Therefore, for each k , we need to find the MLEs for μ_k and σ_k^2 by maximizing the following log-likelihood function:

$$\begin{aligned} & \sum_i \sum_{j=1}^{n_i} \sum_{k=1}^K \log f_k(x_{ij}) P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}') \\ &= \sum_i \sum_{j=1}^{n_i} \sum_{k=1}^K \left[-\frac{1}{2} \log \sigma_k^2 - \frac{1}{2\sigma_k^2} (x_{ij} - \mu_k)^2 \right] P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}'). \end{aligned}$$

Taking derivatives with respect to μ_l and σ_l^2 and equating them to zero, we can get:

$$\begin{aligned} \mu_k^{new} &= \frac{\sum_i \sum_{j=1}^{n_i} x_{ij} P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}')}{\sum_i \sum_{j=1}^{n_i} P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}')}, \\ \sigma_k^{2new} &= \frac{\sum_i \sum_{j=1}^{n_i} (x_{ij} - \mu_l)^2 P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}')}{\sum_i \sum_{j=1}^{n_i} P(\theta_i = 1, \theta_{j|i} = 1, m_{j|i} = k | \mathbf{x}, \boldsymbol{\beta}')}. \end{aligned}$$

A.3. More simulation results on One-Way GATE 1

In this section we present more simulation results on One-Way GATE 1.

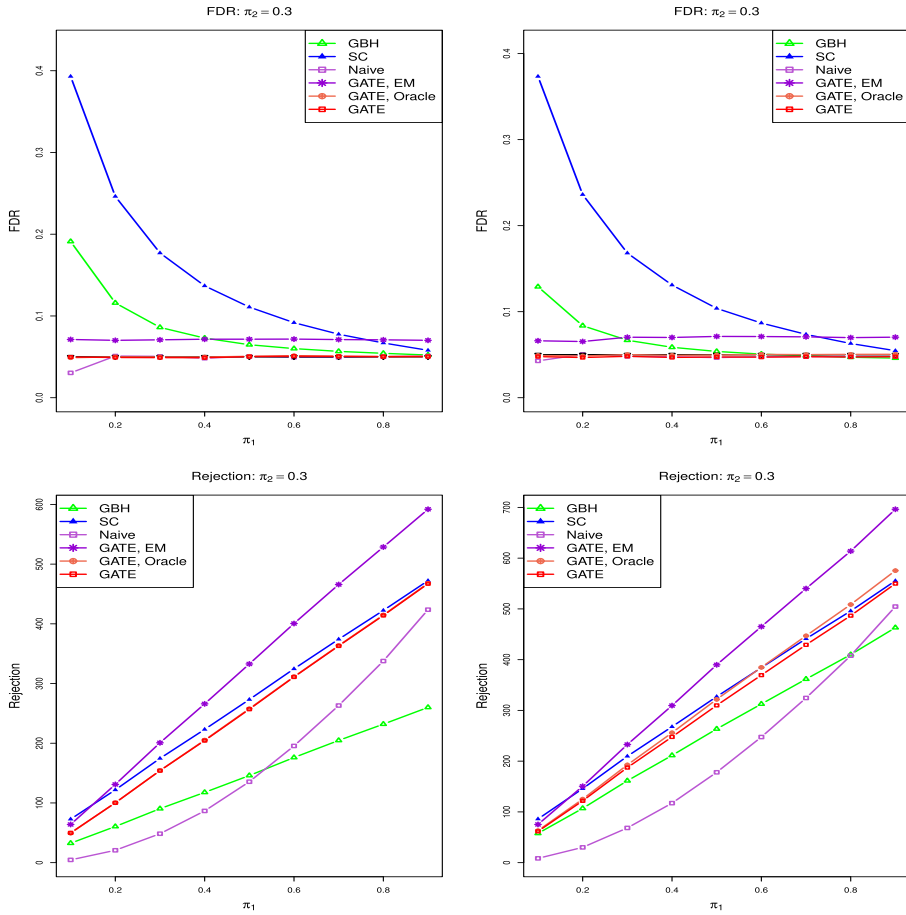


FIG 10. One-Way GATE 1: $m = 100, n = 50, \pi_2 = 0.3$. The left and right panels correspond to $K = 1$ and 2, respectively.

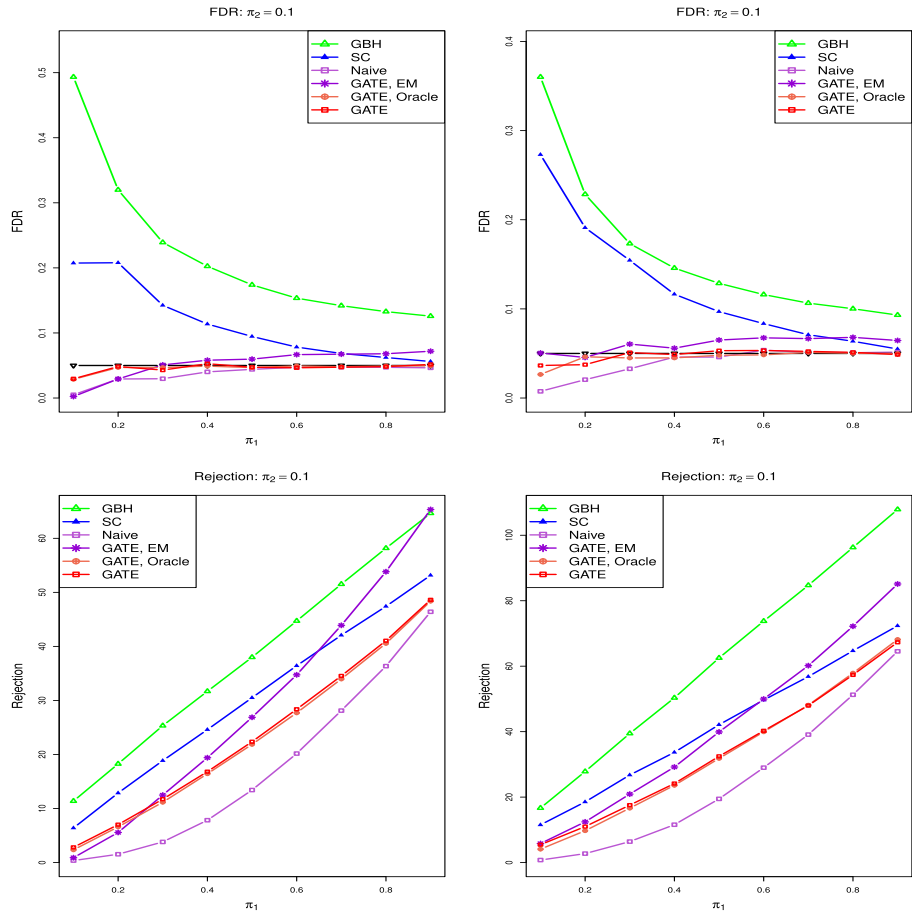


FIG 11. One-Way GATE 1: $m = 100, n = 50, \pi_2 = 0.1$. The left and right panels correspond to $K = 1$ and 2 , respectively.

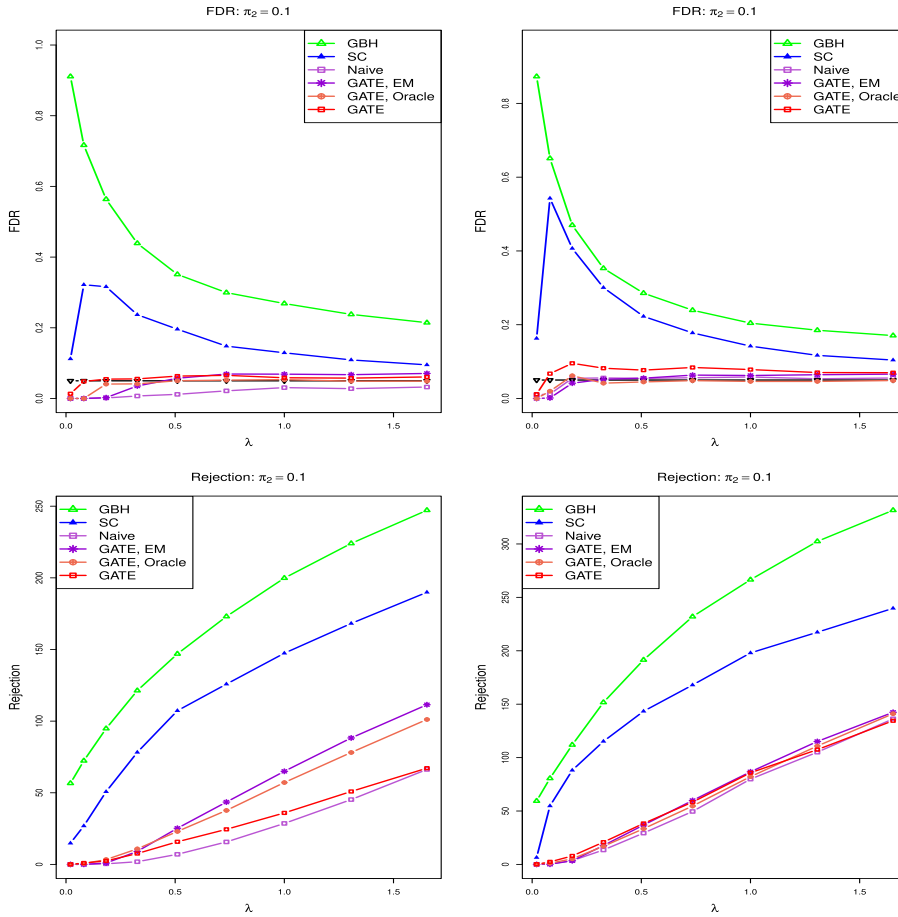


FIG 12. One-Way GATE 1: $m = 1000, n = 5, \pi_2 = 0.1$. The left and right panels correspond to $K = 1$ and 2, respectively.

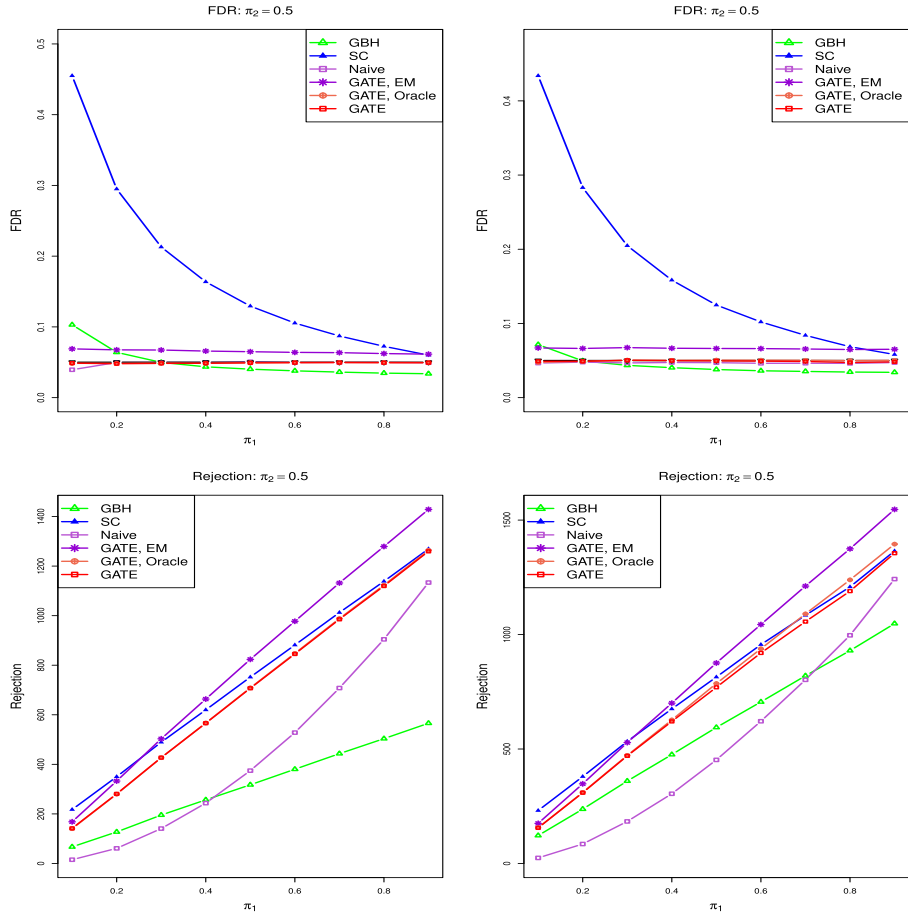


FIG 13. One-Way GATE 1: $m = 100, n = 50, \pi_2 = 0.5$. The left and right panels correspond to $K = 1$ and 2 , respectively.

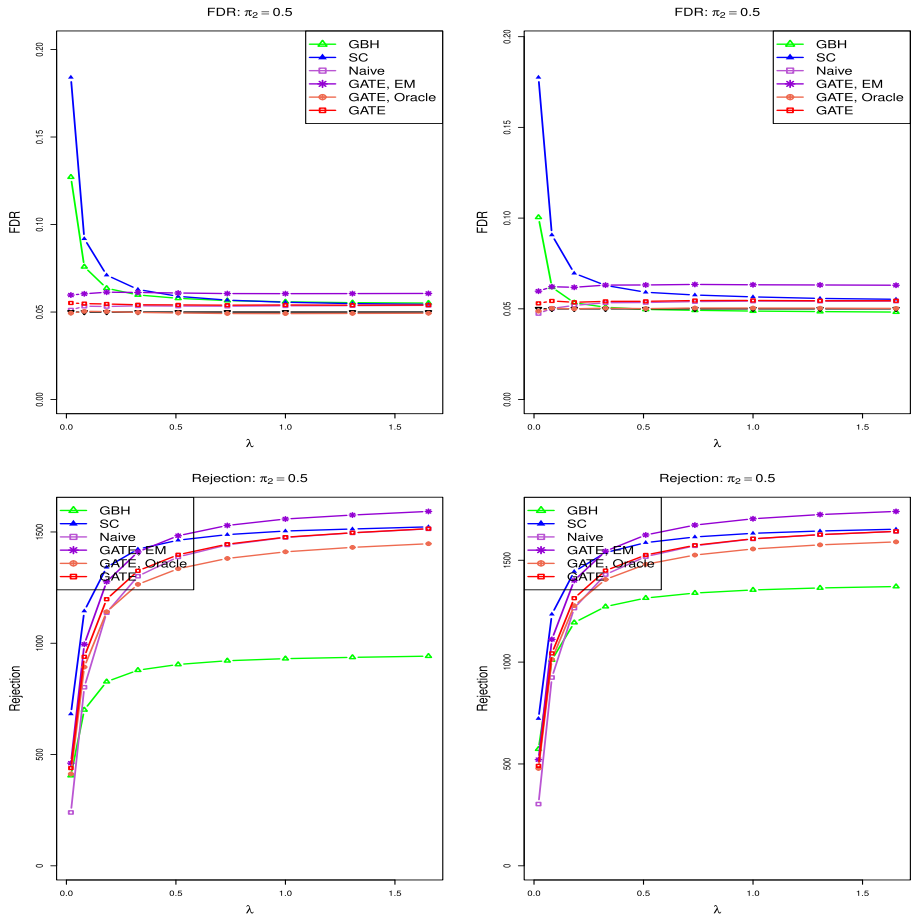


FIG 14. One-Way GATE 1: $m = 1000, n = 5, \pi_2 = 0.5$. The left and right panels correspond to $K = 1$ and 2, respectively.

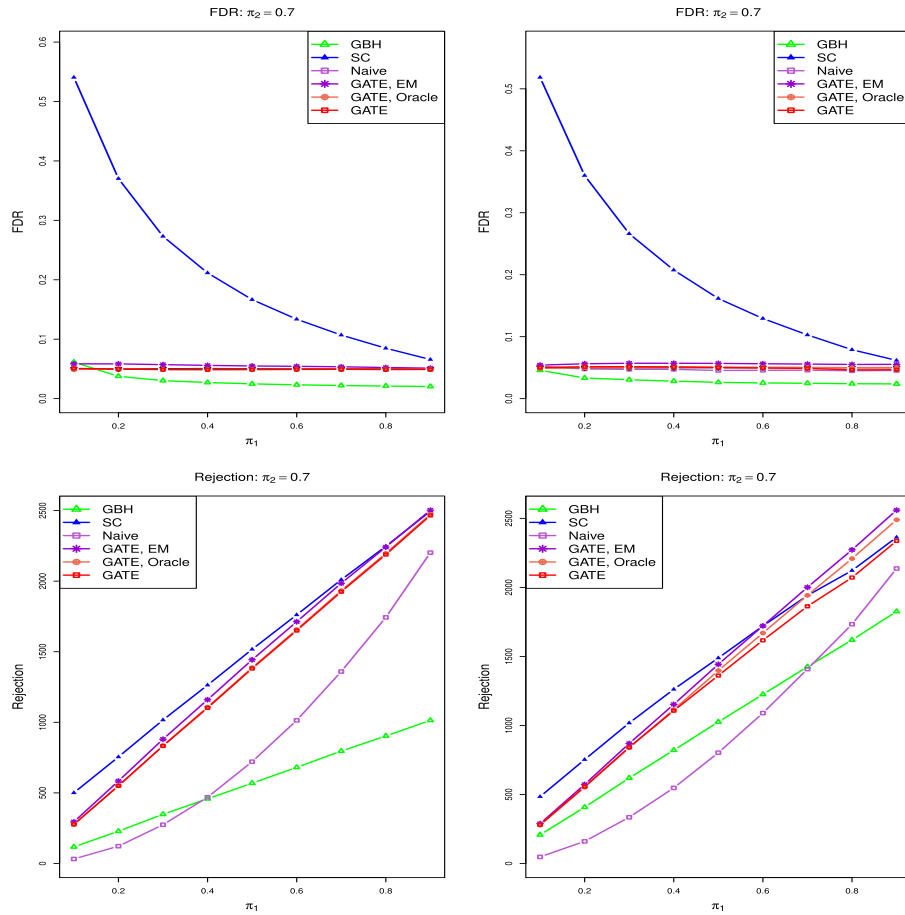


FIG 15. One-Way GATE 1: $m = 100, n = 50, \pi_2 = 0.7$. The left and right panels correspond to $K = 1$ and 2 , respectively.

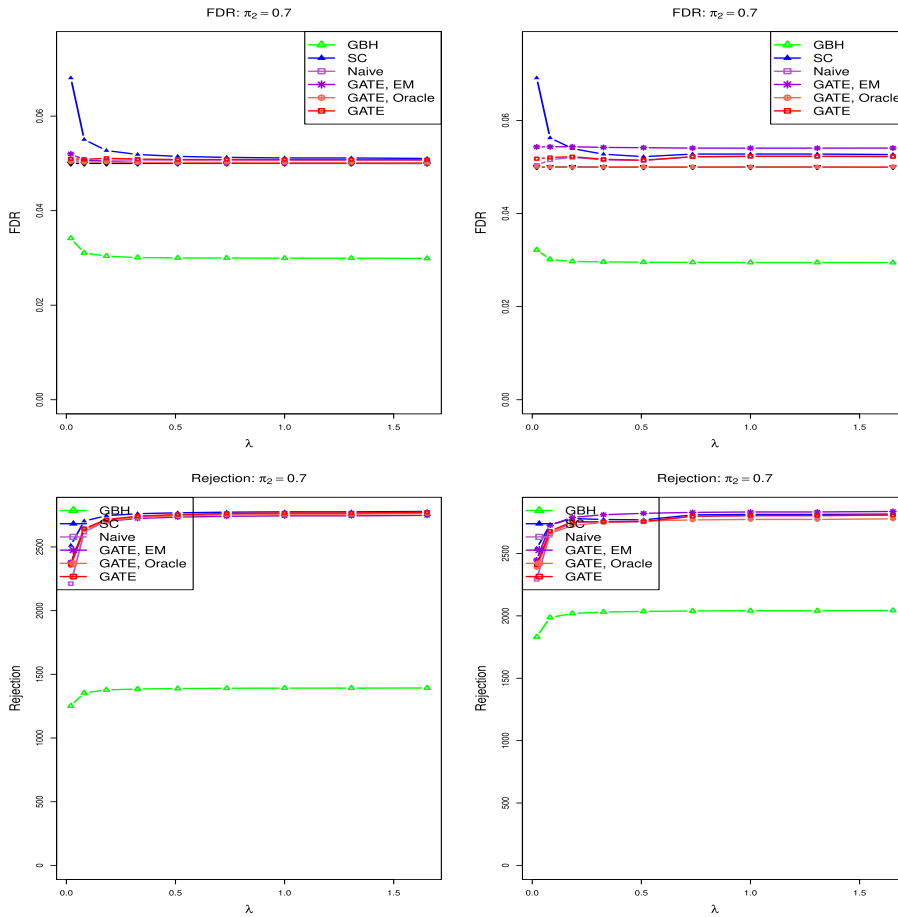


FIG 16. One-Way GATE 1: $m = 1000, n = 5, \pi_2 = 0.7$. The left and right panels correspond to $K = 1$ and 2 , respectively.

A.4. More simulation results on One-Way GATE 2

This section presents more simulation results on One-Way GATE 2.

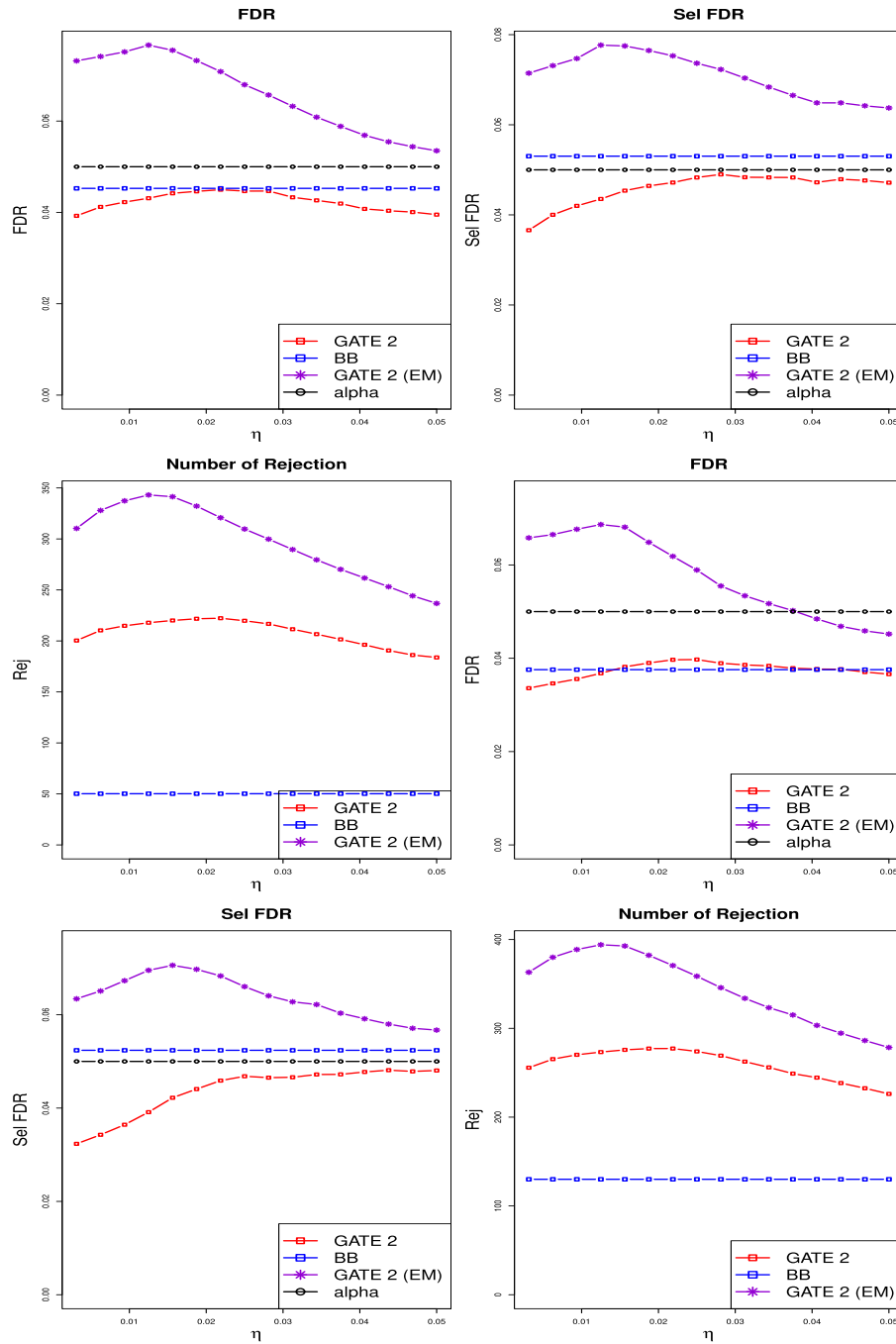


FIG 17. Performance of One-Way GATE 2 when $m = 500, n = 20, \pi_1 = 0.48$. The top panels correspond to cases when $K = 1$ and the bottom ones correspond to $K = 2$.

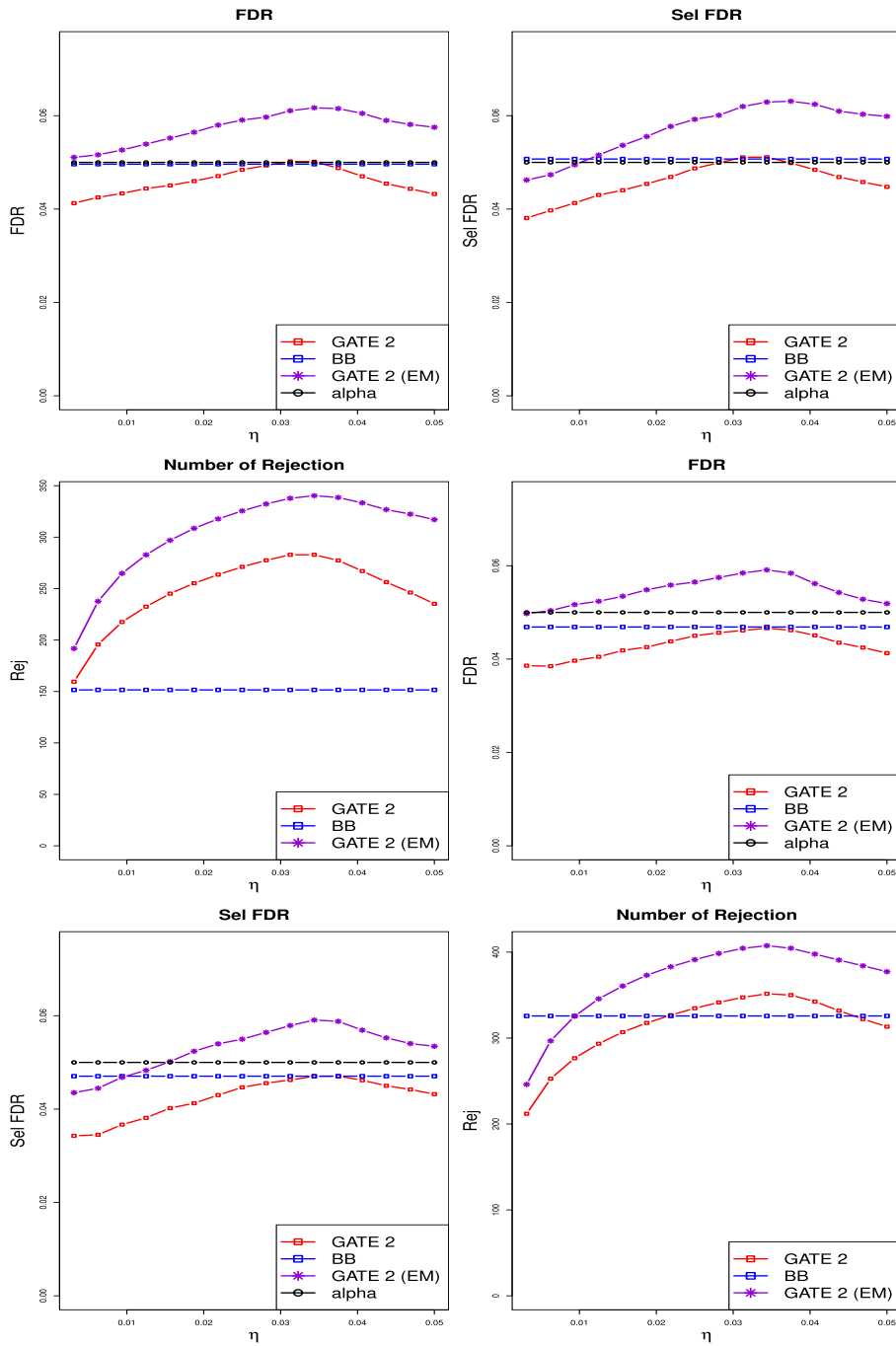


FIG 18. Performance of One-Way GATE 2 when $m = 1000, n = 5, \pi_1 = 0.165$. The top panels correspond to cases when $K = 1$ and the bottoms ones correspond to $K = 2$.

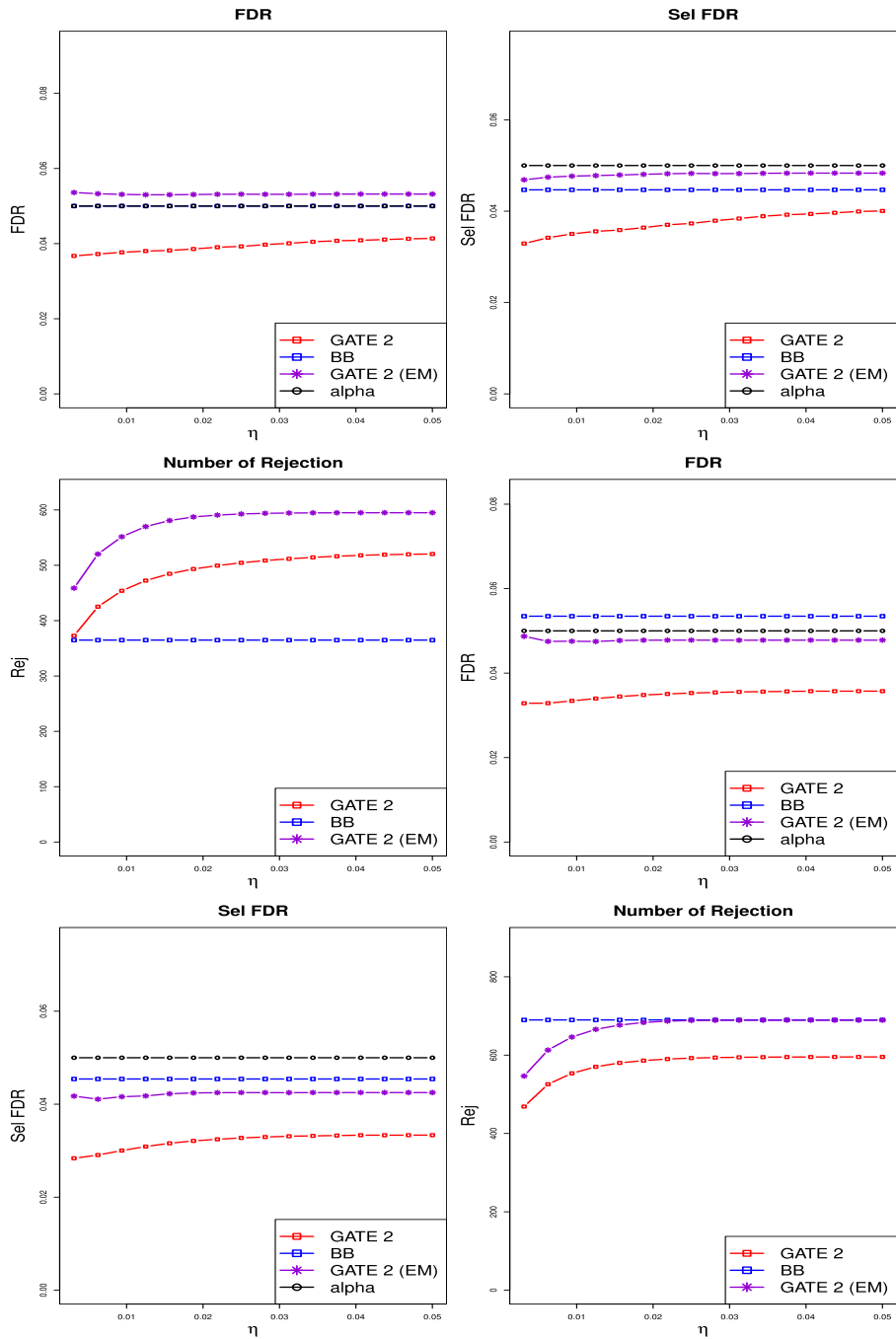


FIG 19. Performance of One-Way GATE 2 when $m = 1000, n = 5, \pi_1 = 0.308$. The top panels correspond to cases when $K = 1$ and the bottom ones correspond to $K = 2$.

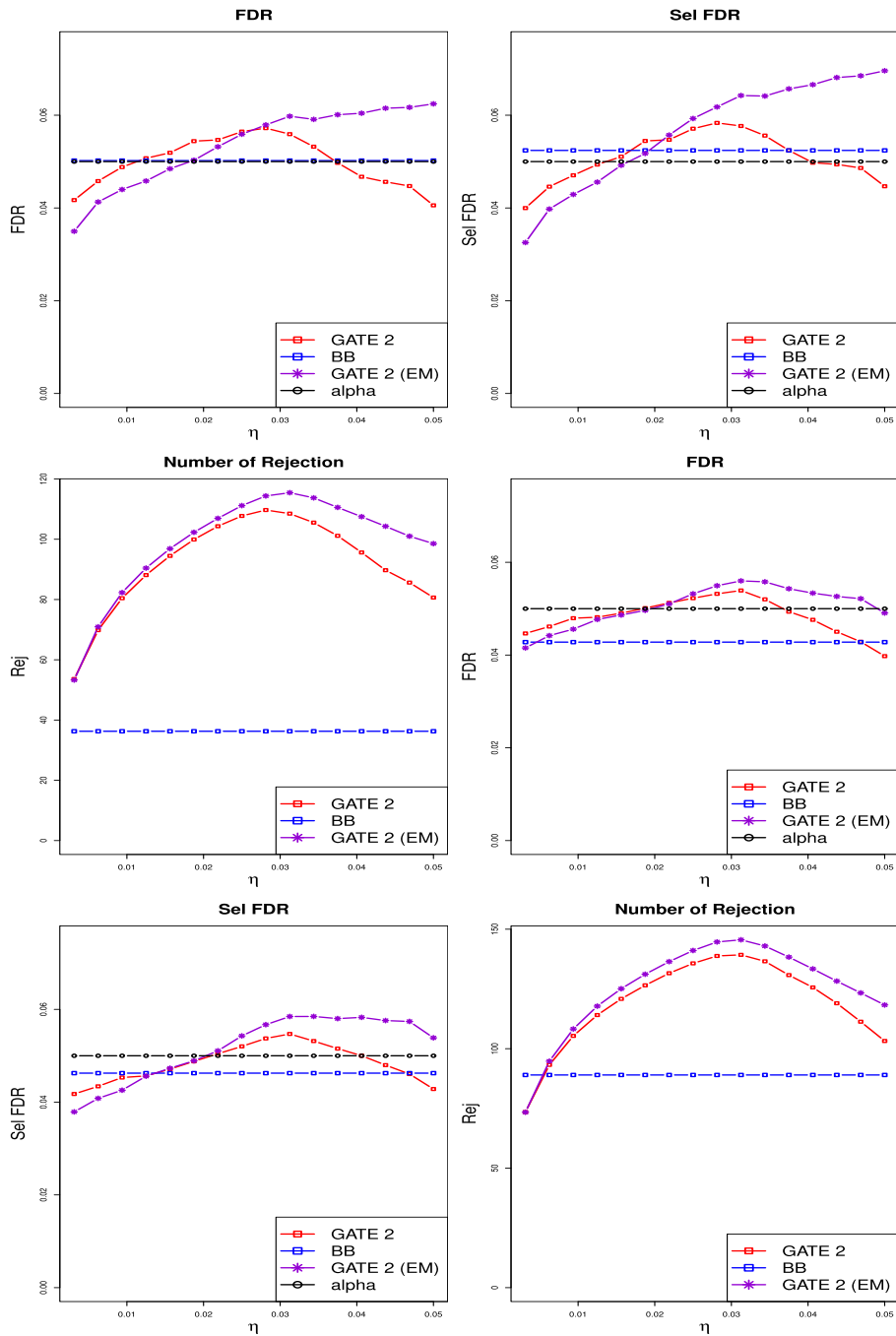


FIG 20. Performance of One-Way GATE 2 when $m = 1000, n = 5, \pi_1 = 0.47$. The top panels correspond to cases when $K = 1$ and the bottom ones correspond to $K = 2$.

A.5. Additional results on the comparison of estimated local fdrs

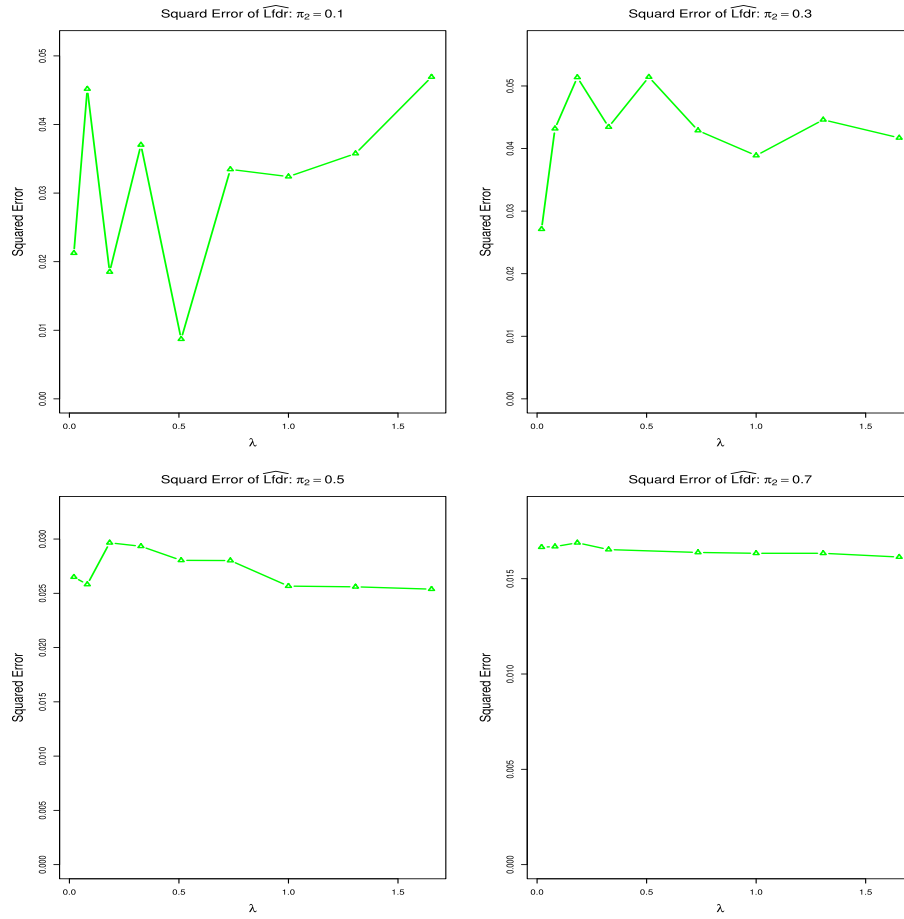


FIG 21. The mean squared error for the estimation of the local fdr scores using the proposed method: $m = 1000, n = 5, L = 2, \pi_2 = 0.1, 0.3, 0.5$ and 0.7 respectively.

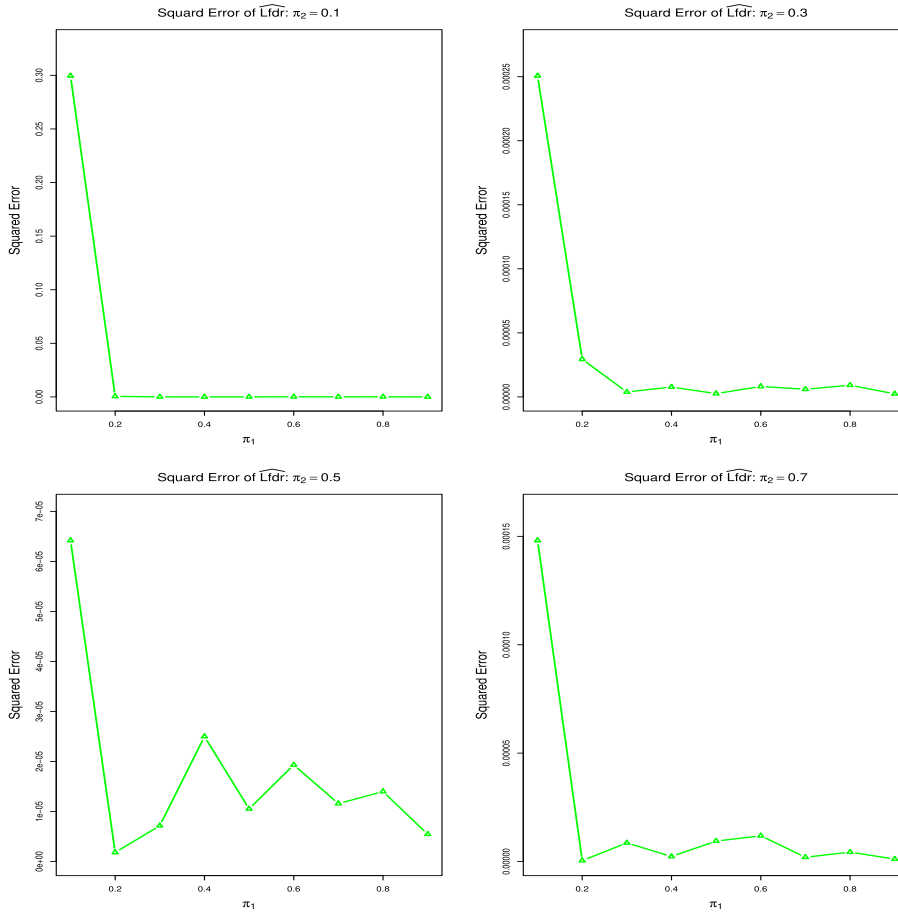


FIG 22. The mean squared error for the estimation of the local fdr scores using the proposed method: $m = 100, n = 50, L = 1, \pi_2 = 0.1, 0.3, 0.5$ and 0.7 respectively.

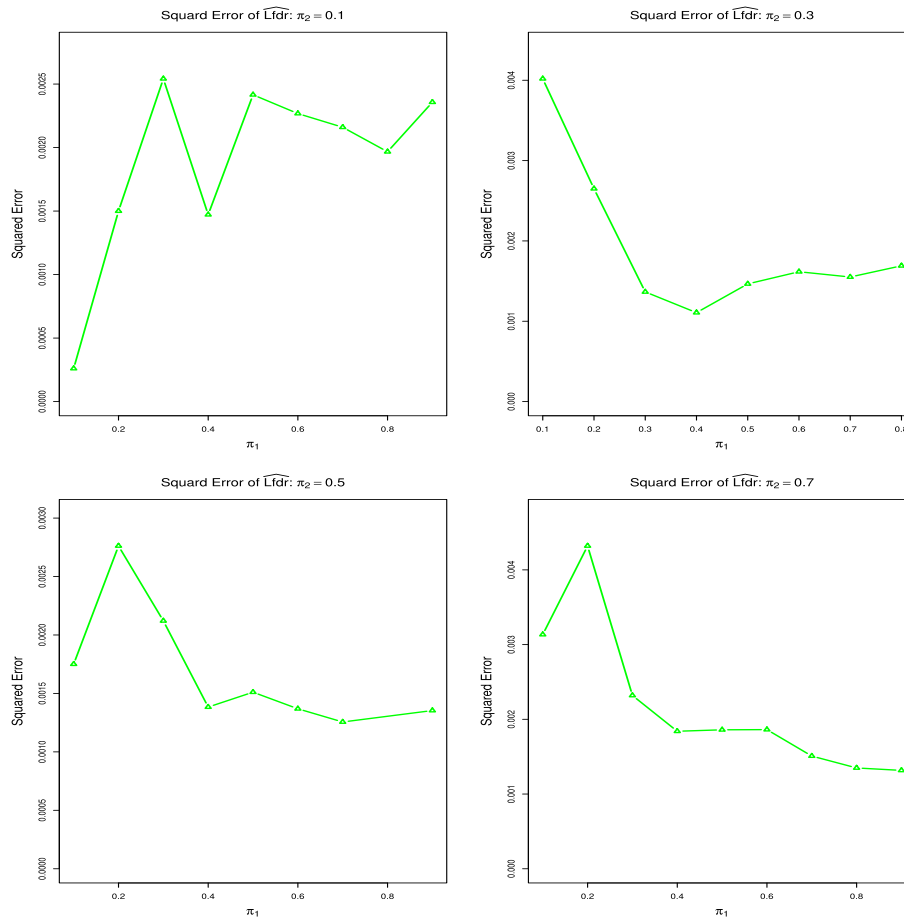


FIG 23. The mean squared error for the estimation of the local fdr scores using the proposed method: $m = 100, n = 50, L = 2, \pi_2 = 0.1, 0.3, 0.5$ and 0.7 respectively.

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