Statistica Sinica **18**(2008), 925-945

A GENERAL DECISION THEORETIC FORMULATION OF PROCEDURES CONTROLLING FDR AND FNR FROM A BAYESIAN PERSPECTIVE

Sanat K. Sarkar, Tianhui Zhou and Debashis Ghosh

Temple University, Wyeth Pharmaceuticals and Penn State University

Abstract: A general decision theoretic formulation is given to multiple testing, allowing descriptions of measures of false discoveries and false non-discoveries in terms of certain loss functions even when randomized decisions are made on the hypotheses. Randomized as well as non-randomized procedures controlling the Bayes false discovery rate (BFDR) and Bayes false non-discovery rate (BFNR) are developed. These are applicable in any situation, unlike the corresponding frequentist procedures that control the BFDR or BFNR, but do so under certain dependence structures of the test statistics. Even in the presence of such dependence, as simulations show, the proposed procedures perform much better than the corresponding frequentist procedures. They provide better control of the BFDR or BFNR than those for which control is achieved through local FDR or local FNR.

Key words and phrases: One-step randomized procedures, posterior false discovery rate, posterior false non-discovery rate.

1. Introduction

A tremendous growth of research has taken place recently in the area of multiple testing because of its increased relevance in analyzing high-dimensional data. Among measures of overall error rates, the false discovery rate (FDR) and false non-discovery rate (FNR) have received the most attention, and procedures controlling them have been developed from both frequentist and Bayesian perspectives (Benjamini and Hochberg (1995), Benjamini and Yekutieli (2001), Efron (2003), Efron, Tibshirani, Storey and Tusher (2001), Genovese and Wasserman (2002, 2004), Sarkar (2002, 2004, 2006), Storey (2002, 2003) and Storey, Taylor and Siegmund (2004)).

The Bayesian theory of false discoveries and false non-discoveries has been developed to a large extent under a simple model, the so-called i.i.d. mixture model, in which the test statistics are assumed i.i.d. given a set of null hypotheses that are all true or all false, with the null hypotheses being true or false according to i.i.d. Bernoulli random variables. This theory has been further developed here using a more general framework, starting with a decision theoretic formulation of multiple testing and using a model where the underlying test statistics and the associated parameters are assumed dependent. We consider, in particular, the problems of controlling the Bayes FDR (BFDR) and Bayes FNR (BFNR).

We provide procedures that control the BFDR or BFNR at a designated level α. The non-randomized version of our BFDR (or BFNR) procedure rejects (or accepts) every family of null hypotheses with the average posterior probability of the null (or alternative) hypotheses less (or greater) than α, while the corresponding randomized version, a one-step randomized procedure, allows one additional random rejection (for BDFR control) or acceptance (for BFNR control), providing a slightly better control of the BFDR or BFNR. Our non-randomized BFDR procedure is same as that in Muller, Parmigiani, Robert and Rousseau (2004).

A control of the BFDR at α can be achieved by rejecting every null hypothesis whose posterior probability is less than α (see, for example, Efron et al. (2001)). However, it is more conservative than our proposed BFDR procedure in that it allows less rejections of the null hypotheses. Our procedure has a more general applicability than the most commonly used BH frquentist FDR procedure (Benjamini and Hochberg (1995)). The BH procedure also controls the BFDR but does so under certain type of positive dependence among the test statistics given the parameters (Benjamini and Yekutieli (2001) and Sarkar (2002, 2004)). As noted through simulation, our procedure is more *powerful* than the BH procedure and the one which controls the Bayesian FDR (Efron (2003)), especially when there is dependence in the tests. Efron's Bayesian FDR is different from the present BFDR. Moreover, our procedure motivates one to formulate a new FDR-based Bayesian variable selection procedure.

To compare different BFDR controlling procedures, we use as performance measures both the BFNR and a Bayesian version of a frequentist notion of Average Power defined in Dudoit, Shaffer and Boldrick (2003), we call the BAP. In some applications, controlling false negatives may be of primary importance; our BFNR controlling procedure would be an appropriate multiple testing method in such a situation from a Bayesian perspective. Of course, there are frequentist FNR procedures (Sarkar (2002, 2004)) which also control the BFNR; they require specific distributional assumptions. The present BFNR procedure is an alternative to theses procedures having a more general applicability. The BFDR, in these situations, can be used as a performance measuring criterion.

The layout of this paper is as follows. The decision theoretic formulation of multiple testing, with representations of false discovery and false non-discovery rates in terms of loss functions, is presented in Section 2. Bayesian measures related to false discoveries, false non-discoveries, and power are given in Section 3. A one-step randomized procedure is introduced in Section 4, along with the

BFDR and BFNR of this and some non-randomized stepwise procedures. Procedures controlling BFDR and BFNR are developed in Section 5. Assuming normal distributions of the test statistics conditional on the parameters, results of simulation studies comparing our proposed BFDR controlling procedure with the BH procedure and the procedure controlling the Bayesian FDR (Efron (2003)) are presented in Section 6. A brief explanation of the new FDR-based Bayesian variable selection procedure is given in Section 7. There are some final remarks in Section 8.

2. A Decision Theoretic Formulation of Multiple Testing

Suppose that we have a set of random variables $\mathbf{X} = (X_1, \ldots, X_n) \sim P_{\boldsymbol{\theta}}$, $\boldsymbol{\theta} = (\theta_1, \ldots, \theta_n) \in \Theta \subset \mathcal{R}^n$, being used to test $H_i : \theta_i \in \Theta_{i0}$ against $K_i : \theta_i \in \Theta_{i1}$, simultaneously for $i = 1, \ldots, n$. Let $\mathbf{d} = (d_1, \ldots, d_n)$, with $d_i = 0$ or 1 according as H_i is accepted or rejected, represent the decision vector, with $\mathcal{D} = \{(d_1, \ldots, d_n) : \ d_i = 0 \text{ or } 1 \ \forall \ i\}$ being the decision space. Given $\mathbf{X} = \mathbf{x}$, we consider choosing the decision vector $\mathbf{d}$ according to the following probabilities:

$$\boldsymbol{\delta}(\mathbf{d} \mid \mathbf{x}) = \prod_{i=1}^{n} \{\delta_i(\mathbf{x})\}^{d_i} \{1 - \delta_i(\mathbf{x})\}^{1-d_i}, \quad \mathbf{d} \in \mathcal{D},$$

for some $0 \le \delta_i(\mathbf{X}) \le 1$, $i = 1, \ldots, n$. The vector $\boldsymbol{\delta}(\mathbf{X}) = (\delta_1(\mathbf{X}), \ldots, \delta_n(\mathbf{X}))$ is referred to as a multiple decision rule or multiple testing procedure. If $0 < \delta_i(\mathbf{X}) < 1$, for at least one i, then $\boldsymbol{\delta}(\mathbf{X})$ is randomized; otherwise, it is non-randomized.

The main objective in a multiple testing problem is to determine $\boldsymbol{\delta}(\mathbf{X})$, the choice of which is typically assessed based on a risk measured by averaging a loss $L(\boldsymbol{\theta}, \boldsymbol{\delta})$ it incurs in selecting $\mathbf{d}$ over uncertainties. In a frequentist approach, only the uncertainty in $\mathbf{X}$ given $\boldsymbol{\theta}$ is considered, while in a Bayesian approach, prior information on $\boldsymbol{\theta}$ is further utilized.

Let $\mathbf{h} = (h_1, \ldots, h_n)$, with $h_i = 0$ or 1 according as $\theta_i \in \Theta_{i0}$ or $\theta_i \in \Theta_{i1}$, represent the unknown configuration of true or false null hypotheses. Given $Q(\mathbf{h}, \mathbf{d})$, a measure of error providing an overall discrepancy between $\mathbf{h}$ and $\mathbf{d}$, the loss is $L(\boldsymbol{\theta}, \boldsymbol{\delta}(\mathbf{X})) = \sum_{\mathbf{d} \in \mathcal{D}} Q(\mathbf{h}, \mathbf{d}) \boldsymbol{\delta}(\mathbf{d}|\mathbf{X})$. The corresponding frequentist risk is $R_{\boldsymbol{\delta}}(\boldsymbol{\theta}) = E_{\mathbf{X}|\boldsymbol{\theta}} L(\boldsymbol{\theta}, \boldsymbol{\delta}(\mathbf{X}))$ and, given a prior distribution on $\boldsymbol{\theta}$, the posterior and Bayes risks are $\pi_{\boldsymbol{\delta}}(\mathbf{X}) = E_{\boldsymbol{\theta}|\mathbf{X}} L(\boldsymbol{\theta}, \boldsymbol{\delta}(\mathbf{X}))$ and $r_{\boldsymbol{\delta}} = E_{\boldsymbol{\theta}} R_{\boldsymbol{\delta}}(\boldsymbol{\theta}) = E_{\mathbf{X}} \pi_{\boldsymbol{\delta}}(\mathbf{X})$, respectively.

Among several possible choices of $Q(\mathbf{h}, \mathbf{d})$ providing different frequentist concepts of error rate in multiple testing, we concentrate on the False Discovery, Proportion (FDP),

$$Q_1(\mathbf{h}, \mathbf{d}) = \frac{\sum_{i=1}^n d_i(1-h_i)}{\left\{\sum_{i=1}^n d_i\right\} \vee 1},$$

and the False Non-Discovery Proportion (FNP),

$$Q_2(\mathbf{h}, \mathbf{d}) = \frac{\sum_{i=1}^n (1-d_i)h_i}{\left\{\sum_{i=1}^n (1-d_i)\right\} \vee 1}.$$

and consider determining $\boldsymbol{\delta}$ controlling the corresponding Bayes risks, the Bayes False Discovery Rate (BFDR) and the Bayes False Non-Discovery Rate (BFNR), respectively. Often in practice, where controlling false positives is of primary importance, finding a $\boldsymbol{\delta}$ that controls the BFDR would be the main objective, and the BFNR could be used as a performance measuring criterion to compare different BFDR controlling procedures. In some applications, however, one wants to control false negatives, rather than false positives. The roles of the BFDR and BFNR can be switched in these situations.

Remark 2.1. When $\boldsymbol{\delta}$ is non-randomized it can be replaced by $\mathbf{d}$.

3. The BFDR and BFNR

The frequentist risk corresponding to Q_1, the false discovery rate (FDR), is

$$\begin{aligned}
\mathrm{FDR} &= E_{\mathbf{X}|\boldsymbol{\theta}}\left[\sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n d_i(1-h_i)}{\left\{\sum_{i=1}^n d_i\right\} \vee 1}\delta(\mathbf{d}|\mathbf{X})\right] \\
&= \sum_{I:|I|>0}\left[\frac{1}{|I|}\sum_{i\in I}(1-h_i)E_{\mathbf{X}|\boldsymbol{\theta}}\left\{\prod_{i\in I}\delta_i(\mathbf{X})\prod_{i\in I^c}[1-\delta_i(\mathbf{X})]\right\}\right] \\
&= \sum_{I:|I|>0}\left[\frac{1}{|I|}\sum_{i\in I}(1-h_i)E_{\mathbf{X}|\boldsymbol{\theta}}\{\phi_I(\mathbf{X})\}\right], \qquad (1)
\end{aligned}$$

where $I \subseteq \{1, \ldots, n\}$, and $\phi_I(\mathbf{X}) = \prod_{i\in I}\delta_i(\mathbf{X})\prod_{i\in I^c}[1-\delta_i(\mathbf{X})]$ is the probability of rejecting the set of null hypotheses $\{H_i, i \in I\}$ and accepting the rest.

Under a prior distribution of $\boldsymbol{\theta}$, the posterior FDR (PFDR) is

$$\begin{aligned}
\mathrm{PFDR} &= E_{\boldsymbol{\theta}|\mathbf{X}}\left[\sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n d_i(1-h_i)}{\left\{\sum_{i=1}^n d_i\right\} \vee 1}\delta(\mathbf{d}|\mathbf{X})\right] \\
&= \sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n d_i r_i(\mathbf{X})}{\left\{\sum_{i=1}^n d_i\right\} \vee 1}\delta(\mathbf{d}|\mathbf{X}) = \sum_{I:|I|>0}\left[\frac{1}{|I|}\sum_{i\in I} r_i(\mathbf{X})\phi_I(\mathbf{X})\right], \qquad (2)
\end{aligned}$$

where $r_i(\mathbf{X}) = E\{(1-h_i) \mid \mathbf{X}\} = P\{\theta_i \in \Theta_{i0}|\mathbf{X}\}$, the posterior probability of H_i being true.

The Bayes FDR (BFDR) is the expectation of (1) with respect to $\boldsymbol{\theta}$, or the expectation of (2) with respect to $\mathbf{X}$. The BFDR has been referred to as the Average FDR in Chen and Sarkar (2006). Often in the literature, the BFDR is treated as a frequentist FDR under a mixture model (Storey (2002, 2003), Genovese and Wasserman (2002) and Efron (2003)).

Analogously, the frequentist risk corresponding to Q_2, the false non-discovery rate (FNR), is

$$\begin{aligned} \mathrm{FNR} &= E_{\mathbf{X}|\boldsymbol{\theta}}\left\{ \sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n (1-d_i)h_i}{\left\{\sum_{i=1}^n (1-d_i)\right\} \vee 1} \delta(\mathbf{d}|\mathbf{X}) \right\} \\ &= \sum_{I:|I^c|>0} \left[\frac{1}{|I^c|} \sum_{i\in I^c} h_i E_{\mathbf{X}|\boldsymbol{\theta}}\{\phi_I(\mathbf{X})\} \right]. \end{aligned} \tag{3}$$

The posterior FNR (PFNR) is

$$\begin{aligned} \mathrm{PFNR} &= E_{\boldsymbol{\theta}|\mathbf{X}}\left[\sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n (1-d_i)h_i}{\left\{\sum_{i=1}^n (1-d_i)\right\} \vee 1} \delta(\mathbf{d}|\mathbf{X}) \right] \\ &= \sum_{I:|I^c|>0} \left[\frac{1}{|I^c|} \sum_{i\in I^c} [1-r_i(\mathbf{X})]\phi_I(\mathbf{X}) \right], \end{aligned} \tag{4}$$

where $1-r_i(\mathbf{X}) = E\{h_i|\mathbf{X}\} = P\{\theta_i \in \Theta_{i1}|\mathbf{X}\}$ is the posterior probability of H_i being false.

The Bayes FNR (BFNR) is the expectation of (3) with respect to θ, or the expectation of (4) with respect to $\mathbf{X}$.

These FNR-related measures are equivalently described in terms of quantities that can be interpreted as measures of power in the same spirit as in single testing. For instance, when controlling frequentist FDR is of importance, $1-$ FNR, which Genovese and Wasserman (2002) call the Correct Non-Discovery Rate (CNR), can be considered as a frequentist measure of power. Similar measures can be defined from a Bayesian perspective; for instance, Posterior CNR (PCNR) $= 1 -$ BFNR and Bayes CNR (BCNR) $= 1 -$ BFNR.

Another frequentist concept of power that is frequently used in multiple testing is the Sensitivity, also known as the Average Power (Dudoit et al. (2003)), defined as the expected proportion of false null hypotheses that are rejected, i.e.,

$$\textit{Average Power} = E_{\mathbf{X}|\boldsymbol{\theta}}\left\{ \sum_{\mathbf{d}\in\mathcal{D}} \frac{\sum_{i=1}^n d_i h_i}{\sum_{i=1}^n h_i} \delta(\mathbf{d}|\mathbf{X}) \right\} = \frac{\sum_{i=1}^n h_i E_{\mathbf{X}|\boldsymbol{\theta}}\{\delta_i(\mathbf{X})\}}{\sum_{i=1}^n h_i}, \tag{5}$$

assuming $\sum_{i=1}^n h_i > 0$. For a Bayesian version of this, we need to properly define the ratio in (5) to incorporate the situation of no false null hypotheses, which can happen with positive probability; we take this ratio to be 1 when $\sum_{i=1}^n h_i = 0$, which makes it consistent with the BCNR concept of power. Thus, the Posterior Average Power is given by

$$E_{\boldsymbol{\theta}|\mathbf{X}}\left\{\frac{\sum_{i=1}^n h_i\delta_i(\mathbf{X})}{\sum_{i=1}^n h_i} I\Big(\sum_{i=1}^n h_i > 0\Big)\right\} + P_{\boldsymbol{\theta}|\mathbf{X}}\left\{\sum_{i=1}^n h_i = 0\right\}. \tag{6}$$

The Bayes Average Power (BAP) is the expectation of (5) with respect to $\boldsymbol{\theta}$ or of (6) with respect to $\mathbf{X}$.

4. The BFDR and BFNR of One-Step Randomized Stepwise Procedures

Let $r_{1:n}(\mathbf{X}) \le \cdots \le r_{n:n}(\mathbf{X})$ be the ordered values of $r_1(\mathbf{X}), \ldots, r_n(\mathbf{X})$, and $(H_{i:n}, \delta_{i:n}(\mathbf{X}))$, $i = 1, \ldots, n$, be the corresponding pairs of the null hypotheses and their rejection probabilities given $\mathbf{X}$. We consider the following type of one-step randomized multiple testing procedure, as a function of a discrete random variable $K(\mathbf{X})$ with probability distribution defined on the set $\{0, 1, \ldots, n\}$. Given $K(\mathbf{X}) = k$, let

$$\delta_{i:n}(\mathbf{X}) = \begin{cases} 1 & \text{if} \quad i \le k \\ \delta_{k+1:n}(\mathbf{X}) & \text{if} \quad i = k+1 \\ 0 & \text{if} \quad i > k+1, \end{cases} \tag{7}$$

with $\delta_{i:n} = 1 \ \forall\ i$ if $K(\mathbf{X}) = n$. Let $\{i_1, \ldots, i_n\}$ be the set of indices such that $r_{i_j}(\mathbf{X}) \equiv r_{j:n}(\mathbf{X})$, $j = 1, \ldots, n$. Note that for this procedure, given $K(\mathbf{X}) = k$,

$$\prod_{i\in I}\delta_i(\mathbf{X})\prod_{i\in I^c}[1-\delta_i(\mathbf{X})] = \begin{cases} 1-\delta_{i_{k+1}}(\mathbf{X}) & \text{if} \quad I = \{i_1, \ldots, i_k\} \\ \delta_{i_{k+1}}(\mathbf{X}) & \text{if} \quad I = \{i_1, \ldots, i_{k+1}\} \\ 0 & \text{otherwise.} \end{cases}$$

Theorem 4.1. *The BFDR of the one-step randomized procedure* (7) *is*

$$\mathrm{BFDR} = \mathrm{E}_{\mathbf{X}}\sum_{\mathrm{k}=0}^{\mathrm{n}}\left\{\Big[(1-\delta_{\mathrm{k+1:n}}(\mathbf{X}))\mathrm{A_k}(\mathbf{X})+\delta_{\mathrm{k+1:n}}(\mathbf{X})\mathrm{A_{k+1}}(\mathbf{X})\Big]\mathrm{I}(\mathrm{K}(\mathbf{X})=\mathrm{k})\right\}, \tag{8}$$

where $\delta_{n+1:n} = 0$, $A_k(\mathbf{X}) = (1/k)\sum_{i=1}^k r_{i:n}(\mathbf{X})$, $k = 1, \ldots, n$, *and* $A_0 = 0$.

Let $X_{1:n} \le \cdots \le X_{n:n}$ be the ordered values of $X_1, \ldots, X_n$. Consider now a multiple testing procedure (7) with

$$K_{SD}(\mathbf{X}) = \max\{1 \le i \le n : X_{i:n} \le c_{i:n}\} \tag{9}$$

if the maximum exists, and $= 0$ otherwise, given some critical values $c_{1:n} \le \cdots \le c_{n:n}$. This is a one-step randomized stepdown procedure in terms of the X_i's. The following theorem provides a more explicit expression for the BFDR of this procedure under the i.i.d. set-up.

Theorem 4.2. *Consider testing $H_i : \theta_i = \theta^{(0)}$ against $K_i : \theta_i = \theta^{(1)}$, $i = 1, \ldots, n$, for some fixed $\theta^{(0)} < \theta^{(1)}$. Let (X_i, θ_i), $i = 1, \ldots, n$, be i.i.d. as (X, θ), where $X|\theta \sim f_\theta(x)$ and $\theta \sim \pi_0 I(\theta = \theta^{(0)}) + (1 - \pi_0) I(\theta = \theta^{(1)})$. Assume that the ratio $f_{\theta'}(x)/f_\theta(x)$ is decreasing in x for any $\theta < \theta'$. Then, the BFDR of the randomized stepdown procedure $\boldsymbol{\delta}$ with $K(\mathbf{X})$ given in* (9) *and $\delta_{k+1:n}$ independent of $\mathbf{X}$ is*

$$\begin{aligned}\text{BFDR} = {} & \pi_0 \sum_{k=1}^{n} \Big(1 - \frac{\delta_{k+1:n}}{k+1}\Big) \frac{F_0(c_{k:n})}{F(c_{k:n})} P\{K_{SD}(\mathbf{X}) = k\} \\ & + \pi_0 \sum_{k=0}^{n-1} \frac{\delta_{k+1:n}}{k+1} E_{\mathbf{X}} \Big\{ \frac{f_0(X_{k+1:n})}{f(X_{k+1:n})} I(K_{SD}(\mathbf{X}) = k) \Big\}, \end{aligned} \tag{10}$$

where $F_i(x) = P\{X \le x | \theta = \theta^{(i)}\}$, $i = 0, 1$, $F(x) = P\{X \le x\} = \pi_0 F_0(x) + (1 - \pi_0) F_1(x)$, with f_0 and f being the densities of F_0 and F, respectively.

Proof. First note that, since $r_i(\mathbf{X}) = \pi_0 f_0(X_i)/f(X_i)$ is an increasing function of X_i, $r_{i:n}(\mathbf{X}) = \pi_0 f_0(X_{i:n})/f(X_{i:n})$. Therefore,

$$\begin{aligned} & E_{\mathbf{X}}\{A_k(\mathbf{X}) I(K_{SD}(\mathbf{X}) = k)\} \\ & = \pi_0 E_{\mathbf{X}} \Big\{ \frac{1}{k} \sum_{i=1}^{k} \frac{f_0(X_{i:n})}{f(X_{i:n})} I(X_{k:n} \le c_{k:n}, X_{k+1:n} > c_{k+1:n}, \ldots, X_{n:n} > c_{n:n}) \Big\}. \end{aligned}$$

Since the X_i's are i.i.d. as f, conditional on the event $\{X_{k:n} \le c_{k:n}, X_{k+1:n} > c_{k+1:n}, \ldots, X_{n:n} > c_{n:n}\}$, $X_{1:n} \le \cdots \le X_{k:n}$ are the order components of k i.i.d. random variables each having the density $f(x) I(x \le c_{k:n})/F(c_{k:n})$. Hence,

$$\begin{aligned} & E_{\mathbf{X}} \Big\{ \frac{1}{k} \sum_{i=1}^{k} \frac{f_0(X_{i:n})}{f(X_{i:n})} \Big| X_{k:n} \le c_{k:n}, X_{k+1:n} > c_{k+1:n}, \ldots, X_{n:n} > c_{n:n} \Big\} \\ & \quad = \int_{-\infty}^{c_{k:n}} \frac{f_0(x)}{f(x)} \frac{f(x)}{F(c_{k:n})} dx = \frac{F_0(c_{k:n})}{F(c_{k:n})}. \end{aligned}$$

Thus,

$$E_{\mathbf{X}}\{A_k(\mathbf{X}) I(K_{SD}(\mathbf{X}) = k)\} = \pi_0 \frac{F_0(c_{k:n})}{F(c_{k:n})} P\{K_{SD}(\mathbf{X}) = k\}.$$

The expression (10) then follows from Theorem 4.1 by noting that

$$A_{k+1}(\mathbf{X}) = \frac{k}{k+1} A_k(\mathbf{X}) + \frac{1}{k+1} \frac{\pi_0 f_0(X_{k+1:n})}{f(X_{k+1:n})}.$$

Remark 4.1. In the above theorem, we could have considered $K_i : \theta_i > \theta^{(0)}$, $i = 1, \ldots, n$, assumed that $\theta \sim \pi_0 I(\theta = \theta^{(0)}) + (1-\pi_0)\eta(\theta)I(\theta > \theta^{(0)})$ for some probability density $\eta(\theta)$ on $\theta > \theta^{(0)}$, and defined F_1 as

$$F_1(x) = \int_{\theta^{(0)}}^{\infty} P\{X \le x|\theta\}\eta(\theta)d\theta.$$

When $\delta_{k+1:n} = 0$ in Theorem 4.2, that is, for the non-randomized stepdown procedure with critical values $c_{1:n} \le \cdots \le c_{n:n}$, the BFDR simplifies to

$$\begin{aligned} \text{BFDR} &= \pi_0 \sum_{k=1}^{n} \frac{F_0(c_{k:n})}{F(c_{k:n})} P\{K_{SD}(\mathbf{X}) = k\} \\ &= \pi_0 \sum_{k=1}^{n} \frac{n}{k} F_0(c_{k:n}) P\{K_{SD}^*(\mathbf{X}) = k-1\}, \end{aligned} \tag{11}$$

where $K_{SD}^*(\mathbf{X}) = \max\{1 \le i \le n-1 : X_{i:n-1} \le c_{i+1:n}\}$, if the maximum exists, and $= 0$ otherwise, with $X_{1:n-1} \le \cdots \le X_{n-1:n-1}$ being the ordered versions of any $n-1$ components of $\mathbf{X}$.

For a non-randomized single-step procedure with the critical value c, the BFDR in Theorem 4.2 simplifies to

$$\text{BFDR} = \frac{\pi_0 F_0(c)}{F(c)} P\{K_{SD}(\mathbf{X}) > 0\}. \tag{12}$$

The first factor in (12), the conditional probability $P\{h_1 = 0|d_1 = 1\}$, is the Bayesian FDR defined by Efron (2003). It is also the positive FDR (pFDR) due to Storey (2002, 2003) under the i.i.d. setup considered in Theorem 4.2.

As seen from the second formula in (11), the BFDR of the non-randomized stepdown procedure with the $c_{k:n}$'s satisfying $F_0(c_{k:n}) = k\alpha/n$ is

$$\text{BFDR} = \pi_0 \alpha \sum_{k=0}^{n-1} P\{K_{SD}^*(\mathbf{X}) = k\} = \pi_0\alpha. \tag{13}$$

This is the Benjamini and Hochberg (1995) (BH) procedure. It is not surprising that the BFDR of the BH-procedure under the the above i.i.d. set-up is $\pi_0\alpha$, as it is known that, conditional on $\boldsymbol{\theta}$, the FDR of the BH-procedure under this setup is equal to $p_0\alpha$, where p_0 is the proportion of true null hypotheses (Benjamini and Yekutieli (2001) and Sarkar (2002)).

The above two results on single-step and the BH procedures have been extended to certain positively dependent distributions in Benjamini and Yekutieli (2001) and in Sarkar (2002, 2004, 2006)).

Analogous to the results on the BFDR, we have the following results related to the BFNR.

Theorem 4.3. *For a one-step randomized procedure* (7), *we have*

$$\mathrm{BFNR} = \mathrm{E}_{\mathbf{X}} \sum_{\mathrm{k}=0}^{\mathrm{n}-1} \Big\{ \Big[(1-\delta_{\mathrm{k:n}}(\mathbf{X}))\mathrm{B}_{\mathrm{k}-1}(\mathbf{X}) + \delta_{\mathrm{k:n}}(\mathbf{X})\mathrm{B}_{\mathrm{k}}(\mathbf{X}) \Big] \mathrm{I}(\mathrm{K}(\mathbf{X}) = \mathrm{k}) \Big\},$$

where $\delta_{1:n} = 1$, $B_k(\mathbf{X}) = (n-k)^{-1} \sum_{i=k+1}^{n} (1 - r_{i:n}(\mathbf{X}))$, $k = 0, \ldots, n-1$, *and* $B_n = 0$.

Theorem 4.4. *For the multiple testing problem in Theorem* 4.2, *and under the model considered therein, the BFNR of the one-step randomized stepup procedure* $\boldsymbol{\delta}$ *with* $\delta_{k:n}$ *independent of* $\mathbf{X}$, *and* $K_{SU}(\mathbf{X}) = \min\{1 \leq i \leq n : X_{i:n} \geq d_{i:n}\} - 1$ *if the minimum exists and* $= n$ *otherwise, is*

$$\begin{aligned} \mathrm{BFNR} = \pi_1 &\sum_{k=0}^{n-1} \Big(1 - \frac{1-\delta_{k:n}}{n-k+1}\Big) \frac{\bar{F}_1(d_{k+1:n})}{\bar{F}(d_{k+1:n})} P\{K_{SU}(\mathbf{X}) = k\} \\ &+ \pi_1 \sum_{k=0}^{n} \frac{1-\delta_{k:n}}{n-k+1} E_{\mathbf{X}} \Big\{ \frac{f_1(X_{k+1:n})}{f(X_{k+1:n})} I(K_{SU}(\mathbf{X}) = k) \Big\}, \end{aligned}$$

where $\pi_1 = 1 - \pi_0$, $\bar{F}_i = 1 - F_i$, $i = 0, 1$, $\bar{F} = 1 - F$, *and* f_1 *is the density of* F_1.

When $\delta_{k:n} = 1$ in Theorem 4.4, that is, for the non-randomized stepup procedure with critical values $d_{1:n} \leq \cdots \leq d_{n:n}$, the BFNR is

$$\begin{aligned} \mathrm{BFNR} &= \pi_1 \sum_{k=0}^{n-1} \frac{\bar{F}_1(d_{k+1:n})}{\bar{F}(d_{k+1:n})} P\{K_{SU}(\mathbf{X}) = k\} \\ &= \pi_1 \sum_{k=0}^{n-1} \frac{n}{n-k} \bar{F}_1(d_{k+1:n}) P\{K^*_{SU}(\mathbf{X}) = k\}, \end{aligned}$$

where $K^*_{SU}(\mathbf{X}) = \min\{1 \leq i \leq n-1 : X_{i:n-1} \geq d_{i+1:n}\}$ if the minimum exists and $= 0$ otherwise, with $X_{1:n-1} \leq \cdots \leq X_{n-1:n-1}$ being the ordered versions of any $n-1$ components of $\mathbf{X}$.

For the non-randomized single-step procedure with the critical value d, we have

$$\mathrm{BFNR} = \pi_1 \frac{\bar{F}_1(d)}{\bar{F}(d)} P\{K_{SU}(\mathbf{X}) < n\};$$

for the non-randomized stepup procedure with the $d_{k:n}$'s satisfying $\bar{F}(d_{k+1:n}) = (n-k)\beta/n$, $k = 0, \ldots, n-1$, we have

$$\mathrm{BFNR} = \pi_1 \beta \sum_{k=0}^{n-1} P\{K^*_{SU}(\mathbf{X}) = k\} = \pi_1 \beta.$$

The fact that this latter procedure controls the BFNR at β also follows from the fact that it controls the frequentist FNR at β (Sarkar (2004)).

5. BFDR and BFNR Controlling Procedures

We now present in this section some procedures that control the BFDR or BFNR.

Theorem 5.1. *Let* $K(\mathbf{X}) = \max\{0 \le j \le n : A_j(\mathbf{X}) \le \alpha\}$. *Then, the one-step randomized procedure*

$$\delta_{i:n}(\mathbf{X}) = \begin{cases} 1 & \text{if} \quad i \le k \\ \frac{\alpha - A_k(\mathbf{X})}{A_{k+1}(\mathbf{X}) - A_k(\mathbf{X})} & \text{if} \quad i = k+1 \\ 0 & \text{otherwise,} \end{cases} \tag{14}$$

given $K = k$, *with* $\delta_{i:n} = 1 \ \forall \ i$ *when* $k = n$, *controls the BFDR at* α.

Proof. From Theorem 4.1,

$$\begin{aligned} \text{BFDR} = E_{\mathbf{X}} \sum_{k=0}^{n-1} \Big\{ \Big[(1 - \delta_{k+1:n}(\mathbf{X})) A_k(\mathbf{X}) + \delta_{k+1:n}(\mathbf{X}) A_{k+1}(\mathbf{X}) \Big] I(K(\mathbf{X}) = k) \Big\} \\ + E_{\mathbf{X}} \Big\{ A_n(\mathbf{X}) I(K(\mathbf{X}) = n) \Big\} \\ = \alpha P\{0 \le K(\mathbf{X}) < n\} + E_{\mathbf{X}}\{A_n(\mathbf{X}) I(K(\mathbf{X}) = n)\}, \end{aligned}$$

which is less than or equal to α.

Remark 5.1. The above procedure does not require any particular dependence structure in the conditional distribution of $\mathbf{X}$ given θ. Procedures that control the frequentist FDR and hence the BFDR, on the other hand, need certain dependence assumptions. For instance, the BFDR of the BH procedure is equal to $\pi_0\alpha$ when the (X_i, θ_i)'s are i.i.d., and is less than $\pi_0\alpha$ when $\mathbf{X}$, given θ, has some type of positive dependence structure. Without such independence or positive dependence assumptions, the BH procedure may fail to control the BFDR at α (Benjamini and Hochberg (1995), Benjamini and Yekutieli (2001) and Sarkar (2002)). Thus, the above procedure is applicable in more general situations, offering an alternative approach to controlling the BFDR when the BH procedure fails to work. The non-randomized version of the procedure in Theorem 5.1 also controls BFDR, though more conservatively.

Under the i.i.d. set-up in Theorem 4.2, the conditional probability $r_i(\mathbf{X})$ simplifies to

$$r_i(\mathbf{X}) = \frac{\pi_0 f_0(X_i)}{f(X_i)} = \frac{\pi_0 f_0(X_i)}{\pi_0 f_0(X_i) + (1 - \pi_0) f_1(X_i)}.$$

This has been referred to as the local FDR by Efron et al. (2001). Suppose that the ratio $f_{\theta'}(x)/f_\theta(x)$ is decreasing in x for any $\theta < \theta'$. Writing $r_i(\mathbf{X})$ simply as $r(X_i)$, we then see that $A_k(\mathbf{X}) = (1/k)\sum_{i=1}^k r(X_{i:n})$ for $k = 1, \ldots, n$. Since $\max\{j : A_j(\mathbf{X}) \le \alpha\} \ge \max\{j : r(X_{j:n}) \le \alpha\}$, the BFDR procedure in Theorem 5.1 rejects more null hypotheses. Thus, under the i.i.d. set-up, this BFDR procedure is more *powerful* than the procedure where the PFDR is controlled by rejecting the null hypotheses whose posterior probabilities are less than or equal to α. This latter idea was suggested in Efron et al. (2001) in their Bayesian approach to multiple testing.

Alternative procedures controlling the BFDR at α can be obtained under the i.i.d. set-up, as discussed in Section 4. First, note from (12) that the BFDR of a non-randomized single-step procedure with critical value c is

$$\mathrm{BFDR} = \frac{\pi_0 F_0(c)}{F(c)}\{1 - [1 - F(c)]^n\}. \tag{15}$$

When the ratio $f_{\theta'}(x)/f_\theta(x)$ is decreasing in x for any $\theta < \theta'$, it can be proved that $P\{X \le x|\theta'\}/P\{X \le x|\theta\}$ is also decreasing in x. Thus, the BFDR in (16) is increasing in c, which suggests that the procedure $\boldsymbol{\delta}$ in Theorem 5.1 with

$$K(\mathbf{X}) = \max\Big\{j : \frac{\pi_0 F_0(X_{j:n})}{F(X_{j:n})}\{1 - [1 - F(X_{j:n})]^n\} \le \alpha\Big\}$$

if the maximum exists, $= 0$ otherwise, and $\delta_{k+1:n} = 0$, controls the BFDR at α. A slightly conservative version of this with

$$K(\mathbf{X}) = \max\Big\{j : \frac{\pi_0 F_0(X_{j:n})}{F(X_{j:n})} \le \alpha\Big\} \tag{16}$$

if the maximum exists, $= 0$ otherwise, and $\delta_{k+1:n} = 0$, is the procedure that controls the Bayesian FDR of Efron (2003).

Since $r(X_i)$ is an increasing function of X_i, the BH-procedure is equivalently described in terms of the $r(X_i)$'s by using the $\boldsymbol{\delta}$ with

$$K(\mathbf{X}) = \max\{1 \le j \le n : r(X_{j:n}) \le c_{j:n}\},$$

if the maximum exists, $= 0$ otherwise, and $\delta_{k+1:n} = 0$, where the constants $c_{1:n} \le \cdots \le c_{n:n}$ are subject to $P\{r(X_1) \le c_{j:n}|\theta_1 = \theta_0\} = j\alpha/n$.

Remark 5.2. Under the i.i.d. setup in Theorem 4.2, our proposed BFDR procedure is asymptotically (as $n \to \infty$) equivalent to the BH procedure, rejecting all H_i with $X_i \le X_{K:n}$, where K is defined by

$$K = \max\Big\{1 \le j \le n : \frac{n}{j}\pi_0 F_0(X_{j:n}) \le \alpha\Big\}. \tag{17}$$

This can be proved as follows:

$$A_j(\mathbf{X}) = \frac{\pi_0}{j}\sum_{i=1}^{j}\frac{f_0(X_{i:n})}{f(X_{i:n})} = \frac{\pi_0 n}{j}\frac{1}{n}\sum_{i=1}^{n}\frac{f_0(X_i)}{f(X_i)}I(X_i \le X_{j:n}) \overset{P}{\approx} \frac{\pi_0 n}{j}F_0(X_{j:n}),$$

since

$$\frac{1}{n}\sum_{i=1}^{n}\frac{\pi_0 f_0(X_i)}{f(X_i)}I(X_i \le x) \xrightarrow{P} \pi_0 E\Big\{\Big(\frac{f_0(X_1)}{f(X_1)}\Big)I(X_1 \le x)\Big\} = \pi_0 F_0(x).$$

Analogous to the result in Theorem 5.1, we also can derive a BFNR-controlling procedure under general dependence conditions.

Theorem 5.2. *Let $K(\mathbf{X}) = \min\{0 \le j \le n : B_j(\mathbf{X}) \le \beta\} - 1$. Then, the one-step randomized procedure*

$$\delta_{i:n}(\mathbf{X}) = \begin{cases} 1 & \text{if} \quad i < k \\ \frac{B_{k-1}(\mathbf{X})-\beta}{B_{k-1}(\mathbf{X})-B_k(\mathbf{X})} & \text{if} \quad i = k \\ 0 & \text{otherwise,} \end{cases}$$

$\boldsymbol{\delta}$ defined as follows given $K = k$, with $\delta_{i:n} = 0 \ \forall \ i$ when $k = -1$, controls the BFNR at β.

Remark 5.3. This BFNR controlling procedure has similar properties as the BFDR controlling procedure proposed in Theorem 5.1, that is, it does not depend on any dependence structure.

Alternative procedures controlling the BFNR at β can be obtained under the i.i.d. set-up. For instance, the $\boldsymbol{\delta}$ in Theorem 5.2 with

$$K(\mathbf{X}) = \min\Big\{j : \frac{\pi_1 \bar{F}_1(X_{j:n})}{\bar{F}(X_{j:n})}\{1 - [F(X_{j:n})]^n\} \le \beta\Big\} - 1$$

if the minimum exists, $= n$ otherwise, and $\delta_{k:n} = 1$ controls the BFNR at β. A slightly conservative version of this; that is, the $\boldsymbol{\delta}$ with

$$K(\mathbf{X}) = \min\Big\{j : \frac{\pi_1 \bar{F}_1(X_{j:n})}{\bar{F}(X_{j:n})} \le \beta\Big\} - 1$$

if the minimum exists, $= n$ otherwise, and and $\delta_{k:n} = 1$, controls the Bayesian FNR.

Since $r(X_i)$ is an increasing function of X_i, the FNR procedure by Sarkar (2004) can be equivalently described in terms of the $r(X_i)$'s by using the $\boldsymbol{\delta}$ with

$$K(\mathbf{X}) = \min\{1 \le j \le n : r(X_{j:n}) \ge d_{j:n}\} - 1,$$

if the maximum exists, $= 0$ otherwise, and $\delta_{k:n} = 0$, where the constants $d_{1:n} \le \cdots \le d_{n:n}$ are subject to $P\{r(X_1) \ge d_{j:n} | \theta_1 = \theta_0\} = (n - j + 1)\beta/n$.

6. Simulations

We numerically studied how our proposed BFDR procedure performs compared to other BFDR procedures, such as the Benjmanini-Hochberg procedure and the procedure controlling the Bayesian FDR defined in Efron (2003). Recall from Section 4 (see (13)) that the BH procedure is a non-randomized stepwise procedure, the BFDR of which is exactly $\pi_0\alpha$ under independence and less than or equal to $\pi_0\alpha$ under certain types of positive dependence of the test statistics. So the compatible version of the BH procedure we should be comparing with is the one that corresponds to (17). While our procedure will not beat this version of the BH procedure under independence, we expect our procedure to perform much better when there is substantial dependence, positive or not, than the other test statistics. Also, recall that the procedure controlling Efron's Bayesian FDR is the one discussed following (16) and controls the BFDR conservatively under the i.i.d. setup. Whether or not it controls the BFDR under a general dependence situation is not known.

Assuming normal distributions of the test statistics, conditional on the parameters, we ran simulations under three different assumptions about the dependence structure of the test statistics.

- Assumption 1: *The X_i's are independent and $X_i \mid \theta_i \overset{i.i.d.}{\sim} N(\theta_i, 1)$.*
- Assumption 2: *The X_i's are multivariate normal with a common positive correlation $\rho = 0.5$:*
$$\mathbf{X} \mid \boldsymbol{\theta} \sim N_n[\boldsymbol{\theta}; (1-\rho)I_n + \rho J_n].$$
- Assumption 3: *The X_i's are paired multivariate normal with negative correlations $\rho = -0.5$:*
$$\mathbf{X} \mid \boldsymbol{\theta} \sim N_n\left[\boldsymbol{\theta}; I_{\frac{n}{2}} \otimes \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix}\right].$$

6.1. One-sided alternatives

Consider testing $H_i : \theta_i = 0$ against $K_i : \theta_i = \gamma > 0$, $i = 1, \ldots, n$, with the following prior for the parameters: $\theta_i \overset{i.i.d.}{\sim} \pi_0 I(\theta = 0) + (1-\pi_0) I(\theta = \gamma)$, for some fixed π_0 and $\gamma > 0$. With independent X_i's, we have

$$r_i(\mathbf{X}) = r(X_i) = Pr(H_i = 0 \mid X_i) = \frac{\pi_0\phi(X_i; 0, 1)}{\pi_0\phi(X_i; 0, 1) + (1-\pi_0)\phi(X_i; \gamma, 1)},$$

where $\phi(x; \mu, \sigma^2)$ is the normal density at x. Notice that r_i is decreasing in X_i for $\gamma > 0$, and hence $A_j(\mathbf{X}) = (1/j)\sum_{i=1}^{j} r(X_{n-i+1:n})$, $j = 1, \ldots, n$. When the

X_i's are multivariate normal with a common positive correlation ρ, they can be represented as $X_i = \theta_i + \sqrt{(1-\rho)}Z_i + \sqrt{\rho}Z_0$ with i.i.d. standard normals Z_i, $i = 0, 1, \ldots, n$. Hence, in this case we have

$$r_i(\mathbf{X}) = \frac{\int_{-\infty}^{\infty} f(\mathbf{X}, H_i = 0|z)\phi(z; 0, 1)dz}{\int_{-\infty}^{\infty} f(\mathbf{X}|z)\phi(z; 0, 1)dz},$$

where

$$\begin{aligned} f(\mathbf{X}|z) &= \prod_{j=1}^{n} \{\pi_0\phi(X_j; \sqrt{\rho}z, 1-\rho) + (1-\pi_0)\phi(X_j; \gamma + \sqrt{\rho}z, 1-\rho)\}, \\ f(\mathbf{X}, H_i = 0|z) &= \pi_0\phi(X_i; \sqrt{\rho}z, 1-\rho) \times \prod_{j \neq i} \{\pi_0\phi(X_j; \sqrt{\rho}z, 1-\rho) \\ &\qquad + (1-\pi_0)\phi(X_j; \gamma + \sqrt{\rho}z, 1-\rho)\}. \end{aligned}$$

We simulated the X_i's under each of the above three assumptions with $n = 100, \gamma = 2$, and $\pi_0 = 0.25, 0.5, 0.7, 0.8$ and 0.9. Posterior probabilities $r_i(X)$ were then calculated based on the above formulas. We applied the BH procedure in (17), Efron's Bayesian procedure in (16), and the proposed randomized BFDR procedure in Theorem 5.1, and calculated the BFDR, BCNR and BAP for each of them. Each simulated value is based on 25,000 replications. The simulated BFDR and BCNR for these three procedures are compared in Figures 1, 2 and 3, respectively, under Assumption 1, in Figures 4, 5 and 6, respectively, under Assumption 2, and in Figures 7, 8 and 9, respectively, under Assumption 3.

Under Assumption 1, all three procedures control the BFDR and there is not much difference in terms of power. Under Assumption 2, the BH and Efron's Bayesian procedures both control the BFDR conservatively, while the new BFDR procedure controls it exactly at α; moreover, in this case, the proposed BFDR procedure is more powerful than the other two procedures. When Assumption 3 holds, Efron's Bayesian procedure and the new BFDR procedure both control the BFDR, but the BH procedure fails to control it when π_0 is close to 1. Also, the new BFDR procedure in this case is more powerful than the other two procedures.

6.2. Two-sided alternatives

Consider testing $H_i : \theta_i = 0$ against $K_i : \theta_i \neq 0$, $i = 1, \ldots, n$, with the following prior for the parameters: $\theta_i \overset{i.i.d.}{\sim} \pi_0 I(\theta = 0) + (1-\pi_0)N(0, \tau^2)$, for some π_0 and τ^2.

Under Assumption 1, we have

$$r_i(\mathbf{X}) = r(X_i) = Pr(H_i = 0|X_i) = \frac{\pi_0\phi(X_i; 0, 1)}{\pi_0\phi(X_i; 0, 1) + (1-\pi_0)\phi(X_i; 0, 1+\tau^2)},$$

which is decreasing in $|X_i|$. Hence, $A_j(\mathbf{X}) = (1/j)\sum_{i=1}^{j} r(|X|_{n-i+1:n})$, $j = 1, \ldots, n$. Under Assumption 2, the conditional probability r_i is as given in (18), but with

$$f(\mathbf{X}|z) = \prod_{j=1}^{n}\{\pi_0\phi(X_j;\sqrt{\rho}z, 1-\rho) + (1-\pi_0)\phi(X_j;\sqrt{\rho}z, 1-\rho+\tau^2)\},$$
$$f(\mathbf{X}, H_i = 0|z) = \pi_0\phi(X_i;\sqrt{\rho}z, 1-\rho) \times \prod_{j\neq i}\{\pi_0\phi(X_j;\sqrt{\rho}z, 1-\rho) + (1-\pi_0)\phi(X_j;\sqrt{\rho}z, 1-\rho+\tau^2)\}.$$

Again, we simulated the BFDR, BCNR (1-BFNR) and BAP of the BH, Efron's Bayesian FDR, and the proposed BFDR procedures with $n = 100$, $\tau = 0.5, 1, 4$ and 10 and $\pi_0 = 0.25, 0.5, 0.7, 0.8, 0.9$ and 0.95 under each of the three

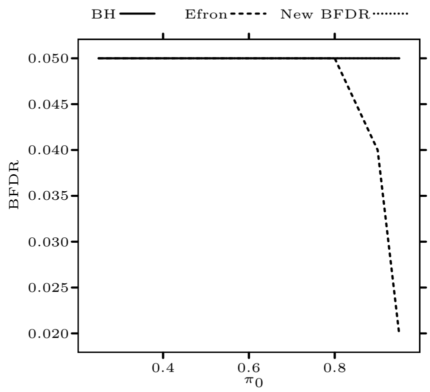

Figure 1. The BFDR in mixture model with one-sided alternatives and $\rho = 0$.

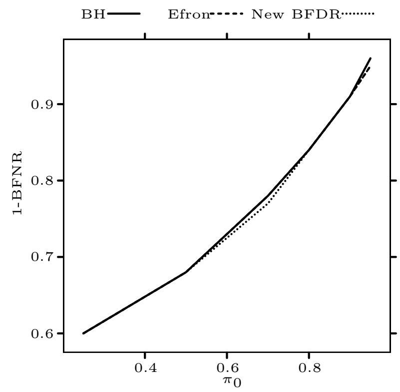

Figure 2. The BCNR in mixture model with one-sided alternatives and $\rho = 0$.

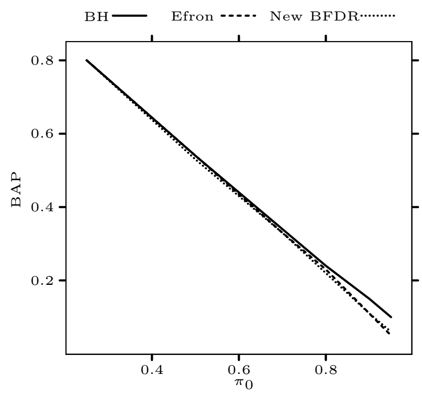

Figure 3. The BAP in mixture model with one-sided alternatives and $\rho = 0$.

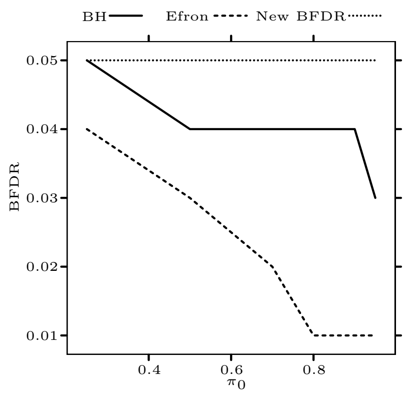

Figure 4. The BFDR in mixture model with one-sided alternatives and $\rho = 0.5$.

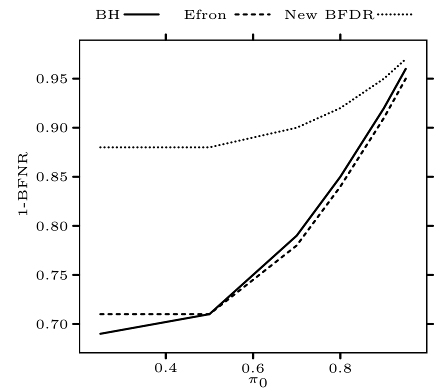

Figure 5. The BCNR in mixture model with one-sided alternatives and $\rho = 0.5$.

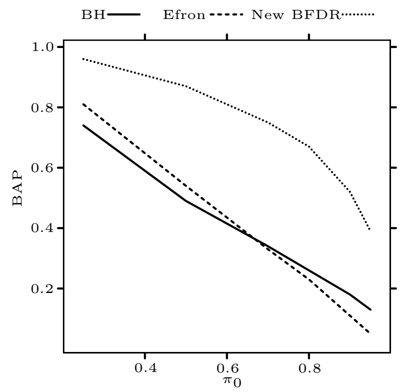

Figure 6. The BAP in mixture model with one-sided alternatives and $\rho = 0.5$.

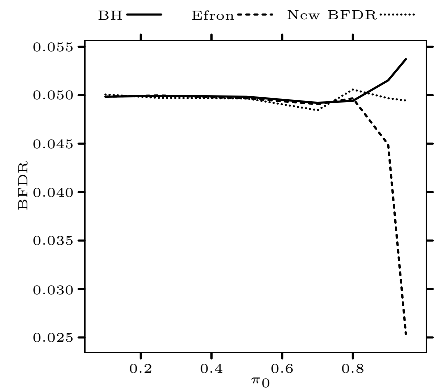

Figure 7. The BFDR in mixture model with one-sided alternatives and $\rho = -0.5$.

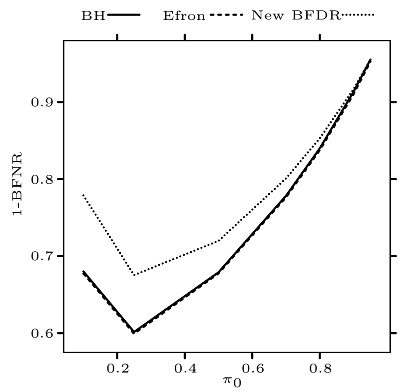

Figure 8. The BCNR in mixture model with one-sided alternatives and $\rho = -0.5$.

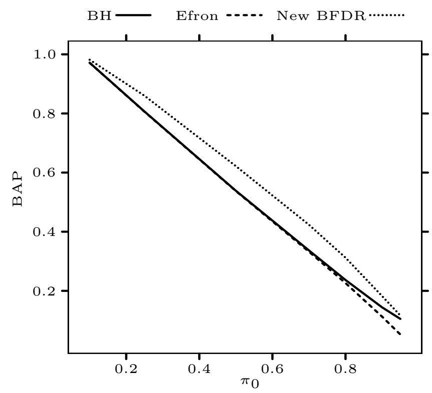

Figure 9. The BAP in mixture model with one-sided alternatives and $\rho = -0.5$.

assumptions regarding the conditional distributions of the X_i's. This time, each simulated value was based on 10,000 replications. The simulated BFDR, BCNR and BAP for these three procedures are now compared in Figures 10, 11 and 12, respectively, under Assumption 1, in Figures 13, 14 and 15, respectively, under Assumption 2, and in Figures 16, 17 and 18, respectively, under Assumption 3.

All three procedures apparently control the BFDR, although the proposed procedure performs better than the other two under dependence. Interestingly, between the BH and Efron's procedures, the latter is now more conservative, particularly when τ is large. In terms of the BFNR and BAP, there is not much difference among the three procedures.

7. FDR-based Variable Selection

Motivated by Theorem 5.1, we briefly describe an FDR-based Bayesian variable selection procedure. More specifically, we develop a BFDR-controlling procedure under a model more specific to variable selection, and incorporate a Bayesian variable selection procedure (George and McCulloch (1993)) into this framework. We need, however, the full data rather than the test statistics $(X_1, \ldots, X_n)$. Denote this as $(Y_i, \mathbf{V}_i)$, $i = 1, \ldots, p$, where Y_i is a binary random variable and $\mathbf{V}_i$ is an n-dimensional random vector. We can then consider a hierarchical binary regression model for analysis. At the first stage of the model, $P(Y_i = 1) \overset{ind}{\sim} \Phi(\mathbf{V}_i^T \boldsymbol{\beta})$, for some $\boldsymbol{\beta} = (\beta_1, \ldots, \beta_n)$. For the second stage of the model, we introduce binary-valued latent variables $\gamma_1, \ldots, \gamma_n$, conditional on which we have, $\beta_i | \gamma_i \sim (1 - \gamma_i) N(0, \tau_i^2) + \gamma_i N(0, c_i^2 \tau_i^2)$, where $c_1^2, \ldots, c_p^2$ and $\tau_1^2, \ldots, \tau_p^2$ are variance components. If $\gamma_j = 1$, this indicates that the jth covariate should be included in the model, while $\gamma_j = 0$ implies that it should be excluded

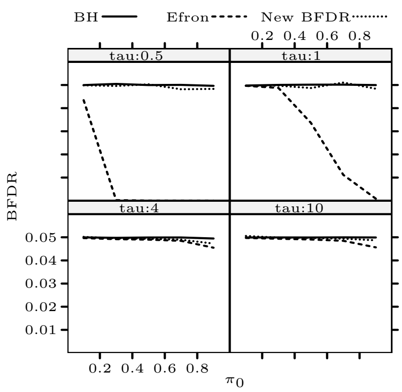

Figure 10. The BFDR in mixture model with two-sided alternatives and $\rho = 0$.

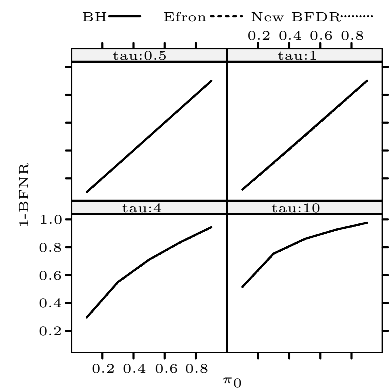

Figure 11. The BCNR in mixture model with two-sided alternatives and $\rho = 0$.

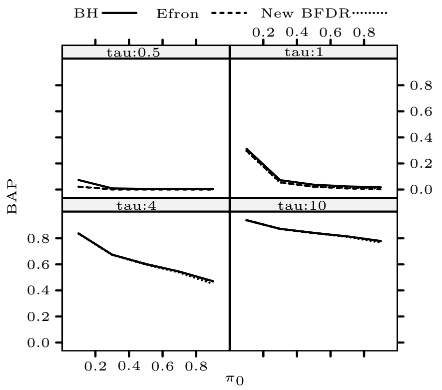

Figure 12. The BAP in mixture model with two-sided alternatives and $\rho = 0$.

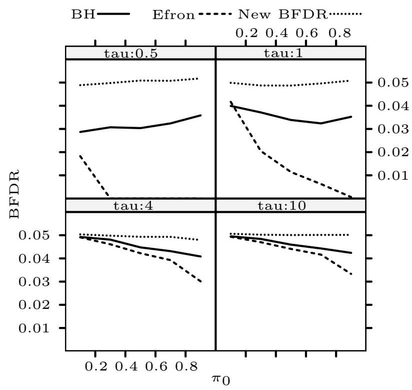

Figure 13. The BFDR in mixture model with two-sided alternatives and $\rho = 0.5$.

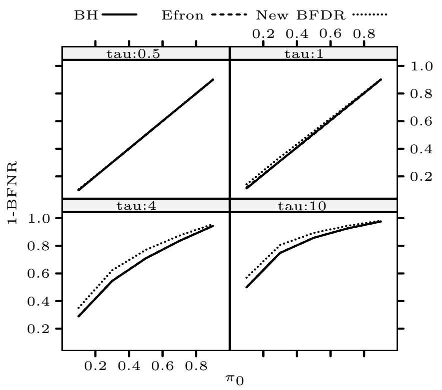

Figure 14. The BCNR in mixture model with two-sided alternatives and $\rho=0.5$.

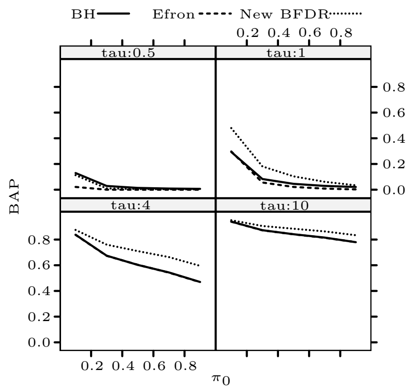

Figure 15. The BAP in mixture model with two-sided alternatives and $\rho=0.5$.

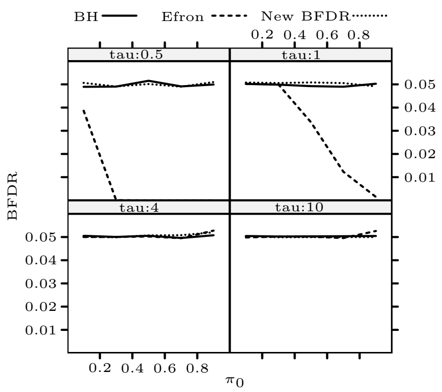

Figure 16. The BFDR in mixture model with two-sided alternatives and $\rho=-0.5$.

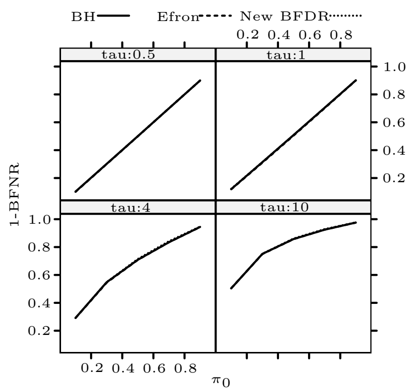

Figure 17. The BCNR in mixture model with two-sided alternatives and $\rho=-0.5$.

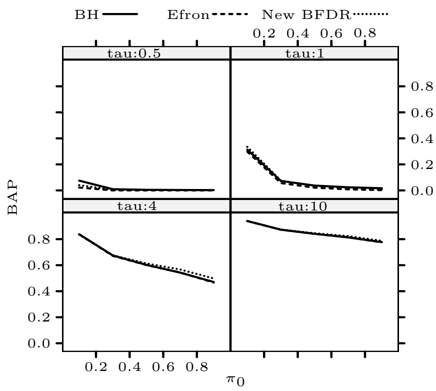

Figure 18. The BCNR in mixture model with two-sided alternatives and $\rho = -0.5$.

from the model. The conditional distributions can be easily computed using Gibbs sampling and data augmentation procedures (Albert and Chib (1993)) for calculating the posterior distribution.

Thus, in this framework, rejecting the null hypothesis $H_i : \gamma_i = 0$ in favor of the corresponding alternative $K_i : \gamma_i = 1$, using a multiple testing procedure, is equivalent to selecting the jth covariate for inclusion in the model. The Bayesian point of view for selecting variables requires us to focus on the posterior distributions of $\gamma_1, \ldots, \gamma_p$. The BFDR-controlling procedure would be based on $P(\gamma_i = 0 \mid \mathbf{Y})$, $i = 1, \ldots, n$, where $\mathbf{Y} = (Y_1, \ldots, Y_p)$. In particular, Theorem 5.1 motivates the following FDR-based procedure.

(a) Set the level to be α.

(b) Find the posterior distribution for the hierarchical regression using Markov Chain Monte Carlo (MCMC) methods.

(c) Based on the MCMC output, calculate the posterior probabilities $r_i(\mathbf{Y}) = P\{\gamma_i = 0 \mid \mathbf{Y}\}$, $i = 1, \ldots, n$, and sort them in increasing order as $r_{(1)}(\mathbf{Y}) \leq \cdots \leq r_{(n)}(\mathbf{Y})$.

(d) Calculate $A_j(\mathbf{Y}) = (1/j) \sum_{i=1}^{j} r_{(i)}(\mathbf{Y})$, $j = 1, \ldots, n$.

(e) Find $K(\mathbf{Y}) = \max\{1 \leq j \leq n : A_j(\mathbf{Y}) \leq \alpha\}$.

(f) Given $K(\mathbf{Y}) = k$, determine the probabilities

$$\delta_{(i)}(\mathbf{Y}) = \begin{cases} 1 & \text{if} \quad i \leq k \\ \frac{\alpha - A_k(\mathbf{Y})}{A_{k+1}(\mathbf{Y}) - A_k(\mathbf{Y})} & \text{if} \quad i = k+1 \\ 0 & \text{otherwise,} \end{cases}$$

with $\delta_{(i)} = 1 \; \forall \; i$ if $k = n$.

(g) Include the variables in the model with the corresponding probabilities in (19).

Notice that this procedure requires one to average posterior probabilities across the models explored in the MCMC iterations. This controls the BFDR at level α. Also, one can produce a BFNR-controlling procedure from Theorem 5.2 based on the MCMC output for $P(\gamma_i = 1 \mid \mathbf{Y})$, $i = 1, \ldots, n$.

8. Concluding Remarks

We have developed a general Bayesian procedure for controlling false discovery and nondiscovery rates that allow for arbitrary dependence of the test statistics. The decision theoretic framework allows for exploration of these error rates from both Bayesian and frequentist perspectives.

If one subscribes to the notion of BFDR or BFNR, we recommend using the proposed procedures, as opposed to the BH and Efron's FDR procedures or their FNR analogs, for any dependence model that considers one-sided or two-sides alternatives. It is proper to point out that our recommendation relies on simulations with 100 tests; in multiple testing applications, one often encounters tens of thousands of tests, and it would be realistic to use a much larger value of n than 100 in the simulations. This is extremely time-consuming, but in increasing n from 100 to 200 we have not noticed any significant difference in the performance of our procedures relative to the BH and Efron's procedures. We think our procedures will perform well for n in the hundreds, but are unable to make a more global statement without numerical evidence.

Acknowledgements

The research of the first author was supported by NSF Grants DMS-0306366 and DMS-0603868, and of the second author by NSF Grant DMS-0306366. We thank an AE and two referees for many helpful comments and suggestions.

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Department of Statistics, Fox School of Business and Management, Temple University, Speakman 319, 1810 North 13th Street, Philadelphia, PA 19122-60, U.S.A.

E-mail: sanat@temple.edu

Wyeth Pharmaceuticals, 500 Arcola Rd, A5035, Collegeville, PA 19426, U.S.A.

E-mail: zhout2@wyeth.com

Departments of Statistics and Public Health Sciences, Penn State University, University Park, PA 16802, U.S.A.

E-mail: ghoshd@psu.edu

(Received October 2006; accepted July 2007)