

A Bayesian Decision Theoretic Approach to Directional Multiple Hypotheses Problems

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Abstract

A multiple hypothesis problem with directional alternatives is considered in a decision theoretic framework. Skewness in the alternatives is considered, and it is shown that this skewness permits the Bayes rules to possess certain advantages when one direction of the alternatives is more important or more probable than the other direction. Bayes rules subject to constraints on certain directional false discovery rates are obtained, and their performances are compared with a traditional FDR rule through simulation. We also analyzed a gene expression data using our methodology, and compare the results to that of a FDR method.

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1 Introduction

Multiple hypotheses problems have received a significant amount of attention in the recent literature due to its use in microarray data analysis, imaging analysis, and other biological applications. In these applications, typically, data can be formulated in the form of a $m \times n$ matrix \mathbf{X} whose i th row \mathbf{x}_i is a sample from a probability model $P(\cdot|\theta_i, \eta)$, where θ_i is a parameter of interest, and η is a nuisance parameter.

Most of the work in literature focuses on the two-tail hypotheses $H_0^i : \theta_i = 0$ vs. $H_a^i : \theta_i \neq 0$, $i = 1, 2, \dots, m$. In this paper, we consider the following hypotheses with directional alternatives

$$H_0^i : \theta_i = 0 \quad vs \quad H_-^i : \theta_i < 0 \quad or \quad H_+^i : \theta_i > 0, \quad i = 1, 2, \dots, m. \quad (1)$$

Earlier work on this problem was based on the familywise error rate, FWER [4, 5]. However, since this approach controls false discovery of even one null, such an approach is not practical for higher dimensional problem, i.e., when m is very large. Shaffer [10], Lewis and Thayer [6] and Sarkar and Zhou [11] focussed on directional false discovery rate (DFDR), an analogous version of the false discovery rate (FDR) for the directional hypotheses. We focus on a Bayesian decision theoretical formulation of this problem with emphasis on the directional false discoveries with skewed alternatives as described in Section 2.

The loss function, we consider, is of the form

$$L(\boldsymbol{\theta}, \mathbf{d}^X) = \sum_{i=1}^m L_i(\theta_i, d_i^X), \quad (2)$$

where $L_i(\theta_i, d_i^X)$ is the loss for each individual hypothesis H_0^i vs. H_-^i or H_+^i , and $\mathbf{d}^X = (d_1^X, d_2^X, \dots, d_m^X)$, with $d_i^X \in \{-1, 0, 1\}$. Here, $d_i^X = -1$ means that H_-^i is selected, $d_i^X = 0$ means that H_0^i is selected, and $d_i^X = 1$ means that H_+^i is selected.

One of the advantages of the Bayesian decision theoretic approach is that it allows us to incorporate the prior information on the direction of θ_i s as it may be relevant in many applications. We consider the prior of the form

$$\pi(\boldsymbol{\theta}) = p_- \pi_-(\boldsymbol{\theta}) + p_0 I(\boldsymbol{\theta} = \mathbf{0}) + p_+ \pi_+(\boldsymbol{\theta}), \quad (3)$$

where p_- , p_0 , and p_+ are some preassigned or estimated probabilities with $p_- + p_0 + p_+ = 1$, and $\pi_-(\cdot)$ and $\pi_+(\cdot)$ are densities with support $(-\infty, 0)$ and $(0, \infty)$, respectively. This prior allows skewness in the distribution of θ_i s. If, for example, $p_- > p_+$, then chances are higher that more of θ_i s are generated with H_- than with H_+ . This may be important in many applications. In particular, consider a genetic experiment in which a microRNA (a non-coding gene) is transfected in cells of interest to test if it suppresses the gene expressions of target mRNAs (coding genes). The biological theory is that certain non-coding genes get attached to a subsequence of specific coding genes

and thus suppress their expressions. This has many ramifications in cancer and other disease research [7]. We consider the data cited in [7] in Section 6, and analyze it using methodology developed in this paper.

The theorem below shows the importance of skewness in the prior (3), which is a straightforward generalization of Theorem 1 of [1], and thus stated without proof.

Theorem 1 *Let $\pi(\theta)$ and $\pi'(\theta)$ be two priors given by*

$$\begin{aligned}\pi(\theta) &= p_- \pi_-(\theta) + p_0 I(\theta = 0) + p_+ \pi_+(\theta) \\ \pi'(\theta) &= p'_- \pi_-(\theta) + p_0 I(\theta = 0) + p'_+ \pi_+(\theta),\end{aligned}$$

where $p_- > p'_-$ and thus $p_+ < p'_+$, and let δ_B and δ'_B denote the Bayes rules under the loss (2) with respect to π and π' respectively. Then

$$r_-^{\delta_B} \leq r_-^{\delta'_B}, \tag{4}$$

but

$$r_+^{\delta_B} \geq r_+^{\delta'_B}, \tag{5}$$

where r_-^δ and r_+^δ are the expected Bayes risk of the rule δ with respect to π_- and π_+ respectively.

If $\pi(\theta)$ is the true prior with $p_- > p_+$, but the prior $\pi'(\theta)$ is considered instead with $p'_- = p'_+$. Then the Theorem 1 implies that the Bayes rule so obtained performs poorly in the left tail of θ_i s which occurs more frequently. If $L_i(\theta_i, d_i)$ is the "0-1" loss, then this implies that the expected number of false discoveries, when θ_i s are negative, will be higher by δ'_B than by δ_B . For the genetic example above, this would mean that there will be more false discoveries if the true skewness in the prior is not taken into account.

Note that the optimal Bayes rule based on the loss (2) may not control false discovery rates. Thus a constrained Bayes rule may be more appropriate as advocated by Muller, Parmigiani and Rice [9]. We thus impose different notions of directional false discovery rates (DFDRs) to obtain constrained Bayes decision rules. The main advantage of this approach is that a specific prior information, in particular the skewness in the prior, can be utilized to obtain better decision rules.

The rest of the paper is as organized as follows. In Section 2, we present the definitions of the false discovery rates for the directional multiple hypotheses. We present a general methodology of Bayes rule in Section 3. Computational aspects of

the Bayes rules is discussed in Section 4, including an example of normal populations. Simulation results with comparisons of the Bayes rules and a traditional FDR rule (adjusted for directional alternatives) are discussed in Section 5. A real example based on the data of [7] is considered in Section 6. We end with some concluding remarks in Section 7.

2 False Discovery Rates

Let m_0 , m_- , and m_+ be true numbers of H_0 , H_- , and H_+ hypotheses, respectively, and let U , V , and W be the number of H_0 , H_- , and H_+ selected by a decision rule \mathbf{d}^X . The Table 1 shows different possibilities of the decisions. Different types of false discoveries are made; for example, V_0 and V_+ together represent the total number of falsely selected H_- hypotheses. Similarly, W_0 and W_+ together represent the total number of falsely selected H_+ . Following Shaffer (2002), we define the directional false discovery rate $DFDR$ as

$$DFDR = E \left[\frac{V_0 + V_+ + W_0 + W_-}{V + W + I(V = 0)I(W = 0)} \right].$$

Table 1

	Select H_0	Select H_-	Select H_+	Total
H_0 is true	U_0	V_0	W_0	m_0
H_- is true	U_-	V_-	W_-	m_-
H_+ is true	U_+	V_+	W_+	m_+
	U	V	W	m

A different variation of this false discovery rate can be defined. Suppose, one is interested in controlling false discoveries of H_- and H_+ separately. In that case, one may like to control the following left and right false discovery rates, respectively:

$$LFDR = E \left[\frac{V_0 + V_+}{V + I(V = 0)} \right] \quad \text{and} \quad RFDR = E \left[\frac{W_0 + W_-}{W + I(W = 0)} \right]$$

The quantities $DFDR$, $LFDR$, and $RFDR$ above are defined in a frequentist manner. In other words, the expectations are with respect to \mathbf{X} given $\boldsymbol{\theta}$ and η . A Bayesian analogue of this can be defined if the expectation is with respect to both \mathbf{X} given $\boldsymbol{\theta}$ and η , and with respect to $\boldsymbol{\theta}$ and η . We will call these error rates as $BDFDR$, $BLFDR$,

and *BRFDR*, respectively. Posterior versions of these with respect to the posterior distribution will be denoted by *PDFDR*, *PLFDR*, and *PRFDR*.

Note that $V_0 + V_+ = \sum_{i=1}^m I(\theta_i \geq 0)I(d_i^X = -1)$ and $W_0 + W_- = \sum_{i=1}^m I(\theta_i \leq 0)I(d_i^X = 1)$. Thus, it is easy to see that

$$PDFDR = \frac{\sum(\nu_i^0 + v_i^+)I(d_i^X = -1) + \sum(\nu_i^0 + v_i^-)I(d_i^X = 1)}{V + W + I(V = 0)I(W = 0)}. \quad (6)$$

and

$$PLFDR = \frac{\sum(\nu_i^0 + v_i^+)I(d_i^X = -1)}{V + I(V = 0)}, \quad PRFDR = \frac{\sum(\nu_i^0 + v_i^-)I(d_i^X = 1)}{W + I(W = 0)}, \quad (7)$$

where

$$\nu_i^- = P(\theta_i < 0|\mathbf{x}), \quad \nu_i^+ = P(\theta_i > 0|\mathbf{x}), \quad \nu_i^0 = P(\theta_i = 0|\mathbf{x}) \quad (8)$$

3 Bayesian Decision Theoretic Methodology

3.1 Bayes Rules under the "0-1" Loss Function

Many special cases of the loss (2) can be considered to reflect the loss in terms of number of false discoveries or false discovery rates. The simplest loss is the "0-1" loss

$$L_0(\boldsymbol{\theta}, d) = \sum I(d_i^X \geq 1)I(\theta_i < 0) + \sum I(d_i^X \leq 1)I(\theta_i > 0) + \sum I(d_i^X \neq 0)I(\theta_i = 0). \quad (9)$$

Note that the expected loss $E[L(\boldsymbol{\theta}, d(\mathbf{X}))]$ is the expected number of total false decisions, $(V_0 + W_0) + (V_+ + W_-) + (U_- + U_+)$. The Bayes rule can be obtained by minimizing the posterior expected loss,

$$E[L_0(\boldsymbol{\theta}, d)|\mathbf{x}] = E[(m_- + m_+)|\mathbf{x}] - \sum(v_i^- - \nu_i^0)I(d_i^X = -1) - \sum(v_i^+ - \nu_i^0)I(d_i^X = 1), \quad (10)$$

From (10), it is easy to see that the Bayes rule selects H_0^i if $\nu_i^0 \geq \nu_i^-$ and $\nu_i^0 \geq \nu_i^+$, selects H_-^i if $\nu_i^- > \nu_i^0$ and $\nu_i^- > \nu_i^+$, and selects H_+^i if $\nu_i^+ > \nu_i^0$ and $\nu_i^+ > \nu_i^-$. Thus with the notations

$$D_1^- = \{i : \nu_i^- > \nu_i^0, \nu_i^- > \nu_i^+\}, \quad D_1^+ = \{i : \nu_i^+ > \nu_i^0, \nu_i^+ > \nu_i^-\}, \quad (11)$$

the Bayes rule can be stated as

$$\delta_B^{(0)} = \begin{cases} \text{Select } H_-^i & \text{for } i \in D_1^- \\ \text{Select } H_+^i & \text{for } i \in D_1^+ \\ \text{Select } H_0^i & \text{for } i \notin D_1^- \cup D_1^+ \end{cases} \quad (12)$$

Note that the Bayes rule $\delta_B^{(0)}$ does not control any false discovery rates. We define the constrained Bayes rule $\delta_B^{(1)}$ as the rule that minimizes the posterior expected loss (10) subject to constrain that $PDFDR \leq \alpha$, where $PDFDR$ is given by (6). Note that $PDFDR \leq \alpha$ also implies that $BDFDR \leq \alpha$.

Now, define $\psi_i = \nu_i^+ + \nu_i^0$ if $i \in D_1^-$ and $\psi_i = \nu_i^- + \nu_i^0$ if $i \in D_1^+$, and rank $\{\psi_i, i \in D_1^- \cup D_1^+\}$ from the lowest to the highest. Suppose the ranked values are denoted $\psi_{[1]} \leq \psi_{[2]} \leq \dots \leq \psi_{[|D_1^- \cup D_1^+|]}$, where notation $|\cdot|$ is used to denote the cardinality of a set. Denote

$$i_0 = \max\{j \leq |D_1^- \cup D_1^+| : \frac{1}{j} \sum_{i=1}^j \psi_{[i]} \leq \alpha\}. \quad (13)$$

If $D_{1\psi} \subseteq D_1^- \cup D_1^+$ denotes the set of indices corresponding to $[1], [2], \dots, [i_0]$, then it is easy to see, from (6) and (12), that the constrained Bayes rule $\delta_B^{(1)}$ is given by

$$\delta_B^{(1)} = \begin{cases} \text{Select } H_-^i & \text{if } i \in D_1^- \cap D_{1\psi} \\ \text{Select } H_+^i & \text{if } i \in D_1^+ \cap D_{1\psi} \\ \text{Select } H_0^i & \text{if } i \notin (D_1^- \cup D_1^+) \cap D_{1\psi}. \end{cases} \quad (14)$$

In many applications, there may be a need for controlling the false discovery of left and right tail hypotheses H_-^i and H_+^i separately. The constrained Bayes rule $\delta_B^{(2)}$ in this case can be obtained by minimizing (10) subject to $PLFDR \leq \alpha_L$ and $PRFDR \leq \alpha_R$, where α_L and α_R are some pre-assigned error rates depending upon the risks associated with selecting H_-^i and H_+^i , respectively. To obtain $\delta_B^{(2)}$, first rank $\{\nu_i^{0+} = \nu_i^+ + \nu_i^0, i \in D_1^-\}$ from the lowest to the highest and rank $\{\nu_i^{0-} = \nu_i^- + \nu_i^0, i \in D_1^+\}$ from the lowest to the highest. Let the ranked values be, respectively, denoted by $v_{[1],-}^{0+} \leq v_{[2],-}^{0+} \leq \dots \leq v_{[|D_1^-|],-}^{0+}$ and $v_{[1],+}^{0-} \leq v_{[2],+}^{0-} \leq \dots \leq v_{[|D_1^+|],+}^{0-}$, respectively. Now,

define

$$i_0^- = \max\{j \leq |D_1^-| : \frac{1}{j} \sum_{i=1}^j v_{[i],-}^{0+} \leq \alpha_L\}, \quad (15)$$

$$i_0^+ = \max\{j \leq |D_1^+| : \frac{1}{j} \sum_{i=1}^j v_{[i],+}^{0-} \leq \alpha_R\}. \quad (16)$$

Denoting $D_{1\nu}^- \subseteq D_1^-$ as the set of indices corresponding to $\nu_{[1],-}^+, \dots, \nu_{[i_0^-],-}^+$ and $D_{1\nu}^+ \subseteq D_1^+$ as the set of indices corresponding to $v_{[1],+}^{0-}, \dots, v_{[i_0^+],+}^{0-}$, it is easy to see from (12), (15), and (16), that the constrained Bayes rule $\delta_B^{(2)}$ can be described as

$$\delta_B^{(2)} = \begin{cases} \text{Select } H_-^i & \text{if } i \in D_{1\nu}^- \\ \text{Select } H_+^i & \text{if } i \in D_{1\nu}^+ \\ \text{Select } H_0^i & \text{if } i \notin D_{1\nu}^- \cup D_{1\nu}^+. \end{cases} \quad (17)$$

3.2 Bayes Rules under a General Loss Function

The "0-1" loss gives equal loss of 1 for misclassifying a true H_- as H_0 or H_+ , and a true H_+ as H_0 or H_- . It may be more appropriate to give higher loss for selecting a true H_- as H_+ than selecting it as H_0 , and likewise for selecting a true H_+ as H_- than selecting it as H_0 . More generally, we may allow the loss to depend on the actual value of θ .

$$\begin{aligned} L_i(\theta_i, d_i^X = -1) &= \begin{cases} 0 & \text{if } \theta_i < 0 \\ l_0 & \text{if } \theta_i = 0 \\ l_0 + l(\theta_i) & \text{if } \theta_i > 0 \end{cases} \\ L_i(\theta_i, d_i^X = 0) &= \begin{cases} l_1 + l(\theta_i) & \text{if } \theta_i < 0 \\ 0 & \text{if } \theta_i = 0 \\ l_1 + l(\theta_i) & \text{if } \theta_i > 0 \end{cases} \\ L_i(\theta_i, d_i^X = 1) &= \begin{cases} l_0 + l(\theta_i) & \text{if } \theta_i < 0 \\ l_0 & \text{if } \theta_i = 0 \\ 0 & \text{if } \theta_i > 0 \end{cases}, \end{aligned} \quad (18)$$

where l_0 and l_1 are some positive constants, and $l(\theta) \geq 0$ is a function that is symmetric around 0 and is increasing in $|\theta|$. Note that $l_0 = l_1 = 1$ and $l(\cdot) = 0$ lead to the "0-1" loss.

The posterior loss, in this case, is given by

$$\begin{aligned} E[\sum L_i(\theta_i, d_i)|\mathbf{x}] &= \sum E[(l_1 + l(\theta_i))I(\theta_i \neq 0)|\mathbf{x}] \\ &\quad - \sum (w_i^- + l_0 v_i^- + l_1 - l_0 - l_1 v_i^0) d_i^- \\ &\quad - \sum (w_i^+ + l_0 v_i^+ + l_1 - l_0 - l_1 v_i^0) d_i^+, \end{aligned}$$

where

$$w_i^- = E[l(\theta_i)I(\theta_i < 0)|\mathbf{x}] \quad \text{and} \quad w_i^+ = E[l(\theta_i)I(\theta_i > 0)|\mathbf{x}] \quad (19)$$

The analogous versions of $\delta_B^{(0)}$, $\delta_B^{(1)}$ and $\delta_B^{(2)}$ can now be obtained, in a similar manner as discussed in Subsection 3.1, by replacing D_1^- and D_1^+ , in (11), by

$$\begin{aligned} D_{1l}^- &= \{i : w_i^- + l_0 \nu_i^- > l_0 - l_1 + l_1 \nu_i^0, \quad w_i^- + l_0 \nu_i^- > w_i^+ + l_0 \nu_i^+\}, \\ D_{1l}^+ &= \{i : w_i^+ + l_0 \nu_i^+ > l_0 - l_1 + l_1 \nu_i^0, \quad w_i^+ + l_0 \nu_i^+ > w_i^- + l_0 \nu_i^-\}, \end{aligned} \quad (20)$$

respectively.

3.3 A Bayes Rule with Exact $BDFDR = \alpha$

Note that if $l_1 = l_0$ in the loss (18), then from (20), $i \in D_{1l}^- \cup D_{2l}^+$ if $w_i^- > l_0(\nu_i^0 - \nu_i^-)$ or $w_i^+ > l_0(\nu_i^0 - \nu_i^+)$. Thus, $i \in D_1^- \cup D_2^+$ implies $i \in D_{1l}^- \cup D_{2l}^+$, which implies that the Bayes rule based on the loss (18) enlarges the rejection region (of rejecting H_0^i) in comparison to the "0-1" loss. Moreover, if $l(\theta) = l_a$ (some fixed positive value), then it can be seen from (19) and (20) that

$$D_{1l}^- = \{i : \nu_i^- > c_0 \nu_i^0, \quad \nu_i^- > \nu_i^+\}, \quad D_{1l}^+ = \{i : \nu_i^+ > c_0 \nu_i^0, \quad \nu_i^+ > \nu_i^-\},$$

where $c_0 = l_0/(l_0 + l_a)$. This c_0 now can be used as an instrument so that the Bayes rule is of particular false discovery rate. For example, we can find c_0 ($0 < c_0 < 1$) such that

$$BDFDR = E\left[\frac{\sum(\nu_i^0 + \nu_i^+)I(d_i^X = -1) + \sum(\nu_i^0 + \nu_i^-)I(d_i^X = 1)}{V + W + I(V = 0)I(W = 0)}\right] = \alpha, \quad (21)$$

where the expectation is with respect to the marginal distribution of \mathbf{X} . It may be interesting to know the property of $BDFDR$ as a function of c_0 . Of particular interests would be to know whether $BDFDR$ is a monotonic function of c_0 . If so, c_0 can be

found through simulation as we illustrate in the next section. This yields a new Bayes rule with exact $BDFDR = \alpha$, which selects H_-^i if $i \in D_{1l}^-$, selects H_+^i if $i \in D_{1l}^+$, and selects H_0^i for all other i .

4 Computation of the Bayes rules

In this section, we discuss the computation of the Bayes rules under the prior (3). We will assume that \mathbf{X} can be reduced to a sufficient statistics (\mathbf{Y}, S) such that $\mathbf{Y} = (Y_1, Y_2, \dots, Y_m)^T$ is a vector of independent variates with $Y_i \sim f(y_i; \theta_i, \eta)$, $i = 1, \dots, m$, the distribution of S is independent of $\boldsymbol{\theta}$, and where \mathbf{Y} and S are independently distributed. A typical example, where this can be done, is $X_{ij} = \theta_i + \varepsilon_{ij}$, $j = 1, 2, \dots, n$, $i = 1, 2, \dots, m$, where $\varepsilon_{ij} \sim N(0, \sigma^2)$. In this case, $Y_i = \bar{X}_i$, and $S = \sum \sum (X_{ij} - \bar{X}_i)^2$.

As discussed in Section 2, the Bayes rules are determined by the posterior distribution of $\boldsymbol{\theta}$ given $\mathbf{X} = \mathbf{x}$. When there is a nuisance parameter η , the posterior expected loss can be computed by first computing the expectation with respect to the posterior distribution of $\boldsymbol{\theta}$ given $\mathbf{X} = \mathbf{x}$, η and then with respect to the posterior distribution of η given $\mathbf{X} = \mathbf{x}$. Note that based on the assumption on (\mathbf{Y}, S) , the posterior distribution of $\boldsymbol{\theta}$ given $\mathbf{X} = \mathbf{x}$, η requires only the consideration of the distribution $Y_i \sim f(y_i; \theta_i, \eta)$, $i = 1, \dots, m$ and the prior distribution (3). We show in the Appendix that a good approximation can be obtained, when m is large, by only considering the distribution $Y_i \sim f(y_i; \theta_i, \eta)$, $i = 1, \dots, m$ with the prior (3), and then by replacing η by the mode of the posterior distribution of η given $S = s$. Thus, from now on, we will assume that η is known with the understanding that, in the case of unknown η , η can be replaced by the posterior mode of η given $S = s$.

Conditionally, given $\mathbf{X} = \mathbf{x}$, the $\theta_1, \theta_2, \dots, \theta_m$ are independently distributed with marginal densities (suppressing η for simplicity)

$$\pi(\theta_i|y_i) = \pi(H_-^i|y_i)\pi(\theta_i|H_-^i, y_i) + \pi(H_0^i|y_i)I(\theta_i = 0) + \pi(H_+^i|y_i)\pi(\theta_i|H_+^i|y_i), \quad (22)$$

where $\pi(\theta_i|H_-^i, y_i)$ and $\pi(\theta_i|H_+^i, y_i)$ are the posterior distributions with respect to the priors $\pi_-(\theta_i)$ and $\pi_+(\theta_i)$ respectively, and

$$\pi(H_-^i|y_i) \propto p_- f(y_i|H_-^i), \quad \pi(H_0^i|y_i) \propto p_0 f(y_i|H_0^i), \quad \pi(H_+^i|y_i) \propto p_+ f(y_i|H_+^i),$$

where $f(y_i|H_0^i) = f(y_i|0)$, and $f(y_i|H_-^i)$, $f(y_i|H_+^i)$ are the marginal densities under the

priors π_- and π_+ , respectively. Note that the proportionality constant above is the inverse of $[p_-f(y_i|H_-^i) + p_0f(y_i|H_0^i) + p_+f(y_i|H_+^i)]$.

Clearly,

$$v_i^- = \pi(H_-^i|y_i), \quad v_i^0 = \pi(H_0^i|y_i), \quad v_i^+ = \pi(H_+^i|y_i). \quad (23)$$

The Bayes decision rule and the constrained Bayes rules $\delta_B^{(0)}$, $\delta_B^{(1)}$, and $\delta_B^{(2)}$, as defined in (12), (14), and (17), can now be obtained from (23). For the loss function (18), the Bayes rule requires, in addition to (23), the computation of $w_i^- = E[l(\theta)I(\theta < 0)|\mathbf{X}]$ and $w_i^+ = E[l(\theta)I(\theta > 0)|\mathbf{X}]$, which are given by

$$w_i^- = \pi(H_-^i|y_i)E[l(\theta_i)|H_-^i, y_i], \quad w_i^+ = \pi(H_+^i|y_i)E[l(\theta_i)|H_+^i, y_i]. \quad (24)$$

Denoting $T_+(y_i) = f(y_i|H_-^i)/f(y_i|0)$ and $T_-(y_i) = f(y_i|H_+^i)/f(y_i|0)$, it can be seen that

$$\begin{aligned} \nu_i^- &= \frac{p_-T_-(y_i)}{p_-T_-(y_i) + p_+T_+(y_i) + p_0}, & \nu_i^+ &= \frac{p_+T_+(y_i)}{p_-T_-(y_i) + p_+T_+(y_i) + p_0} \\ \nu_i^0 &= \frac{p_0}{p_-T_-(y_i) + p_+T_+(y_i) + p_0}. \end{aligned}$$

Thus, from (11),

$$\begin{aligned} D_1^- &= \{i : T_-(y_i) > p_0/p_-, p_-T_-(y_i) > p_+T_+(y_i)\} \\ D_1^+ &= \{i : T_+(y_i) > p_0/p_+, p_+T_+(y_i) > p_-T_-(y_i)\}. \end{aligned} \quad (25)$$

Note that

$$T_-(y_i) = \int_{-\infty}^0 \frac{f(y_i|\theta_i)}{f(y_i|0)} \pi_-(\theta_i) d\theta_i \quad \text{and} \quad T_+(y_i) = \int_0^{\infty} \frac{f(y_i|\theta_i)}{f(y_i|0)} \pi_+(\theta_i) d\theta_i. \quad (26)$$

Thus if $f(y_i|\theta_i)$ has monotone likelihood ratio (MLR) property in y_i , then $T_-(y_i)$ ($T_+(y_i)$) is a decreasing (increasing) function of y_i . In that case, it is easy to see that $\delta_B^{(0)}$, $\delta_B^{(1)}$, and $\delta_B^{(2)}$ hold simplified forms as stated in the following Theorem.

Theorem 2 *Suppose the pdf of y_i , $f(y_i|\theta)$, is MLR in y_i . Let k_- be the largest integer i such that $y_{[i]} < T_-^{-1}(p_0/p_-)$ and $p_-T_-(y_{[i]}) > p_+T_+(y_{[i]})$, and let k_+ be the smallest integer i such that $y_{[i]} > T_+^{-1}(p_0/p_+)$ and $p_+T_+(y_{[i]}) > p_-T_-(y_{[i]})$, where T_- and T_+ are defined by (26). Then the Bayes rule $\delta_B^{(0)}$ selects H_-^i for all i associated with $y_{[1]}, \dots, y_{[k_-]}$, selects H_+^i for all i associated with $y_{[k_+]}, \dots, y_{[m]}$, and selects H_0^i for all*

other i .

Additionally, suppose the $\max\{\frac{1}{j_1+j_2}(\sum_{i_1=1}^{j_1}\nu_{[i_1]}^{0+} + \sum_{i_2=1}^{j_2}\nu_{[i_2]}^{0-}) : j_1 \leq k_-, j_2 \leq m - k_+ + 1\}$, subject to the constrain that it is $\leq \alpha$, is attained by the indices $j_1 = i_{10}^-$ and $j_2 = m - i_{20}^+ + 1$. Then the constrained Bayes rule $\delta_B^{(1)}$ selects H_-^i for all i associated with $y_{[1]}, \dots, y_{[i_{10}^-]}$, selects H_+^i for all i associated with $y_{[i_{20}^+]}, \dots, y_{[m]}$, and selects H_0^i for all other i .

In addition, if $i_0^- = \max\{j : \frac{1}{j} \sum_{i=1}^j \nu_{[i]}^{0+} \leq \alpha_L, i \leq k_-\}$ and $i_0^+ = \min\{m - j + 1 : \frac{1}{j} \sum_{i=1}^j \nu_{[j]}^{0-} \leq \alpha_R, j \leq m - k_+ + 1\}$, then the constrained Bayes rule $\delta_B^{(2)}$ selects H_-^i for all i associated with $y_{[1]}, \dots, y_{[i_0^-]}$, selects H_+^i for all i associated with $y_{[i_0^+]}, \dots, y_{[m]}$, and selects H_0^i for all other i .

Note that, Theorem 2 implies that $T_+(y_i)$ and $T_-(y_i)$ need not be computed for all y_i . This will save a lot of computation time when m is very large. Some more simplification in the computation is possible if $\pi_-(\theta_i)$ and $\pi_+(\theta_i)$ are such that $\pi_+(\theta_i) = \pi_-(-\theta_i)$, and if $f(y_i|\theta_i) = f(y_i'|-\theta_i)$ for some y_i' . Then it can be seen that $T_-(y_i) = T_+(y_i')$. For example, in the binomial case, where $y_i \sim b(n, p_i)$, $i = 1, 2, \dots, m$, consider the problem of testing $H_0^i : \theta_i = 0$ vs. $H_-^i : \theta_i < 0$ or $H_+^i : \theta_i > 0$, where $\theta_i = \log p_i / (1 - p_i)$. If $\pi_+(\theta_i) = \pi_-(-\theta_i)$, then $T_-(y_i) = T_+(n - y_i)$. A similar point can be made about the normal distributions as shown later.

4.1 Determination of p_- , p_+ , and p_0

The Bayes rules as described above are sensitive to the choice of (p_-, p_0, p_+) . If the true values of these probabilities are not available, they need to be estimated from the data itself. The EM algorithm can be used to estimate (p_-, p_0, p_+) by maximizing the marginal likelihood function. Note that the marginal likelihood is given by

$$L(p_-, p_0, p_+|y) = \prod_{i=1}^m [p_- f(y_i|H_-^i) + p_0 f(y_i|0) + p_+ f(y_i|H_+^i)].$$

It is easy to see that the iterative solution of the EM algorithm is given by

$$\hat{p}_-^{(j+1)} = \frac{1}{m} \sum_{i=1}^m \frac{\hat{p}_-^{(j)} T_-(y_i)}{\hat{p}_-^{(j)} T_-(y_i) + \hat{p}_+^{(j)} T_+(y_i) + \hat{p}_0^{(j)}}$$

$$\begin{aligned}\hat{p}_0^{(j+1)} &= \frac{1}{m} \sum_{i=1}^m \frac{\hat{p}_0^{(j)}}{\hat{p}_-^{(j)} T_-(y_i) + \hat{p}_+^{(j)} T_+(y_i) + \hat{p}_0^{(j)}} \\ \hat{p}_+^{(j+1)} &= \frac{1}{m} \sum_{i=1}^m \frac{\hat{p}_+^{(j)} T_+(y_i)}{\hat{p}_-^{(j)} T_-(y_i) + \hat{p}_+^{(j)} T_+(y_i) + \hat{p}_0^{(j)}}\end{aligned}$$

4.2 Normal Populations

Let $y_i \sim N(\theta_i, \sigma^2/n)$. We consider the priors π_- and π_+ as the left and the right truncated $N(0, \sigma^2/\omega)$ priors, where ω is some positive constant. Then $\pi_+(\theta_i) = \pi_-(-\theta_i)$, and thus it is easy to see that $T_-(y_i) = T_+(-y_i)$, where

$$T_+(y_i) = 2\sqrt{\frac{\omega}{n+\omega}} \exp\left\{\frac{n^2 y_i^2}{2(n+\omega)\sigma^2}\right\} \Phi\left(\frac{ny_i}{\sigma\sqrt{n+\omega}}\right) \quad (27)$$

Since the density of Y_i is MLR in y_i , Theorem 2 can be applied. Thus, from Theorem 2, the Bayes rule $\delta_B^{(0)}$ can be stated as follows:

Let

$$\begin{aligned}k_- &= \max\left\{i : y_{[i]} < -c_p \frac{\sigma\sqrt{n+\omega}}{n}, p_- T_+(-y_{[i]}) > p_0\right\} \\ k_+ &= \min\left\{i : y_{[i]} > -c_p \frac{\sigma\sqrt{n+\omega}}{n}, p_+ T_+(y_{[i]}) > p_0\right\},\end{aligned} \quad (28)$$

where c_p is the $p_+/(p_+ + p_-)$ th percentile of $N(0, 1)$. Then select H_-^i for all i associated with $y_{[1]}, \dots, y_{[k_-]}$; select H_+^i for all i associated with $y_{[k_+]}, \dots, y_{[m]}$; and select H_0^i for all other i .

The constrained Bayes rules $\delta_B^{(1)}$ and $\delta_B^{(2)}$ can also be computed as described in Theorem 2 with

$$\nu_{[i]}^{0-} = \frac{p_- T_+(-y_{[i]}) + p_0}{p_- T_+(-y_{[i]}) + p_+ T_+(y_{[i]}) + p_0}, \text{ for } i \geq k_+$$

and

$$\nu_{[i]}^{0+} = \frac{p_+ T_+(y_{[i]}) + p_0}{p_- T_+(y_{[i]}) + p_+ T_+(y_{[i]}) + p_0}, \text{ for } i \leq k_-,$$

Note that, because of monotonicity of $T_+(\cdot)$, $\nu_{[1]}^{0+} \leq \dots \leq \nu_{[k_-]}^{0+}$ and $\nu_{[m]}^{0-} \leq \dots \leq \nu_{[k_+]}^{0-}$.

From Subsection 3.3, the following Bayes rule attains exact $BDFDR = \alpha$:

Select H_0^i if $\nu_i^- > c_0 \nu_i^0$ and $\nu_i^- > \nu_i^+$; select H_+^i if $\nu_i^+ > c_0 \nu_i^0$ and $\nu_i^+ > \nu_i^-$;

otherwise, select H_0^i .

Here the constant c_0 is such that the (21) is satisfied. Using the same arguments as in the proof of Theorem 2, it can be seen that the Bayes rule selects H_-^i for all i associates with $y_{[1]}, \dots, y_{[k_-(c_0)]}$; selects H_+^i for all i associated with $y_{[k_+(c_0)]}, \dots, y_{[m]}$; and selects H_0^i for all other i , where

$$k_-(c_0) = \max\left\{i : y_{[i]} < -c_p \frac{\sigma\sqrt{n+\omega}}{n}, p_-T_+(-y_{[i]}) > c_0p_0\right\}$$

$$k_+(c_0) = \min\left\{i : y_{[i]} > -c_p \frac{\sigma\sqrt{n+\omega}}{n}, p_+T_+(y_{[i]}) > c_0p_0\right\}.$$

The constant c_0 does not depend on σ , and thus a general table can be created for a specific sample size for this cut-off point. For example, when sample size $n = 10$ for all i with $\omega = 1$, Figure 1 shows the graph of $BDFDR$ (computed through simulation) as a function of c_0 for $p_+ = 0.4$ and $p_- = 0.1$. From this, for $\alpha = 0.05$, we obtain $c_0 = 2.896$. The Table 2 shows c_0 values for comparison purpose for different configuration of n and (p_-, p_0, p_+) . As we see that a smaller c_0 value is required for a larger n .

Table 2: c_0 value for an exact $BDFDR = 0.05$

(p_-, p_0, p_+)	$n = 5$	$n = 10$	$n = 20$
(0.4, 0.5, 0.1)	4.435	2.896	1.921
(0.1, 0.8, 0.1)	4.020	2.595	1.678
(0.08, 0.90, 0.02)	3.985	2.584	1.645

[Figure 1]

5 Simulation Results

We now use simulation to illustrate the performance of $\delta_B^{(0)}, \delta_B^{(1)}, \delta_B^{(2)}$ and compare them to the Benjamini-Hochberg (BH) procedure. We generated y_i from $N(\theta_i, 1/n)$, and θ_i from (3) with π_- and π_+ as left and right truncated standard normal densities, respectively, for different choices of (p_-, p_0, p_+) . Note that the Benjamini-Hochberg procedure is based on two-tailed test. Thus, to adapt it to the directional hypothesis (1), upon rejecting H_0^i , we select H_-^i if $y_i < 0$, and H_+^i if $y_i > 0$. The following quantities will be used to compare the results: left-tailed correct discovery rate ($LCDR$), right-tailed correct discovery rate ($RCDR$), left-tailed false non-discovery rate ($LFNDR$),

and right-tailed false non-discovery rate (*RFNDR*), defined by

$$\begin{aligned} LCDR &= E\left[\frac{V_-}{V}\right], \quad RCDR = E\left[\frac{W_+}{W}\right], \\ LFNDR &= E\left[\frac{U_-}{U}\right], \quad RFNDR = E\left[\frac{U_+}{U}\right]. \end{aligned} \quad (29)$$

Note that the expectations above are with respect to both \mathbf{X} and $\boldsymbol{\theta}$. *LCDR* and *RCDR* reflects the power of the tests for the proportion of correct discoveries of left tail and right tail hypotheses, respectively. *LFNDR* and *RFNDR* reflects the false non-discoveries in left and right directions, respectively. The reason the latter rates are important is that a poor test might have a high proportion of correct discoveries but too many of true left and right tails might be declared null. A large error rates of *LFNDR* and *RFNDR* will clearly reflect this.

Note that all quantities in (29) depend on the k_- and k_+ of (28) and $T_+(y_i)$ as defined in (27). It is easy to see that k_- , k_+ and $T_+(y_i)$ are all invariant with respect to σ . Thus, without loss of generality, all comparisons made here can be stated for any σ .

Tables 3-5 are based on the simulation of 5,000 repetitions with $m = 1000$ and $n = 10$. In Table 3, the *BH* procedure is based on *FDR* level of 0.05. In Table 4, the constrained Bayes rule $\delta_B^{(1)}$ is based on *BDFDR* ($= \alpha$) of 0.05, and in Table 5, the constrained Bayes rule $\delta_B^{(2)}$ is based on *BLFDR* ($= \alpha_L$) of 0.025 and *BRFDR* ($= \alpha_R$) of 0.025.

[Tables 3-5]

Note that in all cases we have chosen $p_+ > p_-$. The results of *BH* are highly non-symmetrical depending upon the values of p_- and p_+ . Generally for the *BH* rules, the correct discovery rates *LCDRs* for the left tails are much lower than correct discovery rates *RCDRs* for the right tails. However, for both $\delta_B^{(1)}$ and $\delta_B^{(2)}$, both rates are balanced and very high. For example when $(p_-, p_+) = (0.05, 0.3)$, the *BH* rule has a correct discovery rate of 0.7429 in the left tail as compared to the correct discovery rate of 0.9547 for $\delta_B^{(1)}$ and 0.9789 for $\delta_B^{(2)}$. For the microarray data analysis this would mean that if a particular cell-line generate more of overexpressed genes than underexpressed gene, then the *BH* rule would falsely select underexpressed genes with high proportion in comparison to $\delta_B^{(1)}$ or $\delta_B^{(2)}$. A similar point can be made about false non-discoveries. When $p_+ > p_-$, *RFNDR* is relatively large for *BH*, meaning a high percentage of right tails are declared null. For the microarray data analysis, this means that a higher

percentage of overexpressed genes are declared null under BH rule when compared to $\delta_B^{(1)}$ or $\delta_B^{(2)}$. Overall conclusion is that if the selection of overexpressed genes is more likely, then $\delta_B^{(1)}$ or $\delta_B^{(2)}$ outperform BH rule. When comparing $\delta_B^{(1)}$ and $\delta_B^{(2)}$, $\delta_B^{(2)}$ has a better correct discovery rates than the $\delta_B^{(1)}$, but false non-discovery rates are mostly higher for $\delta_B^{(2)}$.

6 Microarray analysis for an experiment involving microRNA

Biologists believe that certain noncoding RNAs, called microRNAs, regulate gene expressions of coding genes in plants and animals [3]. Several microRNAs have been found to have links to some types of cancer [8]. Lim et al. [7] discuss an experiment in which a microRNA, miR-124, is transfected into HeLa cells. Gene expression data of this experiment is available through <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSM37600>. We analyze this data through the methodology developed in this paper and compare the results with that of BH's FDR. The data presents the average \log_{10} ratios of gene expressions for 23,401 mRNAs including standard error estimates. Lim et al. [7] hypothesized that miR-124 downregulates a large number of target mRNAs. If this hypothesis is true, then it can be expected that more of the genes will be underexpressed than overexpressed. Descriptively, this can be seen from the boxplot of the z-values (Figure 2), where z-values are the normalized \log_{10} ratio, normalized by the standard error estimates.

[Figure 2]

We assume that

$$Z_i \sim N(\theta_i, 1), \quad i = 1, 2, \dots, 23,401$$

For the prior on θ_i , We assume that θ_i s are generated from the prior

$$\pi(\theta) = p_- \pi_-(\theta) + p_0 I(\theta = 0) + p_+ \pi_+(\theta),$$

where $\pi_-(\cdot)$ and $\pi_+(\cdot)$ are the truncated $N(0, \sigma_a^2)$ densities.

All of the computations were carried out using MATLAB R2012b. We used method of moments to estimate σ_a^2 . Using the EM algorithm as discussed in subsection 4.1, we estimated p_- , p_+ , and p_0 . The estimates of p_- , p_+ , and p_0 are given by

$$\hat{p}_- = 0.0201, \quad \hat{p}_+ = 0.0057, \quad \hat{p}_0 = 1 - \hat{p}_- - \hat{p}_+ = 0.9742$$

These estimates suggest that a higher percentage of genes are underexpressed than overexpressed. The Table 6 shows the selected number of underexpressed, overexpressed, and non-expressed genes based on BH’s FDR methodology, and the constrained Bayesian methodology as presented in Section 4. Both FDR and PDFDR were controlled at the level of 0.05. For BH’s FDR methodology we declared the selected genes as underexpressed if the z-values were negative and overexpressed if the z-values were positive.

Table 6: Number of selected genes using constrained Bayes rule with PDFDR=0.05, and BH with FDR of 0.05

Selection	Constrained Bayes Rule	BH rule
Underexpressed	116	101
Non-expressed	23,263	23,264
Overexpressed	22	36

We see in Table 6 that the constrained Bayes rule selected a few more genes as underexpressed than the BH’s rule. While the opposite is true for the selection of overexpressed genes. Note that if the estimates \hat{p}_- , \hat{p}_+ , and \hat{p}_0 are the true values of p_- , p_+ , and p_0 respectively, then the expected number of false discoveries for the constrained Bayes rule would be lower than that of BH rule, since it is a Bayes rule. And, since m is very large, it can be expected that the maximum likelihood estimates \hat{p}_- , \hat{p}_+ , and \hat{p}_0 are closed to the true values of p_- , p_+ , and p_0 , respectively. In addition, although, more genes are selected as underexpressed by Bayes rule, more of these are expected to be true in expectation as we pointed out in the remark following Theorem 1.

7 Concluding Remarks

In this paper, we provided a general framework of computing Bayes decision rule for the directional multiple hypothesis problem when the left and the right hypotheses are asymmetrically generated. The decision rules we derived attain Bayesian optimality with a controlled directional false discovery rates. The false discovery rates we considered can be controlled in left and right directions combined, or separately. The methodologies presented here are useful in many practical situations where it is expected that one direction is more probable than the other. We show through simulation that taking this information into account yields better decision rules than a traditional FDR

rule. We also show for a microarray analysis that more of the genes were selected in the region of interest, which might have been missed if the skewness in the prior was not taken into account. We also showed that if the densities have monotone likelihood ration (MLR) property, then the Bayes rule takes a very simple form. In that case, the Bayes rule can be obtained in the form of the ranked values of the sufficient statistics; and additionally, only a simple non-linear computation is required to find the cut-off points.

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A Appendix

A.1 Estimation of $E[g(\theta_i, \eta)|\mathbf{x}]$ for a non-linear function g

Here, we assume that \mathbf{X} can be reduced to a sufficient statistic (\mathbf{Y}, S) such that $\mathbf{Y} = (Y_1, Y_2, \dots, Y_m)^T$ is a vector of independent variates with $Y_i \sim f(y_i; \theta_i, \eta)$, $i = 1, \dots, m$, and where \mathbf{Y} and S are independently distributed, and the distribution of S is independent of $\boldsymbol{\theta}$. When η is kept fixed, the computation of $E[g(\theta_i, \eta)|\mathbf{x}]$ is based on the posterior distribution of θ_i given y_i and η . Suppose the resulting expression is $h(\eta|y_i)$. It can be seen that the posterior expectation of $h(\eta|y_i)$ is

$$E[h(\eta|y_i)|\mathbf{x}] = \frac{f_*(s)}{f_*(y_i, s)} \int h(\eta|y_i) f_*(y_i|\eta) \pi(\eta|s) d\eta, \quad (30)$$

where $f_*(s)$, $f_*(y_i, s)$ are the marginal densities of S and (Y_i, S) respectively; $f_*(y_i|\eta)$ is the marginal density of y_i given η ; and $\pi(\eta|s)$ is the posterior density of η given $S = s$. Note that $\pi(\eta|s)$ does not depend on $\boldsymbol{\theta}$. Now, suppose $\pi(\eta|s) \propto \exp(-mg_m(\eta))$, where g_m is of order $O(1)$. In this case, using Laplace approximation, it can be shown (Severini [12], section 2.11) that

$$\int h(\eta|y_i) f_*(y_i|\eta) \pi(\eta|s) d\eta \doteq h(\hat{\eta}|y_i) f_*(y_i|\hat{\eta}) \frac{\sqrt{2\pi}}{\sqrt{mg_m''(\hat{\eta})}} \exp\{-mg_m''(\hat{\eta})\}$$

with the remainder term of order $O(1/m)$, where $\hat{\eta}$ the posterior mode. Thus, from (30), we have

$$E[h(\eta|y_i)|\mathbf{x}] \doteq \frac{f_*(s)}{f_*(y_i, s)} f_*(y_i|\hat{\eta}) h(\hat{\eta}|y_i) \frac{\sqrt{2\pi}}{\sqrt{mg_m''(\hat{\eta})}} \exp\{-mg_m''(\hat{\eta})\} \quad (31)$$

A.2 Bayes rule in the presence of the nuisance parameter η

Since $f_*(s)$, $f_*(y_i, s)$ and $f_*(y_i|\hat{\eta})$ does not depend on the function h and since the Bayes rules only depend on the ratios of the expressions (31) for different h functions, the Bayes rule can be expressed approximately in terms of $h(\hat{\eta}|y_i)$ alone for large m . Regarding the assumption that $\pi(\eta|s) \propto \exp(-mg_m(\eta))$, this would typically be the case if S is composed of *i.i.d.* copies (S_i , $i = 1, 2, \dots, m$). In many practical cases, this would be the case; for example, when the observed variables are $X_{ij} = \theta_i + \varepsilon_{ij}$, where ε_{ij} are independently and identically distributed with distribution independent of θ_i , $i = 1, 2, \dots, m$. In this case $S_i = \sum_j (X_{ij} - \bar{X}_i)^2$, and in this case the posterior distribution $\pi(\eta|s)$ satisfies the desired condition.

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Table 3: Left- and right-tailed correct discovery rates and false non-discovery rates of BH

(p_-, p_+)	$LCDR$	$RCDR$	$LFNDR$	$RFNDR$
(0.1, 0.8)	0.9260	0.9938	0.0899	0.7185
(0.1, 0.6)	0.8403	0.9735	0.0734	0.4423
(0.1, 0.4)	0.8337	0.9548	0.0652	0.2611
(0.05, 0.4)	0.7162	0.9553	0.0318	0.2551
(0.1, 0.3)	0.8456	0.9441	0.0626	0.1879
(0.05, 0.3)	0.7429	0.9471	0.0308	0.1853
(0.1, 0.2)	0.8670	0.9298	0.0612	0.1223
(0.05, 0.2)	0.7846	0.9373	0.0302	0.1217
(0.1, 0.1)	0.8987	0.8990	0.0607	0.0607
(0.05, 0.1)	0.7831	0.9362	0.0304	0.1215
(0.05, 0.05)	0.8926	0.8928	0.0313	0.0313

Table 4: Left- and right-tailed correct discovery rates
and false non-discovery rates of $\delta_B^{(1)}$

(p_-, p_+)	<i>LCDR</i>	<i>RCDR</i>	<i>LFNDR</i>	<i>RFNDR</i>
(0.1, 0.8)	0.9568	0.9496	0.1807	0.5445
(0.1, 0.6)	0.9560	0.9495	0.0992	0.3920
(0.1, 0.4)	0.9539	0.9496	0.0794	0.2513
(0.05, 0.4)	0.9547	0.9502	0.0414	0.2465
(0.1, 0.3)	0.9535	0.9500	0.0734	0.1873
(0.05, 0.3)	0.9547	0.9503	0.0386	0.1841
(0.1, 0.2)	0.9520	0.9506	0.0690	0.1263
(0.05, 0.2)	0.9532	0.9509	0.0360	0.1242
(0.1, 0.1)	0.9512	0.9518	0.0656	0.0656
(0.05, 0.1)	0.9542	0.9503	0.0362	0.1240
(0.05, 0.05)	0.9538	0.9531	0.0339	0.0339

Table 5: Left- and right-tailed correct discovery rates
and false non-discovery rates of $\delta_B^{(2)}$

(p_-, p_+)	<i>LCDR</i>	<i>RCDR</i>	<i>LFNDR</i>	<i>RFNDR</i>
(0.1, 0.8)	0.9766	0.9750	0.1459	0.6177
(0.1, 0.6)	0.9769	0.9752	0.0968	0.4293
(0.1, 0.4)	0.9768	0.9754	0.0816	0.2728
(0.05, 0.4)	0.9788	0.9753	0.0425	0.2679
(0.1, 0.3)	0.9769	0.9756	0.0766	0.2023
(0.05, 0.3)	0.9789	0.9756	0.0401	0.1989
(0.1, 0.2)	0.9771	0.9760	0.0728	0.1354
(0.05, 0.2)	0.9793	0.9760	0.0379	0.1334
(0.1, 0.1)	0.9771	0.9771	0.0697	0.0697
(0.05, 0.1)	0.9805	0.9755	0.0381	0.1331
(0.05, 0.05)	0.9805	0.9799	0.0359	0.0359

