Classes of Multiple Decision Functions Strongly Controlling FWER and FDR\footnote{The authors acknowledge support from National Science Foundation (NSF) Grant DMS 0805809, National Institutes of Health (NIH) Grant RR17698, and Environmental Protection Agency (EPA) Grant RD-83241902-0 to University of Arizona with subaward number Y481344 to the University of South Carolina.}

Edsel A. Peña\footnote{E. Peña is Professor, Department of Statistics, University of South Carolina, Columbia. E-Mail: pena@stat.sc.edu.} \hspace{0.5cm} Joshua D. Habiger\footnote{J. Habiger is a PhD student in the Department of Statistics, University of South Carolina, Columbia. E-Mail: habigerj@mailbox.sc.edu.} \hspace{0.5cm} Wensong Wu\footnote{W. Wu is a PhD student in the Department of Statistics, University of South Carolina, Columbia. E-Mail: wu26@mailbox.sc.edu.}

Department of Statistics
University of South Carolina
Columbia, SC 29208 USA

July 16, 2010
Abstract

This paper provides two general classes of multiple decision functions where each member of the first class strongly controls the family-wise error rate (FWER), while each member of the second class strongly controls the false discovery rate (FDR). These classes offer the possibility that an optimal multiple decision function with respect to a pre-specified criterion, such as the missed discovery rate (MDR), could be found within these classes. Such multiple decision functions can be utilized in multiple testing, specifically, but not limited to, the analysis of high-dimensional microarray data sets.
Keywords and Phrases: false discovery rate; family wise error rate; missed discovery rate; multiple decision problem; multiple testing; strong control.

1 Introduction

Consider the situation which arises in the analysis of high-dimensional data, epitomized by a microarray data, where $M$ pairs of null and alternative hypotheses, $(H_{m0}, H_{m1}), m = 1, 2, \ldots, M$, are simultaneously tested; see, for instance, [5, 6] for concrete examples of such situations. Two commonly-used Type I error rates for this multiple testing problem are the family-wise error rate (FWER), which is the probability of at least one false discovery, where discovery means rejecting (accepting) a null (an alternative) hypothesis, and the false discovery rate (FDR), which is the expectation of the ratio of the number of false discoveries over the number of discoveries. The usual testing paradigm employed in these situations is to decide on the collection of statistical tests for the $M$ pairs of hypotheses, e.g., a $t$-test for each pair, obtain the $p$-value for each test, and then use the resulting $M$ $p$-values in the FWER-controlling sequential Šidák procedure, provided an independence condition is satisfied, or the FDR-controlling procedure in [1]. In this conventional approach, there appears to be no leeway in the choice of the multiple testing procedure the moment the individual test procedures have been chosen.

However, we pose the following question. If we are given the $M$ test procedures for each of the $M$ pairs of hypotheses, could we obtain classes of multiple testing procedures whose elements either control the FWER or the FDR? If the answer to this question is in the affirmative, then we may be able to find a multiple testing procedure within these classes which is optimal with respect to some chosen Type II error rate. And, we may then be able to choose the starting collection of test functions that will provide the best multiple testing procedure.

This paper is in this spirit. We will demonstrate that, under certain conditions, when given a collection of test functions for the $M$ pairs of hypotheses, that we can generate classes of multiple testing procedures controlling the FWER or the FDR. The results have important implications in the search for optimal multiple testing procedures that control either of these Type I error rates as we will see later. We shall investigate these issues in a general, but not surprisingly, more abstract framework. The main results in this paper were motivated by those in [14, 15] which did not deal with classes of multiple testing procedures, but instead focused in developing improved FWER and FDR-controlling procedures from the Neyman-Pearson most powerful tests for each of the $M$ pairs of hypotheses.
2 Mathematical Setting

Let \((\mathcal{X}, \mathcal{F}, \mathcal{P})\) be a statistical model, so \((\mathcal{X}, \mathcal{F})\) is a measurable space and \(\mathcal{P}\) is a collection of probability measures on \((\mathcal{X}, \mathcal{F})\). Though not needed in the abstract development, for concreteness we may adopt the usual interpretation that \(\mathcal{X}\) is the space of possible realizations of an observable random entity \(X\) from an experiment or a study. In decision problems with action space \(\mathfrak{A} = \{0, 1\}\), such as in hypothesis testing, a nonrandomized decision function is a \(\delta : (\mathcal{X}, \mathcal{F}) \to (\mathfrak{A}, \sigma(\mathfrak{A}))\). In the hypothesis testing setting, given \(X = x \in \mathcal{X}\), a decision \(\delta(x) = 0\) corresponds to deciding in favor of a null hypothesis \((H_0)\), whereas a decision of \(\delta(x) = 1\), a 
\textit{discovery}, corresponds to rejecting \(H_0\) in favor of an alternative hypothesis \((H_1)\).

It suffices to restrict ourselves to nonrandomized decision functions since, through the use of an auxiliary randomizer which is usually a standard uniform variable \(U\) that is independent of \(X\), we can always convert a randomized decision function \(\delta^* : (\mathcal{X}, \mathcal{F}) \to ([0, 1], \sigma([0, 1]))\) into a nonrandomized decision function \(\delta : (\mathcal{X} \times [0, 1], \mathcal{F} \otimes \sigma[0, 1]) \to (\mathfrak{A}, \sigma(\mathfrak{A}))\) via \(\delta(x, u) = I\{u \leq \delta^*(x)\}\) with \(I\{\cdot\}\) the indicator function.

Thus, in our general formulation, the sample space \(\mathcal{X}\) may actually represent a product space between a data space and \([0, 1]\). This framework is appropriate, for instance, when dealing with discrete data or when using nonparametric decision functions. For more discussions on this matter, see [14, 10].

Decision or test functions typically depend on a size parameter \(\alpha \in [0, 1]\). For example, when testing the null hypothesis \(H_0 : \mu = 0\) versus the alternative hypothesis \(H_1 : \mu \neq 0\) based on a random observable \(X \sim N(\mu, 1)\), the size-\(\alpha\) test \(\delta : \mathcal{X} \equiv \mathbb{R} \to \{0, 1\}\) has \(\delta(x; \alpha) = I\{|x| > \Phi^{-1}(1 - \alpha/2)\}\), where \(\Phi^{-1}(\cdot)\) is the quantile function of the standard normal distribution. Henceforth, in order to simplify our notation, we shall adopt a functional notation where \(\delta(\alpha)\) represents the statistic defined on \(\mathcal{X}\) according to \(x \mapsto \delta(x; \alpha)\). Now, when viewed as a process in \(\alpha\), we then obtain the notion of a (nonrandomized) decision process introduced in [13], which is a stochastic process \(\Delta = \{\delta(\alpha) : \alpha \in [0, 1]\}\) where, \(\forall \alpha \in [0, 1]\), \(\delta(\alpha)\) is a decision function, and such that the following conditions are satisfied.

\begin{enumerate}
  \item[(D1)] \(\delta(0) = 0\) and \(\delta(1) = 1\) a.e.-\(\mathcal{P}\).
  \item[(D2)] The sample paths \(\alpha \mapsto \delta(\alpha)\) are, a.e.-\(\mathcal{P}\), \(\{0, 1\}\)-valued step-functions which are nondecreasing and right-continuous.
\end{enumerate}

Let \(\mathcal{M}\) be a finite set with \(|\mathcal{M}| = M\). An \(\mathcal{M}\)-indexed multiple decision problem is one whose action space is \(\mathfrak{A}^M\). In the context of a multiple hypotheses testing problem, for each \(m \in \mathcal{M}\), there is a pair of hypotheses \(H_{m0}\) and \(H_{m1}\). Of interest is to simultaneously decide between \(H_{m0}\) and \(H_{m1}\) for each \(m \in \mathcal{M}\). A multiple decision function (MDF) for such a problem is a \(\delta = (\delta_m : m \in \mathcal{M})\) where \(\delta_m\) is a decision function, so that \(\delta : (\mathcal{X}, \mathcal{F}) \to (\mathfrak{A}^M, \sigma(\mathfrak{A}^M))\). A multiple decision process (MDP) is a \(\Delta = (\Delta_m : m \in \mathcal{M})\) where \(\Delta_m = \{\delta_m(\alpha) : \alpha \in [0, 1]\}\) is a decision process.
For each $P \in \mathcal{P}$, let there be subsets $\mathcal{M}_0(P)$ and $\mathcal{M}_1(P)$ of $\mathcal{M}$ such that

$$\mathcal{M} = \mathcal{M}_0(P) \cup \mathcal{M}_1(P) \quad \text{and} \quad \mathcal{M}_0(P) \cap \mathcal{M}_1(P) = \emptyset.$$ 

We shall assume that the following condition holds.

(D3) Under $P$, the subcollections $\{\Delta_m : m \in \mathcal{M}_0(P)\}$ and $\{\Delta_m : m \in \mathcal{M}_1(P)\}$ are independent of each other, and the elements of $\{\Delta_m : m \in \mathcal{M}_0(P)\}$ are independent.

In the multiple hypotheses testing situation, $H_{m_0}$ is true under $P$ if and only if $m \in \mathcal{M}_0(P)$. Observe that the elements of $\{\Delta_m : m \in \mathcal{M}_1(P)\}$ need not be independent of each other, under $P$. We shall also assume that

(D4) With $E_P(\cdot)$ denoting the expectation operator under $P$, then $\forall P \in \mathcal{P}, \forall m \in \mathcal{M}_0(P), \forall \alpha \in [0,1]$, we have $E_P\{\delta_m(\alpha)\} = \alpha$.

The collection of all $\mathcal{M}$-indexed multiple decision processes satisfying conditions (D1)–(D4) will be denoted by $\mathcal{D}$. We remark that the requirement of equality in (D4) given by $E_P\{\delta_m(\alpha)\} = \alpha$ will usually be fulfilled in many situations since an auxiliary randomizer is incorporated in our framework, though there may still be situations when dealing with non-regular families of distributions where this condition may not be satisfied. The latter will manifest itself when the decision functions already have power equal to one but without yet requiring their sizes to equal one.

Let $A = (A_m : m \in \mathcal{M})$ be an $\mathcal{M}$-indexed collection of measurable functions with $A_m : ([0,1], \sigma[0,1]) \to ([0,1], \sigma[0,1])$. We assume that, for each $m \in \mathcal{M}$, the following conditions are satisfied:

(A1) $A_m(0) = 0$ and $A_m(1) = 1$.

(A2) The mapping $\alpha \mapsto A_m(\alpha)$ is continuous and strictly increasing.

(A3) $\forall \alpha \in [0,1], \prod_{m \in \mathcal{M}}[1 - A_m(\alpha)] \geq 1 - \alpha$.

(A4) $\forall \alpha \in [0,1], \forall P \in \mathcal{P} : |\mathcal{M}_0(P)| \max_{m \in \mathcal{M}_0(P)} A_m(\alpha) \leq \sum_{m \in \mathcal{M}} A_m(\alpha)$.

Such an $A$ will be called a multiple decision size function. The collection of all $\mathcal{M}$-indexed multiple decision size functions will be denoted by $\mathcal{S}$. A particular element of $\mathcal{S}$ is the Sidak multiple decision size function (cf., [22]) $A^S_m = (A^S_m : m \in \mathcal{M})$ with

$$A^S_m(\alpha) = 1 - (1 - \alpha)^{1/M}, \quad \alpha \in [0,1], m \in \mathcal{M}. \quad (2.1)$$

Another particular element of $\mathcal{S}$ is the Bonferroni size function $A^B = (A^B_m : m \in \mathcal{M})$ with

$$A^B_m(\alpha) = \alpha/M, \quad \alpha \in [0,1], m \in \mathcal{M}. \quad (2.2)$$
Before proceeding we also recall the notion of generalized $P$-value statistics; see [14].

Given a $\Delta \in \mathcal{D}$ and an $A \in \mathcal{S}$, we define for $m \in \mathcal{M}$ the random variable

$$\alpha_m \equiv \alpha_m(\Delta, A) = \inf \{ \alpha \in [0, 1] : \delta_m(A_m(\alpha)) = 1 \}.$$  \hfill (2.3)

The collection $(\alpha_m(\Delta, A) : m \in \mathcal{M})$ is called the vector of generalized $P$-value statistics associated with the pair $(\Delta, A)$. Observe that the usual $P$-value statistic associated with $\delta_m$ is $P_m = A_m(\alpha_m)$, hence the use of the adjective generalized for the $\alpha_m$s. We shall assume without much loss of generality that these generalized $P$-values are a.e. $[\mathcal{P}]$ distinct.

### 3 Main Theorems and Classes of MDFs

We shall present in this section the two main results that will enable the construction of the classes of multiple decision functions controlling FWER and FDR.

Given a $\Delta = \{ \Delta_m : m \in \mathcal{M} \} \in \mathcal{D}$, an $A = \{ A_m : m \in \mathcal{M} \} \in \mathcal{S}$, a $P \in \mathcal{P}$, and an $\alpha \in [0, 1]$, define the stochastic processes

$$S_0(\alpha) \equiv S_0(\alpha; \Delta, A, P) = \sum_{m \in \mathcal{M}_0(P)} \delta_m(A_m(\alpha));$$  \hfill (3.1)

$$S(\alpha) \equiv S(\alpha; \Delta, A) = \sum_{m \in \mathcal{M}} \delta_m(A_m(\alpha));$$  \hfill (3.2)

$$F(\alpha) \equiv F(\alpha; \Delta, A, P) = S_0(\alpha)I\{ S(\alpha) > 0 \},$$  \hfill (3.3)

with the convention that $0/0 = 0$. These quantities have the following interpretations. Given an $\alpha \in [0, 1]$, for each $m \in \mathcal{M}$, the decision function whose size is $A_m(\alpha)$ is chosen from $\Delta_m$, and the MDF $\delta(\alpha) \equiv (\delta_m[A_m(\alpha)] : m \in \mathcal{M})$ will be employed in the decision-making. For this MDF $\delta(\alpha)$, then $S_0(\alpha)$ is the number of false discoveries, $S(\alpha)$ is the number of discoveries, and $F(\alpha)$ is the proportion of false discoveries among all discoveries. Observe, however, that since $P$ is unknown, both $S_0$ and $F$ are unobservable, whereas $S$ is observable.

For $q \in [0, 1]$, let us also define the random variables

$$\alpha^\dagger(q) \equiv \alpha^\dagger(q; \Delta, A) = \inf \left\{ \alpha \in [0, 1] : \prod_{m \in \mathcal{M}_0(P)} [1 - A_m(\alpha)]^{1 - \delta_m(A_m(\alpha))} < 1 - q \right\};$$  \hfill (3.4)

and

$$\alpha^*(q) \equiv \alpha^*(q; \Delta, A) = \sup \left\{ \alpha \in [0, 1] : \sum_{m \in \mathcal{M}} A_m(\alpha) \leq qS(\alpha; \Delta, A) \right\}.$$  \hfill (3.5)
In essence, $\alpha^\dagger(q)$ is a first crossing-time random variable, whereas $\alpha^\ast(q)$ is a last crossing-time random variable. The forms of these two random variables were motivated and justified in Sections 6 and 7 in \cite{14} for a specific multiple decision size function, but the justifications in that paper carry over to the more general setting considered here.

The two main results of this paper are contained in Theorem 3.1 and Theorem 3.2. We present the statements of these theorems, but defer their proofs to Section 4 after some discussions about their implications and potential usefulness.

Theorem 3.1 Under conditions (D1)–(D4) for $\mathcal{D}$ and (A1)–(A3) for $\mathcal{S}$, we have that $\forall P \in \mathcal{P}, \forall \Delta \in \mathcal{D}, \forall A \in \mathcal{S}, \forall q \in [0, 1]$,

$$E_P \{ I \{ S_0(\alpha^\dagger(q; \Delta, A); \Delta, A, P) \geq 1 \} \} \leq q.$$  

Observe that $E_P \{ I \{ S_0(\alpha^\dagger(q; \Delta, A); \Delta, A, P) \geq 1 \} \}$ is the FWER since it is the probability of committing at least one false discovery when the true underlying probability measure is $P$. Thus, Theorem 3.1 shows that for any $q \in [0, 1]$, any multiple decision process $\Delta \in \mathcal{D}$, and any multiple decision size function $A \in \mathcal{S}$, the MDF defined via

$$\delta^\dagger(q) \equiv \delta^\dagger(q; \Delta, A) = (\delta_m[A_m(\alpha^\dagger(q; \Delta, A))]) : m \in \mathcal{M},$$  

strongly controls the FWER at $q$.

Theorem 3.2 Under conditions (D1)–(D4) for $\mathcal{D}$ and (A1)–(A4) for $\mathcal{S}$, we have that $\forall P \in \mathcal{P}, \forall \Delta \in \mathcal{D}, \forall A \in \mathcal{S}, \forall q \in [0, 1]$,

$$E_P \{ F(\alpha^\ast(q; \Delta, A); \Delta, A, P) \} \leq q.$$  

Note that $E_P \{ F(\alpha^\ast(q; \Delta, A); \Delta, A, P) \}$ is the FDR as introduced in the seminal paper of \cite{1}. The implication of Theorem 3.2 is that if, for each $q \in [0, 1]$, and for any multiple decision process $\Delta \in \mathcal{D}$ and multiple decision size function $A \in \mathcal{S}$, we define the MDF

$$\delta^\ast(q) \equiv \delta^\ast(q; \Delta, A) = (\delta_m[A_m(\alpha^\ast(q; \Delta, A))]) : m \in \mathcal{M},$$  

then $\delta^\ast(q)$ is an MDF that controls the FDR at $q$.

The importance of the preceding results is that each multiple decision process $\Delta \in \mathcal{D}$ may have an associated multiple decision size process $A \equiv A(\Delta) \in \mathcal{S}$ such that the resulting multiple decision functions $\delta^\dagger(q)$ or $\delta^\ast(q)$ possess some optimality property, for example, with respect to the missed discovery rate. To define this rate, let

$$M(\alpha) \equiv M(\alpha; \Delta, A, P) = \frac{\sum_{m \in \mathcal{M}_1(P)} (1 - \delta_m[A_m(\alpha)])}{|\mathcal{M}_1(P)|} I\{|\mathcal{M}_1(P)| > 0\}.$$
The quantity $M(\alpha)$ has the interpretation of being the proportion of missed discoveries relative to the number of correct alternative hypotheses. Then, for instance, the missed discovery rate (MDR) of the MDF in (3.7) is

$$E_P \{M(\alpha^*(q); \Delta, A, P)\}.$$ 

For the given $\Delta$, with proper choice of $A$, we may be able to find an MDF that strongly controls the FWER or the FDR, while at the same time possessing an optimal property with respect to another criterion, such as having a small, possibly maximally over $P$, MDR. This idea was implemented in a more restricted setting in [14, 15] when each of the pairs of hypotheses contained simple null and simple alternative hypotheses.

We note that previous works usually focussed in developing a particular MDF and then verifying that it controls the FWER or the FDR, such as, for example, in [1]; more comprehensively, see [4]. It is our hope that by providing a class of MDFs where each member strongly controls the FWER, given by

$$\mathcal{C}^\dagger = \{\delta^\dagger(q; \Delta, A) : \Delta \in \mathcal{D}, A \in \mathcal{G}\}; \quad (3.9)$$

or a class of MDFs where each member controls the FDR, given by

$$\mathcal{C}^* = \{\delta^*(q; \Delta, A) : \Delta \in \mathcal{D}, A \in \mathcal{G}\}, \quad (3.10)$$

then we will acquire the possibility of selecting from these classes MDFs possessing other desirable properties with respect to Type II error rates. More discussion of this issue will be provided in Section 6.

4 Proofs of the Main Theorems

The proofs of the two theorems are analogous to those of Theorem 6.1 and Theorem 7.1 in [14] which can be found in the supplemental article [15]. Note that those proofs were for special forms of the multiple decision process and multiple decision size function, whereas in the current paper we are dealing with an arbitrary element $\Delta \in \mathcal{D}$ and an arbitrary element $A \in \mathcal{G}$. In the proofs below, we assume that $\Delta \in \mathcal{D}$ and $A \in \mathcal{G}$ have been chosen and are fixed. Also, $q \in [0, 1]$ and $P \in \mathcal{P}$ denotes the unknown underlying probability measure. The dependence on $(\Delta, A, P)$ of some of the relevant processes and quantities below will not be explicitly written for brevity, unless needed for clarity.

4.1 Of Theorem 3.1

Proof: We start by defining the stochastic process $H_1 = \{H_1(\alpha) : \alpha \in [0, 1]\}$ via

$$H_1(\alpha) \equiv H_1(\alpha; \Delta, A) = \prod_{m \in \mathcal{M}} [1 - A_m(\alpha)]^{1-\delta_m(A_m(\alpha))}. \quad (4.1)$$
The sample paths of this process are, a.e. \([P]\), left-continuous with right-hand limits \((caglad)\), are piecewise nonincreasing, and with

\[
1 - \alpha \leq H_1(\alpha-) = H_1(\alpha) \leq H_1(\alpha+)
\]

for every \(\alpha \in (0, 1)\), where the first inequality is due to property (A3). In fact, by virtue of property (A1) and property (D1), note that

\[
\lim_{\alpha \downarrow 0} H_1(\alpha) = 1 \quad \text{and} \quad \lim_{\alpha \uparrow 1} H_1(\alpha) = 1.
\]

Now, in terms of \(H_1\), we have that

\[
\alpha^\dagger(q) = \inf \{ \alpha \in [0, 1] : H_1(\alpha) < 1 - q \}.
\]

Since, as pointed out above, we have \(1 - \alpha \leq H_1(\alpha)\), then by its definition, we must have \(\alpha^\dagger(q) \geq q\). This implies that

\[
H_1(\alpha^\dagger(q)) \geq 1 - q. \tag{4.2}
\]

For the quantity of main interest in the theorem, we now have

\[
E_P \left[ I \{ S_0(\alpha^\dagger(q)) \geq 1 \} \right] = P \{ S_0(\alpha^\dagger(q)) \geq 1 \} = 1 - P \{ S_0(\alpha^\dagger(q)) = 0 \} = 1 - P \left\{ \bigcap_{m \in \mathcal{M}_0(P)} [\delta_m(A_m(\alpha^\dagger(q))) = 0] \right\}.
\]

The last probability cannot, however, be written as a product of probabilities since the \(\delta_m(A_m(\alpha^\dagger(q)))\) for \(m \in \mathcal{M}_0(P)\) need not be independent owing to the dependence on \(\alpha^\dagger(q)\) which is determined by all the \((\Delta_m, m \in \mathcal{M})\). On the other hand, we do have the set equality

\[
\bigcap_{m \in \mathcal{M}_0(P)} [\delta_m(A_m(\alpha^\dagger(q))) = 0] = \left\{ \alpha^\dagger(q) < \min_{m \in \mathcal{M}_0(P)} \alpha_m \right\}, \tag{4.3}
\]

where the \(\alpha_m\)s are the generalized \(p\)-value statistics defined in \((2.3)\).

Next, define the stochastic process \(H_2 = \{ H_2(\alpha) : \alpha \in [0, 1] \}\) via

\[
H_2(\alpha) \equiv H_2(\alpha; \Delta, A, P) = \left( \prod_{m \in \mathcal{M}_0(P)} [1 - A_m(\alpha)] \right) \left( \prod_{m \in \mathcal{M}_1(P)} [1 - A_m(\alpha)]^{1 - \delta_m(A_m(\alpha)-)} \right).
\]
Analogously to the $H_1$ process, this has caglad sample paths. Let us then define the quantity
\[ \alpha^\#(q) \equiv \alpha^\#(q; \Delta, A, P) = \inf \{ \alpha \in [0, 1] : H_2(\alpha) < 1 - q \}. \]

Note that this is not a random variable since this depends on the unknown probability measure $P$, in contrast to $\alpha^\dagger(q)$. Furthermore, also note that
\[ H_2(\alpha^\#(q)) \geq 1 - q. \] (4.4)

From their definitions, $H_1(\alpha) \geq H_2(\alpha)$, so that $H_1(\alpha) < 1 - q$ implies $H_2(\alpha) < 1 - q$. Consequently,
\[ \alpha^\dagger(q) \geq \alpha^\#(q). \] (4.5)

Now, the importance of the quantity $\alpha^\#(q)$ arises because of the crucial set equality
\[ \left\{ \alpha^\dagger(q) < \min_{m \in M_0(P)} \alpha_m \right\} = \left\{ \alpha^\#(q) < \min_{m \in M_0(P)} \alpha_m \right\}. \] (4.6)

To see this equality, first observed that the inclusion $\subseteq$ immediately follows from (4.5). To prove the reverse inclusion, since
\[ \{ \alpha^\#(q) < \min_{m \in M_0(P)} \alpha_m \}, \]
implies that, for some $\alpha_0 < \min_{m \in M_0(P)} \alpha_m$, we have $H_2(\alpha_0) < 1 - q$. But for such an $\alpha_0$, we will have $\delta_m(A_m(\alpha_0)-) = 0$ for all $m \in M_0(P)$, so that
\[ \alpha_0 \in \{ \alpha \in [0, 1] : H_1(\alpha) < 1 - q \}. \]

Consequently,
\[ \alpha^\dagger(q) = \inf \{ \alpha \in [0, 1] : H_1(\alpha) < 1 - q \} \leq \alpha_0 < \min_{m \in M_0(P)} \alpha_m. \]

The reverse inclusion $\supseteq$ thus follows, completing the proof of (4.6).

By (4.3), (4.6), and the iterated expectation rule, it now follows that
\[
P \left\{ \bigcap_{m \in M_0(P)} \left[ \delta_m(A_m(\alpha^\dagger(q))) = 0 \right] \right\}
= P \left\{ \alpha^\dagger(q) < \min_{m \in M_0(P)} \alpha_m \right\}
= P \left\{ \alpha^\#(q) < \min_{m \in M_0(P)} \alpha_m \right\}
= E_P \left[ P \left\{ \alpha^\#(q) < \min_{m \in M_0(P)} \alpha_m \mid \alpha^\#(q) \right\} \right].
\]
Since $\alpha^\#(q)$ is measurable with respect to the sub-$\sigma$-field $\sigma(\delta_m : m \in M_1(P))$, whereas $\min_{m \in M_0(P)} \alpha_m$ is measurable with respect to the sub-$\sigma$-field $\sigma(\delta_m : m \in M_0(P))$, then by condition (D3), $\alpha^\#(q)$ and $\min_{m \in M_0(P)} \alpha_m$ are independent. Furthermore, by condition (D3), we obtain

$$P \left\{ \min_{m \in M_0(P)} \alpha_m > w \right\} = P \left\{ \bigcap_{m \in M_0(P)} [\delta_m(A_m(w)) = 0] \right\}$$

$$= \prod_{m \in M_0(P)} P\{\delta_m(A_m(w)) = 0\}$$

$$= \prod_{m \in M_0(P)} [1 - A_m(w)],$$

with the last equality a consequence of condition (D4). Therefore,

$$P \left\{ \bigcap_{m \in M_0(P)} [\delta_m(A_m(\alpha^\dagger(q))) = 0] \right\}$$

$$= E_P \left\{ \prod_{m \in M_0(P)} [1 - A_m(\alpha^\#(q))] \right\}$$

$$\geq E_P \left\{ \left( \prod_{m \in M_0(P)} [1 - A_m(\alpha^\#(q))] \right) \times \left( \prod_{m \in M_1(P)} [1 - A_m(\alpha^\#(q))]^{1 - \delta_m(A_m(\alpha^\#(q))) -} \right) \right\}$$

$$= E_P\{H_2(\alpha^\#(q))\}$$

$$\geq E_P(1 - q)$$

$$= 1 - q$$

with the last inequality following from (4.4). Thus, finally, we have

$$E_P \left[ I \{S_0(\alpha^\dagger(q)) \geq 1\} \right] = 1 - P \left\{ \bigcap_{m \in M_0(P)} [\delta_m(A_m(\alpha^\dagger(q))) = 0] \right\}$$

$$\leq 1 - (1 - q)$$

$$= q.$$
This completes the proof of Theorem 3.1. We remark that condition (D4) can be weakened to just having

$$\forall m \in M_0(P), \forall \alpha \in [0, 1]: \quad P\{\delta_m(\alpha)\} \leq \alpha$$

(4.7)

to still get the desired strong FWER control. This is so since in the portion of the proof where we have

$$\prod_{m \in M_0(P)} P\{\delta_m(A_m(w)) = 0\} = \prod_{m \in M_0(P)} [1 - A_m(w)],$$

we simply replace the second = sign by ≥ and then the proof of the theorem goes through.

4.2 Of Theorem 3.2

Proof: This proof closely mimics that of Theorem 7.1 in [14] as presented in [15]. As an aside, we mention that the seed of the idea of providing a class of FDR-controlling multiple decision functions was planted upon the realization that the proof of this Theorem 7.1 is independent of the choice of the multiple decision size function.

The case with $q = 0$ is trivial since then $\alpha^*(0) = 0$, so that $F(\alpha^*(0)) = 0$. Thus we restrict to $q \in (0, 1]$. By the defining property of $\alpha^*(q)$ given in (3.5), we have that

$$S(\alpha^*(q)) \geq \frac{1}{q} A_\bullet(\alpha^*(q))$$

(4.8)

where $A_\bullet(\alpha) = \sum_{m \in M} A_m(\alpha)$. Consequently, from (3.3),

$$F(\alpha^*(q)) \leq q \frac{S_0(\alpha^*(q))}{A_\bullet(\alpha^*(q))} I\{S(\alpha^*(q)) > 0\} \leq q \frac{S_0(\alpha^*(q))}{A_\bullet(\alpha^*(q))}. \quad (4.9)$$

For $\alpha \in [0, 1]$, define the sub-σ-field

$$\mathcal{F}_\alpha \equiv \mathcal{F}_\alpha(\Delta, A) = \sigma \{\delta_m(A_m(\beta)) : \beta \in [\alpha, 1], m \in M\}. \quad (4.10)$$

Observe that $\mathcal{F} = (\mathcal{F}_\alpha : \alpha \in [0, 1])$ is a decreasing collection of sub-σ-fields of $\mathcal{F}$. By its definition $\alpha^*(q)$ is an $\mathcal{F}$-stopping time.

Let us define the process $T_0(\alpha) = (T_0(\alpha) : \alpha \in [0, 1])$ according to

$$T_0(\alpha) \equiv T_0(\alpha; \Delta, A, P) = \sum_{m \in M_0(P)} \frac{\delta_m(A_m(\alpha))}{A_m(\alpha)}.$$
Fix $0 \leq \alpha \leq \beta \leq 1$. Then, since $\delta_m \in \{0,1\}$, we have

$$E_P\{T_0(\alpha)|\mathcal{F}_\beta\}$$

$$= \sum_{m \in \mathcal{M}_0(P)} E_P\left\{ \frac{\delta_m(A_m(\alpha))}{A_m(\alpha)} | \mathcal{F}_\beta \right\}$$

$$= \sum_{m \in \mathcal{M}_0(P)} \left[ \frac{1}{A_m(\alpha)} \right] P\{\delta_m(A_m(\beta)) = 1 | \mathcal{F}_\beta\} \times E_P\{\delta_m(A_m(\alpha))|\delta_m(A_m(\beta)) = 1\}$$

$$= \sum_{m \in \mathcal{M}_0(P)} \delta_m(A_m(\beta)) \frac{1}{A_m(\alpha) A_m(\beta)}, \text{ a.e. } [P]$$

$$= T_0(\beta).$$

The second equality follows from (D3), whereas the second-to-last equality follows since

$$E_P\{\delta_m(A_m(\alpha))|\delta_m(A_m(\beta)) = 1\}$$

$$= \frac{P\{\delta_m(A_m(\alpha)) = 1, \delta_m(A_m(\beta)) = 1\}}{P\{\delta_m(A_m(\beta)) = 1\}}$$

$$= \frac{P\{\delta_m(A_m(\alpha)) = 1\}}{P\{\delta_m(A_m(\beta)) = 1\}}$$

$$= \frac{A_m(\alpha)}{A_m(\beta)}$$

because of condition (A2) for the $A_m(\cdot)$s and conditions (D2) and (D4) for the $\delta_m(\cdot)$s. The above results show that, under $P$,

$$\{(T_0(\alpha), \mathcal{F}_\alpha) : \alpha \in [0,1]\}$$

forms a reverse martingale process. Further, observe that $T_0(1) = |\mathcal{M}_0(P)|$ a.e. $[P]$ due to conditions (D1) and (A1). Thus,

$$E_P(T_0(1)) = |\mathcal{M}_0(P)|.$$
From the inequality in (4.9), we obtain

\[
E_P[F(\alpha^*(q))] \leq q E_P\left[ \frac{S_0(\alpha^*(q))}{A^*(\alpha^*(q))} \right] 
= q \sum_{m \in \mathcal{M}_0(P)} E_P\left[ \frac{\delta_m(\alpha^*(q))}{A^*(\alpha^*(q))} \right] 
= q \sum_{m \in \mathcal{M}_0(P)} E_P\left[ \frac{\delta_m(\alpha^*(q)) \cdot A_m(\alpha^*(q))}{A_m(\alpha^*(q)) \cdot A^*(\alpha^*(q))} \right] 
\leq q \left[ \sup_{\alpha \in [0,1]} \max_{m \in \mathcal{M}_0(P)} \frac{A_m(\alpha)}{A^*(\alpha)} \right] E_P[T_0(\alpha^*(q))] 
\leq q \frac{1}{|\mathcal{M}_0(P)|} E_P[T_0(1)] 
= q \frac{1}{|\mathcal{M}_0(P)|} 
= q,
\]

where the last inequality is obtained using condition (A4) and by invoking the Optional Sampling Theorem for (reverse) martingales (cf., [3]), and the second-to-last equality because of \( E_P[T_0(1)] = |\mathcal{M}_0(P)| \).

Note that, in particular, since the Šidák multiple decision size function \( A^S \) always satisfies condition (A4) for all \( P \in \mathcal{P} \), then \( \forall \Delta \in \mathcal{D}, \forall P \in \mathcal{P} \), we have the property

\[
E_P\left\{ F(\alpha^*(q; \Delta, A^S); \Delta, A^S) \right\} \leq q. \tag{4.11}
\]

Let us denote by \( \mathcal{P}_0 = \{ P \in \mathcal{P} : \mathcal{M}_0(P) = \mathcal{M} \} \). Observe that for \( P \in \mathcal{P}_0 \), condition (A4) will not be satisfied unless the multiple decision size function \( A \) has identical components, in essence, a Šidák multiple decision size function form. We still therefore need to establish that for an arbitrary \( A \in \mathcal{S} \) and a \( P \in \mathcal{P}_0 \),

\[
E_P\left\{ F(\alpha^*(q; \Delta, A); \Delta, A) \right\} \leq q.
\]

For such a \( P \in \mathcal{P}_0 \), we have \( F(\alpha; \Delta, A) = I\{ S(\alpha; \Delta, A) > 0 \} \), so that

\[
E_P[F(\alpha^*(q; \Delta, A); \Delta, A)] 
= P\{ S(\alpha^*(q; \Delta, A); \Delta, A) > 0 \} 
= P\{ \alpha^*(q; \Delta, A) > 0 \}.
\]

We have, for any \( \Delta \in \mathcal{D} \) and any \( A \in \mathcal{S} \), that

\[
\{ \alpha^*(q; \Delta, A) > 0 \} = \bigcup_{\alpha \in (0,1]} \left\{ \frac{S(\alpha; \Delta, A)}{A^*(\alpha)} \geq \frac{1}{q} \right\}. \tag{4.12}
\]
In Lemma D.1 of [15] it was established, using an inequality of [11], that for $W_m(\eta_m), m \in \mathcal{M}$, independent Bernoulli($\eta_m$) random variables with $\eta_m \in [0, 1]$ and satisfying $\prod_{m \in \mathcal{M}} (1 - \eta_m) = 1 - \alpha$, for each $t \geq 1$,

$$
P \left\{ \frac{\sum_{m \in \mathcal{M}} W_m(\eta_m)}{\sum_{m \in \mathcal{M}} \eta_m} \geq t \right\} \leq P \left\{ \frac{\sum_{m \in \mathcal{M}} W_m(\eta_m^S)}{\sum_{m \in \mathcal{M}} \eta_m^S} \geq t \right\},$$

(4.13)

where $\eta_m^S = 1 - (1 - \alpha)^{1/M}, m \in \mathcal{M}$.

Noting that, under $P \in P_0$, $\delta_m(A_m(\alpha))$s are independent Bernoulli($A_m(\alpha)$), then by using the inequality in (4.13) and condition (A3), it follows that for $q \in (0, 1]$,

$$
P \left\{ \frac{S(\alpha; \Delta, A)}{A^*(\alpha)} \geq \frac{1}{q} \right\} \leq P \left\{ \frac{S(\alpha; \Delta, A^{S+})}{A^{S+}(\alpha)} \geq \frac{1}{q} \right\},$$

(4.14)

where the Šidák sizes $A^{S+} = (A_m^{S+}, m \in \mathcal{M})$ in (4.14) have components

$$A_m^{S+} = 1 - (1 - \alpha^+)^{1/M}, m \in \mathcal{M},$$

with $\alpha^+$ satisfying $\prod_{m \in \mathcal{M}} [1 - A_m(\alpha)] = 1 - \alpha^+$. Observe that by (A3), we have necessarily that $\alpha^+ \leq \alpha$. Combining the results in (4.12) and (4.14), we obtain

$$P\{\alpha^*(q; \Delta, A) > 0\} \leq P\{\alpha^*(q; \Delta, A^{S+}) > 0\}.$$

But since we have already established that, for $P \in P_0$, we have

$$P\{\alpha^*(q; \Delta, A^{S+}) > 0\} \leq q,$$

then it follows that $P\{\alpha^*(q; \Delta, A) > 0\} \leq q$. This implies finally that

$$E_P\{F(\alpha^*(q; \Delta, A); \Delta, A)\} \leq q$$

for any $P \in P_0$, thereby completing the proof of Theorem 3.2.

In contrast to Theorem 3.1 where we were able to have the weaker version of condition (D4) given in (4.7), we could not do this for Theorem 3.2. The reason is that we could not conclude under this weaker condition that the process $\{(T_0(\alpha), F_\alpha) : \alpha \in [0, 1]\}$ is a reverse supermartingale, which would have allowed us to get the desired result. It may be possible that under certain situations we do have this supermartingale property, but the weaker condition (4.7) appears not sufficient for this property to hold in general.
5 Representations of MDFs in Terms of the Generalized $P$-Values

This section expresses the MDFs $\delta^\dagger(q)$ in (3.6) and $\delta^*(q)$ in (3.7) in terms of the generalized $p$-value statistics defined in (2.3). Define the anti-rank statistics vector via

$$((1), (2), \ldots, (M)) : (\mathcal{M}, \mathcal{F}) \to (\mathfrak{M}, \sigma(\mathfrak{M}))$$

(5.1)

where $\mathfrak{M}$ is the space of all possible permutations of $\mathcal{M}$, and such that

$$\alpha(1) < \alpha(2) < \ldots < \alpha(M).$$

Let us first consider the random variable $\alpha^\dagger(q)$ in (3.4). We see from its definition and those of the generalized $p$-value statistics that, for some $J \in \bar{\mathcal{M}} \equiv \{0\} \cup \mathcal{M}$, we have

$$\alpha^\dagger(q) \in [\alpha(J), \alpha(J+1))$$

if and only if

$$\forall j \in \{1, 2, \ldots, J\} : \prod_{m \in \mathcal{M}} [1 - A_m(\alpha(j))]^{1 - \delta_m[A_m(\alpha(j))]} \geq 1 - q;$$

$$\prod_{m \in \mathcal{M}} [1 - A_m(\alpha(J+1))]^{1 - \delta_m[A_m(\alpha(J+1))]} < 1 - q.$$

From the definition of the generalized $p$-value statistics we further have

$$\delta_m[A_m(\alpha(j)) -] = I\{m \leq j - 1\}.$$

Consequently, by defining the $\bar{\mathcal{M}}$-valued random variable

$$J^\dagger(q) = \max \left\{ k \in \mathcal{M} : \prod_{m=j}^{M} [1 - A_m(\alpha(j))] \geq 1 - q, j = 1, 2, \ldots, k \right\},$$

(5.2)

we have the result that

$$\alpha^\dagger(q) \in [\alpha(J^\dagger(q)), \alpha(J^\dagger(q)+1)).$$

Consequently, we obtain the representation of $\delta^\dagger(q)$ in (3.6) in terms of the $\alpha_m$s given by

$$\delta^\dagger(q) \equiv (\delta_m(A_m(\alpha^\dagger(q))), m \in \mathcal{M}) = (\delta_m(A_m(\alpha(J^\dagger(q)))), m \in \mathcal{M})$$

(5.3)

where we used the fact that, for each $m \in \mathcal{M}$, $\delta_m$ is constant in the interval

$$[A_m(\alpha(J^\dagger(q))), A_m(\alpha(J^\dagger(q)+1)).$$
Next let us consider the random variable $\alpha^*(q)$ in (3.5). We may re-express its defining equation via

$$\alpha^*(q) = \sup \left\{ \alpha \in [0, 1] : \sum_{m \in \mathcal{M}} A(m)(\alpha) \leq q \sum_{m \in \mathcal{M}} \delta(m)[A(m)(\alpha)] \right\}.$$ 

But, since $\sum_{m \in \mathcal{M}} \delta(m)[A(m)(\alpha(j))] = j$, then

$$\alpha^*(q) \in [\alpha(j), \alpha(j+1)]$$

if and only if

$$\sum_{m \in \mathcal{M}} A(m)(\alpha(j)) \leq qj; \forall j \in \{J + 1, J + 2, \ldots, M\} : \sum_{m \in \mathcal{M}} A(m)(\alpha(j)) > qj.$$ 

Defining the $\tilde{\mathcal{M}}$-valued random variable

$$J^*(q) = \max \left\{ k \in \mathcal{M} : \sum_{m \in \mathcal{M}} A(m)(\alpha(k)) \leq q \right\}, \quad (5.4)$$

we then have that

$$\alpha^*(q) \in [\alpha(J^*(q)), \alpha(J^*(q)+1)].$$

As a consequence, an equivalent representation of the MDF $\delta^*(q)$ in (3.7) in terms of the $\alpha_m$s is provided by

$$\delta^*(q) \equiv (\delta_m(A_m(\alpha^*(q))), m \in \mathcal{M}) = (\delta_m(A_m(\alpha(J^*(q)))), m \in \mathcal{M}). \quad (5.5)$$

The representations in (5.3) for $\delta^l(q)$ and (5.5) for $\delta^*(q)$ provide alternative computational approaches since, instead of computing $\alpha^l(q)$ and $\alpha^*(q)$, we may simply compute the generalized $p$-values, then $J^l(q)$ and $J^*(q)$, and then finally the realizations of the decision functions.

For a simple application, let us see what becomes of the MDFs $\delta^l(q)$ and $\delta^*(q)$ if we use the Šidák multiple decision size function $A^S$ given in (2.1). We use the alternate representations just obtained above. By simple manipulations, we immediately obtain that

$$J^l(q) = \max \left\{ k \in \mathcal{M} : \alpha(j) \leq 1 - (1 - q)^{M/(M-j+1)}, j = 1, 2, \ldots, k \right\}; \quad J^*(q) = \max \left\{ k \in \mathcal{M} : M[1 - (1 - \alpha(k))]^{1/M} \leq qk \right\}.$$ 

But, for these Šidák size functions, the (ordinary) $p$-value statistics are given by

$$P_m = A^S_m(\alpha_m) = 1 - (1 - \alpha_m)^{1/M}, m \in \mathcal{M}.$$
Re-expressing the $J^\dagger(q)$ and $J^\ast(q)$ in terms of these $p$-values, we easily obtain by simple manipulations that

$$J^\dagger(q) = \max \{ k \in \mathcal{M} : P_{(j)} \leq 1 - (1 - q)^{1/(M-j+1)}, j = 1, 2, \ldots, k \}; \quad (5.6)$$

$$J^\ast(q) = \max \{ k \in \mathcal{M} : P_{(k)} \leq q k / M \}. \quad (5.7)$$

Observe that $J^\dagger(q)$ in (5.6) leads to the step-down sequential Šidák FWER-controlling procedure, see [4]; whereas, $J^\ast(q)$ in (5.7) is the usual form of the step-up Benjamini-Hochberg FDR-controlling procedure in [1]. Thus, through the Šidák sizes, we are able to obtain from our formulation two popular MDFs for FWER and FDR control as special cases of the MDFs $\delta^\dagger(q)$ and $\delta^\ast(q)$.

### 6 Towards the Development of Optimal MDFs

Finally, in this subsection, we indicate, without going into much detail, the potential utility of the classes of MDFs arising from Theorems 3.1 and 3.2 in the context of obtaining MDFs with some optimality properties, especially in non-exchangeable multiple hypotheses testing settings, which are those where the power characteristics of the $M$ test functions are not identical.

Let us fix a multiple decision process $\Delta \in \mathfrak{D}$ and fix a probability measure $P_1 \in \mathcal{P}$.

Define the mappings $\pi_m : [0,1] \to [0,1]$ for $m \in \mathcal{M}$ according to

$$\pi_m(\alpha; P_1) = E_{P_1}[\delta_m(\alpha)], \; \alpha \in [0,1]. \quad (6.1)$$

When viewed as a function of $P_1$, $\pi_m(\alpha; \cdot)$ is the power function of $\delta_m$ when it is allocated a size of $\alpha$. Of interest to us, though, is to view it as a function of $\alpha$ for the fixed $P_1$. In this case, $\pi_m(\cdot; P_1)$ is the receiver operating characteristic curve (ROC) of the $m$th test function. Assume that for each $m \in \mathcal{M}$, the mapping $\alpha \mapsto \pi_m(\alpha; P_1)$ is strictly increasing with $\pi_m(1; P_1) = 1$ and twice-differentiable.

Suppose it is desired to strongly control the overall FWER or FDR at some pre-specified level $q \in [0,1]$, but at the same time maximize the total (or average) power at $P = P_1$. Our idea, partly implemented in [14], is to first obtain the optimal multiple decision size function for weak FWER control associated with $\Delta$, denoted by $A^* = (A^*_m(\alpha), m \in \mathcal{M}) \in \mathfrak{S}$. This is the multiple decision size function $A$ satisfying the condition

$$\forall \alpha \in [0,1] : \prod_{m \in \mathcal{M}} [1 - A_m(\alpha)] = 1 - \alpha,$$

and such that the total power at $P = P_1$, given by $\sum_{m \in \mathcal{M}} \pi_m(A_m(\alpha); P_1)$, is maximized. Under regularity conditions on the ROC functions, the optimal $A^*$ function could be obtained using Lagrangian optimization, for instance, see Theorem 4.3 in [14] which is an
implementation when the individual test functions coincide with the Neyman-Pearson most powerful tests.

Now, having determined the optimal multiple decision size function $A^*$ associated with $\Delta$, which is at this point optimal only in the sense of weak FWER control, we can then apply Theorem 3.1 to obtain the MDF $\delta^t(q; \Delta, A^*)$ which will strongly control the FWER at $q$; or apply Theorem 3.2 to obtain the MDF $\delta^s(q; \Delta, A^*)$ which will control the FDR at $q$.

By virtue of the choice of the size process $A^*$, which is tied-in to the multiple decision process $\Delta$ and the target probability measure $P_1$, we expect that the MDFs $\delta^t(q; \Delta, A^*)$ and $\delta^s(q; \Delta, A^*)$ will perform better with respect to overall power at $P_1$ relative to, for example, the sequential Šidák MDF or the BH MDF, which we saw from the preceding section are MDFs arising from the Šidák multiple decision size function, a size function that may not be optimal for the chosen multiple decision size process $\Delta$. For instance, results of a modest simulation study in [14] demonstrated the improvement over the BH procedure of the MDF $\delta^s$ in a specific setting. Further improvements in power performances could be achieved by proper choice of the multiple decision process $\Delta$, such as, for example, choosing it to have components that are uniformly most powerful (UMP) or uniformly most powerful unbiased (UMPU) test functions. These issues, however, will be deferred for future work, but we expect that the classes of MDFs presented here will play a central role in dealing with these more complex multiple hypotheses testing problems.

We close by pointing out that other approaches have also been proposed for obtaining MDFs possessing certain optimality properties. Relevant papers pertaining to optimality are [26, 25, 7, 8, 23, 24, 20, 12, 16]. Procedures with a Bayes or an empirical Bayes flavor can be found in [13, 21, 5, 9]. In addition, it is also of interest to extend our results to settings where the components of $\{\delta_m : m \in M_0(P)\}$ are dependent as in [19, 2]; see also the review article [18]. Another possible extension is to consider generalized FWER and FDR as in [17]. However, we defer consideration of such extensions for future work.

Acknowledgements

The authors are grateful to Professor Sanat Sarkar for many discussions which were highly beneficial to this work.

References

[1] Benjamini, Y. and Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. Roy. Statist. Soc. Ser. B 57, 1, 289–300.
[2] Benjamini, Y. and Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *Ann. Statist.* 29, 4, 1165–1188.

[3] Doob, J. L. (1953). *Stochastic processes*. John Wiley & Sons Inc., New York.

[4] Dudoit, S. and van der Laan, M. J. (2008). *Multiple testing procedures with applications to genomics*. Springer Series in Statistics. Springer, New York.

[5] Efron, B. (2008a). Microarrays, empirical Bayes and the two-groups model. *Statist. Sci.* 23, 1, 1–22.

[6] Efron, B. (2008b). Simultaneous inference: When should hypothesis testing problems be combined? *The Annals of Applied Statistics* 1, 197–223.

[7] Genovese, C. and Wasserman, L. (2003). Bayesian and frequentist multiple testing. In *Bayesian statistics, 7* (Tenerife, 2002). Oxford Univ. Press, New York, 145–161. With discussions by Merlise A. Clyde and Christian P. Robert and Judith Rousseau, and a reply by the authors.

[8] Genovese, C. R., Roeder, K., and Wasserman, L. (2006). False discovery control with p-value weighting. *Biometrika* 93, 3, 509–524.

[9] Guindani, M., Muller, P., and Zhang, S. (2009). A Bayesian discovery procedure. *JRSS B* 71, 905–925.

[10] Habiger, J. and Peña, E. A. (2010). Randomized P-values and nonparametric procedures in multiple testing. *Journal of Nonparametric Statistics* (iFirst article), 1–22. DOI: 10.1080/10485252.2010.482154.

[11] Hoeffding, W. (1956). On the distribution of the number of successes in independent trials. *Ann. Math. Statist.* 27, 713–721.

[12] Kang, G., Ye, K., Liu, N., Allison, D., and Gao, G. (2009). Weighted multiple hypothesis testing procedures. *Statistical Applications in Genetics and Molecular Biology* 8, 1–21.

[13] Müller, P., Parmigiani, G., Robert, C., and Rousseau, J. (2004). Optimal sample size for multiple testing: the case of gene expression microarrays. *J. Amer. Statist. Assoc.* 99, 468, 990–1001.

[14] Peña, E., Habiger, J., and Wu, W. (2010a). Power-enhanced multiple decision functions controlling family-wise error and false discovery rates. *Annals of Statistics* (to appear).

[15] Peña, E., Habiger, J., and Wu, W. (2010b). Supplement to ‘Power-Enhanced Multiple Decision Functions Controlling Family-Wise Error and False Discovery Rates’. *Annals of Statistics* (to appear as an online supplement).

[16] Roquain, E. and van de Wiel, M. A. (2009). Optimal weighting for false discovery rate control. *Electronic Journal of Statistics* 3, 678–711.
[17] Sarkar, S. K. (2007). Stepup procedures controlling generalized FWER and generalized FDR. *Ann. Statist.* **35**, 6, 2405–2420.

[18] Sarkar, S. K. (2008). On methods controlling the false discovery rate. *Sankhyā* **70**, 2, Ser. A, 135–168.

[19] Sarkar, S. K., and Chang, C.-K. (1997). The Simes method for multiple hypothesis testing with positively dependent test statistics. *J. Amer. Statist. Assoc.* **92**, 440, 1601–1608.

[20] Sarkar, S. K., Zhou, T., and Ghosh, D. (2008). A general decision theoretic formulation of procedures controlling FDR and FNR from a Bayesian perspective. *Statist. Sinica* **18**, 3, 925–945.

[21] Scott, J. and Berger, J. (2006). An exploration of aspects of Bayesian multiple testing. *Journal of Statistical Planning and Inference* **136**, 2144–2162.

[22] Šidák, Z. (1967). Rectangular confidence regions for the means of multivariate normal distributions. *J. Amer. Statist. Assoc.* **62**, 626–633.

[23] Storey, J. (2007). The optimal discovery procedure: a new approach to simultaneous significance testing. *Journal of the Royal Statistical Society, Series B* **69**, 347–368.

[24] Sun, W. and Cai, T. (2007). Oracle and adaptive compound decision rules for false discovery rate control. *Journal of the American Statistical Association* **102**, 901–912.

[25] Westfall, P. H. and Krishen, A. (2001). Optimally weighted, fixed sequence and gatekeeper multiple testing procedures. *J. Statist. Plann. Inference* **99**, 1, 25–40.

[26] Westfall, P. H., Krishen, A., and Young, S. S. (1998). Using prior information to allocate significance levels for multiple endpoints. *Statistics in Medicine* **17**, 2107–2119.