Z-VALUE DIRECTIONAL FALSE DISCOVERY RATE CONTROL WITH
DATA MASKING

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ABSTRACT. We revisit the fundamental “normal-means” problem, where independent normal
test statistics $z_i \sim N(\mu_i, 1)$, $i = 1, \ldots, m$, also known as “z-values”, are observed for the mean
effects $\mu_1, \ldots, \mu_m$. While there is extensive literature on testing the point null hypotheses $\mu_i = 0$
with false discovery rate control, the problem of declaring whether $\mu_i$ is positive or negative
with directional false discovery rate (dFDR) control has been much underserved. Leveraging
the recently invented “data masking” technique, we propose a computationally efficient testing
algorithm, called ZDIRECT, that seeks to mimic the optimal discovery procedure motivated by
a Bayesian perspective yet provides exact dFDR control under minimal pure frequentist assump-
tions. In our simulation studies, ZDIRECT has demonstrated an apparent power advantage over
the directional Benjamini and Hochberg procedure, which, to the best of our knowledge, is the
only other existing procedure that offers dFDR control for the normal-means problem.

1. Introduction

In the past two decades, multiple hypothesis testing with false discovery rate (FDR) control has
arguably become one of the most popular paradigms for exploratory analysis of modern large-scale
datasets where many potential discoveries can be made; see [Benjamini (2020)] for a recent review
on the related practices. While many new testing methods tailored for different structural settings
have emerged in recent years, much of the development in FDR methodologies begins with the
simple yet fundamental “normal-means” problem, in which one observes independent normalized
statistics $z_1, \ldots, z_m$, each distributed as $z_i \sim N(\mu_i, 1)$ with an unknown mean effect $\mu_i$.

A typical goal is to test the null hypotheses

$$H_i : \mu_i = 0, i = 1, \ldots, m,$$

in such a way that the false discovery rate

$$FDR = \mathbb{E} \left[ \frac{\{i : H_i \text{ is rejected and } \mu_i = 0\}}{1 \lor \{i : H_i \text{ is rejected }\}} \right]$$

is controlled under a desired level $q \in (0, 1)$, where a rejection of $\mu_i = 0$ amounts to a “discovery”.

As a standard example in genomics, each $z_i$ may correspond to a differential expression statistic
for a gene $i$ under two experimental conditions, making FDR a suitably scalable Type 1 error rate
to control since the total number of genes $m$ usually measures in the thousands. There is a sizable
literature on methods for controlling the FDR; these include the standard BH procedure [Benjamini
and Hochberg (1995)], its immediate sparsity-adaptive variants [Benjamini and Hochberg (2000),
Storey et al. (2004)], as well as optimal procedures based on local false discovery rates [Heller and
Rosset (2021), Sun and Cai (2007)].

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In this paper, we exclusively refer to these original test statistics as “z-values”. Other works may call a probit-
tranformed p-value as such; see [Efron (2007) p.1353].
Tukey (1991), however, argued that it is not meaningful to test the point nulls in (1.1), as effects in many real applications, however small they might be, are almost never exactly zero; one should instead test the direction/sign of the effect, by declaring either $\mu_i > 0$ or $\mu_i < 0$ as a “discovery”, or making no declaration (and hence no discovery) about the sign of $\mu_i$ at all if the data do not contain enough evidence to support either direction Williams et al. (1999). Here we adopt the more accommodating view of Benjamini and Yekutieli (2005), who allow possibly some $\mu_i$’s to be exactly zero, and a false discovery, also known as a Type S error Gelman and Tuerlinckx (2000), occurs for $i$ if one declares $\mu_i < 0$ when the truth is $\mu_i \geq 0$, or vice versa. Under this framework, a generic discovery procedure consists of two components:

(i) $\mathcal{R} \subseteq [m]$, the set of indices for which sign declarations (discoveries) are made, and
(ii) $\tilde{sgn}_i$, the positive or negative sign declared for each $i \in \mathcal{R}$. (Note that $\tilde{sgn}_i \neq 0$.)

We denote such a procedure, or its associated decisions, by $(\tilde{sgn}_i)_{i \in \mathcal{R}}$. Its Type S error rate analogous to the FDR is the directional false discovery rate (dFDR), defined as

$$dFDR[(\tilde{sgn}_i)_{i \in \mathcal{R}}] = \mathbb{E}\left[\sum_{i \in \mathcal{R}} \mathbf{1}(sgn(\mu_i) \neq \tilde{sgn}_i) / |\mathcal{R}|\right],$$

and its power can be measured by the expected number of true discoveries (ETD)

$$ETD[(\tilde{sgn}_i)_{i \in \mathcal{R}}] = \mathbb{E}\left[\sum_{i \in \mathcal{R}} \mathbf{1}(sgn(\mu_i) = \tilde{sgn}_i)\right].$$

Compared to the FDR literature, methods for controlling the dFDR under our normal-means setting are understudied. To the best of our knowledge, the only existing procedure that provably controls the dFDR under a desired level $q \in (0, 1)$ is what we call the directional BH (dBH) procedure, an adaptation of the standard level-$q$ BH procedure that, upon rejecting the null hypotheses in (1.1) using the two-sided $p$-values, further declares the sign of each rejected $\mu_i$ as that of its corresponding $z$-value $z_i$ (Benjamini and Yekutieli 2005, Definition 6). In this paper, we propose a new procedure, called ZDIRECT, that offers exact dFDR under no stronger assumptions, by leveraging a recently proposed “data masking” technique (Lei and Fithian 2018, Leung and Sun 2021). In short, it promises to improve upon the power of the dBH procedure by circumventing the information reduction step of transforming the $z$-values into the two-sided $p$-values; in particular, it shares the same spirit as the optimal procedures for point null FDR testing of (1.1) which directly summarize the significance of different hypotheses from the $z$-values via the local false discovery rates (Heller and Rosset 2021, Sun and Cai 2007), and hence its name. We believe this is the first time that data masking has been employed to devise a dFDR controlling procedure.

The rest of our work is organized as follows. Section 2 introduces the preliminaries on optimal procedures for dFDR testing under a Bayesian formulation of the problem, where the means $\mu_i$ are assumed to be independently and identically generated, as well as the Empirical Bayes approach to dFDR testing proposed in the same paper. These will lay the groundwork for developing our ZDIRECT algorithm in Section 3. Section 4 demonstrates the numerical performance of ZDIRECT alongside other methods, and Section 5 discusses possible extensions of our work and other related problems.

Notation. We use the shorthand $[m] = \{1, \ldots, m\}$. $\phi(\cdot)$ and $\Phi(\cdot)$ are respectively the standard normal density and distribution functions, $\mathbf{1}(\cdot)$ is the indicator function, and $sgn(\cdot)$ is the usual
sign function defined as

\[
\text{sgn}(x) = \begin{cases} 
1 & \text{if } x > 0 \\
0 & \text{if } x = 0 \\
-1 & \text{if } x < 0
\end{cases}
\]

For two numbers \(a, b \in \mathbb{R}\), \(a \land b\) and \(a \lor b\) respectively represent \(\min(a, b)\) and \(\max(a, b)\), and \(U(; a, b)\) denotes a uniform density on an interval \([a, b] \subseteq \mathbb{R}\).

2. Optimal discovery procedure based on local false sign rates

The two-group model [Efron et al. (2001)] for FDR testing, which assumes that the \(\mu_i\)’s are generated from a mixture distribution with a point mass at zero, has existed for almost as long as the BH procedure. It is not until quite recently that the analogous construct for dFDR testing is explicitly stated in [Stephens (2017)], who assumes that the mean parameters

\[
\mu_i \sim i.i.d. g(\mu)
\]

are independently and identically generated from a common distribution \(g(\cdot)\) that does not necessarily have any point mass.

Under the formulation in (2.1), for a given \(i\), if one had the knowledge of the distribution \(g\) and was obliged to declare a non-zero sign for \(\mu_i\) based on the observation \(z_i\), to minimize the probability of making a Type S error, or equivalently, to maximize that of making a correct sign declaration, he/she would adopt the following strategy:

| If \(P(\mu_i < 0 | z_i) < P(\mu_i > 0 | z_i)\)\) | Then \(\text{declare } \mu_i > 0\)\)
| --- | --- |
| \(P(\mu_i > 0 | z_i) < P(\mu_i < 0 | z_i)\)\) | \(\text{declare } \mu_i < 0\)\)
| \(P(\mu_i > 0 | z_i) = P(\mu_i < 0 | z_i)\)\) | \(\text{declare either } \mu_i > 0 \text{ or } \mu_i < 0\)\)

Table 1. Optimal sign declaration strategy for each \(i\)

This motivates the local false sign rates, defined as

\[
lfsr_i = \min\{P(\mu_i \leq 0 | z_i), P(\mu_i \geq 0 | z_i)\},
\]

which is the probability of making a Type S error for \(i\) according to the optimal strategy in Table 1. Since a smaller \(lfsr_i\) suggests higher confidence in the sign of \(\mu_i\), when attempting to make multiple discoveries with dFDR control, the intuition is to prioritize making sign declarations for those \(i\)’s with the smallest local false sign rates. This in fact defines the optimal discovery procedure (ODP) that maximizes the ETD subject to a dFDR constraint, as stated in the following theorem:

**Theorem 2.1.** For a given level \(q \in (0, 1)\), suppose \((\hat{\text{sgn}}_{O_{\text{DP}}})_{i \in \mathcal{R}_{O_{\text{DP}}}}\) is the optimal discovery procedure such that

\[
dFDR\left(\left(\hat{\text{sgn}}_{O_{\text{DP}}}\right)_{i \in \mathcal{R}_{O_{\text{DP}}}}\right) \leq q
\]

and

\[
ETD\left(\left(\hat{\text{sgn}}_{O_{\text{DP}}}\right)_{i \in \mathcal{R}_{O_{\text{DP}}}}\right) \geq ETD\left(\left(\hat{\text{sgn}}_{i}\right)_{i \in \mathcal{R}}\right)
\]

for any procedure \((\hat{\text{sgn}}_i)_{i \in \mathcal{R}}\) with \(dFDR\left(\left(\hat{\text{sgn}}_i\right)_{i \in \mathcal{R}}\right) \leq q\). It must be true that

(i) \(lfsr_i \leq lfsr_j\) for any \(i \in \mathcal{R}_{O_{\text{DP}}}\) and \(j \in [m] \setminus \mathcal{R}_{O_{\text{DP}}}\), and...
(ii) For each $i \in \mathcal{RODP}$, $\text{sgn}_{i}^{\text{ODP}}$ is declared in accordance with Table 4.

Here, the expectations defining the dFDR and ETD quantities are with respect to both the data $\{z_{i}\}_{i=1}^{m}$ and random parameters $\{\mu_{i}\}_{i=1}^{m}$ under (2.1).

The proof of Theorem 2.1 (Appendix C) extends the arguments in Heller and Rosset (2021, Theorem 2.1) who studied the point null testing problem (1.1). However, to implement the ODP, one must first compute the local false sign rates in (2.2); this is in turn predicated on the oracle knowledge of the unknown distribution $g$, which has to be estimated from the data $\{z_{1}, \ldots, z_{m}\}$ in practice. This poses a very hard nonparametric deconvolution problem with notoriously slow convergence rates, and Efron (2016) suggests more aggressive parametric modeling on $g$ to give a more reasonable estimate.

Stephens (2017)'s choice is to assume that $g(\cdot)$ is a unimodal distribution about 0; in particular, he proposed the finite-mixture form:

\[
g(\cdot; \pi) = \pi_{0}\delta_{0}(\cdot) + \sum_{k=-K, \ldots, -1, 1, \ldots, K} \pi_{k}f_{k}(\cdot),
\]

where $\pi = \{\pi_{-K}, \ldots, \pi_{-1}, \pi_{0}, \pi_{1}, \ldots, \pi_{K}\}$ are mixing probabilities that sum to 1 and parametrize the model, $\delta_{0}(\cdot)$ denotes the delta function at zero, and $f_{k}^{+}$ and $f_{k}^{-}$ are uniform distributions of the forms

\[
f_{k}(\cdot) = \begin{cases} U(\cdot; 0, a_{k}) & \text{if } k = 1, \ldots, K \\ U(\cdot; a_{k}, 0) & \text{if } k = -1, \ldots, -K \end{cases}
\]

for $a_{1}, \ldots, a_{K} > 0$ and $a_{-1}, \ldots, a_{-K} < 0$. By increasing the number of components $K$ and expanding the supporting intervals defined by $a_{k}$, (2.3) can approximate any unimodal distribution about zero (Feller, 2008, p.158). While unimodality seems somewhat restrictive, Stephens (2017) argues, in favor of its plausibility in real applications, that most effects are close to zero while larger effects are decreasingly likely. On a related note, the model also covers Tukey (1991)'s contention of “no exactly zero effects”, as the point mass $\pi_{0}$ in (2.3) can be zero. Moreover, penalized maximum likelihood estimates $\hat{\pi}$ of the mixing probabilities can be reliably obtained with very efficient interior point methods (Stephens, 2017, Supplementary information). By adopting the assumption in (2.3), the ODP can then proceed with the local false sign rates computed based on the estimate $g(\cdot; \hat{\pi})$.

3. A z-value method for directional false discovery rate control

The dBH procedure (Benjamini and Yekutieli, 2005, Definition 6) first determines the rejected subset of $[m]$ based on the two-sided $p$-values $p_{i} = 2\Phi(-|z_{i}|)$, $i = 1, \ldots, m$, and only uses the original $z$-values to declare the signs after. The use of $p_{1}, \ldots, p_{m}$ to make rejection decisions entails information loss, as each $p_{i}$ is a reduction of its corresponding $z_{i}$ via the non-bijective transformation $2\Phi(-|z|)$; in particular, knowing $p_{i}$ alone cannot recover $z_{i}$. At a high level, one reason for the power improvement of the ODP over the dBH procedure is that the former summarizes confidence in the signs of the $\mu_{i}$'s directly from the $z$-values via the local false sign rates (2.2), thereby avoiding the use of two-sided $p$-values. This phenomenon has been observed in the earlier works of Sun and Cai (2007) and Storey (2007) on FDR testing of (1.1), and is also analogous to the fact suggested by the Neyman-Pearson lemma (Lehmann and Romano, 2006, Chapter 3) that, the most powerful (MP) test for a single point null hypothesis is not defined by the two-sided $p$-value. Therefore, we will develop a dFDR controlling algorithm, ZDIRECT, that is potentially more powerful than the dBH procedure by directly operating on the $z$-values.
To do so, we will leverage the data masking technique introduced in [Lei and Fithian (2018)] and subsequently extended in [Leung and Sun (2021)] for z-value based FDR testing. Similarly to the latter work, ZDIRECT is an iterative algorithm that can be presented in terms of the transformed data

\[ u_i = \Phi(z_i), \quad i = 1, \ldots, m. \]

Unlike the two-sided tail function \( 2\Phi(-|\cdot|) \), \( \Phi(\cdot) \) is a bijective transformation that doesn’t collapse the original z-values, so any algorithm operating on the \( u_i \)'s is rightfully considered as “z-value based”. At each step \( t = 0, 1, \ldots, \) our algorithm constructs two disjoint subsets of \([m] \)

\[ \mathcal{R}_t = \{ i : u_i \in (0, s_{i,l,t}) \cup (s_{i,r,t}, 1) \} \quad \text{and} \quad \mathcal{A}_t = \{ i : u_i \in (0.5 - s_{i,l,t}, 1.5 - s_{i,r,t}) \} , \]

to serve, respectively, as a candidate “rejection set” and “acceptance set”, where \( s_{i,l,t} \) and \( s_{i,r,t} \) are thresholding numbers in the “left” and “right” half intervals \((0, 0.5)\) and \((0.5, 1)\) that must satisfy, for all \( i \) and \( t \),

\[ 0 < s_{i,l,t} < 0.25 \quad \text{and} \quad 0.75 < s_{i,r,t} < 1. \]

Specifically, at step \( t \), the ratio

\[ \text{dFDR}_t = \frac{1 + |\mathcal{A}_t|}{|\mathcal{R}_t| \vee 1} \]

is used to as an estimate of the dFDR that would incur if we declared \( \text{sgn}(\mu_i) \) as \( \text{sgn}(z_i) \) for each \( i \in \mathcal{R}_t \). If \( \text{dFDR}_t \leq q \), the target dFDR level, the algorithm will terminate and takes \( \text{sgn}(z_i) \) as the final discovery decisions, where any sign declared is non-zero because \( P(\{\text{sgn}(z_i) = 0\}) = 0 \) under the “normal-means” setting. To make sense of \( \text{dFDR}_t \) as a dFDR estimate, first note that \( \Phi(\cdot) \) is an increasing and sigmoid-like odd function with \( \Phi(0) = 0.5 \), and hence the set \( \mathcal{R}_t \) generally contains the \( i \)'s with large absolute z-values, strong evidence for a negative or positive \( \mu_i \). An \( i \in \mathcal{R}_t \) constitutes a false discovery if either

\[ u_i \in (0, s_{i,l,t}) \quad \text{and} \quad \text{sgn}(\mu_i) \geq 0, \]

or

\[ u_i \in (s_{i,r,t}, 1) \quad \text{and} \quad \text{sgn}(\mu_i) \leq 0. \]

Suppose we are in a Type S error-prone scenario where all the \( \mu_i \)'s are very close to zero, so that all \( u_i \)'s stochastically behave like uniform random variables as a result of the \( z_i \)'s behaving stochastically like mean-zero standard normals. If \( \mu_i \geq 0 \) for a given \( i \), the event \( \{ u_i \in (0, s_{i,l,t}) \} \) and \( \{ u_i \in (0.5 - s_{i,l,t}, 0.5) \} \) are approximately equally likely, so the set size \(|\{ i : u_i \in (0.5 - s_{i,l,t}, 0.5) \}|\) is a conservative estimate of the number of false discoveries by way of (3.2). Analogously, \(|\{ i : u_i \in [0.5, 1.5 - s_{i,r,t}) \}|\) is a conservative estimate of the number of false discoveries by way of (3.3). As such, \(|\mathcal{A}_t|\) makes sense as a conservative estimate of the number of false discoveries in \( \mathcal{R}_t \), where the additive one in the numerator of (3.1) is a theoretical adjustment factor.

If \( \text{dFDR}_t > q \), the algorithm will iterate to step \( t + 1 \) by updating \( \{ \mathcal{R}_t, \mathcal{A}_t \} \) to \( \{ \mathcal{R}_{t+1}, \mathcal{A}_{t+1} \} \), and continues doing so until termination when the dFDR estimate is below \( q \). Each update must follow these two conditions:

\[ \text{(C1)} \] The update must be based on the “partially masked” data \( \{ \tilde{u}_{i,t} \}_{i \in [m]} \) available at step \( t \), where for each \( i \),

\[ \tilde{u}_{i,t} = \begin{cases} 
    u_i & \text{if } u_i \notin \mathcal{M}_t \\
    \overbrace{u_i, \tilde{u}_i} & \text{if } u_i \in \mathcal{M}_t
\end{cases} \]
is a singleton or a two-element set depending on whether \( u_i \) is in the set \( \mathcal{M}_t \equiv \mathcal{A}_t \cup \mathcal{R}_t \), and
\[
\tilde{u}_i \equiv (1.5 - u_i)I(u_i > 0.5) + (0.5 - u_i)I(u_i \leq 0.5),
\]

is the reflection of \( u_i \) about the middle axis at \( u = 0.75 \) of the right interval \((0.5, 1)\), or about the middle axis \( u = 0.25 \) of the left interval \((0, 0.5)\), depending on whether \( u_i \) is greater than or the midpoint of the unit interval \((0, 1)\).

(C2) \( s_{i,t,t+1} \leq s_{i,t,t} \) and \( s_{i,r,t+1} \geq s_{i,r,t} \) for all \( i \), in such a way that at least one of the inclusions \( \mathcal{R}_{t+1} \subseteq \mathcal{R}_t \) and \( \mathcal{A}_{t+1} \subseteq \mathcal{A}_t \) is strict.

Essentially, (C1) means that any computer routine employed to update \( \{\mathcal{R}_t, \mathcal{A}_t\} \) to \( \{\mathcal{R}_{t+1}, \mathcal{A}_{t+1}\} \) can only know that the true value of \( u_i \) is one of the two values in \( \{\tilde{u}_i, u_i\} \) but not which, for all \( i \) in the “masked” set \( \mathcal{M}_t \). (C2) ensures that the elements in \( \mathcal{M}_t \) are gradually “unmasked”, so the algorithm will eventually terminate. Readers familiar with the data masking technique should not be surprised by the construct of ZDIRECT; in a nutshell, that basing the update of the candidate rejection and acceptance sets on the partially masked data \( \mathcal{R}_t \) can only know that the true value of \( u_i \) is in the set \( \mathcal{M}_t \), we have
\[
\min\{\tilde{u}_i, u_i\} \in \{\tilde{u}_i, u_i\}.
\]

To achieve that, for each update that satisfies (C1) and (C2), we aim to get rid of exactly one element from the masked set \( \mathcal{M}_t \), which potentially has the largest local false sign rate, since only elements remaining in the next \( \mathcal{M}_{t+1} \) may eventually be rejected. We propose to first obtain an estimate \( \hat{g}_t(\cdot) \) of the hypothetical mean-generating distribution in (2.1) with the partially masked data \( \{\tilde{u}_{i,t}\}_{i \in [m]} \), and then compute estimated local false sign rates
\[
\hat{\text{f}}_{\text{str},t,i} = \min \left( \frac{\int_{\mu \leq 0} \phi(z_i' - \mu)\hat{g}_t(\mu)d\mu}{\int \phi(z_i' - \mu)\hat{g}_t(\mu)d\mu}, \frac{\int_{\mu > 0} \phi(z_i' - \mu)\hat{g}_t(\mu)d\mu}{\int \phi(z_i' - \mu)\hat{g}_t(\mu)d\mu} \right)
\]
for all \( i \in \mathcal{M}_t \), where by defining the reflected value \( \tilde{z}_i \equiv \Phi^{-1}(\tilde{u}_i) \) on the z-value scale,
\[
z_i' \equiv I(z_i < 0)z_i \wedge \tilde{z}_i + I(z_i \geq 0)z_i \lor \tilde{z}_i
\]

Theorem 3.1 (Exact dFDR control of ZDIRECT). Suppose \( z_i \sim N(\mu_i, 1), i = 1, \ldots, m \), are independent normal variables with means \( \mu_1, \ldots, \mu_m \). Then ZDIRECT, as described above, controls the dFDR at level \( q \in (0, 1) \). Specifically, if the algorithm terminates at step \( t = \min\{t : \text{dFDR}_t \leq q\} \), we have
\[
\mathbb{E}_{\mu} \left[ \left| \left\{ i : \text{sgn}(\mu_i) \neq \text{sgn}(z_i) \text{ and } i \in \mathcal{R}_i \right\} \right| \right] \leq q
\]
where \( \mathbb{E}_{\mu}[\cdot] \) means a (frequentist) expectation with respect to fixed values of \( \mu_1, \ldots, \mu_m \).

The proof of Theorem 3.1 (Appendix D) resembles that of the data masking algorithms for FDR point null testing [Lei and Fithian 2018; Leung and Sun 2021], but also combines an argument similar to that of Barber et al. (2019), which establishes the dFDR controlling property of the knockoff filter in the different context of linear model variable selection; also see Duan et al. [2020] for how masking techniques can be applied to control the familywise error rate (FWER).

3.1. Update with Stephens (2017)’s unimodal model. That the dFDR is presented as an expectation conditional on fixed \( \mu_i \)’s in (3.4) suggests that ZDIRECT provides dFDR control in the pure frequentist sense just like the dBH procedure [Benjamini and Yekutieli 2005, Corollary 3]. However, our original motivation is to devise a more powerful algorithm which can mimic some operational characteristic of the ODP based on the random parameter formulation in (2.1). To achieve that, for each update that satisfies (C1) and (C2), we aim to get rid of exactly one element from the masked set \( \mathcal{M}_t \) which potentially has the largest local false sign rate, since only elements remaining in the next \( \mathcal{M}_{t+1} \) may eventually be rejected. We propose to first obtain an estimate \( \hat{g}_t(\cdot) \) of the hypothetical mean-generating distribution in (2.1) with the partially masked data \( \{\tilde{u}_{i,t}\}_{i \in [m]} \), and then compute estimated local false sign rates
is whichever $z_i$ or $\tilde{z}_i$ closer to the “infinity end” of the half interval $(0, \infty)$ or $(-\infty, 0)$, depending on where $z_i$ lies. That these estimated local false sign rates are evaluated at the $z'_i$’s presumes that any given masked element in $\mathcal{M}_t$ comes from the rejection set $\mathcal{R}_t$. From there, we can identify the element $\hat{i}_t = \arg\max_{i \in \mathcal{M}_t} \frac{1}{2} s_{i,t} + \frac{1}{2} s_{i,t+1}$ and update $\{s_{i,t,t}, s_{i,t,t+1}\}$ to $\{s_{i,t,t+1}, s_{i,t,t+1}\}$ accordingly so that $\hat{i}_t$ is unmasked at step $t + 1$; other thresholds can stay the same by setting $s_{i,t,t+1} = s_{i,t,t}$ and $s_{i,t,t+1} = s_{i,t,t}$ for $i \in \mathcal{M}_t \setminus \{\hat{i}_t\}$.

Our recommendation is to obtain $\hat{g}_t(\cdot)$ by employing (2.3) as a working model, whose log-likelihood with respect to the partial data $\{\tilde{u}_{i,t}\}_{i \in [m]}$ can be written as

$$l_t(\pi) = \sum_{i \in [m]} \log \pi_0 l_{0,i,t} + \sum_{k = -K, -1, 1, \ldots, K} \pi_k l_{k,i,t}$$

for component likelihoods $l_{k,i,t}$ with forms spelt out in Appendix A; in particular, we take $\hat{g}_t(\mu) = g(\mu; \hat{\pi}_t)$, where $\hat{\pi}_t$ is the solution to the penalized maximum likelihood estimation problem

$$(3.6) \quad \max_\pi \left[ l_t(\pi) + \sum_{k = -K}^K (\lambda_k - 1) \log \pi_k \right],$$

where the last term is a Dirichlet penalty with tuning parameters $\lambda_k > 0$. The details of how these tuning parameters are selected, as well as how the number of components $K$ and the end points $a_k$ of the component supports are determined based on the partial data $\{\tilde{u}_{i,t}\}_{i \in [m]}$, are deferred to the next section. Although (2.3) may be misspecified for the hypothetical generating density $g(\cdot)$ in (2.1), the dFDR control is guaranteed by Theorem 3.1 since conditions (C1) and (C2) are met. While many other working models are possible, our choice of Stephens’ (2017)’s model carries two main advantages:

(a) Speed: The optimization problem of the form in (3.6), as explained in Stephens (2017), is convex and can be solved by fast and reliable interior point methods. This is a huge advantage to ZDIRECT which is by default computationally intensive, because many updates are required before the algorithm terminates. Due to their choices of the working model, previous FDR works on data-masking Lei and Fithian (2018), Leung and Sun (2021) have to resort to an EM algorithm for their model update, which is usually substantially slower.

(b) Appropriate flexibility: The unimodality of (2.3) is flexible enough to capture asymmetry in the distribution of the $\mu_i$’s. This is a preferable aspect since, among other things, optimal $z$-value based procedures are known to be able to capitalize on the asymmetry in the distribution of the z-values to improve the power for testing the point nulls in (1.1); see Storey et al. (2007) or Sun and Cai (2007) p.904 for a detailed discussion on this phenomenon; the same is true for sign testing under the current dFDR paradigm. On the other hand, since one can only get the estimate $\hat{g}_t$ with the masked data $\{\tilde{u}_{i,t}\}_{i \in [m]}$, overfitting is generally more of a concern than with the full data and can severely harm the power of the resulting algorithm. Having a relatively simple model like (2.3), which is a form of regularization, can keep overfitting in check.

4. Simulations

In our simulation studies, we compare these four methods for dFDR control:

(a) dBH: The directional BH procedure in Benjamini and Yekutieli (2005), which declares the sign of each $\mu_i$ rejected by a standard level-$q$ BH procedure as $\text{sign}(z_i)$.
(b) LFSR: A version of the optimal procedure based on the \(lfsr\)'s computed with the true mean-generating distribution \(g(\cdot)\). Instead of the ODP described in Theorem 2.1 whose implementation involves solving a more complex infinite linear programming problem to find a threshold for the \(lfsr\)'s (see Heller and Rosset (2021)), we opt for a computationally simpler substitute which goes back to the earlier work of Sun and Cai (2007). This procedure also controls the dFDR under the Bayesian formulation (2.1) and often has power comparable to the ODP; we defer its details to Appendix B.

(c) ASH: A procedure analogous to LFSR, except that the \(lfsr\)'s are computed with \(g(\cdot; \hat{\pi})\) by solving for a penalized maximum likelihood estimate of \(\pi\) based on the unimodal mixture model (2.3), with respect to the full data \(\{z_i\}_{i=1}^m\). All tuning parameters involved are chosen exactly as the default described in Stephens (2017) Supplementary information); ASH stands for “adaptive shrinkage”, as Stephens (2017) called it.

(d) ZDIRECT: Our proposal described in Section 3, where at each step \(t\) we have to solve for \(\tilde{\pi}_t\) in (3.6) with respect to the partial data \(\{a_{i,t}\}_{i=1}^m\). The points \(\alpha_k\) are picked to give a large and dense grid; in particular, for the positive supports, the minimum and maximum are set as \(a_1 = 10^{-1}\) and \(a_K = 2\sqrt{\max_i z_i^2 - 1}\), with the rest set as \(a_k+1 = \sqrt{2}a_k\) based on the multiplicative factor \(\sqrt{2}\) (so the number of components \(K\) is also implicitly determined). The negative supports are set by taking \(a_{-1} = -a_1, \ldots, a_{-K} = -a_K\). This grid follows the recommendation of Stephens (2017), except that we have replaced \(z_i\) with \(z_i^\ast\) since the masking condition (C1) must be observed. Moreover, we set \(\lambda_k = 0.8\) for all \(k = -K, \ldots, 0, \ldots, K\); this further regularizes the maximum likelihood estimation by encouraging sparsity in the mixing proportions \(\pi\). Lastly, to speed up the algorithm, \(\hat{g}_t(\cdot)\) is only re-estimated by (3.6) for every \([m/200]\) steps, i.e., the same \(\hat{g}_t(\cdot)\) is used \([m/200]\) times to update the candidate rejection and acceptance sets before the algorithm terminates, which certainly does not violate the condition (C1).

We simulate \(m = 1000\) independent \(z\)-values \(z_i \sim N(\mu_i, 1)\), where the means \(\mu_1, \ldots, \mu_m\) are generated from a mixture density of the form
\[
g(\mu) = w_0f_0(\mu) + w_1g_1(\mu),
\]
with the mixing proportions \(w_0\) and \(w_1\) summing to 1. The “null” proportion \(w_0\) ranges in \(\{0.8, 0.5, 0.2\}\) to give three level of effect sparsity. We remark that taking \(w_0 = 0.2\) renders a situation close to Tukey (1991)'s conception of “no exactly zero effects”. We also consider two choices for the “alternative” density \(g_1(\mu)\):

(S1) With the unimodal skew normal density (Azzalini 2013)
\[
f(\mu) = 2 \frac{1}{\omega} \phi\left(\frac{\mu}{\omega}\right) \Phi\left(\frac{\alpha \mu}{\omega}\right),
\]
we take \(g_1(\mu) = f(\mu - \arg \max_{\mu} f(\mu))\), i.e., \(g_1\) is a shifted version of \(f\) with a mode at 0. The “slant” parameter \(\alpha\) controls the skewness; if \(\alpha = 0\), the normal distribution with mean 0 and standard deviation \(\omega\) is recovered from (4.1), otherwise a more positive (negative) \(\alpha\) gives a more right skewed (left skewed) distribution. We make \(\alpha\) take values from the set \(\{0, 20, 40, 60, 80\}\) to adjust the skewness, and \(\omega\) take values from \(\{4, 6, 8\}\) to adjust the dispersion.

(S2) The alternative density is itself a bimodal mixture of the form
\[
g_1(\mu) = (1 - w)\phi(\mu + \xi) + w\phi(\mu - \xi).
\]
Here, $\xi$ is an average effect size in absolute value that ranges in $\{0.5, 1, 1.5, 2, 2.5\}$, and $w$ is a mixing proportion for the positively centered means that ranges in $\{0.5, 0.75, 1\}$ to adjust the level of asymmetry of $g_1(\cdot)$.

The empirical dFDR and power of the different methods implemented for the target dFDR level $q = 0.1$ are evaluated with 200 sets of repeatedly generated $\{z_i, \mu_i\}_{i \in [m]}$. The results are shown in Figure 4.1, where the power is shown as the true positive rate, defined as $E \left[ \frac{\sum_{i \in \mathcal{R}} \mathbb{1}(\text{sgn}(\mu_i) \neq \text{sgn}(\hat{\mu}_i))}{|\mathcal{R}|} \right]$ for a generic procedure $(\text{sgn}(\hat{\mu}_i))_{i \in \mathcal{R}}$, which some would consider to be more illustrative than the ETD. The following observations are made:

(a) The LFSR method, which requires oracle knowledge of the underlying distribution $g(\cdot)$ and serves as benchmark for power, displays empirical dFDR that tightly aligns with the target level 0.1 in the two left panels, as expected.

(b) For both (S1) and (S2), all the three z-value based methods (LFSR, ASH, ZDIRECT) display greater improvements in power over dBH as the effects become denser. This is because via leveraging the true underlying density $g(\cdot)$ or its estimate, these methods implicitly account for the proportion of null effects $w_0$, a feature not possessed by dBH. This is analogous to how the sparsity-adaptive variants of the original BH procedure can improve the power (Storey et al., 2004) for testing the points nulls in (1.1). We will discuss this aspect further in Section 5.

(c) For (S1), since the true $g(\cdot)$ is unimodal at zero, we expect ASH to have power comparable to LFSR; this is true, except that the dFDR of ASH is seen to be slightly above the desired level 0.1 for two of the graphs in the upper-left panel of Figure 4.1 when the effects are sparse; after all, the finite mixture in (2.3) only approximates the true unimodal $g(\cdot)$. In contrast, ZDIRECT, which also employs (2.3) as a working model, has the data-masking mechanism (C1) in place to ensure that the dFDR is controlled under 0.1. Despite being more conservative than ASH, it consistently outperform dBH, the only other practical procedure that guarantees exact dFDR control.

(d) For (S2), $g(\cdot)$ is no longer unimodal. It is not surprising to see that ASH severely violates the desired dFDR level in the lower-left panel since (2.3) is very much misspecified with respect to $g(\cdot)$, while ZDIRECT has its dFDR kept in check as guaranteed by Theorem 3.1. Moreover, ZDIRECT still has better power than dBH; in particular, for any given effect sparsity level, we can see from the lower right panel that the power of ZDIRECT (red curve) gradually pulls away from that of dBH (blue curve) as the effects become more asymmetric. This attests to the usefulness of (2.3), even as a misspecified working model, in capturing the asymmetry in the effect distribution to boost the power, as we have mentioned in Section 3.1.

5. Discussion

We have devised an algorithm with strong theoretical guarantee for dFDR control that can improve upon the power of the dBH procedure. As with other algorithms based on data masking (Lei and Fithian 2018, Leung and Sun 2021), the success of ZDIRECT hinges on the working model employed for the iterative updates. To render a powerful data masking method, a good working model should strike a balance between flexibility and simplicity; a working model that is flexible enough can provide good approximation for the unknown generating density $g(\cdot)$, while an overly flexible model can lead to severe overfitting, particularly when the fitting can only be done using the partial data $\{\tilde{u}_{i,t}\}_{i \in [m]}$.

Our choice of Stephens (2017)’s working model, paired with the sparsity-inducing regularization $\lambda_k = 0.8$, has demonstrated consistent power advantage over the dBH procedure, even in other
Figure 4.1. Empirical directional false discovery rate and true positive rates of the four compared methods implemented for a target dFDR level $q = 0.1$. \texttt{sparse}, \texttt{denser} and \texttt{densest} correspond to $w_0 = 0.8, 0.5, 0.2$ respectively. The upper panels are for the skewed normal setup (S1); the x-axis marks different values of the slant parameter $\alpha$, and \texttt{least dispersed}, \texttt{more dispersed} and \texttt{most dispersed} correspond respectively to $\omega = 4, 6, 8$. The lower panels are for the bimodal setup (S2); the x-axis marks different values of the average effect $\xi$, and \texttt{symmetric}, \texttt{more asymmetric} and \texttt{most asymmetric} correspond respectively to $w = 0.5, 0.75, 1$.

undisclosed simulations we have experimented with. The parametric exponential family model for $g(\cdot)$ proposed by Efron (2016) could be another good choice when estimated with appropriate regularization. However, unlike the convex problem in (3.6) which can be solved by very fast interior point methods, the maximum likelihood estimation of that model requires the use of
possibly much slower Newton-type algorithms [Efron 2016, p.9]. This can severely bring down the speed of ZDIRECT, which ideally requires repeated re-estimations of the model to perform quality updates.

Another probable route is to devise a sparsity-adaptive variant of the dBH procedure, much like how sparsity-adaptive variant of the original BH procedure is devised for point null testing [Storey et al., 2004]. It is likely that one can modify the proof argument of [Storey et al., 2004, Theorem 3] to render a procedure with exact dFDR control under our normal-means setting. However, such a procedure is bound to be based on the two-sided p-values; this means that it cannot leverage aspects of the z-value distribution such as its asymmetry to boost the power, like what ZDIRECT has achieved in our simulations (S2).

Finally, an interesting dual problem is to construct, for each $i$ in a data-dependent selected subset $\mathcal{R} \subseteq [m]$, a confidence interval $CI_i \subseteq \mathbb{R}$ such that

(a) each $CI_i$ is sign-determining, i.e. $CI_i \subseteq (-\infty, 0]$ or $CI_i \subseteq (0, \infty)$, and
(b) the false coverage rate (FCR)

$$\mathbb{E} \left[ \frac{|\{i : \mu_i \in CI_i\}|}{1 \lor |\mathcal{R}|} \right]$$

is controlled under a desired level $q \in (0,1)$.

This paradigm of inference has been recently suggested in [Weinstein and Yekutieli, 2020]. Note that ZDIRECT corresponds to such a procedure, which constructs the trivial long interval $CI_i = \begin{cases} \{0, \infty\} & \text{if } z_i > 0 \\ (-\infty, 0] & \text{if } z_i < 0 \end{cases}$ for each $i \in \mathcal{R}$ (Theorem 3.1). A valid procedure that constructs non-trivial selective sign-determining confidence intervals has been proposed in [Weinstein and Yekutieli, 2020, Definition 2], but we speculate the possibility of developing another procedure which can construct more and shorter intervals by a z-value based approach.

**Appendix A. Forms of Component Likelihoods**

Since $z_i = \Phi^{-1}(u_i)$ and $\bar{z}_i = \Phi^{-1}(\bar{u}_i)$, we equivalently express the component likelihoods of $l_i(\pi)$ in terms of $z_i$ and $\bar{z}_i$:

$$l_{0,i,t} = \begin{cases} \phi(z_i) + \phi(\bar{z}_i) & \text{if } i \in \mathcal{M}_t \\ \phi(z_i) & \text{if } i \in [m] \setminus \mathcal{M}_t \end{cases}$$

For $k = -K, \ldots, -1, 1, \ldots, K$,

$$l_{k,i,t} = \begin{cases} \left[ [\phi(z_i - \mu) + \phi(\bar{z}_i - \mu)]f_k(\mu)d\mu \right. & \text{if } i \in \mathcal{M}_t \\ \phi(z_i - \mu)f_k(\mu)d\mu & \text{if } i \in [m] \setminus \mathcal{M}_t \end{cases}$$

with the exact analytic forms

$$l_{k,i,t} = \begin{cases} \frac{\Phi(z_i) - \Phi(z_i - a_k)}{a_k} + \frac{\Phi(\bar{z}_i) - \Phi(\bar{z}_i - a_k)}{a_k} & \text{if } i \in \mathcal{M}_t \text{ and } k \geq 1 \\ \frac{\Phi(z_i - a_k) - \Phi(z_i)}{-a_k} & \text{if } i \in [m] \setminus \mathcal{M}_t \text{ and } k \geq 1 \\ \frac{\Phi(z_i - a_k) - \Phi(z_i)}{-a_k} & \text{if } i \in \mathcal{M}_t \text{ and } k \leq -1 \\ \frac{\Phi(z_i) - \Phi(z_i - a_k)}{a_k} & \text{if } i \in [m] \setminus \mathcal{M}_t \text{ and } k \leq -1 \end{cases}$$
APPENDIX B. **Sun and Cai** (2007)’s Implementation of An Oracle Procedure

An exact implementation of the ODP described in Theorem 2.1 involves solving a rather complex infinite integer programming problem [Heller and Rosset 2021] to determine a threshold for the local false sign rates. As an alternative, in Section 3, LFSR is a similar oracle procedure with an attractively simpler implementation first suggested by [Sun and Cai 2007], and it suffices to serve as a benchmark for the power of our compared procedures. Suppose we denote this procedure as \( \text{LFSR} \) and the discovery set is defined by

\[
\mathcal{R}_{SC} \equiv \{i : \text{lf}sr_i \leq \text{lf}sr(j)\}
\]

with the index

\[
j = j(q) \equiv \max \left\{ i' \in [m] : \sum_{i=1}^{i'} \text{lf}sr(i) \leq q \right\},
\]

where \( \text{lf}sr(1) \leq \cdots \leq \text{lf}sr(m) \) are the order statistics of true local false sign rates, and \( \mathcal{R}_{SC} \) is the empty set if \( j \) is not well-defined. The ratio \( \frac{\sum_{i=1}^{i'} \text{lf}sr(i)}{j} \) in the definition of \( j \) is precisely the conditional dFDR

\[
E \left[ \frac{\{i : \text{sgn}_i^{SC} \neq \text{sgn}(\mu_i) \text{ and } \text{lf}sr_i \leq \text{lf}sr(i')\}}{\mathcal{R}_{SC} \neq \emptyset} \right] P(\mathcal{R}_{SC} \neq \emptyset),
\]

of optimally declaring the signs for the subset \( \{i : \text{lf}sr_i \leq \text{lf}sr(i')\} \) given the data, which also implies the dFDR of \( (\text{sgn}_i^{SC})_{i \in \mathcal{R}_{SC}} \),

\[
E \left[ \frac{\sum_{i=1}^{j} \text{lf}sr(i)}{j} \right] P(\mathcal{R}_{SC} \neq \emptyset),
\]

is less than \( q \) under the Bayesian formulation (2.1).

The procedure ASH is implemented the same way, except that the true \( \text{lf}sr_i \)'s are replaced with their estimates constructed with \( g(\cdot; \hat{\pi}) \) by solving for a penalized estimate of (2.3).

APPENDIX C. Proof of Theorem 2.1

For two procedures \( (\text{sgn}_i^{(1)})_{i \in \mathcal{R}(1)} \) and \( (\text{sgn}_i^{(2)})_{i \in \mathcal{R}(2)} \), \( (\text{sgn}_i^{(2)})_{i \in \mathcal{R}(2)} \) is said to improve upon \( (\text{sgn}_i^{(1)})_{i \in \mathcal{R}(1)} \) if \( ETD[(\text{sgn}_i^{(2)})_{i \in \mathcal{R}(2)}] \geq ETD[(\text{sgn}_i^{(1)})_{i \in \mathcal{R}(1)}] \) and \( dFDR[(\text{sgn}_i^{(2)})_{i \in \mathcal{R}(2)}] \leq dFDR[(\text{sgn}_i^{(1)})_{i \in \mathcal{R}(1)}] \).

Let \( \mathbf{z} = (z_1, \ldots, z_m) \), and let \( (\text{sgn}_i)_{i \in \mathcal{R}} \) be a certain procedure with \( dFDR[(\text{sgn}_i)_{i \in \mathcal{R}}] \leq q \). We also write \( \mathcal{R} = \mathcal{R}(\mathbf{z}) \) and \( \text{sgn}_i = \text{sgn}_i(\mathbf{z}) \) to emphasize that both are functions in \( \mathbf{z} \). It suffices to show that the two statements below are true:

(i) Statement 1: If there exists \( j \in [m] \) such that one or both of the disjoint events

\[
Z_j^{(1)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & j \in \mathcal{R}(\mathbf{z}); \\
\text{sgn}_j(\mathbf{z}) < 0 & P(\mu_j \leq 0|z_j) < P(\mu_j \geq 0|z_j);
\end{array} \right. \quad \text{and} \quad Z_j^{(2)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & j \in \mathcal{R}(\mathbf{z}); \\
\text{sgn}_j(\mathbf{z}) = 1 & P(\mu_j \leq 0|z_j) > P(\mu_j \geq 0|z_j);
\end{array} \right.
\]

(ii) Statement 2: If \( j \in [m] \), then for any \( \mathbf{z} \),

\[
Z_j^{(3)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & \text{sgn}_j(\mathbf{z}) < 0; \\
\text{sgn}_j(\mathbf{z}) > 0 & P(\mu_j \leq 0|z_j) > P(\mu_j \geq 0|z_j);
\end{array} \right.
\]

\[
Z_j^{(4)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & \text{sgn}_j(\mathbf{z}) = 1; \\
\text{sgn}_j(\mathbf{z}) < 0 & P(\mu_j \leq 0|z_j) < P(\mu_j \geq 0|z_j);
\end{array} \right.
\]

\[
Z_j^{(5)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & \text{sgn}_j(\mathbf{z}) > 0; \\
\text{sgn}_j(\mathbf{z}) = 1 & P(\mu_j \leq 0|z_j) < P(\mu_j \geq 0|z_j);
\end{array} \right.
\]

\[
Z_j^{(6)} \equiv \left\{ \begin{array}{ll}
\mathbf{z} & \text{sgn}_j(\mathbf{z}) < 0; \\
\text{sgn}_j(\mathbf{z}) > 0 & P(\mu_j \leq 0|z_j) > P(\mu_j \geq 0|z_j);
\end{array} \right.
\]

have non-zero probabilities, the procedure \((\tilde{y}r_n)_i \in \mathcal{R}'\) defined by
\[
\mathcal{R}'(z) = \mathcal{R}(z) \text{ for all } z
\]
and, for \(i \in \mathcal{R} = \mathcal{R}'\),
\[
\tilde{y}r_n_i(z) = \begin{cases} 
1 & \text{if } i = j \text{ and } z \in \mathcal{Z}_j^{(1)} \\
-1 & \text{if } i = j \text{ and } z \in \mathcal{Z}_j^{(2)} \\
\tilde{y}r_n_i(z) & \text{if otherwise}
\end{cases}
\]

improves upon \((\tilde{y}r_n)_i \in \mathcal{R}\).

(ii) Statement 2: If there exist two distinct \(j, l \in [m]\) such that the event
\[
\mathcal{Z}_{jl} = \{z : f s_{r_j} < f s_{r_l}, l \in \mathcal{R} \text{ and } j \notin \mathcal{R}\}
\]
has non-zero probability, then it is possible to construct an improved procedure \((\tilde{y}r_n)_i \in \mathcal{R}'\)
with the property that
\[
\mathcal{R}'(z) = \begin{cases} 
(\mathcal{R}(z) \setminus \{l\}) \cup \{j\} & \text{if } z \in \mathcal{Z}_{jl} \\
\mathcal{R}(z) & \text{if } z \notin \mathcal{Z}_{jl}
\end{cases}
\]

Suppose both statements can be shown. Then any procedure can be improved by repeatedly
applying Statement 2, until we end up with a procedure for which \(P(\mathcal{Z}_{jl}) = 0\) for all \((j, l)\) pairs. We
can then further improve this procedure by applying Statement 1, and end up with a procedure
for which \(P(\mathcal{Z}_j^{(1)}) = P(\mathcal{Z}_j^{(2)}) = 0\) for all \(j\), and hence satisfying the conditions (i) and (ii) in
Theorem 2.1 since the ODP cannot be improved, it must also have the latter two conditions satisfied.

\[\text{Proof of Statement 1.} \] We write
\[
ETD[\{(\tilde{y}r_n)_i \in \mathcal{R}'\}] - ETD[\{(\tilde{y}r_n)_i \in \mathcal{R}\}]
\]
\[= \int \sum_{i \in \mathcal{R}'(z)} P(\tilde{y}r_n_i(z) = \text{sgn}(\mu_i)|z)P(z)dz - \int \sum_{i \in \mathcal{R}(z)} P(\tilde{y}r_n_i(z) = \text{sgn}(\mu_i)|z)P(z)dz
\]
\[= \int_{\mathcal{Z}_j^{(1)} \cup \mathcal{Z}_j^{(2)}} \sum_{i \in \mathcal{R}(z)} [P(\tilde{y}r_n_i(z) = \text{sgn}(\mu_i)|z) - P(\tilde{y}r_n_i(z) = \text{sgn}(\mu_i)|z)]P(z)dz
\]
\[= \int_{\mathcal{Z}_j^{(1)}} [P(\tilde{y}r_n_j(z) = \text{sgn}(\mu_j)|z) - P(\tilde{y}r_n_j(z) = \text{sgn}(\mu_j)|z)]P(z)dz + \int_{\mathcal{Z}_j^{(2)}} [P(\tilde{y}r_n_j(z) = \text{sgn}(\mu_j)|z) - P(\tilde{y}r_n_j(z) = \text{sgn}(\mu_j)|z)]P(z)dz
\]
\[= \int_{\mathcal{Z}_j^{(1)}} [P(\mu_j > 0|z_j) - P(\mu_j < 0|z_j)]P(z)dz + \int_{\mathcal{Z}_j^{(2)}} [P(\mu_j < 0|z_j) - P(\mu_j > 0|z_j)]P(z)dz > 0,
\]
where the second and third equalities come from the fact that \((\tilde{y}r_n)_i \in \mathcal{R}'\) and \((\tilde{y}r_n)_i \in \mathcal{R}\) differ only
on \(\mathcal{Z}_j^{(1)} \cup \mathcal{Z}_j^{(2)}\) and for \(j\), the fourth equality is from the disjointness of \(\mathcal{Z}_j^{(1)}\) and \(\mathcal{Z}_j^{(2)}\), and the
last equality is from how \(\tilde{y}r_n_j\) is defined on \(\mathcal{Z}_j^{(1)}\) and \(\mathcal{Z}_j^{(2)}\) as well as the independence across all
we leave the details to the reader.

□

Since $R$ has been defined, we only have to define $\tilde{\text{sgn}}_i$ for each $i \in \mathcal{R}'$, as

$$
\tilde{\text{sgn}}_i(z) = \begin{cases} 
1 & \text{if } i = j \text{ and } z \in Z_{jl}^{(1)} \\
-1 & \text{if } i = j \text{ and } z \in Z_{jl}^{(2)} \\
\text{sgn}_i(z) & \text{if otherwise}
\end{cases}
$$

One can then write

$$
ETD[(\tilde{\text{sgn}}_i)_{i \in \mathcal{R}'_l}] - ETD[(\text{sgn}_i)_{i \in \mathcal{R}}] = \int_{Z_{jl}^{(1)}} [P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_j)|z) - P(\text{sgn}_i(z) = \text{sgn}(\mu_l)|z)] P(z) dz + \\
\int_{Z_{jl}^{(2)}} [P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_j)|z) - P(\text{sgn}_i(z) = \text{sgn}(\mu_l)|z)] P(z) dz
$$

(C.1)

$$
= \int_{Z_{jl}^{(1)}} [P(\mu_j > 0|z) - P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_l)|z)] P(z) dz + \\
\int_{Z_{jl}^{(2)}} [P(\mu_j < 0|z) - P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_l)|z)] P(z) dz.
$$

(C.2)

by a similar train of equalities as in the proof for Statement 1. For $z \in Z_{jl}^{(1)}$, $P(\mu_j < 0|z) = lfsr_j < lfsr_\ell \leq P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_l)|z)$, where the last inequality comes from the fact that $lfsr_\ell = P(\mu_l \leq 0|z) \wedge P(\mu_j > 0|z)$ is the smallest conditional probability of making a false discovery that can possibly be achieved by $\tilde{\text{sgn}}_i(z)$. This in turns implies $P(\mu_j > 0|z) > P(\tilde{\text{sgn}}_i(z) = \text{sgn}(\mu_l)|z)$, which means that the term in (C.1) is greater than 0. Similarly one can show that the term in (C.2) is also greater than 0, which gives $ETD[(\tilde{\text{sgn}}_i)_{i \in \mathcal{R}'_l}] - ETD[(\text{sgn}_i)_{i \in \mathcal{R}}] > 0$.

We can also show that $dFDR[(\tilde{\text{sgn}}_i)_{i \in \mathcal{R}'_l}] < dFDR[(\text{sgn}_i)_{i \in \mathcal{R}}]$ similarly; to avoid repetitions, we leave the details to the reader.

□
Appendix D. Proof of Theorem 3.1

We first quote Lei and Fithian (2018, Lemma 2), a fundamental tool for proving false discovery validity of data-masking algorithms.

Lemma D.1. Suppose that, conditionally on the $\sigma$-field $G_{-1}$, $b_1, \ldots, b_m$ are independent Bernoulli random variables with $P(b_i = 1 | G_{-1}) = \rho_i \geq \rho > 0$, almost surely. Also suppose that $[m] \supseteq C_0 \supseteq C_1 \supseteq \cdots$, with each subset $C_{t+1}$ measurable with respect to $G_t = \sigma\left(G_{-1}, C_t, (b_i)_{i \in C_t}, \sum_{i \in C_t} b_i\right)$.

If $i$ is an almost-surely finite stopping time with respect to the filtration $(G_t)_{t \geq 0}$, then

$$E\left[\frac{1 + |C_i|}{1 + \sum_{i \in C_i} b_i} \mid G_{-1}\right] \leq \rho^{-1}.$$ 

To begin our proof, write

$$dFDP(i) = \left|\left\{i : \text{sgn}(\mu_i) \neq \text{sgn}(z_i) \text{ and } i \in R_i\right\}\right| \leq \frac{1 + |A_i|}{1 \lor |R_i|} \left|\left\{i : \text{sgn}(\mu_i) \neq \text{sgn}(z_i) \text{ and } i \in R_i\right\}\right| \frac{1 + |A_i|}{1 \lor |R_i|}.$$ 

Since $dFDR_i = \frac{1 + |A_i|}{1 \lor |R_i|} \leq q$ by definition, it suffices to show that

$$E_{\mu}\left[\frac{\left|\left\{i : \text{sgn}(\mu_i) \neq \text{sgn}(z_i) \text{ and } i \in R_i\right\}\right|}{1 + |A_i|}\right] \leq 1.$$ 

For each $i$, we define the variable

$$E_i = \begin{cases} +1 & \text{if } |z_i| > |\tilde{z}_i| \\ -1 & \text{if } |\tilde{z}_i| > |z_i| \end{cases},$$

which, by recalling the relationships $\Phi(z_i) = u_i$ and $\Phi(\tilde{z}_i) = \tilde{u}_i$, is equal to $+1$ if $u_i$ is closer than $\tilde{u}_i$ to the “endpoints” of the unit interval $[0,1]$, or equal to $-1$ otherwise. In particular, since $s_{i,t,t} < 0.25$ and $s_{i,r,t} > 0.75$ for all $i$ and $t$, it must be that $R_i \subseteq \{i : E_i = +1\}$, i.e., an element $i$ can possibly be a discovery only if $E_i = +1$. Define

$$S_i = \text{sgn}(z_i)E_i,$$

which will take on the same sign as $z_i$ if $u_i$ is closer than $\tilde{u}_i$ to the endpoints of the unit interval $[0,1]$ and let $S = (S_1, \ldots, S_m)$. We will define the set $\mathcal{H}_0 := \{i : S_i \neq \text{sgn}(\mu_i)\}$, which acts like a “null set” since discovering any $i \in \mathcal{H}_0 \cap \{i : E_i = +1\}$ constitutes a Type S error, in light of $R_i \subseteq \{i : E_i = +1\}$. Conditioning on the knowledge of $S$, one will get that

$$E_{\mu}\left[\frac{\left|\left\{i : \text{sgn}(\mu_i) \neq \text{sgn}(z_i) \text{ and } i \in R_i\right\}\right|}{1 + |A_i|}\right|S\right] = E_{\mu}\left[\frac{|R_i \cap \hat{R}_0|}{1 + |A_i|}\right|S\right] \leq E_{\mu}\left[\frac{|R_i \cap \hat{R}_0|}{1 + |A_i \cap \hat{R}_0|}\right].$$

The last inequality in the preceding display implies that (D.1) can be proved if it is true that

$$E_{\mu}\left[\frac{|R_i \cap \hat{R}_0|}{1 + |A_i \cap \hat{R}_0|}\right] \leq 1,$$

which, in turn, we will prove by showing

$$E_{\mu}\left[\frac{|R_i \cap \hat{R}_0|}{1 + |A_i \cap \hat{R}_0|}\right] \leq 1.$$ 

Before finishing proving (D.2), we emphasize that knowledge of the set $\mathcal{H}_0$ does not imply knowing the parameters $\mu_1, \ldots, \mu_m$, even though $\mathcal{H}_0$ is defined with them. Moreover, the expectation
operator $\mathbb{E}_\mu[\cdot]$ simply suggests that the $\mu_1, \ldots, \mu_m$ are considered fixed (but still unknown), as opposed to the random parameter formulation in (2.1).

The rest of the proof follows by setting the scene to apply Lemma D.1. First we define the indicator variables

$$b_i = 1(u_i \in [0.25, 0.75]), i \in [m],$$

and let $\mathcal{G}_t = \{\hat{\mathcal{H}}_0, (u_i)_{i \in [m]}, (b_i)_{i \notin \hat{\mathcal{H}}_0}\}$, where $u_i' = \Phi(z_i')$ for $z_i'$ defined in (3.5), and is the more “extreme” value between $u_i$ and $\tilde{a}_i$. For $t = 0, 1, \ldots$, define

$$C_t = \{i : i \in \hat{\mathcal{H}}_0 \text{ and } u_i \in (0, s_{i,l,t}) \cup (1 - s_{i,r,t}, 1) \cup (0.5 - s_{i,l,t}, 1.5 - s_{i,r,t})\} = \mathcal{H}_0 \cap \mathcal{M}_t,$$

and the filtrations

$$\mathcal{G}_t = \mathcal{F} \left\{ \mathcal{G}_t, (b_i)_{i \notin \mathcal{C}_t}, \sum_{i \in \mathcal{C}_t} b_i \right\}.$$

Since since $s_{i,l,t} < 0.25$ and $s_{i,r,t} > 0.75$ for all $i$ and $t$ we must have that

$$|\mathcal{A}_t \cap \hat{\mathcal{H}}_0| = \sum_{i \in \mathcal{C}_t} b_i \text{ and } |\mathcal{R}_t \cap \hat{\mathcal{H}}_0| = |\mathcal{C}_t| - \sum_{i \notin \mathcal{C}_t} b_i.$$

Writing

$$|\mathcal{A}_t| = |\mathcal{A}_t \cap \hat{\mathcal{H}}_0| + \sum_{i \notin \mathcal{C}_t} |\mathcal{B}_i| \text{ and } |\mathcal{R}_t| = |\mathcal{R}_t \cap \hat{\mathcal{H}}_0| + \sum_{i \notin \mathcal{C}_t} |\mathcal{B}_i|,$$

one see that $|\mathcal{A}_t|, |\mathcal{R}_t| \in \mathcal{G}_t$, so $\hat{t}$ is a stopping time with respect to our filtrations and almost surely finite because ZDIRECT guarantees to terminate. Moreover, $\mathcal{C}_{t+1} \in \mathcal{G}_t$ since $\mathcal{H}_t \in \mathcal{G}_{t-1}$ and the thresholds $s_{i,l,t}$ and $s_{i,r,t}$ are determined by the partial data only.

Lastly, by writing

$$\mathbb{E}_\mu \left[ \frac{|\mathcal{R}_t \cap \hat{\mathcal{H}}_0|}{1 + |\mathcal{A}_t \cap \hat{\mathcal{H}}_0|} \right] = \mathbb{E}_\mu \left[ \frac{|\mathcal{C}_t| - \sum_{i \in \mathcal{C}_t} b_i}{1 + \sum_{i \in \mathcal{C}_t} b_i} \right] \hat{\mathcal{H}}_0 = \mathbb{E}_\mu \left[ \frac{1 + |\mathcal{C}_t|}{1 + \sum_{i \in \mathcal{C}_t} b_i} \right] \hat{\mathcal{H}}_0 - 1.$$

one only need to show that

$$P(b_i = 1 \mid \mathcal{G}_{t-1}) \geq 0.5 \text{ for each } i \in \hat{\mathcal{H}}_0$$

to wrap up the proof. We can break this into two cases:

- **Case 1:** $\mu_i \geq 0$. Since $i \in \hat{\mathcal{H}}_0$, it must be that $S_i = -1$. This can be true with either $u_i \in (0.5, 0.75)$ or $u_i \in (0, 0.25)$, only the former of which can give $b_i = 1$. These two events respectively have probability $\int_{\Phi^{-1}(0.5)} \phi(z_i - \mu_i) \, dz_i$ and $\int_{\Phi^{-1}(0.25)} \phi(z_i - \mu_i) \, dz_i$, and since $\mu \geq 0$, $P(u_i \in (0.5, 0.75)) \geq P(u_i \in (0, 0.25))$. Hence,

$$P(b_i = 1 \mid \mathcal{G}_{t-1}) = \frac{P(u_i \in (0.5, 0.75))}{P(u_i \in (0.5, 0.75)) + P(u_i \in (0, 0.25))} \geq 0.5.$$

- **Case 2:** $\mu_i < 0$. The derivations are completely analogous to that of Case 1.

(It is important to clarify, the above argument only assesses the stochastic behavior of $b_i$ under two different scenarios with $\mu_i$ taking on different signs, and is not conditioning on the knowledge of $\mu_i$; the knowledge of $\mu_i$ implies the knowledge of $S_i$, which will take away any randomness in $b_i$ when combined with the knowledge of $\mathcal{G}_{t-1}$. Putting it another way, the probability $P(b_i = 1 \mid \mathcal{G}_{t-1})$ above can be more appropriately written as $P_{\mu_i}(b_i = 1 \mid \mathcal{G}_{t-1})$ in our style of notation.)
Azzalini, A. (2013). *The skew-normal and related families*, volume 3. Cambridge University Press.
Barber, R. F., Candès, E. J., et al. (2019). “A knockoff filter for high-dimensional selective inference.” *The Annals of Statistics*, 47(5): 2504–2537.
Benjamini, Y. (2020). “Selective inference: The silent killer of replicability.” *Harvard Data Science Review*, 2(4).
Benjamini, Y. and Hochberg, Y. (1995). “Controlling the false discovery rate: a practical and powerful approach to multiple testing.” *Journal of the Royal statistical society: series B (Methodological)*, 57(1): 289–300.
— (2000). “On the adaptive control of the false discovery rate in multiple testing with independent statistics.” *Journal of educational and Behavioral Statistics*, 25(1): 60–83.
Benjamini, Y. and Yekutieli, D. (2005). “False discovery rate–adjusted multiple confidence intervals for selected parameters.” *Journal of the American Statistical Association*, 100(469): 71–81.
Duan, B., Ramdas, A., and Wasserman, L. (2020). “Familywise error rate control by interactive unmasking.” In *International Conference on Machine Learning*, 2720–2729. PMLR.
Efron, B. (2007). “Size, power and false discovery rates.” *The Annals of Statistics*, 35(4): 1351–1377.
— (2016). “Empirical Bayes deconvolution estimates.” *Biometrika*, 103(1): 1–20.
Efron, B., Tibshirani, R., Storey, J. D., and Tusher, V. (2001). “Empirical Bayes analysis of a microarray experiment.” *Journal of the American statistical association*, 96(456): 1151–1160.
Feller, W. (2008). *An introduction to probability theory and its applications, vol 2*. John Wiley & Sons.
Gelman, A. and Tuerlinckx, F. (2000). “Type S error rates for classical and Bayesian single and multiple comparison procedures.” *Computational statistics*, 15(3): 373–390.
Heller, R. and Rosset, S. (2021). “Optimal control of false discovery criteria in the two-group model.” *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 83(1): 133–155.
Lehmann, E. L. and Romano, J. P. (2006). *Testing statistical hypotheses*. Springer Science & Business Media.
Lei, L. and Fithian, W. (2018). “AdaPT: an interactive procedure for multiple testing with side information.” *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 80(4): 649–679.
Leung, D. and Sun, W. (2021). “ZAP: Z-value Adaptive Procedures for False Discovery Rate Control with Side Information.” *arXiv preprint arXiv:2108.12623*.
Stephens, M. (2017). “False discovery rates: a new deal.” *Biostatistics*, 18(2): 275–294.
Storey, J. D. (2007). “The optimal discovery procedure: a new approach to simultaneous significance testing.” *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 69(3): 347–368.
Storey, J. D., Dai, J. Y., and Leek, J. T. (2007). “The optimal discovery procedure for large-scale significance testing, with applications to comparative microarray experiments.” *Biostatistics*, 8(2): 414–432.
Storey, J. D., Taylor, J. E., and Siegmund, D. (2004). “Strong control, conservative point estimation and simultaneous conservative consistency of false discovery rates: a unified approach.” *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 66(1): 187–205.
Sun, W. and Cai, T. T. (2007). “Oracle and adaptive compound decision rules for false discovery rate control.” *Journal of the American Statistical Association*, 102(479): 901–912.
Tukey, J. W. (1991). “The philosophy of multiple comparisons.” *Statistical science*, 100–116.
Weinstein, A. and Yekutieli, D. (2020). “Selective sign-determining multiple confidence intervals with FCR control.” *Statistica Sinica*, 30(1): 531–555.
Williams, V. S., Jones, L. V., and Tukey, J. W. (1999). “Controlling error in multiple comparisons, with examples from state-to-state differences in educational achievement.” *Journal of educational and behavioral statistics*, 24(1): 42–69.