Contextual Online False Discovery Rate Control

Shiyun Chen
Amazon, Seattle, USA

Shiva Kasiviswanathan
Amazon, Sunnyvale, USA

Abstract

Multiple hypothesis testing, a situation when we wish to consider many hypotheses, is a core problem in statistical inference that arises in almost every scientific field. In this setting, controlling the false discovery rate (FDR), which is the expected proportion of type I error, is an important challenge for making meaningful inferences. In this paper, we consider a setting where an ordered (possibly infinite) sequence of hypotheses arrives in a stream, and for each hypothesis we observe a p-value along with a set of features specific to that hypothesis. The decision whether or not to reject the current hypothesis must be made immediately at each timestep, before the next hypothesis is observed. This model provides a general way of leveraging the side (contextual) information in the data to help maximize the number of discoveries while controlling the FDR.

We propose a new class of powerful online testing procedures, where the rejection thresholds are learned sequentially by incorporating contextual information and previous results. We prove that any rule in this class controls online FDR under some standard assumptions. We then focus on a subclass of these procedures, based on weighting the rejection thresholds, to derive a practical algorithm that learns a parametric weight function in an online fashion to gain more discoveries. We also theoretically prove that our proposed procedures, under some easily verifiable assumptions, would lead to an increase of statistical power over a popular online testing procedure proposed by (Javanmard and Montanari, 2018). Finally, we demonstrate the superior performance of our procedure, by comparing it to state-of-the-art online multiple testing procedures, on both synthetic data and real data generated from different applications.

1 Introduction

Multiple hypotheses testing - controlling overall error rates when performing multiple hypothesis tests - is a well-established area in statistics with applications in a variety of scientific disciplines (Dudoit and van der Laan, 2007; Dickhaus, 2014; Roquain, 2011). This problem has become even more important with modern data science, where standard data pipelines involve performing a large number of hypotheses tests on complex datasets, e.g., does this change to my webpage improve my click-through rate, or is this gene mutation associated with certain trait?

Typically, each hypothesis is summarized to one p-value, and is rejected (or claimed as a non-null) if the p-value is below some significance level. The rejected hypotheses are called *discoveries*, and those that were true nulls but mistakenly rejected are called *false discoveries*. The *false discovery rate* (FDR) namely, the expected fraction of discoveries that are false positives is the criterion of choice for statistical inference in multiple hypothesis testing problems. The traditional multiple testing research has focused on the offline setting, where we have an entire batch of hypotheses and the corresponding p-values, and (Benjamini and Hochberg, 1995) developed a standard procedure (called *BH procedure*) to control FDR below a preassigned level. However, the fact that offline FDR control techniques require aggregating p-values from all the tests and processing them jointly, makes it impossible to utilize them for a number of applications which are best modeled as an *online hypothesis testing* problem (Foster and Stine, 2008) (a formal definition will be provided later). In this scenario, we assume that an infinite sequence of hypotheses arrive sequentially in a stream, and decisions are made only based on previous decisions before next hypothesis arrives, without access to the number of hypotheses in the stream or future p-values. For example, in marketing research a sequence of A/B tests can be carried out in an online fashion, or in a pharmaceutical drug test a sequence of clinical trials are conducted over time, or with publicly available datasets where new hypotheses are tested in an on-going fashion by different researchers.

Foster and Stine (2008) designed the first online alpha-

Preliminary work. Under review by AISTATS 2020. Do not distribute.

investing procedures that use and earn alpha-wealth to control a modified variant of FDR (referred to as *mFDR*), which was later extended to a class of *generalized alpha-investing* (GAI) rules by (Aharoni and Rosset, 2014). Javanmard and Montanari (2015, 2018) showed that a monotone class of GAI rules can control online FDR as opposed to the modified FDR controlled in (Foster and Stine, 2008; Aharoni and Rosset, 2014). Within this class, of a special note is a procedure called *LORD* that performs consistently well in practice. Ramdas et al. (2017b) modified the GAI class (referred as to GAI++) to improve its statistical power (uniformly) while still controlling FDR, and the improved LORD++ method arguably represents the current state-of-the-art in the area. Very recently, (Ramdas et al., 2018) empirically demonstrated that using adaptiveness, some further improvements in the power over LORD++ can be obtained. In this paper, we mostly focus on GAI/GAI++ class, but certain results also carry over to the SAFFRON procedure.

All above online testing procedures take p-values as input and make decisions based on previous outcomes. However, these procedures ignore additional information that is often available in modern applications. In addition to the p-value P_i, each hypothesis H_i could also have a feature vector $X_i \in \mathcal{X} \subseteq \mathbb{R}^d$, which encodes contextual[1] information related to the tested hypothesis. The feature vector X_i only carries indirect information about the likelihood of the hypothesis H_i to be false but the relationship is not fully known ahead of time. For example, when conducting an A/B test for a logo size change in a website, contextual information such as text, layouts, images and colors in this specific page can be useful in making a more informative decision. Similarly another example arises when testing whether a mutation is correlated with the trait, here contextual information about both the mutation and the trait such as its location, epigenetic status, etc., could provide valuable information that can increase the power of these tests.

The problem of using side information in testing has been considered in offline setting (Ignatiadis et al., 2016; Genovese et al., 2006; Li and Barber, 2016; Ramdas et al., 2017a; Xia et al., 2017; Lei and Fithian, 2018). We review some relevant prior work in offline setting in detail in Appendix A. In this paper we focus on the more natural online setting, where p-values and contextual features are not available at the onset, and a decision about a hypothesis should be made when it is presented. To the best of our knowledge, this generalization of the online testing problem has not been considered before. Our main contributions in this paper are as follows.

(1) Incorporating Contextual Information. We propose a new broad class of powerful online testing rules, referred to as *contextual generalized alpha-investing* (CGAI) rules, which incorporates the available contextual features in the testing process. We also prove that any monotone rule from this class can control online FDR under some standard assumptions. Formally, we assume each hypothesis H is characterized by a tuple (P, X) where $P \in (0,1)$ is the p-value, and X is the contextual feature vector from some generic space $\mathcal{X} \subseteq \mathbb{R}^d$. We consider a sequence of hypotheses $(H_1, H_2, \dots)$ that arrive sequentially in a stream at each timestep $t = 1, 2, \dots$, with corresponding $((P_1, X_1), (P_2, X_2), \dots)$. Our testing rule generates a sequence of significance levels $(\alpha_1, \alpha_2, \dots)$ at each time based on previous decisions and contextual information seen so far. The test for each hypothesis H_t takes the form $\mathbb{1}\{P_t \leq \alpha_t\}$. Under the independence of p-values, and mutual independence between the p-values and the contextual features for null hypotheses, we show that any monotone rule from this class controls FDR below a preassigned level at any time. We also show that a variant of FDR (mFDR) can be controlled under a weaker assumption on p-values.

(2) Context Weighting. We focus on a subclass of CGAI rules, referred to as *context-weighted generalized alpha-investing* (CwGAI) rules, for designing a practical online FDR control procedure. In particular, we take a parametric function $\omega(;\theta)$ with parameters θ, and at time t use $\omega(X_t;\theta)$ as a weight on α_t generated through GAI rules, with the intuition that larger weights should reflect an increased willingness to reject the null. Since the parameter set θ is unknown, a natural idea here will be to learn it in an online fashion to maximize the number of empirical discoveries. This gives rise to a new class of online testing rules that incorporates the context weights through a learnt parametric function.

(3) Statistical Power Analysis. We then look into the effect of context weighting in discovering true positives. Considering a general model of random weighting, and under the assumption that weights are positively associated with false null hypotheses, we derive a natural sufficient condition under which the weighting improves the power in an online setting, while still controlling FDR. In addition, we also discuss techniques for verifying this power improvement condition in practice. This is the first result that demonstrates the benefits of appropriate weighting in the online setting. Prior to this such results were only known in the offline setting (Genovese et al., 2006).

(4) A Practical Procedure. To design a practical online FDR control procedure with good performance, we model the context weight using a parametric function $\omega(;\theta)$ of a neural network (multilayer perceptron), and train it in an online fashion to maximize the number of empirical discoveries. Our experiments on synthetic and real datasets show that our procedure makes substantially more correct decisions compared to state-of-the-art online testing procedures.

2 Related Online FDR Control Rules

We start with a review of online multiple testing model which was first introduced by (Foster and Stine, 2008). Considering a setting where an ordered (possibly infinite)

[1] Also sometimes referred to as *prior* or *side* information.

sequence of hypotheses arriving in a stream, denoted by $\mathcal{H} = (H_1, H_2, H_3, \dots)$, we have to decide at each timestep t whether to reject H_t having only access to previous decisions. $H_t \in \{0, 1\}$ indicates if tth hypothesis is a true *null* ($H_t = 0$) or *alternative* ($H_t = 1$). Each hypothesis is associated with a p-value P_t. The results in this paper do not depend on the actual test used for generating the p-value. By definition of a *valid* p-value, if the hypothesis H_t is *truly null*, then the corresponding p-value (P_t) is stochastically larger than the uniform distribution, i.e.,

$$\Pr[P_t \le u] \le u, \text{ for all } u \in [0,1]. \tag{1}$$

The marginal distribution of the p-values under alternative (non-null) hypotheses can be arbitrary. The only requirement is that they should be stochastically smaller than the uniform distribution, which means they carry signal that can differentiate them from nulls. Let $\mathcal{H}^0 = \{t : H_t = 0\}$ ($\mathcal{H}^1 = \{t : H_t = 1\}$) index the true (false) null hypotheses.

An online multiple testing procedure is defined as a *decision rule* which provides a sequence of significance levels $\{\alpha_t\}$ and makes the corresponding decisions:

$$R_t := \mathbb{1}\{P_t \le \alpha_t\} = \begin{cases} 1 & P_t \le \alpha_t \quad \Rightarrow \text{reject } H_t, \\ 0 & \text{otherwise} \quad \Rightarrow \text{accept } H_t. \end{cases} \tag{2}$$

A rejection of the null hypothesis H_t indicated by the event $R_t = 1$ is also referred to as a *discovery*. Let us define the false discovery rate (FDR), and true discovery rate (TDR) formally in the online setting. For any time T, denote the first T hypotheses in the stream by $\mathcal{H}(T) = (H_1, \dots, H_T)$. Let $R(T) = \sum_{t=1}^{T} R_t$ be the total number of discoveries (rejections) made by the online testing procedure till time T, and let $V(T) = \sum_{t \in \mathcal{H}^0} R_t$ be the number of false discoveries. Then the online false discovery proportion and rate till time T are defined as:

$$\text{FDP}(T) := \frac{V(T)}{R(T) \vee 1}, \qquad \text{FDR}(T) := \mathbb{E}[\text{FDP}(T)],$$

where $R(T) \vee 1 = \max\{R(T), 1\}$. The expectation is over the underlying randomness. Similarly, let $S(T) = \sum_{t \in \mathcal{H}^1} R_t$ be the number of true discoveries and let $N_1(T)$ be the number of true non-nulls till time T. Then online true discovery proportion and rate till time T are defined as:

$$\text{TDP}(T) := \frac{S(T)}{N_1(T) \vee 1}, \qquad \text{TDR}(T) := \mathbb{E}[\text{TDP}(T)].$$

The true discovery rate is also referred to as *power*. In online hypothesis testing, our goal is to design a sequence of significance levels $(\alpha_t)_{t \in \mathbb{N}}$ such that we can control the online FDR at a desired level α at any time $T \in \mathbb{N}$, i.e.,

$$\sup_T \text{FDR}(T) \le \alpha.$$

Note that none of these above four metrics can be computed without the underlying true labels (ground truth). A variant of FDR studied in early online testing works (Foster and Stine, 2008) is the *marginal FDR*, defined as: $\text{mFDR}(T)_\eta = \frac{\mathbb{E}[V(T)]}{\mathbb{E}[R(T)] + \eta}$, with a special case of $\text{mFDR}(T) = \frac{\mathbb{E}[V(T)]}{\mathbb{E}[R(T)] + 1}$ when $\eta = 1$. Note that the gap between FDR and mFDR can be very significant, and controlling mFDR does not ensure controlling FDR at a similar level (Javanmard and Montanari, 2018). We will also provide a guarantee on mFDR control in a contextual setting under some weaker assumptions on p-values.

Generalized Alpha-Investing Rules. Foster and Stine (2008) proposed the first class of online multiple testing rules (referred to as alpha-investing rules) to control mFDR, which was extended by (Aharoni and Rosset, 2014) to generalized alpha-investing (GAI) rules. The GAI rules covers most of the online testing rules in the current literature.

Any rule of GAI class generates the significance level α_t at time t based on past decisions of the rule till time $t - 1$: $\alpha_t = \alpha_t(R_1, \dots, R_{t-1})$. This means that α_t does not directly depend on the observed p-values but only on past decisions. Let $\mathcal{F}^t = \sigma(R_1, \dots, R_t)$ be the sigma-field of decisions till time t. In GAI rules, we require that $\alpha_t \in \mathcal{F}^{t-1}$.

Specifically, it begins with a wealth of $W(0) > 0$, which is under the desired control level, and keeps track of the available wealth $W(t)$ after t steps. At each time t, an amount of ϕ_t, which is the *penalty* of testing the tth hypothesis at level α_t, will be deducted from the remaining wealth. If the tth hypothesis is rejected, i.e., $R_t = 1$, then an extra wealth of amount ψ_t is *rewarded* to the current wealth. This can be explicitly stated as:

$$W(0) = w_0, \quad 0 < w_0 < \alpha \tag{3}$$
$$W(t) = W(t-1) - \phi_t + R_t \cdot \psi_t, \tag{4}$$

where w_0 and the nonnegative sequences $\alpha_t, \phi_t, \psi_t \in \mathcal{F}^{t-1}$ are user-defined. The wealth $W(t)$ is required to be always non-negative, and thus $\phi_t \le W(t-1)$. Once the wealth ever equals zero, the procedure is not allowed to make any further rejections since it has to set $\alpha_t = 0$ from then on. An additional restriction is needed for the goal to control FDR, in that the reward ψ_t has to be bounded whenever a rejection takes place. Formally, the constraints are:

$$\phi_t \le W(t-1), \tag{5}$$
$$\psi_t \le \min\{\phi_t + b_t, \frac{\phi_t}{\alpha_t} + b_t - 1\}. \tag{6}$$

Javanmard and Montanari (2015, 2018) defined b_t as a user-chosen constant $b_0 = \alpha - w_0$ and proved the FDR control for monotone GAI rules under independence of p-values. The monotonicity of a rule is defined as:

$$\text{If } \tilde{R}_i \le R_i \text{ for all } i \le t-1, \text{ then}$$
$$\alpha_t(\tilde{R}_1, \dots, \tilde{R}_{t-1}) \le \alpha_t(R_1, \dots, R_{t-1}). \tag{7}$$

Recently, (Ramdas et al., 2017b) demonstrated that setting $b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\}$ could potentially lead to larger statistical power. Here, ρ_k defined as $\rho_k := \min_{i \in \mathbb{N}} \{\sum_{t=1}^{i} R_t = k\}$, is the time of kth rejection. Ramdas et al. (2017b) refer to this class of rules as GAI++ rules. Unless otherwise specified, we use this b_t (from GAI++) throughout this paper.

Level based On Recent Discovery (LORD) Rules. One popular subclass of GAI rules (proposed by (Javanmard and Montanari, 2015, 2018)) that is LORD, where significance level α_t is a function based only on *most recent discovery time*. Formally, we choose any sequence of non-increasing nonnegative constants $\gamma = (\gamma_t)_{t=1}^{\infty}$ with $\sum_{t=1}^{\infty} \gamma_t = 1$. At each time t, let τ_t be the last time a discovery was made before t, i.e., $\tau_t := \max\{i \in \{1, \dots, t-1\} : R_i = 1\}$, with $\tau_t = 0$ for all t before the first discovery. The LORD (Javanmard and Montanari, 2015, 2018) rule defines α_t, ϕ_t, ψ_t in the following generalized alpha-investing fashion.

$$\textbf{LORD: } W(0) = w_0,$$

$$\phi_t = \alpha_t = \begin{cases} \gamma_t w_0 & \text{if } t \le \rho_1 \\ \gamma_{t-\tau_t} b_0 & \text{if } t > \rho_1, \end{cases}$$

$$\psi_t = b_0 = \alpha - w_0.$$

Javanmard and Montanari (2018) defined three versions of LORD that slightly vary in how they set the significance levels. In this paper, we stick to one version (though much of the discussion in this paper also holds for the other versions), and we set $b_0 = w_0 = \alpha/2$, in which case, the above rule could be simplified as $\phi_t = \alpha_t = \gamma_{t-\tau_t} b_0$. As with any GAI rule, (Ramdas et al., 2017b) defined LORD++ by replacing b_0 with $b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\}$ and showed it achieves a power increase while still controls online FDR at same level α. We describe LORD and LORD++ in little more detail in Appendix B. Note that both LORD and LORD++ rules satisfy the monotonicity condition from (7).

SAFFRON Procedure. This is a very recently proposed online FDR control procedure by (Ramdas et al., 2018). The main difference between SAFFRON (Serial estimate of the Alpha Fraction that is Futilely Rationed On true Null hypotheses) and the previously discussed LORD/LORD++ procedures comes in that SAFFRON is an adaptive method, based on adaptively estimating the proportion of true nulls. SAFFRON can be viewed as an online extension of Storey's adaptive version of BH procedure from the offline setting. SAFFRON does not belong to the GAI class. See Appendix G for more details about SAFFRON, where we also extend the FDR control results of SAFFRON from (Ramdas et al., 2018) to a weighted version. Our experiments with SAFFRON that suggests that contextual information could potentially help here too.

3 Contextual Online FDR Control

While these online FDR procedures are widely used, a major shortcoming of them is that they ignore additional information that is often available during testing. Each hypothesis, in addition to the p-value, could have a feature vector which encodes contextual information related to the tested hypothesis. For example, in genetic association studies, each hypothesis tests the correlation between a variant and the trait. We have contextual features for each variant (e.g., its location, conservation, epigenetics, etc.) which could inform how likely the variant is to have a true association. Missing details from section are collected in Appendix C.

To deal with such situations, we now assume that a p-value $P_t \in (0,1)$ and a vector of contextual features $X_t \in \mathcal{X} \subseteq \mathbb{R}^d$ are observed for each hypothesis H_t. At each step t, we have to decide whether to reject H_t having access to previous decisions and contextual information seen so far. The overall goal is to control online FDR under a given level α at any time, and improve the number of correct discoveries by using the contextual information. Under the alternative, we denote the density (PDF) of p-values as $f_1(p \mid X)$ (depending on the feature vector $X \in \mathcal{X}$) and the corresponding cumulative distribution (CDF) as $F_1(p \mid X)$. Here $f_1(p \mid X)$ can be any arbitrary unknown function, as long as the p-values are stochastically smaller than those under the null. Note that $f_1(p \mid X)$ is not identifiable from the data as we never observe H_t's directly. This can be illustrated through a simple example described in Appendix C.

Definition 1 (Contextual Online FDR Control). *Given a (possibly infinite) sequence of (P_t, X_t)'s ($t \in \mathbb{N}$) where $P_t \in (0,1)$ and $X_t \in \mathcal{X}$, generate a significance levels α_t's as a function of prior decisions and contextual features $\alpha_t = \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)$, and a corresponding set of decisions $R_t = \mathbb{1}\{P_t \le \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}$ such that $\sup_T$ FDR$(T) \le \alpha$.*

We now define a contextual extension of GAI rules, that we refer to as *Contextual Generalized Alpha-Investing* (contextual GAI or CGAI) rules. In the presence of contextual information, we consider the sigma-field of decisions till time t as $\mathcal{F}^t = \sigma(R_1, \dots, R_t)$, and the sigma-field of features till time t as $\mathcal{G}^t = \sigma(X_1, \dots, X_t)$.

Definition 2 (Contextual GAI Rule). *A contextual GAI rule is defined through three functions, $\alpha_t, \phi_t, \psi_t \in \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)$, that are all computable at time t, with the GAI conditions (3), (4), (5), (6) satisfied.*

We set $b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\}$ as proposed by (Ramdas et al., 2017b). Similar to that in GAI rules (7), we define monotonicity property for contextual GAI rules as follows:

Monotoncity: If $\tilde{R}_i \le R_i$ for all $i \le t-1$, then

$$\alpha_t(\tilde{R}_1, .., \tilde{R}_{t-1}, X_1, .., X_t) \le \alpha_t(R_1, .., R_{t-1}, X_1, .., X_t), \quad \text{for any fixed } \mathbf{X}^t = (X_1, .., X_t). \tag{8}$$

A contextual GAI rule satisfying the monotonicity condition is referred to as *monotone contextual GAI*.

The following theorem establishes the FDR control for any monotone contextual GAI rule under an independence assumption between p-values and between p-values and contextual features for the null hypotheses. As mentioned above, the p-values (P_t) could be arbitrary related to the contextual features (X_t) under the alternative (when $H_t = 1$). These assumptions are standard in multiple testing literature (see, e.g., (Ramdas et al., 2017b; Javanmard and Montanari, 2018; Xia et al., 2017) among others).[2] The proof is based on a *leave-one-out* technique, a variant of which was also used by (Ramdas et al., 2017b) (and also by (Javanmard and Montanari, 2018)) in their analyses. The main distinction for us comes in that we consider the sigma-field at each time t as $\sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)$ including the information of contextual features till time t, instead of just $\mathcal{F}^{t-1}$.

Theorem 1 (FDR Control)**.** *Consider a sequence of* $((P_t, X_t))_{t\in\mathbb{N}}$ *of p-values and contextual features. If the p-values* P_t*'s are independent, and additionally* P_t *are independent of all* $(X_t)_{t\in\mathbb{N}}$ *under the null* $($*whenever* $H_t = 0)$*, then for any monotone contextual generalized alpha-investing rule* $($*satisfying conditions* (3), (4), (5), (6), (8)$)$*, we have online FDR control,* $\sup_{T\in\mathbb{N}} \mathrm{FDR}(T) \le \alpha$*.*

Turning to mFDR, we can also prove a guarantee for mFDR control under a weaker condition than that in Theorem 1 by relaxing the independence assumptions to a weaker conditional super-uniformity assumption.

Conditional super-uniformity: If $H_t = 0$, then

$$\Pr[P_t \le \alpha_t \mid \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)] \le \alpha_t. \quad (9)$$

By definition of the marginal super-uniformity of p-values under the null (1), means that for independent p-values the conditional super-uniformity in (9) holds. So the assumption (9) is indeed weaker than the Theorem 1 assumptions. Our next theorem proves mFDR control for any contextual GAI rule (not necessarily monotone) under this weaker condition.

Theorem 2 (mFDR Control)**.** *Consider a sequence of* $((P_t, X_t))_{t\in\mathbb{N}}$ *of p-values and contextual features. If the p-values* P_t*'s are conditionally super-uniform distributed (as in* (9)*), then for any contextual generalized alpha-investing rule* $($*satisfying conditions* (3), (4), (5), (6)$)$*, we have online mFDR control,* $\sup_{T\in\mathbb{N}} \mathrm{mFDR}(T) \le \alpha$*.*

Remark 1. *For arbitrary dependent p-values and contextual features, the FDR control can be obtained by using a modified LORD rule defined in (Javanmard and Montanari, 2018), under a special case where the contextual features are transformed into weights satisfying certain conditions. See Proposition 2 (Appendix E) for a formal statement.*

4 Context-weighted GAI Rules

The contextual GAI rules form a very general class of online multiple testing rules. In this section, we focus on a subclass of these rules, which we refer to as *Context-weighted Generalized Alpha-Investing* (context-weighted GAI or CwGAI) rules. Specifically, it considers α_t to be a product of two functions with the first one of previous decisions and second one based on the current contextual feature,

$$\alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t) := \alpha_t(R_1, \dots, R_{t-1}) \cdot \omega(X_t; \theta), \quad (10)$$

where $\omega(X_t;\theta)$ is a parametric *weight function* with parameters $\theta \in \Theta$. Since CwGAI is a subclass of CGAI rules, the above FDR and mFDR control theorems from previous section are valid for this class too. Applying this idea of context-weighting to LORD++ (resp. LORD) give rise to a new class of testing procedure that we refer to as CwLORD++ (resp. CwLORD) (defined in Appendix D).

Our reasons for considering this subclass include: (a) We obtain a simpler form of α_t by separating the contextual features from that of previous outcomes, making it easier to design functions that satisfy the monotonicity requirement of the GAI rules. (b) It is convenient to model the weight function by any parametric function, and (c) we can learn the parameters of the weight function empirically by maximizing the number of discoveries. This forms the basis of a practical algorithm for contextual online FDR control that we describe in Section 6. Note that the GAI rules are context-weighted GAI rules when the weight function equals 1. We illustrate the relationship among various classes of testing rules in Figure 3 of Appendix D.

The idea of weighting p-values using prior information has been widely studied in offline multiple testing setup (Genovese et al., 2006; Ignatiadis et al., 2016; Li and Barber, 2016; Lei and Fithian, 2018; Xia et al., 2017; Ramdas et al., 2017a). In many applications, contextual information can provide some prior knowledge about the true underlying state at current time, which may be incorporated in by a weight $\omega_t = \omega(X_t;\theta)$. Intuitively, the weights indicate the strength of a prior belief whether the underlying hypothesis is null or not. A larger weight $\omega_t > 1$ provides more belief of a hypothesis being an alternative which makes the procedure to reject it more aggressively, while a smaller weight $\omega_t < 1$ indicates a higher likelihood of a true null which makes the procedure reject it more conservatively.

Weighting in Online vs. Offline Setting with FDR Control. In the offline setting, prior weights are usually rescaled to have unit mean, and then existing offline FDR control algorithm is applied to the weighted p-values P_i/ω_i instead of P_i (Genovese et al., 2006). However, in the online setting, the weights are computed at each timestep without knowing the total number of hypothesis or contextual information, thus cannot be rescaled to have unit mean in advance. Instead, as presented in (10), we consider weighting the significance levels α_t's, as was also considered by (Ramdas et al., 2017a). Note that weighting p-values is equivalent

[2] Note that a standard assumption in hypothesis testing is that the p-values under the null are uniformly distributed in $(0, 1)$, which does not depend on the contextual features. That means the mutual independence of p-values and contextual features is valid.

to weighting significance levels in terms of decision rules conditioning on the same significance levels, i.e., given the same α_t's, we have $\{P_t/\omega_t \leq \alpha_t\} \equiv \{P_t \leq \alpha_t\omega_t\}$ for all t. The subtle difference is that when α_t's are weighted, the penalty ϕ_t's and rewards ψ_t's are also adjusted according to the GAI constraints. For example, as dictated by (6), if we overstate our prior belief in the hypothesis being alternative by assigning a large $\omega_t > 1$, the penalty will need to be more or the reward will need to be less.

5 Power of Weighted Online Rules

In this section, we answer the question whether weighting helps in an online setting in terms of increased power. We answer this question in affirmative, in the context of the popular LORD procedure of (Javanmard and Montanari, 2018). The benefits of weighting in the offline setting, in terms of increased power was first studied by (Genovese et al., 2006), who showed that a weighted BH procedure improves the power over the corresponding unweighted procedure if weighting is *informative*, which roughly means that the weights are positively associated with the non-nulls. Missing details from this section are collected in Appendix E.

We consider a mixture model where each null hypothesis is false with a fixed probability π_1, and the p-values are all independent. While the mixture model is *idealized*, it does offer a natural ground for comparing the power of various testing procedures (Genovese et al., 2006; Javanmard and Montanari, 2018). The rest of the discussion in this section will be with respect to this mixture model.

Mixture Model. For any $t \in \mathbb{N}$, let

$$\begin{gathered} H_1, \dots, H_t \overset{\text{i.i.d.}}{\sim} \text{Bernoulli}(\pi_1), \\ X_t \mid H_t = 0 \sim \mathcal{L}_0(\mathcal{X}), \quad X_t \mid H_t = 1 \sim \mathcal{L}_1(\mathcal{X}), \\ P_t \mid H_t = 0, X_t \sim \text{Uniform}(0,1), \\ P_t \mid H_t = 1, X_t \sim F_1(p \mid X_t). \end{gathered}$$

where $0 < \pi_1 < 1$ and where $\mathcal{L}_0(\mathcal{X})$, $\mathcal{L}_1(\mathcal{X})$ are two probability distribution on the contextual feature space $\mathcal{X}$. Let $F = \int F_1(p \mid X) \mathrm{d}\mathcal{L}_1(\mathcal{X})$ be the marginal distribution of p-value under alternative. Marginally, the p-values are i.i.d. from the CDF $G(a) = (1-\pi_1)U(a)+\pi_1 F(a)$, where $U(a)$ is the CDF of Uniform(0,1). We do not require that the contextual features X_t's be independent, but only that they be identically distributed as $\mathcal{L}_0(\mathcal{X})$ (under null) or $\mathcal{L}_1(\mathcal{X})$ (under alternative).

General Weighting Scheme. We consider the general weighting as in (Genovese et al., 2006) where weight is a random variable and conditionally independent of P_t given H_t. We assume that weight ω_t has different marginal distributions under null and alternative,

$$\omega_t \mid H_t = 0 \sim Q_0, \quad \omega_t \mid H_t = 1 \sim Q_1, \tag{11}$$

with Q_0, Q_1 unknown continuous distributions on $(0, \infty)$. Under the mixture setup,

$$\omega_t \overset{\text{i.i.d.}}{\sim} (1 - \pi_1)Q_0 + \pi_1 Q_1, \tag{12}$$

with P_t and ω_t being conditionally independent given H_t for all $t = 1 \dots, \infty$.

Contextual Weighting Scheme. This framework of weighting in (11) is very general. For example, it includes as a special case, the following contextual weighting scheme, where we assume that there exists a weight function of contextual features $\omega : \mathcal{X} \times \Theta \to \mathbb{R}$, and the distributions of weights are defined as:

$$\begin{aligned} \omega_t \mid H_t = 0 &\sim \omega(X;\theta), \text{ with } X \sim \mathcal{L}_0(\mathcal{X}), \\ \omega_t \mid H_t = 1 &\sim \omega(X;\theta), \text{ with } X \sim \mathcal{L}_1(\mathcal{X}). \end{aligned} \tag{13}$$

Now Q_0 and Q_1 are defined as the distributions of $\omega(X;\theta)$ under the null and alternative, respectively. Given Q_0 and Q_1, the weight ω_t is sampled as in (12).[3] Note that while the distributions Q_0 and Q_1 for weights are defined through X_t's distribution, the weight ω_t is sampled i.i.d. from the mixture model $(1-\pi_1)Q_0+\pi_1 Q_1$, regardless of the value of X_t. Note that the independence assumption on p-values can still be satisfied even when the $X_t' s$ are dependent.[4] Since this contextual weighting scheme is just a special case of the above general weighting scheme, in the remainder of this section, we work with the general weighting scheme.

Informativeness. Under (11), the marginal distribution of ω is $Q = (1 - \pi_1)Q_0 + \pi_1 Q_1$. For $j = 0, 1$, let $u_j = \mathbb{E}[\omega \mid H_t = j]$ be the means of Q_0 and Q_1 respectively. We assume that the weighting is *informative*, based on the following definition from (Genovese et al., 2006) in the offline setting,

$$u_0 < 1,\ u_1 > 1,\ u = \mathbb{E}[\omega] = (1 - \pi_1)u_0 + \pi_1 u_1 = 1. \tag{14}$$

Remark 1. *Informative-weighting places a natural condition on the weights. Roughly it means that the weight should be positively associated to true alternatives (or the weight under alternative is more likely to be larger than that under the null). The marginal mean of weight $\mathbb{E}[\omega]$ is not necessary to be one. But for the theoretical power comparison of different procedures, it is convenient to scale the weight to have unit mean so that we can use the p-value reweighting akin to the offline setting. For empirical experiments, we will use an instantiation of CwLORD++ (see Section 6), that does not require the weight to have mean one.*

Comparison of Power. In order to compare different procedures, it is important to estimate their statistical power. Here

[3] In case , $X_t \overset{\text{i.i.d.}}{\sim} (1-\pi_1)\mathcal{L}_0+\pi_1\mathcal{L}_1$, then one can define ω_t directly as $\omega_t = \omega(X_t;\theta)$ with Q_0 and Q_1 defined as the distributions of $\omega(X_t;\theta)$ under the null and alternative, respectively.

[4] In practice it is common that the contextual features are dependent (e.g., same genes or genetic variants may be tested in multiple independent experiments at different time), but as long as the tests are carried out independently the p-values are still independent.

we establish sufficient conditions under which a weighting could lead to a power increase for LORD. We work with (a version of) the popular LORD procedure from (Javanmard and Montanari, 2018), which sets

$$W(0) = w_0 = b_0 = \alpha/2,\ \phi_t = \alpha_t = b_0\gamma_{t-\tau_t},\ \psi_t = b_0. \quad (15)$$

As shown by (Javanmard and Montanari, 2018), the power of LORD, under the mixture model, almost surely equals[5]

$$\liminf_{T\to\infty} \mathrm{TDP}(T) = \Big(\sum_{m=1}^{\infty}\prod_{j=1}^{m}(1 - G(b_0\gamma_j))\Big)^{-1}, \quad (16)$$

where $G(a) = (1 - \pi_1)U(a) + \pi_1 F(a)$ as defined earlier.

Definition 3 (Weighted LORD)**.** *Given a sequence of p-values* $(P_1, P_2, \dots)$ *and weights* $(\omega_1, \omega_2, \dots)$*, apply LORD* (15) *to the weighted p-values* $(P_1/\omega_1, P_2/\omega_2, \dots)$*.*

Weighted LORD is not strictly a contextual GAI rule (see discussion in Appendix E), however we establish FDR control of weighted LORD through Proposition 1(Appendix E). Assume F is differentiable and let $f = F'$ be the PDF of p-values under alternative. Due to the fact that p-values under alternative are stochastically dominated by the uniform distribution, there exists some $a_0 > 0$ such that $f(a) > 1$ for all $0 \le a < a_0$. The following theorem is based on comparing the power of weighted LORD (from Theorem 6 in Appendix E) with the power bound of LORD (16).

Theorem 3 (Power Separation)**.** *Suppose that the parameters in LORD* (15) *satisfy* $b_0\gamma_1 < a_0$*, and the weight distribution satisfies* $\Pr[\omega < a_0/(b_0\gamma_1) \mid H_t = 1] = 1$ *for every* $t \in \mathbb{N}$ *and the informative-weighting property in* (14)*. Then, the average power of weighted LORD is greater than or equal to that of LORD almost surely.*

The results show that using the informative context-weighting in the LORD rules will help in making more true discoveries. It also indicates that we can check the informative-weighting property by checking whether the mean of the weight distribution under alternative (Q_1) is greater than that of the corresponding distribution under null (Q_0), which can be done under various scenarios as we describe in detail in Appendix F. We now conclude this section with a simple example of how the conditions of Theorem 3 are easily satisfied in a common statistical model.

Example 1. *To interpret the weight condition in Theorem 3, let's take a concrete example and consider the hypotheses* $(H_1, \dots, H_T)$ *concerning the means of normal distributions (referred to as* normal means model*) with test statistics* $Z_t \sim \mathcal{N}(\mu, 1)$*. So the two-sided p-values are* $P_t = 2\Phi(-|Z_t|)$*. Suppose under the null hypothesis* $\mu = 0$*, and under the alternative* $0 < \mu \le 4$*. Then we can compute that* $a_0 > 0.022$ *for any* μ *such that* $0 < \mu \le 4$*. In fact,* a_0 *increases as* μ *decreases. Setting* $\alpha = 0.05$*,* $T = 10^5$*, and* $\{\gamma_t\}_{t\in\mathbb{N}}$ *as suggested by (Javanmard and Montanari, 2018), we get that as long as the weight* ω *is less than* $a_0/(b_0\gamma_1) \approx 7.52$*, the condition for Theorem 3 is satisfied.*

6 Experimental Evaluation

Now we propose a practical procedure for contextual online FDR control based on context-weighted GAI rules, which sets $\alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t) := \alpha_t(R_1, \dots, R_{t-1}) \cdot \omega(X_t; \theta)$, and present numerical experiments to illustrate the performance with this procedure. In the following, we use $\alpha_t(X_t; \theta)$ as a short to represent $\alpha_t(R_1, \dots, R_{t-1}) \cdot \omega(X_t; \theta)$. Technically, we can use any parametric function $\omega(X_t; \theta)$ (with parameter set $\theta \in \Theta$) to model the weight function. Here we choose a deep neural network (multilayer perceptron) due to its expressive power, as noted in a recent batch FDR control result by (Xia et al., 2017). Given this, a natural goal will be to find $\theta \in \Theta$ that maximizes the number of empirical discoveries (or discovery rate), while controlling the FDR. Note that if the function $\alpha_t(R_1, \dots, R_{t-1})$ is monotone (such as with LORD or LORD++) with respect to R_i's, the function $\alpha_t(R_1, \dots, R_{t-1}) \cdot \omega(X_t; \theta)$ is also monotone with respect to R_i's.

Training the Network, Setting θ. Given a stream $((P_t, X_t))_{t\in\mathbb{N}}$, the algorithm processes the stream in batches, in a single pass. Let $b \ge 1$ denote the batch size. Let θ_j be the parameter obtained before batch j is processed, thus θ_j is only based on all previous p-values and contextual features which are assumed to be independent of all future batches. For each batch, the algorithm fixes the parameters to compute the significance levels for hypothesis in that batch. Define, the empirical discovery rate for batch j as follows: $\mathrm{EDR}_j = \sum_{i=jb+1}^{(j+1)b} \mathbb{1}\{P_i \le \alpha_i(X_i; \theta_j)\}/b$. Since the above function is not differentiable, we use the sigmoid function σ to approximate the indicator function, and define $\mathrm{EDR}_j = \sum_{i=jb+1}^{(j+1)b} \sigma(\lambda(\alpha_i(X_i; \theta_j) - P_i))/b$. Here λ is a large positive hyperparameter. With this, the parameter set θ can now be optimized by using standard (accelerated) gradient methods in an online fashion. Note that we are only maximizing empirical discovery rate subject to empirical FDR control, and the training does not require any ground truth labels on the hypothesis. We state the training procedure in Algorithm 1 (Appendix F).

In all our experiments, we use a multilayer perceptron to model the weight function, which is constructed by 10 layers and 10 nodes with ReLU as the activation function in each layer, and exponential function of the output layer, since the weight has to be non-negative. In the following, we use context-weighted LORD++ (**CwLORD++**) to denote the testing rule obtained by using LORD++ as the monotone GAI rule to set $\alpha_t(R_1, \dots, R_{t-1})$ in $\alpha_t(X_t; \theta)$.

Verifying Informativeness. One last point to note is that we can add the verification of the informative-weighting property (14) to the above procedure under various realistic

[5] Javanmard and Montanari (2018) proposed multiple versions of LORD, and as noted by them, the bound in (16) lower bounds the power on all the versions of LORD under the mixture model.

scenarios such as in presence of feedback or in presence of a validation set. We defer this discussion to Appendix F.

Experimental Results. We now discuss results for numerical experiments with both synthetic and real data to compare the performance of our proposed CwLORD++ with a state-of-the-art online testing rule LORD++ (Ramdas et al., 2017b). Due to space limitations, we present the synthetic data experiments based on the normal means model in Appendix F.1, with results clearly showing that while FDR is always controlled for both LORD++ and CwLORD++, the power of our CwLORD++ uniformly dominates that of LORD++. Our real data experiments focus on a diabetes prediction problem and gene expression data analyses. Experiments with the SAFFRON procedure are presented in Appendix G. The experimental code is also attached as part of the supplementary material for reproducibility.

Diabetes Prediction Problem. We apply our online multiple testing rules to a real-life application of diabetes prediction. Specifically, we want to test if patients are at risk of developing diabetes, i.e., for each patient i, we form the null hypothesis H_i as the "patient will not develop diabetes" versus its alternative. Machine learning algorithms are now commonly used to construct predictive health scores for patients. A high predicted risk score can trigger an intervention (such as medical follow-up), which can be expensive and sometimes unnecessary, and thus it is important to control the fraction of false alerts. The dataset was released as part of a Kaggle competition[6], which contains de-identified medical records of 9948 patients. For each patient, we have a response variable that indicates if the patient is diagnosed with Type 2 diabetes mellitus, along with patient's biographical information and details on medications, lab results, immunizations, allergies, and vital signs.

We train a predictive score based on the available records, and then apply our online multiple testing rule rules to control FDR on test set. Our overall methodology is similar to that of (Javanmard and Montanari, 2018) in their FDR control experiments on this dataset. We regard the biographical information of patients as contextual features. Such choice is loosely based on the idea of *personalization* common in machine learning applications. Note that in theory, for our procedure, one could use any set of features as context. We describe the dataset and the ML training process in detail in Appendix F.2. Here are the results when $\alpha = 0.2$.

Table 1: Diabetes Dataset Results, $\alpha = 0.2$

Procedure	FDR	Power
LORD++	0.147	0.384
CwLORD++	0.176	0.580

Notice that FDR is under control for both procedures, and the power of CwLORD++ is substantially more (about 51%) than LORD++. This improvement shows the benefits of using contextual features for improving the power with FDR control in a machine learning setup. We probe the reasons for this improvement, and present results with different nominal FDR levels from 0.1 to 0.5 in Appendix F.2.

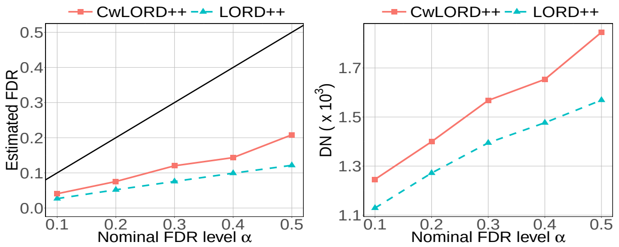


Figure 1: FDR and discovery numbers on Airway RNA-Seq.

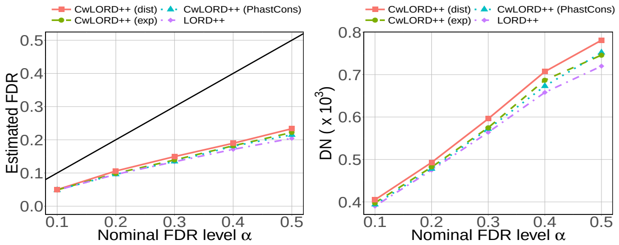


Figure 2: FDR and discovery numbers on GTEx.

Gene Expression Data. Our final set of experiments are on gene expression datasets. In particular, we use the Airway RNA-Seq and GTEx datasets[7] as also studied by (Xia et al., 2017). For both experiments, we use the original ordering of hypotheses as provided in the datasets. Since we don't know the ground truth, we only report the empirical FDR and the empirical discovery rate number in the experiments.

The Airway RNA-Seq dataset contains $n = 33469$ genes, with the aim to identify glucocorticoid responsive (GC) genes that modulate cytokine function in airway smooth muscle cells. The p-values are obtained in two-sample differential analysis of gene expression levels. Log counts of each gene serves as the contextual feature. Figure 1 reports the empirical FDR and the discovery number. We see that our CwLORD++ procedure make about 10% more discoveries than the LORD++ procedure.

In the GTEx study, the question is to quantify the expression Quantitative Trait Loci (eQTLs) in human tissues. In the eQTL analysis, the association of each pair of single nucleotide polymorphism (SNP) and nearby gene is tested. The p-value is computed under the null hypothesis that the SNP genotype is not correlated with the gene expression. The GTEx dataset contains 464,636 pairs of SNP-gene combination from chromosome 1 in a brain tissue. Besides, we consider three contextual features studied by (Xia et al., 2017): 1) the distance (GTEx-dist) between the SNP and the gene (measured in log base-pairs); 2) the average expression (GTEx-exp) of the gene across individuals (measured in log rpkm); and 3) the evolutionary conservation measured by the standard PhastCons scores (GTEx-PhastCons). We apply LORD++ to the p-values, and CwLORD++ to

[6] http://www.kaggle.com/c/pf2012-diabetes

[7] https://www.dropbox.com/sh/wtp58wd60980d6b/AAA4wA60ykP-fDfS5BNsNkiGa?dl=0.

the p-value, contextual feature vector pairs. Figure 2 reports the empirical FDR and the discovery number where for CwLORD++ we use each contextual feature separately. This results in CwLORD++, having an increase in discovery number by 5.5%, 2.6%, 2.9% using GTEx-dist, GTEx-exp, and GTEx-PhastCons as the contextual feature respectively, compared to the LORD++ procedure. We provide additional experimental results with multi-dimensional feature vectors in Appendix F.3, and draw a similar conclusion.

References

Aharoni, E. and Rosset, S. (2014). Generalized α-investing: definitions, optimality results and application to public databases. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 76(4):771–794.

Arias-Castro, E. and Chen, S. (2017). Distribution-free multiple testing. *Electronic Journal of Statistics*, 11(1):1983–2001.

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.

Benjamini, Y. and Hochberg, Y. (1997). Multiple hypotheses testing with weights. *Scandinavian Journal of Statistics*, 24(3):407–418.

Carothers, N. L. (2000). *Real analysis*. Cambridge University Press.

Cox, D. R., Cox, D. R., Cox, D. R., and Cox, D. R. (1967). *Renewal theory*, volume 1. Methuen London.

Dickhaus, T. (2014). *Simultaneous statistical inference*. Springer.

Dobriban, E. (2016). A general convex framework for multiple testing with prior information. *arXiv preprint arXiv:1603.05334*.

Dobriban, E., Fortney, K., Kim, S. K., and Owen, A. B. (2015). Optimal multiple testing under a gaussian prior on the effect sizes. *Biometrika*, 102(4):753–766.

Dudoit, S. and van der Laan, M. J. (2007). *Multiple testing procedures with applications to genomics*. Springer Science & Business Media.

Foster, D. P. and Stine, R. A. (2008). α-investing: a procedure for sequential control of expected false discoveries. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 70(2):429–444.

Foygel-Barber, R. and Candès, E. J. (2015). Controlling the false discovery rate via knockoffs. *The Annals of Statistics*, 43(5):2055–2085.

Genovese, C. and Wasserman, L. (2002). Operating characteristics and extensions of the false discovery rate procedure. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 64(3):499–517.

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

G'Sell, M. G., Wager, S., Chouldechova, A., and Tibshirani, R. (2016). Sequential selection procedures and false discovery rate control. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 78(2):423–444.

Hu, J. X., Zhao, H., and Zhou, H. H. (2010). False discovery rate control with groups. *Journal of the American Statistical Association*, 105(491):1215–1227.

Ignatiadis, N., Klaus, B., Zaugg, J. B., and Huber, W. (2016). Data-driven hypothesis weighting increases detection power in genome-scale multiple testing. *Nature methods*, 13(7):577.

Javanmard, A. and Montanari, A. (2015). On online control of false discovery rate. *arXiv preprint arXiv:1502.06197*.

Javanmard, A. and Montanari, A. (2018). Online rules for control of false discovery rate and false discovery exceedance. *The Annals of statistics*, 46(2):526–554.

Lei, L. and Fithian, W. (2016). Power of ordered hypothesis testing. *arXiv preprint arXiv:1606.01969*.

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.

Li, A. and Barber, R. F. (2016). Multiple testing with the structure adaptive benjamini-hochberg algorithm. *arXiv preprint arXiv:1606.07926*.

Li, A. and Barber, R. F. (2017). Accumulation tests for fdr control in ordered hypothesis testing. *Journal of the American Statistical Association*, 112(518):837–849.

Ramdas, A., Barber, R. F., Wainwright, M. J., and Jordan, M. I. (2017a). A unified treatment of multiple testing with prior knowledge using the p-filter. *arXiv preprint arXiv:1703.06222*.

Ramdas, A., Yang, F., Wainwright, M. J., and Jordan, M. I. (2017b). Online control of the false discovery rate with decaying memory. In *Advances In Neural Information Processing Systems*, pages 5650–5659.

Ramdas, A., Zrnic, T., Wainwright, M., and Jordan, M. (2018). Saffron: an adaptive algorithm for online control of the false discovery rate. *arXiv preprint arXiv:1802.09098*.

Roquain, E. (2011). Type i error rate control in multiple testing: a survey with proofs. *Journal de la Société Française de Statistique*, 152(2):3–38.

Storey, J. D. (2002). A direct approach to false discovery rates. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 64(3):479–498.

Xia, F., Zhang, M. J., Zou, J. Y., and Tse, D. (2017). Neuralfdr: Learning discovery thresholds from hypothesis features. In *Advances in Neural Information Processing Systems*, pages 1541–1550.

Supplementary Material for “Contextual Online False Discovery Rate Control”

A Related Work in the Offline Setting

In the offline setting, where we have access to the entire batch of p-values at one time instant, a number of procedures have been proposed to take advantage of the available auxiliary information to increase the power of test (to make more true discoveries). As we note below, the modeling of auxiliary information varies.

Storey (2002) proposed an adaptive FDR-control procedure based on estimating the proportion of true nulls from data. Reweighting the p-values by applying priors was considered by (Benjamini and Hochberg, 1997; Genovese et al., 2006; Dobriban, 2016; Dobriban et al., 2015). In scenarios where priors are about spatial or temporal structure on hypotheses, *Independent Hypothesis Weighting* procedure was proposed by (Ignatiadis et al., 2016), which clusters similar hypotheses into groups and assigns different weights to these groups. Hu et al. (2010) utilized the idea of both grouping and estimating the true null proportions within each group. Some more procedures in (Foygel-Barber and Candès, 2015; G’Sell et al., 2016; Li and Barber, 2017; Lei and Fithian, 2016) incorporate a prior ordering as the auxiliary information to focus on more promising hypotheses near the top of the ordering. This motivation underlies also the first online multiple testing paper of (Foster and Stine, 2008).

Structure-adaptive BH algorithm (SABHA) (Li and Barber, 2016) and *Adaptive p-value Thresholding* (AdaPT) (Lei and Fithian, 2018) are two recent FDR control adaptive methods which derive the feature vector dependent decision rules. SABHA first censors the p-values below a fixed level, and then uses the censored p-values to estimate the non-null proportion (using non-parametric methods in practice), and then applies the weighted BH procedure of (Genovese et al., 2006). AdaPT is based on adaptively estimating a Bayes-optimal p-value rejection threshold. At each iteration of AdaPT, an analyst proposes a significance threshold and observes partially censored p-values, then estimates the false discovery proportion (FDP) below the threshold, and proposes another threshold, until the estimated FDP is below the desired level.

The offline testing algorithm mostly related to our results is the *NeuralFDR* procedure proposed by (Xia et al., 2017), which uses a neural network to parametrize the decision rule. This procedure in the offline setting, with access to all the p-values and the contextual features, comes up with a single decision rule $t(X)$ based on training a neural network for optimizing on the number of discoveries. In contrast, our method is in online multiple testing setup where we do not know all the p-values or the contextual features at once, and decision rules are different at each time, and varies as a function of previous outcomes and features.

B Missing Details from Section 2

The idea behind LORD (and LORD++) rules is that the significance level α_t is a function based only on *most recent discovery time*. Formally, we start with any sequence of nonnegative numbers $\gamma = (\gamma_t)_{t=1}^{\infty}$, which is monotonically non-increasing with $\sum_{t=1}^{\infty} \gamma_t = 1$. At each time t, let τ_t be the last time a discovery was made before t, i.e.,

$$\tau_t := \max\{i \in \{1, \dots, t-1\} : R_i = 1\},$$

with $\tau_t = 0$ for all t before the first discovery. The LORD rule defines α_t, ϕ_t, ψ_t in the following generalized alpha-investing fashion.

Level based On Recent Discovery (LORD) (Javanmard and Montanari, 2018, 2015):

$$W(0) = w_0,$$

$$\phi_t = \alpha_t = \begin{cases} \gamma_t w_0 & \text{if } t \le \rho_1 \\ \gamma_{t-\tau_t} b_0 & \text{if } t > \rho_1, \end{cases}$$

$$\psi_t = b_0,$$

$$b_0 = \alpha - w_0.$$

Typically, we will set $w_0 = \alpha/2$, in which case, the above rule could be simplified as $\phi_t = \alpha_t = \gamma_{t-\tau_t} b_0 = \gamma_{t-\tau_t} \alpha/2$.

As with any GAI rule, (Ramdas et al., 2017b) showed that one could replace b_0 with $b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\}$ to achieve potentially better power, while still achieving online FDR control at level α. With this replacement, we defined LORD++ as follows.

Improved Level based On Recent Discovery (LORD++) (Ramdas et al., 2017b):

$$W(0) = w_0 \geq \alpha/2,$$
$$\phi_t = \alpha_t = \gamma_{t-\tau_t} b_t,$$
$$\psi_t = b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\}.$$

C Missing Details from Section 3

Identifiability of $f_1(p \mid X)$. We present a simple example from (Lei and Fithian, 2018) that illustrates why $f_1(p \mid X)$ (distribution of p under the alternate) is not identifiable. Consider the following mixture model:

$$H_t \mid X_t \overset{\text{i.i.d.}}{\sim} \text{Bernoulli}(\pi_1),$$
$$P_t \mid H_t, X_t = \begin{cases} \text{Uniform(0,1)} & \text{if } H_t = 0, \\ f_1(p \mid X_t) & \text{if } H_t = 1. \end{cases}$$

Now consider the conditional mixture density $f(p \mid X) = (1-\pi_1) + \pi_1 f_1(p \mid X)$. Note that the H_t's are not observed. Thus, while f is identifiable from the data, π_1 and f_1 are not: for example, $\pi_1 = 0.5$, $f_1(p \mid X) = 2(1-p)$ and $\pi_1 = 1$, $f_1(p \mid X) = 1.5 - p$ result in exactly the same mixture density $f(p \mid X)$.

C.1 Proofs of Theorems 1 and 2

Here we present the proof of the online FDR control for any monotone contextual GAI rule. We start by presenting the following lemma, which is an intermediate result for the proof of FDR later. Recall that $R_t = \mathbb{1}\{P_t \leq \alpha_t\}$, where $\alpha_t \in \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)$ is a coordinatewise non-decreasing function of $R_1, \ldots, R_{t-1}$ for any fixed $\mathbf{X}^t = (X_1, \ldots, X_t)$. Due to the marginal super-uniformity (1), we immediately for independent p-values under the null, the following super-uniformity condition (noted in (9)).

$$\Pr[P_t \leq \alpha_t \mid \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)] \leq \alpha_t.$$

Lemma 1 states a more general result about super-uniformity of independent p-values under the null. The proof is based on a *leave-one-out* technique which is common in the multiple testing. A variant of this result was also used by (Ramdas et al., 2017b) and (Javanmard and Montanari, 2018) in their analysis of GAI rules. The main distinction for us comes in that we consider the sigma-field at each time t as $\sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)$ including the information of contextual features till time t, instead of just $\mathcal{F}^{t-1}$.

Lemma 1 (Super-uniformity). *Let $g : \{0,1\}^T \to \mathbb{R}$ be any coordinatewise non-decreasing function such that $g(\mathbf{R}) > 0$ for any vector $\mathbf{R} \neq (0, \ldots, 0)$. Then for any index $t \leq T$ such that $t \in \mathcal{H}^0$, we have*

$$\mathbb{E}\left[\frac{\mathbb{1}\{P_t \leq \alpha_t(R_1, \ldots, R_{t-1}, X_1, \ldots, X_t)\}}{g(R_1, \ldots, R_T) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right] \leq \mathbb{E}\left[\frac{\alpha_t(R_1, \ldots, R_{t-1}, X_1, \ldots, X_T)}{g(R_1, \ldots, R_T) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right].$$

Proof. Let $\mathbf{P} = (P_1, \ldots, P_T)$ be the sequence of p-values, and $\mathbf{X} = (X_1, \ldots, X_T)$ be the sequence of the contextual feature vectors until sometime T. We define a "leave-one-out" vector of p-value as $\widetilde{\mathbf{P}}^{-t} = (\widetilde{P}_1, \ldots, \widetilde{P}_T)$, which was obtained from $\mathbf{P}$ by setting $P_t = 0$, i.e.,

$$\widetilde{P}_i = \begin{cases} P_i & \text{if } i \neq t, \\ 0 & \text{if } i = t. \end{cases}$$

Let $\mathbf{R} = (R_1, \ldots, R_T)$ be the sequence of decisions on the input $\mathbf{P}$ and $\mathbf{X}$, and $\widetilde{\mathbf{R}}^{-t} = (\widetilde{R}_1, \ldots, \widetilde{R}_T)$ be the sequence of decisions by applying the same rule on the input $\mathbf{P}^{-t}$ and $\mathbf{X}$. Note here we just set one p-value as zero but are not changing the contextual feature vectors.

By the construction of p-values, we have that $R_i = \widetilde{R}_i$ for $i < t$, and hence

$$\alpha_i(R_1, \dots, R_{i-1}, X_1, \dots, X_i) = \alpha_i(\widetilde{R}_1, \dots, \widetilde{R}_{i-1}, X_1, \dots, X_i), \quad \text{for all } i \leq t.$$

We also know that $\widetilde{R}_t = 1$ always holds due to the fact $\widetilde{P}_t = 0 \leq \alpha_t$. Therefore, if the event $\{P_t \leq \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}$ occurs, we have $R_t = \widetilde{R}_t$ and thus $\mathbf{R} = \widetilde{\mathbf{R}}^{-t}$.

From the above arguments, we conclude that

$$\frac{\mathbb{1}\{P_t \leq \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}}{g(\mathbf{R}) \vee 1} = \frac{\mathbb{1}\{P_t \leq \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}}{g(\widetilde{\mathbf{R}}^{-t}) \vee 1}.$$

Due to the fact that $t \in \mathcal{H}^0$ ($H_t = 0$), P_t is independent to all contextual features $\mathbf{X}$ by assumption (as P_i's and X_i's are independent under the null), which gives that P_t is independent of $\sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)$. And since P_t is independent of $\widetilde{\mathbf{R}}^{-t}$, we have,

$$\begin{aligned}
&\mathbb{E}\left[\frac{\mathbb{1}\{P_t \leq \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}}{g(\mathbf{R}) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right] \\
&= \mathbb{E}\left[\frac{\mathbb{1}\{P_t \leq \alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)\}}{g(\widetilde{\mathbf{R}}^{-t}) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right] \\
&\leq \mathbb{E}\left[\frac{\alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)}{g(\widetilde{\mathbf{R}}^{-t}) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right] \qquad (17) \\
&\leq \mathbb{E}\left[\frac{\alpha_t(R_1, \dots, R_{t-1}, X_1, \dots, X_t)}{g(\mathbf{R}) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right] \qquad (18)
\end{aligned}$$

where inequality (17) follows by taking expectation with respect to P_t and using super-uniformity, and inequality (18) is derived by the following observation.

Since $\widetilde{P}_t = 0 \leq \alpha_t$, we have $\widetilde{R}_t = 1 \geq R_t$. Due to the monotonicity of the significance levels, we have

$$\alpha_i(\widetilde{R}_1, \dots, \widetilde{R}_{i-1}, X_1, \dots, X_i) \geq \alpha_i(R_1, \dots, R_{i-1}, X_1, \dots, X_i), \quad \text{for all } i > t,$$

ensuring $\widetilde{R}_i \geq R_i$ for all i, and thus $g(\widetilde{\mathbf{R}}^{-t}) \geq g(\mathbf{R})$ by the non-decreasing assumption on the function g. □

Theorem 4 (Theorem 1 Restated)**.** *Consider a sequence of $((P_t, X_t))_{t \in \mathbb{N}}$ of p-values and contextual features. If the p-values P_t's are independent, and additionally P_t are independent of all $(X_t)_{t \in \mathbb{N}}$ are independent under the null (whenever $H_t = 0$), then for any monotone contextual generalized alpha-investing rule (i.e., satisfying conditions (3), (4), (5), (6), and (8)), we have online FDR control,*

$$\sup_{T \in \mathbb{N}} \mathrm{FDR}(T) \leq \alpha.$$

Proof. Note that the number of false discoveries is $V(T) = \sum_{t=1}^{T} R_t \mathbb{1}\{t \in \mathcal{H}^0\}$ and the amount of wealth is $W(T) = w_0 + \sum_{t=1}^{T}(-\phi_t + R_t\psi_t)$.

We can derive the following expression by using the tower property of conditional expectation

$$\begin{aligned}
\mathbb{E}\left[\frac{V(T) + W(T)}{R(T) \vee 1}\right] &= \sum_{t=1}^{T} \mathbb{E}\left[\frac{R_t \mathbb{1}\{t \in \mathcal{H}^0\} + \frac{w_0}{T} - \phi_t + R_t\psi_t}{R(T) \vee 1}\right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t \in \mathcal{H}^0\}) - \phi_t}{R(T) \vee 1}\right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t \in \mathcal{H}^0\}) - \phi_t}{R(T) \vee 1} \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t)\right]\right] \qquad (19)
\end{aligned}$$

We split the analysis in two cases based on whether $H_t = 0$ or $H_t = 1$.

- Case 1: Suppose that $t \in \mathcal{H}^0$. By applying Lemma 1, we have

$$\mathbb{E}\left[\frac{R_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right] = \mathbb{E}\left[\frac{\mathbb{1}\{P_t \le \alpha_t\}}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right] \le \mathbb{E}\left[\frac{\alpha_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]. \tag{20}$$

  Since $\psi_t \le \frac{\phi_t}{\alpha_t} + b_t - 1$, we further obtain

$$\begin{aligned}\mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t\in\mathcal{H}^0\}) - \phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right] &\le \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\frac{\phi_t}{\alpha_t} + b_t) - \phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right]\\ &= \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t b_t + \frac{\phi_t}{\alpha_t}(R_t - \alpha_t)}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right]\\ &\le \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t b_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right],\end{aligned}$$

  where the last inequality follows by applying (20).

- Case 2: Suppose that $t \notin \mathcal{H}^0$. Using the fact that $\psi_t \le \phi_t + b_t$, we have

$$\begin{aligned}\mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t\in\mathcal{H}^0\}) - \phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right] &\le \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\phi_t + b_t) - \phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right]\\ &= \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t b_t + (R_t - 1)\phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right]\\ &\le \mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t b_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right].\end{aligned}$$

Combining the bound on $\mathbb{E}\left[\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t\in\mathcal{H}^0\}) - \phi_t}{R(T)\vee 1}\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right]\right]$ from both cases in (19) and using the definition of b_t, we obtain that,

$$\begin{aligned}\mathbb{E}\left[\frac{V(T)+W(T)}{R(T)\vee 1}\right] &\le \sum_{t=1}^{T}\mathbb{E}\left[\frac{\frac{w_0}{T} + R_t b_t}{R(T)\vee 1}\right] = \mathbb{E}\left[\frac{w_0 + \sum_{t=1}^{T} R_t b_t}{R(T)\vee 1}\right]\\ &\le \mathbb{E}\left[\frac{w_0 + \sum_{t=1}^{T} R_t\alpha - w_0\mathbb{1}\{T \ge \rho_1\}}{R(T)\vee 1}\right] = \mathbb{E}\left[\frac{w_0 + \alpha R(T) - w_0\mathbb{1}\{T\ge\rho_1\}}{R(T)\vee 1}\right] \le \alpha.\end{aligned}$$

This concludes the proof of the theorem. □

Theorem 5 (Theorem 2 Restated)**.** *Consider a sequence of* $((P_t, X_t))_{t\in\mathbb{N}}$ *of p-values and contextual features. If the p-values* P_t*'s are conditionally super-uniform distributed (as in* (9)*), then for any contextual generalized alpha-investing rule* (*i.e., satisfying conditions* (3)*,* (4)*,* (5)*, and* (6))*, we have online mFDR control,*

$$\sup_{T\in\mathbb{N}} \text{mFDR}(T) \le \alpha.$$

Proof. The conditional super-uniformity implies that under null

$$\mathbb{E}\left[R_t\middle|\sigma(\mathcal{F}^{t-1}\cup\mathcal{G}^t)\right] \le \alpha_t.$$

Now using a proof technique similar to Theorem 4, for any $T \in \mathbb{N}$, we get

$$\begin{aligned}
\mathbb{E}[V(T)] &\leq \mathbb{E}[V(T) + W(T)] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[R_t \mathbb{1}\{t \in \mathcal{H}^0\} + \frac{w_0}{T} - \phi_t + R_t \psi_t \right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t \in \mathcal{H}^0\}) - \phi_t \right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{w_0}{T} + R_t(\psi_t + \mathbb{1}\{t \in \mathcal{H}^0\}) - \phi_t \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t) \right] \right] \\
&\leq \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{w_0}{T} + R_t b_t \middle| \sigma(\mathcal{F}^{t-1} \cup \mathcal{G}^t) \right] \right] \\
&= \mathbb{E}\left[w_0 + \sum_{t=1}^{T} R_t b_t \right] = \mathbb{E}\left[w_0 + \alpha R(T) - w_0 \mathbb{1}\{T \geq \rho_1\} \right] \\
&\leq \alpha \, \mathbb{E}\left[R(T) \vee 1 \right],
\end{aligned}$$

where for the second inequality we used an analysis similar to that used in the first case in the proof of Theorem 4. Therefore, for any $T \in \mathbb{N}$,

$$\text{mFDR}(T) = \frac{\mathbb{E}[V(T)]}{\mathbb{E}[R(T) \vee 1]} \leq \alpha.$$

This concludes the proof of the theorem. □

D Missing Details from Section 4

Let us see how the principle of context weighting (from Section 4) can be applied to LORD++ rules defined in Section 2. Given a weight function, $\omega : \mathcal{X} \times \Theta \to \mathbb{R}$, we define the context-weighted LORD++ (CwLORD++) testing rule as follows.

Context-weighted LORD++ (CwLORD++):

$$\begin{gathered}
W(0) = w_0, \\
\phi_t = \alpha_t = \min\{\gamma_{t-\tau_t} b_t \cdot \omega(X_t; \theta), W(t-1)\}, \\
\psi_t = b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t - 1\}.
\end{gathered}$$

Similarly, given the function ω, we can also define context-weighted LORD using the LORD rules from Section 2. As pointed out before, when α_t's are reweighted, the penalty ϕ_t's are also adjusted accordingly. This provides a clean way of incorporating the weights in an online setup without having to rescale the weights to have unit mean.

We illustrate the relationship among various classes of testing rules in Figure 3.

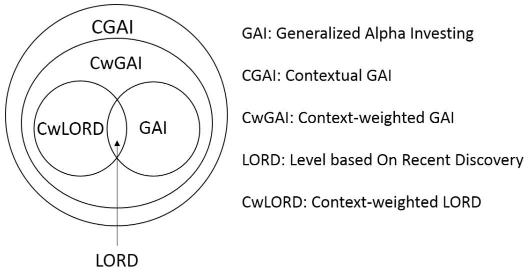

CGAI
CwGAI
CwLORD
GAI
LORD
GAI: Generalized Alpha Investing
CGAI: Contextual GAI
CwGAI: Context-weighted GAI
LORD: Level based On Recent Discovery
CwLORD: Context-weighted LORD

Figure 3: Relationship among various testing rules. One could replace LORD with LORD++ (resp. CwLORD with CwLORD++).

E Missing Details from Section 5

In this section, we present missing details from Section 5 which provides theoretical support of the increased power through proper weighting in an online setting. For completeness, we repeat a few definitions from Section 5.

Mixture Model. For any $t \in \mathbb{N}$, let

$$\begin{gathered} H_1, \dots, H_t \overset{\text{i.i.d.}}{\sim} \text{Bernoulli}(\pi_1), \\ X_t \mid H_t = 0 \sim \mathcal{L}_0(\mathcal{X}), \quad X_t \mid H_t = 1 \sim \mathcal{L}_1(\mathcal{X}), \\ P_t \mid H_t = 0, X_t \sim \text{Uniform}(0, 1), \\ P_t \mid H_t = 1, X_t \sim F_1(p \mid X_t). \end{gathered}$$

where $0 < \pi_1 < 1$ and where $\mathcal{L}_0(\mathcal{X})$, $\mathcal{L}_1(\mathcal{X})$ are two probability distribution on the contextual feature space $\mathcal{X}$. Let $F = \int F_1(p \mid X) \mathrm{d}\mathcal{L}_1(\mathcal{X})$ be the marginal distribution of p-value under alternative. Marginally, the p-values are i.i.d. from the CDF $G(a) = (1 - \pi_1)U(a) + \pi_1 F(a)$, where $U(a)$ is the CDF of Uniform(0,1). We do not require that the contextual features X_t's be independent, but only that they be identically distributed as $\mathcal{L}_0(\mathcal{X})$ (under null) or $\mathcal{L}_1(\mathcal{X})$ (under alternative).

General Weighting Scheme. We consider the general weighting as in (Genovese et al., 2006) where weight is a random variable and conditionally independent of P_t given H_t. We assume that weight ω_t has different marginal distributions under null and alternative,

$$\omega_t \mid H_t = 0 \sim Q_0, \quad \omega_t \mid H_t = 1 \sim Q_1, \tag{21}$$

with Q_0, Q_1 unknown continuous distributions on $(0, \infty)$. Under the mixture setup,

$$\omega_t \overset{\text{i.i.d.}}{\sim} (1 - \pi_1)Q_0 + \pi_1 Q_1, \tag{22}$$

with P_t and ω_t being conditionally independent given H_t for all $t = 1 \dots, \infty$.

Contextual Weighting Scheme. This framework of weighting in (21) is very general. For example, it includes as a special case, the following contextual weighting scheme, where we assume that there exists a weight function of contextual features $\omega : \mathcal{X} \times \Theta \to \mathbb{R}$, and the distributions of weights are defined as:

$$\begin{aligned} \omega_t \mid H_t = 0 &\sim \omega(X; \theta), \text{ with } X \sim \mathcal{L}_0(\mathcal{X}), \\ \omega_t \mid H_t = 1 &\sim \omega(X; \theta), \text{ with } X \sim \mathcal{L}_1(\mathcal{X}). \end{aligned} \tag{23}$$

Now Q_0 and Q_1 are defined as the distributions of $\omega(X; \theta)$ under the null and alternative, respectively. Given Q_0 and Q_1, the weight ω_t is sampled as in (22).[8] A reader might notice that that while the distributions Q_0 and Q_1 for weights are defined through X_t's distribution, the weight ω_t is sampled i.i.d. from the mixture model $(1 - \pi_1)Q_0 + \pi_1 Q_1$, regardless of the value of X_t. Note that the independence assumption on p-values can still be satisfied even when the $X_t's$ are dependent.[9] Since this contextual weighting scheme is just a special case of the above general weighting scheme, in the remainder of this section, we work with the general weighting scheme.

Informativeness. Under (21), the marginal distribution of ω is $Q = (1 - \pi_1)Q_0 + \pi_1 Q_1$. For $j = 0, 1$, let $u_j = \mathbb{E}[\omega \mid H_t = j]$ be the means of Q_0 and Q_1 respectively. We also assume that the weighting is *informative*, based on the following definition from (Genovese et al., 2006) in the offline setting,

$$\textbf{Informative-weighting: } u_0 < 1, \, u_1 > 1, \, u = \mathbb{E}[\omega] = (1 - \pi_1)u_0 + \pi_1 u_1 = 1. \tag{24}$$

Remark 2. *Informative-weighting places a very natural condition on the weights. Roughly it means that the weight should be positively associated to the true alternatives, or equivalently, the weight under alternative is more likely to be larger than that under the null. The marginal mean of weight $\mathbb{E}[\omega]$ is not necessary to be one. But for the theoretical comparison of the power of different procedures, it is convenient to scale the weight to have unit mean so that we can use the p-value reweighting akin to the offline setting. For empirical experiments, we will use an instantiation of CwLORD++, that does not require the weight to have mean one.*

We now focus on the establishing power separation under this property.

[8] In case , $X_t \overset{\text{i.i.d.}}{\sim} (1 - \pi_1)\mathcal{L}_0 + \pi_1 \mathcal{L}_1$, then one can define ω_t directly as $\omega_t = \omega(X_t; \theta)$ with Q_0 and Q_1 defined as the distributions of $\omega(X_t; \theta)$ under the null and alternative, respectively.

[9] For example, in practice it is common that the contextual features are dependent (e.g., same genes or genetic variants may be tested in multiple independent experiments at different time), but as long as the tests are carried out independently the p-values are still independent.

Weighted LORD++. Let the weights ω_t's be random variables that are drawn i.i.d. from this mixture model with marginal distribution Q. Taking the LORD++ rule from Section 2, we define a weighted LORD++ rule as follows.

Definition 4 (Weighted LORD++)**.** *Given a sequence of p-values, $(P_1, P_2, \dots)$ and weights $(\omega_1, \omega_2, \dots)$, apply LORD++ with level α to the weighted p-values $(P_1/\omega_1, P_2/\omega_2, \dots)$.*

We want to emphasize that the weighted LORD++ rule actually reweights the p-values (as done in the offline weighted BH procedure (Genovese et al., 2006)) and then applies the original LORD++ to these reweighted p-values. So this is slightly different from the idea of CwLORD++, that we mentioned above, which reweights the significance levels and then applies it to the original p-values. To understand the difference, let us start from their definitions.

In LORD++, the penalty is $\phi_t = \alpha_t = \gamma_{t-\tau_t} b_t < W(t-1)$, which is always less than current wealth due to the construction of γ_t's and w_0. So in weighted LORD++, we are comparing reweighted p-value P'_t to the level $\alpha_t = \gamma_{t-\tau_t} b_t$, which is equivalent to comparing the original p-value P_t to the level $\alpha'_t = \gamma_{t-\tau_t} b_t \omega_t$.

On the other hand, in CwLORD++, we take a penalty of the form $\tilde{\phi}_t = \tilde{\alpha}_t = \min\{\gamma_{t-\tau_t} b_t \omega_t, W(t-1)\}$. We take the minimum of reweighted significance level and the current wealth, to prevent the penalty $\gamma_{t-\tau_t} b_t \omega_t$ from exceeding the current wealth which would violate a tenet of the alpha-investing rules.

A simple corollary is that the actual significance levels used in weighted LORD++ are greater than those in CwLORD++, i.e.,

$$\alpha'_t = \gamma_{t-\tau_t} b_t \omega_t \geq \min\{\gamma_{t-\tau_t} b_t \omega_t, W(t-1)\} = \tilde{\alpha}_t.$$

That implies the power of weighted LORD++ is equal to or greater than the power of CwLORD++, whereas the FDR of weighted LORD++ may also be higher than that of CwLORD++. From Theorem 1, we know that we have FDR control with CwLORD++, however that result does not hold for weighted LORD++ (as weighted LORD++ is not strictly a contextual GAI rule) We now show that the above weighted LORD++ can still control online FDR at any given level α under the condition $\mathbb{E}[\omega] = 1$, which we do in the following proposition. The FDR control guarantee also holds for weighted LORD (Definition 3).

Proposition 1. *Suppose that the weight distribution satisfies the informative-weighting property in (24). Suppose that p-values P_t's are independent, and are conditionally independent of the weights ω_t's given H_t's. Then the weighted LORD++ rule can control the online FDR at any given level α, i.e.,*

$$\sup_{T \in \mathbb{N}} \mathrm{FDR}(T) \leq \alpha.$$

Proof. We start with a frequently used estimator of FDR that is defined as:

$$\widehat{\mathrm{FDP}}(T) := \frac{\sum_{t=1}^{T} \alpha_t}{R(T) \vee 1}.$$

As established in Section 4 in (Ramdas et al., 2017b), LORD++ applied to any sequence of p-values will ensure that $\sup_T \widehat{\mathrm{FDP}}(T) \leq \alpha$. We apply LORD++ with the sequence of p-values defined as $\boldsymbol{P'} = (\frac{P_1}{\omega_1}, \frac{P_2}{\omega_2}, \frac{P_3}{\omega_3} \dots)$. Let $P'_t = P_t/\omega_t$ for any $t \in \mathbb{N}$. Then it follows that,

$$\sup_{T \in \mathbb{N}} \widehat{\mathrm{FDP}}(T) = \sup_{T \in \mathbb{N}} \frac{\sum_{t=1}^{T} \alpha_t}{R(T) \vee 1} = \sup_{T \in \mathbb{N}} \frac{\sum_{t=1}^{T} \alpha_t}{(\sum_{t=1}^{T} \mathbb{1}\{P'_t \leq \alpha_t\}) \vee 1} \leq \alpha. \tag{25}$$

We denote the sigma-field of decisions based on the weighted p-values $\boldsymbol{P'}$ till time t as $\mathcal{C}^t = \sigma(R_1, \dots, R_t)$. By using the "leave-one-out" method used in Theorem 4, the FDR of the weighted LORD++ at any time T can be written as,

$$\begin{aligned}
\mathrm{FDR}(T) &= \mathbb{E}\left[\frac{\sum_{t=1}^{T} \mathbb{1}\{t \in \mathcal{H}^0 : P'_t \leq \alpha_t\}}{(\sum_{t=1}^{T} \mathbb{1}\{P'_t \leq \alpha_t\}) \vee 1}\right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\frac{\mathbb{1}\{t \in \mathcal{H}^0 : \frac{P_t}{\omega_t} \leq \alpha_t\}}{R(T) \vee 1}\right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\Big[\frac{\mathbb{1}\{t \in \mathcal{H}^0 : \frac{P_t}{\omega_t} \leq \alpha_t\}}{R(T) \vee 1}\Big|\mathcal{C}^{t-1}\Big]\right] \\
&= \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\Big[\frac{\mathbb{1}\{t \in \mathcal{H}^0 : \frac{P_t}{\omega_t} \leq \alpha_t\}}{R^{-t}(T) \vee 1}\Big|\mathcal{C}^{t-1}\Big]\right],
\end{aligned}$$

where $R^{-t}(T) = \sum_{i=1}^{T} \mathbb{1}\{P_i/\omega_i \le \alpha_i\}$ is obtained by setting $P_t = 0$, while keeping all ω_t's unchanged. The last equality holds due to the fact that $R^{-t}(T) = R(T)$ given the event $\{P_t/\omega \le \alpha_t\}$.

Since $\alpha_t \in \mathcal{C}^{t-1}$, and P_t, ω_t are independent of $R^{-t}(T)$ and $\mathcal{C}^{t-1}$, we can take the expectation of the numerator inside the brackets and obtain that

$$\begin{aligned}
\Pr[P_t/\omega_t \le \alpha_t \mid \mathcal{C}^{t-1}, H_t = 0] &= \int \Pr[P_t/\omega_t \le \alpha_t \mid \mathcal{C}^{t-1}, \omega_t = w, H_t = 0]\, \mathrm{d}Q(w \mid H_t = 0) \\
&= \int w\alpha_t dQ(w \mid H_t = 0) \\
&= u_0\alpha_t,
\end{aligned}$$

where $u_0 = \mathbb{E}[\omega \mid H_t = 0]$. Plugging this in the bound on $\mathrm{FDR}(T)$ from above gives,

$$\begin{aligned}
\mathrm{FDR}(T) &= \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{u_0\alpha_t}{R^{-t}(T) \vee 1}\middle|\mathcal{C}^{t-1}\right]\right] \\
&\le \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{\alpha_t}{R^{-t}(T) \vee 1}\middle|\mathcal{C}^{t-1}\right]\right] &(26)\\
&\le \sum_{t=1}^{T} \mathbb{E}\left[\mathbb{E}\left[\frac{\alpha_t}{R(T) \vee 1}\middle|\mathcal{C}^{t-1}\right]\right] &(27)\\
&= \mathbb{E}\left[\frac{\sum_{t=1}^{T} \alpha_t}{R(T) \vee 1}\right] = \mathbb{E}\left[\widehat{\mathrm{FDP}}(T)\right] \le \alpha,
\end{aligned}$$

where inequality (26) is due to the assumption that $u_0 < 1$, (27) follows by the fact that $R^{-t}(T) \ge R(T)$ due to monotonicity of LORD++, and the last equality is based on (25). □

Weakening the Assumptions from Proposition 1. In most applications, the independence between p-values and weights needed in Proposition 1 is not guaranteed. Javanmard and Montanari (2018) achieved the FDR control under dependent p-values by using a modified LORD rule, which sets $\psi_t = b_0$ and $\alpha_t = \phi_t = \gamma_t W(\tau_t)$ with the fixed sequence (γ_t) satisfying $\sum_{t=1}^{\infty} \gamma_t(1 + \log(t)) \le \alpha/b_0$.

We can extend the FDR control results to the dependent weighed p-values. In particular, as long as the following condition is satisfied, i.e., for each weighted p-value (P_t/ω_t) marginally

$$\Pr[P_t/\omega_t \le u \mid H_t = 0] \le u, \quad \text{for all } u \in [0, 1], \tag{28}$$

then the upper bound of FDR stated in Theorem 3.7 in (Javanmard and Montanari, 2018) is valid for weighted p-values. Specifically, if the modified LORD rule in Example 3.8 of (Javanmard and Montanari, 2018) is applied to the weighted p-values under the assumption in (28), then the FDR can be controlled below level α.

We formally state the results in the following proposition.

Proposition 2. *Suppose that the weight distribution satisfies the informative-weighting property in (24). And weighted p-values (P_t/ω_t) marginally satisfy (28). Then the modified LORD++ rule that applies to the weighted p-values can control the online FDR at any given level α, i.e.,*

$$\sup_{T \in \mathbb{N}} \mathrm{FDR}(T) \le \alpha.$$

The proofs of these extension are almost the same as those in (Javanmard and Montanari, 2018) and are omitted here.

Lower Bound on Statistical Power of Weighted LORD++. In order to compare different procedures, it is important to estimate their statistical power. Here, we analyze the power of the weighted LORD++. Define $D(a) = \Pr[P/\omega \le a]$ as the marginal distribution of weighted p-values. Under the assumptions on the weight distribution from (21), the marginal distribution of weighted p-value equals,

$$
\begin{aligned}
D(a) = \Pr[P/\omega \le a] &= \int \Pr[P/\omega \le a \mid \omega = w] \,\mathrm{d}Q(w) \\
&= \int \sum_{h\in\{0,1\}} \Pr[P/\omega \le a \mid \omega = w, H = h] g(h \mid w) \,\mathrm{d}Q(w) \\
&= \int \sum_{h\in\{0,1\}} \Pr[P/w \le a \mid H = h] g(h \mid w) \,\mathrm{d}Q(w) \\
&= \int \sum_{h\in\{0,1\}} ((1-h)aw + hF(aw)) g(h \mid w) \,\mathrm{d}Q(w) \\
&= \int \sum_{h\in\{0,1\}} ((1-h)aw + hF(aw)) \,\mathrm{d}Q(w \mid h) g(h) \\
&= \sum_{h\in\{0,1\}} \int ((1-h)aw + hF(aw)) \,\mathrm{d}Q(w \mid h) g(h) \\
&= (1-\pi_1) \int awdQ(w \mid h = 0) + \pi_1 \int F(aw) \,\mathrm{d}Q(w \mid h = 1) \\
&= (1-\pi_1)\mu_0 a + \pi_1 \int F(aw) \mathrm{d}Q_1(w). \qquad (29)
\end{aligned}
$$

The proof of the following Theorem 6 uses the similar technique as the proof of the statistical power of LORD in (Javanmard and Montanari, 2018). The main distinction is that we replace the marginal distribution of p-values by the marginal distribution of weighted p-values. The proof of Theorem 6 goes through by analyzing the weighted LORD procedure (Definition 3).

Theorem 6. *Let $D(a) = \Pr[P/\omega \le a]$ be the marginal distribution of weighted p-values as in (29). Then, the average power of weighted LORD++ rule is almost surely bounded as follows:*

$$\liminf_{T\to\infty} \mathrm{TDR}(T) \ge \Big(\sum_{m=1}^{\infty} \prod_{j=1}^{m} (1 - D(b_0\gamma_j))\Big)^{-1}.$$

Proof. Since we are interested in lower bounds, we consider a version of LORD (as also considered in (Javanmard and Montanari, 2018)) which that is based on the following rule,

$$\textbf{LORD:} W(0) = w_0 = b_0 = \alpha/2, \quad \phi_t = \alpha_t = b_0\gamma_{t-\tau_t}, \quad \psi_t = b_0.$$

Note that since $b_t = \alpha - w_0 \mathbb{1}\{\rho_1 > t-1\} > b_0$ in LORD++, the test level in LORD++ is at least as large to the test level in LORD. Therefore, for any p-value sequence the power of the LORD from is also a lower bound on the power of LORD++. In the rest of this proof, we focus on LORD for the weighted p-value sequence $\{P_1/\omega_1, P_2/\omega_2, \dots\}$. The bound established below is in fact *tight* for LORD under this p-value sequence.

Denote by ρ_i as the time of the ith discovery (rejection), with $\rho_0 = 0$, and $\Delta_i = \rho_i - \rho_{i-1}$ as the ith time interval between the $(i-1)$st and ith discoveries. Let $r_i := \mathbb{1}\{\rho_i \in \mathcal{H}^1\}$ be the reward associated with inter-discovery Δ_i. Since the weighted p-values are i.i.d. it can be seen that the times between successive discoveries are i.i.d. according to the testing procedure LORD, and the process $R(T) = \sum_{l=1}^{T} R_l$ is a *renewal process* (Cox et al., 1967). In fact, for each i, we have

$$\Pr[\Delta_i \ge m] = \Pr[\cap_{l=\rho_{i-1}}^{\rho_{i-1}+m} \{P_l/\omega_l > \alpha_l\}] = \prod_{l=\rho_{i-1}}^{\rho_{i-1}+m} (1 - D(\alpha_l)) = \prod_{l=\rho_{i-1}}^{\rho_{i-1}+m} (1 - D(b_0\gamma_{l-\rho_{i-1}})) = \prod_{l=1}^{m} (1 - D(b_0\gamma_l)).$$

The above expression is same for every i. Therefore,

$$\mathbb{E}[\Delta_i] = \sum_{m=1}^{\infty} \Pr[\Delta_i \ge m] = \sum_{m=1}^{\infty} \prod_{l=1}^{m} (1 - D(b_0\gamma_l)).$$

Applying the strong law of large numbers for renewal-reward processes (Cox et al., 1967), we obtain that the following statement holds almost surely,

$$\lim_{T\to\infty} \frac{1}{T} \sum_{i=1}^{R(T)} r_i = \frac{\mathbb{E}(r_i)}{\mathbb{E}(\Delta_1)} = \pi_1 \Big(\sum_{m=1}^{\infty} \prod_{l=1}^{m} (1 - D(b_0\gamma_l))\Big)^{-1}.$$

Let $|\mathcal{H}^1(T)|$ be the number of true alternatives till time T. Since $\lim_{T\to\infty} |\mathcal{H}^1(T)|/T = \pi_1$ almost surely, we have

$$\lim_{T\to\infty} \frac{1}{|\mathcal{H}^1(T)|} \sum_{i\in\mathcal{H}^1(T)} R_i = \lim_{T\to\infty} \frac{1}{|\mathcal{H}^1(T)|} \sum_{i=1}^{R(T)} r_i = (\sum_{m=1}^{\infty} \prod_{l=1}^{m} (1 - D(b_0\gamma_l)))^{-1}.$$

Now by using the definition of TDP(T), almost surely, we have that for any weighted LORD++,

$$\liminf_{T\to\infty} \text{TDP}(T) \geq (\sum_{m=1}^{\infty} \prod_{j=1}^{m} (1 - D(b_0\gamma_j)))^{-1}.$$

As discussed above, this bound translates into a lower bound for weighted LORD++. Furthermore, by using the Fatou's lemma (Carothers, 2000), we can extend the same result for TDR(T) almost surely,

$$\liminf_{T\to\infty} \text{TDR}(T) = \liminf_{T\to\infty} \mathbb{E}[\text{TDP}(T)] \geq \mathbb{E}[\liminf_{T\to\infty} \text{TDP}(T)] \geq (\sum_{m=1}^{\infty} \prod_{j=1}^{m} (1 - D(b_0\gamma_j)))^{-1}.$$

□

Comparison of Power. Next, we establish conditions under which a weighting could lead to increased power for LORD. We work with (a version of) the popular LORD procedure from (Javanmard and Montanari, 2018), which sets

$$W(0) = w_0 = b_0 = \alpha/2, \ \phi_t = \alpha_t = b_0\gamma_{t-\tau_t}, \ \psi_t = b_0. \tag{30}$$

As shown by (Javanmard and Montanari, 2018), the average power of LORD, under the mixture model, almost surely equals[10]

$$\text{For LORD: } \liminf_{T\to\infty} \text{TDR}(T) = (\sum_{m=1}^{\infty} \prod_{j=1}^{m} (1 - G(b_0\gamma_j)))^{-1}, \tag{31}$$

where $G(a) = (1 - \pi_1)U(a) + \pi_1 F(a)$ as defined earlier. From the proof of Theorem 6, the average power of weighted LORD almost surely equals

$$\text{For weighted LORD: } \liminf_{T\to\infty} \text{TDR}(T) = \sum_{m=1}^{\infty} \prod_{j=1}^{m} (1 - D(b_0\gamma_j))^{-1}. \tag{32}$$

Assume F is differentiable and let $f = F'$ be the PDF of p-values under alternative. Due to the fact that p-values under alternative are stochastically dominated by the uniform distribution, there exists some $a_0 > 0$ such that $f(a) > 1$ for all $0 \leq a < a_0$. The following theorem is based on comparing this power on weighted LORD from (32) with the power on LORD from from (31).

Theorem 7 (Power Separation)**.** *Suppose that the parameters in LORD* (30) *satisfy* $b_0\gamma_1 < a_0$*, and the weight distribution satisfies* $\Pr[\omega < a_0/(b_0\gamma_1) \mid H_t = 1] = 1$ *for every* $t \in \mathbb{N}$ *and the informative-weighting property in* (24)*. Then, the average power of weighted LORD is greater than equal to that of LORD almost surely.*

Proof. We compare the average power bound of weighted LORD and LORD. It is equivalent to comparing $D(a)$ and $G(a)$ for $a = b_0\gamma_l$, for $l = 1, \ldots, \infty$. Since $u = (1 - \pi_1)u_0 + \pi_1 u_1 = 1$, we have $(1 - \pi_1)u_0 = 1 - \pi_1 u_1$. This means that

$$\begin{aligned} D(a) - G(a) &= (1 - \pi_1)u_0 a + \pi_1 \int F(aw) \, \mathrm{d}Q_1(w) - (1 - \pi_1)a - \pi_1 F(a) \\ &= (1 - \pi_1)(u_0 - 1)a + \pi_1(\int F(aw) \, \mathrm{d}Q_1(w) - F(a)) \\ &= \pi_1(1 - u_1)a + \pi_1(\int F(aw) \, \mathrm{d}Q_1(w) - F(a)). \end{aligned}$$

So we just need to compare $(\mu_1 - 1)a$ and $\int F(aw) \, \mathrm{d}Q_1(w) - F(a)$, for any $a = b_0\gamma_l$, for $l = 1, \ldots, \infty$. Due to the fact that $\{\gamma_l\}$ is a non-increasing sequence, we have $a = b_0\gamma_l \leq b_0\gamma_1$. Since $b_0\gamma_1 < a_0$ and $\Pr[\omega < a_0/(b_0\gamma_1) \mid H = 1] = 1$ by assumption, then $\Pr[\max(a, aw) < a_0 \mid H = 1] = 1$.

[10] Javanmard and Montanari (2018) proposed multiple versions of LORD, and as noted by them the bound in (16) lower bounds the average power on all the versions of LORD for the above mixture model.

For any fixed $a = b_0\gamma_l > 0$, we have

$$\begin{aligned}
\frac{\int F(aw)\,\mathrm{d}Q_1(w) - F(a)}{a} &= \int \frac{F(aw) - F(a)}{a}\,\mathrm{d}Q_1(w) \\
&= \int \frac{F(aw) - F(a)}{(w-1)a}(w-1)\,\mathrm{d}Q_1(w) \\
&= \int f(\xi)(w-1)\,\mathrm{d}Q_1(w) && (33) \\
&\geq \int (w-1)\,\mathrm{d}Q_1(w) && (34) \\
&= \mathbb{E}[W \mid H = 1] - 1 = u_1 - 1,
\end{aligned}$$

for some $\xi \in (\min(a, aw), \max(a, aw))$. Note we assume Q_1 is a continuous distribution, so $\Pr[w = 1 \mid H = 1] = 0$. The equality (33) is achieved by applying the Intermediate Value Theorem, and the inequality (34) is obtained by the fact that $\Pr[\xi < a_0 \mid H = 1] = 1$, i.e., $\Pr[f(\xi) > 1 \mid H = 1] = 1$.

Therefore, we prove that $\int F(aw)\,\mathrm{d}Q_1(w) - F(a) \geq u_1 - 1$, which implies that $D(a) \geq G(a)$ for $a = b_0\gamma_l$, for $l = 1, \ldots, \infty$. □

As discussed earlier since the general weighting scheme includes the context-weighting scheme, so the results here indicate that using the informative context-weighting in the LORD rules will help in making more true discoveries.

Remark 3. *Intuitively, the condition implies that to achieve higher power while controlling FDR, the weights given to alternate hypotheses cannot be too large. Let us discuss this point in the context of weighted LORD++ and context-weighted LORD++.*

In weighted LORD++, we can always assign large weights to make the reweighted p-values small enough to be rejected, in order to achieve high power. But this can lead to a loss in FDR control which is why we need the restriction of $\mathbb{E}[\omega] = 1$ for proving the FDR control in Proposition 1. Therefore, it is natural to have weights not too large.

If we consider reweighting the significance levels as in CwLORD++, assigning a large weight will not affect the FDR control (we prove that FDR is controlled for any choice of weights in Theorem 1). However, the price is paid in terms of power. When we use a large weight, the penalty ϕ_t increases and therefore the wealth might go quickly down to zero. Once the wealth is exhausted, the significance levels afterwards must all be zero and thus preventing any further discoveries.

F Missing Details from Section 6

In this section, we provide additional experimental results. The results demonstrate the increased power (under FDR control) in online multiple testing setup that can be obtained with our proposed contextual weighting in various scenarios.

Informative-Weighting Property. A natural question to ask is whether one can check for the informative-weighting property (24). If we assume the feedback (true labels) are given after testing each batch, then this condition can be verified in the online learning process. With the feedback after each batch, we can compute the average weights of the true alternatives and nulls, to see whether the former is greater than the latter. If so, then the weights learned so far are informative and can be utilized further. If not, for next batch we can revert to previous informative weights, or even start over from the baseline unweighted procedure.

However, the requirement of having feedback after testing each batch is too strict, so in practice the assumption can be relaxed. That is, we can still verify the informative weighting condition in practice if we have a fixed set of contextual features from the same mixture model with known labels (from null or alternative) for validation. Similarly, after testing each batch and updating the parameters of the weight function, we apply the updated weight function to the contextual features of the validation set and compare the average weights of the features from alternatives and nulls. If the former one is greater than the latter, we will keep going on with next batch. Otherwise, we will revert to the previous step of the weight function updates. Please see Section F.1.1 for the numerical comparison of the algorithm implementation with and without validation set. If the labels of the validation set of the contextual features are not available to us, we need to first figure out their labels. One possible way to do so is to apply some powerful offline hypothesis testing rule to first test whether they are from null or alternative. Getting this right require more rigorous assumptions. For example, if the dimension of each contextual feature vector is one, and they are assumed to be normal distributed with mean zero under the null and with mean

Algorithm 1: Online FDR Control with a Context-Weighted GAI Procedure

```
Model the weight function as a multi-layer perceptron (MLP);
Input: A sequence of p-value, contextual feature vector pairs $((P_1, X_1), (P_2, X_2), \dots)$, a monotone GAI rule (such as
       LORD++) denoted by $\mathbb{G}$ with desired FDR control, batch size $b$, learning rate $\eta$
Output: Neural network model parameter set $\theta \in \Theta$
Randomly initialize the parameter set $\theta_0$; batch index $j = 0$
repeat
    for $i = 1$ to $b$ do
        Consider the pair $(P_{jb+i}, X_{jb+i})$ ($i$th hypothesis in the $j$th batch)
        Let $\tilde{\alpha} \leftarrow \alpha_{jb+i}(R_1, \dots, R_{jb+i-1})$ (computed as defined by the GAI rule $\mathbb{G}$)
        Accept/reject this hypothesis with significance level $\alpha_{jb+i}(X_{jb+i}; \theta_j)) := \tilde{\alpha} \cdot \omega(X_{jb+i}; \theta_j)$
    end
    Use the decisions in the $j$th batch to update the empirical discovery proportion $(\mathrm{EDR}_j)$
    Compute the gradient with respect to the parameter set $\frac{\partial\,\mathrm{EDR}_j}{\partial\,\theta}$
    Update the parameter set: $\theta_{j+1} \leftarrow \theta_j + \eta \frac{\partial\,\mathrm{EDR}_j}{\partial\,\theta}$
    $j \leftarrow j + 1$
until convergence or end-of-stream;
Return $\theta_j$
```

greater than zero under the alternative, and with the same known variance. Then we can compute the corresponding p-values and apply the BH procedure to them. From previous works of (Genovese and Wasserman, 2002) and (Arias-Castro and Chen, 2017), the BH procedure is powerful and optimal (with power tending to 1 and FDR controlled) asymptotically under mixture Gaussian model with some conditions. So the test results of BH can be considered as accurate if those conditions are satisfied and provided the size of validation set is large enough. We can further use the labels returned by BH method to validate the informative weighting condition as described above.

Algorithm 1 deals with the case when there is no feedback or validation set. The algorithm learns the weight function in an online fashion, by regarding the previous decisions as ground truth, informally meaning that it will regard previously rejected hypotheses as true alternatives and thereby assigning a larger weighting in CwLORD++ for future hypothesis with contextual features similar to those of previously rejected hypotheses. Online FDR control is always guaranteed by Algorithm 1. The hope is that by maximizing the number of empirical discoveries, the algorithm can learn an informative-weighting (as possibly corroborated by our experiments).

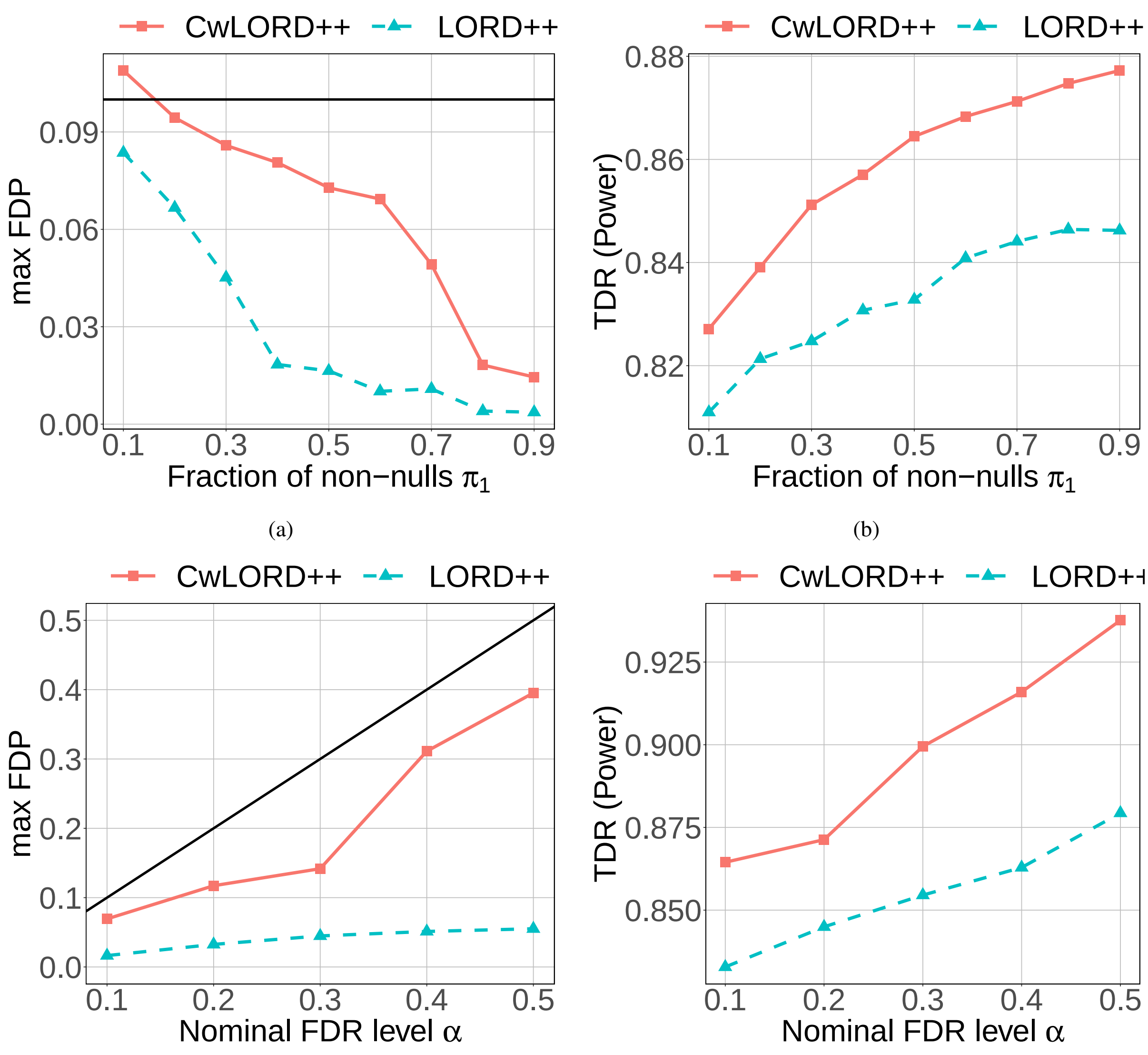
F.1 Synthetic Data Experiments

For the synthetic data experiments, we consider the hypotheses $\mathcal{H}(T) = (H_1, \dots, H_T)$ coming from the normal means model. The setup is as follows: for $t \in [T]$, under the null hypothesis, $H_t : \mu_t = 0$, versus under the alternative, $\mu_t = \mu(X_t)$ is a function of X_t. We observe test statistics $Z_t = \mu_t + \varepsilon_t$, where ε_t's are independent standard normal random variables, and thus the two-sided p-values are $P_t = 2\Phi(-|Z_t|)$. For simplicity, we consider a linear function $\mu(X_t) = \langle \boldsymbol{\beta}, X_t \rangle$ for $\boldsymbol{\beta}$ unknown to the testing setup. We choose the dimension of the features X_t's as $d = 10$ in all following experiments.

We set the total number of hypotheses as $T = 10^5$. We generate each d-dimensional vector X_t independently from $\mathcal{L}_0 = \mathcal{N}(0, \sigma^2 I_d)$ under the null ($H_t = 0$), and from $\mathcal{L}_1 = \mathcal{N}(0.1, \sigma^2 I_d)$ under the alternative ($H_t = 1$) with $\sigma^2 = 2 \log T$. The choice of the σ^2 is to put the signals in a detectable (but not easy) region. This is because under the global null hypothesis where $Z_t \sim \mathcal{N}(0,1)$ for all $t = 1, \dots, T$, we have $\max_{t \in [T]} Z_t \sim \sqrt{2 \log T}$ with high probability. Here, $\boldsymbol{\beta}$ is a deterministic parameter vector of dimension $d = 10$, we generate the ith coordinate in $\boldsymbol{\beta}$ as $\beta_i \sim \mathrm{Uniform}(-2, 2)$ and fix $\boldsymbol{\beta}$ throughout the following experiments. Let π_i denote the fraction of non-null hypotheses. For LORD++, we choose the sequence of hyperparameters $\{\gamma_t\}$ (where $\gamma_t = 0.0722 \log(t \vee 2)/(t \exp(\sqrt{\log t}))$) as suggested by (Javanmard and Montanari, 2018).

In Figure 4, we report the maximum FDP and the statistical power of the two compared procedures as we vary the fraction of non-nulls π_1 and desired level α. The average is taken over 20 repeats.

In the first set of experiments (Figures 4(a) and 4(b)), we set $\alpha = 0.1$, and vary the fraction of non-nulls π_1 from 0.1 to 0.9. We can see that FDP of both rules (CwLORD++ and LORD++) are almost always under the set level $\alpha = 0.1$ and are



(a)

(b)

(c)

(d)

Figure 4: The top rows plots the average of max FDP and TDR (power) for our proposed CwLORD++ and LORD++ as we vary the fraction of non-nulls (π_1) under the normal means model. The nominal FDR control level $\alpha = 0.1$. The bottom row plots the same with varying nominal FDR levels. In this case, we set the fraction of non-nulls $\pi_1 = 0.5$. As mentioned in the text, the average of max FDP is an overestimate of FDR.

decreasing with the increasing fraction of non-nulls. As expected, the power increases with increasing π_1, however the power of CwLORD++ uniformly dominates that of LORD++.

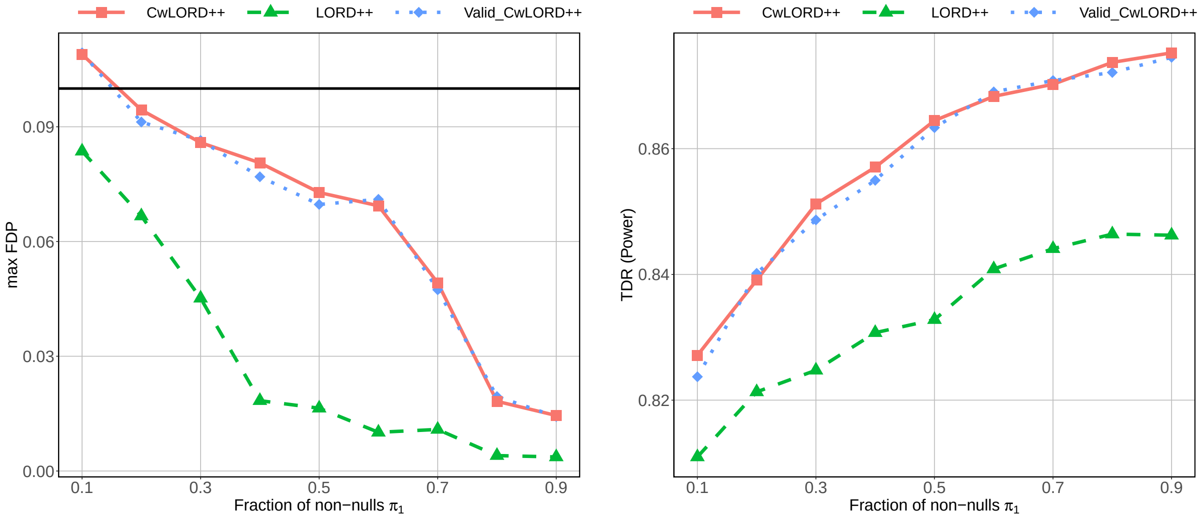
Note that we take the average of maximum FDP over 20 repeats, which is an estimate for $\mathbb{E}[\sup \text{FDP}]$. Due to the fact that $\mathbb{E}[\sup \text{FDP}] \geq \sup \mathbb{E}[\text{FDP}] = \sup \text{FDR}$, the reported average of maximum FDP is probably higher than the true maximum FDR. In Figure 4(a), we see that the average of maximum FDP is almost always controlled under the black line, which means the true maximum FDR should be even lower than that level. When π_1 is really small (like 0.1), the number of non-nulls is too sparse to make a high proportion of true discoveries, which leads to a higher average of maximum FDP that also have a higher variance in Figure 4(a).

In the second set of experiments (Figures 4(c) and 4(d)), we vary the nominal FDR level α from 0.1 to 0.5. The fraction of non-nulls is set as 0.5. Again we observe while both rules have FDR controlled under nominal level (the black line), and our proposed CwLORD++ is more powerful than the LORD++ with respect to the true discovery rate. On average, we notice about 3-5$\%$ improvement in the power with CwLORD++ when compared to LORD++.

F.1.1 Synthetic Data Experiments with Validation of Informative-Weighting

The setting of the numerical experiments are similar to that in Section F.1. The only difference is that here we additionally generate a fixed set of feature vectors $X'_1, \dots, X'_s$ from the same mixture model $(1 - \pi_1)\mathcal{L}_0 + \pi_1\mathcal{L}_1$ with size s, and their labels $H'_1, \dots, H'_s$ are visible to the procedure. We use this set as a prior information to validate the informative-weighting condition of the procedure. As mentioned before, the experiments with the validation set is implemented as follows. After each batch is tested and the parameters of the weight function is updated, we apply the updated weight function to the contextual features $X'_1, \dots, X'_s$ of the validation set. Since the labels of the validation set is visible to us, we compute and compare the average weights of the features from alternatives (with $H = 1$) and nulls (with $H = 0$). If the former one is greater than the latter, we will keep going on testing next batch with the up-to-date weight function. Otherwise, we will revert to the previous step of the weight function updates and use that version to continue with next batch.

In Figure 5, we report the maximum FDP and the statistical power of the LORD++, CwLORD++ and CwLORD++ with validation set (Valid_CwLORD++) as we vary the fraction of non-nulls π_1. The average is taken over 20 repeats.



(a)

(b)

Figure 5: The plots show the average of max FDP and TDR (power) for LORD++, CwLORD++ and CwLORD++ with validation set (Valid_CwLORD++) as we vary the fraction of non-nulls (π_1) under the normal means model. The nominal FDR control level $\alpha = 0.1$.

We can see that the performance of CwLORD++ with the validation set is very close to, and sometimes a bit conservative than that without validation set. The main reason is that the former one converges slower because it will occasionally revert back to previous procedure with weights which have been verified as informative weighting. In particular, it will update very slowly in the first several steps if the random initialization is not informative at all. But on the other hand, the fact that performance with or without checking for informative-weighting are very close is also a strong evidence to show that our proposed CwLORD++ algorithm can gain the informative weighting during the training process.

F.2 Diabetes Prediction Problem

In this section, we apply our online multiple testing rules to a real-life application of diabetes prediction. For completeness, we repeat some of the discussion from Section 6.

Machine learning algorithms are now commonly used to construct predictive health scores for patients. In this particular problem, we want a test to identify patients that are at risk of developing diabetes. A high predicted risk score can trigger an intervention (such as medical follow-up, medical tests), which can be expensive and sometimes unnecessary, and therefore it is important to control the fraction of alerts that are false discoveries. That is, for each patient i, we form the null hypothesis H_i as the "patient will not develop diabetes" versus its alternative. The dataset was released as part of a Kaggle competition[11], which contains de-identified medical records of 9948 patients (labeled as $1, 2, \dots$). For each patient, we

[11] http://www.kaggle.com/c/pf2012-diabetes

have a response variable Y that indicates if the patient is diagnosed with Type 2 diabetes mellitus, along with information on medications, lab results, immunizations, allergies, and vital signs. In the following, we train a predictive score based on the available records, and then will apply our online multiple testing rule rules to control FDR on test set. Our overall methodology is similar to that used by (Javanmard and Montanari, 2018) in their FDR control experiments on this dataset. We proceed as follows. We construct the following features for each patient.

1. Biographical information: Age, height, weight, BMI (Body Mass Indicator), etc.
2. Medications: We construct TF-IDF vectors from the medication names.
3. Diagnosis information: We derive 20 categories from the ICD-9 codes and construct an one-hot encoded vector.
4. Physician specialty: We categorize the physician specialties and create features that represents how many times a patient visited certain specialist.

We regard the biographical information of patients as treated as contextual features. The choice of using biographical information as context is loosely based on the idea of *personalization* common in machine learning applications. In theory, one could use other features too as context.

Second, we split the dataset into four parts **Train1**, comprising 40% of the data, **Train2**, 20% of the data, **Test1**, 20% of the data and **Test2**, 20% of the data. The **Train** sets are used for training a machine learning model (**Train1**) and for computing the null distribution of test statistics (**Train2**), which allows us to compute the p-values in the **Test** sets. We first learn the neural network parameters in the CwLORD++ procedure in an online fashion by applying it to p-values in **Test1**, and then evaluate the performance of both LORD++ and CwLORD++ on **Test2**. This process is explained in more detail below.

We note that our experimental setup is not exactly identical to that of (Javanmard and Montanari, 2018), since we are using a slightly different set of features and data cleaning for the logistic regression model. We also split the data to four subsets instead of three as they did, which gives less training data for the predictive model. Our main focus, is to compare the power of LORD++ and CwLORD++, for a reasonable feature set and machine learning model.

Training Process. We start by training a logistic model similar to (Javanmard and Montanari, 2018).[12] Let $\boldsymbol{x_i}$ denote the features of patient i. We use all the features to model the probability that patient does not have diabetes through a logistic regression model as

$$\Pr[Y_i = 0 \mid \boldsymbol{x} = \boldsymbol{x_i}] = \frac{1}{1 + \exp(\langle \boldsymbol{\beta}, \boldsymbol{x_i} \rangle)}.$$

The parameter $\boldsymbol{\beta}$ is estimated from the **Train1** set.

Construction of the p-values. Let S_0 be the subset of patients in **Train2** set with labels as $Y = 0$, and let $n_0 = |S_0|$. For each $i \in S_0$, we compute its predictive score as $q_i = 1/(1 + \exp(\langle \boldsymbol{\beta}, \boldsymbol{x_i} \rangle))$. The empirical distribution of $\{q_i : i \in S_0\}$ serves as the null distribution of the test statistic, which allows for computation of the p-values. Explicitly, for each j in either **Test1** or **Test2** sets, we compute $q_j^{\text{Test}} = 1/(1 + \exp(\langle \boldsymbol{\beta}, \boldsymbol{x_j} \rangle))$, and construct the p-value P_j by

$$P_j = \frac{1}{n_0} \left| \{ i \in S_0 : q_i \leq q_j^{\text{Test}} \} \right|.$$

Smaller p-value indicates that the patient has higher risk of developing diabetes. We use the p-values computed on the patients in **Test1** to train the weight function in CwLORD++, and the p-values on the patients in **Test2** to the compare performance of CwLORD++ and LORD++. Note that the training of the neural network does not utilize the labels of the hypothesis in the **Test1** set. Since the dataset does not have timestamps of hypotheses, we consider an ordering of hypotheses in the ascending order of corresponding p-values, and use this ordering for both LORD++ and CwLORD++. Note that, since the **Train** and **Test** sets are exchangeable, the null p-values will be uniform in expectation (and asymptotically uniform under mild conditions).

Online Hypothesis Testing Process and Results. We set the desired FDR control level at $\alpha = 0.2$. The set of hyperparameters $\{\gamma_t\}$ is chosen as in the synthetic data experiments. For the patients in **Test1** set, we use their biographical information of patients as contextual features in the training process for CwLORD++ for learning the neural network parameters. We apply the LORD++ and CwLORD++ procedures to the p-values in the **Test2** set and compute the false discovery proportion and statistical power. Let T_2 be the set of patients in **Test2** set. Note that for a patient in **Test2** set, for both CwLORD++ and LORD++, the p-values are identically computed from all the features (including the patient's biographical information). This generates a sequence of p-values $(P_i)_{i \in T_2}$. Now, while LORD++ is applied to this p-value sequence directly, CwLORD++

[12] Even though the chosen logistic model is one of the best performing models on this dataset in the Kaggle competition, in this paper, we do not actively optimize the prediction model in the training process.

	FDR	Power
LORD++	0.147	0.384
CwLORD++	0.176	0.580

Table 2: Results from diabetes dataset with nominal FDR control level $\alpha = 0.2$.

is applied to the sequence of (P_i, X_i) where X_i is the biographical information of patient $i \in T_2$. For CwLORD++, the neural network parameters are fixed in this testing over the **Test2** set.

We repeat the whole process and average the results over 30 random splittings of the dataset. Table 2 presents our final result. We can use biographical information again as contextual features in training CwLORD++ because the p-values under the null are uniformly distributed, no matter which features are used in logistic modeling. This guarantees that the p-values under the null are independent to any features, which is the only condition we need to have a FDR control, assuming the p-values themselves are mutually independent.

Notice that while FDR is under control for both procedures, the statistical power of CwLORD++ is substantially more (about 51%) than LORD++. This improvement illustrates the benefits of using contextual features for improving the power with FDR control in a typical machine learning setup. A possible reason for the observed increase in power with CwLORD++ is that in addition to using the labeled data in the Train1 set for training a supervised model, CwLORD++ uses in an unsupervised way (i.e., without considering labels) some features of the data in the **Test1** set in its online training process with the intent of maximizing discoveries.

One could also see the effect of training LORD++ on larger dataset. For example, previously we trained LORD++ only on **Train1** set (40% of the data) and we completely ignored the **Test1** set for LORD++. Suppose, we instead train logistic model for LORD++ (but not for CwLORD++) on the union of **Train1** and **Test1** set to make the baseline method stronger, with the same splits of the datasets. With this change, LORD++ has FDR at 0.143 and power at 0.427. While this is not completely a fair comparison for CwLORD++ as we have now used more labeled data in training the logistic model for LORD++ than CwLORD++, we observe that CwLORD++ still beats this stronger baseline with over 35% power increase.

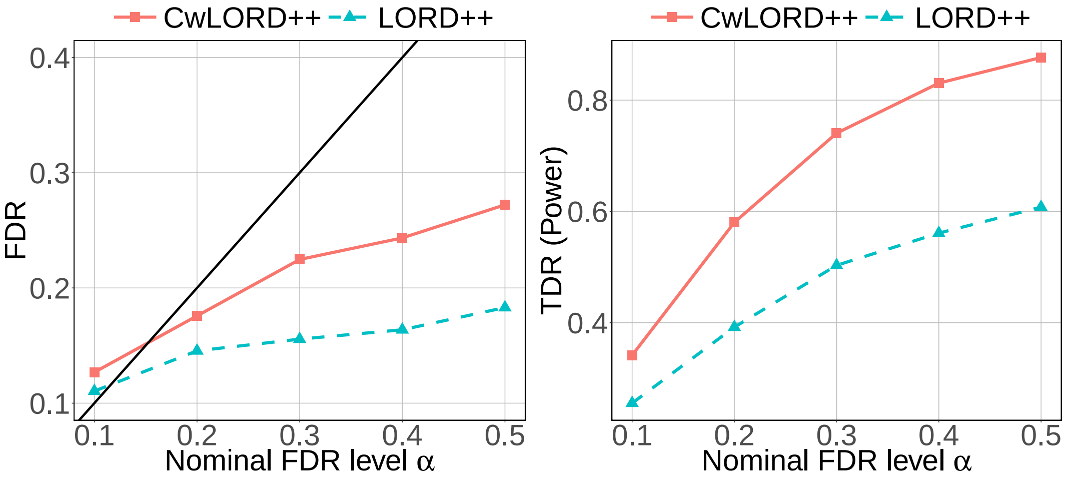


Figure 6: FDR and TDR results on diabetes dataset as we vary the nominal FDR level α. Note that the power of CwLORD++ uniformly dominates that of LORD++, with an average improvement in power of about 44%.

In order to further probe some of these improvements, we repeated the experiment with different nominal FDR levels ranging from 0.1 to 0.5. The results (see Figure 6) demonstrate that our CwLORD++ procedure achieves more true discoveries than the LORD++ procedure while controlling FDR under the same level. The FDR is controlled exactly under the desired level starting around $\alpha \geq 0.15$, while it is close to the desired level even when α is as small as 0.1. This phenomenon can also be observed in (Javanmard and Montanari, 2018), where the FDR is 0.126 for LORD under the target level $\alpha = 0.1$. This is probably because both the experiments here and in (Javanmard and Montanari, 2018) do not adjust for the dependency among the p-values, which violates the theoretical assumption behind the FDR control proof, and is more of a concern when target α level is small.

F.3 Gene Experiments

Here we discuss some additional experiments on GTEx dataset. As mentioned in Section 6, in the GTEx study, we consider three contextual features studied by (Xia et al., 2017): 1) the distance (GTEx-dist) between the SNP and the gene (measured in log base-pairs); 2) the average expression (GTEx-exp) of the gene across individuals (measured in log rpkm); and 3) the evolutionary conservation measured by the standard PhastCons scores (GTEx-PhastCons). In Figure 2 (Section 6), we presented results on using CwLORD++ procedure with each of these three features used separately. Now we discuss what happens when we combine these features.

In Figure 7, the GTEx-dist and GTEx-exp features are used together as a two-dimensional vector, and here CwLORD++ procedure makes about 6.1% more discoveries than the LORD++ procedure. In Figure 8, CwLORD++ uses all the three available features and makes about 6.4% more discoveries than LORD++. These results indicate that additional contextual information could be helpful in making more discoveries.

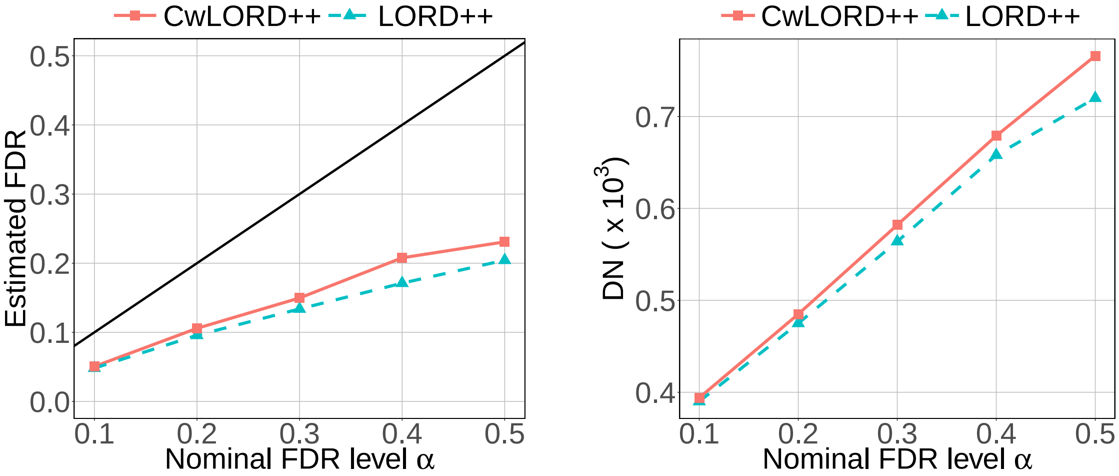


Figure 7: Results on GTEx dataset with GTEx-dist and GTEx-exp used together as a 2-dimensional contextual feature vector in CwLORD++.

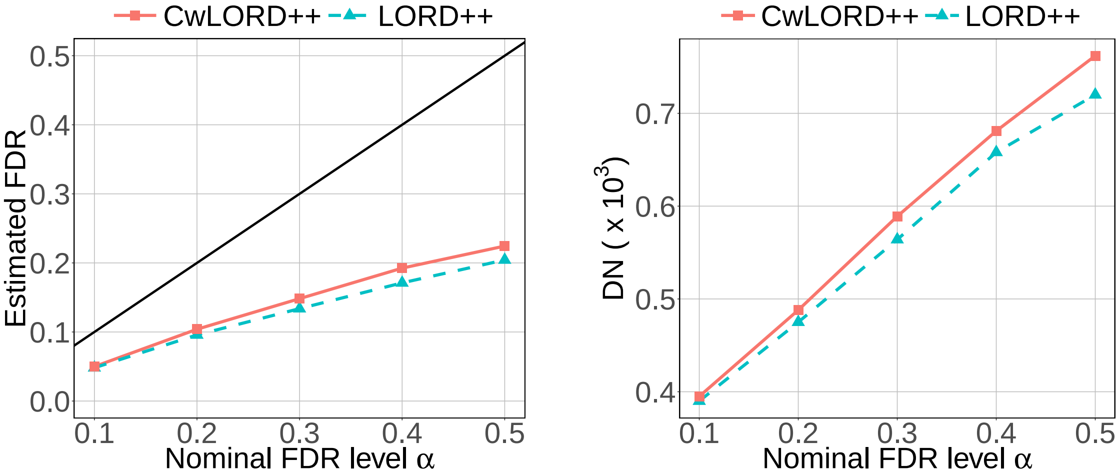


Figure 8: Results on GTEx dataset with GTEx-dist, GTEx-exp, and GTEx-PhastCons used together as a 3-dimensional contextual feature vector in CwLORD++.

G SAFFRON Procedure

Let us start with a quick introduction to the SAFFRON procedure proposed by (Ramdas et al., 2018). Since SAFFRON can be viewed as an online analogue of the famous offline Storey-BH adaptive procedure (Storey, 2002), we start a description of the Storey-BH procedure.

In the offline setting where p-values are all available, the rejection rule is to reject all p-values below some threshold s, meaning that $\mathcal{R}(s) = \{i \mid P_i \leq s\}$. Thus an oracle estimate for FDP is given by

$$\text{FDP}^*(s) := \frac{|\mathcal{H}^0| \cdot s}{|\mathcal{R}(s)| \vee 1}.$$

The world oracle means that FDP* cannot be calculated, since $\mathcal{H}^0$ is unknown. The BH method overestimates $\text{FDP}^*(s)$ by the empirically computable quantity

$$\widehat{\text{FDP}}_{\text{BH}}(s) := \frac{n \cdot s}{|\mathcal{R}(s)| \vee 1},$$

and chooses the threshold $\hat{s}_{\text{BH}}(s) = \max\{s : \widehat{\text{FDP}}_{\text{BH}}(s) \leq \alpha\}$. However, (Storey, 2002) noted that the estimate of $\widehat{\text{FDP}}_{\text{BH}}(s)$ is conservative, and thus proposed a different estimate (referred to as Storey-BH) as

$$\widehat{\text{FDP}}_{\text{St-BH}}(s) := \frac{n \cdot s \cdot \hat{\pi}_0}{|\mathcal{R}(s)| \vee 1},$$

where the fraction of nulls $\hat{\pi}_0$ is estimated by

$$\hat{\pi}_0 := \frac{1 + \sum_{i=1}^{n} \mathbb{1}\{P_i > \lambda\}}{n(1-\lambda)},$$

with a well-chosen λ. There is a bias-variance trade-off in the choice of λ. When λ grows larger, the bias of $\hat{\pi}_0$ grows smaller while the variance becomes larger. Through numerical simulations (Storey, 2002) demonstrated that there could be an increase in power (over the BH procedure) with this adaptivity.

Similarly, in the online setting, the oracle FDP estimate now is

$$\text{FDP}^*(T) := \frac{\sum_{t \in [T], t \in \mathcal{H}^0} \alpha_t}{R(T) \vee 1}$$

The connection between SAFFRON and LORD/LORD++ is the same as that between Storey-BH and BH. Empirically, LORD/LORD++ overestimates the oracle $\text{FDP}^*(T)$ as

$$\widehat{\text{FDP}}_{\text{LORD}}(T) := \frac{\sum_{t \in [T]} \alpha_t}{R(T) \vee 1}$$

SAFFRON estimates the amount of alpha-wealth that was spent testing nulls so far, which is analogous to the proportion of nulls in the offline setting, and controls the following overestimate of oracle FDP,

$$\widehat{\text{FDP}}_{\text{SAFFRON}}(T) := \frac{\sum_{t \in [T]} \alpha_t \frac{\mathbb{1}\{P_t > \lambda_t\}}{(1-\lambda_t)}}{R(T) \vee 1},$$

where $\{\lambda_t\}_{t=1}^{\infty}$ is predictable sequence of user-chosen parameters in interval $(0, 1)$. Note that when $\lambda_t = 0$, it recovers $\widehat{\text{FDR}}_{\text{LORD}}(T)$. When λ_t is chosen to be a constant λ for all t, then SAFFRON procedure can be viewed as an instance of the GAI framework. It starts off with some alpha-wealth $(1-\lambda)W_0 < (1-\lambda)\alpha$, and only loses wealth when testing candidate with p-values $P_t > \lambda$, and gains wealth of $(1-\lambda)\alpha$ on every rejection except the first.

Ramdas et al. (2018) proved that, under some constraints, SAFFRON can control online FDR at given level α by showing that

$$\text{FDR}(T) \leq \mathbb{E}[\widehat{\text{FDP}}_{\text{SAFFRON}}(T)].$$

These results can also be extended to a weighted version of SAFFRON. Akin, to weighted LORD++, we can define weighted SAFFRON as follows.

Definition 5 (Weighted SAFFRON)**.** *Given a sequence of p-values, $(P_1, P_2, \dots)$ and weights $(\omega_1, \omega_2, \dots)$, apply SAFFRON with level α and the parameters $\{\lambda_t\}$ to the weighted p-values $(P_1/\omega_1, P_2/\omega_2, \dots)$.*

Next proposition shows that the above weighted SAFFRON can still control online FDR at any given level α under the condition (24).

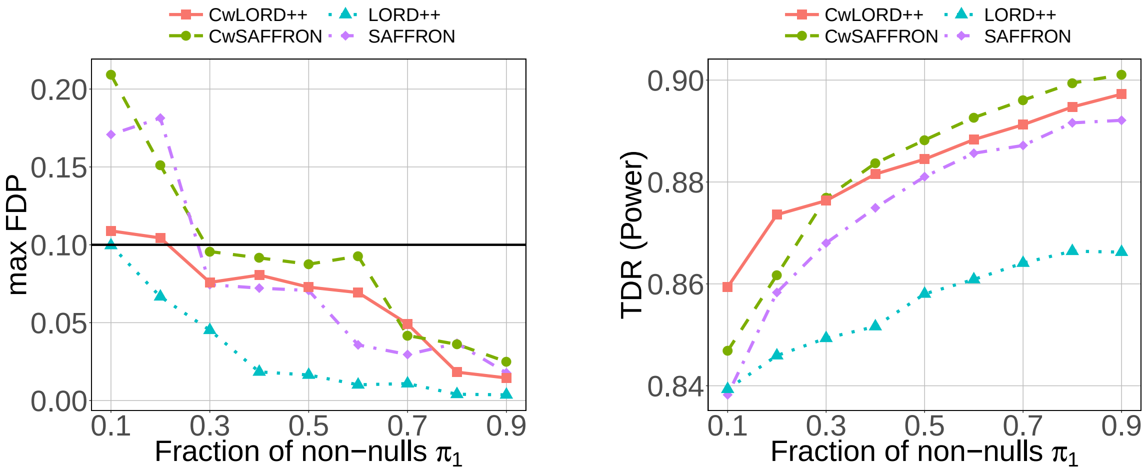
Proposition 3. *Suppose that the weight distribution satisfies the informative-weighting property in* (24)*. Suppose that p-values P_t's are independent, and are conditionally independent of the weights ω_t's given H_t's. Considering the weighted SAFFRON rule with monotone α_t and λ_t, we have*

$$\mathrm{FDR}(T) \leq \mathbb{E}[\widehat{\mathrm{FDP}}_{\text{weighted-SAFFRON}}(T)].$$

The proofs of Proposition 3 of weighted SAFFRON are just simple extensions of the proofs of Lemma 2 and Theorem 1 in (Ramdas et al., 2018), and the techniques of extension are almost the same as that in the proof of 1, thus they are omitted here.

We now present some empirical evidence that contextual information could help with SAFFRON too.

Experiments with SAFFRON. We consider exactly the same setting as with the synthetic data experiments in synthetic data experiments, and train a context-weighted SAFFRON (referred to as CwSAFFRON) in the same way as CwLORD++. With varying fraction of non-nulls, Figure 9 reports the maximum FDP and statistical power (TDP) of CwSAFFRON along with three other procedures, SAFFRON, CwLORD++, and LORD++. We observe that SAFFRON and CwSAFFRON have FDR greater than the nominal level of 0.1 when the fraction of non-nulls π_1 is small (less than 0.3), but is below the nominal level when π_1 gets larger. And the FDR of both LORD++ and CwLORD++ are generally much smaller than that of SAFFRON and CwSAFFRON. On the other hand, the power of CwSAFFRON dominates that of SAFFRON for all π_1, and is larger than that of CwLORD++ when π_1 exceeds 0.3. As the fraction of non-nulls increases, CwSAFFRON achieves a faster increase in power than CwLORD++. A similar phenomenon can be also seen between SAFFRON and LORD++ (which was also noted by (Ramdas et al., 2018)).



(a)

(b)

Figure 9: The average of max FDP and TDR (power) for our proposed CwSAFFRON, CwLORD++, along with SAFFRON and LORD++ with varying the fraction non-nulls (π_1) under the normal means model. The nominal FDR control level $\alpha = 0.1$. As mentioned in the description of the synthetic data experiments, the average of max FDP is an overestimate of FDR.