

EXACT CALCULATIONS FOR FALSE DISCOVERY PROPORTION WITH APPLICATION TO LEAST FAVORABLE CONFIGURATIONS¹

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In a context of multiple hypothesis testing, we provide several new exact calculations related to the false discovery proportion (FDP) of step-up and step-down procedures. For step-up procedures, we show that the number of erroneous rejections conditionally on the rejection number is simply a binomial variable, which leads to explicit computations of the c.d.f., the s th moment and the mean of the FDP, the latter corresponding to the false discovery rate (FDR). For step-down procedures, we derive what is to our knowledge the first explicit formula for the FDR valid for any alternative c.d.f. of the p -values. We also derive explicit computations of the power for both step-up and step-down procedures. These formulas are “explicit” in the sense that they only involve the parameters of the model and the c.d.f. of the order statistics of i.i.d. uniform variables. The p -values are assumed either independent or coming from an equicorrelated multivariate normal model and an additional mixture model for the true/false hypotheses is used. Our approach is then used to investigate new results which are of interest in their own right, related to least/most favorable configurations for the FDR and the variance of the FDP.

1. Introduction. When testing simultaneously m null hypotheses, the false discovery proportion (FDP) is defined as the proportion of errors among all the rejected hypotheses and the false discovery rate (FDR) is defined as the average of the FDP. Since its introduction by Benjamini and Hochberg [1], the FDR has become a widely used Type I error criterion, because it is adaptive to the number of rejected hypotheses. However, the randomness of the denominator in the FDP expression makes the study of the FDP distribution and of the FDR mathematically challenging.

There is a considerable number of papers that deal with the FDR control under different dependency conditions between the p -values (see, e.g., [1, 3–5, 30]). In the latter, the goal is, given a prespecified level α , to provide a procedure with a FDR smaller than α (for any value of the data law in a given distribution subspace,

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e.g., for some dependency assumptions). For instance, the famous linear step-up procedure (LSU), also called the Benjamini–Hochberg procedure [1] (based on the Simes’s line [33]), has been proved to control the FDR under independence and under a positive dependence assumption (see [1, 3]). While controlling the FDR, one wants to maximize the power of the procedure, the power being generally defined as the averaged number of correct rejections divided by the number of false hypotheses.

In this paper, we deal with the “reversed” approach: given the procedure, we aim to compute the corresponding FDR, or more generally the s th moment and the c.d.f. of the FDP, and the Power. For procedures using a constant thresholding and under a mixture model assuming independence between the p -values, Storey [34] addressed these questions, while introducing the positive false discovery rate (pFDR) (see also Chi and Tan [7]). Considering step-up or step-down methods requires more efforts: when the p -values are all i.i.d. uniform, the exact distribution of the rejection number has been computed by Finner and Roters [16] for step-up and step-down procedures, which leads to a computation of the FDR in the degenerate case where all the hypotheses are true [16]. When the p -values follow the particular “Dirac-uniform” configuration, that is, when the p -values associated to false hypotheses are equal to 0 and when the p -values associated to true hypotheses are i.i.d. uniform, the FDP distribution has been computed by Dickhaus [8] for general step-up-down procedures (see Section 3.7 in [8]). For an arbitrary distribution of the p -values under the alternative, Ferreira and Zwinderman [13] gave a first exact expression for the moment of the FDP of the LSU procedure under independence [13]. Together with other recent approaches (see, e.g., [4, 26, 27, 30]), this puts forward a connection between the FDR expression and the rejection number distribution in the step-up case, under independence of the p -values. Additionally, Sarkar [29] found an exact formula for the FDR, which is valid for any step-up-down procedure [29]. However, it involves the c.d.f. of ordered components of dependent variables. This contrasts with [8, 16] and the present paper which use the c.d.f. of ordered components of i.i.d. uniform variables and thus lead to substantially more explicit formulas.

Meanwhile, some of these approaches have also been investigated from the asymptotic point of view, when the number of hypotheses m tends to infinity; Chi [6] computed the asymptotic rejection number distribution of the LSU procedure by introducing the criticality phenomenon [6], while Finner, Dickhaus and Roters [15] computed the asymptotic FDR of the LSU procedure for positively correlated p -values (following an equicorrelated multivariate normal model) in the particular Dirac-uniform configuration [15]. In this paper, the point of view will be mainly nonasymptotic.

The new contributions of the present paper are as follows:

- For a step-up procedure using a threshold $(t_k)_k$, we proved that the distribution of the number of erroneous rejections conditionally on k rejections is a binomial

variable of parameters k and $\text{pFDR}(t_k) = \pi_0 t_k / G(t_k)$, where π_0 is the (averaged) proportion of true nulls and G is the c.d.f. of the p -values. This provides new explicit formulas for the c.d.f. of the FDP, the s th moment of the FDP (providing a correction with respect to [13] for $s \geq 3$) and for the FDR, for any alternative distribution of the p -values. We also give an expression for the power, which yields a considerably less complex calculation than in [20]; see Section 3.1.

- Considering a step-down procedure, a new explicit formula for the FDR and the power is presented under any alternative distribution of the p -values. To our knowledge, this expression is the first one that clearly relates the FDR to (joint) rejection number distribution in the case of a step-down procedure and that is valid under any alternative; see Section 3.1.
- All the previous results, valid under independence between the p -values, can be easily extended to the case where the p -value family follows an equicorrelated multivariate normal model, by using a simple modification; see Section 3.2. However, this requires the use of a nonnegative correlation. The case of a possibly negative correlation is considered when only two hypotheses are tested; see Section 3.3.
- Our formulas corroborate the classical multiple testing results while they give rise to several new results. The two main corollaries hold under independence and are as follows. First, in Section 4.1.1, for the linear step-down procedure, we prove that the Dirac-uniform configuration is a p -value configuration maximizing the FDR, that is, is a least favorable configuration (LFC) for the FDR. Additionally, considering a general step-down procedure, we define a new condition on the threshold ensuring that the Dirac-uniform configuration is still a LFC. As discussed in Section 4.1.1, this condition is different from the one of the step-up case. Second, we find an exact expression of the minimum and the maximum of the variance of the FDP of the LSU, these extrema being taken over some p -value configuration sets of interest. The latter allows to better understand the behavior of the FDP around the FDR. In particular, this puts forward that the convergence of the FDP toward the FDR is particularly slow in the sparse case; see Section 4.2.

For mathematical convenience, most of these results stand in “unconditional” models (also called “two-groups mixture models”; see [10, 12]), which assume that each null hypothesis is true with probability π_0 , independently from the other hypotheses (the case of the more traditional “conditional” models is discussed in Section 5.3). Next, all our formulas are valid nonasymptotically, that is, they hold for each $m \geq 2$. As a counterpart, they inevitably have a general form that can appear somewhat complex at first sight. For instance, denoting by Ψ_m the c.d.f. of the order statistics of m i.i.d. uniform variables on $(0, 1)$, the FDR formula for step-up procedures requires the computation of Ψ_m at a given point of \mathbb{R}^m (at most), while the FDR formula for step-down procedures requires the computation of Ψ_m at $2m$ different points of \mathbb{R}^m (at most). However, let us underline what are to our opinion the two main interests of this exact approach:

- For some model parameter configurations and after possible simplifications, the formulas are usable for further theoretical studies (monotonicity with respect to a parameter, convergence when m tends to infinity, ...), see Theorems 4.1 and 4.3.
- For m not too large (say $m \leq 1000$), these formulas can be fully computed numerically, for example, plotting exact graphs. Thus, they avoid using cumbersome and less accurate simulation experiments (extensively used in multiple testing literature); see, for instance, Section 4.1.2.

2. Preliminaries.

2.1. *Models for the p -value family.* On a given probability space, we consider a finite set of $m \geq 2$ null hypotheses, tested by a family of m p -values $\mathbf{p} = (p_i, i \in \{1, \dots, m\})$. In this paper, for simplicity, we skip somewhat the formal definition of p -values by defining directly a p -value model, that is, by specifying the joint distribution of \mathbf{p} .

In what follows, we denote by \mathcal{F} the set containing c.d.f.'s from $[0, 1]$ into $[0, 1]$ that are continuous and by $F_0(t) = t$ the c.d.f. of the uniform distribution over $[0, 1]$ [we restricted our attention to the case where $F_0(t) = t$ only for simplicity, all our formulas will be valid for an arbitrary increasing $F_0 \in \mathcal{F}$].

DEFINITION 2.1 (Conditional p -value models).

- The p -value family \mathbf{p} follows the *conditional independent model* with parameters $H = (H_i)_{1 \leq i \leq m} \in \{0, 1\}^m$ and $F_1 \in \mathcal{F}$, that we denote by $\mathbf{p} \sim P_{(H, F_1)}^I$, if $\mathbf{p} = (p_i, i \in \{1, \dots, m\})$ is a family of mutually independent variables and for all i ,

$$p_i \sim \begin{cases} F_0, & \text{if } H_i = 0, \\ F_1, & \text{if } H_i = 1. \end{cases}$$

- The p -value family \mathbf{p} follows the *conditional equicorrelated multivariate normal model* (conditional EMN model for short) with parameters $H = (H_i)_{1 \leq i \leq m} \in \{0, 1\}^m$, $\rho \in [-(m - 1)^{-1}, 1]$ and $\mu > 0$, that we denote by $\mathbf{p} \sim P_{(H, \rho, \mu)}^N$, if for all i , $p_i \sim \overline{\Phi}(X_i + \mu H_i)$, where the vector $(X_i)_{1 \leq i \leq m}$ is distributed as a \mathbb{R}^m -valued Gaussian vector with zero means and a covariance matrix having 1 on the diagonal and ρ elsewhere and where $\overline{\Phi}$ denotes the standard Gaussian distribution tail, that is, $\overline{\Phi}(z) = \mathbb{P}[Z \geq z]$ for $Z \sim \mathcal{N}(0, 1)$. In that model, the marginal distributions of the p -values are thus given by

$$p_i \sim \begin{cases} F_0, & \text{if } H_i = 0, \\ F_1(t) = \overline{\Phi}(\overline{\Phi}^{-1}(t) - \mu), & \text{if } H_i = 1. \end{cases}$$

The two models above are said to be “conditional” because the distribution of the p -values are defined conditionally on the value of the parameter $H =$

$(H_i)_{1 \leq i \leq m} \in \{0, 1\}^m$. The latter determines which hypotheses are true or false: $H_i = 0$ (resp., 1) if the i th null hypothesis is true (resp., false). We then denote by $\mathcal{H}_0(H) := \{i \in \{1, \dots, m\} \mid H_i = 0\}$ the set corresponding to the true null hypotheses and by $m_0(H) := |\mathcal{H}_0(H)|$ its cardinal. Analogously, we define $\mathcal{H}_1(H) := \{i \in \{1, \dots, m\} \mid H_i = 1\}$ and $m_1(H) := |\mathcal{H}_1(H)| = m - m_0(H)$.

To each one of the above models, we associate the “unconditional” version in which we endow the parameter H with the prior distribution $\mathcal{B}(1 - \pi_0)^{\otimes m}$, making $(H_i)_{1 \leq i \leq m} \in \{0, 1\}^m$ a sequence of i.i.d. Bernoulli with parameter $1 - \pi_0$. From an intuitive point of view, this means that each hypothesis is true with probability π_0 , independently from the other hypotheses. We thus define the following models for \mathbf{p} [or more precisely for (H, \mathbf{p})].

DEFINITION 2.2 (Unconditional p -value models).

- The couple (H, \mathbf{p}) follows the unconditional independent model with parameters $\pi_0 \in [0, 1]$ and $F_1 \in \mathcal{F}$, which we denote by $(H, \mathbf{p}) \sim \overline{P}^I_{(\pi_0, F_1)}$ if $H \sim \mathcal{B}(1 - \pi_0)^{\otimes m}$ and the distribution of \mathbf{p} conditionally to H is $P^I_{(H, F_1)}$, that is, conditionally on H , \mathbf{p} follows the conditional independent model with parameters H and F_1 . In that model, the p -values are i.i.d. with common c.d.f. $G(t) = \pi_0 F_0(t) + (1 - \pi_0) F_1(t)$.
- The couple (H, \mathbf{p}) follows the unconditional equicorrelated multivariate normal model (unconditional EMN model for short) with parameters $\pi_0 \in [0, 1]$, $\rho \in [-(m - 1)^{-1}, 1]$ and $\mu > 0$, that we denote by $(H, \mathbf{p}) \sim \overline{P}^N_{(\pi_0, \rho, \mu)}$, if $H \sim \mathcal{B}(1 - \pi_0)^{\otimes m}$ and the distribution of \mathbf{p} conditionally on H is $P^N_{(H, \rho, \mu)}$, that is, conditionally on H , \mathbf{p} follows the conditional EMN model with parameters H , ρ and μ .

An important point is that the quantities $m_0(H)$ and $m_1(H)$ are deterministic in the conditional models P^I, P^N , while they become random in the unconditional models $\overline{P}^I, \overline{P}^N$ with $m_0(H) \sim \mathcal{B}(m, \pi_0)$ and $m_1(H) \sim \mathcal{B}(m, 1 - \pi_0)$.

The conditional independent model is one of the most standard p -value models and was, for instance, considered in the seminal paper of Benjamini and Hochberg [1]. Its unconditional version, also called the “two-groups mixture model,” is very convenient and has been widely used since its introduction by Efron et al. [12]; see, for instance, [10, 19, 34].

The conditional EMN model is a simple instance of model introducing dependencies between the p -values. It corresponds to a one-sided testing on the mean of $X_i + \mu H_i$, simultaneously for all $1 \leq i \leq m$. It has become quite standard in recent FDR multiple testing literature; for instance, it was used in [15] with $\mu = \infty$ and it has been considered in [2, 5] for numerical experiments. Furthermore, Efron [11] recently showed that the EMN model may also be viewed as an approximation for some nonequicorrelated models, which reinforces its interest for a practical

use [11]. In this model, provided that $\rho \geq 0$, the p -values are positively regression dependent on each one on the subset $\mathcal{H}_0(H)$ [PRDS on $\mathcal{H}_0(H)$] which is one dependency condition that suffices for FDR control (see [3]). The unconditional version of this model is convenient because it provides exchangeable p -values (although not independent when $\rho \neq 0$).

Additionally, we will sometimes consider the “Dirac-uniform configuration” for the above models. In that configuration, all the p -values corresponding to false nulls ($H_i = 1$) are equal to zero, that is, F_1 is constantly equal to 1 for the independent model and $\mu = \infty$ for the EMN model. This configuration was introduced in [15] to increase the FDR as much as possible for the linear step-up procedures and thus appears as a “least favorable configuration” for the FDR (see also Section 4.1).

2.2. Multiple testing procedures, FDP, FDR and power. A multiple testing procedure R is defined as an algorithm which, from the data, aims to reject part of the null hypotheses. Below, we will consider, as is usually the case, multiple testing procedures which can be written as a function of the p -value family $\mathbf{p} = (p_i, i \in \{1, \dots, m\})$. More formally, we define a multiple testing procedure as a measurable function R , which takes as input a realization of the p -value family $\mathbf{p} \in [0, 1]^m$ and which returns a subset $R(\mathbf{p})$ of $\{1, \dots, m\}$, corresponding to the rejected hypotheses [i.e., $i \in R(\mathbf{p})$ means that the i th hypothesis is rejected by R for the observed p -values \mathbf{p}].

Particular multiple testing procedures are step-up and step-down procedures. First, define a *threshold* as any nondecreasing sequence $\mathbf{t} = (t_k)_{1 \leq k \leq m} \in [0, 1]^m$ (with $t_0 = 0$ by convention). Next, for any threshold \mathbf{t} , the *step-up procedure* of threshold \mathbf{t} , denoted here by $SU(\mathbf{t})$, rejects the i th hypothesis if $p_i \leq t_{\hat{k}}$, with $\hat{k} = \max\{k \in \{0, 1, \dots, m\} \mid p_{(k)} \leq t_k\}$, where $p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(m)}$ denote the ordered p -values (with the convention $p_{(0)} = 0$). In particular, the procedure $SU(\mathbf{t})$ using $t_k = \alpha k/m$ corresponds to the standard linear step-up procedure of Benjamini and Hochberg [1], denoted here by LSU. In addition, for any threshold \mathbf{t} , the *step-down procedure* of threshold \mathbf{t} , denoted here by $SD(\mathbf{t})$, rejects the i th hypothesis if $p_i \leq t_{\tilde{k}}$, with $\tilde{k} = \max\{k \in \{0, 1, \dots, m\} \mid \forall k' \leq k, p_{(k')} \leq t_{k'}\}$. Analogously to the step-up case, the procedure $SD(\mathbf{t})$ using $t_k = \alpha k/m$ is called the linear step-down procedure and is denoted here by LSD.

Next, associated to any multiple testing procedure R and any configuration of true/false hypotheses $H \in \{0, 1\}^m$, we introduce the false discovery proportion (FDP) of R as the proportion of true hypotheses in the set of the rejected hypotheses, that is,

$$(1) \quad \text{FDP}(R, H) = \frac{|\mathcal{H}_0(H) \cap R|}{|R| \vee 1},$$

where $|\cdot|$ denotes the cardinality function. The FDP definition can be traced back to [31]. Then, while for any multiple testing procedure R , the false discovery rate

(FDR) is defined as the mean of the FDP (see [1]), the power is (generally) defined as the expected number of correctly rejected hypotheses divided by the number of false hypotheses. Of course, the FDR and the power depend on the distribution that generates the p -values, and we may use the models defined in Section 2.1. Formally, for any distribution P coming from a conditional model using parameter $H \in \{0, 1\}^m$, we let

$$(2) \quad \text{FDR}(R, P) = \mathbb{E}_{\mathbf{p} \sim P}[\text{FDP}(R(\mathbf{p}), H)],$$

$$(3) \quad \text{Pow}(R, P) = m_1(H)^{-1} \mathbb{E}_{\mathbf{p} \sim P}[|\mathcal{H}_1(H) \cap R(\mathbf{p})|].$$

Similarly, for any p -value distribution \bar{P} coming from an unconditional model, the FDR and the Power use an additional averaging over $H \sim \mathcal{B}(1 - \pi_0)^{\otimes m}$ and are defined by

$$(4) \quad \text{FDR}(R, \bar{P}) = \mathbb{E}_{(H, \mathbf{p}) \sim \bar{P}}[\text{FDP}(R(\mathbf{p}), H)],$$

$$(5) \quad \text{Pow}(R, \bar{P}) = (\pi_1 m)^{-1} \mathbb{E}_{(H, \mathbf{p}) \sim \bar{P}}[|\mathcal{H}_1(H) \cap R(\mathbf{p})|].$$

Note that, for convenience, (5) is not exactly defined as the expectation of (3), because of the denominator. It corresponds precisely to the expected number of correctly rejected hypotheses divided by the *expected* number of false hypotheses.

In the paper, to simplify the notation, we sometimes drop the explicit dependency in \mathbf{p} , H or P , writing, for example, R instead of $R(\mathbf{p})$, \mathcal{H}_0 instead of $\mathcal{H}_0(H)$, $\text{FDP}(R)$ instead of $\text{FDP}(R, H)$ and $\text{FDR}(R)$ instead of $\text{FDR}(R, P)$.

2.3. *Some notation and useful results.* For any $k \geq 0$ and any threshold $\mathbf{t} = (t_1, \dots, t_k)$, we denote

$$(6) \quad \Psi_k(\mathbf{t}) = \Psi_k(t_1, \dots, t_k) = \mathbb{P}[U_{(1)} \leq t_1, \dots, U_{(k)} \leq t_k],$$

where $(U_i)_{1 \leq i \leq k}$ is a sequence of k variables i.i.d. uniform on $(0, 1)$ and with the convention $\Psi_0(\cdot) = 1$. In practice, quantity (6) can be evaluated using Bolshev's recursion $\Psi_k(\mathbf{t}) = 1 - \sum_{i=1}^k \binom{k}{i} (1 - t_{k-i+1})^i \Psi_{k-i}(t_1, \dots, t_{k-i})$ or Steck's recursion $\Psi_k(\mathbf{t}) = (t_k)^k - \sum_{j=0}^{k-2} \binom{k}{j} (t_k - t_{j+1})^{k-j} \Psi_j(t_1, \dots, t_j)$ (see [32], pages 366–369). Additionally, the following relation holds (see Lemma 2.1 in [16]): for all $k \in \mathbb{N}$ and $v_1, v_2 \in \mathbb{R}$ such that $0 \leq v_1 + v_2 \leq v_1 + kv_2 \leq 1$:

$$(7) \quad \Psi_k(v_1 + v_2, \dots, v_1 + kv_2) = (v_1 + v_2)(v_1 + (k + 1)v_2)^{k-1}.$$

From the Ψ_k 's, we define the following useful quantities: for any threshold $\mathbf{t} = (t_k)_{1 \leq k \leq m}$ and $k \geq 0, k \leq m$, we let

$$(8) \quad \mathcal{D}_m(\mathbf{t}, k) = \binom{m}{k} (t_k)^k \Psi_{m-k}(1 - t_m, \dots, 1 - t_{k+1}),$$

$$(9) \quad \tilde{\mathcal{D}}_m(\mathbf{t}, k) = \binom{m}{k} (1 - t_{k+1})^{m-k} \Psi_k(t_1, \dots, t_k).$$

Above, note that $(t_k)^k$ and $(1 - t_{k+1})^{m-k}$ are correct when $k = 0$ and $k = m$, even if $(t_j)_j$ is only defined for $1 \leq j \leq m$. Note that Bolshev’s recursion provides $\sum_{k=0}^m \mathcal{D}_m(\mathbf{t}, k) = \sum_{k=0}^m \widehat{\mathcal{D}}_m(\mathbf{t}, k) = 1$ for any threshold \mathbf{t} .

Finally, we will use the so-called Stirling numbers of the second kind, defined as coefficients $\left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\}$ for $s, \ell \geq 1$ by $\left\{ \begin{smallmatrix} s \\ 0 \end{smallmatrix} \right\} = 0$, $\left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\} = 0$ for $\ell > s$, $\left\{ \begin{smallmatrix} 1 \\ 1 \end{smallmatrix} \right\} = 1$ and the recurrence relation: for all $1 \leq \ell \leq s + 1$, $\left\{ \begin{smallmatrix} s+1 \\ \ell \end{smallmatrix} \right\} = \ell \left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\} + \left\{ \begin{smallmatrix} s \\ \ell-1 \end{smallmatrix} \right\}$. For instance, $\left\{ \begin{smallmatrix} 3 \\ 1 \end{smallmatrix} \right\} = 1$, $\left\{ \begin{smallmatrix} 3 \\ 2 \end{smallmatrix} \right\} = 3$, $\left\{ \begin{smallmatrix} 3 \\ 3 \end{smallmatrix} \right\} = 1$, $\left\{ \begin{smallmatrix} 4 \\ 1 \end{smallmatrix} \right\} = 1$, $\left\{ \begin{smallmatrix} 4 \\ 2 \end{smallmatrix} \right\} = 7$, $\left\{ \begin{smallmatrix} 4 \\ 3 \end{smallmatrix} \right\} = 6$, $\left\{ \begin{smallmatrix} 4 \\ 4 \end{smallmatrix} \right\} = 1$. From a combinatorial point of view, the coefficient $\left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\}$ counts the number of ways to partition a set of s elements into ℓ (nonempty) subsets. The latter is useful to compute the s th moment of a binomial distribution: if $X \sim \mathcal{B}(n, q)$, we have $\forall s \geq 1$, $\mathbb{E}[X^s] = \sum_{\ell=1}^{s \wedge n} \frac{n!}{(n-\ell)!} \left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\} q^\ell$.

3. New formulas.

3.1. Unconditional independent model, $m \geq 2$.

3.1.1. *Step-up case.* Let us consider the unconditional independent model. Finner and Roters [16] derived the exact distribution of the rejection number of any step-up procedure in the case of i.i.d. uniform p -values (i.e., when all the hypotheses are true) [16]. In the unconditional model, the latter can be generalized as follows: denoting $G(t) = \pi_0 F_0(t) + (1 - \pi_0) F_1(t)$ the common c.d.f. of the p -values, we have for $0 \leq k \leq m$ that

$$(10) \quad \mathbb{P}[|\text{SU}(\mathbf{t})| = k] = \mathcal{D}_m([G(t_j)]_{1 \leq j \leq m}, k)$$

(this is straightforward from [16] because G is continuous increasing).

Next, for the procedure $R(t) = \{i \mid p_i \leq t\}$ using a *constant* threshold $t \in [0, 1]$, Storey [34] proved that the distribution of $|\mathcal{H}_0(H) \cap R(t)|$ conditionally on $|R(t)| = k$ is a binomial distribution $\mathcal{B}(k, \pi_0 F_0(t)/G(t))$ (see proof of Theorem 1 in [34], see also Proposition 2.1 in [7]). Later, Chi [6] proved that the distribution of $|\mathcal{H}_0(H) \cap \text{LSU}|$ conditionally on $|\text{LSU}| = k$ is asymptotically binomial (in a particular “supercritical” framework); see [6]. Here, we show that the latter holds nonasymptotically, for any step-up procedure, which, by using (10), gives exact formulas for the c.d.f. of the FDP, the s th moment of the FDP, the FDR and the Power.

THEOREM 3.1. *When testing $m \geq 2$ hypotheses, consider a step-up procedure $\text{SU}(\mathbf{t})$ with threshold \mathbf{t} and the notation of Section 2.3. Then for any parameter $\pi_0 \in [0, 1]$ and $F_1 \in \mathcal{F}$, denoting $G(t) = \pi_0 F_0(t) + \pi_1 F_1(t)$, we have under the generating distribution $(H, \mathbf{p}) \sim \overline{P}_{(\pi_0, F_1)}^I$ of the unconditional independent model, for any $k \geq 1$,*

$$(11) \quad |\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t})| \text{ conditionally on } |\text{SU}(\mathbf{t})| = k \quad \sim \quad \mathcal{B}\left(k, \frac{\pi_0 F_0(t_k)}{G(t_k)}\right).$$

In particular, we derive the following formulas, for any $x \in (0, 1)$, for any $s \geq 1$, denoting by $\left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\}$ the Stirling number of second kind and by $\lfloor z \rfloor$ the largest integer smaller than or equal to z :

$$\begin{aligned}
 & \mathbb{P}[\text{FDP}(\text{SU}(\mathbf{t}), H) \leq x] \\
 (12) \quad &= \sum_{k=0}^m \sum_{j=0}^{\lfloor xk \rfloor} \binom{k}{j} \left(\frac{\pi_0 F_0(t_k)}{G(t_k)} \right)^j \left(\frac{\pi_1 F_1(t_k)}{G(t_k)} \right)^{k-j} \\
 & \quad \times \mathcal{D}_m([G(t_j)]_{1 \leq j \leq m}, k); \\
 & \mathbb{E}[\text{FDP}(\text{SU}(\mathbf{t}), H)^s] \\
 (13) \quad &= \sum_{\ell=1}^{s \wedge m} \frac{m!}{(m-\ell)!} \left\{ \begin{smallmatrix} s \\ \ell \end{smallmatrix} \right\} \pi_0^\ell \\
 & \quad \times \sum_{k=\ell}^m \frac{F_0(t_k)^\ell}{k^s} \mathcal{D}_{m-\ell}([G(t_{j+\ell})]_{1 \leq j \leq m-\ell}, k-\ell);
 \end{aligned}$$

$$\begin{aligned}
 & \text{FDR}(\text{SU}(\mathbf{t}), \bar{P}_{(\pi_0, F_1)}^I) \\
 (14) \quad &= \pi_0 m \sum_{k=1}^m \frac{F_0(t_k)}{k} \\
 & \quad \times \mathcal{D}_{m-1}([G(t_{j+1})]_{1 \leq j \leq m-1}, k-1);
 \end{aligned}$$

$$\begin{aligned}
 & \text{Pow}(\text{SU}(\mathbf{t}), \bar{P}_{(\pi_0, F_1)}^I) \\
 (15) \quad &= \sum_{k=1}^m F_1(t_k) \mathcal{D}_{m-1}([G(t_{j+1})]_{1 \leq j \leq m-1}, k-1).
 \end{aligned}$$

We can apply Theorem 3.1 in the case where $t_k = \alpha k/m$ to deduce the following results for the LSU procedure of Benjamini and Hochberg [1]: first, (14) leads to $\text{FDR}(\text{LSU}) = \pi_0 \alpha$, recovering the well-known result of Benjamini and Yekutieli [3] in the unconditional model. Second, (15) provides the exact expression

$$\begin{aligned}
 \text{Pow}(\text{LSU}) &= \sum_{k=1}^m F_1(\alpha k/m) \binom{m-1}{k-1} (G(\alpha k/m))^{k-1} \\
 & \quad \times \Psi_{m-k}(1 - G(\alpha m/m), \dots, 1 - G(\alpha(k+1)/m)).
 \end{aligned}$$

Glueck et al. [20] have obtained an exact expression for the power of the LSU under independence (in the conditional model) [20], but the corresponding formula was reported to have a complexity exponential in m , which is intractable for large m . Here, we obtained a much less complex formula, requiring (at most) the computation of the function Ψ_m at one point of \mathbb{R}^m . Third, formula (13) used with $t_k = \alpha k/m$ is similar to expression (2.1) in Theorem 2.1 of [13], in which a

formula for the s th moment of the FDP of the LSU was investigated (in the conditional model). Our formula (13) uses additional factors $\{\ell^s\}$. As soon as $s \geq 3$, they are definitely needed and they seem forgotten in [13]; for instance, taking $\alpha = 1$, the corresponding linear step-up procedure rejects all the hypotheses and (13) reduces to the computation of the s th moment of a binomial distribution, which uses at least one $\{\ell^s\} > 1$, see Section 2.3.

Fourth, expression (12) used with $t_k = \alpha k/m$ yields what is to our knowledge the first exact expression for the c.d.f. of FDP(LSU), valid for any $m \geq 2$ and for any alternative c.d.f. F_1 . For instance, taking a typical Gaussian setting where $F_1(t) = \overline{\Phi}(\overline{\Phi}^{-1}(t) - \mu)$, we are able to evaluate the probability $\mathbb{P}(\text{FDP}(\text{LSU}) \leq c\alpha)$ for $c \geq 1$; for $\mu = 3$, $\alpha = 0.05$, $\pi_0 = 1 - 1/\sqrt{m}$, expression (12) provides $\mathbb{P}(\text{FDP}(\text{LSU}) \leq \alpha) \simeq 0.724$, $\mathbb{P}(\text{FDP}(\text{LSU}) \leq 2\alpha) \simeq 0.787$ for $m = 100$ and $\mathbb{P}(\text{FDP}(\text{LSU}) \leq \alpha) \simeq 0.557$, $\mathbb{P}(\text{FDP}(\text{LSU}) \leq 2\alpha) \simeq 0.826$ for $m = 1000$. This means that the LSU procedure, designed to control the FDR at level α , can have a FDP larger than 2α with a “nonnegligible” probability, for some admittedly quite standard values of the model parameters. As m tends to infinity while the model parameters stay constant with m , the FDP converges to the FDR and the latter effect vanishes (see, e.g., [23]). However, we show in Section 4.2 that the convergence can be slow in the sparse case.

Alternatively, some authors are interested in procedures R controlling the FDP, that is, satisfying $\mathbb{P}[\text{FDP}(R) \leq \alpha] \geq 1 - \gamma$; see, for example, [19, 22]. By using (11), we directly deduce that the latter FDP control is satisfied by the step-up procedure $\text{SU}(\mathbf{t}^*)$ using the oracle threshold defined by $t_{m+1}^* = 1$ (by convention) and for any $1 \leq k \leq m$,

$$t_k^* = \max\{t \in [0, t_{k+1}^*] \mid \mathbb{P}[X \leq \alpha k] \geq 1 - \gamma \text{ for } X \sim \mathcal{B}(k, \pi_0 t/G(t))\},$$

with $t_k^* = 0$ if the above set is empty. However, the latter threshold is unknown in practice because it depends on the c.d.f. G and an interesting issue is to estimate it. Chi and Tan [7] introduced the threshold $t_k^{\text{CT}} = \max\{t \in [0, t_{k+1}^{\text{CT}}] \mid \mathbb{P}[X \leq \alpha k] \geq 1 - \gamma \text{ for } X \sim \mathcal{B}(k, 1 \wedge (mt/k))\}$ (with the convention $t_{m+1}^{\text{CT}} = 1$). As a matter of fact, the latter can be seen as the empirical substitute of t_k^* , because $G(t_k) \simeq \widehat{G}_m(t_k) = \widehat{k}/m$ for any step-up procedure rejecting \widehat{k} hypotheses (\widehat{G}_m denoting the e.c.d.f. of the p -values). Using the latter threshold, they established an asymptotic FDP control (as m tends to infinity). Here, a plausible explanation is that their procedure correctly mimics the oracle $\text{SU}(\mathbf{t}^*)$ (asymptotically).

3.1.2. *Step-down case.* In this section, we still consider the unconditional independent model, but we focus on the step-down case. By contrast with the step-up case, for a step-down procedure, the distribution of $|\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t})|$ conditionally on $|\text{SD}(\mathbf{t})| = k$ is not binomial in general. For instance, we prove in the supplementary file [28] the following: for any $k \geq 1$, $k \leq m$,

$$(16) \quad \mathbb{P}[|\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t})| = k \mid |\text{SD}(\mathbf{t})| = k] = \pi_0^k \frac{\Psi_k(F_0(t_1), \dots, F_0(t_k))}{\Psi_k(G(t_1), \dots, G(t_k))} =: a^k;$$

$$\begin{aligned}
 \mathbb{P}[\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t}) = 0 \mid |\text{SD}(\mathbf{t})| = k] &= \pi_1^k \frac{\Psi_k(F_1(t_1), \dots, F_1(t_k))}{\Psi_k(G(t_1), \dots, G(t_k))} \\
 (17) \qquad \qquad \qquad &=: (1 - b)^k,
 \end{aligned}$$

and it turns out that $a = b$ only for particular situations, such as $t_1 = \dots = t_k$, $F_1(x) = x$ or $\pi_0 \in \{0, 1\}$. Also, in the Dirac-uniform configuration $F_1 = 1$ [and thus $G(t) = \pi_0 t + \pi_1$], we establish in the supplementary file [28] the following: for any $1 \leq j \leq k$, $1 \leq k \leq m$,

$$\begin{aligned}
 \mathbb{P}[\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t}) = j \mid |\text{SD}(\mathbf{t})| = k] \\
 (18) \qquad \qquad \qquad &= \binom{k}{j} \pi_0^j \pi_1^{k-j} \frac{\Psi_j(t_{k-j+1}, \dots, t_k)}{\Psi_k(\pi_0 t_1 + \pi_1, \dots, \pi_0 t_k + \pi_1)},
 \end{aligned}$$

and the latter does not correspond to a binomial distribution in general. As a matter of fact, we derived an exact expression for $\mathbb{P}[\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t}) = j \mid |\text{SD}(\mathbf{t})| = k]$, valid for any j, \mathbf{t} and F_1 , but involving functions more complex than the Ψ_k (see formula (1) in the supplement [28]).

As a consequence, we now investigate the calculation of the FDR and of the power directly without using this exact FDP distribution expression. For this, let us recall the exact formula for the distribution of $|\text{SD}(\mathbf{t})|$: for all $k \in \{0, \dots, m\}$,

$$\mathbb{P}[|\text{SD}(\mathbf{t})| = k] = \tilde{\mathcal{D}}_m([G(t_j)]_{1 \leq j \leq m}, k). \tag{19}$$

(see formula (4), page 344 of [32], which can be directly generalized in the unconditional independent model because G is continuous increasing). The next result, based on the calculation of the distribution of $|\text{SD}(\mathbf{t}')|$ conditionally on $|\text{SD}(\mathbf{t})| = k$ (with $t'_j = t_{j+1}$), connects the FDR to distributions of the type (19) (see the proof in Section 6.2).

THEOREM 3.2. *For $m \geq 2$ hypotheses, consider the unconditional independent model $\bar{P}_{(\pi_0, F_1)}^I$, a step-down procedure $\text{SD}(\mathbf{t})$ with threshold \mathbf{t} and the notation of Section 2.3. Then for any parameter $\pi_0 \in [0, 1]$ and $F_1 \in \mathcal{F}$ [denoting $G(t) = \pi_0 F_0(t) + \pi_1 F_1(t)$], we have*

$$\begin{aligned}
 \text{FDR}(\text{SD}(\mathbf{t}), \bar{P}_{(\pi_0, F_1)}^I) \\
 (20) \qquad \qquad \qquad &= \pi_0 m \sum_{k=1}^m \sum_{k'=k}^m \frac{F_0(t_k)}{k'} \tilde{\mathcal{D}}_{m-1}([G(t_j)]_{1 \leq j \leq m-1}, k-1) \\
 &\qquad \qquad \qquad \times \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{G(t_{k+j}) - G(t_k)}{1 - G(t_k)} \right)_{1 \leq j \leq m-k}, k' - k \right);
 \end{aligned}$$

$$\begin{aligned}
 \text{Pow}(\text{SD}(\mathbf{t}), \bar{P}_{(\pi_0, F_1)}^I) \\
 (21) \qquad \qquad \qquad &= \sum_{k=1}^m F_1(t_k) \tilde{\mathcal{D}}_{m-1}([G(t_j)]_{1 \leq j \leq m-1}, k-1).
 \end{aligned}$$

To the best of our knowledge, (20) is the first exact expression for a step-down procedure that relies the FDR to the (joint) distribution of rejection numbers for any p -value alternative distribution. Furthermore, this result can be extended to the more general case of step-up-down procedures; see Section 5.2. The main tool to get (20) is Lemma 7.2.

One straightforward consequence of (20) is that, for a given threshold \mathbf{t} such that t_k/k is nondecreasing in k , the FDR of the step-down procedure of threshold \mathbf{t} is always smaller than the FDR of the step-up procedure of threshold \mathbf{t} :

COROLLARY 3.3. *In the same setting as Theorem 3.2, consider a threshold \mathbf{t} such that t_k/k is nondecreasing in k . Then we have*

$$\begin{aligned} \text{FDR}(\text{SD}(\mathbf{t})) &\leq \pi_0 m \sum_{k=1}^m \frac{t_k}{k} \tilde{\mathcal{D}}_{m-1}([G(t_j)]_{1 \leq j \leq m-1}, k-1) \\ &\leq \text{FDR}(\text{SU}(\mathbf{t})). \end{aligned}$$

While the latter result should probably be considered as well known, it is not trivial because when increasing the rejection number, both numerator and denominator are increasing within the FDP expression (for further developments on this issue, see Theorem 2 in [36]).

Next, by taking $t_k = \alpha k/m$ in (20), we may compute exactly the FDR of the LSD procedure. In the Dirac-uniform model $\bar{P}^I_{(\pi_0, F_1=1)}$ and using (7), we deduce the following expression:

$$\begin{aligned} \text{FDR}(\text{LSD}) &= \pi_0 \frac{\alpha^2}{m} \left(\pi_1 + \pi_0 \frac{\alpha}{m} \right) \\ &\times \sum_{k=1}^m \sum_{j=k}^m \frac{k}{j} \binom{m-1}{k-1} \binom{m-k}{j-k} \pi_0^{m-k} \\ (22) \quad &\times \left(\pi_1 + \pi_0 \frac{\alpha k}{m} \right)^{k-2} \left(\frac{\alpha(j-k+1)}{m} \right)^{j-k-1} \\ &\times \left(1 - \frac{\alpha(j+1)}{m} \right)^{m-j}. \end{aligned}$$

Finally, let us emphasize that expression (20) is also useful to investigate least favorable configurations for the FDR of step-down procedures (see Section 4.1.1).

REMARK 3.4. If we only focus on the Dirac-uniform configuration, the FDP distribution of a given procedure R (rejecting any p -value equals to 0) only depends on the distribution of $|R \cap \mathcal{H}_0(H)|$ (conditionally on H), because $|R \cap \mathcal{H}_0(H)| = |R| - m_1(H)$. As shown in Section 3.7 of [8], this leads to exact computations of the FDR for step-up, step-down and more general step-up-down

procedures in the particular Dirac-uniform configuration. In comparison, Theorem 3.2 is valid for an arbitrary alternative c.d.f. F_1 , while it intrinsically uses the exchangeability of the p -values (which requires to use an unconditional model).

3.2. *Unconditional EMN model with nonnegative correlation $m \geq 2$.* In this subsection, our goal is to obtain results similar to Theorems 3.1 and 3.2, but this time in the unconditional EMN model of parameters π_0 , ρ and μ , with a nonnegative correlation $\rho \in [0, 1]$. In that case, we easily see that the joint distribution of the p -values can be realized as follows: for all i , $p_i = \overline{\Phi}(\sqrt{\rho}\overline{\Phi}^{-1}(U) + \sqrt{1-\rho}\overline{\Phi}^{-1}(U_i) + \mu H_i)$, where U , $(U_i)_i$ are all i.i.d. uniform on $(0, 1)$ [and independent of $(H_i)_i$]. This idea can be traced back to Stuart [35] and Owen and Steck [24]. As a consequence, conditionally on $U = u$, the p -values follow the unconditional independent model of parameters π_0 , $F_0(\cdot|u, \rho)$ and $F_1(\cdot|u, \rho)$ where we let

$$\begin{aligned}
 (23) \quad F_0(t|u, \rho) &= \overline{\Phi}\left(\frac{\overline{\Phi}^{-1}(t) - \sqrt{\rho}\overline{\Phi}^{-1}(u)}{\sqrt{1-\rho}}\right), \\
 F_1(t|u, \rho) &= \overline{\Phi}\left(\frac{\overline{\Phi}^{-1}(t) - \sqrt{\rho}\overline{\Phi}^{-1}(u) - \mu}{\sqrt{1-\rho}}\right)
 \end{aligned}$$

for $\rho \in [0, 1)$ and $F_0(t|u, 1) = \mathbf{1}\{u \leq t\}$, $F_1(t|u, 1) = \mathbf{1}\{u \leq \overline{\Phi}(\overline{\Phi}^{-1}(t) - \mu)\}$ for $\rho = 1$. As a result, to obtain formulas valid in the unconditional EMN model, we may directly use formulas holding in the unconditional independent model (with the above modified c.d.f.'s) and using an additional integration over $u \in (0, 1)$. Hence, we deduce from Theorems 3.1 and 3.2 the following result (the formulas are not fully written for short).

COROLLARY 3.5. *For $m \geq 2$ hypotheses, consider the unconditional EMN model $\overline{P}_{(\pi_0, \rho, \mu)}^N$ with parameters $\pi_0 \in [0, 1]$, $\mu > 0$ and $\rho \in [0, 1]$ and let $G(t | u, \rho) = \pi_0 F_0(t | u, \rho) + \pi_1 F_1(t | u, \rho)$ using notation (23). Then, for any threshold \mathbf{t} , under the generating distribution $(H, \mathbf{p}) \sim \overline{P}_{(\pi_0, \rho, \mu)}^N$, the quantity $\mathbb{P}[\text{FDP}(\text{SU}(\mathbf{t})) \leq x]$ (resp. $\mathbb{E}[\text{FDP}(\text{SU}(\mathbf{t}))^s]$; $\text{FDR}(\text{SU}(\mathbf{t}))$; $\text{Pow}(\text{SU}(\mathbf{t}))$) is given by the right-hand side of (12) [resp. (13); (14); (15)], by replacing $F_0(\cdot)$ by $F_0(\cdot|u, \rho)$, $F_1(\cdot)$ by $F_1(\cdot|u, \rho)$ and $G(\cdot)$ by $G(\cdot|u, \rho)$, and by integrating over u with respect to the Lebesgue measure on $(0, 1)$. Additionally, a similar result holds for step-down procedures using (20) and (21).*

Applying Corollary 3.5 for the LSU procedure, we obtain

$$\begin{aligned}
 (24) \quad & \text{FDR}(\text{LSU}, \overline{P}_{(\pi_0, \rho, \mu)}^N) \\
 &= \pi_0 \sum_{k=1}^m \binom{m}{k} \int_0^1 F_0(\alpha k/m | u, \rho) G(\alpha k/m | u, \rho)^{k-1} \\
 & \quad \times \Psi_{m-k}((1 - G(\alpha(m - j + 1)/m | u, \rho))_{1 \leq j \leq m-k}) du.
 \end{aligned}$$

An expression for $\lim_m \text{FDR}(\text{LSU}, \bar{P}_{(\pi_0, \rho, \mu)}^N)$ was provided by Finner, Dickhaus and Roters [15], by considering the asymptotic framework where m tends to infinity [15]. We compared the latter to the formula (24) by plotting the graph corresponding to their Figure 3 (not reported here). The results are qualitatively the same for $\pi_0 < 1$, but present major differences when $\pi_0 = 1$ and ρ is small. This is in accordance with the simulations reported in the concluding remarks of Section 5 in [15]. Hence, the asymptotic analysis may not reflect what happens for a realistically finite m , which can be seen as a limitation with respect to our nonasymptotic approach. For instance, when $\pi_0 = 1$, Finner, Dickhaus and Roters [15] proved that $\lim_{\rho \rightarrow 0} \lim_m \text{FDR}(\text{LSU}) = \Phi(\sqrt{-2 \log \alpha}) < \alpha$ whereas we have for any $m \geq 2$ that $\lim_{\rho \rightarrow 0} \text{FDR}(\text{LSU}) = \alpha$, as remarked in [15] using simulations and as proved formally in the next result.

COROLLARY 3.6. *For any $m \geq 2$ and for any threshold \mathbf{t} , the quantities $\text{FDR}(\text{SU}(\mathbf{t}), \bar{P}_{(\pi_0, \rho, \mu)}^N)$ and $\text{FDR}(\text{SD}(\mathbf{t}), \bar{P}_{(\pi_0, \rho, \mu)}^N)$ are continuous in any $\pi_0 \in [0, 1]$, any $\rho \in [0, 1]$ and any $\mu > 0$.*

Corollary 3.6 is a straightforward consequence of Corollary 3.5; to prove the continuity in $\rho = 1$, we may remark that for any u outside the set $\mathcal{S} = \{t_k, 1 \leq k \leq m\} \cup \{\Phi(\Phi^{-1}(t_k) - \mu), 1 \leq k \leq m\}$ of zero Lebesgue measure, the functions $F_0(t \mid u, \rho)$ and $F_1(t \mid u, \rho)$ are continuous in $\rho = 1$.

In particular, Corollary 3.6 shows that the limit of the FDR when ρ tends to 1 is given by the degenerated case $\rho = 1$. In the latter case, the FDR is particularly easy to compute because only one Gaussian variable is effective: for step-up procedures, $\text{FDR}(\text{SU}(\mathbf{t})) = \pi_0 t_m$; and for step-down procedures, $\text{FDR}(\text{SD}(\mathbf{t})) = \sum_{k=1}^m \binom{m}{k} \pi_0^k \pi_1^{m-k} \frac{k}{m} \min\{t_{m-k+1}, \Phi(\Phi^{-1}(t_1) - \mu)\}$ (the proof is left to the reader). For instance, under the special p -value configuration where $\rho = 1$ and $\pi_0 = 1$, the above FDR expressions yield $\text{FDR}(\text{SU}(\mathbf{t})) = t_m$ and $\text{FDR}(\text{SD}(\mathbf{t})) = t_1$. Thus, as $\rho \simeq 1$, the FDR value may considerably change as one considers a step-up or a step-down algorithm.

Going back to Corollary 3.5, let us mention that the latter can be used in order to evaluate the FDR control robustness under Gaussian equicorrelated positive dependence for any procedure (step-up or step-down) that controls the FDR under independence. For instance, the *adaptive* procedures of Blanchard and Roquain [5] [step-up using $t_k = \alpha \min\{1, (1 - \alpha)k/(m - k + 1)\}$] and Finner, Dickhaus and Roters [14] [step-up based on a modification of $t_k = \alpha k/(m - (1 - \alpha)k)$] have been proved to control the FDR at level α under independence (asymptotically for [14]). A simulation study was done in [5] in order to check if their respective FDR is still below α (or at least close to α) in the EMN model. Using our exact approach, we are able to reproduce their analysis without the errors due to the Monte–Carlo approximation. However, we underline that our approach uses *non-random* thresholds \mathbf{t} ; this is not always the case for adaptive procedures (see, e.g., [2, 5]).

Finally, let us underline that the main theoretical obstacle brought by the EMN model ($\rho \geq 0$) with respect to the independent model is that the functions $F_0(t | u, \rho)$ and $F_1(t | u, \rho)$ [$u \in (0, 1)$] are much more difficult to study than the original c.d.f.'s F_0 and F_1 . As illustration, the concavity property is lost (see [15], Figure 1), while the latter is often required in studies like the analysis of the least favorable configurations (see Section 4.1.1) or the convergence of the FDP (see, e.g., [23]).

REMARK 3.7. As described in Section 2 of [15], the device that we used to establish Corollary 3.5 also works for suitable test statistics of the form $T_i = g(X_i, U)$ where $(X_i)_i$ is a family of independent variables and the “disturbance variable” U is independent from the X_i 's. Therefore, our methodology would also apply in such framework.

3.3. *EMN model with a general correlation and $m = 2$.* When the correlation ρ is negative, the approach presented in the last section is not valid anymore and the problem seems much more difficult to tackle. We propose in this section to focus on the case where only two hypotheses are tested, which should hopefully give some hints concerning the behavior of the FDR under negative correlations for larger m . The next result follows from elementary integration and does not require the use of an unconditional model (see the proof in the supplementary file [28]).

PROPOSITION 3.8. *For $m = 2$ hypotheses, consider the conditional EMN model $P_{(H, \rho, \mu)}^N$ with parameters $H = (H_1, H_2) \in \{0, 1\}^2$ (generating $m_0 \in \{1, 2\}$ true null hypotheses), $\rho \in [-1, 1]$ and $\mu > 0$. Consider a threshold $\mathbf{t} = (t_1, t_2)$. Let $z_1 = \bar{\Phi}^{-1}(t_2)$ and $z_2 = \bar{\Phi}^{-1}(t_1)$. Then $\text{FDR}(\text{SU}(\mathbf{t}), P_{(H, \rho, \mu)}^N)$ is given by*

$$\begin{array}{l}
 \rho \in (-1, 1), \quad \frac{1}{2} \int_0^{\bar{\Phi}(z_1 - \mu)} \bar{\Phi}\left(\frac{z_1 - \rho \bar{\Phi}^{-1}(w)}{\sqrt{1 - \rho^2}}\right) dw \\
 m_0 = 1 \quad \quad \quad + \int_{\bar{\Phi}(z_1 - \mu)}^1 \bar{\Phi}\left(\frac{z_2 - \rho \bar{\Phi}^{-1}(w)}{\sqrt{1 - \rho^2}}\right) dw \\
 \rho \in (-1, 1), \quad t_1 + \int_{t_1}^{t_2} \bar{\Phi}\left(\frac{z_1 - \rho \bar{\Phi}^{-1}(w)}{\sqrt{1 - \rho^2}}\right) dw \\
 m_0 = 2 \quad \quad \quad + \int_{t_2}^1 \bar{\Phi}\left(\frac{z_2 - \rho \bar{\Phi}^{-1}(w)}{\sqrt{1 - \rho^2}}\right) dw \\
 \rho = -1, m_0 = 1 \quad \begin{cases} t_1, & \text{if } 0 < \mu \leq 2z_1, \\ t_1 + \frac{1}{2}t_2 - \frac{1}{2}\bar{\Phi}(\mu - z_1), & \text{if } 2z_1 < \mu < z_1 + z_2, \\ \frac{1}{2}t_2 + \frac{1}{2}\bar{\Phi}(\mu - z_1), & \text{if } \mu \geq z_1 + z_2, \end{cases} \\
 \rho = -1, m_0 = 2 \quad \begin{cases} 2t_1, & \text{if } 1/2 \geq t_2, \\ 2(t_1 + t_2) - 1, & \text{if } 1/2 < t_2, t_1 + t_2 \leq 1, \\ 1, & \text{if } 1/2 < t_2, t_1 + t_2 > 1, \end{cases} \\
 \rho = 1, m_0 = 1 \quad \frac{1}{2}t_2 \\
 \rho = 1, m_0 = 2 \quad t_2
 \end{array}
 \tag{25}$$

and $FDR(SD(\mathbf{t}), P_{(H,\rho,\mu)}^N)$ is given by

	$\rho \in (-1, 1), \quad \frac{1}{2} \int_0^{\overline{\Phi}(z_2-\mu)} \overline{\Phi}\left(\frac{z_1-\rho\overline{\Phi}^{-1}(w)}{\sqrt{1-\rho^2}}\right) dw$
$m_0 = 1$	$+ \frac{1}{2} \int_{\overline{\Phi}(z_2-\mu)}^{\overline{\Phi}(z_1-\mu)} \overline{\Phi}\left(\frac{z_2-\rho\overline{\Phi}^{-1}(w)}{\sqrt{1-\rho^2}}\right) dw$ $+ \int_{\overline{\Phi}(z_1-\mu)}^1 \overline{\Phi}\left(\frac{z_2-\rho\overline{\Phi}^{-1}(w)}{\sqrt{1-\rho^2}}\right) dw$
$\rho \in (-1, 1),$	$t_1 + \int_{t_1}^1 \overline{\Phi}\left(\frac{z_2-\rho\overline{\Phi}^{-1}(w)}{\sqrt{1-\rho^2}}\right) dw$
$m_0 = 2$	
$\rho = -1, m_0 = 1$	$\begin{cases} t_1, & \text{if } 0 < \mu \leq z_1 + z_2, \\ \frac{1}{2}(t_1 + t_2) - \frac{1}{2}\overline{\Phi}(\mu - z_2) \\ \quad + \frac{1}{2}\overline{\Phi}(\mu - z_1), & \text{if } z_1 + z_2 < \mu < 2z_2, \\ \frac{1}{2}t_2 + \frac{1}{2}\overline{\Phi}(\mu - z_1), & \text{if } \mu \geq 2z_2, \end{cases}$
$\rho = -1, m_0 = 2$	$\min(2t_1, 1)$
$\rho = 1, m_0 = 1$	$\frac{1}{2} \min(t_2, \overline{\Phi}(z_2 - \mu))$
$\rho = 1, m_0 = 2$	t_1

4. Application to least/most favorable configurations.

4.1. *Least favorable configurations for the FDR.* In order to study the FDR control, an interesting multiple testing issue is to determine which are the values of the model parameter F_1 (or μ) for which the FDR is maximum. The latter is called a least favorable configuration (LFC) for the FDR.

4.1.1. *Independent model.* Let us focus on the unconditional independent model. For a *step-up* procedure, expression (14) can be seen as $\pi_0 m \mathbb{E}_0[t_{\hat{k}}/\hat{k}]$ (where $\hat{k} = |\text{SU}([G(t_{j+1})]_{1 \leq j \leq m-1})| + 1$ and \mathbb{E}_0 denotes the expectation with respect to $m - 1$ i.i.d. uniform p -values). This shows that the behavior of the function $k \mapsto t_k/k$ is crucial to determine the LFCs of the FDR. Namely, if F_1 and F'_1 are two c.d.f.'s such that for all $t \in [0, 1]$, $F_1(t) \leq F'_1(t)$, then we have $FDR(\text{SU}(\mathbf{t}), \overline{P}_{(\pi_0, F_1)}^I) \leq FDR(\text{SU}(\mathbf{t}), \overline{P}_{(\pi_0, F'_1)}^I)$ when t_k/k is nondecreasing, while we have $FDR(\text{SU}(\mathbf{t}), \overline{P}_{(\pi_0, F_1)}^I) \geq FDR(\text{SU}(\mathbf{t}), \overline{P}_{(\pi_0, F'_1)}^I)$ when t_k/k is nonincreasing. The latter recovers a well-known result of Benjamini and Yekutieli [3] which was initially established in the conditional model; see Theorem 5.3 in [3]. As a consequence, the LFC for the FDR is either $F_1 = 1$ (Dirac-uniform) when t_k/k is nondecreasing, or $F_1 = 0$ [$F_1(x) = x$ if we only consider concave c.d.f.'s] when t_k/k is nonincreasing. In the border case of a linear threshold, the FDR does not

depend on F_1 (e.g., it is equal to $\pi_0\alpha$ for the LSU), hence any configuration is a LFC.

An open problem is to determine the LFCs of a *step-down* procedure using a given threshold $\mathbf{t} = (t_j)_{1 \leq j \leq m}$. Here, we introduce a new condition on the threshold \mathbf{t} which provides that the Dirac-uniform configuration is a LFC for the FDR of the corresponding *step-down* procedure. We define for any threshold $\mathbf{t} = (t_j)_{1 \leq j \leq m}$ the following condition:

$$(A) \quad k \in \{1, \dots, m\} \mapsto \sum_{i=0}^{m-k} \frac{t_k}{k+i} \tilde{D}_{m-k} \left(\left(\frac{t_{k+j} - t_k}{1 - t_k} \right)_{1 \leq j \leq m-k}, i \right)$$

is nondecreasing.

We now present the main result of this section which uses Theorem 3.2 and is proved in Section 6.3.

THEOREM 4.1. *For $m \geq 2$ hypotheses, consider the unconditional independent model $\bar{P}_{(\pi_0, F_1)}^I$ and a step-down procedure $\text{SD}(\mathbf{t})$ with a threshold $\mathbf{t} = (t_j)_{1 \leq j \leq m}$ satisfying (A). Then for any $\pi_0 \in [0, 1]$ and concave c.d.f. $F_1 \in \mathcal{F}$, we have*

$$(27) \quad \text{FDR}(\text{SD}(\mathbf{t}), \bar{P}_{(\pi_0, F_1)}^I) \leq \text{FDR}(\text{SD}(\mathbf{t}), \bar{P}_{(\pi_0, F_1=1)}^I),$$

meaning that the Dirac-uniform distribution is a least favorable configuration for the FDR of $\text{SD}(\mathbf{t})$. Moreover, for $\alpha \in (0, 1)$, the linear threshold $\mathbf{t} = (\alpha j / m)_{1 \leq j \leq m}$ satisfies (A) and thus (27) holds for the linear step-down procedure LSD.

While condition (A) may be somehow difficult to state formally, it is very easy to check numerically because it only involves a finite set of real numbers. For instance, considering the threshold of Gavrilov, Benjamini and Sarkar [17] $t_k = \alpha k / (m + 1 - (1 - \alpha)k)$ (for which the step-down procedure controls the FDR, see [17]), we may see that $(t_k)_k$ satisfies (A) for each $(\alpha, m) \in \{0.01, 0.05, 0.1, 0.2, 0.5, 0.9\} \times \{5, 10, 50, 100\}$, for instance. In fact, we were not able to find a value of (α, m) for which the corresponding threshold does not satisfy (A) [unfortunately, we have yet no formal argument proving (A) for any value of (α, m)]. As a consequence, Theorem 4.1 states that the LFC for the procedure of Gavrilov, Benjamini and Sarkar [17] is still the Dirac-uniform configuration (over the class of concave c.d.f.’s), at least for the previously listed values of (α, m) , which is a new interesting finding.

In comparison with the step-up case, for which the standard condition “ $k \mapsto t_k/k$ nondecreasing” provides that the Dirac-uniform configuration is a LFC, the new sufficient condition (A) in the step-down case may be written as “ $k \mapsto \zeta(\mathbf{t}, k) \times t_k/k$ is nondecreasing,” where $\zeta(\mathbf{t}, k) = \sum_{i=0}^{m-k} (1 + i/k)^{-1} \times \tilde{D}_{m-k} \left(\left(\frac{t_{k+j} - t_k}{1 - t_k} \right)_{1 \leq j \leq m-k}, i \right)$. It turns out that the additional function $\zeta(\mathbf{t}, \cdot)$ has a

quite complex behavior, not necessarily connected to the one of t_k/k , so that there is no general relation between (A) and “ $k \mapsto t_k/k$ nondecreasing”; for instance, on the one hand, (A) does not hold for the piecewise linear threshold defined by $t_k = \alpha pk/m$ for $1 \leq k \leq a$ and by $t_k = \alpha(pa - m)((a - m)m)^{-1}k + \alpha(1 - (pa - m)(a - m)^{-1})$ for $a + 1 \leq k \leq m$ (using, e.g., $m = 50, p = 0.6, a = 4, \alpha = 0.5$), while t_k/k is nondecreasing. On the other hand, (A) holds for $t_k = 0.9(k/m)^{9/10}$ (using, e.g., $m = 50$) while t_k/k is decreasing. In particular, for the latter threshold and considering only the set of concave c.d.f.’s, a LFC for $FDR(SU(\mathbf{t}))$ is $F_1(x) = x$ while a LFC for $FDR(SD(\mathbf{t}))$ is $F_1 = 1$ [and we checked numerically using Gaussian models that $F_1(x) = x$ is not a LFC for $FDR(SD(\mathbf{t}))$]. This puts forward the complexity of the issue: whether we consider a step-up or a step-down procedure, the LFCs for the FDR may be different for some thresholds [e.g., $t_k = 0.9(k/m)^{9/10}, m = 50$] and they may coincide for some other thresholds (e.g., the one of [17] for suitable (α, m)).

4.1.2. *EMN model.* When the p -values follow the EMN model, we would like to determine whether the Dirac-uniform distribution is still a LFC for the FDR of the LSU. Here, this claim is supported when $\rho \geq 0$ (corroborating the simulation described in Section 1 of [15]) but disproved when $\rho < 0$.

In order to investigate this issue, we reported on Figure 1 the FDR of the LSU procedure against μ in the EMN model when $\rho > 0$ (left) and when $\rho < 0$ (right), by using Corollary 3.5 and Proposition 3.8. Under positive correlation, although each curve is not necessarily nondecreasing (e.g., for $\rho = 0.2$), the case $\mu = \infty$, close to the right most point of Figure 1, seems to be a LFC. A challenging problem

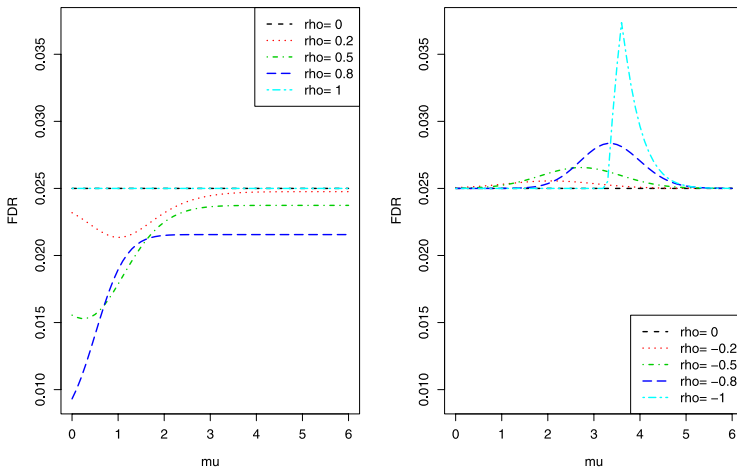


FIG. 1. $FDR(LSU)$ against the mean μ . Left: $\rho \geq 0$ unconditional EMN model $m = 100$ and $\pi_0 = 0.5$. Right: $\rho < 0$ conditional EMN model with $m = 2$ and $m_0 = 1, \alpha = 0.05$.

would be to state the latter formally. Under negative correlation and $m = 2$, however, $\mu = \infty$ is not a LFC anymore. As a matter of fact, in the case where $m = 2$, $m_0 = 1$ and $\mu = \infty$, the two p -values are independent (one p -value equals 0), so that the FDR equals $\alpha/2 = \alpha m_0/m$ which is not a maximum for the FDR, as we will show below.

Qualitatively, we observed the same behavior concerning the FDR of the LSD procedure.

Under negative correlation, the Dirac-uniform is not a LFC for the FDR and we can therefore legitimately ask what are the LFCs in that case. Here, we propose to solve this problem when $m = 2$ in the conditional EMN model. Let $z_1 = \overline{\Phi}^{-1}(\alpha)$ and $z_2 = \overline{\Phi}^{-1}(\alpha/2)$ and first consider the LSU procedure. Its FDR is plotted in Figure 2 (top). When $m_0 = 1$, we can check that $(\rho, \mu) = (-1, z_1 + z_2)$ is a LFC be-

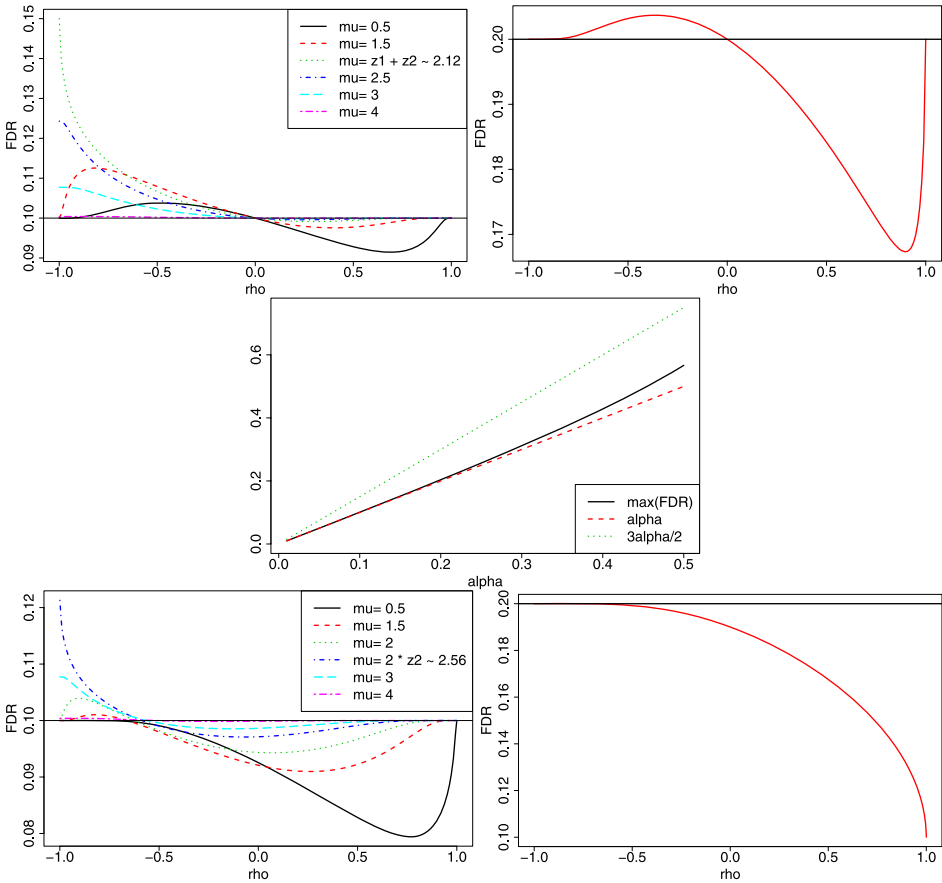


FIG. 2. Top/bottom: FDR against the correlation $\rho \in [-1, 1]$ in the conditional EMN model. $m = 2$; $\alpha = 0.2$. Left: $m_0 = 1$, right: $m_0 = 2$. Top: LSU, bottom: LSD. Middle: $\max_{\rho} \text{FDR}(\text{LSU})$ against $\alpha \in (0, 1/2)$. Conditional EMN model with $m = m_0 = 2$.

cause applying (25), the corresponding FDR is $3\alpha/4$, which equals the Benjamini–Yekutieli’s (BY) upper-bound $(1 + 1/2 + \dots + 1/m)\alpha m_0/m$ [3] (valid under any dependency). Interestingly, in general, Guo and Rao [21] state that the BY bound can be fulfilled using very specific dependency structures between the p -values (not necessarily including those coming from a EMN model) [21]. Here, we remark that the maximum value of the FDR still equals the BY bound for $m_0 = 1$, even for p -values coming from a EMN model. Next, for $m_0 = 2$, we may differentiate the corresponding expression in (25) in order to obtain that, assuming $\alpha \leq 1/2$, the FDR (that does not depend on μ) attains its maximum in $\rho = (-z_1(z_1 - z_2) - \{(z_1^2 - z_1z_2)^2 + 2\log(2)(z_1^2 - z_2^2) + 4(\log(2))^2\}^{1/2}) / (2\log(2)) \in (-1, 0)$. In that case, the BY bound is far from being fulfilled; see Figure 2 (middle).

Second, we consider the LSD procedure, whose FDR is plotted in Figure 2 (bottom). In the case where $m_0 = 2$, by differentiating the corresponding expression in (25) (that does not depend on μ), we are able to state that the FDR attains its maximum at $\rho = -1$ and that the value of the maximum is α . Furthermore, when $m_0 = 1$ the FDR is smaller than $3\alpha/4$ (applying Corollary 3.3). Hence, the FDR of the LSD procedure is always smaller than α when $m = 2$ in the conditional EMN model (for any m_0) and thus also in the unconditional EMN model, even for a negative correlation. An interesting open problem is to know whether this holds for larger m .

REMARK 4.2. Reiner-Benaim [25] also studied the value of μ maximizing the FDR in the case $m = 2$ in the (conditional) EMN model with possibly negative correlation [25]. The latter work focused on the two-sided testing with $\rho \in \{-1, 1\}$, $m_0 = 1$ and $m = 2$.

4.2. *Least/most favorable configurations for the variance of the FDP.* We focus here on the unconditional independent model and on the LSU procedure. Using (13) with $s = 2$, we easily derive the following expression for the variance of the FDP:

$$\begin{aligned}
 \mathbb{V}[\text{FDP}(\text{LSU})] &= \alpha\pi_0 \sum_{k=1}^m \frac{1}{k} \mathcal{D}_{m-1}([G(\alpha(j+1)/m)]_{1 \leq j \leq m-1}, k-1) \\
 (28) \qquad \qquad \qquad &\quad - (\alpha\pi_0)^2/m.
 \end{aligned}$$

As a consequence, by contrast with the FDR which is constantly equal to $\pi_0\alpha$ in that case, the variance of the FDP depends on the alternative p -value c.d.f. F_1 . Moreover, since the sum in (28) equals $\mathbb{E}_0[(|\text{SU}([G(\alpha(j+1)/m)]_{1 \leq j \leq m-1})| + 1)^{-1}]$ (where \mathbb{E}_0 denotes the expectation with respect to $m - 1$ i.i.d. uniform p -values), the smaller F_1 (point-wise), the larger the variance. Therefore, over the set $F_1 \in \mathcal{F}$, the least favorable configuration for the variance (i.e., the configuration where the variance is the largest) is given by $F_1 = 0$ while the most favorable configuration (i.e., the configuration where the variance is the smallest)

is the Dirac-uniform configuration $F_1 = 1$. Over the more “realistic” c.d.f. sets $\mathcal{F}' = \{F_1 \in \mathcal{F} \mid \forall x \in (0, 1), F_1(x) \geq x\}$ and $\mathcal{F}_\varepsilon = \{F_1 \in \mathcal{F} \mid \forall x \in (0, 1), F_1(x) \geq \varepsilon\}$, $0 < \varepsilon \leq 1$, the least favorable configurations for the variance are given, respectively, by $F_1(x) = x$ and $F_1(x) = \varepsilon$. For these extreme configurations, expression (28) can be simplified by using the next formula (proved in the supplementary file [28]): for any threshold of the form $t_k = \beta + k\gamma$, $1 \leq k \leq m$, with $\beta, \gamma \geq 0$,

$$(29) \quad \begin{aligned} & \mathbb{E}_0[(|\text{SU}(\mathbf{t})| + 1)^{-1}] \\ &= \frac{1}{\gamma - \beta} \left[\frac{(1 + \gamma - \beta)^{m+1} - 1}{m + 1} - \gamma[(1 + \gamma - \beta)^m - 1] \right], \end{aligned}$$

for $\gamma \neq \beta$ and $\mathbb{E}_0[(|\text{SU}(\mathbf{t})| + 1)^{-1}] = 1 - m\gamma$ otherwise (where \mathbb{E}_0 denotes the expectation with respect to m i.i.d. uniform p -values). This leads to the following result.

THEOREM 4.3. *Consider the linear step-up procedure LSU in the unconditional independent model with parameters π_0 and F_1 . Then for any $m \geq 2$, $\alpha \in (0, 1)$, $\pi_0 \in [0, 1]$ and $\varepsilon \in (0, 1]$, under the generating distribution $(H, \mathbf{p}) \sim \overline{P}_{(\pi_0, F_1)}^1$, the following holds:*

$$(30) \quad \begin{aligned} \min_{F_1 \in \mathcal{F}} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} &= \min_{F_1 \in \mathcal{F}'} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} \\ &= \min_{F_1 \in \mathcal{F}_\varepsilon} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} \\ &= \frac{\alpha\pi_0}{m} \frac{1 - \pi_0^m}{1 - \pi_0} - \frac{(\alpha\pi_0)^2}{m} \left(\frac{1 - \pi_0^{m-1}}{1 - \pi_0} + 1 \right); \\ \max_{F_1 \in \mathcal{F}} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} &= \alpha\pi_0(1 - \alpha\pi_0); \\ \max_{F_1 \in \mathcal{F}'} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} &= \alpha\pi_0(1 - \alpha) + (1 - \pi_0) \frac{\pi_0\alpha^2}{m}; \\ \max_{F_1 \in \mathcal{F}_\varepsilon} \{\mathbb{V}[\text{FDP}(\text{LSU})]\} &= \frac{\alpha\pi_0}{m} \frac{1 - (1 - (1 - \pi_0)\varepsilon)^m}{(1 - \pi_0)\varepsilon} \\ &\quad - \frac{(\alpha\pi_0)^2}{m} \left(\frac{1 - (1 - (1 - \pi_0)\varepsilon)^{m-1}}{(1 - \pi_0)\varepsilon} + 1 \right). \end{aligned}$$

The proof is made in Section 6.4. Using Theorem 4.3, we are able to investigate the following asymptotic issue: does the FDP converge to the FDR as m grows? Establishing the latter is crucial because when one establishes $\text{FDR} \leq \gamma$, one implicitly wants that for the observed realization ω , the control $\text{FDP}(\omega) \leq \gamma'$ still holds for $\gamma' \simeq \gamma$ (at least with high probability and when m is large). Here, the variance measure the L^2 distance between the FDP and the FDR, and since

FDP $\in [0, 1]$ the latter distance tends to zero if and only if the FDP converges to the FDR in probability. First, if $\pi_0 \in (0, 1)$ does not depend on m , the convergence holds over the set of c.d.f.'s \mathcal{F}_ε , with a distance $(\mathbb{E}(\text{FDP} - \text{FDR})^2)^{1/2}$ converging to zero at rate $1/\sqrt{m}$. This corroborates previous asymptotic studies in the so-called “subcritical” case (see [6, 7]). By contrast, when considering the classes \mathcal{F} and \mathcal{F}' the convergence does not hold in the least favorable configurations $F_1(x) = 0$ and $F_1(x) = x$, respectively. The latter is quite intuitive because the denominator in the FDP does not converge to infinity anymore in that cases (see, e.g., [16]), so these configurations can probably be considered as “marginal.” Second, our nonasymptotic approach allows to make π_0 depends on m in the following way $1 - \pi_0 = 1 - \pi_{0,m} \sim m^{-\beta}$ with $0 < \beta \leq 1$, which corresponds to a classical “sparse” setting (see, e.g., [9]). Expression (30) implies in this sparse case that the variance is always larger than a quantity of order $1/m^{1-\beta}$. In particular, when $1 - \pi_{0,m} \sim 1/m$, for any alternative c.d.f. F_1 , the FDP does not converge to the FDR, and when $1 - \pi_{0,m} \sim m^{-\beta}$ with $0 < \beta < 1$, for all F_1 , the convergence of the FDP toward the FDR is of order slower than $1/m^{(1-\beta)/2}$ (in L^2 norm). As illustration, for $m = 10,000$, $1 - \pi_0 = 1/100$ and $\alpha = 0.05$, expression (30) gives $(\mathbb{E}(\text{FDP} - \text{FDR})^2)^{1/2} \geq 0.0217$, so the FDP has a distribution somewhat spread around the FDR equalling $\pi_0\alpha \simeq 0.05$. As a conclusion, considering a sparse signal slows down the convergence of the FDP to the FDR, so any FDR control should be interpreted with cautious, even in this very standard framework (independent p -values with the LSU procedure).

5. Extensions and discussions.

5.1. *Calculations for false nondiscovery proportion.* Our approach is also useful to study the false nondiscovery proportion (FNP; see [18, 30]), that is, the proportion of false null hypotheses among the nonrejected hypotheses, and in particular the false nondiscovery rate (FNR), defined as the average of the FNP. For this, we use the following “duality” property between step-up and step-down procedures (which is straightforward but has not been noticed before to our knowledge): point-wise, the hypotheses rejected by $\text{SD}(\mathbf{t}, \mathbf{p})$ are exactly the hypotheses nonrejected by $\text{SU}(\bar{\mathbf{t}}, \bar{\mathbf{p}})$ with $\bar{p}_i = 1 - p_i$ and $\bar{t}_r = 1 - t_{m-r+1}$. Hence, the distribution of the FNP of a step-down procedure can be deduced from the distribution of the FDP of a step-up procedure. Precisely, for $0 \leq k \leq m - 1$, property (11) implies that the distribution of the erroneous nonrejection number $|\mathcal{H}_1(H) \cap (\text{SD}(\mathbf{t}))^c|$ conditionally on $|\text{SD}(\mathbf{t})| = k$ is binomial with parameters $m - k$ and $\pi_1(1 - F_1(t_{k+1})) / (1 - G(t_{k+1}))$. In particular, this leads to

$$\text{FNR}(\text{SD}(\mathbf{t}), \bar{P}_{\pi_0, F_1}^I) = m\pi_1 \sum_{k=0}^{m-1} \frac{1 - F_1(t_{k+1})}{m - k} \tilde{\mathcal{D}}_{m-1}((G(t_j))_{1 \leq j \leq m-1}, k).$$

Moreover, applying once more the duality property between step-up and step-down, we deduce from Section 3.1.2 that for a step-up procedure, the distribution

of the erroneous nonrejection number conditional on the rejection number is not binomial, in general, while we can still obtain an explicit expression for the FNR.

5.2. *Step-up-down procedures.* Our methodology can also be used to calculate the FDR of the so-called generalized step-up-down procedure of order $\lambda \in \{1, \dots, m\}$ (see, e.g., [14, 29]). The latter, denoted here by $\text{SUD}_\lambda(\mathbf{t})$, is defined as rejecting the i th hypothesis if $p_i \leq t_{\check{k}}$, with $\check{k} = \max\{k \in \{\lambda, \dots, m\} \mid \forall k' \in \{\lambda, \dots, k\}, p_{(k')} \leq t_{k'}\}$ if $p_{(\lambda)} \leq t_\lambda$ and $\check{k} = \max\{k \in \{0, \dots, \lambda\} \mid p_{(k)} \leq t_k\}$ if $p_{(\lambda)} > t_\lambda$. We easily check that

$$\text{SUD}_\lambda(\mathbf{t}) = \begin{cases} \text{SD}((t_\lambda \vee t_j)_{1 \leq j \leq m}), & \text{if } |\text{SD}((t_\lambda \vee t_j)_{1 \leq j \leq m})| \geq \lambda, \\ \text{SU}((t_\lambda \wedge t_j)_{1 \leq j \leq m}), & \text{if } |\text{SU}((t_\lambda \wedge t_j)_{1 \leq j \leq m})| < \lambda. \end{cases}$$

Therefore, by combining the proofs of formulas (14) and (20) and under the setting of Theorem 3.1 (distribution $\bar{P}_{(\pi_0, F_1)}^I$), we obtain the following expression:

$$\begin{aligned} & \text{FDR}(\text{SUD}_\lambda(\mathbf{t})) \\ &= \pi_0 m \sum_{k=1}^{\lambda-1} \frac{F_0(t_k)}{k} \mathcal{D}_{m-1}((G(t_\lambda \wedge t_{j+1}))_{1 \leq j \leq m-1}, k-1) \\ & \quad + \pi_0 m \sum_{k=\lambda}^m \sum_{k'=k}^m \frac{F_0(t_k)}{k'} \tilde{\mathcal{D}}_{m-1}((G(t_\lambda \vee t_j))_{1 \leq j \leq m-1}, k-1) \\ & \quad \quad \quad \times \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{G(t_{k+j}) - G(t_k)}{1 - G(t_k)} \right)_{1 \leq j \leq m-k}, k' - k \right) \end{aligned}$$

(for the SD part, we should note that even if the rejection number index is k' and not k , the sum may start at $k = \lambda$ as soon as $k' \geq \lambda$).

5.3. *Formulas in the conditional model.* We may legitimately ask whether we may obtain similar explicit formulas for the FDP in the conditional model, that is, conditionally on the vector $H = (H_i)_i$ [in fact, for studying the FDP of procedures of the kind $\{i \mid p_i \leq \hat{t}(\mathbf{p})\}$, with $\hat{t}(\cdot)$ invariant by permutation of the p -values, it is sufficient to work conditionally on the number of true hypotheses m_0]. In the conditional model (regarding, say, the independent case), while some of the technics used in this paper can clearly be used (e.g., the lemmas of Section 7), the p -value i.i.d. property is not true anymore, or more precisely, is only true within the set $\{p_i, i \in \mathcal{H}_0\}$ and $\{p_i, i \in \mathcal{H}_1\}$. Nevertheless, using technics similar to those proving (11) and (18), we can derive the following formulas, holding in the conditional independent model: for any $0 \leq j \leq m_0$ and $j \leq \ell \leq m_1 + j$,

$$\begin{aligned} & \mathbb{P}[\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t}) = j, |\text{SU}(\mathbf{t})| = \ell] \\ &= \binom{m_0}{j} \binom{m_1}{\ell - j} (t_\ell)^j (F_1(t_\ell))^{\ell - j} \\ & \quad \times \Psi_{m-\ell, m_0-j, \bar{F}_1}(1 - t_m, \dots, 1 - t_{\ell+1}); \end{aligned}$$

$$\begin{aligned} &\mathbb{P}[|\mathcal{H}_0(H) \cap \text{SD}(\mathbf{t})| = j, |\text{SD}(\mathbf{t})| = \ell] \\ &= \binom{m_0}{j} \binom{m_1}{\ell - j} (1 - t_{\ell+1})^{m_0 - j} \\ &\quad \times (1 - F_1(t_{\ell+1}))^{m_1 - \ell + j} \Psi_{\ell, j, F_1}(t_1, \dots, t_\ell), \end{aligned}$$

where we let $\overline{F}_1(t) = 1 - F_1(1 - t)$ and $\Psi_{k, k_0, F_1}(t_1, \dots, t_k) = P(p_{(1)} \leq t_1, \dots, p_{(k)} \leq t_k)$, in which the probability is taken over p -values such that $(p_i)_{1 \leq i \leq k_0}$ are i.i.d. uniform, independently of $(p_i)_{k_0+1 \leq i \leq k}$ i.i.d. of c.d.f. F_1 . In particular, the distributions of $|\text{SU}(\mathbf{t})|$ and $|\text{SD}(\mathbf{t})|$ are also depending on functions of the form Ψ_{k, k_0, F_1} .

From the above formulas, the exact calculation of the FDP distribution in the conditional model is feasible as soon as we can calculate the functions Ψ_{k, k_0, F_1} . As a matter of fact, compared to the calculation of the Ψ_k , computing the Ψ_{k, k_0, F_1} is more complex. This issue will be investigated in a forthcoming paper.

6. Proofs.

6.1. *Proof of Theorem 3.1.* Let us first prove (11) by computing the joint distribution of $|\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t})|$ and $|\text{SU}(\mathbf{t})|$. In the independent unconditional model, we may use the exchangeability of $(H_i, p_i)_i$ to obtain for any $0 \leq j \leq \ell \leq m$,

$$\begin{aligned} &\mathbb{P}[|\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t})| = j, |\text{SU}(\mathbf{t})| = \ell] \\ &= \binom{\ell}{j} \binom{m}{\ell} \mathbb{P}[\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t}) = \{1, \dots, j\}, \text{SU}(\mathbf{t}) = \{1, \dots, \ell\}] \\ &= \binom{\ell}{j} \binom{m}{\ell} \mathbb{P}[\text{SU}(\mathbf{t}) = \{1, \dots, \ell\}, H_1 = \dots = H_j = 0, \\ &\quad H_{j+1} = \dots = H_\ell = 1]. \end{aligned}$$

Next, by definition of a step-up procedure, we have $\text{SU}(\mathbf{t}) = \{i \mid p_i \leq t_{\hat{k}}\}$ with $\hat{k} = |\text{SU}(\mathbf{t})|$ (this expression is related to the ‘‘self-consistency’’ condition introduced in [4]). Using Lemma 7.1, if $\hat{k}'_{(\ell)}$ denotes the number of rejections of the step-up procedure of threshold $(t_{j+\ell})_{1 \leq j \leq m-\ell}$ over $m - \ell$ hypotheses and using the p -values $p_{\ell+1}, \dots, p_m$, we have

$$\begin{aligned} \text{SU}(\mathbf{t}) = \{1, \dots, \ell\} &\iff p_1 \leq t_\ell, \dots, p_\ell \leq t_\ell, & \hat{k} &= \ell \\ &\iff p_1 \leq t_\ell, \dots, p_\ell \leq t_\ell, & \hat{k}'_{(\ell)} &= 0. \end{aligned}$$

Therefore,

$$\begin{aligned} &\mathbb{P}[|\mathcal{H}_0(H) \cap \text{SU}(\mathbf{t})| = j, |\text{SU}(\mathbf{t})| = \ell] \\ &= \binom{\ell}{j} \binom{m}{\ell} \mathbb{P}[p_1 \leq t_\ell, \dots, p_\ell \leq t_\ell, \hat{k}'_{(\ell)} = 0, H_1 = \dots = H_j = 0, \\ &\quad H_{j+1} = \dots = H_\ell = 1] \end{aligned}$$

$$\begin{aligned}
 &= \binom{\ell}{j} \binom{m}{\ell} \mathbb{P}[p_1 \leq t_\ell, \dots, p_j \leq t_\ell, H_1 = \dots = H_j = 0] \\
 &\quad \times \mathbb{P}[p_{j+1} \leq t_\ell, \dots, p_\ell \leq t_\ell, H_{j+1} = \dots = H_\ell = 1] \mathbb{P}[\hat{k}'_{(\ell)} = 0] \\
 &= \binom{\ell}{j} \binom{m}{\ell} (\pi_0 F_0(t_\ell))^j (\pi_1 F_1(t_\ell))^{\ell-j} \\
 &\quad \times \Psi_{m-\ell}(1 - G(t_m), \dots, 1 - G(t_{\ell+1})),
 \end{aligned}$$

where we used the independence between the (H_i, p_i) in the second equality. This leads to (11) and then to (12). For (13), we use the Stirling numbers of second kind and the formula of the s th moment of a binomial distribution of Section 2.3. Expression (14) is a direct consequence of (13) for $s = 1$. For the power computation, from (11), the distribution of $|\mathcal{H}_1(H) \cap \text{SU}(\mathbf{t})|$ conditionally on $\hat{k} = |\text{SU}(\mathbf{t})|$ is binomial with parameters \hat{k} and $\pi_1 F_1(t_{\hat{k}})/G(t_{\hat{k}})$. Therefore, $\mathbb{E}[|\mathcal{H}_1(H) \cap \text{SU}(\mathbf{t})|] = \mathbb{E}[\pi_1 \hat{k} F_1(t_{\hat{k}})/G(t_{\hat{k}})]$ and (15) follows.

6.2. *Proof of Theorem 3.2.* Let us prove the FDR expression (the proof for the power is similar). Define $\tilde{k} = |\text{SD}(\mathbf{t})|$ and $\tilde{k}_{(1)}, \tilde{k}'_{(1)}$ as in Lemma 7.2. We get by exchangeability of $(H_i, p_i)_i$ and independence of the p -values,

$$\begin{aligned}
 \text{FDR}(R) &= \sum_{i=1}^m \mathbb{E} \left[\frac{\mathbf{1}\{p_i \leq t_{\tilde{k}}\}}{\tilde{k} \vee 1} \mathbf{1}\{H_i = 0\} \right] = m \mathbb{E} \left[\frac{\mathbf{1}\{p_1 \leq t_{\tilde{k}}\}}{\tilde{k} \vee 1} \mathbf{1}\{H_1 = 0\} \right] \\
 &= m \mathbb{E} \left[\frac{\mathbf{1}\{p_1 \leq t_{\tilde{k}_{(1)}+1}\}}{\tilde{k}'_{(1)} + 1} \mathbf{1}\{H_1 = 0\} \right] = \pi_0 m \mathbb{E} \left[\frac{F_0(t_{\tilde{k}_{(1)}+1})}{\tilde{k}'_{(1)} + 1} \right].
 \end{aligned}$$

Therefore, expression (20) will be proved as soon as we state that for any k, k' with $0 \leq k \leq m$ and $k \leq k' \leq m$, that we have

$$\begin{aligned}
 &\mathbb{P}[|\text{SD}(\mathbf{t})| = k, |\text{SD}(\mathbf{t}')| = k'] \\
 (31) \quad &= \tilde{\mathcal{D}}_m((G(t_j))_{1 \leq j \leq m}, k) \\
 &\quad \times \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{G(t_{k+1+j}) - G(t_{k+1})}{1 - G(t_{k+1})} \right)_{1 \leq j \leq m-k}, k' - k \right),
 \end{aligned}$$

for any threshold $(t_j)_{1 \leq j \leq m+1}$ and letting $\mathbf{t} = (t_j)_{1 \leq j \leq m}$ and $\mathbf{t}' = (t_{j+1})_{1 \leq j \leq m}$. Expression (31) is proved in the supplement [28].

6.3. *Proof of Theorem 4.1.* For any $t \in [0, 1]$, let $G(t) = \pi_0 t + \pi_1 F_1(t)$ and $G_1(t) = \pi_0 t + \pi_1$. First, since F_1 is concave, we have for $t < t' \leq 1$, that $(F_1(t') - F_1(t))/(t' - t) \geq (1 - F_1(t))/(1 - t)$ and thus for $t \leq t'$, we obtain the inequality

$$(32) \quad (G(t') - G(t))/(1 - G(t)) \geq (G_1(t') - G_1(t))/(1 - G_1(t))$$

(by convention, the left-hand side (resp., right-hand side) of (32) is equal to 0 if $G(t) = 1$ [resp., $G_1(t) = 1$]). From expression (20), we obtain

$$\begin{aligned} & \text{FDR}(\text{LSD}, \bar{P}_{(\pi_0, F)}^I) \\ &= \pi_0 m \sum_{k=1}^m \tilde{\mathcal{D}}_{m-1}((G(t_j))_{1 \leq j \leq m-1}, k-1) \\ &\quad \times \sum_{i=0}^{m-k} \frac{t_k}{k+i} \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{G(t_{k+j}) - G(t_k)}{1 - G(t_k)} \right)_{1 \leq j \leq m-k}, i \right) \\ &\leq \pi_0 m \sum_{k=1}^m \tilde{\mathcal{D}}_{m-1}((G(t_j))_{1 \leq j \leq m-1}, k-1) \\ &\quad \times \sum_{i=0}^{m-k} \frac{t_k}{k+i} \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{G_1(t_{k+j}) - G_1(t_k)}{1 - G_1(t_k)} \right)_{1 \leq j \leq m-k}, i \right) \\ &= \pi_0 m \sum_{k=1}^m \tilde{\mathcal{D}}_{m-1}((G(t_j))_{1 \leq j \leq m-1}, k-1) \\ &\quad \times \sum_{i=0}^{m-k} \frac{t_k}{k+i} \tilde{\mathcal{D}}_{m-k} \left(\left(\frac{t_{k+j} - t_k}{1 - t_k} \right)_{1 \leq j \leq m-k}, i \right), \end{aligned}$$

where the inequality comes from (32) and because for a fixed k , the sum over i can be seen as the expectation of $t_k/(k + I)$ where I is the rejection number of a step-down procedure (point-wise nondecreasing in the threshold). Next, considering this time the sum over k as an expectation, since $G \leq G_1$ and since a step-down procedure is point-wise nondecreasing in the threshold, the proof is finished by using condition (A). The reasoning proving that the linear threshold satisfies (A) is done in the supplementary file [28].

6.4. *Proof of Theorem 4.3.* We combine (28) and (29), the latter using $m - 1$ hypotheses and some special values for β and γ : $\beta = \gamma = \pi_0 \alpha / m$ for $F_1(x) = 0$; $\beta = \gamma = \alpha / m$ for $F_1(x) = x$; $\beta = \pi_0 \alpha / m + (1 - \pi_0) \varepsilon$ and $\gamma = \pi_0 \alpha / m$ for $F_1(x) = \varepsilon$.

7. **Useful lemmas.** The following lemma is related to the proof of Theorem 2.1 in [13] and to Lemma 8.1(i) in [27].

LEMMA 7.1. *Consider a step-up procedure $\text{SU}(\mathbf{t})$ using a given threshold \mathbf{t} testing m null hypotheses with p -values p_1, \dots, p_m and rejecting $\hat{k} = |\text{SU}(\mathbf{t})|$ hypotheses. For a given $1 \leq \ell \leq m$, denote by $\hat{k}'_{(\ell)}$ the number of rejections of the*

step-up procedure of threshold $(t_{j+\ell})_{1 \leq j \leq m-\ell}$ over $m - \ell$ hypotheses and using the p -values $p_{\ell+1}, \dots, p_m$. Then we have point-wise

$$\begin{aligned} \forall i, 1 \leq i \leq \ell \quad p_i \leq t_{\hat{k}} &\iff \forall i, 1 \leq i \leq \ell, \quad p_i \leq t_{\hat{k}'_{(\ell)} + \ell} \\ &\iff \hat{k} = \hat{k}'_{(\ell)} + \ell. \end{aligned}$$

For step-down procedures, we use the next lemma.

LEMMA 7.2. Consider a step-down procedure $\text{SD}(\mathbf{t})$ using a given threshold \mathbf{t} testing m null hypotheses with p -values p_1, \dots, p_m and rejecting $\tilde{k} = |\text{SD}(\mathbf{t})|$ hypotheses. Denote by $\tilde{k}_{(1)}$ (resp., $\tilde{k}'_{(1)}$) the number of rejections of the step-down procedure of threshold $(t_j)_{1 \leq j \leq m-1}$ [resp., $(t_{j+1})_{1 \leq j \leq m-1}$] over $m - 1$ hypotheses and using the p -values p_2, \dots, p_m . Then we have point-wise

$$p_1 \leq t_{\tilde{k}} \iff p_1 \leq t_{\tilde{k}_{(1)}+1} \iff \tilde{k} = \tilde{k}'_{(1)} + 1.$$

In the above lemma, we underline that the assertion $p_1 \leq t_{\tilde{k}'_{(1)}+1} \implies p_1 \leq t_{\tilde{k}}$ is not true in general.

These lemmas are proved in the supplementary material [28].

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SUPPLEMENTARY MATERIAL

Supplement to “Exact calculations for false discovery proportion with application to least favorable configurations” (DOI: [10.1214/10-AOS847SUPP](https://doi.org/10.1214/10-AOS847SUPP); .pdf). Supplement which provides some proofs for the present paper.

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