FDR-control: Assumptions, a unifying proof, least favorable configurations and FDR-bounds

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Overview

Reference:

Finner, H., **D**ickhaus, T. and **R**oters, M. (2007).

On the false discovery rate and an asymptotically optimal rejection curve.

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Notation & Definition of FDR

Θ parameter space

$H_1, \ldots, H_n$ null-hypotheses; $p_1, \ldots, p_n$ p-values

$\varphi_{(n)} = (\varphi_1, \ldots, \varphi_n)$ multiple test procedure

$V_n = |\{i : \varphi_i = 1 \text{ and } H_i \text{ true }\}| =$ number of true hypotheses rejected

$R_n = |\{i : \varphi_i = 1\}| =$ number of hypotheses rejected

$\text{FDR}_\vartheta(\varphi_{(n)}) = \mathbb{E}_\vartheta[\frac{V_n}{R_n \vee 1}]$ actual FDR given $\vartheta \in \Theta$

Definition. Let $\alpha \in (0, 1)$ be fixed.

$\varphi_{(n)}$ controls the false discovery rate (FDR) at level α if

$$\text{FDR}(\varphi_{(n)}) = \sup_{\vartheta \in \Theta} \text{FDR}_\vartheta(\varphi_{(n)}) \leq \alpha.$$

The FDR-Theorem: Benjamini & Hochberg (1995)

H_i true for $i \in I_{n,0}$, H_i false for $i \in I_{n,1}$

$I_{n,0} + I_{n,1} = I_n = \{1, \ldots, n\}$, $n_0 = |I_{n,0}|$

$p_i \sim \mathrm{U}([0,1])$, $i \in I_{n,0}$, independent

$(p_i : i \in I_{n,0})$, $(p_i : i \in I_{n,1})$ independent

$p_{1:n} \leq \cdots \leq p_{n:n}$ ordered p-values

Linear step-up procedure $\varphi_{(n)}^{\mathrm{LSU}}$ based on Simes' crit. val. $\alpha_{i:n} = i\alpha/n$:

Reject all H_i with $p_i \leq \alpha_{m:n}$, where $m = \max\{i : p_{i:n} \leq \alpha_{i:n}\}$.

Then

$$\mathrm{FDR}_\vartheta(\varphi_{(n)}^{\mathrm{LSU}}) = \mathbb{E}_\vartheta\left[\frac{V_n}{R_n \vee 1}\right] = \frac{n_0}{n}\alpha$$

Linear step-up in terms of ecdf

Let F_n denote the empirical cdf (ecdf) of the p-values, that is,

$$F_n(t) = \frac{1}{n} \sum_{i=1}^{n} I_{[0,t]}(p_i).$$

Rejection curve: Simes-line defined by $r(t) = t/\alpha$.

Define

$$t^* = \sup\{t \in [0, \alpha] : F_n(t) \geq r(t)\}$$

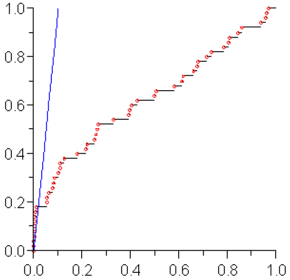
and reject all H_i with $p_i \leq t^*$.

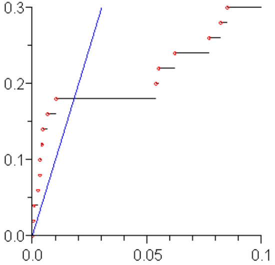
Call t^* the **largest crossing point** (LCP).

Simes-line and ecdf, $\alpha = 0.1$

$$X_i \sim N(\mu_i, 1),\ H_i : \mu_i = 0,\ i = 1, \ldots, n,$$

$$n = 50,\ n_0 = 40,\ \zeta_n = n_0/n = 0.8,\ X_i \sim N(2, 1) \text{ for } i \in I_{n,1}$$





FDR-control under Dependency

- Benjamini, Y. & Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *Ann. Statist.* **29**, 1165-1188.
- Sarkar, S. K. (2002). Some results on false discovery rate in stepwise multiple testing procedures. *Ann. Statist.* **30**, 239-257.

FDR-control for special dependent test statistics:

$$\mathrm{FDR}_\vartheta(\varphi_{(n)}) \leq \frac{n_0}{n}\alpha$$

Key assumptions: **MTP$_2$ or PRDS**

Linear step-up-down procedure (LSUD), Sarkar 2002

LSUD with parameter $\lambda \in [0, \alpha]$:

(1) $F_n(\lambda) \geq r(\lambda) \Rightarrow t^* = \inf\{p_i > \lambda : F_n(p_i) < f_\alpha(p_i)\}$ (SD-part).

Reject all H_i with $p_i < t^*$.

(2) $F_n(\lambda) < r(\lambda) \Rightarrow t^* = \sup\{p_i < \lambda : F_n(p_i) \geq f_\alpha(p_i)\}$ (SU-part).

Reject all H_i with $p_i \leq t^*$.

Remark: SU for $\lambda = \alpha$ and SD for $\lambda = 0$

Proof: FDR-control for SU, SD and SUD $(\alpha_{j:n} = j\alpha/n)$

$$
\begin{aligned}
\mathrm{FDR}_\vartheta(\varphi) &= \mathbb{E}_\vartheta\left[\frac{V_n}{R_n \vee 1}\right] \\
&= \sum_{i\in I_{n,0}} \sum_{j\in I_n} \frac{1}{j} P_\vartheta(R_n = j, \varphi_i = 1) \\
&= \sum_{i\in I_{n,0}} \sum_{j\in I_n} \left[\frac{1}{j} P_\vartheta(p_i \le \alpha_{j:n}) \cdot P_\vartheta(R_n = j \mid p_i \le \alpha_{j:n})\right] \\
&\underset{(i)}{\le} \sum_{i\in I_{n,0}} \sum_{j\in I_n} \frac{\alpha_{j:n}}{j} P_\vartheta(R_n = j \mid p_i \le \alpha_{j:n}) \\
&\underset{(ii)}{\le} \sum_{i\in I_{n,0}} [\alpha_{1:n} P_\vartheta(R_n \ge 1 \mid p_i \le \alpha_{1:n}) \\
&\qquad + \sum_{j=2}^{n} \left(\frac{\alpha_{j:n}}{j} - \frac{\alpha_{j-1:n}}{j-1}\right) P_\vartheta(R_n \ge j \mid p_i \le \alpha_{j:n})] \\
&\underset{(iii)}{\le} \frac{n_0}{n}\alpha.
\end{aligned}
$$

Proof: FDR-control for SU, SD and SUD ($\alpha_{j:n} = j\alpha/n$)

ad (i): "=" holds if $p_i \sim U(0,1), i \in I_{n,0}$.

ad (ii): "$\leq$" holds if

$$(1) \qquad \forall i \in I_{n,0} : P_\vartheta(R_n \geq j \mid p_i \leq t) \text{ is non-increasing in } t \in (0, \alpha_{j:n}].$$

$$\text{"=" holds if} \qquad \begin{cases} \varphi \text{ is a LSU-test,} \\ p_i,\ i \in I_{n,0},\ \text{iid,} \\ (p_i :\in I_{n,0}),\ (p_i :\in I_{n,1}) \text{ independent.} \end{cases}$$

ad (iii): (iii) holds if $\forall i \in I_{n,0} :\ P_\vartheta(R_n \geq 1 \mid p_i \leq \alpha_{1:n}) = 1$.

Note: MTP_2 or PRDS implies (1).

Condition (1)

Condition (1) is the most important assumption and applicable for SU- and SUD-tests.

(1) $\forall i \in I_{n,0} : P_\vartheta(R_n \geq j \,|\, p_i \leq t)$ is non-increasing in $t \in (0, \alpha_{j:n}]$.

Suppose that the p_i's , $i \in I_{n,0}$ are iid uniform

and $(p_i :\in I_{n,0})$, $(p_i :\in I_{n,1})$ are independent.

Then, we have for SU-tests that

$$\forall i \in I_{n,0} : P_\vartheta(R_n \geq j \,|\, p_i \leq t) \text{ is constant in } t \in (0, \alpha_{j:n}].$$

For SUD-test,

$$P_\vartheta(R_n \geq j \,|\, p_i \leq t) \text{ is typically decreasing in } t \in (0, \alpha_{j:n}].$$

Question

What happens with the FDR if we use

non-linear critical values / a non-linear rejection curve

for a SU- or SUD-procedure of order $\lambda < 1$?

Critical value functions

Let $\rho : [0,1] \to [0,1]$ be non-decreasing and continuous with $\rho(0) = 0$ and positive values on $(0,1]$.

Define critical values

$$\alpha_{i:n} = \rho(i/n) \in (0,1],\ i = 1, \ldots, n.$$

We call ρ a **critical value function.**

Define r by

$$r(x) = \inf\{u \in [0,1] : \rho(u) = x\} \text{ for } x \in [0,1] \ \ (\text{with } \inf \emptyset = \infty).$$

We call r a **rejection curve.**

Often: $r(x) = \rho^{-1}(x)$.

SU based on ρ

From **Benjamini and Yekutieli (2001)** we get the following.

Consider a SU-procedure based on ρ.

If $\rho(x)/x$ is non-decreasing in $x \in (0, 1]$ and if the p_i's under the nulls are iid uniform and independent of the alternative p-values,

then the FDR is largest if $p_i = 0$ a.s. for all alternative p-values,

i.e., Dirac-uniform configurations are least favorable (LFC) for the FDR.

FDR bound for SU

Let $\vartheta \in \Theta$ such that $n_0 = |I_{n,0}| =$ number of true nulls.

$I'_{n,0} = I_{n,0} \setminus \{i_0\}$ for some $i_0 \in I_{n,0}$.

Then the FDR of the SU-test $\varphi_{(n)}^{\text{SU},\rho}$ based on ρ is bounded by

$$\text{FDR}_\vartheta(\varphi_{(n)}^{\text{SU},\rho}) \leq \frac{n_0}{n} \mathbb{E}_{I'_{n,0}} \left[\frac{\rho(R_n/n)}{R_n/n} \right],$$

with " $=$ " for the Dirac-uniform configuration.

Moreover, if

$$\lim_{n\to\infty} \frac{n_0}{n} = \zeta \text{ and } \lim_{n\to\infty} \frac{R_n}{n} = \gamma_\zeta \text{ a.s. (w.r.t. DU)},$$

then the FDR is asymptotically bounded by

$$\zeta \frac{\rho(\gamma_\zeta)}{\gamma_\zeta}.$$

Idea: Optimize ρ for a SU procedure

Try to find a ρ such that

$$\zeta \frac{\rho(\gamma_\zeta)}{\gamma_\zeta} \equiv \min\{\zeta, \alpha\}$$

for as many ζ's as possible !

In other words, try to find a SU-test such that the FDR-level α is (asymptotically) exhausted under DU-configurations.

Solution:

In the next talk by Thorsten Dickhaus.

FDR bound for SUD(λ)

Let $\vartheta \in \Theta$ such that $n_0 =$ number of true nulls.

$I'_{n,0} = I_{n,0} \setminus \{i_0\}$ for some $i_0 \in I_{n,0}$.

Then the FDR of the SUD-test $\varphi_{(n)}^{\text{SUD},\rho}$ based on ρ is bounded by

$$\text{FDR}_\vartheta(\varphi_{(n)}^{\text{SUD},\rho}) \leq \frac{n_0}{n} \mathbb{E}_{I'_{n,0}} \left[\frac{\rho(R_n/n)}{R_n/n} \right].$$

This bound is not sharp for SUD ($\lambda < 1$).

However, if

$$\lim_{n\to\infty} \frac{n_0}{n} = \zeta \text{ and } \lim_{n\to\infty} \frac{R_n}{n} = \gamma_\zeta \text{ a.s. (w.r.t. DU),}$$

then the FDR is asymptotically sharply bounded by

$$\zeta \frac{\rho(\gamma_\zeta)}{\gamma_\zeta}.$$

Now: Optimize ρ for a SUD procedure

Try to find a ρ such that

$$\zeta \frac{\rho(\gamma_\zeta)}{\gamma_\zeta} \equiv \min\{\zeta, \alpha\}$$

for as many ζ's as possible !

In other words, try to find a SUD-test such that the FDR-level α is exhausted under DU-configurations.

Solution:

In the next talk by Thorsten Dickhaus.

Optimal procedure ?

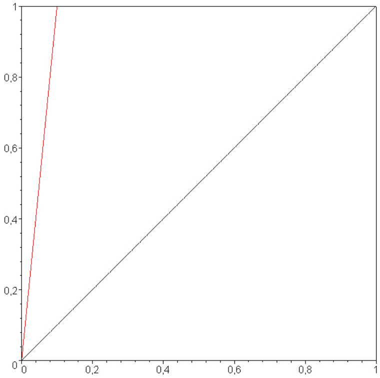
Does there exist an

asymptotically optimal rejection curve ?

Does there exist an

asymptotically optimal SU- or SUD-procedure ?

Which rejection curve is optimal ?



Which rejection curve is optimal ?

There are so many other curves $r : [0,1] \to [0,1]$!