



New adaptive procedures that control the FDR

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Setting



- $(\mathcal{X}, \mathfrak{X}, \mathbf{P})$ probability space.
- \mathcal{H} a finite set of hypotheses for \mathbf{P} , $m := |\mathcal{H}|$ (**known**)

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- For each $h \in \mathcal{H}$, **p-value**: $p_h : \mathcal{X} \rightarrow [0, 1]$ (measurable) such that

If $h \in \mathcal{H}_0$, $\forall t \in [0, 1]$, $\mathbf{P}(p_h \leq t) \leq t$

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- A **multiple testing procedure**: a (measurable) function

$$R : \mathbf{p} = (p_h)_{h \in \mathcal{H}} \in [0, 1]^{\mathcal{H}} \mapsto R(\mathbf{p}) \subset \mathcal{H}$$

(returns the rejected hypotheses)

Type I error



R makes a **type I error** for h :

$$h \in \mathcal{H}_0 \cap R$$

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False Discovery Rate of R [Benjamini and Hochberg (1995)]:

$$\text{FDR}(R) := \mathbf{E} \left[\frac{|\mathcal{H}_0 \cap R|}{|R|} \mathbf{I}\{|R| > 0\} \right]$$

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How to build R with $\text{FDR}(R) \leq \alpha$?

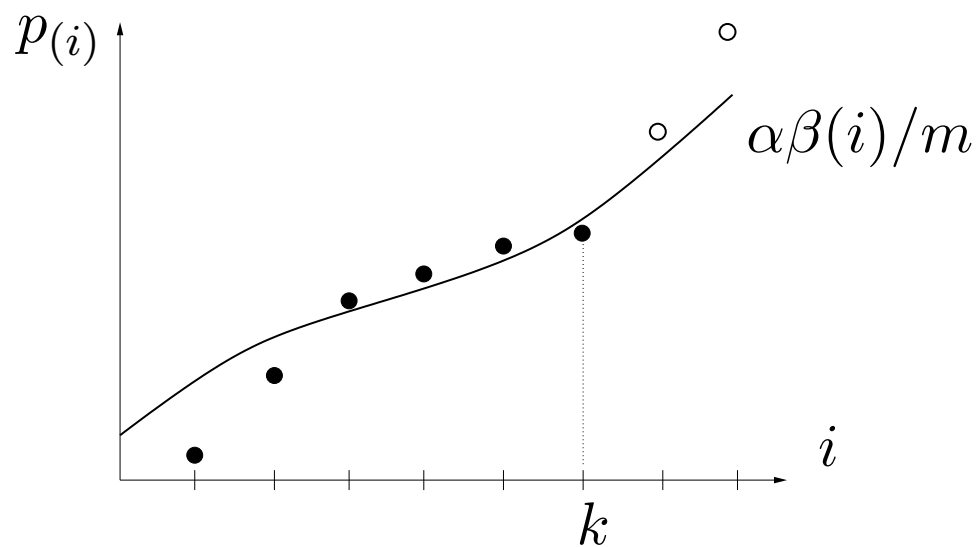
Step-up procedure



If $p_{(1)} \leq \dots \leq p_{(m)}$ are the ordered p -values
and $\beta : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ non-decreasing: **threshold function**

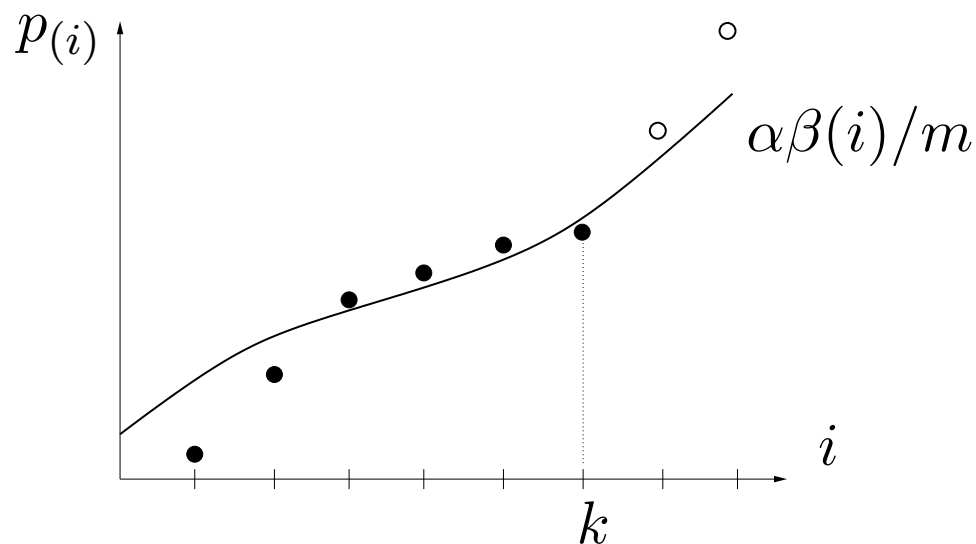
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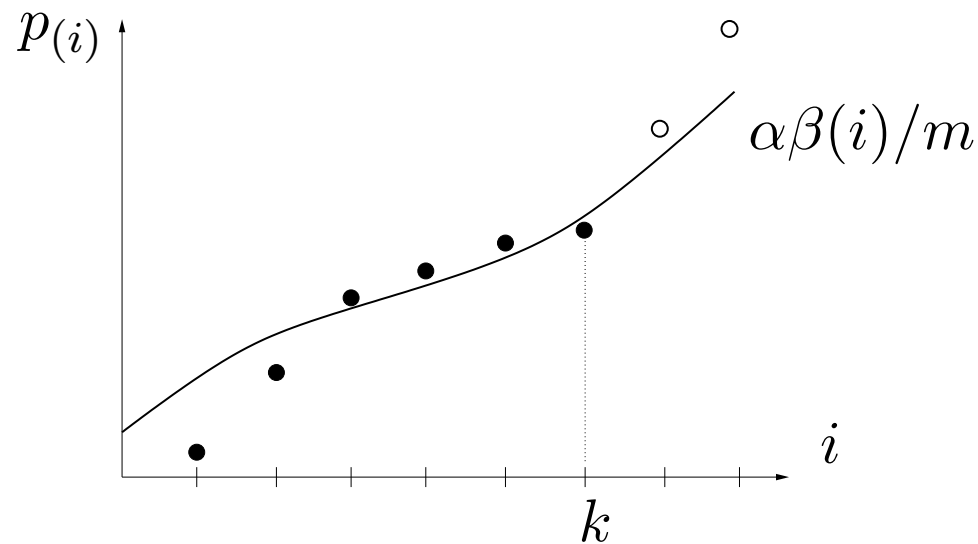


Definition (step-up procedure with threshold function β)

$$R_\beta := \{h \in \mathcal{H} \mid p_h \leq p_{(k)}\} \quad \text{where} \quad k := \max\{i \mid p_{(i)} \leq \alpha\beta(i)/m\}$$

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Linear step-up procedure: R_β where $\beta(i) = i$.

Goal in step-up FDR control



Find a threshold function β such that

$$\text{FDR}(R_\beta) \leq \alpha$$

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With β as "large" as possible

Known FDR control results



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Benjamini and Hochberg (1995), Benjamini and Yekutieli (2001):

Theorem 1 *p-values independent or positively dependent (PRDS):*

The linear step-up procedure has a FDR smaller than $\pi_0\alpha$, i.e. for $\beta(i) = i$,

$$\text{FDR}(R_\beta) \leq \pi_0\alpha.$$

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Benjamini and Yekutieli (2001):

Theorem 2 *p-values with general dependencies:*

The step-up procedure with threshold function $\beta(i) = i/(1 + 1/2 + \dots + 1/m)$ satisfies

$$\text{FDR}(R_\beta) \leq \pi_0\alpha.$$

Known FDR control results (2)



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Theorem 3 *p-values with general dependencies:*

If β of the form:

$$\beta(i) = \int_0^i u d\nu(u),$$

and ν is some distribution on $(0, \infty)$,

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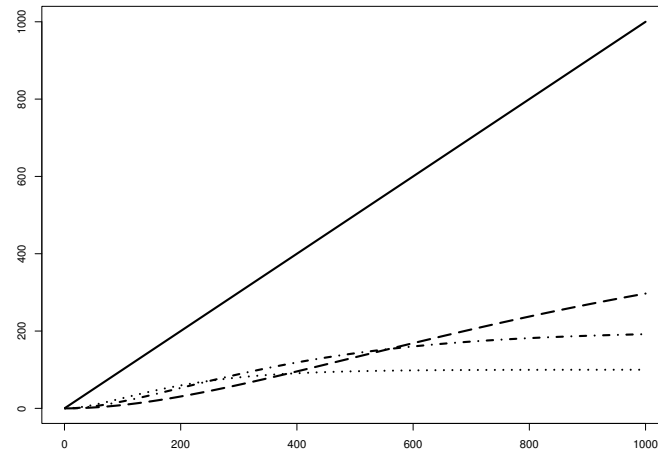
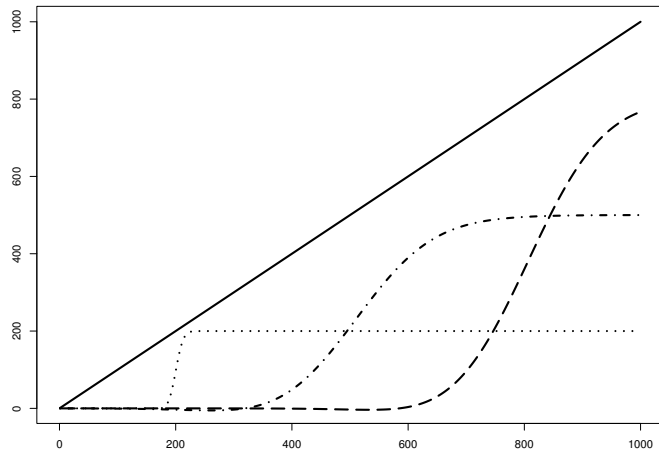
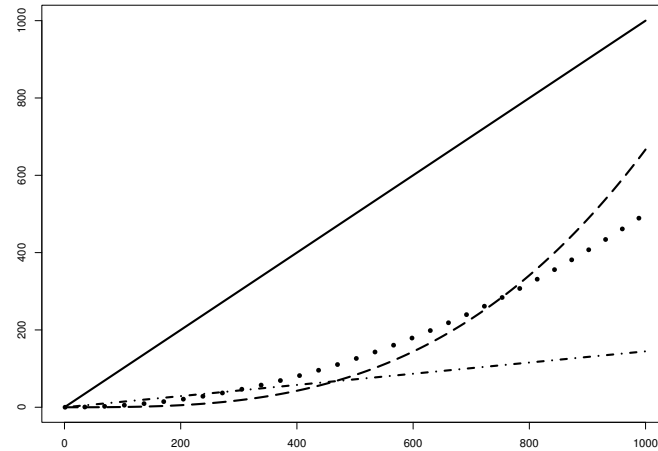
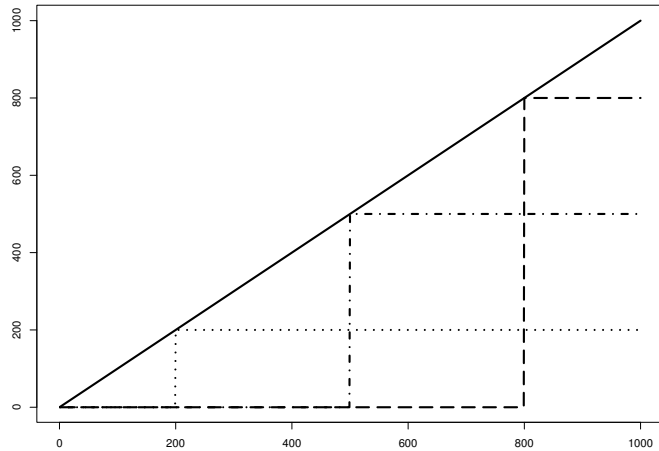
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- $\nu(\{k\}) \propto k$ gives $\beta(i) = \frac{i(i+1)(2i+1)}{3m(m+1)}$

Some choices for β (general dependencies)



\Rightarrow no uniformly-optimal choice (it depends on the data)

To control FDR under gen. dep.: **not only BY's procedure !**

Introduction to adaptive procedures



Summary: we have $\text{FDR}(R_\beta) \leq \pi_0 \alpha$ when

1. The p -values are independent or positively dependent and $\beta(i) = i$
2. The p -values with general dependencies and $\beta(i) = \int_0^i u d\nu(u) \leq i$,
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(π_0) -Adaptive step-up procedures: $R_{\hat{\beta}}$ with $\hat{\beta} \simeq \beta^*$

Our Goal



Find $\hat{\beta} \geq \beta$ such that $\text{FDR}(R_{\hat{\beta}}) \leq \alpha$ and $\hat{\beta}$ "close to" $\beta\pi_0^{-1}$

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Under several dependence cases :

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One-stage procedure: $\hat{\beta}$ is deterministic

Outline



- I. When the p -values are independent
 - Some existing adaptive procedures
 - New adaptive procedures

- II. When the p -values are dependent
 - New (and first ?) adaptive procedures

I. Existing adaptive procedures with FDR control



[Benjamini, Krieger and Yekutieli (2006)] **BKY06**:

1. Apply the standard step-up linear procedure R_0 at level $\alpha/(1 + \alpha)$ and put $\hat{F} = \frac{m}{m - |R_0|}$
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Using [Storey (2001)] **Storey- λ** :

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Benjamini, Krieger and Yekutieli (2006):

Theorem 4 *p-values independent*

These two procedures satisfy $\text{FDR}(R) \leq \alpha$

I. New one-stage adaptive procedure



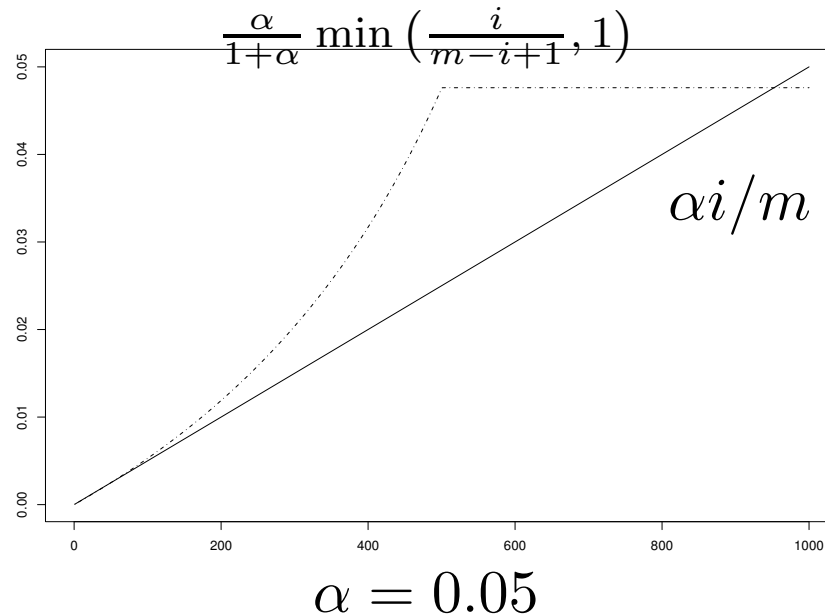
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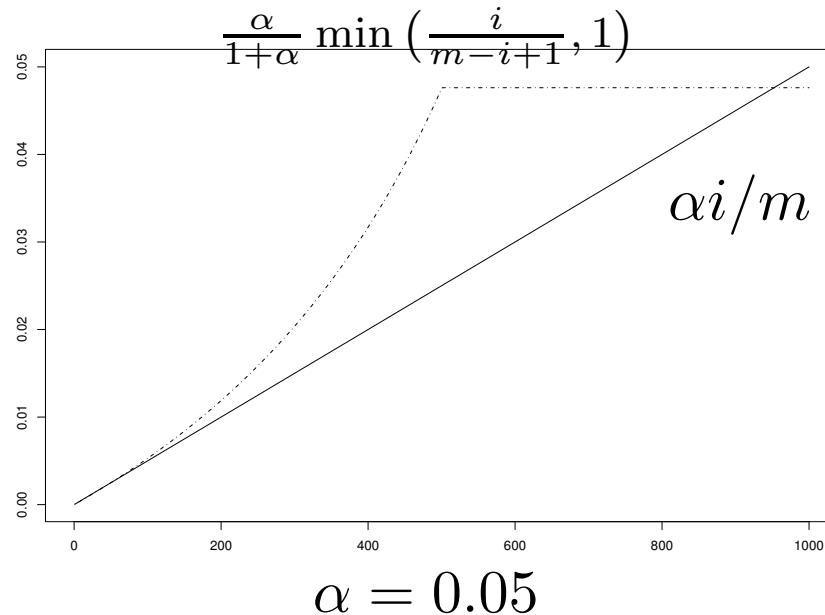
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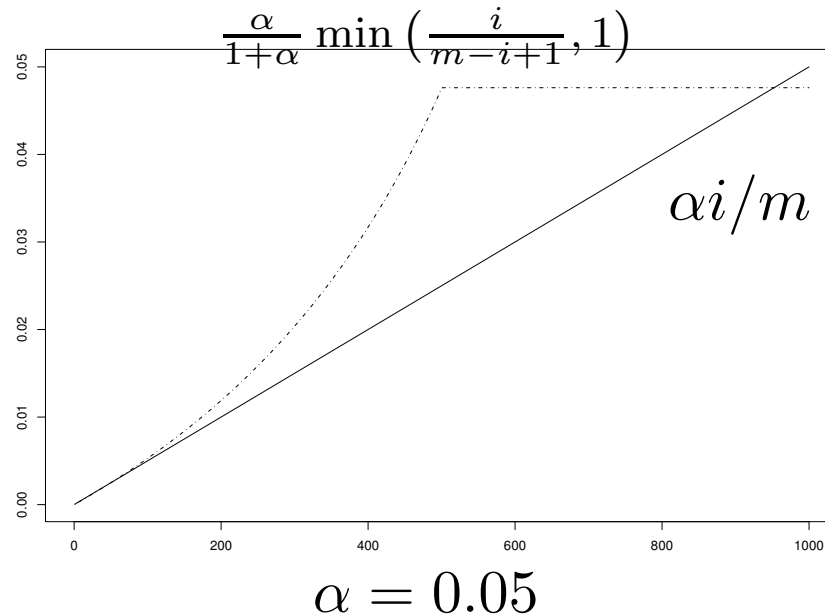
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Idea: use this procedure in the first step !

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Theorem 6 *p-values independent*: consider the two-stage procedure :

1. Apply the new one-stage adaptive procedure R'_0 at level α

and put $\hat{F} = \frac{m}{m - |R'_0| + 1}$

2. Take the step-up procedure R with global threshold $\frac{\alpha}{1+\alpha} \frac{i}{m} \hat{F}$

Then $\text{FDR}(R) \leq \alpha$.

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On simulations:

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Storey-1/2 \gg BR07-2S \gg BKY06

- *positively dependent case*: FDR control?

Storey-1/2 is **not robust!**

New two-stage procedure *seems robust* to positive correlations

I I. Under dependence



Recall: FDR control for step-up procedures with $\alpha\beta(i)/m$ in the cases:

- positive dependencies with $\beta(i) = i$
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Theorem 7 two-stage adaptive procedure:

1. Non-adaptive step-up procedure R_0 with threshold $\frac{\alpha}{4} \frac{\beta(i)}{m}$
and put $\hat{F} = \frac{1}{1 - \sqrt{(2|R_0|/m - 1)_+}}$
2. Step-up procedure R with threshold $\frac{\alpha}{2} \frac{\beta(i)}{m} \hat{F}$

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Loss/ indep case: $\frac{\alpha}{2}, \frac{\alpha}{4}$ and $\frac{1}{1 - \sqrt{(2x-1)_+}} \leq \frac{1}{1-x}$

I I. Under dependence (2)



Remarks :

- Estimation based on Markov's inequality (conservative device)

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(m_0 small and $p_h, h \notin \mathcal{H}_0$ small)

I I. Under dependence (2)



Remarks :

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⇒ interest **more theoretical than practical.**

Conclusion and future works



New adaptive procedures that control the FDR:

- * when the p -values are independent:
 - one-stage explicit and better than LSU
 - two-stage → better than BKY06
 - seems robust to positive correlations.
- * when the p -values have positive or general dependencies:
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Choose the prior ν from an estimator of π_0 ?



Thank you for your attention!

A preprint is available on: <http://genome.jouy.inra.fr/~eroquain>



Appendix

I. Simulations



For $k = 1, \dots, m$,

$$Y_k \sim \mathcal{N}(\mu_k, 1)$$

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With 10000 simulations, $m = 100$, mean = 3:

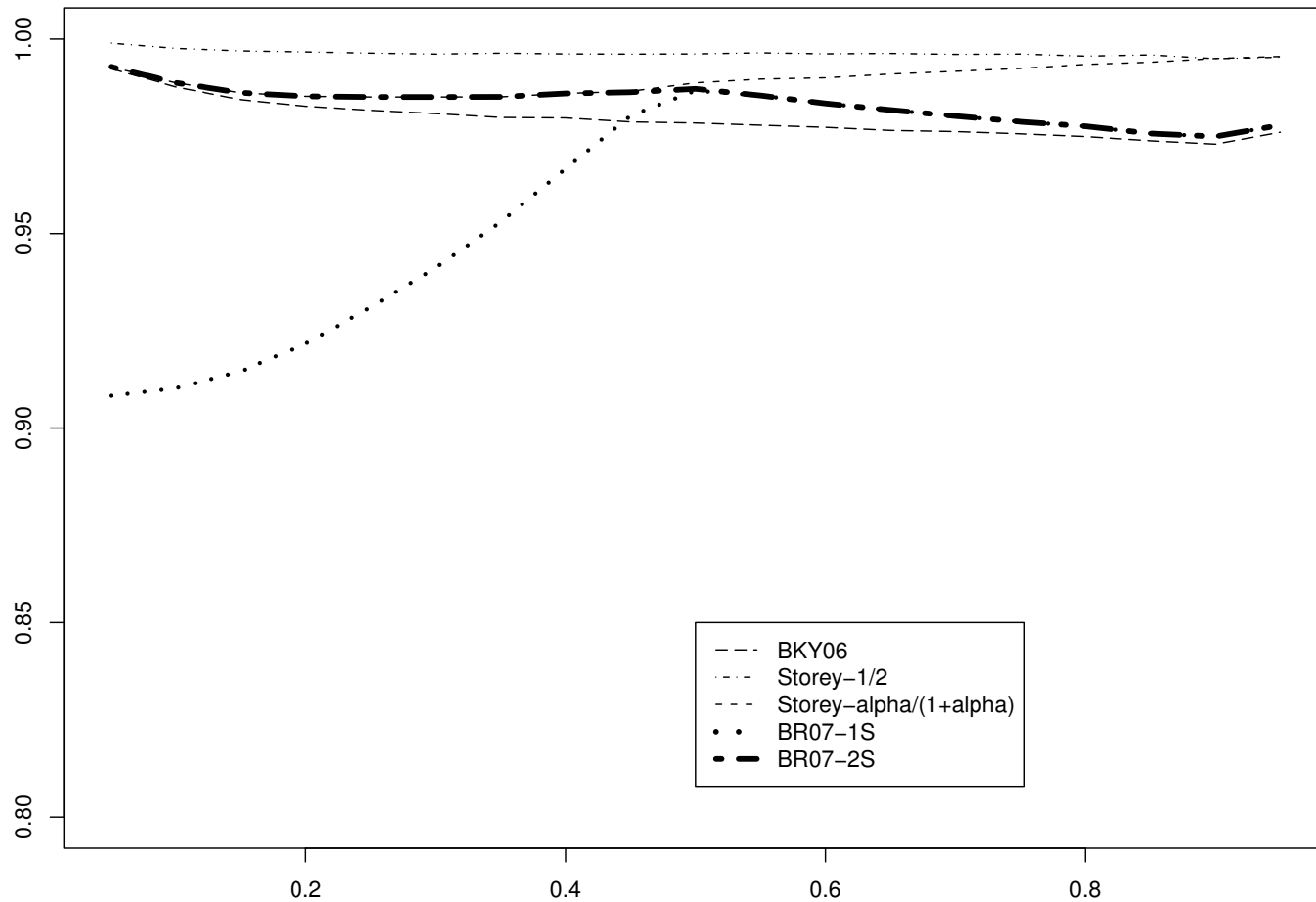
- **Power** (in independent case) :

nb of correct rejections / nb of correct rejections of the oracle procedure

- **FDR estimation** (in the positive dependent case)

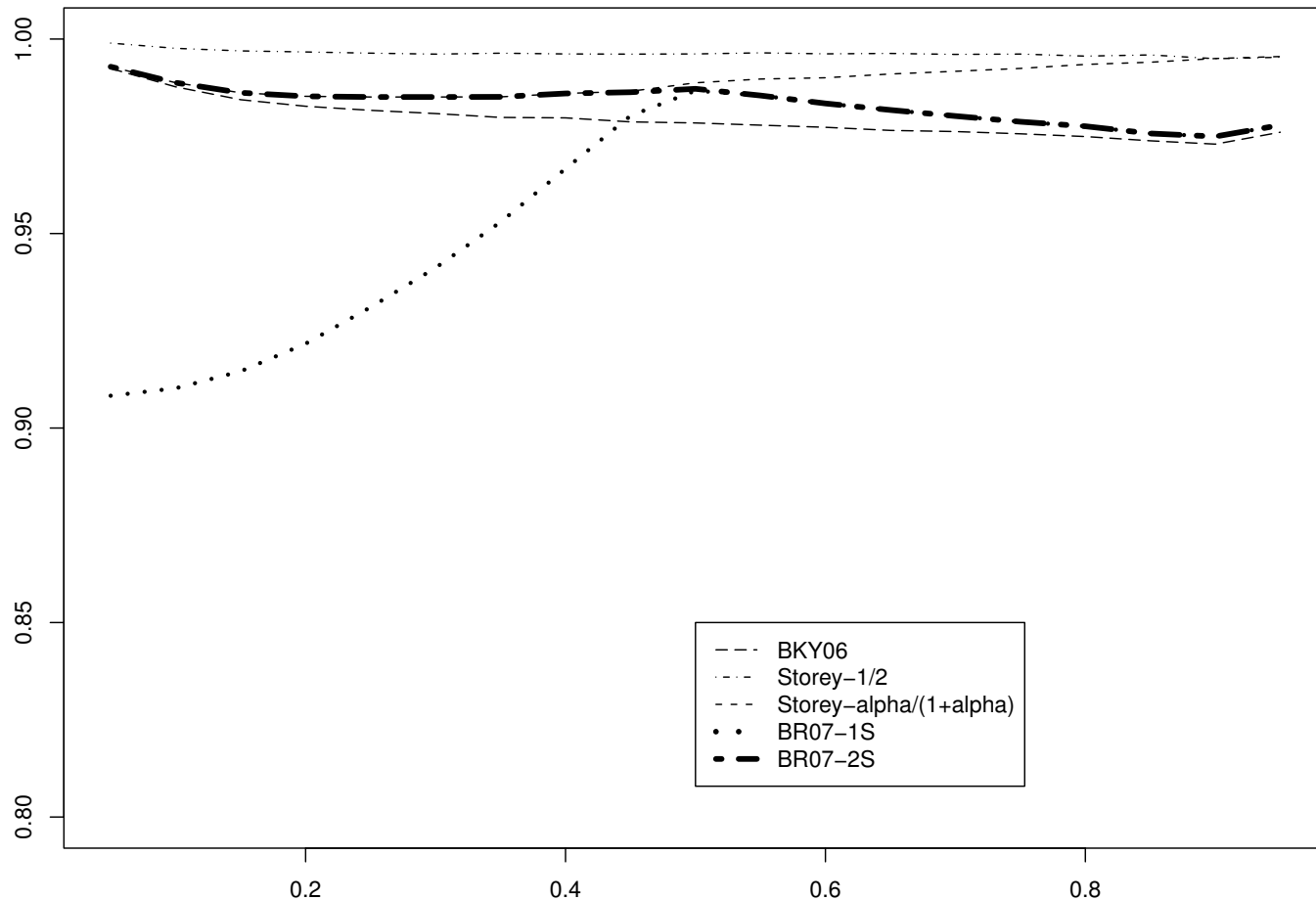
I. Simulations, Power, indep. case

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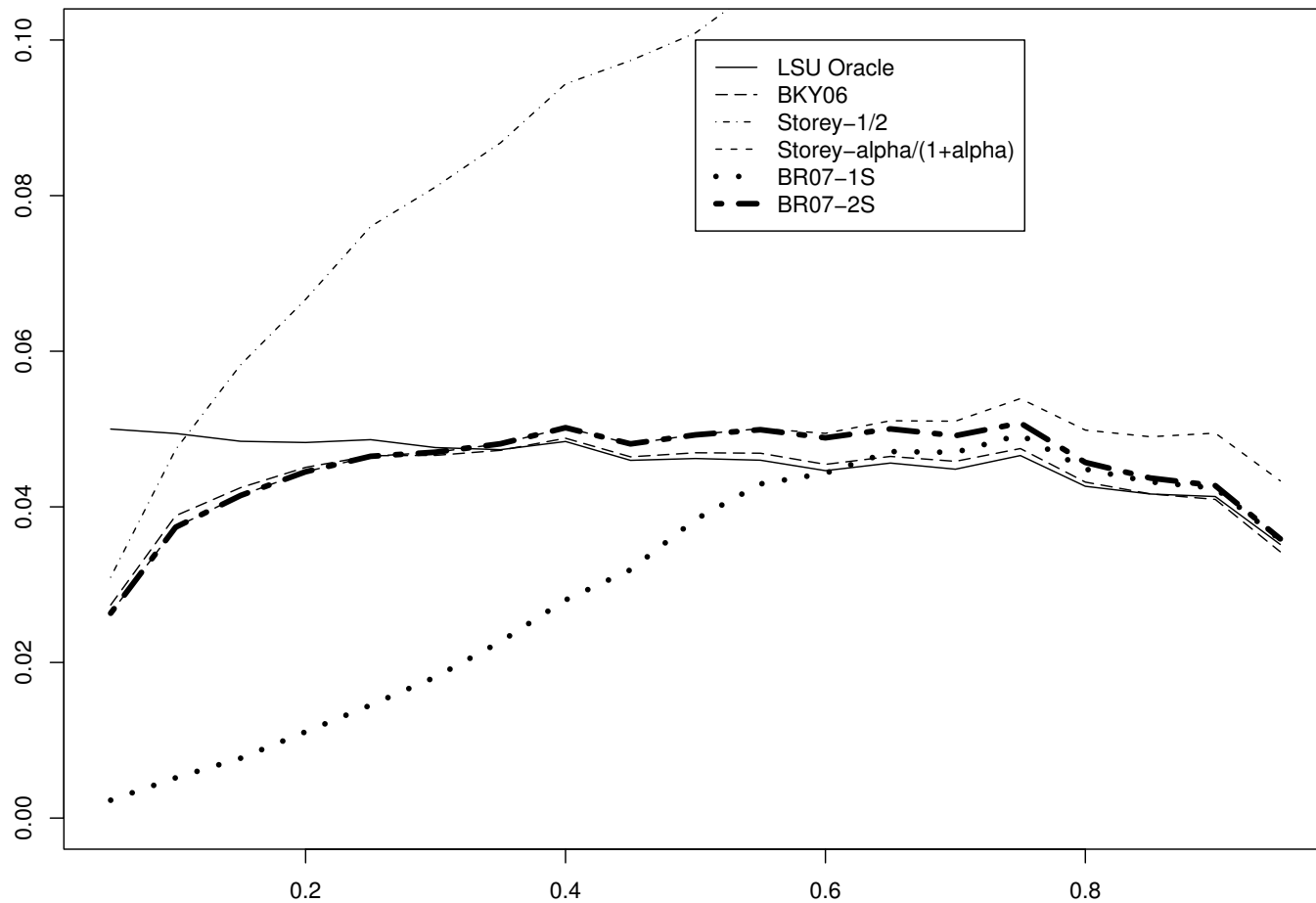
$\rho = 0$ (independent case) :



Storey-1/2 \gg Storey- $\alpha/(1 + \alpha)$ \gg BR07-2S \gg BKY06

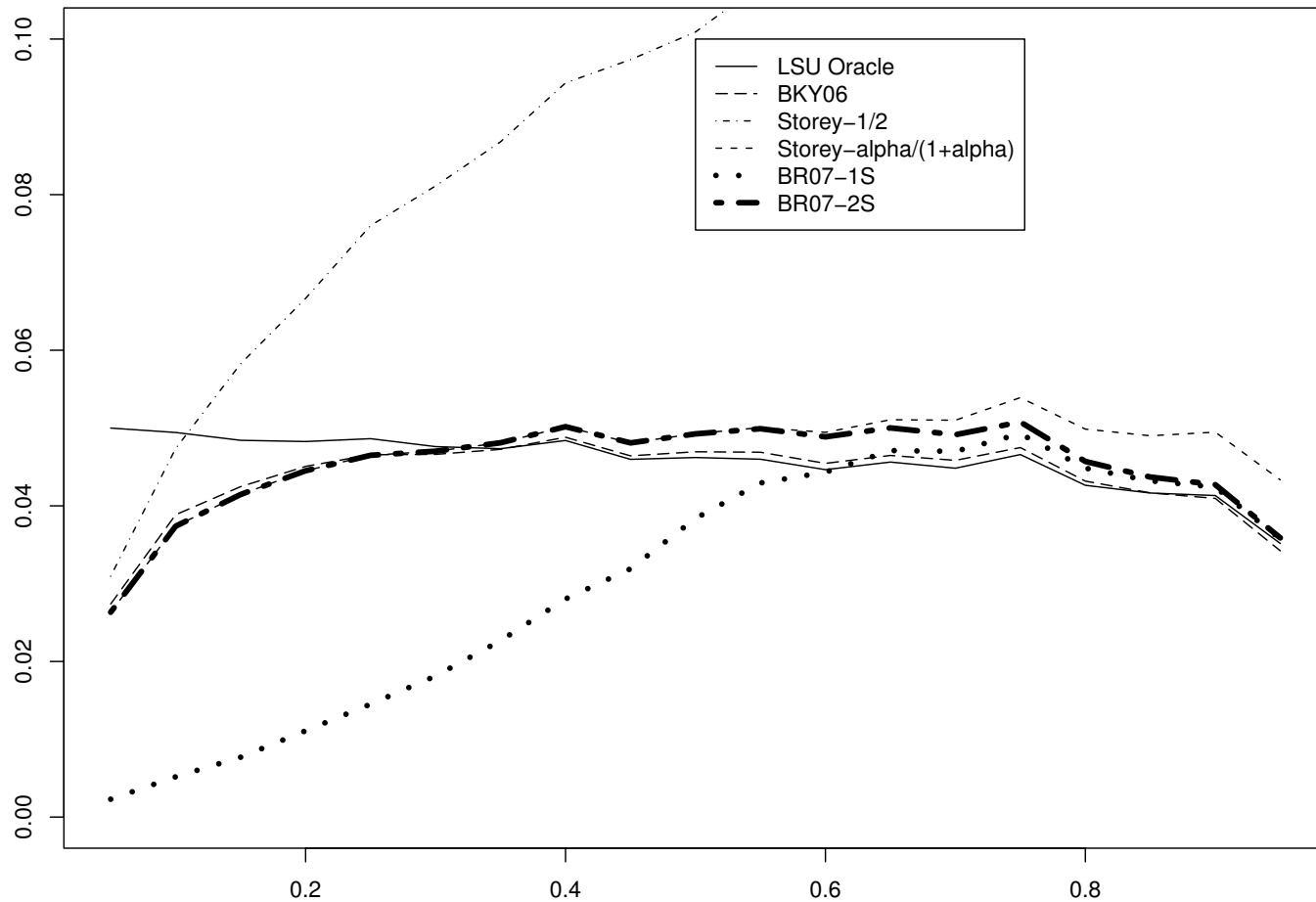
I. Simulations, FDR, with corr

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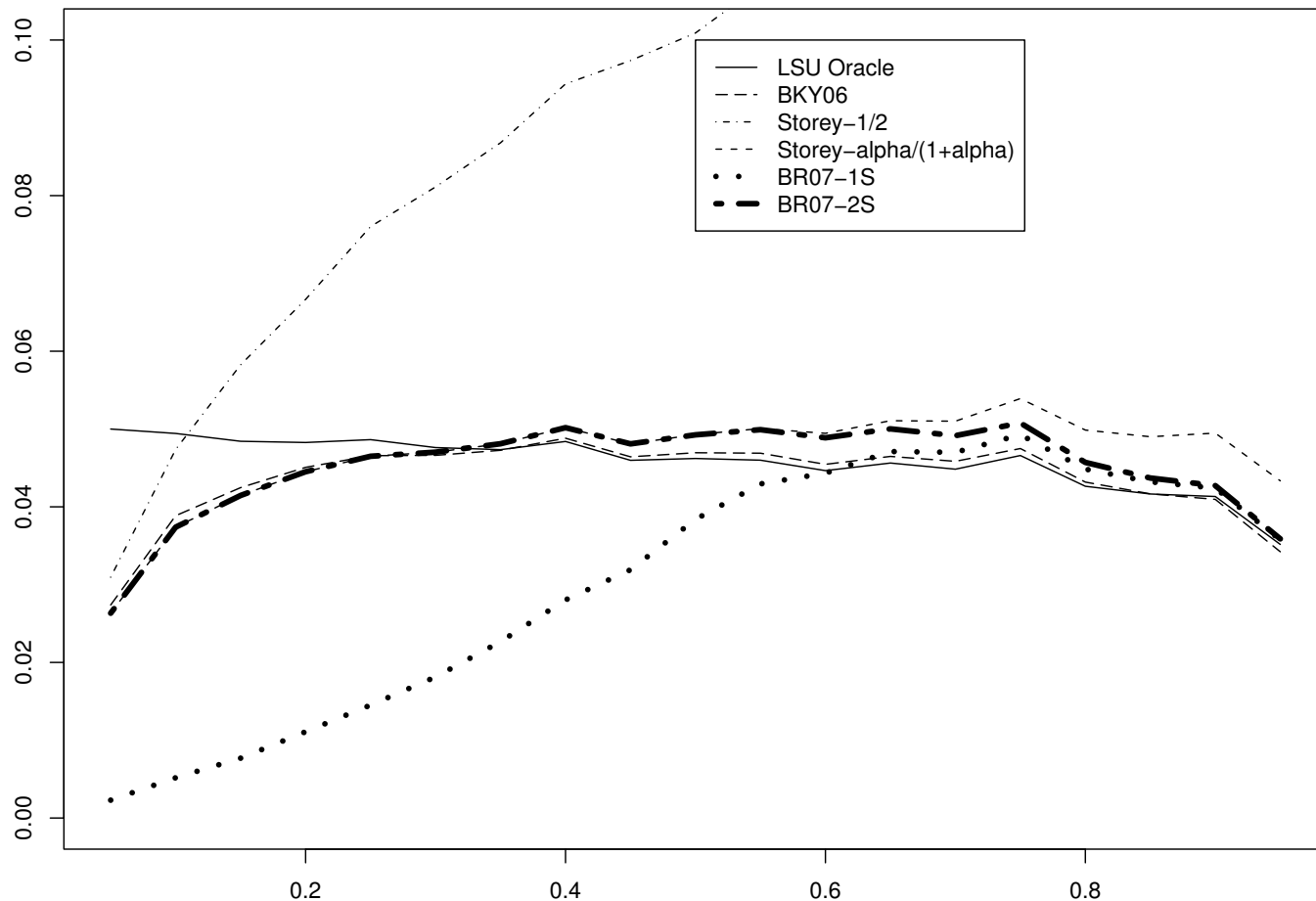
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⇒ Storey-1/2 is **not robust!** Storey- $\alpha/(1 + \alpha)$ not robust? (max $\simeq 0.054$)

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$\rho = 0.5$ (positive correlate case) :



⇒ Storey-1/2 is **not robust!** Storey- $\alpha/(1 + \alpha)$ not robust? (max $\simeq 0.054$)

⇒ New procedures **seem robust** to positive correlations

I I. Simulations

$m = 100, m_0 = 5, \rho = 0.1, 2 \leq \text{mean} \leq 5$

