A set-output point of view on FDR control

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Outline

I **A set-output point of view on classical procedures**

1. The "cardinal control" condition $\Rightarrow$ FDR control
2. The step-up procedures satisfy the "cardinal control" condition

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II **New adaptive procedures**

1. New adaptive procedures under independence
2. A first two-stage adaptive procedure under general dependence

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  No hypotheses for p_h if $h \in \mathcal{H}_1$.
- A multiple testing procedure : a (measurable) function

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

(return the rejected hypotheses)

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- A "careful" type I error for A: Family Wise Error Rate

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- A "more permissive" type I error [Benjamini and Hochberg (1995)] : False Discovery Rate of A

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

$\mathrm{FDR}(A) \leq \alpha \Rightarrow A$ contains (on average) less than α percent errors.

Goal in FDR control

Find multiple testing procedures A such that

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Remarks :
- m is fixed (non asymptotic)
- $\mathcal{H}_0$ is not random (frequentist approach)

Part I

A set-output point of view
on classical procedures

I.1. The "cardinal control" condition

Natural multiple testing procedure :

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$$\mathrm{FDR}(A) = \mathbf{E}\left[\frac{|\mathcal{H}_0 \cap A|}{|A|}\mathbf{I}\{|A| > 0\}\right] = \sum_{h \in \mathcal{H}_0} \mathbf{E}\left[\frac{\mathbf{I}\{p_h \leq t\}}{|A|}\right]$$

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Idea : include in t the feedback $|A|$

$\Rightarrow$ Consider $t = \alpha\beta(|A|)/m$, where $\beta : \mathbb{R}_+ \to \mathbb{R}_+$ non-decreasing.

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Condition introduced by Blanchard and Fleuret (2007) on A :

$$A \subset \{h \in \mathcal{H} |\, p_h \leq \alpha\beta(|A|)/m\} \quad (*)$$

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If A satisfies $(*)$,

$$\begin{aligned} \mathrm{FDR}(A) &= \mathbf{E}\left[\frac{|\mathcal{H}_0 \cap A|}{|A|}\mathbf{I}\{|A| > 0\}\right] \\ &\leq \sum_{h\in\mathcal{H}_0} \mathbf{E}\left[\frac{\mathbf{I}\{p_h \leq \alpha\beta(|A|)/m\}}{|A|}\right] \end{aligned}$$

I.1. Condition $(*) \Rightarrow$ FDR control

Lemma 1 (p-values satisfy PRDS) For a procedure A such that $|A|$ is non-increasing in each p-value and

$$A \subset \{h \in \mathcal{H} |\, p_h \leq \alpha |A|/m\},$$

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Lemma 2 (distribution free) For a procedure A such that :

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Remarks :
- the price of distribution-free : $\beta(|A|) \leq |A|$.
- Lemma 1 : new result adapted from Benjamini and Yekutieli (2001)
- Lemma 2 : result of Blanchard and Fleuret (2007)

I.1. Proof of Lemma 1

$$\begin{aligned}
\mathrm{FDR}(A) &\le \sum_{h\in\mathcal{H}_0} \mathbf{E}\left[\frac{\mathbf{I}\{p_h \le \alpha|A|/m\}}{|A|}\right] \\
&= \sum_{h\in\mathcal{H}_0} \sum_{k=1}^{m} \frac{1}{k}\mathbf{E}\left[\mathbf{I}\{p_h \le \alpha k/m\}\mathbf{I}\{|A| = k\}\right] \\
&\le \frac{\alpha}{m} \sum_{h\in\mathcal{H}_0} \left[\sum_{k=1}^{m} \mathbf{P}(|A| = k|\, p_h \le \alpha k/m)\right]
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\end{aligned}$$

$$\sum_{k=1}^{m}\mathbf{P}(|A| = k|\, p_h \leq \alpha k/m)$$

$$= \sum_{k=1}^{m}\left[\mathbf{P}(|A| \leq k|\, p_h \leq \alpha k/m) - \mathbf{P}(|A| \leq k-1|\, p_h \leq \alpha k/m)\right]$$

$$\leq \sum_{k=1}^{m}\left[\mathbf{P}(|A| \leq k|\, p_h \leq \alpha k/m) - \mathbf{P}(|A| \leq k-1|\, p_h \leq \alpha (k-1)/m)\right] \leq 1\Box$$

I.1. Proof of Lemma 2

Since for any $z > 0$ $\int_{y \geq z} y^{-2} dy = 1/z$,

$$
\begin{aligned}
\mathrm{FDR}(A) &\leq \sum_{h \in \mathcal{H}_0} \mathbf{E}\left[\frac{\mathbf{I}\{p_h \leq \alpha\beta(|A|)/m\}}{|A|} \right] \\
&= \sum_{h \in \mathcal{H}_0} \mathbf{E}\left[\int_{y \geq |A|} y^{-2} \mathbf{I}\{p_h \leq \alpha\beta(|A|)/m\} dy \right] \\
&\leq \sum_{h \in \mathcal{H}_0} \mathbf{E}\left[\int_{y > 0} y^{-2} \mathbf{I}\{p_h \leq \alpha\beta(y)/m\} dy \right] \\
&= \sum_{h \in \mathcal{H}_0} \int_{y > 0} y^{-2} \mathbf{P}(p_h \leq \alpha\beta(y)/m) dy \\
&\leq \alpha/m \sum_{h \in \mathcal{H}_0} \int_{y > 0} y^{-2} \beta(y) dy = \alpha m_0/m,
\end{aligned}
$$

using Fubini's theorem $\square$.

I.2. Step-up procedures satisfy $(*)$

If $p_{(1)} \leq \cdots \leq p_{(m)}$ are the ordered p-values :

Definition (step-up procedure with threshold $\alpha\beta(r)/m$)
If $\overline{r} := \max\{r \geq 0 |\, p_{(r)} \leq \alpha\beta(r)/m\}$, this is $\{h \in \mathcal{H} |\, p_h \leq \alpha\beta(\overline{r})/m\}$

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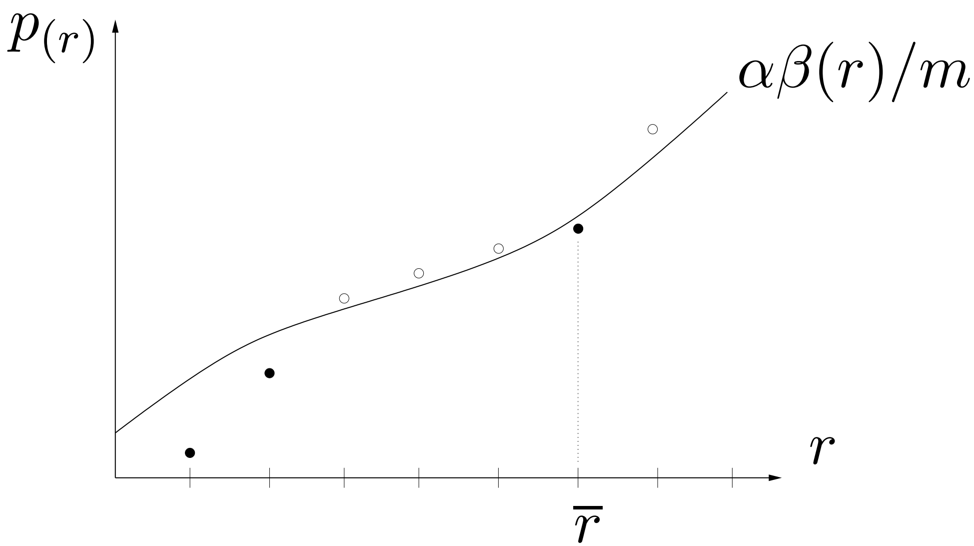

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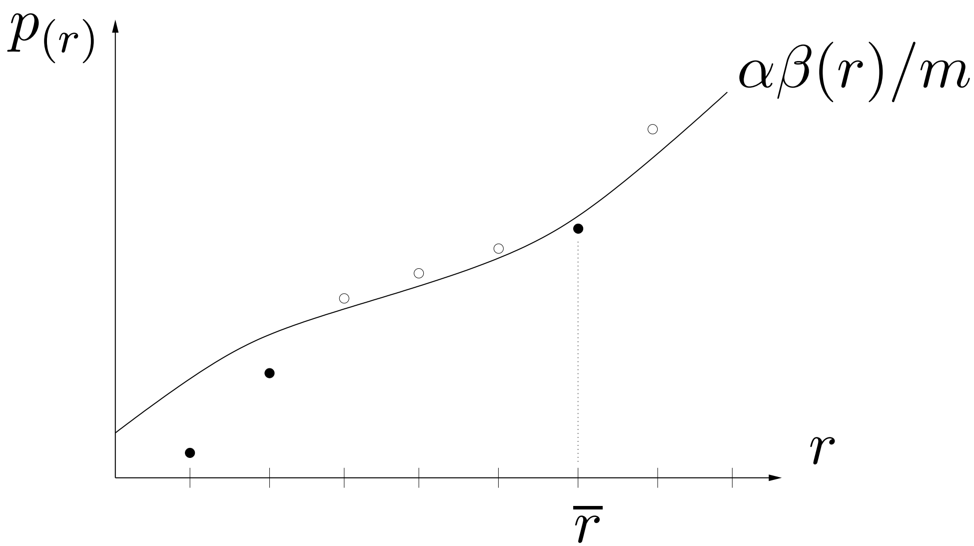

Proposition The step-up procedure A with threshold $\alpha\beta(r)/m$ satisfies

$$A \subset \{h \in \mathcal{H} |\, p_h \leq \alpha\beta(|A|)/m\} \;\; (*).$$

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We let

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The step-up procedure is $A(\overline{r})$. We apply this with $r = \overline{r}$. $\square$

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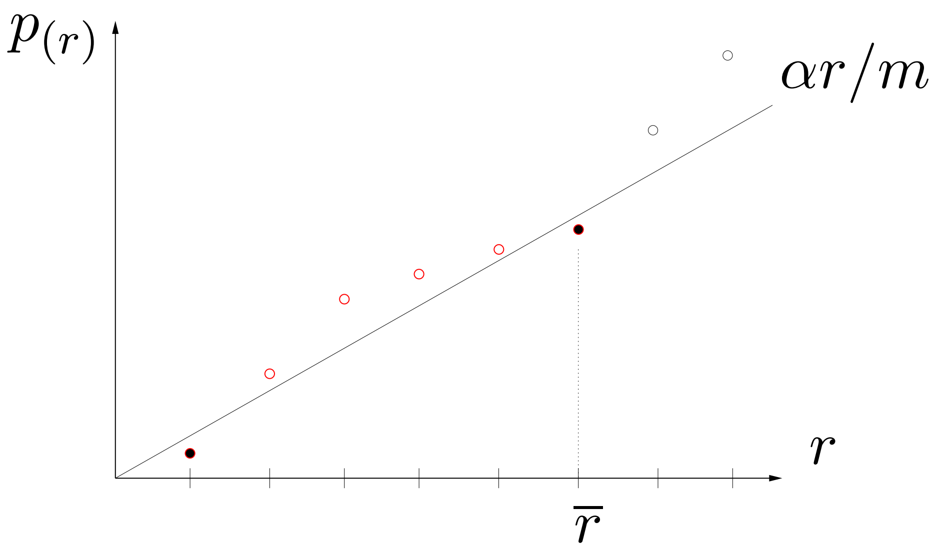

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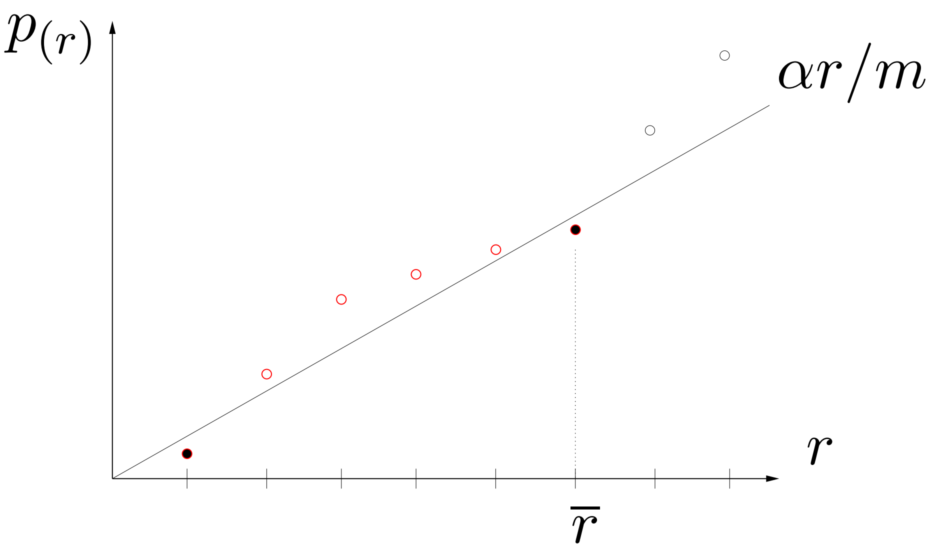

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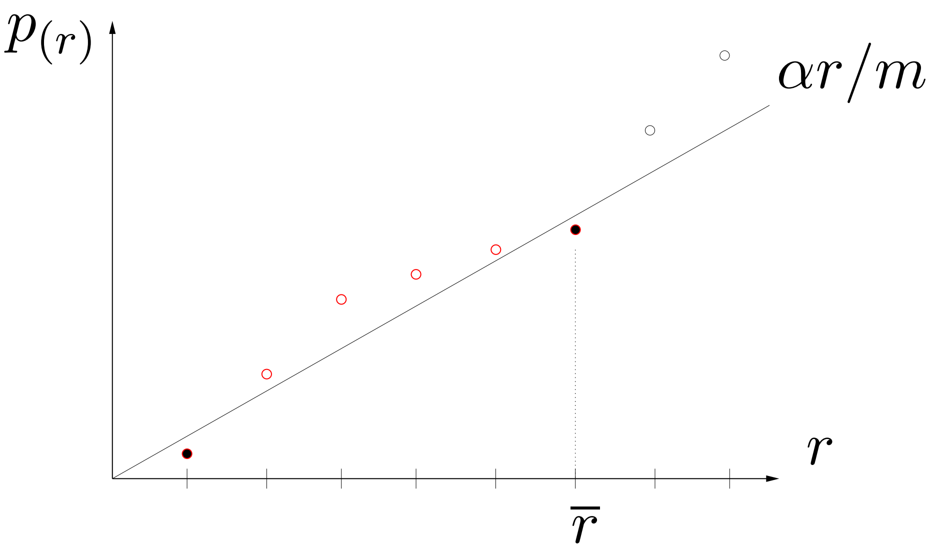

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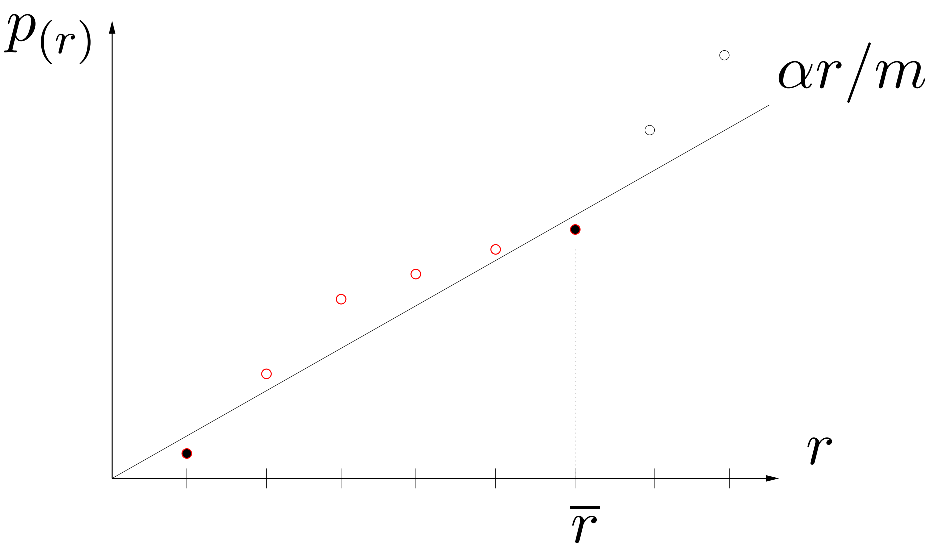

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- In the independent case : $\text{FDR}(A) = \alpha m_0/m$ (if p-values continuous)

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Theorem 2 (distribution free) :
For A the step-up procedure with threshold $\alpha\beta(r)/m$,
where $\beta(r) = \int_0^r u d\nu(u)$, and ν is some distribution on $(0, \infty)$,
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- This is a result of Blanchard and Fleuret (2007)
- The case $\beta(r) = \frac{r}{1+1/2+\cdots+1/m}$ is found with $\nu(\{k\}) = C/k$.
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  Different $\nu \Rightarrow$ different threshold functions β
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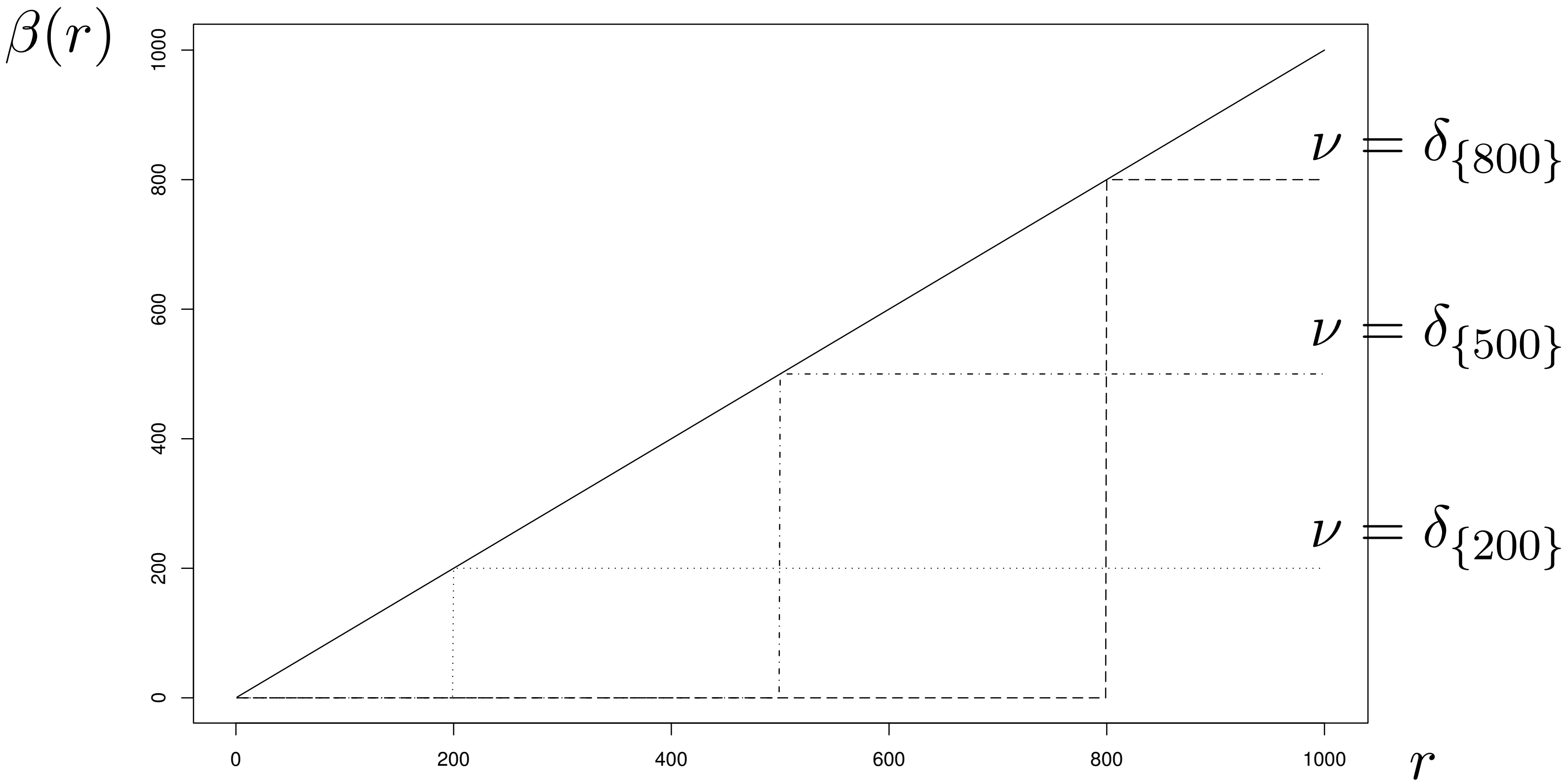
Question : Choice for ν ? i.e. choice for β?

I.2. Threshold functions with Dirac prior



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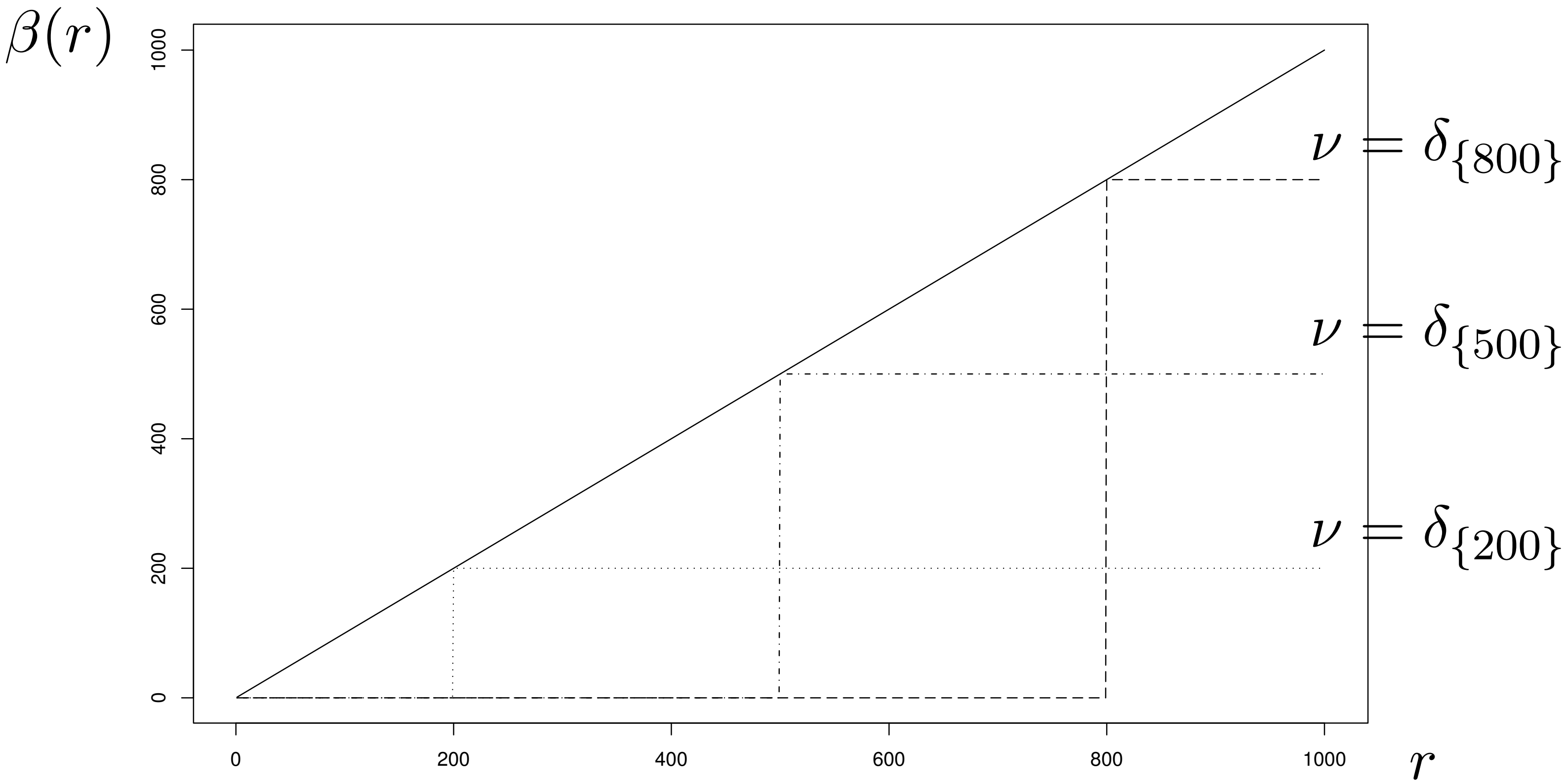
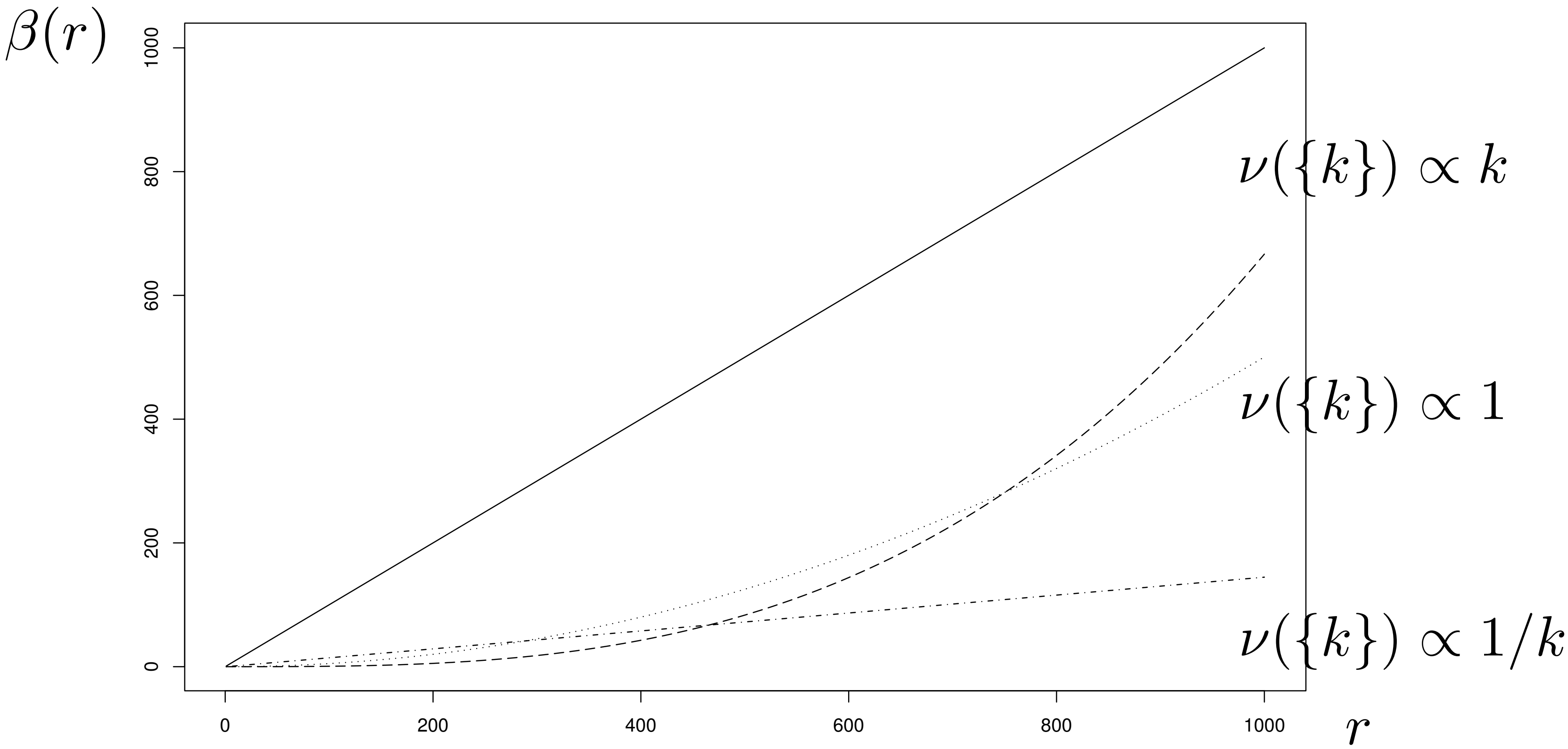


$\Rightarrow$ very effective in few cases and very bad in other cases.
$\Rightarrow$ very risky (ν very concentrated)

I.2. Threshold functions with power prior



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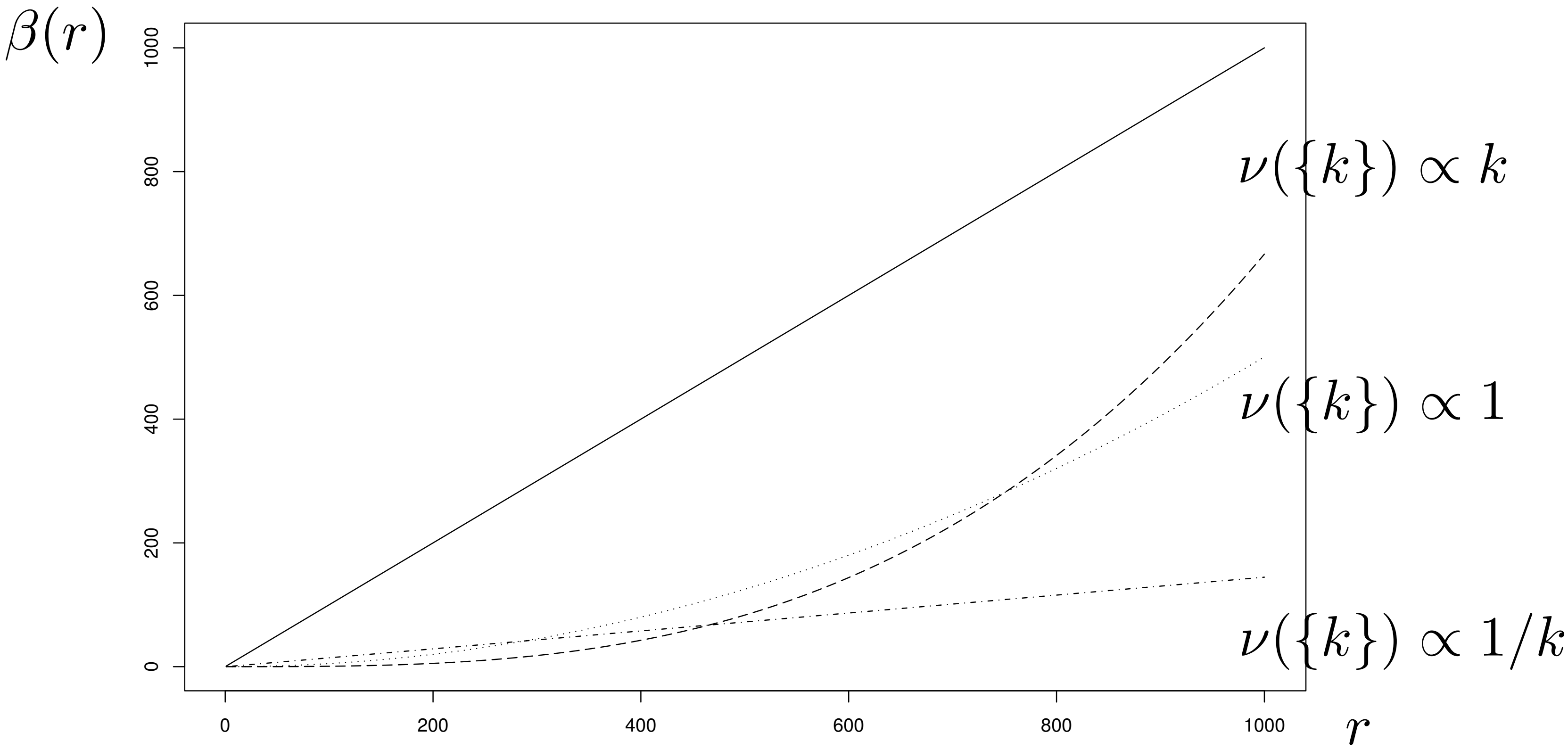

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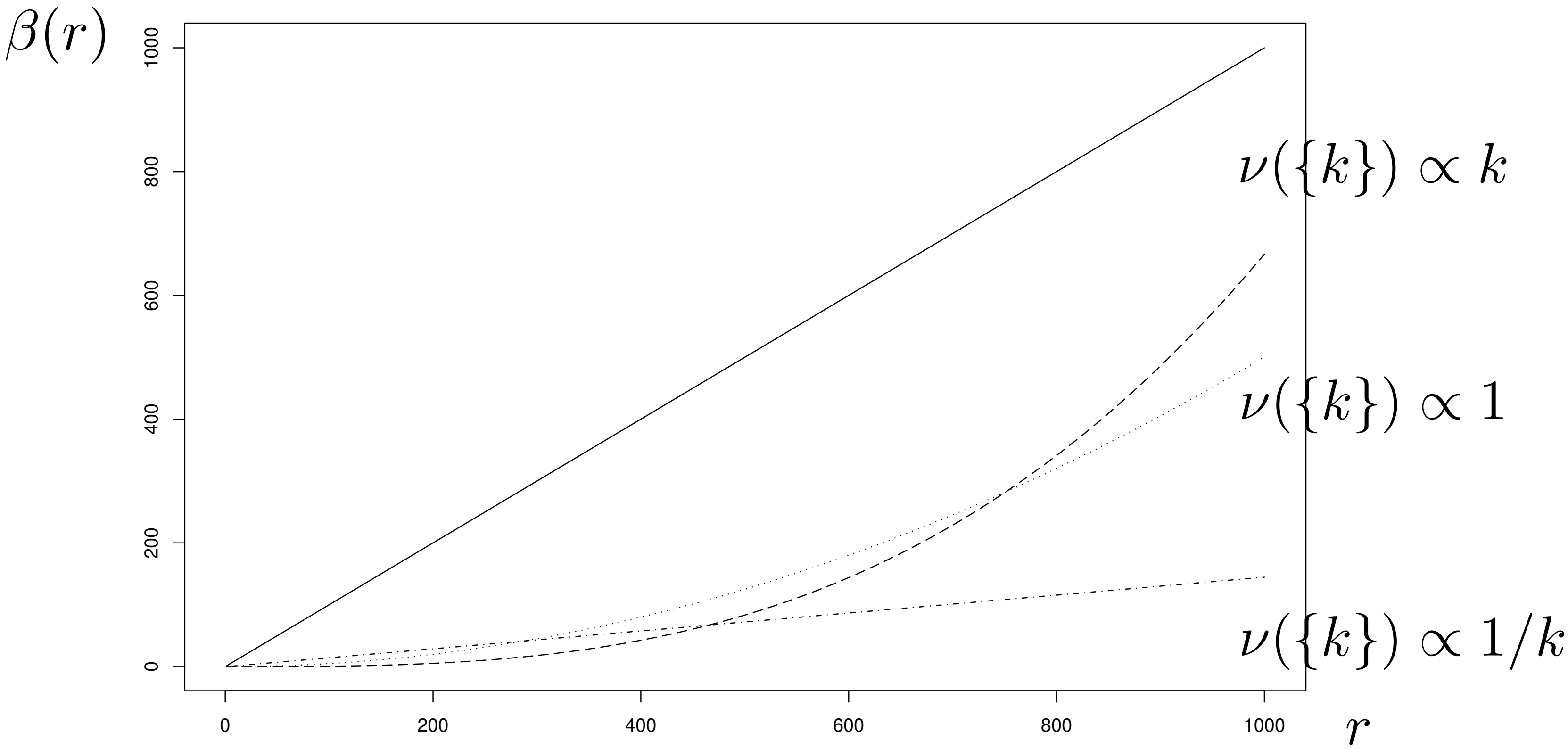

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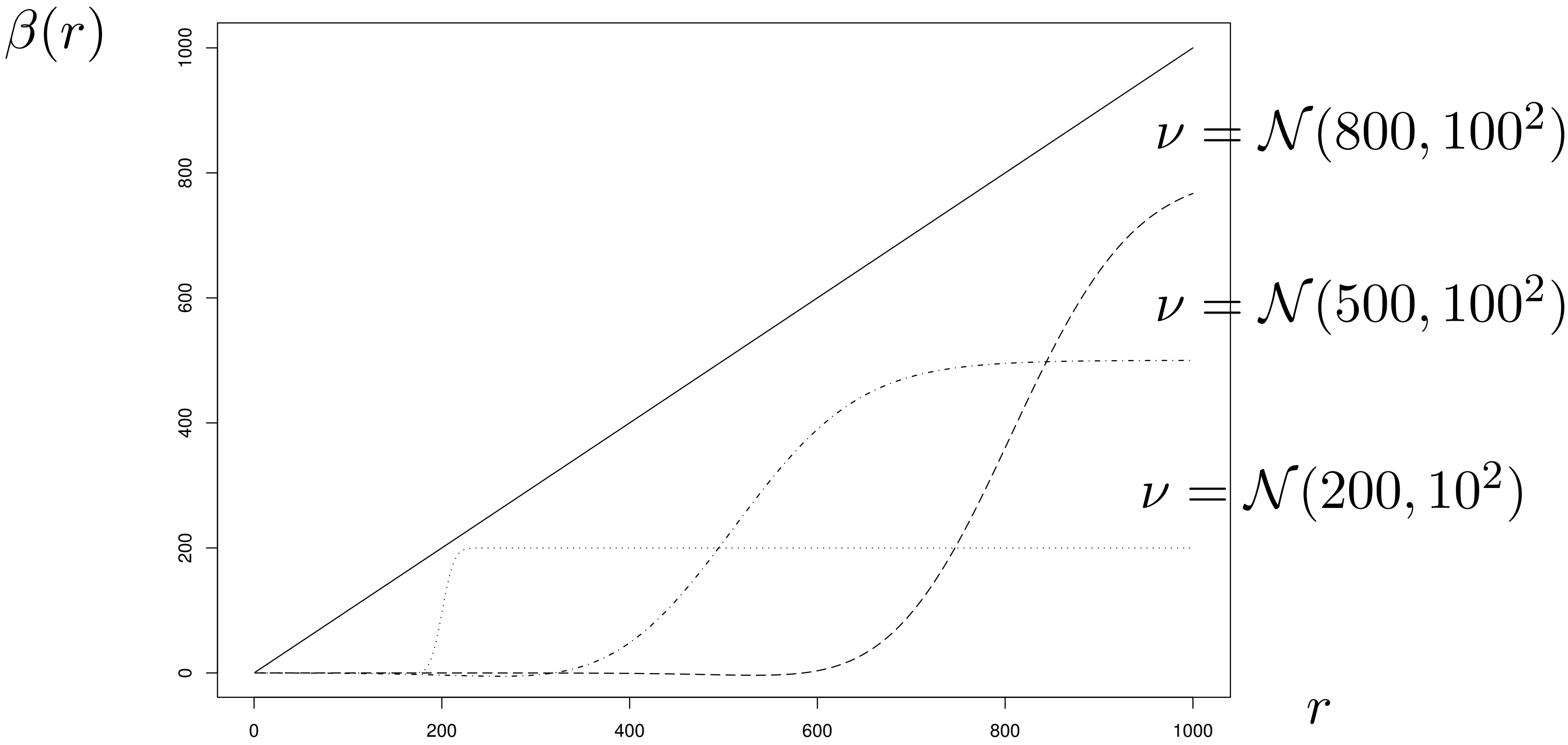
BY2001 ($\nu(\{k\}) \propto 1/k$) :

- more effective for "small" number of rejections cases
- less effective for "large" number of rejections cases

I.2. Threshold functions with Gaussian prior



The mean : the prior idea on the number of rejections

The variance : choose the risk.

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Choose $\nu = \nu(\mathbf{p})$ and still provide FDR control ?

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Theorems 1 and 2 provide that

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with $\beta \leftrightarrow$ dependency contexts.

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I I.1. π_0-adaptive procedures

Notations :
- $A_{\alpha,\beta}$ the step-up procedure with threshold $\alpha\beta(.)/m$
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- One-stage : β' is a deterministic threshold function.
- Two-stages : first $F(\mathbf{p}) \geq 1$ (under-)estimates π_0^{-1}, then $\beta' = \beta F$.

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The two-stages adaptive procedure Storey-λ :

1. $F = \frac{(1-\lambda)m}{|\{h \in \mathcal{H} | p_h > \lambda\}|+1}$ (modified Storey Estimator)
2. Take the step-up procedure A with threshold $\alpha Fr/m$

Classical choice : $\lambda = 1/2$.

I I.1. New π_0-adaptive procedures

Our new adaptive procedures that control FDR :

1. Under independence :
- First one-stage adaptive procedure.
- New two-stages adaptive procedure

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- First one-stage adaptive procedure.
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2. Under general dependence : first two-stages adaptive procedure.

I I.1. New one-stage adaptive procedure

Theorem 3 (p-values independent) : The step-up procedure with threshold

$$\frac{\alpha}{1+\alpha}\min\left(\frac{r}{m-r+1},1\right)$$

has a FDR smaller than α.

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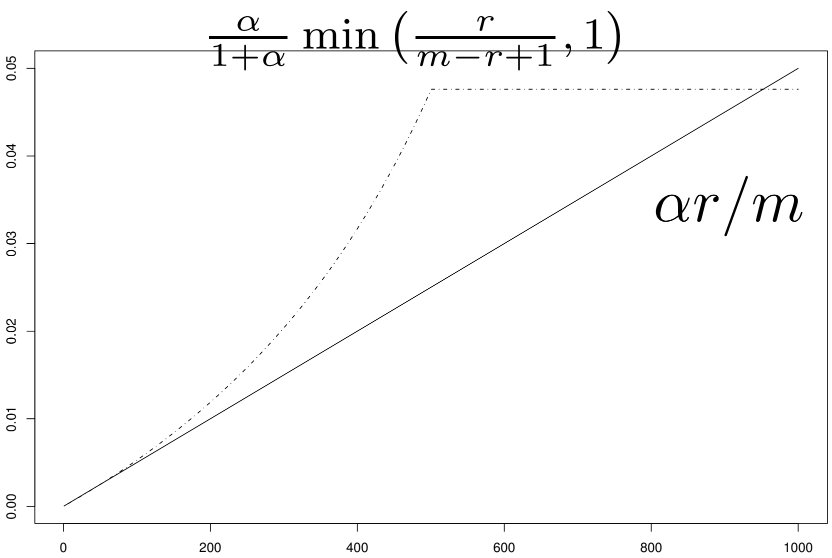

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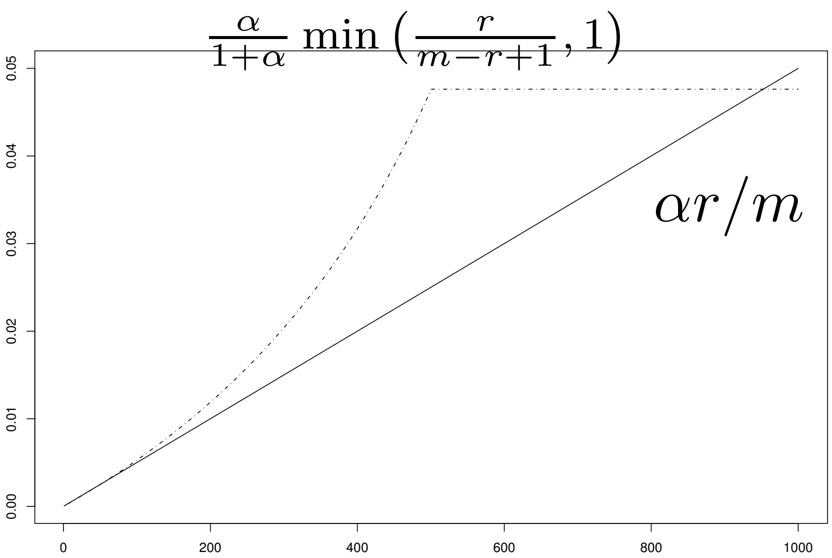

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Remarks :

- better than the linear step-up procedure (up to extrem cases)
- better than BKY06 for less than 50% of rejections (up to the "+1")

I I.1. New two-stages adaptive procedure

Theorem 4 (p-values independent) : Consider the two-stages procedure :

1. Apply the new one-stage adaptive procedure A_0 at level α and put $F = \frac{m}{m-|A_0|+1}$
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How these new results work on simulated data?
- independant case : comparison with Storey1/2?
- robustness to positive correlations ?

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For $k = 1, \ldots, m$, $Y_k \sim \mathcal{N}(\mu_k, 1)$, null hypotheses : "$\mu_k \leq 0$"

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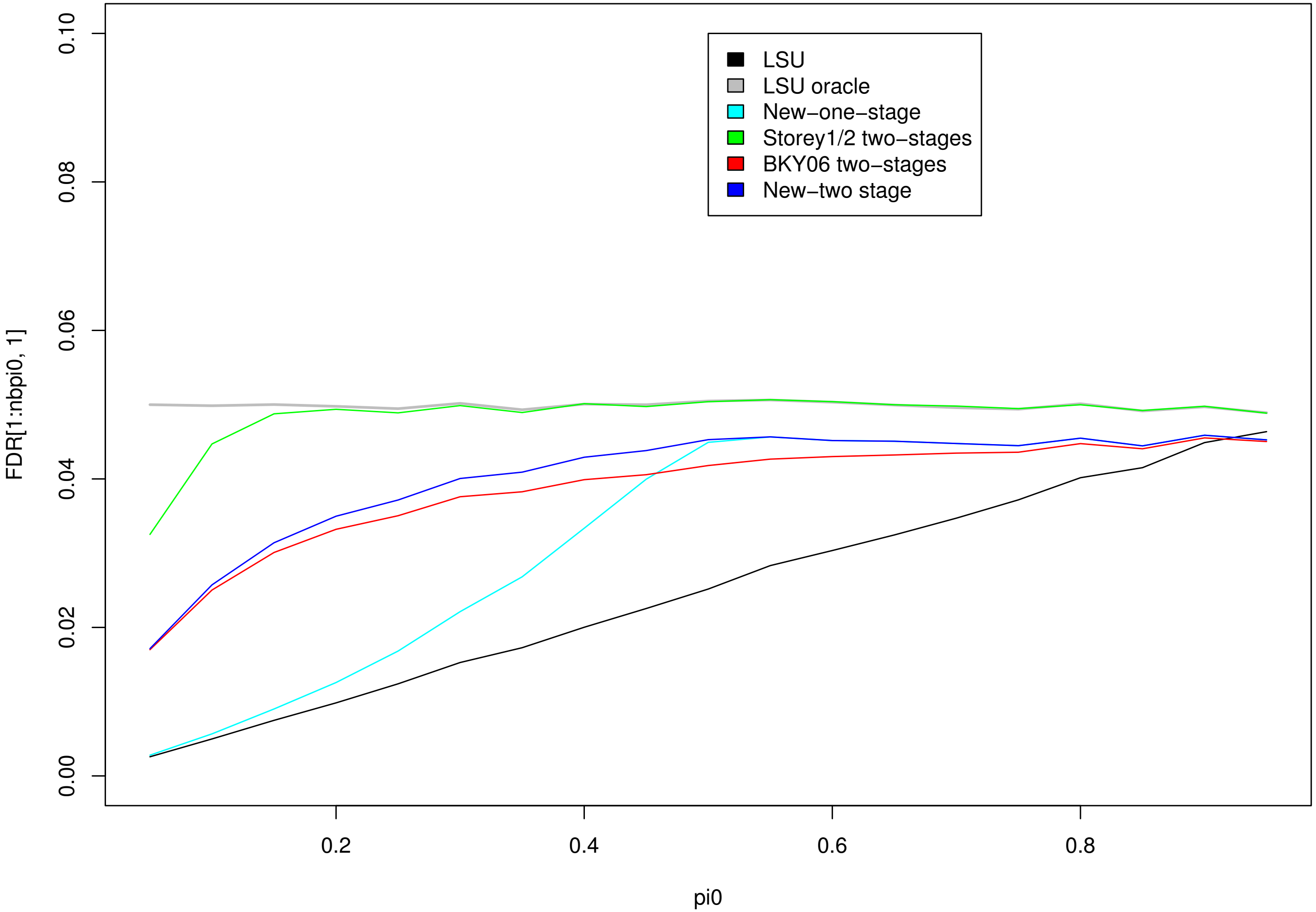
With 10000 simulations, $m = 100$:

- FDR estimation

- Power (in independent case) :
number of true rejections / number of true rejections of the oracle procedure (when we know π_0)

I I.1. Simulations, FDR, indep

$\rho = 0$ (independant case) :



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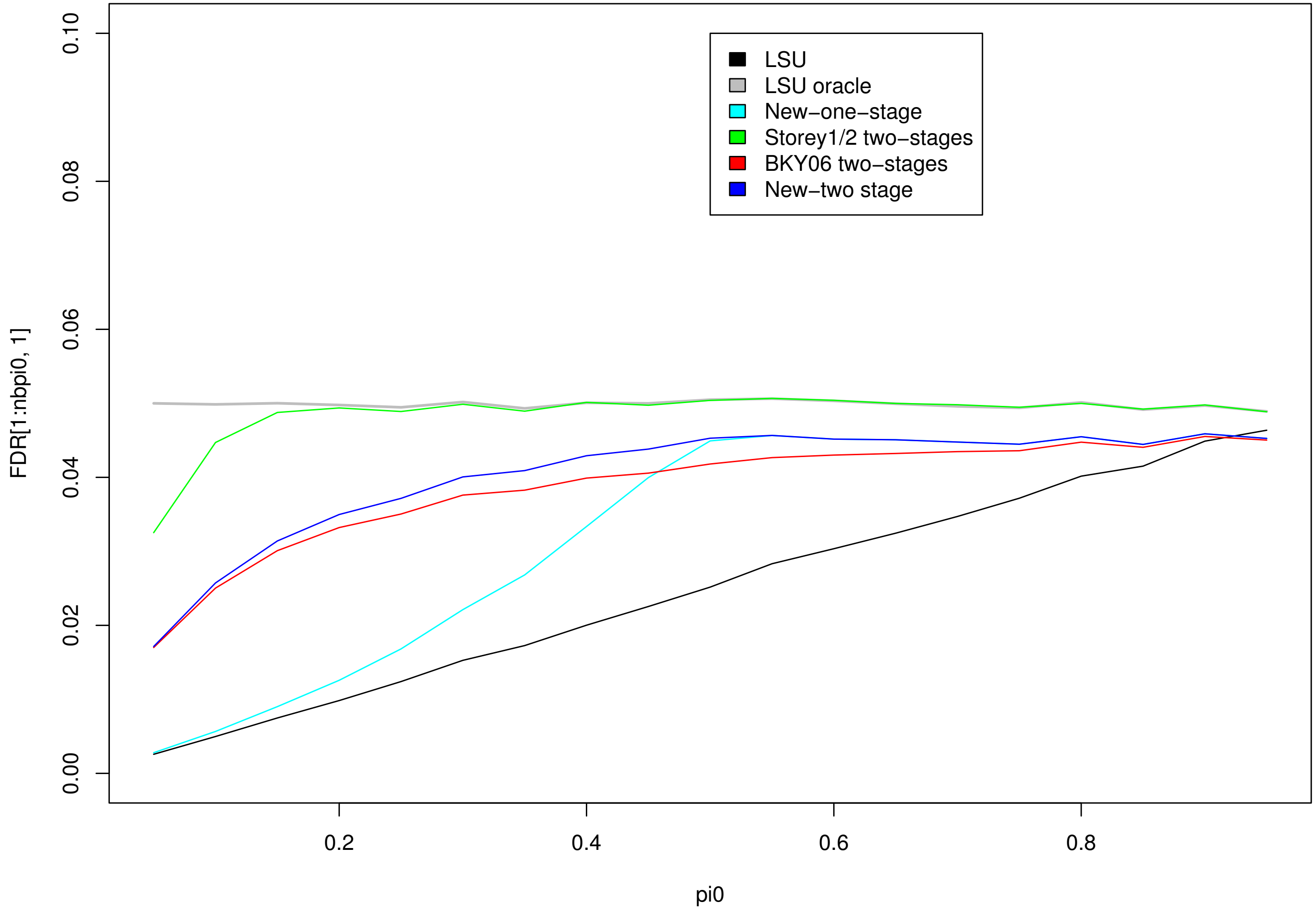

Accuracy of the FDR control :

$\Rightarrow$ New two-stages better than BKY06

$\Rightarrow$ Storey1/2 two-stages better.

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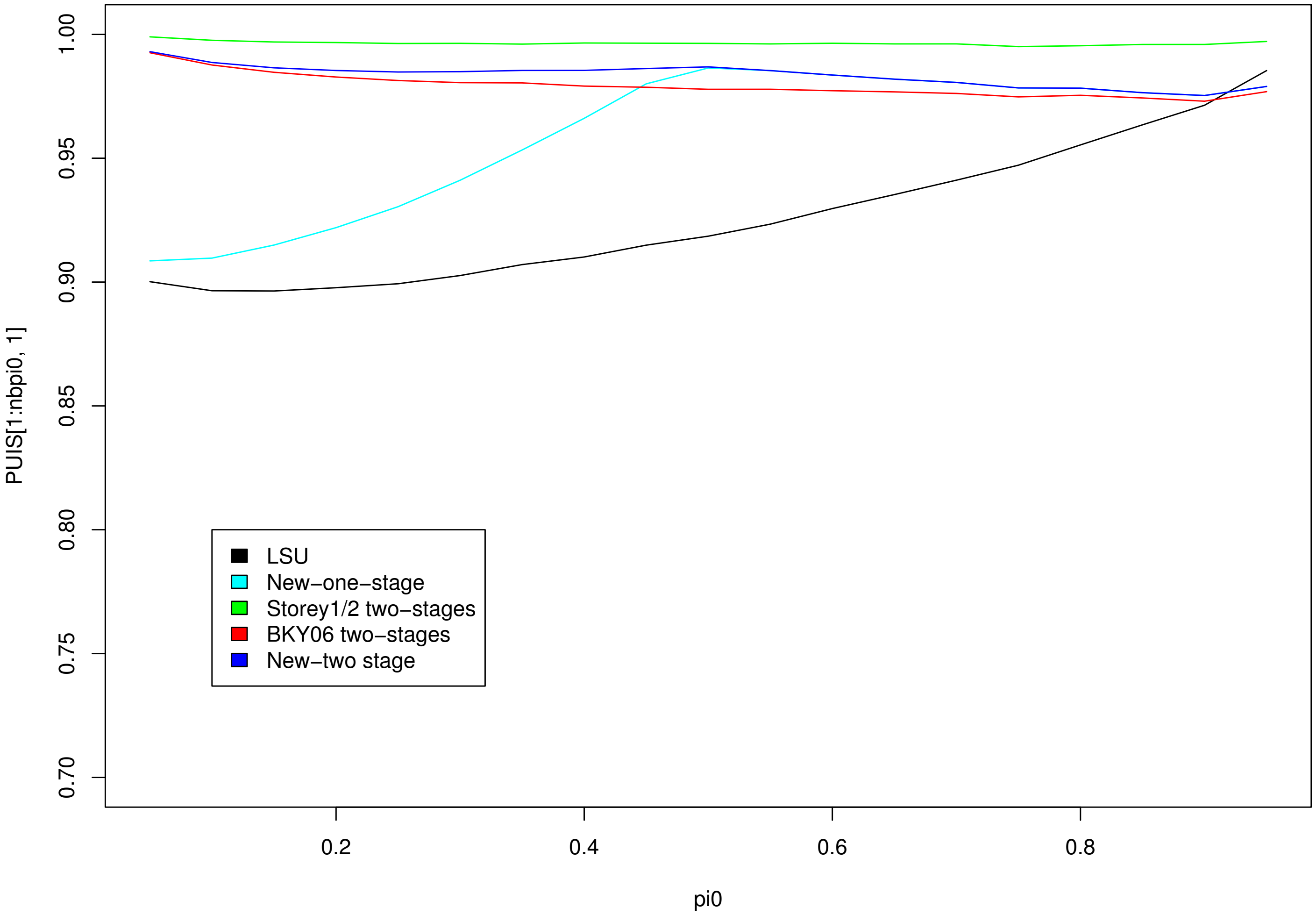

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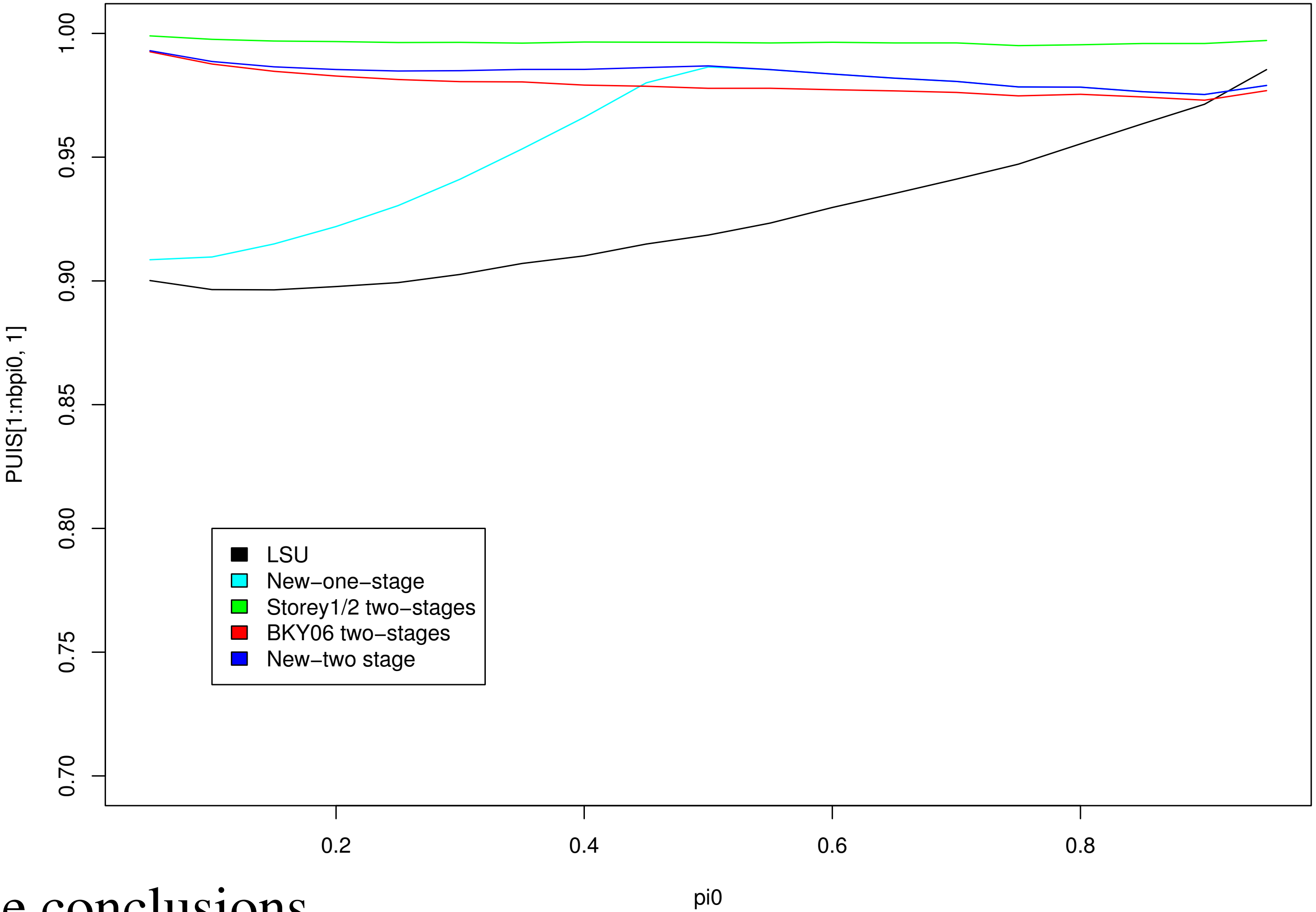
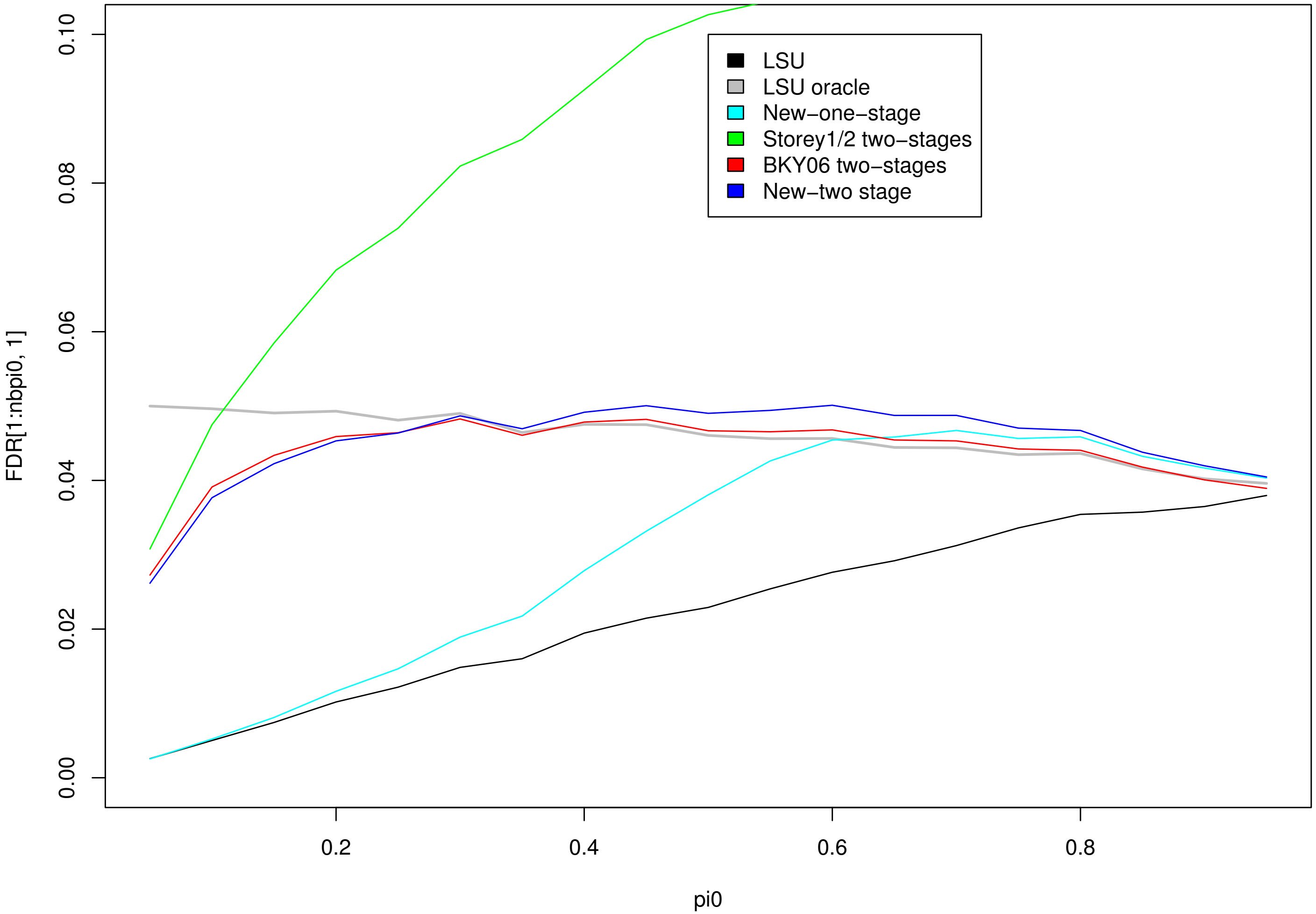


$\Rightarrow$ same conclusions.

I I.1. Simulations, FDR, with corr

$\rho = 0.5$ (correlate case) :



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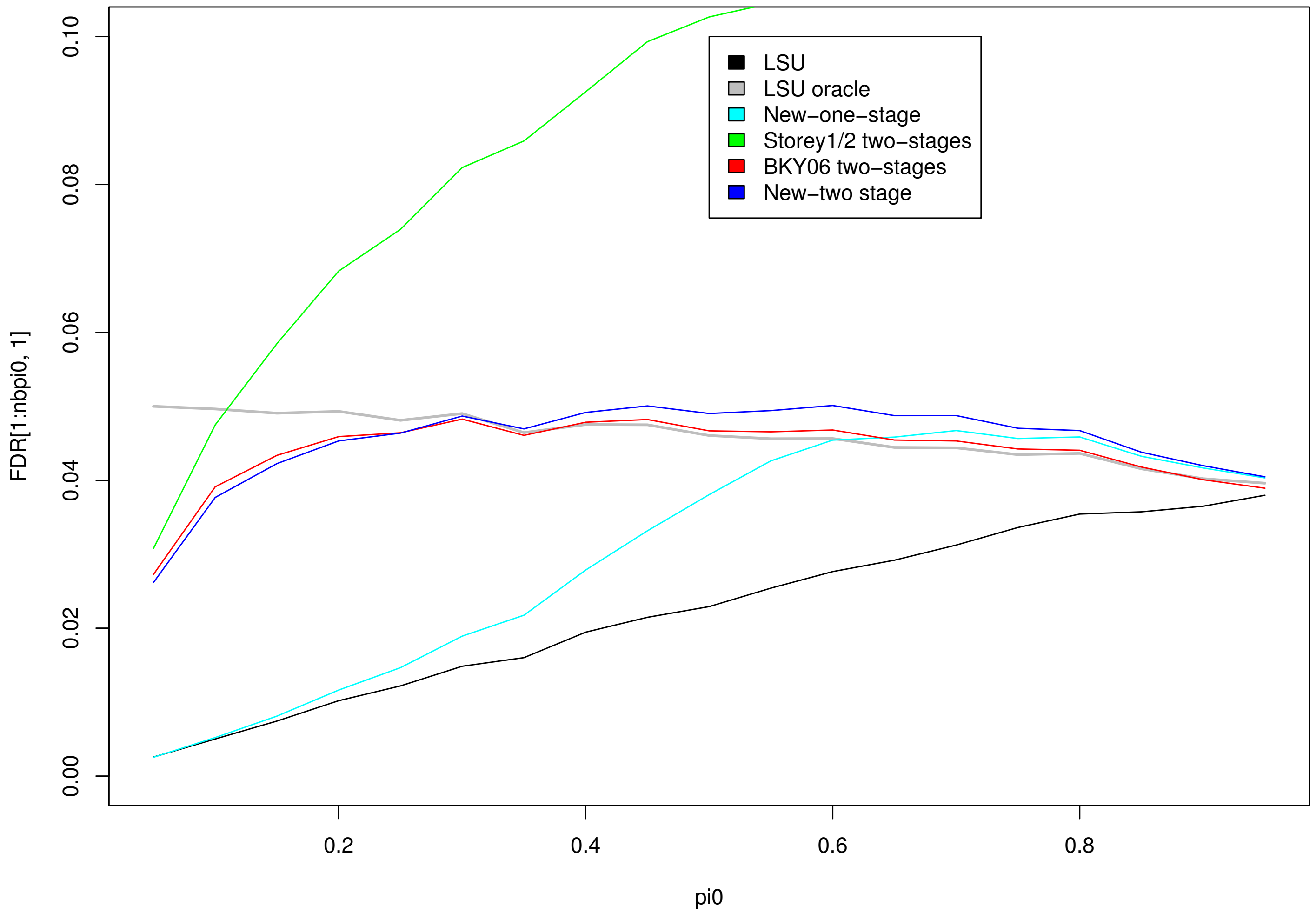

$\Rightarrow$ New procedures seems robust to positive correlations

$\Rightarrow$ Storey1/2 is not robust.

I I.2. Under general dependence

Recall Theorem 2 : $\mathrm{FDR}(A) \leq \alpha$ if A step-up with threshold $\alpha\beta(.)/m$, where $\beta \leftarrow$ prior distribution ν.

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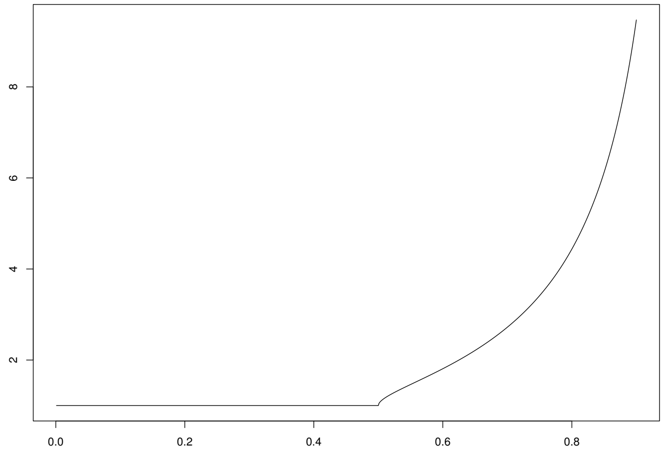
Theorem 5 (distribution free) : consider the two-stages procedure :

1. Apply the non-adaptive step-up procedure A_0 with threshold $(\alpha/4)\beta(.)/m$ and put $F = \frac{1}{1-\sqrt{(2|A_0|/m-1)_+}}$.
2. Take the step-up procedure A with threshold $(\alpha/2)\beta(.)F/m$

Then A satisfies $\mathrm{FDR}(A) \leq \alpha$.

I I.2. New two-stages adaptive procedure

$F(x) = \frac{1}{1 - \sqrt{(2x-1)_+}}$:



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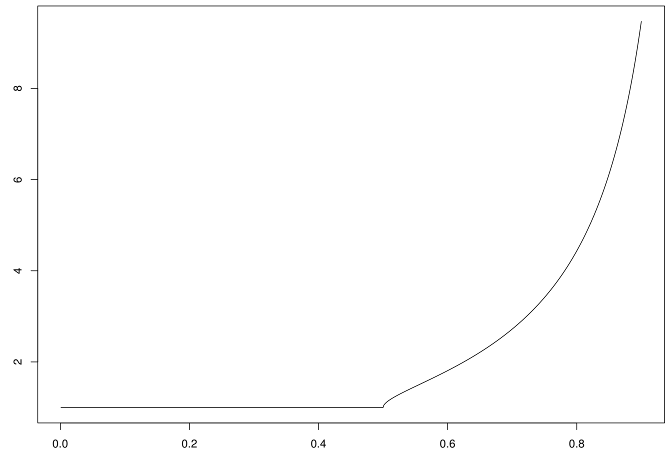

Remarks :
- new procedure better than non-adaptive if $F(|A_0|/m) \geq 2$ i.e $|A_0|/m \geq 62.5\%$ (and $|A_0|$ at level $\alpha/4$).

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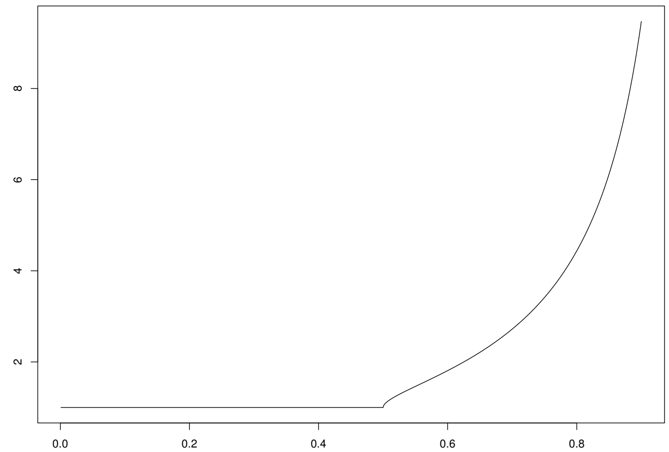

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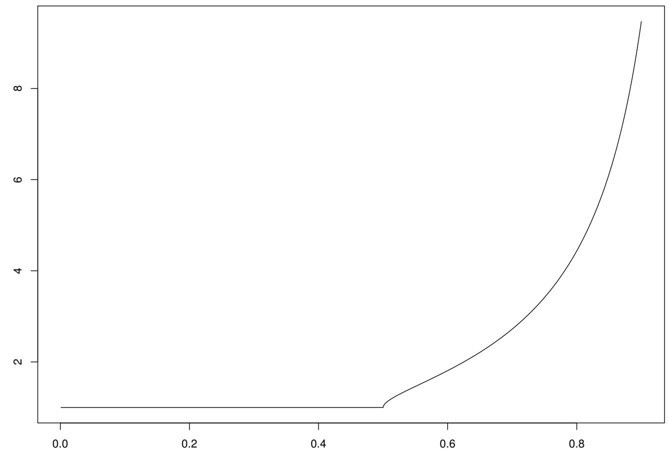

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$\Rightarrow$ interest more theoretical than practical.

Conclusion

We present :

- A set-output point of view $\Rightarrow$ shorter proofs for classical FDR control (+ some extension).
- New adaptive procedures (to π_0) :
  - $*$ in the independent case : one-stage (with explicit threshold) and then two-stages, better than BKY06 and seems robust to PRDS.
  - $*$ in the general dependent case : first two-stages procedure but only relevant when large number of rejections.

Future works

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- Choice of the prior ν ($\rightarrow \beta$) for the general dependent case

Thank you for your attention!

Appendix

I.1. The PRDS property

Benjamini and Yekutieli (2001) :
A subset $D \subset [0,1]^{\mathcal{H}}$ is called nondecreasing if for $\mathbf{p} \leq \mathbf{p}' \in [0,1]^{\mathcal{H}}$,

$$\mathbf{p} \in D \Rightarrow \mathbf{p}' \in D.$$

Then $\mathbf{p} = (p_h, h \in \mathcal{H})$ is PRDS on $\mathcal{H}_0$ if for all $h \in \mathcal{H}_0$ and nondecreasing set D,

$$u \in [0,1] \mapsto \mathbf{P}(\mathbf{p} \in D |\, p_h = u) \text{ is non-decreasing}$$

Examples :
- independent case
- p-value associated to Gaussian vector with positive correlations

Remark : if $|A(.)| \downarrow$, this implies for k fixed

$$u \in [0,1] \mapsto \mathbf{P}(|A(\mathbf{p})| \leq k |\, p_h \leq u) \text{ is non-decreasing}$$

Recent two-stage adaptive procedures

In Benjamini, Krieger and Yekutieli (2006) : main estimation procedures :

- "Modified" Storey Estimator $\alpha' = \alpha$ and $F(\mathbf{p}) = \frac{(1-\lambda)m}{|\{h \in \mathcal{H} | p_h > \lambda\}|+1}$
  Intuition : for λ "sufficiently large",

$$\frac{|\{h \in \mathcal{H} | p_h > \lambda\}|}{(1-\lambda)} \simeq \frac{|\{h \in \mathcal{H}_0 | p_h > \lambda\}|}{(1-\lambda)} \simeq m_0$$

  Choice for $\lambda \in (0,1)$? $\lambda = 1/2$ classically.

- Estimation with the linear procedure at level $\alpha' = \alpha/(1+\alpha)$: A_0
  Take $F(\mathbf{p}) = \frac{m}{m-|A_0|}$ for $|A_0| < m$ and $F(\mathbf{p}) = 1$ otherwise.

Theorem (BKY 2006) : In the two preceding cases, under independence,

the (two-stage) procedure with threshold $r \mapsto \alpha' r F(\mathbf{p})/m$ has a FDR $\leq \alpha$.

Summary

Non-adaptive : FDR controlled by $\alpha\pi_0$:

- in the independent case : LSU with equality
- in the dependent case :
  * if PRDS case : "worse" than independent so FDR control for LSU still provided
  * if general case : procedures β-SU robust to any dependence

Adaptive : FDR controlled by α :

- in the independent case : with accuracy with Storey 1/2, with a little less accuracy for new one-stage or BKY06 two-stages
- in the dependent case : new two-stages procedure only efficient when a lot of rejections.
  On simulations in PRDS case : new one-stage, BKY06 two-stages FDR$\leq\simeq \alpha$.