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# New FDP controlling procedures under dependence

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*Joint work with S. Delattre*<sup>2</sup>

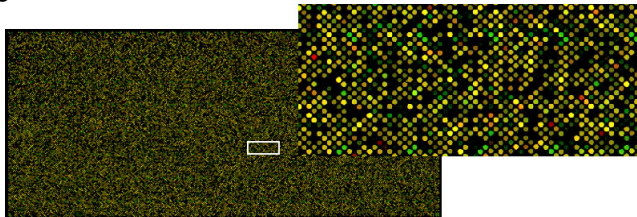
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<sup>2</sup>Laboratory LPMA, Université Paris Diderot (Paris 7), France

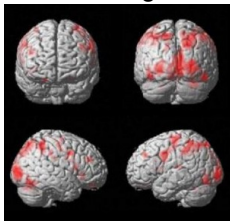
MCP 2017, 21-th June 2017, Riverside

# Massive and complex data

- ▶ **Microarray**  
interesting genes?



- ▶ **Neuroimaging (fMRI)**  
activated regions?



- ▶ **Astronomy**  
directions with stars?



# Adaptative procedures

- ▶ Model:  $P = (H, \Gamma)$  with  $H \in \{0, 1\}^m$  and  $\Gamma$  some “parameter”
- ▶ Type I error rates: Crit = FWER, FDR,  $\mathbf{P}(FDP > \gamma)$
- ▶ Build classical procedure  $R$ :

$$\sup_P \{\text{Crit}(R, P)\} \leq \text{ and } \approx \alpha$$

- ▶ Build adaptive procedure  $R = R(\hat{\Gamma})$  :

$$\forall P, \text{ Crit}(R, P) \leq \text{ and } \approx \alpha$$

- ★  $\Gamma$  = proportion of signal: [Holm (1979)], [Storey (2002)], [Benjamini et al (2006)], [Sarkar (2008)], [Blanchard and R. (2009)], [Finner et al (2009)], [Li and Barber (2017)], ...
- ★  $\Gamma$  = effect sizes of signal: [Wasserman and Roeder (2006)], [R. and van de Wiel (2009)],...
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# Dependence and multiple testing

- ▶ non-adaptive: survive to dependence
- ▶ adaptive: learn dependence
- ▶ FWER:
  - non-adaptive: [Bonferroni (1935)], [Benditkis et al (2015)], ...
  - adaptive: [Westfall and Young (1993)], [Romano and Wolf (2005)], ...
- ▶ FDR:
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- ▶ FDP:
  - non-adaptive: [Lehmann and Romano (2005)], [Romano and Shaikh (2006)]...
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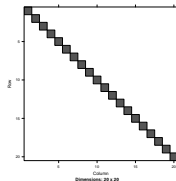
# Setting

We observe

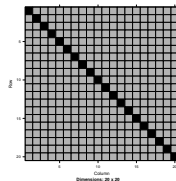
$$\begin{pmatrix} X_1 \\ X_2 \\ \vdots \\ X_m \end{pmatrix} = \begin{pmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_m \end{pmatrix} + \mathcal{N}(0, \Gamma)$$

- ▶ Mean : some  $\mu_i = 0$ , some  $\mu_i \neq 0$  ( $\mu_i > 0$ )
- ▶ Noise : various covariance  $\Gamma$  here **known** !

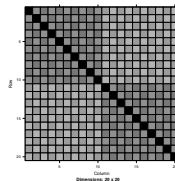
Indep.



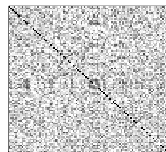
Equicorrelated



3-factor



Real Life



# FDP approach

## Procedure:

Step-up or step-down procedure with some critical values  $\tau_\ell, \ell = 1, \dots, m$ .  
Crossing point  $\hat{\ell}$ , thresholding at  $\tau_{\hat{\ell}}$

$$\text{FDP} = \frac{\# \text{ false rejections}}{1 \vee \# \text{ rejections}} = \frac{V(\tau_{\hat{\ell}})}{1 \vee R(\tau_{\hat{\ell}})}$$

## Aim

- Control the FDP : derive critical values  $\tau_\ell, 1 \leq \ell \leq m$ , s.t.

$$\mathbf{P}(\text{FDP}(\tau_{\hat{\ell}}) > \alpha) \leq \zeta \text{ (and } \approx \zeta) \text{ for all } (\mu, \Gamma)$$

- Choose  $\tau_\ell = \tau_\ell(\Gamma)$ , here  $\Gamma$  known

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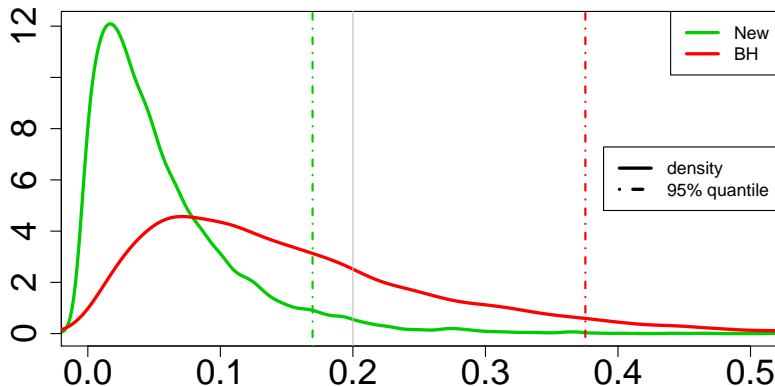
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# Limitation of BH procedure

$m = 1000$ ,  $\alpha = 0.2$ ,  $\zeta = 0.05$ , Equi-correlated  $\rho = 0.1$



[Korn et al. (2004)], among others

# Romano-Wolf's heuristic revisited

Calibrate critical values  $\tau_\ell$ 's :

Crossing point  $R(\tau_{\hat{\ell}}) = \hat{\ell}$  assume  $\hat{\ell} = \ell_0$

$$\mathbf{P}(\text{FDP}(\tau_{\ell_0}) > \alpha) = \mathbf{P}(V(\tau_{\ell_0}) > \alpha R(\tau_{\ell_0})) = \mathbf{P}(V(\tau_{\ell_0}) \geq \lfloor \alpha \ell_0 \rfloor + 1) \leq \zeta$$

e.g. using Markov's inequality

$$\mathbf{P}(V(\tau_{\ell_0}) \geq \lfloor \alpha \ell_0 \rfloor + 1) \leq \frac{m_0 \tau_{\ell_0}}{\lfloor \alpha \ell_0 \rfloor + 1} \leq \frac{m \tau_{\ell_0}}{\lfloor \alpha \ell_0 \rfloor + 1} \text{ gives } \tau_\ell = \frac{\zeta(\lfloor \alpha \ell \rfloor + 1)}{m}$$

Several other "bounding devices" adapting to dependence

▶  $K$ -Markov

▶ Exact: for  $Z \sim \mathcal{N}(0, \Gamma)$ ,

$$\mathbf{P}(V(t) \geq k) \leq \mathbf{P}(V'(t) \geq k) \text{ for } V'(t) = \sum_{i=1}^m \mathbf{1}\{\bar{\Phi}(Z_i) \leq t\},$$

⇒ Many new critical values !

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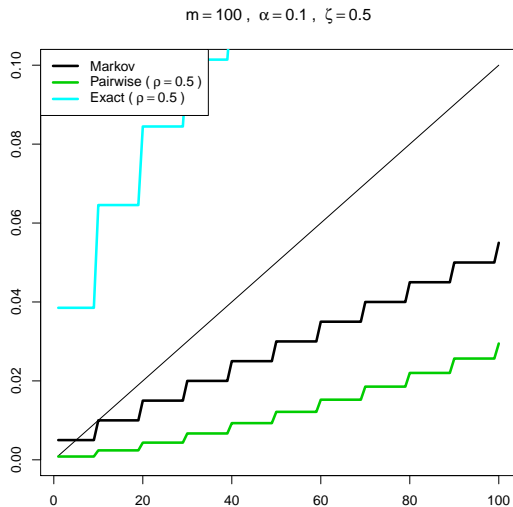
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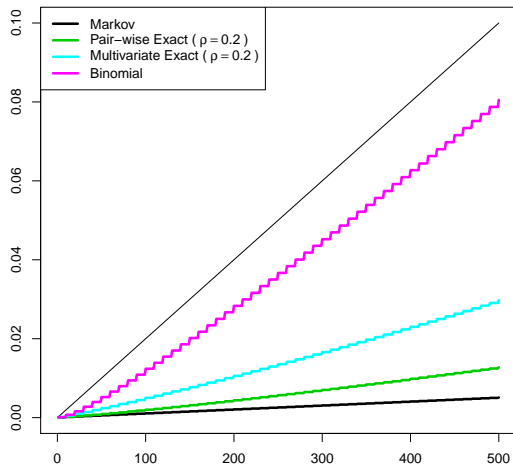


# RW heuristic critical values



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$m = 500$ ,  $\alpha = 0.1$ ,  $\zeta = 0.05$



# Theoretical study of RW's heuristic

Finite sample:

$$\mathbf{P}(\text{FDP} > \alpha) \leq \zeta$$

- ▶ validation under indep. between null  $p$ -values and alternative  $p$ -values  
[Guo et al (2014)], [Guo and Romano (2007)], [Romano and Wolf (2007)]
- ▶ counter-example under equi-correlation
- ▶ two theoretically valid modifications of RW's heuristic

Asymptotic:

$$\limsup_m \{\mathbf{P}(\text{FDP} > \alpha)\} \leq \zeta$$

- ▶ validation under weak-dependence (CLT for  $p$ -value process)
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# A finite sample valid correction

Let  $I_\ell = \mathbf{1}\{V'(\tau_\ell) \geq \lfloor \alpha \ell \rfloor + 1\}$  and

$$V'(t) = \sum_{i=1}^m \mathbf{1}\{\Phi(Z_i) \leq t\}, \quad Z \sim \mathcal{N}(0, \Gamma)$$

Now bound

$$\begin{aligned} \mathbf{P}(\text{FDP}(\tau_{\hat{\ell}}) > \alpha) &= \mathbf{P}(V(\tau_{\hat{\ell}}) \geq \lfloor \alpha \hat{\ell} \rfloor + 1) \\ &\leq \sum_{\ell=1}^m \mathbf{E}(I_\ell \mathbf{1}\{\hat{\ell} = \ell\}) \\ &= \sum_{\ell=1}^m \mathbf{E}(I_\ell \mathbf{1}\{\hat{\ell} \geq \ell\}) - \sum_{\ell=1}^{m-1} \mathbf{E}(I_\ell \mathbf{1}\{\hat{\ell} \geq \ell + 1\}) \\ &= \sum_{\ell=1}^m \mathbf{E}((I_\ell - I_{\ell-1}) \mathbf{1}\{\hat{\ell} \geq \ell\}) \\ &\leq \sum_{\ell=1}^m \mathbf{E}((I_\ell - I_{\ell-1})_+) := B(\tau, m, \Gamma) \end{aligned}$$

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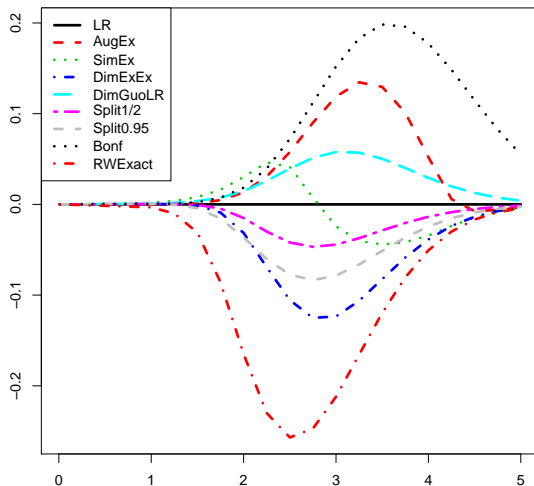
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# Illustration : FNR relative to LR

$m = 200$ ,  $\alpha = 0.2$ ,  $\zeta = 0.05$ ,  $\rho = 0.2$ ,  $\pi_0 = 0.5$



# RW heuristic made asymptotical

## Equi-correlated case

$$X_i = \mu_i + \rho^{1/2} W + (1 - \rho)^{1/2} \zeta_i, \quad 1 \leq i \leq m.$$

Then,

$$\mathbf{P}(V(\tau_\ell) \geq \lfloor \alpha \ell \rfloor + 1) \leq \mathbf{P}(V'(\tau_\ell) \geq \lfloor \alpha \ell \rfloor + 1) \approx \mathbf{P}(F(\tau_\ell, W) \geq \alpha \ell / m)$$

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$$F(t, W) = \overline{\Phi} \left( (\overline{\Phi}^{-1}(t) - \rho^{1/2} W) / (1 - \rho)^{1/2} \right) \text{ increasing w.r.t. } W$$

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New critical values

$$\tau_\ell = \overline{\Phi} \left( \rho^{1/2} \overline{\Phi}^{-1}(\zeta) + (1 - \rho)^{1/2} \overline{\Phi}^{-1}(\alpha \ell / m) \right)$$

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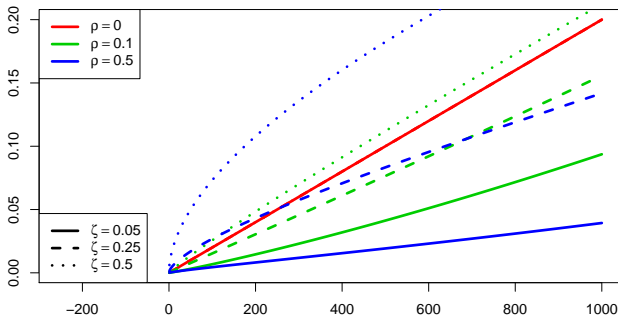
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# Result



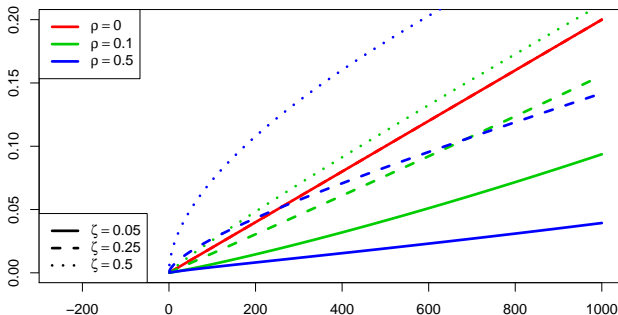
## Theorem [Delattre and R. (2015)]

One-sided Gaussian  $\rho$ -equi-correlation;  $\rho \in [0, 1)$ ,  $m_0/m \rightarrow \pi_0 \in (0, 1)$ , then

$$\limsup_m \mathbf{P}(\text{FDP}(\text{New}) > \alpha) \leq \zeta.$$

Can be generalized to  $Y_i = c_i W + \xi_i$ ,  $c_i \geq 0$

# Result



## Theorem [Delattre and R. (2015)]

One-sided Gaussian  $\rho$ -equi-correlation;  $\rho \in [0, 1)$ ,  $m_0/m \rightarrow \pi_0 \in (0, 1)$ , then

$$\limsup_m \mathbf{P}(\text{FDP}(\text{New}) > \alpha) \leq \zeta.$$

Can be generalized to  $Y_i = c_i W + \xi_i$ ,  $c_i \geq 0$

# Outlook

## Conclusions : FDP control

- ▶ incorporating known dependence is possible
- ▶ RW's heuristic can be justified in some cases
- ▶ and corrected otherwise

## Perspectives

- ▶ more justifications of RW's heuristic?
- ▶ unknown dependence (permutation?)
- ▶  $p$ -value correction under equi-correlation

## Advertising

2-year postdoc position in France about post hoc inference

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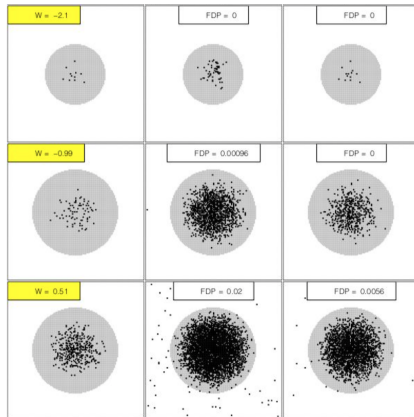
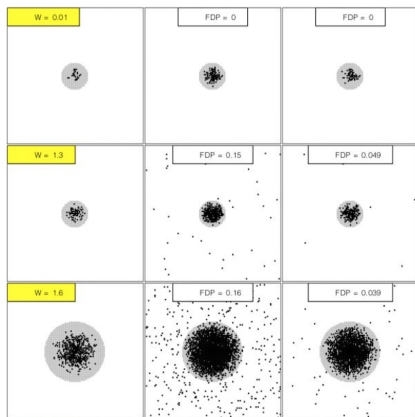
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# Illustration



# On going work: $p$ -value correction

Under equi-correlation

$$X_i = \mu_i + \rho^{1/2}W + (1 - \rho)^{1/2}\zeta_i, \quad 1 \leq i \leq m.$$

How to “kill”  $W$ ?

- ▶  $X_i^* = X_i - \bar{X}$  (add bias)
- ▶  $X_i^* = X_i - \rho^{1/2}\hat{W}$

Semi-parametric estimation of  $W$ :

- ▶  $\mu \in \mathbb{R}^m$  unknown sparse signal  $m_0/m \geq 1 - c m^{-\beta}$ ,  $\beta \in [0, 1)$
- ▶ minimax estimation rate of  $W$  is

$$m^{-\beta}(\log m)^{-\gamma}$$

with  $\gamma = 1/2$  (two-sided)  $\gamma = 3/2$  (one-sided).

Todo: properties of BH based on  $X_i^* = X_i - \rho^{1/2}\hat{W}$ ?

[Leek and Storey (2008)], [Friguet et al. (2009)], [Fan et al. (2012)]

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