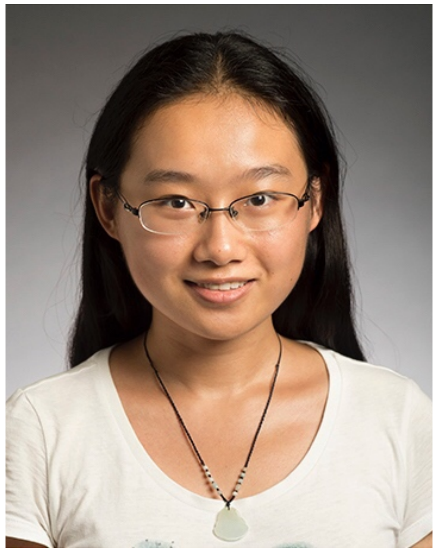
Dept. of Statistics and Data Science
Carnegie Mellon University

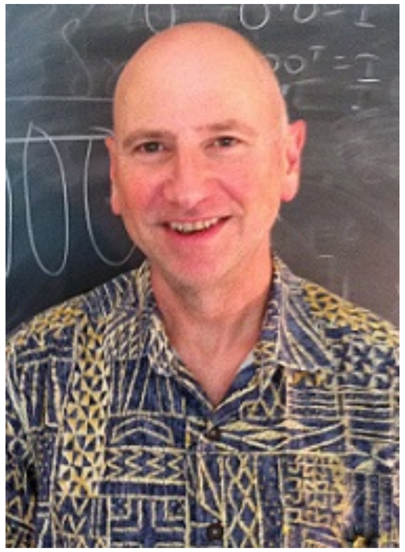
Familywise error rate control by interactive unmasking

Boyan Duan

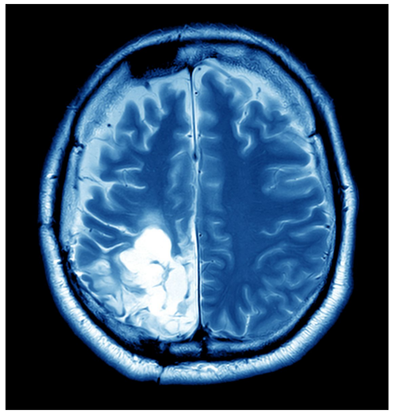
Aaditya Ramdas

Larry Wasserman





Motivating example: tumor detection in brain image



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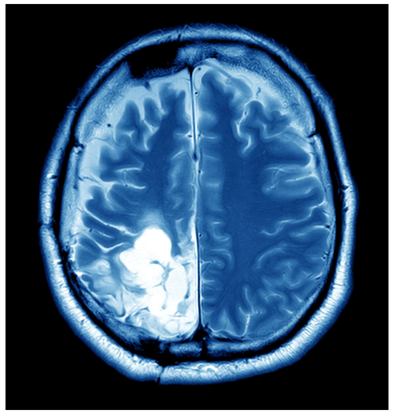

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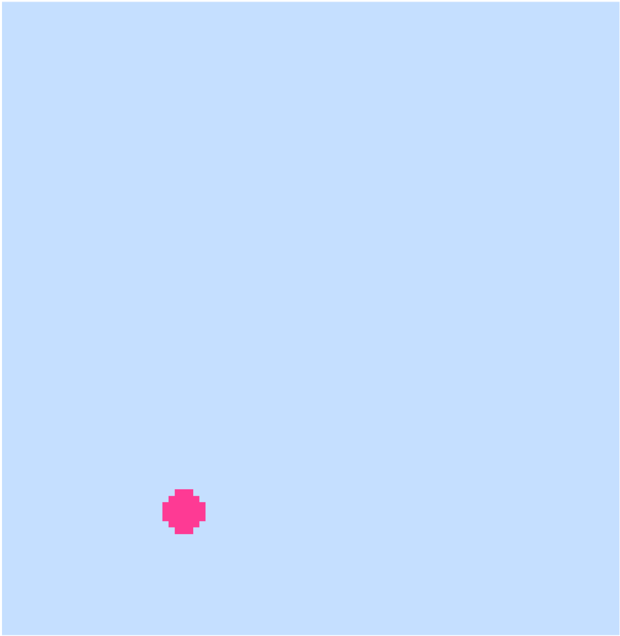

Underlying true μ_i

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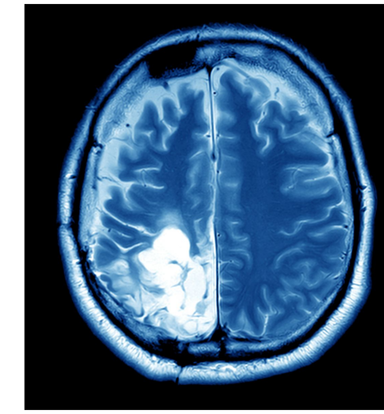

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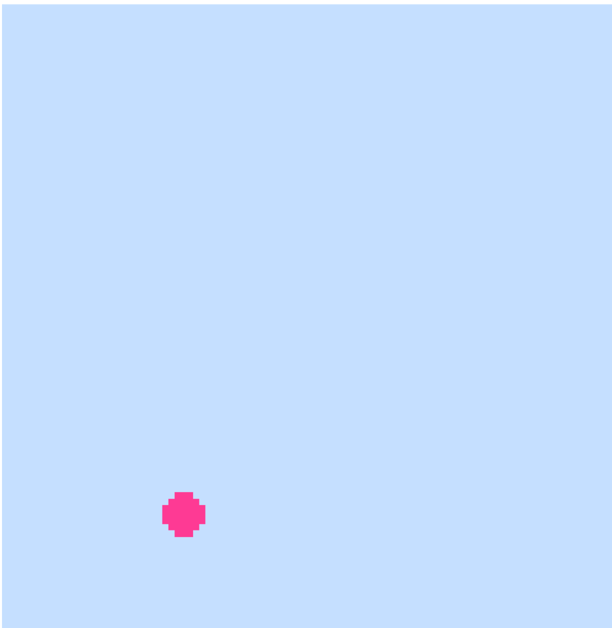

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Observed p-values

$$P_i = 1 - \Phi(Z_i)$$

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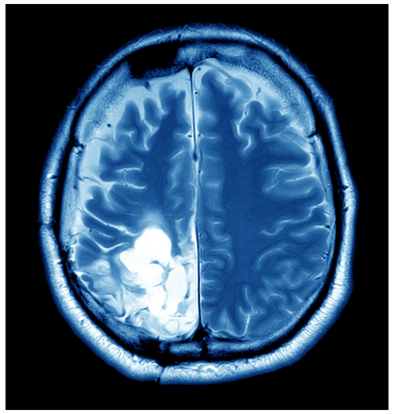

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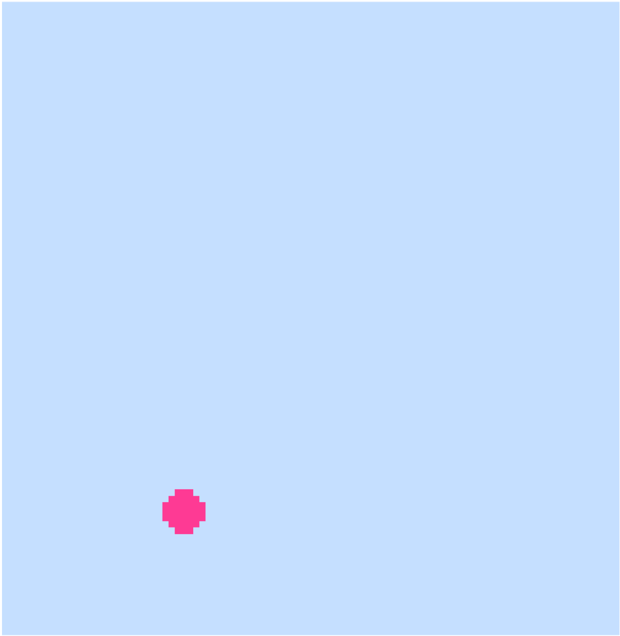

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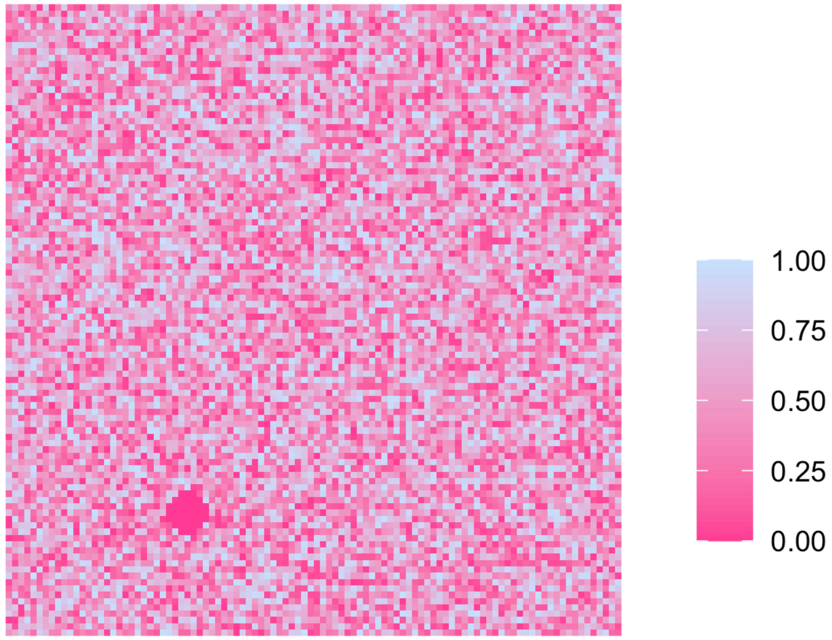

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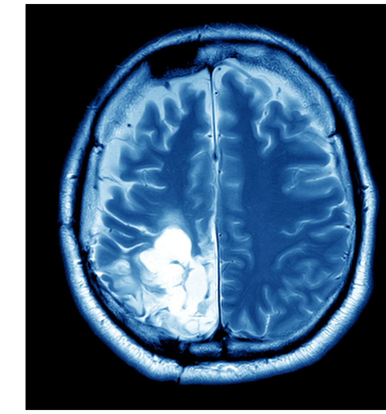

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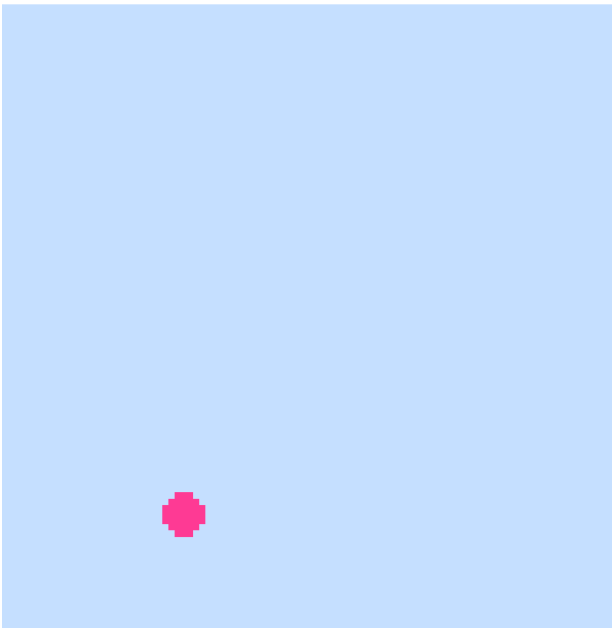

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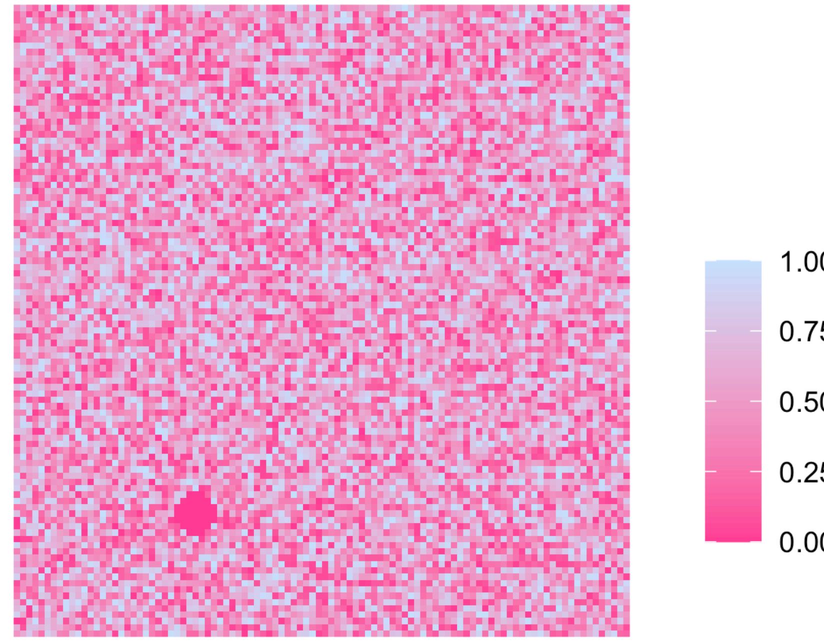

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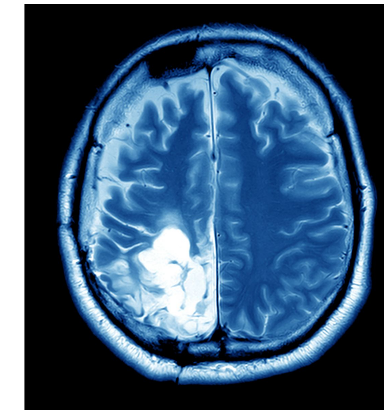

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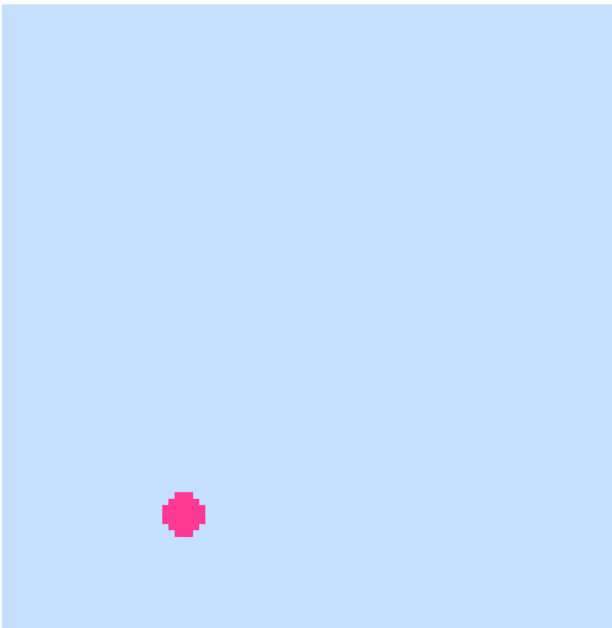

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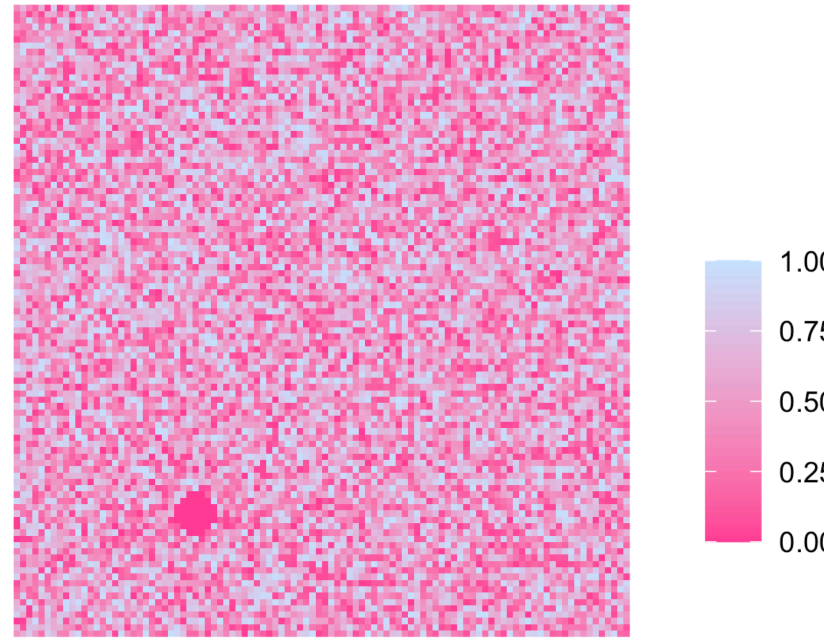

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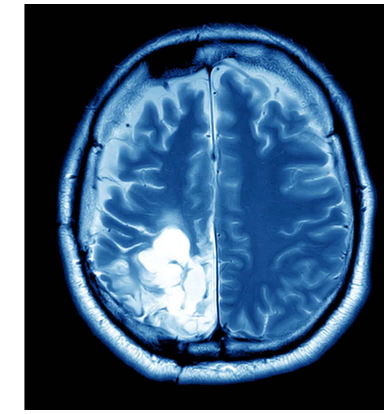

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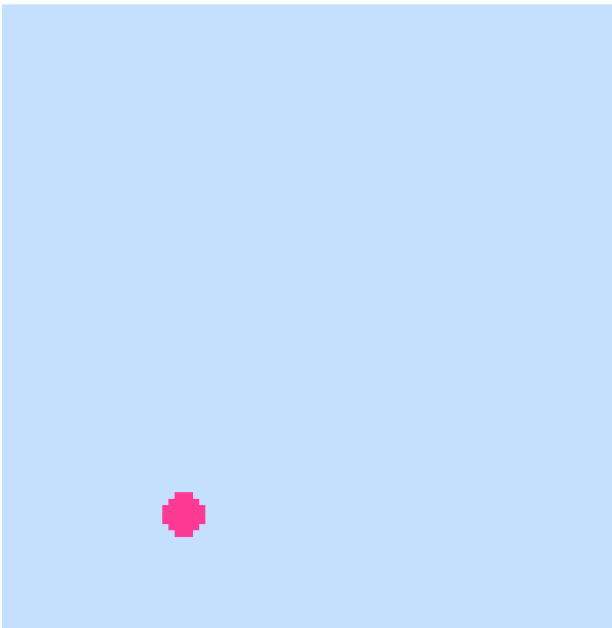

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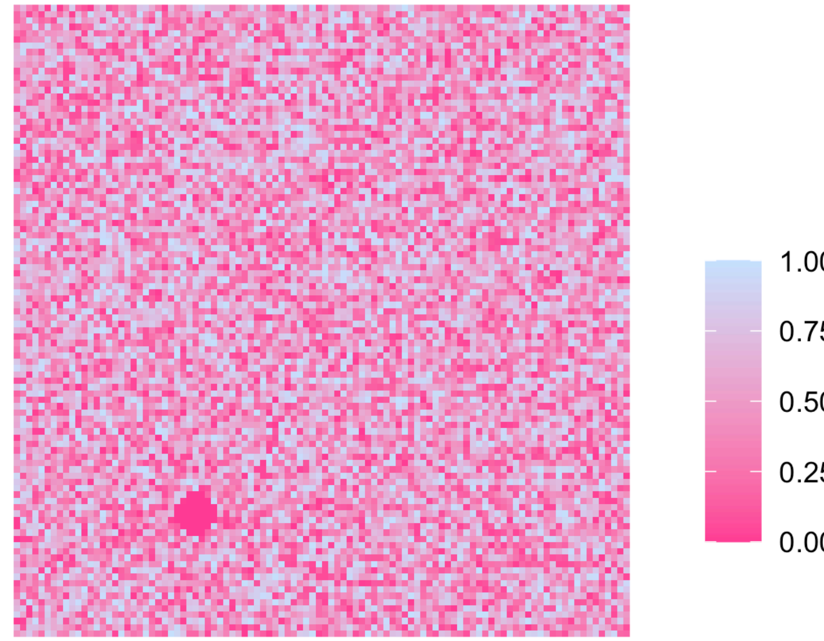

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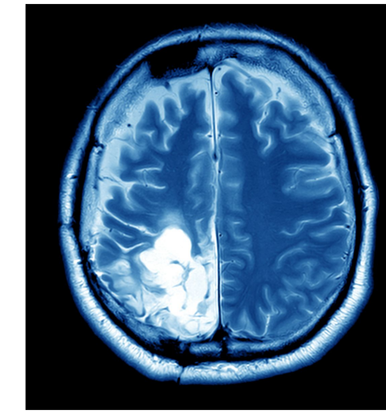

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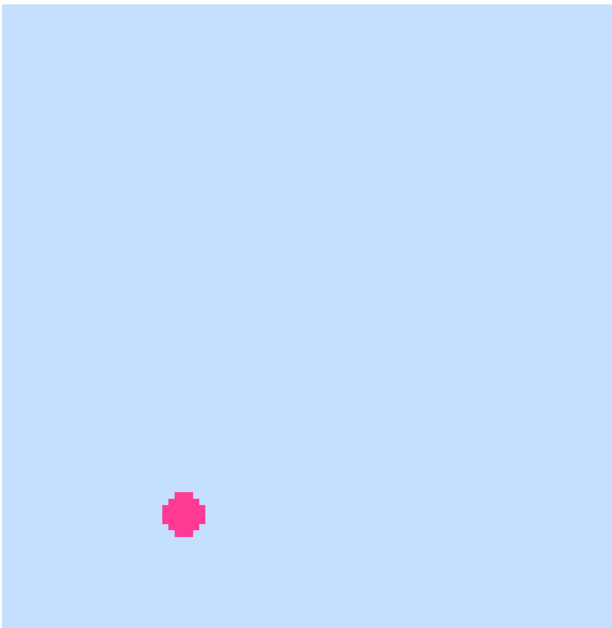

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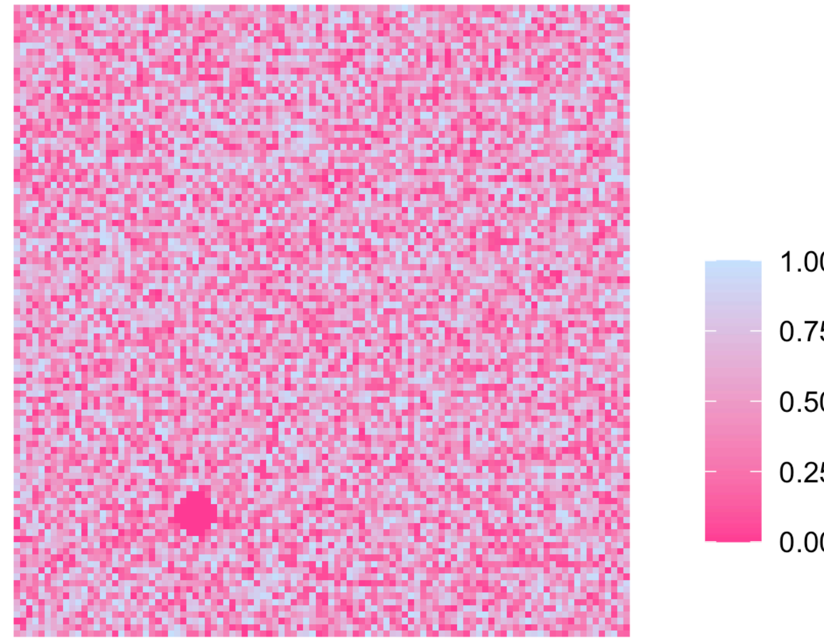

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taking account of <u>side information</u>. Eg. structure, covariates…

Classical testing

Pre-fixed procedure. Eg. weighted Bonferroni: reject H_i if $P_i/w_i \leq \alpha/n$.

Interactive tests with FDR control:
Lei, Fithian (2018); Lei, Ramdas, Fithian (2019)

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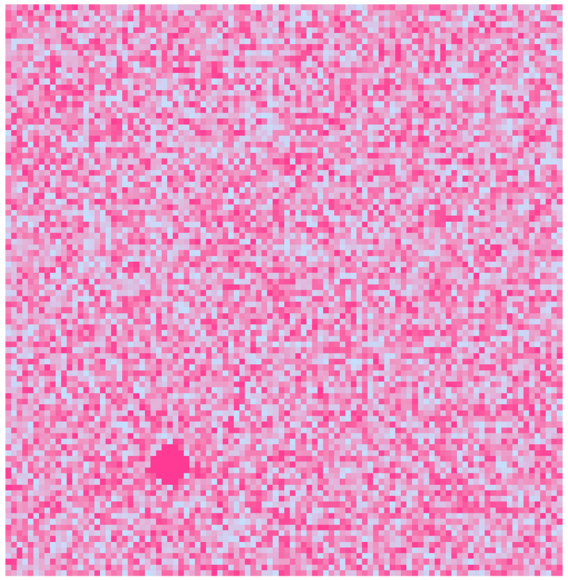

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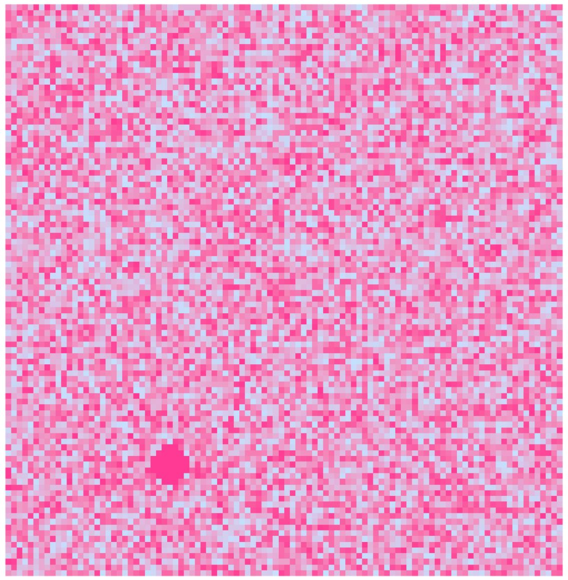

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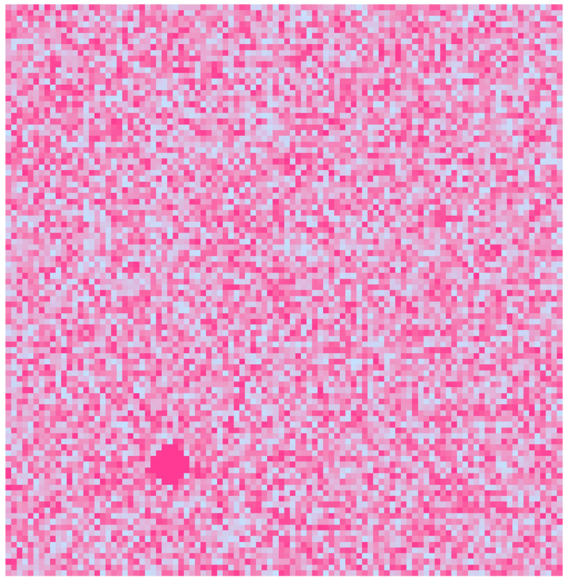

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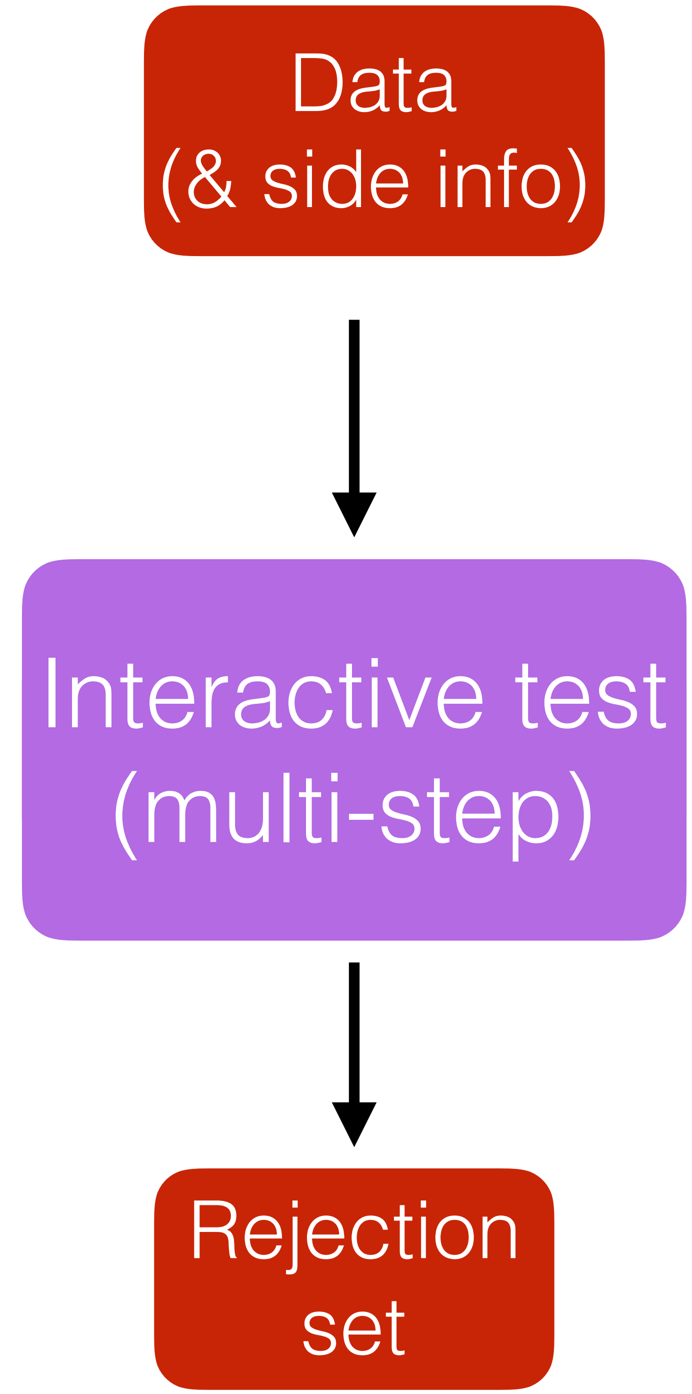

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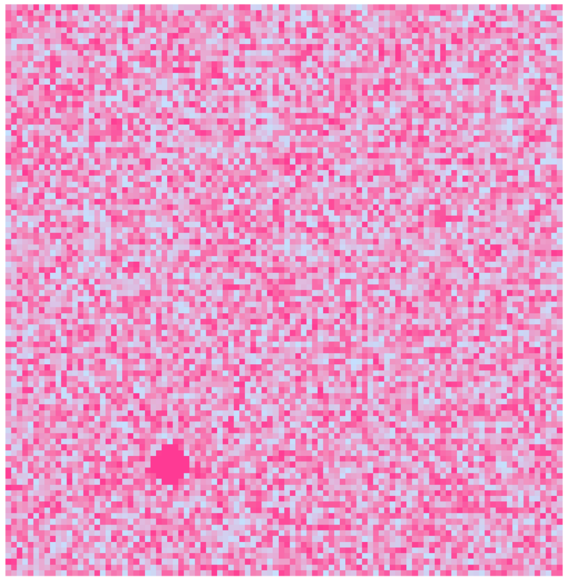

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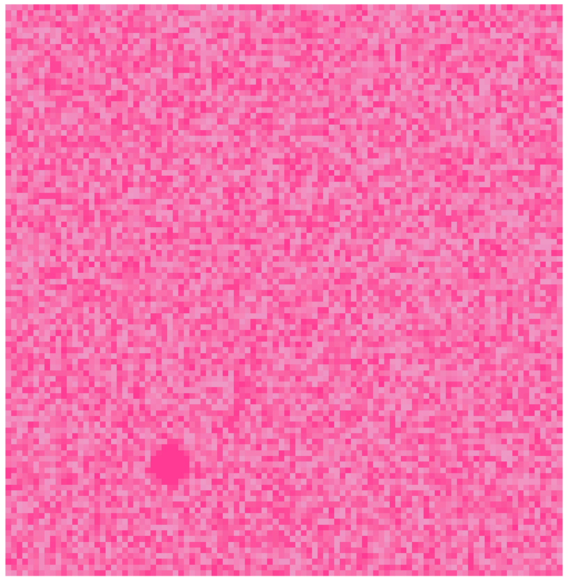
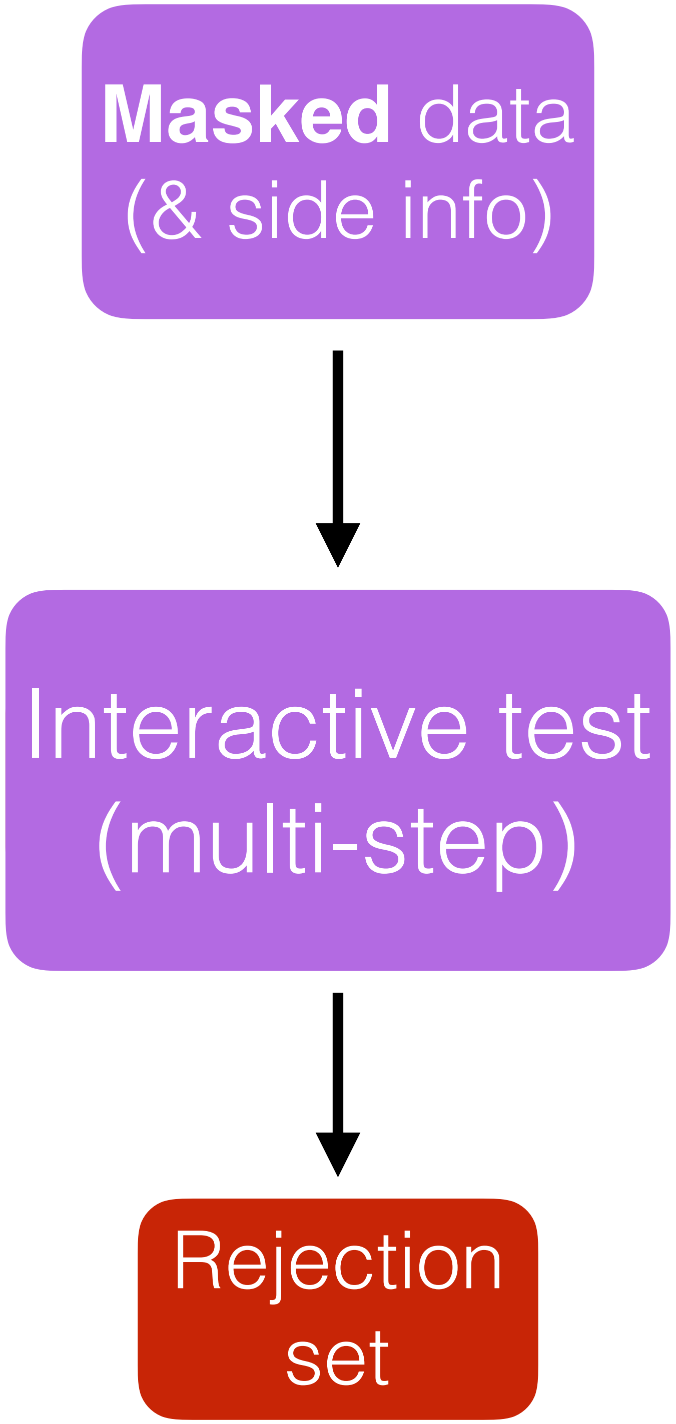


masked p-values



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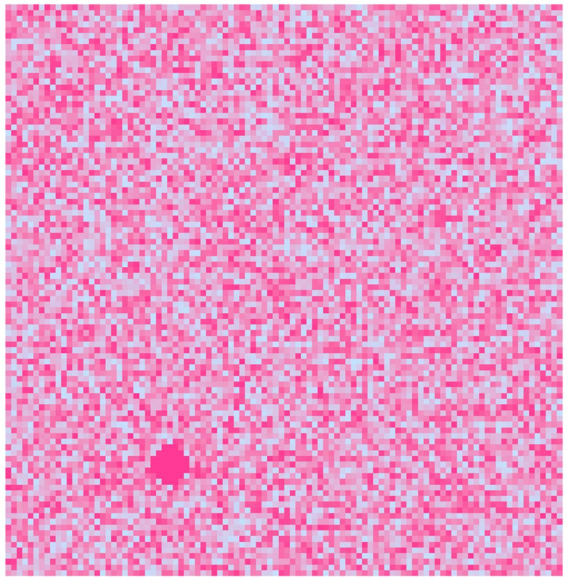

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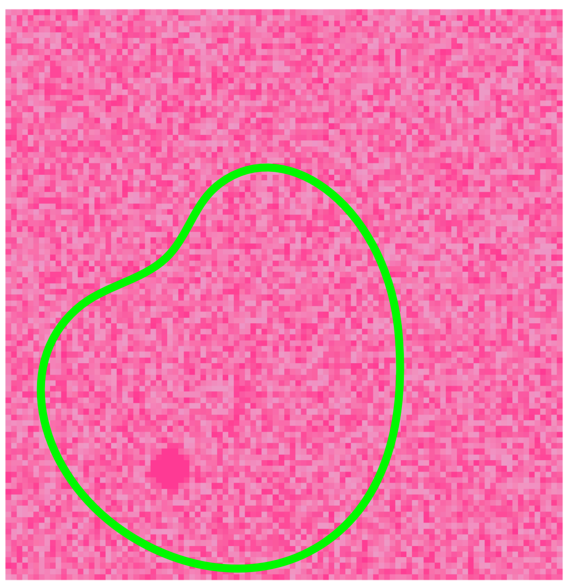

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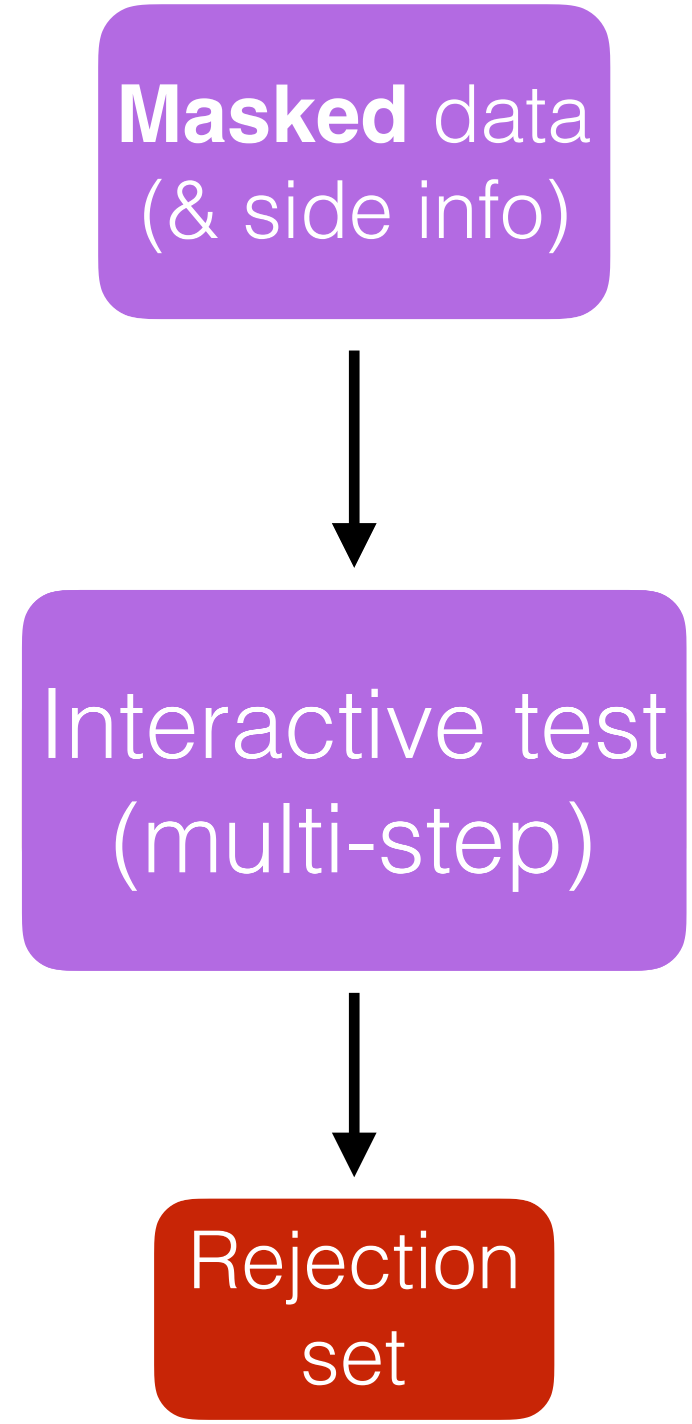

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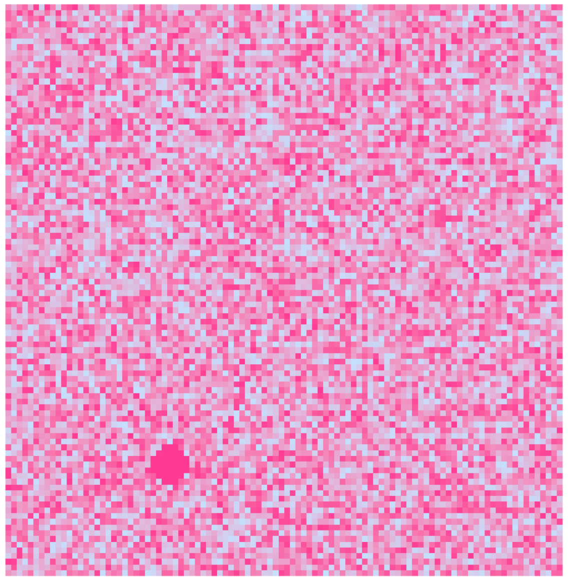

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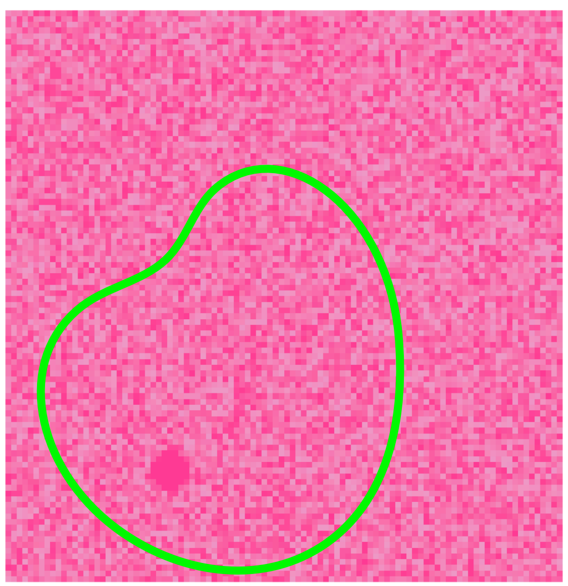

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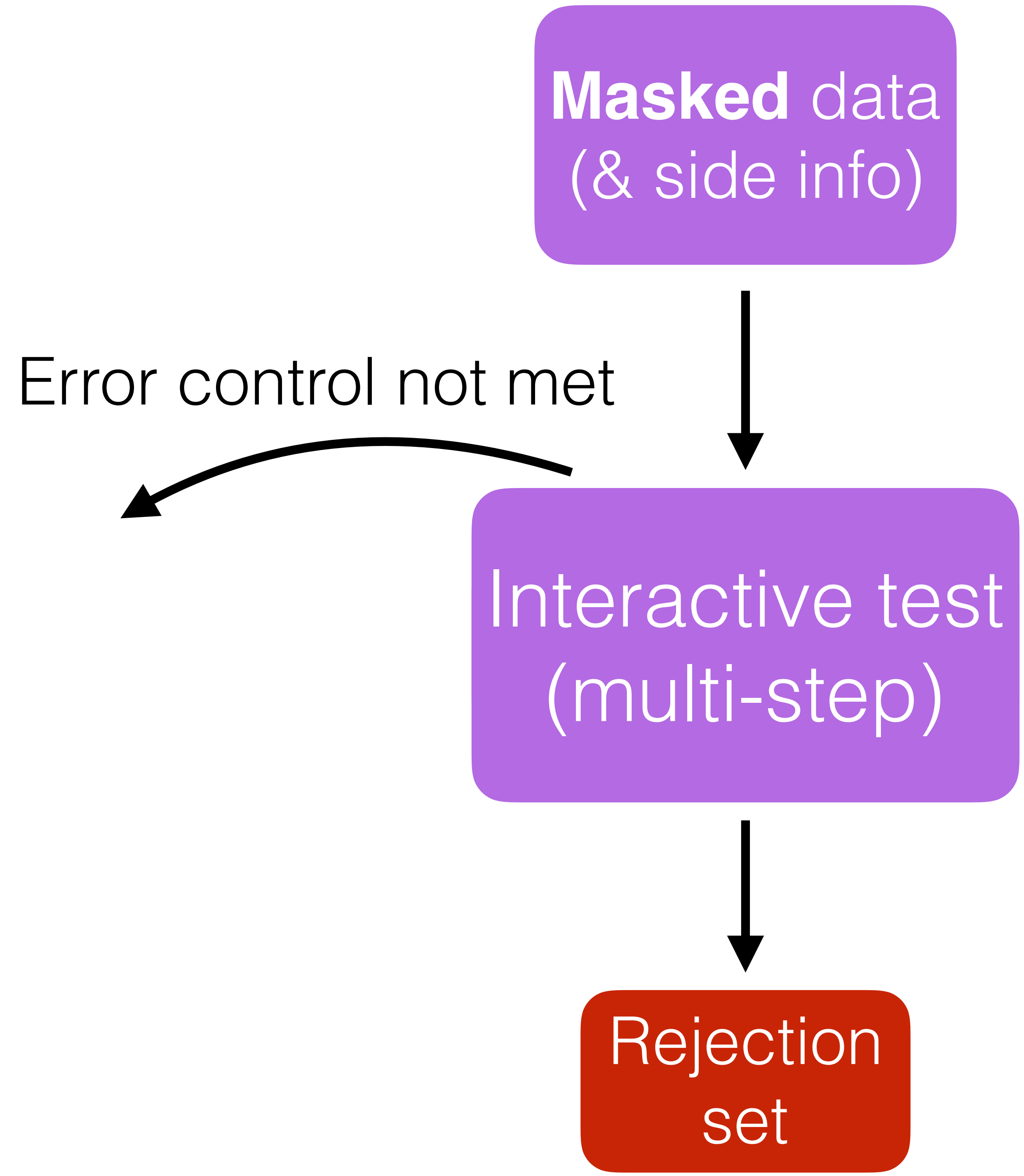

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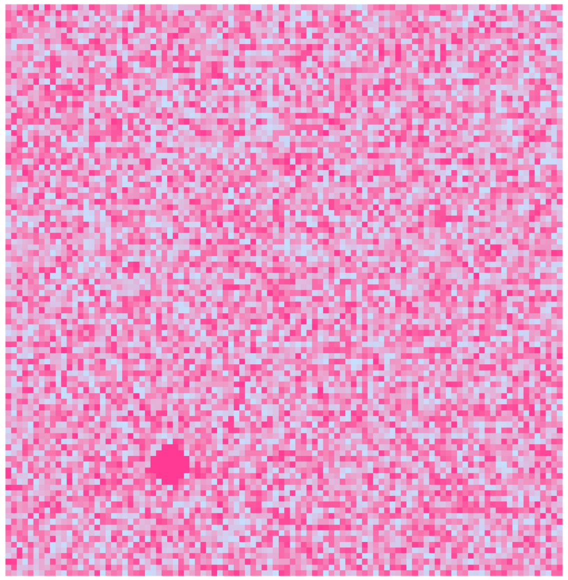

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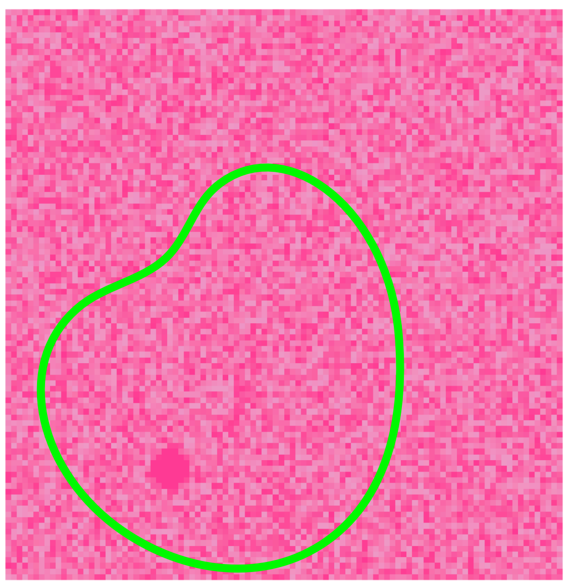

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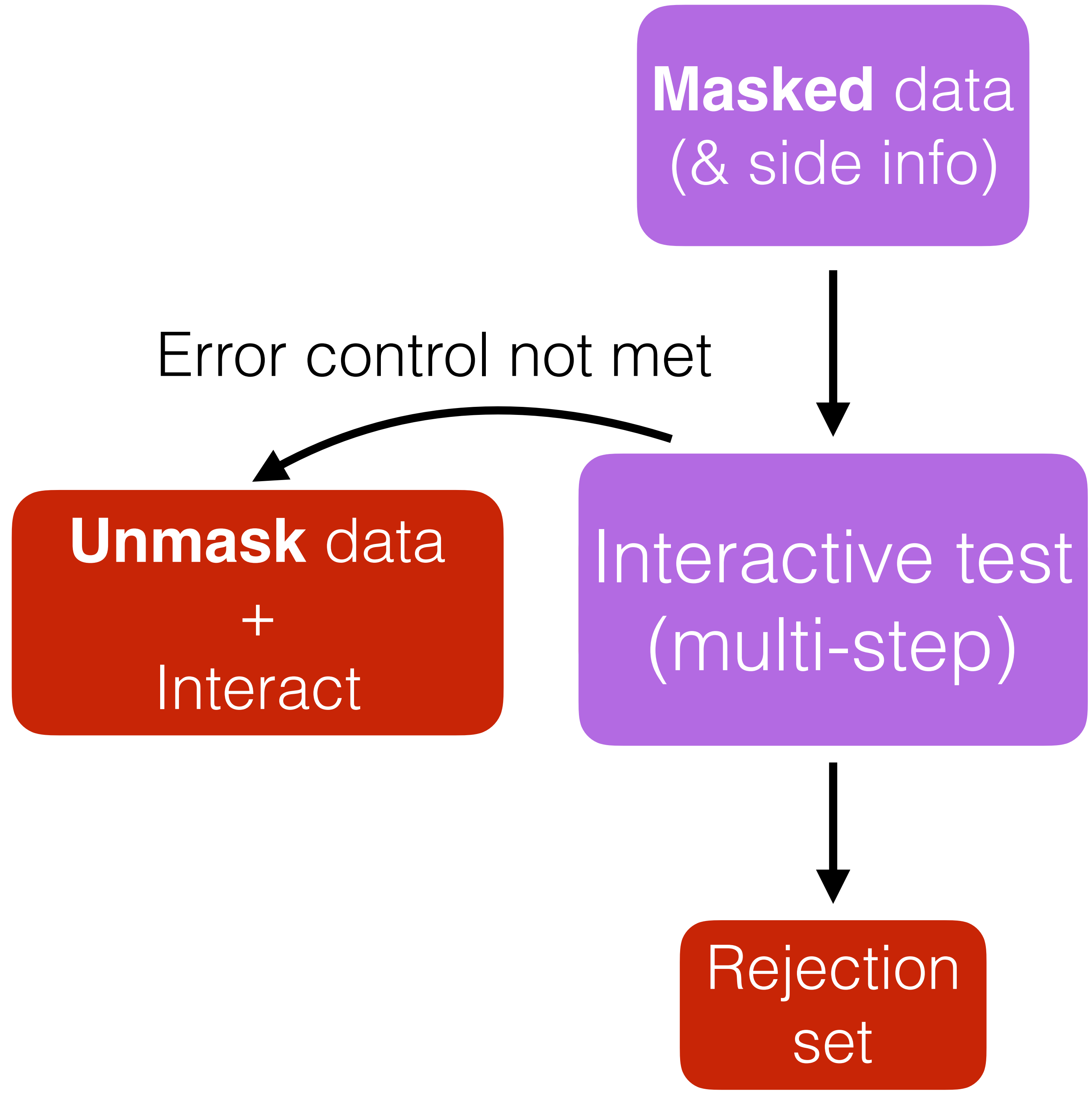

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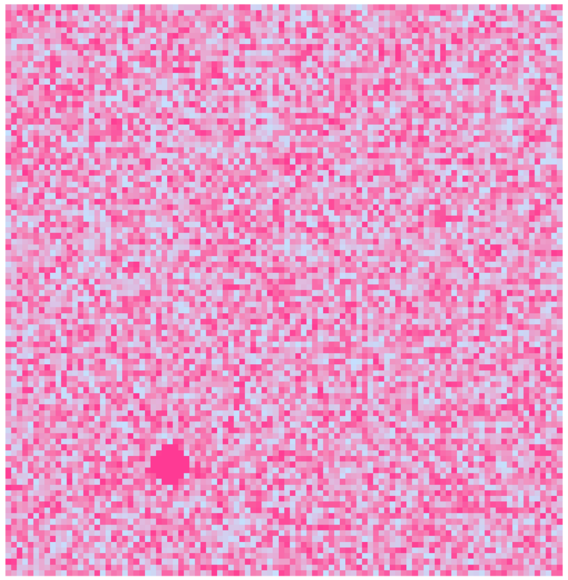

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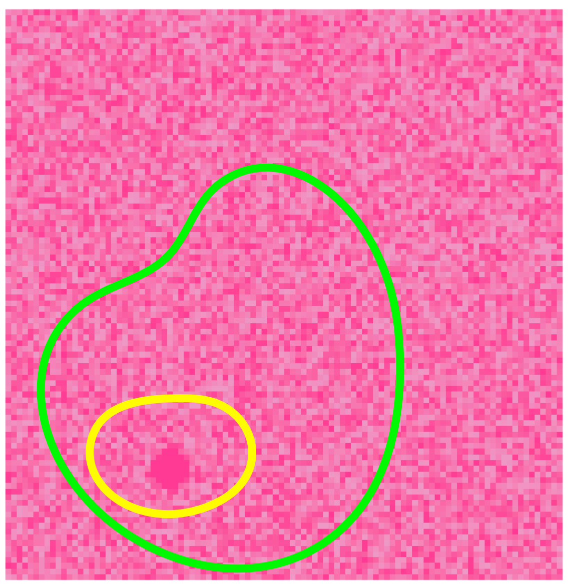

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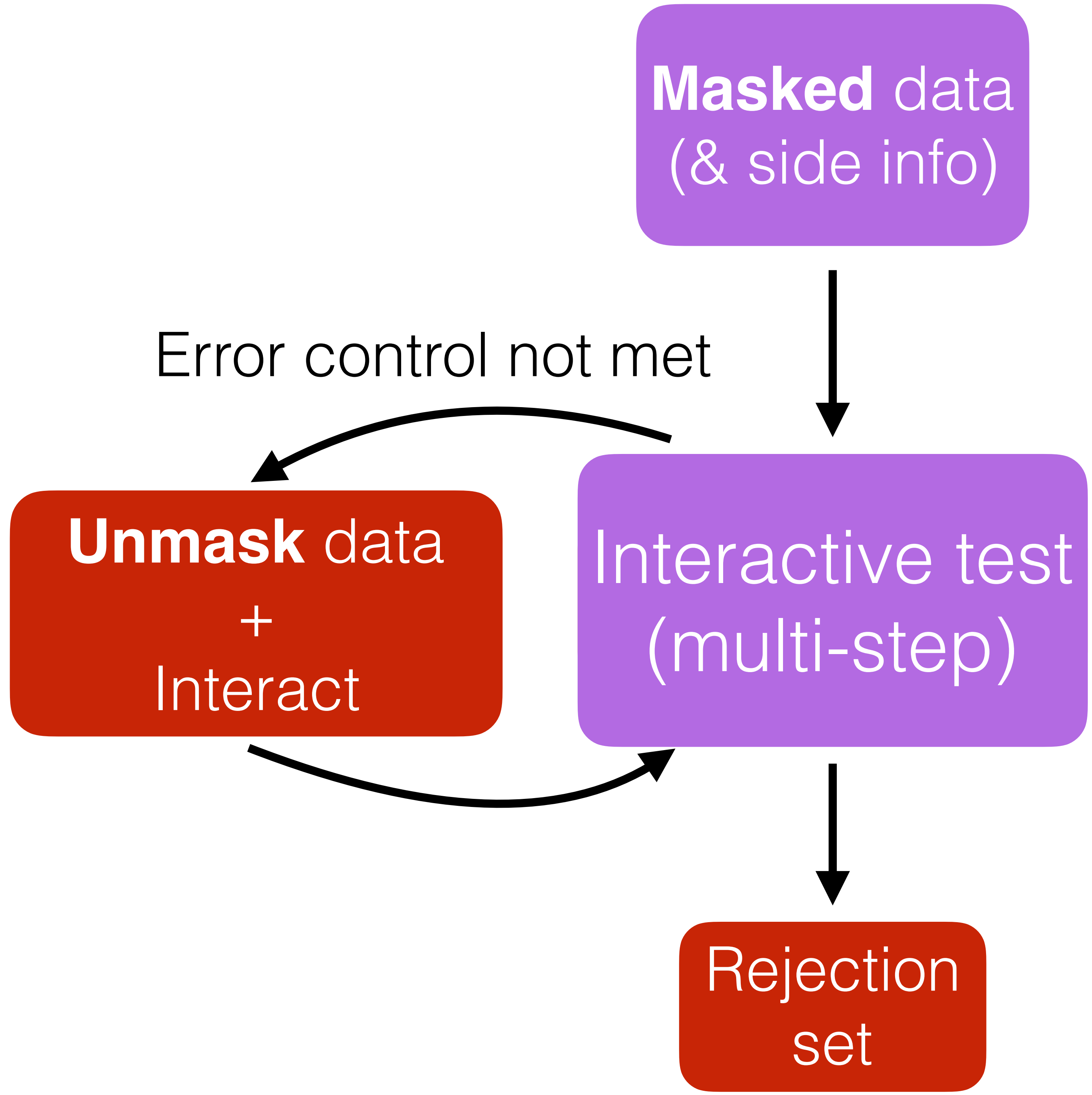

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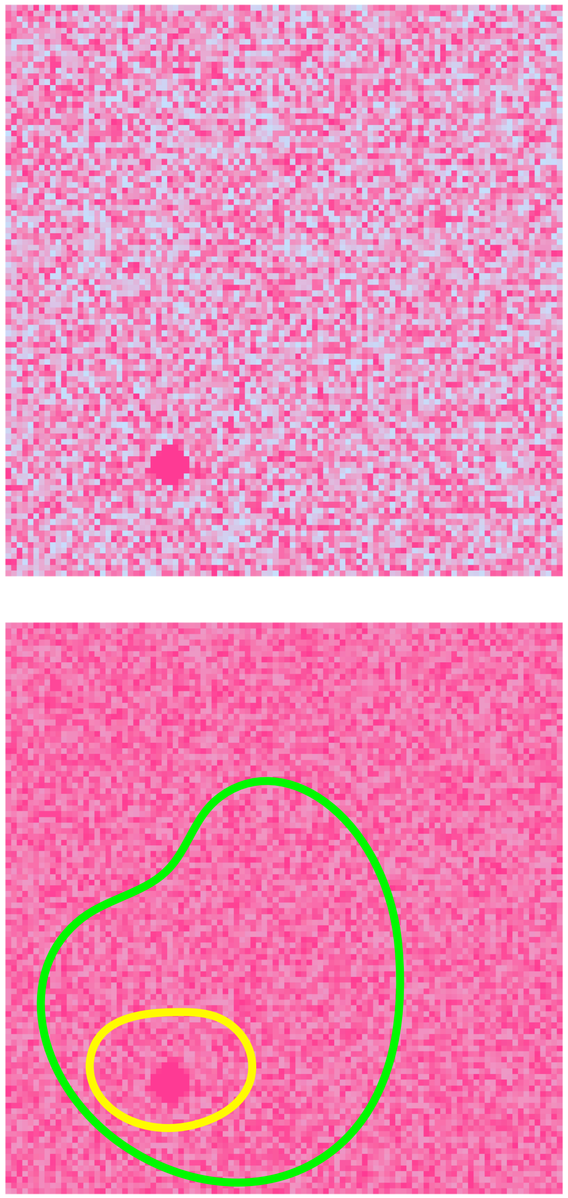

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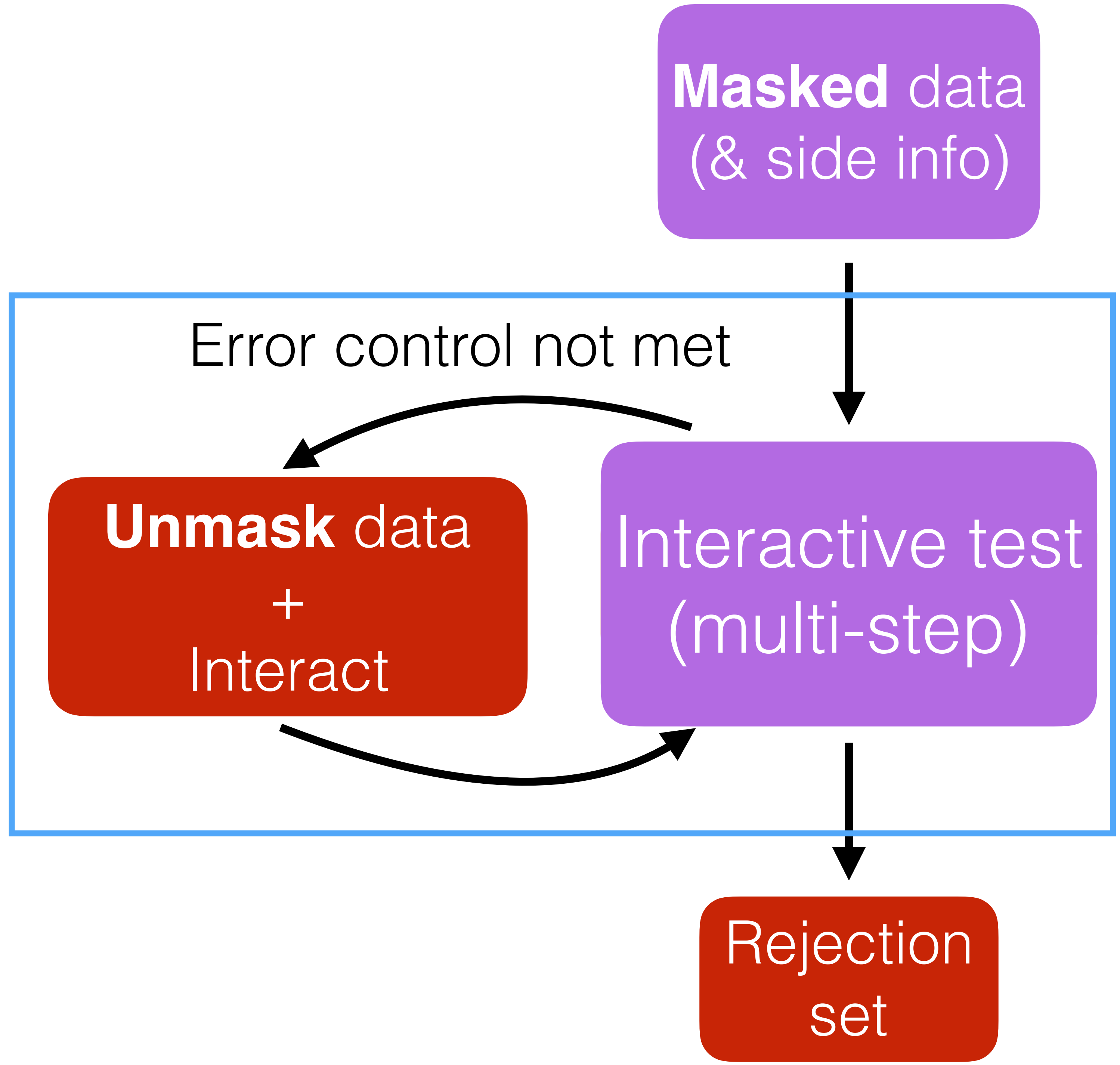

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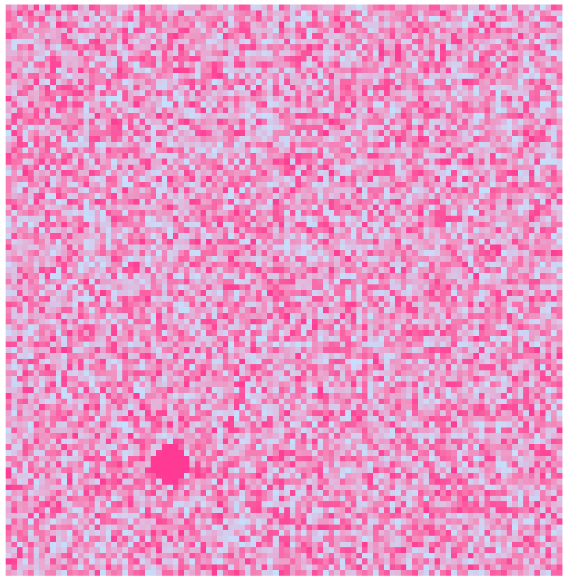

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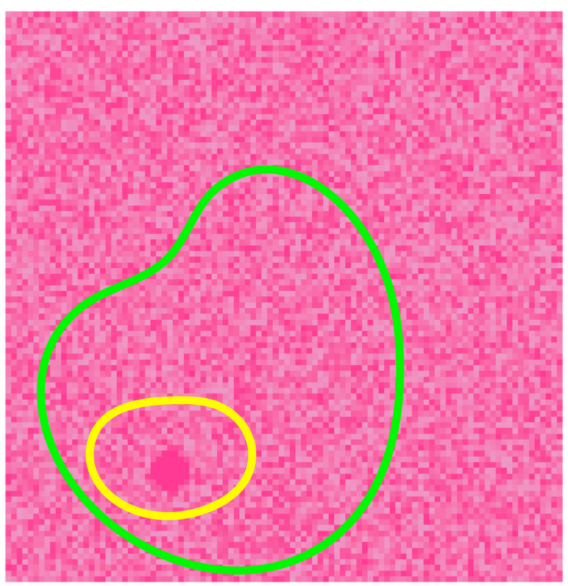

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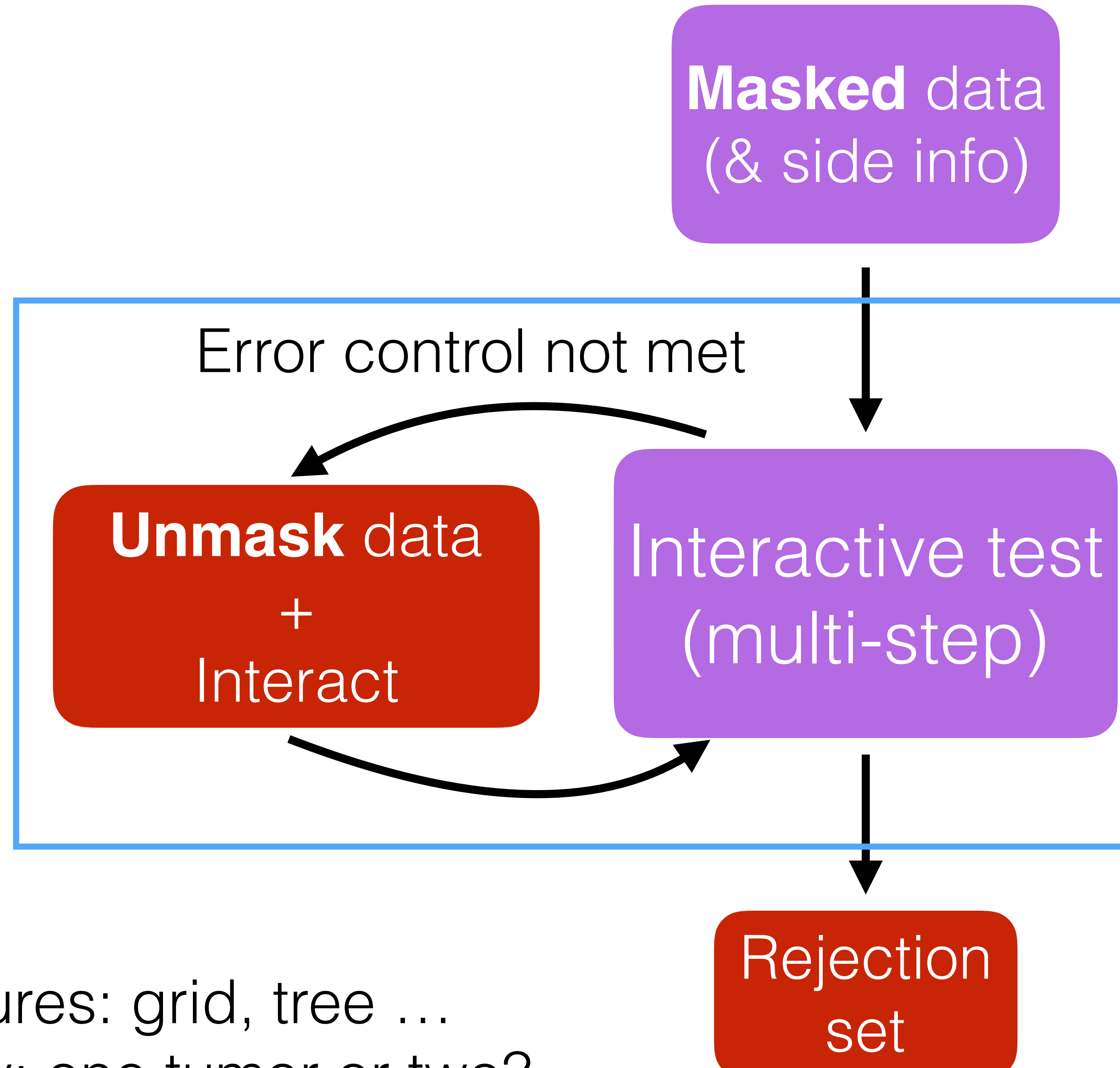

Interactive testing

- Accommodate various structures: grid, tree …
- Be revised manually on the fly: one tumor or two?

Interactive tests with FDR control:
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Component 1: mask p-values

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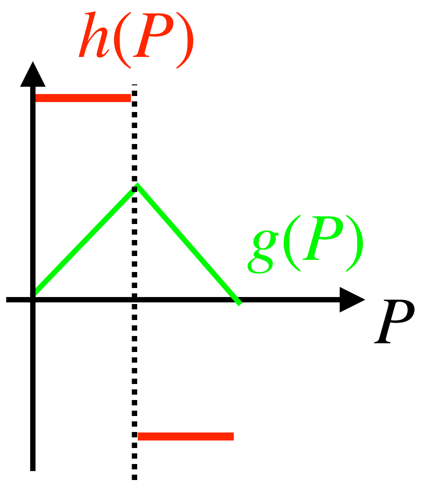
$$P \longrightarrow \begin{cases} g(P) = \min\{P, 1 - P\} \\ h(P) = 2 \cdot 1\{P < 0.5\} - 1 \end{cases}$$



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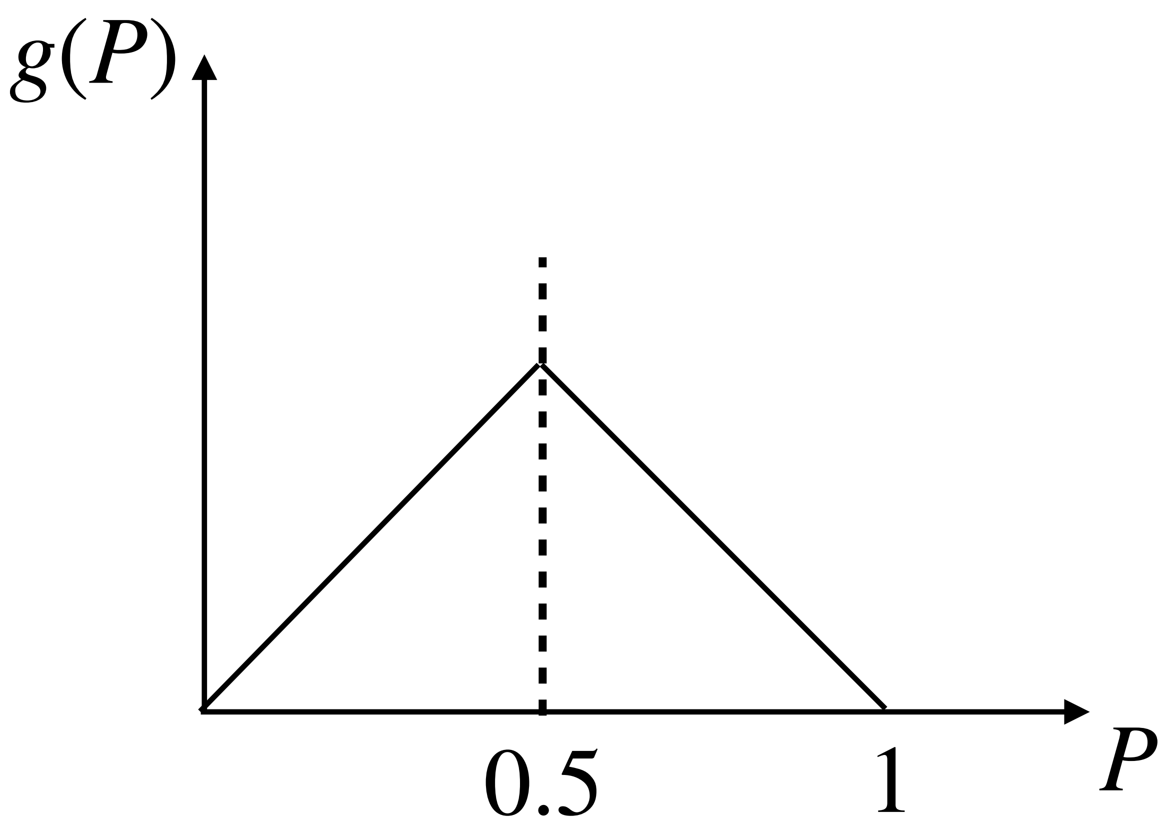
Small $g(P)$ indicate non-nulls



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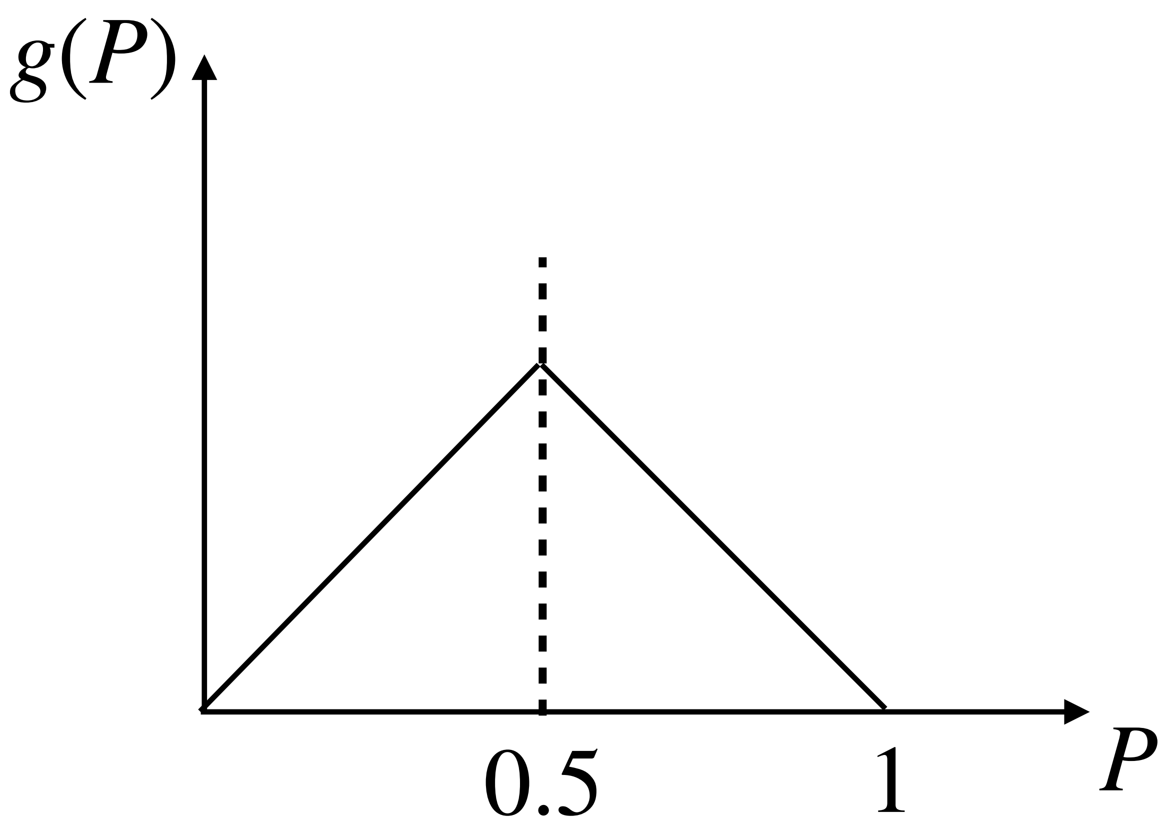

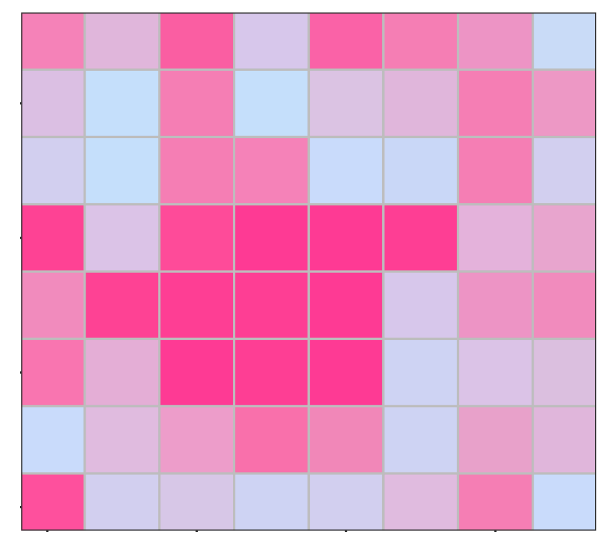

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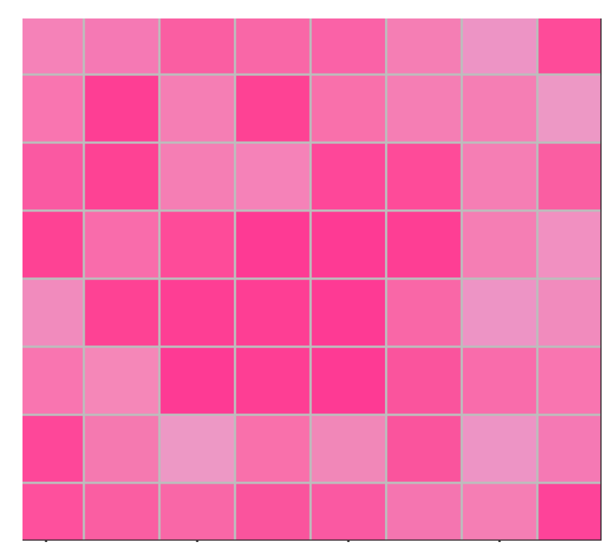

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Note: above masking works for FDR control, but not *FWER* control.

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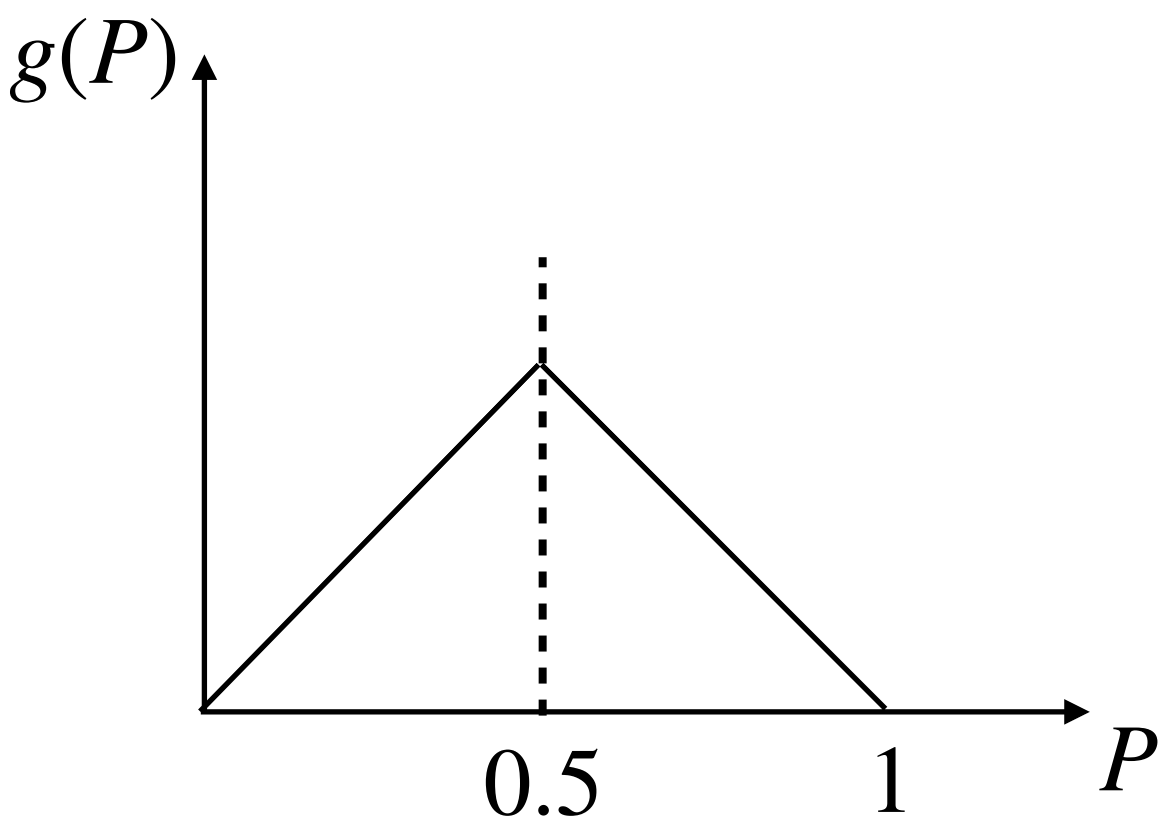

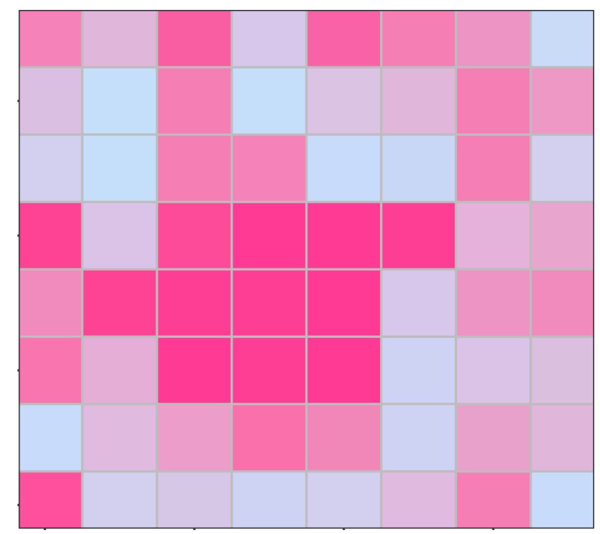

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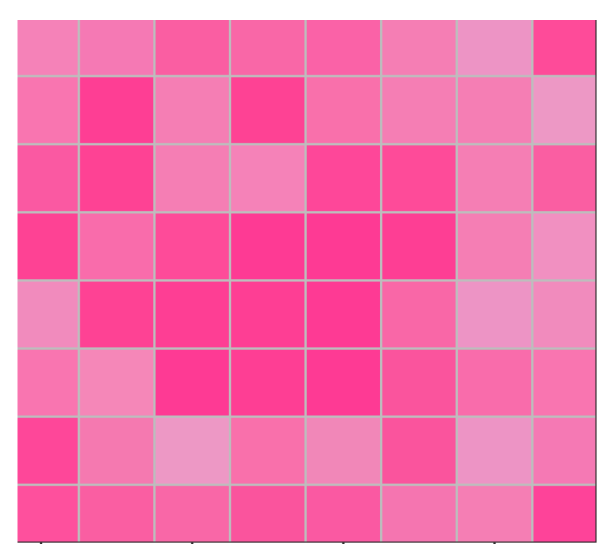

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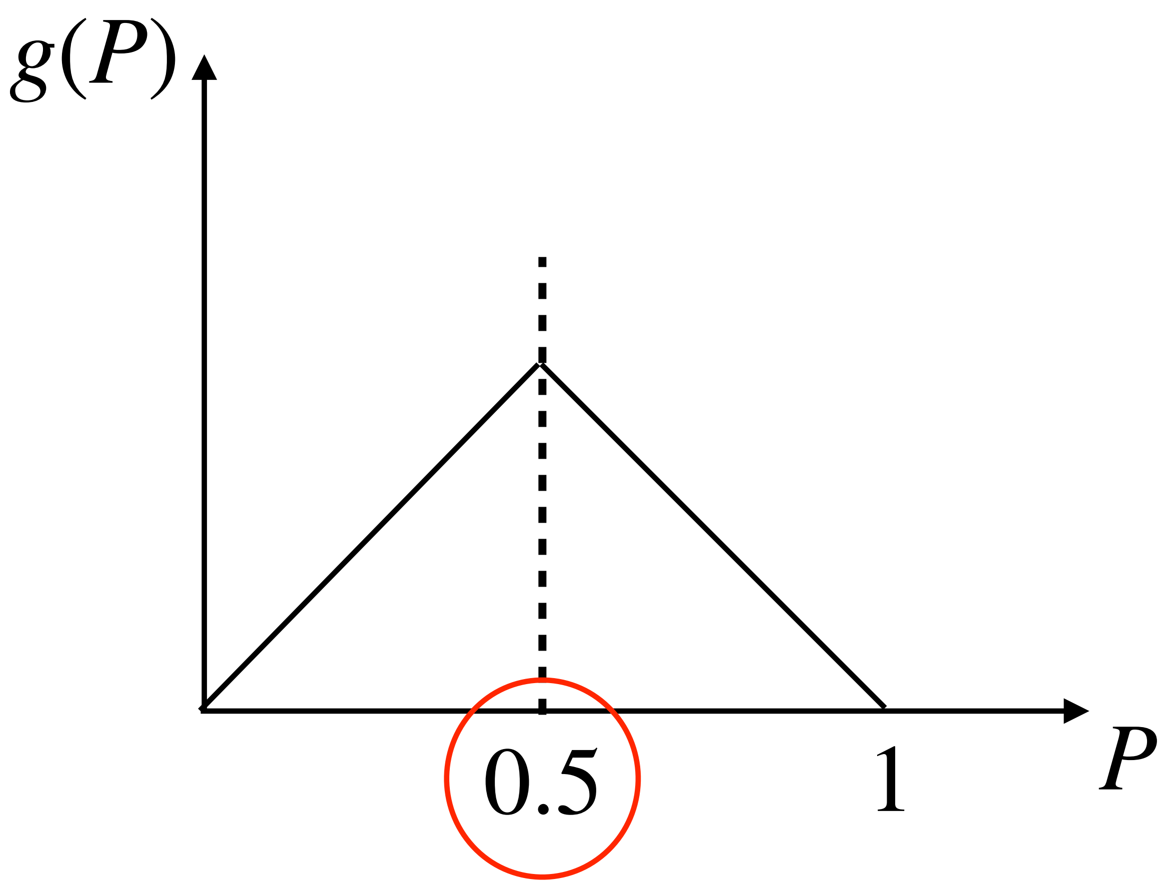
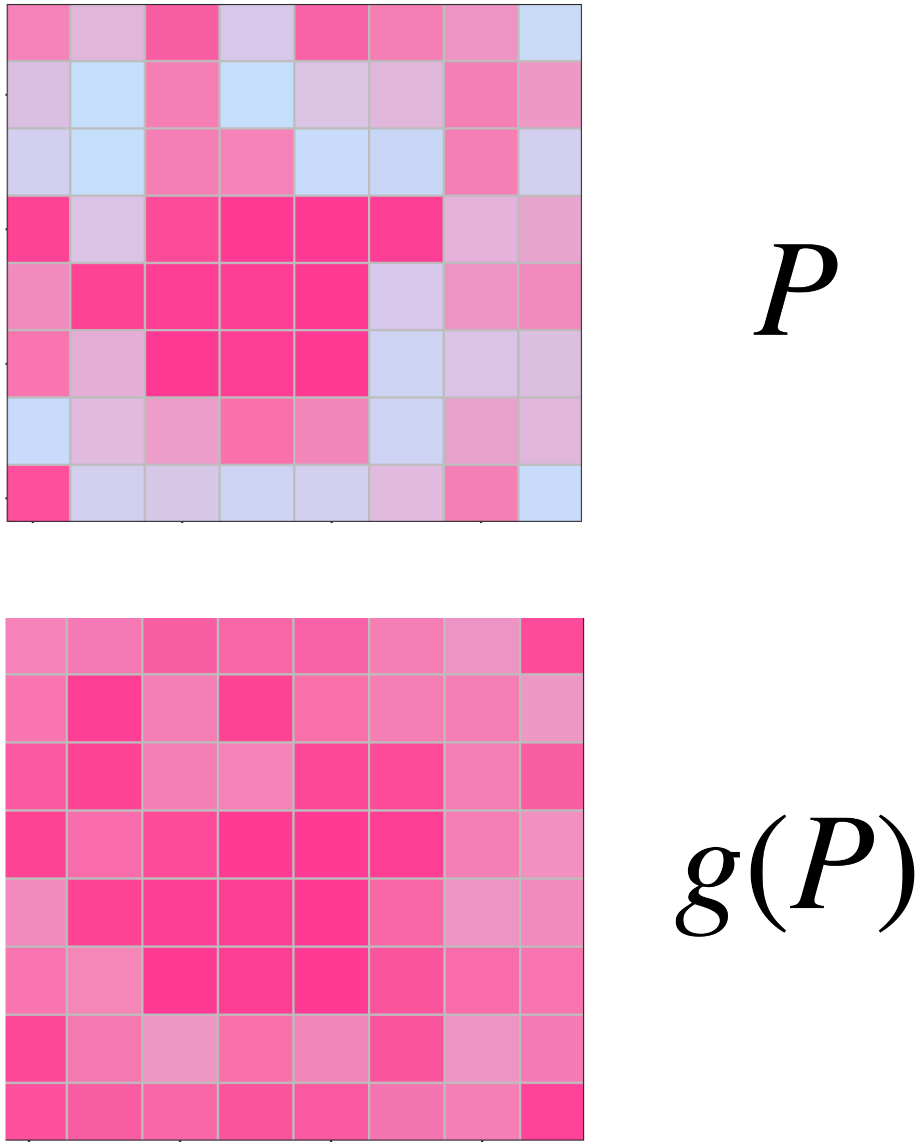




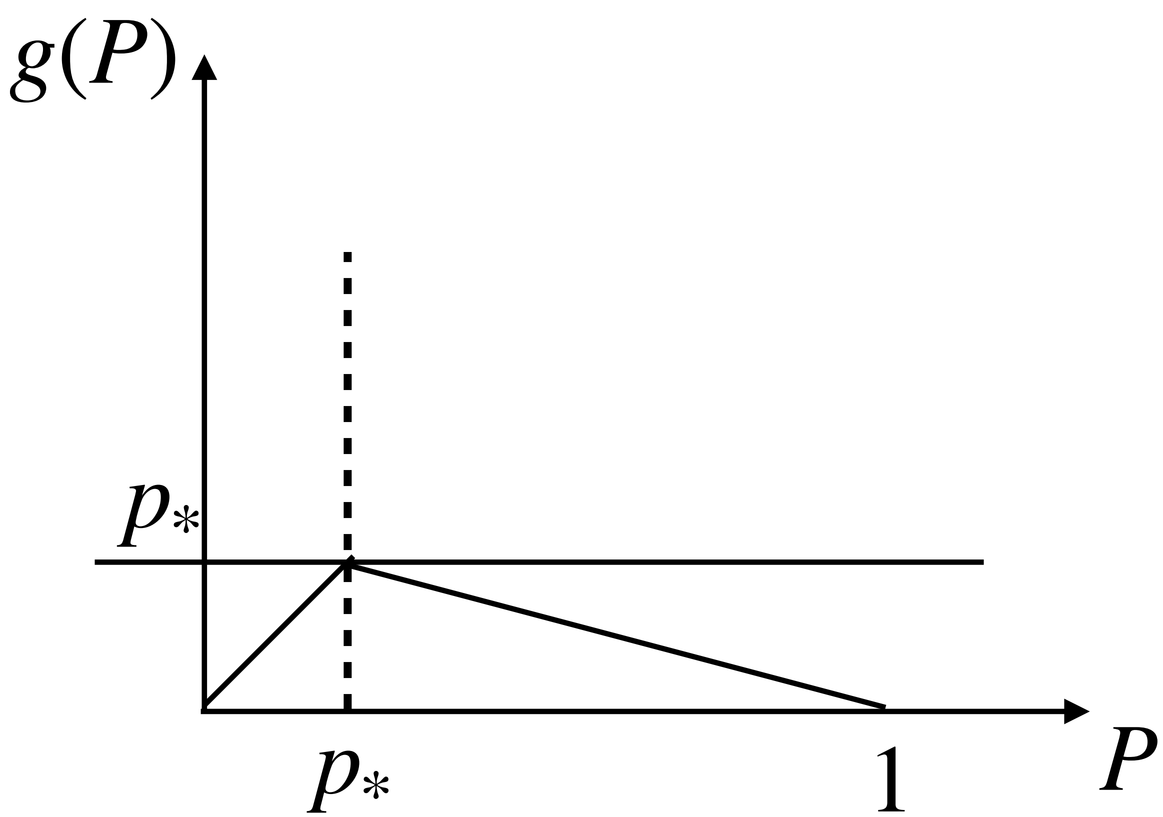
Component 1: mask p-values

$$P \longrightarrow \begin{cases} g(P) = \min\{P, 1 - P\} \\ h(P) = 2 \cdot 1\{P < 0.5\} - 1 \end{cases}$$

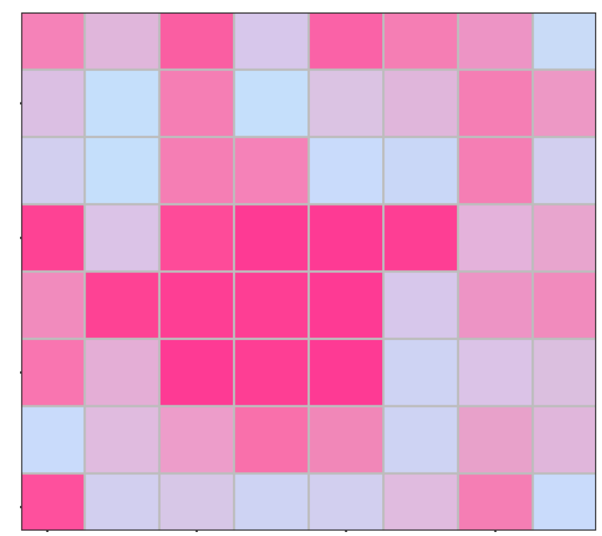
Independent for nulls

Note: above masking works for FDR control, but not *FWER* control.

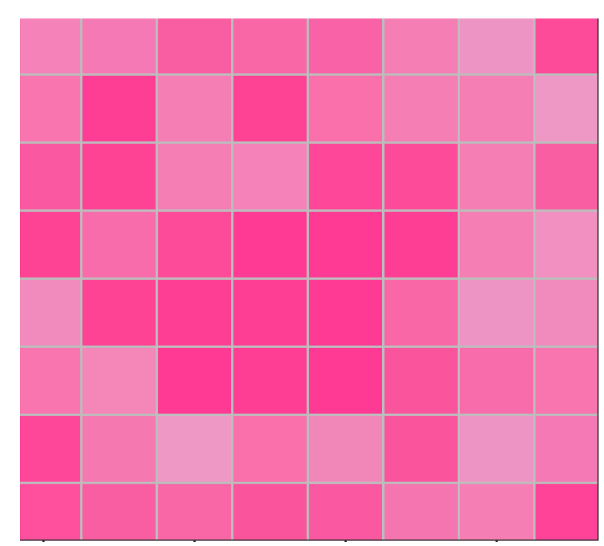
Small $g(P)$ indicate non-nulls



(Default $p_* = \alpha/2$)



P



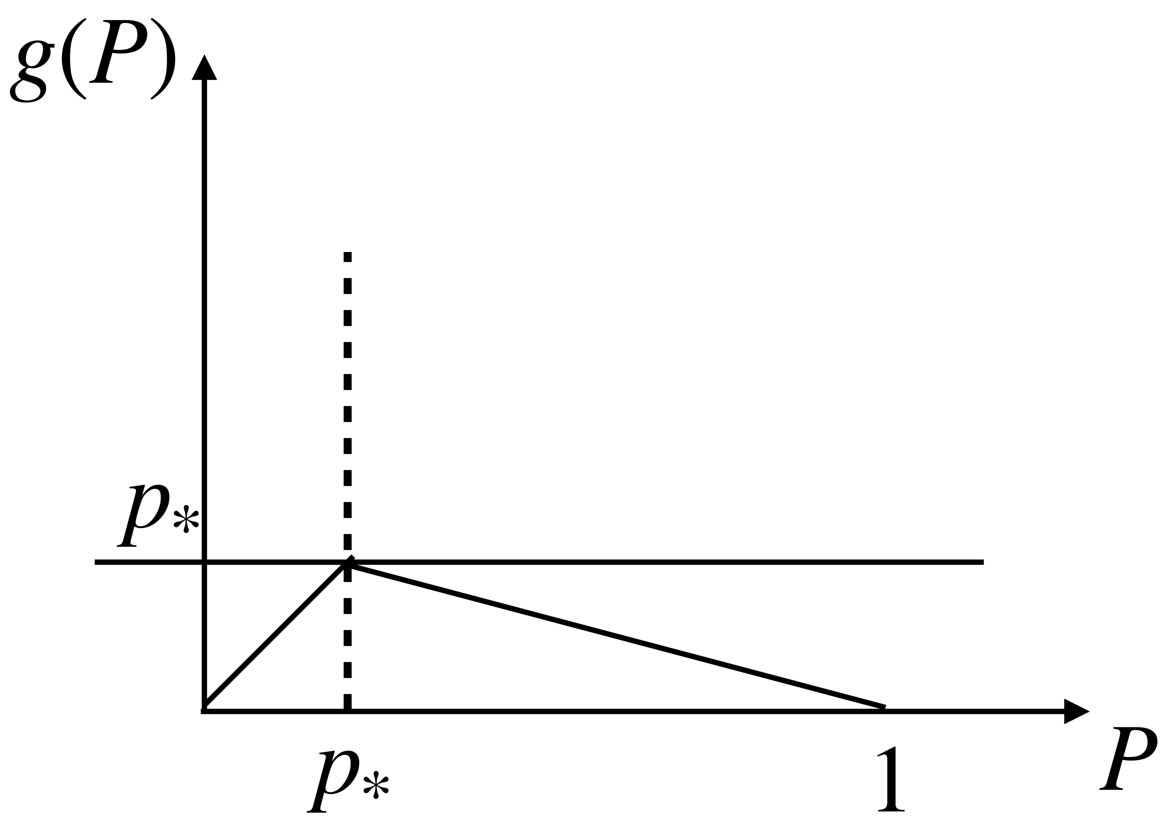
$g(P)$

Component 1: mask p-values

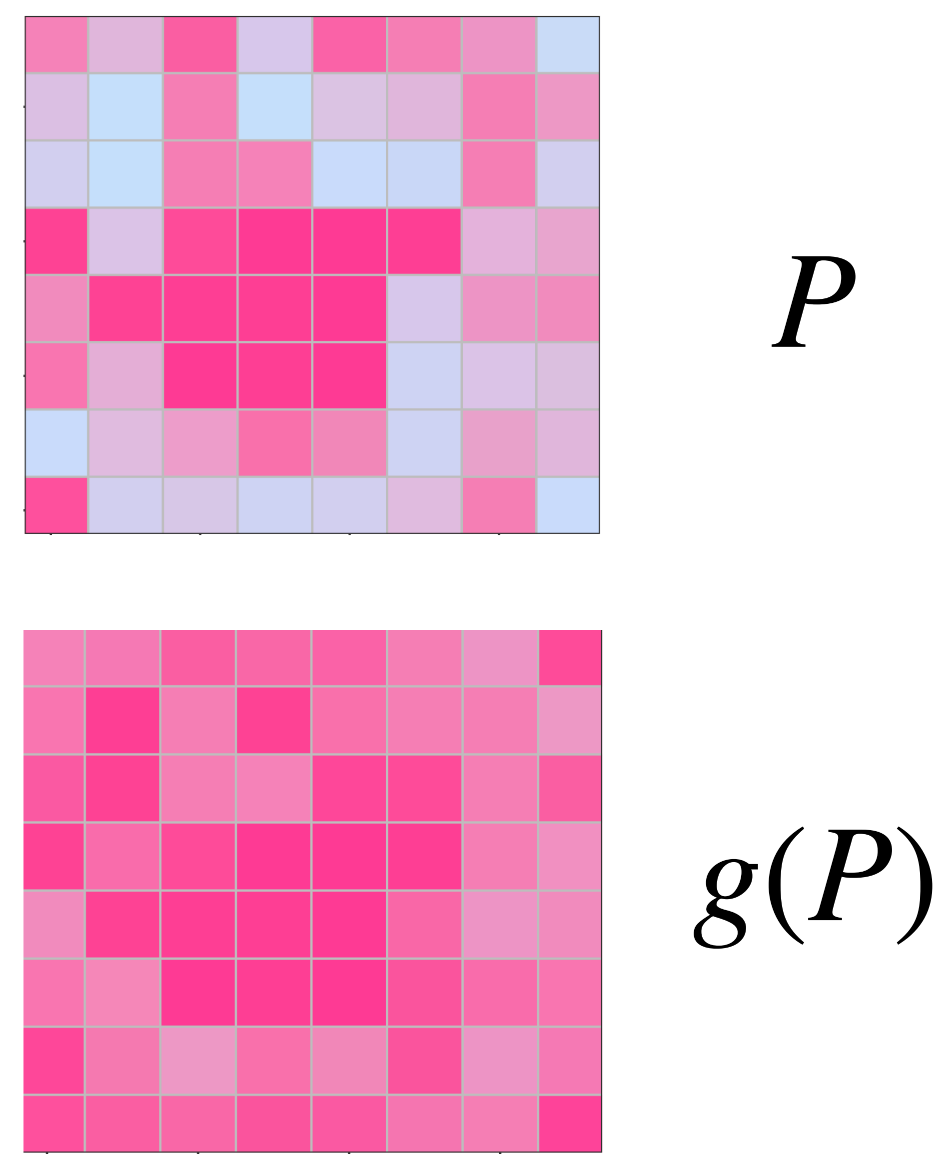
$$P \longrightarrow \begin{cases} g(P; p_*) = \min\{P, \frac{p_*}{1-p_*}(1-P)\} \\ h(P; p_*) = 2 \cdot 1\{P < p_*\} - 1 \end{cases}$$

Independent for nulls

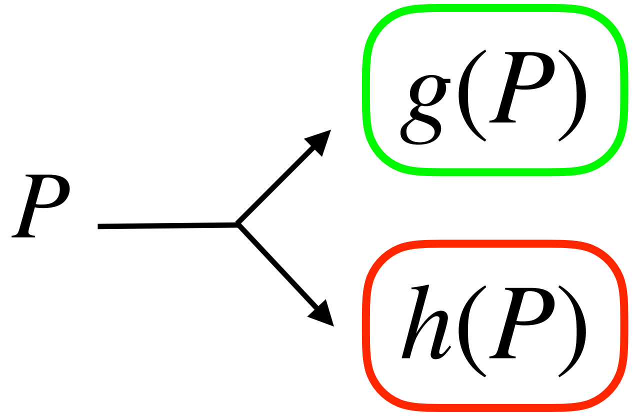
Small $g(P)$ indicate non-nulls



(Default $p_* = \alpha/2$)

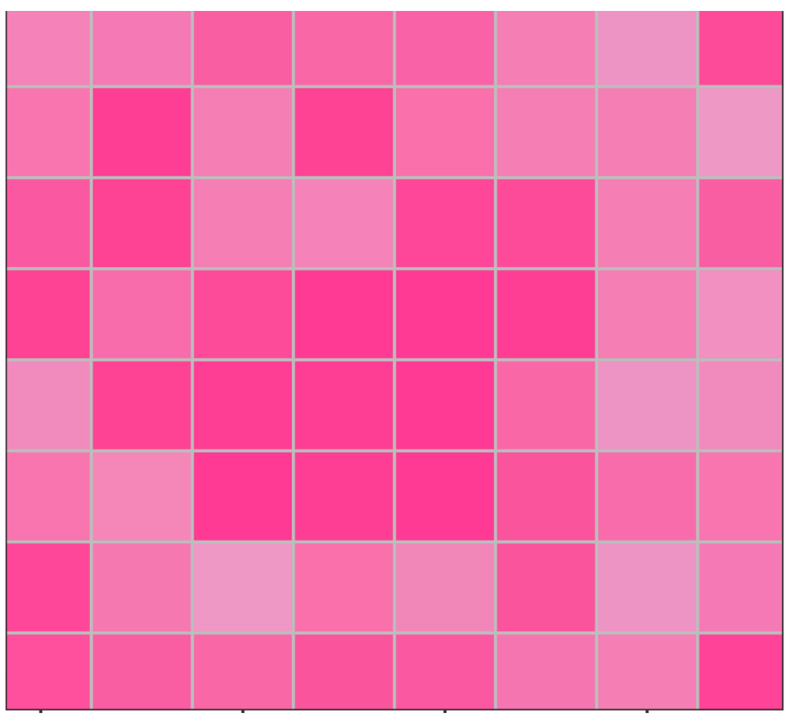


Component 2: select candidate set interactively

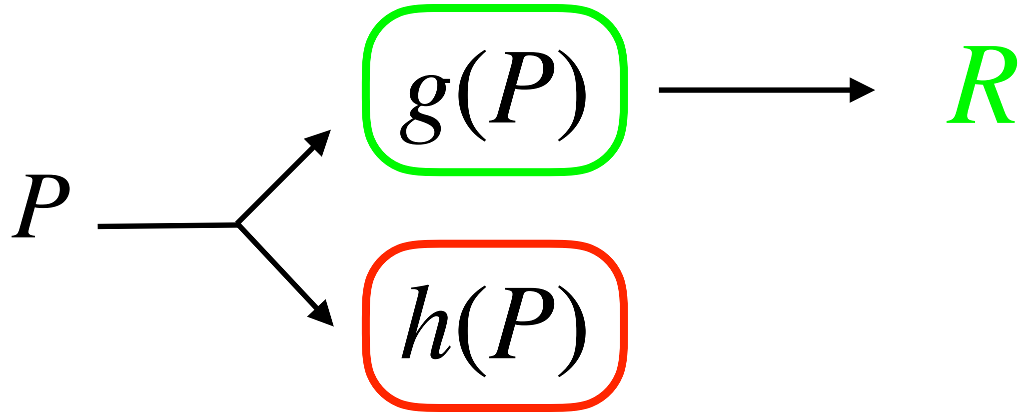


for cand. set selection

for error control

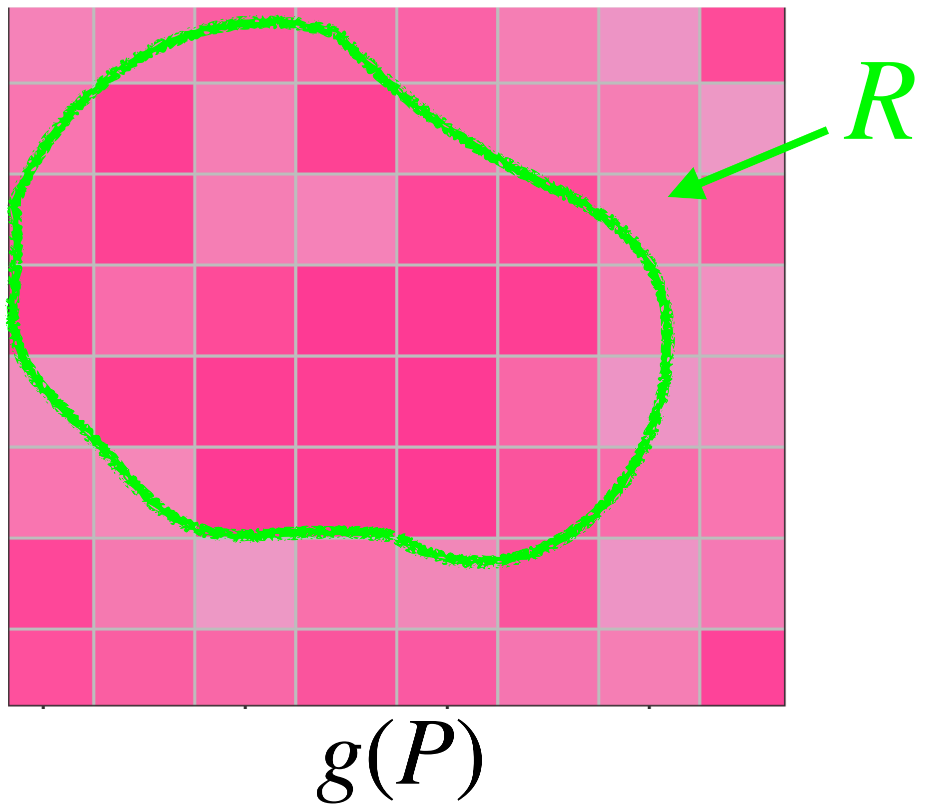


Component 2: select candidate set interactively



for cand. set selection

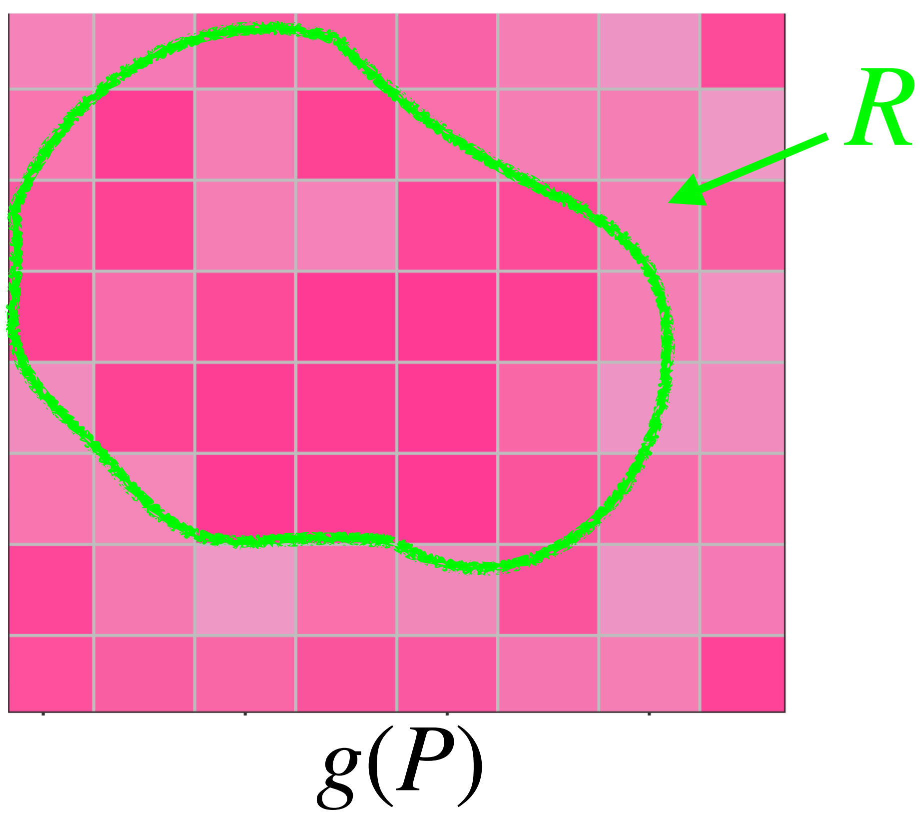
for error control



Component 2: select candidate set interactively

$P \to g(P) \to R$ for cand. set selection

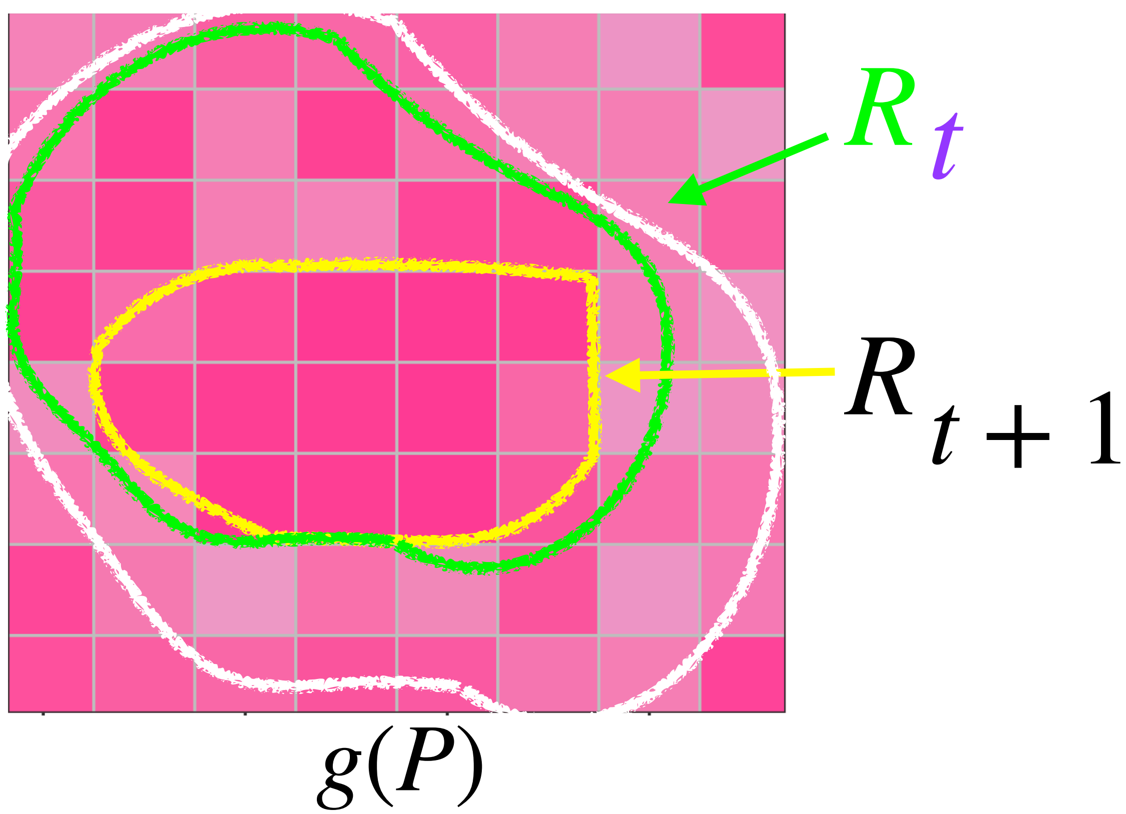
$P \to h(P) \to \widehat{\text{FWER}} \overset{?}{\leq} \alpha$ for error control



Component 2: select candidate set interactively

$P \to g(P) \longrightarrow R_t$ for cand. set selection

$P \to h(P) \longrightarrow \widehat{\text{FWER}}_t \overset{?}{\leq} \alpha$ for error control



$R_0 = \{1, \ldots, n\}$

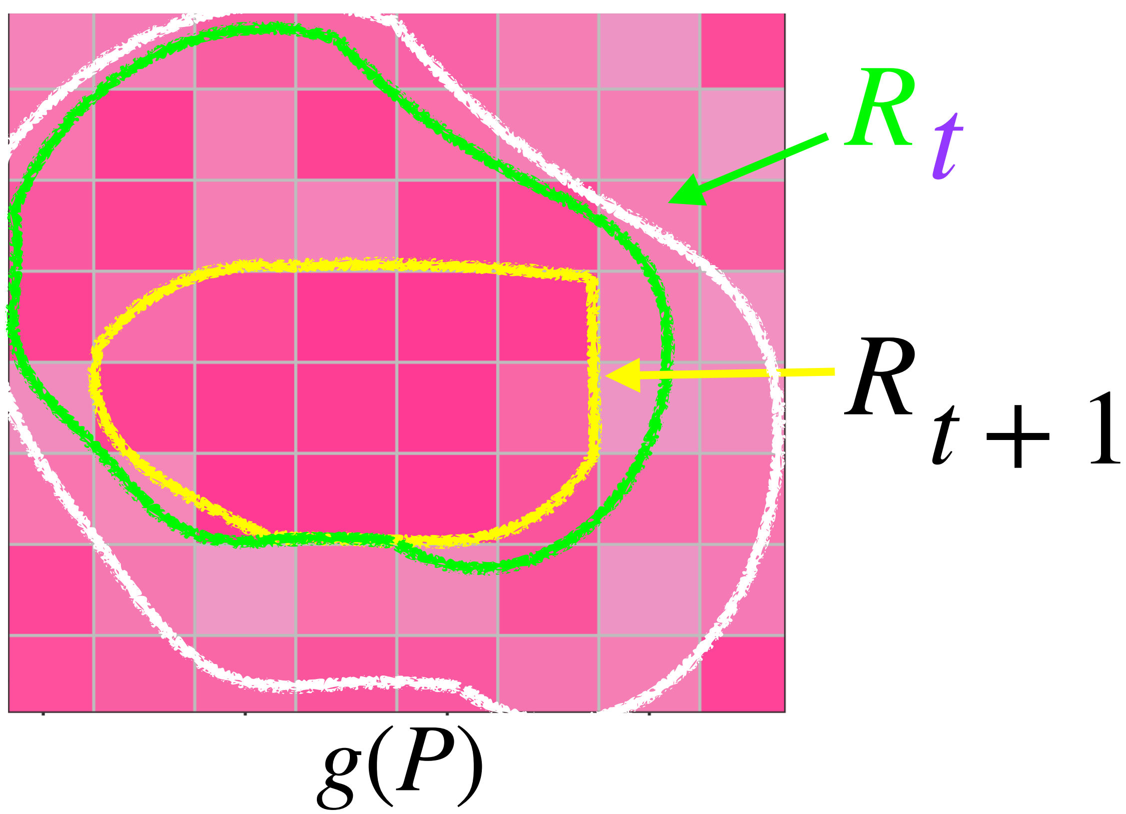
$R_0 \supseteq R_1 \supseteq \ldots$

progressively shrink R_t

Component 2: select candidate set interactively

$P \to g(P) \to R_t$ for cand. set selection

$P \to h(P) \to \widehat{\text{FWER}}_t \overset{?}{\leq} \alpha$ for error control



$R_0 = \{1, \ldots, n\}$

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progressively shrink R_t

$\{g(P_i)\}_{i=1}^n$

Component 2: select candidate set interactively

$P \to g(P) \to R_t$ for cand. set selection

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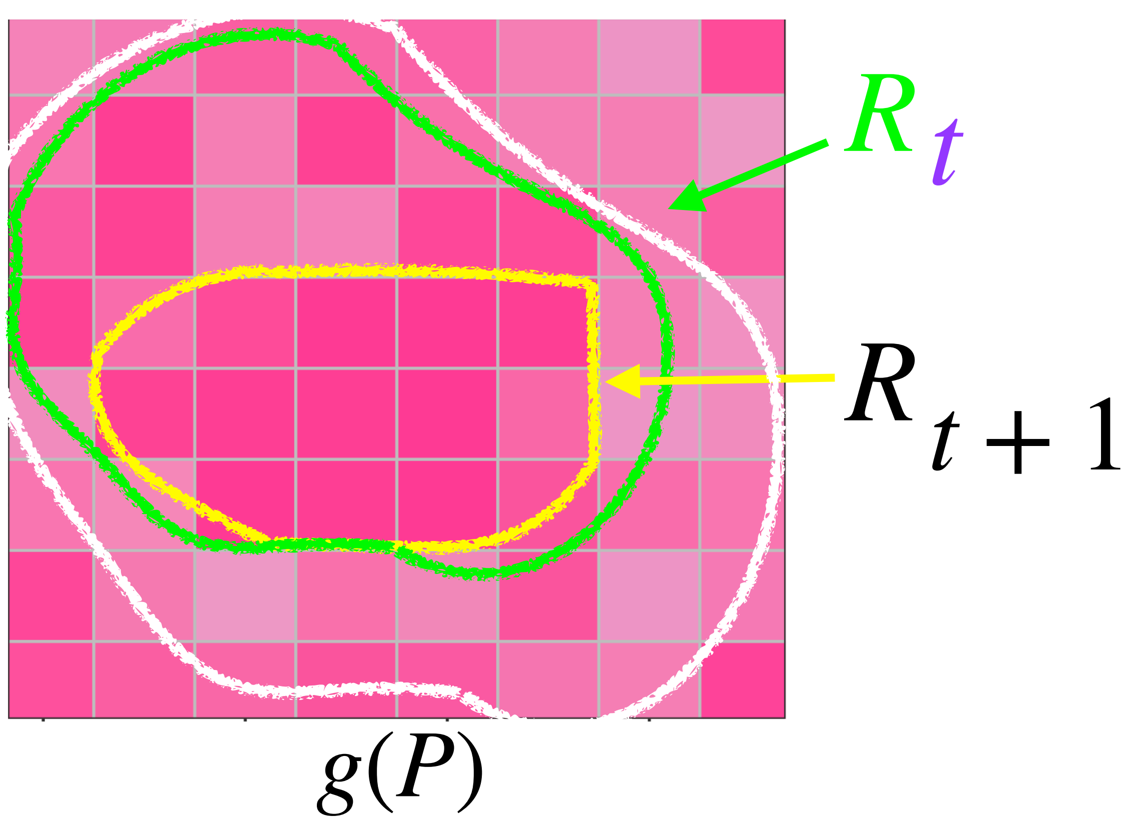

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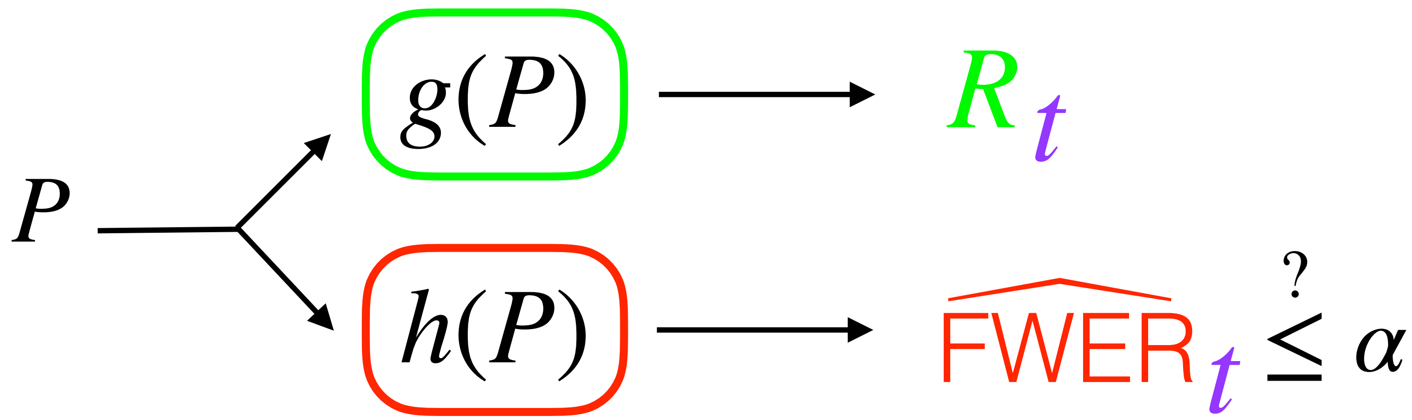
progressively shrink R_t

$\{g(P_i)\}_{i=1}^n$

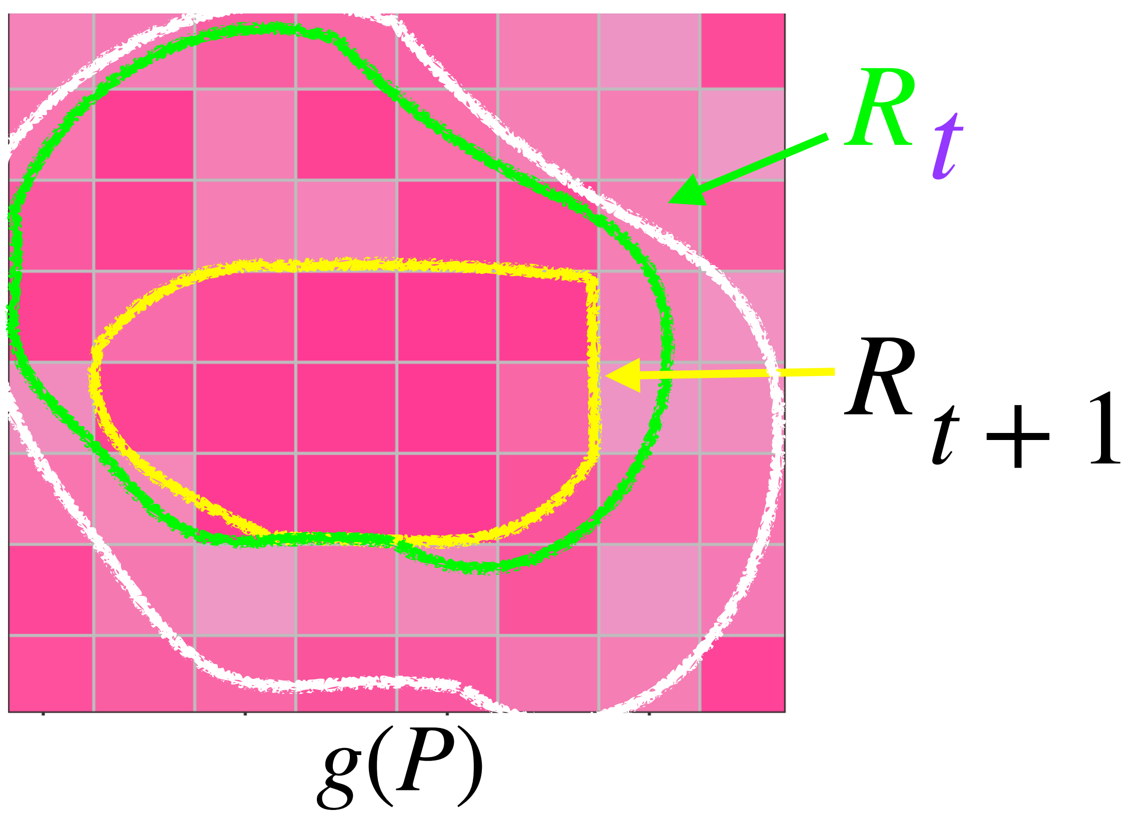
+ coordinates

Component 2: select candidate set interactively



for cand. set selection

for error control



$R_0 = \{1, \ldots, n\}$
$R_0 \supseteq R_1 \supseteq \ldots$

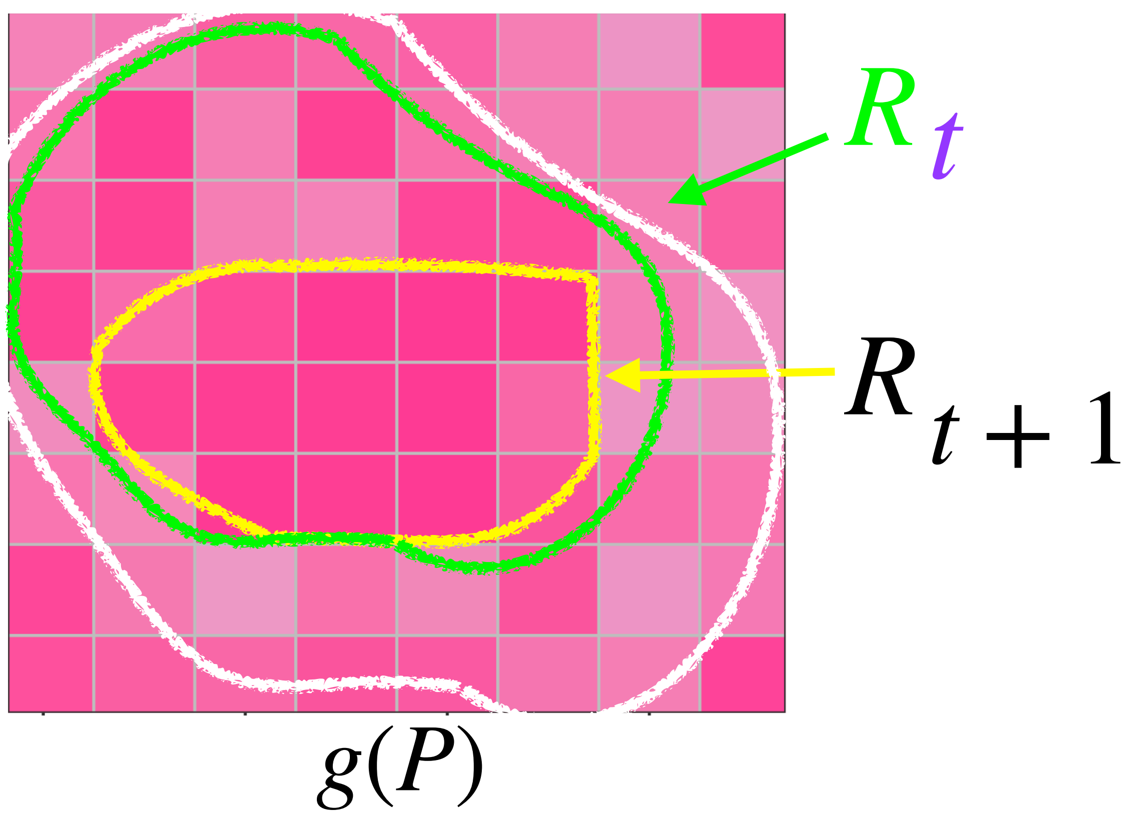
progressively shrink R_t

$\{g(P_i)\}_{i=1}^n$
\+ coordinates
(side information $\{x_i\}_{i=1}^n$)

Component 2: select candidate set interactively

$P \to g(P) \to R_t$ for cand. set selection

$P \to h(P) \to \widehat{\text{FWER}}_t \overset{?}{\leq} \alpha$ for error control

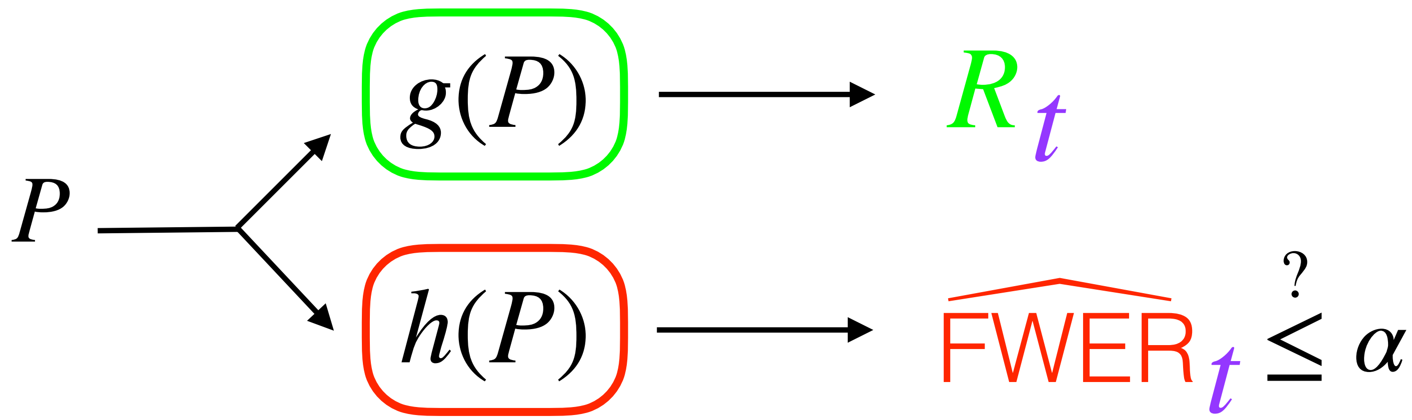


$R_0 = \{1, \ldots, n\}$
$R_0 \supseteq R_1 \supseteq \ldots$

progressively shrink R_t

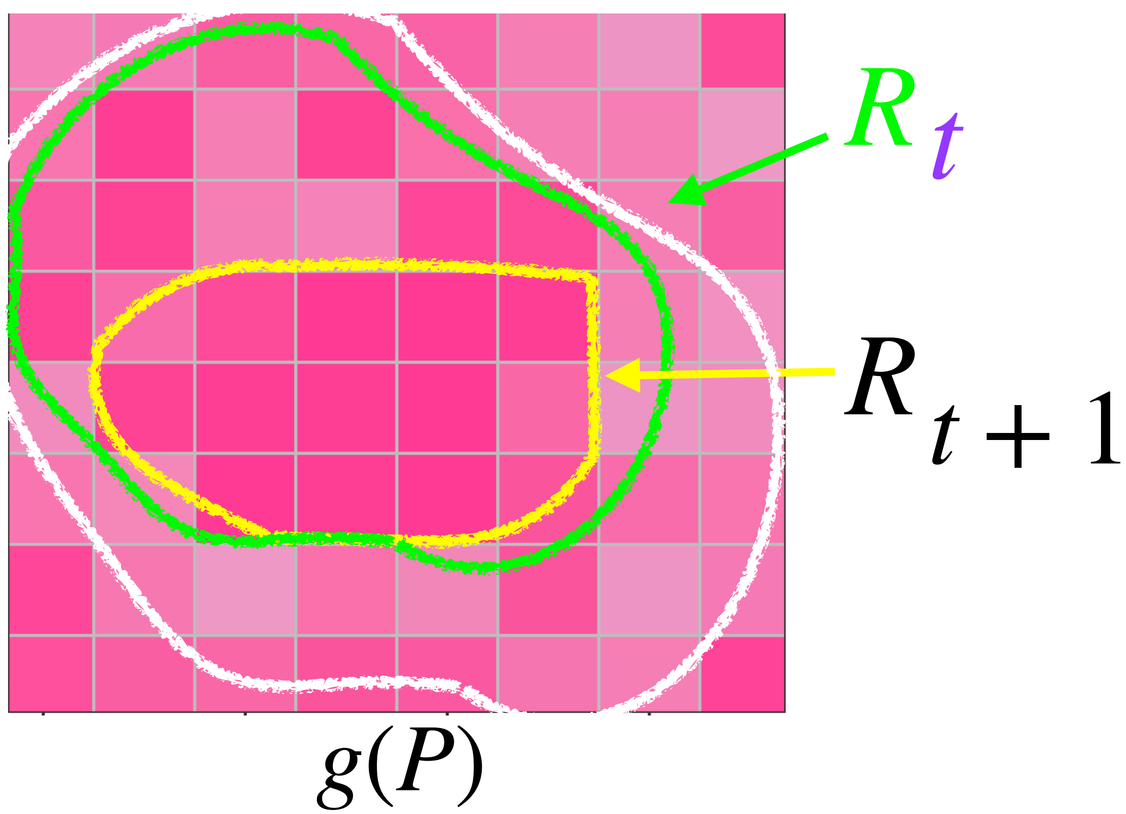
$\{g(P_i)\}_{i=1}^n$
+ coordinates
(side information $\{x_i\}_{i=1}^n$)
+ $\{h(P_i)\}_{i \notin R_t}$

Component 2: select candidate set interactively



for cand. set selection

for error control



$R_0 = \{1, \ldots, n\}$

$R_0 \supseteq R_1 \supseteq \ldots$

progressively shrink R_t using increasing information:

$\{g(P_i)\}_{i=1}^n$

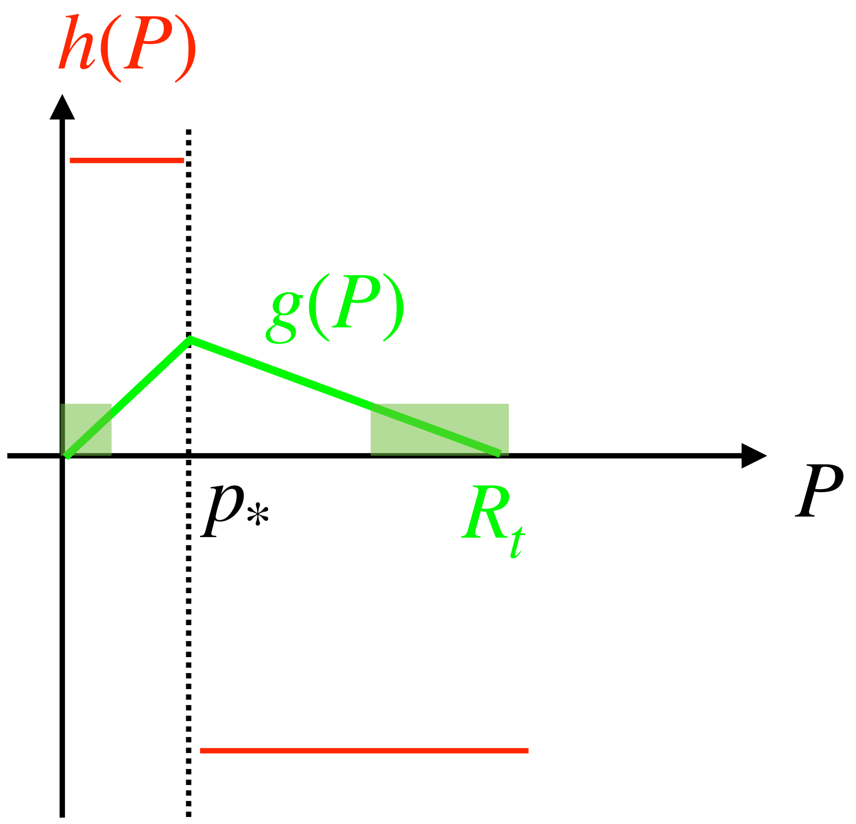
+ coordinates

(side information $\{x_i\}_{i=1}^n$)

+ $\{h(P_i)\}_{i \notin R_t}$

Component 3: error control

FWER := $\mathbb{P}$(#false rejections ≥ 1)



Component 3: error control

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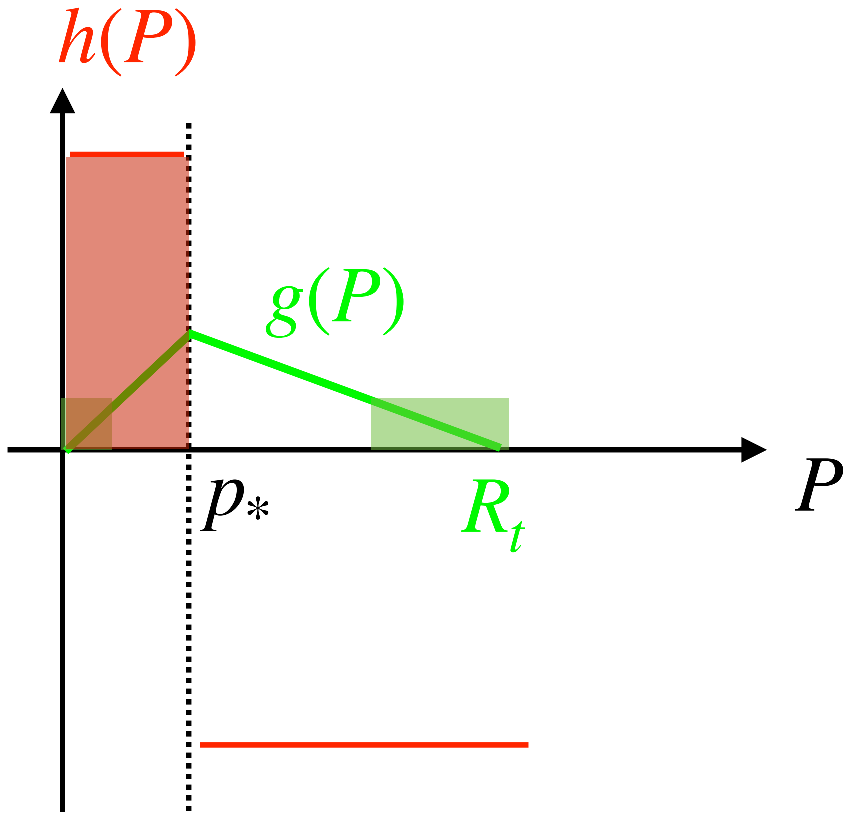
Reject the set

$$\{H_i \in R_t : h(P_i) = 1\}.$$



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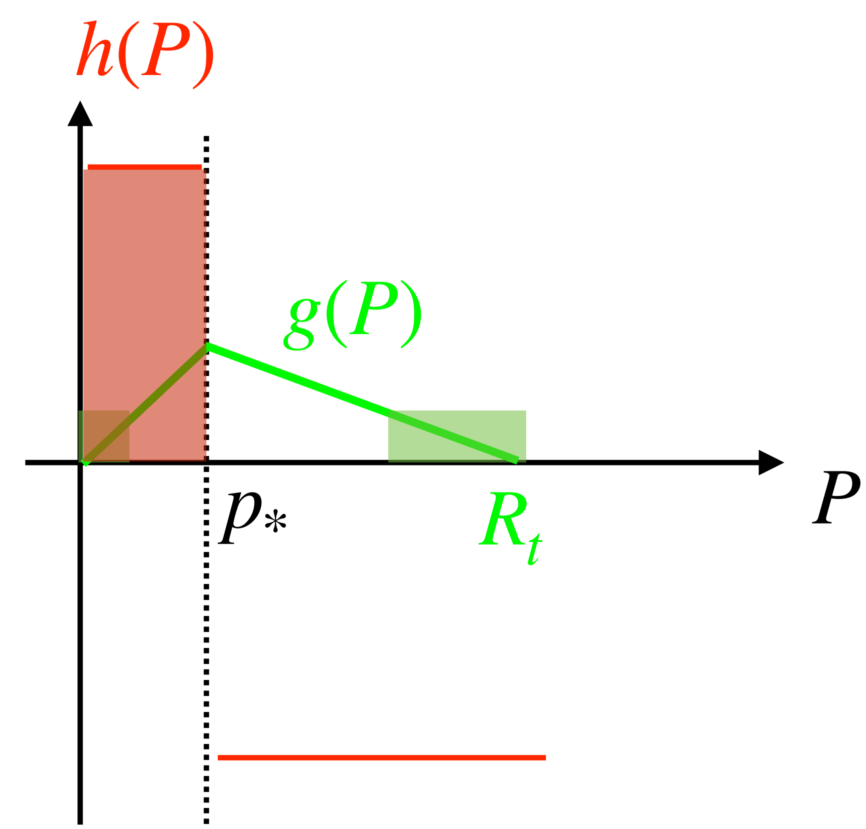
Count

$$R_t^- := |\{H_i \in R_t : h(P_i) = -1\}|$$

$h(P_i) \sim \mathrm{Ber}(p_*)$ if H_i is null



FWER control using binary var.: Janson & Su (2016)

Component 3: error control

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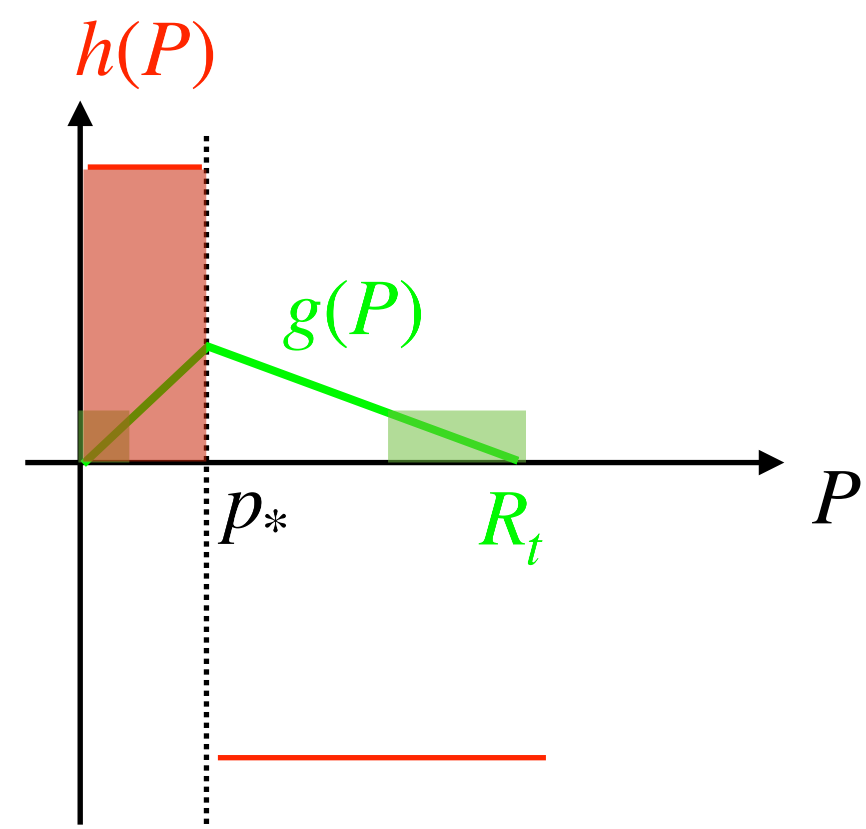
Stop shrinking when

$$\widehat{\text{FWER}}_t := 1 - (1 - p_*)^{R_t^- + 1} \leq \alpha.$$



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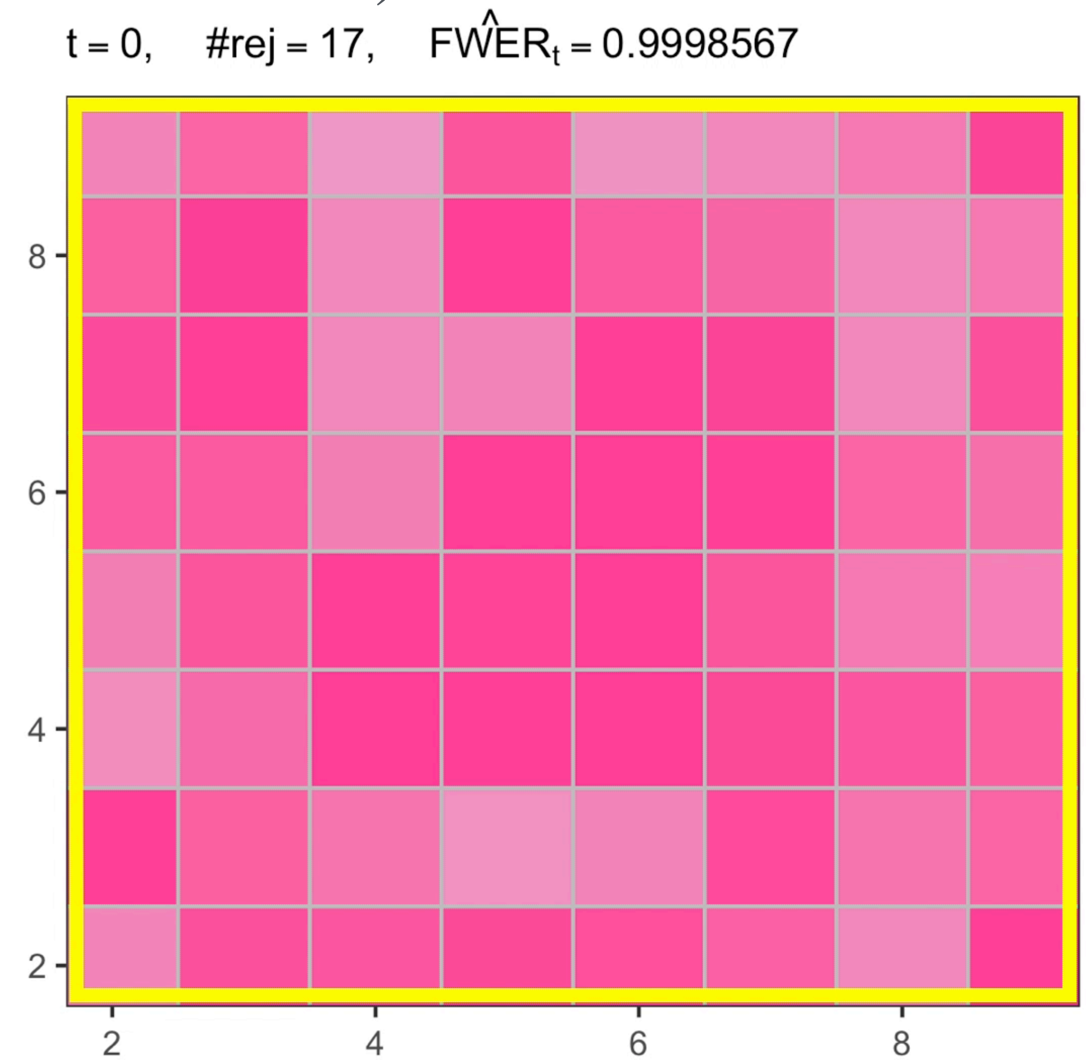

10×10 hypotheses with 9 non-nulls ($\alpha = 0.2$)

FWER control using binary var.: Janson & Su (2016)

Component 3: error control

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Reject the set

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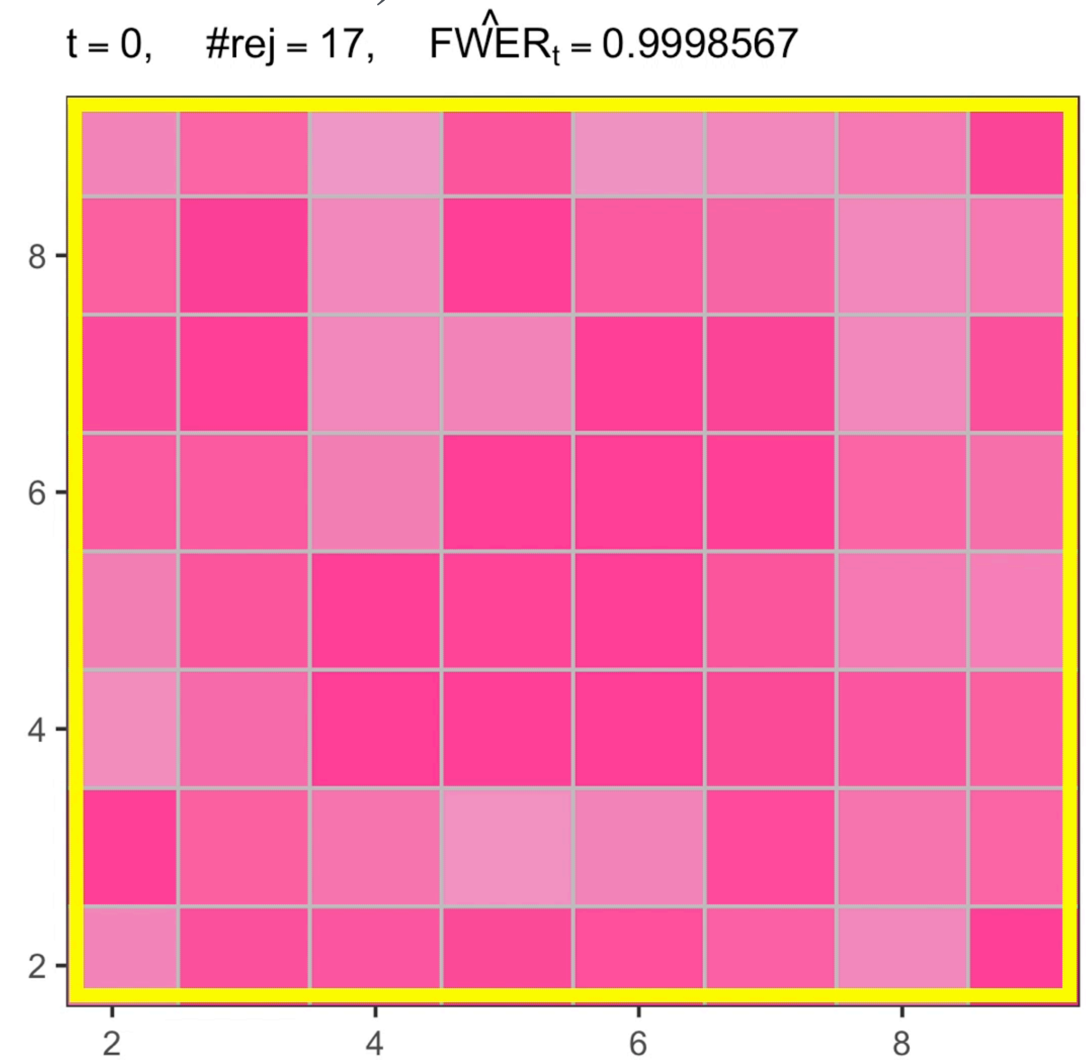

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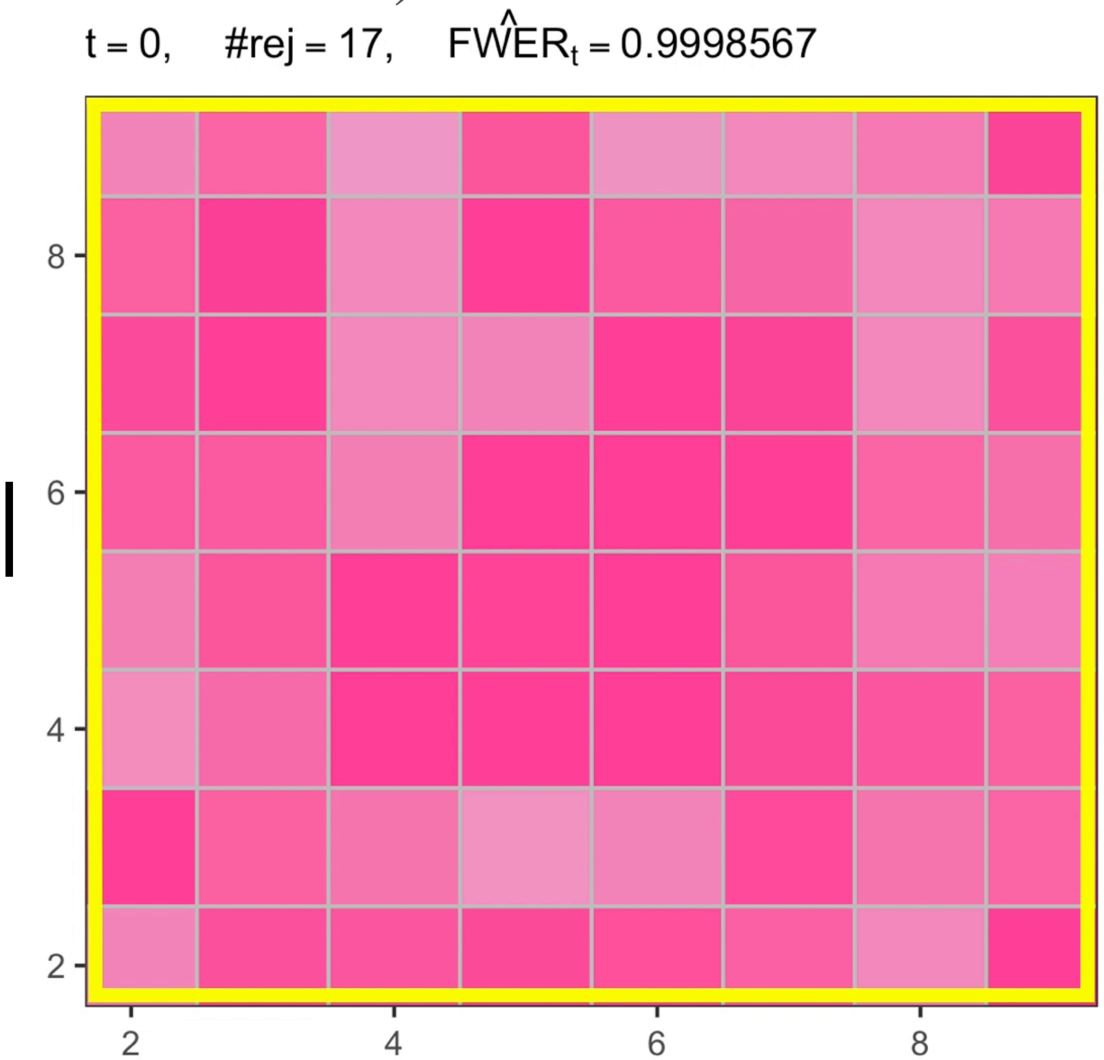


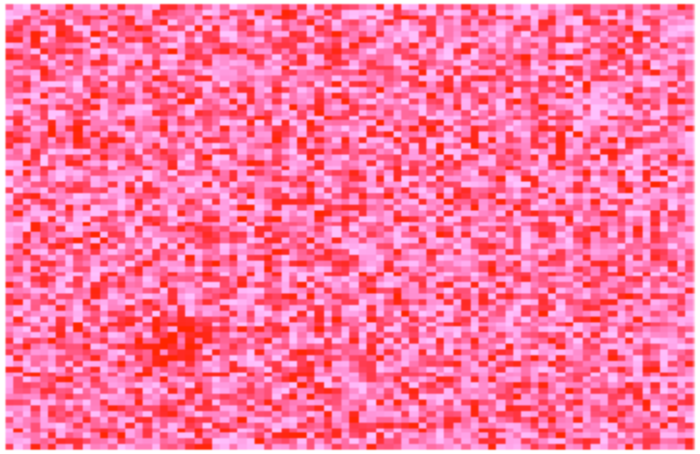
10×10 hypotheses with 9 non-nulls
($\alpha = 0.2$)

Theorem: the i-FWER method control FWER if null p-values are mutually independent, and are independently of the non-nulls.

FWER control using binary var.:
Janson & Su (2016)

Strategies to shrink R_t

- Estimate the probability of being non-null.

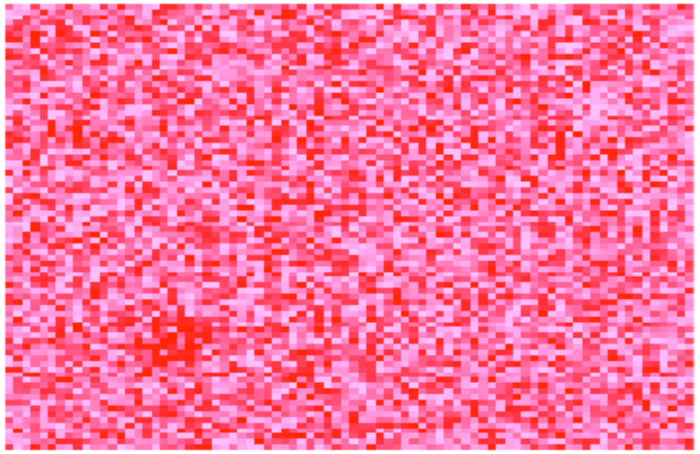


$g(P)$

smoothed probability

Strategies to shrink R_t

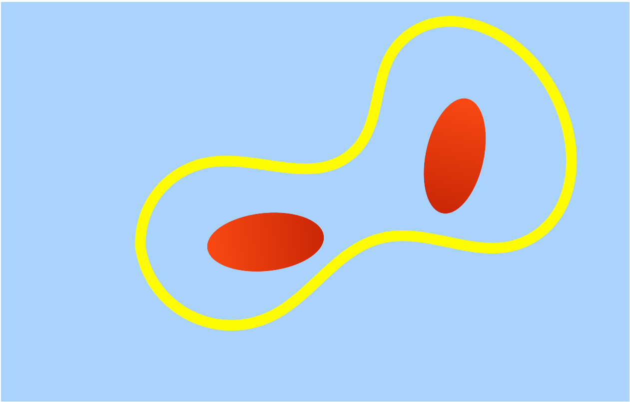
- Estimate the probability of being non-null.



$g(P)$

smoothed probability

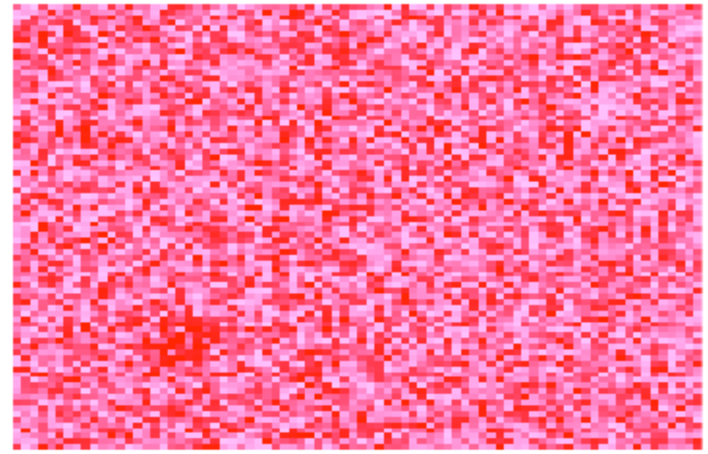
- Change the strategy at any step.



single center?

Strategies to shrink R_t

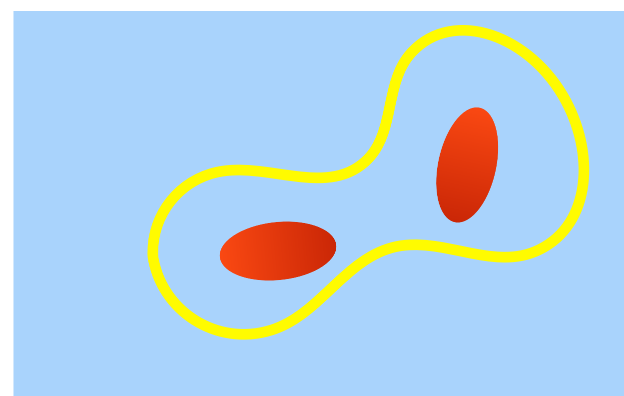
- Estimate the probability of being non-null.



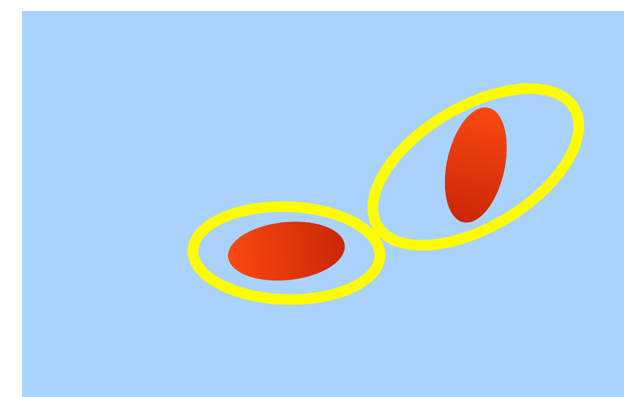
$g(P)$

smoothed probability

- Change the strategy at any step.



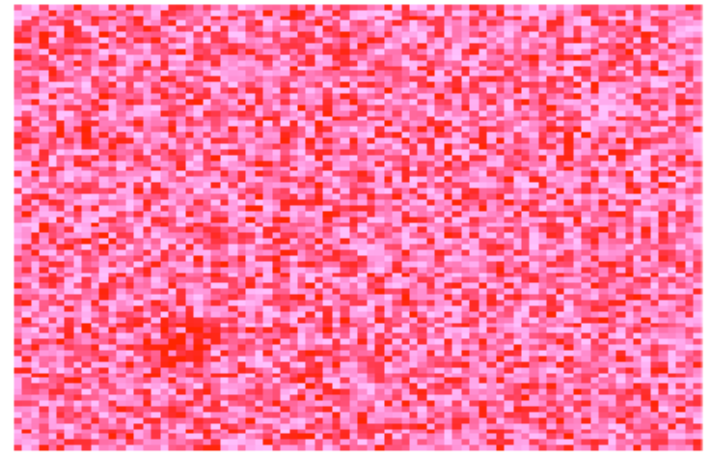
single center?



two centers

Strategies to shrink R_t

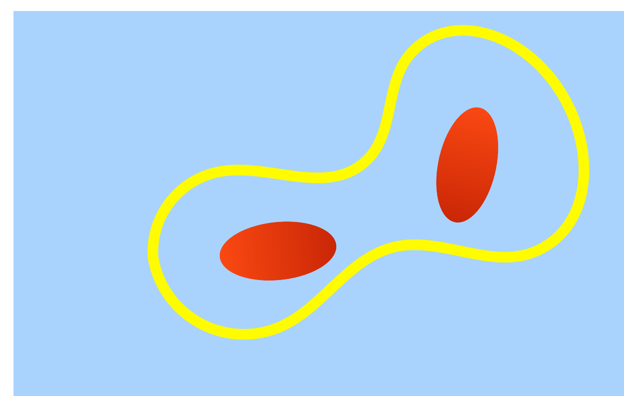
- Estimate the probability of being non-null.



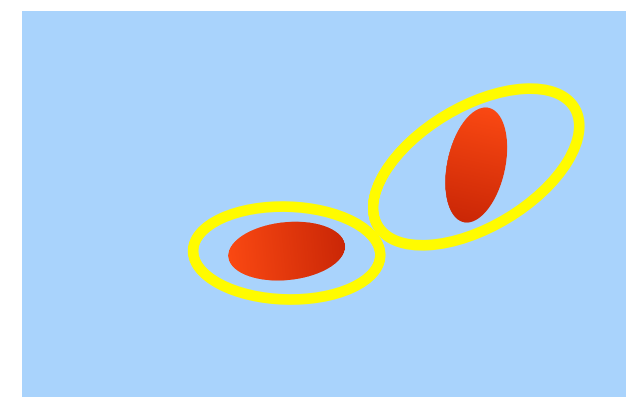
$g(P)$

smoothed probability

- Change the strategy at any step.

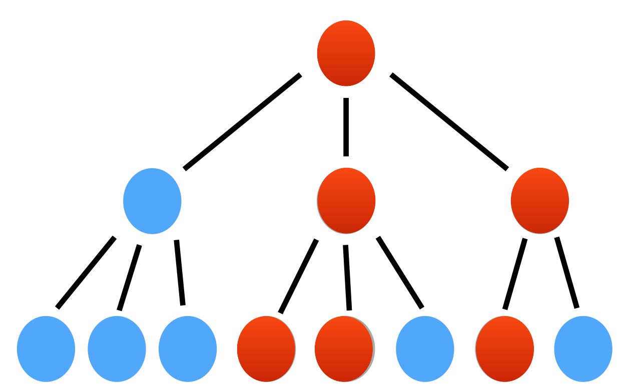


single center?



two centers

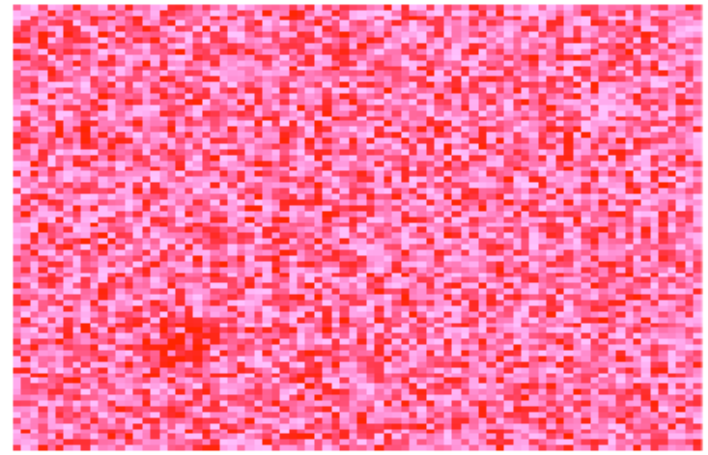
- Customize the strategy to different structures.



Hierarchical structure

Strategies to shrink R_t

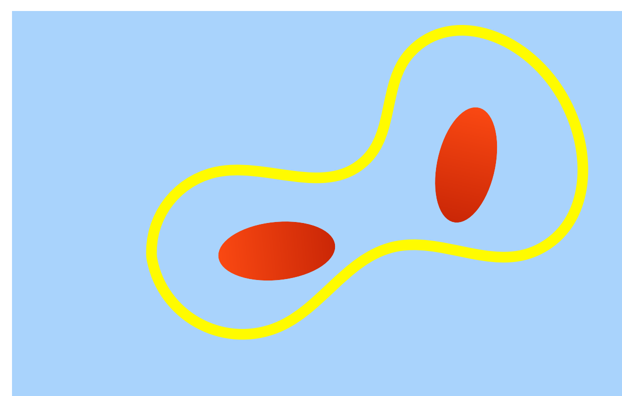
- Estimate the probability of being non-null.



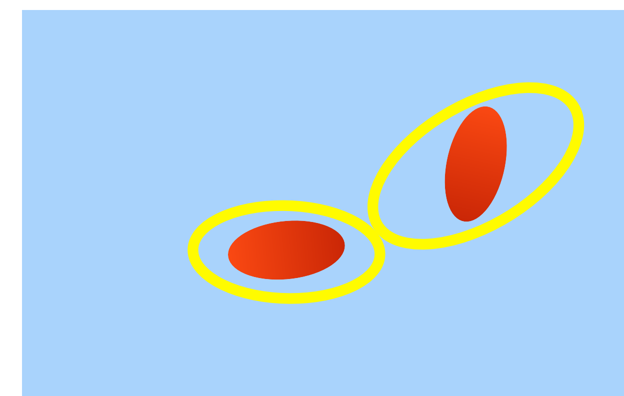
$g(P)$

smoothed probability

- Change the strategy at any step.

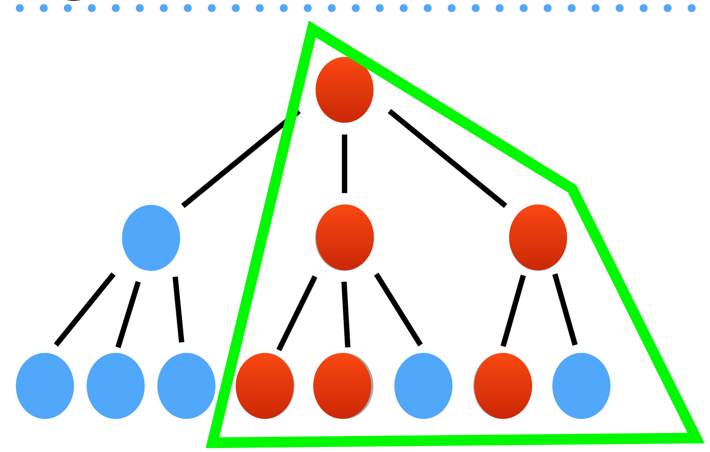


single center?



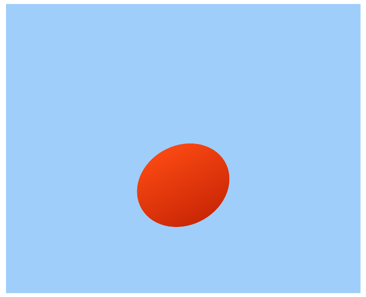
two centers

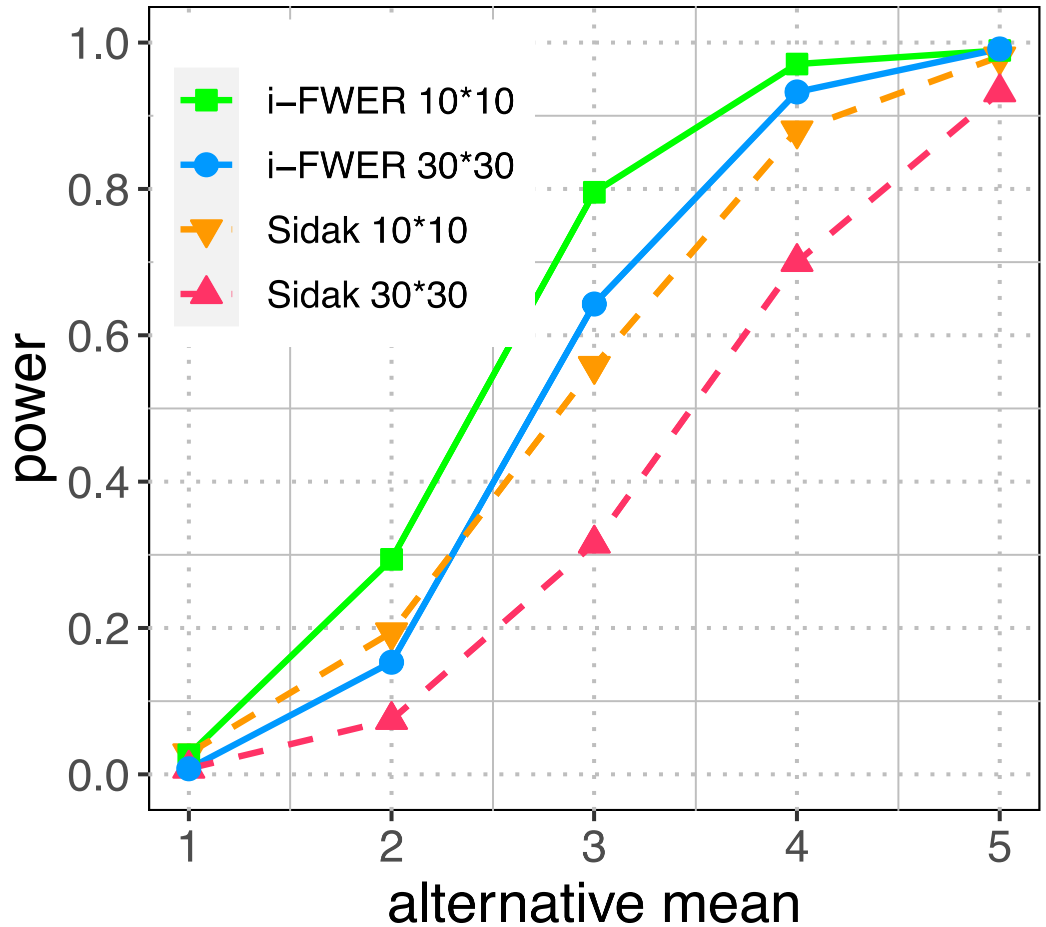
- Customize the strategy to different structures.



Hierarchical structure

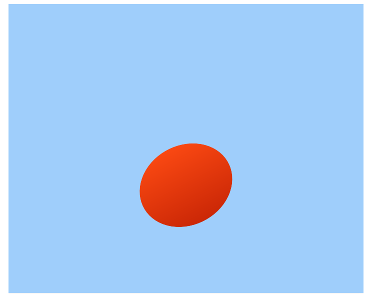
Grid

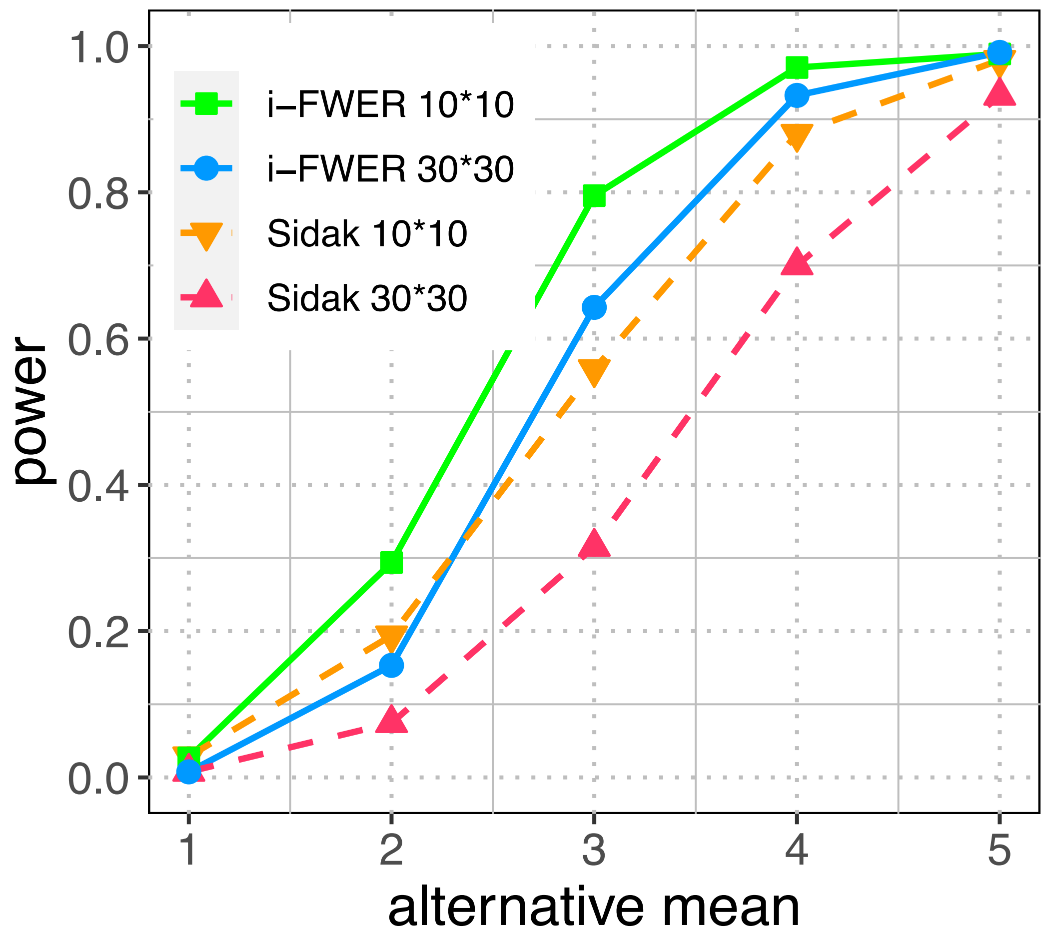




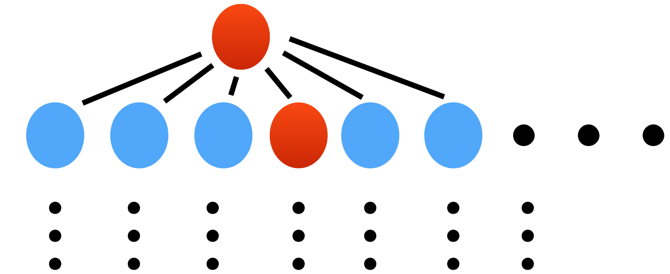
Meinshausen (2008); Goeman and Finos (2012); Ignatiadis et al. (2016); Lei, Fithian (2018)

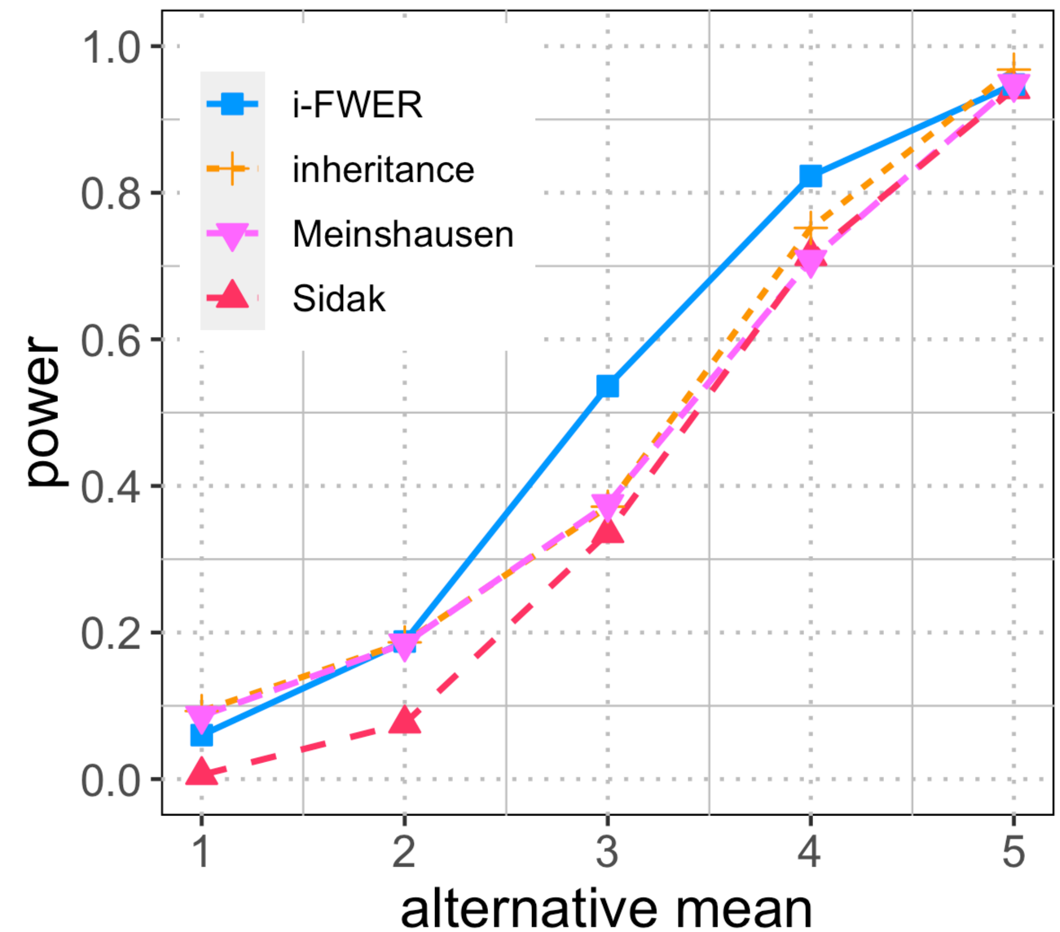
Grid





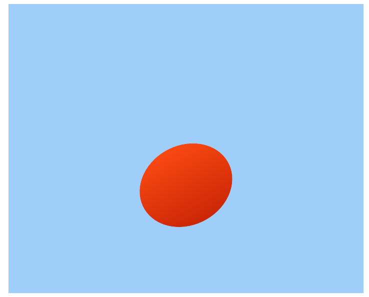
Tree

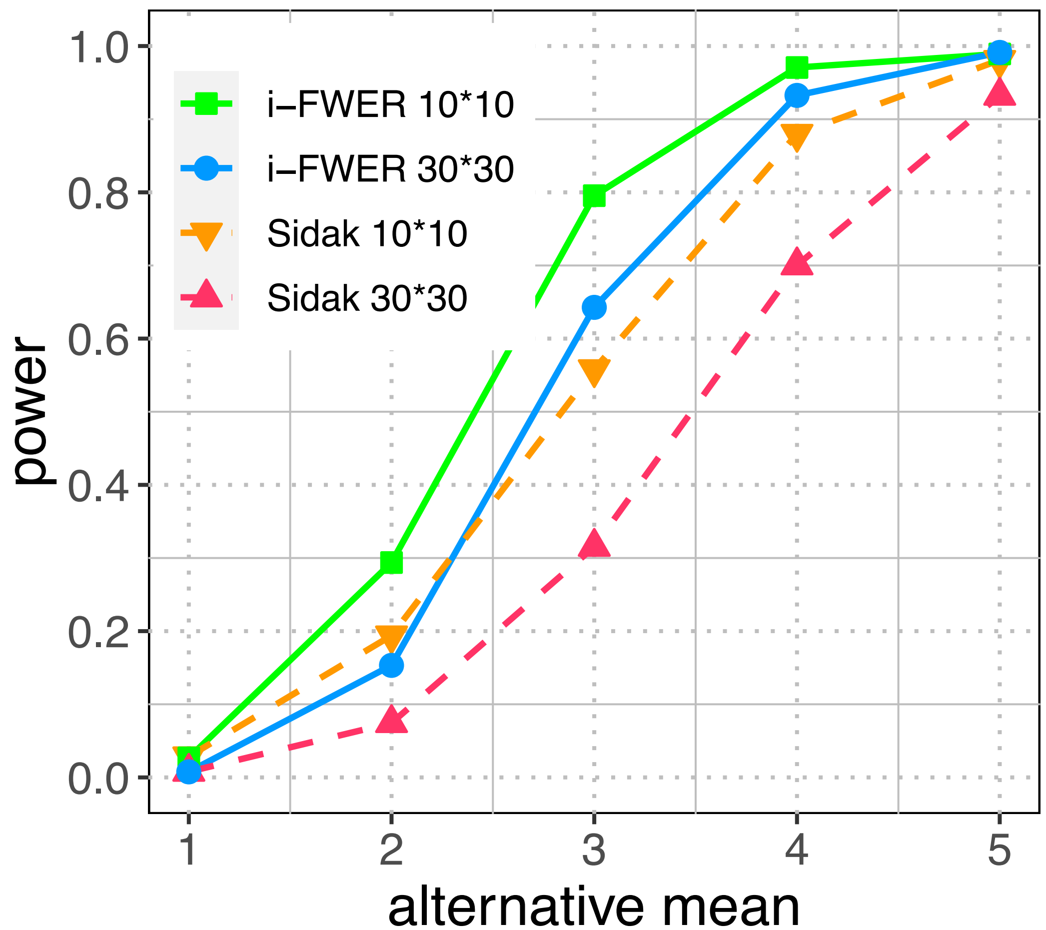




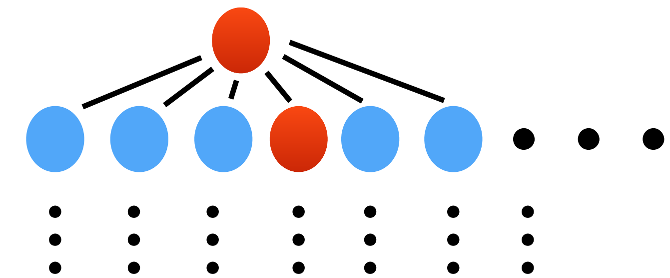
Meinshausen (2008); Goeman and Finos (2012); Ignatiadis et al. (2016); Lei, Fithian (2018)

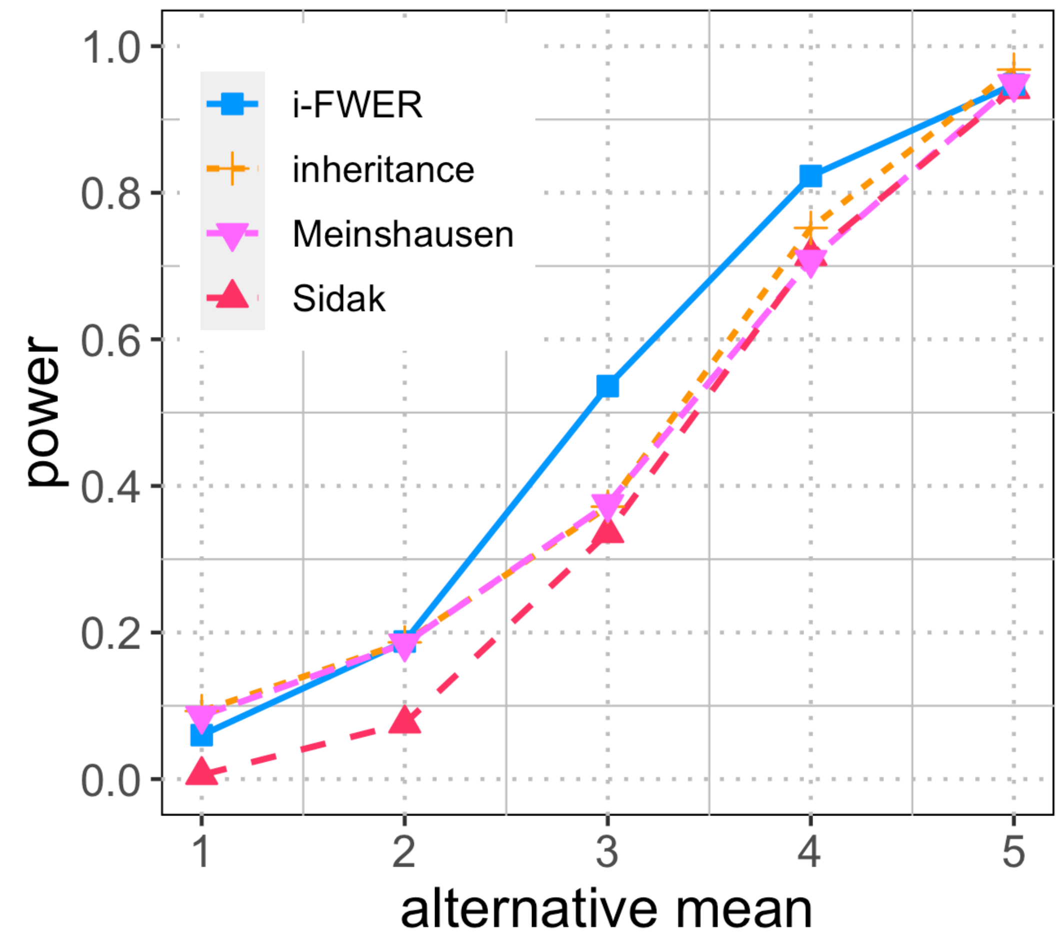
Grid





Tree





Real data: RNA sequence

FWER level	IHW★	i-FWER
0.1	1552	1613
0.2	1645	1740
0.3	1708	1844

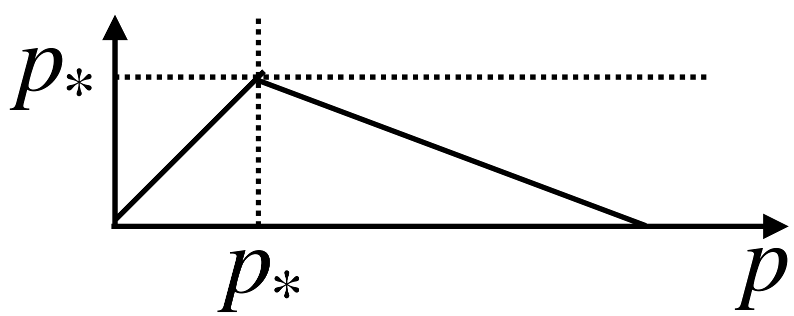
differentially expressed genes
in airway smooth muscle cell lines
in response to dexamethasone

Meinshausen (2008); Goeman and Finos (2012);
★Ignatiadis et al. (2016); Lei, Fithian (2018)

Extensions

Masking functions

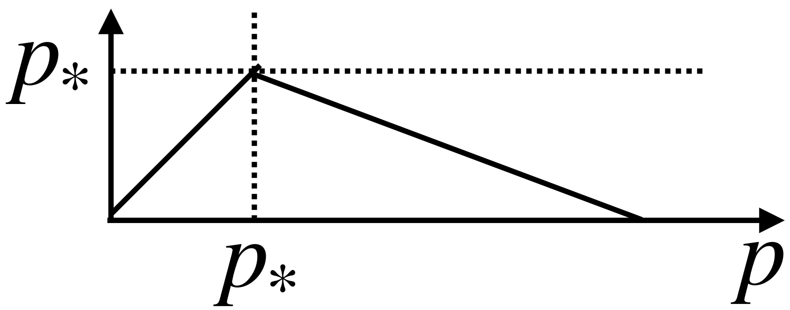
Tent function



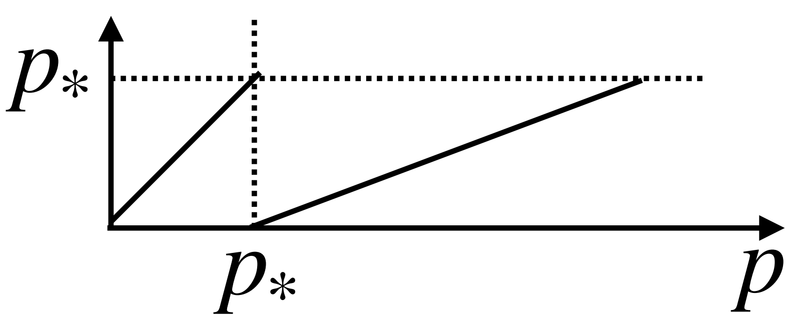
Extensions

Masking functions

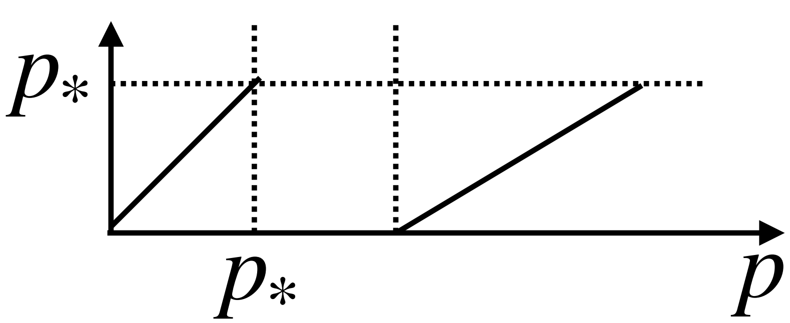
Tent function



Railway function



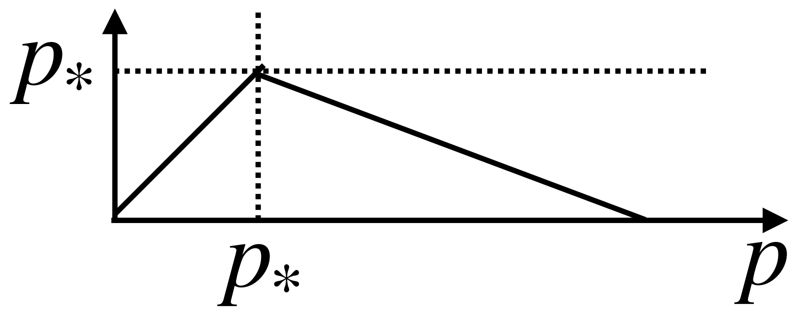
Gap function



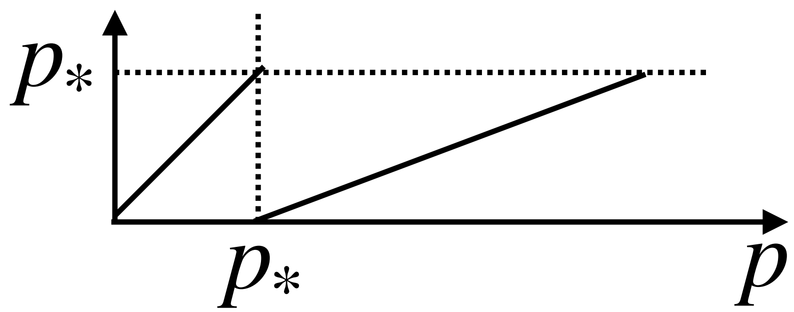
Extensions

Masking functions

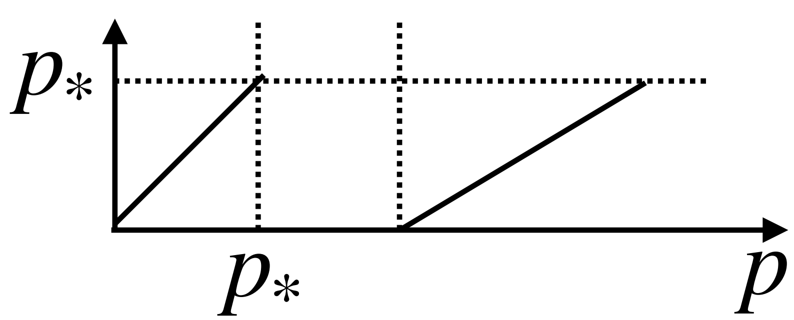
Tent function



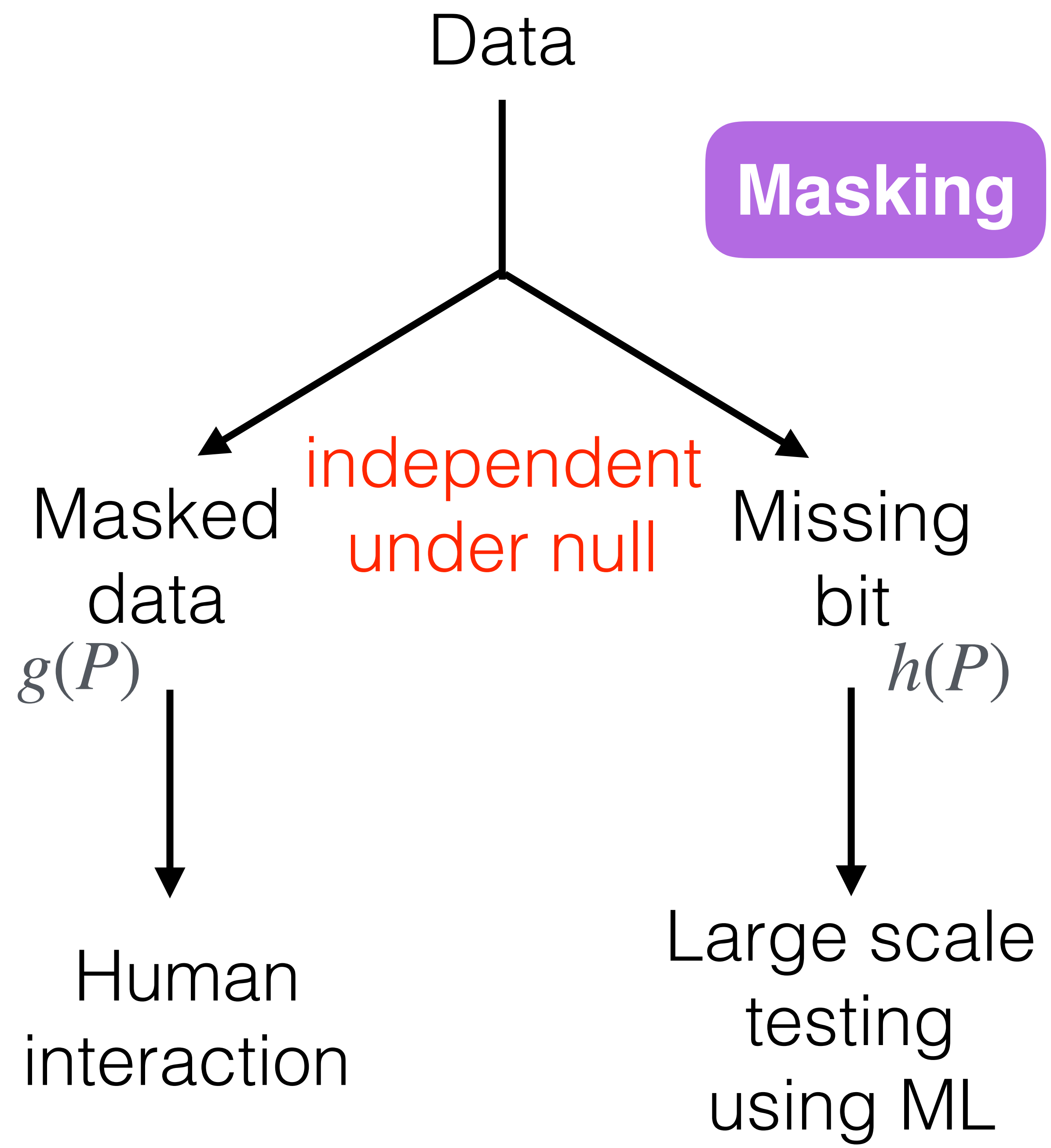
Railway function



Gap function



Interactive testing



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Familywise error rate control by interactive unmasking

Boyan Duan

Aaditya Ramdas

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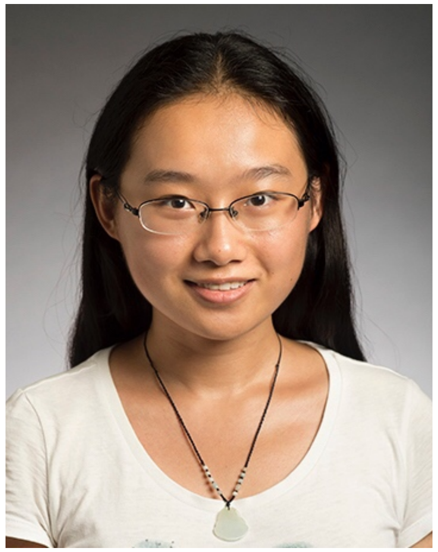

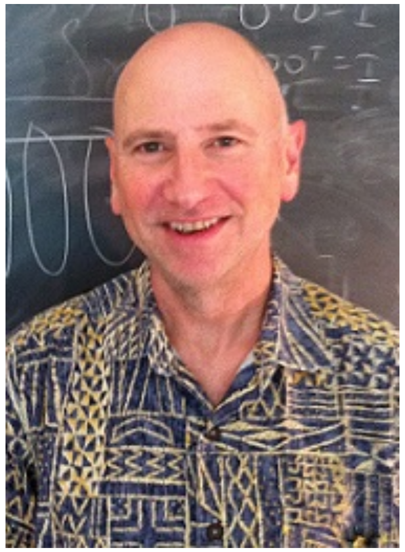

Thank you!