Non-consonant rejections in Hommel's procedure

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FWER and FDR for large problems

Large hypothesis testing problems

Behavior of FWER and FDR-controlling methods is very different

As number of hypotheses $m \to \infty$

Let $|R|$ be the number of rejected hypotheses

Typical behavior FWER

$|R|/m \to 0$ (e.g. Bonferroni)

Typical behavior FDR

$|R|/m \to c \geq 0$ where $c > 0$ if enough signal present (e.g. BH)

How about FDP confidence?

G&S 2011

Proposed simultaneous confidence for FDP based on closed testing

Confidence bound $q_\alpha(S)$ for every S

Upper confidence bound for FDP in set S simultaneous over all S

Question of this talk

How do these bounds scale if $m \to \infty$?

- Simultaneous and based on closed testing, so like FWER?
- FDP is the criterion, so like FDR?

Two perspectives

Sizes of the problem

Number of hypotheses m; sample size n

Large problems

Finite n; $m \to \infty$

Uniform consistency

Let $n \to \infty$, but look at behavior uniform in m

Closed testing, Simes

Setup

Elementary hypotheses $H_1, \dots, H_m$ with p-values $p_1 \leq \dots \leq p_m$

Intersection hypothesis

Define $H_I = \bigcap_{i \in I} H_i$ for all $I \subseteq \{1, \dots, m\}$

Simes local test

Reject H_I iff $|I| p_{(i:I)} \leq i\alpha$ where $p_{(i:I)}$ ith smallest among $\{p_j\}_{j \in I}$

Closed testing

Reject H_I iff Simes test rejects H_J for all $J \supseteq I$

FDP confidence

FDP of $S \subseteq \{1, \ldots, m\}$

FDP $\pi(S) = |T \cap S|/|S|$ where $T \subseteq \{1, \ldots, m\}$ true hypotheses

FDP confidence bound

$q_\alpha(S) = \max\{|I| \colon I \subseteq S, H_I \text{ not rejected by CT}\}/|S|$

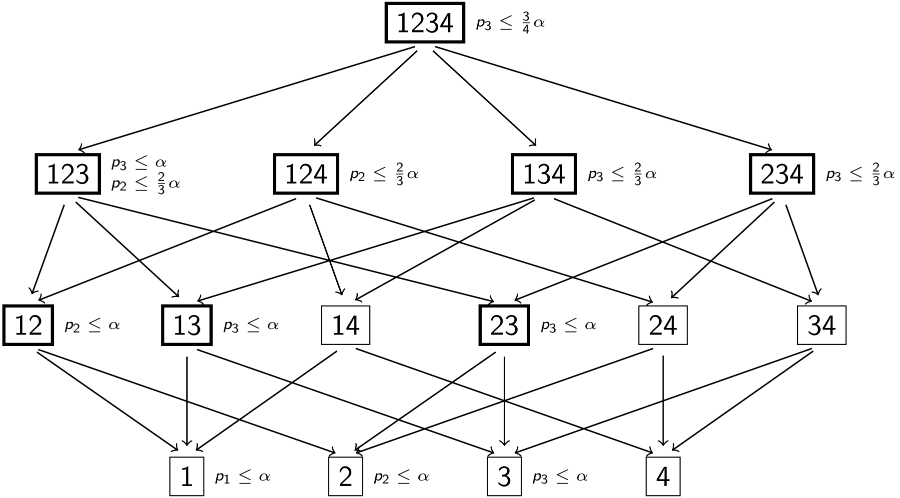
Simultaneous

$\mathrm{P}(\pi(S) \leq q_\alpha(S) \text{ for all } S \subseteq \{1, \ldots, m\}) \geq 1 - \alpha$

Huge simultaneity

2^m simultaneous confidence statements

Example ($\alpha/2 < p_1 \leq p_2 \leq p_3 \leq 2\alpha/3$, and $p_4 > \alpha$)



Non-consonance

Non-consonant rejection

Rejection of H_I not implied by rejection of some H_i, $i \in I$

FWER rejections (Hommel)

Reject $R = \{1 \leq i \leq m \colon H_i \text{ rejected by CT}\}$

FWER perspective

Non-consonant rejection = waste of resources

FDP confidence perspective

Non-consonant rejections: we may have $q_\alpha(S) < |S \setminus R|/|S|$

Computation for large problems

Shortcut

Fast algorithm for closed testing

Shortcut for $q_\alpha(S)$

We improved the quadric shortcut of Hommel

- in speed
- extension to non-elementary hypotheses and $q_\alpha(S)$

Complexity

- $O(m \log m)$ for calculating h
- $O(|S|)$ for $q_\alpha(S)$ if h is known

Setup

Power for large problems

What are the properties of the method as m gets large?

Model that allows $m \to \infty$

Property that new p-values are 'like' previous ones

Efron model

Test statistics drawn i.i.d. from a mixture distribution
$F(x) = \gamma F_0(x) + (1 - \gamma) F_1(x)$

p-value distribution

Also a mixture distribution $P(x)$

Known FDR and FWER results

FDR: Benjamini and Hochberg

Let B be the index set of hypotheses rejected by BH at α

Chi

$|B|/m \to c > 0$ if P is Simes-detectable at α

Simes-detectable

$P^{-1}(x) < x\alpha$ for at least one $x > 0$

For Hommel rejected set R

$|R|/m \to 0$ however much signal there is

Equivalent Chi-result

Note

$|R|/m \to 0$ implies $|S \setminus R|/|S| \to 1$ if $|S|/m \not\to 0$

Theorem

If P is Simes-detectable at level $q\alpha$ for some $q \in (0, 1)$, then there is a set S with $|S|/m \to x$ for some $x \in (0, 1)$ such that $q_\alpha(S) \to q' < q$.

Clearly

Many non-consonant rejections as $m \to \infty$

Change of perspective

Classical asymptotics

We let sample size $n \to \infty$. Assume $p_i \to 0$ as $n \to \infty$ if $i \notin T$

Finite m asymptotics

- $\mathrm{P}(R = T^c) \to 1 - \alpha$ (consistent if $\alpha \to 0$ slowly)
- same for BH
- How about FDP bounds?

Large problems

How about consistency uniformly in m?

Uniform consistency of $q_\alpha(S)$

Theorem

If $|S|/m \to c > 0$ when $m \to \infty$ then as $n \to \infty$, $q_\alpha(S) \to \pi(S)$ uniformly in m

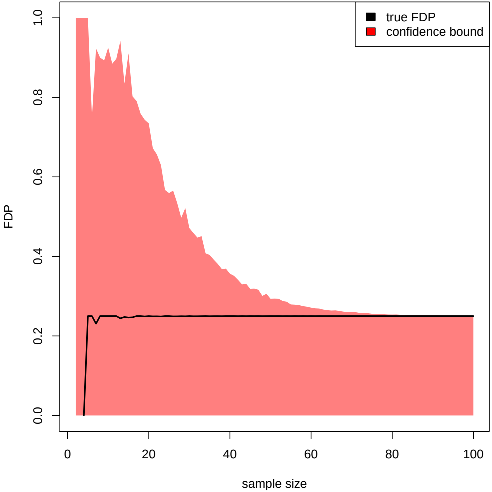
Interpretation

Consistency for sets that are 'large enough'

Note

Consistency for every $\alpha \in (0, 1)$

Illustration by simulation: $m = n^3$



Discussion

All-resolution inference

Simultaneous upper bound for 2^m FDPs is uniformly consistent

Small versus large sets

Consistency fails for vanishing sets

Detection vs pinpointing

It's much easier to detect (quantify amount) than to pinpoint

Non-consonant rejections with Simes

Rare for small m; ubiquitous for large m

Read more?

Goeman JJ and Solari A (2011)
Multiple Testing for Exploratory Research.
Statistical Science 26 (4) 584–597

Chi Z (2007)
On the performance of FDR control: constraints and a partial solution
Annals of Statistics, 35 (4) 1409–1431

Goeman JJ, Meijer RJ, Krebs, T
`hommel` R package
`cran.r-project.org`

My Multiple Testing Group

Diaa al Mohamad

Confidence intervals for ranks based on partitioning

Jesse Hemerik

Permutation-based simultaneous confidence bounds for the FDP

Jakub Pecanka

Conditionalized testing for inflated p-values

Mitra Ebrahimpoor

All-resolution inference for gene sets

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Comparison of different variable selection methods

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