Analysis of Error Control in Large Scale Two-Stage Multiple Hypothesis Testing

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Outline

What is a Two-stage Procedure?

In large-scale multiple testing, a natural testing strategy is to

- **Stage 1.** reduce the number of tested hypotheses by some selection (screening or filtering) process;
- **Stage 2.** simultaneously test the selected hypotheses by using some conventional multiple testing method.

Practical Application Examples

Two-stage procedures have been extensively used in various practical applications (McClintick and Edenberg, 2006; Talloen et al., 2007; Hackstadt and Hess, 2009). Examples include

- Detecting differentially expressed genes across conditions in microarray experiments.
- Detecting brain voxels associated with a task in fMRI studies.
- Detecting adverse events associated with a new drug in clinical trials.
- Detecting genetic variants associated with a trail in genome-wide association studies.

Related Methods

- **Independent filtering:** Bourgon et al. (2010), Dai et al. (2012), and Kim and Schliekelman (2016).
- **Sample splitting:** Cox (1975), Rubin et al. (2006), and Wasserman and Roeder (2009).
- **Data-driven weighted methods:** Fino and Salmaso (2007), Ignatiadis et al (2016), Li and Barber (2016), and Lei and Fithian (2016).
- **Selective inference methods:** Benjamin and Yekutieli (2005), Taylor and Tibshirani (2015), Berk et al (2013), Barber and Candés (2015), Lee et al (2016), Fithian et al. (2014), etc.
- **Other methods exploiting covariate information:** Cai and Sun (2009), Yoo et al. (2010), Hu et al. (2010), Du and Zhang (2014), etc.

Advantages of Independent Filtering

In this talk, we mainly focus on the method of independent filtering. It has several advantages:

- completely removes the selection effect in the control of type 1 error rate;
- reduces the multiplicity effect;
- does not “waste” data while carrying out both selection and testing.

The Key Issues

It has also several key issues remaining for independent filtering:

- Asymptotic power analysis;
- Construction of selection rules, including choice of selection statistics and determination of selection thresholds;
- Comparison with the corresponding conventional (one-stage) multiple testing methods;
- Type 1 error rate control under dependence;
- Statistical interpretation: quantifying the effects of various factors on performance of independent filtering.

Outline

Basic Setup

Consider a stylized Gaussian model:

- Assume that for $i = 1, \ldots, m$, a sample of size n from a normal population with unknown mean μ_i and variance σ_i^2 is observed; that is, data
$$X_{ij} \overset{i.i.d}{\sim} N(\mu_i, \sigma_i^2), \quad ; j = 1, \ldots, n.$$
- The m samples are assumed to be mutually independent.
- For $i = 1, \ldots, m$, consider testing hypotheses
$$H_i : \mu_i = 0 \quad vs. \quad H_i' : \mu_i \neq 0 \ .$$

Basic Setup (Cont.)

- Define the selection and test statistics

$$S_{n,i} = \sum_{j=1}^{n} X_{i,j}^2 \quad \text{and} \quad T_{n,i} = \frac{\sqrt{n}\bar{X}_{n,i}}{\hat{\sigma}_{n,i}}.$$

- The **basic two-stage strategy** for our method: the statistics $S_{n,i}$ are first used to "select" which of the hypotheses to "test" in the second stage, at which point the statistics $T_{n,i}$ are used.
- **Basic facts:** under $H_i : \mu_i = 0$, we have that

$$S_{n,i}/\sigma_i^2 \sim \chi_n^2 \quad \text{and} \quad T_{n,i} \sim t_{n-1} \ .$$

  But, the more important reason motivating our choice is that, by Basu's theorem, $S_{n,i}$ **and** $T_{n,i}$ **are independent under** H_i (Lehmann and Romano, 2005).

Basic Setup (Cont.)

- In our asymptotic analysis, the following is always assumed.

  Assumption A1: $\lim_{m\to\infty} \frac{\log m}{n} = d, 0 \leq d < \infty$, where d is a nonnegative constant.

- Let $|I_{m,1}|$ denote the number of false null hypotheses. In our asymptotic power analysis, some degree of sparsity regarding $|I_{m,1}|$ is often assumed.

  Assumption A2: $|I_{m,1}| \asymp m^{1-\epsilon}$ for some $0 < \epsilon \leq 1$.

Two-stage Single Hypothesis Testing

- For selecting and detecting **single true null hypothesis** $H_i : \mu_i = 0$ by using independent filtering, **the type 1 error rate** of rejecting H_i is

$$\begin{aligned} & \Pr_{\mu_i=0}\{H_i \text{ selected and detected}\} \\ = \quad & \Pr_{\mu_i=0}\{H_i \text{ selected}\} \cdot \Pr_{\mu_i=0}\{H_i \text{ detected}\}. \end{aligned} \tag{1}$$

  In (1), the first and second terms are type 1 error rates of selection and detection, respectively.

- **For example**, in order to ensure the type 1 error rate controlled at level α, it is enough to control type 1 error rate of detection at level 5α if the chance of selecting H_i is 20%.

Two-stage Single Hypothesis Testing (Cont.)

- For selecting and detecting **single false null hypothesis** H_i by using independent filtering, **the power** of rejecting H_i is

$$\begin{aligned} & \Pr_{\mu_i}\{H_i \text{ selected and detected}\} \\ = \; & \Pr_{\mu_i}\{H_i \text{ selected}\} \cdot \Pr_{\mu_i}\{H_i \text{ detected} | H_i \text{ selected}\}, \end{aligned}$$

  where $\Pr_{\mu_i}\{H_i \text{ selected}\}$ is the power of selection and $\Pr_{\mu_i}\{H_i \text{ detected} | H_i \text{ selected}\}$ is the conditional power of detection based on the event of H_i being selected.
- Thus, selection affects the overall power of independent filtering.

Outline

Basic Two-stage Bonferroni-type Procedure

Firstly, we consider two-stage procedures where the selection thresholds are fixed.

Procedure 1

1. ***Stage 1.*** *For $i = 1, \ldots, m$, given a fixed threshold u_i, H_i is selected iff $S_{n,i} \geq u_i$. Let $\hat{S}_n$ denote the indices of selected hypotheses.*
2. ***Stage 2.*** *Apply the Bonferroni test to selected hypotheses H_i with $i \in \hat{S}_n$; that is, reject H_i iff $|T_{n,i}| \geq t_{n-1}(1 - \frac{\alpha}{2|\hat{S}_n|})$, the $1 - \alpha/2|\hat{S}_n|$ quantile of the t-distribution with $n-1$ degrees of freedom.*

Theorem 1

For any choice of the sequence of fixed selection thresholds u_i, the above Procedure 1 controls the FWER at level α.

Remarks on Procedure 1

- The sequence of selection thresholds u_i is fixed but arbitrary.
- No matter the variances σ_i^2 are known or unknown, Procedure 1 always controls the FWER at level α.
- The FWER control of Procedure 1 only requires that any test statistic $T_{n,i}$ be independent of the selection statistics $S_{n,1}, \ldots, S_{n,m}$, if H_i is true.
- More generally, the FWER control of Procedure 1 even holds outside our stylized Gaussian model.

Two-stage Holm-type Procedure

Let $\hat{p}_{n,i}$ denote the marginal p-value when testing H_i based on $|T_{n,i}|$. Let $\tilde{p}_{n,i}$ be one if H_i is not selected and equal to $\hat{p}_{n,i}$ if it is selected. Let $\tilde{p}_{n,r_1} \leq \tilde{p}_{n,r_2} \leq \cdots \leq \tilde{p}_{n,r_m}$ denote the ordered p-values.

Procedure 2

1. ***Stage 1.*** *For $i = 1, \ldots, m$, given a fixed threshold u_i, H_i is selected iff $S_{n,i} \geq u_i$. Let $\hat{S}_n$ denote the indices of selected hypotheses.*
2. ***Stage 2.*** *Apply Holm's procedure to selected hypotheses H_i with $i \in \hat{S}_n$; that is, reject H_i iff $\tilde{p}_{n,r_j} \leq \alpha/(|\hat{S}_n| - j + 1)$ for $j = 1, \ldots, i$.*

Theorem 2

For any choice of the sequence of fixed selection thresholds u_i, the above Procedure 2 controls the FWER at level α.

Choice of Selection Thresholds

Depending on **different assumptions regarding the variances** σ_i^2, we choose different forms of selection thresholds:

- **Known variance:** For $i = 1, \ldots, m$, let the selection threshold $u_i = \sigma_i^2 \chi_n^2(1 - \beta)$ and common parameter $\beta = m^{\gamma - 1}$ with $0 < \gamma \leq 1$, which is **fixed.** Such selection thresholds ensure that roughly $\beta m = m^\gamma$ hypotheses are selected for testing.
- **Unknown and unequal variance:** For $i = 1, \ldots, m$, let the selection threshold $u_i = \hat{\sigma}_i^2 \chi_n^2(1 - \beta)$ and $\beta = m^{\gamma - 1}$ with $0 < \gamma \leq 1$, where $\hat{\sigma}_i^2$ is an estimate of σ_i^2 independent of the selection and test statistics.

Choice of Selection Thresholds (Cont.)

- **Unknown but equal variance:** Assume $\sigma_i^2 = \sigma^2$ for $i = 1, \ldots, m$. Let $\hat{\sigma}^2$ denote an overall estimator of σ^2, which satisfies

$$\hat{\sigma}^2 - \sigma^2 = O_P\left(\frac{1}{\sqrt{mn}}\right) .$$

- For $i = 1, \ldots, m$, let the selection threshold $u_i = \hat{\sigma}^2 \chi_n^2(1 - \beta)$ and $\beta = m^{\gamma - 1}$ with $0 < \gamma \leq 1$. Note that u_i **is the same but random.** Such selection thresholds ensure that roughly $\beta m = m^\gamma$ hypotheses are selected for testing.

Modified Two-stage Bonferroni-type Procedure

Based on the **random selection threshold** set for **the case of unknown but equal variance**, we develop a modified two-stage Bonferroni-type procedure, **for which Theorem 1 is not applicable.**

Procedure 3

1. ***Stage 1.*** *Given a random threshold* $\hat{u} = \hat{\sigma}^2 \chi^2_n(1-\beta)$ *and* $\beta = m^{\gamma-1}$ *with* $0 < \gamma \leq 1$, H_i *is selected iff* $S_{n,i} \geq \hat{u}$. *Let* $\hat{S}_n$ *denote the indices of selected hypotheses.*
2. ***Stage 2.*** *Apply the Bonferroni test to selected hypotheses* H_i *with* $i \in \hat{S}_n$*; that is, reject* H_i *iff* $|T_{n,i}| \geq t_{n-1}(1 - \frac{\alpha}{2|\hat{S}_n|})$, *the* $1 - \alpha/2|\hat{S}_n|$ *quantile of the t-distribution with* $n-1$ *degrees of freedom.*

Modified Two-stage Bonferroni-type Procedure (Cont.)

Theorem 3

Assume Assumption A1.
(i) For $\gamma > 1/2$, the above Procedure 3 asymptotically controls the FWER as $m \to \infty$.
(ii) For $\gamma = 1/2$ and $d > 0$, the above Procedure 3 asymptotically controls the FWER as $m \to \infty$. In fact, the same is true if

$$\gamma > \frac{1}{2}\left[1 - \frac{\epsilon^*}{d} + \frac{\log(1+\epsilon^*)}{d}\right],$$

where

$$\epsilon^* = 2(1-\gamma)d + c^*(\gamma, d)\sqrt{(1-\gamma)d},$$

and $c^*(\gamma, d)$ will be defined later.

Outline

Basic Idea of Power Analysis

- We break up the power analysis of two-stage procedures in two parts: the first part analyzes the probability of “selection” in the first stage, while the second will analyze the probability of “detection” in the second stage.
- Rejection of false null H_i then occurs when both H_i has been selected at the first stage and then detection occurs at the second stage.

Two Technical Results

To perform asymptotic power analysis, we need to derive bounds on extreme t-distributed and Chi-squared quantiles (Fujikoshi and Mukaihata, 1993; Inglot, 2010).

Lemma 1

Fix any $0 < \alpha < 1$ and $\delta > 0$. Then, for all m large enough,

$$t_{n-1}(1 - \frac{\alpha}{m}) \geq \sqrt{n-1}\left[\exp(\frac{(1-\delta)2\log(m)}{n-1}) - 1\right]^{1/2}$$

and

$$t_{n-1}(1 - \frac{\alpha}{m}) \leq \sqrt{n-1}\left[\exp(\frac{2\log(m)}{n-1.5}) - 1\right]^{1/2}.$$

Two Technical Results (Cont.)

Let $g(x) = \frac{e^x - 1 - x}{x^2}$, which is increasing on $(0, \infty)$. Then, define $a(c) = \left[g^{-1}\left(2/c^2\right)/c\right]^2$, which is decreasing in c.

Lemma 2

Given the value γ used in stage one for selection with $\beta_m = m^{\gamma - 1}$, and d in Assumption A1, with $d > 0$, define $c^* = c^*(\gamma, d)$ to be the solution of the equation $a(c) = (1 - \gamma)d$.
(i) For any $c > c^*$ and sufficiently large n,

$$\chi_n^2(1 - \beta_m) \leq n + 2\log\left(\frac{1}{\beta_m}\right) + c\sqrt{n\log\left(\frac{1}{\beta_m}\right)}.$$

(ii) For any $c < c^*$ and sufficiently large n,

$$\chi_n^2(1 - \beta_m) \geq n + 2\log\left(\frac{1}{\beta_m}\right) + c\sqrt{n\log\left(\frac{1}{\beta_m}\right)}.$$

Power Analysis: Known Variance

Firstly, we study the power of our two-stage Bonferroni-type procedure **under known variance.**

- For each H_i, its selection threshold u_i is of the form $u_i = \sigma_i^2 \chi_n^2(1-\beta)$ and $\beta = m^{\gamma-1}$, where $0 < \gamma \leq 1$.
- Hypothesis H_i is selected iff $S_{n,1} > \sigma_i^2 \chi_n^2(1 - m^{\gamma-1})$.

The Probability of Selecting Non-Null μ_i

Lemma 3

(i) Under Assumption A1, if

$$\mu_i^2/\sigma_i^2 > 2(1-\gamma)d + c^*(\gamma, d)\sqrt{(1-\gamma)d}\ , \tag{2}$$

then $\lim_{m\to\infty} P_{\mu_i}\{H_i \textit{ selected}\} = 1$.
(ii) Under Assumption A1, if

$$\mu_i^2/\sigma_i^2 < 2(1-\gamma)d + c^*(\gamma, d)\sqrt{(1-\gamma)d}\ , \tag{3}$$

then $\lim_{m\to\infty} P_{\mu_i}\{H_i \textit{ selected}\} = 0$.

Remark: if $d = 0$, then the condition (2) always holds, while in (ii) if $d = 0$ the condition (3) never holds, which implies H_i is selected with probability tending to one.

The Probability of Detecting Non-Null μ_i

We now consider the probability that μ_i is detected at the second stage using the t-statistic $T_{n,i}$.

Lemma 4

Under Assumptions A1 and A2, we have

(i) *when* $\mu_i^2/\sigma_i^2 > e^{2\gamma d} - 1$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ detected}\} = 1$;

(ii) *when* $\mu_i^2/\sigma_i^2 < e^{2\gamma d} - 1$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ detected}\} = 0$.

Remark: If $d = 0$, then $P_{\mu_i}\{H_i \text{ detected}\} \to 1$ for any $\mu_i > 0$.

Asymptotic Power Analysis: Known Variance

Combining Lemma 3 and 4, we have

Theorem 4

Under Assumptions A1 and A2, we have

(i) *when* $\mu_i^2/\sigma_i^2 > \max\{e^{2\gamma d} - 1, 2(1-\gamma)d + c^*(\gamma, d)\sqrt{(1-\gamma)d}\}$,

$$\lim_{m \to \infty} P_{\mu_i}\{H_i \text{ rejected}\} = 1 \ ;$$

(ii) *when* $\mu_i^2/\sigma_i^2 < \max\{e^{2\gamma d} - 1, 2(1-\gamma)d + c^*(\gamma, d)\sqrt{(1-\gamma)d}\}$,

$$\lim_{m \to \infty} P_{\mu_i}\{H_i \text{ rejected}\} = 0 \ .$$

Remarks on Asymptotic Power Analysis

- The **asymptotic average power** of this two-stage procedure is roughly the proportion of non-null means μ_i satisfying the inequality in Theorem 4 (i).
- Specifically, if $d = 0$, then $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ rejected}\} = 1$ for any given $0 < \gamma \leq 1$ and any $\mu_i \neq 0$. The fact implies that the **asymptotic average power** of this two-stage procedure is equal to one when $d = 0$.

Determination of Selection Threshold: Known Variance

- By minimizing the right-hand side of the inequality in Theorem 4 (i) or (ii) with respect to γ, one can determine **an optimal value** γ^* of γ for each given value of *d*, which maximizes probability of detecting any false null or average power asymptotically.
- For the optimal value γ^* of γ, one can determine **an optimal detection threshold** for Procedure 1 under known variance, which is equal to the corresponding value of the right-hand side of the inequality in Theorem 4 (i) or (ii).
- Figure 1 depicts the graphs of the optimal value γ^* of γ and the above optimal detection threshold with respect to *d*.

Determination of Selection Threshold: Known Variance (Cont.)

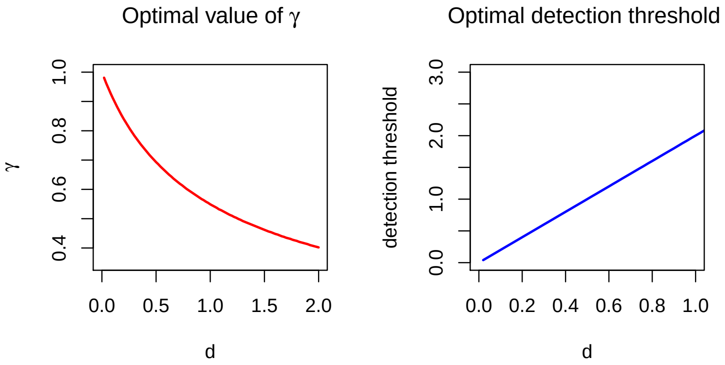

Figure 1: The optimal value (left) of γ and the optimal detection threshold (right) of μ_i^2/σ_i^2 for Procedure 1 under known variance.

Asymptotic Power Analysis: Unknown Variance

Next, we study the power of our two-stage Bonferroni-tyle procedure **under unknown and unequal variance.**

- For each H_i, its selection threshold u_i is of the form $u_i = \hat{\sigma}_i^2 \chi_n^2(1-\beta)$ and $\beta = m^{\gamma-1}$, where $0 < \gamma \leq 1$ and $\hat{\sigma}_i^2$ is an estimate of σ_i^2 constructed based on some pilot data or by using sample splitting method.
- Hypothesis H_i is selected iff $S_{n,1} > \hat{\sigma}_i^2 \chi_n^2(1 - m^{\gamma-1})$.
- Under certain conditions on $\hat{\sigma}_i^2$, one can derive a similar result of asymptotic power analysis as Theorem 4.
- By using a similar way as in the case of known variance, one can determine an optimal value γ^* of γ for each given value of d.

Outline

Method Comparison: Known Variance

- **Under known variance**, we compare our Procedure 1 with the original Bonferroni method based on Z-statistics through asymptotic power analysis.
- Let $Z_{n,i} = \frac{\sqrt{n}\bar{X}_{n,i}}{\sigma_i}$. Consider the Bonferroni method based on Z-statistic $Z_{n,i}$, which rejects H_i if $|Z_{n,i}| > z_{(1-\frac{\alpha}{2m})}$.

Result 1

Under Assumption A1, for the original Bonferroni method based on Z-statistics, we have
(i) when $\mu_i^2/\sigma_i^2 > 2d$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ rejected}\} = 1$.
(ii) when $\mu_i^2/\sigma_i^2 < 2d$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ rejected}\} = 0$.

Method Comparison: Known Variance (Cont.)

- Result 1 shows the detection threshold of the original Bonferroni procedure based on Z-statistics is an exact linear function of d with the slope of 2.0.
- Figure 1 demonstrates that the optimal detection threshold of our Procedure 1 under known variance is almost linear in terms of d with the slope being about 2.001.
- The above two facts shows that Procedure 1 has almost the same asymptotic power performance as the original Bonferroni based on Z-statistics if its selection threshold is optimally determined.
- The original Bonferroni procedure based on Z-statistics is optimal in some sense (Candes, Stats 300C, Lecture Note 2, Stanford 2016). Thus, **our two-stage Bonferroni is almost optimal under known variance**, although t-statistics are used as the test statistics for tested hypotheses.

Method Comparison: Unknown Variance

- **Under unknown variance**, we compare our Procedure 1 with the original Bonferroni method based on t-statistics and the split sample method.
- Consider the original Bonferroni method based on t-statistics, which rejects H_i if $|T_{n,i}| > t_{n-1}(1 - \frac{\alpha}{2m})$.

Result 2

Assume Assumption A1. For the original Bonferroni method based on t-statistics,
(i) when $\mu_i^2/\sigma_i^2 > e^{2d} - 1$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ rejected}\} = 1$.
(ii) when $\mu_i^2/\sigma_i^2 < e^{2d} - 1$, $\lim_{m\to\infty} P_{\mu_i}\{H_i \text{ rejected}\} = 0$.

Split Sample Method

- Split the sample in two $n = n_1 + n_2$ independent parts. For $k = 1, 2$, suppose $T_{n,i}^{(k)}$ denotes the t-statistic computed on the kth subsample of size n_k for testing H_i.
- H_i is selected in the first stage if $|T_{n,i}^{(1)}| > u$, for some threshold u. Let $|\hat{S}_n|$ denote the number of selected hypotheses.
- H_i is rejected at the second stage if also

$$|T_{n,i}^{(2)}| > t_{n_2-1}(1 - \frac{\alpha}{2|\hat{S}_n|}) \ .$$

- For any cutoff u used for selection, this procedure controls the FWER at level α.

Split Sample Method (Cont.)

Taking the selection threshold u to be of the form $u = t_{n_1-1}(1 - m^{\gamma-1}/2)$ for some $0 < \gamma \leq 1$, we have

Result 3

Assume Assumption A1 and A2. Also assume $n_1/n \to r$. For the above split sample method,

(i) when $\mu_i^2/\sigma_i^2 > \max\left[\exp(\frac{2(1-\gamma)d}{r}), \exp(\frac{2\gamma d}{1-r})\right] - 1$,

$$\lim_{m\to\infty} P_{\mu_1}\{H_1 \text{ rejected}\} = 1 .$$

(ii) when $\mu_i^2/\sigma_i^2 < \max\left[\exp(\frac{2(1-\gamma)d}{r}), \exp(\frac{2\gamma d}{1-r})\right] - 1$,

$$\lim_{m\to\infty} P_{\mu_1}\{H_1 \text{ rejected}\} = 0 .$$

Remarks on Method Comparison

- Ideally, the optimal detection threshold of our Procedure 1 under unknown variance is almost a linear function with the slope of 2.001.
- Based on Result 2 and 3, one can find out that the optimal detection thresholds of the original Bonferroni based on t-statistics and the split sample method are both exponential functions of d.
- The above facts implies that our two-stage procedure is more powerful than the original Bonferroni based on t-statistics asymptotically if its selection threshold is optimally determined.
- Figure 2 shows comparison of their optimal detection thresholds.

Comparison of Optimal Detection Thresholds

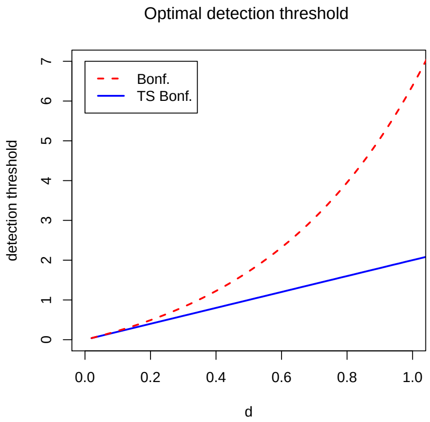

Figure 2: The optimal detection thresholds of our Procedure 1 (TS Bonf.) and the original Bonferroni procedure (Bonf.) based on t-statistics.

Outline

Weak Dependence

- We consider Procedure 1 in the case of known variance, where the selection thresholds $u_i = \sigma_i^2 \chi_n^2(1 - m^{\gamma-1})$.
- Let $|I_{m,0}|$ and $|\hat{S}_{n,0}|$ denote the numbers of all true nulls and selected true nulls, respectively. We make the following assumptions regarding $|I_{m,0}|$ and $|\hat{S}_{n,0}|$.

  Assumption B1: $\frac{|I_{m,0}|}{m} \to \pi_0$ as $m \to \infty$, where $0 < \pi_0 \leq 1$ is a fixed constant.

  Assumption B2: $\frac{|\hat{S}_{n,0}|}{m^\gamma} \xrightarrow{P} \pi_0$ as $m \to \infty$.

Theorem 5

Assume Assumptions B1 and B2. Procedure 1 with the selection thresholds $u_i = \sigma_i^2 \chi_n^2(1 - m^{\gamma-1})$ *for* $i = 1, \ldots, m$*, asymptotically controls the FWER at level* α*.*

Arbitrary Dependence

We still consider Procedure 1 in the case of known variance. By modifying its **random detecting threshold** at the second stage, we can develop an improved version of Procedure 1 below.

Procedure 4

1. *Given a fixed threshold* $u_i = \sigma_i^2 \chi_n^2(1-\beta)$*,* H_i *is selected iff* $S_{n,i} \geq u_i$*, where* $0 < \beta \leq 1$ *is any give positive constant.*
2. *Apply a single-step test with common critical value* $\alpha/\beta m$ *to the selected hypotheses; that is, reject* H_i *iff* $|T_{n,i}| \geq t_{n-1}(1 - \frac{\alpha}{2\beta m})$*, the* $1 - \frac{\alpha}{2\beta m}$ *quantile of the* t*-distribution with* $n-1$ *degrees of freedom.*

Arbitrary Dependence (Cont.)

Theorem 6

For any choice of the value of β, the above Procedure 4 strongly controls the FWER at level α under arbitrary dependence.

Remarks:

1. Note that $E[|\hat{S}_n|] \geq \beta m$, thus Procedure 4 is on average more powerful than Procedure 1 under known variance.
2. Compared with Procedure 1, one limitation of Procedure 4 is that its FWER control is more dependent on the assumption of known variance. For Procedure 1, even though the assumption does not hold, its FWER control is still valid for any fixed selection thresholds.

Outline

Conclusion

- Introduce a selection rule by using the idea of independent filtering.
- Develop two-stage Bonferroni-type procedures by combining conventional Bonferroni procedure with the selection rule, along with different forms of selection thresholds to adapt to different settings.
- Discuss some important theoretical and practical problems, including FWER control, asymptotic power analysis, determination of selection thresholds, and the dependence issue.
- Through asymptotic power analysis, compare the two-stage procedures with other related procedures and obtain two interesting findings.
- The same idea and techniques are being applied to develop two-stage BH-type procedures for controlling the FDR.