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Controlling Error Rates with Multiple Positively-Dependent Tests

by

Abdullah Al Masud

A Report submitted in partial fulfillment

of the requirement for the degree

of

MASTER OF SCIENCE

in

Statistics

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Abstract

It is a typical feature of high dimensional data analysis, for example a microarray study, that a researcher allows thousands of statistical tests at a time. All inferences for the tests are determined using the p-values; a smaller p-value than the α -level of the test signifies a statistically significant test. As the number of tests increases, the chance of observing some small p-values is very high even when all null hypotheses are true. Consequently, we make wrong conclusions on the hypotheses. This type of potential problem frequently happens when we test several hypotheses simultaneously, i.e., the multiple testing problem. Adjustment of the p-values can redress the problem that arises in multiple hypothesis testing. P-value adjustment methods control error rates [type I error (i.e. false positive) and type II error (i.e. false negative)] for each hypothesis in order to achieve high statistical power while keeping the overall Family Wise Error Rate (FWER) no larger than α , where α is most often set to 0.05. However, researchers also consider the False Discovery Rate (FDR), or Positive False Discovery Rate (pFDR) instead of the type I error in multiple comparison problems for microarray studies. The methods involved in controlling the FDR always provide higher statistical power than the methods involved in controlling the type I error rate while keeping the type II error rate low. In practice, microarray studies involve dependent test statistics (or p-values) because genes can be fully dependent on each other in a complicated biological structure. However, some of the p-value adjustment methods only deal with independent test statistics. Thus, we carry out a simulation study with several methods involved in multiple hypothesis testing.

Our result suggests a suitable method given that the test statistics are dependent with a particular covariance structure while allowing different values of the underlying parameters in the alternative hypotheses.

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Chapter 1

Introduction

The most common biological question in a DNA microarray data analysis is identifying genes whose expression levels change with the different levels of the variable of interest such as a covariate, or the response variable. The response variable could be clinical outcome or censored survival time; the covariate can be the dose of a drug, time, treatment/control group, and so forth (Dudoit et al., 2003). Multiple hypothesis testing is often applied to identify differentially expressed genes in the presence of different levels of the variable of interest. The null hypothesis for each gene is that the expression levels are not associated with the variable of interest. We have the same number of alternative hypotheses in the study. And each null hypothesis has the same type I error rate. Therefore, it becomes difficult to control the overall type I error rate at level α in order to achieve desired statistical power (= 1-type II error rate). Because of the mixture of null and alternative hypotheses, the obtained p-values follow different types of distributions, for example Beta distributions, instead of the Uniform distribution. Multiple comparison p-value adjustment procedures control the type I error, FDR, or pFDR to achieve higher power while minimizing the type II error rate. In microarray studies, most often controlling the FDR, or pFDR ensures more statistical power rather than controlling the type I error rate (Dudoit et al., 2003; Pounds and Cheng, 2004).

Microarray data always deal with a large number of genes. Each gene has a complex network involving other genes with known and unknown dependence structures. When we execute hypothesis testing of gene expression levels, the natural dependency phenomena of genes results in wrong conclusions. But if we know the number of correlated genes in a given system, how strongly they are correlated with each other, and their differential expression value under the alternative hypotheses, then we may be able to determine a reasonable adjusted p-value method. A reasonable method can improve the statistical power with increasing numbers of correlated genes, increasing correlation value, and increasing differential expression value of genes under the alternative hypotheses while controlling the FDR. Although all of the conventional p-value adjustment methods can work with dependent test statistics (or p-values), very few of them accomplish good statistical power.

In Chapter 2 we summarize several procedures in the literature to control error rates in multiple comparisons and the positive regression dependency condition. In Chapter 3 we propose methods and analyze several multiple comparison procedures with results. We finish with a conclusion and remaining questions in Chapter 4. The R code for this report is included in Appendix. All computations were done with R (R Development Core Team, 2009), using packages MASS (Venables and Ripley, 2002), Matrix (Bates and Maechler, 2010), Biobase (Gentleman et al., 2004), multtest (Pollard et al., 2009), qvalue (Dabney et al., 2010), and lattice (Sarkar, 2010).

Chapter 2

Controlling the error rates

Suppose a study involves testing simultaneously m hypotheses H_k , $k=1,2,\dots,m$. In a microarray experiment, each H_k stands for testing the differential expression of a gene k .

An unknown parameter m_0 (i.e. the number of true null hypothesis) along with some random variables of the m specific hypotheses can be summarized by Table 2.1, in accordance with Benjamini and Hochberg (1995). We always encounter four unknown random variables when we test m hypotheses simultaneously. The variables are S, T, U, and V presented in Table 2.1. Also we can observe a random variable, R, presented in Table 2.1 in the decision status. Here R is the total number of significant tests (and in a microarray study R is the total number of declared significant genes). Generally we want to minimize the number V of false positives (or type I errors), and the number T of false negatives (or type II errors) in all multiple hypothesis testing. So controlling V while minimizing T ensures maximum achievement of power.

Table 2.1: Number of errors that occurred in m hypotheses

Hypotheses	Declared tests		Total
	Insignificant	Significant	
Null (H_0)	U	V	m_0
Alternative (H_1)	T	S	$m-m_0$
Total	$m-R$	R	m

2.1 Methods involved in controlling family wise error rate (FWER)

The FWER is defined as the probability of one or more false positive events (or type I errors). That is,

$$\text{FWER} = P[V > 0]. \quad (2.0)$$

2.1.1 Bonferroni correction in multiple testing (or the Bonferroni procedure)

In multiple comparisons, the Bonferroni correction is widely used to control the probability that a true null hypothesis is incorrectly rejected, although it gives a conservative upper bound on the FWER. Let p_1, p_2, \dots, p_n be random p-values of a set of given hypotheses H_1, H_2, \dots, H_n . The Bonferroni procedure (Dudoit and Van der Laan, 2007, page 113) gives significant hypothesis H_i when $p_i \leq \{\alpha/n\}$, using the Bonferroni inequality,

$$P\left\{\bigcap_{i=1}^n (p_i \leq \alpha/n)\right\} \leq \alpha, \quad 0 \leq \alpha \leq 1. \quad (2.1)$$

That is, given all true null hypotheses, the probability of type I error does not exceed the desired level α .

2.1.2 Šidák's single step and step-down procedures

Šidák (1967) proposed an alternative method of multiple comparison for controlling FWER at level α . The main motivation was the conservative result of the Bonferroni correction. Based on the Bonferroni inequality (Equation 2.1) it is obvious we compare the p-values to a very small significance level when there is a large number of hypotheses. So, in order to improve the conservative result of multiple comparisons, at first the Šidák Single Step (SS) procedure (Dudoit and Van der Laan, 2007, page 115; Šidák, 1967) declares a hypothesis H_i statistically significant when $p_i \leq 1 - (1 - \alpha)^{1/n}$, for $i = 1, 2, \dots, n$.

When a study allows several tests at a time, the Šidák Step-down (SD) procedure (Dudoit and Van der Laan, 2007, page 123) declares a hypothesis H_i statistically significant if $p_i \leq 1 - (1 - \alpha)^{1/(n-j+1)}$ for $j=1,2,\dots,i$ and $i=1,2,\dots,n$.

2.1.3 A simple sequentially rejective multiple test procedure (or the Holm procedure)

Holm (1979) demonstrated a new procedure of multiple comparisons that controls the type I error rate at level α , and this procedure is called the Holm procedure. Regardless of various combinations of true and false null hypotheses, this procedure considers significance tests sequentially (i.e., 'one at a time') as long as the previous result rejects. Because Bonferroni first used the Bonferroni inequality (Equation 2.1) in the multiple hypothesis setting and Holm used also the same inequality, it was called 'the sequentially rejective Bonferroni test.' Order-

ing the p-values as $p_1 \leq p_2 \leq p_3 \leq \dots \leq p_n$ of the corresponding null hypotheses H_1, H_2, \dots, H_n ; then one can execute this step-down procedure for given α level test as follows:

Step 1: Reject H_1 if $p_1 \leq \alpha/n$

Step 2: Reject H_2 if $p_2 \leq \alpha/(n - 1)$

...

Step n: Reject H_n if $p_n \leq \alpha$.

Generally, the Holm method rejects hypothesis H_i when $p_i \leq \alpha/(n - i + 1)$. The procedure stops at the smallest i for which H_i is accepted (or not rejected). This method gains more power than the Bonferroni method, but this power gain is not large (Holm, 1979). Another advantage of the Holm procedure is this procedure is a closed testing procedure. An idea of closed testing procedure (Westfall and Wolfinger, 2000) is below:

Suppose there are n hypotheses H_1, H_2, \dots, H_n and the overall type I error rate is α . If not only any of these elementary hypotheses, say H_k , is significant but also all of the intersection hypotheses that include H_k are significant, then H_k will be declared significant based on the closed testing principle.

But Holm (1979) mentioned that the test statistics need to be independent not only for ‘computational reasons’ but also ‘a good experimental design requires the different hypotheses to be tested by variables.’

2.1.4 A stage wise rejective multiple test procedure (or the Hommel procedure)

Consider the p-values (p_1, p_2, \dots, p_n) of the test statistics (Y_1, Y_2, \dots, Y_n) for n hypotheses H_1, H_2, \dots, H_n . Based on Rüger's (1978) inequality, regarding the overall hypothesis $H_0 = \bigcap_{i=1}^n H_i$ and level α test, one can reject H_0 when $p_i \leq \{i\alpha/n\}$ for $i = 2, 3, \dots, n$, where p_i is the i^{th} smallest of the p-values. The index i is determined before executing the n tests. In contrast, Hommel (1983) proposed an alternative inequality to reject overall hypothesis H_0 at level α if $p_i \leq \{i\alpha/(n \sum_{k=1}^n \frac{1}{k})\}$ for at least one i ($i = 1, 2, \dots, n$). In fact, Hommel's inequality does not require calculation of the index i in advance because this inequality is a combination of the Bonferroni test and all $(n-1)$ possible Rüger tests (Hommel, 1988). But this inequality can not make inference on individual tests (Hommel, 1988). Therefore, Hommel (1988) proposed a multiple testing procedure combining the idea of an overall test H_0 and the principle of closed testing procedure. Considering the overall hypothesis H_0 , Simes (1986) described a modified Bonferroni method, which controls the FWER at level α when the test statistics are independent. The Simes procedure (Simes, 1986) has higher statistical power than the classical Bonferroni method if several hypotheses are correlated. In the Simes procedure, the rejection criterion is obtained for hypotheses $H_0 = \{H_{(1)}, H_{(2)}, \dots, H_{(n)}\}$ corresponding to $\{p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(n)}\}$ with $p_{(i)} \leq i\alpha/n$ for at least one i . Although Simes did not provide a clear idea about how to draw inferences on an individual hypothesis in H_0 , it was recommended that the classical Bonferroni procedure or the Holm procedure be used to make statements on individual hypotheses when H_0 is rejected (Hochberg, 1988).

On the other hand, considering the same overall hypothesis H_0 , Hommel (1988) presented another approach of multiple testing in order to make inference on individual hypothesis in overall hypothesis H_0 . Inference for H_i depends on an index j , where $j = \max\{i \in \{1, 2, \dots, n\} :$

$p_{n-i+k} > \{k\alpha/i\}; k \in \{1, 2, \dots, i\}$. Then H_i is declared significant when $p_i \leq \{\alpha/j\}$. Otherwise, reject all H_i if j does not exist.

In general if test statistics are independent, then the Hommel (1988) method controls the FWER at α level.

2.1.5 A sharper Bonferroni method (or the Hochberg procedure)

Hochberg (1988) suggested a modified Bonferroni procedure for multiple testing extending Simes (1986) idea, but based on the closed test procedure. Suppose $H_0 = \bigcap_{i=1}^m H_i$ and

$H'_0 = \bigcap_{n=i(1)}^{i(m')}$ H'_n , where $H_0 \supseteq H'_0$ of $m' \leq m$ individual hypotheses. Based on the closure test theorem (Alt, 1991, page 3) rejection of at least one hypothesis H'_n at level α indicates the rejection of H_0 . So Hochberg (1988) proposed the statement that the FWER will be strongly controlled when the Bonferroni inequality (Equation 2.1) is applied on hypothesis H'_0 instead of H_0 for all $H_0 \supseteq H'_0$.

In order to resolve the issue of making the statements on hypotheses, after Hommel (1988) Hochberg as well simplified Simes's idea based on the closure principal of tests. Then Hochberg (1988) demonstrated a new step-up procedure of multiple testing in the following way:

Order the p-values of H'_0 as $p_{i(1)}, p_{i(2)}, \dots, p_{i(m')}$. The Hochberg procedure rejects any hypothesis in H'_0 when $p_{i(j)} \leq \{j\alpha/m''\}$ for all $H''_0 \supseteq H'_0$ and for any hypothesis $H_{i(j)} \in H''_0$, where $H''_0 = \bigcap_{k=i(1)}^{i(m'')} H''_k$. So Hochberg (1988) again reinforced that the Hochberg procedure controls 'the family wise error rate in strong sense under any H'_0 ' (see Equation 2.1).

The Hochberg procedure makes inference on individual hypotheses in the following way: applying the step-up technique in which, for the ordered p-values as $(p_m \geq p_{m-1} \geq \dots \geq p_1)$, one rejects all $H_{i'}$ with $p_{(i)} \leq \alpha/(m - i + 1)$ for $(i' \leq i)$ and $i = m, m-1, \dots, 1$. At the initial stage, if $p_m \leq \alpha$, then reject all $H_{i'}$ ($i' = m, m-1, \dots, 1$). Otherwise, H_m is accepted; then the procedure rejects the rest of hypotheses, $H_{i'}$ ($i' = m-1, m-2, \dots, 1$) compared to $p_{m-1} \leq \{\alpha/2\}$ and so on. Like the Hommel procedure, this procedure also performs well on independent test statistics. But the Hommel procedure increases the power of the tests while controlling the FWER. Sarkar (1998) showed that the Hochberg procedure controls the FWER when test statistics follow the multivariate total positivity of order 2 (that is, MTP_2) condition [described in Section 2.4].

2.2 Methods controlling the false discovery rate (FDR)

Recalling Table 2.1 and according to Benjamini and Hochberg (1995), the False Discovery Proportion (FDP) is the number of false positives (or false rejections) divided by the number of rejections. That is,

$$Q = \frac{V}{R}. \tag{2.2}$$

And the FDR is the expected FDP. That is,

$$\text{FDR} = E(Q). \tag{2.3}$$

2.2.1 Controlling the FDR rate (or the Benjamini and Hochberg procedure)

Benjamini and Hochberg (1995) provided a completely different idea of controlling error rates of multiple hypothesis testing. The procedure involves a step-up technique for non-parametric statistics in order to control the error rates. They suggested the multiplicity problem will be reduced if we only consider the FDP instead of the usual idea of the probability of making at least one type I error among all tests. Also the exact controlling will be accomplished by the FDR while providing a smaller type II error rate.

They proposed a linear step-up technique, considering the Simes (1986) test, that ensures the FDP converges to a desired level α in the 1st order mean. Also their proposed method, referred to as the BH procedure, provides a non-parametric and finite sample method for choosing the p-value threshold, which is often more powerful than the traditional methods associated with controlling the FWER.

The linear step-up BH procedure works in the following way: consider the ordered p-values as $p_{(m)} \geq p_{(m-1)} \geq \dots \geq p_{(1)}$ of the hypotheses, $\{H_m, H_{m-1}, \dots, H_1\}$. The BH procedure rejects all hypotheses H_k starting with $p_{(m)}$ when $k = \max \{i : p_{(i)} \leq (i\alpha/m)\}$. Otherwise the process stops when k does not exist. For independent tests the BH procedure controls the FDR at level α .

Following Table 2.1 and Equation 2.3, one of the important features of this error rate mentioned by Benjamini and Hochberg (1995) is that it will not be controlled at level α if $m_0 = m$ even if $Q = 1$. Also controlling $(V/R|R > 0)$ is not possible when $Q = 1$. Thus, the alternative formulation of the FDR is

$$P(R > 0)E(V/R|R > 0). \tag{2.4}$$

2.2.2 The control of the FDR in multiple testing under dependency (or the Benjamini and Yekutieli procedure)

A follow-up paper extended the work of the original BH procedure when the test statistics or the p-values are dependent. Benjamini and Yekutieli (2001) pointed out that the BH procedure controls the FDR at level α when the test statistics have positively dependent structure [described in Section 2.4]. However when the test statistics are negatively correlated or a different dependency exists, the modified BH procedure, referred to as the BY procedure (Benjamini and Yekutieli, 2001), controls the FDR with upper bound $m_0\alpha/(m \sum_{i=1}^m \frac{1}{i})$. But the error rate gives a conservative bound.

2.2.3 The adaptive linear step-up procedure of the BH procedure (or the adaptive Benjamini and Hochberg procedure)

Benjamini et al. (2006) reported a gain in power can be expected when the procedure involves the estimation of m_0 (i.e. the number of true nulls). In addition the same authors recommended the improvement of controlling the FDR based on the ‘knowledge of m_0 ’.

Assuming independent tests to estimate m_0 by the original BH procedure, the adaptive BH procedure, referred to as the ABH procedure by Benjamini et al. (2006), involves the following steps:

- Step 1: Use the linear step-up procedure (that is, original BH procedure) at α ,
and if no hypothesis is rejected stop; otherwise, proceed.

Step 2: Estimate $m_0(k)$ by $(m + 1 - k)/(1 - p_{(k)})$, where $k = \max\{i : p_{(i)} \leq (i\alpha/m)\}$ for which we reject all $H_{(i)}$ ($i = 1, 2, \dots, k$).

Step 3: Starting with $k = 2$ stop when for the first time $m_0(k) > m_0(k - 1)$.

Step 4: Estimate $\hat{m}_0 = \min\{m_0(k), m\}$ rounding up to the next highest integer.

Step 5: Use the linear step-up procedure with $\alpha' = m\alpha/\hat{m}_0$.

Benjamini et al. (2006) suggested the following calculation that involves Step 2 above. Suppose $r(\alpha) =$ number of significant tests. Then $m - r(\alpha)$ is the number of true null hypotheses except that $m_0\alpha$ true null hypotheses are expected to be among the $r(\alpha)$ rejected. For m_0 solve the following equation

$$m_0 \simeq m - \{r(\alpha) - m_0\alpha\} \tag{2.5}$$

$$m_0 \simeq \{m - r(\alpha)\}/(1 - \alpha). \tag{2.6}$$

Then use $\alpha = p_{(k)}$ in Equation 2.6 to approximate $m_0(k)$.

The ABH procedure controls the FDR exactly at level α , while the original BH procedure was shown to provide a slightly conservative upper bound. Besides the ABH procedure has greater power than the original BH procedure (Benjamini and Hochberg, 2000; Benjamini et al., 2006).

2.2.4 The two stage procedure of controlling the FDR (or the two stage Benjamini and Hochberg procedure)

According to Benjamini et al. (2006), the two stage linear step up procedure of the BH procedure, which is referred to as the TSBH procedure, is summarized in the following way:

Step 1: Use the linear step-up procedure (or the original BH procedure) at level $\alpha' = \alpha/(1 + \alpha)$. Let r_1 be the number of rejected hypotheses. If $r_1 = 0$ do not reject any hypothesis and stop; also if $r_1 = m$ reject all m hypotheses and stop; otherwise proceed.

Step 2: Assume $\hat{m}_0 = m - r_1$.

Step 3: Use again the linear step-up procedure with $\alpha'' = m\alpha'/\hat{m}_0$.

In Step 2 the TSBH procedure, by Benjamini et al. (2006), involves estimating m_0 following Table 2.1 and constraint,

$$m_0 \leq m - (R - V). \quad (2.7)$$

The BH procedure is used in the initial stage, ensuring $E(V/R) \leq \{m\alpha/m_0\}$, so that $V \leq \{\alpha m_0 R/m\}$. Putting V in Equation 2.7 above we obtain the following equations:

$$m_0 \leq m - (R - \frac{\alpha m_0 R}{m}) \quad (2.8)$$

$$m_0 \leq \frac{(m-R)}{1 - \frac{R\alpha}{m}} \leq \frac{(m-R)}{(1-\alpha)} \leq (m-R)(1+\alpha). \quad (2.9)$$

The right-most bound of Equation 2.9 is inherently used in the TSBH procedure. This procedure also controls the FDR at level α when test statistics are independent. Benjamini et al. (2006) showed that the TSBH procedure controls the FDR below but close to the nominal level α and provides higher power than the original BH procedure when tests are correlated.

2.3 A direct approach to FDR (or the q-value method)

In the original BH procedure, the rejection of all hypotheses $H_{(i)}$ ($i = 1, 2, \dots, k$) is determined with $p_{(i)} \leq i\alpha/m$, where k is the largest number of rejected nulls. Storey (2002) mentioned the missing information about the estimation process that is involved in selecting the maximum number of rejected hypotheses, (i.e., ' \hat{k} ') from each possible combination of hypotheses in the BH procedure. Benjamini and Hochberg (1995), mentioned the usual estimation process involves finding \hat{k} . But Storey (2002) again pointed out that the original BH process may be unreliable for choosing a reliable estimate of \hat{k} when a large number of hypotheses are considered, because the original BH procedure requires an estimation process to control the FDR. Another flaw of the BH procedure addressed by Storey (2002) was that the procedure controls the FDR at the level α 'for all values of m_0 (i.e., the number of true null hypotheses) simultaneously.' Perhaps there was also missing information about m_0 in the original BH procedure. In fact, Benjamini and Hochberg (2000) and Benjamini et al. (2006), proposed the adaptive procedure of controlling the FDR and the two stage procedure of controlling FDR. Indeed these methods estimate m_0 prior to adjusting the FDR.

Storey (2002) demonstrated a new way of controlling the error rates with the pFDR at the desired level α . The error rate, pFDR, preserves information about m_0 by applying point estimation techniques and a Bayesian framework. Storey introduced a new term 'q-value' that

quantifies the pFDR. Storey (2002) defined the positive false discovery rate as follows:

$$\text{pFDR} = E(V/R|R > 0). \quad (2.10)$$

That is the expected portion of erroneously rejected hypotheses among all rejected hypotheses when positive findings have occurred.

Again Storey (2002) indicated the problem of controlling the FDR for the BH procedure is that the BH procedure literally controlled the error rate at $\alpha/P(R > 0)$ instead of at α level given any significant result (that is, $R > 0$) regarding Equation 2.4. In fact since the estimation process of pFDR sets the error bounds after allocating the rejection region to each test, the q-value method proposed by Storey (2002) achieves higher statistical power than the original BH method while controlling the pFDR.

The estimation of the error rate can be obtained, in accordance with Storey (2002), for independent tests H_i with statistics $T = \{T_1, T_2, \dots, T_m\}$ and for the same rejection region Γ of each statistic in the following way. Let $H_i = 0$ when null hypothesis i is true, and $H_i = 1$ otherwise.

$$pFDR(\Gamma) = \frac{\pi_0 P(T \in \Gamma | H_i = 0)}{P(T \in \Gamma)} = P(H_i = 0 | T \in \Gamma). \quad (2.11)$$

Here, $P(T \in \Gamma) = \pi_0 P(T \in \Gamma | H_i = 0) + \pi_1 P(T \in \Gamma | H_i = 1)$,

$\pi_0 = P(H_i = 0)$, and $\pi_1 = P(H_i = 1)$; they are prior knowledge.

Storey (2002) defined the ‘q-value’ as for an observed statistic, $T = t$

$$q(t) = \min_{\{\Gamma:t \in \Gamma\}} \text{pFDR}(\Gamma) = \min_{\{\Gamma:t \in \Gamma\}} P(H_i = 0 | T \in \Gamma).$$

That is, ‘The q-value is a measure of the strength of an observed statistic with respect to pFDR - it is the minimum pFDR rejecting a statistic with value t for the set of nested rejection regions.’

On the other hand, the P-value is defined as

$$p(t) = \min_{\{\Gamma:t \in \Gamma\}} P(T \in \Gamma | H_0 = 0).$$

The q-value measures the error rate with respect to the pFDR, but the p-value measures the error rate with respect to the type I error. Thus, Storey (2002) said the q-value is analogous to the p-value.

2.4 Positive regression dependency

Benjamini and Yekutieli (2001) showed that the original BH procedure controls FDR at level α when the joint distribution of the test statistics corresponding to the true null hypotheses has “Positive Regression Dependency on each one from the Subset (PRDS).” A technical definition of PRDS is as follows. Let D be the entire set of test statistics and it is an increasing set. Let X and Y be two subsets of D , and $X \leq Y$ as well. Also the random elements of X (say X_1, X_2, \dots, X_n) correspond to the true null test statistics. If $P(X_1, X_2, \dots, X_n \in D | X_i = x)$ is increasing in each X for any $i \in \{1, 2, \dots, n\}$ then X is called the PRDS on each one from the subset of X . In the context of microarrays, conditioning on each hypothesis (i.e., gene), each time, the PRDS is required to hold for a subset of the test statistics corresponding to the true null hypotheses.

Based on Benjamini and Yekutieli (2001), another type of positive dependency is explained in the following way. Let $X = \{X_1, X_2, \dots, X_n\}$ and $Y = \{Y_1, Y_2, \dots, Y_m\}$ be random test statistics. X is multivariate total positivity of order 2 (MTP_2) if, for all X and Y ,

$$f(x)f(y) \leq f(\min(x, y))f(\max(x, y)). \quad (2.12)$$

Here, f is the joint density function or the joint probability function. MTP_2 is widely used to follow the notion of positive regression dependency of the tests corresponding to the null hypotheses, because it is easier to prove (Benjamini and Yekutieli, 2001). ‘Positive regression dependence implies in turn that X is positively associated, in the sense that for any two functions f and g , which are both increasing (or both decreasing) in each of the coordinates, $cov(f, g) \geq 0$.’ Benjamini and Yekutieli (2001) mentioned that PRDS has two properties in which it is different from the above concept, MTP_2 . First, monotonicity is required after conditioning only on one test at a time. Second, the conditioning is done only on any one from a subset of the tests. Thus, if X is MTP_2 then it follows that X is PRDS.

2.5 Abbreviation of relevant procedures

All the abbreviations of multiple comparison procedures are shown with their sections in below Table 2.2. These methods are used in our simulation study [Section 3.1] in order to adjust p-values. And their abbreviations are used in our simulation results [Section 3.2] to make plots.

Table 2.2: Abbreviations of the multiple comparison procedures with sections

Procedures	Abbreviations	Section
The Bonferroni procedure	Bonferroni procedure	2.1.1
The Šidák single step	Sidak SS procedure	2.1.2
The Šidák step down	Sidak SD procedure	2.1.2
The Holm procedure	Holm procedure	2.1.3
The Hommel procedure	Hommel procedure	2.1.4
The Hochberg procedure	Hochberg procedure	2.1.5
The Benjamini and Hochberg procedure	BH procedure	2.2.1
The Benjamini and Yekutieli procedure	BY procedure	2.2.2
The adaptive Benjamini and Hochberg procedure	ABH procedure	2.2.3
The two stage Benjamini and Hochberg procedure	TSBH procedure	2.2.4
The q-value method	q-value method	2.3

Chapter 3

Methods and results

3.1 Simulation

Simulation study is a fundamental part of the data analysis process. Such a study is useful to verify theoretical as well as large sample properties of statistical methods and test statistics. Then we can connect the results obtained from large samples with the small sample properties of statistical methods. We simulate 2000 test statistics Z (corresponding to 2000 genes in a microarray study), assuming $Z \sim N(\mu, \Sigma)$. Moreover, we investigate the performance of multiple comparison procedures involved in adjusting the p-values under various dependence scenarios through Monte Carlo simulation study generating several sets of p-values of size 2000. Each p-value associates with a test statistic. Our main dependent scenario of test statistics (or p-values) is present in the covariance matrix (i.e., Σ) with different numbers of correlated tests and their varying correlations. We also focus on different mean values of the non-true nulls' test statistics in order to see the pattern of performance of multiple comparison procedures. Our general hypothesis as follows:

$$H_i^0 : \mu = 0 \text{ vs } H_i^1 : \mu \neq 0 \text{ for } i = 1, 2, \dots, 2000.$$

In our study our first and the most important dependency scenarios are in the covariance matrix ($\Sigma_{2000 \times 2000}$) of test statistics (Zs). Thus the construction of Σ includes two issues: (1) number of total correlated Zs (corresponding to genes) and (2) correlation value (r) of dependent Zs. Regarding the first issue, our main motivation is to examine the pattern of change of various multiple comparison procedures for increasing the total number of correlated Zs. So we consider two different total numbers of correlated Zs. In addition, in order to define the total number of correlated Zs out of 2000 Zs we consider two different groups. The first group has 120 dependent Zs and the second group has 360 dependent Zs. Again in order to distribute the number of dependent Zs for each group into several symmetrical matrices we consider some blocks. For the first group we have six blocks and each block has twenty dependent Zs. In terms of second group, we consider six blocks of sixty dependent Zs. Besides, for the two groups, the dependent Zs of the first three blocks always associate with the alternative hypotheses, and the dependent Zs of the remaining three blocks represent the null hypotheses. We reinforce our first dependency phenomena of the Σ matrix for both groups in that we have always the same number of blocks associated with the alternative hypotheses as associated with the null hypotheses. Then we assume all remaining hypotheses are independent. Therefore the diagonal elements of the entire $\Sigma_{2000 \times 2000}$ matrix consist of six blocks with the remaining elements being ones, and the off diagonal elements being zeros. So it seems that all blocks under a specific total number of correlated Zs always appear at diagonal positions of the entire Σ matrix. Indeed each block is a symmetric matrix inside the Σ matrix. In our study for the first group we allow six matrices with dimension 20×20 , but for the second group we have six 60×60 dimensional matrices. Because of the symmetric matrix all diagonal elements of the blocks are ones, but the off-diagonal elements represent the degree of correlation between Zs.

We choose four arbitrary non-negative correlation coefficients, that is $r \in \{0, 0.20, 0.50, 0.99\}$. The values of r are chosen to represent a reasonable range of values. Non-negative value of r ensures that covariance between Z s is always non-negative. So we satisfy the condition of positive regression dependency of correlated Z s [Section 2.4 of this report]. These correlation values r measure how much dependent Z s are correlated with each other. Specifically $r = 0$ indicates genes are completely independent; by contrast $r = 0.99$ indicates that the linear association between genes are almost to 1. The main motivation of our study is to understand how various multiple comparison methods are affected by the correlation values (or r) of Z s. Based on the preceding paragraph, we put the same correlation value r in the off-diagonal positions of each block (or symmetric matrix) so that we can explain the performance of various multiple comparison procedures when the same degree of dependency is present in the same number of alternative hypotheses as well as in the same number of null hypotheses. Changing the r values we obtain different off-diagonal elements in the blocks. Thus we summarize the construction of our general $\Sigma_{2000 \times 2000}$ matrix in such a way so that under a given number of correlated Z s all blocks (or symmetrical sub-matrices) appear at the diagonal position of entire Σ matrix and the off-diagonal elements of the blocks preserve the degree of dependency of correlated Z s. The following is the general form of our $\Sigma_{2000 \times 2000}$ matrix:

$$\Sigma = \begin{bmatrix} \begin{bmatrix} 1 & r \\ r & 1 \end{bmatrix} & & & & 0 \\ & \begin{bmatrix} 1 & r \\ r & 1 \end{bmatrix} & & & \\ & & 0 & & \begin{bmatrix} 1 & r \\ r & 1 \end{bmatrix} \\ \dots & \dots & \dots & \dots & \dots & 1 \end{bmatrix}$$

The block-diagonal structure of the Σ matrix affects the construction of our mean vector μ . For null hypothesis, $\mu_i = 0$, while for alternative hypothesis, $\mu_i = A$ for some $A > 0$. We use the same A for all alternative hypotheses to allow an inspection of the effect of A , and consider separately $A \in \{0.5, 1.5, 3, 4.7\}$. Here these values of A are chosen to represent a reasonable range of values.

Three of the six dependent blocks in the Σ matrix correspond to null hypotheses (so their corresponding $\mu_i = 0$), and the remaining three dependent blocks correspond to alternative hypotheses (so their corresponding $\mu_i = A$). In all our simulations we have total 200 alternative hypotheses (out of 2000 hypotheses), thus we have either 140 ($= 200 - 3 \times 20$) or 20 ($= 200 - 3 \times 60$) completely independent alternative hypotheses, depending on the dependence group size. Notice that implicit in our simulation is the assumption that a group of dependent hypotheses will have a shared truth (nulls all true or all false). This assumption is made for computational convenience and to facilitate interpretation. The following is our general form of $\mu_{1 \times 2000}$ vector.

$$\mu = \begin{bmatrix} A & A & \dots & A & 0 & 0 & 0 & \dots & A \end{bmatrix}.$$

For any total number of dependent Zs and for each simulation we replicate 2000 Zs under a specific A with four different r in the $\Sigma_{2000 \times 2000}$ matrix. Each $\Sigma_{2000 \times 2000}$ matrix will be distinguishable from each other in the off-diagonal elements of the blocks under a given number of total dependent Zs. We run our simulation 6000 times considering a given number of total dependent Zs. Then for each combination of $\mu_{1 \times 2000}$ vector and $\Sigma_{2000 \times 2000}$ matrix we generate 6000 sets of 2000 p-values. Next we adjust these p-values with the multiple comparison methods described in Section 2.1 and 2.2 of this report. Finally we calculate power, FDR

and type I error for the corresponding multiple comparison procedures, averaging for each procedure across simulations for each combination of r , A , and a specific total number of dependent Z s.

3.2 Simulation results

Figures 3.1 through 3.4 show the average FDR value and Figures 3.5 through 3.8 show the average power of different A values for the two group sizes, with panels representing the r values. The average here is taken across all simulations. 360 dependent tests are defined with red color and open triangle, and 120 dependent tests are defined with blue color and open circle. The filled circle and triangle are used to highlight the q-value method. Rows, representing the different methods, in each panel are sorted in decreasing order (from top to bottom) based on the results when $r = 0.5$ for 120 dependent tests. We order the methods based on the ranks of the average FDR for $r = 0.5$ because it is the middle of each figure, and we can see the effect of higher and lower r values by comparison with that middle panel.

Referring to Figure 3.1 and 3.2, it is obvious that all of the procedures involved in controlling not only the FWER but also the FDR, control the FDR level above the usual desired level 0.05 when A is below or equal to 1.5 under the alternative hypotheses. The procedures tend to increase their average FDR levels with increasing value of r when there are a large number of dependent tests, for example 360 dependent genes in our study, for the value of A at level 0.5 compared with the value at 1.5 (Figure 3.1 and 3.2). But at $r = 0.2$, for 360 dependent tests all methods, except the BY procedure, provide smaller average FDR rate compared with 120 dependent tests when A is 0.5 (Figure 3.1). In general for $r \approx 1$ and for a large number of dependent tests, all methods involved in controlling the FWER, such as the

Bonferroni, Holm, Sidak SD procedures and so forth, have a higher value of the average FDR level than the methods involved in controlling the FDR when A is small (Figure 3.1 and 3.2). In Figure 3.2, all plots show that the BY procedure usually gives lower average FDR measures than the remaining procedures, though for $r \approx 1$ and for a larger number of dependent tests this procedure can increase the average FDR value. Due to our positive regression condition of dependent tests, the BY procedure gives a small FDR rate. Actually increasing value of A decreases the average FDR level for all methods (Figure 3.2).

When we start increasing the value of A from 1.5 the TSBH, ABH, BH and q-value methods can control the FDR at level 0.05, and all the remaining multiple comparison procedures control the average FDR level below 0.01 (Figure 3.3 and 3.4). All methods involved in controlling the FWER show that they have higher average FDR values than the BY procedure when A is 3 and there are 360 dependent tests with $r \approx 1$ (the top panel of Figure 3.3). As the value of A rises from 3, actually the BY procedure as well as the methods involved in controlling the FWER are very conservative. The estimated FDR values are close to zero (Figure 3.4).

Regardless of the increasing number of dependent tests and increasing r , for $A = 3$ and 4.7 the q-value method usually provides higher FDR values compared with the TSBH, and ABH methods (Figure 3.3 and 3.4). The gap between their obtained FDR values is a meager amount. For increasing r and for all numbers of dependent tests, the q-value method is always able to retain its average FDR level exactly at 0.05 (Figure 3.3 and 3.4). By contrast when A is equal to 3, for 360 dependent tests the ABH, and TSBH methods have a small amount of average FDR value at $r = 0.99$ compared at $r = 0$ (Figure 3.3). The BH procedure also has a downward trend towards $r = 0.99$ for controlling FDR with increasing number of dependent tests when A is equal to 3 (Figure 3.3). Moreover an average FDR value of the

BH procedure is between 0.04 and 0.05 when A is more than or equal to 3 (Figure 3.3 and 3.4).

In a microarray study, controlling the type I error rate is not useful because the calculation of it involves the number of true false positives over the number of total true null hypotheses. So we always obtain a very conservative type I error measure to compare the p-values given the true null hypotheses. It often fails to detect alternative hypotheses (i.e., genes). Even though we are able to reject some true null genes using an estimated conservative type I error measure, power becomes low to reject the alternative genes in a microarray study. Therefore we will not continue to discuss type I error rate control in this section.

When A is below 2, none of the procedures give very good power (Figure 3.5 and 3.6). Increasing the value of A we can expect a power improvement for the BH, TSBH, ABH and q-value methods if we consider a large number of dependent tests with $r \approx 1$ (top panels in Figure 3.5 and 3.6). Of course all methods gain power when A is around 4.7 (Figure 3.8). Also it is noticeable that for $A = 4.7$ only the BH, TSBH, ABH and q-value methods accomplish power of about 98% (Figure 3.8); whereas the methods involved in controlling the FWER achieve power of about 70%. Under the positive regression dependent situation and for $A = 4.7$, the BY procedure is also able to increase power by 4.5 times compared with the power when A is 3 (Figure 3.7 and 3.8). Increasing the value of A from 3, the BH, TSBH, ABH and q-value methods always increase power, and their observed powers are very close to each other (Figure 3.8).

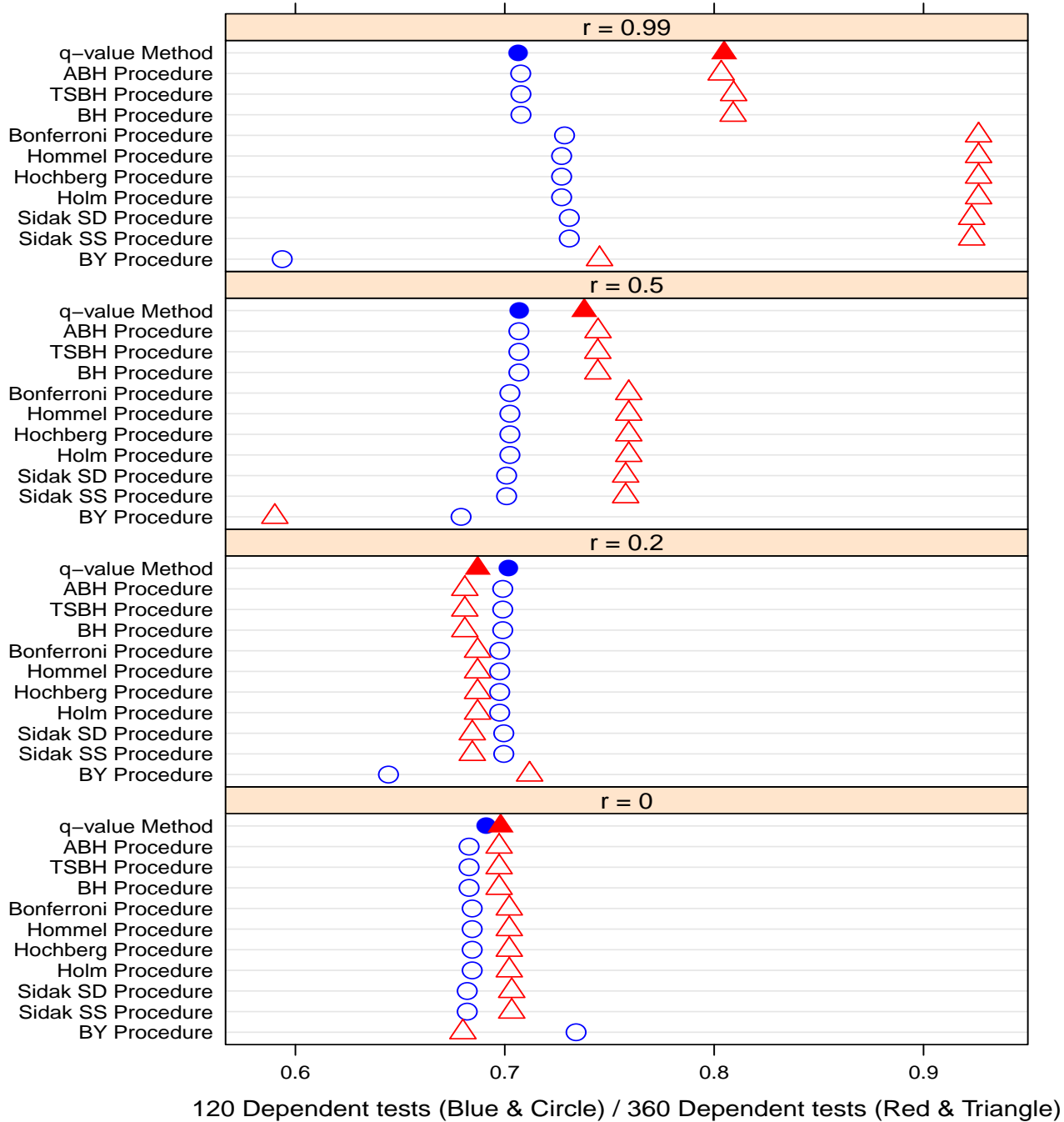


Figure 3.1: Average FDR of $A = 0.5$

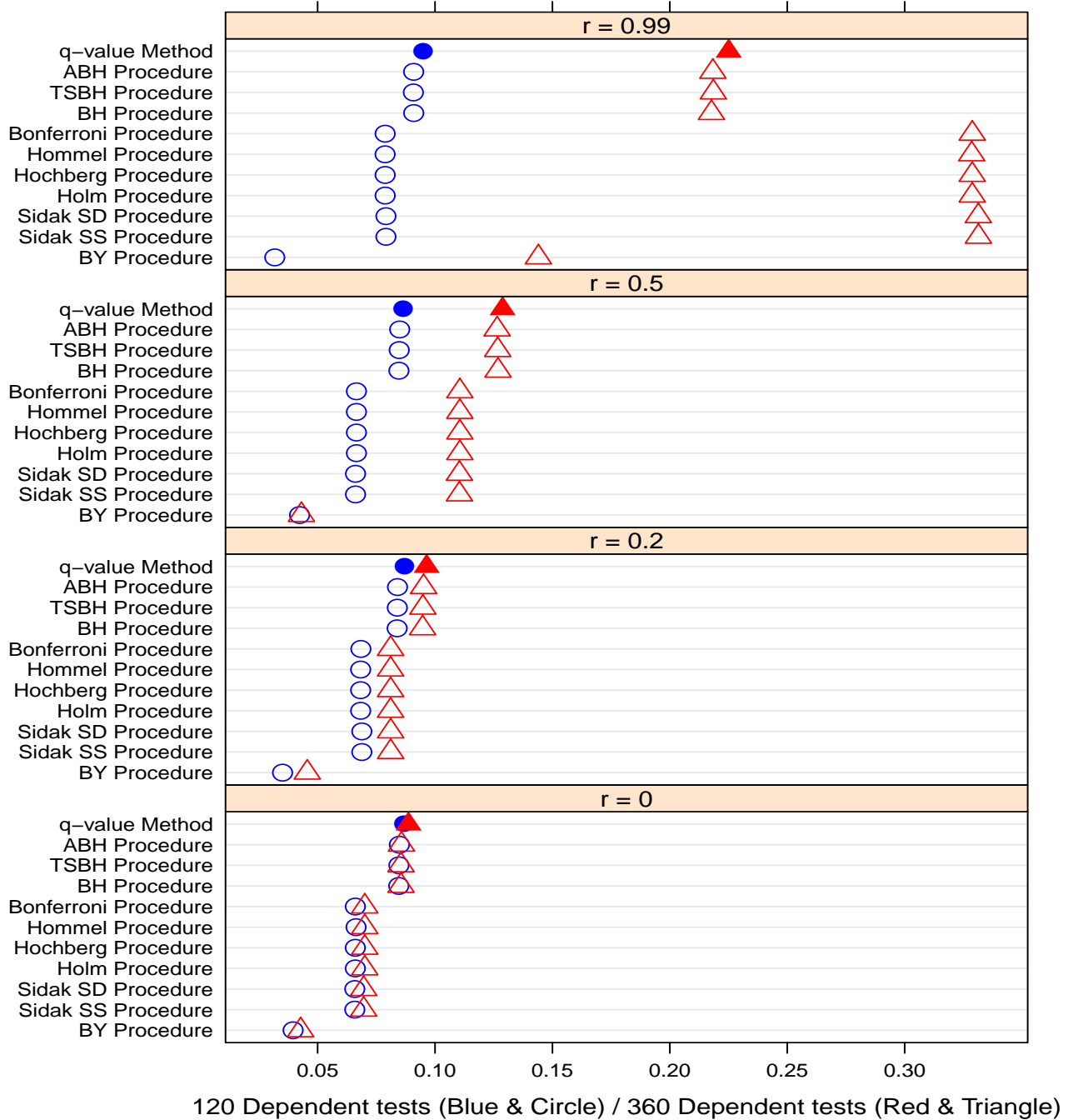


Figure 3.2: Average FDR of $A = 1.5$

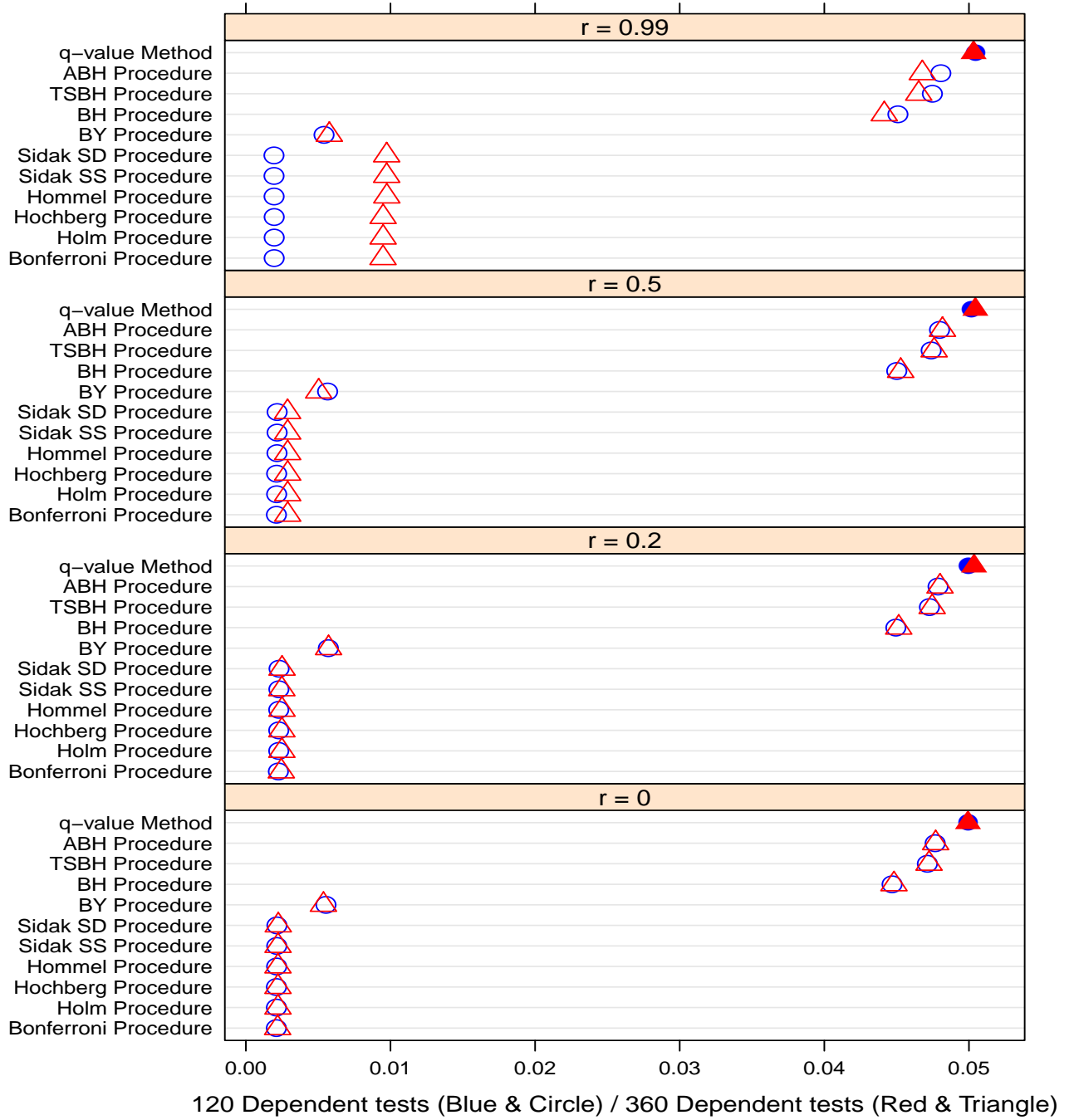


Figure 3.3: Average FDR of $A = 3$

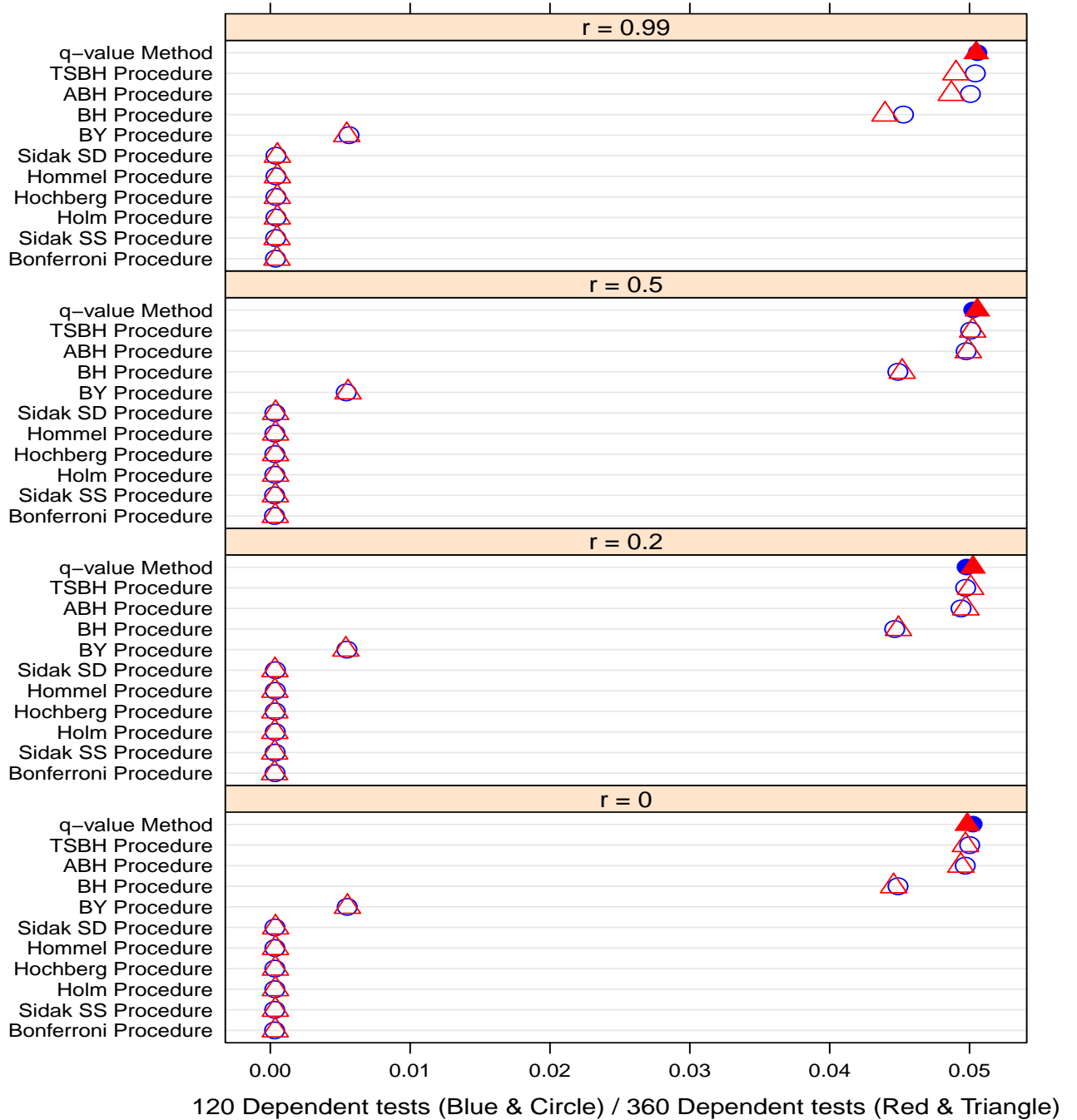


Figure 3.4: Average FDR of $A = 4.7$

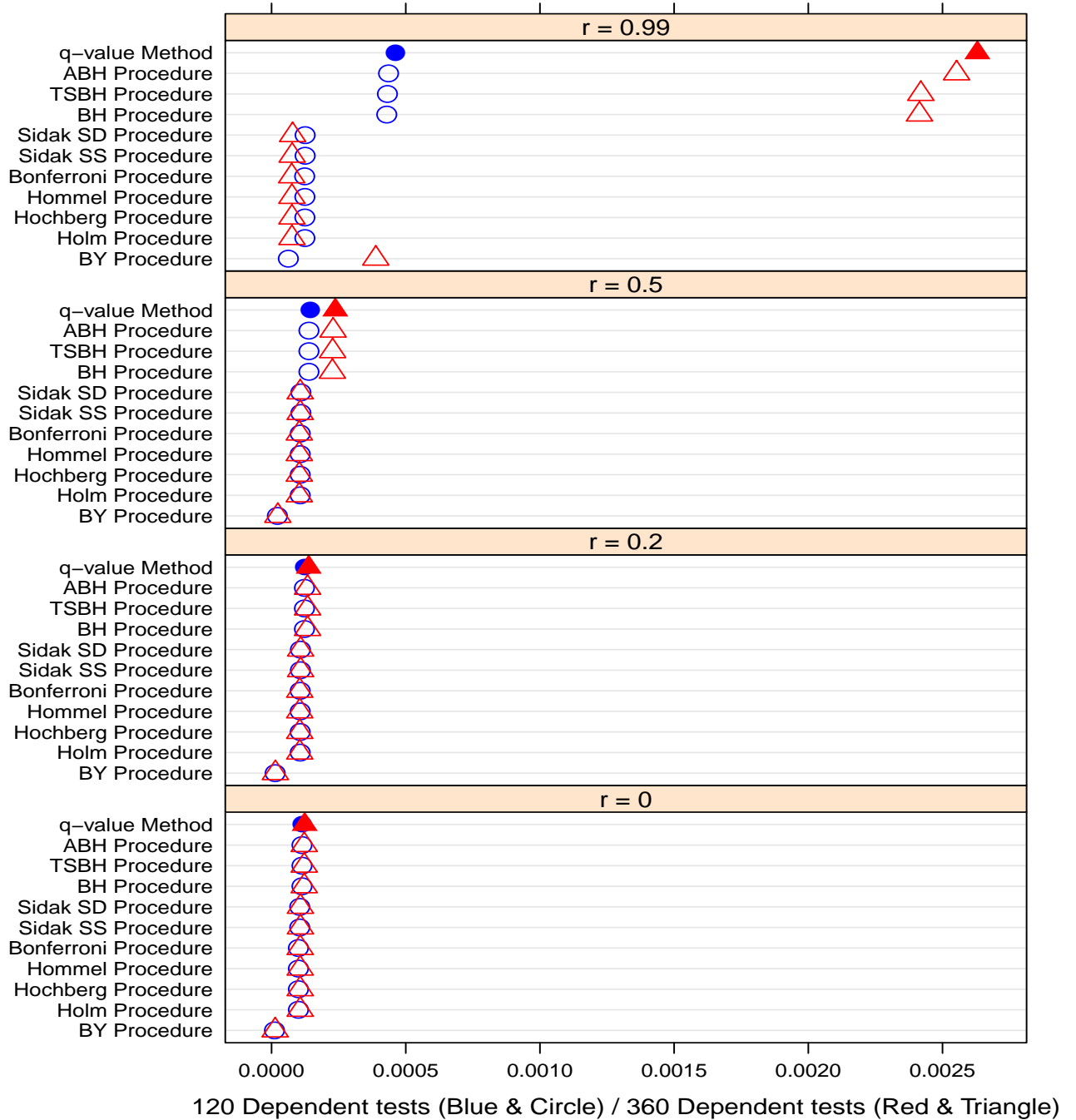


Figure 3.5: Average power of $A = 0.5$

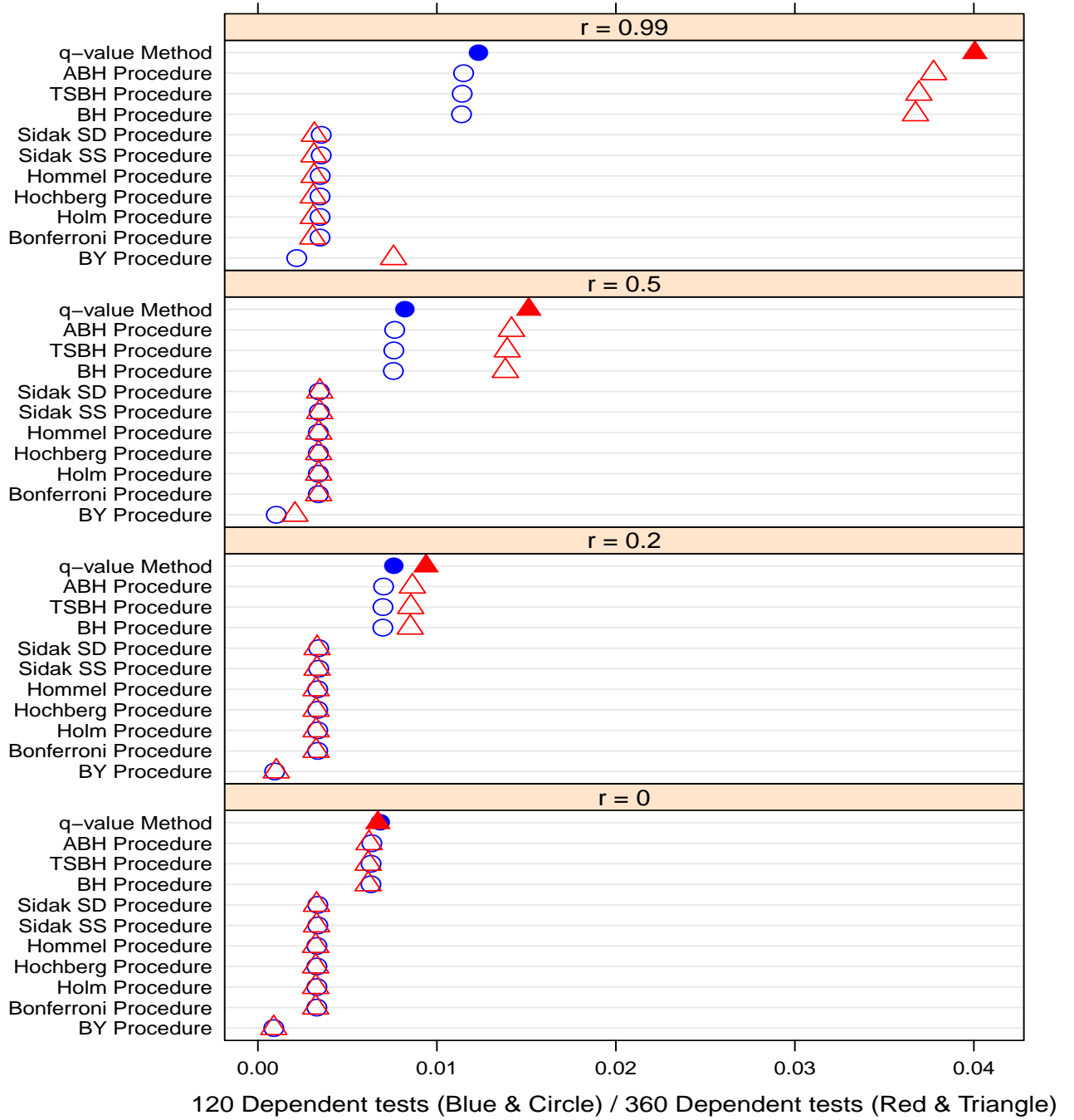


Figure 3.6: Average power of $A = 1.5$

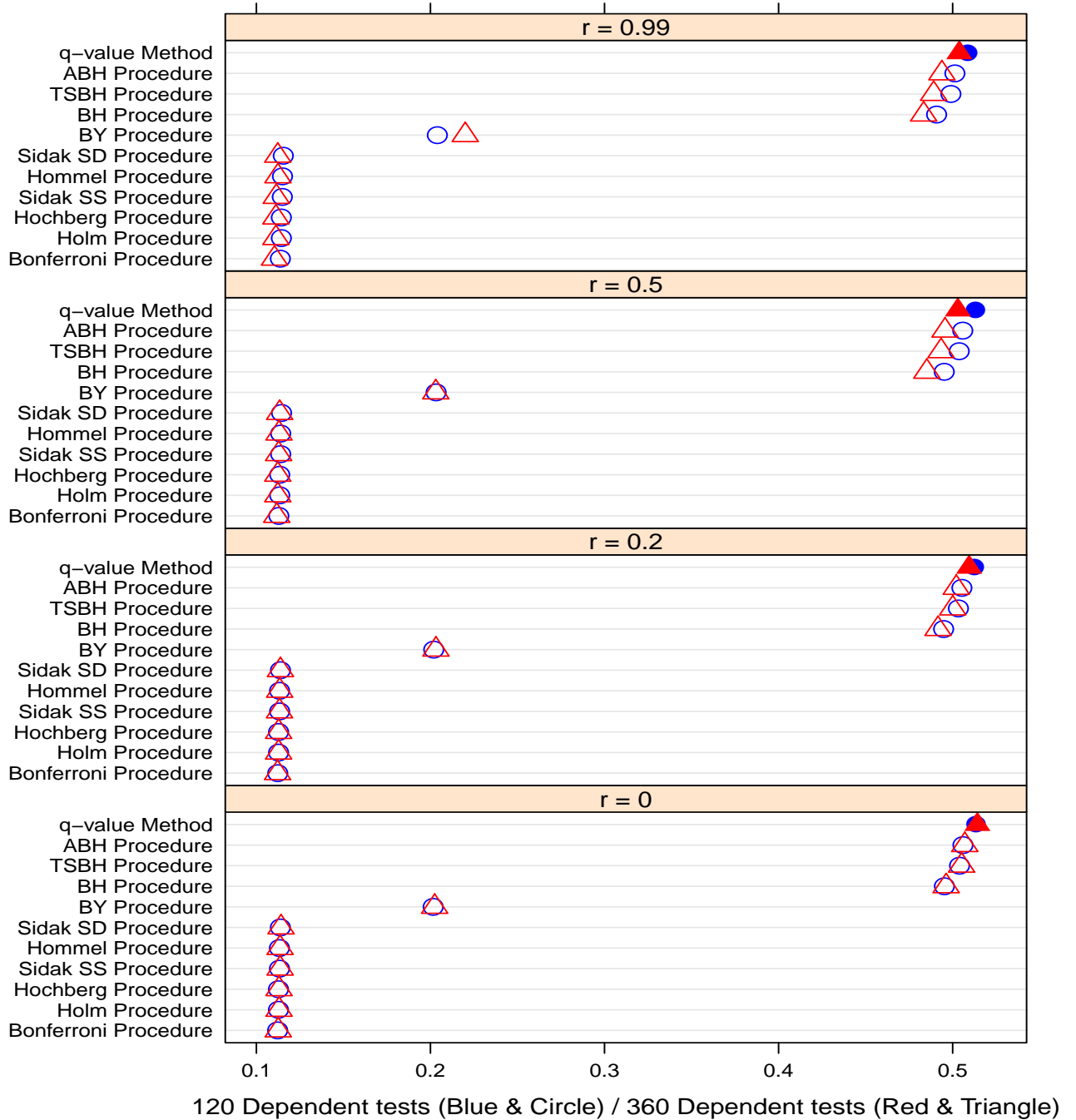


Figure 3.7: Average power of $A = 3$

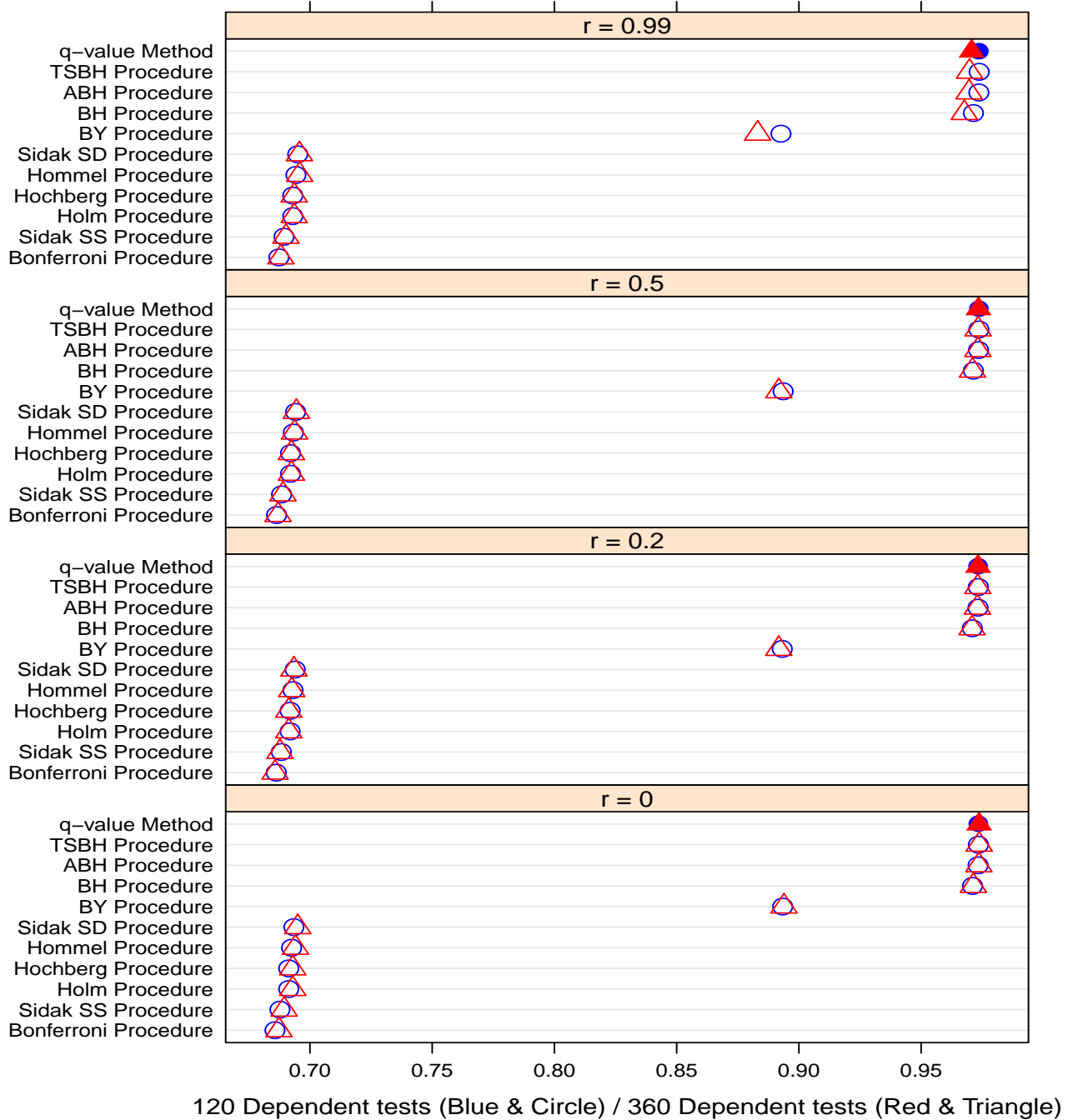


Figure 3.8: Average power of $A = 4.7$

Chapter 4

Conclusion and remaining questions

Based on our results, we conclude when gene expression value of alternative genes is small (for example approximately 2) the FDR value increases with respect to increasing number of dependent genes as well as increasing correlation values. Also the intrinsic nature of the q-value method proposed by Storey (2002) has the flexible ability to allow for dependency of hypotheses in a microarray study. In general, the q-value method has the ability to provide a satisfactory amount of power while controlling the FDR at level α especially when the gene expression value of non-true null genes is around 3. The q-value method ensures gains in power for a larger number of dependent genes or a higher positive correlation value. For a large gene expression value, such as 4, of alternative genes, the typical methods ABH, and TSBH can also gain in power to about 97% while controlling the FDR. If we consider gene expression value of non-true null genes of below 1.5, the q-value method still can provide a satisfactory FDR measure under a positive dependence condition. Indeed, our calculated FDR by the q-value method completely depends on the process that at first controls the pFDR. This is the main difference of the common methods BH, ABH, TSBH, and BY that involve controlling the FDR. So we can expect better results (power and error rate) considering our dependency conditions if we apply the q-value method to control the FDR in a microarray study.

It is not necessary that genes in a microarray study always follow positive regression dependence condition. If the genes are negatively correlated, then another method proposed by Yekutieli (2008) may work. However the method will again give a conservative FDR (Yekutieli, 2008). In order to eliminate the conservative error rate, we may apply gate keeping techniques (Dmitrienko and Tamhane, 2007; Dmitrienko et al., 2008). We can also consider the p-value weighting approach by Genovese et al. (2006). The crucial question still unresolved under the dependent genes in microarray study is determining which strategy will provide a higher power when genes are both positively and negatively correlated.

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Appendix A

Appendix

A.1 R script for the big block issue

```
.libPaths("/home/A01382510/R")
cat('Starting script',date(),'\n')
library(MASS);library(Biobase);library(multtest);library(qvalue)
rho<-c(0,.2,.5,.99);mu<-c(0.5,1.5,3,4.7);num_sim<-6000
Matrix1<-array(dim=c(length(rho),33,length(mu)))
alternative<-c(1:180,400:419)
MU<-rep(0,2000)
null<-which(MU==0)
n_true_null<-length(null);n_true_alternative<-length(alternative)
for(i in 1:length(mu))
{
  MU[alternative]<-mu[i]
  for(j in 1:length(rho))
  {
```

```

block<- matrix(rho[j],ncol=60,nrow=60);diag(block) <- 1
Sigma1 <- as.matrix(bdiag(block,block,
                           block,block,block,diag(2000-360)))
z<-mvrnorm(num_sim,mu=matrix(MU,ncol=1),Sigma1,tol=.1,empirical=F)
# get p-values
# p.mat is a matrix, with row for each simulation;
# so dim(p.mat) will be Num.Sim x 2000
p.mat<- 2*(1-pnorm(abs(z)))
sim.mat<-matrix(nrow=num_sim,ncol=33)
for( sim in 1: num_sim)
  {
    if((floor(sim/100)==(sim/100)) | (is.element(sim,c(1:5))))
    { cat('Starting simulation',sim,'of',num_sim,date()),'\n') }
    p.values<-p.mat[sim,]
    adj_p_value_BY<-p.adjust(p.values,method='BY')
    adj_p_value_BH<-p.adjust(p.values,method='BH')
    adj_p_value_hochberg<-p.adjust(p.values,method='hochberg')
    adj_p_value_hommel<-p.adjust(p.values,method='hommel')
    adj_p_value_holm<-p.adjust(p.values,method='holm')
    adj_p_value_bonferroni<-p.adjust(p.values,method='bonferroni')
    ## To run the following function need to load the 'multtest'
    adj_p_value_SidakSS<- mt.rawp2adjp(p.values,proc='SidakSS')
    adj_p_value_SidakSD<- mt.rawp2adjp(p.values,proc='SidakSD')
    adj_p_value_TSBH<- mt.rawp2adjp(p.values,proc='TSBH')
    adj_p_value_ABH<- mt.rawp2adjp(p.values,proc='ABH')
    Adj_p_value_SidakSS<-adj_p_value_SidakSS$adjp[,2]
                                     [order(adj_p_value_SidakSS$index)]
  }

```

```

Adj_p_value_SidakSD<-adj_p_value_SidakSD$adjp[,2]
      [order(adj_p_value_SidakSD$index)]
Adj_p_value_TSBH<-adj_p_value_TSBH$adjp[,2]
      [order(adj_p_value_TSBH$index)]
Adj_p_value_ABH<-adj_p_value_ABH$adjp[,2]
      [order(adj_p_value_ABH$index)]
q_value<-qvalue(p.values)
adj_q_value<-q_value$qvalues
true_false_positive_q_value<-length(which(adj_q_value
      [null]<=0.05))
sig_alternative_q_value<-length(which(adj_q_value
      [alternative]<=0.05))
true_false_positive_SidakSS<-length(which(Adj_p_value_SidakSS
      [null]<=0.05))
sig_alternative_SidakSS<-length(which(Adj_p_value_SidakSS
      [alternative]<=0.05))
true_false_positive_SidakSD<-length(which(Adj_p_value_SidakSD
      [null]<=0.05))
sig_alternative_SidakSD<-length(which(Adj_p_value_SidakSD
      [alternative]<=0.05))
true_false_positive_TSBH<-length(which(Adj_p_value_TSBH[null]
      <=0.05))
sig_alternative_TSBH<-length(which(Adj_p_value_TSBH[alternative]
      <=0.05))
true_false_positive_ABH<-length(which(Adj_p_value_ABH[null]
      <=0.05))
sig_alternative_ABH<-length(which(Adj_p_value_ABH[alternative]

```

```

                                <=0.05))
true_false_positive_BY<-length(which(adj_p_value_BY[null]
                                <=0.05))
sig_alternative_BY<-length(which(adj_p_value_BY[alternative]
                                <=0.05))
true_false_positive_BH<-length(which(adj_p_value_BH[null]
                                <=0.05))
sig_alternative_BH<-length(which(adj_p_value_BH[alternative]
                                <=0.05))
true_false_positive_hommel<-length(which(adj_p_value_hommel
                                [null]<=0.05))
sig_alternative_hommel<-length(which(adj_p_value_hommel
                                [alternative]<=0.05))
sig_alternative_bonferroni<-length(which(adj_p_value_bonferroni
                                [alternative]<=0.05))
true_false_positive_bonferroni<-length(which(adj_p_value_bonferroni
                                [null]<=0.05))
true_false_positive_hochberg<-length(which(adj_p_value_hochberg
                                [null]<=0.05))
sig_alternative_hochberg<-length(which(adj_p_value_hochberg
                                [alternative]<=0.05))
true_false_positive_holm<-length(which(adj_p_value_holm[null]
                                <=0.05))
sig_alternative_holm<-length(which(adj_p_value_holm[alternative]
                                <=0.05))
## The following functions print out the type I error rate, and power
type_I_error_q_value<-true_false_positive_q_value/n_true_null

```

```

type_I_error_holm<-true_false_positive_holm/n_true_null
type_I_error_hochberg<-true_false_positive_hochberg/n_true_null
type_I_error_bonferroni<-true_false_positive_bonferroni/n_true_null
type_I_error_hommel<-true_false_positive_hommel/n_true_null
type_I_error_BH<-true_false_positive_BH/n_true_null
type_I_error_BY<-true_false_positive_BY/n_true_nul
type_I_error_TSBH<-true_false_positive_TSBH/n_true_null
type_I_error_SidakSS<-true_false_positive_SidakSS/n_true_null
type_I_error_SidakSD<-true_false_positive_SidakSD/n_true_null
type_I_error_ABH<-true_false_positive_ABH/n_true_null
power_q_value<-sig_alternative_q_value/n_true_alternative
power_holm<-sig_alternative_holm/n_true_alternative
power_hommel<-sig_alternative_hommel/n_true_alternative
power_bonferroni<-sig_alternative_bonferroni/n_true_alternative
power_hochberg<-sig_alternative_hochberg/n_true_alternative
power_BH<-sig_alternative_BH/n_true_alternative
power_BY<-sig_alternative_BY/n_true_alternative
power_TSBH<-sig_alternative_TSBH/n_true_alternativ
power_ABH<-sig_alternative_ABH/n_true_alternative
power_SidakSS<-sig_alternative_SidakSS/n_true_alternative
power_SidakSD<-sig_alternative_SidakSD/n_true_alternative
significant.test.BY<-length(which(adj_p_value_BY<=0.05))
significant.test.BH<-length(which(adj_p_value_BH<=0.05))
significant.test.hochberg<-length(which(adj_p_value_hochberg<=0.05))
significant.test.hommel<-length(which(adj_p_value_hommel<=0.05))
significant.test.holm<-length(which(adj_p_value_holm<=0.05))
significant.test.bonferroni<-length(which(adj_p_value_bonferroni

```

```

                                <=0.05))
significant.test.SidakSS<-length(which(adj_p_value_SidakSS$adjp[,2]
                                <=0.05))
significant.test.SidakSD<-length(which(adj_p_value_SidakSD$adjp[,2]
                                <=0.05))
significant.test.TSBH<-length(which(adj_p_value_TSBH$adjp[,2]
                                <=0.05))
significant.test.ABH<-length(which(adj_p_value_ABH$adjp[,2]
                                <=0.05))
fdr_q_value<-true_false_positive_q_value/length(which(adj_q_value
                                <=0.05))

fdr_BH<-true_false_positive_BH/significant.test.BH
fdr_BY<-true_false_positive_BY/significant.test.BY
fdr_Holm<-true_false_positive_holm/significant.test.holm
fdr_Hochberg<-true_false_positive_hochberg/significant.test.hochberg
fdr_Hommel<-true_false_positive_hommel/significant.test.hommel
fdr_bonferroni<-(true_false_positive_bonferroni/
                significant.test.bonferroni)
fdr_SidakSS<-(true_false_positive_SidakSS/
                significant.test.SidakSS)
fdr_SidakSD<-(true_false_positive_SidakSD/
                significant.test.SidakSD)
fdr_ABH<-true_false_positive_ABH/significant.test.ABH
fdr_TSBH<-true_false_positive_TSBH/significant.test.TSBH
vec <
c(type_I_error_holm,type_I_error_hochberg,type_I_error_hommel,
type_I_error_BH,type_I_error_BY,type_I_error_TSBH,type_I_error_ABH,

```

```

type_I_error_SidakSS,type_I_error_SidakSD,type_I_error_bonferroni,
type_I_error_q_value,power_holm,power_hochberg,power_hommel,power_BH,
power_BY,power_TSBH,power_ABH,power_SidakSS,power_SidakSD,
power_bonferroni,power_q_value,fdr_Holm,fdr_Hochberg,fdr_Hommel,
fdr_BH,fdr_BY,fdr_TSBH,fdr_ABH,fdr_SidakSS,fdr_SidakSD,fdr_bonferroni,
fdr_q_value)
    sim.mat[sim,]<- vec
}

# now get error rate, power, fdr -- all averaged over simulations
ave.vec<-apply(sim.mat,2,mean,na.rm=T)
Matrix1[j,,i]<-ave.vec

# this is a length 33 vector for mu level i, rho level j;
}
}

Colum<-c('ty_I_holm','ty_I_hoch','ty_I_hom','ty_I_BH','ty_I_BY','ty_I_TSBH','ty_I_ABH',
'ty_I_SS','ty_I_SD','ty_I_bon','ty_I_q','p_holm','p_hoc','p_hom','p_BH','p_BY',
'p_TSBH','p_ABH','p_SS','p_Sd','p_bon','p_q','fdr_Holm','fdr_Hoc','fdr_Hom','fdr_BH',
'fdr_BY','fdr_TSBH','fdr_ABH','fdr_SS','fdr_SD','fdr_bon','fdr_q')
Row<-c('r=0','r=0.2','r=0.5','r=0.99')
mu.mat.3.1<- Matrix1[,,1] # this is matrix of results for mu level 0.5
rownames(mu.mat.3.1)<-Row
colnames(mu.mat.3.1)<-Colum
write.csv(mu.mat.3.1,"/home/A01382510/hpc_03162011/Result_0.5_bigblock.csv")
mu.mat.3.2<- Matrix1[,,2] # this is matrix of results for mu level 1.5
rownames(mu.mat.3.2)<-Row
colnames(mu.mat.3.2)<-Colum
write.csv(mu.mat.3.2,"/home/A01382510/hpc_03162011/Result_1.5_bigblock.csv")

```



```

mu.mat.3.3<- Matrix1[, ,3] # this is matrix of results for mu level 3
rownames(mu.mat.3.3)<-Row
colnames(mu.mat.3.3)<-Colum
write.csv(mu.mat.3.3, "/home/A01382510/hpc_03162011/Result_3_bigblock.csv")
mu.mat.3.4<- Matrix1[, ,4] # this is matrix of results for mu level 4.7
rownames(mu.mat.3.4)<-Row
colnames(mu.mat.3.4)<-Colum
write.csv(mu.mat.3.4, "/home/A01382510/hpc_03162011/Result_4.7_bigblock.csv")
cat('Completed script',date(),'\n')

```

A.2 R script for the small block issue

```

.libPaths("/home/A01382510/R")
cat('Starting script',date(),'\n')
library(MASS);library(Biobase);library(multtest);library(qvalue)
rho<-c(0, .2, .5, .99);mu<-c(0.5, 1.5, 3, 4.7);num_sim<-6000
Matrix1<-array(dim=c(length(rho), 33, length(mu)))
alternative<-c(1:180, 400:419)
MU<-rep(0, 2000)
null<-which(MU==0)
n_true_null<-length(null);n_true_alternative<-length(alternative)
for(i in 1:length(mu))
{
  MU[alternative]<-mu[i]
  for(j in 1:length(rho))
  {

```

```

block<- matrix(rho[j],ncol=20,nrow=20);diag(block) <- 1
Sigma1 <- as.matrix(bdiag(block,block,
                           block,block,block,block,diag(2000-120)))
z<-mvrnorm(num_sim,mu=matrix(MU,ncol=1),Sigma1,tol=.1,empirical=F)
# get p-values
# p.mat is a matrix, with row for each simulation;
# so dim(p.mat) will be Num.Sim x 2000
p.mat<- 2*(1-pnorm(abs(z)))
sim.mat<-matrix(nrow=num_sim,ncol=33)
for( sim in 1: num_sim)
  {
    if((floor(sim/100)==(sim/100)) | (is.element(sim,c(1:5))))
    { cat('Starting simulation',sim,'of',num_sim,date(),'\n') }
    p.values<-p.mat[sim,]
    adj_p_value_BY<-p.adjust(p.values,method='BY')
    adj_p_value_BH<-p.adjust(p.values,method='BH')
    adj_p_value_hochberg<-p.adjust(p.values,method='hochberg')
    adj_p_value_hommel<-p.adjust(p.values,method='hommel')
    adj_p_value_holm<-p.adjust(p.values,method='holm')
    adj_p_value_bonferroni<-p.adjust(p.values,method='bonferroni')
    ## To run the following function need to load the 'multtest'
    adj_p_value_SidakSS<- mt.rawp2adjp(p.values,proc='SidakSS')
    adj_p_value_SidakSD<- mt.rawp2adjp(p.values,proc='SidakSD')
    adj_p_value_TSBH<- mt.rawp2adjp(p.values,proc='TSBH')
    adj_p_value_ABH<- mt.rawp2adjp(p.values,proc='ABH')
    Adj_p_value_SidakSS<-adj_p_value_SidakSS$adjp[,2]
                                [order(adj_p_value_SidakSS$index)]
  }

```

```

Adj_p_value_SidakSD<-adj_p_value_SidakSD$adjp[,2]
                    [order(adj_p_value_SidakSD$index)]
Adj_p_value_TSBH<-adj_p_value_TSBH$adjp[,2]
                    [order(adj_p_value_TSBH$index)]
Adj_p_value_ABH<-adj_p_value_ABH$adjp[,2]
                    [order(adj_p_value_ABH$index)]
q_value<-qvalue(p.values)
adj_q_value<-q_value$qvalues
true_false_positive_q_value<-length(which(adj_q_value
                    [null]<=0.05))
sig_alternative_q_value<-length(which(adj_q_value
                    [alternative]<=0.05))
true_false_positive_SidakSS<-length(which(Adj_p_value_SidakSS
                    [null]<=0.05))
sig_alternative_SidakSS<-length(which(Adj_p_value_SidakSS
                    [alternative]<=0.05))
true_false_positive_SidakSD<-length(which(Adj_p_value_SidakSD
                    [null]<=0.05))
sig_alternative_SidakSD<-length(which(Adj_p_value_SidakSD
                    [alternative]<=0.05))
true_false_positive_TSBH<-length(which(Adj_p_value_TSBH[null]
                    <=0.05))
sig_alternative_TSBH<-length(which(Adj_p_value_TSBH[alternative]
                    <=0.05))
true_false_positive_ABH<-length(which(Adj_p_value_ABH[null]
                    <=0.05))
sig_alternative_ABH<-length(which(Adj_p_value_ABH[alternative]

```

```

                                <=0.05))
true_false_positive_BY<-length(which(adj_p_value_BY[null]
                                <=0.05))
sig_alternative_BY<-length(which(adj_p_value_BY[alternative]
                                <=0.05))
true_false_positive_BH<-length(which(adj_p_value_BH[null]
                                <=0.05))
sig_alternative_BH<-length(which(adj_p_value_BH[alternative]
                                <=0.05))
true_false_positive_hommel<-length(which(adj_p_value_hommel
                                [null]<=0.05))
sig_alternative_hommel<-length(which(adj_p_value_hommel
                                [alternative]<=0.05))
sig_alternative_bonferroni<-length(which(adj_p_value_bonferroni
                                [alternative]<=0.05))
true_false_positive_bonferroni<-length(which(adj_p_value_bonferroni
                                [null]<=0.05))
true_false_positive_hochberg<-length(which(adj_p_value_hochberg
                                [null]<=0.05))
sig_alternative_hochberg<-length(which(adj_p_value_hochberg
                                [alternative]<=0.05))
true_false_positive_holm<-length(which(adj_p_value_holm[null]
                                <=0.05))
sig_alternative_holm<-length(which(adj_p_value_holm[alternative]
                                <=0.05))
## The following functions print out the type I error rate, and power
type_I_error_q_value<-true_false_positive_q_value/n_true_null

```

```

type_I_error_holm<-true_false_positive_holm/n_true_null
type_I_error_hochberg<-true_false_positive_hochberg/n_true_null
type_I_error_bonferroni<-true_false_positive_bonferroni/n_true_null
type_I_error_hommel<-true_false_positive_hommel/n_true_null
type_I_error_BH<-true_false_positive_BH/n_true_null
type_I_error_BY<-true_false_positive_BY/n_true_nul
type_I_error_TSBH<-true_false_positive_TSBH/n_true_null
type_I_error_SidakSS<-true_false_positive_SidakSS/n_true_null
type_I_error_SidakSD<-true_false_positive_SidakSD/n_true_null
type_I_error_ABH<-true_false_positive_ABH/n_true_null
power_q_value<-sig_alternative_q_value/n_true_alternative
power_holm<-sig_alternative_holm/n_true_alternative
power_hommel<-sig_alternative_hommel/n_true_alternative
power_bonferroni<-sig_alternative_bonferroni/n_true_alternative
power_hochberg<-sig_alternative_hochberg/n_true_alternative
power_BH<-sig_alternative_BH/n_true_alternative
power_BY<-sig_alternative_BY/n_true_alternative
power_TSBH<-sig_alternative_TSBH/n_true_alternativ
power_ABH<-sig_alternative_ABH/n_true_alternative
power_SidakSS<-sig_alternative_SidakSS/n_true_alternative
power_SidakSD<-sig_alternative_SidakSD/n_true_alternative
significant.test.BY<-length(which(adj_p_value_BY<=0.05))
significant.test.BH<-length(which(adj_p_value_BH<=0.05))
significant.test.hochberg<-length(which(adj_p_value_hochberg<=0.05))
significant.test.hommel<-length(which(adj_p_value_hommel<=0.05))
significant.test.holm<-length(which(adj_p_value_holm<=0.05))
significant.test.bonferroni<-length(which(adj_p_value_bonferroni

```

```

                                <=0.05))
significant.test.SidakSS<-length(which(adj_p_value_SidakSS$adjp[,2]
                                <=0.05))
significant.test.SidakSD<-length(which(adj_p_value_SidakSD$adjp[,2]
                                <=0.05))
significant.test.TSBH<-length(which(adj_p_value_TSBH$adjp[,2]
                                <=0.05))
significant.test.ABH<-length(which(adj_p_value_ABH$adjp[,2]
                                <=0.05))
fdr_q_value<-true_false_positive_q_value/length(which(adj_q_value
                                <=0.05))

fdr_BH<-true_false_positive_BH/significant.test.BH
fdr_BY<-true_false_positive_BY/significant.test.BY
fdr_Holm<-true_false_positive_holm/significant.test.holm
fdr_Hochberg<-true_false_positive_hochberg/significant.test.hochberg
fdr_Hommel<-true_false_positive_hommel/significant.test.hommel
fdr_bonferroni<-(true_false_positive_bonferroni/
                significant.test.bonferroni)
fdr_SidakSS<-(true_false_positive_SidakSS/
                significant.test.SidakSS)
fdr_SidakSD<-(true_false_positive_SidakSD/
                significant.test.SidakSD)
fdr_ABH<-true_false_positive_ABH/significant.test.ABH
fdr_TSBH<-true_false_positive_TSBH/significant.test.TSBH
vec <
c(type_I_error_holm,type_I_error_hochberg,type_I_error_hommel,
type_I_error_BH,type_I_error_BY,type_I_error_TSBH,type_I_error_ABH,

```

```

type_I_error_SidakSS,type_I_error_SidakSD,type_I_error_bonferroni,
type_I_error_q_value,power_holm,power_hochberg,power_hommel,power_BH,
power_BY,power_TSBH,power_ABH,power_SidakSS,power_SidakSD,
power_bonferroni,power_q_value,fdr_Holm,fdr_Hochberg,fdr_Hommel,
fdr_BH,fdr_BY,fdr_TSBH,fdr_ABH,fdr_SidakSS,fdr_SidakSD,fdr_bonferroni,
fdr_q_value)
    sim.mat[sim,]<- vec
}

# now get error rate, power, fdr -- all averaged over simulations
ave.vec<-apply(sim.mat,2,mean,na.rm=T)
Matrix1[j,,i]<-ave.vec

# this is a length 33 vector for mu level i, rho level j;
}

}

Colum<-c('ty_I_holm','ty_I_hoch','ty_I_hom','ty_I_BH','ty_I_BY','ty_I_TSBH','ty_I_ABH',
'ty_I_SS','ty_I_SD','ty_I_bon','ty_I_q','p_holm','p_hoc','p_hom','p_BH','p_BY',
'p_TSBH','p_ABH','p_SS','p_Sd','p_bon','p_q','fdr_Holm','fdr_Hoc','fdr_Hom','fdr_BH',
'fdr_BY','fdr_TSBH','fdr_ABH','fdr_SS','fdr_SD','fdr_bon','fdr_q')
Row<-c('r=0','r=0.2','r=0.5','r=0.99')
mu.mat.3.1<- Matrix1[,,1] # this is matrix of results for mu level 0.5
rownames(mu.mat.3.1)<-Row
colnames(mu.mat.3.1)<-Colum
write.csv(mu.mat.3.1,"/home/A01382510/hpc_03162011/Result_0.5_smallblock.csv")
mu.mat.3.2<- Matrix1[,,2] # this is matrix of results for mu level 1.5
rownames(mu.mat.3.2)<-Row
colnames(mu.mat.3.2)<-Colum
write.csv(mu.mat.3.2,"/home/A01382510/hpc_03162011/Result_1.5_smallblock.csv")

```

```

mu.mat.3.3<- Matrix1[, ,3] # this is matrix of results for mu level 3
rownames(mu.mat.3.3)<-Row
colnames(mu.mat.3.3)<-Colum
write.csv(mu.mat.3.3, "/home/A01382510/hpc_03162011/Result_3_smallblock.csv")
mu.mat.3.4<- Matrix1[, ,4] # this is matrix of results for mu level 4.7
rownames(mu.mat.3.4)<-Row
colnames(mu.mat.3.4)<-Colum
write.csv(mu.mat.3.4, "/home/A01382510/hpc_03162011/Result_4.7_smallblock.csv")
cat('Completed script',date(),'\n')

```

A.3 R script for Figure 3.1 to 3.8

```

install.packages('lattice')
library(lattice)

#Date: May 5/2011
MU_0.5_smallblock<-read.csv("E:\\MS thesis result\\Result_0.5_smallblock.csv")
MU_0.5_smallblock<-MU_0.5_smallblock[,-1]
MU_0.5_bigblock<-read.csv("E:\\MS thesis result\\Result_0.5_bigblock.csv")
MU_0.5_bigblock<-MU_0.5_bigblock[,-1]
row_names<-c('Holm Procedure', 'Hochberg Procedure', 'Hommel Procedure', 'BH Procedure',
'BY Procedure', 'TSBH Procedure', 'ABH Procedure', 'Sidak SS Procedure',
'Sidak SD Procedure', 'Bonferroni Procedure', 'q-value Method')
r<-c('r = 0', 'r = 0.2', 'r = 0.5', 'r = 0.99')
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{

```



```

    FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+22)]))
  }
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
           FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+22)]))
  }
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
           FDR[9,],FDR[10,],FDR[11,]),ncol=1)
# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
       rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
       rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
       rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
       rep('q-value Method',4))
Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)

```

```

summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\FDR_A_0.5.pdf',height=9,width=7.2)
dotplot(Alg ~ Val |object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
        / 360 Dependent tests (Red & Triangle)",cex=1.5,
panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()
## Following code for power A = 0.5
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+11)]))
}
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+11)]))
}
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],

```

```

FDR[9,],FDR[10,],FDR[11,]),ncol=1)

# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)

# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
      rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
      rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
      rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
      rep('q-value Method',4))

Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\power_A_0.5.pdf',height=9,width=7.2)
## This is the correct plot and done
dotplot(Alg ~ Val | object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
      / 360 Dependent tests (Red & Triangle)",cex=1.5,
panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

```

```

## Following code FDR A =1.5
MU_0.5_smallblock<-read.csv("E:\\MS thesis result\\Result_1.5_smallblock.csv")
MU_0.5_smallblock<-MU_0.5_smallblock[,-1]
MU_0.5_bigblock<-read.csv("E:\\MS thesis result\\Result_1.5_bigblock.csv")
MU_0.5_bigblock<-MU_0.5_bigblock[,-1]
row_names<-c('Holm Procedure','Hochberg Procedure','Hommel Procedure','BH Procedure',
'BY Procedure','TSBH Procedure','ABH Procedure','Sidak SS Procedure',
'Sidak SD Procedure','Bonferroni Procedure','q-value Method')
r<-c('r = 0','r = 0.2','r = 0.5','r = 0.99')
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
  FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+22)]))
}
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
  FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+22)]))
}
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
FDR[9,],FDR[10,],FDR[11,]),ncol=1)

```

```

# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
      rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
      rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
      rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
      rep('q-value Method',4))
Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == r = 0.5])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\FDR_A_1.5.pdf',height=9,width=7.2)
dotplot(Alg ~ Val |object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
      / 360 Dependent tests (Red & Triangle)",cex=1.5,
panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

```

```

## Following code for power A = 1.5
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+1)]))
  }
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
            FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+1)]))
  }
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
            FDR[9,],FDR[10,],FDR[11,]),ncol=1)
# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
        rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
        rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
        rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
        rep('q-value Method',4))

```

```

Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\power_A_1.5.pdf',height=9,width=7.2)
dotplot(Alg ~ Val |object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
        / 360 Dependent tests (Red & Triangle)",cex=1.5,
panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

## Following code for FDR A =3

MU_0.5_smallblock<-read.csv("E:\\MS thesis result\\Result_3_smallblock.csv")
MU_0.5_smallblock<-MU_0.5_smallblock[,-1]
MU_0.5_bigblock<-read.csv("E:\\MS thesis result\\Result_3_bigblock.csv")
MU_0.5_bigblock<-MU_0.5_bigblock[,-1]
row_names<-c('Holm Procedure','Hochberg Procedure','Hommel Procedure','BH Procedure',
'BY Procedure','TSBH Procedure','ABH Procedure','Sidak SS Procedure',
'Sidak SD Procedure','Bonferroni Procedure','q-value Method')

```

```

r<-c('r = 0','r = 0.2','r = 0.5','r = 0.99')
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+22)]))
  }
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
            FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+22)]))
  }
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
            FDR[9,],FDR[10,],FDR[11,]),ncol=1)
# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
        rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
        rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
        rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
        rep('q-value Method',4))
Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))

```



```

dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)

dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\FDR_A_3.pdf',height=9,width=7.2)
dotplot(Alg ~ Val |object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
        / 360 Dependent tests (Red & Triangle)",cex=1.5,
panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

## Following code for power A = 3
FDR<-matrix(0,ncol=length(r),nrow=11)

for(i in 1:11)
{
  FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+11)]))
}

# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],

```

```

        FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+11)]))
  }
# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
            FDR[9,],FDR[10,],FDR[11,]),ncol=1)
# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
        rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
        rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
        rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
        rep('q-value Method',4))
Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\power_A_3.pdf',height=9,width=7.2)
dotplot(Alg ~ Val | object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)

```

```

/ 360 Dependent tests (Red & Triangle)",cex=1.5,

panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

## Following code for FDR A =4.7
MU_0.5_smallblock<-read.csv("E:\\MS thesis result\\Result_4.7_smallblock.csv")
MU_0.5_smallblock<-MU_0.5_smallblock[,-1]
MU_0.5_bigblock<-read.csv("E:\\MS thesis result\\Result_4.7_bigblock.csv")
MU_0.5_bigblock<-MU_0.5_bigblock[,-1]
row_names<-c('Holm Procedure','Hochberg Procedure','Hommel Procedure','BH Procedure',
'BY Procedure','TSBH Procedure','ABH Procedure','Sidak SS Procedure',
'Sidak SD Procedure','Bonferroni Procedure','q-value Method')
r<-c('r = 0','r = 0.2','r = 0.5','r = 0.99')
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+22)]))
}
# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)

```

```

for(i in 1:11)
  {
    FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+22)]))
  }

# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
            FDR[9,],FDR[10,],FDR[11,]),ncol=1)

# Make an object set to use panel, and they are correlation values
object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)

# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
       rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
       rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
       rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
       rep('q-value Method',4))

Alg<-rep(alg,2)

speed<-c(rep("120",44),rep("360",44))

dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)

summary(dat32$Alg)

pdf('C:\\ABDULLAH\\Ressult\\FDR_A_4.7.pdf',height=9,width=7.2)
dotplot(Alg ~ Val | object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)

```

```

/ 360 Dependent tests (Red & Triangle)",cex=1.5,panel=function(x,y){

panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

## Following code for power A = 4.7
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
  FDR[i,]<-matrix(c(MU_0.5_smallblock[, (i+11)]))
}

# Make Matrix with 120 tests
x<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],FDR[9,],
           FDR[10,],FDR[11,]),ncol=1)
FDR<-matrix(0,ncol=length(r),nrow=11)
for(i in 1:11)
{
  FDR[i,]<-matrix(c(MU_0.5_bigblock[, (i+11)]))
}

# Make Matrix with 360 tests
y<-matrix(c(FDR[1,],FDR[2,],FDR[3,],FDR[4,],FDR[5,],FDR[6,],FDR[7,],FDR[8,],
           FDR[9,],FDR[10,],FDR[11,]),ncol=1)

# Make an object set to use panel, and they are correlation values

```

```

object<-rep(c('r = 0','r = 0.2','r = 0.5','r = 0.99'),22)
# Make Methods, that send in the y-axis
alg<-c(rep('Holm Procedure',4),rep('Hochberg Procedure',4),rep('Hommel Procedure',4),
      rep('BH Procedure',4),rep('BY Procedure',4),rep('TSBH Procedure',4),
      rep('ABH Procedure',4),rep('Sidak SS Procedure',4),
      rep('Sidak SD Procedure',4),rep('Bonferroni Procedure',4),
      rep('q-value Method',4))
Alg<-rep(alg,2)
speed<-c(rep("120",44),rep("360",44))
dat32 = data.frame(object,Alg,Val = rbind(x,y),speed)
dat32$Alg = factor(dat32$Alg,levels = dat32$Alg[dat32$object == "r = 0.5"]
                  [order(dat32$Val[dat32$object == "r = 0.5"])])
dat32$Alg<-factor(dat32$Alg)
summary(dat32$Alg)
pdf('C:\\ABDULLAH\\Ressult\\power_A_4.7.pdf',height=9,width=7.2)
dotplot(Alg ~ Val | object, data = dat32, groups = speed,layout = c(1,4),
xlab = "120 Dependent tests (Blue & Circle)
      / 360 Dependent tests (Red & Triangle)",cex=1.5,panel=function(x,y){
panel.dotplot(x, y,cex = 1.5,pch = c(c(rep(1,10),16),c(rep(2,10),17)),
col=c(rep('blue',11),rep('red',11) ))
}
)
dev.off()

```