International Journal of Statistical Sciences *ISSN 1683-5603*
Vol. 24(2) Special, December, 2024, pp 123-136
DOI: https://doi.org/10.3329/ijss.v24i20.78218

Controlling the k-FWER by Adaptive Modified Bonferroni Methods under the Discrete Framework

Prapti Giri[1], Aniket Biswas[2] and Gaurangadeb Chattopadhyay[1*]

[1]Department of Statistics, University of Calcutta, Kolkata, India
[2]Department of Statistics, St. Xavier's University, Kolkata, India
[*]Correspondence should be addressed to Gaurangadeb Chattopadhyay
(Email: gcdhstat@gmail.com)

[Received July 7, 2024; Accepted December 1, 2024]

Abstract

Family wise error rate (FWER) is an important measure of the overall Type-I error when multiple tests are performed simultaneously. For a positive integer k, k-FWER is the probability of rejecting at least k true null hypotheses. In this article, we present an adaptive version of the Bonferroni and the modified Bonferroni procedure for controlling k-FWER by plugging-in an estimator of the proportion of true null hypotheses. We verify k-FWER control of the adaptive methods empirically. Extensive simulation experiments exhibit the gain in power by the proposed methods over the existing methods for multiple discrete tests. We demonstrate applications of the proposed methods through two benchmark real-world datasets.

Keywords: Fisher's exact test, Binomial test, Multiple hypotheses testing, Gene expression, Amino acids.

AMS Classification: 62F03.

1. Introduction

The problem of multiple hypotheses testing has become relevant in large scale biological experiments due to the advent of high-throughput devices. Multiple hypotheses testing generally refers to any instance that involves the testing of more than one hypotheses simultaneously. For a single hypothesis testing problem, we control the probability of Type-I error, that is, the probability of rejecting a true null hypothesis. There are different measures of over-all Type-I error for a multiple hypotheses testing problem. One such measure is the family-wise error rate (FWER) which is the probability of at least one false rejection [Lehmann and Romano (2005)]. It can be generalized by considering the probability of at least k false rejections [Lehmann and Romano (2005)]. This measure is popularly known as the k-FWER. Another popular measure of overall Type-I error is the false discovery rate (FDR) [Benjamini and Hochberg (1995)]. In the existing literature, most of the FWER controlling procedures are developed for continuous data. However, these procedures might not be satisfactory when they are used for discrete data. One such extensively used method is the Bonferroni procedure [Lehmann and Romano (2005)]. The Bonferroni procedure is based on the union bound consists of choosing $\alpha_B = k\alpha/m$, where α_B is individual cutoff point for p-values, α is the cutoff point below which overall Type-I error needs to be controlled and m is the total number of hypotheses taken under consideration for testing [Wang (2022)]. It provides strong control of k-FWER without any assumption on the set of available p-

values. Several attempts have been made for improvement of the Bonferroni procedure in discrete setups. Tarone (1990) proposed a modified Bonferroni procedure for discrete data, the proposed procedure reduces the number of tested hypotheses by eliminating the hypotheses with relatively large minimal attainable p-values. Tarone's procedure is more powerful than the conventional Bonferroni procedure, but it lacks α-consistency, that is, a hypothesis which does not get rejected at a given level α may get rejected at a lower level than α. Hommel and Krummenauer (1998) further improved the Boneferroni procedure. The authors developed modified versions of the Tarone procedure, which not only control the FWER, but also satisfy the desired property of α-consistency. Zhu and Guo (2019) developed a more powerful procedure which is a modified version of the Bonferroni procedure by using known marginal distributions of true null p-values. It is shown that the modified Bonferroni procedure strongly controls the FWER under arbitrary dependence and it is more powerful than the existing Tarone-type procedures. Wang (2022) improved the modified version of the Bonferroni procedure following the same idea in the line of Zhu and Guo (2019) for controlling the k-FWER. In this paper, we propose an adaptive version of the Bonferroni method and modified Bonferroni method used for controlling k-FWER under the discrete framework. We present the adaptive versions of the multiple testing procedure by plugging-in an estimator of the proportion of true null hypotheses. We verify k-FWER control of the adaptive methods empirically. Prior to delving into this method, we briefly discuss two popular testing problems under the discrete setup, namely, the Fisher's exact test (FET) and binomial test (BT).

Here we are discussing the FET procedure for testing equality of two proportions. Let X_i follow binomial distribution with index N_i and parameter ξ_i, independently for each $i = 1,2$. To test for the equality of the success probabilities, that is, $\xi_1 = \xi_2$. Suppose, x_i is the count realized on X_i for each $i = 1,2$. The test statistic is as follows:

$$T_1 = x_1 | x. \qquad (1)$$

Here, $x = x_1 + x_2$ is the total observed count. Under the null hypotheses $\xi_1 = \xi_2$, T_1 has hypergeometric distribution as given below:

$$P(T_1 = t | N_1, N_2, x) = \frac{\binom{N_1}{t}\binom{N_2}{x-t}}{\binom{N_1+N_2}{x}} \quad \text{for } t = \max\{0, x - N_2\}, \ldots, \min\{x, N_1\}. \qquad (2)$$

Now, we briefly discuss the BT. Let Y_i be Poisson random variable with mean θ_i , independently for each $i = 1,2$. To test for the equality of the means, i.e., $\theta_1 = \theta_2$. Similar to FET, let y_i be the realized count of Y_i for each $i = 1,2$. The test statistic is as follows:

$$T_2 = y_1 | y. \qquad (3)$$

Here, $y = y_1 + y_2$ denotes the total observed count. T_2 has binomial distribution with index x and parameter $\theta_1/(\theta_1 + \theta_2)$. Thus, we refer to this test as the BT. Under null $\theta_1 = \theta_2$, T_2 has binomial distribution with index x and parameter $1/2$. In contrast to the continuous tests, in case of discrete tests, the p-values corresponding to the true null hypotheses have different distributions.

Zhu and Guo (2019) suggested use of known marginal distributions of true null p-values for strongly controlling FWER in their modified Bonferroni procedure. For motivating the proposed method, we discuss the Bonferroni method by Lehmann and Romano (2005) and the modified Bonferroni method by Wang (2022) in Section 2. In this section, we also prove that the modified Bonferroni method strongly controls the k-FWER. We present our adaptive method in the empirical Bayesian setup by using Storey's estimator of the proportion of true null hypotheses [Storey (2002), Storey et al. (2004)] in Section 3. The numerical findings from simulation studies are reported in Section 4. Two real-life applications, one related to the study of HIV and the other related to methylation study are analysed in Section 5 for demonstration purposes. We conclude the article by pointing out the limitations and the future scopes of the current work.

2. Generalization of the Bonferroni method

Here, we give a brief outline of the problem of multiple hypotheses testing. Let $H_1, H_2, \dots, H_m$ be the m null hypotheses to be tested. Let p_i be the p-value corresponding to H_i for each $i = 1,2,\dots,m$. For multiple hypotheses testing problem, one measure of overall Type-I error is the family wise error rate (FWER), which is the probability of rejecting at least one true null hypothesis. Let V be the number of false rejections. FWER $= \Pr\ (V \geq 1)$. For $k = 1,2,\dots,m$, we define

$$k\text{-FWER} = \Pr\ (V \geq k). \tag{4}$$

Here we use p as the notation for p-value, irrespective of it being a random variable or a fixed realization. Let $\mathbb{I} = \{1,2,\dots,m\}$ and $\mathbb{T}$ be the index set of true null hypotheses. Also let $\mathbb{P}_i$ be the support of p_i for all $i \in \mathbb{I}$. For more details, see Dickhaus (2014).

Assumption 1: [Super-uniformity]: The marginal distribution functions F_i of all true null p-values p_i are known and for each $i \in \mathbb{I}$, $F_i(u) = u$ if $u \in \mathbb{P}_i$ and $F_i(u) < u$ if $u \in [0,1] \setminus \mathbb{P}_i$.

Method 1: [Bonferroni method]: Let $\alpha_B = k\alpha/m$. For any $i \in \mathbb{I}$, reject H_i if and only if its corresponding p-value $p_i \leq \alpha_B$. The adjusted p-values for H_i corresponding to this method can be derived as

$$\tilde{p}_{i,B} = \min\left\{1, \frac{m\,p_i}{k}\right\} \text{ for each } i \in \mathbb{I}. \tag{5}$$

This method was originally proposed by Lehmann and Romano (2005). For $k = 1$, this method boils down to the Bonferroni method for controlling the FWER.

Result 1: [Lehmann and Romano (2005)]: Under superuniformity, Bonferroni method strongly controls the k-FWER at level α.

Method 2: [Modified Bonferroni method]: Let

$$\alpha^*_B = \max\left\{p \in \cup_{i \in \mathbb{I}} \mathbb{P}_i : \sum_{i \in \mathbb{I}} F_i(p) \leq k\alpha\right\} \tag{6}$$

if the maximum exists. Otherwise, set $\alpha^*_B = \alpha_B = k\alpha/m$. For any $i \in \mathbb{I}$, reject H_i, if and only if $p_i \leq \alpha^*_B$. The adjusted p-values for H_i corresponding to this method are defined as

$$\tilde{p}_{i,MB} = \min\left\{1, \frac{\sum_{r=1}^{m} F_r(p_i)}{k}\right\} \text{ for each } i \in \mathbb{I}. \tag{7}$$

Result 2: Under the assumption of superuniformity, the modified Bonferroni method strongly controls the k-FWER at level α.

Proof: Let V be the number of falsely rejected null hypotheses. Corresponding to the modified Bonferroni method,

$$\begin{aligned} k\text{-FWER} &= \Pr\ (V \geq k) \\ &\leq \frac{E(V)}{k} \\ &= \frac{1}{k} E\left[\sum_{i \in \mathbb{T}} I(p_i \leq \alpha^*_B)\right] \\ &= \frac{1}{k} \sum_{i \in \mathbb{T}} F_i(\alpha^*_B) \end{aligned}$$

$$\leq \frac{1}{k} \sum_{i \in \mathbb{I}} F_i(\alpha^*{}_B) \quad (8)$$

The first inequality is the well-known Markov's inequality. The last inequality follows from the fact that $\mathbb{T} \subseteq \mathbb{I}$.

If $\max\{ p \in \cup_{i \in \mathbb{I}} \mathbb{P}_i : \sum_{i \in \mathbb{I}} F_i(p) \leq k\alpha \}$ exists, then, from the definition of $\alpha^*{}_B$ in (6), it follows that

$$\sum_{i \in \mathbb{I}} F_i(\alpha^*{}_B) \leq k\alpha. \quad (9)$$

Using (9) in (8), we get the result.

When $\max\{ p \in \cup_{i \in \mathbb{I}} \mathbb{P}_i : \sum_{i \in \mathbb{I}} F_i(p) \leq k\alpha \}$ does not exist, we put $\alpha^*{}_B = k\alpha/m$ in (8) and get

$$k\text{-FWER} \leq \frac{1}{k} \sum_{i \in \mathbb{I}} F_i(\alpha^*{}_B)$$
$$\leq \frac{1}{k} m \frac{k\alpha}{m} = \alpha.$$

The inequality directly follows from the assumption of superuniformity of the p-values corresponding to the true null hypotheses.

Remark 1: The modified Bonferroni method for controlling the k-FWER is at least as powerful as the Bonferroni method for controlling the k-FWER in the sense that if any H_i is rejected by the Bonferroni method, then it is also rejected by the modified Bonferroni method. Assumption 1 holds when null hypotheses are boundary sets of the parameter spaces under the true and false null hypotheses. From Assumption 1, for any $i \in \mathbb{I}$, it is easy to check that

$$\sum_{j \in \mathbb{I}} F_j(p_i) \leq m p_i. \quad (10)$$

Using (10) in (5) and (7), we get $\tilde{p}_{i,MB} \leq \tilde{p}_{i,B}$ for each $i \in \mathbb{I}$. Since H_i is rejected by a particular method when its adjusted p-value is less than or equal to the overall k-FWER level α, the proposed method is an improvement over the existing k-FWER controlling method when the test-statistics are discrete.

3. Adaptive method

Consider the problem of simultaneously testing m null hypotheses $H_1, H_2, \ldots, H_m$, among which there are m_0 true and m_1 false null hypotheses. Here, the test-statistics are discrete. Let π_0 denote the proportion of true null hypotheses. Consider, $H = \{ H_i, i \in \mathbb{I} \}$, a set of m related but independent hypotheses such that $H_i = 1$ and $H_i = 0$ correspond to the true and false null hypotheses, respectively. Thus, H_i's follow a Bernoulli distribution with success probability $\pi_0 \in (0,1)$. Thus $\mathbb{T} = \{ i \in \mathbb{I} : H_i = 1 \}$ and $\mathbb{F} = \{ i \in \mathbb{I} : H_i = 0 \}$ denote the set of indices corresponding to the true and false null hypotheses, respectively. The number of true null hypotheses $m_0 = \sum_{i \in \mathbb{T}} H_i$ follows the binomial distribution with index m and parameter π_0. For implementing the proposed adaptive procedures, we use the aforementioned setup along with the estimator of π_0 introduced by Storey (2002), Storey et al. (2004). In particular, Storey (2002) introduced the following estimator of π_0.

$$\hat{\pi}_0(\tau) = \frac{\sum_{i \in \mathbb{I}} I(p_i > \tau)}{m(1-\tau)} \quad (11)$$

where $\tau \in (0,1)$ is chosen such that $P(p_i > \tau) = 0$ for each $i \in \mathbb{F}$.

Storey et al. (2004) introduced a slightly modified estimator of π_0 as follows:

$$\hat{\pi}_0{}^s(\tau) = \frac{1 + \sum_{i \in \mathbb{I}} I(p_i > \tau)}{m\,(1-\tau)}. \quad (12)$$

Although this estimator was originally proposed under the continuous framework, it is also valid for the discrete setup. In simulation experiments and real data analysis, we set $\tau = 0.5$. Under the discrete setup, it has high upward bias [Chen (2018), Biswas and Chattopadhyay (2024)]. Thus, practitioners often use this estimator with randomized p-values and mid p-values instead of the conventional p-values under discrete setups. Now, we briefly discuss the randomized and mid p-values used in this discrete framework. Let T be a discrete test-statistic and t_0 be the observed value of T. Define

$$p_{right} = P_{H_0}(T > t_0),$$
$$p_{left} = P_{H_0}(T < t_0),$$
$$p_{equal} = P_{H_0}(T = t_0).$$

For a right-sided test, a left-sided test, and a two-sided test, the conventional p-values are $p_{right} + p_{equal}$, $p_{left} + p_{equal}$ and $2 \times \min\{ p_{right} + p_{equal}, p_{left} + p_{equal}\}$ respectively. Let u be a random observation from Uniform$(0,1)$. For a right-sided test, a left-sided test, and a two-sided test, the randomized p-values are $p_{right} + u \times p_{equal}$, $p_{left} + u \times p_{equal}$ and $2 \times \min\{ p_{right} + u \times p_{equal}, p_{left} + u \times p_{equal}\}$ respectively. For a right-sided test, a left-sided test, and a two-sided test, the mid p-values are $p_{right} + 0.5 \times p_{equal}$, $p_{left} + 0.5 \times p_{equal}$ and $2 \times \min\{ p_{right} + 0.5 \times p_{equal}, p_{left} + 0.5 \times p_{equal}\}$ respectively. The conventional p-value is superuniform, whereas the randomized p-value and mid p-value are subuniform [Chen (2020)]. Using these three variants of p-values, we implement three adaptive procedures as discussed below.

Method 3: [Adaptive Bonferroni]**:** Let $\alpha_{AB} = k\alpha/m\,\hat{\pi}_0{}^s(0.5)$. For any $i \in \mathbb{I}$, reject H_i if and only if its corresponding p-value $p_i \le \alpha_{AB}$. The adjusted p-values for H_i corresponding to this method can be derived as

$$\tilde{p}_{i,AB} = \min\left\{1, \frac{m\,\hat{\pi}_0{}^s(0.5)\,p_i}{k}\right\} \text{ for each } i \in \mathbb{I}. \quad (13)$$

Assumption 2: The p-values corresponding to the true null hypotheses $\{p_i : i \in \mathbb{T}\}$ are independent. Moreover, $\{p_i : i \in \mathbb{T}\}$ and $\{p_i : i \in \mathbb{F}\}$ are also independent.

Let $\mathbb{P} = \{p_1, p_2, \dots, p_m\}$ and $\mathbb{P}^{(-i)} = \{p_1, \dots, p_{i-1}, p_{i+1}, \dots, p_m\}$. For notational convenience, we denote $\hat{\pi}_0{}^s(\tau)$ by $\hat{\pi}_0(\tau)$ here, in Lemma 1 and in the proof of Result 3. Note that, $\hat{\pi}_0(\tau)$ is a function of $\mathbb{P}$. We denote $\hat{\pi}_0{}^{(-i)}(\tau)$ to be the same estimator when $\mathbb{P}^{(-i)}$ is used instead of $\mathbb{P}$. Note that,

$$\hat{\pi}_0{}^{(-i)}(\tau) \le \hat{\pi}_0(\tau)\text{, a.s.}$$

Lemma 1: Under Assumption 1 and Assumption 2, for $i \in \mathbb{T}$,

$$E\left[\frac{1}{\hat{\pi}_0{}^{(-i)}(\tau)}\right] \le \frac{1}{\pi_0}.$$

Blanchard and Roquain (2009) provided a more general statement and proof of Lemma 1.

Result 3: Suppose, Assumption 1 and Assumption 2 hold. Adaptive Bonferroni method strongly controls the k-FWER at level α, when conventional p-values are used.

Proof:

Conditionally on $\mathbb{T}$,

$$\begin{aligned}
k\text{-FWER} &= \Pr\ (V \geq k) \\
&\leq \frac{E(V)}{k} \\
&= \frac{1}{k}\ E\ \left[\sum\nolimits_{i\,\in\,\mathbb{T}} I(p_i \leq \alpha_{AB})\right] \\
&= \frac{1}{k}\ E\ \left[\sum\nolimits_{i\,\in\,\mathbb{T}} I\left(p_i \leq \frac{k\alpha}{m\,\hat{\pi}_0(0.5)}\right)\right] \\
&\leq \frac{1}{k}\ E\ E\left[\sum\nolimits_{i\,\in\,\mathbb{T}} I\left(p_i \leq \frac{k\alpha}{m\,\hat{\pi}_0{}^{(-i)}(0.5)}\,\middle|\,\mathbb{P}^{(-i)}\right)\right] \\
&= \frac{1}{k}\ E\ \left[\sum\nolimits_{i\,\in\,\mathbb{T}} \left(\frac{k\alpha}{m\,\hat{\pi}_0{}^{(-i)}(0.5)}\right)\right] \\
&= \frac{\alpha}{m}\ \sum\nolimits_{i\,\in\,\mathbb{T}} E\ \left(\frac{1}{\hat{\pi}_0{}^{(-i)}(0.5)}\right) \\
&\leq \frac{\alpha m_0}{m\pi_0}
\end{aligned}$$

The fourth equality follows from Assumption 1 and Assumption 2. The last inequality follows from Lemma 1.

Unconditionally,

$$\begin{aligned}
k\text{-FWER} &\leq \frac{\alpha}{m\,\pi_0} E(m_0) \\
&= \frac{\alpha}{m\,\pi_0} (\,m\pi_0) \\
&= \alpha
\end{aligned}$$

The first equality follows from the fact that $m_0 \sim \text{Binomial}(m, \pi_0)$.

Method 4: [Adaptive modified Bonferroni]: Let

$$\alpha^*{}_{AB} = \max\ \{\,p\ \in \cup_{i\,\in\,\mathbb{I}}\, \mathbb{P}_i :\ \sum\nolimits_{i\,\in\,\mathbb{I}} F_i(p) \leq\ \frac{k\alpha}{\hat{\pi}_0{}^{s}(0.5)}\} \tag{14}$$

if the maximum exists. Otherwise, set $\alpha^*{}_{AB} = \alpha_{AB} = k\alpha/m\,\hat{\pi}_0{}^{s}(0.5)$. For any $i\ \in\ \mathbb{I}$, reject H_i, if and only if $p_i \leq\ \alpha^*{}_{AB}$. The adjusted p-values for H_i corresponding to this method can be derived as

$$\tilde{p}_{i,AMB} = \min\{\,1, \frac{\hat{\pi}_0{}^{s}(0.5)\ \sum_{r=1}^{m} F_r(p_i)}{k}\}\ \text{ for each }\ i \in\ \mathbb{I}. \tag{15}$$

There is an extensive literature on the problem of estimating π_0 under the continuous framework. See, e.g., Benjamini et al. (2006), Sarkar (2008), Sarkar et al. (2012), Cheng et al. (2015), Biswas (2022), Biswas et al. (2021), Biswas et al. (2022).

4. Simulation study

In this section, we perform extensive simulation studies to investigate the performances of the proposed adaptive procedures in terms of the k-FWER control (for k=1,2,3,5) and power, defined as:

$$\text{Power} = \frac{\text{Cardinality of } (\mathbb{R}\ \cap \mathbb{F}\,)}{m - m_0} \tag{16}$$

where $\mathbb{R}$ is the set of indices corresponding to the rejected null hypotheses.

We consider multiple Fisher's exact tests (FETs) and binomial exact tests (BTs). By using the true null distribution of the FET or BT statistic, one can calculate the p-value p_i and its support $\mathbb{P}_i$ for each $i \in \mathbb{I}$. Then the simulated k-FWER and power are calculated by taking the average over 1000(=N) iterations.

4.1 Simulation setting

We consider multiple FETs and multiple BTs to study the different aspects of an estimator of π_0, as described in Section 3. For both discrete multiple testing scenarios we set $m = 100$ and $m = 250$ and vary π_0 over the set {0.1, 0.2, …, 0.9}. For Bonferroni, modified Bonferroni and their adaptive versions, the level of significance is fixed at $\alpha = 0.1$. For a fixed value of π_0, we find $m_0 = \lfloor m\pi_0 \rfloor$, a fixed value which is less than m. To perform m FETs, we simulate the data as follows. First, we construct two different arrays of parameters, namely, ξ_1 and ξ_2. Let the i^{th} element of ξ_i be ξ_{ji}, $j = 1,2$ and $i \in \mathbb{I}$. To include the true-null cases, we set $\xi_i = \xi_{1i} = \xi_{2i}$ and generate ξ_i from Uniform(0.15,0.20), independently, for each $i = 1,2, \ldots, m_0$. To include the false-null cases, set $\xi_{1i} = 0.2$ and $\xi_{2i} = 0.5$ for each $i = m_0 + 1, m_0 + 2, \ldots, m$. X_{ji} is generated from the binomial distribution with index 20 and parameter ξ_{ji}, $j = 1,2$ and $i \in \mathbb{I}$. For each $i \in \mathbb{I}$, we test the following:

$$H_{0i}:\ \xi_{1i} = \xi_{2i} \text{ versus } H_{1i}:\ \xi_{1i} \neq \xi_{2i.} \tag{17}$$

To perform m BTs, we simulate the data in a similar manner. Two different arrays of parameters, namely, θ_1 and θ_2, are constructed. Let the i^{th} element of θ_j be $\theta_{ji}, j = 1,2$ and $i \in \mathbb{I}$. To include the true-null cases, we set $\theta_i = \theta_{1i} = \theta_{2i}$ and generate θ_i from the Pareto distribution with the location parameter 3 and the scale parameter 8, independently, for each $i = 1,2, \ldots, m_0$. To include the false-null cases, we set $\theta_{2i} = \rho_i\theta_{1i}$ where ρ_i is generated from Uniform(1.5,4.5), for each $i = m_0 + 1, m_0 + 2, \ldots, m$. Y_{ji} is generated from the Poisson distribution with mean $\theta_{ji}, j = 1,2$ and $i \in \mathbb{I}$. For each $i \in \mathbb{I}$, we test the following:

$$H_{0i}:\ \theta_{1i} = \theta_{2i} \text{ versus } H_{1i}:\ \theta_{1i} \neq \theta_{2i.} \tag{18}$$

4.2 Simulation results

We denote the Bonferroni procedure by B, its adaptive versions with conventional p-values, randomized p-values and mid p-values by ABS, ABR and ABM, respectively**.** We denote the modified Bonferroni procedure by MB, its adaptive versions with conventional p-values, randomized p-values and mid p-values by AMBS, AMBR and AMBM, respectively. Here we report the power for $m = 100$ and $m = 250$ for multiple FETs and BTs. For all the computations, we set $\alpha = 0.1$. We also simulate the k-FWER for FETs and BTs for both $m = 100$ and $m = 250$ and observe that for different values of k, the procedures considered here control the k-FWER at the desired level. Due to the conservative nature of k-FWER, under the discrete framework, all the simulated values are found to be much smaller than 0.1. Thus we refrain from reporting it in this paper.

Table 1: Simulated power of different multiple testing procedures when multiple FETs are performed for $m = 100$.

π_0	B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
$k = 1$								
0.1	0.045689	0.078078	0.111667	0.107533	0.087600	0.133700	0.177089	0.170456
0.2	0.044850	0.068413	0.090913	0.088638	0.092575	0.122713	0.155200	0.152950
0.3	0.046129	0.067886	0.080700	0.079871	0.100186	0.119429	0.147486	0.147143
0.4	0.044867	0.062367	0.070800	0.070733	0.100383	0.111617	0.138067	0.138617
0.5	0.043600	0.051560	0.067840	0.067720	0.100200	0.106300	0.132040	0.132720
0.6	0.045300	0.047375	0.066875	0.067225	0.102900	0.105600	0.131200	0.132475
0.7	0.045600	0.045800	0.063433	0.064533	0.106000	0.106533	0.127833	0.131900
0.8	0.046100	0.046100	0.057800	0.059150	0.115750	0.115750	0.133900	0.137500
0.9	0.041500	0.041500	0.045700	0.049200	0.121800	0.121800	0.133600	0.138700
$k = 2$								
0.1	0.068311	0.123022	0.159867	0.152733	0.122767	0.191400	0.241678	0.234111
0.2	0.067400	0.109675	0.133613	0.131550	0.125163	0.173938	0.215388	0.212825
0.3	0.068329	0.094514	0.125643	0.125186	0.135871	0.166543	0.202543	0.202114
0.4	0.067633	0.085250	0.114733	0.115617	0.141017	0.161800	0.189617	0.190467
0.5	0.067380	0.077480	0.100960	0.101360	0.148060	0.159080	0.178200	0.178580
0.6	0.067950	0.070850	0.091400	0.092975	0.161425	0.163700	0.175300	0.175775
0.7	0.068133	0.068367	0.083567	0.085733	0.167500	0.167667	0.170667	0.172100
0.8	0.068900	0.068900	0.082150	0.084000	0.167700	0.167700	0.170100	0.170900
0.9	0.062500	0.062500	0.068700	0.071100	0.164100	0.164100	0.165200	0.165500
$k = 3$								
0.1	0.084878	0.146367	0.201333	0.195322	0.151100	0.227778	0.291122	0.282922
0.2	0.084175	0.129213	0.167188	0.164775	0.160550	0.209588	0.259463	0.255825
0.3	0.085129	0.124686	0.150014	0.148971	0.167443	0.200386	0.243429	0.242957
0.4	0.084767	0.118267	0.133683	0.134667	0.169033	0.189717	0.230467	0.232900
0.5	0.082720	0.105520	0.123760	0.124660	0.168920	0.178700	0.219860	0.221040
0.6	0.083875	0.093225	0.122325	0.122500	0.172200	0.175700	0.216075	0.218375
0.7	0.083867	0.085433	0.115933	0.117733	0.174767	0.175200	0.209400	0.213800
0.8	0.086800	0.086850	0.112200	0.115400	0.181800	0.181850	0.209350	0.214450
0.9	0.077600	0.077600	0.092400	0.097000	0.185300	0.185300	0.204600	0.211100
$k = 5$								
0.1	0.122233	0.202778	0.258167	0.247456	0.202178	0.288689	0.357011	0.347456
0.2	0.121363	0.176975	0.219775	0.217163	0.201675	0.264225	0.323850	0.320188
0.3	0.124143	0.155443	0.204343	0.203629	0.206757	0.253057	0.301257	0.299871
0.4	0.122033	0.142433	0.186183	0.187300	0.213767	0.243533	0.282250	0.282817
0.5	0.120680	0.129640	0.164940	0.166380	0.219880	0.235640	0.267900	0.267960
0.6	0.121750	0.123325	0.152550	0.154275	0.230925	0.237250	0.264250	0.264900
0.7	0.121133	0.121133	0.140533	0.143167	0.247667	0.248233	0.263533	0.264600
0.8	0.123300	0.123300	0.137300	0.139300	0.257250	0.257250	0.261300	0.262050
0.9	0.115900	0.115900	0.120200	0.123400	0.256600	0.256600	0.258000	0.258600

Table 2: Simulated power of different multiple testing procedures when multiple FETs are performed for $m = 250$.

$k = 1$								
π_0	B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
0.1	0.025849	0.044947	0.066840	0.065556	0.055867	0.083169	0.111596	0.108120
0.2	0.026240	0.037540	0.055375	0.053670	0.057885	0.075950	0.100995	0.099725
0.3	0.026011	0.035297	0.045920	0.045560	0.058680	0.070126	0.094097	0.093474
0.4	0.025940	0.035140	0.040773	0.040833	0.060107	0.068693	0.092060	0.092173
0.5	0.026712	0.034000	0.036176	0.036512	0.064960	0.068632	0.090592	0.091888
0.6	0.025710	0.026930	0.034860	0.034840	0.066340	0.067110	0.090930	0.092120
0.7	0.025027	0.025027	0.033880	0.033880	0.072360	0.072467	0.093533	0.094467
0.8	0.027280	0.027280	0.035360	0.036020	0.089900	0.089900	0.098300	0.098680
0.9	0.027120	0.027120	0.030720	0.032440	0.098840	0.098840	0.099200	0.099200
$k = 2$								
0.1	0.045044	0.068133	0.094182	0.090551	0.076182	0.120782	0.154822	0.150347
0.2	0.045000	0.067730	0.079275	0.077705	0.083570	0.113285	0.140235	0.137830
0.3	0.045269	0.058817	0.068714	0.068766	0.084171	0.103474	0.128577	0.127686
0.4	0.045340	0.048327	0.068013	0.068020	0.094000	0.101660	0.124667	0.124593
0.5	0.045880	0.045944	0.066088	0.066576	0.099792	0.100568	0.121192	0.121992
0.6	0.044630	0.044630	0.056080	0.057830	0.099990	0.100110	0.116130	0.117740
0.7	0.044093	0.044093	0.047560	0.049200	0.099227	0.099227	0.111160	0.114067
0.8	0.045960	0.045960	0.046440	0.047100	0.100380	0.100380	0.110760	0.113820
0.9	0.044760	0.044760	0.044800	0.044800	0.102440	0.102440	0.110680	0.113440
$k = 3$								
0.1	0.052627	0.086631	0.122036	0.120400	0.099973	0.145236	0.191618	0.186516
0.2	0.052880	0.076500	0.108180	0.105805	0.100625	0.135725	0.173200	0.170885
0.3	0.053166	0.067771	0.088000	0.087297	0.101349	0.125817	0.160823	0.159709
0.4	0.052927	0.068040	0.080980	0.081067	0.105833	0.123853	0.156233	0.156933
0.5	0.053312	0.067688	0.071552	0.072424	0.112728	0.122384	0.153024	0.154768
0.6	0.052560	0.058510	0.066710	0.066950	0.118350	0.120100	0.150270	0.152590
0.7	0.051440	0.051600	0.066680	0.066680	0.122200	0.122320	0.151453	0.154613
0.8	0.053400	0.053400	0.067660	0.067800	0.136100	0.136100	0.160480	0.164180
0.9	0.052360	0.052360	0.063520	0.065320	0.159320	0.159320	0.164080	0.165920
$k = 5$								
0.1	0.067644	0.121378	0.155507	0.150449	0.121364	0.192067	0.238431	0.231987
0.2	0.068080	0.113290	0.133600	0.131515	0.124410	0.175925	0.217820	0.215165
0.3	0.067611	0.091897	0.121497	0.121314	0.135383	0.166749	0.202491	0.201434
0.4	0.068040	0.084827	0.119533	0.119553	0.144573	0.166280	0.192527	0.193573
0.5	0.068120	0.080784	0.106280	0.108720	0.149192	0.166160	0.181104	0.182584
0.6	0.066660	0.068200	0.089630	0.091920	0.165480	0.167010	0.173110	0.174020
0.7	0.066680	0.066707	0.083920	0.084613	0.167720	0.167720	0.168853	0.169680
0.8	0.067860	0.067860	0.082240	0.083040	0.170960	0.170960	0.171360	0.171740
0.9	0.067120	0.067120	0.074520	0.076320	0.167320	0.167320	0.167520	0.167800

Table 3: Simulated power of different multiple testing procedures when multiple BTs are performed for $m = 100$.

$k = 1$								
π_0	B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
0.1	0.072578	0.089533	0.108244	0.105567	0.114844	0.141000	0.166789	0.163100
0.2	0.073638	0.083538	0.100838	0.098538	0.118775	0.136100	0.161213	0.157450
0.3	0.070886	0.075529	0.091429	0.088786	0.119071	0.129071	0.154043	0.150571
0.4	0.072067	0.073150	0.087300	0.084767	0.124533	0.130450	0.155067	0.151267
0.5	0.073540	0.073600	0.082820	0.080520	0.124800	0.127980	0.151020	0.147420
0.6	0.071575	0.071575	0.077000	0.075575	0.129400	0.130650	0.153400	0.149300
0.7	0.073100	0.073100	0.075367	0.074100	0.136833	0.136900	0.154733	0.150100
0.8	0.070950	0.070950	0.072050	0.071050	0.145400	0.145400	0.157100	0.152800
0.9	0.067000	0.067000	0.067100	0.067100	0.158000	0.158000	0.164800	0.161000
$k = 2$								
0.1	0.097044	0.122578	0.149456	0.146089	0.150422	0.188256	0.214667	0.210067
0.2	0.097800	0.116550	0.139175	0.135013	0.154013	0.183300	0.207538	0.202825
0.3	0.094543	0.107157	0.126043	0.122114	0.155800	0.178329	0.199043	0.195857
0.4	0.096783	0.102300	0.121067	0.118483	0.167767	0.181633	0.200583	0.197567
0.5	0.097100	0.098260	0.114980	0.112780	0.173160	0.178040	0.193960	0.191560
0.6	0.096650	0.096750	0.111100	0.108100	0.185550	0.186300	0.196025	0.193800
0.7	0.096800	0.096800	0.105533	0.102000	0.185567	0.185567	0.191800	0.189700
0.8	0.094800	0.094800	0.098600	0.096550	0.185350	0.185350	0.190600	0.188450
0.9	0.090100	0.090100	0.091900	0.090700	0.186400	0.186400	0.192400	0.189200
$k = 3$								
0.1	0.114822	0.149700	0.178111	0.172911	0.177611	0.215267	0.250856	0.245756
0.2	0.115988	0.141575	0.164513	0.159925	0.184600	0.208163	0.242600	0.238025
0.3	0.112629	0.126757	0.151429	0.148200	0.186671	0.199943	0.233714	0.228843
0.4	0.115333	0.121700	0.149150	0.145467	0.193783	0.201867	0.233350	0.228150
0.5	0.114340	0.115660	0.139440	0.134720	0.192580	0.195480	0.225440	0.221300
0.6	0.114600	0.114650	0.131275	0.126750	0.199150	0.200425	0.227350	0.222525
0.7	0.112633	0.112667	0.123500	0.119467	0.202733	0.202867	0.226067	0.220233
0.8	0.111400	0.111400	0.117550	0.114600	0.213550	0.213550	0.224950	0.221950
0.9	0.107400	0.107400	0.109800	0.108600	0.227700	0.227700	0.231400	0.228800
$k = 5$								
0.1	0.150111	0.189056	0.221133	0.215067	0.210400	0.260089	0.299244	0.293378
0.2	0.150788	0.176025	0.206200	0.201288	0.217275	0.251825	0.288875	0.282350
0.3	0.147100	0.159029	0.192843	0.189414	0.222671	0.242529	0.276757	0.271471
0.4	0.151050	0.154583	0.189017	0.183333	0.234833	0.243350	0.273283	0.268183
0.5	0.148240	0.148680	0.174780	0.168720	0.235260	0.237120	0.264560	0.259220
0.6	0.149425	0.149450	0.164750	0.159000	0.239175	0.239725	0.261975	0.257050
0.7	0.148000	0.148000	0.155533	0.151800	0.237967	0.238000	0.256800	0.251300
0.8	0.146000	0.146000	0.148450	0.147000	0.240400	0.240400	0.254050	0.249600
0.9	0.142800	0.142800	0.144000	0.143300	0.249200	0.249200	0.258200	0.254700

Table 4: Simulated power of different multiple testing procedures when multiple BTs are performed for $m = 250$.

π_0	B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
$k = 1$								
0.1	0.038596	0.055204	0.070227	0.068253	0.07924	0.097138	0.117133	0.115338
0.2	0.037875	0.052160	0.061695	0.059145	0.083035	0.093090	0.111920	0.109445
0.3	0.037811	0.049229	0.056686	0.055206	0.084920	0.092360	0.110526	0.107749
0.4	0.038033	0.043460	0.053947	0.053227	0.089667	0.092920	0.110113	0.106820
0.5	0.037600	0.040600	0.052120	0.051424	0.092352	0.092824	0.109832	0.106776
0.6	0.037690	0.038360	0.049510	0.047370	0.090760	0.090880	0.108560	0.105490
0.7	0.038213	0.038227	0.046813	0.044160	0.100227	0.100227	0.113413	0.110960
0.8	0.036120	0.036120	0.040960	0.039380	0.111000	0.111000	0.116440	0.114380
0.9	0.040280	0.040280	0.043720	0.042400	0.123800	0.123800	0.124680	0.124240
$k = 2$								
0.1	0.058182	0.079653	0.097836	0.094956	0.102520	0.127804	0.153800	0.150689
0.2	0.057010	0.072105	0.087550	0.085005	0.107705	0.122405	0.145110	0.141295
0.3	0.057069	0.069623	0.081697	0.079211	0.113189	0.122103	0.142223	0.137817
0.4	0.057687	0.064740	0.077287	0.075033	0.115927	0.121820	0.139420	0.134633
0.5	0.057024	0.058528	0.072176	0.070880	0.121120	0.121928	0.137336	0.132128
0.6	0.056210	0.056350	0.069680	0.068140	0.119250	0.119300	0.133600	0.128620
0.7	0.058360	0.058360	0.068827	0.065840	0.122787	0.122787	0.137707	0.132720
0.8	0.056220	0.056220	0.062100	0.059240	0.127100	0.127100	0.141220	0.136360
0.9	0.059160	0.059160	0.061680	0.060120	0.146920	0.146920	0.154160	0.150000
$k = 3$								
0.1	0.072191	0.097333	0.117271	0.115484	0.122529	0.153493	0.182760	0.178129
0.2	0.071075	0.08804	0.108275	0.105020	0.121795	0.146725	0.172750	0.168505
0.3	0.070674	0.082949	0.100034	0.097166	0.124297	0.144914	0.169349	0.164971
0.4	0.071713	0.078513	0.094460	0.092153	0.127647	0.142353	0.167547	0.162740
0.5	0.070696	0.072632	0.088864	0.086128	0.135520	0.141544	0.165784	0.161168
0.6	0.070180	0.070240	0.082930	0.081070	0.141780	0.142160	0.165220	0.159470
0.7	0.072627	0.072627	0.082053	0.079467	0.151160	0.151160	0.171920	0.166867
0.8	0.070120	0.070120	0.076480	0.073440	0.164360	0.164360	0.179400	0.174300
0.9	0.072920	0.072920	0.075400	0.073560	0.186760	0.186760	0.187840	0.187280
$k = 5$								
0.1	0.096698	0.122040	0.150533	0.148311	0.150596	0.189751	0.217173	0.211524
0.2	0.094690	0.113370	0.138445	0.133260	0.149775	0.182905	0.203545	0.199170
0.3	0.095006	0.109851	0.126646	0.122251	0.157851	0.180789	0.198703	0.195560
0.4	0.095707	0.101253	0.118820	0.116007	0.165033	0.180607	0.196040	0.193220
0.5	0.095264	0.095768	0.114328	0.113056	0.174560	0.180712	0.193376	0.191280
0.6	0.092700	0.092720	0.108620	0.105650	0.181980	0.182100	0.189190	0.187050
0.7	0.095400	0.095400	0.105507	0.100973	0.186640	0.186640	0.191880	0.190000
0.8	0.093840	0.093840	0.098520	0.095480	0.186500	0.186500	0.192000	0.189660
0.9	0.098360	0.098360	0.099240	0.098440	0.194240	0.194240	0.197680	0.195320

From Table 1, Table 2, Table 3 and Table 4, we observe that, for all values of π_0, AMBR and AMBM are more powerful than all the other procedures considered here for any fixed value of k. Also, as k increases, the power increases gradually for both FETs and BTs for all the methods. From Table 1 and Table 2, MB, AMBS, AMBR, AMBM appear to be more powerful than B, ABS, ABR, ABM respectively. From Table 3 and Table 4, we note that MB is more powerful than B, ABS, ABR and ABM and similarly the other adaptive modified procedures AMBS, AMBR, AMBM are more powerful than B, ABS, ABR and ABM.

5. Data analysis

We now apply the k-FWER controlling procedures discussed in section 4 to two important real life datasets. We set $\alpha = 0.1$.

The first study is related to HIV vaccine efficacy. From the aspect of multiple testing, the objective of analysing this "HIV dataset" [Gilbert, (2005)] is to identify differentially polymorphic positions among the total 118 positions. In this dataset, two sequence sets were obtained from 73 individuals infected with sub type C HIV and another 73 individuals with subtype B HIV, respectively. The null hypothesis corresponding to each position is "the probability of a nonconsensus amino acid does not differ between the two amino acid sequence sets". Here, for each $i \in \mathbb{I}$, X_{1i} and X_{2i} are the number of nonconsensus amino acids in i^{th} patient for subtype C and subtype B, respectively. Similarly, for each $i \in \mathbb{I}$, ξ_{1i} and ξ_{2i} are probabilities of a nonconsensus amino acids at i^{th} position for subtype C and subtype B patients, respectively. To identify the positions where the probability of a nonconsensus amino acid differs between the two amino acid sequence sets, we test $H_{0i} : \xi_{1i} = \xi_{2i}$ versus $H_{1i} : \xi_{1i} \neq \xi_{2i}$ for $i = 1,2, \dots, 118$ and apply multiple testing procedures. Out of the 118 two-sided p-values that we find for the FETs, 50 p-values are noninformative in a sense that the marginal totals, $X_{1i} + X_{2i}$ are identically equal to 1. Thus, we remove those rows from the data set and work with the remaining $m = 68$ hypotheses. The following table shows the number of differentially polymorphic positions identified by 8 different procedures taken under study for this dataset.

Table 5: Number of differentially polymorphic positions identified for HIV dataset.

$k = 1$							
B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
10	10	11	11	14	15	15	15
$k = 2$							
11	11	12	12	15	16	16	16
$k = 3$							
11	12	14	14	16	16	16	16
$k = 5$							
15	15	15	15	16	18	20	20

From the aspect of multiple testing, the main objective of studying the "Methylation dataset" [Lister et al., (2008)] is to identify differentially methylated cytosines between two unreplicated lines of *Arabidopsis thaliana*, wild-type (Col-0), and mutant defective (Met1-3). The null hypothesis corresponding to each cytosine is "the cytosine is not differentially methylated between the two lines." There are around 22,000 cytosines, each of which is under two conditions. For each cytosine under each condition, there is only one replicate. Here, each $i \in \mathbb{I}$, Y_{1i} and Y_{2i} are the counts for each cytosine in i^{th} wild-type and mutant defective, respectively. Similarly, for each $i \in \mathbb{I}$, θ_{1i} and θ_{2i} correspond to the i^{th} unknown means of the counts. To identify the differentially methylated cytosines, we test $H_{0i} : \theta_{1i} = \theta_{2i}$ versus $H_{1i} : \theta_{1i} \neq \theta_{2i}$ for $i = 1,2, \dots ,22000$ and apply multiple testing procedures. The discrete count for each replicate is modelled by a Poisson distribution and BET is applied. We only keep cytosines whose total counts for both lines are greater than 5 and whose count for each line does not exceed 25 to filter out the unreliable genes and to better utilize for multiple testing, jumps in the p-value distributions. Finally, we perform 3525 BTs. The following table shows the number of differentially methylated cytosines identified by 8 different procedures taken under study for this dataset.

Table 6: Number of differentially methylated cytosines identified for Methylation dataset.

			$k = 1$				
B	ABS	ABR	ABM	MB	AMBS	AMBR	AMBM
37	40	54	47	73	74	76	76
			$k = 2$				
54	60	69	69	80	86	96	96
			$k = 3$				
63	73	76	74	86	111	118	118
			$k = 5$				
74	80	86	86	118	120	138	138

6. Conclusion

The main objective of the work is to control the k-FWER by adaptive versions of the original Bonferroni and the modified Bonferroni procedures at a prefixed level for any positive integer k [Zhu and Guo (2019), Wang (2022)]. To control the k-FWER by adaptive methods, we plug-in an threshold-based estimator of the proportion of true null hypotheses. In the estimator, we use the set of conventional p-values as well as randomized and mid p-values. Thus, in total, we consider eight k-FWER controlling procedures. Using extensive simulation studies, we find that the adaptive modified Bonferroni procedures with randomized and mid p-values are the most powerful and also see that the k-FWER of these adaptive procedures are below the nominal level. Thus the practitioners may use these procedures to bring out more interesting features in large-scale inferential problems without losing control over the k-FWER for any appropriate choice of k. However, the theoretical proof of k-FWER control by the adaptive procedures remains a challenging problem and further research in this direction is warranted. Another extension of this work pertains to the study of the properties of the adaptive procedures when the estimates of the proportion of true null hypotheses originally proposed under the discrete framework [Chen et al. (2018), Biswas and Chattopadhyay (2024)] are used.

Acknowledgement

The authors thank one of the guest editors and reviewer for their helpful suggestions and comments on an earlier version of the manuscript.

References

[1] Benjamini, Y. and Hochberg, Y. (1995). “Controlling the false discovery rate: A practical and powerful approach to multiple testing,” Journal of the Royal Statistical Society Series B (Methodological), 57, 289–300.

[2] Benjamini, Y., Krieger, A. M., and Yekutieli, D. (2006). “Adaptive linear step-up procedures that control the false discovery rate,” Biometrika, 93, 491–507.

[3] Biswas, A., Chattopadhyay, G., and Chatterjee, A. (2021). “Bias-corrected estimators for proportion of true null hypotheses: application of adaptive FDR controlling in segmented failure data,” Journal of Applied Statistics, 49, 3591 3613.

[4] Biswas, A., Chakraborty, S., and Baruah, V. J. (2022). “Estimation of the propor tion of true null hypotheses under sparse dependence: Adaptive FDR controlling in microarray data,” Statistical Methods in Medical Research, 31, 917–927.

[5] Biswas, A. (2022a). "Estimating the proportion of true null hypotheses with application in microarray data," Communications in Statistics- Simulation and Computation, 51, 6294–6308.

— (2022b). "Model free bias reduction of Storey's estimator for the proportion of true null hypotheses," Calcutta Statistical Association Bulletin, 27–41, 74.

[6] Biswas, A., and Chattopadhyay, G. (2024). "Estimating the proportion of true null hypotheses and adaptive false discovery rate control in discrete paradigm," Biometrical Journal, 66, 2200204.

[7] Blanchard, G. and Roquain, E. (2009). "Adaptive false discovery rate control under independence and dependence," Journal of Machine Learning Research, 10, 2837–2871.

[8] Chen, X. (2020), "False discovery rate control for multiple testing based on discrete p-values," Biometrical Journal, 2020; 1–20.

[9] Chen, X., Doerge, R. W., and Heyse, J. F. (2018). "Multiple testing with discrete data: proportion of true null hypotheses and two adaptive FDR procedures," Biometrical Journal, 60, 761–779.

[10] Cheng, Y., Gao, D., and Tong, T. (2015). "Bias and variance reduction in estimating the proportion of true-null hypotheses," Biostatistics, 16, 189–204.

[11] Dickhaus, T. (2014), Simultaneous statistical inference with applications in the life sciences, Springer.

[12] Gilbert, Peter B. (2005). "A modified false discovery rate multiple comparisons procedure for discrete data, applied to human immunodeficiency virus genetics," Appl. Statist. 54, Part 1,pp. 143–158.

[13] Hommel, G. and Krummenauer, F. (1998). "Improvements and modifications of Tarone's multiple test procedure for discrete data," Biometrics Vol. 54, No. 2, pp. 673-681.

[14] Lehmann, E. L., Romano, J. P., and Casella, G. (2005). Testing statistical hypotheses (Vol. 3), Springer.

[15] Lister, R., O'Malley, R., Tonti-Filippini, J., Greogory, B. D., Berry, C. C., Miller, A. H., and Ecker, J. R. (2008). "Highly integrated single-base resolution maps of the epigenome in arabidopsis," Cell, 133, 523–536.

[16] Sarkar, S. K. (2008), "On methods controlling the false discovery rate," Sankhya: The Indian Journal of Statistics, Series A, 70, 135–168.

[17] Sarkar, S. K., Guo, W., and Finner, H. (2012). "On adaptive procedures controlling the family wise error rate," Journal of Statistical Planning and Inference, 142, 65–78.

[18] Storey, J. D. (2002). "A direct approach to false discovery rates," Journal of the Royal Statistical Society Series B (Methodological), 64, 479–498.

[19] Storey, J. D., Taylor, J. E., and Siegmund, D. (2004). "Strong control, conservative point estimation and simultaneous conservative consistency of false discovery rates: A unified approach," Journal of the Royal Statistical Society Series B (Methodological), 66, 187–205.

[20] Tarone, R.E. (1990). "A Modified Bonferroni Method for Discrete Data," Biometrics Vol. 46, No. 2, pp. 515-522.

[21] Wang, Li. (2022). "New testing procedures with k-FWER control for discrete data," Statistics and Probability Letters, 180, 109236.

[22] Zhu, Yalin. and Guo, Wenge. (2019). "Family-Wise Error Rate Controlling Procedures for Discrete Data," Statistics in Biopharmaceutical Research, Vol. 00, No. 0, 1–12.