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Supplementary material to: A non-randomized procedure for discrete multiple testing based on randomized tests

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Appendix A: Proof of Theorem 3.1

Without loss of generality, assume that among the m tests, the null hypotheses from the first k tests are true and the alternative hypotheses from the other tests are true, i.e.

$$\Delta_i = 0, i = 1, ..., k, \qquad \text{and} \qquad \Delta_i = 1, i = k+1, ..., m.$$

Then for $i = 1, ..., k$, suppose that the p-value P_i from the ith test follows the discrete null distribution with cdf H_{0i} and support $\mathcal{P}_i$. Then $H_{0i}(p_i) = p_i$, for any $p_i \in \mathcal{P}_i$ (Westfall and Wolfinger, 1997). And for $i = k+1, ..., m$, suppose that P_i has the alternative cdf H_{1i} and support $\mathcal{P}_i$.

For the ith test, let $b_{i\lambda} = \min\{p : p \geqslant \lambda, p \in \mathcal{P}_i\}$ and $a_{i\lambda} = \max\{p : p < \lambda, p \in \mathcal{P}_i \cup \{0\}\}$,

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i.e. $a_{i\lambda} < \lambda \leqslant b_{i\lambda}$ are two consecutive values in $\mathcal{P}_i$ around λ. Then, based on the definition 1, for $i = 1, ..., m$, the conditional MCF for the ith test, r_i, follows the discrete distribution with density

$$g(r_i) = \begin{cases} Pr(p_i \leqslant a_{i\lambda}) = H_{\Delta_i i}(a_{i\lambda}), & \text{if } r_i = 1, \\ Pr(p_i = b_{i\lambda}) = H_{\Delta_i i}(b_{i\lambda}) - H_{\Delta_i i}(a_{i\lambda}), & \text{if } r_i = w_i(\lambda), \\ Pr(p_i > b_{i\lambda}) = 1 - H_{\Delta_i i}(b_{i\lambda}), & \text{if } r_i = 0, \end{cases}$$

where we let $w_i(\lambda) = \frac{\lambda - a_{i\lambda}}{b_{i\lambda} - a_{i\lambda}}$.

So marginally the MCF follows the average distribution G^m with p.m.f

$$g^m(r) = \begin{cases} \frac{1}{m}\sum_{i=1}^m H_{\Delta_i i}(a_{i\lambda}), & \text{if } r = 1, \\ \frac{1}{m}[H_{\Delta_i i}(b_{i\lambda}) - H_{\Delta_i i}(a_{i\lambda})], & \text{if } r = w_i(\lambda), \qquad i = 1, ..., m, \\ 1 - \frac{1}{m}\sum_{i=1}^m H_{\Delta_i i}(b_{i\lambda}), & \text{if } r = 0. \end{cases}$$

When a MCF r comes from a true null test, it follows which we denote by G_0^m with p.m.f

$$g_0^m(r) = \begin{cases} \frac{1}{k}\sum_{i=1}^k H_{\Delta_i i}(a_{i\lambda}) = \frac{1}{k}\sum_{i=1}^k a_{i\lambda}, & \text{if } r = 1, \\ \frac{1}{k}[H_{\Delta_i i}(b_{i\lambda}) - H_{\Delta_i i}(a_{i\lambda})] = \frac{1}{k}[b_{i\lambda} - a_{i\lambda}], & \text{if } r = w_i(\lambda), \qquad i = 1, ..., k, \\ 1 - \frac{1}{k}\sum_{i=1}^k H_{\Delta_i i}(b_{i\lambda}) = 1 - \frac{1}{k}\sum_{i=1}^k b_{i\lambda}, & \text{if } r = 0. \end{cases}$$

Similarly, when r comes from a true non-null test, it follows G_1^m with p.m.f

$$g_1^m(r) = \begin{cases} \frac{1}{m-k}\sum_{i=k+1}^m H_{1i}(a_{i\lambda}), & \text{if } r = 1, \\ \frac{1}{m-k}[H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})], & \text{if } r = w_i(\lambda), \qquad i = k+1, ..., m, \\ 1 - \frac{1}{m-k}\sum_{i=k+1}^m H_{1i}(b_{i\lambda}), & \text{if } r = 0. \end{cases}$$

In our method, among the total m tests, we reject the tests with the largest $n_m = \lfloor m(\pi_0\lambda + \pi_1 F_1(\lambda))\rfloor$ MCFs r_i. Thus if denote the $(1 - n_m/m)$-th quantile of the empirical distribution of $(r_1, ..., r_m)$ by $\tilde{q}_{n(m)/m}(r_1, ..., r_m)$, it is equivalent to rejecting the ith test if $r_i > \tilde{q}_{n_m/m}(r_1, ..., r_m)$. Note that

$$\frac{n_m}{m} = \frac{\lfloor m(\pi_0\lambda + \pi_1 F_1(\lambda))\rfloor}{m} \to \pi_0\lambda + \pi_1 F_1(\lambda), \qquad m \to \infty.$$

So if we let $u = \pi_0\lambda + \pi_1 F_1(\lambda)$ and let q_u^m denote the $(1-u)$-th quantile of G^m, by the Glivenko-Cantelli theorem in Billingsley (2013), we have

$$\tilde{q}_{n_m/m}(r_1, ..., r_m) - q_u^m \to 0, \qquad as \qquad m \to \infty.$$

Recall that pFDR(m, λ) is the pFDR corresponding to our method, then based on Theorem 1 in (Storey, 2003), we have

$$\begin{aligned} &\text{pFDR}(m,\lambda) - \frac{\pi_0 \text{Pr}(r > q_u^m | r \sim G_0^m)}{u} \\ = &\frac{\pi_0 \text{Pr}(r > \tilde{q}_{n/m}(r_1, ..., r_m) | r \sim G_0^m, r_i \sim G^m)}{n_m/m} - \frac{\pi_0 \text{Pr}(r > q_u^m | r \sim G_0^m)}{u} \to 0, \qquad \text{as} \;\; m \to \infty. \quad (1)\end{aligned}$$

Next we consider $\Pr(r > q_u^m | r \sim G_0^m)$. Without loss of generality, we first assume that

$$w_1(\lambda) \geqslant ... \geqslant w_t(\lambda) > q_u^m \geqslant w_{t+1}(\lambda) \geqslant ... \geqslant w_k(\lambda),$$

$$w_{k+1}(\lambda) \geqslant ... \geqslant w_s(\lambda) > q_u^m \geqslant w_{s+1}(\lambda) \geqslant ... \geqslant w_m(\lambda).$$

Thus,

$$\text{Pr}(r > q_u^m | r \sim G_0^m) = \frac{1}{k}[\sum_{i=1}^{k} a_{i\lambda} + \sum_{i=1}^{t}(b_{i\lambda} - a_{i\lambda})]. \qquad (2)$$

On the other hand,

$$\begin{aligned} \pi_0\lambda + \pi_1 F_1(\lambda) = \quad & u = Pr(r > q_u^m | r \sim G^m) \\ &= \frac{1}{m}\Big[\sum_{i=1}^{k} a_{i\lambda} + \sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) \\ &\quad + \sum_{i=1}^{t}(b_{i\lambda} - a_{i\lambda}) + \sum_{i=k+1}^{s}(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda}))\Big]. \qquad (3)\end{aligned}$$

Also note that MCF represents the probability that the randomized p-value is less than λ, and F_1 is the cdf of the limit alternative distribution of the randomized p-value when $m \to \infty$, so

$$\frac{1}{m-k}[\sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) + \sum_{i=k+1}^{m} w_i(\lambda)(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda}))] = E(r | r \sim G_1^m) \to F_1(\lambda), \qquad \text{as} \;\; m \to \infty.$$

Note that $\frac{k}{m} \to \pi_0$ and $\frac{m-k}{m} \to \pi_1$ as $m \to \infty$, then we have

$$
\begin{aligned}
& \frac{k}{m}\lambda + \frac{1}{m}\sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) + \frac{1}{m}\sum_{i=k+1}^{m} w_i(\lambda)[H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})] \\
\to & \frac{k}{m}\lambda + \frac{m-k}{m}F_1(\lambda) \\
\to & \pi_0\lambda + \pi_1 F_1(\lambda), \qquad \text{as} \qquad m \to \infty.
\end{aligned}
$$

So combining (3),

$$
\begin{aligned}
& \lim_{m\to\infty} \frac{\sum_{i=1}^{k} a_{i\lambda} + \sum_{i=1}^{t}(b_{i\lambda} - a_{i\lambda})}{k} \\
= & \lim_{m\to\infty} \{\frac{m}{k}(\pi_0\lambda + \pi_1 F_1(\lambda)) - \frac{1}{k}[\sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) + \sum_{i=k+1}^{s} H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})]\} \\
= & \lim_{m\to\infty} \frac{m}{k}\{\frac{k}{m}\lambda + \frac{1}{m}\sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) + \frac{1}{m}\sum_{i=k+1}^{m} w_i(\lambda)[H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})]\} \\
& - \lim_{m\to\infty} \frac{1}{k}[\sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) + \sum_{i=k+1}^{s} H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})]\} \\
= & \lambda + \lim_{m\to\infty}\{\frac{1}{k}\sum_{i=s+1}^{m} w_i(\lambda)(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})) - \frac{1}{k}\sum_{i=k+1}^{s}(1 - w_i(\lambda))(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda}))\} \\
\leqslant & \lambda + \lim_{m\to\infty}\frac{1}{k}\sum_{i=s+1}^{m} w_i(\lambda)(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})) \\
\leqslant & \lambda + \lim_{m\to\infty}\frac{m-s}{k} q_u^m \cdot c \\
\leqslant & \lambda + \lim_{m\to\infty}\frac{m-k}{k} q_u^m \cdot c \\
\leqslant & \lambda + \frac{\pi_1}{\pi_0} q_u c, \qquad (4)
\end{aligned}
$$

where $q_u = \lim_{m\to\infty} q_u^m$. The second inequality is due to that $q_u^m \geqslant w_i(\lambda)$ for $i = s+1, ..., m$ and $H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda}) \leqslant c$, as H_{1i} satisfy Condition 3.1.

On the other hand, for $i = 1, 2, ..., t$, $\frac{\lambda - a_{i\lambda}}{b_{i\lambda} - a_{i\lambda}} = w_i(\lambda) \geqslant q_u^m$. So

$$
b_{i\lambda} \leqslant a_{i\lambda} + \frac{\lambda - a_{i\lambda}}{q_u^m} \leqslant \frac{\lambda}{q_u^m}, \qquad i = 1, 2, ..., t
$$

So if we let $\rho = \lim_{m\to\infty} \Pr(r > q_u^m | r \sim G_0^m) = \lim_{m\to\infty} \frac{\sum_{i=1}^k a_{i\lambda} + \sum_{i=1}^t (b_{i\lambda} - a_{i\lambda})}{k}$, then

$$\begin{aligned}
\rho &= \lim_{m\to\infty} \frac{\sum_{i=k+1}^t a_{i\lambda} + \sum_{i=1}^t b_{i\lambda}}{k} \\
&\leqslant \lim_{m\to\infty} \frac{(t-k)\lambda + t\cdot\lambda/q_u^m}{k} \\
&\leqslant \lim_{m\to\infty} \frac{k\cdot\lambda/q_u^m}{k} = \frac{\lambda}{q_u}. \qquad (5)
\end{aligned}$$

From (4) and (5), we get

$$\rho \leqslant \lambda + \frac{\pi_1}{\pi_0} q_u c \leqslant \lambda + \frac{c\pi_1}{\pi_0}\frac{\lambda}{\rho}. \qquad (6)$$

So,

$$\rho \leqslant \frac{\lambda + \sqrt{\lambda^2 + \frac{4c\pi_1}{\pi_0}\lambda}}{2}.$$

Combining with (1) and (2), we proved

$$\limsup_{m\to\infty} \mathrm{pFDR}(m,\lambda) \leqslant \frac{\pi_0 \rho}{u} \leqslant \frac{\pi_0 \frac{\lambda + \sqrt{\lambda^2 + \frac{4c\pi_1}{\pi_0}\lambda}}{2}}{\pi_0\lambda + \pi_1 F_1(\lambda)}.$$

Appendix B: Proof of Theorem 3.2

All the notations we used are the same as in the proof of Theorem 3.1.

Similarly to the proof of Theorem 3.1 and from

$$\mathrm{pFNR} = \Pr(\Delta = 1 | T \notin \Gamma) = \frac{\Pr(\Delta = 1)\Pr(T \notin \Gamma | \Delta = 1)}{\Pr(T \notin \Gamma)},$$

we have

$$\mathrm{pFNR}(m,\lambda) - \frac{\pi_1 \Pr(r < q_u^m | r \sim G_1^m)}{1 - (\pi_0\lambda + \pi_1 F_1(\lambda))} \to 0 \qquad \text{as} \quad m \to \infty. \qquad (6)$$

And

$$\begin{aligned}
\Pr(r < q_u^m | r \sim G_1^m) &= \sum_{i=s+1}^m \frac{1}{m-k}[H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda})] + 1 - \frac{1}{m-k}\sum_{i=k+1}^m H_{1i}(b_{i\lambda}) \\
&= 1 - \frac{1}{m-k}[\sum_{i=s+1}^m H_{1i}(a_{i\lambda}) + \sum_{i=k+1}^s H_{1i}(b_{i\lambda})].
\end{aligned}$$

Let $\gamma = \sum_{i=s+1}^{m} H_{1i}(a_{i\lambda}) + \sum_{i=k+1}^{s} H_{1i}(b_{i\lambda})$, then based on equation (3) from the proof of theorem 3.1, we have

$$\begin{aligned}\pi_0\lambda + \pi_1 F_1(\lambda) &= \frac{1}{m}[\sum_{i=1}^{k} a_{i\lambda} + \sum_{i=k+1}^{m} H_{1i}(a_{i\lambda}) \\ &\quad + \sum_{i=1}^{t}(b_{i\lambda} - a_{i\lambda}) + \sum_{i=k+1}^{s}(H_{1i}(b_{i\lambda}) - H_{1i}(a_{i\lambda}))] \\ &= \frac{1}{m}(\sum_{i=t+1}^{k} a_{i\lambda} + \sum_{i=1}^{t} b_{i\lambda} + \gamma).\end{aligned}$$

So

$$\begin{aligned}\Pr(r < q_u^m | r \sim G_1^m) &= 1 - \frac{1}{m-k}\gamma \\ &= 1 - \frac{1}{m-k}[m(\pi_0\lambda + \pi_1 F_1(\lambda)) - (\sum_{i=t+1}^{k} a_{i\lambda} + \sum_{i=1}^{t} b_{i\lambda})] \\ &= 1 - \frac{m}{m-k}[\pi_0\lambda + \pi_1 F_1(\lambda)] + \frac{k}{m-k}\frac{\sum_{i=t+1}^{k} a_{i\lambda} + \sum_{i=1}^{t} b_{i\lambda}}{k}.\end{aligned}$$

Note that $\frac{k}{m} \to \pi_0$ and $\frac{m-k}{m} \to \pi_1$ as $m \to \infty$, then we have

$$\begin{aligned}\limsup_{m\to\infty} \Pr(r < q_u^m | r \sim G_1^m) &= 1 - \frac{1}{\pi_1}[\pi_0\lambda + \pi_1 F_1(\lambda)] + \frac{\pi_0}{\pi_1}\rho \\ &\leqslant 1 - \frac{1}{\pi_1}[\pi_0\lambda + \pi_1 F_1(\lambda)] + \frac{\pi_0}{\pi_1}\frac{\lambda + \sqrt{\lambda^2 + \frac{4c\pi_1}{\pi_0}\lambda}}{2}.\end{aligned}$$

where $\rho = \lim_{m\to\infty} \frac{\sum_{i=1}^{k} a_{i\lambda} + \sum_{i=1}^{t}(b_{i\lambda} - a_{i\lambda})}{k}$, and the inequality is due to (6) from the proof of Theorem 3.1. Combining with (1) from the proof of Theorem 3.1, we get

$$\begin{aligned}\limsup_{m\to\infty} \mathrm{pFNR}(m, \lambda) &\leqslant \frac{\pi_1\{1 - \frac{1}{\pi_1}[\pi_0\lambda + \pi_1 F_1(\lambda)] + \frac{\pi_0}{\pi_1}\frac{\lambda + \sqrt{\lambda^2 + \frac{4c\pi_1}{\pi_0}\lambda}}{2}\}}{1 - [\pi_0\lambda + \pi_1 F_1(\lambda)]} \\ &= \frac{\pi_1(1 - F_1(\lambda)) + \pi_0\frac{\sqrt{\lambda^2 + \frac{4c\pi_1}{\pi_0}\lambda} - \lambda}{2}}{1 - [\pi_0\lambda + \pi_1 F_1(\lambda)]}.\end{aligned}$$

Appendix C: Proof of Theorem 3.3

Assume that, for the ith test, the discrete p-value follows the two-component model

$$p_i|\Delta_i \sim (1-\Delta_i)G_{0i} + \Delta_i G_{1i},$$

where $\Delta_i \sim Bernoulli(\pi_1)$, and G_{0i}, G_{1i} are the null and alternative distribution.

Denote the corresponding alternative distribution for randomized p-value by F_{1i}, then

$$\tilde{p}_i|\Delta_i \sim (1-\Delta_i)U[0,1] + \Delta_i F_{1i}.$$

So marginally,

$$P \sim \pi_0 G_0 + \pi_1 G_1,$$

$$\tilde{P} \sim \pi_0 U[0,1] + \pi_1 F_1,$$

where $G_0 = \frac{1}{m}\sum_{i=1}^m G_{0i}$, $G_1 = \frac{1}{m}\sum_{i=1}^m G_{1i}$ and $F_1 = \frac{1}{m}\sum_{i=1}^m F_{1i}$.

The q-value method defines q-value for the ith test as

$$q(p_i) = \inf\{\frac{\pi_0\lambda}{\pi_0\lambda + \pi_1 G_1(\lambda)} : \lambda \geqslant p_i\},$$

and for a nominal FDR level α, we identify the ith test as significant if $q(p_i) \leqslant \alpha$.

Therefore this rejection rule is equivalent to identifying the ith test as significant if $p_i \leqslant \lambda^*$, where

$$\lambda^* = \sup\{\lambda : \frac{\pi_0\lambda}{\pi_0\lambda + \pi_1 G_1(\lambda)} \leqslant \alpha\}.$$

Next we consider the MCF-based method. In step 2, for the same nominal FDR level α, we define

$$\tilde{\lambda}^* = \sup\{\lambda : \frac{\pi_0\lambda}{\pi_0\lambda + \pi_1 F_1(\lambda)} \leqslant \alpha\}.$$

and then calculate MCF values for each test corresponding to $\tilde{\lambda}^*$.

For the single ith test, Lehmann and Romano (2006) showed that F_{1i} is stochastically larger than G_{1i}. So its average distribution F_1 is stochastically larger than G_1. Then $\frac{\pi_0\lambda^*}{\pi_0\lambda^* + \pi_1 F_1(\lambda^*)} \leqslant \frac{\pi_0\lambda^*}{\pi_0\lambda^* + \pi_1 G_1(\lambda^*)} \leqslant \alpha$. Therefore $\lambda^* \leqslant \tilde{\lambda}^*$.

Suppose the ith test is identified as significant by the q-value method, i.e. $p_i \leqslant \lambda^*$. Then

$$p_i^- < \tilde{p}_i < p_i \leqslant \lambda^* \leqslant \tilde{\lambda}^*.$$

So by the definition of MCF, the MCF of the ith test corresponding to $\tilde{\lambda}^*$ is always 1. So the ith test will also be rejected by the MCF-based method.

Lemma 1

Lemma 1 If F_1 is strictly concave, then $\frac{\pi_0\lambda}{\pi_0\lambda+\pi_1 F_1(\lambda)}$ is non-decreasing in terms of λ.

Proof:

Showing that $\frac{\pi_0\lambda}{\pi_0\lambda+\pi_1 F_1(\lambda)}$ is non-decreasing in λ is equivalent to showing that $\frac{\partial}{\partial\lambda}(\frac{\pi_0\lambda}{\pi_0\lambda+\pi_1 F_1(\lambda)}) > 0 \iff F_1(\lambda) > \lambda F_1'(\lambda)$. So it suffices to show $F_1(\lambda) > \lambda F_1'(\lambda)$, i.e. $\int_0^\lambda f_1(t)dt > \lambda f_1(\lambda)$, where f_1 is the density of F_1. And it suffices to show f_1 is strictly decreasing. And this is a direct result given that F_1 is strictly concave.

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