A Appendix

A.1 Mathematical proofs

First we introduce the basic setup and notation.

**Model A.1.** Let \( (\Omega, \mathcal{F}, \{\mathbb{P}_\vartheta : \vartheta \in \Theta\}) \) be a statistical experiment and let \( \mathcal{H} = \{H_1, \ldots, H_m\} \) denote a set of null hypotheses of interest with \( \emptyset \neq H_i \subset \Theta \) for all \( i \in \{1, \ldots, m\} \). Let \( p_i, i \in \{1, \ldots, m\} \), denote the marginal p-value for testing \( H_i \) versus \( K_i : \Theta \setminus H_i \). A (non-randomized) multiple test procedure \( \varphi_{(m)} = (\varphi_1, \ldots, \varphi_m)^\top \) for testing \( H_m \) is a vector of measurable mappings (individual tests) from the sample space into \( \{0, 1\}^m \). In this, the event \( \varphi_i = 1 \) means rejection of the \( i \)-th null hypothesis \( H_i \). As convention, the index \( \ell \) will be used to index families, while \( i \) is used to index individual hypotheses.

Relevant quantities.

**Definition A.1.** Under the assumptions of Model A.1, we let the total number of rejections, the number of erroneous rejections, the number of correct rejections, and the FDR, respectively, of \( \varphi_{(m)} \) be defined as

\[
R_m(\varphi_{(m)}) = |\{i \in \{1, \ldots, m\} : \varphi_i = 1\}|, \quad (A.1)
\]

\[
V_m(\varphi_{(m)}) = |\{i \in \{1, \ldots, m\} : \varphi_i = 1 \text{ and } H_i \text{ is true}\}|, \quad (A.2)
\]

\[
S_m(\varphi_{(m)}) = |\{i \in \{1, \ldots, m\} : \varphi_i = 1 \text{ and } H_i \text{ is false}\}|, \quad (A.3)
\]

\[
\text{FDR}_\vartheta(\varphi_{(m)}) = \mathbb{E}_\vartheta \left[ \frac{V_m(\varphi_{(m)})}{R_m(\varphi_{(m)}) \lor 1} \right]. \quad (A.4)
\]

The multiple test \( \varphi_{(m)} \) is said to control the FDR at level \( \alpha \in (0, 1) \) if

\[
\sup_{\vartheta \in \Theta} \text{FDR}_\vartheta(\varphi_{(m)}) \leq \alpha.
\]

It is said to control the FDR asymptotically at level \( \alpha \) as \( m \to \infty \) if

\[
\lim_{m \to \infty} \sup_{\vartheta \in \Theta} \text{FDR}_\vartheta(\varphi_{(m)}) \leq \alpha.
\]

If the \( m \) hypotheses are structured in disjoint families \( \mathcal{H}_1, \ldots, \mathcal{H}_k \) with \( |\mathcal{H}_\ell| = m_\ell \) for \( 1 \leq k \leq m \), a multiple test \( \varphi_{(m_\ell)} \) is applied within each family, and we set \( \varphi_{(m)} = (\varphi_{(m_1)}, \ldots, \varphi_{(m_k)})^\top \), we define the global FDR of \( \varphi_{(m)} \) by

\[
g\text{FDR}_\vartheta(\varphi_{(m)}) = \mathbb{E}_\vartheta \left[ \frac{\sum_{\ell=1}^k V_{m_\ell}(\varphi_{(m_\ell)})}{\{\sum_{\ell=1}^k R_{m_\ell}(\varphi_{(m_\ell)})\} \lor 1} \right].
\]

In the sequel, all considered multiple test procedures are such that the quantities in (A.1) - (A.4) actually only depend on the joint distribution of the (random) p-values \( p_1, \ldots, p_m \), and one may assume that \( (\Omega, \mathcal{F}) = ([0, 1]^m, B([0, 1]^m)) \) without loss of generality.
Critical value functions and rejection curves. The critical values \( \alpha_{i,m} \) from Definition 2 may be defined in terms of a critical value function \( \rho : [0,1] \to [0,1] \), where \( \rho \) is non-decreasing and continuous, \( \rho(0) = 0 \) and \( \alpha_{i,m} = \rho(i/m) \), \( i \in \{1, \ldots, m\} \). For a given critical value function \( \rho \), the function \( r \) defined by \( r(t) = \inf\{u : \rho(u) = t\} \) for \( t \in [0,1] \) is called the rejection curve corresponding to \( \rho \).

The AORC \( r_\alpha : [0,1] \to [0,1] \) is defined by
\[
r_\alpha(t) = \frac{t}{t(1 - \alpha) + \alpha}, \quad t \in [0,1],
\]
and the corresponding critical value function is given by \( r_\alpha^{-1}(t) = 1 - r_\alpha(1 - t) \), see Finner et al. (2009). The critical values induced by this critical value function are the ones given in Definition 3.

**Lemma A.1** (Sen 1999). Denote the empirical cumulative distribution function (ecdf) of the \( p \)-values \( p_1, \ldots, p_m \) by \( \hat{F}_m \), given by
\[
\hat{F}_m(t) = \sum_{i=1}^{m} I_{[0,t]}(p_i).
\]
Assume that \( \alpha_{i,m} = \rho(i/m), i \in \{1, \ldots, m\} \) for a critical value function \( \rho \) with corresponding rejection curve \( r \). Then it holds
\[
p_{i,m} \leq \alpha_{i,m} \text{ if and only if } \hat{F}_m(p_{i,m}) \geq r(p_{i,m}).
\]

Additional technical assumptions. Let \( m_{1,\ell} \) denote the number and \( q_{N,\ell}(m_{\ell}) = m_{N,\ell}/m_\ell \) the proportion of true null hypotheses in family \( \ell \in \{1, \ldots, k\} \). Define \( \pi_\ell(m) = m_\ell/m \) as the proportion of hypotheses belonging to family \( \ell \). Consider an asymptotic setting such that \( \forall \ell \in \{1, \ldots, k\} : m_\ell \to \infty \). For convenience, we assume \( \pi_\ell(m) \to \pi_\ell \in (0,1) \) and \( q_{N,\ell}(m_\ell) \to q_{N,\ell} \in [0,1] \).

Let \( \theta^* = \theta^*(m_{N1}, \ldots, m_{Nk}) \) denote a parameter value such that for every family \( \mathcal{H}_\ell, 1 \leq \ell \leq k \), the \( m_\ell \) \( p \)-values corresponding to true null hypotheses are uniformly distributed on \([0,1]\) and jointly stochastically independent, and that the remaining \( (m_\ell - m_{N,\ell}) \) \( p \)-values corresponding to false null hypotheses are almost surely equal to zero. Such a parameter value is commonly referred to as a Dirac-uniform configuration, see, e.g., Section 2.2.2 of Dickhaus (2014) and references therein.

Notice that \( \theta^* \) does not necessarily have to be contained in \( \Theta \). Under \( \theta^* \), the ecdf of the \( m_\ell \) \( p \)-values in family \( \mathcal{H}_\ell \), say \( \hat{F}_{m,\ell} \), converges in the Glivenko-Cantelli sense to \( \hat{F}_{\infty,\ell} \), given by \( \hat{F}_{\infty,\ell}(t) = (1 - q_{N,\ell}) + q_{N,\ell}I(t \in [0,1]) \). Furthermore, \( r_\alpha \) and \( \hat{F}_{\infty,\ell} \) possess a unique point of intersection on \([0,1]\), cf. Figure 5.2 of Dickhaus (2014). We denote by \( q_{N,\ell} \) the abscissa of this point of intersection.

In general \( t = \alpha_{i,m} \) is called a crossing point between \( \hat{F}_m \) and \( r \) if it satisfies \( \hat{F}_m(p_{i,m}) \geq r(p_{i,m}) \) and \( \hat{F}_m(p_{i+1,m}) < r(p_{i+1,m}) \) for \( i \in \{1, \ldots, m - 1\} \) or \( \hat{F}_m(p_{m,m}) \geq r(p_{m,m}) \) for \( i = m \).

Finally, we introduce the following assumption regarding the type I error behavior of \( \hat{\theta} \) with respect to the parameter \( \theta \) of the statistical model.

**Assumption A.1.** For given numbers \( m_{N1}, \ldots, m_{Nk} \), the parameter value \( \theta^* = \theta^*(m_{N1}, \ldots, m_{Nk}) \) is a least favorable parameter configuration (LFC) for the FDR of \( \hat{\theta} \). This means that FDR\( \theta(\hat{\theta}(m_{i})) \leq \text{FDR}_{\theta^*}(\hat{\theta}(m_{i})) \) for all \( \theta \) which are such that exactly \( m_{N,\ell} \) null hypotheses are true in family \( \mathcal{H}_\ell, 1 \leq \ell \leq k \).

Assumption A.1 is a standard assumption in FDR theory; see, among others, Blanchard et al. (2014) and Bodnar and Dickhaus (2014) and references therein.
Main results.

Theorem A.1. Let \( \theta \in \Theta \) and assume that for \( 1 \leq \ell \leq k \) the multiple test \( \varphi_{(m)} \) is an SUD test based on the critical value function \( \rho \leq r_{\alpha}^{-1} \) (with corresponding rejection curve \( r \)). Furthermore, let the assumptions from above be fulfilled and let \( \varphi_{(m)} = (\varphi_{(m_1)}, \ldots, \varphi_{(m_k)})^T \). For notational convenience, let \( R_{m_\ell} = R_{m_\ell}(\varphi_{(m)}) \) and \( V_{m_\ell} = V_{m_\ell}(\varphi_{(m)}) \).

If

\[
\forall \ell \in \{1, \ldots, k\} : \lim_{m_{\ell} \to \infty} \mathbb{P}_\theta \left( \frac{R_{m_{\ell}}}{m_{\ell}} \in (0, r_{q_{N}(m_{\ell})}) \right) = 1,
\]

then it holds that

\[
\limsup_{m \to \infty} gFDR_\theta(\varphi_{(m)}) \leq \alpha.
\]

Proof. The global FDR computes as

\[
gFDR_\theta(\varphi_{(m)}) = \mathbb{E}_\theta \left[ \frac{\sum_{\ell=1}^{k} V_{m_\ell}}{\left\{ \frac{\sum_{\ell=1}^{k} R_{m_\ell}}{\sum_{\ell=1}^{k} R_{m_\ell}} \right\}} \vee 1 \right] = \mathbb{E}_\theta \left[ \frac{m^{-1} \sum_{\ell=1}^{k} V_{m_\ell}}{m^{-1} \left\{ \frac{\sum_{\ell=1}^{k} R_{m_\ell}}{\sum_{\ell=1}^{k} R_{m_\ell}} \right\}} \right]. \tag{A.5}
\]

Let \( t_{m_{\ell}} \in [0, 1] \) denote the random crossing point between \( r \) and the ecdf of the \( p \)-values \( \hat{F}_{m_{\ell}, \ell} \) characterizing the rejection rule of \( \varphi_{(m)} \). This allows for the representation \( R_{m_{\ell}}/m_{\ell} = r(t_{m_{\ell}}) = \hat{F}_{m_{\ell}, \ell}(t_{m_{\ell}}) \) and \( V_{m_{\ell}} = m_{\ell} r_{q_{N}(m_{\ell})}(t_{m_{\ell}}) \). This means that the right-hand side of (A.5) equals

\[
\mathbb{E}_\theta \left[ \frac{\sum_{\ell=1}^{k} \pi_{\ell}(m) q_{N} \hat{F}_{N m_{\ell}, \ell}(t_{m_{\ell}})}{\sum_{\ell=1}^{k} \pi_{\ell}(m) r(t_{m_{\ell}})} \right] = \mathbb{E}_\theta \left[ \frac{\sum_{\ell=1}^{k} \pi_{\ell}(m) q_{N} \hat{F}_{N m_{\ell}, \ell}(t_{m_{\ell}}) r(t_{m_{\ell}})}{\sum_{\ell=1}^{k} \pi_{\ell}(m) r(t_{m_{\ell}})} \right]. \tag{A.6}
\]

An argumentation analogous to the one in the proof of Theorem 4.5 in Gontscharuk [2010] allows us to find an asymptotic non random upper bound for \( q_{N} \hat{F}_{N m_{\ell}, \ell}(t_{m_{\ell}}) / r(t_{m_{\ell}}) \). According to (5) in Definition 5, we can choose a \( \delta > 0 \) and \( m_{\ell} \) large enough such that \( \sup_{t \in [0, 1]} |\hat{F}_{N m_{\ell}}(t) - F_{N}(t)| \leq \delta \). Then it holds that

\[
q_{N} \hat{F}_{N m_{\ell}}(t_{m_{\ell}}) / r(t_{m_{\ell}}) \leq q_{N} t_{q_{N}} / r_{a}(t_{q_{N}}) + \mathcal{O}(\delta) \leq q_{N} t_{q_{N}} / r_{a}(t_{q_{N}}) + \mathcal{O}(\delta).
\]

By design of the function \( r_{a} \), it holds that \( q_{N} t_{q_{N}} / r_{a}(t_{q_{N}}) = \min\{\alpha, q_{N}\} \). Thus, it holds that the right-hand side of (A.6) can for eventually all large \( m_{\ell} \) be bounded from above by

\[
\mathbb{E}_\theta \left[ \frac{\sum_{\ell=1}^{k} \pi_{\ell}(m) r_{a}(t_{m_{\ell}}) \min\{\alpha, q_{N}\}}{\sum_{\ell=1}^{k} \pi_{\ell}(m) r_{a}(t_{m_{\ell}})} \right] + \mathcal{O}(\delta).
\]

Since \( \delta \) can be chosen arbitrarily small, this entails

\[
\limsup_{m \to \infty} gFDR_\theta(\varphi_{(m)}) \leq \alpha.
\]

Theorem A.2 (Statistical properties of the procedure \( \varphi^{HO} \)). Assume that the assumptions from above are fulfilled. Then, the proposed procedure \( \varphi^{HO} \) defined by Algorithm 2 controls the FWER at the stage of the families at level \( \alpha \). Furthermore, the global FDR of \( \varphi^{HO} \) and the FDR of \( \varphi^{HO} \) within each family are asymptotically bounded by \( \alpha \).
We conclude that
\[ \limsup \] of
\[ 1 \] we have
Asymptotic FDR control within each family can be established as follows. If a family
\[ H_\ell \] completes the argumentation.
Thus, if the family
\[ \ell \] is rejected, the SUD procedure which is applied in family \( H_\ell \) in the second stage of \( \varphi_{H_\ell}^{\text{HO}} \),
1 ≤ \( \ell \) ≤ \( k \). This follows from the fact that \( \kappa \) and hence, \( \ell \), are fixed constants and the rejection rule of \( \varphi_{H_\ell}^{\text{HO}} \) involves the additional condition regarding \( p_{\ell}^{u}/m_\ell \). Hence, \( R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) \leq R_{m_\ell}(\varphi_{H_\ell}^{\text{AORC}}) \).
Under \( \theta^* \) (cf. Assumption [A.1]) and by construction of \( R_\alpha \), we have, by setting \( t_{\bar{q}_{N\ell}} = 1 \) for \( q_{N\ell} < \alpha \), that \( R_{m_\ell}(\varphi_{H_\ell}^{\text{AORC}}) / m_\ell \rightarrow r_\alpha(t_{\bar{q}_{N\ell}}) \) almost surely, cf. Corollary 5.1.(i) of [Finner et al. 2009].
We conclude that \( \lim \sup_{m_\ell \rightarrow \infty} R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) / m_\ell \leq r_\alpha(t_{\bar{q}_{N\ell}}) \) for all \( \theta^* \in \Theta \). On the other hand, consider for each 1 ≤ \( \ell \) ≤ \( k \) such that \( H_\ell \) has been selected at the first stage of analysis the following chain of inequalities:

\[ p_{\ell; m_\ell} \leq \min_{j=1, \ldots, (m_\ell - \ell + 1)} \left\{ p_{(\ell - 1 + j); m_\ell} \right\} \leq p_{\ell}/m_\ell = \min_{j=1, \ldots, (m_\ell - \ell + 1)} \left\{ \frac{(m_\ell - \ell + 1)}{j} \right\} \]
\[ \leq \frac{\alpha}{\kappa} \leq \frac{1}{\kappa} \frac{m_\ell}{m_\ell} \leq r_\alpha^{-1} \frac{1/\kappa \cdot m_\ell}{m_\ell} \leq r_\alpha^{-1} \frac{u_\ell}{m_\ell}. \]

Thus, if the family \( H_\ell \) is rejected, the SUD procedure \( \varphi^{\text{AORC}}_{H_\ell} \) will reject at least \( u_\ell \) hypotheses within \( H_\ell \). Notice that, by definition of \( u_\ell \), we have that \( u_\ell / m_\ell \geq \kappa^{-1} \). We conclude that, in each selected family \( H_\ell \), \( \inf_{m_\ell \rightarrow \infty} R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) / m_\ell > 0 \). Thus, Theorem A.1 can be applied with \( k \) replaced by \( |\{1 \leq \ell \leq k : H_\ell \text{ has been rejected}\}| \) in this case.

However, if for some \( \ell \in \{1, \ldots, k\} \) we have \( q_{N\ell} = 1 \), we can find a number \( m_\ell \) which is large enough such that \( \mathbb{P}_\theta(p^{u_\ell}/m_\ell \leq \alpha/\kappa) \leq \alpha/\kappa \) due to the assumed validity of the conjunction p-value. Hence, letting \( x \) denote all observed data, straightforward calculation yields for \( \theta^* \), which is such that \( q_{N\ell} = 1 \), that

\[ \mathbb{E}_\theta \left[ \frac{V_{m_\ell}}{R_{m_\ell} \vee 1} \right] = \int \frac{V_{m_\ell}(x)}{R_{m_\ell}(x) \vee 1} d\mathbb{P}_\theta(x) \leq \int \frac{V_{m_\ell}(x)}{R_{m_\ell}(x) \vee 1} d\mathbb{P}_\theta(x) + \int \frac{V_{m_\ell}(x)}{R_{m_\ell}(x) \vee 1} d\mathbb{P}_\theta(x) \]
\[ \leq \int \frac{1}{R_{m_\ell}(x) \vee 1} d\mathbb{P}_\theta + 0 \]
\[ = \mathbb{P}_\theta(p^{u_\ell}/m_\ell \leq \alpha/\kappa) \leq \alpha/\kappa, \]
which completes the argumentation.

Asymptotic FDR control within each family can be established as follows. If a family \( H_\ell \) is not rejected, we have \( R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) = V_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) = 0 \). On the other hand, in each selected family \( H_\ell \), it holds
\[ V_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) \leq V_{m_\ell}(\varphi_{H_\ell}^{\text{AORC}}), \] by the same argumentation as for \( R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) \). Under the LFC \( \theta^* \), this also entails that
\[ \frac{V_{m_\ell}(\varphi_{H_\ell}^{\text{HO}})}{R_{m_\ell}(\varphi_{H_\ell}^{\text{HO}}) \vee 1} \leq \frac{V_{m_\ell}(\varphi_{H_\ell}^{\text{AORC}})}{R_{m_\ell}(\varphi_{H_\ell}^{\text{AORC}}) \vee 1} \]
almost surely, because the structure of an SUD test yields that, as soon as \( V_{m,\ell}(\varphi_{\text{HO}}^{H}) \geq 1 \), we have 
\[
R_{m,\ell}(\varphi_{\text{HO}}^{H}) = V_{m,\ell}(\varphi_{\text{HO}}^{H}) + (m_{\ell} - m_{N\ell}),
\]
and the mapping \( x \mapsto x/(x+a) \) is isotone in \( x > 0 \) for \( a \geq 0 \). Since \( \varphi_{\text{AORC}}^{H} \) asymptotically controls the FDR under \( \vartheta^{*} \), this implies the assertion. ■

### A.2 The tuning parameter \( \kappa \)

Here, we report results of a power study regarding the tuning parameter \( \kappa \). The study was done in two setups for the normal means problem with effect size \( \mu^{*} \) and variance 1, analogous to the simulations in “Computer simulations regarding the power of \( \varphi_{\text{HO}}^{H} \). Our theoretical investigations indicate that we can expect the power of the procedure \( \varphi_{\text{HO}}^{H} \) within one selected family \( \mathcal{H}_{\ell} \) (in our case of size \( m_{\ell} = 2,000 \)) to depend on the ratio of true null hypotheses \( q_{N\ell} \) within the family. To this end, we considered a balanced and a highly unbalanced case by setting \( q_{N\ell} \in \{0.5, 0.99\} \). In both cases the power of \( \varphi_{\text{HO}}^{H} \) has been estimated as a function of \( \mu^{*} \in [0, 5] \), and we let the parameter \( \kappa \) range from 1 to 10,000,000 on a \( \log_{10} \) scale.

The plots in S1 Fig. indicate that small values of \( \kappa \) lead to a high specificity in case of a large value of \( q_{N\ell} \), while large values of \( \kappa \) lead to a good sensitivity in case of a moderate value of \( q_{N\ell} \). This is line with the recommendation that \( \kappa \) should be chosen according to the amount of signals within a family which is considered relevant.

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