

A Supplementary Material

This supplementary material contains proofs of Theorems 3 and 4 from the main text, as well as a counterexample showing that procedures that use an estimate of the proportion of true null hypotheses may not control FDR when applied to average significance level controlling p -values.

A.1 Proof of Theorem 4.1

We begin with a lemma regarding uniform convergence.

Lemma S1. *If (12) holds, then*

$$\inf_{t \in [0,1]} [t - V(t)/m] \geq o_P(1). \quad (\text{S14})$$

If (13) holds for continuous functions F and G , then

$$\sup_{t \in [0,1]} |V(t)/m - G(t)| \xrightarrow{P} 0 \quad \text{and} \quad \sup_{t \in [0,1]} |R(t)/m - F(t)| \xrightarrow{P} 0. \quad (\text{S15})$$

Proof. The result follows by arguing as in the proof of the Glivenko-Cantelli Theorem. Let $\bar{t}_K(t)$ be the least element in $\{0, 1/K, \dots, (K-1)/K, 1\}$ that is greater than or equal to t . To show (S14), note that $t - V(t)/m \geq t - V(\bar{t}_K(t))/m \geq \bar{t}_K(t) - V(\bar{t}_K(t)/m) - 1/K$. Thus, $\inf_{t \in [0,1]} [t - V(t)/m] \geq \min_{t \in \{0, 1/K, \dots, (K-1)/K, 1\}} [t - V(t)/m] - 1/K$. Applying (12) and taking $K \rightarrow \infty$ gives (S14).

Similarly, to show that (S15) holds so long as (13) holds for continuous G and F , note that $V(t)/m - G(t) \leq V(\bar{t}_K(t))/m - G(t) \leq V(\bar{t}_K(t))/m - G(\bar{t}_K(t)) + \omega(1/K)$ where $\omega(\varepsilon) = \sup_{s,t \in [0,1], |s-t| \leq \varepsilon} |G(s) - G(t)|$ satisfies $\lim_{\varepsilon \rightarrow 0} \omega(\varepsilon) = 0$ by uniform continuity of G on the interval $[0, 1]$. From this and an analogous lower bound, it follows that $\sup_{t \in [0,1]} |V(t)/m - G(t)| \leq \max_{t \in \{0, 1/K, \dots, (K-1)/K, 1\}} |V(t)/m - G(t)| + \omega(1/K)$. Applying (13) and taking $K \rightarrow 0$ gives the first part of (S15). The same arguments applied to $R(t)/m - F(t)$ give the second part of (S15). □

We now prove Theorem 4.1. We begin by showing that the first claim in the theorem holds under (12). For any $\varepsilon > 0$, the event $\inf_{t \in [t, 1]} \left[\widehat{\text{FDR}}(t) - \text{FDP}(\mathcal{R}_t^{\text{fixed}}, \mathcal{H}_0) \right] < -\varepsilon$ implies that there exists $t \in [t, 1]$ such that $t - V(t)/m < -\varepsilon(R(t) \vee 1)/m \leq -\varepsilon(R(\underline{t}) \vee 1)/m$.

This implies $\inf_{t \in [\underline{t}, 1]} [t - V(t)/m] \leq -\varepsilon \cdot \eta/2$ on the event $R(\underline{t})/m = \frac{1}{m} \sum_{i=1}^m I(p_i \leq \underline{t}) \geq \eta/2$, which holds with probability approaching one by assumption. The first claim of Theorem 4.1 now follows by noting that the probability of this event converges to zero by (S14).

Next, we show that the second claim of the theorem holds if (12) holds and (13) holds for some continuous F and G . The first part of the second claim follows immediately from (S15), using uniform continuity of the function $(a, b) \mapsto a/b$ over $b \in [F(\underline{t}), 1]$ since $F(\underline{t}) \geq \eta > 0$. The second part of the second claim then follows immediately from the dominated convergence theorem. The third part of the second claim follows from combining the first claim in the theorem with the first and second part of the second claim in the theorem.

A.2 Proof of Theorem 4.2

We have

$$\text{FDP}(\mathcal{R}_{\text{BH},q}, \mathcal{H}_0) = \frac{V(\hat{t}_{\text{BH},q})/m}{[R(\hat{t}_{\text{BH},q}) \vee 1]/m} \leq \widehat{\text{FDR}}(\hat{t}_{\text{BH},q}) + I(\hat{t}_{\text{BH},q} < t^*) + o_P(1)$$

using the fact that $\sup_{t \in [t^*, 1]} \left[\frac{V(t)/m}{[R(t) \vee 1]/m} - \widehat{\text{FDR}}(t) \right] \leq o_P(1)$ by Theorem 4.1. Since $\widehat{\text{FDR}}(\hat{t}_{\text{BH},q}) \leq q$ by construction, it suffices to show $P(\hat{t}_{\text{BH},q} \geq t^*) \rightarrow 1$. But this follows since $\widehat{\text{FDR}}(t^*) \leq q$ implies $\hat{t}_{\text{BH},q} \geq t^*$, and $\widehat{\text{FDR}}(t^*) \xrightarrow{P} G(t^*)/F(t^*) < q$ by (13). This shows that $\text{FDP}(\mathcal{R}_{\text{BH},q}, \mathcal{H}_0) \leq q + o_P(1)$, from which it also follows that $\text{FDR}(\mathcal{R}_{\text{BH},q}, \mathcal{H}_0, P) \leq q + o(1)$ by dominated convergence.

A.3 Counterexample for adaptive procedures

As noted in the main text, procedures that attempt to incorporate estimates $\hat{\pi}$ of $\#\mathcal{H}_0/m$ will in not, in general, lead finite sample or asymptotic FDR control under weak dependence conditions on the p -values. As a counterexample, consider the procedure $\mathcal{R}_{\hat{\pi}, \beta(\cdot), q}$ with $\beta(t) = t$ that uses the estimate $\hat{\pi} = (\sum_{i=1}^m I(p_i > \lambda) + 1)/((1 - \lambda)m)$ of π_0 for some $\lambda \in (0, 1)$ as in Storey et al. (2004) and suppose that $\#\mathcal{H}_0/m \rightarrow \pi_0$ where $q < \pi_0 < \lambda$. Suppose that p_i is independent over i and follows a uniform distribution on $[0, \pi_0]$ for $i \in \mathcal{H}_0$, and that p_i follows some other distribution with support contained in $[0, \pi_0)$ for $i \notin \mathcal{H}_0$. Then (12) and (13) hold. However, note that the cutoff $\hat{t}_{\hat{\pi}, \beta(\cdot), q}$ in (10) will be equal to 1 so long as $q \geq \hat{\pi}m \cdot 1/R(1) = \hat{\pi}$, which holds for large enough m with probability one since $\hat{\pi} = 1/((1 - \lambda)m) \rightarrow 0$ with probability one. Since the FDP is equal to $\#\mathcal{H}_0/m$ on the event that $\hat{t}_{\hat{\pi}, \beta(\cdot), q} = 1$, this implies that the FDP is equal to $\#\mathcal{H}_0/m \rightarrow \pi_0 > q$ with probability

one for large enough m , so that the FDR is equal to $\#\mathcal{H}_0/m > q$ for large enough m . Note that the FDP is also equal to $\#\mathcal{H}_0/m$ on the event that $\hat{t}_{\hat{\pi},\beta(\cdot),q} \geq \lambda$, since the p -values are all supported on $[0, \lambda)$. Thus, the same argument goes through for the modification of the procedure in which $\hat{t}_{\hat{\pi},\beta(\cdot),q}$ is replaced by λ when $\hat{t}_{\hat{\pi},\beta(\cdot),q} > \lambda$.

Note also that the oracle version of this procedure ($\mathcal{R}_{\pi_0,\beta(\cdot),q}$ with $\beta(t) = t$ and π set to the true asymptotic null proportion π_0) also fails to control FDR asymptotically. For this procedure, the cutoff $\hat{t}_{\pi_0,\beta(\cdot),q}$ is equal to 1 so long as $q \geq \pi_0$, which holds by assumption. Thus, this oracle procedure has FDP equal to π_0 with probability one, which means that it has FDR equal to π_0 for all m .