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A fast algorithm to compute a curve of confidence upper bounds for the False Discovery Proportion using a reference family with a forest structure

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Abstract

This paper presents a new algorithm (and an additional trick) that allows to compute fastly an entire curve of post hoc bounds for the False Discovery Proportion when the underlying bound $V^*_{\mathfrak{R}}$ construction is based on a reference family $\mathfrak{R}$ with a forest structure à la Durand et al. (2020). By an entire curve, we mean the values $V^*_{\mathfrak{R}}(S_1), \dots, V^*_{\mathfrak{R}}(S_m)$ computed on a path of increasing selection sets $S_1 \subsetneq \cdots \subsetneq S_m$, $|S_t| = t$. The new algorithm leverages the fact that going from S_t to S_{t+1} is done by adding only one hypothesis.

Keywords: multiple testing, algorithmic, post hoc inference, false discovery proportion, confidence bound

Contents

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1 Introduction

Multiple testing theory is often used for exploratory analysis, like Genome-Wide Association Studies, where multiple features are tested to find promising ones. Classical multiple testing theory like Family-Wise Error Rate (FWER) control or False Discovery Rate (FDR) control (Benjamini and Hochberg, 1995) can be used, but a more recent trend consists in the computation of post hoc bounds, also named post selection bounds or confidence envelopes, for the number of false positives, or, equivalently, for the False Discovery Proportion (FDP). This approach is notably advocated for in the context of exploratory research by (Goeman and Solari, 2011, Section 1).

Mathematically speaking, a confidence upper bound (we prefer to say upper bound instead of envelope for obvious reasons) is a function $\hat{V} : \mathscr{P}(\mathbb{N}_m^*) \to \mathbb{N}_m$, where $\mathbb{N}_m = \{0, \dots, m\}$, $\mathbb{N}_m^* = \{1, \dots, m\}$ and m is the number of hypotheses, such that

$$\forall \alpha \in]0, 1[, \mathbb{P}\left(\forall S \subseteq \mathbb{N}_m^*, |S \cap \mathscr{H}_0| \leq \hat{V}(S)\right) \geq 1 - \alpha. \tag{1}$$

Here, α is a target error rate and $\mathscr{H}_0$ is the set of hypotheses indices that are true null hypotheses. Note that the construction of $\hat{V}$ depends on α and on the random data X and the dependence is omitted to lighten notation and because there is no ambiguity. The meaning of Equation 1 is that $\hat{V}$ provides an upper bound of the number of null hypotheses in S for any selection set $S \subseteq \mathbb{N}_m^*$, which allows the user to perform post hoc selection on their data without breaching the statistical guarantee. Also note that by dividing by $|S| \vee 1$ in Equation 1 we also get a confidence bound for the FDP:

$$\forall \alpha \in]0, 1[, \mathbb{P}\left(\forall S \subseteq \mathbb{N}_m^*, \mathrm{FDP}(S) \leq \frac{\hat{V}(S)}{|S| \vee 1}\right) \geq 1 - \alpha. \tag{2}$$

So post hoc bounds provide ways to construct FDP-controlling sets instead of FDR-controlling sets, which is much more desirable given the nature of the FDR as an expected value. See for example (Bogdan et al., 2015, Figure 4) for a credible example where the FDR is controlled but the FDP has a highly undesirable behavior (either 0 because no discoveries at all are made, either higher than the target level).

The first confidence bounds are found in (Genovese and Wasserman, 2006) and (Meinshausen, 2006), although, in the latter, only for selection sets of the form $\{i \in \mathbb{N}_m : P_i \leq t\}$ where P_i is the p-value associated to the null hypothesis $H_{0,i}$. In (Goeman and Solari, 2011) the authors re-wrote the generic construction of (Genovese and Wasserman, 2006) in terms of closed testing (Marcus et al., 1976), proposed several practical constructions and sparked a new interest in multiple testing procedures based on confidence envelopes. This work was followed by a prolific series of works like (Meijer et al., 2015) and (Vesely et al., 2023). In (Blanchard et al., 2020), the authors introduce the new point of view of references families (see Section 2.2) to construct post hoc bounds, and show the links between this meta-technique and the closed testing one, along with new bounds.

Following the reference family trail, in (Durand et al., 2020) the authors introduce new reference families with a special set-theoretic constraint that allows an efficient computation of the bound denoted by $V_{\mathfrak{R}}^*$ on a single selection set S. The problem is that one often wants to compute $V_{\mathfrak{R}}^*$ on a whole path of selection sets $(S_t)_{t \in \mathbb{N}_m^*}$, for example the hypotheses attached to the t smallest p-values. Whereas the algorithm provided the aforementioned work (Durand et al., 2020, Algorithm 1) is fast for a single evaluation, it is slow and inefficient to repeatedly call it to compute each $V_{\mathfrak{R}}^*(S_t)$. If the S_t's are nested, and growing by one, that is $S_1 \subsetneq \cdots \subsetneq S_m$ and $|S_t| = t$, there is a way to efficiently compute $\left(V_{\mathfrak{R}}^*(S_t)\right)_{t \in \mathbb{N}_m}$ by leveraging the nested structure.

This is the main contribution of the present paper: a new and fast algorithm computing the curve $\left(V_{\mathfrak{R}}^*(S_t)\right)_{t \in \mathbb{N}_m}$ for a nested path of selection sets, that is presented in Section 3.2. An additional algorithm that can speed up computations both for the single-evaluation algorithm and the new curve-evaluation algorithm is also presented, in Section 3.1. In Section 2.1, all necessary notation and vocabulary is re-introduced, most of it being the same as in (Durand et al., 2020). Finally, a few numerical experiments are presented in Section Section 4 to demonstrate the computation time gain.

2 Notation and reference family methodology

2.1 Multiple testing notation

2.2 Post hoc bounds with reference families

2.3 Deterministic regions with a forest structure

3 New algorithms

3.1 Pruning the forest

Algorithm 1 Pruning of $\mathfrak{R}$

procedure PRUNING($\mathfrak{R} = (R_k, \zeta_k)_{k \in \mathcal{K}}$ with $\mathfrak{R}$ complete)
    $\mathcal{K}^{\mathfrak{pr}} \leftarrow \mathcal{K}$
    $H \leftarrow \max_{k \in \mathcal{K}} \phi(k)$ ▷ maximum depth
    for $h = H - 1, \dots, 1$ **do**
        $\mathcal{K}^h \leftarrow \{k \in \mathcal{K} \ : \ \phi(k) = h\}$
        $newVec \leftarrow (0)_{k \in \mathcal{K}^h}$
        for $k \in \mathcal{K}^h$ **do**
            $Succ_k \leftarrow \{k' \in \mathcal{K}^{h+1} \ : \ R_{k'} \subseteq R_k\}$
            if $Succ_k = \varnothing$ **then**
                $newVec_k \leftarrow \zeta_k$
            else
                if $\zeta_k \geq \sum_{k' \in Succ_k} Vec_{k'}$ **then**
                    $\mathcal{K}^{\mathfrak{pr}} \leftarrow \mathcal{K}^{\mathfrak{pr}} \setminus \{k\}$
                end if
                $newVec_k \leftarrow \min\left(\zeta_k, \sum_{k' \in Succ_k} Vec_{k'}\right)$
            end if
        end for
        $Vec \leftarrow newVec$
    end for
    return $(\mathcal{K}^{\mathfrak{pr}}, \sum_{k \in \mathcal{K}^1} Vec_k)$
end procedure

Tip

Proposition 3.1 (Pruning).

3.2 Fast algorithm to compute a curve of confidence bounds on a path of selection sets

Theorem 3.1 (Fast curve computation).

Algorithm 2 Formal computation of $(V^*_{\mathfrak{R}}(S_t))_{0\le t\le m}$

procedure $\textsc{Curve}(\mathfrak{R} = (R_k, \zeta_k)_{k\in\mathscr{K}}$ with $\mathfrak{R}$ complete, path $(S_t)_{1\le t\le m}$ with $S_t = \{i_1, \dots, i_t\})$
  $\mathscr{P}^0 \leftarrow \{(i,i) : 1 \le i \le n\}$ ▷ the set of all atoms indices
  $\mathscr{K}_0^- \leftarrow \{k \in \mathscr{K} : \zeta_k = 0\}$
  $\eta_k^0 \leftarrow 0$ for all $k \in \mathscr{K}$
  for $t = 1, \dots, m$ **do**
    if $i_t \in \bigcup_{k\in\mathscr{K}_{t-1}^-} R_k$ **then**
      $\mathscr{P}^t \leftarrow \mathscr{P}^{t-1}$
      $\mathscr{K}_t^- \leftarrow \mathscr{K}_{t-1}^-$
      $\eta_k^t \leftarrow \eta_k^{t-1}$ for all $k \in \mathscr{K}$
    else
      for $h = 1, \dots, h_{\max}(t)$ **do**
        $\eta^t_{k^{(t,h)}} \leftarrow \eta^{t-1}_{k^{(t,h)}} + 1$
        if $\eta^t_{k^{(t,h)}} < \zeta_k$ **then**
          Pass
        else
          $h_t^f \leftarrow h.$
          $\mathscr{P}^t \leftarrow \left(\mathscr{P}^{t-1} \setminus \{k \in \mathscr{P}^{t-1} : R_k \subseteq R_{k^{(t,h_t^f)}}\}\right) \cup \{k^{(t,h_t^f)}\}$
          $\mathscr{K}_t^- \leftarrow \mathscr{K}_{t-1}^- \cup \{k^{(t,h_t^f)}\}$
          Break the loop
        end if
      end for
      if the loop has been broken **then**
        $\eta_k^t \leftarrow \eta_k^{t-1}$ for all $k \in \mathscr{K}$ not visited during the loop, that is all $k \notin \{k^{(t,h)}, 1 \le h \le h_t^f\}$
      else
        $\mathscr{P}^t \leftarrow \mathscr{P}^{t-1}$
        $\mathscr{K}_t^- \leftarrow \mathscr{K}_{t-1}^-$
        $\eta_k^t \leftarrow \eta_k^{t-1}$ for all $k \in \mathscr{K}$ not visited during the loop, that is all $k \notin \{k^{(t,h)}, 1 \le h \le h_{\max}(t)\}$
      end if
    end if
  end for
  return $\mathscr{P}^t, \eta_k^t$ for all $t = 1, \dots, m$ and $k \in \mathscr{K}$
end procedure

Proof. Content □

Corollary 3.1 (Easy implementation)**.**

4 Numerical experiments

5 Conclusion

6 Acknowledments

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Algorithm 3 Implementation of $(V^*_{\mathfrak{R}}(S_t))_{0\leq t\leq m}$

procedure CURVE($\mathfrak{R} = (R_k, \zeta_k)_{k\in\mathcal{K}}$ with $\mathfrak{R}$ complete, path $(S_t)_{1\leq t\leq m}$ with $S_t = \{i_1, \dots, i_t\}$)
 $V_0 \leftarrow 0$
 $\mathcal{K}^- \leftarrow \{k \in \mathcal{K} \,:\, \zeta_k = 0\}$
 $\eta_k \leftarrow 0$ for all $k \in \mathcal{K}$
 for $t = 1, \dots, m$ **do**
  if $i_t \in \bigcup_{k\in\mathcal{K}^-} R_k$ **then**
   $V_t \leftarrow V_{t-1}$
  else
   for $h = 1, \dots, h_{\max}(t)$ **do**
    find $k^{(t,h)} \in \mathcal{K}^h$ such that $i_t \in R_{k^{(t,h)}}$
    $\eta_{k^{(t,h)}} \leftarrow \eta_{k^{(t,h)}} + 1$
    if $\eta_{k^{(t,h)}} < \zeta_k$ **then**
     pass
    else
     $\mathcal{K}^- \leftarrow \mathcal{K}^- \cup \{k^{(t,h)}\}$
     break the loop
    end if
   end for
   $V_t \leftarrow V_{t-1} + 1$
  end if
 end for
 return $(V_t)_{1\leq t\leq m}$
end procedure

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Session information

```
R version 4.4.0 (2024-04-24)
Platform: x86_64-pc-linux-gnu
Running under: Ubuntu 22.04.4 LTS

Matrix products: default
BLAS:   /usr/lib/x86_64-linux-gnu/openblas-pthread/libblas.so.3
LAPACK: /usr/lib/x86_64-linux-gnu/openblas-pthread/libopenblasp-r0.3.20.so;  LAPACK version 3.10.0

locale:
 [1] LC_CTYPE=C.UTF-8       LC_NUMERIC=C           LC_TIME=C.UTF-8
 [4] LC_COLLATE=C.UTF-8     LC_MONETARY=C.UTF-8    LC_MESSAGES=C.UTF-8
 [7] LC_PAPER=C.UTF-8       LC_NAME=C              LC_ADDRESS=C
[10] LC_TELEPHONE=C         LC_MEASUREMENT=C.UTF-8 LC_IDENTIFICATION=C

time zone: UTC
tzcode source: system (glibc)

attached base packages:
[1] stats     graphics  grDevices datasets  utils     methods   base

loaded via a namespace (and not attached):
 [1] compiler_4.4.0    fastmap_1.1.1     cli_3.6.2         htmltools_0.5.8.1
 [5] tools_4.4.0       yaml_2.3.8        rmarkdown_2.26    knitr_1.46
 [9] jsonlite_1.8.8    xfun_0.43         digest_0.6.35     rlang_1.1.3
[13] renv_1.0.7        evaluate_0.23
```