Merging p-values under arbitrary dependence

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Agenda

Simple question

Suppose that we are testing the same hypothesis using $K \geqslant 2$ tests and obtain p-values $p_1, \ldots, p_K$. How can we combine them into a single p-value?

A question of a long history

- Tippett'31, Pearson'33, Fisher'48: assume independence
- The Bonferroni correction: minimum $\times$ correction (K)
- We are interested in the case of no dependence assumption
- Can be used to test multiple hypotheses

Meta-analysis

A typical example from meta-analysis

TABLE 1
Data on 10 Studies of Sex Differences in Conformity Using the Fictitious Norm Group Paradigm

Study	Sample size: Control n^C	Sample size: Experimental n^E	Effect size d	Student's t	Significance level p	$-2\log p$	$\Phi^{-1}(p)$	$\log[p/(1-p)]$
1	118	136	0.35	2.78	0.0029	11.682	−2.758	−5.838
2	40	40	0.37	1.65	0.0510	5.952	−1.635	−2.923
3	61	64	−0.06	−0.33	0.6310	0.921	0.335	0.537
4	77	114	−0.30	−2.03	0.9783	0.044	2.020	3.809
5	32	32	0.70	2.80	0.0034	11.367	−2.706	−5.680
6	45	45	0.40	1.90	0.0305	6.978	−1.873	−3.458
7	30	30	0.48	1.86	0.0341	6.760	−1.824	−3.345
8	10	10	0.85	1.90	0.0367	6.608	−1.790	−3.266
9	70	71	−0.33	−1.96	0.9740	0.053	1.942	3.622
10	60	59	0.07	0.38	0.3517	2.090	−0.381	−0.612

The sex differences dataset, from p.35 of Hedges/Olkin'85

The value of no assumption

Why no independence assumption?

- A set of p-values is only one vector: no hope to test/verify any dependence model among them
- Non-identifiability: are we rejecting independence or the scientific hypothesis?
- Efron'10, Large-scale Inference, p50-p51:
  "*independence among the p-values ... usually an unrealistic assumption. ... even PRD* [positive regression dependence] *is unlikely to hold in practice.*"

Merging functions

Let $\mathcal{H}$ be a collection of atomless probability measures ...

Definition (p-variables and merging functions)

(i) A p-variable is a random variable P that satisfies

$$\sup_{\mathbb{P}\in\mathcal{H}} \mathbb{P}(P \leqslant \varepsilon) \leqslant \varepsilon, \quad \varepsilon \in (0,1).$$

(ii) A p-merging function is an increasing Borel function $F : [0,\infty)^K \to [0,\infty)$ such that $F(P_1,\dots,P_K)$ is a p-variable for all p-variables $P_1,\dots,P_K$.

- Controlled type I error under arbitrary dependence

Merging functions

- $\mathcal{U}$: the set of all uniform $[0,1]$ random variables under $\mathbb{P}$

For an increasing Borel $F:[0,\infty)^K \to [0,\infty)$, equivalent are:

- F is a p-merging function w.r.t. some collection $\mathcal{H}$
- F is a p-merging function w.r.t. all collections $\mathcal{H}$
- fixing $\mathbb{P}$, $F(\mathbf{P})$ is a p-variable for all $\mathbf{P} \in \mathcal{U}^K$
- fixing $\mathbb{P}$, for all $\varepsilon \in (0,1)$, $\overline{\mathbb{P}}(F \leqslant \varepsilon) \leqslant \varepsilon$, where

$$\overline{\mathbb{P}}(F \leqslant \varepsilon) = \sup\left\{\mathbb{P}(F(\mathbf{P}) \leqslant \varepsilon) : \mathbf{P} \in \mathcal{U}^K\right\}$$

It suffices to consider $\mathcal{H} = \{\mathbb{P}\}$ for a generic $\mathbb{P}$ and $\mathcal{U}^K$

- Multi-marginal OT problem: $\sup\{\mathbb{E}[\mathbb{1}_{\{F(\mathbf{P}) \leqslant \varepsilon\}}] : \mathbf{P} \in \mathcal{U}^K\}$

Existing methods

Without any assumptions on the p-values $p_1, \ldots, p_K$

- $p_{(1)}, \ldots, p_{(K)}$ are the ascending order statistics
- The Bonferroni method

$$F(p_1, \ldots, p_K) = Kp_{(1)}$$

- Order-family (O-family) Rüger'78

$$G_{k,K} = (p_1, \ldots, p_K) = \frac{K}{k} p_{(k)}$$

- Simes–Hommel Hommel'83

$$H(p_1, \ldots, p_K) = \ell_K \bigwedge_{k=1}^{K} \frac{K}{k} p_{(k)}; \qquad \ell_K = \sum_{k=1}^{K} \frac{1}{k}$$

Precise merging functions

Definition (precise merging functions)

A p-merging function F is precise if, for all $\varepsilon \in (0,1)$, $\overline{\mathbb{P}}(F \leqslant \varepsilon) = \varepsilon$.

The Bonferroni method $F(p_1, \dots, p_K) = Kp_{(1)}$

$$\mathbb{P}\left(\bigwedge_{k=1}^{K} p_k \leqslant \varepsilon/K\right) = \mathbb{P}\left(\bigcup_{k=1}^{K} \{p_k \leqslant \varepsilon/K\}\right)$$

$$\leqslant \sum_{k=1}^{K} \mathbb{P}(Kp_k \leqslant \varepsilon) = \sum_{k=1}^{K} \frac{\varepsilon}{K} = \varepsilon.$$

- Equality if $\{Kp_k \leqslant \varepsilon\},\ k \in [K]$ are mutually exclusive

Merging p-values via averaging

- Generalized mean — Kolmogorov'30

$$M_{\phi,K}(p_1,\dots,p_K)=\phi^{-1}\left(\frac{\phi(p_1)+\cdots+\phi(p_K)}{K}\right),$$

where $\phi:[0,1]\to[-\infty,\infty]$ is continuous & strictly monotone

- M-family: for $r\in\mathbb{R}\setminus\{0\}$,

$$M_{r,K}(p_1,\dots,p_K)=\left(\frac{p_1^r+\cdots+p_K^r}{K}\right)^{1/r}.$$

- $\phi(x)=\tan((x-\frac{1}{2})\pi)$: Cauchy combination — Liu/Xie'20

Merging p-values via averaging

Special cases:

- Arithmetic: $M_{1,K}(p_1, \ldots, p_K) = \frac{1}{K}\sum_{k=1}^{K} p_k$
- Harmonic: $M_{-1,K}(p_1, \ldots, p_K) = \left(\frac{1}{K}\sum_{k=1}^{K} \frac{1}{p_k}\right)^{-1}$
- Quadratic: $M_{2,K}(p_1, \ldots, p_K) = \sqrt{\frac{1}{K}\sum_{k=1}^{K} p_k^2}$

Limiting cases:

- Geometric: $M_{0,K}(p_1, \ldots, p_K) = \left(\prod_{k=1}^{K} p_k\right)^{1/K}$
- Maximum: $M_{\infty,K}(p_1, \ldots, p_K) = \max(p_1, \ldots, p_K)$
- Minimum: $M_{-\infty,K}(p_1, \ldots, p_K) = \min(p_1, \ldots, p_K)$

The cases $r \in \{-1, 0, 1\}$ are known as Platonic means.

Merging p-values via averaging

The arithmetic average $M_{1,K}(p_1, \ldots, p_K) = \frac{1}{K}\sum_{k=1}^{K} p_k$ is not a p-merging function

Rüschendorf'82, Meng'93

$$\overline{\mathbb{P}}(M_{1,K} \leqslant \varepsilon) = \min(2\varepsilon, 1).$$

- $\Rightarrow 2M_{1,K}$ is a precise p-merging function

Task. Find $b_{r,K} > 0$ such that (the M-family)

$$F_{r,K} = b_{r,K} M_{r,K} \text{ is precise}$$

- $M_{r,K}$ increases in $r \Longrightarrow b_{r,K}$ should decrease in r.

Translation to a risk aggregation problem

For $\alpha \in (0,1]$ and a random variable X, define

$$Q_\alpha(X) = \inf\{x \in \mathbb{R} : \mathbb{P}(X \leqslant x) \geqslant \alpha\}$$

and for a function $F : [0,1]^K \to [0,\infty)$, define

$$\underline{Q}_\alpha(F) = \inf\left\{Q_\alpha(F(\mathbf{P})) : \mathbf{P} \in \mathcal{U}^K\right\}.$$

Translation to a risk aggregation problem

Lemma 1

For $a > 0$, $r \in [-\infty, \infty]$, and $F = aM_{r,K}$, equivalent are:

(i) *F is a p-merging function, i.e., $\overline{\mathbb{P}}(F \leqslant \varepsilon) \leqslant \varepsilon$ for all $\varepsilon \in (0,1)$;*

(ii) *$\underline{Q}_\varepsilon(F) \geqslant \varepsilon$ for all $\varepsilon \in (0,1)$;*

(iii) *$\overline{\mathbb{P}}(F \leqslant \varepsilon) \leqslant \varepsilon$ for some $\varepsilon \in (0,1)$;*

(iv) *$\underline{Q}_\varepsilon(F) \geqslant \varepsilon$ for some $\varepsilon \in (0,1)$.*

The same conclusion holds if all $\leqslant$ and $\geqslant$ are replaced by $=$.

- In statistical practice one only needs to have $\overline{\mathbb{P}}(F \leqslant \varepsilon) \leqslant \varepsilon$ for a specific ε, e.g. 0.05, 0.01, ...

Translation to a risk aggregation problem

It boils down to calculate $\underline{Q}_\varepsilon(M_{r,K})$, or equivalently:

(i) for $r > 0$, aggregation of Beta risks

$$(\underline{Q}_\varepsilon(M_{r,K}))^r = \inf_{U_1,\dots,U_K \in \mathcal{U}} \left\{ Q_\varepsilon \left(\frac{1}{K} (U_1^r + \cdots + U_K^r) \right) \right\}$$

(ii) for $r = 0$, aggregation of exponential risks

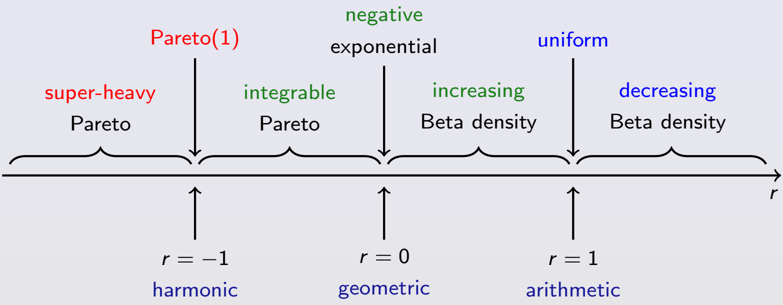
$$\log(\underline{Q}_\varepsilon(M_{r,K})) = \inf_{U_1,\dots,U_K \in \mathcal{U}} \left\{ Q_\varepsilon \left(\frac{1}{K} (\log U_1 + \cdots + \log U_K) \right) \right\}$$

(iii) for $r < 0$, aggregation of Pareto risks

$$(\underline{Q}_\varepsilon(M_{r,K}))^r = \sup_{U_1,\dots,U_K \in \mathcal{U}} \left\{ Q_{1-\varepsilon} \left(\frac{1}{K} (U_1^r + \cdots + U_K^r) \right) \right\}$$

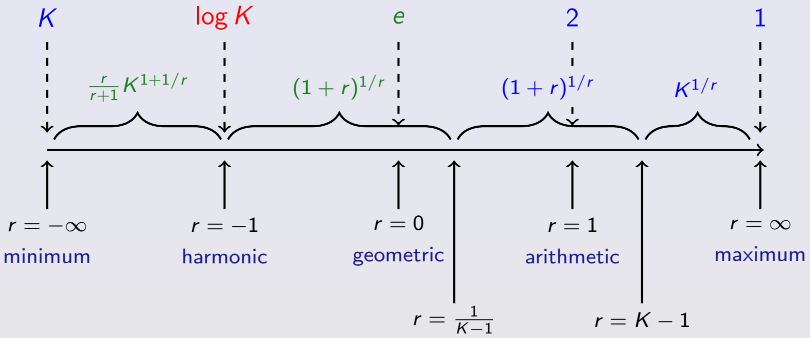
Translation to a risk aggregation problem

Breakdown of U^r (or $\log U$) for $r \in \mathbb{R}$



Main results summary

Constant multiplier in front of $M_{r,K}$



blue: precise; green: asymptotically precise; red: limit

Admissible p-merging functions

For p-merging functions F and G:

- F is symmetric if $F(\mathbf{p})$ is invariant under permutation of $\mathbf{p}$
- F is homogeneous if $F(\lambda \mathbf{p}) = \lambda F(\mathbf{p})$ for all $\lambda \in (0,1]$ and $\mathbf{p}$ with $F(\mathbf{p}) \leqslant 1$
- F dominates G if $F \leqslant G$
- F is admissible if it is not dominated by any other one

Properties

- Admissible $\Longrightarrow$ precise, lower semicontinuous, grounded
- Any p-merging function is dominated by an admissible one

Simes function

The Simes function

$$S_K(p_1, \dots, p_K) = \bigwedge_{k=1}^{K} \frac{K}{k} p_{(k)}$$

Theorem 1

The Simes function S_K is the minimum over all symmetric p-merging functions.

- S_K is not valid p-merging (only valid under some assumptions)
- $H_K = \ell_K S_K$ is precise
- S_K is a lower bound for any symmetric improvement

Simes function

Proof sketch.

- Take any symmetric p-merging function F and $\mathbf{p} = (p_1, \dots, p_K)$
- Let $\alpha := S_K(\mathbf{p})/K \implies p_{(k)} \geqslant k\alpha$ for each k
- Symmetry and monotonicity of $F \implies$

$$F(\mathbf{p}) = F(p_{(1)}, \dots, p_{(K)}) \geqslant F(\alpha, 2\alpha, \dots, K\alpha) =: \beta$$

- Let Π be the set of all permutations of $(\alpha, 2\alpha, \dots, K\alpha)$, and $\mu = \mathrm{U}(\Pi)$
- Take $(P_1, \dots, P_K) \sim K\alpha\mu + (1 - K\alpha)\delta_{(1,\dots,1)}$
- For each k, $P_k \sim \sum_{k=1}^{K} \alpha\delta_{k\alpha} + (1 - K\alpha)\delta_1 \implies P_k$ is a p-variable
- F is a p-merging function $\implies$

$$\beta \geqslant \mathbb{P}(F(P_1, \dots, P_K) \leqslant \beta) \geqslant \mathbb{P}((P_1, \dots, P_K) \in \Pi) = K\alpha$$

- $F(\mathbf{p}) \geqslant K\alpha = S_K(\mathbf{p}) \implies S_K$ dominates all symmetric p-merging functions
- $S_K = \bigwedge_{k=1}^{K} G_{k,K}$

Rejection regions of admissible p-merging functions

- The rejection region of a p-merging function F at level $\varepsilon \in (0,1)$:

$$R_\varepsilon(F) := \left\{ \mathbf{p} \in [0,\infty)^K : F(\mathbf{p}) \leqslant \varepsilon \right\}$$

- A collection $\{R_\varepsilon \subseteq [0,\infty)^K : \varepsilon \in (0,1)\}$ of increasing Borel lower sets induces a function $F : [0,\infty)^K \to [0,1]$ via

$$F(\mathbf{p}) = \inf\{\varepsilon \in (0,1) : \mathbf{p} \in R_\varepsilon\} \quad \text{with } \inf \varnothing = 1$$

- F is p-merging $\iff \mathbb{P}(\mathbf{P} \in R_\varepsilon) \leqslant \varepsilon$ for all $\varepsilon \in (0,1)$, $\mathbf{P} \in \mathcal{U}^K$
- F is homogeneous $\implies R_\varepsilon(F) = \varepsilon A$ for some $A \subseteq [0,\infty)^K$.

Rejection regions of admissible p-merging functions

Admissibility $\iff$ rejection region cannot be enlarged

- Precision of p-merging $\iff$ classic OT

$$\text{Compute } \sup_{\mathbf{P}\in\mathcal{U}^K} \mathbb{E}[\mathbb{1}_A(\mathbf{P})]$$

- Admissibility (or optimality) $\iff$ "reverse OT"

$$\text{Given } \sup_{\mathbf{P}\in\mathcal{U}^K} \mathbb{E}[\mathbb{1}_A(\mathbf{P})] \leqslant \varepsilon, \text{ find the largest } A \subseteq [0,1]^K$$

- Such A needs to be nested
- Techniques in OT can be very helpful

Rejection regions of admissible p-merging functions

Using e-values Vovk/W.'21

- A calibrator is a decreasing function $f : [0, \infty) \to [0, \infty]$ satisfying $f = 0$ on $(1, \infty)$ and $\int_0^1 f(x)\mathrm{d}x \leqslant 1$
- A calibrator f is admissible if it is upper semicontinuous, $f(0) = \infty$, and $\int_0^1 f(x)\mathrm{d}x = 1$

Representation theorems

Let Δ_K be the standard K-simplex and write $\mathbf{p} = (p_1, \dots, p_K)$.

Theorem 2

For any admissible homogenous p-merging function F, there exist $(\lambda_1, \dots, \lambda_K) \in \Delta_K$ and admissible calibrators $f_1, \dots, f_K$ such that

$$R_\varepsilon(F) = \varepsilon \left\{ \mathbf{p} \in [0,\infty)^K : \sum_{k=1}^{K} \lambda_k f_k(p_k) \geqslant 1 \right\} \text{ for } \varepsilon \in (0,1). \quad (1)$$

Conversely, for any $(\lambda_1, \dots, \lambda_K) \in \Delta_K$ and calibrators $f_1, \dots, f_K$, (1) induces a homogenous p-merging function.

Representation theorems

Proof sketch.

- For decreasing functions $g_1, \ldots, g_K$ on $[0, \infty)$, denote by

$$\left(\bigoplus_{k=1}^{K} g_k\right)(x_1, \ldots, x_K) := \sum_{k=1}^{K} g_k(x_k)$$

- Classic duality ($R_\varepsilon(F)$ is closed and F is precise)

$$\min\left\{\sum_{k=1}^{K}\int_0^1 g_k(x)\mathrm{d}x : \bigoplus_{k=1}^{K} g_k \geqslant \mathbb{1}_{R_\varepsilon(F)}\right\} = \max_{\mathbf{P}\in\mathcal{U}} \mathbb{P}(\mathbf{P} \in R_\varepsilon(F)) = \varepsilon$$

- Take $(g_1^\varepsilon, \ldots, g_K^\varepsilon)$ such that $\bigoplus_{k=1}^{K} g_k^\varepsilon \geqslant \mathbb{1}_{R_\varepsilon(F)}$ and $\sum_{k=1}^{K}\int_0^1 g_k^\varepsilon(x)\mathrm{d}x = \varepsilon$
- Choose g_k^ε to be non-negative and left-continuous
- Monotonicity

$$\max_{\mathbf{P}\in\mathcal{U}^K} \mathbb{P}(\mathbf{P} \in R_\varepsilon(F)) = \varepsilon \implies \max_{\mathbf{P}\in\mathcal{U}^K} \mathbb{P}(\varepsilon\mathbf{P} \in R_\varepsilon(F)) = 1$$

Representation theorems

Proof sketch (continued).

- Using duality again

$$\min\left\{\sum_{k=1}^{K}\frac{1}{\varepsilon}\int_0^{\varepsilon} g_k(x)\mathrm{d}x : \bigoplus_{k=1}^{K} g_k \geqslant \mathbb{1}_{R_\varepsilon(F)}\right\} = 1$$

$\Longrightarrow \sum_{k=1}^{K}\int_0^{\varepsilon} g_k^{\varepsilon}(x)\mathrm{d}x \geqslant \varepsilon \Longrightarrow g_k^{\varepsilon}(x) = 0$ for $x > \varepsilon$

- Define the set $A_\varepsilon := \{\mathbf{p} \in [0,\infty)^K : \sum_{k=1}^{K} g_k^{\varepsilon}(p_k) \geqslant 1\}$
- $\bigoplus_{k=1}^{K} g_k^{\varepsilon} \geqslant \mathbb{1}_{R_\varepsilon(F)} \Longrightarrow R_\varepsilon(F) \subseteq A_\varepsilon$
- By Markov's inequality,

$$\sup_{\mathbf{P}\in\mathcal{U}^K} \mathbb{P}\left(\bigoplus_{k=1}^{K} g_k^{\varepsilon}(\mathbf{P}) \geqslant 1\right) \leqslant \sup_{P\in\mathcal{U}} \sum_{k=1}^{K} \mathbb{E}[g_k^{\varepsilon}(P)] = \varepsilon$$

- Define a function F' with rejection region $R_\delta(F') = \delta\varepsilon^{-1}A_\varepsilon$ for $\delta \in (0,1)$
- F' is a valid homogeneous p-merging function and $F' \leqslant F$

Representation theorems

Proof sketch (continued).

- Admissibility of $F \implies F = F'$, thus

$$R_\varepsilon(F) = A_\varepsilon = \varepsilon\left\{\mathbf{p} \in [0,\infty)^K : \sum_{k=1}^K g_k^\varepsilon(\varepsilon p_k) \geqslant 1\right\} \quad \text{for each } \varepsilon \in (0,1)$$

- $\varepsilon^{-1} R_\varepsilon(F) = \varepsilon^{-1} A_\varepsilon$ does not depend on $\varepsilon \in (0,1)$
- For a fixed $\varepsilon \in (0,1)$ and each k, let $\lambda_k := \varepsilon^{-1}\int_0^\varepsilon g^\varepsilon(x)\mathrm{d}x$ and $f_k : (0,\infty) \to \mathbb{R}$, $x \mapsto g_k^\varepsilon(\varepsilon x)/\lambda_k$ (if $\lambda_k = 0$, then let $f_k := 1$), and further set $f_k(0) = \infty$
- For each k with $\lambda_k \neq 0$,

$$\int_0^1 f_k(x)\mathrm{d}x = \frac{\int_0^1 \varepsilon g_k^\varepsilon(\varepsilon x)\mathrm{d}x}{\int_0^1 g_k^\varepsilon(x)\mathrm{d}x} = \frac{\int_0^\varepsilon g_k^\varepsilon(x)\mathrm{d}x}{\int_0^1 g_k^\varepsilon(x)\mathrm{d}x} = 1$$

$\implies f_k$ is an admissible calibrator

- Converse statement: Markov's inequality

Representation theorems

Theorem 3

For any F that is admissible within the family of homogenous symmetric p-merging functions, there exists an admissible calibrator f such that

$$R_\varepsilon(F) = \varepsilon \left\{ \mathbf{p} \in [0,\infty)^K : \frac{1}{K}\sum_{k=1}^{K} f(p_k) \geqslant 1 \right\} \text{ for } \varepsilon \in (0,1). \quad (2)$$

Conversely, for any calibrator f, (2) induces a homogenous symmetric p-merging function.

- We say f induces F if (2) holds
- Converse: not true; calibrator: not unique

Examples

Example 1

The p-merging function $F := G_{k,K}$, $k \in \{1, \ldots, K\}$, is induced by the calibrator $f : x \mapsto (K/k)\mathbb{1}_{\{x \in [0,k/K]\}}$.

Example 2

In case $K = 2$, the p-merging function

$F : \mathbf{p} \mapsto 2M_{1,2}(\mathbf{p})\mathbb{1}_{\{\min(\mathbf{p})>0\}}$ is induced by the admissible calibrator $f : x \mapsto (2 - 2x)_+$ on $(0, \infty)$ and $f(0) = \infty$.

- F is the zero-adjusted version of the arithmetic merging function
- F is not admissible (dominated by Bonferroni)

Connection to joint mixability

A necessary and sufficient condition for a calibrator f to induce a precise p-merging function via (1) is

$$\mathbb{P}\left(\frac{1}{K}\sum_{k=1}^{K} f(P_k) = 1\right) = 1 \quad \text{for some } P_1, \dots, P_K \in \mathcal{U}. \qquad (3)$$

- $\Longrightarrow$ Joint mixability (f specifies the quantile) Wang/W.'11'16
- Difficult to check for a given f in general
- For a convex f, (3) holds if and only if $f \leqslant K$ on $(0, 1]$
- Weaker than admissibility

Connection to e-tests

Connecting a p-test to an e-test: For a fixed $\varepsilon \in (0,1)$, and an admissible p-merging function F:

$$\mathbf{p} \in R_\varepsilon(F) \iff \sum_{k=1}^{K} \lambda_k f_k\left(\frac{p_k}{\varepsilon}\right) \geqslant 1 \iff \sum_{k=1}^{K} \lambda_k f'_k(p_k) \geqslant \frac{1}{\varepsilon},$$

where $f'_k(x) := f_k(x/\varepsilon)/\varepsilon$. Four steps:

(i) Calibrate all p-values to e-values via admissible calibrators $f'_1, \dots, f'_n$

(ii) Merge the e-values via a weighted arithmetic average

(iii) Calibrate the merged e-value to a p-value via $e \mapsto 1/e$

(iv) Use the resulting p-value and the threshold ε for the test

Sufficient conditions for admissibility

Theorem 4

Suppose that an admissible calibrator f is strictly convex or strictly concave on $(0,1]$, $f(0+) \in (K/(K-1), K]$, and $f(1) = 0$. The p-merging function induced by f is admissible.

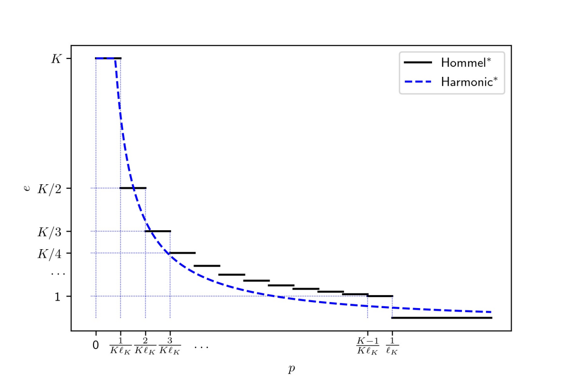
- Proof based on joint mixability
- Open question: can strict convexity be reduced to convexity?
- Conditions of this type are not necessary
- Admissibility holds true also for

$$g : x \mapsto f\left(\frac{x-\eta}{1-K\eta}\right) \mathbb{1}_{\{x\in(\eta,1-(K-1)\eta]\}} + K\mathbb{1}_{\{x\in[0,\eta]\}}$$

Hommel's function

Define the Hommel* calibrator f by

$$f : x \mapsto \frac{K \mathbb{1}_{\{\ell_K x \leqslant 1\}}}{\lceil K \ell_K x \rceil}.$$



Hommel's function and the O-family

Theorem 5

The p-merging function $H_K \wedge 1$ is dominated (strictly if $K \geqslant 4$) by the p-merging function H_K^* induced by the Hommel calibrator f,*

$$R_\varepsilon(H_K^*) = \varepsilon \left\{ \mathbf{p} \in [0,\infty)^K : \frac{1}{K} \sum_{k=1}^{K} f(p_k) \geqslant 1 \right\}, \quad \varepsilon \in (0,1).$$

Moreover, H_K^* is always admissible among symmetric p-merging functions, and it is admissible if K is not a prime number.

- Primality appears in the proof due to factoring the set $[K]$
- H_K^* is not admissible for $K = 2, 3$ (we guess also 5)

Hommel's function and the O-family

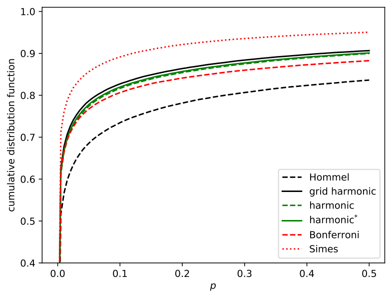
- The Bonferroni method is admissible
- Members $G_{k,K}$ of the O-family are admissible after truncation at 1 except for $k = K$
- Members $F_{r,K}$ of the M-family are not admissible except for $r = -\infty$
- $F_{r,K}$ can be strictly improved to $F^*_{r,K}$
- $F^*_{r,K}$ are admissible unless $r = 1 \Leftarrow$ non-strict convexity
- $F^*_{-1,K}$ is similar to H^*_K

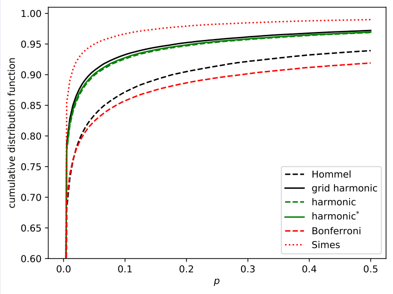
1. Merging p-values
2. Admissibility
3. Rejection regions
4. Constructing admissible p-merging functions
5. Simulation results and summary

Simulation results

- Correlated z-tests
- $K = 10^6$ observations from $\mathrm{N}(\mu, 1)$
- Pairwise correlation: 0.9
- Last observation: -0.9 correlation with all others
- $\mu = 0$ for null and $\mu = -5$ for alternative
- K_1 observations are drawn from the alternative; the rest from the null
- P-values are $\Phi(x)$
- $F_{-\infty,K}$ (Bonferroni); H_K (Hommel); $F_{-1,K}$ (harmonic); $F^*_{-1,K}$ (harmonic*'); H^*_K (grid harmonic'); S_K (Simes),

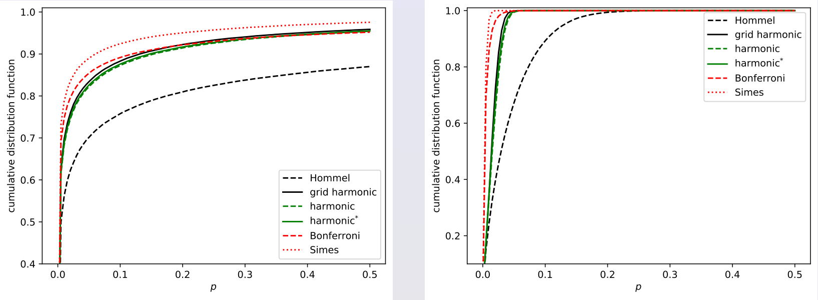
Simulation results





$K_1 = 10^3$ (left panel) and $K_1 = 10^4$ (right panel)

Simulation results



$K_1 = 10^5$ with correlation 0.5 (left panel) and 0 (right panel) in place of 0.9

Simulation results

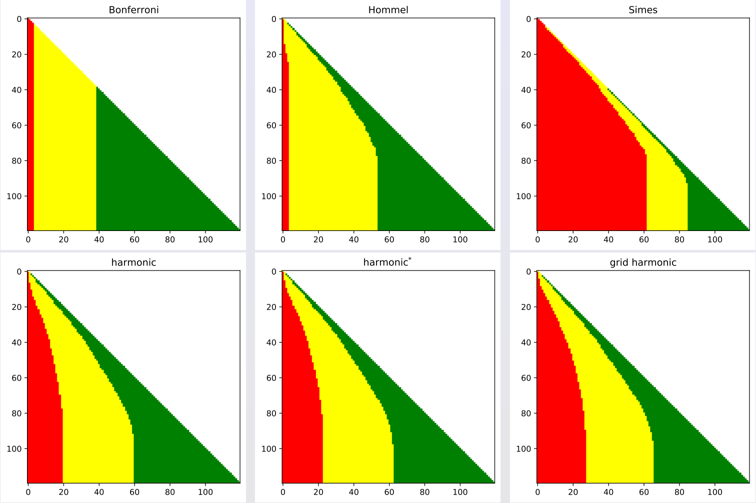
- GWGS discovery matrix Genovese/Wasserman'04; Goeman/Solari'11
- $\mathrm{DM}_{i,j}$: a p-value for testing "there are less than j true discoveries among the i rejected hypotheses"
- $\mathcal{N} \subseteq [K]$: nulls
- Jointly validity: for each $\alpha \in (0,1)$,

$$\mathbb{P}\left(\exists (i,j) \in D_\alpha : \#(R_i \setminus \mathcal{N}) < j\right) \leqslant \alpha$$

where R_i is the set of i hypotheses with smallest p-values and

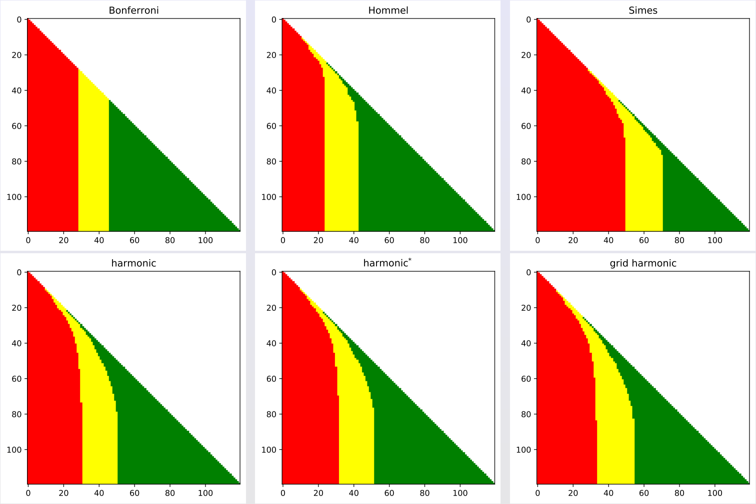
$$D_\alpha = \{(i,j) : \mathrm{DM}_{i,j} \leqslant \alpha\}$$

Simulation results



GWGS discovery matrices with correlation 0.9 and significance levels 1% and 5%

Simulation results



GWGS discovery matrices with correlation 0.5 and significance levels 1% and 5%

Summary

Unsolved mathematical questions

- Homogeneity assumption in the representation results
- Strict convexity of calibrator in the sufficient condition for admissibility and $F^*_{-1,K}$
- Whether H^*_K is inadmissible for all prime K

More applications of multi-marginal OT and reverse OT?

Thank you

Thank you for your kind attention

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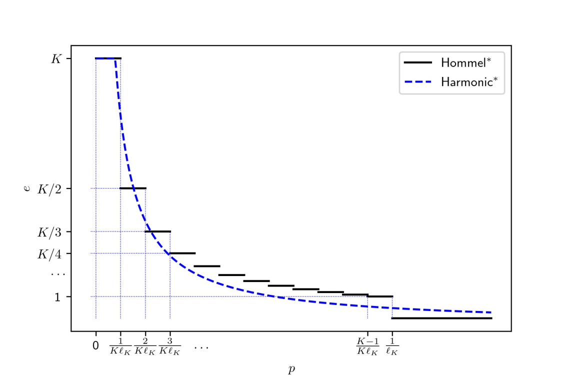
- Vovk/W., Combining p-values via averaging — Biometrika, 2020
- Vovk/Wang/W., Admissible ways of merging p-values under arbitrary dependence — Annals of Statistics, 2022

Hommel's function and the O-family

Define the Hommel* calibrator f by

$$f : x \mapsto \frac{K \mathbb{1}_{\{\ell_K x \leqslant 1\}}}{\lceil K \ell_K x \rceil}.$$



Hommel's function and the O-family

Theorem 6

The p-merging function $H_K \wedge 1$ is dominated (strictly if $K \geqslant 4$) by the p-merging function H_K^* induced by the Hommel calibrator f,*

$$R_\varepsilon(H_K^*) = \varepsilon \left\{ \mathbf{p} \in [0,\infty)^K : \frac{1}{K}\sum_{k=1}^{K} f(p_k) \geqslant 1 \right\}, \quad \varepsilon \in (0,1).$$

Moreover, H_K^* is always admissible among symmetric p-merging functions, and it is admissible if K is not a prime number.

Hommel's function and the O-family

Proof sketch.

- Recall: $H_K(\mathbf{p}) = \ell_K \bigwedge_{k=1}^K \frac{K}{k} p_{(k)}$ where $\ell_K = \sum_{i=1}^K \frac{1}{k}$.
- Induced by the calibrator $f \implies H_K^*$ is a p-merging function.
- Verify $H_K \geqslant H_K^*$: $H_K(\mathbf{p}) \leqslant \varepsilon \implies$ there exists m such that $K\ell_K p_{(m)} \leqslant \varepsilon$ $\implies \#\{k : K\ell_K p_k/m \leqslant \varepsilon\} \geqslant m \implies$

$$\sum_{k=1}^K \frac{\mathbb{1}_{\{\ell_K p_k \leqslant \varepsilon\}}}{\lceil K\ell_K p_i/\varepsilon \rceil} \geqslant \sum_{k=1}^K \frac{1}{m} \mathbb{1}_{\{K\ell_K p_k/\varepsilon \leqslant m\}} = \frac{1}{m}\#\{k : K\ell_K p_k/m \leqslant \varepsilon\} \geqslant 1$$

$\implies R_\varepsilon(H_K) \subseteq R_\varepsilon(H_K^*) \implies H_K \geqslant H_K^*$.
- Check $H_K = H_K^*$ if and only if $K \leqslant 3$.

Hommel's function and the O-family

Proof sketch (continued).

- Suppose H_K^* is not admissible among symmetric p-merging functions.
- There exists a calibrator g satisfying

$$\left\{\mathbf{p} \in [0,\infty)^K : \frac{1}{K}\sum_{k=1}^{K} f(p_k) \geqslant 1\right\} \subsetneq \left\{\mathbf{p} \in [0,\infty)^K : \frac{1}{K}\sum_{k=1}^{K} g(p_k) \geqslant 1\right\}.$$

- Denote by $\tau := 1/(K\ell_K)$. For $x \in (0, K\tau]$, set $p_1 = \cdots = p_m = x$ and $p_{m+1} = \cdots = p_K > 1$, where $m := \lceil \tau x \rceil$.
- $f(x) = K/m \Longrightarrow \sum_{k=1}^{K} f(p_k) = K \Longrightarrow K \leqslant \sum_{k=1}^{K} g(p_k) = mg(x) \Longrightarrow g(x) \geqslant K/m = f(x)$.
- $\int_0^{K\tau} g(x)\mathrm{d}x \geqslant \int_0^{K\tau} f(x)\mathrm{d}x = 1 \Longrightarrow g = f$ almost everywhere on $[0,1]$.
- f is left-continuous $\Longrightarrow g \leqslant f$, a contradiction.
- The admissibility statement for non-prime K is much more complicated.

Hommel's function and the O-family

- $S_K \leqslant H_K^* \leqslant H_K \implies 1/\ell_K \leqslant H_K^*/H_K \leqslant 1$
- H_K^* may not be admissible for a prime K

Example 3

In case $K = 2$, $H_2^* = H_2 : (p_1, p_2) \mapsto (3p_{(1)}) \wedge (\frac{3}{2}p_{(2)})$ is strictly dominated by $F : (p_1, p_2) \mapsto (3p_1) \wedge (\frac{3}{2}p_2)$, which is a (non-symmetric) p-merging function because

$$\mathbb{P}(F(P_1, P_2) \leqslant \alpha) \leqslant \mathbb{P}\left(P_1 \leqslant \frac{1}{3}\alpha\right) + \mathbb{P}\left(P_2 \leqslant \frac{2}{3}\alpha\right) \leqslant \alpha.$$

Hommel's function and the O-family

Theorem 7

The p-merging function $\mathbf{p} \mapsto G_{k,K}(\mathbf{p}) \wedge \mathbb{1}_{\{\min(\mathbf{p})>0\}}$ *is admissible for* $k = 1, \dots, K-1$*, and it is admissible among symmetric p-merging functions for* $k = K$*.*

The M-family

- $F_{r,K} = (b_{r,K} M_{r,K}) \wedge 1$
- For $r \neq \{-1, 0\}$ and $r < 1/(K-1)$, denote by c_r the unique number $c \in (0, 1/K)$ solving the equation

$$\frac{(K-1)(1-(K-1)c)^r + c^r}{K} = \frac{(1-(K-1)c)^{r+1} - c^{r+1}}{(r+1)(1-Kc)}$$

- c_{-1} and c_0 are limits of c_r
- Set $c_r := 0$ for $r \geqslant 1/(K-1)$
- Write $d_r := 1 - (K-1)c_r$

The M-family

Proposition 1

For $K \geqslant 3$ and $r \in (-\infty, \frac{1}{K-1})$,

$$b_{r,K} = 1/M_{r,K}(c_r, d_r, \dots, d_r).$$

- If $r < s$ and $rs > 0$, then

$$K^{1/s-1/r} b_{r,K} \leqslant b_{s,K} \leqslant b_{r,K}$$

The M-family

For $r < 0$:

- Rejection region

$$R_\varepsilon(F_{r,K}) = \varepsilon\left\{\mathbf{p} \in [0,\infty)^K : \frac{\sum_{k=1}^K p_k^r}{c_r^r + (K-1)d_r^r} \geqslant 1\right\}$$
$$= \varepsilon\left\{\mathbf{p} \in [0,\infty)^K : \sum_{k=1}^K \frac{p_k^r - d_r^r}{c_r^r - d_r^r} \geqslant 1\right\}.$$

- Define a calibrator

$$f_r : x \mapsto K\left(\frac{x^r - d_r^r}{c_r^r - d_r^r} \wedge 1\right)_+ .$$

- f_r is strictly convex on $[c_r, d_r]$.

The M-family

Let $F^*_{r,K}$ be the p-merging function induced by f_r, i.e.,

$$R_\varepsilon(F^*_{r,K}) = \varepsilon \left\{ \mathbf{p} \in [0,\infty)^K : \sum_{k=1}^{K} \left(\frac{p_k^r - d_r^r}{c_r^r - d_r^r} \right)_+ \geqslant 1 \right\}, \ \varepsilon \in (0,1).$$

- $R_\varepsilon(F_{r,K}) \subset R_\varepsilon(F^*_{r,K})$
- $F^*_{r,K}$ is admissible

The M-family

Theorem 8

For $K \geqslant 3$ and $r \in (-\infty, K-1)$, $F_{r,K}$ is strictly dominated by the p-merging function $F^*_{r,K}$ defined via, for $\mathbf{p} \in (0,\infty)^K$ and $\varepsilon \in (0,1)$,

$$F^*_{r,K}(\mathbf{p}) \leqslant \varepsilon \iff F_{r,K}(\mathbf{p} \wedge (\varepsilon d_r \mathbf{1})) \leqslant \varepsilon \ \ \text{or} \ \ \min(\mathbf{p}) = 0.$$

Moreover, $F^*_{r,K}$ is admissible unless $r = 1$.

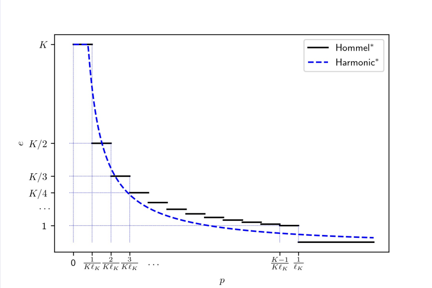
The M-family

Recall

$$f_{-1} : x \mapsto K\left(\frac{x^{-1} - d_{-1}^{-1}}{c_{-1}^{-1} - d_{-1}^{-1}} \wedge 1\right)_+ ;$$

the Hommel* calibrator

$$f : x \mapsto \frac{K\mathbb{1}_{\{\ell_K x \leqslant 1\}}}{\lceil K\ell_K x \rceil}.$$



- When taking values in $(0, K)$:

$$f_{-1}(x) = a/x - b \quad \text{vs} \quad f(y) = a'/\lceil b'y \rceil$$

The M-family

Proposition 2

For $K \geqslant 3$ *and* $\mathbf{p} \in [0,\infty)^K$, *we have, if* $r \in (-\infty, 1/(K-1))$,

$$F^*_{r,K}(\mathbf{p}) = \left(\bigwedge_{m=1}^{K} \frac{M_{r,m}(p_{(1)},\dots,p_{(m)})}{M_{r,m}(c_r, d_r, \dots, d_r)} \right) \wedge 1,$$

and, if $r \in [1/(K-1), K-1)$, *with the convention* $\cdot/0 = \infty$,

$$F^*_{r,K}(\mathbf{p}) = \left(\bigwedge_{m=1}^{K} \frac{M_{r,m}(p_{(1)},\dots,p_{(m)})}{(1 - \frac{rK}{(r+1)m})_+} \right) \wedge \mathbb{1}_{\{p_{(1)}>0\}}.$$

The M-family

Proposition 3

For $r < s$, $K \geqslant 2$ and $a, b > 0$, the following statements hold.

(i) $aM_{r,K} \leqslant bM_{s,K}$ *if and only if* $a \leqslant b$.

(ii) $bM_{s,K} \leqslant aM_{r,K}$ *if and only if* $rs > 0$ *and* $aK^{-1/r} \geqslant bK^{-1/s}$.

Proposition 4

Suppose $r \neq s$. *If* $K = 2$, $F_{r,K} \geqslant F_{s,K}$ *if and only if* $1 \leqslant r < s$ *or* $s < r \leqslant 1$. *If* $K \geqslant 3$, $F_{r,K} \geqslant F_{s,K}$ *if and only if* $K - 1 \leqslant r < s$.

Magnitude of improvement

Proposition 5

For $K \geqslant 3$, we have

$$\inf_{\mathbf{p}>\mathbf{0}} \frac{F^*_{1,K}(\mathbf{p})}{F_{1,K}(\mathbf{p})} = \inf_{\mathbf{p}>\mathbf{0}} \frac{F^*_{0,K}(\mathbf{p})}{F_{0,K}(\mathbf{p})} = 0, \quad \inf_{\mathbf{p}>\mathbf{0}} \frac{F^*_{-1,K}(\mathbf{p})}{F_{-1,K}(\mathbf{p})} = 1 - (K-1)c_{-1},$$

and

$$\min_{\mathbf{p}>\mathbf{0}} \frac{H^*_K(\mathbf{p})}{H_K(\mathbf{p})} = \min\left\{ t > 0 : \sum_{k=1}^{K} \frac{\mathbb{1}_{\{t \geqslant k/K\}}}{\lceil k/t \rceil} \geqslant 1 \right\} =: \gamma_K.$$

Moreover, $c_{-1} \sim 1/(K \log K)$ and $\gamma_K \sim 1/\log K$ as $K \to \infty$.

Magnitude of improvement

- $F^*_{-1,K}$ improves $F_{-1,K}$ only by a factor $1 - 1/\log K \sim 1$
- H^*_K can improve H_K by a significant factor of $1/\log K$
- $H^*_K(\mathbf{p})/H_K(\mathbf{p}) = \gamma_K$ is attained by $\mathbf{p} = (\alpha, 2\alpha, \cdots, K\alpha)$ for $\alpha \in (0, 1/K\ell_K]$.
- Since $H_K = \ell_K S_K$ and

$$\gamma_K \sim 1/\log K \sim 1/\ell_K,$$

H^*_K performs similarly to the Simes function S_K for some values of $\mathbf{p}$ above