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Article

Meta-Analysis of Genuine and Fake *p*-Values

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Abstract: For Sir Ronald Fisher, it is important to consistently obtain significant *p*-values to support an experimental hypothesis. So, replicating experiments to obtain independent *p*-values is a legitimate and desirable research practice. Several simple statistics have been proposed to meta-analyze *p*-values, all assuming that they are genuine, i.e. observations from independent standard Uniform random variables. But, as publication bias favors the studies that report "significant" *p*-values, when a $p > 0.05$ is obtained for the outcome of an experiment, some researchers will "fall into temptation" and decide to replicate the experiment in the hope of getting a smaller second *p*-value, ideally a significant one. Consequently, if the smallest of two *p*-values is reported, this is a Beta(1,2) distributed "fake" *p*-value, not a uniformly distributed genuine *p*-value. This is an unacceptable scientific research practice, and moreover the detection of fake *p*-values is unpractical. Even when it is possible, the analytic results to accommodate their existence in combined tests are cumbersome. For an informed decision, inclusive when the presence of fake *p*-values in a sample of *p*-values to be meta-analyzed is probable, tables with simulated critical values for the usual combined testing are supplied. This will also allow comparisons to be made between several combined tests.

Keywords: combined *p*-values; fake *p*-values; Mendel random variables; meta-analysis

1. Introduction

The use of *p*-values, defined as the probability of obtaining a result equal to or more extreme than what was actually observed, under a null hypothesis of no effect or no difference, is generally credited to Pearson [1], although Kennedy-Shaffer [2] extensively lists its previous use, tracing it back to Arbuthnott [3].

Fisher [4,5] popularized the concept, which plays a central role in his theory of significance testing. According to Fisher [6], a *p*-value should function as an informal index to evaluate the discrepancy between the data and the hypothesis under investigation. This closely matches the meaning of significance of Edgeworth [7], who considered a difference to be "significant and not accidental" if it was unlikely to have resulted from chance alone. On the other hand, a *p*-value smaller than 0.05, considered by Fisher [4,5] to be a threshold for a significant value, only hints that the experiment should be repeated. If subsequent studies also generate significant *p*-values, then it is fair to conclude that the observed effects are unlikely to result from chance alone. In this regard, Fisher [8] states that "*A scientific fact should be regarded as experimentally established only if a properly designed experiment rarely fails to give this* [P=0.05] *level of significance*". Therefore, a significant *p*-value just indicates that further experiments should be carried out.

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Obtaining significant p-values raises the issue of reproducibility (cf. Utts [9], Greenwald et al. [10], or Colquhoun [11]), which in turn requires that the p-values obtained from the repeated experiments must be summarized into a combined p-value. Being well-aware of this, Fisher [6] was one of the first to meta-analyze p-values. Note, however, that a combined p-value is not, in general, a p-value in the strict sense of the definition (Vovk and Wang [12]).

Taking a different approach, Neyman and Pearson [13,14] developed a theory for hypothesis testing. Significance testing and hypothesis testing were in Fisher's [15] and E. Pearson's [16] points of view incompatible, but they have become so intertwined that they are regarded by most users as part of a single and coherent approach to statistical inference (Lehman [17]). The work of Cox et al. [18] is an excellent critical overview of significance testing, with stimulating discussions and reply.

Despite the original Neyman-Pearson standpoint that hypothesis testing limits the number of mistaken conclusions in the long run, the discomforting price of abandoning the ability to measure evidence and assess the truth from a single experiment was soon forgotten in favor of the methodology of using p-values. In other words, taking for granted that each study originates conclusions with certain error rates instead of adding evidence to that provided by other sources and other studies. This clearly generated plenty of bad science, raising doubts on many scientific papers, with p-values adding nothing to true scientific knowledge (Ioannidis [19,20]).

The editorials in *The American Statistician* vol. 70 (Wasserstein and Lazar [21]) and vol. 73 (Wasserstein et al. [22]), introducing issues discussing the dangers of abuse when using p-values and significance testing, summarize, to a certain extent, the fierce debate on the matter and have originated a warning on p-values in *Nature* (Baker [23]). To cite some highlights of the debate, while Goodman [24,25] and Kühberger et al. [26] warn on the fallacies and misconceptions of p-values, Benjamini [27] claims that the abuse is not the fault of the p-values, and Greenland [28] states that valid p-values behave exactly as they should. Critics of the p-values question why is it so hard to get rid of significance testing and p-values (Goodman [29]; Halsey [30]), or to put forward the need to complement p-values with effect size, sample size, or Bayes factors (Colquhoun [31]; Goodman et al. [32]; Rougier [33]), or even to recommend lowering the significance threshold to 0.005, cf. Di Leo and Sardanelli [34]. Murdoch et al. [35] emphasize that p-values are random variables and the innovating paper of Fraser [36] argues that the p-value function should be used instead of p-values.

The heart of the matter is that a single p-value should not be used as a sound basis for decision. As already mentioned, a low p-value is just an indication that the experiment should be repeated, and that only consistently obtaining low p-values uphold the conviction that the null hypothesis should be rejected, as both Fisher and Neyman and Pearson originally defended, although on opposite sides when it comes to statistical inference understanding. Therefore, replicating to obtain independent p-values in such contexts is legitimate, even desirable, and the resulting combined p-values are relevant for decision making under uncertainty.

The classical test statistics $T(P_1, \ldots, P_n)$ for combining p-values assume that the p-values are all genuine (or *bona fide*), i.e. that under a null hypothesis the P_k's are independent and identically distributed standard Uniform random variables. The combination of genuine p-values either relies on algebraic properties of Uniform random variables (order statistics, sums, products), or on transformations of standard Uniform random variables. In Section 2, a preliminary discussion of combining genuine p-values is undertaken.

However, the assumption that all p_k's are genuine can be false, namely since the bias that results from some publication policies is the source of selective reporting of scientific findings. The greater opportunity researchers have to publish significant results than non-significant ones originates a so-called file drawer problem, thus exacerbating the publication bias phenomenon, which is discussed in Section 3. In addition to censoring p-values above traditional thresholds, publication bias can increase the temptation to replicate experiments in the hope of obtaining significant results.

Such scientific malpractice originates the report of fake p-values, as described in Section 4, where Mendel random variables, inspired by the Mendel-Fisher controversy, discussed in Fisher [37],

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Franklin et al. [38], and Pires and Branco [39], are introduced. While it is acceptable to think that the replication of p-values may strengthen the confidence in the idea that observed effects are unlikely to result from chance alone, the replication of p-values with the sole purpose of keeping only the most favorable ones is methodologically wrong, even possibly fraud, as Fisher [37] hinted in his discussion of Mendel's results. The new trend of retaining only the p-values less than some specified cut-off value (Zaykin [40]; Neuhäuser and Bretz [41]; Zhang et al. [42]), or to use the product of the most significant p-values (Dudbridge and Koeleman [43]), have a similar effect of favoring the rejection of an overall null hypothesis, which in our opinion biases the conclusions. An extension of Deng and George's [44] contraction, considered in *Subsection 4.1*, leads to ways of testing independence *versus* correlated P-values, in *Subsection 4.2*. In *Subsection 4.3*, the combination of genuine and fake p-values is investigated. This is a simple issue using Tippett's [45] minimum method, but the analytical results for other ways of combining p-values, exemplified in *Subsection 4.3*, are complex to work with, even in the simplest case of just one fake p-value being present, making them useless from a practical point of view.

In these complex settings, simulation is a good tool for obtaining estimates of critical values for combined tests. Tables are supplied as Supplementary Materials, and in Section 5 their usefulness for an overall informed decision is illustrated. Section 6 summarizes the main findings with a comparison of different scenarios.

2. Combining Genuine p-Values

Let us assume that the p-values p_k, $1 \leq k \leq n$, are known for testing H_{0k} *versus* H_{Ak}, $k = 1, \ldots, n$, in n independent studies on some common topic, and that the objective is to achieve a decision on the overall problem H_0^*: all of the H_{0k} are true *versus* H_A^*: some of the H_{Ak} are true.

As there are many different ways in which H_0^* can be false, selecting an appropriate test is in general unfeasible. On the other hand, combining the available p_k's so that $T(p_1, \ldots, p_n)$ is the observed value of a random variable whose sampling distribution under H_0^* is known is a simple issue, since under H_0^*, $\boldsymbol{p} = (p_1, \ldots, p_n)$ is the observed value of a random vector $\boldsymbol{P} = (P_1, \ldots, P_n)$ with independent Uniform$(0,1)$ univariate margins, i.e. genuine p-values.

The classical statistics $T(P_1, \ldots, P_n)$ for combining independent genuine p-values use:

— transformations of the $P_k \sim Uniform(0,1)$ random variables, namely $-2 \ln P_k \sim \chi^2_2$, $\Phi^{-1}(P_k) \sim Gaussian(0,1)$, where Φ is the standard Gaussian cumulative distribution function, or $\ln\left(\frac{P_k}{1-P_k}\right) \sim Logistic(0,1)$ (*Subsection 2.1*), or
— sums, products and order statistics of $P_1, \ldots, P_n$, namely the Pythagorean harmonic, geometric and arithmetic means (*Subsection 2.2*).

Note, however, that there are good reasons to believe that not all p_k's are genuine, either because some of the H_{Ak} are true, or because there is truncation (Zaykin et al. [40]; Neuhäuser and Bretz [41]; Zhang et al. [42]) or censoring due to publication bias (two issues that will be addressed in Section 3), or even because of poor scientific methodology (possibly fraud) leading to the generation of fake p-values, as described in Section 4 in the context of the Mendel-Fisher controversy (Fisher [37]; Franklin et al. [38]; Pires and Branco [39]) and Mendel random variables.

2.1. Combining Transformed Genuine p-Values

In 1932, Fisher [6] (Section 21.1), from the fact that $-2 \ln P_k \sim \chi^2_2$ when $P_k \sim Uniform(0,1)$, used the statistic

$$T_F(P_1, \ldots, P_n) = -2 \sum_{k=1}^{n} \ln P_k \big| H_0^* \sim \chi^2_{2n}.$$

Thus, the overall hypothesis H_0^* is rejected at a significance level α if $-2\sum_{k=1}^{n} \ln p_k > \chi^2_{2n,1-\alpha}$, where $\chi^2_{m,q}$ denotes the q-th quantile of the chi-square distribution with m degrees of freedom.

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In what concerns the use of Gaussian transformed p-values, Stouffer et al. [46] used as a test statistic

$$T_S(P_1,\ldots,P_n) = \sum_{k=1}^{n} \frac{\Phi^{-1}(P_k)}{\sqrt{n}}.$$

As

$$\sum_{k=1}^{n} \frac{\Phi^{-1}(P_k)}{\sqrt{n}} \Big| H_0^* \sim Gaussian(0,1),$$

H_0^* is rejected at a significance level α if $\left|\sum_{k=1}^{n} \frac{\Phi^{-1}(p_k)}{\sqrt{n}}\right| > z_{1-\alpha}$, with z_q denoting the q-th quantile of the standard Gaussian distribution.

Since $[\Phi^{-1}(P_k)]^2 \big| H_0^* \sim \chi_1^2$, an alternative to Fisher's method is to use the statistic

$$T_C(P_1,\ldots,P_n) = \sum_{k=1}^{n} \left[\Phi^{-1}(P_k)\right]^2 \Big| H_0^* \sim \chi_n^2,$$

as observed in Chen [47]. Note that Liu et al. [48] and Cinar and Viechtbauer [49] prefer an inverse chi-square method, more precisely,

$$T_L(P_1,\ldots,P_n) = \sum_{k=1}^{n} F_{\chi_1^2}^{-1}(1-P_k),$$

where $F_{\chi_1^2}^{-1}$ is the inverse cumulative distribution function of the chi-square distribution with one degree of freedom.

Mudholkar and George [50] propose the use of the statistic

$$T_{MG}(P_1,\ldots,P_n) = -\sum_{k=1}^{n} \ln\left(\frac{P_k}{1-P_k}\right),$$

based on the logit transformation $\ln\left(\frac{P_k}{1-P_k}\right) \big| H_0^* \sim Logistic(0,1)$, and which combines together $1-P_k$ and P_k.

Due to the approximation

$$T_{MG}^* = -\frac{\sum_{k=1}^{n} \ln\left(\frac{P_k}{1-P_k}\right)}{\sqrt{\frac{n\,\pi^2(5n+2)}{3(5n+4)}}} \approx t_{5n+4},$$

H_0^* is rejected at significance level α if

$$t_{MG}^* = \frac{\left|\sum_{k=1}^{n} \ln\left(\frac{p_k}{1-p_k}\right)\right|}{\sqrt{\frac{n\,\pi^2(5n+2)}{3(5n+4)}}} > t_{5n+4,1-\alpha},$$

where $t_{m,q}$ represents the q-th quantile of Student's t-distribution with m degrees of freedom. Or alternatively, as

$$\ln\left(\frac{P_k}{1-P_k}\right) \Big| H_0^* \approx Gaussian\left(0, \tfrac{\pi^2}{3}\right),$$

H_0^* is rejected if $-\sum_{k=1}^{n} \ln\left(\frac{p_k}{1-p_k}\right) \Big/ \pi\sqrt{\frac{n}{3}} > z_{1-\alpha}$.

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2.2. *Should You Mean It?*

An interesting way of combining p-values is to consider an average-like function

$$M_{\Psi,n}(P_1,\ldots,P_n) = \Psi^{-1}\left(\frac{\sum_{k=1}^{n}\Psi(P_k)}{n}\right), \tag{1}$$

where $\Psi : [0,1] \to [-\infty,\infty]$ is a continuous strictly monotonic function (Kolmogorov [51]).

If in (1), $\Psi(p) = p^r$, $r \in [-\infty,\infty]$, this is the so-called mean of order r

$$T_r(P_1,\ldots,P_n) = M_{r,n}(P_1,\ldots,P_n) = \left(\frac{\sum_{k=1}^{n}P_k^r}{n}\right)^{1/r}, \tag{2}$$

with the understanding that the case $r = 0$ is the limit as $r \to 0$, i.e.

$$T_0(P_1,\ldots,P_n) = M_{0,n}(P_1,\ldots,P_n) = \exp\left(\frac{\sum_{k=1}^{n}\ln P_k}{n}\right) = \left(\prod_{k=1}^{n}P_k\right)^{1/n}.$$

If $r_1 \le r_2$, then $T_{r_1}(p_1,\ldots,p_n) \le T_{r_2}(p_1,\ldots,p_n)$ (Theorem 16 in Hardy et al. [52]). The means of order r for combining p-values are invariant for any permutation of $p_1,\ldots,p_n$, which is a useful property for the simulations carried out to obtain the results in **Section 5**.

The most used means of order r, defined in (2), are the Pythagorean means, namely

— Harmonic mean:

$$T_{-1}(P_1,\ldots,P_n) = \frac{n}{\sum_{k=1}^{n}1/P_k} = T_{\mathcal{H}_n}(P_1,\ldots,P_n) \qquad (\Psi(P) = 1/P);$$

— Geometric mean:

$$T_0(P_1,\ldots,P_n) = \left(\prod_{k=1}^{n}P_k\right)^{1/n} = T_{\mathcal{G}_n}(P_1,\ldots,P_n) \qquad (\Psi(P) = \ln P);$$

— Arithmetic mean:

$$T_1(P_1,\ldots,P_n) = \frac{\sum_{k=1}^{n}P_k}{n} = \overline{P}_n \qquad (\Psi(P) = P).$$

Other special cases are

$$T_{-\infty}(P_1,\ldots,P_n) = \min\{P_1,\ldots,P_n\} = P_{1:n}$$

and

$$T_{+\infty}(P_1,\ldots,P_n) = \max\{P_1,\ldots,P_n\} = P_{n:n}.$$

From now on, we shall use the notations $T_{-\infty}$=T_T, T_1=T_E and $T_\infty = T_W$, due to their use in the combined tests of Tippett [45], Edgington [53] and Wilkinson [54], respectively.

Tippett [45] was the first one to meta-analyze p-values using the statistic

$$T_T(P_1,\ldots,P_n) = P_{1:n}.$$

As $P_{1:n}|H_0^* \sim Beta(1,n)$, the decision is to reject H_0^* at a significance level α if the minimum observed p-value $p_{1:n} < 1-(1-\alpha)^{1/n}$.

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Tippett's minimum method is a special case of Wilkinson's method (Wilkinson [54]), which recommends the rejection of H_0^* if some order statistic $p_{k:n} < c$. As

$$T_{W_k}(P_1, \ldots, P_n) = P_{k:n} | H_0^* \sim Beta(k, n+1-k),$$

the cut-of-point c to reject H_0^* at a significance level α is the solution of

$$\int_0^c u^{k-1}(1-u)^{n-k} \mathrm{d}u = \alpha\, B(k, n+1-k).$$

Note that Tippett's and Wilkinson's methods use drastically restricted information, contrasting with the efficient way in which Fisher's and Stouffer's methods use all available information.

In 1933, Pearson [55] expressed the distribution of

$$T_P(P_1, \ldots, P_n) = \prod_{k=1}^{n} P_k$$

as a function of the upper incomplete Beta function,

$$\mathcal{B}_z(p, q) = \int_z^1 x^{p-1}(1-x)^{q-1}\mathrm{d}x,\ p, q > 0,\ z \in (0, 1).$$

In fact, the product of n independent random variables $P_k \sim Uniform(0, 1)$ verifies

$$\prod_{k=1}^{n} P_k \overset{\mathrm{d}}{=} Y_{1,1,1,n} \sim BetaBoop(1, 1, 1, n),$$

where $Y_{p,q,P,Q} \sim BetaBoop(p, q, P, Q)$ is a random variable with probability density function

$$f_{Y_{p,q,P,Q}}(x) = \frac{x^{p-1}(1-x)^{q-1}[-\ln(1-x)]^{P-1}(-\ln x)^{Q-1}}{\int_0^1 t^{p-1}(1-t)^{q-1}[-\ln(1-t)]^{P-1}(-\ln t)^{Q-1}\mathrm{d}t}\, \mathbb{I}_{(0,1)}(x),$$

with $p, q, P, Q > 0$ such that $\int_0^1 t^{p-1}(1-t)^{q-1}[-\ln(1-t)]^{P-1}(-\ln t)^{Q-1}\mathrm{d}t < \infty$, cf. Brilhante et al. [56] and Brilhante and Pestana [57].

As $Y_{p,1,1,Q}^{1/\alpha} \overset{\mathrm{d}}{=} Y_{\alpha p,1,1,Q}$, $p, Q, \alpha > 0$, we conclude that the geometric mean

$$\mathcal{G}_n = T_0(P_1, \ldots, P_n) = \left(\prod_{k=1}^{n} P_k\right)^{1/n}$$

of n independent $P_k \sim Uniform(0, 1)$ is a BetaBoop$(n, 1, 1, n)$ random variable with probability density function

$$f_{\mathcal{G}_n}(x) = \frac{n^n}{\Gamma(n)}\, x^{n-1}\, (-\ln x)^{n-1}\, \mathbb{I}_{(0,1)}(x),$$

where $\Gamma(\alpha) = \int_0^\infty x^{\alpha-1}\mathrm{e}^{-x}\mathrm{d}x,\ \alpha > 0$, is the Euler's Gamma function, being $\mathbb{I}_A$ the indicator function of A.

Therefore, the cumulative distribution function of $\mathcal{G}_n$ is

$$F_{\mathcal{G}_n}(x) = \frac{\Gamma(n,\, -n\, \ln x)}{\Gamma(n)}\, \mathbb{I}_{(0,1)}(x) + \mathbb{I}_{[1,\infty)}(x),$$

where $\Gamma(\alpha, z) = \int_z^\infty x^{\alpha-1}\mathrm{e}^{-x}\mathrm{d}x,\ \alpha, z > 0$, is the upper incomplete Gamma function. Critical quantiles $g_{n,1-\alpha}$ for $\mathcal{G}_n$ can easily be computed from the critical quantiles $g^*_{n,1-\alpha}$ of $\mathcal{G}_n^n = \prod_{k=1}^n P_k$, where $\int_0^{g^*_{n,1-\alpha}} \frac{(-\ln x)^{n-1}}{(n-1)!}\, \mathrm{d}x = 1-\alpha$, since $g_{n,1-\alpha} = (g^*_{n,1-\alpha})^{1/n}$.

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Observe, however, that using products of standard uniform random variables, or adding their exponential logarithms, provides essentially the same information. Pearson [55] acknowledged that combining p-values using

$$T_P(P_1,\ldots,P_n) = [\mathcal{G}_n(P_1,\ldots,P_n)]^n = \prod_{k=1}^{n} P_k$$

is equivalent to Fisher's [6] earlier combination method based on

$$T_F(P_1,\ldots,P_n) = -2\sum_{k=1}^{n} \ln P_k,$$

as described in *Subsection 2.1*.

In 1934, Pearson [58] observed that in bilateral contexts it would be more adequate to combine $\prod_{k=1}^{n} P_k$ and $\prod_{k=1}^{n}(1-P_k)$, namely using

$$T_{P^*}(P_1,\ldots,P_n) = \min\left\{\prod_{k=1}^{n} P_k, \prod_{k=1}^{n}(1-P_k)\right\}. \tag{3}$$

As already observed, T_P is equivalent to T_F. Similarly, using Fisher's transformation, T_{P^*} defined in (3) is equivalent to

$$\begin{aligned} T_{PF} &= \max\left\{-2\ln\left(\prod_{k=1}^{n} P_k\right), -2\ln\left(\prod_{k=1}^{n}(1-P_k)\right)\right\} \\ &= \max\left\{-2\sum_{k=1}^{n}\ln P_k, -2\sum_{k=1}^{n}\ln(1-P_k)\right\}, \end{aligned} \tag{4}$$

which clearly is not χ^2_{2n}-distributed. Owen [59] used the Bonferroni's correction

$$\alpha - \tfrac{\alpha^2}{4} \leq \mathbb{P}\left(T_{PF} \geq \chi^2_{2n,1-\alpha/2}\right) \leq \alpha$$

to establish lower and upper bounds.

Instead of (3), we suggest the use of the minimum of the geometric means,

$$T_{\min\{\mathcal{G}_n,\mathcal{G}_n^*\}} = \min\left\{\left(\prod_{k=1}^{n} P_k\right)^{1/n}, \left(\prod_{k=1}^{n}(1-P_k)\right)^{1/n}\right\}.$$

Combining p-values through their sum (Edgington [53]), or arithmetic mean,

$$T_E(P_1,\ldots,P_n) = \overline{P}_n,$$

is also feasible, but much less appealing than Fisher's chi-square transformation method, since $\overline{P}_n$ has a very cumbersome probability density function,

$$f_{\overline{P}_n}(x) = \frac{n}{\Gamma(n)}\left[\sum_{j=0}^{\lfloor nx\rfloor}(-1)^j\binom{n}{j}(\max\{0,nx-j\})^{n-1}\right]\mathbb{I}_{(0,1)}(x),$$

where $\lfloor x\rfloor$ is the largest integer not greater than x. However, for moderately large values of n, an approximation based on the central limit theorem can be used to perform an overall test on H_0^* *versus* H_A^*. But this procedure is not consistent, in the sense that it can fail to reject the overall test's null hypothesis, even though the results of some of the individual p-values are extremely significant.

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Wilson [60] recommends the use of the harmonic mean $T_{\mathcal{H}_n}(P_1,\ldots,P_n)$ for combining mutually exclusive tests, not necessarily independent, assuming that the p-values being combined are valid. It was shown that $T_{\mathcal{H}_n}(P_1,\ldots,P_n)$ effectively controls the strong-sense familywise error rate, i.e. the probability of falsely rejecting a null hypothesis in favor of an alternative hypothesis in one or more of all tests performed. The harmonic mean of p-values, whose distribution is in the domain of attraction of the heavy-tailed Landau skewed additive (1,1)-stable law [61], is robust to positive dependency between p-values and also to the distribution of weights w used in its computation, being as well insensitive to the number of tests, aside from being mainly influenced by the smallest p-values. Based on recent developments in robust risk aggregation techniques, Vovk and Wang [12], without making any assumptions on the dependence structure of the p-values to be combined, extended those results to generalized means and showed that n p-values can be combined by scaling up the harmonic mean $T_{\mathcal{H}_n}(P_1,\ldots,P_n)$ by a factor $\ln n$.

2.3. Which Combining Rule Should Be Used?

To illustrate the application of different combined methods, Examples 1 and 2 are considered using data taken from Hartung et al. [62]. The tables in the Supplementary Materials, containing critical values for each combined method, are used (case $n_f = 0$, i.e. no fake p-values, compared with $n_f = 1,\ldots,\lfloor n/3 \rfloor$ fake p-values) to decide whether the hypothesis H_0^* should be rejected or not.

Example 1 (Table 3.1, [62], p. 31)**.** *For the meta-analysis of $n = 19$ case-control studies on the risk of lung cancer in women in relation to exposure to environmental tobacco smoke the p-values are*

0.0669	0.2740	0.6844	0.8460	0.0623	0.1805	0.0990	0.0143
0.0580	0.0690	0.6572	0.0571	0.0027	0.0127	0.4747	0.1760
0.2855	0.0056	0.2411,					

The observed values for the above combined tests statistics are:

$$
\begin{aligned}
&T_F(0.0669,\ldots,0.2411) = 90.0426\\
&T_S(0.0669,\ldots,0.2411) = -4.7198\\
&T_{MG}(0.0669,\ldots,0.2411) = 38.4946 \quad (t^*_{MG} = 4.9189)\\
&T_C(0.0669,\ldots,0.2411) = 41.7048\\
&T_T(0.0669,\ldots,0.2411) = 0.0027\\
&T_{\mathcal{H}_{19}}(0.0669,\ldots,0.2411) = 0.0233\\
&T_{\mathcal{G}_{19}}(0.0669,\ldots,0.2411) = 0.0935\\
&T_{\min\{\mathcal{G}_{19},\mathcal{G}^*_{19}\}}(0.0669,\ldots,0.2411) = 0.0935\\
&T_E(0.0669,\ldots,0.2411) = 0.2246\\
&T_W(0.0669,\ldots,0.2411) = 0.8460\,.
\end{aligned}
$$

In this case, H_0^* is rejected at the usual significance level 0.05 using all combined tests, with the exception of Tippett's method, as expected, since only 4 of the 19 p-values are smaller than 0.05. As can be noted, Tippett's rule drastically discards most of the information and therefore should not be considered a reliable test to make an overall decision.

Example 2 (Table 13.1, [62], p. 172)**.** *For the meta-analysis of $n = 20$ validity studies examining the correlation between ratings of the instructor and student achievement the p-values are:*

0.0153	0.0051	0.2248	0.0007	0.0041	0.5491	0.0529	0.0247
0.0046	0.2878	0.7385	0.0096	0.0720	0.00004	0.0010	0.0312
0.0053	0.0988	0.0674	0.2502				

The observed values for the combined tests statistics are:

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$$
\begin{aligned}
&T_F(0.0153,\ldots,0.2502) = 154.5968\\
&T_S(0.0153,\ldots,0.2502) = -8.0553\\
&T_{MG}(0.0153,\ldots,0.2502) = 73.8730 \quad (t^*_{MG} = 9.1960)\\
&T_C(0.0153,\ldots,0.2502) = 90.1191\\
&T_T(0.0153,\ldots,0.2502) < 0.0000\\
&T_{\mathcal{H}_{20}}(0.0153,\ldots,0.2502) = 0.0007\\
&T_{\mathcal{G}_{20}}(0.0153,\ldots,0.2502) = 0.0210\\
&T_{\min\{\mathcal{G}_{20},\mathcal{G}^*_{20}\}}(0.0153,\ldots,0.2502) = 0.0210\\
&T_E(0.0153,\ldots,0.2502) = 0.1222\\
&T_W(0.0153,\ldots,0.2502) = 0.7385\,.
\end{aligned}
$$

The overall rejection of H_0^* seems more consistent in this example. However, a closer look at the data shows that 9 *out of* 20 *p-values are greater than the usual significance level* 0.05*, which is an exceptional case, since p-values greater than* 0.05 *often lead to the non-publication of the studies, thus creating a phenomenon known as publication bias. Four of the p-values are much greater than* 0.05*, which causes the rejection of H_0^* when using the combined tests based on the transformations of p-values T_F, T_S, T_{MG} and T_C, whereas the rejection using the mean of order r tests T_T, $T_{\mathcal{H}_{20}}$, $T_{\mathcal{G}_{20}}$, $T_{\min\{\mathcal{G}_{20},\mathcal{G}^*_{20}\}}$, T_E and T_W is due to the existence of some very small p-values.*

Both previous examples raise some concern on the validity and efficiency of combined tests and on the question of which one should actually be used. A common understanding on this matter is that any rational combining procedure $T(p_1,\ldots,p_n)$ should be monotone, in the sense that if one set of p-values $(p_1,\ldots,p_n)$ leads to the rejection of the overall null hypothesis H_0^*, any set of componentwise smaller p-values $(p'_1,\ldots,p'_n)$, $p'_k \leq p_k$, $k = 1,\ldots,n$, must also lead to its rejection.

Birnbaum [63] has shown that every monotone combined test procedure is admissible, i.e. provides a most powerful test against some alternative hypothesis for combining some collection of tests, and therefore is optimal for some combined testing situation whose goal is to harmonize eventually conflicting evidence, or to pool inconclusive evidence. In the context of social sciences, Mosteller and Bush [64] recommend Stouffer et al.'s [46] method, which is also preferred by Whitlock [65], while Littell and Folks [66,67] have shown that, under mild conditions, Fisher's method is optimal for combining independent tests. Owen [59], showing that Birnbaum's statement on the inadmissibility of Pearson's two-sided combined test was wrong, recommends Pearson's two-sided combination rule, given in (4). Marden [68], using the concepts of sensitivity and sturdiness, orders from best to worst $T_F \succ T_T \succ T_S \succ T_E \succ T_W$, warning that all statistics perform worse as n increases.

The thorough comparison performed by Loughin [69] concludes that the normal combining function has a good performance in problems where evidence against the combined null hypothesis is spread among more than a small fraction of the individual tests. Moreover, when the total evidence is weak, Fisher's method is the best choice if the evidence is at least moderately strong and is concentrated in a relatively small fraction of the individual tests. The Mudholkar and George's [50] logistic combination method provides a compromise between the two. When the total evidence against the combined null hypothesis is concentrated in one or in a very few of the tests to be combined, Tippett's minimum function can be useful as well. See also Won et al. [70] on how to choose an optimal method to combine p-values.

Since there is no unanimity among researchers as to which procedure should be used, a reasonable approach is to compare the results for a variety of tests. For this purpose, tables with critical values for the combined test statistics discussed earlier are presented as Supplementary Materials.

For more details on the early developments of combining one-sided tests, see the first chapter of Oosterhoff [71]. In what regards recent advances on combining tests, namely in a dependence framework, or using e-values, defined by expectations, instead of p-values, defined by probabilities, see recent developments in Vovk and Wang [72], Vovk et al. [73], and Vuursteen et al. [74].

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3. Publication Bias

Published results have in general significant p-values, typically less than 0.05, and this publication bias is one of the ill-resolved problems in the meta-analysis of p-values. In fact, many published studies deal with significant p-values, see for instance the insistence on $p \leq 0.05$ in Zintaras et al. [75].

The influential International Committee of Medical Journal Editors (ICMJE) [76] in its Uniform Requirements for Manuscripts states that

> "*Editors should seriously consider for publication any carefully done study of an important question, relevant to their readers, whether the results for the primary or any additional outcome are statistically significant. Failure to submit or publish findings because of lack of statistical significance is an important cause of publication bias*".

The *Journal of Articles in Support of the Null Hypothesis* [77] offers "*an outlet for experiments that do not reach the traditional significance levels (p < .05)* [...] *reducing the file drawer problem, and reducing the bias*", considering that "*without such a resource researchers could be wasting their time examining empirical questions that have already been examined*".

As with many other techniques used in meta-analysis, publication bias can easily lead to erroneous conclusions in combined testing (Pestana et al. [78]). Indeed, if the set of available p-values comes mainly from studies considered worthy of publication because the observed p-values are small, thus pointing out to significant results, then the rejection of H_0^* can be due to publication bias. Often, the assumption that the p_k's are observations of independent Uniform(0,1) random variables is questionable, since they are frequently a set of low order statistics, given that p-values greater than 0.05 are less published.

Example 3 (Table B1, p. 726 in van Aert et al. [79] assessment of meta-analysis)**.** *For the set of the $n = 25$ p-values*

0.0489	0.0690	0.0133	0.0372	0.0188	0.0457	0.0307	0.0428
0.0335	0.0274	0.0030	0.0531	0.0335	0.0254	0.0240	0.0023
0.0254	0.0263	0.0429	0.0172	0.0365	0.0287	0.0200	0.0498
0.0134							

the observed values for the combined test statistics are:

$$
\begin{aligned}
&T_F(0.0489,\ldots,0.0134) = 184.4354\\
&T_S(0.0489,\ldots,0.0134) = -9.7083\\
&T_{MG}(0.0489,\ldots,0.0134) = 91.4336 \quad (t^*_{MG} = 10.1611)\\
&T_C(0.0489,\ldots,0.0134) = 96.6378\\
&T_T(0.0489,\ldots,0.0134) = 0.0023\\
&T_{\mathcal{H}_{25}}(0.0489,\ldots,0.0134) = 0.0156\\
&T_{\mathcal{G}_{25}}(0.0489,\ldots,0.0134) = 0.0250\\
&T_{\min\{\mathcal{G}_{25},\mathcal{G}^*_{25}\}}(0.0489,\ldots,0.0134) = 0.0250\\
&T_E(0.0489,\ldots,0.0134) = 0.0308\\
&T_W(0.0489,\ldots,0.0134) = 0.0690\,.
\end{aligned}
$$

H_0^* is rejected, as expected, whatever combined test is used. In fact, the meta-analysis of these p-values is a pointless exercise, since it is obvious that they cannot be a random sample from the standard Uniform distribution.

As a matter of fact, it seems reasonable to assume for the set of p-values in Example 3 that the distribution of the underlying P_k's is a Uniform$(0, 0.0718)$, where the right endpoint is the unbiased estimate $p_{25:25} \times 26/25$. Consequently, dividing the values by 0.0718 we obtain a genuine standard Uniform sample, i.e. 0.6814, 0.9615, 0.1853, 0.5184, 0.2620, 0.6368, 0.4278, 0.5964, 0.4668, 0.3818, 0.0418,

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0.7400, 0.4668, 0.3540, 0.3344, 0.0321, 0.3540, 0.3665, 0.5978, 0.2397, 0.5086, 0.3999, 0.2787, 0.6940, 0.1867, and the observed values of the combined tests statistics for these new values are:

$$\begin{aligned}
&T_F(0.6814,\ldots,0.1867) = 52.7130\\
&T_S(0.6814,\ldots,0.1867) = -1.0837\\
&T_{MG}(0.6814,\ldots,0.1867) = 9.2157 \quad (t^*_{MG} = 1.0241)\\
&T_C(0.6814,\ldots,0.1867) = 14.3117\\
&T_T(0.6814,\ldots,0.1867) = 0.0321\\
&T_{\mathcal{H}_{25}}(0.6814,\ldots,0.1867) = 0.2181\\
&T_{\mathcal{G}_{25}}(0.6814,\ldots,0.1867) = 0.3485\\
&T_{\min\{\mathcal{G}_{25},\mathcal{G}^*_{25}\}}(0.6814,\ldots,0.1867) = 0.3484\\
&T_E(0.6814,\ldots,0.1867) = 0.4285\\
&T_W(0.6814,\ldots,0.1867) = 0.9615\,.
\end{aligned}$$

So there is no reason to reject the hypothesis that the sample of expanded values is from the standard Uniform distribution.

It is worth noting that under H_0^* the moment of order k of the geometric mean is

$$\mathbb{E}\left(\mathcal{G}_n^k\right) = \left(1/\left(1+\frac{k}{n}\right)\right)^n \xrightarrow[n\to\infty]{} \mathrm{e}^{-k}.$$

Hence,

$$\mathbb{E}(\mathcal{G}_n) = \left(\frac{n}{n+1}\right)^n \underset{n\to\infty}{\downarrow} \frac{1}{\mathrm{e}} \approx 0.3679,$$

the standard deviation decreases to zero, the skewness steadily decreases after a maximum 0.2645 for $n = 5$, and the kurtosis increases from -0.8541 (for $n = 2$) towards 0. Observe that for $n \geq 14$, the expected value of $\mathcal{G}_n$ is greater than 0.36 and the standard deviation is smaller than 0.1. Therefore, whenever $p_{n:n}$ is smaller than a threshold $c \ll 1/\mathrm{e}$, the test based on $T_{\mathcal{G}_n}$ will lead to the rejection of H_0^*, as it happens with the data from van Aert et al. [79], but a $p_{n:n}$ smaller than a low threshold can just be a consequence of publication bias.

The assessment of publication bias is often performed computing the number of non-significant p-values that would be needed to reverse the decision to reject H_0^* based on the available p-values, which is illustrated with Examples 4 and 5.

Example 4. *For the seven p-values in* Fogacci *et al.* [80] *from studies on the effect of vitamin D supplements administered to pregnant women with risk of preeclampsia incidents:*

$$0.039 \quad 0.324 \quad 0.057 \quad 0.001 \quad 0.324 \quad 0.105 \quad 0.003$$

it follows that $T_F(p_1,\ldots,p_7) = -2\sum_{k=1}^7 \ln p_k = 46.667$. *As* $\mathbb{P}(T_F > 46.667|H_0^*) = 0.0000218$, H_0^* *is rejected. In this example,* p_2, p_3, p_5 *and* p_6 *are greater than* 0.05, *and the rejection of* H_0^* *is caused by the very small* p_4 *and* p_7 *values, thus raising some doubts as to whether the p-values are truly genuine. According to* Hartung et al. [62], p. 177, *to reverse the decision to reject* H_0^* *at the significance level* 0.05, *it is necessary to compute the number* n_0 *of non-significant additional p-values such that*

$$-2\sum_{k=1}^{7} \ln p_k - 2n_0 \ln \widetilde{p} \leq \chi^2_{2(7+n_0),0.95}\,,$$

where for simplicity it is assumed that $p_8 = \ldots = p_{7+n_0} = \widetilde{p}$. *The solution of* $46.667 - 2n_0 \ln \widetilde{p} \leq \chi^2_{2(7+n_0),0.95}$ *depends on the value of* $\widetilde{p}$. *For instance, if* $\widetilde{p} = 0.4$, *then* $n_0 = 46$, *if* $\widetilde{p} = 0.5$, *then* $n_0 = 23$, *and if* $\widetilde{p} = 0.6$, *then* $n_0 = 17$.

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Example 5. *The p-values in* Table 2 *of* Zintaras et al.'s [75] *investigation of heterogeneity-based genome search for preeclampsia are:*

0.010	0.015	0.025	0.029	0.032	0.034	0.044	0.047	0.049
0.053	0.055	0.060	0.162					

Since $T_F(0.010,\ldots,0.162) = 85.0524$, H_0^* *is also rejected* ($\mathbb{P}[T_F > 85.0524] = 0.0000000342$). *In this case, to observe* $-2\sum_{k=1}^{13} \ln p_k - 2n_0 \ln \widetilde{p} \leq \chi^2_{2(13+n_0),0.95}$, *it will be needed* $n_0 = 120$ *if* $\widetilde{p} = 0.4$, $n_0 = 52$ *if* $\widetilde{p} = 0.5$, *and* $n_0 = 36$ *if* $\widetilde{p} = 0.6$. *Even if* $\widetilde{p} = 0.9$, *it will require* $n_0 = 22$.

In Zintaras et al.'s [75] example, the high number of non-significant studies needed to reverse the rejection of H_0^* seems to indicate that the decision is the consequence of having consistently low p-values, or possibly moderate censoring of non-significant p-values (note that $p_{13:13} = 0.162 > 0.05$). In Fogacci et al.'s [80] example, the rejection of H_0^* was due to $p_{1:7}$, although 4 out of 7 p-values are greater than 0.05, and the fact that $p_{2:7}$ is quite small, can be considered suspicious.

Begg and Mazumdar [81] and Egger et al. [82] devised tests to detect publication bias. Jin et al. [83] and Lin and Chu [84] present interesting overviews, and Givens et al. [85] provide a deep insight on publication bias in meta-analysis, namely using data-augmentation techniques.

It is also worth mentioning that Zaykin et al. [40], Neuhäuser and Bretz [41] and Zhang [42] advocate the use of a truncated product combination statistic of only those p-values smaller than some specified cut-off value, which in practice dismisses publication bias. Dudbridge and Koeleman [43] go even further, proposing the combination of the most significant p-values. This recommendation clearly favors the rejection of H_0^*, therefore increasing the probability of false positive results, and contributing to the misconception that significance implies importance.

4. Mendel Random Variables — Combined Tests with Genuine and Fake *p*-Values

The assumption $P_k|H_0 \sim Uniform(0,1)$, $k = 1,\ldots,n$, is rather naive. In fact, the alternative hypothesis H_A^* states that some of the H_{Ak} are true, and so a meta-decision on H_0^* implicitly assumes that some of the P_k's may have non-uniform distribution, cf. Hartung et al. [62], pp. 81–84; Kulinskaya et al. [86], pp. 117–119. Thus, the uniformity of the P_k's is solely the consequence of assuming that the null hypothesis is true, and this far-fetched assumption led Tsui and Weerahandi [87] to introduce the concept of generalized p-values. See also Weerahandi [88], Hung et al. [89] and Brilhante [90], and references therein, on the promising concepts of generalized and of random p-values. Moreover, a consequence of publication bias is that most of the published studies point out to the rejection of H_0. Hence, instead of combining p-values, it would be more reasonable to combine either generalized p-values or random p-values. Assuming that the p-values being combined can come from a combination of null and alternative hypotheses, Dai and Charnigo [91] investigated a Beta mixture adjustment. For large exploratory studies, an extreme-value distribution adjustment for fixed numbers of combined evidence and a Beta distribution adjustment for the most significant evidence are accurate and efficient (Dudbridge and Koeleman [92]).

Moreover, when the result of an experiment leads to a p-value which is not highly significant or significant, there is the possibility of the researcher carrying out a new experiment, in the hope of obtaining a "better" p-value that favors the publication of his study.

Such malpractice of trying to obtain results more attuned with the researcher's expectations (or wishes) is scientifically wrong, eventually fraud, leading to results "*too good to be true*", as Fisher [37] observed in his appraisal of Mendel's data: "*the data of most, if not all, of the experiments have been falsified so as to agree closely with Mendel's expectations*". For more details on the (in)famous Mendel-Fisher controversy, see Franklin et al. [38], and Pires and Branco [39].

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If a reported p_k is the "best" of ℓ observed p-values in ℓ independent repetitions of an experiment, such "fake p-value" comes from the minimum of ℓ independent Uniform(0,1) random variables, so that $P_k \sim \text{Beta}(1,\ell)$ with probability density function

$$f_{P_k}(x) = \ell(1-x)^{\ell-1}\mathbb{I}_{(0,1)}(x).$$

On the other hand, fake p-values demand substantial changes in the computation of combined p-values. For instance, with regard to Fisher's method, for fake p-values $P_k \sim \text{Beta}(1,\ell_k)$, it implies that $-2\ell_k \ln(1-P_k) \sim \chi^2_2$. Therefore, for $\ell_k = 1$, i.e. for genuine p-values $P_k \sim \mathit{Uniform}(0,1)$, it follows that $-2\ln P_k \overset{\text{d}}{=} -2\ln(1-P_k) \sim \chi^2_2$. Hence, the existence of fake p-values requires the following adjustment to Fisher's combined test:

$$T_F^f(P_1,\ldots,P_n) = -2\sum_{k=1}^{n} \ell_k \ln P_k | H_0^* \sim \chi^2_{2n},$$

but the problem is that the values ℓ_k are actually unknown.

Using the integral transform theorem, $1-(1-P_k)^{\ell_k} \sim \mathit{Uniform}(0,1)$, and as far as Stouffer et al.'s method is concerned,

$$\frac{\sum_{k=1}^{n} \Phi^{-1}\left(1-(1-P_k)^{\ell_k}\right)}{\sqrt{n}} \sim \mathit{Gaussian}(0,1),$$

while for Chen's T_C statistic,

$$\sum_{k=1}^{n} \left[\Phi^{-1}\left(1-(1-P_k)^{\ell_k}\right)\right]^2 \sim \chi^2_n.$$

In what concerns Mudholkar and George's T_{MG} statistic, if $P_k \sim \mathit{Beta}(1,\ell_k)$, then the cumulative distribution function and probability density function of $Y = \ln\left(\frac{P_k}{1-P_k}\right)$ are, respectively,

$$F_Y(y) = \left[1 - \frac{1}{(1+\mathrm{e}^y)^{\ell_k}}\right]\mathbb{I}_{\mathbb{R}}(y) \quad \text{and} \quad f_Y(y) = F_Y'(y) = \frac{\ell_k\,\mathrm{e}^y}{(1+\mathrm{e}^y)^{\ell_k+1}}\mathbb{I}_{\mathbb{R}}(y)\,.$$

The central limit theorem can be used to obtain an approximation of $\sum_{k=1}^{n} \ln\left(\frac{P_k}{1-P_k}\right)$, as long as we know which of the p-values are the fake ones and their corresponding ℓ_k values.

In fact, the main problem here is that there is no information on whether some of the reported p-values are in fact fake p-values, and if so, how many and which ones are. In the classical framework, the number n of p-values $(p_1,\ldots,p_n)$ to be combined is generally small, and if the overall null hypothesis is true, it seems reasonable to expect that the number n_f of fake p-values with $\text{Beta}(1,\ell)$ distribution, $\ell = 2,3,\ldots$, to be much smaller than the number $n-n_f$ of genuine standard Uniform distributed p-values. For what follows, it is assumed that the proportion of fake p-values among the observed p-values being combined is $\frac{n_f}{n} = \frac{m}{2}$, $m \in [0,2]$.

With regard to fake p-values, it is likely that in most cases $\ell = 2$, especially when the second experiment provides a smaller p-value that supports the researcher's expectations. Actually, if the second p-value is again non-significant, there is a good chance that this would continue to happen with other similar experiments, which have a cost attached (at least they are time-consuming). In this situation, the researcher will most likely decide to give up carrying out further experiments and no p-value will be reported.

For what follows, it is also assumed that the model for the p-values to be combined is $P_k \sim \mathit{Beta}(1,\ell)$, with $\ell \in \{1,2\}$, i.e. P_k is a genuine p-value if $\ell = 1$, or a fake one if $\ell = 2$. As it is unknown whether P_k is genuine or fake, the distribution of P_k is a mixture of the minimum of two independent Uniform(0,1) random variables and of a Uniform(0,1) random variable, with weights $\frac{m}{2}$ and $1-\frac{m}{2}$, respectively.

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Therefore, P_k has probability density function

$$f_{P_k}(x) = \tfrac{m}{2} f_{U_{1:2}}(x) + (1 - \frac{m}{2}) f_U(x) = \left(\tfrac{m}{2} 2(1-x) + 1 - \frac{m}{2}\right) \mathbb{I}_{(0,1)}(x),$$

where $U_{1:2}$ denotes the minimum of two standard uniform random variables U_1, U_2, and $U \sim Uniform(0,1)$. In other words,

$$f_{P_k}(x) = \left(m(1-x) + 1 - \frac{m}{2}\right)\mathbb{I}_{(0,1)}(x).$$

More generally, tilting the probability density function of $U \sim Uniform(0,1)$ with pole $\left(\frac{1}{2}, 1\right)$, for $m \in [-2,2]$, we obtain the probability density function of a random variable X_m given by

$$f_{X_m}(x) = \left(mx + 1 - \frac{m}{2}\right) \mathbb{I}_{(0,1)}(x),$$

and thus we shall say that $X_m \sim Mendel(m)$ when $m \in [-2,2]$.

Note that $X_0 \sim Uniform(0,1)$, $X_{-2} \sim Beta(1,2)$ is the minimum of two independent standard uniform random variables, and $X_2 \sim Beta(2,1)$ is the maximum of two independent standard uniform random variables. For intermediate values of $m \in (-2,0)$, X_m is a mixture of a standard uniform random variable, with weight $1 - \frac{|m|}{2}$, and a Beta(1,2) random variable, and for $m \in (0,2)$, it is a mixture of a standard uniform random variable and a Beta(2,1) random variable, i.e. with cumulative distribution function

$$F_{X_m}(x) = \left(1 - \tfrac{|m|}{2}\right) F_U(x) + \tfrac{|m|}{2} F_{U_{i:2}}(x),$$

where $i = 1$ if $m \in [-2,0]$ and $i = 2$ if $m \in (0,2]$, and $U_{1:2}$ and $U_{2:2}$ denote, respectively, the minimum and maximum of two independent standard uniform random variables.

4.1. Deng and George's Contractions with Mendel Random Variables

Let X and Y be independent random variables with support $\mathcal{S}_X = \mathcal{S}_Y = [0,1]$. The support extension resulting from $\frac{X}{Y}$ or $\frac{1-X}{1-Y}$ [respectively $X+Y$] followed by the contraction $V = \min\left\{\frac{X}{Y}, \frac{1-X}{1-Y}\right\}$ [respectively $W = X + Y - \lfloor X + Y \rfloor$], so that $\mathcal{S}_V = \mathcal{S}_W = [0,1]$, restores the unit $[0,1]$ support. These contractions have been used by Deng and George [44], with $X \sim Uniform(0,1)$ — i.e. $X \sim Mendel(0)$ — to obtain a useful characterization of the standard Uniform distribution. **Theorem 1** extends their results to Mendel(m), $m \in [-2,2]$, random variables.

Theorem 1. *If $X_m \sim Mendel(m)$ and Y, with support $[0,1]$, are independent random variables, then*

$$V = \min\left\{\frac{X_m}{Y}, \frac{1-X_m}{1-Y}\right\} \sim Mendel\big((2\mathbb{E}[Y] - 1)m\big).$$

In particular, if $X_{m_1} \sim Mendel(m_1)$ and $X_{m_2} \sim Mendel(m_2)$ are independent, then

$$V_{m_1,m_2} = \min\left\{\frac{X_{m_1}}{X_{m_2}}, \frac{1-X_{m_1}}{1-X_{m_2}}\right\} \sim Mendel\big(\tfrac{m_1 m_2}{6}\big), \tag{5}$$

and the cumulative distribution function of

$$W_{m_1,m_2} = X_{m_1} + X_{m_2} - \lfloor X_{m_1} + X_{m_2} \rfloor$$

is

$$F_{W_{m_1,m_2}}(x) = (1 - \tfrac{m_1 m_2}{12}) F_U(x) + \frac{m_1 m_2}{12} F_{X_{2,2}}(x),$$

where $U \sim Uniform(0,1)$ and $X_{2,2} \sim Beta(2,2)$.

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Proof. The probability density function of $X \sim Mendel(m)$ is $f_X(x) = m\,x + 1 - \frac{m}{2}$, so for $x \in [0,1]$, $F_X(x) = \frac{m}{2}x^2 + (1-\frac{m}{2})x$. If $\widetilde{X} = 1 - X$ and $\widetilde{Y} = 1 - Y$, then $F_{\widetilde{X}}(x) = 1 - F_X(1-x)$, $\mathbb{E}(\widetilde{Y}) = 1 - \mathbb{E}(Y)$ and $\mathbb{E}(\widetilde{Y}^2) = 1 - 2\,\mathbb{E}(Y) + \mathbb{E}(Y^2)$. Therefore, for $v \in [0,1]$,

$$\begin{aligned} F_V(v) &= \mathbb{P}[X \le vY] + \mathbb{P}[\widetilde{X} \le v\widetilde{Y}] \\ &= \mathbb{E}[F_X(vY)] + \mathbb{E}\left[F_{\widetilde{X}}(v\widetilde{Y})\right] \\ &= \mathbb{E}[F_X(vY)] + \mathbb{E}\left[1 - F_X(1 - v\widetilde{Y})\right] \\ &= \frac{m}{2}\left[2\,\mathbb{E}(Y) - 1\right]v^2 + \left[1 + \tfrac{m}{2} - m\,\mathbb{E}(Y)\right]v\,, \end{aligned}$$

and consequently,

$$f_V(v) = \left[(2\mathbb{E}(Y) - 1)mv + 1 - \frac{m(2\mathbb{E}(Y)-1)}{2}\right]\mathbb{I}_{[0,1]}(v).$$

In what regards the random variable V_{m_1,m_2} defined in (5),

$$\mathbb{E}[X_{m_2}] = \int_0^1 x\,(m_2 x + 1 - \tfrac{m_2}{2})\,\mathrm{d}x = \tfrac{1}{2} + \tfrac{m_2}{12},$$

and hence $\left[2(\frac{1}{2} + \frac{m_2}{12}) - 1\right] m_1 = \frac{m_1 m_2}{6}$, i.e. $V_{m_1,m_2} \sim Mendel(\frac{m_1 m_2}{6})$.

On the other hand, for $w \in [0,1]$,

$$\begin{aligned} F_{W_{m_1,m_2}}(w) &= \mathbb{P}\left[X_{m_1} + X_{m_2} \le w\right] + \mathbb{P}\left[1 < X_{m_1} + X_{m_2} \le 1 + w\right] \\ &= \int_{-\infty}^{\infty} F_{X_{m_1}}(w-y) f_{X_{m_2}}(y)\,\mathrm{d}y + \int_{-\infty}^{\infty}\left[F_{X_{m_1}}(1+w-y) - F_{X_{m_1}}(1-y)\right] f_{X_{m_2}}(y)\,\mathrm{d}y \\ &= \int_0^w F_{X_{m_1}}(w-y) f_{X_{m_2}}(y)\,\mathrm{d}y + \int_w^1 F_{X_{m_1}}(1+w-y) f_{X_{m_2}}(y)\,\mathrm{d}y - \mathbb{E}[F_{X_{m_2}}(1-Y)] \\ &= \left(1 - \frac{m_1 m_2}{12}\right)w + \frac{m_1 m_2}{12}\left(3w^2 - 2w^3\right), \end{aligned}$$

and therefore

$$\begin{aligned} f_{W_{m_1,m_2}}(w) &= \left(1 - \frac{m_1 m_2}{12} + \frac{m_1 m_2}{12}\,6w(1-w)\right)\mathbb{I}_{[0,1]}(w) \\ &= \left(1 - \frac{m_1 m_2}{12}\right) f_U(x) + \frac{m_1 m_2}{12} f_{X_{2,2}}(x)\,, \end{aligned}$$

with $X_{2,2} \sim Beta(2,2)$. □

4.2. Testing Independence

The extension of classical methods of combining independent p-values to a more general framework of combining correlated p-values is nowadays an active area of research, with far-reaching consequences in dealing with taxa and investigation in Genomics and, more generally, with Big Data. Therefore, testing the independence of a sequence of standard uniform random variables *versus* autoregressive Mendel processes is relevant in the context of meta-analyzing p-values.

Let $\{X_{m,i}\}$, $i \in \mathbb{N}$, be a sequence of replicas of independent Mendel random variables X_m, $m \in [-2,2]$. For $1 \le i \le n$ and $\rho \in [0,1)$, define

$$Y_{m,0} = X_{m,0}, \;\; Y_{m,i} = \rho\, Y_{m,i-1} + (1-\rho)\, X_{m,i}.$$

If $\rho = 0$, then the sequence $\{Y_{m,i}\}$, $i \ge 0$, is the initial one, but if $\rho > 0$, then there is serial correlation.

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The inverse transformation $X_{m,i}=\frac{Y_{m,i}-\rho\, Y_{m,i-1}}{1-\rho}$, with $i=1\ldots,n$ and $J=\left(\frac{1}{1-\rho}\right)^n$, leads to

$$f_{\boldsymbol{Y_m}}(\boldsymbol{y})=\prod_{i=1}^{n}\left(m\,\frac{y_i-\rho\,y_{i-1}}{1-\rho}+\frac{2-m}{2}\right)\frac{1}{1-\rho}\mathbb{I}_S(\boldsymbol{y}),$$

where $\boldsymbol{Y_m}=(Y_{m,1},\ldots,Y_{m,n})$, $\boldsymbol{y}=(y_1,\ldots,y_n)$, $0\le y_i\le 1$, and

$$\boldsymbol{S}=\bigcap_{i=1}^{n}\left\{(y_1,\ldots,y_n):0<\frac{y_i-\rho\,y_{i-1}}{1-\rho}<1\right\}.$$

Since

$$0<\frac{y_i-\rho\,y_{i-1}}{1-\rho}<1\iff\begin{cases}\rho<\frac{y_i}{y_{i-1}}\\ \rho<\frac{1-y_i}{1-y_{i-1}}\end{cases}\iff\rho<\min\left\{\frac{y_i}{y_{i-1}},\frac{-1y_i}{1-y_{i-1}}\right\},$$

for all $i\in\{1,\ldots,n\}$, this is equivalent to

$$\rho<\min_{1\le i\le n}\min\left\{\frac{y_i}{y_{i-1}},\frac{1-y_i}{1-y_{i-1}}\right\}=A(\boldsymbol{y}).$$

The following cases are considered.

— $\rho=0$:
If $\rho=0$ ($\boldsymbol{y}=\boldsymbol{x}$), the sequence $\{Y_{m,i}\}$, $i\ge 0$, is the initial one, and so the joint probability density function of $Y_1,\ldots,Y_n$ is

$$f_{Y_1,\ldots,Y_n}(\boldsymbol{y})=f_{X_1,\ldots,X_n}(\boldsymbol{x})=\left(\tfrac{1}{1-\rho}\right)^n\mathbb{I}_{\{\boldsymbol{x}\in[0,1]^n:\rho<A(\boldsymbol{x})\}}(\boldsymbol{x}),$$

which requires solving the equation

$$\min_{1\le i\le n}\min\left\{\frac{X_{0,i}}{X_{0,i-1}},\frac{1-X_{0,i}}{1-X_{0,i-1}}\right\}=\min_{1\le i\le n}\{U_1,\ldots,U_n\},$$

where $\{U_1,\ldots,U_n\}$ is a sequence of independent standard uniform random variables, and therefore $\min\limits_{1\le i\le n}\{U_1,\ldots,U_n\}\sim Beta(1,n)$.

— $\rho\in(0,1)$, $m=0$:
If $\rho\in(0,1)$ and $m=0$, then $X_{0,i}\overset{\mathrm{d}}{=}U_i$, and

$$\begin{aligned}\min\left\{\frac{Y_{0,i}}{Y_{0,i-1}},\frac{1-Y_{0,i}}{1-Y_{0,i-1}}\right\}&=\min\left\{\rho+(1-\rho)\frac{U_i}{Y_{0,i-1}},\rho+(1-\rho)\frac{1-U_i}{1-Y_{0,i-1}}\right\}\\&=\rho+(1-\rho)\,\min\left\{\frac{U_i}{Y_{0,i-1}},\frac{1-U_i}{1-Y_{0,i-1}}\right\}\\&=\rho+(1-\rho)U_i^*,\end{aligned}$$

with $U_i^*\sim Uniform(0,1)$, and so $\min\left\{\frac{Y_{0,i}}{Y_{0,i-1}},\frac{1-Y_{0,i}}{1-Y_{0,i-1}}\right\}=V_{i,\rho}\sim Uniform(\rho,1)$. On the other hand, $V=\min\limits_{1\le i\le n}V_{i,\rho}$ is the maximum likelihood estimator of ρ, which is also sufficient for ρ. The likelihood function is $L(\rho)=\left(\frac{1}{1-\rho}\right)^n\mathbb{I}_{\{\rho\le V\}}(\rho)$. Therefore, the hypothesis of independence should be rejected if $V>1-\alpha^{1/n}$, with the power of the test being equal to $\frac{\alpha}{(1-\rho)^n}$ if $\rho\le 1-\alpha^{1/n}$, or 1 otherwise.

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— $\rho \in (0,1)$, $m \in [-2,2]$:
For a general $m \in [-2,2]$, it follows from $\frac{Y_{m,i}}{Y_{m,i-1}} = \rho + (1-\rho)\,\frac{X_{m,i}}{Y_{m,i-1}}$ and $\frac{1-Y_{m,i}}{1-Y_{m,i-1}} = \rho + (1-\rho)\,\frac{1-X_{m,i}}{1-Y_{m,i-1}}$ that

$$\min\left\{\frac{Y_{m,i}}{Y_{m,i-1}}, \frac{1-Y_{m,i}}{1-Y_{m,i-1}}\right\} = \rho + (1-\rho)\,\min\left\{\frac{X_{m,i}}{Y_{m,i-1}}, \frac{1-X_{m,i}}{1-Y_{m,i-1}}\right\},$$

and with the independence of the $X_{m,i}$'s implying that

$$\min\left\{\frac{Y_{m,i}}{Y_{m,i-1}}, \frac{1-Y_{m,i}}{1-Y_{m,i-1}}\right\} \stackrel{\mathrm{d}}{=} \rho + (1-\rho)\,X_{\frac{m^2}{6},i}\,.$$

As $F_{X_{\frac{m^2}{6},i}}(x) = \left((1-\frac{m^2}{12})x + \frac{m^2}{12}x^2\right)\mathbb{I}_{(0,1)}(x) + \mathbb{I}_{[1,\infty)}(x)$, the cumulative distribution function of

$$W = \min_{1\le i\le n}\left\{\rho + (1-\rho)\,X_{\frac{m^2}{6},i}\right\} = \rho + (1-\rho)\,\min_{1\le i\le n} X_{\frac{m^2}{6},i}$$

is

$$F_W(x) = \begin{cases} 0\,, & x < \rho \\ 1 - \left[1 - (1-\frac{m^2}{12})\frac{x-\rho}{1-\rho} - \frac{m^2}{12}\left(\frac{x-\rho}{1-\rho}\right)^2\right]^n, & \rho \le x < 1 \\ 1\,, & x \ge 1 \end{cases}.$$

4.3. Combined Tests with Genuine and Fake p-values — Some Analytic Results

4.3.1. Tippett's $T_T(P_1,\ldots,P_n)$

Provided the number n_f of fake p-values is known, it is straightforward to obtain the exact distribution of Tippett's combined test statistic: If there are n_f fake Beta(1,2) p-values among the n available p_k's to be combined, $T_T(P_1,\ldots,P_n) = P_{1:n+n_f}$. Therefore, the decision rule is to reject H_0^* at a significance level α if the minimum observed p-value $p_{1:n+n_f} < 1-(1-\alpha)^{1/(n+n_f)}$.

Tippett's case is quite unique, since the analytical results for the test statistics of the other combination methods are cumbersome.

4.3.2. Pearson's $T_P(P_1,\ldots,P_n)$

The computation of the probability density function of Pearson's statistic $T_P(P_1,\ldots,P_n) = \prod_{k=1}^n P_k$ when all P_k's are independent genuine p-values is a straightforward exercise of multiplicative algebra of random variables, since

$$f_{T_P}(x) = \frac{(-\ln x)^{n-1}}{\Gamma(n)}\,\mathbb{I}_{(0,1)}(x).$$

To accommodate fake p-values in the analysis, the first step is to obtain the cumulative distribution function of $\prod_{k=1}^n P_k$ when there exists just one fake p-value in the sample, and the remaining $n-1$ p-values are genuine ones (note that it is irrelevant to know which P_k is actually the fake one).

— Probability density function of $Z_{n,1} = Y\prod_{k=1}^{n-1} P_k$, with independent $P_k \sim \mathit{Uniform}(0,1)$ and $Y \sim \mathit{Beta}(1,2)$

Let $Z_{n,1} = YP_1\cdots P_{n-1}$, where $P_k \sim \mathit{Uniform}(0,1)$, $k = 1,\ldots,n-1$, and $Y \sim \mathit{Beta}(1,2)$ are independent random variables, and define $S = -\ln Z_n$. Therefore,

$$S = -\ln Y + \sum_{k=1}^{n-1}(-\ln P_k) \stackrel{d}{=} W + X,$$

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where $W = -\ln Y$ and $X = \sum_{k=1}^{n-1}(-\ln P_k) \sim Gamma(n-1,1)$ are independent random variables. Since the joint probability density function of the random pair (W,X) is

$$f_{(W,X)}(w,x) = \frac{2}{(n-2)!}x^{n-2}(1-\mathrm{e}^{-w})\mathrm{e}^{-(x+w)}\,\mathbb{I}_{(0,\infty)\times(0,\infty)}(w,x)\,,$$

for $s > 0$,

$$\begin{aligned} f_S(s) &= \int_0^s f_{(W,X)}(s-x,x)\mathrm{d}x = \frac{2}{(n-2)!}\mathrm{e}^{-s}\int_0^s x^{n-2}(1-\mathrm{e}^{-s+x})\mathrm{d}x \\ &= \frac{2}{(n-2)!}\mathrm{e}^{-s}\left[\int_0^s x^{n-2}\mathrm{d}x - \int_0^s x^{n-2}\mathrm{e}^{-s+x}\mathrm{d}x\right] \\ &= \frac{2}{(n-2)!}\mathrm{e}^{-s}\left\{\frac{s^{n-1}}{n-1} - \mathrm{e}^{-s}(-1)^n\left[\Gamma(n-1,-s) - \Gamma(n-1)\right]\right\} \\ &= \frac{2}{(n-2)!}\left\{\frac{s^{n-1}\mathrm{e}^{-s}}{n-1} + (-1)^n\mathrm{e}^{-2s}\left[(n-2)! - \Gamma(n-1,-s)\right]\right\}. \end{aligned}$$

Consequently, for $z \in (0,1)$,

$$\begin{aligned} f_{Z_{n,1}}(z) &= \frac{2}{(n-2)!}\left[\frac{(-\ln z)^{n-1}z}{n-1} + (-1)^n z^2\left[(n-2)! - \Gamma(n-1,\ln z)\right]\right]\frac{1}{z} \\ &= \frac{2}{(n-2)!}\left[\frac{(-\ln z)^{n-1}}{n-1} + (-1)^n z\left[(n-2)! - \Gamma(n-1,\ln z)\right]\right]. \end{aligned} \tag{6}$$

Noting that $\Gamma(\alpha,z) = \Gamma(\alpha)(1-P(\alpha,z))$, where $P(\alpha,z) = \frac{1}{\Gamma(\alpha)}\int_0^z t^{\alpha-1}\mathrm{e}^{-t}\mathrm{d}t$, $\alpha,z > 0$, and in particular, $P(n,z) = 1-\mathrm{e}^{-z}\sum_{k=0}^{n-1}\frac{z^k}{k!}$, $n \in \mathbb{N}$ (cf. Abramowitz and Stegun [93], 6.5.1–6.5.3 and 6.5.13), we get

$$\Gamma(n-1,\ln z) = \frac{\Gamma(n-1)}{z}\sum_{k=0}^{n-2}\frac{(\ln z)^k}{k!} = \frac{(n-2)!}{z}\sum_{k=0}^{n-2}\frac{(\ln z)^k}{k!}\,.$$

Therefore, substituting the above expression in (6), it follows that

$$\begin{aligned} f_{Z_{n,1}}(z) &= \frac{2(-\ln z)^{n-1}}{(n-1)!} + 2(-1)^n z\left[1 - \frac{1}{z}\sum_{k=0}^{n-2}\frac{(\ln z)^k}{k!}\right] \\ &= 2(-1)^{n-1}\left[\frac{(\ln z)^{n-1}}{(n-1)!} - z + \sum_{k=0}^{n-2}\frac{(\ln z)^k}{k!}\right] \\ &= 2(-1)^{n-1}\left[1 - z + \sum_{k=1}^{n-1}\frac{(\ln z)^k}{k!}\right]. \end{aligned}$$

Note that due to the contraction resulting from multiplying random variables with support $[0,1]$,

$$\sum_{k=1}^{n-1}\frac{(\ln z)^k}{k!} \xrightarrow[n\to\infty]{} \mathrm{e}^{\ln z} - 1 = z - 1\,,$$

and therefore for all $z > 0$, $f_{Z_{n,1}}(z) \xrightarrow[n\to\infty]{} 0$. In other words, $f_{Z_{n,1}}(z) \xrightarrow[n\to\infty]{} \delta_0$, the Dirac degenerate at 0 "density", and $F_{Z_{n,1}}(z) \xrightarrow[n\to\infty]{} H_0(z) = \begin{cases} 0, & x < 0 \\ 1, & x \geq 0 \end{cases}$, i.e. the Heaviside function.

— Probability density function of $Z_{n,2} = Y_1 Y_2 \prod_{k=1}^{n-2} P_k$, with independent $Y_1, Y_2 \sim Beta(1,2)$ and $P_k \sim Uniform(0,1)$

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Let $Y_1 \overset{\mathrm{d}}{=} Y_2 \sim Beta(1,2)$ be independent random variables. The probability density function of $Z_{2,2} = Y_1 Y_2$ is

$$f_{Z_{2,2}}(z) = -4\left[2(1-z) + (1+z)\,\ln z\right] \mathbb{I}_{(0,1)}(z)\,,$$

and from which we easily obtain the probability density function of $Z_{3,2} = Y_1 Y_2 P_1$,

$$f_{Z_{3,2}}(z) = 4\left[3 - 3z + (z+2)\ln z + \frac{(\ln z)^2}{2}\right] \mathbb{I}_{(0,1)}(z).$$

Applying recursive methods, the probability density function of $Z_{n,2}$ is

$$f_{Z_{n,2}}(z) = 4(-1)^{n-1}\left[n(1-z) + z\ln z + \sum_{k=1}^{n-1} \frac{(n-k)(\ln z)^k}{k!}\right] \mathbb{I}_{(0,1)}(z).$$

4.3.3. Fisher's Statistic Sampling Distribution for Combining p-Values from a Mendel(m) Population

If $X_1, \ldots, X_n$ are independent and identically distributed random variables with probability density function f, the probability density function of the sum $X_1 + \cdots + X_n$ is the n-fold convolution of f, denoted by f^{n*}, and defined as

$$f^{n*} = f^{(n-1)*} * f = f * f^{(n-1)*}\,,$$

with $f^{1*} = f$ and $f^{0*} * f = f$. As for the n-fold convolution of a finite mixture of probability density functions $f_1, \ldots, f_k$, i.e. with probability density function $f(t) = \sum_{j=1}^{k} \pi_j f_j(t)$, where $\pi_j \geq 0$ and $\sum_{j=1}^{k} \pi_j = 1$, it is

$$f^{n*}(t) = \sum_{n_1+\cdots+n_k=n} \frac{n!}{n_1!\ldots n_k!}\, \pi_1^{n_1} \ldots \pi_k^{n_k} f_1^{n_1*} * \cdots * f_k^{n_k*}(t)\,, \tag{7}$$

(Sarabia et al. [94]), which is also a mixture.

Let $(X_1, \ldots, X_n)$ be a random sample with $X_k \overset{d}{=} X \sim Mendel(m),\ m \in (-2,2),\ k = 1, \ldots, n$, i.e. with probability density function

$$f_X(x) = \left(mx + 1 - \tfrac{m}{2}\right)\mathbb{I}_{(0,1)}(x)\,,$$

and define $T_{n;m} = -2\sum_{k=1}^{n} \ln X_k$.

If $m = 0$, then $T_{n;0} = T_F \sim \chi^2_{2n}$ since $X_k \sim Uniform(0,1)$, $k = 1, \ldots, n$. If $m \in (-2,0) \cup (0,2)$, define $Y_k = -2\ln X_k$, $k = 1, \ldots, n$. Therefore, for $t > 0$, the probability density function of Y_k can be expressed as

$$f_{Y_k}(t) = \frac{m}{2}\,\mathrm{e}^{-t} + \left(1 - \frac{m}{2}\right)\frac{1}{2}\,\mathrm{e}^{-t/2} = \left(1 + \frac{m}{2}\right)\frac{1}{2}\mathrm{e}^{-t/2} - \frac{m}{2}\left(\mathrm{e}^{-t/2} - \mathrm{e}^{-t}\right).$$

Consequently, if $m \in (0,2)$, the distribution of Y_k is a convex mixture of two exponential distributions, more precisely,

$$f_{Y_k}(t) = \tfrac{m}{2} f_{E_1}(t) + \left(1 - \tfrac{m}{2}\right) f_{E_2}(t)\,, \tag{8}$$

where E_j denotes an exponential random variable with scale parameter $j > 0$. On the other hand, if $m \in (-2,0)$, then the distribution of Y_k is also a convex mixture since its probability density function can be expressed as

$$f_{Y_k}(t) = \left(1 + \tfrac{m}{2}\right) f_{E_2}(t) + \left(-\tfrac{m}{2}\right) f_W(t)\,, \tag{9}$$

where W has probability density function $f_W(t) = \left(\mathrm{e}^{-t/2} - \mathrm{e}^{-t}\right)\mathbb{I}_{(0,\infty)}(t)$.

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Note that if $m \in (-2,0)$ (respectively, $m \in (0,2)$), probability density function (8) (respectively, probability density function (9)) can be considered a general mixture. Hence, the probability density function of $T_{n;m}$ is the n-fold convolution of a finite mixture when $m \in (-2,0) \cup (0,2)$.

Although Theorem 1 in Sarabia et al. [94] only deals with convex mixtures, it is extended in Theorem 2 to general finite mixtures, i.e. mixtures where some mixing weights are allowed to be negative.

Theorem 2. *Let f_j, $j = 1,\ldots,k$, be probability density functions and X a random variable with probability density function defined by*

$$f(x) = \sum_{j=1}^{k} a_j f_j(x)\,,$$

where $a_1,\ldots,a_k$ are real constants subject to $\sum_{j=1}^{k} a_j = 1$. The probability density function of the n-fold convolution of f is

$$f^{n*}(x) = \sum_{n_1+\cdots+n_k=n} \frac{n!}{n_1!\cdots n_k!} a_1^{n_1}\ldots a_n^{n_k} f_1^{n_1*} * \cdots * f_k^{n_k*}(x)\,.$$

Proof. Denoting by ψ_j the characteristic function of the probability density function f_j, $j = 1,\ldots,k$, the characteristic function of f^{n*}, the probability density function of the n-fold convolution of f, is

$$\begin{aligned}\psi(t) &= \left[\mathbb{E}\left(\mathrm{e}^{itX}\right)\right]^n = \left[\sum_{j=1}^{k} a_j \psi_j(t)\right]^n \\ &= \sum_{n_1+\cdots+n_k=n} \frac{n!}{n_1!\cdots n_k!} a_1^{n_1}\ldots a_k^{n_k} \psi_1^{n_1}(t)\cdots\psi_k^{n_k}(t)\,.\end{aligned}$$

As $\psi_1^{n_1}\cdots\psi_k^{n_k}$ is the characteristic function of the convolution $f_1^{n_1*} * \cdots * f_k^{n_k*}$, the probability density function of the n-fold convolution of f is

$$f^{n*}(x) = \sum_{n_1+\cdots+n_k=n} \frac{n!}{n_1!\cdots n_k!} a_1^{n_1}\ldots a_k^{n_k} f_1^{n_1*} * \cdots * f_k^{n_k*}(x)\,,$$

which is an immediate consequence of the inversion formula for characteristic functions. □

Therefore, from Theorem 2 it follows that $T_{n;m}$ is a finite mixture when $m \in (-2,0) \cup (0,2)$.

Since probability density functions (8) and (9) are formally equivalent, for what follows, it suffices to work with probability density function (8). Thus applying (7), we get for $t > 0$,

$$f_{T_{n;m}}(t) = \sum_{k=0}^{n} \binom{n}{k} \left(\tfrac{m}{2}\right)^k \left(1-\tfrac{m}{2}\right)^{n-k} f_{E_1}^{k*} * f_{E_2}^{(n-k)*}(t)\,,$$

where $f_{E_1}(t) = \mathrm{e}^{-t}\,\mathbb{I}_{(0,\infty)}(t)$ and $f_{E_2}(t) = \frac{1}{2}\,\mathrm{e}^{-t/2}\,\mathbb{I}_{(0,\infty)}(t)$.

Noticing that f_j^{m*} is the m-convolution of an exponential probability density function with scale parameter j, in other words, f_j^{m*} is the probability density function of the sum of m independent and identically distributed exponential random variables with scale parameter j, $j = 1,2$, it follows that f_j^{m*} is the probability density function of the Gamma distribution with shape parameter m and scale parameter j, and therefore

$$f_1^{k*}(t) = \frac{t^{k-1}\mathrm{e}^{-t}}{\Gamma(k)}\,\mathbb{I}_{(0,\infty)}(t) \quad \text{and} \quad f_2^{(n-k)*}(t) = \frac{t^{n-k-1}\mathrm{e}^{-t/2}}{2^{n-k}\Gamma(n-k)}\,\mathbb{I}_{(0,\infty)}(t)\,.$$

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Hence,

$$\begin{aligned} f_1^{k*} * f_2^{(n-k)*}(t) &= \int_{-\infty}^{\infty} f_1^{k*}(x) f_2^{(n-k)*}(t-x)dx \\ &= \int_0^t \frac{x^{k-1}\mathrm{e}^{-x}(t-x)^{n-k-1}\mathrm{e}^{-(t-x)/2}}{2^{n-k}\Gamma(k)\Gamma(n-k)}dx \\ &= \frac{\mathrm{e}^{-t/2}}{2^{n-k}\Gamma(k)\Gamma(n-k)} \int_0^t x^{k-1}(t-x)^{n-k-1}\mathrm{e}^{-x/2}dx\,. \end{aligned}$$

Using the formula

$$\int_0^u x^{\nu-1}(u-x)^{\mu-1}\,\mathrm{e}^{\beta x}dx = B(\mu,\nu)u^{\mu+\nu-1}{}_1F_1(\nu;\mu+\nu;\beta u)\,,\ \mu>0,\ \nu>0,$$

(cf. Gradshteyn and Ryzhik [95], 3.383.1), where $B(p,q) = \int_0^1 x^{p-1}(1-x)^{q-1}\mathrm{d}x$, $p,q>0$, is the Beta function and ${}_1F_1(a;b;z) = \sum_{k=0}^{\infty}\frac{(a)_k}{(b)_k}\frac{z^k}{k!}$ the Kummer's confluent hypergeometric function, we obtain

$$\begin{aligned} f_1^{k*} * f_2^{(n-k)*}(t) &= \frac{\mathrm{e}^{-t/2}}{2^{n-k}\Gamma(k)\Gamma(n-k)}B(n-k,k)t^{n-1}{}_1F_1(k;n;-\tfrac{t}{2}) \\ &= \frac{t^{n-1}\mathrm{e}^{-t/2}}{2^{n-k}\Gamma(n)}\,{}_1F_1(k;n;-\tfrac{t}{2})\,. \end{aligned}$$

Therefore, for $t>0$,

$$\begin{aligned} f_{T_{n;m}}(t) &= \sum_{k=0}^{n}\binom{n}{k}(\tfrac{m}{2})^k(1-\tfrac{m}{2})^{n-k}\frac{t^{n-1}\mathrm{e}^{-t/2}}{2^{n-k}\Gamma(n)}{}_1F_1(k;n;-\tfrac{t}{2}) \\ &= \frac{t^{n-1}\mathrm{e}^{-t/2}}{2^n\Gamma(n)}\sum_{k=0}^{n}\binom{n}{k}m^k(1-\tfrac{m}{2})^{n-k}{}_1F_1(k;n;-\tfrac{t}{2})\,. \end{aligned}$$

For example, if $n=2$ and $m=1$,

$$\begin{aligned} f_{T_{2;1}}(t) &= \frac{t\,\mathrm{e}^{-t/2}}{4}\sum_{k=0}^{2}\binom{2}{k}\left(\frac{1}{2}\right)^{2-k}{}_1F_1(k;2;-\tfrac{t}{2}) \\ &= \frac{1}{16}\left[(t+8)\,\mathrm{e}^{-t/2}+4(t-2)\,\mathrm{e}^{-t}\right] \\ &= \frac{1}{4}\frac{t\,\mathrm{e}^{-t/2}}{4}+\frac{1}{4}t\,\mathrm{e}^{-t}+\frac{1}{2}\left(\mathrm{e}^{-t/2}-\mathrm{e}^{-t}\right), \end{aligned}$$

which is a convex mixture, and if $n=2$ and $m=-1$,

$$\begin{aligned} f_{T_{2;-1}}(t) &= \frac{t\,\mathrm{e}^{-t/2}}{4}\sum_{k=0}^{2}\binom{2}{k}(-1)^k\left(\frac{3}{2}\right)^{2-k}{}_1F_1(k;2;-\tfrac{t}{2}) \\ &= \frac{1}{16}\left[3(3t-8)\,\mathrm{e}^{-t/2}+4(t+6)\mathrm{e}^{-t}\right] \\ &= \frac{9}{4}\frac{t\,\mathrm{e}^{-t/2}}{4}+\frac{1}{4}t\,\mathrm{e}^{-t}-\frac{3}{2}\left(\mathrm{e}^{-t/2}-\mathrm{e}^{-t}\right), \end{aligned}$$

which is a general mixture.

In Figure 1 we plot the probability density function of $T_{n;m}$ for $n=2,3$ and $m=-1,0,1$.

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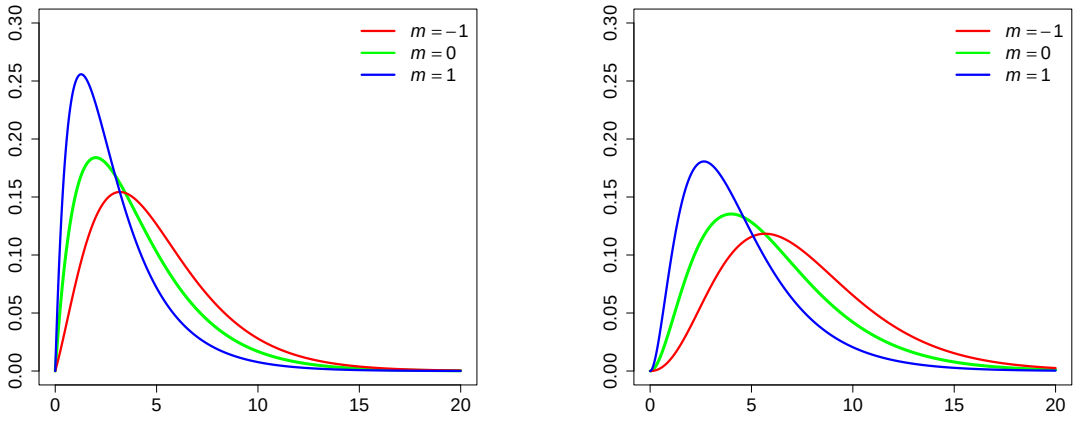

(a) **(b)**

Figure 1. Probability density function of $T_{n;m}$ for $m = -1, 0, 1$: **(a)** $n = 2$. **(b)** $n = 3$.

5. Discussion

With the exception of Tippett's $T_T(P_1, \ldots, P_n) = P_{1:n}$, the other combined test statistics mentioned in Section 2 have a distribution that does not allow a closed-form expression for the cumulative distribution function when there are $n_f \geq 1$ fake p-values in the sample.

As already mentioned, it is in general impossible to know whether there exist or not fake p-values among the set of p-values to be combined. Therefore, a realistic approach is to examine possible scenarios and assess how the existence of fake p-values can affect the decision on the overall hypothesis H_0^*.

For this purpose, a simple simulation was carried out with the software R (version 4.3.1), a language and environment for statistical computing (R Core Team 2023, [96]), to obtain quantile estimates of order q (q = 0.005,0.01,0.025,0.05,0.1,0.9,0.95,0.975,0.99,0.995) for the combined test statistics indicated in Section 2, and when some of the p-values in the sample are fake ones. The guidelines in Davison and Hinkley [97] on how to estimate quantiles (pp. 18-19) were followed here. The tables with the estimated quantiles (in a few cases some are exact) are supplied in the Supplementary Materials for sample sizes $n = 3, \ldots, 28$, and when there exists at most $n_f \leq \lfloor n/3 \rfloor$ fake p-values. These tables are a useful tool to build up an overall picture, as is illustrated with Example 6.

Example 6. *For the set of $n = 18$ fictional p-values:*

$$\begin{array}{cccccccccc} 0.4574 & 0.0223 & 0.0371 & 0.6954 & 0.0549 & 0.2793 & 0.7928 & 0.6917 & 0.3483, \\ 0.0554 & 0.8238 & 0.8583 & 0.3824 & 0.7138 & 0.0423 & 0.0116 & 0.7543 & 0.1438 \end{array}$$

the observed values for the combined test statistics are:

$$\begin{aligned} &T_F(0.4574, \ldots, 0.1438) = 56.9104 \\ &T_S(0.4574, \ldots, 0.1438) = -1.9665 \\ &T_C(0.4574, \ldots, 0.1438) = 26.1606 \\ &T_{MG}(0.4574, \ldots, 0.1438) = 15.9379 \quad (t^*_{MG} = 2.0935) \\ &T_{\mathcal{G}_{18}}(0.4574, \ldots, 0.1438) = 0.2058 \\ &T_{\min \mathcal{G}_{18}, \mathcal{G}^*_{18}}(0.4574, \ldots, 0.1438) = 0.2058 \\ &T_{\mathcal{H}_{18}}(0.4574, \ldots, 0.1438) = 0.0734 \\ &T_E(0.4574, \ldots, 0.1438) = 0.3981 \\ &T_T(0.4574, \ldots, 0.1438) = 0.0116 \\ &T_W(0.4574, \ldots, 0.1438) = 0.8583\,. \end{aligned}$$

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We reproduce below only the part for $n = 18$ from the tables in the Supplementary Materials (without the standard errors), highlighting the critical quantiles that lead to the rejection of H_0^* with an asterisk, as well as indicating the smallest significance level $\alpha \in \{0.005, 0.01, 0.025, 0.05, 0.10\}$ for which this happens.

• Fisher's Statistic $T_F = 56.9104$

n	n_f	0.900	0.950	0.975	0.990	0.995	α
18	0	47.2122∗	50.9985∗	54.4373∗	58.6192	61.5812	0.025
18	1	48.3379∗	52.1229∗	55.5203∗	59.7620	62.7232	0.025
18	2	49.4103∗	53.1857∗	56.6785∗	60.8012	63.7274	0.025
18	3	50.4540∗	54.3029∗	57.7948	62.0427	65.0779	0.05
18	4	51.5281∗	55.3389∗	58.8498	63.1156	66.1164	0.05
18	5	52.5732∗	56.4025∗	59.8978	64.0685	67.2668	0.05
18	6	53.6360∗	57.4945	60.9949	65.3194	68.3048	0.10

• Stouffer's Statistic $T_S = -1.9665$

n	n_f	0.900	0.950	0.975	0.990	0.995	α
18	0	1.2815∗	1.6448∗	1.9600∗	2.3264	2.5758	0.025
18	1	1.1321∗	1.4888∗	1.8005∗	2.1669	2.4111	0.025
18	2	0.9884∗	1.3418∗	1.6537∗	2.0091	2.2655	0.025
18	3	0.8432∗	1.1942∗	1.5043∗	1.8587∗	2.1084	0.01
18	4	0.6997∗	1.0505∗	1.3625∗	1.7079∗	1.9505∗	—
18	5	0.5578∗	0.9073∗	1.2070∗	1.5548∗	1.8026∗	—
18	6	0.4117∗	0.7573∗	1.0546∗	1.3945∗	1.6334∗	—

• Chen's Statistic $T_C = 26.1606$

n	n_f	0.900	0.950	0.975	0.990	0.995	α
18	0	25.9894∗	28.8693	31.5264	34.8053	37.1564	0.10
18	1	26.0050∗	28.8614	31.5476	34.7641	37.2442	0.10
18	2	26.0007∗	28.8603	31.5185	34.7654	37.1842	0.10
18	3	25.9715∗	28.8615	31.5584	34.7827	37.2972	0.10
18	4	25.9611∗	28.8558	31.5221	34.8170	37.2941	0.10
18	5	25.9520∗	28.8359	31.4967	34.8157	37.2759	0.10
18	6	25.9417∗	28.8679	31.5524	34.7698	37.2629	0.10

• Mudholkar and George's Statistic $T_{MG} = 15.9379$

n	n_f	0.900	0.950	0.975	0.990	0.995	α
18	0	9.8535∗	12.6987∗	15.1577∗	18.0717	20.0749	0.025
18	1	10.7808∗	13.6068∗	16.0024	18.9023	20.8850	0.05
18	2	11.6996∗	14.4896∗	16.9051	19.6710	21.6251	0.05
18	3	12.6072∗	15.3900∗	17.8073	20.6821	22.6112	0.05
18	4	13.5400∗	16.2821	18.6795	21.5146	23.4955	0.10
18	5	14.4620∗	17.1581	19.5568	22.3635	24.2301	0.10
18	6	15.3463∗	18.0434	20.4629	23.1753	25.2362	0.10

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• Geometric Mean $T_{\mathcal{G}_{18}} = 0.2058$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.18076	0.19626	0.22044∗	0.24253∗	0.26943∗	0.025
18	1	0.17517	0.19015	0.21392∗	0.23508∗	0.26114∗	0.025
18	2	0.17034	0.18474	0.20715∗	0.22824∗	0.25348∗	0.025
18	3	0.16407	0.17849	0.20082	0.22127∗	0.24623∗	0.05
18	4	0.15941	0.17324	0.19502	0.21499∗	0.23899∗	0.05
18	5	0.15439	0.16871	0.18942	0.20873∗	0.23215∗	0.05
18	6	0.15002	0.16295	0.18373	0.20250	0.22540∗	0.10

• Minimum of Geometric Means $T_{\min\left\{\mathcal{G}_{18},\mathcal{G}_{18}^{*}\right\}} = 0.2058$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.16748	0.18109	0.20234	0.22089∗	0.24268∗	0.05
18	1	0.16771	0.18106	0.20210	0.22066∗	0.24246∗	0.05
18	2	0.16614	0.17955	0.20004	0.21905∗	0.24126∗	0.05
18	3	0.16209	0.17584	0.19665	0.21584∗	0.23835∗	0.05
18	4	0.15833	0.17185	0.19303	0.21195∗	0.23429∗	0.05
18	5	0.15416	0.16818	0.18850	0.20724∗	0.22955∗	0.05
18	6	0.14992	0.16267	0.18340	0.20183	0.22413∗	0.10

• Harmonic Mean $T_{\mathcal{H}_{18}} = 0.0734$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.00484	0.00933	0.02154	0.03932	0.06833	—
18	1	0.00470	0.00892	0.02061	0.03724	0.06481	—
18	2	0.00448	0.00850	0.01953	0.03528	0.06166	—
18	3	0.00433	0.00808	0.01860	0.03350	0.05882	—
18	4	0.00408	0.00772	0.01773	0.03213	0.05639	—
18	5	0.00395	0.00735	0.01702	0.03087	0.05413	—
18	6	0.00374	0.00707	0.01635	0.02967	0.05194	—

• Arithmetic Mean $T_E = 0.3981$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.32566	0.34207	0.36647	0.38733	0.41222∗	0.10
18	1	0.31913	0.33507	0.35886	0.37940	0.40362∗	0.10
18	2	0.31213	0.32820	0.35130	0.37126	0.39516	—
18	3	0.30455	0.31983	0.34308	0.36304	0.38675	—
18	4	0.29747	0.31320	0.33505	0.35499	0.37860	—
18	5	0.28958	0.30480	0.32736	0.34705	0.37017	—
18	6	0.28308	0.29723	0.31931	0.33906	0.36191	—

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• Minimum $T_T = 0.0116$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.00028	0.00056	0.00141	0.00285	0.00584	—
18	1	0.00026	0.00053	0.00133	0.00270	0.00553	—
18	2	0.00025	0.00050	0.00127	0.00256	0.00525	—
18	3	0.00024	0.00048	0.00120	0.00244	0.00500	—
18	4	0.00023	0.00046	0.00115	0.00233	0.00478	—
18	5	0.00022	0.00044	0.00110	0.00223	0.00457	—
18	6	0.00021	0.00042	0.00105	0.00213	0.00438	—

• Maximum $T_W = 0.8583$

n	n_f	0.005	0.010	0.025	0.050	0.100	α
18	0	0.74501	0.77426	0.81470	0.84668	0.87992∗	0.10
18	1	0.73587	0.76506	0.80672	0.83921	0.87388∗	0.10
18	2	0.72414	0.75493	0.79795	0.83189	0.86768∗	0.10
18	3	0.71307	0.74442	0.78830	0.82406	0.86091∗	0.10
18	4	0.70160	0.73412	0.77899	0.81504	0.85338	—
18	5	0.68996	0.72267	0.76825	0.80548	0.84499	—
18	6	0.67754	0.71057	0.75737	0.79515	0.83610	—

Note that the conclusions with T_F and $T_{\mathcal{G}_n}$ are the same, but it is obviously useful to supply both tables. The example has been constructed to have p-values in the range $[0, 1]$, some of them small and some large. This is a situation where T_{MG} and $T_{\min\{\mathcal{G}_n, \mathcal{G}^*\}}$, which use both P_k's and $1 - P_k$'s, may be useful for an informed decision.

In fact, in this example, T_{MG} and $T_{\min\{\mathcal{G}_n, \mathcal{G}_n{}^*\}}$ perform almost as well as T_F (or $T_{\mathcal{G}_n}$) and better than T_S. Moreover, the statistic T_C seems to be less reliable than T_S and T_{MG}, and except for the geometric ($r = 0$) mean $T_{\mathcal{G}_n}$, the means of order $r \in \{-\infty, -1, 1, \infty\}$, i.e. T_T, $T_{\mathcal{H}_n}$, T_E and T_W, do not contribute effectively for a clearcut decision.

This example shows that the existence of fake p-values can influence the overall decision on H_0^*, as expected, and the most recommended Fisher's and Stouffer et al.'s methods are clearly affected by their existence. Aside from the number of fake p-values in the sample, their magnitude has also a bearing on the smallest level α that leads to the rejection of H_0^*.

6. Conclusions

Although significance testing and p-values have these days plenty of bad press and detractors, reporting low p-values still has a mythic standing and influences publication acceptance. Therefore, it is possible that research teams will try to obtain smaller p-values if the first ones obtained are not significant. In these unwanted situations, which were first pointed out by Fisher [37] when denouncing the possibility of fraud in Mendel's theories (cf. also Franklin [38], and Pires and Branco [39]), the most realistic scenarios are:

1. In the first experiment the p-value obtained was greater than 0.05 and the p-value obtained in the second experiment is smaller than 0.05. The first one is "hidden" and the second one is reported. However, the reported p-value is not genuine, it is the fake result of two P, and therefore it is Beta(1,2)-distributed.
2. The p-values obtained in the first and second experiments were both greater than 0.05. This seems to indicate that there are no grounds to reject the null hypothesis and the most plausible

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consequence is the abandonment of the line of research, thus leading to no p-value being published. In fact, replicating experiments has costs, at least it is time consuming, and therefore discarding further experimentation seems to be a reasonable decision.

So, when meta-analyzing p-values via combining them, one must be aware that in the Brave New World of scientific achievements, where the underlying motto is "publish or perish", eventually some — but almost certainly very few — of the the P_k's, $k = 1, \ldots, n$, to be used in statistics $T(P_1, \ldots, P_n)$ are fake $Beta(1, 2)$ p-values, although in an honest world all p-values should be genuine $Beta(1, 1) = Uniform(0, 1)$ values.

It is therefore reasonable to use tools such as the extensive tables supplied in the Supplementary Materials to compare the results of several combined tests, assuming that between the P_k's there are $n_f = 0, 1, \ldots, j \ll n$ fake p-values.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

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