

Monte Carlo Simulations for Assessing the Performance of Permutation of Residuals Methods in One-way ANOVA

Bir Yönlü Varyans Analizinde Artıkların Performansını Belirleyen Yöntemler İçin Monte Carlo Simülasyonları

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ABSTRACT Objective: The current paper aims to assess the relative performance of three permutation methods of residuals where exact probability was used. **Material and Methods:** A total of 198 Monte Carlo simulations were run for the three permutation of residuals considering different population distributions, increasing sample size and variance under the unique scenario of balanced and homoscedastic design in ANOVA framework. **Results:** When residuals follow a lognormal distribution, permutation of residuals under reduced model showed the best performance. In the case of cubed exponential distribution, permutation of residuals under full model revealed satisfactory results. Permutation of residuals under modified model revealed a conservative character. **Conclusion:** The use of the exact probability instead of the approximate value has changed the behaviour of the permutation of residuals in the case of one-way ANOVA. We suggest that the choice of the permutation method in one-way ANOVA should be based on the distribution of the residuals.

Keywords: Permutation test; ANOVA; exact probability; alpha rate; power of test; sample size

ÖZET Amaç: Bu makale, tam olasılığın kullanıldığı üç permütasyon artık değer yönteminin relatif performansını değerlendirmeyi amaçlamaktadır. **Gereç ve Yöntemler:** ANOVA çerçevesinde dengeli ve homoscedastic tasarımın benzersiz senaryosu altında, farklı anakütle dağılımları, artan örneklem büyüklüğü ve varyans göz önüne alındığında, artık değerlerin üç permütasyonu için toplam 198 Monte Carlo simülasyonu gerçekleştirilmiştir. **Bulgular:** Artık değerler lognormal dağılımı izlediğinde indirgenmiş model altında artık değerlerin permütasyonu en iyi performansı göstermiştir. Küp üstel dağılım durumunda, artık değerlerin tam model altında permütasyonu tatmin edici sonuçlar vermiştir. Artık değerlerin modifiye edilmiş modele göre permütasyon işlemi, muhafazakâr bir karakteristik ortaya koymuştur. **Sonuç:** Yaklaşık değer yerine kesin olasılık kullanımı, tek yönlü ANOVA durumunda artık değerlerin permütasyon davranışını değiştirmiştir. Tek yönlü ANOVA'da permütasyon yönteminin seçiminin artık değerlerin dağılımına dayanması gerektiğini öneririz.

Anahtar Kelimeler: Permütasyon testi, ANOVA; tam olasılık; alfa hızı; test gücü; örneklem ölçümü

Inferential statistics aims at providing objects for decision-making, researching optimal value and determining the well-adjusted model based on probability or confidence intervals. Hence, when one considers a dataset constituted by γ samples ($y_1, y_2, \dots, y_\gamma$) for a given factor. A, it is hypothesized that these samples come from the same population y . In other words, the null hypothesis (Eq.1)

$$H_0 : \mu_1 = \mu_2 = \dots = \mu_\gamma \text{ vs. } H_1 : \exists(i, j), \mu_i \neq \mu_j \quad (1)$$

is tested. When $\gamma > 2$, a single factor Analysis of Variance (ANOVA) or the Kruskal Wallis test as non-parametric counterpart is used.^{1,2} The use of the

ANOVA or the Kruskal Wallis test requires the fulfilment of the parametric or the non-parametric assumptions. The violation of such conditions does not guarantee accurate interpretation of test results especially when the sample size is small.^{3,4} Most recently, the use of free distribution methods such as permutation methods emerged as a best alternative when assumptions are disregarded. The permutation tests consist of rearranging data by shifting the treatments labels and computing the statistics of interest. The effectiveness of the method comes from the empirical generation of the null distribution. Actually, no assumption is made regarding the distribution of population from which the samples were taken, and the original data are used rather than the ranks of data.^{5,6} The only one requirement of the permutation method is the exchangeability where the joint density f satisfies (Eq.2)

$$f(z_1, z_2, \dots, z_N) = f(z_{\pi(1)}, z_{\pi(2)}, \dots, z_{\pi(N)}) , \quad (2)$$

where $(\pi_1, \pi_2, \dots, \pi_N)$ is any permutation of $(1, 2, \dots, N)$.

Additionally, permutation methods remain robust when outliers and missing data occur.⁷ The decision is made using the probability computed as the proportion of the statistics greater than the one observed.^{8,9} However, it has been demonstrated that the former procedure of the computation of the probability value is inflated. The procedure generated frequently the value of probability equal to zero though a subset of the overall population was used.¹⁰ To avoid the probability value equal to zero, the authors proposed a computation of exact probability value. So far, the exact probability computation has been rarely implemented for the permutation in the case of ANOVA and regression. Thus, one can hypothesize that the implementation of the exact probability in ANOVA will change the former known rank of the permutation procedures.

It is recorded that the raw data or the residuals could be permuted in ANOVA. Within the permutation of residuals, ter Braaj proved the superiority of full model residuals (PRF) when it was compared with Oja's permutation methods and bootstrapping one.¹¹⁻¹³ Further, simulations studies showed that compared to the overall permutation strategies, the permutation of residuals under reduced model (PRR) was relatively the most robust.¹⁴ Compared to the permutation of residuals under reduced model, the permutation of residuals under modified model (PRM) was the only one which kept the nominal value of type I error.⁹ However, all these studies assessed the relative performance of permutation methods using the approximate probability value.

The current simulation study intends to use the exact probability value for the assessment of PRF, PRR and PRM performance under balanced homoscedastic design.

MATERIAL AND METHODS

This study adapted the simulation plan to address our objective. The detail of the permutation of residuals methods was described on the Annex 1.

SIMULATION PLAN

The simulation was implemented using a code built in R software.¹⁵ Monte Carlo simulations were used to investigate the essential empirical characteristics of the permutation of residuals tests and compare methods sensitivity under the increasing sample size and variance. A total of 198 simulations was run according to the scenario described in Table 1. For each individual simulation, 1000 datasets were used to generate the parameters alpha, power and effect size under known distribution parameters. For each

Annexe 1
 The simulation was based the method described on ⁹
Models in single factor ANOVA

The model for analysis of variance with single error term (ANOVA) can be written as

$$y = X\beta + \varepsilon \tag{5}$$

where y is the response vector, X represents the design matrix, β the vector of parameters that should be estimated and ε the vector of errors ($\sim N(0, \sigma^2)$).

Let suppose that X is based sigma-restricted parameterization. X and β can be split into the two components, the one of interest and the one of no interest:

$$X = \begin{bmatrix} X_1 \\ X_2 \end{bmatrix}; \beta = \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}$$

Eq.(5) becomes

$$y = X_1\beta_1 + X_2\beta_2 + \varepsilon \tag{6}$$

Suppose that the test on part X_2 of the design matrix using the hypothesis

$$H_0 : \beta_2 = 0 \text{ vs. } H_1 : \beta_2 \neq 0 \tag{7}$$

was not significant Eq. (6) could be simply rewritten (Eq.8)

$$y = X_1\beta_1 + \varepsilon \tag{8}$$

In the case of balanced ANOVA model it has been proved⁹ that the Fisher statistics F_R for the test of hypothesis (Eq. 7) is given by Eq.9:

$$F_R = \frac{y'(X_{rr}(X'_{rr}X_{rr})^{-1}X'_{rr})y/(p-q)}{y'(I-X(X'X)^{-1}X')y/(N-p)} \tag{9}$$

With

$$X_{rr} = (I - H_1)X_2 \text{ and } H_1 = X_1(X'_1X_1)^{-1}X'_1$$

Permutation of residual under pooled model

The permutation of residuals under full model consists to reallocate y and recomputed the fisher statistics as in the Eq. (9). At each reallocation a new fisher statistics is computed and the set of new fisher generate the null distribution.

Permutation of residuals under reduced model

After per-multiplication of the equation (Eq. 9), both part by $I - H_1$. The model (Eq. 8) can be rewritten as

$$y_{rr} = X_{rr}\beta_2 + \varepsilon_{rr} \tag{10}$$

where the residuals under reduced model is $y_{rr} = (I - H_1)y$ and $\varepsilon_{rr} = (I - H_1)\varepsilon$. F statistics (Eq. 9) becomes (Eq. 11) as :

$$F_{rr} = \frac{y_{rr}'(X_{rr}(X'_{rr}X_{rr})^{-1}X'_{rr})y_{rr}/(p-q)}{y_{rr}'(I-X(X'X)^{-1}X')y_{rr}/(N-p)} \tag{11}$$

Accordingly, after permutation F_{rr} is denoted F_{rr}^* and y_{rr} becomes y_{rr}^* .

Permutation of residuals under modified model

The modified model is obtained when the matrix V of dimension $N \times (N - q)$ columns forms an orthonormal basis for x_1 . The orthonormality of a given X means $XX' = I_N - H_1$. The model (Eq. 10) becomes

$$y_{mr} = x_{mr}\beta_2 + \varepsilon_{ij} \tag{12}$$

In such model $y_{mr} = V'y_{rr}$ are the residuals under the modified model, $x_{mr} = V'X_{rr}$ and $\varepsilon_{mr} = V'\varepsilon_{rr}$. F is computed as follow (Eq. 13):

$$F_{rr} = \frac{y_{mr}'(x_{mr}(x'_{mr}x_{mr})^{-1}x'_{mr})y_{mr}/(p-q)}{y_{mr}'(I_N - q^{-1}x_{mr}(x'_{mr}x_{mr})^{-1}x'_{mr})y_{mr}/(N-p)} \tag{13}$$

p_{value} is given by the number of F_{rr}^* that exceed the F_{rr} by the number of permutation

TABLE 1: Detailed outline of simulation scenarios conducted for the study.

Type of design	Distribution	Size	variance
Balanced Homoscedastic	Normal $N(0)$	$n=\{3,5,10,15,30,50\}$	$\sigma^2=\{1,1.5,2,3,6\}$
	Lognormal $lnN(0)$	$n=\{3,5,10,15,30,50\}$	$\sigma^2=\{1,1.5,2,3,6\}$
	Cubed Exponential $e^3(1)$	$n=\{3,5,10,15,30,50\}$	$\sigma^2=\{1\}$

simulated dataset, the statistic test and associated p value were calculated for each permutation test using 999 random permutations. The significance level to reject the null hypothesis was set a priori at $\alpha=0.05$ in all cases, and the rejection rate of each test was calculated as the proportion of p value (out of the 1000 simulated datasets) that were less than or equal to α . In addition to the type I error, the power of different permutation procedures was investigated regarding (a) the sample size (b) the residuals normality (c) the type of distribution.

Exact p Value Computation from Monte Carlo Simulation

The purpose of Monte Carlo simulation after permutation test is to estimate $p_{\infty} = P(F > F_{obs})$ where p_{∞} represents the real probability and $P(F > F_{obs})$ the probability after a given permutation to observe the statistics F greater than the test statistics (F_{obs}). However, the known computation of the p value does not take into account the margin error generated by the estimation, and leads to biased estimation of type I error.¹⁰ In concrete case, to compute p_{∞} let us suppose π the number of permutations, F is the Fisher statistics supposed to be continuous, so that p_{∞} is uniformly distributed on $(0, 1)$. F^* denotes all distinct F statistics computed and B is the number of times out of π that $F^* > F_{obs}$, with F_{obs} the initial test statistic. Then, the exact probability (p_u) represents the probability of the random variable B to be inferior to b . $p_u = P(B \leq b)$ for the Monte Carlo coming from marginal distribution of B is given by (Eq.3):

$$p_u = P(B \leq b) = \frac{b+1}{\pi+1} \quad (3)$$

Type I Error Estimation

The empirical probabilities of type I error were studied for the three permutation methods considering:

(a) the sample size $n = \{3,5,10,15,30,50\}$

(b) the distribution of random error $\varepsilon = \{\text{standard normal } (\mathcal{N}(0,1)), \text{ Cubed exponential } (e^3(1)), \text{ log-normal } (\ln\mathcal{N}(0,1))\}$

Standard normal distribution is selected because it represents the ideal case of the distribution of residuals when ANOVA is done. The cubed exponential distribution is used to simulate radically non normal error term.⁵ Furthermore, most of biological data follow lognormal distribution.¹⁶ Residuals variance based on the empirical value of σ as $\hat{\sigma} = \{1, 1.5, 2, 3, 6\}$ for every distribution were used to simulate increasing residuals variance according to sample size.¹⁷ The empirical type I error at 95% confidence interval was calculated for each dataset and for each of the three permutation methods.

STATISTICAL POWER

The investigation of power f (for a given sample size) was indexed uniquely by the measure of the effect size proposed.¹⁸

$$f = \frac{\sqrt{\sum_{i=1}^N (y_i - \bar{y})^2 / N}}{\sigma_{\varepsilon}}, \quad (4)$$

where σ_{ε} is a constant for any dataset of Monte Carlo simulation; $\theta = f \cdot \sigma_{\varepsilon}$ is the measure of effect size, $y_i - \bar{y}$ represents the residuals after the ANOVA and N the total sample size. The Cohen's table was used to detect the statistical power of each method with the R package "pwr".^{19,20} The parameter helped to establish the power curves for different error distributions used in simulations.

In order to see whether there is a meaningful difference between alpha rates, a two-way Analysis of Covariance considering the type of permutation methods, the type of distribution and the cofactor residuals variance were done.

RESULTS

SAMPLE SIZE AND REJECTION RATE TREND

Results of the simulation study (Figure 1) showed that residuals permutation methods were more accurate (alpha reached its asymptotic value) when the sample size increased. When the total sample size is very low 9 (3*3), the rejection rate is generally above the nominal rejection value of 0.05. When residuals followed normal distribution, the PRF and PRR gave value of type I error close to the nominal value of 0.05 when total sample size reaches 15 (3*5). However, the PRM was conservative and stays at 0.01 regardless the sample size.

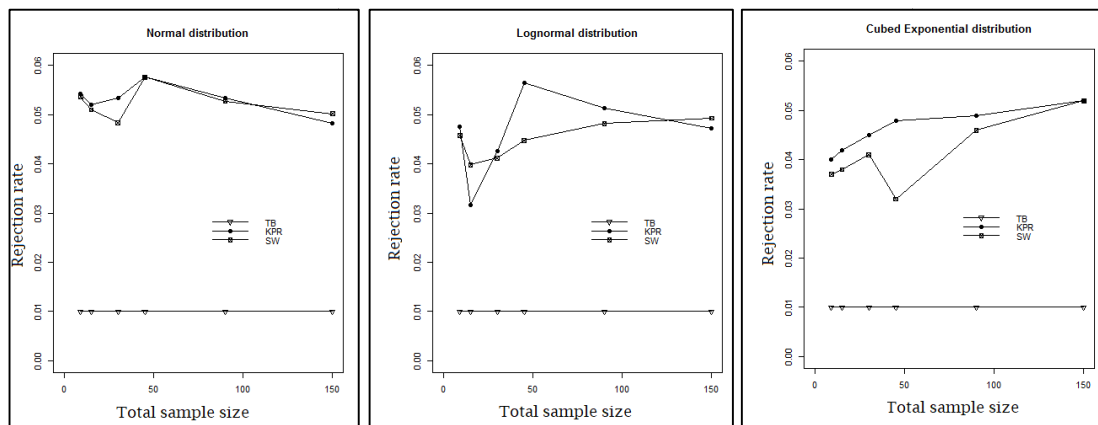


FIGURE 1: Empirical rejection rate for the three permutation of residuals methods.

When residuals follow lognormal distribution, the PRR model gave rejection rate close to the nominal alpha, whereas the PRF was slightly above the nominal value. Similarly, the PRM was conservative.

In the case of cubed exponential distribution of residuals, the PRF had a rejection rate close to 0.05. However, the PRR and PRF were more conservative.

TB: PRF of ter Braak; SW: PRR of Still and White; KPR: PRM Kherad-Pajouh and Renaud^{9,21,22}

INCREASING RESIDUALS VARIANCE EFFECT

The results of two ways Analysis of Covariance (Table 2) showed that there was a significant difference between different values of variances. When the variance increased, the rejection rate of type one error also increased regardless the residuals permutation method that was considered (Figure 2).

TABLE 2: Two ways Analysis of Covariance results.

	Df	Sum Sq	Mean Sq	F value	Pr (>F)
Methods	2	0.122	0.061	16.128	4.00E-07
Distribution	2	0.010	0.005	1.359	2.60E-01
Standard deviation	4	0.008	0.012	6.395	2.39E-01
Methods: Distribution	4	0.024	0.006	1.586	1.80E-01
Methods: Standard deviation	8	0.017	0.002	3.548	4.20E-02
Distribution: Standard deviation	4	0.009	0.267	4.588	4.71E-02
Methods: Distribution :Standard deviation	8	0.016	0.006	1.541	8.24E-03
Residuals	165	0.624	0.004		

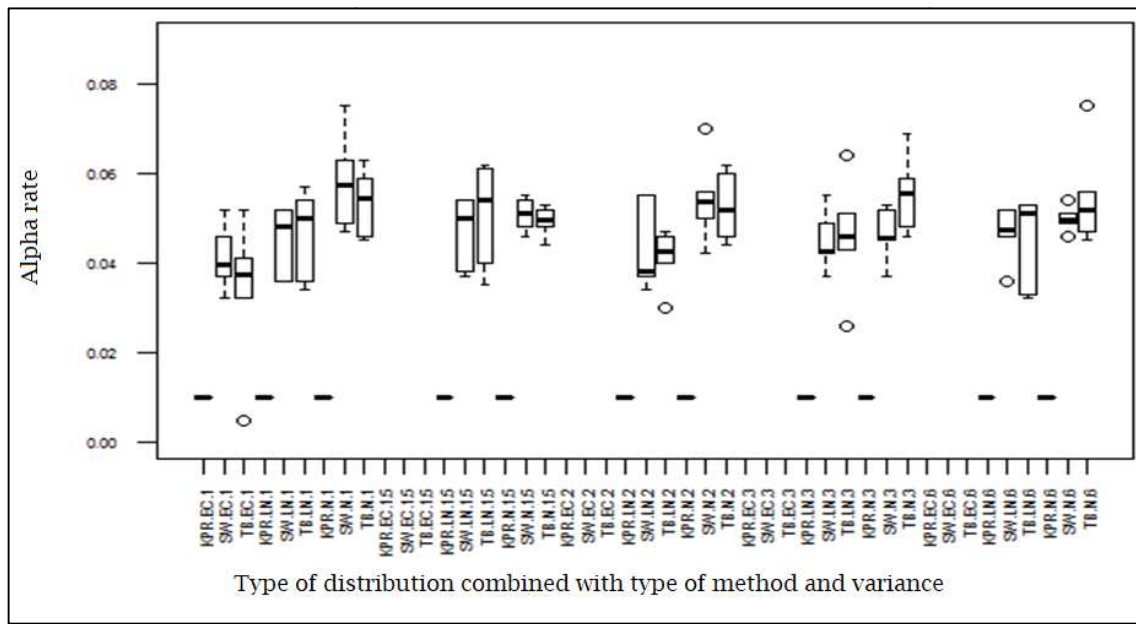


FIGURE 2: Box plots showing the trend of alpha rate with the increasing value of variance.

KPR denotes permutation of residuals under modified model; SW is permutation of residuals under reduced model; TB is the permutation of residuals under pooled model; EC is the cubed exponential distribution; LN: Lognormal distribution; N: normal distribution; the value that follows different combinations of method and distribution types represents the residuals values

POWER OF TESTS

The power curve (Figure 3) showed that there was not a significant difference in terms of group variance. Additionally, it can be noticed that the power of test asymptotically converged to 1 when sample size increased regardless the distribution. When the sample size of population reached 30 individuals, the curve reached a stationary state. This indicated that the best performance for the permutation test was obtained when the total sample size reached at least 30 individuals.

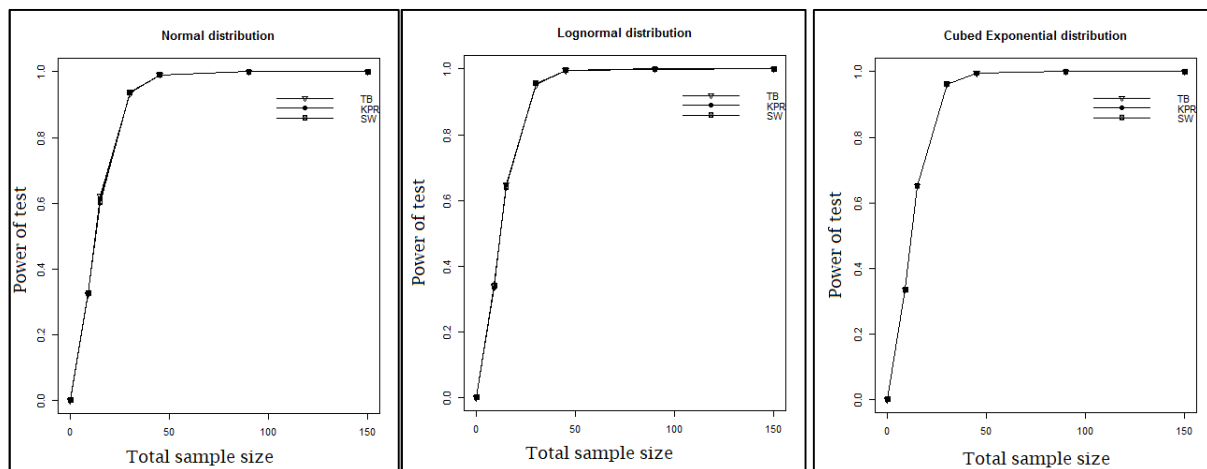


FIGURE 3: Power curve of the three permutation of residuals methods under increasing size of sample.

NUMERICAL RESOLUTION OF THE SIMULATION

The numerical example referred to Manly⁵ and the hypothesis tested in the example was to know whether the consumption of ants by lizard depended on the months. Based on the example dataset (Table 3), the three methods of residuals permutation were applied using the exact probability value. The number of ants consumed followed a Poisson distribution and the raw application of traditional ANOVA cannot be reliable. The permutation of residuals under full, restricted and modified model based on 5000 Monte Carlo resampling were all significant (Table 4). The results implied that the lizard consumption was highly dependent on the period of year.

TABLE 3: Number of ants consume by lizard according to months.

Month	Number	Month	Number	Month	Number	Month	Size
June	13	July	8	August	515	September	18
June	242	July	59	August	488	September	44
June	105	July	20	August	88	September	21
June	182	July	24	August	460	September	140
June	21	July	312	August	1223	September	40
June	7	July	68	August	990	September	27

TABLE 4: Numerical resolution of the simulation considering Manly ⁵ example.

	Pvalue
F test	9.545984
PRF	0.0004
PRR	0.0002
PRM	0.0001

PRF: Permutation of residuals under full model; PRR: Permutation of residuals under restricted model; PRM: Permutation of residuals under modified model.

DISCUSSION

Our simulations showed that permutation of residuals lost in accuracy when the sample size was very low. Similar results were obtained by most of simulation studies.^{18,23} The type I error converged when the sample size increased.²⁴ Then, the character inflated, conservative or accurate of any of the permutation of residuals methods is more highlighted when the sample size increase.

Under normal distribution, PRR performed as better as PRF. Anderson and Ter Braak ¹⁴ showed similar results. According to the authors, when residuals were either normal or uniformly distributed (both symmetric distributions), the normal-theory F-test provided the most powerful test and maintained correct type I error. Thus, when residuals are normally distributed and design is homoscedastic, traditional F-test gives as good results as PRR and PRF.

On contrary to the results of Anderson and Legendre simulation studies, under cubed exponential distribution, the PRR was conservative.²³ The most accurate method from our simulation study was the PRF.²¹ Such performance of PRF confirmed the prediction of Phipson & Smyth who showed a reverse tendency of test when exact probability is used.¹⁰ While the exact value of probability is used, the permutation methods recorded as inflated give value of type I error close to the nominal value of

alpha. The tendency of inflated value of rejection rate was demonstrated by North et al.²⁵ The approximate computation of p-value widely used gathers together not only the real p-value but also the margin error.

In addition, when error rate followed lognormal distribution, the permutation test under the reduced model gives alpha rate close to the nominal value of 0.05. These results are similar to those of Anderson and Ter Braak.¹⁴ According to their findings, this method performed better than the permutation of residuals under full model.

The numerical resolution of the simulation studies did not give additional information than those reported by previous simulation studies.^{5,18,26} Nonetheless, the results confirmed the conservative characters of the permutation of residuals under modified model.

CONCLUSION

The simulation studies revealed that when the exact probability value was used instead of the approximate one, behavior of permutation test changed. Moreover, according to the nature of residuals, there was not a unique applicable method. The numerical resolution, revealed that the real life phenomena distribution can be an asset for an accurate use of the permutation of residuals in ANOVA framework. Therefore, for one-way ANOVA implementation, the choice of the method should be based on the residuals distribution for better accuracy.

Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

Idea/Concept: Merveille Koissi Savi; **Design:** Merveille Koissi Savi; **Control/Supervision:** Romain Glèlè Kakai; **Data Collection:** Merveille Koissi Savi, Elliott Ronald Dossou Yovo; **Analysis and/or Interpretation:** Merveille Koissi Savi, Elliott Ronald Dossou Yovo; **Literature Review:** Merveille Koissi Savi; **Writing the Article:** Merveille Koissi Savi, Elliott Ronald Dossou Yovo, Romain Glèlè Kakai; **Critical Review:** Merveille Koissi Savi, Elliott Ronald Dossou Yovo; **References and Fundings:** Merveille Koissi Savi.

REFERENCES

1. Fisher R. The Design of Experiments. 1st ed. Edinburgh: Oliver & Boyd; 1935. p.252.
2. Kruskal WH, Wallis WA. Use of ranks in one-criterion variance analysis. J Am Stat Assoc 1952;47(260):583-621.
3. Glèlè Kakai R, Sodjinou E, Fonton N. Conditions D'application Des Méthodes Statistiques Paramétriques: Application Sur Ordinateur. 3rd ed. Cotonou: Bibliothèque Natl; 2006. p.93.
4. Mundry R, Fischer J. Use of statistical programs for nonparametric tests of small samples often leads to incorrect P values: examples from Animal Behaviour. Anim Behav 1998;56(1):256-9.
5. Manly BFJ. Randomization, Bootstrap and Monte Carlo Methodology in Biology. 2nd ed. CRC Press; 1997. p.424.
6. Edgington E. Randomization Test. Statistic: Textbooks and Monographs No. 77. 2nd ed. New York: M. Dekker; 1987. p.341.
7. LaFleur BJ, Greevy RA. Introduction to permutation and resampling-based hypothesis tests. J Clin Child Adolesc Psychol 2009;38(2):286-94.
8. Pesarin F. Multivariate Permutation Tests: with Applications to Biostatistics. 1st ed. Chichester: Wiley; 2001. p.432.
9. Kherad-Pajouh S, Renaud O. An exact permutation method for testing all effects for any design of ANOVA. Computational Statistics & Data Analysis 2010;54(7):1881-93.
10. Phipson B, Smyth GK. Permutation P-values should never be zero: calculating exact P-values when permutations are randomly drawn. Stat Appl Genet Mol Biol 2010;9:Article39.
11. ter Braak CJF. Permutation versus bootstrap significance tests in multiple regression and Anova. Bootstrapping and Related Techniques. 1st ed. UK: Springer My Copy; 1992. p.79-86.

12. Oja H. On permutation tests in multiple regression and analysis of covariance analysis problems. *Aust J Stat* 1987;29(1):91-100.
13. Kempthorne O. *The Design and Analysis of Experiments*. 1983.
14. Anderson M, Braak CT. Permutation tests for multi-factorial analysis of variance. *J Stat Comput Simul* 2003;73(2):85-113.
15. R Development Core Team. R Core Team. *R A language and environment for statistical computing*. 2013.
16. Limpert E, Stahel WA, Abbt M. Log-normal distributions across the sciences: keys and clues: on the charms of statistics, and how mechanical models resembling gambling machines offer a link to. *AIBS Bull* 2001.
17. Hahn S, Konietschke F, Salmaso L. A comparison of efficient permutation tests for unbalanced ANOVA in two by two designs--and their behavior under heteroscedasticity. 2013;114(13):267-69.
18. Anderson MJ, Walsh DCI. PERMANOVA, ANOSIM, and the Mantel test in the face of heterogeneous dispersions: what null hypothesis are you testing? *Ecol Monogr* 2013;83(4):557-74.
19. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988. p.474.
20. Champely S, Ekstrom C, Dalgaard P, Gill J, Weibelzahl S, Anandkumar A, et al. *PWR: Basic Functions for Power Analysis*. 2015. p.22.
21. ter Braak CJF. *Update Notes: CANOCO version 3.10*. 1990. p.36.
22. Still A, White A. The approximate randomization test as an alternative to the F test in analysis of variance. *Br J Math* 1981;34(2):243-52.
23. Anderson M, Legendre P. An empirical comparison of permutation methods for tests of partial regression coefficients in a linear model. *J Stat Comput* 1999;62(3):271-303.
24. Stevens JP. *Applied Multivariate Statistics for the Social Sciences*. 5th ed. Routledge; 2012. p.664.
25. North BV, Curtis D, Sham PC. A note on the calculation of empirical P values from Monte Carlo procedures. *Am J Hum Genet* 2002;71(2):439-41.
26. Kherad-Pajouh S, Renaud O. A general permutation approach for analyzing repeated measures ANOVA and mixed-model designs. *Stat Pap* 2014;56(4):947-67.