

LARGE SAMPLE PROPERTIES OF TWO TESTS FOR INDEPENDENT JOINT ACTION OF TWO DRUGS

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Biological models for the independent action of two drugs imply that if the drugs are administered in various combinations of doses, then the corresponding probabilities of response must satisfy certain inequalities if the drugs are acting independently. The hypothesis that the probabilities do satisfy these inequalities can be tested using the likelihood ratio test or using the bootstrap test proposed by Wahrendorf and Brown in 1980. In the simplest dose design, only one dosage of each drug is used. The three combination doses required to test the hypothesis are each drug singly and the combination of the two drugs. The asymptotic distribution of the bootstrap test is derived. The asymptotic distribution of the likelihood ratio test is obtained by applying Feder's results. The calculation of the asymptotic critical values and powers is presented.

1. Introduction. This paper concerns the testing of a set of inequalities implied by a type of joint action, namely, independent joint action. Two test statistics are studied, one is the likelihood ratio test and the other is the bootstrap test proposed by Wahrendorf and Brown (1980).

We now review drug action and tolerances. In the study of the joint action of drugs, various methods of modeling the action have been proposed. The papers by Hewlett and Plackett (1952, 1959, 1964, 1979) and Plackett and Hewlett (1948, 1967) and the papers by Ashford (1958, 1981), Ashford and Smith (1964) and Ashford and Cobby (1974) represent the two main streams of study. Their models are different. In Hewlett and Plackett's classification, the joint action of two drugs is considered *biologically independent* if the joint action is dissimilar and noninteractive. A joint action is dissimilar if the primary sites of action of the drugs are not the same, and the action is noninteractive if the presence of one drug has no influence on the effect of the second drug. Note that biological independence is more general than statistical independence in that statistical independence is a special case of biological independence. Using the concept of drugs competing for receptors, Hewlett and Plackett (1964) gave an example of a joint action which is interactive in the biological sense, but which induces the same response function as the noninteractive model they derived in 1959. Therefore the biological independence of two drugs cannot be identified from the probability of response as a function of the dose combination. Consequently, the testing of independent

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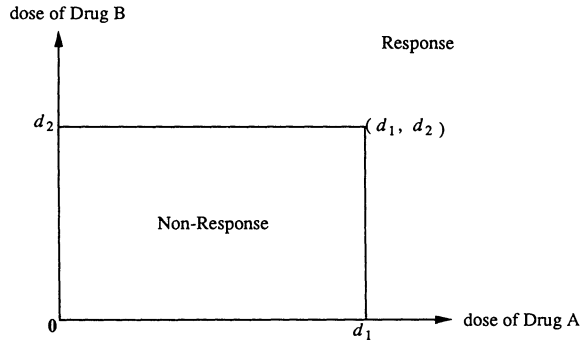


FIG. 1. The dose-response relation of a subject to two drugs of independent joint action: d_1 , tolerance for drug A; d_2 , tolerance for drug B.

action in this paper is not testing the equivalent mathematical formulations of independent joint action, but a set of inequalities implied by the independent joint action. In the papers of Ashford and his coauthors cited previously, the drug actions are classified by the behavior of the probability of response as a function of dose combination, their classifications are not equivalent to those of Hewlett and Plackett. In this paper we are investigating biological independence, as defined by Hewlett and Plackett.

The tolerance of a subject for a drug is the minimum effective dose required to elicit a response. Since the tolerance for a given drug is a characteristic of a subject, the tolerance may vary from individual to individual. Therefore, when a population of subjects is considered, the tolerances of subjects can be thought of as the values of a random variable associated with the probability of response to a given drug. The modeling of the univariate tolerance distribution is well-studied in the literature. For discussion of models for univariate tolerance densities, see Finney (1971) and Hewlett and Plackett (1979).

When two drugs are applied to a subject, the response and nonresponse regions can have various shapes. If the joint action of these two drugs is biologically independent, then the nonresponse region of a subject is a rectangle. The subject will respond if the dose of either one of the two drugs received exceeds the subject's tolerance for the corresponding drug, as in Figure 1. Consequently, for a population of subjects and for a given dose combination (z_1, z_2) of drugs A and B, all subjects whose tolerance pairs are above and to the right of (z_1, z_2) will not respond. See Figure 2. If every individual has a rectangular response region, then it is natural to refer the upper corner of the rectangle, the pair of individual tolerances, as the subject's bivariate tolerance. Then the probability of response to the combination is determined by the joint distribution of the bivariate tolerances. For joint actions that are not independent, the nonresponse region may not be a rectangle. If the region is not known to belong to a two-parameter family of sets, the nonresponse region may not be determined by the univariate tolerances and a bivariate tolerance

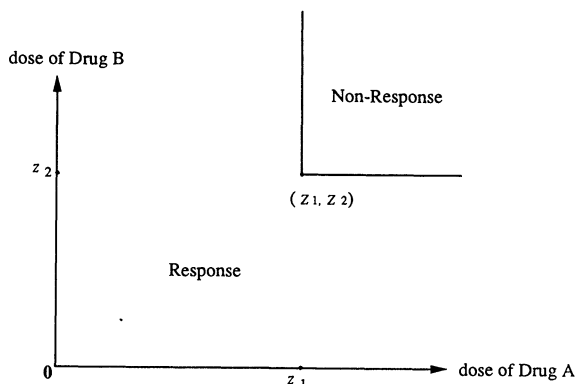


FIG. 2. The dose-response relation of a population to two drugs of independent joint action: z_1 , dose of drug A; z_2 , dose of drug B.

cannot be defined. See Figure 3 for an example of two different nonresponse regions with the same univariate tolerances.

If p_1 and p_2 are the probabilities of response to doses z_1 and z_2 of drugs A and B, respectively, if p_3 is the probability of response to the joint application of both and if there are no spontaneous responses, then independent action implies that p_1 is the probability that the bivariate tolerance lies in the half-plane to the left of the vertical line through (z_1, z_2) . Similarly, p_2 is the probability that the bivariate tolerance lies in the half-plane below the horizontal line through (z_1, z_2) and p_3 is the probability that the bivariate tolerance lies in either of these two half-planes. Elementary probability calculations show that the following inequalities hold:

$$(1.1) \quad \max(p_1, p_2) \leq p_3 \leq \min(p_1 + p_2, 1).$$

These inequalities are equivalent to those of Fréchet (1951) giving bounds for a bivariate distribution function in term of two univariate marginal distributions.

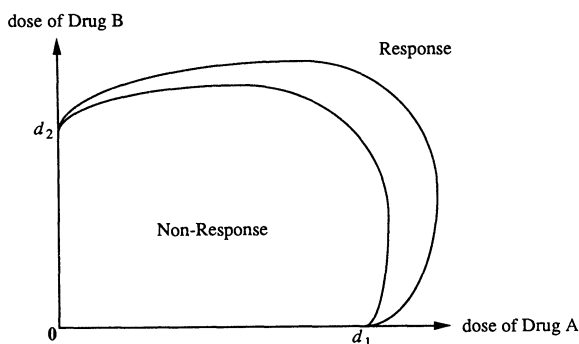


FIG. 3. The dose-response relation of a subject to two drugs of nonindependent joint action: d_1 , tolerance for drug A; d_2 , tolerance for drug B.

Wahrendorf and Brown (1980) applied the bootstrap method [Efron (1979)] to testing the inequalities implied by the independent joint action. However, the distribution of their statistic is not studied in their paper. The likelihood ratio test is a competitor to the bootstrap test for testing the inequalities (1.1). In Section 2, the test statistics of these two tests are discussed. The consistency of maximum likelihood estimators, upon which both the likelihood ratio test and the bootstrap test are based, implies that both test statistics converge in distribution to degenerate random variables when the limit point of the sequence of parameters considered is not on the boundary of the set defined by (1.1). Therefore, in Section 3, the asymptotic distributions of the likelihood ratio test statistic and the bootstrap test statistic are studied for a sequence of parameters converging toward the boundary of the set defined by (1.1). Then in Section 4, the asymptotic critical values and powers are formulated and determined.

2. Two test statistics. The two test statistics considered for testing the inequalities (1.1) are described in this section. When doses z_1 and z_2 of drugs A and B are administered to each of the subjects of two random samples of sizes n_1 and n_2 singly, and to a random sample of size n_3 jointly, those subjects will either respond or fail to respond depending on their tolerances to the drugs. Then the response of the j th subject to drug A, Y_{1j} , has a Bernoulli distribution with parameter p_1 for $j = 1, \dots, n_1$, which we abbreviate as $Y_{1j} \sim B(1, p_1)$. Similarly, the responses to drug B and to the joint application of drugs A and B are $Y_{2j} \sim B(1, p_2)$, for $j = 1, \dots, n_2$, and $Y_{3j} \sim B(1, p_3)$, for $j = 1, \dots, n_3$. Therefore, the likelihood function of Y_{ij} for $i = 1, 2, 3$ and $j = 1, \dots, n_i$ is

$$L_n(\mathbf{y}, \mathbf{p}) = \prod_{i=1}^3 \prod_{j=1}^{n_i} p_i^{y_{ij}} (1 - p_i)^{1-y_{ij}},$$

where $\mathbf{y}^T = (\mathbf{y}_1^T, \mathbf{y}_2^T, \mathbf{y}_3^T)$, $\mathbf{y}_i^T = (y_{i1}, \dots, y_{in_i})$, $\mathbf{p}^T = (p_1, p_2, p_3)$, n is the total sample size and $n = n_1 + n_2 + n_3$. From this point on, we say “ n is large” when n_1, n_2 and n_3 are all large. Define sets Ω , Ω_0 and Ω_A as follows:

$$\Omega_0 = \{\mathbf{p} \in \Omega: \mathbf{p} \text{ satisfies (1.1)}\},$$

$$\Omega = [0, 1]^3$$

and

$$\Omega_A = \Omega - \Omega_0.$$

Then the set Ω_0 (see Figure 4), is the tetrahedron FGHA and its interior in the unit cube Ω . When the functions defining the boundary of a set are given indices, $1, 2, \dots$, the index set $I(\cdot)$ is defined as the set of indices which identify the boundary surfaces that contain a given point. For example, the index set $I(\cdot)$ for a point on the edge AH of tetrahedron FGHA contains the indices of the boundary functions defining surface AGH and surface AFH. Let $\Lambda_n(\mathbf{Y})$ be the likelihood ratio test statistic for testing $H_0: \mathbf{p} \in \Omega_0$ against $H_1:$

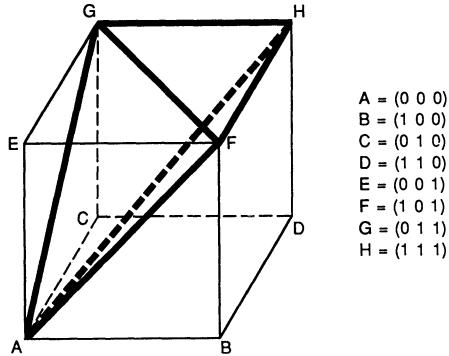


FIG. 4. The tetrahedron $FGHA$ and its interior, which represent the null space Ω_0 for the testing of independent action,

$$\Omega_0 = \{\mathbf{p} \in \Omega : \max(p_1, p_2) \leq p_3 \leq \min(p_1 + p_2, 1)\}.$$

$\mathbf{p} \in \Omega_A$. Then,

$$(2.1) \quad \Lambda_n(\mathbf{Y}) = \frac{\sup_{\mathbf{p} \in \Omega_0} L_n(\mathbf{Y}, \mathbf{p})}{\sup_{\mathbf{p} \in \Omega} L_n(\mathbf{Y}, \mathbf{p})}.$$

Let $X_i = \sum_{j=1}^{n_i} Y_{ij}$, $i = 1, 2, 3$ and $\mathbf{X} = (X_1, X_2, X_3)^T$. Then $X_i \sim B(n_i, p_i)$. Since \mathbf{X} is a sufficient statistic for \mathbf{p} , the likelihood function can be rewritten as

$$L_n(\mathbf{x}, \mathbf{p}) = \prod_{i=1}^3 p_i^{x_i} (1 - p_i)^{n_i - x_i}.$$

Because the denominator of (2.1) is just $L_n(\mathbf{X}, \mathbf{p})$ with \mathbf{p} replaced by $\hat{\mathbf{P}}^{(n)} = \hat{\mathbf{P}}^{(n)}(\mathbf{X}) = (X_1/n_1, X_2/n_2, X_3/n_3)$, the maximum likelihood estimator of \mathbf{p} , $\Lambda_n(\mathbf{Y})$ can be written as

$$(2.2) \quad \Lambda_n(\mathbf{X}) = \frac{\sup_{\mathbf{p} \in \Omega_0} L_n(\mathbf{X}, \mathbf{p})}{L_n(\mathbf{X}, \hat{\mathbf{P}}^{(n)})}.$$

Thus, for any observed \mathbf{x} , the likelihood ratio test statistic requires the maximization of $L_n(\mathbf{x}, \mathbf{p})$ over Ω_0 . The maximization can be achieved either theoretically or numerically.

It is easy to see that when the true \mathbf{p} is in Ω_0 and when n is large, the numerator of (2.2) will tend to be closer to the denominator of (2.2) than when \mathbf{p} is away from Ω_0 . The level α likelihood ratio test for testing $H_0: \mathbf{p} \in \Omega_0$ versus $H_1: \mathbf{p} \in \Omega_A$ rejects H_0 upon observing \mathbf{x} if $\Lambda_n(\mathbf{x})$ is smaller than a critical value $c_{L,n}(\alpha)$, where $c_{L,n}(\alpha)$ is the largest real number that satisfies

$$\sup_{\mathbf{p} \in \Omega_0} \text{Prob}(\Lambda_n(\mathbf{X}) < c_{L,n}(\alpha)) \leq \alpha.$$

The bootstrap test will be introduced next. Testing the hypothesis of the inequalities implied by the independent joint action tests whether the true

parameter \mathbf{p} is in the null set Ω_0 . When \mathbf{p} is in the interior of Ω_0 , by the consistency of the maximum likelihood estimators, the probability that $\hat{\mathbf{P}}^{(n)}$ is in Ω_0 increases to 1 as n increases. Hence, Wahrendorf and Brown (1980) suggested considering

$$\pi_n(\mathbf{p}) = \text{Prob}_{\mathbf{p}}(\hat{\mathbf{P}}^{(n)} \in \Omega_0)$$

as a measure of agreement between \mathbf{p} being in Ω_0 and $\hat{\mathbf{P}}^{(n)}$ being in Ω_0 .

Since $\pi_n(\mathbf{p})$ is defined by the probability of $\hat{\mathbf{P}}^{(n)}$ satisfying (1.1), $\pi_n(\mathbf{p})$ can only have values between 0 and 1. Smaller values of $\pi_n(\mathbf{p})$ suggest that the joint action is not independent. Although this function is meaningful and natural, it requires knowledge of \mathbf{p} , which is an unknown parameter. Nevertheless, one can estimate $\pi_n(\mathbf{p})$ when data are available. Wahrendorf and Brown applied the bootstrap method [Efron (1979)] for estimating $\pi_n(\mathbf{p})$.

Before defining the bootstrap test statistic, a brief discussion on the bootstrap method is given. The bootstrap method applies to the estimation of the distribution of a function of a random variable with an unknown distribution. The bootstrap estimate of the distribution of the function of the random variable is obtained by replacing the unknown distribution of the random variable by the empirical distribution based on a random sample. Then the bootstrap estimate of any property of the function of the random variable can be calculated. In general, it is difficult to implement the bootstrap method without using Monte-Carlo simulations. However, the probability masses of the binomial random vectors are tractable. Consequently, in testing the hypothesis of the binomial parameter that the vector \mathbf{p} satisfies (1.1), Monte-Carlo simulation is not essential for estimating $\pi_n(\mathbf{p})$.

To estimate $\pi_n(\mathbf{p})$, one can enumerate all possible vectors $\hat{\mathbf{p}}^{(n)} = \hat{\mathbf{p}}^{(n)}(\mathbf{x}) = (x_1/n_1, x_2/n_2, x_3/n_3)$ of $\hat{\mathbf{P}}^{(n)}$. Then the bootstrap estimate of $\pi_n(\mathbf{p})$ upon observing \mathbf{x} is

$$\hat{\pi}_n(\mathbf{p}) = \pi_n(\mathbf{x}) = \text{Prob}_{\hat{\mathbf{p}}^{(n)}(\mathbf{x})}(\hat{\mathbf{P}}^{(n)}(\mathbf{X}) \in \Omega_0).$$

In other words, $\pi_n(\mathbf{x})$ is the sum of the probabilities assuming $\hat{\mathbf{p}}^{(n)}$ is the true parameter. Therefore, the bootstrap test statistic for testing $H_0: \mathbf{p} \in \Omega_0$ versus $H_1: \mathbf{p} \in \Omega_A$ is

$$(2.3) \quad \pi_n(\mathbf{X}) = \text{Prob}_{\hat{\mathbf{p}}^{(n)}(\mathbf{X})}(\mathbf{P}^{(n)*} \in \Omega_0),$$

where $\mathbf{P}^{(n)*}$ is the maximum likelihood estimator of \mathbf{p} based on a random sample. The smaller $\pi_n(\mathbf{x})$ is, the less likely it is that the joint action is independent. Therefore, the level α bootstrap test rejects the hypothesis of \mathbf{p} belonging to Ω_0 for all $\pi_n(\mathbf{x})$ smaller than a critical value $C_{B,n}(\alpha)$, where $C_{B,n}(\alpha)$ is the largest number satisfying

$$\sup_{\mathbf{p} \in \Omega_0} \text{Prob}(\pi_n(\mathbf{X}) < C_{B,n}(\alpha)) \leq \alpha.$$

In contrast to calculating $\pi_n(\mathbf{x})$ directly, one can obtain a Monte-Carlo approximation to it. That is, generate a random sample of $\hat{\mathbf{P}}^{(n)}$, called $\mathbf{p}^{(n)*}$, under $\hat{\mathbf{p}}^{(n)}$ first. Then the fraction of $\mathbf{p}^{(n)*}$'s satisfying (1.1) is the Monte-Carlo

approximation to $\pi_n(\mathbf{x})$. This alternative method saves time when exact calculation is computationally too intensive.

3. Asymptotic distributions. The asymptotic distributions of the likelihood ratio test and the bootstrap test are studied under a sequence of local alternatives. Section 3.1 contains the results of the likelihood ratio test based on Feder's (1968) theorem. The asymptotic distribution of the bootstrap test statistic is derived in Section 3.2.

3.1. *Likelihood ratio test statistic.* Feder (1968) gave the asymptotic distribution of the log likelihood ratio test statistic when the true parameter approaches the boundaries of the null set. Feder's theorem is for independent and identically distributed random variables. His results extend trivially to a collection of n independently distributed random variables consisting of k groups of random variables Y_{ij} for $i = 1, \dots, k$ and $j = 1, \dots, n_i$, with distribution function $f_i(Y_{ij})$ when the number of such random variables in each group, n_i , converges to a fixed proportion, λ_i , of the total number of random variables, where $\lambda_i > 0$ and $\lambda_1 + \dots + \lambda_k = 1$.

Feder's theorem does not require that the union of the null and the alternative sets be the entire Euclidean space. In testing the inequalities implied by independent joint action, however, the null set is always the complement of the alternative set. Therefore, Proposition 3.1 is specialized to the likelihood ratio test for testing independent joint action.

The regularity conditions required for Feder's theorem are easily satisfied when considering the Bernoulli distribution. The logit transformation of the Bernoulli parameters, the p_i 's for $i = 1, 2, 3$, gives new parameters $\theta_i = \log(p_i/(1 - p_i))$ and $\theta_i \in R$. Thus, Feder's result implies that when testing whether or not the vector of the logits of the Bernoulli parameters is in a set S , minus twice the log likelihood ratio test statistics will converge to some random variable determined by the limit point of the sequence of the true parameters provided that S is the intersection of subspaces with smooth boundaries. The transformed null set obtained from the logit transformations is

$$S = \{\boldsymbol{\theta} \in R^3: g_i(\boldsymbol{\theta}) \geq 0, i = 1, 2, 3\},$$

where

$$g_i(\boldsymbol{\theta}) = \frac{1}{e^{-\theta_3} + 1} - \frac{1}{e^{-\theta_i} + 1}, \quad i = 1, 2,$$

and

$$g_3(\boldsymbol{\theta}) = \frac{1}{e^{-\theta_1} + 1} + \frac{1}{e^{-\theta_2} + 1} - \frac{1}{e^{-\theta_3} + 1}.$$

The transformed null set S defined above is bounded by three surfaces. One surface never touches either of the other two because $g_3(\boldsymbol{\theta}) = 0$ implies the product of $g_1(\boldsymbol{\theta})$ and $g_2(\boldsymbol{\theta})$ is nonzero. The intersection of the first two surfaces

is the line $\{\theta: \theta_1 = \theta_2 = \theta_3\}$, which is common to surfaces $\{\theta: \theta_1 = \theta_3\}$, and $\{\theta: \theta_2 = \theta_3\}$. Therefore, when considering $\theta^{(0)}$ on the boundary of the transformed null set S , there are two cases: Either $\theta^{(0)}$ is in the interior of the i th boundary surface, where $i = 1, 2, 3$, and in which case the index set $I(\theta^{(0)}) = \{i\}$, or $\theta^{(0)}$ is on the common edge of the two intersecting surfaces, in which case the index set $I(\theta^{(0)}) = \{1, 2\}$. When $\theta^{(0)}$ is on the edge, the situation is more complicated. The asymptotic distribution under local alternatives depends on how the alternative sequence approaches the boundary surfaces. The asymptotic distributions of the likelihood ratio test statistics are summarized below.

PROPOSITION 3.1 [Feder (1968)]. *The likelihood ratio test statistics for testing $H_0: \theta \in S$ versus $H_1: \theta \in R^3 - S$ under a sequence of alternatives*

$$\theta^{(n)} = \theta^{(0)} + \frac{\mathbf{k}}{\sqrt{n}}$$

for some constant vector \mathbf{k} independent of n and for $\theta^{(0)}$ on the i th boundary of S satisfy the following cases, provided that the derivative of g_i with respect to θ is continuous at $\theta^{(0)}$ for $i = 1, 2$ and 3 :

CASE 1. *When $I(\theta^{(0)}) = \{i\}$, $i = 1, 2$ or 3 , then*

$$-2 \log \Lambda_n(\mathbf{X}) \rightarrow_d [\min(0, (Z + \eta_i))]^2,$$

where Z is a univariate standard normal random variable,

$$\mathbf{d}_i = \left. \frac{\partial}{\partial \theta} g_i(\theta) \right|_{\theta = \theta^{(0)}},$$

$$\eta_i = \frac{\mathbf{d}_i^T \mathbf{k}}{(\mathbf{d}_i^T \mathbf{J}^{-1}(\theta^{(0)}) \mathbf{d}_i)^{1/2}}, \quad i = 1, 2, 3$$

and \mathbf{J} is the Fisher information matrix for θ of the entire sample,

$$\mathbf{J}(\theta) = \lim_{n \rightarrow \infty} \frac{1}{n} E_{\theta} \left(\left[\frac{\partial}{\partial \theta} \log \prod_{i=1}^k \prod_{j=1}^{n_i} f_i(Y_{ij}, \theta) \right] \left[\frac{\partial}{\partial \theta} \log \prod_{i=1}^k \prod_{j=1}^{n_i} f_i(Y_{ij}, \theta) \right]^T \right).$$

CASE 2. *When $I(\theta^{(0)}) = \{1, 2\}$, then*

$$-2 \log \Lambda_n(\mathbf{X}) \rightarrow_d \begin{cases} (\mathbf{AZ} + \boldsymbol{\tau})^T (\mathbf{AZ} + \boldsymbol{\tau}) & \text{if } \mathbf{b}_i^T \mathbf{Z} + \gamma_i < 0, i = 1 \text{ and } 2, \\ (\mathbf{a}_i^T \mathbf{Z} + \eta_i)^2 & \text{if } \mathbf{a}_i^T \mathbf{Z} + \eta_i < 0, \mathbf{b}_i^T \mathbf{Z} + \gamma_i \geq 0, \\ 0 & i = 1 \text{ or } 2, \\ & \text{otherwise,} \end{cases}$$

where

$$\mathbf{A} = (a_{ij}), \text{ where } a_{ij} = \begin{cases} 1 - \lambda_i & \text{if } i = j, \\ -\sqrt{\lambda_i \lambda_j} & \text{otherwise, } i, j = 1, 2, 3, \end{cases}$$

$$\mathbf{Z} \sim N(0, I_3), \text{ where } I_3 \text{ is the unit matrix of order three,}$$

$$\boldsymbol{\tau} = \mathbf{A}\mathbf{J}^{1/2}(\boldsymbol{\theta}^{(0)})\mathbf{k},$$

$$\mathbf{a}_i = \frac{\mathbf{J}^{-1/2}(\boldsymbol{\theta}^{(0)})\mathbf{d}_i}{(\mathbf{d}_i^T \mathbf{J}^{-1}(\boldsymbol{\theta}^{(0)})\mathbf{d}_i)^{1/2}} \text{ and } \mathbf{a}_i^T \mathbf{a}_i = 1$$

and \mathbf{b}_i satisfies $\mathbf{a}_i^T \mathbf{b}_i = 0, \mathbf{b}_i^T \boldsymbol{\theta}^{(0)} = 0$ and $\mathbf{b}_i^T \mathbf{b}_i = 1, i = 1, 2, 3,$

$$\gamma_i = \mathbf{b}_i^T \mathbf{J}^{1/2}(\boldsymbol{\theta}^{(0)})\mathbf{k}, \quad i = 1, 2, 3.$$

For verification that this proposition is implied by Feder’s theorem, see Hoffman [(1986), Corollary 4.5, page 59].

Proposition 3.1 shows that the asymptotic distribution of minus twice the likelihood ratio test statistic $-2 \log \Lambda_n(\mathbf{X})$, under a sequence of alternatives depends strongly on the limit point. If the limit point $\boldsymbol{\theta}^{(0)}$ is in the interior of the boundary faces of S , then the asymptotic distribution is the distribution of the square of a truncated normal random variable. It is truncated at a value determined by the sequence of the alternatives.

3.2. *Bootstrap test statistic.* Under a sequence of parameters $\mathbf{p}^{(n)}$, the bootstrap test statistic defined in (2.3) converges in probability to a degenerate random variable when the limit point of the sequence of parameters is not on the boundary of Ω_0 . If the limit point is in the interior of Ω_0 , the consistency of the maximum likelihood estimators implies that the degenerate random variable is equal to 1. If the limit point is in the interior of Ω_A , the degenerate random variable is equal to 0. However, when the limit point is on the boundary of Ω_0 , the bootstrap test statistic converges in distribution to a nonlinear function of normal random variables as described in Theorem 3.2.

THEOREM 3.2. *The bootstrap test statistic $\pi_n(\mathbf{X})$ for testing $H_0: \mathbf{p} \in \Omega_0$ versus $H_1: \mathbf{p} \in \Omega_A$ under a sequence of alternatives*

$$\mathbf{p}^{(n)} = \mathbf{p}^{(0)} + \frac{1}{\sqrt{n}} \mathbf{c},$$

for some constant vector \mathbf{c} independent of n and for $\mathbf{p}^{(0)}$ on the boundary of Ω_0 , satisfies

$$\pi_n(\mathbf{X}) \rightarrow_d \Phi_\rho(V_1 + \xi_1, V_2 + \xi_2),$$

where $\mathbf{V} = (V_1, V_2)$ is a bivariate normal random vector with mean 0 , variances 1 and covariance ρ , Φ_ρ is the joint distribution function of \mathbf{V} , and ρ, ξ_1

and ξ_2 are defined as follows:

CASE 1. When $I(\mathbf{p}^{(0)}) = \{j\}$, $j = 1, 2$ or 3 , then $\xi_1 = \xi_2 = \mu_j$ and $\rho = 1$;

CASE 2. When $I(\mathbf{p}^{(0)}) = \{1, 2\}$, then $\xi_j = \mu_j$ for $j = 1, 2$ and

$$\rho = \left[\frac{\lambda_1 \lambda_2}{(\lambda_1 + \lambda_3)(\lambda_2 + \lambda_3)} \right]^{1/2},$$

where

$$\mu_j = \frac{\mathbf{a}_j^T \mathbf{c}}{(\mathbf{a}_j^T \Sigma(\mathbf{p}^{(0)}) \mathbf{a}_j)^{1/2}},$$

$$\mathbf{a}_1^T = \frac{1}{\sqrt{2}}(-1, 0, 1), \quad \mathbf{a}_2^T = \frac{1}{\sqrt{2}}(0, -1, 1), \quad \mathbf{a}_3^T = \frac{1}{\sqrt{3}}(1, 1, -1)$$

and the matrix $\Sigma(\mathbf{p}^{(0)})$ is a diagonal matrix with $p_j^{(0)}(1 - p_j^{(0)})/\lambda_j$ as the j th diagonal element for $j = 1, 2, 3$.

The proof of the theorem will be stated after some lemmas are discussed.

LEMMA 3.3. Given a positive integer J , for any J vectors \mathbf{b}_j in R^k , define A as the set $\{\mathbf{p} \in (0, 1)^k, \mathbf{b}_j^T \mathbf{p} \geq 0, j = 1, \dots, J, \mathbf{b}_j \in R^k\}$. Then for $\mathbf{p}^{(0)}$ on the boundary of A ,

$$\lim_{n \rightarrow \infty} S_n(\mathbf{p}^{(0)}) = S_0,$$

where

$$S_n(\mathbf{p}^{(0)}) = \sqrt{n} (A - \mathbf{p}^{(0)}),$$

$$S_0 = \{\mathbf{p} \in R^k : \mathbf{b}_i^T \mathbf{p} \geq 0, i \in I(\mathbf{p}^{(0)})\}.$$

Lemma 3.3 says that for any point $\mathbf{p}^{(0)}$ on the boundary of A , the limit set S_0 of $S_n(\mathbf{p}^{(0)})$ can be described in terms of the half-spaces whose intersection defines A . The limit set S_0 is the intersection of the subset of those half-spaces whose boundary planes contain $\mathbf{p}^{(0)}$. The following example illustrates the application of Lemma 3.3.

EXAMPLE 3.4. Let $k = 3$ and let $\mathbf{a}_1, \mathbf{a}_2, \mathbf{a}_3$ and Ω_0 be as in Theorem 3.2. Then when $\mathbf{p}^{(0)}$ is $(0.5, 0.4, 0.5)$, $\mathbf{p}^{(0)}$ is in the interior of the boundary plane of Ω_0 defined by $\mathbf{a}_1^T \mathbf{p} = 0$ and the index set $I(\mathbf{p}^{(0)})$ is $\{1\}$. Lemma 3.3 implies that $\lim_{n \rightarrow \infty} S_n(\mathbf{p}^{(0)})$ is the half-space defined by

$$\{\mathbf{p} \in R^3 : \mathbf{a}_1^T \mathbf{p} \geq 0\} = \{\mathbf{p} \in R^3 : p_3 - p_1 \geq 0\}.$$

When $\mathbf{p}^{(0)}$ is $(0.5, 0.5, 0.5)$, then $\mathbf{p}^{(0)}$ is on the edge of Ω_0 defined by $\mathbf{a}_1^T \mathbf{p} = \mathbf{a}_2^T \mathbf{p} = 0$ and the index set $I(\mathbf{p}^{(0)})$ is $\{1, 2\}$. By Lemma 3.3,

$$\lim_{n \rightarrow \infty} S_n(\mathbf{p}^{(0)}) = \{\mathbf{p} \in R^3: \mathbf{a}_1^T \mathbf{p} \geq 0 \text{ and } \mathbf{a}_2^T \mathbf{p} \geq 0\} = \{\mathbf{p} \in R^3: p_3 \geq \max(p_1, p_2)\}.$$

LEMMA 3.5. *Let \mathbf{W}_n be a random vector in R^k which converges to \mathbf{W} in R^k . That is,*

$$\mathbf{W}_n \rightarrow_d \mathbf{W}.$$

Then for S_n defined in Lemma 3.3,

$$\lim_{n \rightarrow \infty} \text{Prob}(\mathbf{W}_n \in S_n) = \text{Prob}(\mathbf{W} \in S_0).$$

PROOF. By the definition of S_n , $\mathbf{W}_n \in S_n$ is equivalent to

$$(\mathbf{W}_n + \sqrt{n} \mathbf{p}^{(0)})/\sqrt{n} \in A.$$

For all $j = 1, \dots, J$, by the definition of A ,

$$(3.1) \quad \mathbf{a}_j^T (\mathbf{W}_n + \sqrt{n} \mathbf{p}^{(0)}) \geq 0.$$

When j is not in $I(\mathbf{p}^{(0)})$, $\lim_{n \rightarrow \infty} (\mathbf{a}_j^T \mathbf{W}_n + \sqrt{n} \mathbf{a}_j^T \mathbf{p}^{(0)}) \geq 0$ is always true because

$$\mathbf{a}_j^T \mathbf{p}^{(0)} > 0 \text{ and } \mathbf{a}_j^T \mathbf{W}_n \rightarrow_d \mathbf{a}_j^T \mathbf{W}$$

by the continuous mapping theorem. When j is in $I(\mathbf{p}^{(0)})$, then $\mathbf{a}_j^T \mathbf{p}^{(0)} = 0$. Hence, (3.1) becomes

$$\mathbf{a}_j^T \mathbf{W}_n \geq 0.$$

Therefore,

$$(3.2) \quad \text{Prob}(\mathbf{a}_j^T \mathbf{W}_n \geq 0, j \in I(\mathbf{p}^{(0)})) \rightarrow_{n \rightarrow \infty} \text{Prob}(\mathbf{a}_j^T \mathbf{W} \geq 0, j \in I(\mathbf{p}^{(0)})).$$

By (3.2) and Lemma 3.3, this lemma follows. \square

LEMMA 3.6. *Let Y_1, Y_2, \dots, Y_n be a random sample of Bernoulli random variables with parameter p_n , where as n increases, p_n converges to p_0 which is strictly between 0 and 1. Then the maximum likelihood estimator \hat{P}_n of p_n satisfies*

$$\lim_{\varepsilon \rightarrow 0} \sup_{|p_n - p_0| < \varepsilon} \sup_{s \in R} \left| \text{Prob}(\sqrt{n} (\hat{P}_n - p_n) \leq s) - \Phi \left[\frac{s}{(p_n(1 - p_n))^{1/2}} \right] \right| = 0.$$

PROOF. Define Y_n^* as

$$Y_n^* = \frac{\sum_{i=1}^n Y_i - E(\sum_{i=1}^n Y_i)}{[\text{Var}(\sum_{i=1}^n Y_i)]^{1/2}}.$$

Then Y_n^* and \hat{p}_n have the following relation:

$$(3.3) \quad Y_n^* = \frac{\sqrt{n} (\hat{P}_n - p_n)}{(p_n(1 - p_n))^{1/2}}.$$

By the Berry–Esseen theorem [Serfling (1980), page 33], for all n ,

$$(3.4) \quad \sup_{t \in R} |\text{Prob}(Y_n^* \leq t) - \Phi(t)| \leq \frac{33}{4} \frac{p_n^2 + (1 - p_n)^2}{(np_n(1 - p_n))^{1/2}}.$$

Substituting (3.3) into (3.4), the lemma follows because p_n converges to p_0 which is strictly between 0 and 1. \square

Let $\hat{\mathbf{P}}^{(n)}$ be the maximum likelihood estimator of $\mathbf{p}^{(n)}$ which converges to $\mathbf{p}^{(0)}$ as n approaches infinity. Let $\mathbf{P}^{(n)*}$ be the maximum likelihood estimator of $\mathbf{p}^{(n)}$ obtained from the bootstrap replication of the response random variable \mathbf{Y} . For vectors \mathbf{a} and \mathbf{b} in R^k , write $\mathbf{a} \leq \mathbf{b}$ when $a_i \leq b_i$ for $i = 1, 2, \dots, k$. Now we will prove Theorem 3.2.

PROOF OF THEOREM 3.2. By definition, $\pi_n(\mathbf{X})$ can be written as

$$(3.5) \quad \begin{aligned} \pi_n(\mathbf{X}) &= \text{Prob}(\sqrt{n}(\mathbf{P}^{(n)*} - \hat{\mathbf{P}}^{(n)}) \in \sqrt{n}(\Omega_0 - \hat{\mathbf{P}}^{(n)})) \\ &= \text{Prob}(\sqrt{n}(\mathbf{P}^{(n)*} - \hat{\mathbf{P}}^{(n)}) \in \sqrt{n}(\Omega_0 - \mathbf{p}^{(0)}) - \sqrt{n}(\mathbf{p}^{(n)} - \mathbf{p}^{(0)}) \\ &\quad - \sqrt{n}(\hat{\mathbf{P}}^{(n)} - \mathbf{p}^{(n)})). \end{aligned}$$

Define $\mathbf{W}_1^{(n)}$, $\mathbf{W}_2^{(n)}$ and S_n as follows:

$$\begin{aligned} \mathbf{W}_1^{(n)} &= \sqrt{n}(\mathbf{P}^{(n)*} - \hat{\mathbf{P}}^{(n)}), \\ \mathbf{W}_2^{(n)} &= \sqrt{n}(\hat{\mathbf{P}}^{(n)} - \mathbf{p}^{(n)}), \\ S_n &= \sqrt{n}(\Omega_0 - \mathbf{p}^{(0)}). \end{aligned}$$

Then (3.5) becomes

$$(3.6) \quad \pi_n(\mathbf{X}) = \text{Prob}(\mathbf{W}_1^{(n)} \in S_n - \mathbf{c} - \mathbf{W}_2^{(n)}).$$

Define random vector \mathbf{W}_j as $\mathbf{W}_j \sim N(0, \Sigma(\mathbf{p}^{(0)}))$, for $j = 1, 2$. We will now show that $\mathbf{W}_1^{(n)}$ converges in distribution to \mathbf{W}_1 .

Let G_n be the joint cumulative distribution function of $\mathbf{W}_1^{(n)}$. Conditioning on $\hat{\mathbf{P}}^{(n)} = \hat{\mathbf{p}}^{(n)}$, for any \mathbf{w} in R^3 , $G_n(\mathbf{w})$ is the sum of

$$\text{Prob}(\sqrt{n}(\mathbf{P}^{(n)*} - \hat{\mathbf{P}}^{(n)}) \leq \mathbf{w}, \hat{\mathbf{P}}^{(n)} = \hat{\mathbf{p}}^{(n)})$$

over all possible vectors of $\hat{\mathbf{P}}^{(n)}$. Since $\mathbf{P}^{(n)*}$ and $\hat{\mathbf{P}}^{(n)}$ are independent, $G_n(\mathbf{w})$ is the sum of

$$(3.7) \quad \text{Prob}(\sqrt{n}(\mathbf{P}^{(n)*} - \hat{\mathbf{P}}^{(n)}) \leq \mathbf{w} |_{\hat{\mathbf{p}}^{(n)}}) \text{Prob}(\hat{\mathbf{P}}^{(n)} = \hat{\mathbf{p}}^{(n)}).$$

For any given $\varepsilon > 0$, define B as the open ball of radius ε centered at $\mathbf{p}^{(0)}$ and let B^c be the complement of B . Since $\mathbf{p}^{(n)}$ converges to $\mathbf{p}^{(0)}$ which is in B ,

$$\text{Prob}(\hat{\mathbf{P}}^{(n)} \in B^c) \rightarrow 0 \quad \text{as } n \rightarrow \infty.$$

Therefore,

$$\lim_{n \rightarrow \infty} G_n(\mathbf{w}) = \lim_{n \rightarrow \infty} \sum_{\hat{\mathbf{p}}^{(n)} \in B} (3.7).$$

By Lemma 3.6, the first term of (3.7) converges to $\text{Prob}(\mathbf{W}_1 \leq \mathbf{w})$ for all possible realizations of $\hat{\mathbf{P}}^{(n)}$ and \mathbf{w} . Consequently, the following holds:

$$\lim_{n \rightarrow \infty} G_n(\mathbf{w}) = \text{Prob}(\mathbf{W}_1 \leq \mathbf{w}) \lim_{n \rightarrow \infty} \sum_{\hat{\mathbf{p}}^{(n)} \in B} \text{Prob}(\hat{\mathbf{P}}^{(n)} = \hat{\mathbf{p}}^{(n)}) = \text{Prob}(\mathbf{W}_1 \leq \mathbf{w}).$$

We now have proved that

$$\mathbf{W}_1^{(n)} \rightarrow_d \mathbf{W}_1.$$

Lemma 3.3 implies that

$$(3.8) \quad \lim_{n \rightarrow \infty} S_n = \{\mathbf{p} \in R^3: \mathbf{a}_j^T \mathbf{p} \geq 0, j \in I(\mathbf{p}^{(0)})\}.$$

By Lemma 3.6,

$$(3.9) \quad \mathbf{W}_2^{(n)} \rightarrow_d \mathbf{W}_2.$$

Note that the two random vectors \mathbf{W}_1 and \mathbf{W}_2 are independent because they are functions of independent random variables $\mathbf{P}^{(n)*}$ and $\hat{\mathbf{P}}^{(n)}$, respectively. Now, consider the expression in (3.6) as a function of $\hat{\mathbf{P}}^{(n)}$. Then by (3.8) and (3.9) and by Lemma 3.5, $\pi_n(\mathbf{X})$ satisfies the following:

$$(3.10) \quad \pi_n(\mathbf{X}) \rightarrow_d \text{Prob}(\mathbf{W}_1 \in \{\mathbf{p} \in R^3: \mathbf{a}_i^T \mathbf{p} \geq 0, i \in I(\mathbf{p}^{(0)})\} - (\mathbf{c} + \mathbf{W}_2)).$$

1. When $I(\mathbf{p}^{(0)}) = \{i\}$, $i = 1, 2$ or 3 , then by (3.10),

$$\pi_n(\mathbf{X}) \rightarrow_d \text{Prob}(\mathbf{a}_i^T \mathbf{W}_1 \geq -(\mathbf{a}_i^T \mathbf{c} + \mathbf{a}_i^T \mathbf{W}_2)).$$

Dividing $\mathbf{a}_i^T \mathbf{W}_1$ by its standard deviation, $(\mathbf{a}_i^T \Sigma(\mathbf{p}^{(0)}) \mathbf{a}_i)^{1/2}$, (3.10) becomes

$$\pi_n(\mathbf{X}) \rightarrow_d \Phi(V_1 + \mu_i).$$

2. When $I(\mathbf{p}^{(0)}) = \{1, 2\}$, then (3.10) is

$$\pi_n(\mathbf{X}) \rightarrow_d \text{Prob}(\mathbf{a}_i^T \mathbf{W}_1 \geq -(\mathbf{a}_i^T \mathbf{c} + \mathbf{a}_i^T \mathbf{W}_2), i = 1 \text{ and } 2).$$

Dividing $\mathbf{a}_i^T \mathbf{W}_1$ by its standard deviation for each i , this expression becomes

$$\pi_n(\mathbf{X}) \rightarrow_d \Phi_\rho(V_1 + \mu_1, V_2 + \mu_2). \quad \square$$

Theorem 3.2 establishes that $\pi_n(\mathbf{X})$ converges in distribution to a random variable which is the probability that a normal random vector is in a quadrant determined by an independent random vector. The density function of the limiting distribution is presented for $\mathbf{p}^{(0)}$ in Ω_0 and $I(\mathbf{p}^{(0)}) = \{1\}$ in the following corollary.

COROLLARY 3.7. *Let H and h be the cumulative distribution function and the density function, respectively, of $\Phi(V_1 + \mu_1)$. Then for any r in the unit interval $[0, 1]$,*

$$H(r) = \Phi(\Phi^{-1}(r) - \mu_1) \quad \text{and} \quad h(r) = \exp(-\mu_1(-2\Phi^{-1}(r) + \mu_1)/2).$$

When $\mathbf{p}^{(n)}$ is identical to $\mathbf{p}^{(0)}$ and $I(\mathbf{p}^{(0)}) = \{1\}$, then μ_1 is 0. Hence, $h(r)$ reduces to the density of the uniform density on $[0, 1]$. The density function of $\Phi(V_1 + \mu_1)$ is plotted in Figure 5 for $p_i^{(0)} = 0.5$ and $\lambda_i = \frac{1}{3}$ for $i = 1, 2, 3$. In this case, $\mu_1 = (\frac{2}{3})^{1/2}(c_3 - c_1)$.

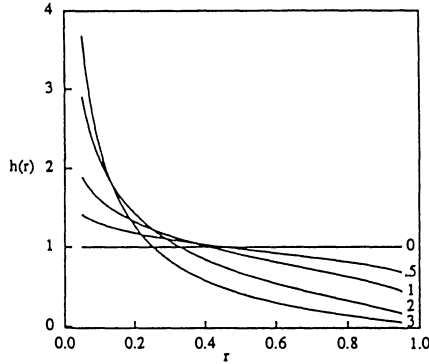


FIG. 5. The asymptotic density function h of the bootstrap test statistic for $c = c_1 - c_3$, $\mathbf{p} = (0.5, 0.5, 0.5)$ and $\lambda_i = \frac{1}{3}$, $i = 1, 2, 3$. Each curve is labeled with the value of c .

4. Asymptotic critical values and powers. In this section a discussion on how the critical values are determined for both tests is included. Then, based on the specified alternative sequence of parameters, the asymptotic powers are formulated.

4.1. *Critical values.* For a given target level α , the exact size and the corresponding critical value of the likelihood ratio test are functions of n . Let $c_{L,n}(\alpha)$ and $C_{L,n}(\alpha)$ be the critical values of $\Lambda_n(\mathbf{X})$ and $-2 \log \Lambda_n(\mathbf{X})$, respectively, for a test of size α_n . That is,

$$\alpha_n = \sup_{\theta \in S} \text{Prob}(\Lambda_n(\mathbf{X}) < c_{L,n}(\alpha)) = \sup_{\theta \in S} \text{Prob}(-2 \log \Lambda_n(\mathbf{X}) > C_{L,n}(\alpha)).$$

Then as n approaches infinity, α_n and $C_{L,n}(\alpha)$ must satisfy

$$\alpha_n \rightarrow \alpha \quad \text{and} \quad C_{L,n}(\alpha) \rightarrow C_L(\alpha)$$

for some $C_L(\alpha)$.

To determine $C_L(\alpha)$, consider $\theta^{(n)} \equiv \theta^{(0)}$. Then $\eta_i = 0$, $\gamma_i = 0$ and $\tau = 0$. First, consider cases when $I(\theta^{(0)}) = \{i\}$, $i = 1, 2$ or 3 ,

$$(4.1) \quad \text{Prob}(-2 \log \Lambda_n(\mathbf{X}) > C_{L,n}(\alpha)) \rightarrow_{n \rightarrow \infty} \text{Prob}([\min(Z, 0)]^2 > C_L(\alpha)).$$

Since the distribution of $[\min(Z, 0)]^2$ is an equal mixture of a chi-square distribution with one degree of freedom and a distribution degenerate at zero, (4.1) is

$$(4.2) \quad \text{Prob}(\chi_1^2 > C_L(\alpha))\text{Prob}(Z \leq 0) = \frac{1}{2}\text{Prob}(\chi_1^2 > C_L(\alpha)).$$

Next, consider the case when $I(\theta^{(0)}) = \{1, 2\}$. By Proposition 3.1,

$$(4.3) \quad \begin{aligned} &\text{Prob}(-2 \log \Lambda_n(\mathbf{X}) > C_{L,n}(\alpha)) \\ &\rightarrow_{n \rightarrow \infty} \sum_{i=1}^2 \text{Prob}((\mathbf{a}_i^T \mathbf{Z})^2 > C_L(\alpha))\text{Prob}(\mathbf{a}_i^T \mathbf{Z} < 0, \mathbf{b}_i^T \mathbf{Z} \geq 0) \\ &\quad + \text{Prob}((\mathbf{AZ})^T (\mathbf{AZ}) > C_L(\alpha))\text{Prob}(\mathbf{b}_i^T \mathbf{Z} < 0, i = 1, 2). \end{aligned}$$

The random variables $(\mathbf{a}_i^T \mathbf{Z})^2$ and $(\mathbf{AZ})^T(\mathbf{AZ})$ have chi-square distributions with one and two degrees of freedom, respectively. The two normal random variables $\mathbf{a}_i^T \mathbf{Z}$ and $\mathbf{b}_i^T \mathbf{Z}$ are independent because $\mathbf{a}_i^T \mathbf{b}_i = 0$. Hence, the following holds:

$$\text{Prob}(\mathbf{a}_i^T \mathbf{Z} < 0, \mathbf{b}_i^T \mathbf{Z} \geq 0) = \text{Prob}(\mathbf{a}_i^T \mathbf{Z} < 0)\text{Prob}(\mathbf{b}_i^T \mathbf{Z} \geq 0) = \frac{1}{4}, \quad i = 1, 2.$$

Thus, (4.3) is now

$$(4.4) \quad \frac{1}{2}\text{Prob}(\chi_1^2 > C_L(\alpha)) + \text{Prob}(\chi_2^2 > C_L(\alpha))\text{Prob}(\mathbf{b}_i^T \mathbf{Z} < 0, i = 1, 2).$$

Because when $\theta^{(0)}$ is not on the boundary of the transformed null set, $-2 \log \Lambda_n(\mathbf{X})$ either converges to zero or diverges, the size of the test must be achieved on the boundary of the transformed null set. Comparing (4.2) and (4.4), one sees that for any given α , the corresponding $C_L(\alpha)$ is determined by (4.4). For example, let $\alpha = 0.05$ and $\lambda_1 = \lambda_2 = \lambda_3 = \frac{1}{3}$. Then the critical value obtained for this example is $C_L(\alpha) = 3.8201$.

Now for a given α level test and the sample size n , let α_n and $C_{B,n}(\alpha)$ be the size and the corresponding critical value of the bootstrap test. Then α_n and $C_{B,n}(\alpha)$ must satisfy

$$(4.5) \quad \alpha = \lim_{n \rightarrow \infty} \alpha_n = \lim_{n \rightarrow \infty} \sup_{\mathbf{p} \in \Omega_0} \text{Prob}(\pi_n(\mathbf{X}) < C_{B,n}(\alpha)).$$

Also, there must exist a constant $C_B(\alpha)$ such that

$$C_{B,n}(\alpha) \rightarrow C_B(\alpha) \quad \text{as } n \rightarrow \infty.$$

There are two cases to be considered in determining the critical value $C_B(\alpha)$ of the bootstrap test. Under the null hypothesis, that is, when $\mathbf{p}^{(n)} \equiv \mathbf{p}^{(0)}$, then $\mu_i = 0$ for $i = 1, 2$ or 3 .

CASE 1. When $I(\mathbf{p}^{(0)}) = \{i\}$, $i = 1, 2$ or 3 , by Theorem 3.2,

$$\lim_{n \rightarrow \infty} \text{Prob}(\pi_n(\mathbf{X}) < C_{B,n}(\alpha)) = \text{Prob}(\Phi(V_1) < C_B(\alpha)) = C_B(\alpha).$$

CASE 2. When $I(\mathbf{p}^{(0)}) = \{1, 2\}$, by Theorem 3.2,

$$(4.6) \quad \lim_{n \rightarrow \infty} \text{Prob}(\pi_n(\mathbf{X}) < C_{B,n}(\alpha)) = \text{Prob}(\Phi_\rho(V_1, V_2) < C_B(\alpha)).$$

The right-hand side of (4.6) is the probability that (V_1, V_2) is below the curve bounded by the contour of Φ_ρ of value $C_B(\alpha)$. Since for any (v_1, v_2) on this curve, the region $\{(x, y) \in R^2: x < v_1, y < v_2\}$ is a subset of the region defined by

$$\Phi_\rho(V_1, V_2) < C_B(\alpha),$$

we have

$$(4.7) \quad \text{Prob}(\Phi_\rho(V_1, V_2) < C_B(\alpha)) > C_B(\alpha).$$

Because $\pi_n(\mathbf{X})$ converges to 1 when $\mathbf{p}^{(0)}$ is in the interior of the null set, by (4.5)–(4.7), the size of the test is determined by Case 2 and

$$\alpha = \text{Prob}(\Phi_\rho(V_1, V_2) < C_B(\alpha)).$$

In other words, to determine the critical value for a given level α test, one needs to inspect only those sequences of $\mathbf{p}^{(n)}$ for which the limit points are on the edge defined by $p_1 = p_2 = p_3$. For example, when $\alpha = 0.05$ and $\lambda_1 = \lambda_2 = \lambda_3 = \frac{1}{3}$, with 1000 replications, the critical value is 0.0154. The standard error of the estimate of the critical value is 0.002957.

4.2. *Asymptotic powers.* Since the asymptotic distribution of $-2 \log \Lambda_n(\mathbf{X})$ under a sequence of alternatives depends on the limit point of the sequence and the limiting sample fractions, so does the asymptotic power β . If the limit point is in the interior of a boundary face of the transformed null set such that g_i is 0 for only one i , then the asymptotic power β_i can be calculated using the formula

$$\begin{aligned} \beta_i &= \text{Prob}([\min(Z + \eta_i, 0)]^2 > C_L(\alpha)) \\ &= \text{Prob}(Z + \eta_i < -\sqrt{C_L(\alpha)}) = \Phi(-\eta_i - \sqrt{C_L(\alpha)}), \quad i = 1, 2, 3. \end{aligned}$$

If the limit point of the alternative sequence is on the edge of the transformed null set defined by $g_1 = g_2 = 0$, then the asymptotic power β is

$$\begin{aligned} (4.8) \quad \beta &= \sum_{i=1}^2 \text{Prob}((\mathbf{a}_i^T \mathbf{Z} + \eta_i)^2 > C_L(\alpha) \text{ and } \mathbf{a}_i^T \mathbf{Z} + \eta_i < 0, \mathbf{b}_i^T \mathbf{Z} + \gamma_i \geq 0) \\ &\quad + \text{Prob}((\mathbf{AZ} + \boldsymbol{\tau})^T (\mathbf{AZ} + \boldsymbol{\tau}) > C_L(\alpha)) \text{Prob}(\mathbf{b}_i^T \mathbf{Z} + \gamma_i < 0, i = 1, 2). \end{aligned}$$

Since \mathbf{a}_i and \mathbf{b}_i are orthogonal, $\mathbf{a}_i^T \mathbf{Z}$ and $\mathbf{b}_i^T \mathbf{Z}$ are two uncorrelated standard normal random variables. The first term of (4.8) is thus

$$\begin{aligned} &\sum_{i=1}^2 \text{Prob}(\mathbf{a}_i^T \mathbf{Z} + \eta_i < -C_L(\alpha)^{1/2} \text{ and } \mathbf{b}_i^T \mathbf{Z} + \gamma_i \geq 0) \\ &= \sum_{i=1}^2 \Phi(-\eta_i - C_L(\alpha)^{1/2})\Phi(\gamma_i). \end{aligned}$$

The second term of (4.8) needs to be evaluated numerically.

Next, we consider the asymptotic power for the bootstrap test. If the limit point of a sequence of parameters $\mathbf{p}^{(n)}$, defined in Theorem 3.2, is either in the interior of the null set or of the alternative set, then the asymptotic power is 1 or 0, due to the consistency of the maximum likelihood estimator. When $\mathbf{p}^{(0)}$ is on the boundary of the null set, then the asymptotic power depends on the location of $\mathbf{p}^{(0)}$.

Given α , the level of the test, the critical value $C_B(\alpha)$ can be approximated. Knowing the value of $C_B(\alpha)$, one can calculate or approximate the power according to where $\mathbf{p}^{(0)}$ is. The powers β are as follows:

CASE 1. When $I(\mathbf{p}^{(0)}) = \{i\}$, $i = 1, 2$ or 3 , by Theorem 3.2, the asymptotic power is

$$\beta_i = \text{Prob}(\Phi(V_1 + \mu_i) < C_B(\alpha)) = \text{Prob}(V_1 \leq -\mu_i + \Phi^{-1}(C_B(\alpha))).$$

Because V_1 is a standard normal random variable, (4.9) is now

$$\beta_i = \Phi(\Phi^{-1}(C_B(\alpha)) - \mu_i).$$

CASE 2. When $I(\mathbf{p}^{(0)}) = \{1, 2\}$, by Theorem 3.2, the asymptotic power is

$$\beta = \text{Prob}(\Phi_p(V_1 + \mu_1, V_2 + \mu_2) < C(\alpha)).$$

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