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Publication Date

2000

A GENERALIZED NONPARAMETRIC TEST FOR LATTICE-ORDERED MEANS

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ABSTRACT. Treatment means in factorial experiments are lattice ordered when there is an increase in mean response as the level of any factor is increased, holding the other factors fixed. Such means occur naturally in many experiments. A nonparametric test for lattice-ordered means involving a Kendall-type statistic will be summarized for k -factor factorial experiments. Specifically, the form of the test statistic and variance under the null hypothesis will be presented. In addition, a normalized version of the test statistic will be discussed and applied to relevant data.

1. INTRODUCTION

Data from factorial experiments have been routinely analyzed using ANOVA for many years. This classical method of inference determines which factors and interaction of factors are statistically significant, and also indicates whether some difference in treatment means exists using an overall F-test. For many experiments a researcher may expect a certain order on the treatment means, thus a more specific test than one for “some difference” may be appropriate. Consider the following examples.

Example 1: Athletes often take anabolic-androgenic steroids (high levels of testosterone) in an attempt to increase their strength. The use of these and other types of steroids in sports has been quite controversial due to potential health risks, and the unfair advantage that they may give athletes over those not taking the drug. However, the efficacy of such drugs has only been determined in recent years. A 2x2 controlled experiment by Bhasin, et. al. (1996) tested the effects of testosterone (no-placebo/yes-600mg) and exercise (no/yes) on muscle size and strength in men with previous weightlifting experience. (The exercises included bench pressing and squatting, and size and strength of the triceps and quadriceps muscles were measured before and after the treatment period.) For both exercise and no-exercise groups, it might be expected that those given the testosterone will have greater increase in mean muscle size than those given the placebo. Similarly, for each of the placebo and testosterone groups, one might expect that average muscle size will have greater increase for those exercising than for those not exercising. It is not as clear how mean response will compare between the

placebo-and-exercise group and the testosterone-and-no-exercise group. Table 1 displays data for change in quadriceps muscle volume over the 10 week treatment period, for which a total of 30 subjects were measured. (The treatment sample sizes were not equal, partially due to the fact that certain subjects that did not complete the experiment.)

Example 2: The rate of growth for bacteria depends largely on its environmental conditions, including such factors as temperature and pH. For example, extreme high and low temperatures are used to either kill or inhibit the growth of bacteria. Water activity (a_w) is another factor related to bacterial growth. In plain water (for which $a_w = 1$), bacteria generally grows most quickly, while increasing the amount of a humectant such as sodium chloride in the solution decreases water activity ($a_w < 1$) and slows down bacterial growth. Buchanan and Bagi (1997) performed an experiment where the growth of Escherichia-coli O157:H7 (E-coli) was observed in a brain-heart infusion (BHI) broth for various levels of temperature ($19^\circ C$, $28^\circ C$), pH (4.5, 5.5, 6.5) and a_w (0.982, 0.985, 0.987), using sucrose as the humectant. (This was actually just a subset of their entire experiment.) For these factors and levels, E-coli growth rate is expected to increase, on average, as one of the factors is increased, holding the others fixed. The justification for this hypothesis comes from previous models showing this particular relationship, but where sodium chloride was used as the humectant (Buchanan and Klawitter, 1992; Buchanan, et. al. 1993; Sutherland, Bayliss and Braxton, 1995). Once again, it is not as clear how an increase in one or two factors but a decrease in one or two of the others will affect mean growth rate. Table 2 contains the means reported for each treatment.

In both experiments one may be interested in carrying out a test where the alternative hypothesis is order restricted. To define this test, let $\mathbf{i} = (i_1, i_2, \dots, i_k)$ and $\mathbf{j} = (j_1, j_2, \dots, j_k)$ denote two treatment indices, and let the relation $\mathbf{i} \leq \mathbf{j}$ denote $i_1 \leq j_1, i_2 \leq j_2, \dots, i_k \leq j_k$. For the testosterone experiment, \mathbf{i} is defined as follows: $i_1 = 1$ and 2 for placebo and testosterone, respectively; $i_2 = 1$ and 2 for no-exercise and exercise, respectively. (The index \mathbf{j} is defined similarly.) For the E-coli experiment, let i_1, i_2 and i_3 be associated with temperature, pH, and a_w , respectively, where $i_1 = 1$ and 2 for low and high temperatures, $i_2 = 1, 2$ and 3 for low, moderate and high pH values, and $i_3 = 1, 2$ and 3 for low, medium and high a_w values, all respectively. (Again, \mathbf{j} is defined similarly.) The test of interest is then $H_0 : \mu_{\mathbf{i}} = \mu$ for all \mathbf{i} versus $H_A = H_1 - H_0$ where

$$(1) \quad H_1 : \mu_{\mathbf{i}} \leq \mu_{\mathbf{j}}, \quad \mathbf{i} \leq \mathbf{j}.$$

The type of order on the treatment means in (1) has been referred to as lattice order (Higgins and Bain, 1999, and Bain, 1994) or matrix order (Robertson, Wright and Dykstra, 1988). This is a kind of partial order on the means since not all pairs of means are comparable. Treatments for which means can be compared under lattice order will be referred to as lattice-comparable treatments.

The development of normal distribution likelihood ratio tests of H_0 vs. H_A are well summarized in Barlow, et. al. (1972) and Robertson, et. al. (1988). (Tests with alternatives that have other types of partial orders are also considered.) The tests exist for the known and unknown variances cases, for which null distributions are mixtures of chi-squared or beta distributions, respectively. These distributions have only been explicitly defined for one-factor and 2x2 experiments, as they are quite complex. Moonesinghe and Wright (1994) simulated components of the null distributions for $k=2$ and various factor levels, allowing one to determine approximate p-values for given test statistic values. These are done for the equal treatment sample sizes case.

Nonparametric tests of H_0 vs. H_A are generally simpler and normal approximations can be employed even with relatively small experiments. One-factor tests started appearing in the literature with Terpstra (1952), Jonckheere (1954) and Chacko (1963). (Note that when $k=1$, lattice order is the same as simple order, which is $\mu_1 \leq \mu_2 \leq \dots \leq \mu_k$.) Bain (1994) and Higgins and Bain (1999) summarized tests for nonreplicated data when $k=2$, using Kendall-type and Spearman-type statistics. The test using the Kendall-type statistic will be generalized to k factors and replicated data in this article.

2. FORM OF THE TEST

2.1. The Test Statistic. For two treatment indices $\mathbf{i} = (i_1, i_2, \dots, i_k)$ and $\mathbf{j} = (j_1, j_2, \dots, j_k)$, let $\mathbf{i} < \mathbf{j}$ denote $i_1 \leq j_1, i_2 \leq j_2, \dots, i_k \leq j_k$, with “ $<$ ” holding for at least one pair. Also, let $Y_{\mathbf{i}r}$ denote the response for replicate r in treatment \mathbf{i} , which has a continuous c.d.f. $F_{Y_{\mathbf{i}r}} = F_{\mathbf{i}}$ and mean $E(Y_{\mathbf{i}r}) = \mu_{\mathbf{i}}$, for $r = 1, \dots, n_{\mathbf{i}}$. The statistic that will be used for the lattice-ordered test is defined as

$$\begin{aligned} (2) \quad L &= \frac{2}{N_{la}} \sum_{\mathbf{i}} \sum_{\mathbf{j} > \mathbf{i}} \left(\sum_{r=1}^{n_{\mathbf{i}}} \sum_{s=1}^{n_{\mathbf{j}}} I(Y_{\mathbf{i}r} \leq Y_{\mathbf{j}s}) \right) - 1 \\ &= \frac{1}{N_{la}} \sum_{\mathbf{i}} \sum_{\mathbf{j} > \mathbf{i}} \left(\sum_{r=1}^{n_{\mathbf{i}}} \sum_{s=1}^{n_{\mathbf{j}}} \left[I(Y_{\mathbf{i}r} < Y_{\mathbf{j}s}) - I(Y_{\mathbf{i}r} > Y_{\mathbf{j}s}) \right] \right), \end{aligned}$$

where

$$(3) \quad N_{la} = \sum_{\mathbf{i}} \sum_{\mathbf{j} > \mathbf{i}} n_{\mathbf{i}} n_{\mathbf{j}}.$$

The test statistic L is the proportion of unique pairs of responses that are consistent with the order that is expected on the respective treatment means, which is then simply rescaled into a range between -1 and +1. (The last step in (2) follows from the fact that the $Y_{\mathbf{i}r}$ ’s are continuous random variables.) Note that only lattice-comparable treatments are considered. The quantity N_{la} in (3) is the total number of response pairs evaluated.

The statistic L is a useful measure of the degree of lattice order in the responses. The closer L is to +1, the more the responses are in agreement with H_A , while values of L that are close to or less than zero occur when the responses do not show strong support of H_A . Now L is closely related to Kendall's correlation statistic (K), particularly when $k = 1$. However, K is defined generally for bivariate (X, Y) data while L is just defined for data where X has fixed levels.

It should be noted that the hypotheses H_0 and H_A previously given in terms of means can be generalized to distributions for this nonparametric test. This will be particularly useful if one can assume that $F_i(y) \geq F_j(y)$ for all y , and for all \mathbf{i} and \mathbf{j} such that $\mathbf{i} \leq \mathbf{j}$, but cannot assume common errors. In such a case the hypotheses are written as $H_0 : F_i(y) = F(y)$ for all \mathbf{i} and some c.d.f. F versus $H_A = H_1 - H_0$ where $H_1 : F_i(y) \geq F_j(y)$ for all $\mathbf{i} \leq \mathbf{j}$.

2.2. Mean and Variance of L Under H_0 . Consider a k -factor experiment for which the treatment means are lattice ordered. If all responses are independent and there exists some c.d.f. F such that $F_i(y) = F(y - \mu_i)$ for all y and for all \mathbf{i} , then the statistic L can be used to test H_0 vs. H_A in terms of the treatment means.

The mean and variance of L under H_0 will be denoted as $E_0(L)$ and $Var_0(L)$, respectively. Now $E_0(L) = 0$ since $E_0[I(Y_{ir} < Y_{js}) - I(Y_{ir} > Y_{js})] = 0$ for each \mathbf{i}, \mathbf{j} such that $\mathbf{i} \leq \mathbf{j}$, and for all r and s . The variance $Var_0(L)$ can be derived using a general expression from Ager and Brent (1978) since L is a special case of the statistic that they consider. (In their paper they propose a Kendall-type statistic that can be used for tests where H_A has any type partial order placed on the means or distributions.) Adapting their variance expression to suit L yields

$$(4) \quad Var_0(L) = \frac{N_{la} + Q}{3N_{la}^2},$$

where N_{la} is as given in (3) and

$$(5) \quad Q = \sum_{\mathbf{i}} n_{\mathbf{i}} \left(\sum_{\mathbf{j} < \mathbf{i}} n_{\mathbf{j}} - \sum_{\mathbf{j} > \mathbf{i}} n_{\mathbf{j}} \right)^2.$$

For numerical calculations, a more tractable form of the variance is obtained when N_{la} in (3) and Q in (5) are rewritten as

$$(6) \quad N_{la} = \sum_{\mathbf{i}} \sum_{\mathbf{j} \geq \mathbf{i}} n_{\mathbf{i}} n_{\mathbf{j}} - \sum_{\mathbf{i}} n_{\mathbf{i}}^2$$

and

$$(7) \quad Q = \sum_{\mathbf{i}} n_{\mathbf{i}} \left(\sum_{\mathbf{j} \leq \mathbf{i}} n_{\mathbf{j}} - \sum_{\mathbf{j} \geq \mathbf{i}} n_{\mathbf{j}} \right)^2,$$

respectively. An existing program to calculate $Var_0(L)$ is available upon request from the author.

2.3. Asymptotic Normality. The lattice-ordered means test can be carried out easily by determining the exact or simulated permutation distribution of L under H_0 and comparing the test statistic with this distribution. A simpler approach is to create a test statistic based on L that is asymptotically standard normal, which should be a good approximation for sufficiently-sized experiments. Bain (1994) and Ager and Brent (1978) showed that the standard normal distribution provides an adequate approximation to the test statistic

$$(8) \quad Z = \frac{L - \frac{1}{2N_{la}}}{\sqrt{Var_0(L)}}$$

when the number of unique treatment comparisons, N_{la} , is as small as 50 to 85. For a 4x4 experiment with nonreplicated data $N_{la} = 84$. For a 2x2 experiment with $n=5$ replicates in each treatment, $N_{la} = 125$. (See Table 3 for more examples.) This reinforces the fact that large data sets are not necessary for the normal approximation to be effective. The test of H_0 vs. H_A based on Z is a right-tailed test, and the term ' $\frac{1}{2N_{la}}$ ' is included as a correction for continuity.

2.4. Simplifications for Balanced Data. Often times a researcher will have nonreplicated data or replicated data with equal treatment sample sizes (with n in each treatment). In such cases, $Var_0(L)$ can be expressed in closed form in terms of the number of levels for each factor, which are denoted by m_h , $h = 1, \dots, k$. Specifically, $Var_0(L)$ is as given in (4), where

$$(9) \quad N_{la} = n^2 \left(\prod_{h=1}^k \binom{m_h + 1}{2} - \prod_{h=1}^k m_h \right)$$

and

$$(10) \quad Q = \frac{2n^3}{3^k} \prod_{h=1}^k \binom{m_h + 1}{2} \left(\prod_{h=1}^k (2m_h + 1) - \prod_{h=1}^k (m_h + 2) \right).$$

The derivation of (9) and (10) are given in Appendices A and B, respectively. One can verify that $Var_0(L)$ reduces to the variance of Kendall's correlation statistic (K) when $k=1$ and $n=1$. Table 3 shows values of N_{la} and $Var_0(L)$ for experiments of certain size and for $n=1$ and 5.

3. APPLICATIONS OF THE TEST

Example 1 (Testosterone experiment, data in Table 1): For the test of H_0 vs. H_A , there are $N_{la} = 281$ pairs of lattice-order comparisons, 265 of which are increasing, as expected. Thus the value of $L = (265 - 16)/281 = 0.886$, denoting a strong positive lattice order among the responses. Using the short program constructed, it was determined that $Var_0(L) = 0.0332274$.

Using the normal approximation to L as given in (8), $z = 4.85$, for which $p < 0.0001$. One would reject the hypothesis of equal means and conclude that exercise and/or testosterone increases mean quadriceps muscle volume.

Example 2 (E-coli experiment, data in Table 2): The test of H_0 vs. H_A was carried out on the treatment sample means. (Each treatment actually had 2 to 3 replicates, but only averages were reported.) The statistic $L = 0.80$ with $N_{la} = 90$. Using the closed form given in section 2.4, with $n = 1$, it was determined that $Var_0(L) = 0.05144$. The normalized test statistic $z = 3.50$, for which $p = 0.0002$. Once again one would reject the equal means hypothesis and conclude that average E-coli growth speeds up as at least one of the three factors (water activity, pH, temperature) are increased, using sucrose as the humectant.

4. REMARKS

The lattice-ordered means test can be applied to data from many factorial experiments where factors are at least ordinal in nature and the responses are expected to be lattice ordered. Unlike the overall F-test for ANOVA, the alternative hypothesis for the lattice-ordered means test involves a partial order on the means. Thus a more specific conclusion is reached when the null hypothesis is rejected. Also, the nonparametric test is a nice alternative for experimental data that is nonreplicated. In such a case the overall ANOVA F-test cannot be performed unless at least one of the interaction effects is assumed to be 0. No such assumption is required for the nonparametric test.

In certain experiments the levels of at least one of the factors may need to be reversed so that lattice-ordered means are expected. For example, within a range of temperatures and levels of humidity, a certain plant may be expected to have more growth as temperature is decreased and humidity is held fixed, or as humidity is increased and temperature is held fixed. In such a case the test can be performed if the levels are simply arranged as needed.

There are a few notes of caution for the researcher, regarding choosing the levels of the factors and making conclusions based on results. (1) The levels of each factor must be considered carefully. In the microbiology example, the ranges of pH and temperature were selected so that levels too high were not included. For example, since foods are cooked at higher temperatures to kill E-coli, the growth rate of this bacteria cannot be expected to continue increasing if very high temperatures are included in the experiment. The danger is that when many but not all treatment means follow lattice order in an experiment, then it is still quite possible to reject the null hypothesis. In such a case a large majority of the responses (or sample means) may still be lattice ordered, leading to a value of L that is big enough to accept H_A . (2) For the lattice-ordered means test performed on data from a k -factor experiment, rejection of the null hypothesis technically does not imply that any individual factor (or subset of factors) is significant. Thus, if H_A is

accepted, one can qualify the conclusion by saying ‘there is a mean increase in response (at least somewhere), as one or more of the factors is increased.’

ACKNOWLEDGEMENTS

The author would like to thank Shalender Bhasin, Tom Storer, Nancy Berman, and their team of researchers for the data from the testosterone experiment. The author would also like to thank James Higgins (Kansas State University) for the initial motivation to write this article.

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APPENDIX A. DERIVATION OF N_{la} FOR BALANCED DATA

$$\begin{aligned}
N_{la} &= n^2 \left(\sum_{\mathbf{i}} \sum_{\mathbf{j} \geq \mathbf{i}} 1 - \sum_{\mathbf{i}} 1 \right) \\
&= n^2 \left(\sum_{i_1=1}^{m_1} \sum_{i_2=1}^{m_2} \dots \sum_{i_k=1}^{m_k} \left[\sum_{j_1=i_1}^{m_1} \sum_{j_2=i_2}^{m_2} \dots \sum_{j_k=i_k}^{m_k} 1 \right] - \sum_{i_1=1}^{m_1} \sum_{i_2=1}^{m_2} \dots \sum_{i_k=1}^{m_k} 1 \right) \\
&= n^2 \left(\sum_{i_1=1}^{m_1} \sum_{i_2=1}^{m_2} \dots \sum_{i_k=1}^{m_k} \left[(m_1 - i_1 + 1)(m_2 - i_2 + 1) \dots (m_k - i_k + 1) \right] \right. \\
&\quad \left. - m_1 m_2 \dots m_k \right) \\
&= n^2 \left(\frac{m_1(m_1 + 1)m_2(m_2 + 1) \dots m_k(m_k + 1)}{2^k} - m_1 m_2 \dots m_k \right) \\
&= n^2 \left(\prod_{h=1}^k \binom{m_h + 1}{2} - \prod_{h=1}^k m_h \right)
\end{aligned}$$

APPENDIX B. DERIVATION OF Q FOR BALANCED DATA

$$\begin{aligned}
Q &= n^3 \sum_{\mathbf{i}} \left(\sum_{j \leq i} 1 - \sum_{j \geq i} 1 \right)^2 \\
&= n^3 \sum_{\mathbf{i}} \left(\left[i_1 i_2 \dots i_k \right] - \left[(m_1 - i_1 + 1)(m_2 - i_2 + 1) \dots (m_k - i_k + 1) \right] \right)^2 \\
&= n^3 \sum_{i_1=1}^{m_1} \sum_{i_2=1}^{m_2} \dots \sum_{i_k=1}^{m_k} \left(i_1 i_2 \dots i_k - (m_1 - i_1 + 1)(m_2 - i_2 + 1) \dots (m_k - i_k + 1) \right)^2 \\
&= n^3 \prod_{h=1}^k \left(\sum_{i_h=1}^{m_h} i_h^2 \right) - 2n^3 \prod_{h=1}^k \left(\sum_{i_h=1}^{m_h} i_h (m_h - i_h + 1) \right) + n^3 \prod_{h=1}^k \left(\sum_{i_h=1}^{m_h} (m_h - i_h + 1)^2 \right) \\
&= n^3 \left(\prod_{h=1}^k \frac{m_h(m_h+1)(2m_h+1)}{6} - 2 \prod_{h=1}^k \frac{m_h(m_h+1)(m_h+2)}{6} \right. \\
&\quad \left. + \prod_{h=1}^k \frac{m_h(m_h+1)(2m_h+1)}{6} \right) \\
&= \frac{2n^3}{3^k} \prod_{h=1}^k \binom{m_h+1}{2} \left(\prod_{h=1}^k (2m_h+1) - \prod_{h=1}^k (m_h+2) \right)
\end{aligned}$$

Table 1: *Androgenic steroid (testosterone) experiment (Bhasin, Storer, Berman et al., 1996): effects of testosterone (placebo, 600mg) and exercise (no, yes) on quadriceps muscle volume for men. Values given express % change over the ten week treatment period. Experiment-wide ranks are given in parentheses.*

Placebo		Testosterone	
no exercise	exercise	no exercise	exercise
-4.51 (1)	-2.12 (3)	5.28 (14)	11.40 (20)
-2.55 (2)	-2.05 (4)	9.57 (16)	11.98 (23)
-1.00 (5)	1.18 (9)	10.12 (17)	13.39 (25)
-0.40 (6)	2.58 (10)	11.24 (19)	13.43 (26)
-0.19 (7)	3.35 (12)	11.45 (21)	13.44 (27)
0.62 (8)	5.12 (13)	12.43 (24)	13.60 (28)
2.99 (11)	5.84 (15)		13.74 (29)
	10.57 (18)		20.02 (30)
	11.46 (22)		

Table 2: *E-coli experiment (Buchanan and Bagi, 1997): observed exponential growth rate [log(cfu/ml) per hour] for E-coli among various levels of water activity (a_w), temperature and pH. Experiment-wide ranks are given in parentheses. (Sucrose was used as the humectant to control the water activity level.)*

Temp	a_w	pH		
		4.5	5.5	6.5
19°C	0.982	0.206 (5)	0.147 (3)	0.146 (2)
	0.985	0.213 (6)	0.227 (7)	0.270 (10)
	0.987	0.120 (1)	0.256 (9)	0.247 (8)
28°C	0.982	0.175 (4)	0.454 (13)	0.498 (15)
	0.985	0.350 (11)	0.476 (14)	0.501 (16)
	0.987	0.418 (12)	0.553 (18)	0.548 (17)

Table 3: N_{la} and $Var_0(L)$ for various-sized experiments, with $n=1$ and $n=5$.

Experiment size	$n=1$		$n=5$	
	N_{la}	$Var_0(L)$	N_{la}	$Var_0(L)$
2x2	5	0.3067	125	0.0507
3x3	27	0.1001	675	0.0181
4x4	84	0.0512	2100	0.0096
5x5	200	0.0317	5000	0.0061
6x6	405	0.0217	10125	0.0042
2x2x2	19	0.1302	475	0.0232
3x3x3	189	0.0343	4725	0.0066
4x4x4	936	0.0148	23400	0.0029