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Gary G. Koch and Pranab Kumar Sen

University of North Carolina, Chapel Hill

Institute of Statistics Mimeo Series No. 500

December 1966

Work partially supported by the National Institute of Health, Public Health Service, Grant GM-12868.

DEPARTMENT OF BIOSTATISTICS

UNIVERSITY OF NORTH CAROLINA

Chapel Hill, N. C.

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Gary G. Koch and Pranab Kumar Sen[1]

University of North Carolina
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SUMMARY

In this paper, the authors discuss the statistical analysis (both parametric and non-parametric) of "mixed model" experiments. The general structure of such experiments involves n randomly chosen subjects who respond once to each of p distinct treatments. The hypothesis of no treatment effects is considered under several different combinations of assumptions concerning the joint distribution of the observations corresponding to each of the particular subjects. For each situation, an appropriate test procedure is discussed and its properties studied.

The different methods considered in the paper are illustrated in detail in two numerical examples. These examples have been chosen to illustrate the relative performances of the different test criteria for a situation in which the null hypothesis is essentially true (Example 1) and for a situation in which the null hypothesis is essentially false (Example 2).

Finally, the section on examples contains algorithms for the efficient computation of the various test criteria. A computer program based on these algorithms has been written and can be made available to any interested persons.

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* Work partially supported by the National Institute of Health, Public Health Service, Grant GM-12868.

[1] On leave of absence from Calcutta University, India

1. INTRODUCTION

In accordance with the familiar "mixed model" experiments (cf. Eisenhart [1947] and Scheffé [1959]), let Y_{ij} be the response of the i-th subject to the j-th treatment for $i=1,2,\ldots,n$; $j=1,2,\ldots,p$. Thus, each subject responds to each of p distinct treatments exactly once. The outcome of the experiment may be represented by the <u>observation matrix</u> $\underset{n\times p}{\tilde{Y}} = (Y_{ij})$ composed of n independent stochastic row vectors

$$\underline{Y}_i' = (Y_{i1},\ldots,Y_{ip}),\ i=1,2,\ldots,n\ . \tag{1.1}$$

It is assumed that $\underline{Y}_i$ has a continuous p-variate cumulative distribution function (c.d.f.) $F_i(\underline{y})$, where

$$F_i(\underline{y}) = G_i(\underline{y}-\underline{m}_i),\ \underline{m}_i' = (m_{i1},\ldots,m_{ip}); \tag{1.2}$$

$$m_{ij} = b_i+t_j,\ i=1,2,\ldots,n;\ j=1,2,\ldots,p. \tag{1.3}$$

Together with (1.2) and (1.3), the basic assumption throughout this paper is

A.1. <u>The joint distribution of any linearly independent set of contrasts among the observations on any particular subject is diagonally symmetric</u>.

Two additional assumptions which may or may not be imposed are

A.2. <u>The "additivity" of subject effects</u>;

A.3. <u>The "compound symmetry" of the error vectors</u>.

The assumptions A.1, A.2, and A.3 will be explained more fully in what follows. In any event, four cases of interest arise; and these may be described by the following table

	Not A.2	A.2
Not A.3	Case I	Case III
A.3	Case II	Case IV

In each of the above cases, the hypothesis of no treatment effects, i.e.,

$$H_o: \quad t_1 = t_2 = \dots = t_p = 0, \tag{1.4}$$

is considered, and appropriate test procedures are given. Various properties of these tests are also studied.

2. THE NORMAL (PARAMETRIC) CASE

In this section, the basic assumptions are A.1, A.2, and

A.4. $G_1 \equiv G_2 \equiv \dots \equiv G_n \equiv G$ is a multinormal c.d.f.; i.e., the error vectors have a common p-variate normal distribution with a null mean vector and a positive definite dispersion matrix Σ.

Note that A.4 implies that the $\underline{Y}_i$, i=1,2,...,n, are independently distributed according to the multivariate normal distributions $N(\underline{m}_i, \Sigma)$, i=1,2,...,n, where the $\underline{m}_i$'s are defined by (1.2) and (1.3). To test H_o in (1.4), we may proceed as follows. Let C be a (p × p) matrix of the following structure

$$C = \begin{bmatrix} p^{-\frac{1}{2}} \underline{j}' \\ C_1 \end{bmatrix} \quad \text{where } \underline{j}' = (1,\dots,1) \text{ and } C_1 \underline{j} = \underline{0}. \tag{2.1}$$

If we let

$$\underline{U}_i = C_1 Y_i, \quad i=1,2,\dots,n; \quad \bar{\underline{U}} = \frac{1}{n} \sum_{i=1}^{n} \underline{U}_i; \tag{2.2}$$

$$S_U = \sum_{i=1}^{n} (\underline{U}_i - \bar{\underline{U}})(\underline{U}_i - \bar{\underline{U}})', \tag{2.3}$$

then the test statistic is

$$T^2 = n(n-1)\ \underline{\bar{U}}'\ \underset{\sim}{S}_U^{-1}\ \underline{\bar{U}}\ . \tag{2.4}$$

Under H_o, $(n-p+1)T^2/(n-1)(p-1)$ has the F-(variance ratio) distribution with $[(p-1),\ (n-p+1)]$ degrees of freedom (d.f.), where it is necessary to presuppose that $n \geq p$. The test procedure based on T^2 represents a parametric solution to Case III. Since T^2 is invariant under any (non-singular) linear transformation on the $\underline{U}_i$, $i=1,2,\ldots,n$, some computational convenience may be gained by basing the test on the contrasts

$$U^*_{ik} = Y_{ik} - Y_{i1} \text{ for } k=2,\ldots,p;\ i=1,2,\ldots,n. \tag{2.5}$$

Now, a sufficient condition (also necessary, if the distribution is multinormal) for A.3 is

$$\underset{\sim}{\Sigma} = \rho\sigma^2\underset{\sim}{J} + (1-\rho)\sigma^2\underset{\sim}{I} \tag{2.6}$$

where $\underset{\sim}{J}$ is the $p \times p$ matrix of 1's and $\underset{\sim}{I}$ is the $p \times p$ identity matrix. Since (2.6) implies that the variability of a subject's response is independent of the treatment given, we shall say that there is <u>no interaction</u> between treatments and subjects in this case. The test of H_o in (1.4) may now be based on the statistic

$$F_t = (n-1)S_t^2/S_e^2 \tag{2.7}$$

where

$$S_t^2 = n\sum_{j=1}^{p}(\bar{Y}_{.j}-\bar{Y}_{..})^2,\quad S_e^2 = \sum_{i=1}^{n}\sum_{j=1}^{p}(Y_{ij}-\bar{Y}_{i.}-\bar{Y}_{.j}+\bar{Y}_{..})^2$$

with

$$\bar{Y}_{i.} = p^{-1}\sum_{j=1}^{p}Y_{ij},\quad \bar{Y}_{.j} = n^{-1}\sum_{i=1}^{n}Y_{ij},\quad \bar{Y}_{..} = (np)^{-1}\sum_{i=1}^{n}\sum_{j=1}^{p}Y_{ij}\ .$$

Under H_o, F_t has the F-distribution with $[(p-1), (n-1)(p-1)]$ d.f. The test based on F_t provides a parametric solution to Case IV.

One may note that the validity of (2.6) may be checked by means of a likelihood ratio test given by Votaw [1948] which is a generalization of one originally due to Wilks [1946] (for the particular case $b_1 = b_2 = \ldots = b_n = 0$). For a further discussion of the parametric case, the reader is referred to Wilks [1946], Scheffé [1959], Imhof [1960], and Geisser [1963].

3. A NON-PARAMETRIC TREATMENT OF CASE I

First, let us clarify the statement of the basic assumption A.1. Suppose $\underline{U}_i$ is defined as in (2.2), and $\underline{m}_i$ as in (1.2); let $\underline{t}' = (t_1, \ldots, t_p)$ where the t_i's are defined by (1.3). Finally, let $\underline{\theta}$ be a $(p-1) \times 1$ vector defined by

$$\underline{\theta} = \underset{\sim}{C}_1 \, \underline{m}_i = \underset{\sim}{C}_1 \, \underline{t} \tag{3.1}$$

where $\underset{\sim}{C}_1$ is defined by (2.1). Then A.1 asserts that for each $i=1,2,\ldots,n$, $(\underline{U}_i - \underline{\theta})$ and $(\underline{\theta} - \underline{U}_i)$ have the same distribution. Under H_o, $\underline{\theta} = \underline{0}$; and hence, in this situation, A.1 implies that $\underline{U}_i$ and $-\underline{U}_i$ have the same distribution. One may note that this is much less restrictive than the usual assumption of multi-normality of the $\underline{U}_i$.

To test H_o, we may proceed as follows.

Let

$$R_{ij} = \text{Rank } \{Y_{ij}: Y_{i1}, \ldots, Y_{ip}\} \quad \begin{matrix} j=1,2,\ldots,p \\ i=1,2,\ldots,n \end{matrix} \tag{3.2}$$

where ties are to be handled by the mid-rank method; i.e.,

$$R_{ij} = 1 + \left\{\begin{matrix}\text{The number of } Y_{ij'} \text{ which} \\ \text{are less than } Y_{ij}\end{matrix}\right\} + \left(\tfrac{1}{2}\right)\left\{\begin{matrix}\text{The number of} \\ Y_{ij'} \text{ equal to } Y_{ij}\end{matrix}\right\} \tag{3.2'}$$

where $j' \neq j$; also $j, j' = 1,2,\ldots,p$; $i=1,2,\ldots,n$.

Let

$$T_{n,j} = \frac{1}{n}\sum_{i=1}^{n} R_{ij} \quad \text{for} \quad j=1,2,\ldots,p; \tag{3.3}$$

$$\underline{T}_n' = (T_{n,1},\ldots,T_{n,p}) \quad . \tag{3.4}$$

We next observe that if $Z_{ij} = Y_{ij}-\bar{Y}_{i\cdot}$, $j=1,2,\ldots,p$, then

$$R_{ij} = \text{Rank}\ \{Z_{ij}\colon Z_{i1},\ldots,Z_{ip}\} \quad \begin{matrix} j=1,2,\ldots,p \\ i=1,2,\ldots,n \end{matrix} \; . \tag{3.5}$$

But the Z_{ij}'s are contrasts; hence, under H_o, the vectors $\underline{Z}_i' = (Z_{i1},\ldots,Z_{ip})$ and $-\underline{Z}_i' = (-Z_{i1},\ldots,-Z_{ip})$ have the same distribution by assumption A.1. This sign-invariance generates a set of 2^n conditionally equally likely realizations; and as a result, the rank vectors

$$\underline{R}_i' = (R_{i1},\ldots,R_{ip}) \text{ and } (p+1)\underline{1}'-\underline{R}_i' = (p+1-R_{i1},\ldots,p+1-R_{ip}) \tag{3.6}$$

are (conditionally) equally likely, each occurring with conditional probability $\frac{1}{2}$ for $i=1,2,\ldots,n$. Thus, under this conditional probability law (say $\mathcal{P}_n$),

$$E\{T_{n,j} \mid \mathcal{P}_n\} = \frac{1}{n}\sum_{i=1}^{n} \frac{R_{ij} - [(p+1)-R_{ij}]}{2} = \frac{p+1}{2} \tag{3.7}$$

$$\text{Cov}\{T_{n,j}, T_{n,j'} \mid \mathcal{P}_n\} = \frac{1}{n^2}\sum_{i=1}^{n} (R_{ij}-\frac{p+1}{2})(R_{ij'}-\frac{p+1}{2}) \equiv v_{n,jj'} \tag{3.8}$$

for all $j,j'=1,2,\ldots,p$. Let us define the matrix

$$\underset{\sim}{V}_n = (v_{n,jj'}) \; . \tag{3.9}$$

Since the $T_{n,j}$'s in (3.3) satisfy the constraint

$$\sum_{j=1}^{p} T_{n,j} = p(p+1)/2, \tag{3.10}$$

$\underset{\sim}{V}_n$ is essentially singular and of rank at most (p-1). However, if $G_i(\underline{y})$ has a "scatter" not confined to any lower dimensional space of the real p-dimensional space (R_p), one may show that n $\underset{\sim}{V}_n$ has rank (p-1) in probability (the argument is similar to that given in Puri and Sen [1966]). Thus, if $\underset{\sim}{C}$ is defined as in (2.1), the test statistic is

$$W_n = \underline{T}_n' \underset{\sim}{C}_1' [\underset{\sim}{C}_1 \underset{\sim}{V}_n \underset{\sim}{C}_1']^{-1} \underset{\sim}{C}_1 \underline{T}_n \quad . \tag{3.11}$$

Under the permutation model $\mathcal{P}_n$, W_n can have 2^n (not necessarily distinct) equally likely (conditionally) realizations; and this may be used as a basis of a permutationally distribution free test of H_o. Moreover, under $\mathcal{P}_n$, $\underline{T}_n$ is the vector of averages over n independent random variables. Hence, by routine methods, $n^{\frac{1}{2}} \underline{T}_n$ can be shown to have asymptotically (under $\mathcal{P}_n$) a multinormal distribution of rank (p-1). Thus, under $\mathcal{P}_n$, W_n has asymptotically a chi-square distribution with (p-1) d.f. From the above remarks, we have the following test procedure

$$\text{reject } H_o \text{ if and only if } W_n \geq \chi^2_{(1-\epsilon)}(p-1) \tag{3.12}$$

where $P\{\chi^2(p-1) \geq \chi^2_{(1-\epsilon)}(p-1)\} = \epsilon$, $0<\epsilon<1$, the desired significance level.

If we now define a kernel

$$\phi(a_i; a_1, \ldots, a_p) = \tfrac{1}{2} + \sum_{j=1}^{p} c(a_i - a_j) \tag{3.13}$$

where c(u) is 1, $\frac{1}{2}$, or 0 according as u is >, =, or < 0, then it may easily be verified that

$$T_{n,j} = \frac{1}{n} \sum_{i=1}^{n} \phi(Y_{ij}; Y_{i1}, \ldots, Y_{ip}) \text{ for } j=1,\ldots,p \ . \tag{3.14}$$

Using the well-known results on U-statistics (cf. Hoeffding [1948], Fraser [1947]) and following some essentially simple steps, one may show that the test in (3.12) is consistent against any heterogeneity of $t_1,\dots,t_p$. Thus, for any fixed $t_1,\dots,t_p$ (not all equal), the power of the test will be asymptotically equal to one. Therefore, to study the asymptotic power of the test, we shall consider a sequence of alternatives for which the power lies in the open interval (0,1). This is specified by

$$t_j = n^{-\frac{1}{2}}\lambda_j,\quad j=1,2,\dots,p;\ \sum_1^p \lambda_j = 0 \tag{3.15}$$

where $\lambda_1,\dots,\lambda_p$ are all real and finite. Here, let us also assume

$$G_1 \equiv G_2 \equiv \dots \equiv G_n \equiv G \text{ and } G \text{ absolutely continuous .} \tag{3.16}$$

Let the marginal c.d.f.'s of G be denoted by $G_{[j]}(x)$, $j=1,2,\dots,p$; and the joint marginal c.d.f.'s (of order 2), by $G_{[j,j']}(x,y)$, $j\neq j'=1,2,\dots,p$. If the elements of the matrix $\underset{\sim}{\nu} = (\nu_{jj'})$ are defined by

$$\nu_{jj'} = 3\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}[2G_{[j]}(x)-1][2G_{[j']}(y)-1]dG_{[j,j']}(x,y) \tag{3.17}$$

then it may be shown that $n\,\underset{\sim}{V}_n$ converges in probability to $\underset{\sim}{\nu}$ and W_n has asymptotically a non-central χ^2-distribution with (p-1) d.f. and non-centrality parameter

$$\eta_W = \underset{\sim}{\lambda}'\underset{\sim}{C}_1'[\underset{\sim}{C}_1\underset{\sim}{\nu}\underset{\sim}{C}_1']^{-1}\underset{\sim}{C}_1\underset{\sim}{\lambda} \tag{3.18}$$

when (3.15) holds - again the reader is referred to Puri and Sen [1966], Theorem 4.2.

Finally, one may note that given the permutation covariance matrix V_n, we may always select $\underset{\sim}{C}_1$ in such a way that $\underset{\sim}{C}_1\underset{\sim}{V}_n\underset{\sim}{C}_1' = \underset{\sim}{D}_n$ = diagonal $(d_{n,1},\dots,d_{n,(p-1)})$. In such a case, W_n reduces to

$$W_n = \sum_{k=1}^{p-1} W_{n,k}^2/d_{n,k} \tag{3.19}$$

where the $W_{n,k}$ are the elements of the vector $\underset{\sim}{C}_1 \underline{T}_n$.

4. A NON-PARAMETRIC TREATMENT OF CASE II

As has been explained in section 2, A.3 really means no interaction between treatments and subjects. Under this condition, $\underset{\sim}{Y}_i$ is composed of p interchangeable random variables (under H_o in (1.4)) for all i=1,...,n; and hence, the distribution of $\underset{\sim}{Y}_i$ remains invariant under any permutation of its coordinates, for i=1,...,n. This leads to a set of $(p!)^n$ equally likely (conditionally) permutations and the associated permutational model is denoted by $\tilde{\mathcal{P}}_n$. In this case, we shall also work with the statistic $\underset{\sim}{T}_n$ in (3.3) and (3.4), but under $\tilde{\mathcal{P}}_n$. Thus, we have

$$E(T_{n,j} \mid \tilde{\mathcal{P}}_n) = (p+1)/2 \tag{4.1}$$

$$\text{cov}(T_{n,j}, T_{n,j'} \mid \tilde{\mathcal{P}}_n) = \frac{(\delta_{ij}p-1)}{(p-1)n} \bar{\sigma}_R^2, \quad j, j'=1,\ldots,p \tag{4.2}$$

where

$$\bar{\sigma}_R^2 = \frac{1}{np} \sum_{i=1}^{n} \sum_{j=1}^{p} (R_{ij} - \frac{p+1}{2})^2, \tag{4.3}$$

R_{ij}'s being defined as in (3.2) or (3.2') and δ_{ij} is the usual Kronecker delta. Hence, we may use the test statistic

$$\tilde{W}_n = [n(p-1)/p\ \bar{\sigma}_R^2] \sum_{j=1}^{p} (T_{n,j} - (p+1)/2)^2 . \tag{4.4}$$

The asymptotic distribution of $n^{\frac{1}{2}}(T_{n,j} - (p+1)/2)$, j=1,...,p, (under $\tilde{\mathcal{P}}_n$) can easily be shown to be multinormal (with the aid of Berry-Essen theorem [cf. Loeve (1962, p. 288)]), and hence, $\tilde{W}_n$ will have asymptotically a chi square distribution with (p-1) d.f. For small values of n, the exact permutation distribution of W_n can be traced with the aid of $(p!)^n$ equally likely intra-block rank permutations (under $\tilde{\mathcal{P}}_n$), and the exact permutation test can be based on $\tilde{W}_n$ (using the right hand tail as the critical region); while for large n, we may proceed as in (3.12). In the particular case, when ties are ignored, $\bar{\sigma}_R^2$ reduces to $(p^2-1)/12$, and our test statistic reduces to Friedman's [1937] test statistic. In this case, the permutation distribution and the unconditional null distribution of $\tilde{W}_n$ agree with each other, and a tabulation of the exact null distribution of $\tilde{W}_n$ for certain specific small values of n and p is contained in Owen [1962]. Moreover, for the sequence of alternatives in (3.15), it follows precisely by the same technique as in Elteren and Noether [1959] that $\tilde{W}_n$ has asymptotically a non-central χ^2 distribution with (p-1) d.f. and the non-centrality parameter

$$\tilde{\eta}_W = [12p/(p+1)](\sum_{j=1}^{p} \lambda_j^2)(\int_{-\infty}^{\infty} g^2(x)dx)^2 \tag{4.4}$$

where g(x) is the density function of Z_{ij}, defined just after (3.4). The efficiency of this test with respect to the classical analysis of variance test (which is incidentally valid for Case IV when normality and homoscedasticity hold) is therefore

$$e_{\tilde{W},F} = \frac{12\ p\sigma^2(1-\rho)}{(p+1)} (\int_{-\infty}^{\infty} g^2(x)dx)^2, \tag{4.5}$$

where ρ is the common correlation between Z_{ij} and $Z_{ij'}$, for $j\neq j'=1,\ldots,p$. If $G(\underset{\sim}{x})$ is a multinormal c.d.f., (4.5) reduces to

$$(3/\pi)\left(\frac{p}{p+1}\right) \tag{4.6}$$

which is the same as in the case of uncorrelated errors considered by Elteren and Noether [1959] and Hodges and Lehmann [1962].

5. A NON-PARAMETRIC TREATMENT OF CASE III

We define a set of random variables $U_{i;jj'}$ by

$$U_{i;jj'} = Y_{ij} - Y_{ij'} \qquad \begin{matrix} j, j'=1,2,\ldots,p \\ i=1,2,\ldots,n \end{matrix} \tag{5.1}$$

where one should note that $U_{i;jj}$ is identically 0. Under H_o in (1.4), each $U_{i;jj'}$ $(j\neq j')$ is distributed symmetrically about 0 and $(U_{i;12},\ldots,U_{i;1p},\ldots, U_{i;p1},\ldots,U_{i;(p-1)p})$ is diagonally symmetric about 0 (although the distribution is singular and of rank (p-1)). Let

$$W_{jj'} = \frac{1}{n}\sum_{i=1}^{n} S_{i;jj'}$$

where (5.2)

$$S_{i;jj'} = \{\mathrm{Sign}(U_{i;jj'})\}\{\mathrm{Rank}[\,|U_{i;jj'}|:|U_{1:jj'}|,\ldots,|U_{n:jj'}|\,]\}$$

for $j\neq j'=1,2,\ldots,p$. In the above definition, ties are handled by the mid-rank method and zero is assigned to zero values. Thus, $W_{jj'}$ is the Wilcoxon [1949] signed-rank statistic; also, $W_{j'j} = -W_{jj'}$ for all $j\neq j'=1,2,\ldots,p$. Finally, either by convention or the definition in (5.2), we write $W_{jj} = 0$ for $j=1,2,\ldots,p$. Now let

$$T^*_{n,j} = \sum_{j'=1}^{p} W_{jj'}, \qquad j=1,2,\ldots,p \tag{5.3}$$

$$\underline{T}^{*\prime}_n = (T^*_{n,1},\ldots,T^*_{n,p}) \tag{5.4}$$

From the definition of the $W_{jj'}$, it follows that

$$\sum_{j=1}^{p} T^*_{n,j} = 0 \tag{5.5}$$

and hence at most (p-1) of the $T^*_{n,j}$ are linearly independent. If we define the scores S_{ij} by

$$S_{ij} = \sum_{j'=1}^{p} S_{i;jj'} \qquad \begin{array}{l} i=1,2,\ldots,n \\ j=1,2,\ldots,p \end{array} \tag{5.6}$$

then $T^*_{n,j}$ may be alternatively written as

$$T^*_{n,j} = \frac{1}{n}\sum_{i=1}^{n} S_{ij} \quad . \tag{5.7}$$

Under the permutation model $\mathcal{P}_n$ of diagonal symmetry, we have when H_o holds

$$E\{T^*_{n,j} \mid \mathcal{P}_n\} = 0 \qquad j=1,2,\ldots,p \tag{5.8}$$

$$E\{T^*_{n,j} T^*_{n,j'} \mid \mathcal{P}_n\} = \frac{1}{n^2}\sum_{i=1}^{n} S_{ij} S_{ij'} \equiv v^*_{n;jj'} \tag{5.9}$$

If $\underset{\sim}{V}^*_n = (v^*_{n;jj'})$ and $\underset{\sim}{C}_1$ is as defined in (2.1), a test of H_o may be based on

$$W^*_n = \underline{T}^{*\prime}_n \underset{\sim}{C}_1' [\underset{\sim}{C}_1 \underset{\sim}{V}^*_n \underset{\sim}{C}_1']^{-1} \underset{\sim}{C}_1 \underline{T}^*_n \tag{5.10}$$

Given the permutational model, the ranks are invariant; only the signs are equally likely and jointly symmetrically distributed. Hence, it can be easily shown that permutationally W^*_n has sensibly a χ^2-distribution with (p-1) degrees of freedom. For small values of n, the exact permutation distribution of W^*_n can be computed by reference to the 2^n conditionally equally likely realizations.

Again, let us denote the marginal c.d.f. of $U_{i;jj'}$ by $G^*_{[jj']}(x)$; the bivariate c.d.f. of $U_{i;jj'}$, $U_{i;\ell\ell'}$ by $G^*_{[jj',\ell\ell']}(x,y)$. Then, proceeding in a way similar to that followed in Case I, we define elements of a matrix $\underset{\sim}{\nu}^* = (\nu^*_{j\ell})$ by

$$\nu^*_{j\ell} = \sum_{\substack{j'=1 \\ j'\neq j}}^{p} \sum_{\substack{\ell'=1 \\ \ell'\neq \ell}}^{p} \nu_{jj';\ell\ell'} \tag{5.11}$$

$$\nu_{jj';\ell\ell'} = 3 \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} [2G^*_{[jj']}(x)-1][2G^*_{[\ell\ell']}(y)-1]dG^*_{[jj',\ell\ell']}(x,y) \ . \tag{5.12}$$

It can be shown that under (3.15), W^*_n has asymptotically a non-central χ^2-distribution with (p-1) d.f. and non-centrality parameter

$$\underline{\delta}'\underset{\sim}{C}_1'[\underset{\sim}{C}_1\underset{\sim}{\nu}^*\underset{\sim}{C}_1']^{-1}\underset{\sim}{C}_1\underline{\delta} \tag{5.13}$$

where $\underline{\delta}' = (\delta_1,\ldots,\delta_p)$; and

$$\delta_j = \sum_{\substack{j'=1 \\ j'\neq j}}^{p} (\lambda_j-\lambda_{j'}) \int_{-\infty}^{\infty} g^{*2}_{[jj']}(x)dx, \tag{5.14}$$

$g^*_{[jj']}$ being the probability density function corresponding to the c.d.f. $G^*_{[jj']}$.

6. A NON-PARAMETRIC TREATMENT OF CASE IV

Here we assume that A.1, A.2, and A.3 hold. Let

$$R^*_{ij} = \text{Rank}\{Z_{ij}:Z_{11},\ldots,Z_{np}\} \quad \begin{matrix} i=1,\ldots,n \\ j=1,\ldots,p \end{matrix} \ ; \tag{6.1}$$

as in the previous sections, ties are to be handled by the mid-rank method. If we then define

$$\tilde{T}^*_{n,j} = \frac{1}{n} \sum_{i=1}^{n} R^*_{ij} \qquad j=1,2,\ldots,p \tag{6.2}$$

and

$$\sigma^2(R^*) = \frac{1}{n(p-1)} \sum_{i=1}^{n} \sum_{j=1}^{p} (R^*_{ij} - \frac{1}{p} \sum_{j=1}^{p} R^*_{ij})^2, \tag{6.3}$$

then it follows from the results of Sen [1966] that a test of H_o can be based on

$$\tilde{W}^*_n = n \sum_{j=1}^{p} (\tilde{T}^*_{n,j} - \frac{np+1}{2})^2/\sigma^2(R^*).$$

For small values of n, the permutation distribution of $\tilde{W}^*_n$ can be traced by reference to the $(p!)^n$ conditionally equally likely intra-subject rank permutations. For large n, $\tilde{W}_n$ has sensibly a χ^2-distribution with (p-1) d.f. Asymptotic power properties of this test also follow from the results of Sen [1966].

7. EXAMPLES

In this section, we shall consider the statistical analysis of two numerical examples. The data are from experiments undertaken at the Department of Pathology, Duke University Medical Center, Durham, North Carolina.

Example 1: Sixteen animals were randomly placed into one of two groups - an experimental group receiving ethionine in their diets and a pair-fed control group. The data for each animal consisted of a measurement of the amount of radioactive iron among various sub-cellular fractions from liver cells. The cell fractions used were nuclei (N), mitochondria (Mit), microsomes (Mic), and supernatant (S). One question of interest to the experimenters was whether the ratio of the measurements for the experimental group to those for the control group was the same for all cell fractions. If matched pairs of animals are regarded as subjects and cell fractions are regarded as treatments, then the above question may be attacked by the methods previously considered in this paper.

The data are as follows:

Pair	N	Mit	Mic	S	Mean
1	1.73	1.08	2.60	1.67	1.77
2	2.50	2.55	2.51	1.80	2.34
3	1.17	1.47	1.49	1.47	1.40
4	1.54	1.75	1.55	1.72	1.64
5	1.53	2.71	2.51	2.25	2.25
6	2.61	1.37	1.15	1.67	1.70
7	1.86	2.13	2.47	2.50	2.24
8	2.21	1.06	0.95	0.98	1.30
Mean	1.89	1.77	1.90	1.76	1.83

First, let us obtain the test statistics appropriate for the situations in which the error vector may be assumed to be normally distributed. The computations leading to the Hotelling T^2 statistic are listed below.

Pair	N - Mit	N - Mic	N - S
1	0.65	-0.87	0.06
2	-0.05	-0.01	0.70
3	-0.30	-0.32	-0.30
4	-0.21	-0.01	-0.18
5	-1.18	-0.98	-0.72
6	1.24	1.46	0.94
7	-0.27	-0.61	-0.64
8	1.15	1.26	1.23
Mean	0.13	-0.01	0.14

$$(n-1)^{-1}\underset{\sim}{S}_u = \begin{bmatrix} 0.68 & 0.59 & 0.51 \\ 0.59 & 0.84 & 0.58 \\ 0.51 & 0.58 & 0.54 \end{bmatrix}$$

$$(n-1)\underset{\sim}{S}_u^{-1} = \begin{bmatrix} 5.34 & -0.82 & -4.15 \\ -0.82 & 4.56 & -4.02 \\ -4.15 & -4.02 & 10.08 \end{bmatrix}$$

$$\bar{\underset{\sim}{u}}' = \begin{bmatrix} 0.13 & -0.01 & 0.14 \end{bmatrix}$$

$$T^2 = 8 \begin{bmatrix} 0.13 & -0.01 & 0.14 \end{bmatrix} \begin{bmatrix} 5.34 & -0.82 & -4.15 \\ -0.82 & 4.56 & -4.02 \\ -4.15 & -4.02 & 10.08 \end{bmatrix} \begin{bmatrix} 0.13 \\ -0.01 \\ 0.14 \end{bmatrix} = 1.16$$

$$\frac{(n-p+1)}{(n-1)(p-1)} T^2 = (5/21)(1.16) = 0.28; \quad d.f. = (3,5) .$$

Since $0.28 \leq F_{0.75}(3,5)$, we may conclude that this test indicates the data to be consistent with H_o (the hypothesis that the ratio is the same for all cell fractions).

The estimated covariance matrix of the cell fractions is

$$(n-1)^{-1}\underset{\sim}{S} = \begin{bmatrix} 0.26 & -0.01 & -0.06 & -0.03 \\ -0.01 & 0.41 & 0.27 & 0.22 \\ -0.06 & 0.27 & 0.47 & 0.23 \\ -0.03 & 0.22 & 0.23 & 0.21 \end{bmatrix} .$$

Since the structure of this matrix does not greatly contradict the assumption that the error vector is symmetrically distributed, the analysis of variance test of H_o is of interest.

Source of Variation	d.f.	Sum of Squares	Mean Square	Var. Ratio
Cell Fractions	3	0.15	0.05	0.21
Pairs	7	4.51	0.64	2.67
Error	21	4.95	0.24	
Total	31	9.61		

Noting that $0.21 \leq F_{0.75}(3,21)$, we may again conclude that the data tend to be consistent with H_o.

Let us now turn to the analysis of the data in terms of the non-parametric statistics associated with each of the Cases I - IV. For Case I, we first compute the within block ranks corresponding to each of the observations where ties are handled by the mid-rank method. These are as follows

Pair	N	Mit	Mic	S
1	3	1	4	2
2	2	4	3	1
3	1	2.5	4	2.5
4	1	4	2	3
5	1	4	3	2
6	4	2	1	3
7	1	2	3	4
8	4	3	1	2
Total	17	22.5	21	19.5

The statistic W_n is obtained by carrying out three steps

i. Select (p-1) = 3 linearly independent contrasts among the cell fractions; then, within each block, transform the ranks into these contrasts. Eg., we have used N - Mit, N - Mic, and N - S.

ii. Compute the sums and sums of products of deviations associated with the contrasts defined in (i).

iii. Compute the matrix product of the row vector of sums, the matrix of sums of products of deviations, and the column vector of sums, all of which were obtained in (ii). This is W_n.

Applying the above procedure to the data, we obtain

Pair	N - Mit	N - Mic	N - S
1	2	-1	1
2	-2	-1	1
3	-1.5	-3	-1.5
4	-3	-1	-2
5	-3	-2	-1
6	2	3	1
7	-1	-2	-3
8	1	3	2
Total	-5.5	-4.0	-2.5

$$n^2 \underset{\sim}{V}_{n,u} = \begin{bmatrix} 30.47 & 21.75 & 16.53 \\ 21.75 & 36.00 & 20.25 \\ 16.53 & 20.25 & 22.47 \end{bmatrix}$$

$$n^{-2} \underset{\sim}{V}^{-1}_{n,u} = \begin{bmatrix} 0.064 & -0.024 & -0.024 \\ -0.024 & 0.066 & -0.041 \\ -0.024 & -0.041 & 0.100 \end{bmatrix}$$

$$n \underline{T}_{n,u} = \begin{bmatrix} -5.5 & -4.0 & -2.5 \end{bmatrix}$$

$$W_n = \begin{bmatrix} -5.5 & -4.0 & -2.5 \end{bmatrix} \begin{bmatrix} 0.064 & -0.024 & -0.024 \\ -0.024 & 0.066 & -0.041 \\ -0.024 & -0.041 & 0.100 \end{bmatrix} \begin{bmatrix} -5.5 \\ -4.0 \\ -2.5 \end{bmatrix} = 1.01; \quad \text{d.f.} = 3.$$

Since $1.01 \leq \chi^2_{0.75}(3)$, we again conclude the data to be consistent with H_o.

The statistic appropriate to Case II is most simply obtained by performing a type of analysis of variance on the set of within-block ranks. If these are denoted by R_{ij}, we proceed as follows.

i. Compute $S_t^2 = (1/n) \sum_{j=1}^{p} \left\{ \sum_{i=1}^{n} R_{ij} \right\}^2 - np(p+1)^2/4$

ii. Compute $S_e^2 = (np\bar{\sigma}_R^2) = \sum_{i=1}^{n} \sum_{j=1}^{p} R_{ij}^2 - np(p+1)^2/4$ and $s_e^2 = S_e^2/n(p-1)$.

iii. Compute $\tilde{W}_n = S_t^2/s_e^2$.

The results for this method are

$$S_t^2 = 202.06 - 200.00 = 2.06$$

$$S_e^2 = 239.50 - 200.00 = 39.50$$

$$s_e^2 = (39.50)/(24) = 1.65$$

$$\tilde{W}_n = (2.06)/(1.65) = 1.25; \quad d.f. = 3.$$

We note that $1.25 \leq \chi^2_{0.75}(3)$ and draw the same conclusions as before.

Case III requires the most extensive computations. However, these may be performed efficiently by proceeding as follows.

i. Within each block compute the $\binom{p}{2}$ differences associated with each possible pair of treatments where the treatment to the right is subtracted from the one to the left. Eg., N - Mit, N - Mic, N - S, Mit - Mic, Mit - S, Mic - S

Pair	N - Mit	N - Mic	N - S	Mit - Mic	Mit - S	Mic - S
1	0.65	-0.87	0.06	-1.52	-0.59	0.93
2	-0.05	-0.01	0.70	0.04	0.75	0.71
3	-0.30	-0.32	-0.30	-0.02	0.00	0.02
4	-0.21	-0.01	-0.18	0.20	0.03	-0.17
5	-1.18	-0.98	-0.72	0.20	0.46	0.26
6	1.24	1.46	0.94	0.22	-0.30	-0.52
7	-0.27	-0.61	-0.64	-0.34	-0.37	-0.03
8	1.15	1.26	1.23	0.11	0.08	-0.03

ii. Each of these new variables has a particular value within each block. Let signed ranks be associated with each of the values associated with a given variable (where ties are handled by the mid-rank method and zero is assigned to zero values).

Pair	N - Mit	N - Mic	N - S	Mit - Mic	Mit - S	Mic - S
1	5	-5	1	-8	-7	8
2	-1	-1.5	5	2	8	7
3	-4	-3	-3	-1	0	1
4	-2	-1.5	-2	4.5	2	-4
5	-7	-6	-6	4.5	6	5
6	8	8	7	6	-4	-6
7	-3	-4	-4	-7	-5	-2.5
8	6	7	8	3	3	-2.5

iii. Within each block, scores are obtained for each cell fraction by adding the sum of the signed ranks associated with variables in which it is the minuend to the negative of the sum of the signed ranks associated with variables in which it is the subtrahend.

Pair	N	Mit	Mic	S
1	1	-20	21	-2
2	2.5	11	6.5	-20
3	-10	3	5	2
4	-5.5	8.5	-7	4
5	-19	17.5	6.5	-5
6	23	-6	-20	3
7	-11	-9	8.5	11.5
8	21	0	-12.5	-8.5
Total	2	5	8	-15

iv. To the scores obtained in (iii), apply the steps of the computational procedure given for Case I.

Pair	N - Mit	N - Mic	N - S
1	21	-20	3
2	-8.5	-4	22.5
3	-13	-15	-12
4	-14	1.5	-9.5
5	-36.5	-25.5	-14
6	29	43	20
7	-2	-19.5	-22.5
8	21	33.5	29.5
Total	-3	-6	17

$$n^2 \underset{\sim}{V}^*_{n,u} = \begin{bmatrix} 3495 & 2706 & 1923 \\ 2706 & 4640 & 2672 \\ 1923 & 2672 & 2686 \end{bmatrix}$$

$$n^{-2} \underset{\sim}{V}^{*-1}_{n,u} = \begin{bmatrix} 5.55 & -2.22 & -1.76 \\ -2.22 & 5.94 & -4.32 \\ -1.76 & -4.32 & 9.28 \end{bmatrix} \times 10^{-4}$$

$$n \underset{-}{T}^*_{n,u} = [\; -3 \quad -6 \quad 17 \;]$$

$$W^*_n = 0.39; \qquad \text{d.f.} = 3.$$

Finally, let us consider Case IV. The test statistic may be computed most simply by performing the following steps.

i. For each observation in a given block, subtract the block mean.

ii. Rank the (np) "residuals" obtained in (i) where ties are handled by the mid-rank method. Let these be denoted by R^*_{ij}.

iii. Compute $S_t^{*2} = (1/n) \sum_{j=1}^{p} \{ \sum_{i=1}^{n} R^*_{ij} \}^2 - np(np+1)^2/4$

iv. Compute $S_e^{*2} = n(p-1)\sigma^2(R^*) = \sum_{i=1}^{n} \sum_{j=1}^{p} R^{*2}_{ij} - (1/p) \sum_{i=1}^{n} \{ \sum_{j=1}^{p} R^*_{ij} \}^2$,

$$s_e^{*2} = S_e^{*2}/n(p-1).$$

v. $\tilde{W}^*_n = S_t^{*2}/s_e^{*2}$

The results associated with this test procedure are given below

Pair	N - Mean	Mit-Mean	Mic-Mean	S - Mean
1	-0.04	-0.69	0.83	-0.10
2	0.16	0.21	0.17	-0.54
3	-0.23	0.07	0.09	0.07
4	-0.10	0.11	-0.09	0.08
5	-0.72	0.46	0.26	0.00
6	0.91	-0.33	-0.55	-0.03
7	-0.38	-0.11	0.23	0.26
8	0.91	-0.24	-0.35	-0.32

Pair	N	Mit	Mic	S
1	15	2	30	12.5
2	23	25	24	4
3	10	18.5	21	18.5
4	12.5	22	14	20
5	1	29	27.5	17
6	31.5	7	3	16
7	5	11	26	27.5
8	31.5	9	6	8
Mean	16.19	15.44	18.94	15.44

$S_t^{*2} = 66.38$

$S_e^{*2} = 2615.62 \qquad s_e^{*2} = 108.98$

$\tilde{W}_n^* = 0.61; \qquad \text{d.f.} = 3.$

From the previous remarks, one can see that all the test procedures lead us to conclude that the data are consistent with H_o. Also, the values of the computed test statistics tend to be more or less similar to one another.

Example 2: Sixteen animals were randomly placed into one of two groups - an experimental group receiving ethionine in their diets and a pair-fed control group. The liver of each animal was split into two parts one of which was treated with radioactive iron and oxygen and the other, with radioactive iron and nitrogen. The data consist of the amounts of iron absorbed by the variously treated liver halves. If matched pairs of animals are regarded as subjects and the combinations ethionine-oxygen (EO), ethionine-nitrogen (EN), control-oxygen (CO), and control-nitrogen (CN) are regarded as treatments, then the hypothesis that neither diet nor gas has any effect may be tested by the methods discussed in this paper.*

Pair	EO	EN	CO	CN	Mean
1	38.43	31.47	36.09	32.53	34.63
2	36.09	29.89	34.01	27.73	31.93
3	34.49	34.50	36.54	29.51	33.76
4	37.44	38.86	39.87	33.03	37.30
5	35.53	32.69	33.38	29.88	32.87
6	32.35	32.69	36.07	29.29	32.60
7	31.54	31.89	35.88	31.53	32.71
8	33.37	33.26	34.17	30.16	32.74
Mean	34.90	33.16	35.75	30.46	33.57

* Note that the structure of the data allows other tests to be considered; eg., equality of diet effects, equality of gas effects, etc. However, we are interested here only in the hypothesis of equality of all treatment effects.

After computations similar to those given in Example 1, we find

$$T^2 = 17.14 \quad \text{and} \quad \frac{(n-p+1)}{(n-1)(p-1)} T^2 = 4.08.$$

Since $4.08 \leq F_{0.95}(3,5)$, the test does not reject H_o. However, T^2 is large enough to recommend additional experimental results to study the differences among the treatment effects.

The estimated covariance matrix for the treatment vector is

$$(n-1)^{-1} \underset{\sim}{S} = \begin{bmatrix} 5.86 & 1.31 & 1.29 & 1.47 \\ 1.31 & 7.13 & 4.35 & 2.60 \\ 1.29 & 4.35 & 4.14 & 2.40 \\ 1.47 & 2.60 & 2.40 & 3.17 \end{bmatrix}$$

Again, the analysis of variance test of H_o is of interest.

Source of Variation	d.f.	Sum of Squares	Mean Square	Var. Ratio
Treatments	3	131.19	43.73	15.40
Pairs	7	82.38	11.77	4.14
Error	21	59.70	2.84	
Total	31	273.27		

Since $15.40 \geq F_{0.99}(3,21)$, we reject H_o and conclude that there are significant differences among the treatment effects.

The non-parametric statistics for Case I and Case II are based on the intra-block rank matrix

Pair	EO	EN	CO	CN
1	4	1	3	2
2	4	2	3	1
3	2	3	4	1
4	2	3	4	1
5	4	2	3	1
6	2	3	4	1
7	2	3	4	1
8	3	2	4	1
Total	23	19	29	9

Case I: $W_n = 600.00$
d.f. = 3

Case II: $\tilde{W}_n = 15.90$
d.f. = 3

In Case III, the score matrix for the treatments is

Pair	EO	EN	CO	CN
1	20	-18	5	-7
2	18	-11	9	-16
3	2	4	14	-20
4	-7	10	16	-19
5	16	-3	-2	-11
6	-8	4	18	-14
7	-11	-1	18	-6
8	4	1	6	-11
Total	34	-14	84	-104

Case III: $W_n^* = 64.27$ d.f. = 3

Finally, for Case IV, the matrix of intra-inter-block ranks of residuals is

Pair	EO	EN	CO	CN
1	31	5	23	8
2	32	9	25	3
3	20	21	28	2
4	16	24	26	1
5	27	14	17	6
6	13	15	30	4
7	11	12	29	10
8	19	18	22	7
Total	169	118	200	41

Case IV: $\tilde{W}_n^* = 16.02$ d.f. = 3

Since the test statistics obtained above all exceed the 99th percentile point of the chi-square distribution with three degrees of freedom, we reject H_o for each of the Cases I-IV.

One may note that the statistic W_n is considerably larger than the others. One reason for this is that with W_n the particular arrangement of the ranks within the blocks not only affects the mean scores associated with a treatment but also the estimated variance-covariance matrix. As a result, for data configurations in which the intra-block ranks show consistent treatment differences, the statistic W_n is likely to be very large. For example, suppose for the case $n = 8$, $p = 4$, we observed a rank matrix in which the arrangement (4 3 2 1) occurred four times and the arrangement (3 4 2 1) occurred four times; the contrast obtained by subtracting the score assigned to the fourth treatment from that assigned to the third treatment has a mean value of one but an estimated variance of zero. Strictly speaking, W_n cannot be computed, but we can argue that its value is infinite.

On the other hand, when we compute $\tilde{W}_n$ and $\tilde{W}_n^*$, the estimated variability of the treatment mean scores depends only on the values of the ranks assigned to a block and not on the particular arrangement of them within the blocks.

For reasons similar to those given previously for W_n, the statistic W_n^* may also be noticeably larger than $\tilde{W}_n$ and $\tilde{W}_n^*$. Since this extreme-type behavior of W_n and W_n^* does not cause us to wrongly accept false hypotheses, we can argue that there is nothing to worry about. On the other hand, when such large values occur, the chi-square distribution may not provide an idea of the exact significance level at which the hypothesis would be rejected. If this were of interest, then one should perform the associated permutation test.

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