ADAPTIVE NONPARAMETRIC DISTRIBUTION-FREE PROCEDURES IN FACTORIAL DATA ANALYSIS

by

RICHARD NZAGONG FERIM

Presented to the Faculty of the Graduate School of

The University of Texas at Arlington in Partial Fulfillment

of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

THE UNIVERSITY OF TEXAS AT ARLINGTON

DECEMBER 2009

ACKNOWLEDGEMENTS

In the pursuit of my highest academic achievement, a lot of people have played a major part in making this dream come true. I first want to thank Professor Sun-Mitchell for thinking through and developing the problem of my research. I appreciate her reading every line of my Dissertation and making the recommended changes. It was a pleasure working with someone who cares, understands and puts in her best for her students.

I want to thank Dr Hawkins DL who mentored me in statistical consulting and inspired me in rigorous statistical problem solving approach and methods. Working at the at the Stat Lab was an experience of a life time. I thank Professor Edgar Brunner for forwarding to me some very valuable material on his work and for answering my questions. Thanks to all my professors and especially my Statistics professors for the thorough training. Special thanks to Dr Han Chien-Pai, Dr Minerva Cordero-Epperson and Dr Danny Dyer for accepting to serve in my committee.

I thank the Mathematics Department for providing me with the needed resources and the atmosphere to carry out my studies. Thanks Professor Zhu

and all the members of the GAANN fellowship for the scholarship and for constantly monitoring my progress.

Special thanks to my wife Crystabelle for her understanding during all this period of my lengthy education. Your patience and love has borne fruits. Thank you Jr and Candace for sacrificing with me to make this dream come true. Special thanks to my Dad (Abraham Ferim) and Mum (Helen Ferim) who instilled in me the passion and value of higher education. Thank you Jesus for the brains to understand some of these concepts .

November 20, 2009

ABSTRACT

ADAPTIVE NONPARAMETRIC DISTRIBUTION-FREE PROCEDURES IN FACTORIAL DATA ANALYSIS

RICHARD NZAGONG FERIM, PhD
The University of Texas at Arlington, 2009

Supervising Professor: SHAN SUN-MITCHEL

Many statisticians have questioned the basic assumptions about underlying models which might dominate the analysis of the data in many cases. The assumption of normality without much thought is of concern to a growing group of statisticians. If wrongly assumed, the assumption of normality can lead in serious flaws in the analysis of data. It therefore becomes important to consider distribution-free procedures that don't have to rely on the normality assumption. This is where the adaptive procedures come into play. When data is skewed or light tailed, these adaptive methods produce better results than the regular Wilcoxon and parametric methods. The problem has been solved for a

c-sample problem (Sun 1997). Our goal here is to extend this method, to the TWO-WAY ANOVA problem.

TABLE OF CONTENTS

APPENDIX

LIST OF ILLUSTRATIONS

Figure Page

LIST OF TABLES

CHAPTER 1

INTRODUCTION

Many statisticians have questioned the basic assumptions about underlying models which might dominate the analysis of the data in many cases. The assumption of normality without much thought is of concern to a growing group of statisticians.

It therefore becomes important to use a more appropriate distribution or to rely on distribution-free procedures. This is where the nonparametric procedure comes into play. Using ranks in the nonparametric case give better results especially when the distribution is not normal. More so, tailoring to the specific sample distribution with respect to its kurtosis and skewness, we can use different scoring methods to obtain optimal outcomes. Means for calculating the statistics for ordered alternatives and confidence interval for multiple comparisons are presented to show the advantage .The problem has been solved for a one-way layout with c-samples. Our challenge is to extend this result to a TWO-WAY layout.

1.1 The Notion of Ranks

A skin research lab wants to test the effectiveness of a new drug that is claimed to have a beneficial effect a particular skin condition. There are 5 patients in the clinic suffering from this disorder to about the same degree (this number is small to provide meaningful results). Of these five, three are selected at random to receive the new drug, and the other two serve as controls (given a placebo, which is a harmless pill not containing any active ingredient). Here, we are dealing with a double blind situation. This eliminates the psychological effects from both the patient and staffers that might result from such knowledge. After some time, a visiting physician interviews the patients and ranks them according to the severity of their condition. The patient whose condition is judged to be most serious is assigned 1, the next most serious rank 2, and so on, up to rank 5. The claim made for the new treatment will be considered warranted if the three treated patients rank sufficiently high in this combined ranking of all five patients.

1.2 One-Way Layout Design

Suppose we have c random samples X_i from continuous distribution functions $F_i(u) = F(u - \theta_i), i = 1,.....,c$ with n_i observations in each, with $X_i = (X_{i1,} X_{i2,} ....., X_{ni})$. Our test null hypothesis is $H_0 : \theta_1 = \theta_2 = \Lambda = \theta_c$. (which implies $F_1(u) = F_2(u) = ... = F_c(u)$).

In a one way layout, we rank the combined c samples, and let R_{ij} denote the rank of observation X_{ij} in this sample and $a(R_{ij})$ is its score , where a(·) is the symbol satisfying $a(1) \le a(2) \le \Lambda \le a(n_1 + n_2 + \Lambda + n_c)$. Here, $N = n_1 + n_2 + \Lambda + n_c$. In this chapter, we describe the adaptive procedure (Sun 1997) for a one way layout c-sample problem.

1.2.1 Adaptive procedures.

The distribution of a function F, in general is unknown. Suppose there is a classification which detects the tail-weight and the amount of skewness of F. Then the rank test suggested by this scheme is going to be superior to the Wilcoxon test and the Student t-test.

We will quantify skewness and kurtosis.In general, since F is unknown , the kurtosis is also unknown. An appropriate indicator of tail weight is $Q_2 = \frac{\overline{U}_{.05} - \overline{L}_{.05}}{\overline{U}_{0.5} - \overline{L}_{0.5}}$ (Hogg 1974), where $\overline{U}_{.05}$ *and* $\overline{U}_{0.5}$ are, respectively, the averages of the largest 5% and 50% of the ordered statistics of the sample(replacing largest by smallest yields the definition of $\overline{L}_{.05}$ *and* $\overline{L}_{0.5}$) .

We work (as in Hill et al.,1988) with $\overline{Q_2} = \frac{n_1 Q_{1,2} + n_2 Q_{2,2} + \Lambda + n_c Q_{c,2}}{n_1 + n_2 + \Lambda + n_c}$, the weighted average of the Q_2 values based on the individual samples.

Using asymptotic theory and Monte Carlo methods, an indicator of skewness, studied by Fisher and explained in Hogg et al. (1975), is

$Q_1 = \frac{\overline{U}_{.05} - \overline{M}_{.5}}{\overline{M}_{0.5} - \overline{L}_{0.05}}$ where $\overline{U}_{.05}$, $\overline{M}_{0.5}$ *and* $\overline{L}_{.05}$ are respectively , the averages of the top 5%, middle 50% and bottom 5% of the order statistics of the combined sample. However, we will work with the average of the weighted Q_i s .

Hence, $\overline{Q}_1 = \frac{n_1 Q_{1,1} + n_2 Q_{2,1} + \Lambda + n_c Q_{c,1}}{n_1 + n_2 + \Lambda + n_c}$, the weighted average of the Q_1 values based on the individual samples.Hogg et al (1975) concluded the following: if $\frac{1}{2} \le \overline{Q}_1 \le 2$, then we have symmetry. $\overline{Q}_1 < \frac{1}{2}$ *and* $\overline{Q}_1 > 2$ then we have skewness to the left and right respectively .

For Kurtosis, $\overline{Q}_2 < 2.24$ we have a light tailed distribution. $2.24 \le \overline{Q}_2 \le 3.8$ we have a not heavy and not light distribution. If $\overline{Q}_2 > 3.8$ then we have a heavy tailed distribution. Also note that if $\overline{Q}_2 < 3.8$ then F is not heavy-tailed (NH).

The studies of Gastwirth (1965) and Randles and Hogg (1973) suggest the statistic h_L (based on the scores a_L) when F is light tailed. Here, $h = \sum a(R_{ij})$.

For example h_L is constructed by discarding the middle one-half of the observations in the combined sample, and assigning Wilcoxon-type scores to the remaining observations. However, further improvement is possible , by employing the modified statistic h_{ML} , based on the scores a_{ML}, obtained by squaring the scores a_L. If the data indicates that F is NH and skewed to the

right, we use the statistic h_{SR} with scores a_{SR} which emphasize the smallest observations. By contrast, h_{SL} with scores a_{SL} is used in the case where F is NH and skewed to the left. Finally, when we simply say 'skewed', we mean 'skewed to the right'. The table below gives a description of the schemes for all cases and when to apply them.

Table 1.1 Indicator Values for Skewness and Kurtosis

Indicator values	For Adaptive Scheme I	For Adaptive Scheme II
$\overline{Q}_2 > 3.8$	h_w	h_w
$\frac{1}{2} \le \overline{Q}_1 \le 2$ $2.24 \le \overline{Q}_2 \le 3.8$	h_W	h_W
$\frac{1}{2} \le \overline{Q}_1 \le 2,$ $\overline{Q}_2 < 2.24$	h_L	h_{ML}
$\overline{Q}_1 < \frac{1}{2},$ $\overline{Q}_2 < 3.8$	h_{SL}	h_{SL}
$\overline{Q}_1 \ge 2,$ $\overline{Q}_2 < 3.8$	h_{SR}	h_{SR}

For any positive number B, let [B] denote the largest integer ≤ B.

Table 1.2 Score Values For Related Statistics

$$i)\quad a_W(i) = \frac{i}{N+1} \qquad if \quad 1 \le i \le N.$$

$$ii)\quad a_L(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{4}\right] - \dfrac{1}{2}}{N+1} & if \quad i \le \left[\dfrac{N+1}{4}\right] \\ \dfrac{i - N + \left[\dfrac{N+1}{4}\right] - \dfrac{1}{2}}{N+1} & if \quad i \ge N - \left[\dfrac{N+1}{4}\right] + 1, \\ 0 & otherwise. \end{cases}$$

$$iii)\quad a_{ML}(i) = \begin{cases} -\dfrac{\left(i - \left[\dfrac{N+1}{4}\right] - \dfrac{1}{2}\right)^2}{(N+1)^2} & if \quad i \le \left[\dfrac{N+1}{4}\right] \\ \dfrac{\left(i - N + \left[\dfrac{N+1}{4}\right] - \dfrac{1}{2}\right)^2}{(N+1)^2} & if \quad i \ge N - \left[\dfrac{N+1}{4}\right] + 1 \\ 0 & otherwise. \end{cases}$$

$$iv)\quad a_{SL}(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{2}\right]}{N} & if \quad i \ge \left[\dfrac{N+1}{2}\right], \\ 0 & otherwise. \end{cases}$$

$$v)\quad a_{SR}(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{2}\right] - 1}{N} & if \quad i \le \left[\dfrac{N+1}{2}\right], \\ 0 & otherwise. \end{cases}$$

$N = n_1 + n_2 + \Lambda + n_c.$

The adaptive procedure can also be applied when tie occurs. Suppose measurements are now rounded off to the nearest integers then $\tilde{X}_{ij}$ is then obtained from X_{ij} and $Y_1 \le Y_2 \le \Lambda \le Y_N$ be the N elements $\tilde{X}_{ij}$, j=1,2,..., n_i, i=1,2,…,c, arranged in ascending order.

Then our nonparametric procedure consists in replacing the N observations by N scores, say $a_N(1), a_N(2), \Lambda, a_N(N)$. A tie of the form $Y_k < Y_{k+1} = Y_{k+2} = \Lambda = Y_{k+s+1}$ is resolved by the average scores method, i.e. each of the s observations $Y_{k+1}, Y_{k+2}, \Lambda, Y_{k+s}$ is assigned the score $(a_N(k+1) + \Lambda + a_N(k+s))/s$. For further discussion, see Gibbons (1971).

1.2.2 Hypothesis Testing

Let $\tilde{F}_i$ be the distribution function of $\tilde{X}_{i1,}\tilde{X}_{i2,}.....,\tilde{X}_{in_i}$ and let $\tilde{a}_N(\cdot)$ denote the scores obtained after applying the average scores method, and $\tilde{R}_{ip}$ denote the rank of the $\tilde{X}_{ip}$ in the combined sample of size N. Write $\tilde{S}_i = \tilde{a}_N(\tilde{R}_{i1}) + \Lambda + \tilde{a}_N(\tilde{R}_{in_i})$. In the case of ties, these ranks may not be uniquely defined. Still $\tilde{S}_i$ makes sense in view of the average score method. Finally, let $\tilde{a}_N$ be the average of the N scores $a_N(1), a_N(2), \Lambda, a_N(N)$.

To test the null hypothesis $H_0 : \theta_1 = \theta_2 = \Lambda = \theta_c$ (same as $\tilde{F}_1 = \tilde{F}_2 = \Lambda = \tilde{F}_c$), we use the statistic

$$S_c = \frac{(N-1)\sum_i n_i \left(\left(\frac{\tilde{S}_i}{n_i} \right) - \tilde{a}_N \right)^2}{\sum_i \left(\tilde{a}_N(i) - \tilde{a}_N \right)^2} \qquad (1.1)$$

Conover (Theorem4.5 1973) implies that under H_0, S_c has asymptotically a chi-square distribution with c-1 degrees of freedom, whose (1-α)th quantile will be denoted by $\chi^2_{1-\alpha}$ (for some preassigned level of significance of α). If the value of S_c computed from the sample exceeds $\chi^2_{1-\alpha}$, then H_0 should be rejected. We then carry out multiple comparisons.

1.2.3 Multiple Comparison.

Here, we assume equal sizes of the c samples for easy analysis. For arbitrary and fixed i and j (i≠j) consider the two samples: $\tilde{X}_i = (\tilde{X}_{i1,}\tilde{X}_{i2,}.....,\tilde{X}_{in_i})$ and $\tilde{X}_j = (\tilde{X}_{j1,}\tilde{X}_{j2,}.....,\tilde{X}_{jn_{ji}})$. Corresponding to the related sample of size $n_i + n_j$, we define the scores $a_{ij}(1),\Lambda\ , a_{ij}(n_i + n_j)$ and some related constants as follows:

$$a_{ij}(p) = J\left(\frac{p}{n_i + n_j + 1} \right), \quad 1 \le p \le n_i + n_j, \qquad (1.2)$$

$$\tilde{a}_{ij}(p) = \frac{1}{n_i + n_j} \sum_{p=1}^{n_i+n_j} a_{ij}(p)$$

Table 1.3 Score Functions for ONE-WAY ANOVA

$$J(u)=\begin{cases} u-\frac{1}{4}, & 0<u<\frac{1}{4} \\ 0 & ,\frac{1}{4}\le u\le\frac{3}{4} \\ u-\frac{3}{4}, & \frac{3}{4}<u<1 \end{cases} \qquad h_L$$

$$J(u)=\begin{cases} -\left(u-\frac{1}{4}\right)^2, & 0<u<\frac{1}{4} \\ 0 & ,\frac{1}{4}\le u\le\frac{3}{4} \\ \left(u-\frac{3}{4}\right)^2, & \frac{3}{4}<u<1 \end{cases} \qquad h_{ML}$$

$$J(u)=u, \qquad 0<u<1 \qquad h_W$$

$$J(u)=\begin{cases} u-\frac{1}{2}, & 0<u\le\frac{1}{2} \\ 0, & \frac{1}{2}<u<1 \end{cases} \qquad h_{SR}$$

$$J(u)=\begin{cases} 0, & 0<u\le\frac{1}{2} \\ u-\frac{1}{2}, & \frac{1}{2}<u<1 \end{cases} \qquad h_{SL}$$

By the proper choice of J, h can become any of the five statistics.

In the combined sample $(\tilde{X}_i, \tilde{X}_j)$, let $\tilde{R}_{ik}^{(i,j)}$ and $\tilde{R}_{jl}^{(i,j)}$ denote respectively, the ranks of $\tilde{X}_{ik}$ and $\tilde{X}_{jl}$. Then we define

$$h(\tilde{X}_{i,}\tilde{X}_j) = \frac{1}{n_i}\sum_{k=1}^{n_i}\tilde{a}_{ij}(\tilde{R}_{ik}{}^{(i,j)}) \quad \text{and} \quad h(\tilde{X}_{j,}\tilde{X}_i) = \frac{1}{n_j}\sum_{l=1}^{n_j}\tilde{a}_{ij}(\tilde{R}_{jl}{}^{(i,j)}) \quad \text{where}$$

$\tilde{a}_{ij}(1), \tilde{a}_{ij}(2), \Lambda\ , \tilde{a}_{ij}(n_i + n_j)$ are obtained from $a_{ij}(1), a_{ij}(2), \Lambda\ , a_{ij}(n_i + n_j)$ when ties are handled by the average score method. The counterparts of the above two equations based on the continuous data (X_i, X_j) are respectively $h(X_i, X_j)$ *and* $h(X_j, X_i)$.

Let $R_{c,\alpha}$ denote the upper 100α% quantile of the range of a sample of size c from a standard normal distribution and define $\mu_n^{(1)} = \bar{a}_{ij} - \frac{1}{2}n^{-\frac{1}{2}}A_{ij}R_{c,\alpha}$, $\mu_n^{(2)} = \bar{a}_{ij} + \frac{1}{2}n^{-\frac{1}{2}}A_{ij}R_{c,\alpha}$ and $X_i - \rho = (X_{i1} - \rho, X_{i2} - \rho, \Lambda\ , X_{in_i} - \rho)$ for any real number ρ. Now calculate:

$$\tilde{\Delta}_{ij,L} = \sup\{\rho : h(X_i - \rho, X_j) > \mu_n^{(2)}\},$$
$$\tilde{\Delta}_{ij,U} = \inf\{\rho : h(X_i - \rho, X_j) < \mu_n^{(1)}\}$$

We then can obtain the 100(1-α)% confidence interval $\tilde{I}_{ij} = [\tilde{\Delta}_{ij,L} - 1, \tilde{\Delta}_{ij,U} + 1]$ for $\Delta_{ij} = \theta_i - \theta_j$.

1.2.4 Other Notions Studied

Simultaneous Confidence interval for contrast (Sun 1997) are discussed.

By a contrast, we mean a linear combination $\sum_{i=1}^{c} l_i \theta_i$ such that $\sum_{i=1}^{c} l_i = 0$.

We start with the point estimate $\tilde{\Delta}_{ij}$ of (Δ_{ij}).

Let $\mu = E[h(X_i, X_j)]$ under H_0. Then define

$$\Delta_{ij}^{*} = \sup\{\rho : h(\tilde{X}_i - \rho, \tilde{X}_j) > \mu\},$$
$$\Delta_{ij}^{**} = \sup\{\rho : h(\tilde{X}_i - \rho, \tilde{X}_j) < \mu\},$$
$$\tilde{\Delta}_{ij} = \frac{1}{2}\left(\Delta_{ij}^{*} + \Delta_{ij}^{**}\right)$$

Then $\tilde{\Delta}_{ij}$ is called a 'raw estimate' (of Δ_{ij}).

Raw estimates have the following drawbacks. $\tilde{\Delta}_{ij} + \tilde{\Delta}_{jk}$ is clearly an estimate of $(\theta_i - \theta_j) + (\theta_j - \theta_k) = \Delta_{ik}$. And $\tilde{\Delta}_{ij}$ is also an estimate of Δ_{ik} (in general, $\tilde{\Delta}_{ij} \neq \tilde{\Delta}_{ij} + \tilde{\Delta}_{jk}$). Thus, although both $\tilde{\Delta}_{ik}$ and $\tilde{\Delta}_{ij} + \tilde{\Delta}_{jk}$ estimate the same parameter, still, the estimates themselves are not the same. The problem arises as to which estimates are to be used.

This was overcome by introducing the concept of 'adjusted estimates'.

$\tilde{\Delta}_{1\bullet} = \frac{1}{c}\left(\tilde{\Delta}_{11} + \tilde{\Delta}_{12} + \Lambda + \tilde{\Delta}_{1c}\right)$ define $\tilde{\Delta}_{11} = 0 = \tilde{\Delta}_{22} = \Lambda = \tilde{\Delta}_{cc}$.

Write $\tilde{\Delta}_{r\bullet} = \frac{1}{c}\left(\tilde{\Delta}_{r1} + \tilde{\Delta}_{r2} + \Lambda \ + \tilde{\Delta}_{rc} \right)$ r=1,2,…c. The estimate $\tilde{Z}_{ij} = \tilde{\Delta}_{i\bullet} - \tilde{\Delta}_{j\bullet}$ is called the 'adjusted estimate'. Hence, the ambiguity above is totally taken care of.

Let $\xi_{ij} = \{\max | \tilde{Z}_{ij} - u |, u \in \tilde{I}_{ij}\}$ and $\tilde{H}_{n,\alpha} = \max_{1 \le i \ne j \le c} \{\xi_{ij}\}$

Simultaneous confidence intervals for all contrasts $\varphi = \sum l_i \theta_i$ can be constructed.

With asymptotic probability $\ge 1 - \alpha$, φ belongs to the interval

$$\left[\sum l_i \tilde{\Delta}_{i\bullet} - \frac{1}{2} \tilde{H}_{n,\alpha} \sum | l_i |, \sum l_k \tilde{\Delta}_{i\bullet} + \frac{1}{2} \tilde{H}_{n,\alpha} \sum | l_i | \right] \qquad (1.3)$$

(See Shan 1997 for proof).

Scheffe multiple comparisons tests are looked at in the c-sample case where the sample sizes are different. Let

$$A^2 = \int_0^1 J^2(u) du - \left(\int_0^1 J(u) du \right)^2 \qquad (1.4)$$

The construction of the simultaneous confidence intervals requires a knowledge of $A^2 \chi^2_{1-\alpha} / B^2(F)$ where $B(F) = \int_{-\infty}^{\infty} \left(d/dx \right)(J(F)) dF(x) \big)$ and $\chi^2_{1-\alpha}$ is the $(1-\alpha)$th quantile of the chi-square distribution with c-1 degrees of freedom. However, B(F) is unknown (since F is unknown) and is estimated as follows:

Let $L_{\alpha/2}$ and $U_{\alpha/2}$ be respectively, the lower and the upper $\frac{1}{2}\alpha th$ quantiles of the limiting normal distribution of $h(X_i, X_j)$. Set

$$\begin{aligned}
\tilde{\Delta}_{ij,u} &= \inf\{\rho : h(\tilde{X}_i - \rho, \tilde{X}_j) < L_{\alpha/2}\}, \\
\tilde{\Delta}_{ij,L} &= \sup\{\rho : h(\tilde{X}_i - \rho, \tilde{X}_j) > U_{\alpha/2}\}, \\
\tilde{D}_{ij} &= \tilde{\Delta}_{ij,u} - \tilde{\Delta}_{ij,L}
\end{aligned} \qquad (1.5)$$

Let $\tau_{\alpha/2}$ denote the upper $\frac{1}{2}\alpha th$ quantile of the standard normal distribution, and for $i \neq j$, write

$\tilde{B}_{ij}(F) = 2A^2\chi^2_{\alpha/2}\sqrt{n_i + n_j}\,/(\sqrt{n_i + n_j}\,(\tilde{D}_{ij} + 2))$. Let $\tilde{B}(F) = \left[1/\binom{c}{2}\right]\sum \tilde{B}_{ij}(F)$, the summation taken over all the distinct pairs (i ,j), with i<j. Then $\tilde{B}_{ij}(F)$ is the required estimate (of B(F)).

Define $\tilde{\delta}^2 = A^2\chi^2_{\alpha/2} / \tilde{B}^2(F)$ and $\psi = \sum |l_i| + \tilde{\delta}^2\left[\sum l_i^2 / n_i\right]^{1/2}$

We can now construct simultaneous confidence intervals applicable to any contrast $\varphi = \sum l_i\theta_i$

For any contrast φ, the asymptotic probability that φ is in

$(\sum l_i \tilde{\Delta}_{i\bullet} - \psi, \sum l_i \tilde{\Delta}_{i\bullet} + \psi)$ is $\geq 1 - \alpha$ (Shan 1997)

Test for ordered alternatives :

$H_0 : \theta_1 = \theta_2 = \Lambda = \theta_c$ against $H_a : \theta_1 \le \theta_2 \le \Lambda \le \theta_c$ *or* $\theta_1 \ge \theta_2 \ge \Lambda \ge \theta_c$ were also looked at.

Shan concluded based on the work of Puri and Sen (1971, p.248) that s*hort confidence intervals are a reflection of high asymptotic relative efficiency (ARE) . Shan* showed in an example that the average lengths of the confidence intervals for the Adaptive procedures are shorter than those of the Wilcoxon and parametric procedure. Hence the Adaptive procedures are more effective.

1.2.5 Conclusion on One-Way Anova

The adaptive procedure gives better results in the one-way ANOVA analysis than the regular parametric or nonparametric Wilcoxon method. Our goal is to extend the Adaptive procedure to the two way ANOVA case with center and treatment effect. This will be done by developing asymptotic results for the score functions, and then applying our data set to obtain optimal results.

CHAPTER 2

OTHER NONPARAMETRIC APPROACHES

Here, we will explore a few approaches to the nonparametric analysis of data with factorial designs. These are methods that have been researched by others and their asymptotic results derived.

2.1 Ignoring Centers

A primitive approach toward the data analysis will be to ignore the centers and analyze the data as a simple two-sample problem in the case where we have two treatments. This approach was discussed by Fleiss (1986). Fleiss mentioned two randomization procedures, one employing separate and independent randomization schedules for the several clinics and the second ignoring the clinics in the random assignment of patients to treatment groups. Fleiss discussed two pooling ideas. Firstly pooling means “averaging within-clinic differences” and is thus used in the same sense as “pooling”variances”. Secondly, “pool the data” is a euphemism for “throw together all the responses to a treatment, ignoring the clinics”. In summary, pooling in the sense of averaging within-clinic differences is almost always justified, and pooling in the sense of throwing together all the data is rarely justified

In this case, the Wilcoxon-Mann-Whitney (WMW) statistics are used here to test the hypothesis $H_0 : F_1 = F_2$ of no treatment effect.

2.2 Van Elteren

Van Elteren (1960) proposes to test a hypothesis of no treatment effect. For i=1,2 treatments and j=1,….a centers, and k=1,……, n_{ij} patients, the hypothesis of no treatment effect $H_0^{tr} : F_{1j} = F_{2j} \quad \forall \quad j = 1,....., a$ with overall treatment effect W defined by $W = \sum_{j=1}^{a} c_j \theta_j$ where

$\theta_j = \Pr\{X_{1jk} \le X_{2jk'}\} + \frac{1}{2}\Pr\{X_{1jk} = X_{2jk'}\}$ is the WMW effect for center j and the quantities c_j's are weights such that the test has certain optimality and efficiency properties. Optimal weights of the form

$$c_j = \frac{n_{1j} n_{2j}}{n_{1j} + n_{2j} + 1} \quad \forall \quad j = 1,....., a .$$

The estimator of the effects θ_j are then given by

$$\hat{\theta}_j = \frac{1}{n_{\cdot j}} = \left(\overline{R}_{2\bullet}^{(j)} - \overline{R}_{1\bullet}^{(j)}\right) + \frac{1}{2}$$

where $R_{ik}^{(j)}$ is the rank of X_{ijk} within the jth center, $n_{\bullet j} = n_{1j} + n_{2j}$ and $\overline{R}_{i\bullet}^{(j)} = \frac{1}{n_{ij}} \sum_{k=1}^{n_{ij}} R_{ik}^{(j)}$. The sum of the weighted WMW effects is standardized and compared with the standard normal distribution to test H_0^{tr}

2.3 Mack and Skillings (MSP)

Mack and Skillings (1980) consider a linear, fixed-effect parametric model defined by

$$X_{ijk} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \varepsilon_{ijk} \qquad \varepsilon_{ijk} \sim \mathrm{F}_{ij} \qquad (2.1)$$

where $\sum_{i=1}^{2} \alpha_i = \sum_{j=1}^{b} \beta_j = \sum_{i=1}^{2} (\alpha\beta)_{ij} = \sum_{j=1}^{b} (\alpha\beta)_{ij} = 0$; $\varepsilon_{ijk} \sim N(0, \sigma^2)$.

Here, α_i denotes the effect of the ith treatment, β_j, the effect of the jth center and $(\alpha\beta)_{ij}$, the interaction between the ith treatment and the jth center.

If we consider the above model without the interaction term, we can present the hypothesis of no treatment effect, i.e., $H_0 : \alpha_i = 0$. MSP uses the the ranks $R_{ik}^{(j)}$ within each center j in the construction of their statistics. In case of no ties, the statistics

$$T = \frac{12}{N(N+1)} \left[n_{1\bullet} \left(R_1^* - \frac{N+4}{2} \right)^2 + n_{2\bullet} \left(R_2^* - \frac{N+4}{2} \right)^2 \right] \sim \chi_1^2 ,$$

is proposed to test H_0, where $R_i^* = \sum_{j=1}^{b} \left(1 / n_{ij} \right) \sum_{k=1}^{n_{ij}} R_{ik}^{(j)}$, $N = \sum_{i=1}^{2} \sum_{j=1}^{b} n_{ij}$ and $n_{i\bullet} = \sum_{j=1}^{b} n_{ij}$. In case of ties, this procedure is modified accordingly.

2.4 Boos and Brownie

Boos and Brownie (1992) also considered the model defined above and then introduced the concept of treatment effect and interaction in a

nonparametric sense nonparametric sense. The concept also is based on the WMW effects defined in by $\theta_j = \Pr\{X_{1jk} \le X_{2jk'}\} + \frac{1}{2}\Pr\{X_{1jk} = X_{2jk'}\}$ and their estimators

$\hat{\theta}_j = \frac{1}{n_{\cdot j}} = \left(\bar{R}_{2\bullet}^{(j)} - \bar{R}_{1\bullet}^{(j)}\right) + \frac{1}{2}$. The average term $\bar{\theta} = \frac{1}{b}\sum_{j=1}^{b}\theta_j$ is considered as the treatment effecting a stratified setup. The hypothesis of no-treatment effect is formulated as $H_0^{tr} : \bar{\theta} - \frac{1}{2} = 0$

For interaction, the hypothesis is $H_0^{\text{int}} : \theta_1 = \theta_2 = ... = \theta_b$.

The estimators for the treatment and interaction effects are given respectively as $\bar{\hat{\theta}} = \frac{1}{b}\sum_{j=1}^{b}\hat{\theta}_j$ and $\hat{\theta}^{\text{int}} = \sum_{j=1}^{b}\left(\hat{\theta}_j - \bar{\hat{\theta}}_j\right)^2$.

The average $\bar{\hat{\theta}}$ is standardized and compared with the standard normal distribution to test H_0^{tr}. The standardized form of $\hat{\theta}^{\text{int}}$ is compared with a χ^2_{b-1} to test H_0^{int}.

All the above mentioned methods are nonparametric, rank based. However, none of the these methods take into consideration the shape of the underlying distribution function F. In the next chapter, we propose adaptive procedures which take into consideration the shape of the distribution.

CHAPTER 3

EXTENDING RESULTS TO THE TWO-WAY LAYOUT

Here we are interested in extending the c-sample analysis of the adaptive method to higher dimensional methods. In particular, we will develop the analysis for a two way factorial analysis with fixed effect.

3.1 TWO-WAY Layout Design

We define a general fixed model, with a treatments groups. Every treatment group i contains k=1,……,n_i independent (randomly chosen) subjects. These $n = \sum_{i=1}^{a} n_i$ subjects are observed under j=1,….,b different (fixed) situations (centers). The general fixed model can be written by independent random vectors X_{ijk} where j=centers and i= treatments.

$$X_{ijk} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \varepsilon_{ijk} \qquad (3.0)$$

where $\sum_{i=1}^{a} \alpha_i = \sum_{j=1}^{b} \beta_j = \sum_{i=1}^{a} (\alpha\beta)_{ij} = \sum_{j=1}^{b} (\alpha\beta)_{ij} = 0$; $\varepsilon_{ijk} \sim F_{ij}(x)$.

Here, α_i denotes the effect of the ith treatment, β_j, the effect of the jth center and $(\alpha\beta)_{ij}$, the interaction between the ith treatment and the jth center.

Here, $X_{ijk} \sim F_{ij}(x) = \frac{1}{2}\left[F_{ij}^{+}(x) + F_{ij}^{-}(x)\right]$ i=1,…r, j=1….,d. Here, $F_{ij}^{+}(x) = P(X_{ijk} \le x)$ is the right continuous version and $F_{ij}^{-}(x) = P(X_{ijk} < x)$ is the left continuous version of the distribution function. We will use the distribution function $F_{ij}(x)$ to describe an effect (eg treatment effect).

3.1.1. Relative Treatment Effect

Let P_{ij} be the treatment effect for treatment i and center j. Then we have

$$P_{ij} = \int H(x)dF_{ij}(x) \text{ where } H(x) = \frac{1}{N}\sum_{i=1}^{a}\sum_{j=1}^{b} n_{ij}F_{ij} \qquad (3.1)$$

The relative effect P_{ij} quantifies the tendency of the marginal distribution F_{is} with respect to the mean distribution H. If F_{is} tends to lie to the right of H, then $p_{is} > \frac{1}{2}$ and if no tendency to the left or right of H exists then $p_{is} = \frac{1}{2}$. The relative effects P_{ij} may be weighted independently of i and j by a score function J(u):$u \in (0,1) \to \Re$ with bounded second derivative that is $\| J'' \|_{\infty} = \underset{0 \le U \le 1}{Sup} | J''(u) | < \infty$ .We then define the relative scored effect $P_{ij} = \int J[H(x)]dF_{ij}(x)$.We denote P(J)= $P(J) = (P_{11}(J), ..., P_{ab}(J))'$ the vector of these relative effects which are estimated by replacing H(x) and F_{ij} by their empirical counterparts. The empirical distributions $\hat{F}_{ij}$ are expressed as:

$\hat{F}_{ij}(x) = \frac{1}{n_{ij}} \sum_{k=1}^{n_{ij}} C(X - X_{ijk})$ .The empirical counterpart of H(x) is given by : $\hat{H}(x) = \frac{1}{N} \sum_{i=1}^{a} \sum_{j=1}^{b} \sum_{k=1}^{n_{ij}} C(X - X_{ijk})$ .Here, $C(u) = \frac{1}{2}[C^{+}(u) + C^{-}(u)]$ is the normalized version of the counting function $C^{+}(u)$ and $C^{-}(u)$ where $C^{+}(u) = 0$ or 1 according as u< or ≥ 0 and $C^{-}(u) = 0$ or 1 according as u≤ or > 0. The relative treatment effects P_{ij} *are estimated by* $\hat{P}_{ij}(J) = \int J[\hat{H}(x)] d\hat{F}_{ij}(x)$. *Here,* $\hat{P}_{ij}(J) = \frac{1}{n_{ij}} \sum_{k=1}^{n_{ij}} J[\hat{H}_{N}(X_{ijk})]$ *where*

$$J[\hat{H}_{N}(X_{ijk}) = J\left[\frac{1}{N}\left(R_{ijk} - \frac{1}{2}\right)\right] \qquad (3.2)$$

$\hat{P}_{ij}(J)$ *then becomes* $\hat{P}_{ij}(J) = \frac{1}{n_{ij}} \sum_{k=1}^{n_{ij}} J\left[\frac{1}{N}\left(R_{ijk} - \frac{1}{2}\right)\right]$*, where J is a score function defined below.* Equation (3.2) is the rank score of X_{ijk} and R_{ijk} is the mid-rank of X_{ijk} among all observations. $J[H(X_{ijk})]$ is called the asymptotic rank-transform of X_{ijk} since $E[J(\hat{H}) - J(H)]^2 \to 0$ under suitable conditions. $\phi_{ijk} = J\left[\hat{H}(X_{ijk})\right] = J\left[\frac{1}{N}\left(R_{ijk} - \frac{1}{2}\right)\right]$ is the rank score of X_{ijk} and R_{ijk} is the mid-rank of X_{ijk} amongst all observations. We then define the score functions for each of the test statistics for the higher way dimension. For any positive number B, let [B] denote the largest integer ≤ B. The scores are defined below.

Table 3.1 Scores For TWO-WAY ANOVA

$$i)\quad a_W(i) = \frac{i}{N+1} \qquad if \quad 1 \le i \le N.$$

$$ii)\quad a_L(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{4}\right]}{N+1} & if \quad i \le \left[\dfrac{N+1}{4}\right] \\ \dfrac{i - N + \left[\dfrac{N+1}{4}\right]}{N+1} & if \quad i \ge N - \left[\dfrac{N+1}{4}\right] + 1, \\ 0 & otherwise. \end{cases}$$

$$iii)\quad a_{ML}(i) = \begin{cases} -\dfrac{\left(i - \left[\dfrac{N+1}{4}\right]\right)^2}{(N+1)^2} & if \quad i \le \left[\dfrac{N+1}{4}\right] \\ \dfrac{\left(i - N + \left[\dfrac{N+1}{4}\right]\right)^2}{(N+1)^2} & if \quad i \ge N - \left[\dfrac{N+1}{4}\right] + 1, \\ 0 & otherwise. \end{cases}$$

$$iv)\quad a_{SL}(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{2}\right] + 0.5}{N+1} & if \quad i \ge \left[\dfrac{N+1}{2}\right], \\ 0.5 & otherwise. \end{cases}$$

$$v)\quad a_{SR}(i) = \begin{cases} \dfrac{i - \left[\dfrac{N+1}{2}\right] - 0.5}{N+1} & if \quad i \le \left[\dfrac{N+1}{2}\right], \\ 0.5 & otherwise. \end{cases}$$

Here $N = n_{11} + n_{12} + n_{21} + n_{22}$

Table 3.2 Score Functions For TWO-WAY ANOVA

$$J(u) = \begin{cases} u - \frac{1}{4}, & 0 < u < \frac{1}{4} \\ 0 & , \frac{1}{4} \le u \le \frac{3}{4} \\ u - \frac{3}{4}, & \frac{3}{4} < u < 1 \end{cases} \qquad h_L$$

$$J(u) = \begin{cases} -\left(u - \frac{1}{4}\right)^2, & 0 < u < \frac{1}{4} \\ 0 & , \frac{1}{4} \le u \le \frac{3}{4} \\ \left(u - \frac{3}{4}\right)^2, & \frac{3}{4} < u < 1 \end{cases} \qquad h_{ML}$$

$$J(u) = u, \qquad 0 < u < 1 \qquad h_W$$

$$J(u) = \begin{cases} u - \frac{1}{2}, & 0 < u \le \frac{1}{2} \\ 0.5, & \frac{1}{2} < u < 1 \end{cases} \qquad h_{SR}$$

$$J(u) = \begin{cases} 0.5, & 0 < u \le \frac{1}{2} \\ u - \frac{1}{2}, & \frac{1}{2} < u < 1 \end{cases} \qquad h_{SL}$$

3.2 Defining Skewness and Kurtosis For Two-Way ANOVA

The definition of skewness and kurtosis will be modified from the one in the c-sample case. In the 2x2 factorial design $N = n_{11} + n_{12} + n_{21} + n_{22}$ is the total size of the sample.

An indicator of skewness, studied by Fisher and explained in Hogg et al.(1975), is $Q_{1ij} = \frac{\overline{U}_{0.05} - \overline{M}_{0.5}}{\overline{M}_{0.5} - \overline{L}_{0.05}}$ where $\overline{U}_{0.05}$, $\overline{M}_{0.5}$ and $\overline{L}_{0.05}$ are respectively , the averages of the top 5%, middle 50% and bottom 5% of the order statistics of the individual sample with treatment i and center j. However, we will work with the average of the weighted Q_{1ij} s .

Hence, $\overline{Q}_1 = \frac{n_{11}Q_{111} + n_{12}Q_{112} + n_{21}Q_{121} + n_{22}Q_{122}}{n_{11} + n_{12} + n_{21} + n_{22}}$, the weighted average of the Q_1 values based on the individual samples for the case where we have two factor for each effect. This result can be further extended for higher dimensions.

Similarly, for kurtosis, we use $Q_{2ij} = \frac{\overline{U}_{0.05} - \overline{L}_{0.05}}{\overline{U}_{0.5} - \overline{L}_{0.5}}$, where $\overline{U}_{0.05}$, $\overline{U}_{0.5}$ and $\overline{L}_{0.05}$ are respectively , the averages of the top 5%, upper 50% and bottom 5% of the order statistics of the individual sample with treatment i and center j. Here also, we will work with the average of the weighted Q_{2ij} s .

Hence, $\overline{Q}_2 = \frac{n_{11}Q_{211} + n_{12}Q_{212} + n_{21}Q_{221} + n_{22}Q_{222}}{n_{11} + n_{12} + n_{21} + n_{22}}$, the weighted average of the Q_2 values based on the individual samples for the case where we have two

factor for each effect. This result can be further extended for higher dimensions. We will use the conclusion of Hogg et al(1975) which states the following : if $\frac{1}{2} \le \overline{Q_1} \le 2$, then we have symmetry. If $\overline{Q_1} < \frac{1}{2}$ *and* $\overline{Q_1} > 2$ then we have skewness to the left and right respectively .

For Kurtosis, $\overline{Q_2}$<2.24 we have a light tailed distribution. $2.24 \le \overline{Q_2} \le 3.8$, we have a not heavy and not light distribution. $\overline{Q_2} > 3.8$ (Heavy tailed). Also note that if $\overline{Q_2} < 3.8$ then F is not heavy-tailed (NH).

3.3 Relative Effects, Hypotheses and Estimators

3.3.1.Hypothesis Test

Here, we will use the following notations throughout. Let $\mu = (\mu_1, ... \mu_d)'$ *be a d-dimensional vector of constants. Hypothesis concerning the components of* μ *are formulated by contrast matrices where a matrix* $C_{r \times d} 1_d = 0_{r \times 1}$ *where* $1_d = (1, ..., 1)'$ *denotes the d-dimensional vector of 1's. In particular, we use the contrast matrix(sometimes called centering matrix)*

$$P_d = I_d - \frac{1}{d} J_d$$

where I_d *is the d-dimensional unit matrix and* $J_d = 1_d 1_d'$ *is the* $d \times d$ *matrix of 1's. Note that* P_d *is a d-dimensional project matrix of rank d-1, i.e.* $P_d{}^2 = P_d$ *and* $P_d' = P_d$

In the two-way classification where A has i=1,…..,a levels and factor B has j=1,…..,b levels with k=1,….., n_{ij} *replications per cell (i,j) and the independent random variables* X_{ijk} have distribution functions

$F_{ij}(x) = \frac{1}{2}\left[F_{ij}^{+}(x) + F_{ij}^{-}(x)\right]$. Let $F = (F_{11},.....,F_{1b},.....,F_{a1},.....,F_{ab})'$ denote the vector of the distribution functions. Let $C_A = P_a \otimes \frac{1}{b}1_b'$, $C_B = \frac{1}{a}1_a' \otimes P_b$ and $C_{AB} = P_a \otimes P_b$ where P_a and P_b are given above and $A \otimes B$ is the Kronecker product defined below.

Let $A_{pxq} = \begin{pmatrix} a_{11} ..... & .a_{1q} \\ . & \\ . & \\ . & \\ a_{p1} ..... & .a_{pq} \end{pmatrix}$ and $B_{rxs} = \begin{pmatrix} b_{11} ..... & .b_{1s} \\ . & \\ . & \\ . & \\ b_{r1} ..... & .b_{rs} \end{pmatrix}$

Then the kronecker-product $A \otimes B$ is defined as :

$$A \otimes B = \begin{pmatrix} a_{11}B ..... & .a_{1q}B \\ . & \\ . & \\ . & \\ a_{p1}B ..... & .a_{pq}B \end{pmatrix}_{prxqs} \qquad (3.2a)$$

Then the nonparametric hypotheses of ‘no main effect A’, ‘no main effect B’ or ‘no interaction AB’ are formulated as follows:

$H_0^F(A): C_A F = 0, \quad H_0^F(B): C_B F = 0, \quad H_0^F(AB): C_{AB} F = 0$

3.3.2. Remark

In a linear model without interaction (i.e. where the main effects are well defined), the hypothesis of no nonparametric main effect A or B, respectively are equivalent to the parametric hypotheses of no main effect A or B, respectively (in the usual linear model).

3.3.3. Asymptotic Results

We will present the asymptotic results for score functions and then apply them to the adaptive case for a TWO-WAY ANOVA.

3.3.3.1 Score functions with bounded derivatives

Here, we will work with the ONE-WAY ANOVA case and then extend it to the TWO-WAY ANOVA.

Assumptions

(a) $N = \sum_{i=1}^{d} n_i \to \infty$,

(b) $\frac{N}{n_i} \le N_0 < \infty$, *i=1,….,d.*

Let J(u), $u \in (0,1) \to \Re^1$, *be a score function with*

(c1) bounded first derivative, i.e. $\| J' \|_\infty = \sup_{0<u<1} | J'(u) | < \infty$.

(c2) bounded second derivative ,i.e. $\| J'' \|_\infty = \sup_{0<u<1} | J''(u) | < \infty$

Note that (c2) $\Rightarrow$ *(c1)* $\Rightarrow \| J \|_{\infty} = \sup_{0<u<1} | J(u) | < \infty$

We will begin by looking at the conditions for the consistency of the estimators $\hat{p}_i(J)$.

Proposition 3.1 Let $X_{ij} \sim F_i(x)$, *i=1,….d, j=1,….,* n_i *be independent random variables and let* $p_i(J) = \int J[H(x)]dF_i(x)$ *and*

$$\hat{p}_i(J) = \int J[\hat{H}]d\,\hat{F}_i = \frac{1}{n_i}\sum_{j=1}^{n_i} J\left[\frac{1}{N}\left(R_{ij} - \frac{1}{2}\right)\right] = \frac{1}{n_i}\sum_{j=1}^{n_i}\phi_{ij} = \overline{\phi_{i\bullet}}.$$

Here, $R_{ij} = \frac{1}{2} + N\hat{H}(X_{ij}) = \frac{1}{2} + \sum_{r=1}^{d}\sum_{s=1}^{n_r} c(X_{ij} - X_{rs})$ *is the mid-rank of all the random variables* X_{ij} *among all the N observations. Note that* $\frac{1}{2}$ *is added in case of ties and* $\phi_{ij} = J\left[\frac{1}{N}\left(R_{ij} - \frac{1}{2}\right)\right]$ *are called rank scores .Then, under assumptions (a),(b) and (c1),* $\hat{p}_i(J) - p_i(J) \xrightarrow{p} 0$

Proof. It suffices to show that $E\left(\hat{p}_i(J) - p_i(J)\right)^2 \to 0$.

Note that, by applying Jensen's inequality we have

$$\left(\hat{p}_i(J) - p_i(J)\right)^2 = \left(\int J\left[\hat{H}\right] d\hat{F}_i - \int J[H] dF_i\right)^2$$

$$= \left(\int J\left[\hat{H}\right] - J[H] d\hat{F}_i + \int J[H] d\left[\hat{F}_i - F_i\right]\right)^2$$

$$\leq \frac{2}{n_i}\sum_{j=1}^{n_i}\left(J\left[\hat{H}(X_{ij})\right] - J\left[H(X_{ij})\right]\right)^2$$

$$+ \frac{2}{n_i^2}\sum_{j=1}^{n_i}\sum_{k=1}^{n_i}\left(J\left[H(X_{ij})\right] - \int J[H] dF_i\right)\left(J\left[H(X_{ik}) - \int J[H] dF_i\right]\right)$$

Taking expectations and using independence and the equation below

$E\left(J\left[\hat{H}(X)\right] - J\left[H(X)\right]\right)^2 \leq \frac{1}{N}\| J' \|_\infty^2$, we obtain

$$E\left(\hat{p}_i(J) - p_i(J)\right)^2 \leq \frac{2}{N}\| J' \|_\infty^2 + \frac{2}{n_i^2}\sum_{j=1}^{n_i} E\left(J\left[H(X_{ij})\right] - \int J[H] dF_i\right)^2$$

$$\leq \frac{2}{n_i}\left(\| J' \|_\infty^2 + \| J \|_\infty^2\right) = O\left(\frac{1}{n_i}\right)$$

This concludes the proof.

Next, we state the basic asymptotic equivalence.

Theorem 3.2.(Brunner 1999) Let $X_{ij} \sim F_i(x)$*, i=1,…,d, j=1,…,* n_i*, be independent random variables. Then under assumptions (a),(b) and (c2),*

$$\sqrt{N}\int J[\hat{H}] d(\hat{F} - F) \doteq \sqrt{N}\int J[H] d(\hat{F} - F).$$

Proof. It suffices to consider the ith component of $\hat{F} - F$ *.We note that*

$$\sqrt{N}\int J[\hat{H}]d(\hat{F}_i - F_i) = \sqrt{N}\int J[H]d(\hat{F}_i - F_i)$$
$$+\sqrt{N}\int (J[\hat{H}] - J[H])d(\hat{F}_i - F_i), \quad i = 1,...,d.$$

Using Taylor's expansion, we obtain

$$J[\hat{H}] - J[H] = J'[H][\hat{H} - H] + \frac{1}{2}J''(\hat{\theta}_N)[H \hat{-} H]^2,$$

where $\hat{\theta}_N$ *is between* $\hat{H}$ *and H. Thus,*

$$\sqrt{N}\int J[\hat{H}]d(\hat{F}_i - F_i) = \sqrt{N}\int J[H]d(\hat{F}_i - F_i) + \sqrt{N}(B_1 + B_2),$$

where

$$B_1 = \int J'[H][\hat{H} - H]d(\hat{F}_i - F_i)$$

$$B_2 = \frac{1}{2}\int J''[\hat{\theta}_N][\hat{H} - H]^2 d(\hat{F}_i - F_i).$$

To complete the prove, we have,

$$E(NB_1^2) = NE\left(\int J'[H][\hat{H} - H]d(\hat{F}_i - F_i)\right)^2 \to 0, \text{ and}$$

$$E(NB_2^2) = NE\left(\frac{1}{2}\int J''[\hat{\theta}_N][\hat{H} - H]^2 d(\hat{F}_i - F_i)\right)^2 \to 0,$$

by Lemma A.4 (Brunner 2002) and assumptions (a) , (b) and (c2).

This completes the proof. (See Brunner 2002)

Next, we define the estimate for the variance matrix V_N

We note that $\sqrt{N}\int J[H]d\hat{F} = \sqrt{N}\,\bar{Y}_{\bullet}(J)$ *is a vector of independent (unobservable) random variables* $\sqrt{N}\,\bar{Y}_{i\bullet}(J) = \sqrt{N}n_i^{-1}\sum_{j=1}^{n_i} Y_{ij}(J), i = 1,...,d,$ *where* $Y_{ij}(J) = J[H(X_{ij})]$ *is called asymptotic rank (score) transform (ART) because* $Y_{ij}(J)$ *is asymptotically equivalent to* $\hat{Y}_{ij}(J) = J[\hat{H}(X_{ij})]$ *and*

$$V_N = Cov(\sqrt{N}\,\bar{Y}.(J)) = N\overset{d}{\oplus}_{i=1}\frac{1}{n_i}\sigma_i^2(J), \tag{3.4}$$

where $\sigma_i^2(J) = Var(J[H(X_{ij})])$, j=1,……, n_i .

The unknown variances $\sigma_i^2(J)$ can be estimated from the rank scores

$$\phi_{ij} = \hat{Y}_{ij}(J) = J[1/N(R_{ij} - \frac{1}{2})].$$

The following theorem states that the estimate of the unknown variances of the distribution converge in probability to the variances of the transformed ranks.

Theorem 3.3. Let $X_{ij} \sim F_i(x), i = 1,...,n_i$ be independent random variables and assume that $\sigma_i^2(J) \geq \sigma_0^2(J) > 0$ where $\sigma_i^2(J)$ is given in (3.4). Then, under the assumptions (a), (b) and (c1), $\hat{\sigma}_i^{\,2}(J)/\sigma_i^2(J) \xrightarrow{p} 1$ where

$$\hat{\sigma}_i^{\,2}(J) = \frac{1}{n_i - 1}\sum_{j=1}^{n_i}(\phi_{ij} - \bar{\phi}_{i\bullet})^2, \qquad \bar{\phi}_{i.} = \frac{1}{n_i}\sum_{j=1}^{n_i}\phi_{ij,} \qquad i = 1,...,d, \tag{3.5}$$

Where $\phi_{ij} = J[1/N(R_{ij} - \frac{1}{2})]$.

Moreover, $\hat{V}_N V_N^{-1} \xrightarrow{P} I_d$ $where \hat{V}_N = N \oplus_{i=1}^{d} (1/n_i) \hat{\sigma}_i^{\,2}(J).$

The proof of this can be found in Brunner 2002.

The next theorem will be important in the derivation of our asymptotic result of the Wilcoxon Type Statistics.

Theorem 3.4

Let $X_{ij} \sim F_i(x)$,i=1,…..,d , j=1,……, n_i be independent random variables and assume that $\sigma_i^2(J) \geq \sigma_0^2(J) > 0$ where $\sigma_i^2(J)$ is given in (3.1). Let V_N be as given in (3.4) and let $\hat{V}$ be as given in Theorem 3.3. Then, under assumptions (a), (b) and (c2) and under hypothesis $H_0^F : CF = 0$,

1. The statistics $\sqrt{N} C \hat{p}(J) = \sqrt{N} C \int J[\hat{H}] d\hat{F}$ has asymptotically a multivariate normal distribution with mean 0 and covariance matrix $CV_N C'$,
2. The quadratic form $Q_N(C) = N \hat{p}'(J) C' [CV_N C']^{-} C \hat{p}(J)$ has asymptotically a central χ_f^2-distribution with f=rank(C) where $[CV_N C']^{-}$ denotes a generalized inverse of $[CV_N C']$
3. If C is a full row rank, then $Q_N(C) = N \hat{p}'(J) C' [CV_N C']^{-} C \hat{p}(J)$ has asymptotically a central χ_f^2-distribution with f=rank(C).

The next theorem will be important in the derivation of the ANOVA Type Statistics which is important when sample size is small.

Theorem 3.5

Let $M = C'(CC')^{-}C$ *and let* V_N *be as given in (3.4). Then, under the assumptions of Theorem 3.4 and under the hypothesis* $H_0^F : CF = 0$ *,the quadratic form* $Q_N(C) = N \hat{p}'(J) M \hat{p}(J)$ has asymptotically the weighted χ^2-distribution as of $\sum_{i=1}^{d} \lambda_i U_i$ where the U_i are independent random variables each having a χ_1^2-distribution and the λ_i are the eigenvalues of MV_NM.

The degree of freedom f for the above asymptotic distribution can be estimated as follows.

Let M be as defined in Theorem 3.5 and assume that the diagonal elements m_{ii} of M are identical to m, say, i.e. $m_{ii} \equiv m$. Further let $\Lambda_d = diag\{n_1, ..., n_d\}$. Then, under the assumptions of Theorem 3.5, the distribution of the statistic

$$T_N(M) = \frac{N}{m \cdot tr(\hat{V}_N)} \cdot \hat{p}'(J) M \hat{p}(J) = \frac{Q_N^*(M)}{m \cdot tr(\hat{V}_N)} \qquad (3.6)$$

can be approximated under H_0^F by the central $F(\hat{f}_1, \hat{f}_0)$ distribution with estimated degrees of freedom.

$$\hat{f}_1 = m^2 \cdot \frac{\left[tr(\hat{V}_N)\right]^2}{tr((M\hat{V}_N M\hat{V}_N))} = (Nm)^2 \cdot \frac{\left(\sum_{i=1}^{d} \hat{\sigma}^2(J)/n_i\right)^2}{tr((M\hat{V}_N M\hat{V}_N))} \qquad (3.7)$$

and

$$\hat{f}_0 = \frac{\left[tr(\hat{V}_N)\right]^2}{tr(\hat{V}_N^2(\Lambda_d - I_d)^{-1})} = \frac{\left(\sum_{i=1}^{d} \hat{\sigma}^2(J)/n_i\right)^2}{\sum_{i=1}^{d} \hat{\sigma}_i^4(J)/\left[n_i^2(n_i-1)\right]} \qquad (3.8)$$

where $\hat{\sigma}_i^2(J)$ is given in (3.3) and $tr(\cdot)$ denotes the trace of a square matrix. See Brunner et al. (1997) .

3.3.3.2 Asymptotic Derivation for the Two-factor Design

We now consider the two-way cross classification where factor A has i=1,….,a levels and B has j=1,….,b levels with k=1,….., n_{ij} replications per cell (i,j) and the independent random variables X_{ijk} have distribution functions $F_{ij}(x) = \frac{1}{2}\left[F_{ij}^+ + F_{ij}^-\right]$. Let $F = (F_{11},....,F_{1b},....,F_{a1},.....,F_{ab})'$ denote the vector of the distribution functions where the second index j is running faster than the first index i. Let $C_A = P_a \otimes \frac{1}{b}1_b'$, $C_B = \frac{1}{a}1_a' \otimes P_b$ and $C_{AB} = P_a \otimes P_b$ where P_a and P_b

are given in section 3.2.2. Then the nonparametric hypotheses of 'no main effect A', 'no main effect B' or 'no interaction AB' are formulated as follows:

$$H_0^F(A): C_A F = 0, \quad H_0^F(B): C_B F = 0, \quad H_0^F(AB): C_{AB} F = 0$$

Let $\hat{F}(x) = (\hat{F}_{11}(x), \ldots\ldots\ldots, \hat{F}_{ab}(x))'$ denote the vector of the empirical distribution functions $\hat{F}_{ij}(x) = n_{ij}^{-1} \sum_{k=1}^{n_{ij}} c(x - X_{ijk})$ and let $\tilde{\phi}_{i\bullet\bullet} = b^{-1} \sum_{j=1}^{b} \bar{\phi}_{ij\bullet}$,i=1,……..,a, denote the unweighted means of the cell means $\bar{\phi}_{ij\bullet} = n_{ij}^{-1} \sum_{k=1}^{n_{ij}} \phi_{ijk}$ where

$\phi_{ijk} = J\left[\frac{1}{N}\left(R_{ijk} - \frac{1}{2}\right)\right]$ and R_{ijk} is the rank of X_{ijk} among all the $N = \sum_{i=1}^{a}\sum_{j=1}^{b} n_{ij}$ observations. To test the hypothesis $H_0^F(\cdot)$ formulated above, consider the statistic $\hat{p}(J) = \int J\left[\hat{H}\right] d\hat{F} = \left(\bar{\phi}_{11\bullet}, \ldots\ldots\ldots, \bar{\phi}_{ab\bullet}\right)'$ under the hypothesis $H_0^F : CF = 0$ using the contrast matrices C_A, C_B, C_{AB}.

Let
$$\hat{\sigma}_{ij}^2(J) = \frac{1}{n_{ij} - 1} \sum_{k=1}^{n_{ij}} \left(\phi_{ijk} - \bar{\phi}_{ij\cdot}\right)^2, \quad \hat{V}_N = N \overset{a}{\underset{i=1}{\oplus}} \overset{b}{\underset{j=1}{\oplus}} \frac{\hat{\sigma}_{ij}^2(J)}{n_{ij}}, \qquad (3.9)$$
$$\hat{\tau}_i^2(J) = \frac{1}{b^2} \sum_{j=1}^{b} \frac{\hat{\sigma}_{ij}^2(J)}{n_{ij}} \quad , \quad \hat{\sum}_a = \overset{a}{\underset{i=1}{\oplus}} \hat{\tau}_i(J)$$

Let $\hat{W}_a = N^{-1}\hat{\Sigma}_a^{-1}\left(I_a - J_a\hat{\Sigma}_a^{-1}/1_a'\hat{\Sigma}_a^{-1}1_a \right)$ and note that $\hat{W}_a$ is a generalized inverse

of $C_A\hat{V}_N C_A' = NP_a\hat{\Sigma}_a P_a$ and that $P_a\hat{W}_a P_a = \hat{W}_a$. Then under $H_0^F(A)$, it follows from Theorem 3.4 that the quadratic form

$$Q_N(C_A) = N\hat{p}'(J)C_A'(C_A\hat{V}_N C_A')^{-}C_A\hat{p}(J) = N\hat{p}'(J)\left[\hat{W}_a \otimes \frac{1}{b}J_b\right]p'(J)$$

$$= \sum_{i=1}^{a}\frac{1}{\hat{\tau}_i^2(J)}\left(\tilde{\phi}_{i\bullet\bullet} - \frac{1}{\sum_{r=1}^{a}\left(1/\hat{\tau}_r^2(J)\right)}\sum_{r=1}^{a}\frac{\tilde{\phi}_{r\bullet\bullet}}{\hat{\tau}_r^2(J)} \right)^2 \qquad (3.10)$$

has asymptotically a central χ_f^2 - distribution with f=a-1.

Next, the statistic for testing the hypothesis $H_0^F(AB)$ of no nonparametric interaction, namely $Q_N(C_{AB}) = N\hat{p}'(J)C_{AB}'(C_{AB}\hat{V}_N C_{AB}')^{-}C_{AB}\hat{p}(J)$, (3.11)

is also derived from Theorem 3.4 and $Q_N(C_{AB})$ has asymptotically a central χ_f^2 distribution with f=(a-1)x(b-1) under $H_0^F(AB)$.

Finally, since rows and columns are interchangeable in this design, the quadratic form $Q_N(C_B)$ for testing $H_0^F(B)$ is obtained by interchanging rows and columns. These statistics (3.10) and (3.11) are referred to as the WILCOXON-TYPE STATISTICS (WTS).

As in section 3 we describe the application of our method to small samples. The hypothesis $H_0^F(A)$ in the cross-classification is equivalently stated as $H_0^F(A): M_A F = 0$ where $M_A = P_a \otimes \frac{1}{b} J_b$ is a projection matrix with constant diagonal elements $m_a = (a-1)/(ab)$. Let $\tilde{\phi}_{i\bullet\bullet} = b^{-1}\sum_{j=1}^{b} \bar{\phi}_{ij\bullet}$ and $\tilde{\phi}_{\bullet\bullet\bullet} = a^{-1}\sum_{i=1}^{b} \tilde{\phi}_{i\bullet\bullet}$. Then under $H_0^F(A)$, the statistics

$$T_N(M_A) = \frac{Nab^2}{(a-1)tr\left(\hat{V}_N\right)} \cdot \sum_{i=1}^{a}\left(\tilde{\phi}_{i\bullet\bullet} - \tilde{\phi}_{\bullet\bullet\bullet}\right)^2 \qquad (3.12)$$

has asymptotically a central $F(\hat{f}_A, \hat{f}_0)$ distribution where the degrees of freedom $\hat{f}_A$ and $\hat{f}_0$ are derived from (3.7) and (3.8) respectively, by replacing M with M_A and $\hat{V}_N$ is given in (3.9). The same derivations follow for the other hypotheses. These results are referred to as the ANOVA-TYPE STATISTICS (ATS).

These results will be used in our next section to analyze data and calculate the significance of various main and interaction effects.

3.4 Power Calculations

The power of a statistical test is the probability of rejecting the null hypothesis when the alternative is in fact true. Power equals one minus the

probability of a Type II error, and is also known as sensitivity or the true positive rate.

There are two types of power calculations: prospective and retrospective power calculations. Prospective power calculations refer to the the power of statistical hypothesis tests for new experiments that are yet to be conducted. Such calculations are critical in determining the size and structure of a new experimental design and in optimizing information gain from experimental units.

Retrospective power calculations are calculations in which power statistics are used to embellish analysis of a data set in hand. Careful considerations must be taken when dealing with this type of analysis. However, power calculations on current data sets can be useful from a pilot study perspective, in the sense that reasonable estimates for required parameters can be obtained from existing data in order to perform an appropriate prospective power calculation.Power calculations for mixed models are more difficult due to their more complex covariance structure . Assuming the hypothesis test of interest is a linear combination $K'\beta$, and knowing that our general t- and F-statistics can be written using the variance matrix $K'\left[X'V^{-1}X\right]^{-1}K$. So the power associated with such tests is a function of the following:

(1) the magnitude of $K'\beta$, also known as the effect size

(2) the design matrix X, including the number of its rows (the sample size) and the structure of its columns (from the fixed effects)

(3) the value of the variance and covariance parameters in V

(4) the test size, commonly known as α, the probability of a Type I error, or one minus the specificity of the test.

Our calculations for power in this paper will be based on retrospective power calculations. In the parametric case, power can be calculated using Proc Glmpower in SAS.

CHAPTER 4

APPLICATIONS

Here, we will apply our method to three cases. The statistics and their asymptotic distributions be given for each section.

4.1 Case where Data is Light-Tailed

A new synthetic erythropoietin-type hormone, Rebligen, which is used to treat chemotherapy-induced anemia in cancer patient, was tested in a study of 48 adult cancer patients undergoing chemo-therapeutic treatment. Half the patients received low-dose administration of Rebligen via intramuscular injection three times at 2-day intervals; half the patients received a placebo in a similar fashion. Patients were stratified according to their type of cancer: cervical, prostate, or colorectal. For study admission, patients were required to have a baseline hemoglobin less than 10 mg/dl and a decrease in hemoglobin of at least 1 mg/dl following the last chemotherapy. Changes in hemoglobin (in mg/dl) from the pre-first injection to one week after last injection (as shown in Table 4.1) were obtained for analysis. Does Rebligen have any effect on the hemoglobin (Hgb) levels? (Common Statistical Methods for Clinical Research with SAS Examples-Glenn A Walker -2002). levels: Active and Placebo.

Table 4.1 Raw Data for the Experiment For Case 1

	----ACTIVE---		PLACEBO	
Cancer Type	*Patient Number*	*Hgb Change*	*Patient Number*	*Hgb Change*
CERVIVAL	*1*	*1.7*	*2*	*2.3*
	3	*-0.2*	*4*	*1.2*
	6	*1.7*	*5*	*-0.6*
	7	*2.3*	*8*	*1.3*
	10	*2.7*	*9*	*-1.1*
	12	*0.4*	*11*	*1.6*
	13	*1.3*	*14*	*-0.2*
	15	*0.6*	*16*	*1.9*
PROSTATE	*22*	*2.7*	*21*	*0.6*
	24	*1.6*	*23*	*1.7*
	26	*2.5*	*25*	*0.8*
	28	*0.5*	*27*	*1.7*
	29	*2.6*	*30*	*1.4*
	31	*3.7*	*32*	*0.7*
	34	*2.7*	*33*	*0.8*
	36	*1.3*	*35*	*1.5*
COLORECTAL	*42*	*-0.3*	*41*	*1.6*
	45	*1.9*	*43*	*-2.2*
	46	*1.7*	*44*	*1.9*
	47	*0.5*	*48*	*-1.6*
	49	*2.1*	*50*	*0.8*
	51	*-0.4*	*53*	*-0.9*
	52	*0.1*	*55*	*1.5*
	54	*1.0*	*56*	*2.1*

Of primary interest is whether the Active treatment shows any effect on hemoglobin relative to any effects shown by the Placebo group. We will go ahead to analyze our data using the parametric, nonparametric Wilcoxon type procedure and the adaptive nonparametric methods listed in chapter three.

Our calculations for skewness and kurtosis based on individual cancer by drug type reveals the following results. For skewness, $\overline{Q_1} = 0.81060$ and $\overline{Q}_2 = 1.68668$. Based on these results, we classify our data as symmetric and light-tailed. Hence, we can use both the h_L and the h_{ML} test statistic with scores a_L and the a_{ML} respectively. Rank means $\overline{R_{ij.}}$, i = 1,2,3; j= 1,2, within the two treatment groups and the three cancer types as well as the unweighted means $\tilde{R}_{i..}$ within the cancer types and $\tilde{R}_{.j.}$ within the two treatments are displayed on table 4.2

Table 4.2 Rank Means and Relative Treatment Effects for Wilcoxon Scores

	Rank Means			Relative Treatment Effects		
Cancer Type	Active	Placebo	$\tilde{R}_{i..}$	Active	Placebo	$\tilde{p}_{i.}$
CERVICAL	26.31	21.00	23.66	0.54	0.43	0.49
PROSTATE	36.44	23.00	29.72	0.75	0.47	0.61
COLORECTAL	20.63	19.63	20.13	0.42	0.40	0.41
$\tilde{R}_{.j.}$	27.79	21.21		0.57	0.43	

Here, the average rank for each treatment by type is given and the average of the average rank for each cancer type and each treatment type is also calculated. For example, the average of the ranks in the Active treatment group for those with cervical cancer is 26.31 while the average rank of those in the placebo group for those with cervical cancer is 21.0.Their average rank (thosewith cervical cancer) is 23.66.

Looking at the relative effects p_{ij} , we see that there is a tendency for the marginal distributions of those with prostate cancer ,taking the active drug and those with cervical cancer taking the active drug to lie to the right of the mean distribution H. There is a tendency for all others to lie to the left of the mean distribution.

We will plot graphs of the relative marginal effects for the two treatment groups. Here, cancer type 1 is cervical, 2 is prostate and 3 is colorectal. Our graph looks like the one in Fig 4.1 below. With this visual view, we will go ahead to look at the main effects and the interaction effects for the parametric procedure, nonparametric with the Wilcoxon method and adaptive methods and then compare the results.

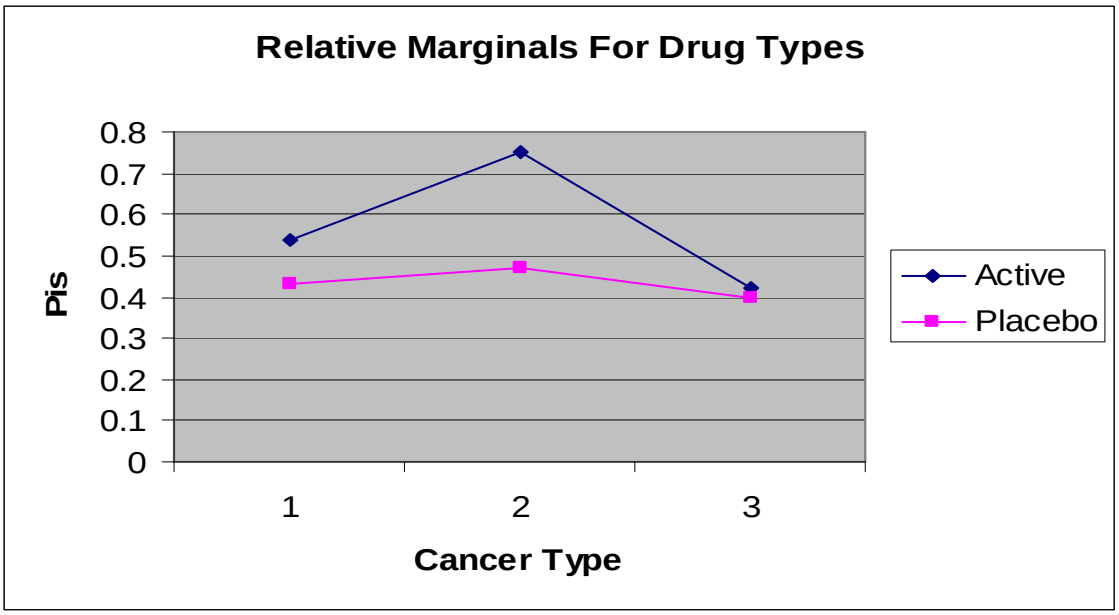

Fig 4.1 Relative Marginal Graph for Different Drug types using Wilcoxon Scores

4.1.1.Test Results For case 1

We obtain the test statistics and p-values for the nonparametric main effects and interaction in the above clinical trial. The results of the test statistics obtained by the all the methods used and the resulting p-values are given in the left part The results obtained by the ATS with the resulting p-values are given in the right part of the table.

A test of the hypothesis normality of the data is not rejected. We will therefore assume that the parametric approach will perform well. However, our data is symmetric and light-tailed. The adaptive procedures do well under these circumstances. Non parametric Wilcoxon test lose power here (page 56).

Table 4.3 Test Statistics and p values for main effects and interactions (case1)

Wilcoxon Test Results (aW)				
	Wald-Type Statistic		ANOVA-Type Statistic	
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A)$ -trt	2.88	0.0899	2.88	0.0982
$H_O^F(B)$ -type	4.82	0.0899	2.08	0.1400
$H_O^F(AB)$ -trt*type	2.05	0.3584	0.88	0.4192
Adaptive Light-Tailed Case (aL)				
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A) - trt$	8.78	0.0030	8.78	0.0050
$H_O^F(B) - type$	11.33	0.0035	5.66	0.0035
$H_O^F(AB) - trt * type$	0.900	0.4059	0.90	0.4136
Adaptive Modified Wilcoxon case (aML)				
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A) - trt$	11.87	0.0006	11.87	0.0013
$H_O^F(B) - type$	13.35	0.0013	6.67	0.0031
$H_O^F(AB) - trt * type$	1.570	0.4550	0.79	0.4616

Table 4.4 Test Statistics and p values for parametric main effects and interactions (case1)

	Type III SS	
Hypothesis	F Value	p-Value
$H_O^F(A)$ -trt	4.11	0.0491
$H_O^F(B)$ -type	3.55	0.0376
$H_O^F(AB)$ -trt*type	0.36	0.7018

4.1.1.1. Wilcoxon Scores Results

For the Wilcoxon scores, results show that there is no interaction effect, no Type effect and no Treatment effect. So the Wilcoxon type scores cannot detect the effect of any of the variables. The large p-value (p=0.4192) for $H_O^F(AB)$ indicates that the results are quite homogeneous within the two drug types (no interaction). There is no evidence for a significant treatment effect for the drug (p=0.0982 and also for the cancer type (p=0.1400). Because the data is assumed to come from a normal distribution, the nonparametric test cannot detect the significant effect on treatment, since it loses power in this case (Table 4.5 page 56)

4.1.1.2. a_L Scores Results

Since our calculations for skewness and kurtosis based on individual cancer by drug type reveals our data as symmetric and light-tailed we can apply the adaptive procedure with the h_L test statistic with scores a_L .The results of the test statistics obtained by the WTS and the ATS with the resulting p-values show that there is no Interaction effect, but there is a Type effect and a Treatment effect. So the a_L type scores can detect a significant treatment effect (p=0.005) and also a significant type effect (p=0.0035) but also concludes that there is no interaction effect (p=0.4136). Hence, the a_L type scores can determine the main effects as being significant while the Wilcoxon scores do not detect any of the effects as being significant.

4.1.1.3. a_{ML} Scores Results

We now use the a_{ML} scores together with the h_{ML} test statistics which is also an adaptive procedure to evaluate our data and get results. The results of the test statistics obtained by the WTS with the resulting p-values are together with those of obtained by the ATS with the resulting p-values show that there is no Interaction effect, but there is a Type effect and a Treatment effect. So the a_{ML} type scores can detect a significant treatment effect (p=0.0013) and also a significant type effect (p=0.0031) but also concludes that there is no

interaction effect (p=0.4616). Hence, the a_{ML} type scores can determine the main effects as being significant while the Wilcoxon scores do not detect any of the effects as being significant.

4.1.1.4. Parametric Test Results

We also did a parametric test result for these effects where normality is assumed and came up with the following results. The parametric procedure detects a significant treatment effect (p=0.0491) and also a significant type effect (p=0.0376) but also concludes that there is no interaction effect (p=0.7018). *Here also, the main effects are significant while the interaction is not significant.*

4.1.2. Comparison of Results

From this example, we see that when skewness and kurtosis are taken into consideration, we are able to detect the treatment effects. But the ordinary Wilcoxon method fails to identify the treatment effect. Although the parametric method does obtain the same result for treatment effect, the adaptive method still have a higher power (see Table 4.5) and shorter confidence lengths (Table 4.6).

4.1.2.1. Power Test and Graphs

Here, we will work on the probability of rejecting the the null hypothesis when the alternative is in fact true. Power equals one minus the probability of a Type II error, and is also known as sensitivity or the true positive rate.

Table 4.5 Power of the Test For All the Test scores (case1)

Obs	Effect		a_L	a_{ML}	a_W	Parametric
1	Treatment	POWER	0.82517	0.91999	0.37946	0.508
2	Type		0.83629	0.89401	0.44067	0.629
3	Trt*Type		0.19516	0.17522	0.20889	0.104

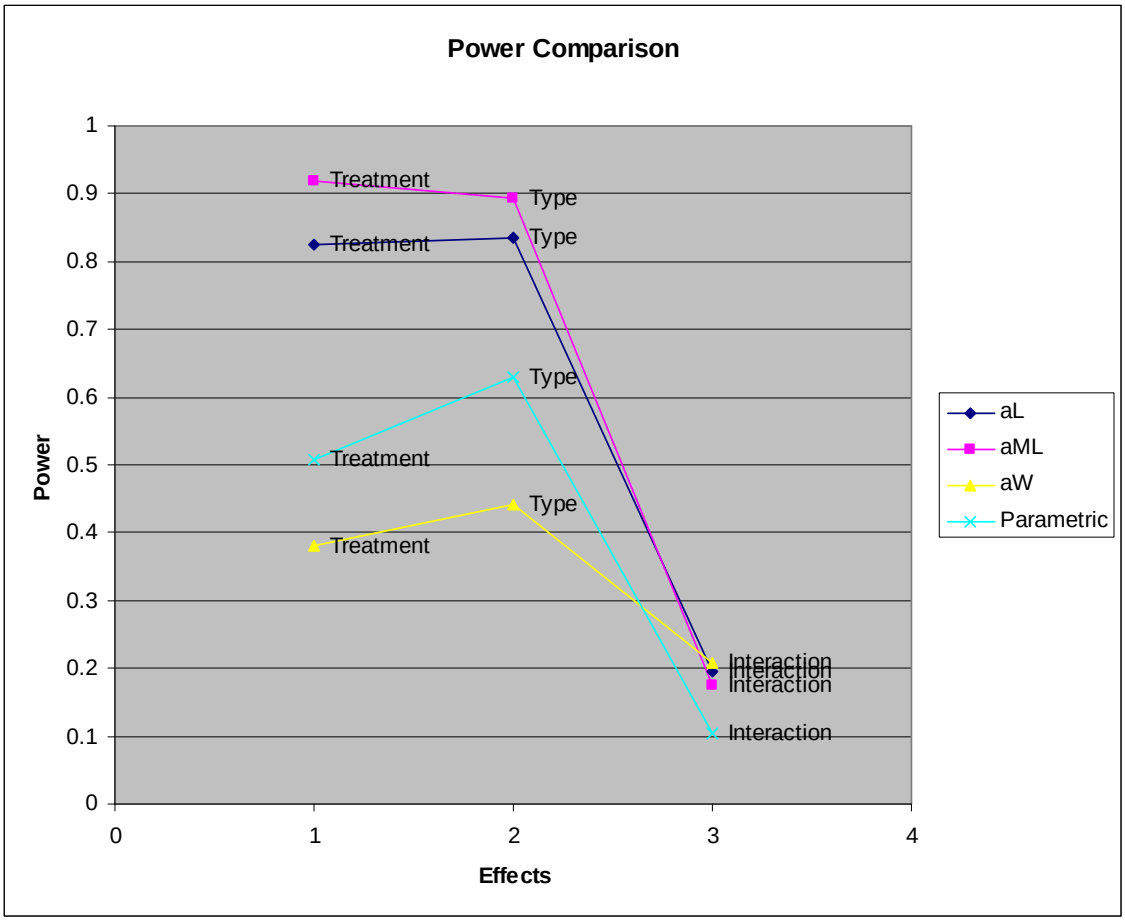

Fig 4.2 Power Comparison For Different Effects (case1)

Here, we see that the power for the detecting the interaction effects is about same for all the score functions except for the Parametric procedure where it is slightly lower. For the main effects, the adaptive scores have higher powers than the Wilcoxon scores and the parametric method.

4.1.2.2. Confidence Intervals and lengths

Table 4.6 Comparing the CI for different Methods (case1)

Method	*Effect*	*Difference b/w 1 and 2*	*Confidence Limits*		*Length of Interval*
			LL	*UL*	
a_L	*Treatment*	*0.07398*	*0.0236*	*0.124*	*0.1008*
a_{ML}	*Treatment*	*0.01571*	*0.0065*	*0.0249*	*0.01841*
a_W	Treatment	*0.1344*	*-0.0261*	*0.2948*	*0.3209*
Parametric	*Treatment*	*0.6625*	*0.0026*	*1.3224*	*1.3198*

Observe that the shortest intervals are provided by the two adaptive schemes, and especially by scheme II (a_{ML}). Short intervals are a reflection of high asymptotic relative efficiency (ARE) as pointed out by (Sun 1997). We can therefore conclude that our adaptive procedures here have better ARE than the Wilcoxon and parametric procedures .Shorter confidence intervals together with

better power than the nonparametric and parametric methods, make the adaptive procedures to be a more appropriate method.

4.2 Case where Data is Skewed to the Right

Table 4.7 Simulated Data For a 2x2 Design (case2)

Center1 Treatment1	Center1 Treatment2	Center2 Treatment1	Center2 Treatment2
51.297	2.594	35.557	2.1
51.423	2.846	35.708	2.37
52.18	4.361	36.616	3.985
52.273	4.545	36.727	4.181
52.413	4.825	36.895	4.48
52.766	5.531	37.319	5.23
53.344	6.688	38.013	6.47
54.443	8.885	39.331	8.81
57.192	14.384	42.63	14.676
57.879	15.759	43.455	16.14
59.821	19.642	45.785	20.285
63.562	27.123	50.274	28.26
66.238	32.476	53.486	33.97
68.499	36.997	56.198	38.8
72.863	45.726	61.435	48.11
76.484	52.969	65.781	55.83
78.014	56.029	67.617	59.1
87.341	74.682	78.809	78.99
96.982	93.963	90.378	99.56
105.584	111.168	100.701	117.91
137.534	175.067	139.04	186.07
157.715	215.429	163.257	229.12
160.479	220.958	166.575	235.02
164.808	229.615	171.769	244.26
167.346	234.692	174.815	249.67
183.937	267.874	194.724	285.07
187.872	275.745	199.447	293.46
491.588	883.177	563.906	941.39
512.016	924.033	588.42	984.97
535.007	970.015	616.009	1034.02

The above set of data was simulated using Monte Carlo simulations. The data was simulated to be non normal. Our calculations for skewness and

kurtosis based on individual treatment by center type reveals the following results. For skewness, $\overline{Q_1} = 12.6501$ and $\overline{Q}_2 = 3.13640$. Based on these results, we classify our data as Skewed to the right and not heavy tailed (note here also that our data is also not light tailed). Hence, we can use the h_{SR} test statistic with scores a_{SR} . We will also use the Wilcoxon scores and then compare with the parametric analysis where normality is assumed.

Rank means $\overline{R}_{ij}$, i = 1,2; j= 1,2, within the two treatment groups and the two centers as well as the unweighted means $\tilde{R}_{i..}$ within the centers and $\tilde{R}_{.j.}$ within the two treatments are displayed on table 4.9

Table 4.8 Rank Means and Relative Treatment Effects For Wilcoxon scores

	Ranks			Relative Treatment Effects		
Cancer Type	Treat 1	Treat 2	$\tilde{R}_{i..}$	Treat 1	Treat 2	$\tilde{p}_{i.}$
Center 1	70.07	54.03	62.05	0.58	0.45	0.52
Center 2	62.67	55.23	58.95	0.52	0.46	0.49
$\tilde{R}_{.j.}$	66.37	54.63		0.55	0.46	

Here, the average rank for each treatment by center is given and the average of the average rank for each center and each treatment type is also calculated. For example, the average of the ranks in the treatment 1 for those in center 1 is 70.07 while the average rank of those in treatment 2 and center 1 is 54.03.Their average rank (those in center 1) is 62.05. Looking at the relative

effects p_{ij} , we see that there is a tendency for the marginal distributions of those taking treatment 1 and in center 1 and those taking treatment 1 and in center 2 to lie to the right of the mean distribution H. There is a tendency for all others to lie to the left of the mean distribution.

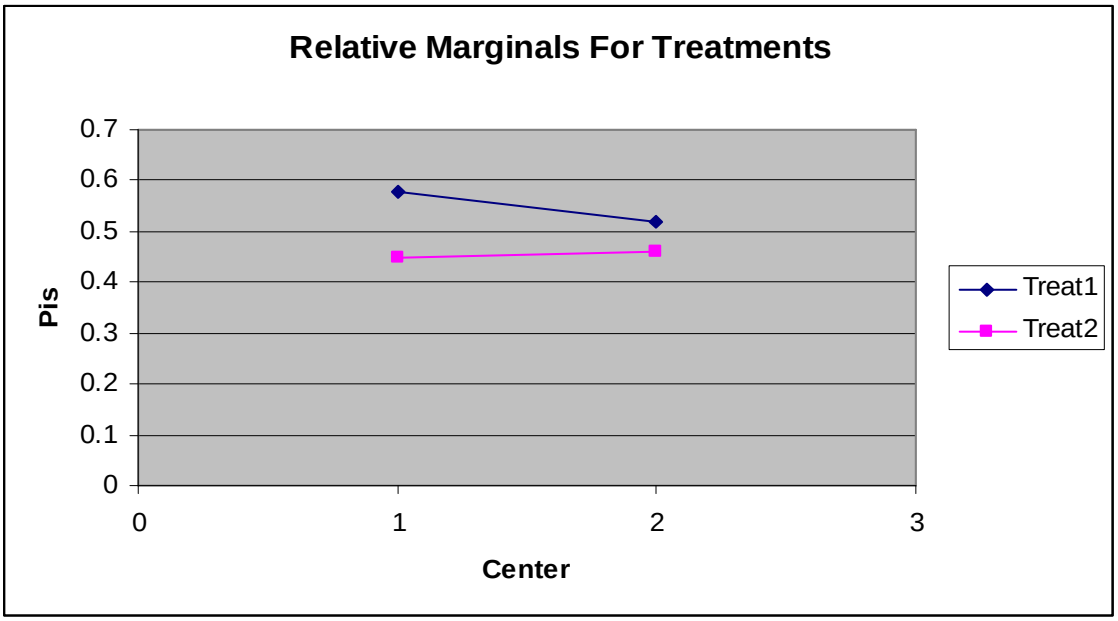

Fig 4.3 Relative Marginal Graph for Treatments using Wilcoxon scores (case 2)

4.2.1. Test Results For case 2

We obtain the test statistics and p-values for the nonparametric main effects and interaction in the above clinical trial. The results of the test statistics obtained by the all the methods used and the resulting p-values are given in the left part. The results obtained by the ATS with the resulting p-values are given in the right part of the table. We simulated our data to be non normal .The parametric approach which assumes the normality of the

underlying distribution should therefore not be appropriate in the analysis of this type of data. We will for comparison however go ahead to use it as one of the methods to analyze our data.

Table 4.9 Test Statistics and p values for main effects and interactions(case 2)

	Wilcoxon Test Results (aW)			
	Wald-Type Statistic		ANOVA-Type Statistic	
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A)$ -treat	3.45	0.0634	3.45	0.0666
$H_O^F(B)$ -center	0.24	0.6238	0.24	0.6250
$H_O^F(AB)$ -treat*center	0.46	0.4963	0.46	0.4980
a_{SR} *Scores Results*				
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A)$ -treat	7.47	0.0063	7.47	0.0074
$H_O^F(B)$ -center	0.82	0.3645	0.82	0.3665
$H_O^F(AB)$ -treat*center	0.85	0.3562	0.85	0.3582

Since our data indicates that F is skewed to the right, we expect that the adaptive procedures will do well under these circumstances.

Table 4.10 Test Statistics and p values for parametric main effects and interaction (case2)

	Type III SS	
Hypothesis	F Value	p-Value
$H_O^F(A)$ -Treatment	0.87	0.3526
$H_O^F(B)$ -Center	0.02	0.8922
$H_O^F(AB)$ -Interaction	0.01	0.9061

4.2.1.1. Wilcoxon Scores Results

The above results are obtained for the Wilcoxon type scores. We obtain the test statistics and p-values for the nonparametric Wilcoxon main effects and interaction in the above simulations. The results of the test statistics obtained by the WTS with the resulting p-values are given in the left part and the results obtained by the ATS with the resulting p-values are given in the right part of the table (table 4.9).

The results show that there is no Interaction effect, no treatment effect and no center effect. So the a_W type scores cannot detect a significant treatment effect (p=0.0666) , cannot detect a significant center effect (p=0.6250) and also cannot detect an interaction effect (p=0.4980)

4.2.1.2. a_{SR} *Scores Results*

We now use the a_{SR} scores (adaptive scores where data is skewed to the right) together with the h_{SR} test statistics to evaluate our data and get results. The results of the test statistics obtained by the WTS with the resulting p-values are given in the left part and the results obtained by the ATS with the resulting p-values are given in the right part of the table.The results show that there is no Interaction effect, but there is a significant treatment effect and no center effect. So the a_{SR} type scores can detect only a significant treatment effect (p=0.0007) while the Wilcoxon cannot detect any effects.

4.2.1.3. Parametric Test Results

We also did a parametric test result for these effects where normality is assumed though our data is non normal, the test statistics show that*, none of the effects (main and interaction) are significant.*

4.2.2. Comparison of Results

. The Wilcoxon and the parametric results do not detect any of the effects as being significant. We will do a comparison test and also compare the lengths of the intervals for the different hypothesis tests together with calculating the power of our test.

4.2.2.1. Power Test and Graphs

Here, we will work on the probability of rejecting the the null hypothesis when the alternative is in fact true. We will compare the power of all three procedures.

Table 4.11 Power Test For All the Test scores (case 2)

Obs	Effect		a_{SR}	a_W	Parametric
1	Treatment	POWER	0.77270	0.45120	0.152
2	Center		0.14641	0.07740	0.052
3	Interaction		0.14991	0.10333	0.052

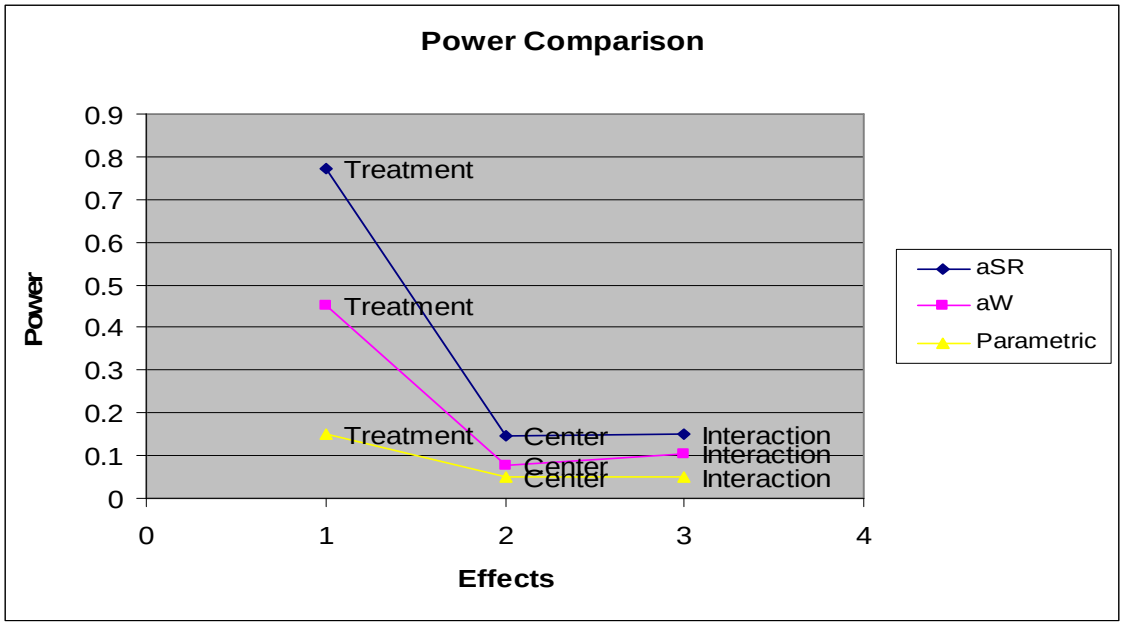

Fig 4.4 Power Comparison For Different Effects (Case 2)

Here, we see that the power for detecting the interaction effect is higher for the adaptive procedure than Wilcoxon and parametric procedures. For the main effects, the adaptive scores have higher powers than the Wilcoxon scores and the parametric method.

4.2.2.2.Confidence Intervals and lengths

Table 4.12 Comparing the CI for different Methods (case2)

Method	*Effect*	*Difference b/w 1 and 2*	*Confidence Limits*		*Length of Interval*
			LL	*UL*	
a_{SR}	*Treatment*	*0.1893*	*0.0519*	*0.327*	*0.2751*
	Center	*0.0628*	*-0.0745*	*0.2001*	*0.2746*
Wilcoxon	*Treatment*	*0.0970*	*-0.0068*	*0.2007*	*0.2075*
	Center	*0.02562*	*-0.0781*	*0.1294*	*0.2075*
Parametric	Treatment	-38.509	-120.22	43.21	163.43
	Center	-5.605	-87.32	76.12	163.44

Here, the parametric procedure perform very poorly with extremely large confidence intervals and confidence lengths. The confidence lengths for the adaptive procedure are slightly larger than those for the Wilcoxon procedure. The Wilcoxon procedure didn't show any main effect significance, so we need to be careful about our conclusions.

Note that the adaptive procedure shows better power values for the main effects and interactions than both the Wilcoxon and parametric methods.

4.3 Case where Data is Skewed to the Left

The data set below was simulated using Monte Carlo simulations. The data was simulated to be non normal. We have the following result:

Table 4.13 Simulated Data For a 2x2 Design (case3)

Center1 Treatment1	Center1 Treatment2	Center2 Treatment1	Center2 Treatment2
236.182	52.734	234.182	22.734
240.208	113.118	238.208	83.118
245.325	189.877	243.325	159.877
245.331	189.963	243.331	159.963
248.931	243.971	246.931	213.971
250.311	264.666	248.311	234.666
251.056	275.836	249.056	245.836
251.114	276.71	249.114	246.71
252.058	290.87	250.058	260.87
252.965	304.471	250.965	274.471
253.016	305.238	251.016	275.238
253.241	308.618	251.241	278.618
253.268	309.018	251.268	279.018
253.527	312.903	251.527	282.903
253.591	313.868	251.591	283.868
253.785	316.771	251.785	286.771
254.043	320.65	252.043	290.65
254.092	321.376	252.092	291.376
254.129	321.93	252.129	291.93
254.254	323.812	252.254	293.812
254.608	329.114	252.608	299.114
254.858	332.866	252.858	302.866
255.025	335.37	253.025	305.37
255.089	336.339	253.089	306.339
255.101	336.513	253.101	306.513
255.14	337.1	253.14	307.1
255.163	337.444	253.163	307.444
255.194	337.911	253.194	307.911
255.202	338.035	253.202	308.035
255.244	338.663	253.244	308.663

We simulated our data to be non normal. The parametric approach which assumes the normality of data should therefore not be appropriate in the analysis of this type of data. For comparison purpose we will however go ahead to use it as one of the methods to analyze our data. Since our data indicates that F is skewed to the left, we expect that the adaptive procedures will do .

Our calculations for skewness and kurtosis based on individual treatment by center type reveals the following results. For skewness, $\overline{Q_1} = 0.099$ and $\overline{Q}_2 = 3.287$. Based on these results, we classify our data as Skewed to the left. Hence, we can use the h_{SL} test statistic with scores a_{SL} . We will also use the Wilcoxon scores and then compare with the parametric analysis where normality is assumed. Rank means $\overline{R_{ij.}}$, i = 1,2; j= 1,2, within the two treatment groups and the two centers as well as the unweighted means $\tilde{R}_{i..}$ within the centers and $\tilde{R}_{.j.}$ within the two treatments are displayed on table 4.15.

Table 4.14 Rank Means and Relative Treatment Effects For Wilcoxon Scores

	Ranks			Relative	Treatment	Effects
Cancer Type	Treat 1	Treat 2	$\tilde{R}_{i..}$	Treat 1	Treat 2	$\tilde{p}_{i.}$
Center 1	50.77	88.30	69.54	0.42	0.73	0.58
Center 2	35.47	67.47	51.47	0.29	0.56	0.43
$\tilde{R}_{.j.}$	43.12	77.89		0.36	0.65	

Here, the average rank for each treatment by center is given and the average of the average rank for each center and each treatment type is also calculated.

For example, the average of the ranks in treatment 1 for those in center 1 is 50.77 while the average rank of those in treatment 2 and center 1 is 8.30.Their average rank (those in center 1) is 69.54.

The relative effects p_{ij} , show a tendency for the marginal distributions of those taking treatment 2 and in center 1 and those taking treatment 2 and in center 2 to lie to the right of the mean distribution H. There is a tendency for all others to lie to the left of the mean distribution

We do a plot of both the Wilcoxon scores and the parametric values (raw means) to get a better picture of what is going on.

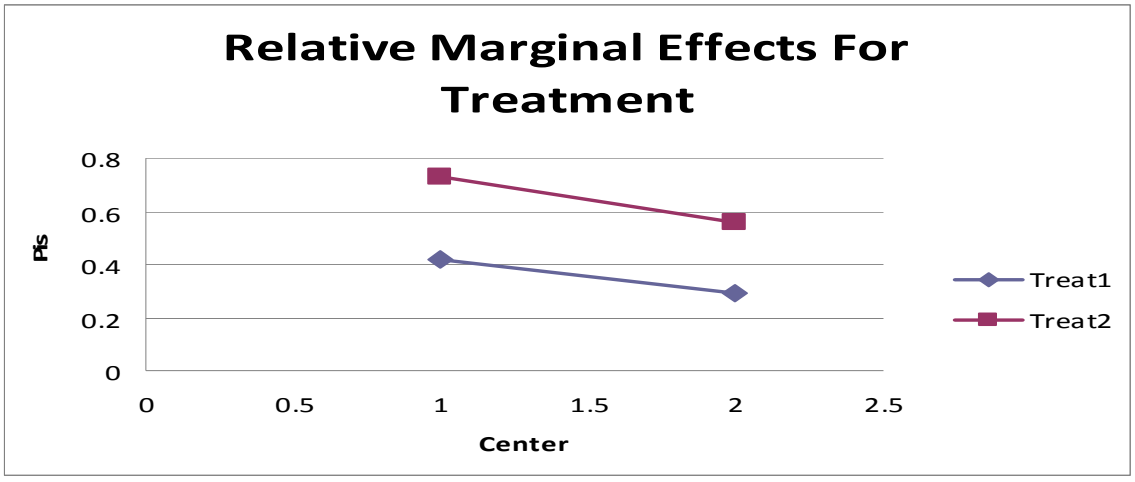

Fig 4.5 Relative Marginal Graph for Different Treatment types using Wilcoxon

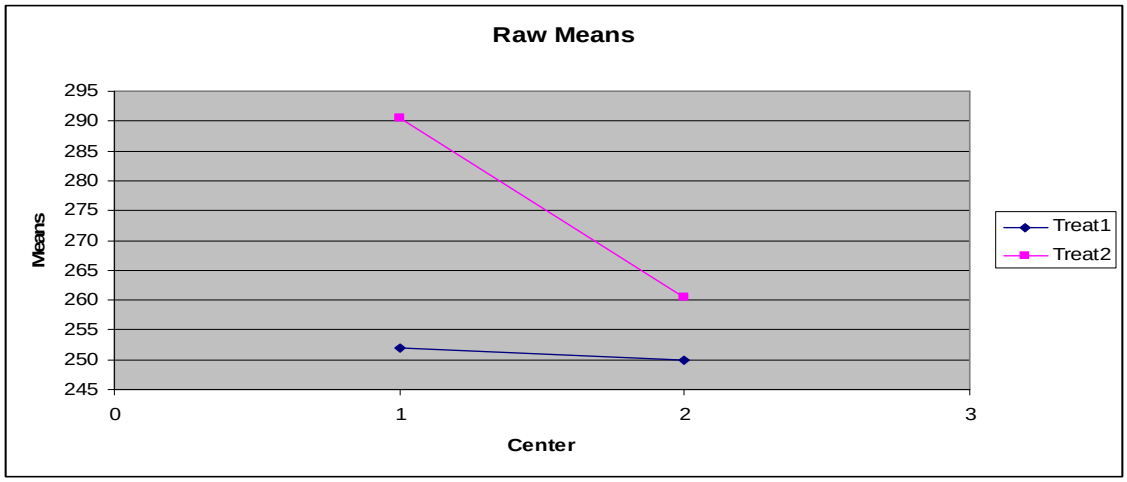

Fig 4.6 Raw Means For simulated Data

4.3.1 .Test Results For case 3

Table 4.15 Test Statistics and p values for main effects and interactions(case3)

Wilcoxon Test Results (aW)				
	Wald-Type Statistic		ANOVA-Type Statistic	
Hypothesis	$Q_N(C)$	p-Value	$F_N(M)$	p-Value
$H_O^F(A)$ -treat	11.63	0.0007	11.63	0.0010
$H_O^F(B)$ -center	43.05	<0.0001	43.05	<0.0001
$H_O^F(AB)$ -treat*center	0.27	0.6016	0.27	0.6030
Adaptive procedure (a_{SL} *-skewed to the left) scores Results*				
$H_O^F(A)$ -treat	3.12	0.0771	3.12	0.0800
$H_O^F(B)$ -center	5.64	0.0176	5.64	0.0193
$H_O^F(AB)$ -treat*center	31.37	<0.0001	31.37	<0.0001

Table 4.16 Test Statistics and p values for parametric main effects and interactions (case3)

	Type III SS	
Hypothesis	F Value	p-Value
$H_O^F(A)$ -Treatment	7.48	0.0072
$H_O^F(B)$ -Center	3.19	0.0767
$H_O^F(AB)$ -Interaction	2.44	0.1208

4.3.1.1. Wilcoxon Scores Results

The results of the test statistics obtained by the WTS with the resulting p-values are given in the left part and the results obtained by the ATS with the resulting p-values are given in the right part of the table above (Table 4.15).

The results show that there is no Interaction effect, but there is a treatment effect and a center effect. So the a_W type scores can detect a significant treatment effect (p=0.0010) and also detect a significant center effect (p< 0.0001) but cannot detect an interaction effect (p=0.6030).

4.3.1.2. a_{SL} Scores Results

We now use the adaptive scores (a_{SL} scores) together with the h_{SL} test statistics to evaluate our data for the case where data is skewed to the left to get results. From table 4.15, the results show that there is a significant

interaction effect (p<0.0001). With a significant interaction effect main effects can be misleading. We will deal more with this under the comparisons section.

4.3.1.3. Parametric Test Results

We also did a parametric test result for these effects where normality is assumed. Note that our data is non normal. Our results show that only the treatment effect is significant (p=0.0072).

4.3.2. Comparison of Results

The Wilcoxon scores detect both main effects as being significant (center p<0.0001 and treatment p=0.0010) but fail to detect any interaction effect. The adaptive procedure detects an interaction effect (p<0.0001) while the parametric procedure detects only a significant treatment effect(p=0.0072). We will do a comparison test and also compare the lengths of the intervals for the different hypothesis tests together with calculating the power of our test.

4.3.2.1. Power Test and Graphs

Here, we will work at the probability of rejecting the null hypothesis when the alternative is in fact true. We will compare the power of all three procedures.

Table 4.17 Power Test For All the Test scores (case 3)

Obs	Effect		a_{SL}	a_W	Parametric
1	Treatment	POWER	0.4177	1.0000	0.774
2	Center		0.6530	0.92041	0.425
3	Interaction		0.9998	0.08099	0.341

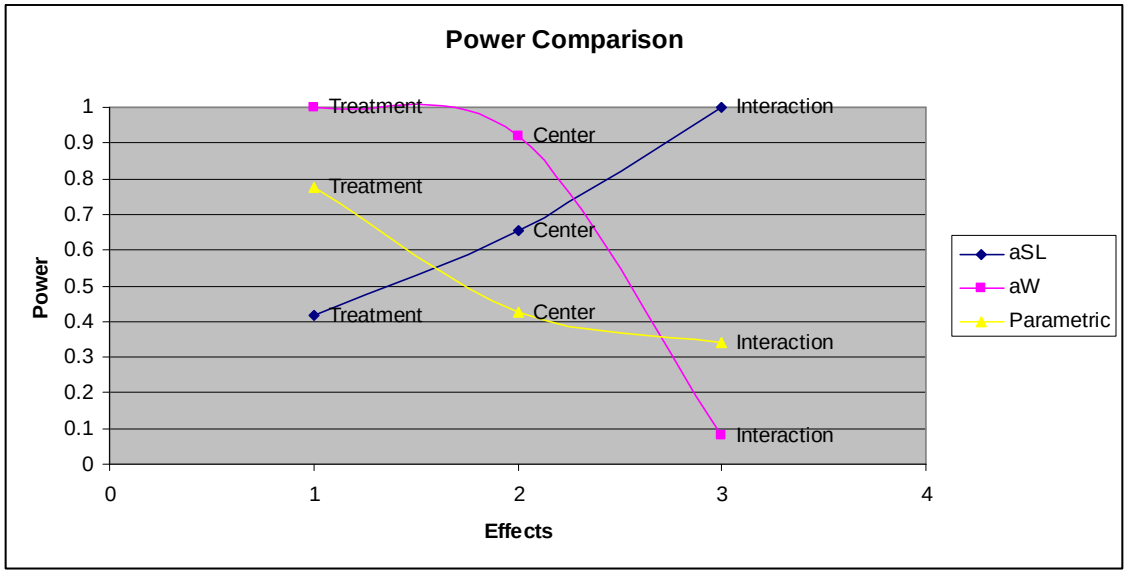

Fig 4.7 Power Comparison For Different Effects

Figure 4.9 shows that adaptive procedure has great power in detecting interaction than the Wilcoxon and parametric procedures.

4.3.2.2.Confidence Intervals and lengths

Since there is an interaction in the a_{SL} *scores case, we will do a comparison of the lengths of the intervals for the various effects. We will then see which of the methods has a shorter interval.*

We can see that from table 4.19 that the adaptive method has shorter estimates for the differences for both the treatment effect and the center effect. *Short intervals are a reflection of high asymptotic relative efficiency (ARE) as pointed out by (Sun 1997). We can therefore conclude that our adaptive procedures here have better ARE than the Wilcoxon and parametric procedures.*

Table 4.18 Comparing the CI for different Methods

Method	*Effect*	*Difference b/w 1 and 2*	*Confidence Limits* *LL*	*UL*	*Length of Interval*
a_{SL}	*Treatment*	*0.04573*	*-0.0056*	*0.097*	*0.1026*
	Center	*-0.06143*	*-0.1127*	*-0.01015*	*0.10255*
Wilcoxon	*Treatment*	*-0.2873*	*-0.3745*	*-0.2002*	*0.1743*
	Center	*0.1493*	*0.0621*	*0.2365*	*0.1744*
Parametric	Treatment	-24.49	-42.23	-6.75	35.48
	Center	16.00	-1.74	33.74	35.48

CHAPTER 5

CONCLUSION

In all three cases, the adaptive methods do really well as compared to the parametric method and the Wilcoxon method. The adaptive method is able to detect effects where the Wilcoxon and parametric are not able to and also the confidence intervals for the adaptive methods are shorter than those of the Wilcoxon. We can therefore improve on the analysis of our data by taking into consideration the skewness and kurtosis of the underlying distribution F and then applying the appropriate adaptive procedure to it.

APPENDIX A

SAS CODES WHEN DATA IS SKEWED TO THE RIGHT

```
data one;
  input obser center treatment score;
  datalines;
DATA,……..
;

 proc means data=one N mean var skewness kurtosis;
var score;
 run;
proc rank data=one out=test1;
var score;
ranks r;
run;
proc sort data=one;
by score;
run;
proc sort data=test1;
by r;
run;
data sR;set test1;
```

```
rnew1=r;
p=floor(0.5*(120+1));
rnewW=rnew1/121;
if rnew1 le p then rnew2=(rnew1-p-0.5)/121;
else rnew2=0.5;
run;
proc print;
proc mixed data=sR ANOVAF;
class center treatment;
model rnew2=center | treatment /chisq ddfm=satterth;
repeated / type=UN(1) Grp=center*treatment ;
lsmeans treatment /pdiff cl;
lsmeans center /pdiff cl;
ods output tests3='F:\Dissertation';
run;

data f_powersR;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
```

```
run;
proc print data=f_powersR;
run;
proc mixed data=sR ANOVAF;
class center treatment;
model rnewW=center | treatment /chisq ddfm=satterth;
repeated / type=UN(1) Grp=center*treatment ;
lsmeans treatment /pdiff cl;
lsmeans center /pdiff cl;
ods output tests3='F:\Dissertation';
run;

data f_powersR;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powersR;
run;
```

```
proc glm data=one;
class center treatment;
model score=center | treatment;
lsmeans treatment/pdiff cl;
lsmeans center/pdiff cl;
run;
proc glmpower data=one;
CLASS center treatment;
MODEL score=center | treatment;
power
    stddev= 225.9886
          ntotal=120
          power=.;
 run;
```

APPENDIX B

SAS CODES WHEN DATA IS SKEWED TO THE LEFT

```
data one;
  input obser center treatment score;
  datalines;
……..
 ;
 proc sort data=one;
 by treatment center;
 run;

proc rank data=one out=test1;
var score;
ranks r;
run;
proc sort data=one;
by score;
run;
proc sort data=test1;
by r;
run;
data W;set test1;
rnewW=r/121;
run;
```

```
data sL;set test1;
rnew1=r;
p=floor(0.5*(120+1));
if rnew1 ge p then rnew2=(rnew1-p+0.5)/121;
else rnew2=0.5;
run;
proc mixed data=sL ANOVAF;
class center treatment;
model rnew2=center | treatment /chisq  ddfm=satterth;
repeated / type=UN(1) Grp=treatment ;
lsmeans treatment /diff cl;
lsmeans center /diff cl;
ods output test3='F:\Dissertation';
run;
data f_powersL;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powersL;
```

```
run;
proc mixed data=W ANOVAF;
class center treatment;
model rnewW=center | treatment /chisq  ddfm=satterth;
repeated / type=UN(1) Grp=treatment*center ;
lsmeans treatment /diff cl;
lsmeans center /diff cl;
ods output test3='F:\Dissertation';
run;

data f_powerW;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powerW;
run;

proc glm data=one;
class center treatment;
```

```
model score=center | treatment;
lsmeans treatment/pdiff cl;
lsmeans center/pdiff cl;
run;


proc glmpower data=one;
CLASS center treatment;
MODEL score=center | treatment;
power
    stddev=49.05778
          ntotal=120
          power=.;
 run;
proc sort data=one;
by score;
run;
```

APPENDIX C

SAS CODES WHEN DATA IS LIGHT-TAILED

```
data hgbds;
  input trt $ type $ patno hgbch @@;
  datalines;
ACT C 1 1.7 ACT C 3 -0.2 ACT C 6 1.7
ACT C 7 2.3 ACT C 10 2.7 ACT C 12 0.4
ACT C 13 1.3 ACT C 15 0.6 ACT P 22 2.7
ACT P 24 1.6 ACT P 26 2.5 ACT P 28 0.5
ACT P 29 2.6 ACT P 31 3.7 ACT P 34 2.7
ACT P 36 1.3 ACT R 42 -0.3 ACT R 45 1.9
ACT R 46 1.7 ACT R 47 0.5 ACT R 49 2.1
ACT R 51 -0.4 ACT R 52 0.1 ACT R 54 1.0
PBO C 2 2.3 PBO C 4 1.2 PBO C 5 -0.6
PBO C 8 1.3 PBO C 9 -1.1 PBO C 11 1.6
PBO C 14 -0.2 PBO C 16 1.9 PBO P 21 0.6
PBO P 23 1.7 PBO P 25 0.8 PBO P 27 1.7
PBO P 30 1.4 PBO P 32 0.7 PBO P 33 0.8
PBO P 35 1.5 PBO R 41 1.6 PBO R 43 -2.2
PBO R 44 1.9 PBO R 48 -1.6 PBO R 50 0.8
PBO R 53 -0.9 PBO R 55 1.5 PBO R 56 2.1

;
```

```
proc freq data=hgbds;
tables type*trt;
run;
proc print;
run;

proc rank data=HGBDS out=test3;
var HGBCH;
ranks r;
run;

proc sort data=HGBDS;
by HGBCH;
run;
proc sort data=test3;
by r;
run;
data L;set test3;
rnew1=r;
rnewW=rnew1/49;
```

```
p=floor(0.25*49);
q=49-p;
if rnew1 le p then rnew2=(rnew1-p)/49;
else if rnew1 ge q then rnew2=(rnew1-48+p)/49;
else rnew2=0.0;
run;
proc print;
data ML;set test3;
rnew1=r;
p=floor(0.25*49);
q=49-p;
if rnew1 le p then rnew2=(-(rnew1-p)**2)/(49*49);
else if rnew1 ge q then rnew2=((rnew1-48+p)**2)/(49*49);
else rnew2=0;
run;

proc mixed data=L ANOVAF;
class TRT TYPE ;
model rnew2=TRT TYPE TRT*TYPE /chisq  ddfm=satterth;
repeated / type=UN(1) Grp=trt ;
lsmeans trt /ADJUST=SCHEFFE  Pdiff cl;
lsmeans type /ADJUST=SCHEFFE Pdiff cl;
```

```
ods output tests3='F:\Dissertation';
run;
data f_powerL;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powerL;
run;
proc mixed data=ML ANOVAF;
class TRT TYPE ;
model rnew2=TRT TYPE TRT*TYPE /chisq solution ddfm=satterth;
repeated / type=UN(1) Grp=trt ;
lsmeans trt /ADJUST=SCHEFFE Pdiff cl;
ods output tests3='F:\Dissertation';
run;
data f_powerML;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
```

```
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powerML;
run;
proc mixed data=L ANOVAF;
class TRT TYPE ;
model rnewW=TRT TYPE TRT*TYPE /chisq solution ddfm=satterth;
repeated / type=UN(1) Grp=trt*type ;
lsmeans trt /ADJUST=SCHEFFE Pdiff cl;
ods output tests3='F:\Dissertation';
RUN;

run;
data f_powerW;
set 'F:\Dissertation';
Noncen =NumDF*Fvalue;
Alpha=0.05;
FCrit=finv(1-Alpha,NumDF,DenDF,0);
Power=1-probf(FCrit,NumDF,DenDF,Noncen);
run;
proc print data=f_powerW;
```

```
run;
PROC GLM DATA=HGBDS;
CLASS TRT TYPE;
MODEL HGBCH=TRT TYPE TRT*TYPE/SS3  ;
LSMEANS TYPE/ ADJUST=SCHEFFE PDIFF  STDERR;
LSMEANS trt/pdiff cl;

RUN;

proc glmpower data=HGBDS;
CLASS TRT TYPE;
MODEL HGBCH=TRT TYPE TRT*TYPE;
power
    stddev=1.132672
          ntotal=48
          power=.;
 run;
RUN;
```

APPENDIX D

MONTE-CARLOS CODES

(1)

```
data A (type=corr); _type_='corr';
  input x1-x2;
cards;
1.00 .
.70 1.0
;
proc factor N=2;
run;
```

(2)

```
proc iml;
skewkurt={2 1,
          .5 0,
         -2.25 1,
          3 0.5};
start Newton;
    run Fun;
  Do ITER=1 to MAXITER
    while (Max(ABS(F))>converge);
```

```
    run DERIV;
    Delta=-SOLVE(J,F);
    COEF=COEF+DELTA;
    run FUN;
  END;
Finish Newton;
Maxiter=25;
converge=.000001;
Start Fun;
X1=COEF[1];
x2=COEF[2];
X3=COEF[3];
 F=(X1**2+6*X1*X3+2*X2**2+15*X3**2-1)//
   (2*X2*(X1**2+24*X1*X3+105*X3**2+2)-SKEWNESS)//
   (24*(X1*X3+X2**2*(1+X1**2+28*X1*X3)+X3**2*
   (12+48*X1*X3+141*X2**2+225*X3**2))-KURTOSIS);
FINISH FUN;
START DERIV;
 J=((2*X1+6*X3) || (4*X2) || (6*X1+30*X3))//
   ((4*X2*(X1+12*X3))||(2*(X1**2+24*X1*X3+105*X3**2+2))
```

```
   ||((4*X2*(12*X1+105*X3)))//
    ((24*(X3+X2**2*(2*X1+28*X3)+48*X3**3))||
    (48*X2*(1+X1**2+28*X1*X3+141*X3**2))||
         (24*(X1+28*X1*X2**2+2*X3*(12+48*X1*X3+141*X2**2+225*X3**2)+X3*
*2*(48*X1+450*X3)))));
FINISH DERIV;
DO;
NUM= NROW(SKEWKURT);
DO VAR=1 TO NUM;
  SKEWNESS=SKEWKURT[VAR,1];
  KURTOSIS=SKEWKURT[VAR,2];
  COEF={1.0,0.0,0.0};
  RUN NEWTON;
  COEF=COEF`;
  SK_KUR=SKEWKURT[VAR,];
  COMBINE=SK_KUR || COEF;
  IF VAR=1 THEN RESULT=COMBINE;
  ELSE IF VAR>1 THEN RESULT=RESULT // COMBINE;
END;
```

```
  PRINT "COEFFICIENTS OF B, C, D FOR FLEISHMAN'S POWER
TRANSFORMATION";
  PRINT "Y=A+BX+CX^2+DX^3";
  PRINT "A=-C";
  MATTRIB RESULT COLNAME=({SKEWNESS KURTOSIS B C D})
              FORMAT=12.9;
  PRINT RESULT;
END;
QUIT;
proc iml;
```

(3)

```
Proc iml;
F={    0.92195        0.38730,
       0.92195       -0.38730};
Data=rannor(J(30,2,0));
data=data`;
z=F*data;
```

```
z=z`;
x1= -4.005524770+-4.154782459*z[,1]+4.005524770*z[,1]##2+-
0.849299806*z[,1]##3;
x11=x1*15+130;
x12=x1*30+160;
X21=X1*18+130;
X22=X1*32+170;
z=x11||X12||X21||X22;
create A from Z [Colname={x11 X12 X21 X22}];
append from z;

proc means data=A N mean var skewness kurtosis;
var x11 X12 X21 X22;
data one; set A;
if x11 then center=1 ;
run;

proc print;
run;
```

REFERENCES

[1] M. Akritas, E. Brunner, A unified approach to rank tests for Mixed models, J. Statist. Plan. and Infer. 61 (1997) 249-277

[2] D. Boos, C. Brownie, A Rank based mixed model approach to multiclinical trials. Biometrics 48 (1992) 61-72

[3] E. Brunner, S. Domhof, F Langer, Nonparametric Analysis of longitudinal Data in Factorial Experiments, Wiley series (2002)

[4] E.Brunner, M. Puri , Nonparametric Methods in Factorial Designs

[5] E. Brunner, U. Munzel, M Puri, Rank-Score tests in Factorial Designs with repeated Measures, J. Multiva. Analys. 70 (1999) 286-317

[6] E. Brunner, M. Puri, A class of rank-score tests in factorial designs, J. Statist. Plan. And infer. 103 (2002) 331-360

[7] E. Brunner, M. Puri,S Shan , Nonparametric Methods for Stratified two-Sample Designs with Application to Multiclinic Trials, J. Amer. Statist Assoc. 90 (1995) 1004-1014

[8] V. Elteren, On the Combination of Independent Two sample tests of Wilcoxon

[9] X. Fan, A. Felsovalyi, S. Sivo, S. Keenan, SAS for monte Carlo Studies, SAS press (2001)

[10] J. Fleiss, Analysis of Data from Multiclinic Trials , Cont. Clinic. Trials , 7 (1986) 267-275

[11] X. Gao, M. Alvo, A Non parametric test for Interaction in Two-way Layouts, Canad. J. of Statist. , 33 (2005) 529-543

[12] N.J. Hill, A.R. Padmanabham, M. Puri, Adaptive Nonparametric Procedures and Applications, Appl. Statist. 37 (1988) 205-218

[13] R. Hogg, D. Fisher, R. Randles, A two-sample adaptive distribution-free test, J. Amer. Statist. Assoc. 70 (1975) 656-661

[14] E. Lehmann, Nonparametrics Statistical methods based on Ranks, Springer (1975).

[15] Ramon Little and al, SAS for Mixed Models, SAS press, (2008)

[16] G. Mack, J. Skillings, A Friedman-type rank test for main effects in a two-factor ANOVA , J. Amer. Statist. Assoc. 75 (1980) 947-951

[17] K.M. Patel, D.G Hoel, A nonparametric Test for interaction in Factorial Experiments, J. Amer. Stat. Assoc. 68 (1973) 615-620

[18] S. Shan , A class of adaptive distribution-free procedure, J. Statist. Plan. and infer. 59 (1997) 191-211

[19] K. Thangavelu, E. Brunner , Wilcoxon-Mann-Whitney test for stratified sample and Efron's paradox dice, J. Statist. Plan. And Infer. 137 (2007) 720-737

[20] G. A. Walker, Common Statistical methods For Clinical Research with SAS Examples, SAS press, (2002)

BIOGRAPHICAL INFORMATION

Richard Ferim was born in Cameroon in West Africa. After completing his undergraduate education in Cameroon, he moved to the United States in 1998. Richard took a lot of computer certification programs including CISCO and Unix and worked for McGraw Hills Companies as a Computer Operator. In 2003 after being laid off, Richard returned to continue his Masters in Numerical Analysis. After his Masters, he made the switch to statistics because he thought it is a much more applicable field. He completed his PhD in Mathematical Sciences (with focus in Statistics) at the University of Texas at Arlington under the direction of Professor Shan Sun-Mitchel.