

 \sim

A STATISTICAL RANK TEST FOR ANALYSING BIOMEDICAL

DATA

Ву

ROBERT ALEXANDER MAGEE, R.T., B.Sc.

A Thesis

Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements

> for the Degree Master of Science

McMaster University

August 1976.

ROBERT ALEXANDER MAGEE 1977

С

MASTER OF SCIENCE (1976) (Health Sciences)

TITLE: A Statistical Rank Test For Analysing Biomedical Data

AUTHOR: Robert Alexander Magee R.T. (Canadian Society of Laboratory Technologists) B.Sc. (McMaster University) ** ****

SUPERVISOR: Dr. Charles W. Dunnett

NUMBER OF PAGES: xiii, 141

ABSTRACT

In the analysis of biomedical data, a question commonly asked by researchers involves the determination of the "best" or "worst" member of a group of results and an associated measure of the probability that this member is the "best" or "worst". Commonly, analysis of variance is suggested as the test of choice. Unfortunately, this test does not exactly answer the original question and further testing must be done to satisfy the question completely. This thesis presents a non-parametric rank test which directly answers the question of "best" or "worst".

Before applying this test to biomedical problems, the probability tables associated with this test are expanded and the methods used are presented and discussed. An analogous parametric test is then described and compared in performance with the non-parametric test throughout the remainder of the thesis. Power curves for both the nonparametric and parametric test are developed for several population distributions and the results compared. The three areas of application are; chromosome frequencies in the culture of human melanoma tissue; scoring patterns among evaluators of letters of applications to medical school; and the determination of outliers when relating

iii

vital capacity to ventilatory response.

It was found that except for cases where the number of objects was less than 10, the parametric test has equal or greater power than the non-parametric test when analysing continuous data, regardless of the population distribution. For less than 10 objects, the non-parametric test had greater power regardless of population distribution. Subsequent to analysis in the three areas cited, it was concluded that the two tests agreed very highly in selecting extreme deviates although the non-parametric test was consistently more conservative in its probability measure. The problem of ties was found to weaken the power of the non-parametric test as did the ranking procedure itself but its ease of application and superior power with small sample sizes is a distinct advantage. The robustness of the parametric test is obvious throughout the examples. Α method of selecting data values which are second or third most extreme was tested and it became obvious that the data must be displayed to show its distributional characteristics before this type of analysis could be carried out or interpreted.

iv

ACKNOWLEDGEMENTS

First of all, I would like to thank Dr. Charles Dunnett for suggesting this topic and for being my supervisor. Without his support and helpful suggestions, this thesis could not have been written. Dr. Stephen Leeder and Mrs. Ruth Milner, both read this document several times, and their insight and constructive criticisms were greatly appreciated. I am also greatful for the information supplied by Dr. Peter McCullogh which is presented in Chapter IV, and for the respirology data supplied by Dr. John Rigq, which appears in Chapter VI. Dr. Barbara Ferrier and Mr. Fred Bradly allowed me to collect information from the Medical School Admissions Office which was used in Chapter V, and I appreciate this very much.

Last, but certainly not least, I would like to thank Mr. Donald Gilchrist of the Computational Services Unit for supplying the computing facilities and to Mrs. Linda Teiml who typed this thesis and drew most of the figures at least twice.

TABLE OF CONTENTS

۱

t ∳

4 1 1

Ι.	INTR	ODUCTION	
	1.1	Aims	1
L.	1.2	Relevance	1
	1.3	Thesis Format	3
	1.4	Research Questions	3
			-
II	REVI	EW OF LITERATURE RELATING TO EXTREME VALUE ANA	LYSIS
	2.1	Development of Extreme Value Analysis	4
	2.2	Nair's Test	7
	2.3	Youden's Test	ıo
	2.4	Current Approaches to Extreme Value Analysis	in
		the Biomedical Sciences	14
III	THE	EXPANSION OF TABLES FOR YOUDEN'S TEST FOR THE	
	EXTR	EME DEVIATE	
	3.1	Introduction	16
	3.2	Techniques for Generating Tables of One-Sided	
		Percentage Points	17
		3.2.1 Introduction	17
		3.2.2 Exhaustive Enumeration	17
		3.2.3 A Probability Generating Function for	•
		the Case $I = 2$	21

vi

	3.2.4	Approximation Using an Iterative	
		Procedure Based on Bonferroni's	
		Inequalities	24
	3.2.5	Approximation by a Normal Distribution	
		for Large J	26
	3.2.6	Approximation by a Uniform Distribution	L
	•	for Large I	28
3.3	The Con	nparison of Youden's Test and Nair's	
	Test		29
	3.3.1	Introduction	29
	3.3.2	A Comparison of Power Curves Derived	
		from a Simulation of Normally Distribu-	
		ted Data	33
	3.3.3	A Comparison of Bias Detection in Non-	
	-	normally Distributed Data-	36
	3.3.4	A Comparison of Bias Detection in Non-	
		normally Distributed Data with Differin	g
	•	Variances	39
AN AI	NALYSIS	OF CHROMOSOMAL CHARACTERISTICS OF HUMAN	I
MELA	NOMA	•	
4.1	Introdu	iction	42

6

IV

ł

4.2	Description of the Data		44
4.3	Analysis and Results		44
4.4	Conclusions	•	49

vii

V AN ANALYSIS OF SCORING PATTERNS AMONG EVALUATORS OF LETTERS OF APPLICATION TO MEDICAL SCHOOL

5.1	Introduction	51
5.2	Description of the Data	53
5.3	Analysis and Results	56
5.4	Conclusions	68

VI THE DETERMINATION OF OUTLIERS IN A STUDY OF VENTILATORY RESPONSE TO CHANGES IN OXYGEN AND CARBON DIOXIDE CONCENTRATION

6.1	Introduction	70
6.2	Description of the Data	74
6.3	Analysis and Results	77
6.4	Conclusions	87

VII DISCUSSION AND CONCLUSIONS

7.1	Introd	uction			90
7.2	Resear	ch Questic	ons		90
	7.2.1	Research	Question	1	9 Q
	7.2.2	Research	Question	2	92
	7.2.3	Research	Question	3	93
7.3	Conclu	sions			95

REFERENCES

- 96

è

viii

APPENDIX A -

Tables Of One-Sided Percentage Points at Nominal Levels of 1, 3, 5 and 10%.

100

127

man and manage as a set of a star

APPENDIX B - Computer Program Documentation 126

- B.1 A FORTRAN program for calculating one-
- sided percentage points for Youden's test by exhaustive enumeration using both Lehmer's method and Well's method of combinatoric enumeration.
- B.2 A FORTRAN program for calculating onesided percentage points for Youden's test in the case of I = 2. This program is based on the binomial theorem. 130
- B.3 A FORTRAN program for calculating onesided percentage points for Youden's test.
 This program uses an iterative procedure based on Bonferroni's inequalities.
- B.4 A FORTRAN program for generating power
 curves for Nair's test and Youden's test under
 specified parent population assumptions.
 B.5 A FORTRAN program for analysing data
- B.5 A FORTRAN program for analysing data
 organized in a two-way classification by
 Youden's test and Nair's test.
 138

ix

LIST OF TABLES AND FIGURES

í

1

2.1	Analysis of Variance for Example 1.	9
2.2	Quality Control Results of Four Laboratories on	-
	Six Unknowns	12
2.3	Quality Control Results of Four Laboratories on	
	Six Unknowns (Modified)	14
3.1	A Mapping of Techniques to Youden's Table of One-	
	Sided Percentage Points	18
3.2	A Comparison of Critical Values Between Tabled	
	Values and the Normal Approximation for $J = 25$	27
3.3	A Comparison of Critical Values Between Tabled	
	Values and the Uniform Approximation for $I = 25$	30
3.4	Power Curves for Nair's and Youden's Tests Based	
	on Normally Distributed Data	34
3.5	Power Curves for Nair's and Youden's Tests Based	
	on Uniformly Distributed Data	37
3.6	Power Curves for Nair's and Youden's Tests Based	
	on Uniformly Distributed Data with Variable	
	Variance	40
4.1	Total Number of Normal Chromosomes Found in 10	
	Cells at Metaphase for Each of the Eight Selected	
	Strains of Melanoma	45

х

{	4.2	The Distribution of Rank Sums for all Chromosomes	
Ĺ		in the Melanoma Data	46
,	4.3	Analysis of Melanoma Data for Extreme Deviate	
		Chromosome Counts, Using Youden's and Nair's	
		Tests	47
	4.4	Analysis of Variance for Melanoma Data	48
	5.1	Total Scores on Five Control Letters Given by	
Å	1	Teams and Reader Types	54.
K ^a .↓	5.2	Mean Scores [,] for Each Team Based on All Letters	
		Read	55
`	5.3	Frequency of Total Scores for 5 Control Letters by	
	~ *	Type of Reader	58
,	5.4	Maximum and Minimum Extreme Deviates in the Three	
, 4		Types of Readers (Mean Scores)	59
۰ ۲	5.5	Absolute Differences Between Group Total and	
		Individual Total by Reader	60
	5.6	Frequency of Total Absolute Differences from	•
	,	Group Mean for 5 Control Letters by Type of	
		Reader	61
,	5.7	Maximum and Minimum Extreme Deviates in the Three	
· ·		Types of Readers (Absolute Differences from the	•
•	•	Group Mean)	62
4	5.8	Frequency of Total Scores for 5 Control Letters	•
_	• ` ·	(All Teams)	64
<i>.</i>	<u>ر</u> • ر		
	• • •		

ŵ

t

xi

5.9	Maximum and Minimum Extreme Deviates in Reading	
	Teams (Mean Scores)	64
5.10	Frequency of Total Absolute Differences from Group	
	Mean for 5 Control Letters (All Teams)	65
5.11	Maximum and Minimum Extreme Deviates in Reading	
	Teams (Dispersion About the Group Mean)	65
5.12	Frequency of Mean Team Scores for All Letters	66
5.13	Frequency of Absolute Differences from the Grand	
	Mean for all Letters, by Team	66
5.14	Summary of Teams, Showing Extreme Deviance Control	
	Letter Data and Comparison with All Letter Data	67
6.1	Rate of Ventilatory Change due to Decreasing O_2	
0	and Fixed CO ₂ Concentrations Plotted Against Vital	
	Capacity	73
6.2	Data Collected to Show Change in Ventilatory	
	Response with Changing O_2 and CO_2 Concentrations	76
6.3	Rate of Ventilatory Change Due to Decreasing O_2	_
	and CO ₂ Concentrations Plotted Against Vital	
	Capacity	78
6.4	Rate of Ventilatory Change Due to Increasing CO ₂	
	and Fixed O2 Concentrations Plotted Against Vital	
	Capacity	78
6.5	Extremeness Values and Associated Rankings for the	
	Eight, Subjects by the 3 Measures of Ventilatory	
	Response when Regressed Against Vital Capacity	80

xii

ł

6.6 Rate of Ventilatory Change Due to Decreasing 02 and CO, Concentrations Plotted Against Change in 81 Frequency of Respirations Rate of Ventilatory Change Due to Decreasing 0, 6.7 and Fixed CO, Concentrations Plotted Against 81 Change in Frequency of Respirations Rate of Ventilatory Change Due to Fixed O_2 and 6.8 Increasing CO₂ Concentrations Plotted Against Change in Frequency of Respirations 82 Extremeness Values and Associated Rankings for 6.9 the 8 Subjects by the 3 Measures of Venilatory Response when Regressed Against Change in 83 Frequency of Breathing 6.10 Rate of Ventilatory Change Due to Decreasing 02 and CO, Concentrations Plotted Against Change 84 in Tidal Volume 6.11 Rate of Ventilatory Change Due to Decreasing O2 and Fixed CO, Concentrations Plotted Against Change in Tidal Volume 84 6.12 Rate of Ventilatory Change Due to Fixed 0, and Increasing CO₂ Concentrations Plotted Against 85 Change in Tidal Volume 6.13 Extremeness Values and Associated Rankings for the 8 Subjects by the 3 Measures of Ventilatory Response when Regressed Against Tidal Volume

xiii

CHAPTER I

INTRODUCTION

1.1 Aims

The aims of this thesis are: -

a) to introduce the idea that many of the problems in the biomedical sciences which are evaluated by analysis of variance can be more successfully analysed by a technique which measures the deviation of the most extreme member of the group from the others;

b) to expand the capabilities of an existing nonparametric technique which measures the deviation of the most extreme member of the group from the others and to compare it with its parametric analog;

c) to show how these tests may be used to analyse various types of biomedical data.

1.2 <u>Relevance</u>

Biomedical researchers are often faced with the problem of determining which of several treatments is "best". Another problem which appears to be unrelated to the selection of "best", is the determination of outliers. These two problems require the researcher to determine the probability that the "best" or most extreme result is dif-

ferent from all the other results in the experiment. Often, a two way analysis of variance is performed with the assumption that the data are normally distributed and that the results will reflect, at least in part, how significantly the best or most extreme member of the data deviates The assumption of normality from the other data values. with respect to biomedical data can at times be very risky and, while statistical methods based on normally distributed data are quite robust, an appropriate non-parametric test should be used in those situations where the data are known to be non-normal. The use of analysis of variance to answer the question of which value is most extreme is not particularly useful. If the extreme data value is not significantly extreme, and the data are approximately normally distributed and all from the same population, then analysis of variance will answer the question regarding extremeness. If, on the other hand, there exists a significantly extreme data value, then traditional analysis of variance would be unable to determine a significance level for this deviant result.

This thesis presents two statistical tests, one parametric and the other non-parametric, which have been developed specifically to solve problems of selecting the most extreme data value in the context of a two way classification of data.

1.3 Thesis Format

The first part of this thesis discusses the need for, and the general approach to extreme value analysis in the biomedical sciences. Also, a general description of the historical development of extreme value analysis is presented and two particular tests are described in detail.

The second part is concerned with the expansion of the non-parametric test for the extreme deviate and a comparison with the parametric analog. The third part presents a detailed analysis of three problems in the biomedical sciences using these methods. The thesis ends with a discussion of the research questions and several general conclusions.

1.4 Research Questions

The following research questions were posed.

 What types of data are most suitable for analysis by the non-parametric test?

2. Under what conditions is the parametric test superior to the non-parametric test?

3. Is it beneficial to use the non-parametric test to determine second or even third most extreme deviates?

3

1

CHAPTER II

REVIEW OF LITERATURE RELATING TO EXTREME VALUE ANALYSIS

2.1 The Development of Extreme Value Analysis

The distant beginning of extreme value analysis is Student's t-test. Here the objective is to determine whether the difference between, say, the number of post-operative infections in two comparable groups of patients is indicative of a true difference in treatments or if the difference is the result of pure chance. A test statistic "t" determined such that, in the absence of a true treatment effect, the Studentized difference will exceed t with a probability of α . Student's t test may not be valid when the data are not normally distributed. This has led to the development of distribution-free methods of assessing the significance of differences between two data sets. The Wilcoxon two sample and paired tests being strong competitors of the t-test for this purpose.

The next level of complexity leads to the comparison of means of several samples. The F-test (one way analysis of variance) provides a test of the equality of several treatment means. The analogous non-parametric method for a one way classification has been developed by

Kruskal and Wallis (1952). The F-test is also useful in a two way classification and the analogous non-parametric methods are Friedman's χ^2 . (Friedman, 1937) and Kendall's concordance coefficient W (Kendall, 1948).

At times it is not sufficient to determine whether the null hypothesis of equal treatment means has been rejected, but it is also necessary to identify which treatment mean leads to the rejection of the null hypothesis. An approach to answering this question is as follows: in scanning the results of an experiment, one's attention will naturally be drawn to the largest contrasts and the smaller ones will not be examined. This may be stated in the following way: what value will be exceeded by a sample contrast with a prescribed conditional probability, the condition being that the contrast was large enough to attract attention in the first place from among a defined set of contrast effects? Techniques which attempt to formulate and answer this question are known as multiple comparison methods. Nemenyi (1963), in his thesis, surveyed the entire subject of distribution free multiple comparisons, providing a comprehensive list of techniques and sample computations for each. He partially expanded several tables of probability values for some of the tests, but individual methods were not examined in detail.

Extreme value analysis is one type of multiple comparison analysis, and is synonymous with "outlier stati-

stics" and "slippage measures".

The Studentized maximum absolute deviate introduced by Halperin et al (1955) is a multiple comparison test used in extreme value analysis. It is a normal theory statistic for one and two way classifications, which may be used to augment the F-test in determining which treatment has a mean different from the rest. A one tailed version of this test has also been developed by Nair (1948). The non-parametric extreme value rank sum test proposed by Doornbos-Prins (1958) and Youden (1960) and developed by Thompson-Willke (1963) and Willke (1964) can be used to augment Friedman's χ^2 or Kendall's concordance coefficient in the same way, but only for a two way classification. A non-parametric extreme value rank sum test which deals with a one way classification has been proposed by Odeh (1967) and developed by MoDonald and Thompson (1967).

In a logical and chronological sense, statistical methods for the analysis of variance have developed from the simple t-test to the F-test and finally to a technique for selecting extreme values. Tests based on normal distribution theory and comparable distribution free methods have developed in parallel. The following two sub-sections will describe Nair's test and Youden's test and will serve as background to the remainder of the thesis.

2.2 Nair's Test

Let x_1, x_2, \ldots, x_k be independent normally distributed variates, each with mean μ and variance σ^2 . Denote the ordered values of the above variates as y_1, y_2, \ldots, y_k ; then the Nair statistics may be defined as

$$d = \frac{y_k - \overline{y}}{s_v} \text{ or } \frac{\overline{y} - y_1}{s_v} ; \overline{y} = \sum_{i=1}^k (y_i) / k$$

where s_v is the sample estimate of σ based on v degrees of freedom and the two expressions provide for the choice of either upper or lower tail for a one tailed test.

The following two examples have been taken from Nair (1948) but the setting has been altered in keeping with the biomedical nature of this thesis.

Example 1.

A randomized block experiment has been designed to select the best of four bacteriocidal methods for purifying drinking water. Five replications gave the following mean bacteria counts per 100 ml. for the methods A; B, C and D

А	В	С	D
34.4	34.8	33.7	28.4

and an error variance of $\sigma^2 = 2.19$ based on 12 d.f. Despite the similarity of the first three means, an analysis of variance (Table 2.1) showed significant differences among the four means.

The variance ratio F for treatments against error is 44.82/2.19 = 20.5 which is much larger than $F_{0.001} = 10.8$. Nair points out that while the large F value is probably attributable largely to the small mean associated with method D, a test of significance of the difference between 28.4 and the mean of 34.4, 34.8 and 33.7 by the usual t-test

$$t = \frac{34.3 - 28.4}{\sqrt{(2.19(1/15 + 1/5))}} = 7.7 ,$$

with 12 degrees of freedom is probably not valid as 28.4 has been selected as the smallest mean instead of being selected at random. The appropriate criterion in this case is the Studentized extreme deviate used by Nair as follows

$$\frac{x-x_1}{s_v} = \frac{32.8-28.4}{\sqrt{1/5}\times 2.19} = 6.7$$

with n = 4 and v = 12. Referring to Hartley and Pearson

(1969) Vol. 1, Table 26 we find that this value far exceeds the critical value at $\alpha = 0.001$ which is 4.1.

Source of Variation	Degrees of Freedom	Sum of Squares	Variance
Replications	4	21.46	5.36
Methods	3	134.45	44.82
Error	12	26.26	2.19
Total	19	182.17	-

Table 2.1

Analysis of Variance for Example 1

Having concluded, by the above procedure, that the smallest mean 28.4 is significantly smaller than the other three means, we are justified in saying that method D is definitely superior to A, B and C.

Example 2.

This is artificially created from example 1 by changing the error variance from 2.19 to 13.00. An error variance of 13.00 gives a standard error per replication of 11% which is high but not unrealistic for this type of procedure. The variance ratio for methods against error is F = 44.82/13.00 = 3.45 which is not significant at the 5% level. One obviously concludes, therefore, that there are

no significant differences among the means of the four procedures A, B, C and D.

But, if we compare the smallest mean against the general mean and calculate the studentized extreme deviate

$$\frac{\bar{x} - x_1}{s_{11}} = \frac{32.8 - 28.4}{\sqrt{1/5 \times 13.00}} = 2.7$$

we find that the probability of getting this or a larger value when n = 4, v = 12 lies between 2.5% and 1%. On the 2.5% level, therefore, 28.4 is significantly smaller than the general mean, indicating that D is superior to A, B, and C. Although this situation was contrived, the possibility of its actual occurrence is real, and care should therefore be taken in using the F test as a screening procedure for the detection of extreme deviation.

2.3 Youden's Test

Youden's extreme rank sum test is the non-parametric analogue of Nair's test and is described by Thompson and Willke (1963) as follows. Let I objects be ranked independently by each of J judges and let r_{ij} denote the rank of object i assigned by judge j. Place r_{ij} in the ith row of the jth column of a table of ranks. Each column of this table will contain a permutation of the first I integers.

.

Let $r_i = \sum_{i=1}^{n} r_{ij}$ denote the sum of the j ranks for the ith object. These rank sums will be our test statistics. Note that $\bar{r} = [r_i/I] = J(I+1)$. The null hypothesis to be tested, is that the ranks are assigned at random by each of the judges. More precisely: H_0 : for each judge, every one of the I! permutations of the ranks is equally likely. If H_0 is true, then $r_1, \ldots r_T$ are identically, but not independently, distributed with expectations \bar{r} , and the marginal distribution of each rank sum is symmetric about r. If, however, one of the objects tends to rank higher (or lower) than the others, then all permutations are not equally likely, and the distribution of the rank sum for that object will be skewed accordingly. Hence the rejection region for the test is taken to be the event that at least one rank sum occurs which is extreme enough to be unlikely under H₀. Example 1.

Four different hospital laboratories have been collaborating on a quality control program. The results shown below indicate the values obtained by each hospital analysing for a particular constituent in each of six unassayed controls labelled, A, B, C, D, E and F. It is required to know whether any of the labs has produced results extremely different from the others. The hospitals are represented as I, II, III and IV, the values in brackets are the within column rankings and the rank sums of each hospital are shown in the far right column.

<u></u>
1

Control Lab	A	В	с	D	E	F	R _S
I	14.8(1)	16.0(1)	12.2(1)	21.3(2)	18.5(2)	22.3(1)	8
II	15.3(3)	16.3(2)	12.7(3)	22.0(3)	18.8(3)	23.0(3)	17
III	15.4(4)	16.7(3)	12.8(4)	21.1(1)	18.9(4)	23.1(4)	20
IV	15.1(2)	17.0(4)	12.3(2)	22.9(4)	18.0(1)	22.5(2)	15

The second	h	٦	\sim	2	2	
тa	ω	1	С.	~	. "	

Quality Control results of four Laboratories on six unknowns

Using the rank sums, Friedman's χ^2 shows

ቋ

$$\chi^{2} = \frac{12}{Nk(k+1)} \int_{j=1}^{k} (R_{j})^{2} - 3N(k+1)$$

= $\frac{12}{4 \times 6 \times (6+1)} \times 978 - 3 \times 4 \times (6+1) = 7.8$

which, with 3 degrees of freedom is significant at the 5% level. Kendall's concordance coefficient also shows significance at the same level.

$$W = \frac{s}{\frac{1}{12}k^2 (N^3 - N)}$$

A VALUE CHART



This degrée of association (0.43) is significant at the 5% level.

By invoking Youden's test and using the same rank sums, we observe (Appendix A, I = 4, J = 6) that a rank sum of 8 or less occurs about 3% of the time under the null hypothesis and therefore it can be said that the minimum rank sum of 8 is significant at the 3% level. This suggests that the results from lab I are significantly different from the other labs. We may also check the other end of the distribution by examining the largest rank sum and here we find that a rank sum of 20 is not significant at the 10% level.

Example 2.

As in section 2.2, this example is a modification of example 1, designed to show using non-parametric statistics that even though overall variance analysis is not significant, there can still exist a significantly extreme deviate.

Suppose the values in column six were modified as

13

ション

in Table 2.3

Control Lab	A	B	С	D	Е	F	Rs
I	14.8(1)	16.0(1)	12.2(1)	21.3(2)	18.5(2)-	22.5(2)	9
II	15.3(3)	16.3(2)	12.7(3)	22.0(3)	18.8(3)	23.0(3)	17
III	15.4(4)	16.7(3)	12.8(4)	21.1(1)	18.9(4)	22.3(1)	17
IV	15.1(2)	17.0(4).	12.3(2)	22.9(4)	18.0(1)	23.1(4)	17

Table 2.3

Quality Control results of four Laboratories on six unknowns (modified)

The rank sums appear to show that lab I varies considerably from the others and yet both Friedman's χ^2 (4.8) and Kendall's W (s = 48) fail to recognize an overall variation significant at the 10% level. On the other hand, Youden's test recognizes a rank sum of 9 as being significantly extreme at the 8% level.

2.4 Current Approaches to Extreme Value Analysis in the Biomedical Sciences

On reviewing current biomedical literature, it is apparent that tests of extremeness are almost never used in data analysis in this area. In the simplest situations, where a test group is compared with a control group and the

t-test applied in determining the probability of a difference, it could also be said that the degree of extremeness of the test group from the control is being assessed. But beyond this, tests of extremeness are rarely employed. Moreover, a large amount of biomedical research today asks such questions as; what is the best ..., what is the largest ..., the smallest ..., the strongest ..., the cheapest ... The search for these superlatives argues for the use of tests of extremeness.

Many of the problems in the biomedical sciences are problems of selection but are not formulated as such. They are formulated instead as hypothesis testing questions, with the result that the real questions are not addressed directly.

Both Youden's test and Nair's test are able to measure extremeness in a two way classification but are not strictly selection techniques as there is an underlying null hypothesis of no difference. They are, though, more specific than the popular analysis of variance methods in that they do specify a significance level for the extreme deviate.

The use of these techniques in the biomedical sciences, with particular attention to Youden's test for one tailed probabilities is developed in the remaining chapters.

CHAPTER III

the approximation of the

-

THE EXPANSION OF TABLES FOR YOUDEN'S TEST FOR THE EXTREME DEVIATE

3.1 Introduction

As far as can be determined, there are only two tables published for Youden's Test for the Extreme Deviate. Thompson and Willke produced a table of two-sided percentage points for nominal one, three and five percent values over the range three to fifteen for both I and J. Subsequently Willke published a table of one-sided percentage points for the same nominal values and ranges of I and J. This chapter will describe the various techniques used to produce a table of one-sided percentage points for one, three, five and ten percent values over the range two to twenty-five for I and three to twenty-five for J. In addition, an attempt has been made to supply four digits of precision as opposed to three, or an upper and lower bound where this degree of precision is unattainable.

The second part of this chapter deals with a comparison of Youden's Test and its parametric analog, a test developed by Nair. A simulation technique is used to compare the two tests in terms of their operating characteristics curves for three different types of parent populations.

16 `

3.2 <u>Techniques For Generating Tables Of One-Sided Percentage</u> <u>Points</u>

3.2.1 Introduction

This section deals with the various methods used to generate the table of one-sided percentage points. Also discussed are two approximation techniques for obtaining percentage points which are beyond the bounds of the table.

Table 3.1 outlines which techniques were used and in what areas of the overall table they were used. The numbers in each of the areas refer to the sub-heading numbers for a description of the techniques found in the text. For example; 3.2.2, which refers to exhaustive enumeration, was used to calculate the values in the table for I from 3 to 11 while J varied from 3 to 8 for each I.

3.2.2 Exhaustive Enumeration

When the problem of developing a table for Youden's test was first approached, this technique was thought of first and while it reflects a basic understanding of the use of Youden's rank sum test, exhaustive enumeration is soon found to be of little use generally.

Consider I objects and J judges. Each of the judges can independently assign I! different rank arrangements to the I objects. Therefore, in total there are (I!)^J different sets of rankings of the I objects by the J judges. For each

17

12.1





A Mapping of Techniques to Youden's Table of One-Sided Percentage Points

of these sets of rankings it is required to produce the I rank sums, determine the size of the smallest or largest rank sum (for the one-sided tables) and increment the appropriate rank sum counter by one. The number of sets can be reduced to (I!) J-1 by setting the first judge's ranking as constant and ultimately dividing the rank sum counts by $(I!)^{J-1}$ rather than $(I!)^{J}$, to produce the individual rank sum probabilities. The limitation of this technique is the sheer amount of calculation required. For example, to calculate the probability distribution for ten objects and eight judges would require the evaluation of more than (10!)⁷ = 8.2 \times 10⁴⁵ sets of rankings of eighty rank values each. The number of arrangements produced by each judge is also greater than 3.6 \times 10⁶. If a computer could evaluate one million sets per second, it would take about 2.6 \times 10³² years to complete the job for this one distribution alone.

The main benefit of exhaustive enumeration lies in the calculation of distributions for very small values of I and J where limiting type approximations are notoriously poor and also to aid the statistician in "getting a feel" for what occurs as these rank sets are produced. The latter benefit is helpful in the development of techniques for approximating the actual distributions.

Example:

....

The case of I = 3, J = 2.

Keeping the first judge constant we have $(3!)^{2-1} = 6$ different sets, from which we extract and tabulate minimum rank sums.

	J	Γ	RSUM				J	RSUM			J		RSUM
	1	1	2*			1	1	2*			1	2	3*
I	2	2	4		I	2	3	5		I	2	1	3
	3	3	6 <i>,</i>			3	2	5			3	3	6
	J	٢	RSUM	_	•		J	RSUM	_		J		RSUM
	1	2	3*			1	3	4			l	3	4*
I	2	3	5		I	2	l	3*		I	2	2	4
	3	1	4			3	2	5			3	1	4

Min. Rank Sum	Frequency	Probability	Cum. Prob.
2	2 [.]	2/6 (.3)	2/6 (3)
3	3	3/6 (.5)	5/6 (.83)
4	1	1/6 (.16)	6/6 (1.0)

As I becomes large it becomes increasingly complicated to produce all possible arrangements of the I ranks. To simplify this, the program described in Appendix B (1) which carries out exhaustive enumeration can use either the transposition method of M.B. Wells to initialize an array

with all arrangements of I ranks, or the lexicographical method of D.H. Lehmer which produces the ith permutation of I integers directly $(l \leq i \leq I!)$.

3.2.3 A Probability Generating Function For The Case I = 2

For the case of two objects (I = 2) and J judges it was possible to develop a probability generating function. In this situation each of the J judges can only assign one of two possible ranks to each of the two objects and therefore we have a binomial or two-class population. The binomial distribution is the sampling distribution of the proportions we might observe in random samples drawn from a two-class population. Since the proportion of cases expected in one of the categories is 1/2, the probability of obtaining a given rank sum R, for either object, is

$$p(R) = {\binom{J}{R-J}} \cdot {(\frac{1}{2})}^{R-J} \cdot {(\frac{1}{2})}^{J-R+J} = {\binom{J}{R-J}} \cdot {(\frac{1}{2})}^{J}$$

for

J < R < 2J

and for the one-tailed situation

$$p(R) = 2(\frac{J}{R-J}) \cdot (\frac{1}{2})^{J}$$

The cumulative sampling distribution is therefore

$$2 \cdot \sum_{i=0}^{x} {J \choose i} \cdot {(\frac{1}{2})}^{J}$$

where

The binomial coefficients can then be used to produce the one-tailed percentage points for any J and I = 2 in the following way:

- Generate the Jth order coefficients using Pascals algorithm.
- 2. Double the first $\left[\frac{J+1}{2}\right]$ coefficients.
- 3. Divide the first $\left[\frac{J}{2}\right] + 1$ coefficients by 2^{J} .
- 4. Accumulate these results such that the ith cumulant is the sum of the first i terms.

Example:

Suppose we wish to generate the cumulative probability distribution for the case I = 2 and J = 6. 1
1. Using Pascal's algorithm ORDER 1 1 l 1 2 1 2 1 3 3 1 3 1 4 6 4 1 4 10 5 1 5 10 1 5 1 6 15 20 15 6 1 6 2. Double the first $\left[\frac{6+1}{2}\right] = 3$ coefficients 20 12 30 2 15 6 1 3. Divide the first $\left[\frac{6}{2}\right] + 1 = 4$ coefficients by 2⁶ (64) 12/64 30/64 20/64 2/64 4. Accumulate these results 2/64 14/64 44/64 64/64

and the resulting distribution for I = 2, J = 6 is:

R _{min}	R _{max}	Probability
. 6	12	2/64 (.03125)
7	11	14/64 (.21875)
8	10	44/64 (.68750)
9	9	64/64 (1.0000)

Appendix B (2) contains a listing of a computer program

ł

ì

•

٤,

which will generate probabilities by the above method for specified values of J.

3.2.4 <u>Approximation Using An Iterative Procedure Based On</u> Bonferroni's Inequalities

This teghnique has been used by Thompson and Willke (1963) to approximate tables of two-sided percentage points and later by Willke (1964) to produce corresponding one-sided tables.

Let $r_i = \sum_{j=1}^{r} r_{ij}$ denote the sum of the ranks for the ith object, where r_{ij} is the rank in the ith row and jth column of a table of ranks. These rank sums become the test statistics for testing the hypothesis H_0 : The I objects are indistinguishable. For each i we have $J \leq r_i \leq IJ$. Let R be defined, so that under the null hypothesis

 $P[A(R)] = 1 - \alpha$

where $A = A(R) = \{r_i: J+R < r_i < IJ-R, i = 1, ..., I\}$ and α is an appropriate significance level. \overline{A} , the complement of Aprovides a two-sided symmetric region for réjecting H_0 .

$$\bar{A} = \{r_i: r_{\min} < J + R \text{ or } r_{\max} > IJ - R\}$$

and a one-sided region for rejecting H_0 is provided by

using r_{min} or r_{max} in the above equation, where r_{min} and r_{max} are respectively the minimum and maximum rank sums. Upper and lower bounds for P[A(R)] can be obtained by the following procedure:

Define the event $A_i\{\dot{r}_i: J+R < r_i < IJ-R\}$ and denote the complement by \bar{A}_i ; then $\bar{A} = \bigcup_i \bar{A}_i$. By Bonferroni's inequalities we have under H_0

$$IP(\overline{A}_{1}) \gg P(\overline{A}) \gg IP(\overline{A}_{1}) - (\frac{1}{2})P(\overline{A}_{1}, \overline{A}_{2}) \quad . \tag{1}$$

To compute the upper bound let $p_J(k) = P(r_1=k)$ for J judges. If p (*i*) is the probability that the first object receives a rank of *i* from the Jth judge, then we have the recursion relationship.

$$p_{J}(k) = \sum_{i} p(i) p_{J-1}(k-i)$$
 (2)

Under the null hypothesis, $p(i) = \frac{1}{I}$. When $k < \frac{J}{2}$ (for J odd) or $k < \frac{J}{2}-1$ (for J even), then the upper bound $(P(\bar{x}_{I}))$ as calculated by $p_{J}(k)$ is the exact probability of a given rank sum occurring. This fact is particularly useful for small I, since the 10% level is usually found before either of these inequalities is violated. When $k > \frac{J}{2}$ (for J odd) or $k > \frac{J}{2}-1$ (for J even) then $IP(\bar{A}_{I})$ as calculated by $p_{J}(k)$ is no longer exact but becomes a conservative upper bound. That is, it will always be higher than the exact value. In -

this case a lower bound is required. In light of the fact that $IP(\bar{A}_1)$ has been shown to be exact under certain conditions, a botter lower bound has been developed. If we let q represent the rank sum beyond which $p_J(k)$ is no longer exact, then the lower bound is defined as

$$I \qquad I-1 \\ p_J(k) - p_J(k-q-1+j)$$

the superscripts I and I-l indicating the number of objects. Appendix $B_{\gamma}(3)$ contains a listing of a computer program which will calculate one-sided probabilities by this technique.

3.2.5 <u>Approximation By A Normal Distribution For Large J</u> Using the moment values

 $Er_{i} = \frac{1}{2}J(I+1) = \overline{r}'$ $var r_{i} = J(I+1)(I-1)/12$ $cov(r_{i},r_{i}') = -J(I+1)/12$

and asymptotic normality we have, according to Thompson and Willke (1963), the following:

For large J the probability is approximately $1 - \alpha$ that all row sums r_i simultaneously lie in the interval whose endpoints are $\frac{1}{2}J(I+1) \pm J^{1/2}a(I,\alpha)$. Here

	1 PEI	RCENT	3 PEF	RCENT
I	YOUDEN	NORMAL	YOUDEN	NORMAL
5	54	55	57	56
10 .	93	93	98	98
15	131	131.	138	138
20	169	168	177	177
25	206	204	216	216

	5 PEI	RCENT	10 PERCENT		
Ι.	YOUDEN	NORMAL	YOUDEN	NORMAL	
5	58	59	60	60	
10	100	101	104	104	
15	. 141 -	141	_ 146	147	
20	182	182	188	189	
25	222	221	230	230	

Table 3.2

A Comparison of Critical Values Between Tabled Values and The Normal Approximation For J = 25

Э

27

1 2

1 / K

$$a(I,\alpha) = \left[\frac{I(I+1)}{12}\right]^{1/2} h(I,\alpha)$$

and $h(I,\alpha)$ is as defined by Halperin <u>et al</u> (1955) as the significance point of the maximum absolute deviate in normal samples. Values for $h(I,\alpha)$ may be found in Biometrika Tables for Statisticians, Hartley and Pearson (1968). Table 3.2 gives an idea of how good the normal approximation is to the tabled values for J = 25 and various values of I. The minimum rank sums for nominal 1, 3, 5 and 10 percent levels are compared.

3.2.6 Approximation By A Uniform Distribution For Large I

Thompson and Willke (1963) have developed the justification for a uniform approximation in the following way. Under H_0 , r_{ij} has a discrete uniform distribution over the integers 1, ..., I. Thus for a large I a continuous uniform distribution ought to provide a good approximation. Also, r_{ij} and $r_{i'j}$ are dependent random variables, but one suspects that this dependency should vanish as $I \neq \infty$. Subsequently, Thompson and Willke derive the following:

$$\alpha_{u} = IP(\overline{A}_{i}) \doteq \frac{I}{J!} \left(\frac{J+2R+1}{2I}\right)^{J}; \frac{J+2R+1}{2I} \leq 1$$

and solving for R,

· 28

$$R \doteq I\left(\frac{\alpha_{u}J!}{I}\right) - \frac{J+1}{2}; \frac{\alpha_{u}J!}{2I} < 1$$

Table 3.3 compares the uniform approximation to tabled values for I = 25 and selected values of J as large as ten. Where J > 10 and I is large, the normal approximation seems superior to the uniform approximation, but this has not been thoroughly investigated.

3.3 The Comparison Of Youden's Test and Nair's Test

3.3.1 Introduction

As a basis for comparison, it was felt that the power curves for the two tests would provide a simple yet useful way of attaining this goal. A simulation technique was used to produce the curves under various conditions, as the derivation of the theoretical curves was beyond the scope of this thesis.

Separate pairs of curves were generated for values of I = 5, 15 and 25 and for values of J = 5, 15 and 25. Alpha levels of both one and five percent were specified. The above specifications were carried out under three separate assumptions regarding the variance of the parent populations. In the first case, both parent populations were normal, with equal variances. In the second case, they were both uniform with equal variances and in the third case the distributions were also uniform, but the variance of the

	~	~		
	1 PEF	RCENT	3 PER	CENT
J	YOUDEN	UNIFORM	YOUDEN	UNI FORM
3	5	4	6	6
4	9	9	12	12
5	16	16	19	19
7	31	31	35	35
10	56	56	63	62

1						
	5 PE	ERCENT	10 PERCENT			
J	YOUDEN	UNIFORM	YOUDEN	UNIFORM		
3	7	7 -	· 8	8		
4	13	13	15 .	15		
5	21	21	24	24		
7	38	38	41	41		
10	66	6 5	70	70		

Table 3.3

A Comparison of Critical Values Between Tabled Values and The Uniform Approximation For I = 25

30

-} -}

۶

...

extreme deviate population increased as the difference between the two means increased.

The simulation was performed in the following manner. Values for I and J were specified prior to execution along with the type of parent population, and the number of separate evaluations to be done at each delta value. All data presented here represent 200 evaluations at each delta The delta value is defined as the true difference level. between the population mean and the mean of the extreme This value is incremented from zero to three in deviate. steps of 0.2, proportionate to the population standard deviation such that a delta of 1.4, for example, indicates that the mean of the extreme deviate is 1.4 standard deviations away from the population mean. The simulation generates and evaluates in turn, each of the 200 separate data sets for each of the specified delta values within the constraints of I, J and alpha. The data sets are selected in a pseudo-random fashion from the specified distribution. Each member of the Ith row is then incremented by an amount equal to delta. This arbitrarily defines the Ith row as the Øextreme deviate with known mean and variance. The data set is then analysed by Nair's and Youden's tests and scores are kept of how often each of these tests, working at a specified alpha level and delta value, correctly identify the known extreme deviate. A percentile version of these scores, plotted against the delta values (0.0 to 3.0 by 0.2) produces

31

the power curves for Nair and Youden under identical conditions.

A source code listing of this simulation program can be found in Appendix B (4).

The actual curves were approximated by fitting a logistic function to the data generated by the simulation. The function was of the form

$$y = \frac{\frac{1}{1-(f(x))}}{\frac{1}{1+e}}$$

where f(x) represents a first, second or third degree polynomial. The transformation

$$f(x) = \ln\left(\frac{y}{1-y}\right)$$

is then subjected to a least squares fit for each of the first three orders of the polynomial. That function with the minimum sum of squared differences based on the original data was selected. Generally, the mean deviation of the data points from the function never exceeded three percent, and this was felt to be acceptable for a comparative demonstration based on a simulation. This also agreed with the maximum binomial standard error for n = 200. In every case, the order of the polynomial was also found to be the same for Nair and Youden, given that the same data had been evaluated.

Only the data for alpha equal to five percent are shown in the following tables, as the one percent values were found to be entirely comparable, but with the usual overall decreases in power.

3.3.2 <u>A Comparison of Power Curves Derived From A Simula-</u> tion of Normally Distributed Data

Figure 3.4 presents the power curves based on normally distributed data. Each graph presents the curves for a different value of I and for J equal to 5, 15 and 25. Where there is only one curve for a particular value of J, the power curves are identical and are both represented by the single line.

Several interesting observations can be made from the curves aside from using them to determine power. For the case of I = 5 and J = 5 we see that the non-parametric test is slightly superior and this is probably due to the low degrees of freedom (16) used in the parametric test. This superiority however is soon overcome as either I or J increases, and the tests show roughly equal power for any value of I or J greater than ten. The observation that power . is generally independent of I except for very small values, is consistent with the findings of Willke. Siegel, also suggests that when N is small, the non-parametric test is usually preferred as the calculated probability values are usually exact and in this instance (I = 5, J = 5) such is the case.

Figure 3.4



Power Curves for Nair's and Youden's Tests Based on Normally Distributed Data



ł

ì

and the second of the



.

and the second se

· ·

· · · ·

3.3.3 <u>A Comparison of Bias Detection in Non-Normally Distri-</u> buted Data

Figure 3.5 presents the power curves based on uniformly distributed data. The uniform distribution was arbitrarily selected as a simple yet representative nonnormal distribution.

The similarity of these power curves with those previously described is somewhat unexpected. Generally, it was felt that once the parent distribution strayed signficantly from normality, that the non-parametric test would show superior power. However, this is obviously not the In fact, not only are the comparisons between case. parametric and non-parametric identical for both distributions, but the actual values of corresponding power curves are essentially the same. This may be accounted for in part by the fact that the uniform distribution and the normal distribution are both symmetrical and that the uniform is a rough approximation to a normal distribution with a large variance. Nevertheless, the apparent robustness of the parametric test is probably the single most impressive aspect of this. comparison.

and the second product of the second



the first the second second



38

÷

3.3.4 <u>A Comparison of Bias Detection in Non-Normally Distri-</u> buted Data With Differing Variances

Figure 3.6 shows the power curves based on uniformly distributed data in which the extreme deviate has a variance which varies directly as the difference between the means. The previous two cases demonstrated a situation known as "slippage" where the extreme deviate has a parent population identical to the other samples, except that the mean is different. By relating the variance of the extreme deviate to the difference between the means (delta) one is able to look at a more complex and probably more realisted situation found in extreme value analysis.

¹ Looking at the power curves, two things are immediately apparent. First, the power curves have a lower "slope" than the previous two cases, indicating that the power-efficiency is decreased. This is predictable, since the overlap between the two distributions decreases more slowly as delta increases, due to increasing variance of the deviant population and consequently it is more difficult to distinguish between distributions.

Second, we see that the relationship between members within a given pair has not changed from the previous two cases. For I = 5 and J = 5, the non-parametric test is still slightly better, and in all other cases the two tests are either identical or the parametric test shows a slight improvement. Again, the robustness of the parametric test is evident.



÷...

÷.

.....



CHAPTER IV

AN ANALYSIS OF CHROMOSOMAL CHARACTERISTICS OF HUMAN MELANOMA

4.1 Introduction

Many experiments in cancer research involve the artificial growth of different types of cancerous tissue and the examination of the cells during this growth. The following discusses such an experiment after a brief description of some of the less common terms and concepts.

With the exception of cells used in sexual reproduction (sperm and ova) all normal human cells contain twentythree pairs of chromosomes which are confined within the nucleus These twenty-three pairs of chromosomes are classified as autosomes (22 pairs, in which the two members of each pair are visually very similar) and sex chromosomes, (1 pair, the female having two X chromosomes and the male having one X and one Y chromosome). Within the human.body, these cells are able to reproduce by a process known as mitosis which results in two daughter cells for each parent cell. During one of the stages of mitosis, called the metaphase, the chromosomes, which are normally a tightly tangled mass within the nucleus become separated and clearly visible under magnification. In the laboratory, it

is possible to cause certain types of human cells to reproduce artificially in a controlled environment (in vitro). It is also possible to stop reproduction at the metaphase, and after certain preparation, the chromosomes are visible for examination. One technique often used is to photograph a cell's chromosomes with suitable magnification, produce a black and white print, then cut out the chromosomes and arrange them into the twenty-three pairs for further examination. This orderly arrangement of pairings is known as a karyotype.

McCulloch et al (1976) have recently completed an experiment designed to select specific chromosomal characteristics of cultured human melanoma. This study was undertaken to characterize several cell lines so that "inhouse" immunological investigations could be performed on pure cultures from a defined origin.

Basically, the experiment consisted of culturing eight different strains of human malignant melanoma and then karyotyping ten of the best of about fifty metaphases from each of the eight strains. Analysis was carried out in two areas. First, within strains, chromosomes were examined for any unusual, strain specific marker conditions. In this case, a marker condition refers to the consistent occurrence of a chromosome which could not be normally classified. Such a unique occurrence, if valid, could be used to identify this strain in other situations. Second, the frequency

of specific chromosomes was examined across strains. The objective in this case was to determine if there was a specific chromosome which occurred much more or less frequently than the others for melanoma, as represented by the eight selected strains. It is this second objective which can benefit from extreme value analysis and was, in fact the exact problem which suggested this thesis.

4.2 Description of the Data

Table 4.1 shows the total counts of normal chromosomes found in ten cells at metaphase for each of the eight selected strains of melanoma. Each row represents a particular autosome as described in the first column. The sex chromosomes were not used in the analysis, as the sex of the original donors was not known for some of the strains. The strains are represented by the columns and are identified in the first row. The column at the right shows the rank sum for each chromosomes. The chromosome counts were ranked from 1 to 22 within each strain and the ranks were summed across strains for each of the chromosomes. To maintain clarity, the individual ranks are not shown.

4.3 Analysis and Results

The objective, as stated by McCulloch et al (1976), was to determine if one or more of the chromosomes occurred significantly more or less than the others. If the findings

CELL LINES CHROMOSOME	M-1	M-2	M-3	M-4	M-5	M-6	M-7	73-61	rank Sum
1	9	29	21	26	26	.48	9	17	93
2	29	22	19	30	18	60	16	20	105
3	5	28	20	32	22	64	27	20	118
4	18	18	12	32	8	30	22	15	61
5	24	22	19	22	16	45	29	10	90
6	22	20	16	28	22	39	29	15	91
7	10	42	32	40	30	71	42	25	157
8	26	16	16	29	17	31	26	10	68
9	19	24	19	11	20	44	30	13	92
10	8	17	15	20	14	36 '	20	10	40
11	13	29	14	11	18	35	18	25	74
12	10	23	24	32	27	42	28	20	115
13	26 -	· 31	20	24	19	25	. 9	10	76
14	20	28	24	39.	22	42	23	20	124
15	11	12	26	20	22	30	20	17	70
16	13	25	18	18	15	35	15	17	60
17	17	13	11	6 `	11	38	23	22	57
18	19	13	18	24	20	50	22	20	87
19	16	15	17	32	16	44	11	17	71
20	22	27	17	28	23	60	26	10	105
21	7	28	26	30	21	34`	39	30	112
22	32	31	31	40	31	66	28	17	158

Table 4.1

\

The second

Total Number of normal chromosomes found in ten cells at metaphase for each of the eight selected strains of melanoma

were positive, then the relative frequency of occurrence of these particular chromosomes could be used to help classify unknown melanoma tissue.

In the case of non-parametric analysis, the rank sums as shown in Table 4.1 have been chosen as the test statistics. A visual representation of the rank sums is shown in Figure 4.2. A real number line is drawn and the integer values from 20 to 160 by 10's are marked. Each of the twenty-two rank sums is located on this line with a vertical mark. In the case of identical rank sums, the marks are placed very close together about the actual rank sum.



Figure 4.2

The distribution of rank sums for all chromosome counts in the melanoma data

This representation of the rank sums allows the investigator to get an intuitive feel for the rank sum distribution and an expectation with regard to those values which will

be selected as extreme.

Both Youden's test and Na r's test were used to analyse Table 4.1 for the occurrence of extremely low or high chromosome counts and the results are shown in Table 4.3.

	DIRECTION OF		YC JD				NAIR		
CHROMOSOME	EXTREMENESS	SIGNIF	F	OWS	COLS	SIGNIF	d	n	df
10	MIN	0.03	ر ہ	22	8	0.08	2.59	22	147
7 22	MAX(1) MAX(2)	<<0.01 <<0.01	158 177	22 21	8 8	<0.001 <0.001	5.21 4.73	22 21	147 140

Table 4.3

Analysis of melanoma data for extre e Ceviate chromosome counts, using Youden's and Nar's tests

Chromosomes which are felt to be extreme (p<0.05) are listed in column one and column two indicates which tail of the distribution was examined. With regard to Youden's test, the significance value of the sel cted row and its rank sum (R_s) are shown along with the number of rows and columns in the data set. For Nair's test, the significance value is also shown as is the test statistic (d), the number of objects under consideration (r_i) and the degrees of freedom (df).

A technique for determining second, third, ..., etc. most extreme deviates was also employed and this is the

reason why two maxima are shown in Table 4.3. After determining the most extreme deviate in the maximum direction, this row of data was then deleted from the data set and the identical calculation was again performed on the modified data set. The two maxima shown are ordered (1) and (2) with (1) being the most extreme. It also accounts for the decrease in the number of rows, n, and degrees of freedom in the bottom line of Table 4.3.

A two way analysis of variance was performed on the complete data set (Table 4.4) for comparison with the results of Nair's test, and Friedmans χ^2 was calculated for comparison with Youden's test.

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	VARIANCE	F
CHROMOSOMES STRAINS ERROR	21 7 147	4031.41 11753. 7069.78	191.97 1679. 48.09	3.99 34.91
TOTAL	175	22854.19	-	-

Table 4.4

Analysis of variance for melanoma data

Looking at figure 4.2 it appears as though there are two maximum extreme deviates and possibly one minimum extreme deviate according to the distribution of the rank sums. The F-test indicates very strongly (Table 4.4) that the chromosome counts are not all from the same distribution

(p << 0.001), and Friedman's $\chi^2 = 58$ (p << 0.001) is in agreement. Table 4.3 indicates that Youden's test and Nair's test agree in selecting the extreme deviates but differ slightly on the level of significance for the extreme minimum, as shown in the first row of the table.

4.4 Conclusions

Interpreting figure 4.2 visually, three different chromosomes are of immediate interest, one occurring less frequently than the others and two which both occur considerably more frequently than the rest. Both the F test and Friedman's χ^2 indicate very strongly that the mean counts for the different chromosomes come from more than one distribution. Nair's test and Youden's test are in agreement with the visual inspection and with the analysis of variance. They also agree with one another as to order and direction of extremeness for the three outlying chromosomes and do not differ appreciably as to the significance level of each.

Given the high degree of consistency among the techniques used and the associated high probability values, the conclusion must be that chromosome numbers seven and twenty-two occur much more frequently than all others for these eight strains of melanoma. Also, chromosome number ten occurs less frequently than all others, although the confidence in this statement is not as great as for the

maximum extreme deviates.

Chromosomes seven, twenty-two, and to a lesser extent, ten could then be used, by virtue of their relative frequencies, as marker chromosomes indicative of melanoma as defined by this selection of cell-lines.

÷.

CHAPTER V

AN ANALYSIS OF SCORING PATTERNS AMONG EVALUATORS OF LETTERS OF APPLICATION TO MEDICAL SCHOOL

5.1 Introduction

Several medical schools in Canada have recently modified their admission procedures by using some nonacademic data, as well as the traditional marks of academic achievement to choose their new students. This change stems from the concept that, given a basic level of academic ability, other characteristics of the applicant may be equally important. These other characteristics are often referred to as personal qualities.

The primary tool used to collect information about these personal qualities at McMaster University is a letter written by the applicant about himself. The letter is up to eight hundred words long and should attempt to answer the questions posed by the medical school. These questions are purposefully left vague and simply ask, "describe who you are, where you are going and how you will get there".

The letters are assessed by three readers working independently. There are commonly fifty teams, each of three readers, to process a total of about twenty-two hundred letters. Each team consists of a faculty person, a

51

medical student and a member of the community; each member having been randomly selected. This three member concept is repeated at each step of the admission process in the belief that admission decisions are not the sole prerogative of the faculty.

The scoring of the letter is centered around a form Which first asks the reader to assess the presence or absence of a set of personal qualities as shown by the letter. The tabulation of these personal qualities assists the reader in selecting a global score which ranges from 1 (poor) to 4 (excellent). No attempt is made to formalize the assignment of a global score from the personal qualities, nor to imply that other factors should not be considered. The sum of the global scores from the three readers of each letter is used in selecting candidates for interview, which is the second step in the admissions procedure.

In an effort to compare readers, five "control" letters are sent to every reader in such a way that they cannot be distinguished from the other letters they are asked to read. The "control" letters are selected from all applicants' letters to provide a representative crosssection. One letter is selected which should be rated very high, another should be scored very low, a third letter is selected because it is highly controversial (readers will tend to score this letter very high or very low) and two other letters are selected which are average.

The readers are non-expert at this method of evaluation and change from year to year. Also, they donate their time and come from all parts of the community near the medical school. With this in mind, evaluation of the readers is vital to ensure that applicants are unlikely to be incorrectly scored by a poor reader or team of readers.

Before an analysis of the readers and teams can be carried out, several assumptions must be made.

1. The best estimate of an applicant's score is the mean score of all readers who read the letter.

2. The overall mean score (3 readers reading 45 randomly assigned letters) should be approximately the same for all teams.

3. The individuals and teams giving the most extreme results with the control letters are most likely to give the most extreme results generally.

With the above assumptions, extreme value analysis can be used to select individual readers and teams which deviate most from the mean (best estimate of the true value) and are therefore most likely to score applicants incorrectly.

5.2 Description of the Data

Table 5.1 lists the forty-eight teams and the total scores for the five control letters by team member. Also shown are the team totals and the totals for each type of

TEAM	FACULTY	STUDENT	COMMUNITY	TOTAL
1	11	1.4	14	39
2	14	11	12	37
3	11	12	10	33
4	13	11	10	34
5	11	14	11	. 36
6	9	10		LO 26
7	13	11	11	. 35
8	15	11	9	35
9	13	13	11	37
10	9	10	15 🚭	34
11	HI 17	13	16	HT 46
12	11	12	8	31
13	13	10	11	34
14	12	13	11	36
15	13	10	. 13	36
16	10	9	9	28
17	11	11	10	. 32
<u>1</u> 8	11	€ .		37
19	13 🦷	8	HI 14	35
20	10	- 13	11	34
21	10	14	11	35
22	13 -	8	10	31
23	12	14	10	36
24	9	8	13.	30
25	13	9	12	34
26	13	15	14	42
27	12	9	12	33
: 28	.11 .	13	11	35
29	11	11	12	34
30	10	11	14	35
31	13	10	13	36
32	14	. 10	13	37
33	13	9	13	35
34	13	13	11	37
35	13	12	9	34
36	- 12	11 .	13	36
37	12	14 [°]	13	39
38	TO - 8,	11	9	28
39	12	14	9.	35
40	11	10	11	32
41	12	13	11	36
42	11	10 ,	15	36
43	12 ·	9	15	36
44	10	12	9	31
45	10	12	13	35
46	10	нт 16	11	37
47	9	10 G	14	29
48	11	~ 9	11	31
FOTAL	560	538	562	1660

Table 5.1 -

Total scores on five control letters given by teams and reader types

1

TEAM	MEAN SCORE	TEAM	MEAN SCORE	TEAM	MEAN SCORE
1	7.02	17	6.28	33	7.48
2	6.98	18	HI 8.10	34	6.88
3	6.39	19	7.41	35	6.93
4	7.80	20	6.72	36	6.27
5	6.26	21	7.40	37	7.28
6	LO 5.27	22	6.95	38	6.02
7	7.30	23	6.41	39	6,45
8	6.82	24	7.24	40	6.50
9	6.64	25	7.02	41	5.79
10	6.65	26	7.42	42	7.20
11	7.93	27	6.55	43	7.63
12	6.90	28	7.07	44	6.75
13	6.19	29	7.43	45	7.17
14	7.00	30	6.56	46	6.41
15	7.28	31	7.91	47	6.49
16	7.07	32	5.75	48	6.15

Table 5.2

Mean scores for each team based on all letters read

.

team member, i.e. student, faculty, community. Although the individual scores of each letter by reader were available, they are not shown because of their great number and minimal use in this discussion. Table 5.2 lists the mean scores of the actual data for the same forty-eight teams. Each team read between forty-one and forty-six letters and the mean is shown in this table to standardize for the number of letters read.

5.3 Analysis and Results

The evaluation of the readers' performance was considered at two levels; the individual reader, and the team. It is most important to know that each of the teams is evaluating correctly, for it is the total, or team score, which is used to determine whether or not the applicant. should be considered further. The measurement of the individual reader's performance is of secondary importance but should be useful in determining weaknesses in the training of the readers or in pinpointing the reason for a poor team performance. Using extreme value analysis, precision and accuracy of both individuals and teams will be measured to determine if any significantly extreme deviates exist for these particular data, Table 5.3 shows Table 5.1 in the form of three histograms. The histograms represent the total scores given to the five control letters by each of the readers. The readers are separated by type

56

into faculty, student and community. The results of analysis by Youden's and Nair's tests are shown in Table The faculty member of team 11, and the community 5.4. member of team 18 both appear to be scoring significantly higher than all other members of their type. These particular individuals are indicated in Figure 5.3 by the hatched areas. It is interesting to note that there are no significantly extreme (p < 0.05) deviates in the minimum direction. The student from team 47 definitely appears to be extreme according to Figure 5.3 and Table 5.1. Nair's test even gives a significance level of 0.02 but this be caused by the more or less consistent skew to could the right shown in these data. Youden's test should not be affected by the nature of the distribution and indicates a significance level of > 0.10.

These results show that two of the individual readers are significantly different from others of their group with respect to accuracy in determining the "true" scores of the five control letters. It is also useful to note that both of these individuals tend to err on the high side of the "true" value.

The other important measure of performance in individual readers is that of precision. In terms of correctly evaluating a letter, it is not so important to measure the spread about an individual reader's mean, but to measure the individual's spread about the group mean or best

57

ħ,

Si or





1.1.1

Frequency of total scores for 5 control letters by type of reader

58

وه و المارين ما الا ماري الاستان الله المعاملات المحملة أوله ما يك محملي المريم ولا يريس

211 X X X V

ŀ

٦.

بمتحقظته الم
TYPE OF READER	MAXIM	JM DEV:	IATE	MINIMUM DEVIATE			
	TEAM	*Y	*N	TEAM	*Y	*N	
FACULTY	11	0.03	0.02	38	>>0.10	>>0.10	
STUDENT	46	0.10	0.03	47	0.10	0.02	
COMMUNITY	18	0.05	0.03	6	>0.10	0.07	

(*Y = YOUDEN, N = NAIR)

Table 5.4

Maximum and Minimum extreme deviates in the three types of readers (Mean Scores)

estimate of the true value. This approach is able to point out not only those who are consistently high or low scorers, but also those who for some reason always seem to score in the opposite direction to everyone else. This type of reader would score good applicants as poor and poor applicants as good and is therefore unlike those who score everyone as good or poor. Table 5.5 shows the absolute differences between the group total and the individual total for each reader. Frequency histograms of these data are found in Figure 5.6. These data are then analysed by Nair's test and Youden's test and the results are displayed in Table 5.7.

The histograms displayed in Figure 5.6° indicate a definite skewing to the right in all three cases which probably invalidates Nair's test as a method of analysing these data. Visually, there appears to be at least one suspect extreme deviate in each case but the results shown

بالالا الجاسية مريشية والمعاد

ГЕАМ	FACULTY	STUDENT	COMMUNITY	TOTAL
1	1.84	2.72	3.17	7.73
2	2.72	1.96	3.17	7.85
3	, 1.84	LQ 1.42	3.30	6.56
4	2.42	3.12	3.75	9.29
5	LO 1.58	2.72	1.58	LO 5.88
6	2.54	2.96	4.54	10.04
1	4.88	3.58	3.59	12.05
8	4.17	3.58	4.75	12.50
9	2.42	1.72	2.75	6.89
בט בור	3.84	4.12	4.1/	12.13
12	5.47	2.42	4.72	12.61
13	HI 0.05	1.42	HI 0.84	
14	3.59	4.12	3.84	11.55
15 ~	2.35	3.90	1.50	1.0/
16	9 84	4.12	2 1 2	3.17
17	3 42	3.50	2.12	0.20
18	3'14	3.39	5 17	
19	1 26	3.50	3,17	^9 97
20	6.00	2.42	3.12	7.54
21	13.30	3.17	1.84	8.31
22	2.17	4.84	2.12	9.13
23	2.33	2.47	2.12	6.92
24 .	3.12	3.54	3.14	9.80
25	2.89	4.30	2.96	10.15
26	3.96	3.72	3.17	10.85
27	1.88	3.12	2.14	.7.14
28	3.14	2.63	2.42	8.19
29	1.58	1.84	2.71	6.13
30	2.00	1.58	3.17	6.75
22 21	2.17	2.96	3.71	8.84
22 .	2.4/	2.58	3.72	8.77
34		2.54	2.42	-/.38
35	5.33	3.71	3.59	
36	2.42	2.90	2.04	6 14
37	1 88	1.30	2.44	7 0/
38	3 54	2 75	3 00	9 29
39	2.14	2.75	3 12	7 98
40	3.14	2.00	3.13	8.27
41	3.87	2.17	LO 1.58	7.62
42	1.58	2.58	3.72	7.88
43	2.33	3.12	3.47	8.92
44	2.84 •	2.58	3:00	8.42
45	3.30	1.42	1.72	6.44
46	3.68	4.47	1,.96	10.11
47	3.38	HI 5.54	2.47	11.39
48	2.75	3.12	4.05	9.92

Table 5.5

Absolute differences between group total and individual total by reader

1. <u>1. 1. 1. 1.</u>



TYPE OF READER	MAXIMUM DEVIATE			MINIMUM DEVIATE			
	TEAM	. *Y	*N	TEAM	*Y	*N	
FACULTY	12	0.01	0.002	5	>>0.10	>>0.10	
STUDENT	47	>0.10	>0.10	3	>>0.10	>>0.10	
COMMUNITY	12	0.03	0.003	41	>>0.10 [•]	>>0.10	

(*Y = YOUDEN, N = NAIR)

Table 5.7

Minimum and Maximum extreme deviates in the three types of readers (absolute differences from the group mean)

in Table 5.7 indicate that this is not exactly true, keeping in mind that Nair's test is weakened by the skewness of the data. Youden's test indicates that both the faculty member of team 12 and the community member of team 12 are significantly extreme from the other members of their groups in respect of the degree of dispersion of their scores about the group mean. Again, there are no extreme members of the student group which appears to contradict a visual interpretation, but this is probably due to the mean student variation being somewhat higher than that in the other two groups of readers. This would tend to keep values of 7.5 - 8.0 more within the body of the distribution.

The selection of the faculty member from team 12 as an extreme variance deviate is of particular interest because it points out that readers can be found who score high when all others score low and vice versa. This reader's total score for all five control letters is 11, which is very close to the group mean of 11.7 indicating that there is no significant difference between this reader and the rest. However, an analysis of the total absolute difference between the group means and the individual reader's scores shows this reader to be significantly different from all other readers. On the other hand, the community member from team 12 whose dispersion measure about the group mean was also significant, can be recognized in the first analysis as having had the second lowest total score.

The analysis of the reading teams is carried out in much the same way as the analysis of individual readers. Figure 5.8 shows the distribution of the total scores given by each team for each of the control letters and Table 5.9 summarizes the analysis of these data by Nair's and Youden's tests. Both tests select team 11 as the maximum extreme deviate and team 6 as the minimum extreme deviate and their relative locations in Figure 5.8 are indicated by shading. Team 26, while appearing suspect as a second most extreme deviate has a significance value in excess of 0.10 according to both tests and is therefore not considered as extreme.

A tabulation of the absolute differences between group mean total and team total was also carried out, and the results are displayed as a histogram in Figure 5.10. The results of analysis for extreme difference show team 11

63

in a star in the second of

\$.





Frequency of total scores for 5 control letters (all teams)

MA	MAXIMUM DEVIATE			MINIMUM DEVIATE			
TEAM	YOUDEN	NAIR	TEAM	YOUDEN	NAIR		
11	<0.01	<0.001	6	0.01	0.01		

Table 5.9

.....

j - #7

Maximum and minimum extreme deviates in reading teams (Mean Scores)

64

3

1

1

11

. . .





МА	MAXIMUM DEVIATE			MINIMUM DEVIATE			
TEAM	YOUDEN	NAIR	TEAM	YOUDEN	NAIR		
11	0.05	<0.01	- 36	>>0.10	>>0.10		

Table 5.11

Maximum and minimum extreme deviates in reading teams (dispersion about the group mean)









 $\boldsymbol{\circ}$

Frequency of absolute differences from the grand mean for all letters, by team

to be the significant maximum deviate with no significant minimum deviate. Analysis of the data for second most extreme deviate in the maximum direction failed to show significance.

Now that the analysis of the control letter data is complete it is worthwhile examining the complete set of letter scores to see how the deviant teams performed overall. Figure 5.12 displays the frequency of mean team scores for all letters and Figure 5.13 shows the frequency of absolute differences from the grand mean for the same data. Table 5.14 summarizes the teams which were extreme in evaluation of both control letters and total letters.

And a second		
ANALYSIS	CONTROL LETTERS	ALL LETTERS
MAXIMUM MÉAN	, team ll	team 18
MINIMUM MEAN	team 6	team 6
MAXIMUM [*] X _g -X	team ll	team 6
minimum [*] x _g -x	none	none

* absolute difference of the team score from the group team

Table 5.14

Summary of teams showing extreme deviance in control letter data and comparison with all letter data

Team 18 is shown to have the maximum mean score for all letters and considering that this team was very close to the mean for both measures of the control letter data, it is reasonable to assume that the letters allocated to this team were unusually good. Team 11, which had the highest mean with the control letters also had the third highest mean for all letters which suggests that team 11 is probably the highest scoring team. On the other hand, team 6, consistent in both control letters and all letters, is definitely the lowest scoring team. The problem now is to decide which team will take honours for being most deviant from the group mean; high scoring team 11 or low scoring team 6. Team 6 was most deviant in the all letters; category and third most deviant in the control letter evaluation while team 11 was most deviant in the control letter study and about average for all letters. Undoubtedly team 6 is the most deviant team from the group mean.

5.4 Conclusion

From the results obtained in this chapter, it is obvious that extreme value analysis can be a useful tool in evaluating letter readers and teams in the context of a medical school admissions procedure. The use of control letters allows for comparison of readers and the results can be used to reasonably predict team performance in the sense of extreme variation. The analysis of absolute differences from the group mean is superior to the analysis of mean scores in the determination of extreme deviates, because extreme value analysis of these measurements will

not only pick out extreme means (consistently low or high) but will also select those who are extremely different from the group (consistently different in the extreme from the group mean). Finally, Youden's test is probably more useful in analysing these data than Nair's test, because of the skewed nature of the distribution of the absolute difference from the group mean.

· · · · · · · · ·

\$7

CHAPTER VI

THE DETERMINATION OF OUTLIERS IN A STUDY OF VENTILATORY RESPONSE TO CHANGES IN OXYGEN AND CARBON DIOXIDE CONCENTRATION

6.1 Introduction

Of particular interest to respirologists is the fact that increasing levels of carbon dioxide and decreasing levels of oxygen in the blood, will stimulate a person to increase their ventilation. This may occur either by a change in the depth (an increase in the tidal volume), or by an increase in the frequency at which they are breathing. In the actual situation, most people will exhibit a response which is mixed with respect to an increase in tidal volume and also an increase in frequency.

The rate at which ventilation increases with either increasing levels of carbon dioxide or decreasing levels of oxygen, exhibits a wide range of variation among subjects. It is possible to regress the change in ventilation against either changing partial pressures of carbon dioxide in the blood or changing levels of oxygen saturation. Within the biologic range of either carbon dioxide tension or oxygen saturation in this context, a linear model appears to be a fairly valid way of describing the data. It is not biologic-

ŧ

cally feasible to interpret the intercept of these regression lines because this would mean extrapolating back to almost zero levels of either carbon dioxide or oxygen in the blood, which clearly do not occur under normal circumstances. However, it is possible to interpret the slope of the regression line and compare it among subjects or even within the same subject under different circumstances. Experimentally this may involve the interposing of some obstruction to breathing, simulating airway obstruction or by restricting the subject's chest movement by applying a chest binder (simulating various "restrictive" disorders of lung and chest wall elasticity).

The factors affecting the slope of the regression line relating change in ventilation to change in either carbon dioxide or oxygen (under conditions where the other variable, be it carbon dioxide or oxygen, is held constant while the test variable is changing) include the person's sex, genetic constitution, vital capacity and athleticism. These biological variations among subjects may be interpreted by looking at the components of the ventilatory change which, as mentioned previously, include tidal volume and frequency responses.

As both increasing levels of carbon dioxide and decreasing levels of oxygen provoke an increase in ventilation, it would be reasonable to assume that there would be a further relationship between the slope of the regression

71.

associating ventilation change with change in both of these variables. This does not necessarily appear to be the case, although there is a loose association. However, some people who have a brisk ventilatory response to increasing levels of carbon dioxide, may have a relatively shallow and slow response to decreasing levels of oxygen. The reasons for this variability of response are not clearly understood, but can be analysed in terms of the components of ventilation, namely the response of tidal volume and the response of frequency to the stimulus. A further way in which they could be examined is by relating the slopes of the regression lines associating ventilation with change in a particular variable, to vital capacity.

The problem investigated in this chapter relates to just such an examination. The slope of the ventilatory response, regressed against changing levels of oxygen saturation was examined in relationship to vital capacity in a group of eight subjects (figure 6.1). Most of the subjects appear to fall within the confidence interval of a regression of ventilatory response against vital capacity. However, two subjects were outside the confidence interval, and the question arose as to whether these subjects constituted a separate subset of the population or whether they were simply indicating that the normal distribution about the fitted line was much wider than had first been assumed and that the error associated with the linear model was

72

とうしょう うちょう ちょう





Rate of ventilatory change due to decreasing 02 and fixed CO2 concentrations plotted against vital capacity

artificially narrow.

The analysis carried out in section 6.3 will attempt to look at the way in which the different components of ventilation, namely tidal volume and frequency response relate to overall ventilatory response in the eight subjects. This will be considered separately for each of the following three sets of conditions:

 concurrent decrease of oxygen and carbon dioxide concentrations;

73

STAR A CARLES

 fixed carbon dioxide concentration and decreasing oxygen concentration;

 fixed oxygen concentration and increasing carbon dioxide concentration.

At each step, a maximum and minimum extreme deviate is selected and the associated probability values determined. Finally, all the results are evaluated for consistency, or lack thereof, among the subjects to determine if the sample, represents more than one population.

6.2 Description of the Data

Table 6.2 is a tabulation of all the data used in this chapter. For each of the eight subjects the following is displayed:

Column 1: subject identification number;

Column 2: vital capacity in litres. Vital capacity is the greatest volume of air which can be exhaled in one breath subsequent to a maximal inhalation:

Column 3:

the change in ventilatory response under conditions of progressively decreasing oxygen and carbon dioxide concentrations. Measured in litres per min per percentage change in oxygen . saturation;

Column 4:

the change in ventilatory response under conditions of progressively decreasing oxygen concen-

trations and fixed carbon dioxide levels. Measured in litres per minute per percentage change in oxygen saturation;

Column 5:

the change in ventilatory response under conditions of increasing carbon dioxide concentration but fixed oxygen saturation. Measured in litres per minute per millimetre of mercury pressure of carbon dioxide;

Column 6:

the change in véntilation frequency under the same conditions as column three. Measured in respirations per minute per percentage change in oxygen saturation;

Column 9: the change in tidal volume under the same conditions as column four. Measured in litres per percentage change of oxygen saturation; Column 10: the change in ventilation frequency under the same conditions as column five. Measured in respirations per minute per millimetre of mercury pressure of carbon dioxide;

75

4.42

ΤI	$\frac{\Delta V_{t}}{\Delta CO_{2}}$	0.042	0.036	0.081	0.084	0.063	0.025	0.050	0.066	
10	$\frac{\Delta f}{\Delta CO_2}$	0.57	0.72	0.32	0.50	0.73	0.41	0.67	0.63	
6	$\frac{\Delta V_{t}}{\Delta S_{a}O_{2}}$ (PCO ₂)	0.032	0.030	0.068	0.055	0.043	0.038	0.038	0.042	
ø	$\frac{\Delta f}{\Delta S_a O_2}$ (PCO ₂)	0.36	0.50	0.12	0.22	0.50	0.35	0.20	0.26	
7	$\frac{\Delta V_{t}}{\Delta S_{a}O_{2}}$ (ET)	0.018	0.025	910.0	0.030	0.022	0.031	0.018	0.070	
Q	$\frac{\Delta f}{\Delta S_a O_2}$ (ET)	0.12	0.22	0.45	0.14	0.19	0.04	0.12	0.10	
Ŋ	sco2	1. 88	2.14	2.08	2.91	3.30	1.06	2.39	2.93	
4	sao2 (Pco2)	1.20	1.30	1.30	1.44	1.84	1.06,	1.20	1.48	
, m	s _a 0 ₂ (ET)	0.46	0.56	0.22	0.53	0.60	0.28	0.44	0.22	
7	AC.	3.8	4.2	6.5	6.2	໌ ຜ ມີ	4.6	.9 . 2	و.1	
Column Noj- 1	Subject No.	, r-1	77	m	4	. ທ.	, O .	, 7 ,	ω	3,3

×.'

Table 6.2

Data collected to show change in ventilatory response with changing 0_2 and $C0_2$ concentrations

76`

Column 11: the change in tidal volume under the same conditions as column five. Measured in litres per millimetre of mercury pressure of carbon dioxide.

6.3 Analysis and Results

The problem described in the introduction and displayed in figure 6.1 is to determine whether the two subjects farthest from the regression line, namely members five and six, are from the same population as the other subjects or from some other population. If it could be shown that these two subjects still appear extreme when another measure of ventilatory change or response is plotted against vital capacity, then the probability of these two subjects belonging to a population different from the other subjects is improved. 7 In fact, two other-measures of ventilatory response have been used; the response to concurrent decrease in oxygen and carbon dioxide concentrations and the response to increasing carbon dioxide concentration with fixed oxygen saturation. The information regarding these two tests is displayed in figures 6.3 and 6.4. The data for figure 6.3 are taken from columns two and three of table 6.2 and the data for figure 6.4 are taken from columns two and five of the same table.

To organize the information from these three measures of ventilatory response in such a way that Youden's test





Rate of ventilatory change due to increasing CO₂ (fixed O₂) concentrations plotted against vital capacity

78

could be applied, it was necessary to develop a two way classification of the eight subjects by the three measures of ventilatory response. This was done by performing a linear regression on each of the three sets of data and using, as a measure of extremeness, the signed difference between the actual ventilatory response and the calculated ventilatory response as a percentage of the calculated ventilatory response.



where: VR_c is the calculated ventilatory response

VR_A is the actual ventilatory response. The measures of extremeness determined by the above formula for all subjects and for all three measures of ventilatory response are shown in table 6.5. Youden's test selected subject number five as the maximum extreme value (p = .016) as did Nair's test (p = .01). The minimum extreme deviate was subject number six according to both tests but the associated probabilities were not as convincing (Youden, $p \ge 0.10$; Nair, p = .05).

Another way of determining those subjects who are extremely different from the rest with regard to ventilatory response is to look at the relationship between change in

	MEASURES OF	MEASURES OF VENTILATORY RESPONSE					
SUBJECT	0 ₂ + co ₂ +	$\begin{array}{c} \circ_2 + \\ \circ_2 + \\ \circ_2 + \end{array}$	$O_2 \leftrightarrow O_2 \pm O_2 \pm O_2 \pm O_2 \pm O_2 \pm O_2 \pm O_2 \oplus O_2 $	RANK . SUMS			
1	- 4.8 (4)*	1.8 (5)	1 <i>6</i> .9 (5)	14			
2	20.4 (6)	6.3 (7)	21.7 (7)	20			
3	-38.4 (2)	-12.2 (3)	-20.5 (3)	8			
4	42.6 (7)	- 0.5 (4)	16.1 (4)	15			
5	53.7 (8)	31.1 (8)	40.0 (8)	24**			
6	-37.2 (3)	-16.4 (1)	-44.4 (2)	6			
7	10.0 (5)	-13.0 (2)	-47.3 (1)	8			
8	-46.8 (1)	2.9 (6)	18.7 (6)	13			

* Numbers in brackets show the rank of each value within column

.

Table 6.5

Extremeness values and associated rankings for the eight subjects by the three measures of ventilatory response when regressed against vital capacity ~**†**

A second and a

و بور و والد

÷

· ` ` ` `

į.

2

ž

e)



of respirations

`;

المقالين المتعلج المراجر المحمد





,	MEASURES OF	1		
SUBJECŢ	0 ₂ + C0 ₂ +		$\begin{array}{c} O_2 \leftrightarrow \\ CO_2 \uparrow \end{array}$	RANK SUMS
1	9.5 (5)*	-12.9 (Ž)	-19.6 (3)	10
2	38.8 (7)	-10.7 (3)	-21.3 (2)	12
3	-39.8 (2)	4.5 (5)	22.1 (7)	14 "
4	4.7 (6)	10.7 (6)	34.6 (8)	20
5	46.9 (8)	26.2 (8)	20.1 (6)	22
6	-35.3 (3)	-22.7 (1)	-45.1 (1)	5
. 7	4.7 (4)	- 6.8 (4)	- 7.8 (4)	12
8	-52.7 (1)	11.9 (7)	17.5 (5)	13
1				

*Numbers in brackets show the rank of each value within column

Table 6.9

Extremeness values and associated rankings for the eight subjects by the three measures of ventilatory response when regressed against change in frequency of breathing



Figure 6.10





Rate of ventilatory change due to decreasing O_2 and fixed CO_2 concentrations plotted against change in tidal volume





i

Rate of ventilatory change due to fixed 0_2 and increasing CO_2 concentrations plotted against change in tidal volume.

	MEASURES O	2		
SUBJECT	0 ₂ ↓ C0 ₂ ↓	$0_2 + 0_2 $	$\begin{array}{c} O_2 \leftrightarrow \\ CO_2 \end{array}$	PANK SUMS
1	0.7 (5)	- 8.3 (4)	- 6.5 (3)	12
2	31.1 (7)	- 0.1 (5)	14.2 (6)	18
3	-52.6 (1)	-10.1 (2)	-28.4 (2)	5
4	30.5 (6)	3.0 (6)	- 2.2 (4)	16
, 5	36.4 (8)	36.1 (8)	32.3 (8)	_ 24**
6	-30.3 (2)	-20,4 (1)	-34.5 (1)	4**
7	- 3.6 (4)	- 9.9 (3)	6.6 (5)	12
8	-15.9 (3)	9.8 (7)	14.3 (7)	17 •

*Numbers in brackets show the rank of each value within the column.

Table 6.13

Extremeness values and associated rankings for the eight subjects by the three measures of ventilatory response when regressed against change in tidal volume

86

frequency of respiration and overall ventilatory response under the same three sets of conditions mentioned previously. Similarly, tidal volume may also be related to overall ventilatory response. Figure 6.6, 6.7 and 6.8 display the data which relate change in frequency of respiration to overall ventilatory response for the three sets of conditions. Table 6.9 shows the extremeness values for the eight subjects under the three sets of conditions. These results are determined by the same methods as those in Table 6.5. Here again subject five is the maximum extreme deviate and subject six the minimum extreme deviate but the probabilities for both subjects is >.10 as determined by both Nair's test and Youden's test.

Figures 6.10, 6.11 and 6.12 display information much the same as that just analysed except that the change in frequency of respirations has been replaced with change in tidal volume. The extremeness values for each subject are similarly summarized in table 6.13.

Here, the evidence points strongly to subject five being the maximum extreme deviate (Nair, p = .0025; Youden, p = .016) and subject six being the minimum extreme deviate (Nair, p = .01; Youden, p = .06).

6.4 Conclusions

The initial problem of determining extreme deviation in subjects when relating ventilatory response to vital

capacity has been approached by developing a two way classification of the eight subjects against three different measures of ventilatory response. The measure of extremeness in each of the three cases was defined as the distance from the measured value of ventilatory response to the calculated value as determined by a linear model showing the relationship between vital capacity and the particular measure of ventilatory response. The data were then analysed using both Youden's and Nair's tests. Subjects number five and six were the original extremes as shown in figure 6.1. Confirmation of this extremeness was supplied when data from the other two measures of ventilatory response were incorporated in the analysis as shown in table 6.5. In particular, subject five was selected as a maximum extreme deviate by both tests ($p \simeq .01$). Subject six was selected as the minimum extreme deviate but with a probability which makes its significance questionable $(.10 \ge p > .05)$. Of the three measures of ventilatory response, the first one (decreasing oxygen and carbon dioxide concentrations), is probably the weakest because both gas concentrations are decreasing at the same time. A rank of three for subject six under these conditions is probably higher than the true value and if a value of two were used instead, then both Youden and Nair would agree that subject six was the minimum extreme deviate with p = .05.

Further analysis has shown how these two subjects

differ from the others in their association of ventilatory response with either change in frequency of breathing or tidal volume. Table 6.9 shows the results of regressing change in frequency of breathing with ventilatory response and measuring for extremeness from the fitted line. Again, subjects five and six are selected as extreme but both Nair's and Youden's tests suggest a probability value->.10 for both subjects.

In the case of regressing change in tidal volume with ventilatory response and measuring for extremeness about the fitted line, table 6.13 shows that the rank sums for subjects five and six are definitely extreme. The probability values determined by Youden's test are; subject five: maximum (p = .016), subject six: minimum (p = .06). Nair's test supplies more extreme values; subject five: maximum (p = .0025)subject six: minimum (p = .01).

In conclusion, subject six appears extreme in the minimum direction with a probability value of 0.05 and subject five extreme in the maximum direction with a probability value of 0.02.

It should be pointed out, however, that this study has been used to demonstrate the application of extreme value analysis and does not lead automatically to more general biological conclusions about the distribution of ventilatory response in the population. This technique and a larger random sample would be needed to determine if a real population subset does, in fact, exist.

CHAPTER VII

DISCUSSION AND CONCLUSIONS

7.1 Introduction

In the previous chapters, Youden's and Nair's tests have been introduced and used in the analysis of three different biomedical problems. Youden's test in particular has been emphasized and chapter two dealt exclusively with the various methods used to increase the range of the associated probability tables and their accuracy. In this chapter, each of the three research questions posed in chapter one will be discussed based on the experience gained in analysing the three problems presented in chapters four, five and six. The final section will draw general conclusions regarding the use of Youden's test in analysing biomedical data.

7.2 <u>Research Questions</u>

7.2.1 Research Question 1

What types of data are most suitable for analysis by the non-parametric test?

In discussing the type of data most suitable for analysis by Youden's test, it is important that we look at both the nature of the distribution of the data and the nature of the values themselves, i.e. whether they are continuous or discrete measurements.

With regard to the nature of the underlying distribution of the data, chapter three presents power curves for comparing Youden's test and Nair's test assuming three different types of population distributions. It is observed that when the number of objects (identified by the letter I) is.small, and the number of judges (identified by the letter J) is small, then Youden's test has the greater power, independent of the data distribution used. As J increases and I remains small, the two tests appear to approach the same power independent of the data distribution. As I increases in value, the parametric test of Nair is either of greater power, or of power equal to, the non-parametric test of Youden for the three distributions examined.

The simulation program which generated these power curves used continuous data as opposed to discrete data putting Youden's test to a slight disadvantage. In this case it is probably correct to conclude that Youden's test has superior power in situations where I is small, otherwise Nair's test has power at least equal to that of Youden's test.

Youden's test, like all other rank tests, suffers from the ranking process which is usually required to transform the data prior to analysis. This process causes a

considerable decrease in power compared to parametric tests when analysing data whose parent population is approximately normally distributed. For example, if two subjects have values of 4.001 and 4.002 they could be ranked 1 and 2, but under different conditions these same two subjects could have values of 4.001 and 86.2 and the ranking would still be 1 and 2. Parametric tests do not have this problem and are able to take into account the magnitude of the difference between subjects. Another problem encountered when using non-parametric tests is the method of solving tied values. Depending on the technique used, either loss of power or additional calculation of a correction factor, is involved.

Although power curves were not calculated using rank data, Youden's test would obviously perform best in this situation as the probability tables are based on approximations of all possible rankings. On the other hand, Nair's test has greater power when analysing continuous data.

7.2.2 Research Question 2

Under what conditions is the parametric test superior to the non-parametric test?

From the simulations performed in chapter three it is obvious that Nair's test is superior in analysing normal-

ly distributed data when the sample size is not small (say greater than 10). The considerable robustness shown when the data were not normally distributed indicates that this test can also be used when the data distribution is strictly non-normal (but similar to a normal distribution), providing the sample size exceeds 10. If the data contain a large number of tied values then Nair's test is probably superior, as the technique used for resolving ties in Youden's test is to randomly assign the N tied values the next N ranks. If the number of judges is small, then there is a high probability of one of the objects attaining an unusually high or low rank sum which could erroneously classify it as a significantly extreme deviate. With Nair's test there is no requirement that the scores be unique and so the problem of ties does not arise.

7.2.3 Research Question 3

Is it beneficial to use the non-parametric test to ' determine second and third most extreme deviates?

When this question was originally formulated, it was thought that it would be useful to develop a technique which would select those objects which were second and third most extreme from the other objects. The technique involves deleting the most extreme object from the two way classification of data and re-ranking to select the most extreme deviate. This object would be the second most extreme deviate. By a similar technique the third most extreme deviate can also be found. The most important thing learned regarding this procedure is that one must display the data in a way which shows its distributional characteristics prior to interpretting the meaning of second and third most extreme deviates. In chapter four, Figure 4.2 displays the melanoma data in such a way that two extreme maximum deviates and one extreme minimum deviate appear obvious. Analysis shows this to be the case (see Table 4.3). The technique worked for this particular set of data because the majority of the values were clustered around the mean with very few far from the mean. However, if the data are more widely spread with no clustering, it is possible to show each value to be significantly extreme from the others as either a first, second, third or more, extreme deviate. Results like this are generally meaningless and may be avoided by visually examining the sample distribution.

Another problem regarding sample distribution is bi-modality or possibly multi-modality. A histogram or graph of some form will usually show several tight clusters of values with relatively vacant areas in between. In this case it is not only questionable as to whether second and third most extreme deviates should be determined, but questionable as to whether extreme value analysis would be meaningful.
7.3 Conclusions

An existing non-parametric test has been expanded by increasing the size and accuracy of the associated probability table. The methods used to expand the table have been described and the updated table presented. Power curves for the non-parametric test and its parametric analog were estimated by a simulation technique, and presented graphically for visual comparison. The ability of this test to solve problems of a biomedical nature has been demonstrated in three separate instances and comparison with its parametric analog has been made throughout. Answers to the research questions were presented and discussed.

As a final comment on the application of Youden's test to biomedical problems, it has been found that reformulation of the problem or reorganization of the data is a very important step in applying this test to situations which at first glance seem inappropriate.

3

REFERENCES

- Barton, D.E. and David, F.N. (1959): Combinatorial Extreme Value Distribution. Mathematika 6: 63-66.
 Doornbos, R. and Prins, H.J. (1958): On Slippage Tests. Indag. Math. 20: I. 39-46, II. 47-55, III. 438-447.
 Feller, W. (1957): An Introduction To Probability Theory And Its Applications. John Wiley and Sons, New York.
- 4. Friedman, M. (1937): The Use Of Ranks To Avoid The Assumptions Of Normality Implicit In The Analysis Of Variance. J.A.S.A. 32: 675-701.
- 5. Halperin, M., Greenhouse, S.W., Cornfield, J. and Zalokar, J. (1955): Tables Of Percentage Points For The Studentized Maximum Absolute Deviate In Normal Samples. J.A.S.A. 50: 185-195.
- Hartley, H.O. and Pearson, E.S. (1969): Biometrika Tables For Statisticians. Biometrika, Vol. 1 and 2 (Third Edition), Cambridge University Press.
- 7. Kendall, M.G. and Babington Smith (1939): The Problem Of M Rankings. Ann. Math. Stats. 10: 275-287.
- Kramer, A. (1956): A Quick Rank Sum Test For Significance Of Differences In Multiple Comparisons. Food Technology 10: 391-392.

- 9. Kruskal, W.H. and Wallis, W.A. (1952): Use Of Ranks In One Criterion Variance Analysis. J.A.S.A. 47: 583-621.
- 10. McCulloch, P.B., Dent, P.B., Hayes, P.R., Liao, S-K. (1976): Common and Individually Specifice Chromosomal Characteristics Of Cultured Human Melanoma. Cancer Research 36: 398-403.
- 11. McDonald, B.J. and Thompson, W.A. (1967): Rank Sum Multiple Comparisons In One And Two-Way Classifications. Biometrika 54: 487.
- 12. McMaster University Medical School Admission's Data (1975): By permission of Dr. B. Ferrier and Mr. F. Bradley.
- 13. Nair, K.R. (1948):- Distribution Of The Extreme Deviate From The Sample Mean. Biometrika 35: 118-144.
- 14. Nemenyi, P. (1963): Distribution-Free Multiple Comparisons. Ph.D. Thesis topic. State University of New York Downstate Medical Centre.
- Odeh, R.E. (1967): The Distribution Of The Maximum Sum Of Ranks. Technometrics 9: 281-289.
- 16. Rebuck, A.S., Jones, N.L., Campbell, E.J.M. (1972): Ventilatory Response To Exercise And To CO₂ Rebreathing In Normal Subjects. *Clinical Sciences* 43: 861-867.
- 17. Saunders, N.A., Leeder, S.R., Rebuck, A.S. (1976): Ventilatory Response To Carbon Dioxide In Young Athletes: A Family Study. American Review Of Respiratory Disease 113: 497-502.

- 18. Siegel, S. (1956): Non-Parametric Statistics For The Behavioural Sciences. McGraw-Hill Book Company, Toronto, Canada.
- 19. Tate, M.W., Clelland, R.C. (1959): Non-Parametric And Shortcut Statistics. Interstate Printers and Publishers Incorporated, Danville, Illinois.
 - 20. Thompson, W.A. (JR.) and Willke, T.A. (1963): On An Extreme Rank Sum Test For Outliers. *Biometrika 50*: 375-383.
- 21. Thompson, W.R. (1935): On A Criterion For The Rejection Of Observations And The Distribution Of The Ratio Of Deviation To Sampling Standard Deviation. Ann. Math. Stats. 6: 214-219.
- 22. Wilcoxon, F., Wilcox, R.A. (1964): Some Rapid Approximate Statistical Procedures. Lederle Laboratories, Pearl River, New Jersey.
- 23. Willke, T.A. (1964): General Application Of Youden's Rank Sum Test For Outliers And One-Sided Percentage Points. Journal of Research of the National Bureau of Standards, Vol. 68B 2: 55-58.
- 24. Youden, W.J. (1963): Ranking Laboratories By Round-Robin Tests. Materials Research and Standards 3: 2-13.
- 25. Youden, W.J. (1964): Statistical Problems Arising In The Establishment Of Physical Standards. Proceedings of the Fourth Berkeley Symposium on Mathematical

Statistics and Probability. University of California Press, Berkeley and Las Angeles, Ú.S.A.

1.

APPENDIX A

TABLES OF ONE-SIDED PERCENTAGE POINTS AT NOMINAL

3

LEVELS OF 1, 3, 5 AND 10%

N

MAX

I. İ 111 NIN

t

α 1

11

7

10 UPPER LOWE: Exact 1 1 1 1 1 1 ŧ. 5% 1 1 XAN 1 そうしょくろうこうこうできょうしょう ŧ ١I そてもちらこからしいはんこかもしのもんららか ともろろろろろろろろろろろ t 1 r ł UPPER LJWEH Exact Ì. 1 1 1 1 1 ŝ MAX l ŧ ł ł 7 I W Ì Ŧ Ì £ JPPER LUWER Exact ¢ .1250 .0355 .0125 .0175 .0175 .0174 .0174 .01225 .01225 .01224 .01224 .01224 .01224 .01224 .01224 I t MAX 1 BON40下4114400411440041440001 1 i 2 ŧ t Σ È

> -

40200000

001

01(

000

0100

.

0004

1000 1000

4

Ì

ار ر . .

3 .

•

* * *

÷.

ĺ

`

٠

;

;

W Warner

ţ

0998 1108 1220 UPPER LOWER 0 0 0 ω •1055 •1205 ;72 i õ 97 0.114 0A97 1111 0370 0741 1152 യന 4 M Θ 4 50 Q õ 10 • 0572 • 0772 • 0779 1 04940718 059 0,896 07,34 ٠ • ٠ 091 • .0999 .1110 .1221 0532210 79 ō ٠ • ٠ • . ٠ к0 ō ---1 õ -. . MAX 00400-mu@00400-munro0400 1 + H H H H N N N N N H H H H H 4 4 4 4 ທ່ານເທົ່າທ 1 i NIM i Ē ſ â 1 PER LONER 1 i 6 N M 4 S O σ UPPE: ŧ ъ 8 P A A σ 1 ź **I セ イ Ci か ご O ら S Ci と し く S か Ci と し と C S Ci と し く S か C と と と と C S Ci と ー し ー ト ー** 1 Ē PER LOWER Exact £ dd £ # MAX 111 2 Ξ ŧ r Ł JPPER LUWER Exact I 1 Ī I 1% うちょうちょうないかかもととをところでももくちょうちょう I XAM VIM 1 ۹ ż 5

11

3

**. 102

•

Ħ

ר		N A X	18 JPPER LOWER Exact		I A X	3* UPPER LJWEK EXACT		AX UP5		ΙΣ ΙΖ ΙΣ ΙΣ	I X	10% UPPER [EXA(
n	m	12	, ,0625	m	12	0625	'n	12	• 0525	ო	12	.063	ហ
\$	•	15	.0156	\$	16	.0155	iU	15	• 0781	ഗ	ן ניין	0.76	
ഗ	Q	19	•0234	Ś	61	.0234	ŝ	61	• 0234	• •-	8	0.90	0
9	~	2 3	•0068	ď	25	.0273	g	22	.0273	6	5	.0820	0818
~	5	26	•0089	10	52	.0293	10	1 10	.0293	11		0789	0788
æ	11	29	.0101	د. 1	28	.0297	27	29	.0297	13	27	.0742	0140
σ	۳ ۲	ი ო	.0108 -] 4	31 3	·0292	<u>ا</u>	30	• 0 5 3 8	5	00	.05	8
10	ות - ר	ω Ω	.0110	16	34	.0280	17	33 .06	633 .0632	16	32	.1289	1280
] _	17	38	.0110	н Ч	37	•0265	6 I	35	.0578	20	35	.1150	1146
5 L	61	41	.0107	20	40	.0243	21	30 • 66	526 .0525	22	38	.1025	1020
6	21	44	.0103	ດ ດາ	4 G	.0231	23	42 .04	+77 .0475	24	4]	.0913	1160
14	3	47	÷000°	やい	\$ \$.0213	50	45 .04	131 .0430	26	44	.0813	0811
5	5 2	5 0	500°.	27	4 B	•0389	27	4 9	• 0389	59	40	.1273	1268
16	27	2 T	•0096	50	51	.0350	30	50 • 06	545 .0644	31	• •	.1125	1119
17	2	56	•0060	31	ທ 4	.0315 .	ς Έ	53 、	• 0575	33	52	• 0660	6993
18	31	ູດີ	• 0 0 7 4	ŝ	57	.0283	. 4 C	56/	.0512	35	5	.0882	0879
19	ო ო	62	•0068	35	60	• 0255	ч С	59 .04	157 .0455	37	58	0781	0780
20	Э6 Э	64	.0123	37	63	•0229	33	62 /	• 0 4 0 7	40	90	.1131	1126
S,	38	67	.0111	4 U	ሪ የ	.0363	4 1	64 .01	515 .0614	42	53	1001	0000
22	40	70	.0100	4 2	с В С	.0324 .0323	43	67 • 05	545 .0545	44	56	0887	0884
23	42	73	.0041	77	71	.0249 .028B	40	70	• 0 4 8 5	46	69	0786	0785
24	44	76	• 0042	4 G	74	.0257	47	73	• 0 4 3 1	. 4	1	1090	1085
22	46	79	•0074	φ. β	77	.0230	64	75 .03	384 .0383	51	74	.0967	0964

ս Ն

0% PPER LOWER EXACT	0000	1200 1188	0896 0894	0672 .0669	1062 1057	0778 0774	1080 1074	AAT0. 5070	1030 1026	0762 0758	8700 2560	1151 1140	0863 0860	1024 1017	1191 . 1911					0404 °0406	1026 .1020	1146 .1140	0890 .0886	0990 0986
	ر ت			י הי הי		 	. 96	. (1 t										•	•	•	0		57	00
	m) vc	ά	20	- m	5	18	20	s S	י ה ו ה ו	2 2 2 2 2 2 2 3	2	. m		0 C	. 4	44		- 0	ר ו ל ו	25	ស្ព	5.7	609
5% UPPE3 LO#E3 EXACT	• 0 4 0 0	• 0400	• 0336	.0672 .0669	• 0502	• 0375	 0572 0571 	•0422 •0421	• 0584 • 0583	.0431 .0430	.0564 .0563	•0419 •0418	• 0529 • 0529	.0395	•0485 •0485	.0584 .05R2	-0441	.0522 .0521			• 0 4 6 4	•0536 •0535	• 0 4 1 1	• 0 4 7 1
1 X X X X X X X X X X X X X X X X X X X	15	10	53	5	30	34	37	41	44	4 0	5	ា ហ	с С	63	. ro	5	22	1		- 6	N D	10 8 1	80 80	<u>6</u>
	m	10	~	10	י ן י	14	17	61	גי 2	4 N	27	23	32	4 C	37	4 0	5 C	- 4	47	- c L	с С	53	ւր Մ	53
38 UPPER LOWER EXACT	.0400	• 0400	• 0335	.0209	.0211	•0375	.0280	.020a	-0312	.0231	.0319	.0237	• 0312	.0232	.0296 .0295	.0365	.0275	• 0333	.0252			• 0354	.0270	•0315
N A X	15	19	23	27	31	9¢	8 9 9	4 4 7	4 10	40	5 25	56	59	63	66	69	73	76	80	c d		ς β	06	63
	m	IJ	7	σ	11	14	15	α Γ	に	ň	25	с, В	31	е С	35	39	41	44	45	0	ר ז ו ו	າ ເ	5	57
1 × JPPER LUWER EXACT	• 0 + 0 0	• 0040	9600.	• 0090	• 0077	• 0063	• 0126	• 0146	• 0073	•0117	• 0088	.0128	• 0096	• 0071	• 0098	• 0073	• 0097	•0125	•0094	-0117	0,000	• 00.90	6010.	• 0082
N A X	15	50	5	ย กา	ი . ო	36	י ע י ע	n 1 t -	47	20	t N	5.7	6 1	69	69	22	75	78	82 82	10 00		n r 0 0	U . 7 (5
	m	. t	ب	æ,	01	2 1	1 r	- :	♪ (22	2 I 4 I	22	י ע ע		ታ . ጦ (36	6 °	4 C	44	47	49	ר ה ה ח	0 × 0 U	t Ω
ר .	ų	Φ ι	۰ ת	0 1	~ "	ະ ເ	N 0) , 1 ,	-4 (21	m ,	4 1		1 6	1	8-	19	50	5	22	5	ט ר אינ	1 t 7 U	2

104 .

S 11

L

7

UPPER LOWER Exact

MAX

NIM

n

10%

i

ŧ

1

ł

.0691

•0694 .0972

.llll

PER LOWEH Exact 1 111 0279 . ٠ lddU å Å MAX ŧ νIν Ì 1 œ

•0694 •0691 •0432 •0594 •0591 • 0441 EXACT i 1 1 1 • 0278 • 0 4 0 4, • 0 4 2 0, • 0 4 3 1 • 0447 • 0442 •0440 •0435 •0435 •0431 .05l2 .0562 .0600 •0439 .0383 .0442 Ś 0 UPPE: .041 .057 .055 1 ນ 8 VAX 8 ł 1 7 そららままららいちゃくこともらまい。 l н У .0260 .0273 .0272 .0282 .0299 .0288 .0293 **,**0224 .0292 .0289 285 .0280 .0277 0320 0355 244 0231 0432 0270 0365 0227 295 295 Ñ 0278 .0293 • ວທ o 0 Q 0220 • • ٠ . . . • • 94 98 102 105 110 JPPER LOWER Exact ŧ .0278 .01623 .01623 .01071 .00107 .00109 .00109 .00108 .00108 .00108 .00108 .00108 .00108 .00108 .00108 .00108 .00085 .00085 .00086 1 11 18 XAM VIN N.60m0440000000000410m00,0 **11-~22~2~~~~~~~~~~~**

のこのやまよどもららしんらいくをもららのでえるののことののことをもちもののです。

•0724 •0821 •0893

0967 0721 0815 0935 0996 0996 0996 0996 0997 0997 0937 0937 0937 0937 .0943 .0976 .0994 .1002 .1002 .0994

105

 \mathbf{o} ິທິທ

.0896 .0870 .1160 .1116 .1073

.0943 .0920

σ ŝ 0 m

•0964 .0981

.1065

5

an

N

0

•

:

۲ ۲

ŧ

• • •

ì

.

1

LOWER	A A A A A A A A A A A A A A A A A A A	0986 1132 0976 1107
10% - UPPEF	••••••••••••••••••••••••••••••••••••••	• 0 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9
X A X	• • • • • • • • • • • • • • • • • • •	100 104 109 133
	4 F O M O O N O O N O O M O O	0 4 7 7 7 0 7 4 7 7 7 0 7 4 7 7 7 7 7 0 7 4 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
LONE? ACT	20 40 40 50 50 50 50 50 50 50 50 50 5	• 0547 • 0547 • 0547
5% UPPE3		. 0540 . 0540 . 0549 . 0749 . 774
X 4 5		
		υ σ σ σ Ρ Σ
38 UPPER LJWEN EXACT	0437 02040437 04360275 02330275 02910291 0290028002800356 02850376 035503170283 $02830283028302830283028302830283$.0292 .0291 .0335 .0292 .0291 .0253
N A X		108 113 128
	10144440000000000000000000000000000000	5 5 7 5 5 5 5 6 7 7 5 5 5 6 7 5 5
1% JPPF3 LUWE? EXACT	.0204 .0140 .0140 .0187 .0125 .0125 .0080 .0080 .0080 .0115 .0102 .0102	•0117 •0102 •0099
N A K	くろくを80 を40 からかる 20 とこと 20 の 40 から 40 から 20 20 10 10 10 10 10 10 10 10 10 10 10 10 10	122
171 14 1 X	10 4 m 0 4 6 4 4 8 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	5 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
ר	<pre>% ************************************</pre>	

106

** ^*

 \mathfrak{D} n

LON FR	625 •0678	.1116	•1169 •0911	.1077 .0833	.0941	.1112	.0861 .0916	.0961	.1033	.1061	.1100	.1111	.0482	.0890 .0898
10% - UPPER	• 0 6 8 4	•1128 •0915	.1182 .0921	.1087 .0840	. 1948	.1122	.0868 .0923	0260.	.1042	.1069	.1108	.1121	.0887	.0896 .0903
MAX	8 8 8 8	4 0 4 0	գ Մ Մ	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	67 72		ດ ຄຸດ ຄຸດ	е 6	103	108	118	123	621	134 139
	4 1-	11	218	5 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	3 C 9 C	14	4 4 4 4	1 5 1	n n n in	6.9	20	75	78	8 9 8 0 8 0
LONE 2 ACT	625 •0679	.0513	.0578	.0453 .0557	.0435 .0503	.0565	• 0 4 9 • • 0 4 8 9	.0520 0520	• • • • • •	.0458	• 0 4 9 9	.0515	.0530	• 0 5 4 2 • 0 5 5 3
5% - UPPE3	• 0 • 0 6 8 4	• 0615 • 0524	• 0 4 3 4 • 0 5 8 2	.0460 .0560	.0437 .0505	.0567	• 0 4 4 0 • 0 4 8 3	.0522	.0434	.0459 .0481	.0500	.0517	• 0532 • 10	• 0 0 4 4 • 0 0 0 0 0
1 X U	ት ት ት	0 4 1 1	4 () (1 () (1 () (ካ ካ ባ	69 46	57	r c r Ø	6 6 6 7	50 10 10	111	121	125	131	141
	46	01	5 C C C	2 2	6 4 C 4	9 E .	4 4	ት ቢ በ ብ	l S S S S S S S S S S S S S S S S S S S	6 0 4	5 C	72	75	0 4 0 6
38	.0293 .0292	.0308 .0307 .0282 .0231	• 0 4 4 4 5 • 0 3 5 4 • 0 3 5 3 0 2 6 6 2 5 2 5	.0353 .0302	.0285 .0341 .034V	.0265 0305	.03424.0341	.0256 .0265 .0292	.0315	.0339 .0264	.0280	• UZ95 • 0294	.0320 .0307	• • • • • • • • • • • • • • • • • • • •
× Ψ Ψ	3 0 0 0 0	6 7 0 0 7 0	្រំ ហេ ។ អំហំ រ	1 4 1	75	81 84	16	97 102	107	112 118	123	128	7 7 7 7 7 7 7 7 7	143
17 1μ 1Σ	6 V M				a N	36	4	4 I 1 1	י טר מ גורי ו	ን ሌ ጉ ዓ	57		2 t	₽
]& JPPER LOWER Exact	.0156 .0098 	• 0151 • 0064 • 0121	.0115 .0115		•0114	.0092 .0091	.0110	•0100 •0100	.0113	2000 ·	.0108	C800.	5600·	.0106 .0105
MAX	4 1 6	- + 0 1 + 1	5.0	10	18	8 8 9 9 9	9 6 7	1050	110	121	125	1 2 2	142	147
	רט מי	100	17	1 T C	- 0 v m	94 94	4]	1 4 4 4	ን የ	ים ערו	63	202	74	78
ר	(ጠ 4 ቢ	n o r	000	10	12		51	140	¥о 14	20	210	9 0 7 0	51	25

:

Ā



.

ø

ţ

.2

1 = 1

2

ŧ

104 UPPER 10WFR	EXACT	• .,	.1235 .1223	.0960 .0946	.1207 .1192	.0847 .0837	.0932 .0924	.0975 .0963	.0987 .097A	•0978 •0968	.0955 .0947	.0922 .0913	.0882 .0876	.1119 .1106	.1050 .1041	.09R2 .0974	1160 . 7190.	.1098 .1087	.1017 .1009	•0941 •0933	.1095 .1096	.1008 .1000	•0929 •0923	.1060 .1052	.0974 .0968
MIN MAX	•		5 25	8 32	12 38	15 45	19 51	23 57	27 63	31 69	35 75	39 81	43 87	48 92	* 52, 98	56 104	60 110	65 115	69 I2I	73 127	78 132	82 138	86 144	91 149	95 155
PEA LOWER	EXACT		• 0494	430 .0477	384 .0383	509 .0505	594 .0591	417 .0415	451 .0449	469 .0467	477 .0475	475 .0473	467 .0466	455 .0453	439 .0437	564 .0562	534 .0532	504 .0502	473 .0472	444 .0443	535 .0534	1640. 664	404 • 0462	545 .0543	504 .0503
11 4AX UP			4 25	7 33 .0	10 40 .0	14 45 •0	19 52 .0	21 59 .0	25 65 .0	0.17 65	33 77 .0	37 83 .0	41 89 .0	45 95 .0	49 101 .0	54 105 .0	53 112 .0	62 119 .0	65 124 •0	0. 051 07	75 135 10	0 141 62	83 147 •0	R9 152 .0	92 159 .0
3% +	EXACT		.0123	.0206 .0205	.U384 .N383	0291 .0290	.0355 .0364	.0251 .0250	.0293	.0315 .n3l+	.0327	• ⁰³³³ •0332	•0332 •0332	.0328 .0327	.0320	.0310 .0309	.0298	-0285 	• 0272 ·	.0340 .0339	.0320 .0319	.0300	.0292 .n281	.0263	.0315 .0314
	I		3 27	б 34	10 40	13 47	17 53	20 60	24 66	59 72	32 78	35 84	40 90	44 96	4A 102	52 10A	55 114	50 120	54 126	59 131	73 137	77 143	91 149	35 155	30 160
18	EXACT		.0123	•0069	• 0085	.0073	.0121	1600.	.0114	.0082	•000*	•0103	.0109	.0113	.0115	.0116 .0115	.0115	.0113	0110.	.0167	.0103	•000	• 0095	•0600 •	.0113
 MIV MAX			3 27	υ Ω	8 42	11 49	15 55	19 62	22 68	- 25 75	29 Å]	33 87	37 93	41 99	45 105	49 111	53 117	57 123	61 129	65 135	69 141	73 147	77 153	81 159	86 164
ت			m	4	Ŋ	Q	2	æ	6	10	11	12	т Т Э	14	15	16	17	18	ó₹	20	21	22	23	24	25

•;

1

•

<u>.</u>

۰. م

.

÷

•

•

R

10
11

	ACT		.0993	.1233	.0786	1610.	.1126	.1017	0160 10	.1101	.0960	.1104	.0952	. 1060	0000° (. 0993	. 1073	. 0914	7790.	.1032	.1085	: 0925	1.0967	. 1003	.1039
10% -	UPPER	•	.1000	.1260	.0792	.0800	.1140	.1030	.0918	.1116	•0469	.1117	• 0959	.1072	.0916	.1002	.1082	2440.	18660。	.1041	•1094	• 0932	•0973	.1011	.1046
	XAM		28	35	4 J	50	56	63	70	76	6) 0)	89	96	102	109	115	121	128	134	140	146	153	159	165	171
1 1 1 1	NIW		ഗ	6	12	16	2]	5 2 2	29	34	38	43	47	52	56	51	66	70	75	80	85	в9	94	66	104
 	LOWER ACT		400	.0349	.0460	•0497	•0499	• 0 4 7 7	•0445	.0577	.0514	.0454	.0549	.0469	.0539	•0464	.0519	•0445	.0489	•0530	•0454	•0447	.0519	.0548	•0469
ت ع	UPPER		0.	.0350	• 0 4 6 2	.0500	.0501	•0480	1440.	.0580	.0515	• 0455	.0542	• 0471	.0540	• 0465	•0520	• 0446	•0430	• 0532	•0425	•0488	• 0520	• 0550	• 0470
1 t 1	VAX		о С	37	44	51	53	60	72	7 ዓ	83	6 0	99	105	111	113	124	131	137	143	150	156	152	169	175
1 7 5 1	78 7 5		4	7	11	ΪĴ	61	ი ი ა	75	ς. Έ	35	4	410	49	ი ჭ	ເບ ຜ	63	57	~ L	77	8 1	д А 5	16	а 25	100
3×	UPPER LOWER Exact	,	.0400	.0350 .0349	• 0252	.0300 .0299	.0318 .0317	<pre>.0316 .0315</pre>	.0302 .0301	.0292 .0291	.0259 .0258	.0329 .0324	-0292	.0258 .0257	.0306 .0305	.0257 .026b	.0305	.0255 .0264	.0297	.0329 .n328	• 0282	.0308 .0307	\$EE0. EE60.	.0285	•0305
	XAM		29	37	4 0	52	5 C	65	73	80	87	63	100	107	113	120	126	133	1 39	145	152	158	164	171	177
; ; ; ;	۸IW		4	7	ΟÎ	14	1 a	さな	ч С	30	34	9 9	43	47	ሌ በ	じん	51	5 S	70	75	61	9 4	66	93	98
1 %	JPPER LUWER Exact	_	.0100	.0150	.0126	• 0092	.0114	.0074 .0075	.0081	.0082	1800.	.0114 .0113	.0105	•0096	.0087 .0086	0107	. 00.95	.0113.	•000•	.0087	.0100	.0087	.0098	•010¥	• 0004
1	MAX		30	38	46	5 4	61	63	, 75	63	.06	96	103	110	11,7	, 1 23	130	135	143	150	155	163	169	175	182
1 1 1 1	MIN '		m	۵	ን	12	, 1 6	61	23	27	31	36	40	4 4	4 B	6 9 9	57	62	66	70	75	62	. 78	89	63
	ר		m	4	S	Q	~	ω	6	10	11	12	13	14 14	15	16	17.	18	19	20.	21	22	23	24	25

:

£

1008 1027 1031 1029 1017 .0932 0980 0957 0930 0930 0902 1052 1012 UPPER LOWER EXACT 0979 1002 0460 0863 0690 1 .1131 1071 82. 260 660 i t t 0 • .0950 0408 •0947 .0879 .1150 .1036 .1038 .1026 .0964 1020 9938 Ĺ .0826 .1086 .0870 •0988 .1019 .1041 .1010 .0989 .1060 .0940 .0937 260 10% 10140001400 1014100140 98 105 112 119 125 133 140 147 154 151 MIN MAX 14 14 œ œ 2551 S 86 97 02 07 ł 45 81 16 N -•0522 •0539 •0539 0505 .0510 .0507 .0492 0494 0445 0441 .0487 .0500 .0507 .0511 .0500 $\boldsymbol{\alpha}$.0468 .0482 a σ 047] • 0 4 5 9 UPPE2 LONE: Exact m S 0 • 033. 11 .0526 .0541 .0538 .0555 • 0470 •0489 .0510 .0513 .0512 .0508 0472 • 0502 0494 .0543 0460 .0497 0484 .0435 •0443 .0502 • 0447 4 ł ŵ 8° 8 õ XVN- VIN 5 7.9 7] œ σ m ŝ T σ o. c C 2 •0321 .0329 .0324 .0254 .0263 .0320 .0319 .0322 .0321 .0322 .0321 .0320 .0319 • 0262 • 0315 .0310 • 0549 .0258 .030/ .0316 .0283 .0311 307 . 0306 UPPER LOWER Exact • 0240 .0296 •0312 300 .0282 .0315 •0331 .0308 .0316 .0311 .0294 .0259 .0297 .0253 SIEU. 0317 .0297 0 ЗÅ 0 . 541 540 540 73 80 1,10 1,24 1,31 1,38 1,38 165 152 155 102 173 XAN VIM ហ α ហ 180 187 -----9 X ō σ 96 51 56 75 75 75 91 95 91 91 10 C ŧ or 07 .0106 JPPER LOWER 0 1 1 1 1 .01 • 0 1 0 4 • 0 0 9 4 • 0 0 9 4 .0113 •0036 0102 0083 01.10 4010. 0102 •0093 .0102 0109 ,0095 ,0098 0100 0087 0092 9900. } 1 1 ₹ 0 .01(10 **%** • 105 t MIN MAX 57 4 ID AL O i i i i 50 r 8 0. 0 ですのの ພະຜູຜ 08 40 V 86 20 81 4 M N N N N N 00 00 S.

I = I

0691 1190 ıα ū 0 UPPER LOWE EXACT õ Ī õ ٠ •0965 •1089 .1116 .1011 •1112 •1022 •1054 •1056 •1056 •1036 694 215 4 1067 0958 1013 114 σ 10% ş -• MAX .82 189 197 204 160 157 175 52 ŝ 4 • 4 Z Ξ r 0530 0481 0525 0474 0513 UPPER LONER Exact 05290474004740051300474 Ė 052A 0481 α • 0533 052.067 1 8 J X MMX V £ 201 209 ď t 1 í h 1 • 0202 • 0222 • 0321 • 0259 JB -----UMPER LOWER EXACT 0320 0323 0335 0335 0335 0329 0320 0329 0329 0329 .0324 .0301 .0278 .0278 .0317 •0327 .0325 .0297 28 .03 .0297 ရပ 0291 0274 • 0203 • 0279 • 0203 • 0 • 02223 • 0 • 03223 • 0 • 0325 • 0325 • 0302 0320 0318 0292 03 æ 1m ï, MAX 203 i 1 7 I W • ŧ FR LOWER 0121 | | | | | .0067 .0121 .0121 .0107 .0108 00094 0098 0110 0057 0105 1600 0104 .0000 1600 060 L 1 1 g d d (010 1 % • MAX ŧ 2 μ 7 - ถึง กัง กัง -

11

c -H

UPPER LOWER EXACT 0940 1038 1038 0974 0924 0924 09251 09251 09251 09251 09551 0930 094 094 095 095 • .0956 .1051 .1043 .0934 •1037 0893 .0959 .1012 .1053 .1085 .0919 e • 0902 .1064 0949 0959 0959 0958 0953 4 118: 098/ 10% • ٠ MIN MAX *** Ł ĩ L UPPER LOWE: Exact 0592 0574 0561 0500 0505 0487 0487 .0484 .0510 .0531 ഗവ 4 • 0465 0484 ł չջ Մ . . чАX 1 フレット 95 101 107 1113 113 125 1 .0333 .0332 .0353 .03352 .0359 .03552 .0310 .0309 .0243 .0309 .0243 .0309 .0243 .0309 .0243 .0309 .0333 .0332 .0313 .0312 .0270 .0237 .0319 .0317 .0277 .0287 .0303 .0316 .0327 UPPER LOWER Exact .0279 .0238 .0304 .0317 .0323 ŝ 49134664902234556488 844555422200984564888 1111111111 ٣AX 195 204 ł 7 1 W 1 -----C . JPPER LOWER EXACT 36 0085 0115 0108 01008 0100 0107 0107 0107 ហ m .010. •0068 •0088 •0081 •0104 •0117 •0084 0059 ±€00 0086 4 ٠ 0 . 10 ¥ • • MI' MAX t のからろ下のものよりらからで下して ろろろろでしてしてしてして 7 m

16.

mo e 113

0939 0929

ഗ S

094 660

നഗ G

> ò 0

.0292 97 .0296

16 • 020

Ň

õ

.

.0286

97

.

212 220 228

> 0094 0098

ຽ 0 - - -

σ 4

049 .64

. 760

		1	1.8			38 11111	1]] 1	1	5% *		1 1 1 1	1	10%	
ר	7 1 W	4AX	JPPER LOWER	7 I E	XAR	UPPER LOWER	ヽ」	хди	UPPE2	LO KER	NIW	MAX	UPPER.	LOWER
			1.7AC1						L X D				F × J	
'n	m	42 24	.0051	4	41	.0204	ŝ	40	.0510	.0503	Ś	96 6	.1020	.1008
4	2	5 S	.0128 .0127	α	52	. b255 . n254	α 1	۲. ۲	-0453	-0456	~	4	1203	1178
ഗ	11	64	.0120	13	62	.0335 .0334	14	61	• 0521	.0519	16	5.0	.1137	1121
9	15	75	• 0093	α.	72	.0345 .0344	19	1	.0504	.0501	21	69	.1008	0994
~	20	8 5 8	.0103	5 N	82	•0325 •0324	24	81	•0459	.0455	26	61	.0866	.0858
80	25	95 26	.0102	6 7	92	.0293 .0292	0 E	6	.0545	.0542	32	98	.0965	.0953
6	30	105	9500.	33	102	.0256 .0255	35	100	•0461	.0459	38	76	.10254	.1014
0	Ω Ω	115	.0087	9 G	111	.0292 .9291	41	109	• 0502	•0499	44	106	.1056	.1043
2	41	124	•0104	า เก	120	.0319 .031d	47	119	.0529	.0525	50	115	.1064	.1054
2	46	134		<u>.</u>	129	.0337 .0336	53	127	.0544	.0541	56	124	.1056	.1045
6	25	143	.0100	τ. Ω	139	. 0275	59	136	.0549	.0547	62	133	.1036	.1027
4	ទ	152	•0109	ሌ ዓ	148	.0293 .0292	500	145	.0547	.0545	68 9	142	.1007	.0997
S	63	162	•0089	5 д	157	.0285 ~	71	154	.0540	.0537	74	151	.0972	.0964
16	69	171	• 0093	74	166	.0246 .02 ⁸⁵	77	163	.0528	.0525	80	160	• 0932	.0925
[]	75	180	•00.96	80	175	.0283	e a	172	.0512	.0510	87	168	.1052	.1053
5	81	189	.00 .	3£	184	.0279	68	181	•0494	• 0 4 9 2	۴6	177	.1006	.0997
6	87	199	8600.	Е¢	192	•0329	60	190	.0475	.0473	66	186	.0950	•0944
0	63	207	.0098	66 6	201	.0317 .0316	102	1 9 A	.0542	.0539	106	194	.1053	.1044
5	66	215	.0097	105	210	.0305 .0304	103	207	.0515	.0513	112	203	.0988	.0981
20	105	225	•0036 •0095	111	219	1950. St50.	114	215 2	•04B9	.0485	119	211	.1078	.1069
ŝ	111	234	•0393	117	228	.0279 .0278	120	ちいて	· 04K1	0460	125	220	.1006	.0999
4	117	243	.0091	124	236	.0314 .0313	127	233	.0511	•0209	131	229	.0939	.0932
ហ	124	251	+0105	130	245	.029A .0297	133	242	.0480	•0479	138	237	.1010	.1004

= 15

۰,

ر.	- 7 W	MAX	1% Jpper Lower Exact		A A ۲	3Å 1}PPER LQWER Exact		- 4 X 4 A X	5% = UPPE? ExA	 LO#ER CT		I X		1010 1010 1010
ო	4	44	.0178	4	44	.0179	'n	43 6	• 0 4 4 4	•0443	so.	42	.0889	.0880
4	7	57	.0104	σ	ີ ໃ	.0373 .0371	10	5 4	.0622	.0615	11	23	.0978	.0961
ហ	11	69	.0091	13	67	. 0254	15	65	.0593	.0589	16	6 4	.0863	•0854
9	16	80	.0105	1 g	78	.0244	20	76	.0510	.0507	22	74	.0982	.0969
~	21	16.	.0102	10 10	88	.0304 .0303	25	85	.0575	.0572	28	84	.1029	.1017
60	26	102	.0091	30	9 A	.0340 .0338	Зl	97	•0455	•0453	34	94	.1027	.1014
	32	112	.010° 6010	33	109	.0210 .0269	37	107	•0463	.0465	401	04	• 0995	• 0985
10,	37	123	•0089	4]	119	.0278 .0277	4 J	117	.0465	•0462	46 l	14	•0945	.0935
11	4 J	133	•0096	47	129	.0277	64	127	•0451	• 0 4 4 9	53 1	23	•1094	.10A3
12	49	143	660Ú.	εc	139	.0271 .0270	55	135	.0537	.0534	59 J	93	.1006	.0996
13	ភូ ភូ	153	.0100	50	148	.0326 .0325	62	145	.0501	•0+99	65 1	43.	.0919	.0912
14	61	163	.0099 .0098	56	158	.0307 .0306	69	155	• 0465	•0463	72 1	52	•1007	.0997
15	6,7	173	• 0096	22	168	·0296 •0285	75	165	.0520	.0519	161	61	•1084	.1074
16	73	183	• 0092	19	177	0323 .0322	۱۶	175	•0474	• 0472	85 1	71	1260.	.0963
17	80	192	.010A	ሌ ቢ	187	.0295	88	184	.0515	.0515	92 1	80	.1027	.1019
1.8	86	202	.0101	<u>5</u> 6	196	.0326 .0325	94	194	.0465	•0465	1 66	6 8	.1074	.1055
19	92	212	+000+	40	-206	.0296 .0295	101	203	•0498	.0497	105 1	66	•0955	•0640
20	6 6	221	.0106	105	215	•031g	109	ςlç	.0527	.0525	112 2	0.8	.0989	1890.
21	105	231	•0098	111	225	.0297 .0286	114	さとく	• 0472	•0470	119 2	17	.1017	.1010
22	112	240	.010H	llg	234	.0305 .0304	121	18ç	•0493	•0491	126 2	26	.1041	.1033
23	118	250	A000.	125	243	.0321 .0320	129	240	.0512	.0511	133 2	5 9 2 2	.1060	.1052
24	125	259	.0106	lil	253	.0287	135	549	.0529	.0527	139 2	1 1 1 1 1	•0937	.0931
25	131	263	•0096	1 3 A	262	.0300 .0249	141	259	• 0470	•0469	146 2	45	•0949	•0944

ł,

16 II

7

-

0976 0956 0932 1041 1076 0963 .1049 1002 0993 .0774 .1183 .0933 4100 0914 0957 09860 1001 0969 UPPER LOWER EXACT 100 106(.10 • • • . . 0921 .0939 .1048 .0781 .1208 0944 0923 0973 .1010 .1000 .1012 .1011 1061 ÷ 4 m ¢ .1090 .1068 7660 1860 .960 .097 10% ٠ • • • 1 51 MIN MAX 50 NNN 80%631440%60%50%60%47%6%42%6 44%72110999994669554422%41 ł ഗ ŧ UPPE3 LOVE3 Exact 0390 0509 498 in a 5 4 œ 4 0 0 С 0 ٠ ٠ ٠0391 .0513 .0513 .0517 .0529 .0510 .0549 .0475 .0549 .0589 .0532 .0464 5 5 5 5 5 4 NNO O σ • 0485 • 0505 • 0523 • 0523 • 0523 .0517 .0489 .0476 .0531 .050 10 •**.** ហ らりららららららららららららららことやをとこすのもの。 ようらやをくしょう ちゅくりょう ちょうし しゅうち オモスー しゅうしょう くろころ くろう くろう Ś VAX 0 こと16 て かんのとりをごこをごうちをとしてこのこうかをござていのののの人人分ごらかどをことです。 <,, ,0320 ,0320 .U257 .0266 .U311 .0310 .0279 .0307 .0324 .0226 .0317 .0313 .0308 .0302 .0285 .0292 .0291 .0299 .0309 .0315 .0319 .0390 .0306 .0304 .0304 UPPER LOWEN Exact • 0263 • 0257 • 02 0391 0308 0308 0259 .0309 .0330 .0297 .0290 .0300 .0316 .0320 Ð σ 4 ۍ • • 0315 • 0314 • 0309 ٠ ŝ • • . . • 249 259 269 279 1 VAY. , 1 1 1 712 **うらどら 5ー かくりをりりを 70 そくしててててて**すりしたりをのうしてい くろう 10 ちょうしし くちち イムクショット くしろ 4 ちょう 10 to 10 t \$.0102 m JPPER LOWER ŧ .010. 1 -01 -0091 -03 0103 0156 0085 0121 0128 0102 008900109 0100 0091 0095 6600 1600 191 6600 0105 0101 104 EXACT . 1049 1 1 40 o 0 • ----C C 1 * ٠ t MIN MAX 1 1 7

116

ហ

I = 17

 $\overline{}$

					i				•					
7	7 ¥	W A K	1%		1 X Y F	3% UPPER LOWER EXACT	7 I. 5		5%	LONER		MAN	10%	LOVER CT
m	4	50	.0138	ហ	49	.0346 .0345	۱۲	4	,03450	2450.	٢	47	1121.	l o l
4	7	6 0	.0071	o	63	.0256 .0255			- 0427	1040 1040	- ^	- 0	1008	0000
ĥ	12	79	• 0095	15	75	.0350 .0358	• •	46	.0523	· 0250	1 1	200	1026	0660. Cloi
Q	17	16	.0087	0	88	.02/3 .0272	· ~	85	.0526	.0522	5 4 1	- 00 - 10	.0948	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
2	23	103	.0102 .0101	2 2 0	100	· 0272	6 0	9.9	• 0490	.0487	31	95	.1079	.1067
ω	59	115	.0104 .0104	ς Γ	111	•0336 •n335	30	103	• 0565	.0561	37	107	.0916	09060
σ	ŝ	127	.0101	39	123	.0297	4]	121	• 0485	•0483	44	118	• 0956	.0947
0	4 1	139	.0093	45	134	 U327 0326 	4 B	132	.0514	1150.	5]	129	.0967	.0957
11	4 8 1	150	.0107	10 V'	146	.0277 .0276	5 5 5	143	.0529	.0526	9 0 0	140	.0958	.0949
21.	10 4	162	•0034	96	157	.0248 .0287	62	154	.0530	.0529	65	151	.0934	.0926
е т ,	61	173	•0101	ን ጉ	168	.0293 .0292	69	165	.0524	.0521	73	151	.1070	.1060
4	20 U 40 I	184	.0105	73	179	.0293 .0292	75	175	.0511	.0509	90	172	.1016	.1007
ა 1.	5 / 2	561	•0109	90	190	.0289 .	83	187	•0493	.0491	97	193	.0959	.0952
16	8 1 8	207	1600.	97	201	.0281	06	199	.0473	.0471	6	193	.1051	.1042
~ :	R B G C	218	.0091	9 0	ミン	.0323 .0322	99	208	.0529	.0527	102	204	.0980	.0973
£0 -	96	228	.0104	102	222	.0309 .0308	105	6lc	6670.	.0497	110	214	.1052	.1043
6 .	103	539	•0106	109	233	.0293	112	230 230	•0469	.0467	117	225	.0973	.0946
202		250	.0103	116	442	.0278 .0277	120	240	•020•	.0507	125	235	.1029	.1021
2		261	.0100	124	254	.0395 .0304	127	251	•0474	.0473	132	246	• 0947	.094]
22	124	272	• 0036	131	ζ65	.0236 .0285	135	26 l	.0507	.0505	140	256	1660.	.0984
53	132	282	• 0107	139.	. 275	.0309	142	272	.0470	•0458	148	256	.1030	.1024
. 1 .	139	293	•0102	146	286	<pre>.0257 .0286</pre>	150	282	•0497	•0495	155	277	• 0943	.0937
2 2	146	304	•0036	154	296	•0305	159	292	• 0522	• 0250	163	287	•0974	.0968

£

117

١

. .

= 18

÷

0976 0968 0958 0958 0944 1 8 UPPER LOWE EXACT 1 0849
1108
0937
0943
0943
0943
0943
1078
1079
1063 0950 0952 0938 0938 0932 0932 0932 0953 0953 .1080 Q 104(10% ٠ MAX 1 1 NIW ÷ j, F o L UPPER LOWER Exact I. i T I I I .0511 10 4 5 G N .050. • 051 .051 -05 ഹ 3% 2% 0 чАX 0 1 L 1 0.0 0.0 t 1 1 フレカ UPPER LJWER Exact ÷ 0 m 0283 0292 0293 0293 0209 0309 0310 .0309 .0286 .0287 .0287 .0287 .0287 .0287 .0287 .0281 .0281 .0281 0296 0303 0317 30 . . • • ų t 0 XAM 269 240 291 302 313 NIN t .0101 .0103 .0100 .0096 .0109 .0109 .0101 .0101 .0101 .0101 .0101 .0104 0120 0123 0122 0098 0096 .0095 .0112 .0095 \$ α JPPER LUWER Exací .0123 * 0 MAX 1 ナニゼ 5

19 tŧ

.0957 .1024 .0882 0918 œ Ŵ UPPER LOWE EXACT t 60 i I I .10970 .1042 .0892 .09930 .09934 .0994 .10940 .10940 .10946 ŧ ო თ Ð 0 00000 1010 560 .104 095(0965 .101. 00 10.5 -1 • . . • MAX ŧ t NIM 91945910100980204552024 9205520100980204552004 9101111111 1 • 0480 • 0523 • 0499 • 0475 I. UPPE2 LOWE3 Exact ന ţ. 1 İ t 0 ł 51 տ Տ 0 1 1 1 чАX Ì フレカ 4 1 ~ 0277 0306 0305 0301 0305 0301 0305 0332 0334 0335 0334 0325 0324 0305 0324 0305 0324 0305 0324 0305 0324 0325 0324 .0299 .0300 .0299 .0295 .0294 .0289 .0294 .0282 .0294 .0313 .02812 .0302 .0301 .0315 .0314 ł UPPER LOWER Exact ł 0277 1 Э¥ . . ٠ . -X٩٤ I ŧ i 21 1 1 Σ JPPER LOWER EXACT 0.0109 I. 1 •000• .0101 .0102 .0102 .0102 .0102 .0033 .0095 .0111 .0102 •0005 •0090 .0103 •0102 .0108 .0095 .0099 •000• ŧ 11 011 13 • 334591647580801869185349514378 332106476582109865379328 3321064765831085379328 3321064765831085310 MIN MAX t 1 1 1 5

119

١

•

1 = 20

J

10% ----1 UPPER LOWER Exact 647 0962 0965 α ŝ 81 58 0957 0865 .080 ŏ .0875 .0894 .0969 .0925 .11.02 .0928 .0928 .1069 .0966 .0966 .0965 .0973 .0963 .0953 0468 1 МДХ I NΙM a t ACT 6.5 1 I Ò 1 . . ٠ ٠ . • ٠ • 500 ŧ ພະ UPPI 5% 0 • ٠ ٠ ٠ . . • • . ちてしいのうちゅうかん しょくりん うくうろう うろう しょうしょう ひんゆう しょう くうくう くうこう I × 6 I E A N 33) t t 34 Ē ŧ 7 ł 15 - 0261 - 0261 5 - 0272 5 - 0314 18 - 0317 - 0299 - 0295 - 0310 - 030 - 0315 - 03' .0313 307 .0306 2297 .0296 3295 .0284 3314 .0313 1 .0311 .0287 .0299 .0310 UPPER LOW-PH t T T EXACT. 0250 .0295 .0317 .0245 4 ω .0253 .0273 .0315 .0318 Ň 0297 0285 0314 t 312 312 310 311 0 ŧ. ٠ я М 0 0 00 ¢ • ٠ . • . XAr 1 ۷IW 1 ŧ ٠ α JPPER LOWER Exact .0100 .0087 .0087 .0085 .0085 .0103 .0108 .0108 .0108 .0108 .0108 .0108 .0108 .0108 .0108 .0108 ~ 4 C ----.0 0104 H€00. .0106 0098 *ن*ه, ŧ ٠ 0 ж 0 -. • ٠ E X M M V 1 μ ł 7

۳.

٤

•

1 = 21

EXACT EXACT • 0091 • 0103 • 0103		C C			× 4 ×	2770	7170-	Z T E	XAM	UPPER	LOWER
• 0091 • 0076 • 0103 • 0103			EXACT	I		СХ Ш Х				EX	ст
• 0091 • 0076 • 0103 • 0095	ŧ										
•0076 •0103 •0095	ſ	61	•UZZ7 •9226	r	60	.0454	•0451	2	с С	.0794	.07A5
•0103 •0095 •0104 •0103	11	77	•0,356 •0354	27	75	.0535	.0530	14	74	.1081	.1062
-0104 -0103	17	63	.0318 .0317	6	0	.0441	043R	. 7	0		
-010, 4010.	5	108	.0330 .0328	2.2	105	.0564	0550.	1 U 1 U	104		
· · · · · · · · · · · · · · · · · · ·	31	123	JJ07 . 0306	, ,	2010	10701	2040 -	2 C 7 L		0040	
.0101	3 я	138	.0270	4	י ע ה ר	よくい 0 · · · · ·		20			
2600	4 5	152	.0285	4	0 4		- 0 1 0 v	ר ה ה ת	1451	0 0 0 0 0 0 0 0 0	
.0102	54	166	- J290 . 1289	5		.0510		2 4			~ ~ ~ ~ ~ ~
.0107	52	180	0294 1283	- 11 1 1		2440.		- 0 - 4		• 1000	0101. 0101.
.0108	17	193	LSEN 4560) -		0 5 5 0 -		- a 			> n n n n n
.0106	79	207	E030.	. d	204	<070 ·		- 4			1 ~ ~ ~ ~ ~ ~
.0102	7 4	221	.0291 .0280	5							アルロー
.0097	36	234	0.301 0.200						v - v - v		1601.
. 010×] o E	1 N 1 N 1 N		* *		• C t O 1	• 0 + 0 •		0 V V	.0438	.0432
			CIC() 01/ ^ •	104	t nt	• 0 + 8 +	• 0 4 8 5	113	239	•0943	.0936
		2 C C C C C C C C C C C C C C C C C C C	. 0784	117	257	•07670	-0495 -	123	251	.1063	.1055
1010	ς γ γ	515	• V 2 9 3 • 0 2 4 2	125	0 L c	6670.	.0497	132	264	.1048	.1040
• 0097	131	287	•029a	135	283	.0501	0 498	141	277	.1028	1021
.0102	140	300	.0302 .0301	144	295	• 0 4 9 7	-0495	150	062	.1004	1000
.0106	149	313	• 0302	153	60°	-0495	1040-	55	203	7790.	0071
• 0095	159	326	• 0302 • 0301	162	222	0445	.0483	941	ט ג ה ה		
.0097	157	339	.0299	171		.0476	0476				· • • •
9600°	176	352	.0295	181	747	0510					1161.
6600.	a ca l	365									+ - r - r

11

.....

.

••

• - '

. *

1 · 4 . 17. 1 4

۰ ، , ی

. . .

0911 1011 1011 0915 0950 0950 10255 09250 09250 09255 09260 1109 .1037 .0971 .1008 .1038 UPPER, LOWER EXACT 1 1137 1004 10% -----1157
0922
0922
0922
0953
0983
0985
0985 .1054 .0994 •1044 •0977 1045 .1014 266 0 6 õ MAX 311111 ZIW 1111111111 984555447589991734487748 99555447389999173448 0 1 r UPPEA LOMER Exact 041] ſ 1 111 0 4 5 8 V 5 8 V s S 0 0 0 VAX t l 1 フルナ 1 .0207 .0206 .0310 .0308 .0254 .0263 .0251 .0260 .0297 .0296 .0284 .0283 .0313 .0312 .0282 .0281 .0295 .0281 .0295 .0294 .0305 .0304 .0303 .0304 .0299 .0308 .0307 .0295 .n294 .0307 296 UPPER LOWER EXACT œ õ .0315. 0299 .029 . .0300 .0282 1620. **C** • 297 а¥ К 0 ٠ ٠ ٠ ٠ . ٠ XAM VIM ŧ ----1 ar ЈРРЕА ĽИМЕЯ Ехаст 1 0105 0101 0098 0094 11111 ж • XAM VIM っ

11

UPPER LOWER EXACT 1029 1042 1102 0030 0030 0993 1021 6760 6760 1032 1014 0960 1023 1071 0915 1054 0 \circ ហ 104 104 10 99 97 i .0955 •1034 •1034 •0523 •1055 .1022 .0968 •1029 .1048 .1058 039 .0941 .0922 .1037 .1000 .1122 .0960 .0954 4 ഹ .1059 021 00 098 10% 345 359 373 387 WIN WAX 4 Ś .0529 .0529 .0515 .0515 .0473 .0504 .0504 .0508 .0508 ~ n 377 .0487 .0497 EN LOMES Exact 0 Ì 0505 0517 0475 0489 0200 0588
0554
0554
0454
0453
0453
0474 .0522 .0522 .0531 .0531 0467 0499 0509 508 .0379 UPPE: 205 1 ហ ស õ ō ٠ • 955. 35.2 83 11.7 133 148 154 173 194 209 523 23B 25,2 295 310 324 365 380 66 184 t L J VAX 39 7] 4 99 ŝ 5 m 1 m 2 m 3 10 4 Ac) ጥ ----¢ x S てで .0304 .0303 .0315 .0314 .0299 .0287 UPPER LJWEH EXACT 299 .0288 290 .0279 315 .0279 290 .0279 292 .0249 292 .0241 20289 290 0279 309 0304 292 0241 .0312 0239 .0298 .0305 .0274 0377 1 ł 0 9 0 9 0 9 .0294 .0240 .0309 .0292 .0306 .0290 .0290 .0315 .0292 .0292 .0290. 0 .0271 ł .0378 . . R ٠ 343 66 85 1102 1135 1135 1151 1165 1165 1165 1197 256 271 314 328 ۲A۲ 512 242 242 285 300 357 371 385 ě NIŴ 11222 t 0 Q c 0144 .0104 α .0104 .0103 .0107 JPPER LOWEI EXACT 0107 .010 • 0084 • 0105 • 0089 0098 0105 0092 0092 0094 0093 0100 0095 0103 .0076 0096 0102 0094 0038 0101 1 ж ٠ . MAX -110 D 381 39 ō 7 I W 105 1125 1125 1155 1152 1162 1191 191 Î M4U02001010495220010149 7

123

.

al design of the second s

L.

Ň

11

6663 0963 0989 1007 0862 606 0948 0460 1074 916 N 0954 1034 1034 UPPER LOWER EXACT 071 2 0 0884 1660 102102102102 40 0 õ õ 0874 .1048 .0928 .0918 0.961 1042 1023 0956 646 1000 1041 0970 995 013 026 033 96 035 ě 20 δÔ 0 0 0 ò ٠ ٠ . • . • MAX 66 00 375 90 10 0 $\overline{\mathbf{v}}$ Ô m f + MAN 98 4 0 1 1 1 0 4 0 0 0 0 0 1 1 1 1 0 4 0 0 208 219230 97 ł .0555 .0555 .0518 .0518 .0518 0481 0501 0513 ø R δ 0510 m 0 in 4 4 NI 0 .0483 .052) .0469 EN LOWE 048 052 050 050 050 050 048] 4 0 0 0 0 0 00 0 UPPE2 L Exac 0458 0521 0486 0515 0511 0560 く870 S Ś • S m N N m 0 048 052 047 048 048 047 020 048 051 048 049 1 C 0 0 0 у Ж 178 194 755 243 200 00° 20° 383 39 я X۵۷ 100100 **O** llż 337 352 367 8 321 m α 0 ~ 4 L. Ņ, 1 211 0319 0315 0315 0297 0302 .0322 .0296 .0341 .0319 •0317 0301 0310 1 UPPER LOWER EXACT 0 30 290 • 03 0100 Ś .0285 0 ¢. ∩ ► 028 ٠ . ٠ ٠ • ٠ ဂဆ 030 .0320 .0317 .0298 .0303 .0320 .0318 .0323 .0311 .0302 .0290 F . m ы У O, KA: 72 92 111 129 129 246 254 254 310 355 357 372 372 372 181 197 214 164 7 くこのてらゅうらくろう 50 ς. 5 μ ~ ~ ~ M N N **3**-2 0 JPPER LUWER Exact Q 0 •01 .010 .0160 .0381 .0112 .0103 .0101 -0092 -0091 .0095 .0076 .0075 .0103 •0096 03 •0] .0107 4600 0198 œ 0104 1600 0103 .0108 111 01 æ $\overline{\mathbf{O}}$ MAX 50441455554194/113 84587086554144/113 7777771444 303 313 335 366 366 398 4 4 4 7 ž No No 5

1 = 25

APPENDIX B

COMPUTER PROGRAM DOCUMENTATION

-

*

• , . .

3

*

SCONTRUL FILE=5,FILE=6 С Ç A FURTRAN PROGRAM FOR CALCULATING ONE-SIDED PERCENTAGE С POINTS FOR YOUDEN'S TEST BY EXHAUSTIVE ENUMERATION С USING BOTH LEHMER'S METHOD AND WELL'S METHOD OF С COMBINATORIC ENUMERATION. С С THE CODING IS SPECIFIC TO THE HP3000 SYSTEM. ·C CHARACTER ANS#1 DIMENSION KOUNT (24) + NSUMS (6) + DIST (80) COMMON LIST (760, 6), NPERM 5 DISPLAY "ENTER NUMBER OF OBJECTS AND JUDGES" ACCEPT NORJ, JUDGES 1F(NOBJ.EQ.0)STOP NPERM=1 DO 7 I=2+NOBJ NPERM=NPERM*I 7 DISPLAY "LEHMER OR WELLS" ACCEPT ANS IF (ANS_EQ. "W") GOTU 10 CALL LEHMER(NOBJ) GOTO 15 CALL MRWELLS(NOBJ) 10 15 DO 20 J=1, JUDGES 20 KOUNT(J) = 100 22 K=1.80 22 DIST(K) = 0.0DO 30 J=1,NUBJ 25 .30 MSUMS(T) = ID0 40 J=1+JUDGES K=KOUNT(J) D0 35 I=1+N08J. 35 NSUMS(I)=NSUMS(I)+LIST(K,I) 40 CONTIN JE MIN=999 00 45 I=1.NUBJ IF (NSUMS(I) .LT.MIN) MIN=NSUMS(I) 45 CONTINUE DIST(MIN)=DIST(MIN)+1.0 DO 50 J=1+JUDGES KOUNT(J) = DOUNT(J) + 1IF (KOUNT(J) .LE.NPERM) GOTO 25 KOUNT(J)=1 50 CONTINUE WRITE(5,100)(DIST(K),K=1,80) 100 FORMAT (" RAW FREQUENCY COUNTS"/. (1x, 10F7.0/)) DO 55 K=2.84 55 UIST(K) = UIST(K) + DIST(K-1)WRITE(6,110)(DIST(K),K=1,80)

110	FORMAT(" ACCUMULATED FREQUENCY COUNTS"/+(1X+)0F7+0/)) P=DIST(80)
	$00 \ 60 \ <=1.80$
60	DISI(K) = DISI(K)/P
	WRITE(6+120)(DIST(K)+K=1+80)
150	FORMAT(" STANUARDIZED FREQUENCY COUNTS"/,(1X,10F7.5/))
	GOTO 5
	END
	SUBROUTINF LEHMER (NOBJ)
	DIMENSION NUIGIIS(6), NDIGIIS2(6)
	LOMMON LIST (760,6) +NPERM
	UQ 30 K=0,NPEPM←1
~	
5	
10	
10	
	NDTGTTS(ND-1) = N2 + M*ND+1
	N2=M
	1F(M.GF.1)GOTO 10
	IF((ND-1).EQ.NOBJ)GOTO 15
	L2=N0-1
	DO 13 1=NOBJ, 1,-1
	1F(L2.E0.0)GOTO 12
	NDIGITS(1)=NDIGITS(L2)
	r5=r5-1
	GOTO 13
12	NDIGIIS(I) = 0
13	
16	
12	
	NDIGITS 2 (1) = NDIGITS (1-1)
	IF (NDIGITS2(U), GF, NDIGITS(U) NDIGITS2(U) =NDIGITS2(U) +1
20	
20	$LIST(K_1+I+1) = NDIGITSP(NOBJ)$
25	CONTINJE
30	CONTINJE
	RETURN
	END
	SUBROUTINE MRWELLS(N)
	$DIMENSION \ A(10) \star XM1(10)$
	COMMON D(720,6),NF
	$\begin{array}{c} \text{DO} 10 1=1 \\ \text{O} 10 \\ \text{O}$
10	4(T)≥∩ [*] Ω
τu	
12	- XM1 (11)
12	
	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

- Q

۲

ł

ŝ

i

	N1=M-1
	J=0
	NH=0
15	J=J+1
	I = J + I
	NQ=N1/T
	$NR = NI - VQ \Rightarrow T$
	IF (NH) 30.20.30
20	IF (NR-1) 25.30.25
25	NH=J
чU	A (J) =N2
	IF (NQ) 35.40.35
35	N1=N2
	GO TO 15
40	IF (NH) 50,45,50
45	NH=J+1
50	L=M
	DO 47 I=1.N
47	D(L,I) = XMI(I)
	NS=NH+1
	IF (NH-(NH/2) #2) 60,55,60
55	IF (A(NH+1)-2,)60,70,70
60	W=XM1(NS)
	XM1(NS)=XM1(NS-1)
	XM1(NS-1)=W "
	GO TO 90
70	NX=NH-A(NH+1)
	IF(NX)75,75,80
75	NX=1
80	W=XM1(NS)
	XM1(NS)=XM1(NX) *
	XMl(NX)=W
90	CONTINJE
	RETURN
	END

۴.

PROGRAM TST(INPUT, UUTPUT, TAPE5=INPUT, TAPE6=0(ITPUT) С С A FORTRAN PROGRAM FOR CALCULATING ONE-SIDED PERCENTAGE С POINTS FOR YOUDENS TEST IN THE CASE OF 1 = 2. С С THIS PROGRAM IS BASED ON THE RINOMIAL THEOREM AND IS С SPECIFIC TO THE CDC6400 SYSTEM. Ç DIMENSION NA(200) +NU(200) 10 READ(5,100)LU,NHI 100 FORMAT(213) IF(EOF(5))1000,20 20 #RITE(5,110) 110 FORMAT(1H1) CALL NAINOM(L()-2, NA) NS=2MS=2*L0+1 DO 80 J=LO,NHI NS=NS#2 K=J-2 00 40 I=1.K 40 NB(I+1) = NA(I) + NA(I+1)NB(1) = 1NB(J) = 100 50 I=1.J 50 NA(I) = vB(I)DO 55 I=1.200 L=J/2 DO 60 I=1,J K=J+I $IF(I \circ GT \cdot L) K = K + J - I - I$ NB(K) = NB(K) + NA(I)60 L=L+J WRITE (5, 120) J.NS 120 FORMAT(* C = 2, J = *, 13 + * SUM = *, 114) C=0.0 MS2=MS DO 70 I=J.L P=FLOAT(NB(I))/FLOAT(NS) C=C+PMS2=M52-1 WRITE(5,130) I + MS2, NB(I) , P, C 70 130 FORMAT(1X,12,2X,12,2X,114,2X+F8.6,2X+F8.6) MS=MS+2 80 CONTINJE GOTO 10 1000 STOP END SUBROUTINE NBINOM (N+LIST) DIMENSION LIST(1)

1

. .

Ę

ž

Ĺ

ł

÷,

í

,
MID=N/2+1 LIST(1)=1 LIST(N+1)=1 IF(MID_LE+1)RETURN DO 10 VX=2+MID LIST(NY)=LIST(NX-1)*(N+NX+1)/NX 10 LIST(N=NX+2)=LIST(NX) RETURN END

٤

.

```
$CONTROL FILF=5, FILE=1, FILE=2, MAP, LABEL
С
    A FORTRAN PROGRAM FOR CALCULATING ONE-SIDED PERCENTAGE
С
    PUINTS FOR YOUDENS TEST USING AN ITERATIVE PROCEDURE
¢
С
    BASED ON BONFERRONI'S INEQUALITIES.
С
    THE CODING IS SPECIFIC TO THE HP3000 SYSTEM.
C
С
      COMMON JUPPER/ CINV+NC+PROB(8400)+MPTR(25)
      COMMON /LOWER/ CINVL, NCL, MLP (R(25)
      DISPLAY "ENTER LOW VALUES FOR C AND J"
 5
      ACCEPT NCLUIJLU
      IF (NCLD. FQ. 0) STOP
      DISPLAY "ENTER HIGH VALUES FOR C AND J"
      ACCEPT NCHI+JHI
      UISPLAY "ENTER LOWER & UPPER CUM. PRUB. VALUES"
      ACCEPT CUMPLO, CUMPHI
      DO 30 NC=NCLO,NCHI
      NCL=NC-1
      MPTK(1) = 1
      MLPTR(1)=1
      UO 7 K=2,25
      MLPIR(\langle) = MLPIR(K-1) + NCL^{*}K-K
      MPTR(K) = MPTR(K-1) + NC^{P}K - K
 7
      `LIMITP=MPTR(25)+NC*26-27
      LIMITL=MLPTR(25)+NCL*26-27
      DO 8 K=1,LIMIIP
      PROB(K) = 0.0
 8
      REWIND 2
      DUM=0.0
      DO 9 K=1,1 IMITL
      WRITE(2)DUM
 9
      C=FLOAT(NC)
      CL = C - 1
      CINV=1./C
      CINVL=1./CL
      1HC+01C=L 05 00
      L+S/([+L)=TJAX3XAM
      KMAX=NC#J
      KHI={KMAX+J}/2+J
      CUMP=0.0
      CUMPL=0.0
      00 10 K=J+KHI
      CALL TAU(J,K,P)
      PR=C*P
      CUMP=CJMP+PR
      ALPHAL = CUMP
      IF (K.LT, MAXEXACT) GO TO 15
      CALL TAL (J, K-MAXEXACT+J,P)
      PRL=CL+P
```

COMPT=COMPT+bKT ALPHAL =CUMP+CUMPL*PR IF (CUMPLI) CUMPLO) GO TO 10 15 1F(CJMD.GT.CUMPHI)GU TO 20 WRITE(1.100)NC.J.K.KWAX.CUMP.ALPHAL FORMAT(12,1X,12,1X,13,1X,13,2F9.6) 100 KMAX=KMAX-1 10 CONTINJE 20 30 CONTINJE 60 TO 5 END SUBROUTINE THU(J+K+P) COMMON /UPPER/ CINV+NC, PROB(8400) + MPTR(25) P=0.0 IF (K.GT.NC.) RETURN IF(J.NE.0) GO TO 15 IF (K.E3.0)P=1.0 RETURN IF(J+NE-1)60 TO 18 15 P=CINV RETURN IF (J.NF.K) G0 TO 20 18 P=CINV##J RETURN $N_1 = M^p T_q(J) + K = 1$ 20 1F(PROR(N1).EQ.0.0)G0 TO 25 P=PROB(N1) KETURN 25 L=K-J+1IF(L.GT.NC)L=NC 00 30 I=1,L CALL TAU(J-1,K-I,PS) P=P+PS 30 P=P*CINV PROB(N1) = PRETURN END SUBROUTINE TWL(J,K,P) COMMON /LOWER/ CINVL, NCL, MLPTR(25) $P=0 \neq 0$ IF (K+GT+NCL*J) RETURN IF (J.NE. 0) GU TO 15 1F(K.E3.0)P=1.0 RETURN 15 IF (J.NE.1) GO TO 18 P=CINVL. RETURN 1F (J+NE.K) GO TO 20 18 P=CINVL##J RETURN

1.5

á,

ţ

é

3

- 20 N1=MLPTR(J)+K-1 READ(20N1)PROBL IF(PROBL:EQ.0.0)GO TO 25 P=PROBL: RETURN
- 25 L=K-J+1 1F(L+GT+NCL)L=NCL DO 30 I=1+L CALL T+L(J-1+K-I+PS)
- 30 P=P+PS P=P*CIVVL *RITE(20N1)P RETURN END

.

1

```
$CONTROL MAP, LAREL , FILE=5, FILE=6
С
С
    A FORTRAN PROGRAM FOR SENERATING POWER CURVES FOR
С
    NAIR'S JEST AND YOUDEN'S UNDER SPECIFIED PARENT
С
    POPULATION ASSUMPTIONS.
С
С
    THE CODING IS HP3000 SPECIFIC.
С
       DIMENSION A(25,25),B(25,25)
 5
       WRITE(5+110)
      FORMAT (" FNTER I, J, # OF SIMULATIONS")
 110
       READ (5. #) I.J. NITER
       1F(1.Eg.0)STOP
      LIM=1-1
      XNITER=FLOAT (NITER)/100.
      WRITE(5, 120)
 120
      FORMAT (" ENTER CRITICAL 1 & 5% VALJES FOR NATE & YOUDEN")
      READ (5, *) C1+C2+NY1+NY2
      WRITE(5+130)
      FORMAT (" ENTER LOWEST DELTA, STEPSIZE & NJMBER OF STEPS")
 130
      REAU(5, *) XLOW, STEP, NJMDELTA
      WRITE(6,140)
      FORMAT (" FNTER SEED")
 140
      READ(5.4)SEED
      ARITE (6+150) I+J+NITER+C1+C2+NY1+NY2+SEED
      FORMAT (" I = "+12," J= "+12," SIMULATIONS = "+14/
 150
     +" CHITICAL POINTS= "+F4+2+3X+F4,2+3X+14+3X+14/
     +" RANDOM NO. SEED= ".F10.5//)
      IF (SEED.EQ.0.0) GO TO 7
      DUM=RAVD(SEED)
 7
      DELTA=XLOW-STEP
      DO 90 ND=1+NUMPELTA
      DELTA=DELTA+STEP
      MINN3=0
      MINN4=0
      MINN]=0
      MINN2=0
      MINY]=0
      MINY2=D
      DO 80 ITER=1+NITER
      DO 20 L=1.J
      00 17 K=1,LIM
С
    CHANGE THE FOLLOWING TWO LINES
С
   TO REFLECT THE PARENT POPULATION DESIRED.
С
С
      A(K,L)=UNIFORM(0.0,1.0,DUM)
17
      A(I+L) = UNIFORM (0.0.1.0.UUM) - UELTA
 20
      CALL NAIR(I)J+A+STATNR,MINOBJ)
      IF (MINDBJ.NE.T) GO TO 30
```

. .

•

IF (STAINR.GE.C1) MINN3=MINN3+1 IF (STATNR.GL.C2) MINN4=MINN4+1 DO 60 L=1.J 30 XM=0.0 DO 50 4=1.1 XM=X4+1. XMIN=99.E70 00 40 <=1+I IF(A(N,L)-XMIN)35,40,40XMIN=A(K+L) 35 NPTR=K CONTINIE 40 A(NPTR.L)=99.E70 B(NPIR.L)=XM 50 CONTINJE 60 CALL NAIR(I+J+B+STATNR+MINOBJ) IF (MINDBJ.NE.I) GO TO 78 IF (STATNR.GE.C]) MINN] = MINN] +1 IF (STATNR.GE.C2) MINN2=MINN2+1 78 CALL YOUDEN (I.J.B.MINOBJ, NOBJSUM) IF (MIN)BJ.NE.I) GO TU 80 IF (NOBJSUM.LE.NY1) MINY1=MINY1+1 IF (NOB JSUM. LE. NY2) MINY2=MINY2+1 CONTINIE 80 YMINI=FLUAT(MINY1)/XNITER YMIN2=FLOAT ('4INY2) /XNITER XMIN1=FLOAT (MINN1) /XNITER XMIN2=FLOAT (MINN2)/XNITER XMIN3=FLOAT (MINN3) /XNITER XMIN4=FLOAT (MINN4) /XNITER WRITE(5,100)DELTA, XMIN], XMINC, YMIN1, YMIN2 FORMAT(1X+F3-1+4F10-1) 100 WRITE(5,105)XMIN3,XMIN4 FORMAT(4X+2F10,1) 105 IF (XMIN1.E0.100..AND.XMIN1.E0.100.)GU TO 5 CONTINJE 90 GO TO 5 END SUBROUTINE NAIR(I, J, D, STATNR, NR) DIMENSION C(25) + D(25,25) Q1=1 ພປະປ SSQRS=0.0 55QCS=0.0 655Q=0.0 GS=V.0 DO 5 L=1.J 5 ((L) = 0.0XMIN=99.E70 DO 20 K=1+1

.)

 \mathcal{O} 137 KS=0.0 00 10 L=1.J $P=D(K \bullet E)$ KS=RS+> C(L) = C(L) + P10 GSSW=GSSQ+P*P GS=GS+2S SSQRS=SSQRS+RS#RS IF (RS. 3E. XMIN) GO TO 20 XMIN=RS NR=K CONTINJE 20 10 30 L=1.J 30 SSQCS=SSQCS+C(L)+C(L)GM=GS/(QI*QJ) EV = (GSSQ - SSUCS/QI - SS3RS/QJ + GS*GS/(QI*QJ))/((QI - 1 +)*(QJ - 1 +)))STATNR=(GM-XMIN/QJ)/SORT(EV/UJ) RETURN END SUBROUTINE YOUDEN(I, J, A, MINOBJ, NOBJSUM) DIMENSION A(25,25), TEMP(25) C 00'3 K=1+1 IEMP(K) = 0.0 ~ 3 DO 50 K=1,1 00 40 L=1,J TEMP(K) = TEMP(K) + A(K+L)40 CONTINUE 50 XMIN=1000. $00 \ 60 \ \kappa = 1 \cdot I$ IF (TEMP(K).GE.XMIN) GO TU 60 XMIN=TEMP(K) MINOBJ=K 60 CONTINJE NOBJSUM=IFIX (XMIN) RETURN END FUNCTION UNIFORM (XMEAN. VARIANCE, DUM) WIDTH=SQRT(12. #VARIANCE) HALFWIDTH=WIDTH/2. UNIFORM=RAND (DUM) *WIDTH+XMEAN-HALFWIDTH RETURN END FUNCTION DNORM (DUM) UNORM=-6.0 DO TU 1=1+15 10 DNORM=DNORM+RAND (DUM) RETURN END

٠,

138

```
$CONTRUL FILE=5,FILE=6
С
С
    A FORTRAN PROGRAM FOR ANALYSING DATA ORGANISED
    IN A THU WAY CLASSIFICATON BY YOUDEN'S TEST AND
С
    NAIRIS TEST.
С
C
С
    THIS PROGRAM WAS WRITTEN FOR THE HP3000 COMPJTER
С
С
    SYSTEM. MODIFICATIONS MAY BE NECESSARY BEFORE
C
    SUCCESSFULLY EXECUTING THIS PROGRAM ON ANOTHER
С
    COMPUTER.
С
      COMMON A (25+25) + XXX + MMM + DUM
      DIMENSION B(25,25)
 10
      DISPLAY "ENTER ROWS & CULUMNS"
С
    BOTH NRON AND NCOL HAVE A MAXIMUM VALUE
С
С
    OF 25 AND DEPEND ON THE DIMENSIONS OF
С
    ARRAYS A AND B.
С
    NROW <= 0 TERMINATES THE PROGRAM.
С
      ACCEPT NROW NCOL
      1F(NRON.LE.0)STOP
      UUM = RAND(17.)
      NC=NCOL
      NR=NRO*
      DO 15 I=1, NROW
      ACCEPT(B(I+J)+J=1+NCOL)
 15
      GOTO 30
      DISPLAY "OPTION?"
 20
      ACCEPT NOP
С
C
    THE OPTIONS ARE:
Ĉ
         ENTRY OF NEW DATA
     1
         REINITIALIZE WITH EXISTING DATA
C
     2
С
         CALCULATE USING NAIR AND YOUDEN'S TESTS.
     3
С
         INVERT MAIRIX
     4
С
     5
         TEMPORARILY DELETE A ROW
С
     6
         DISPLAY PRESENT STATUS.
С
     7
         SPECIFY EITHER MAX OR MIN EXTREME DEVIATE
С
      GOTO(10,30,50,70,90,110,130),NOP
 30
      DO 40 I=1,NKO*
      DO 40 J=1.NCUL 3
      A(I,J) = B(I,J)
 40
      NC=NCOL
      NR=NRU/
      GOTU 20
 50
      CALL YOUDEN (NR, NC, MINROW, MINSUM)
      DISPLAY"YOUUEN .. ROW=" . MINROW . "RANK SUM=" . MINSUM
```

CALL NAIR (NR, NC, STAT, MINROW) DISPLAY"NAIK. . ROW=", MINKOW, "STATISTIC=", STAT 60TO 20 . LARGE=VR .70 IF (NC.GT.NR) LARGE=NC DO 80 1=1+LARGE DO 80 J=I+1+LARGE TEMP=A(I,J) $A(I \bullet J) = A(J \bullet I)$ A(J,I) = TEMP80 NTEMP=VR NR=NC NC=NTEMP GOTO 20 DISPLAY "ROW?" 90 ACCEPT NU DO 100 I=ND + NH-1 DO 100 J=1.NC 100 (L+I+I)A = (L+I+J)NR=NR-1 GOTO 20 DISPLAY"NR/NC", NR, "/", NC, "MINMAX=", MMM 110 DISPLAY $((A(I \cdot J) \cdot J=1 \cdot NC) \cdot I=1 \cdot NR)$ GOTO' 20 130 DISPLAY "MAX=1+MIN=0" ACCEPT NOP С С TO TEST FOR MAX. EXTREME DEVIATE ANSWER 1 С 11 ŧI. 11 MIN. 11 11 Į¢. 2 С THIS WILL STAY IN EFFECT UNTIL CHANGED С BUT MUST BE INITIALIZED WHEN NEW DATA IS ENTERED С $X_{X}X = 1$. MMM=1 IF (NOP, EQ. 0) GOTO 20 $X_X X = -1$. MMM=-1 GOTO 20. END SUBROUTINE NAIR(I, J, STATNR, NR) COMMON D(25,25),XXX, MMM DIMENSION C(25) QI = Iພງ≃ງ SSQRS=0.0 SSQCS=0.0' $G_{5}SQ = 0.0$ $GS = 0 \cdot 0$ 00 5 L=1,J $\mathcal{L}(L)=0.0$

139

2

ş

人民ない

1	XMIN=99.E70
	$00 \ 20 \ x=1,1$
	RS=0.0
10	655Q=655Q+P*P
	65=65+25
	SSQRS=SSQRS+RS#RS
	IF((PS*XXX)+GE,XMIN)GO TO 20
	XMIN=RS*XXX
	NR=K
20	CONTINUE
	XMIN=XVIN*XXX
	DO(30) = 1 + J
30	SSBCS = SSBCS + C(L) + C(L)
00	
	$F_{v=1}(S_{0}) = (S_{0})
	STATUR-($GM_XMIN/0$))/SOPT(FV/0))
	CHODOLINTAE VOLUENTAR NO. MTAOR NOD ICHM)
	DIMENSIUN N125,25) INIEMF(25)
	DO TO JETINK ·
10	$N(I_{3}J)=0$
•	UO 30 LC=1.NC .
	M=0
	NSTRT=FLOAT(NR)*RAND(DUM)+1.
	DO'J0 LR=1,NR .
	M=M+1 *
	XMIN=99,E70
	DO 20 x=1,NR
	K1=MOD(NSTHT+K.NR)+1
	IF (A(K1.LC).GT.XMIN. OR.N(K1.LC).NE.0) 00TO 20
	XMIN=A/KI-IC
	NDTHEKS
20	CONTINIE
20	
30	
	00 40 J=14NC
40	NOD 1011-1000
-	
	NSIKI=FLUAI(NK) *RANU(DUM)+1.
	00 50 1=1+NK
	KI=MUD(NSTRT+1+NR)+1
	IF ((NIEMP (KI) (MMM) .GE, NOBUSUM) GOTO 50

14

140

1

C. 18 . 187 . 187 . 187 .

** *** 5

NOBJSUM=NTEMP(KI)#MMM MINDBJ=KI CONTINJE NOBJSUM=NOBJSUM#MMM DISPLAY"RANKSUM VALUES" DISPLAY (NTEMP(I),I=1,NR) RETURN END

50

Ť,

2.1

ويوجعه والمراجع والمراجع والمراجع والمتعاد المتعاد والمتعاد والمتعاد والمتعاد والمتعاد والمتعاد والمتعاد والمت

>

and the second